

COVID-19 CADTH Horizon Scan

Breath Tests for the Detection of SARS-CoV-2

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Key Messages

- Horizon Scan reports provide brief summaries of information regarding new and emerging health technologies.
- These technologies are identified through the CADTH Horizon Scanning Service as topics of potential interest to health care decision-makers in Canada.
- This Horizon Scan summarizes the available information regarding an emerging technology, breath tests for the detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Headline and Introduction

Testing for SARS-CoV-2 might soon be as easy as waiting to exhale.

As the pandemic continues and travel and larger events begin again, the ability to quickly and accurately screen large groups of people for the SARS-CoV-2 infection becomes even more important.

How it Works

Breath tests for SARS-CoV-2 work by analyzing the volatile organic compounds (VOCs) present in exhaled breath. They do not detect the virus itself. Instead, they detect compounds produced by virus-infected cells.¹ VOCs are the byproducts of physiological processes like cellular metabolism, respiration, and digestion.² An infection or disease can disrupt these processes and result in changes to the typical VOC make up of a person's breath.² Research conducted since the beginning of the COVID-19 pandemic has determined that breath samples from people who had tested positive for infection with SARS-CoV-2 had higher levels of aldehydes and ketones and a lower level of methanol.² In addition to knowing which VOCs to detect in the sample, it is important to know which ones to ignore.³ Smoking and the consumption of alcohol can cause people to emit specific VOCs that should be excluded from the analysis for the detection of SARS-CoV-2.³

Using breath tests for the identification of disease is not a new concept. These technologies have been under development for some time with a focus on gastrointestinal issues, cancers, respiratory infections, and tuberculosis.¹ The analysis can be done using a variety of platforms. Some tests involve the collection of a sample that is run through a mass spectrometer.³ The TracieX test requires the person to blow into the portable, hand-held breathalyzer unit for 10 seconds. The breathalyzer is then disinfected and placed into the portable reader and the analysis is complete in 2 minutes.⁴ The test uses a sensor chip to identify the molecular fingerprint of the VOCs in the breath sample.⁴ The aeoNose device uses metal-oxide sensors that change conductivity when they react with VOCs in the breath.⁵ The Microtox BT test is a modification of an artificial intelligence based water contamination system that uses a nano-optofluidic chip with a secondary antibody to the SARS-CoV-2 spike protein.⁶ These types of tests are intended to be used mostly for screening purposes and a positive or inconclusive breath test result would likely need to be followed with a RT-PCR test to confirm a diagnosis of SARS-CoV-2 infection.^{3,7}

Table 1 provides a summary of some examples of breath tests for SARS-CoV-2 that are currently in development or being used internationally.

Table 1: Examples of Breath Tests in Development for SARS-CoV-2

Test name (Manufacturer)	Sample processing time	Reported accuracy	Regulatory status
aeoNose (eNose Company)	Breathe through the machine for 5 minutes	Sensitivity = 86% NPV = 92% NPV with machine learning = 96% ⁵	Undergoing clinical trials ⁸
BreFence Go (Breathonix)	40 to 60 seconds	Sensitivity = 85.7% Specificity = 97% ³	Provisional approval in Singapore (May 2021) ³
GeNose C19	3 minutes	Sensitivity = 95%	Distribution licence for use in Indonesia (December 2020) ⁹
Microtox BT (DeepVerge)	Not reported	Not reported	Undergoing clinical trials ⁶
SpiroNose (Breathomix)	The manufacturer indicates the results are available "instantaneously" ¹⁰	PPV = 98% ^{a11}	Use by the GGD for broad screening is currently on hold due to questions about accuracy ¹²
TracieX Breathalyser (Silver Factory Technology)	Blow into the mouthpiece for 10 seconds, less than 2 minutes for a result	Sensitivity = 95% Specificity = 97.8% ⁷	Provisional approval in Singapore ¹³

GGD = the municipal health service of the Netherlands; NPV = negative predictive value; PPV = positive predictive value.

^a Clinical study publication is a pre-print and has not yet been peer-reviewed.

Who Might Benefit?

Breath tests for the detection of SARS-CoV-2 infection would likely be most useful as screening tests for large groups of people or for those who need to be tested often. These tests produce results quickly and do not necessarily need to be conducted by health professionals, which makes them suited to use to test a crowd.⁴

In Singapore, breath testing is being trialed at checkpoints to screen trucker drivers and in airports to screen incoming passengers.⁴ The aeoNose is being tested as a screening tool for health care workers.⁸ In May 2021, the SpiroNose was used to screen competitors taking part in the Eurovision Song Contest in the Netherlands for SARS-CoV-2 infection before they were allowed on stage to perform.²

Availability in Canada

At the time this article was published, commercial breath tests for the detection of SARS-CoV-2 infection were not available for use in Canada or the US.

The TracieX Breathalyser¹³ and BreFence Go breath test³ have received provisional approval for distribution in Singapore. The GeNose C19 test received a distribution licence in December 2020 for use in Indonesia.⁹

What Does It Cost?

These testing devices are not currently available for use in Canada and Canadian prices are unavailable.

In Singapore, the BreFence Go test costs about US\$5 to US\$20 per sample, depending on volume of samples being tested.³ The TracieX currently costs about US\$20 per test. The company is currently producing 200,000 tests per month and the price per test is expected to decrease once they reach their production target of 2 million tests per month.⁴ The GeNose costs about US\$1 to US\$2 per sample.⁹

In Canada, most tests currently used for the detection of SARS-CoV-2 are publicly funded, and the costs associated with procurement and administration are not clearly reported. The total cost of administering RT-PCR tests would include the combined cost of testing equipment, testing supplies, and health care worker resources required to take the samples, ship the samples to the lab, and pay the salaries of lab workers to run the tests. Given the lower anticipated per test costs, the availability of breath tests for SARS-CoV-2 screening may represent a reduction in per test cost burden to the health care system if they were to become available. Alternatively, screening large groups of people who might otherwise not present themselves for testing could add additional costs to the system.

Current Practice

Lab-based RT-PCR tests with high sensitivity remain the gold standard for diagnosis of SARS-CoV-2 infection in Canada.¹⁴ RT-PCR testing looks for the presence of viral genetic material in the diagnostic sample and is usually done by trained professionals in a lab or at the point of care.¹⁴ These tests convert single-strand samples of RNA into double-stranded DNA and then amplify the DNA into larger quantities that are easier for the test to detect.¹⁵ PCR tests are not recommended as diagnostic tests for people who are not showing symptoms of COVID-19 or who have not been identified as a close contact of someone diagnosed with COVID-19.¹⁴

The ability to quickly test and diagnose people with COVID-19 is necessary to slow the spread of SARS-CoV-2, benefiting everyone. When a person is accurately diagnosed with COVID-19, they can isolate themselves immediately and minimize the chances of the virus being spread to others. Isolating those who test positive early in the infectious period, and initiating contact tracing immediately, could potentially decrease the rate of community transmission.

Using breath testing also has the potential to increase lab capacity to do confirmatory RT-PCR diagnostic testing, as required, rather than using RT-PCR testing to monitor broad populations of asymptomatic people who want precautionary testing before travel, entering the workplace, or attending a large event. Overall, more testing options provide the opportunity for a greater proportion of the population to be tested and to help curb the spread of the virus.

What is the Evidence?

Much of the research regarding the use of breath tests for the detection of SARS-CoV-2 is still ongoing. The BreFence Go test is currently being evaluated through trials at border crossings and in airports in Dubai and Singapore. The test is being used to test hundreds of truck drivers per day at a bridge crossing in Singapore.⁷ The TracieX is being used to screen inbound passengers at the Changi Airport, in a partnership with the National Centre for Infectious Diseases of Singapore.⁴ Participants in the study will be tested with both the TracieX and a RT-PCR test to evaluate the accuracy of the breath test.⁴ The aeoNose is undergoing a multi-centre validation study in ten hospitals in the Netherlands with the intention of using it as a screening tool for health care staff.⁸

In Canada, researchers with the BC Cancer Foundation are working on a breath test where a person's breath would be captured in a tube, which would then be analyzed for the markers of SARS-CoV-2 infection.¹⁶ Clinical studies are currently under way. As of March 2021, 300 of 1,000 study participants had been tested using the device.¹⁶ The researchers anticipate the test will be portable, inexpensive, and will produce results quickly.¹⁶ Work is ongoing at Hamilton Health Sciences and McMaster University assessing the Picomole breath analyzer.¹⁷ The study will examine samples from 100 people with confirmed COVID-19 and 100 people with negative RT-PCR test results. The breath samples will be concentrated, frozen, and sent to the Picomole lab in New Brunswick for analysis.¹⁷

The [ClinicalTrials.gov](https://www.clinicaltrials.gov) registry lists many more studies that are under way regarding the evaluation of breath tests for the detection of SARS-CoV-2 infection.

Safety

No known safety issues have emerged with the use of tests for SARS-CoV-2. The main concern with testing done outside of a laboratory is the potential for human error. An improperly conducted test could provide a false-negative result. A false-negative result is a negative-test result in a person who is positive for the presence of the virus.¹⁴ One of the ways this can happen is when the test is performed too soon after exposure to the virus and there is not enough viral antigen in the sample to result in a positive test.¹⁴ False-negative tests may result in further spread of the virus by people who have received a negative-test result despite being unknowingly infectious to others.¹⁴

In real-world use, the SpiroNose test produced more false negatives than expected, though those results were ultimately attributed to user error.² Clinical studies of the SpiroNose test also resulted in a higher than expected number of false-positive test results.² Because of this, the test is now being used in the Netherlands for screening, not diagnosis. Any result other than "negative" from the test requires follow-up with a RT-PCR test to confirm a diagnosis.²

A risk of providing people more frequent results from tests with lower sensitivity is the potential for behaviour modification based on those results. Compliance with public health measures may be decreased due to a false sense of security in the receipt of a negative-test result that may be incorrect.¹⁸

Issues to Consider

Breath tests, as with most COVID-19 tests, have the potential to create a lot of waste. Each sample collected for these tests required the use of a disposable mouthpiece, face mask, or entire breathalyzer unit that will be discarded after use. When considered as a part of broad screening of crowds at events, borders, and workplaces, these tests could produce a lot of excess waste.

Eating, drinking, smoking, and other behaviours can alter the accuracy of breath tests. In clinical studies, participants had to refrain from eating for at least 4 hours before their sample was collected.¹⁹ Smoking, oral hygiene, and medications were also avoided before sampling.²⁰ Participation could be low or results inaccurate if individuals are required to avoid other substances or behaviours to ensure the accuracy of the commercial versions of these tests.

Related Developments

Engineers at the Massachusetts Institute of Technology and Harvard University have developed a face mask that contains a sensor that can detect whether the wearer has an active SARS-CoV-2 infection within 90 minutes of wear.²¹ A biosensor is attached to the inside of the mask that is able to detect viral nucleic acids in the breath. The visual display of the test's result is on the inside of the mask to maintain the wearer's privacy.²¹ The researchers envision these types of tests being used for health care workers and first responders who are exposed to SARS-CoV-2 and other airborne pathogens or toxins.²¹

Researchers at RMIT University in Melbourne, Australia have partnered with Soterius to create a wearable biosensor that can detect SARS-CoV-2 within a minute.²² The biosensor is housed in a fob that can be scanned at entry checkpoints to allow access to users with negative results and prevent entry for those whose breath contains markers of SARS-CoV-2 infection. The prototype is being refined with an anticipated entry on to the market in early 2022.²²

Looking Ahead

Testing is an important and evolving factor in the management of the pandemic. For testing to be an effective part of public health strategy, it must be easily and equitably available to all who need it. This would include both the location of, and access to, testing locations and ensuring enough tests, equipment, and people have been secured to provide an adequate number of tests relative to demand. The COVID-19 pandemic has magnified existing direct and indirect societal inequities. Public health measures like quarantine, physical distancing, and testing do not have the same impact on everyone. These factors are important when assessing interventions related to testing for SARS-CoV-2.

Despite the success of ongoing vaccination campaigns around the world, testing for SARS-CoV-2 and diagnosis of COVID-19 will continue to remain an important part of public health measures, particularly as access to travel and larger events begin to increase once again.²³

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