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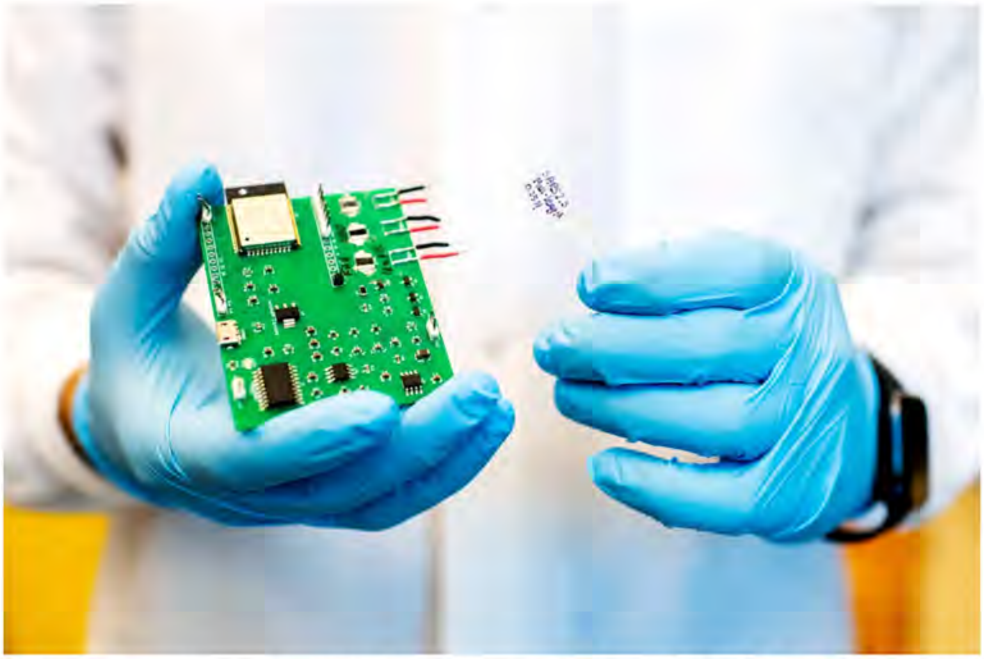
Could Breathalyzers Make Covid Testing Quicker and Easier?

A breath test would offer advantages over throat and nose swabs, but the technology is novel, and early trials with volunteers are still ongoing.



Nian Sun's lab at Northeastern University is developing a handheld breathalyzer test for Covid-19. PHOTOGRAPH: RUBY WALLAU/NORTHEASTERN UNIVERSITY

SIX MONTHS INTO battling the Covid-19 pandemic, it's clear that the US still needs better testing. Backlogs have caused unbearably long wait times for results, and the coming flu season might further encumber test processing. But what if our coronavirus-carrying breath could be harnessed to detect Covid-19? That's the hope of some researchers at Ohio State University and Northeastern University, who are developing Covid-19 breathalyzer devices.

Most people know breathalyzers as the handheld tools toted by police officers for determining alcohol intoxication; but scientists wield them too—just not for sobriety tests. Researchers have explored using them, and similar devices, to analyze exhaled breath for indicators of diabetes, certain cancers, respiratory diseases, and many other conditions.

Now, researchers like Ohio State University engineering professor Perena Gouma say a similar approach might work for Covid-19 and could offer key advantages over the current gold standard, polymerase chain reaction (PCR) tests based on throat or nose swabs. A breathalyzer needs no reagents nor laboratory processing and could provide rapid results. This kind of test "is noninvasive and nonintrusive," Gouma says. "You can deploy it wherever, whenever." While there aren't any on the market yet for Covid-19 testing, her lab and others are conducting trials on people and hope to gain approval from the Food and Drug Administration for broader use.

Gouma has been studying breath analysis, sensors, and diagnostic devices for years. In 2017, she invented a breath-monitoring device aimed at early detection of the flu by primarily targeting the exhaled chemical compound isoprene. Building on this work, she's now developed a prototype Covid-19 breathalyzer that uses ceramic sensors to detect volatile organic compounds in a person's breath that she believes act as Covid-19 biomarkers, or disease indicators. Since this work is still unpublished, Gouma won't say specifically which gaseous molecules her device looks for, only that she and her collaborators came to their conclusions about the likely indicators for Covid-19 after studying the medical literature on other coronavirus diseases and their related biomarkers.

The breathalyzer's sensors incorporate nanomaterials with high affinity for these biomarkers, meaning the sensors respond only to the target chemical compounds. When users exhale into a disposable mouthpiece attached to the device, the presence of these chemicals in their breath triggers a change in electrical resistance, which the device measures in order to give a reading.

The results take only 15 seconds, Gouma says, and can be transmitted wirelessly or read directly on the device. About a minute later, the breathalyzer is ready for another go. "With this technology, you can monitor the next day and the day after," Gouma says. "Nothing prevents you from knowing your state of health at any time."

While the breathalyzer could be used in hospitals or other health care settings, it wouldn't require specialized training or health care workers to operate, so people at theaters, airports, schools, and other places could also use it, Gouma says. "I envision ubiquitous use of the breathalyzer. That's what we strive for," she says.

Development of her breathalyzer received support from a National Science Foundation grant in June. Earlier this summer, Gouma began running a clinical study to test the device at the Ohio State Wexner Medical Center, which included people who had Covid-19 and those who did not. Additional testing is underway that involves participants from various Covid-19 testing sites around Columbus, Ohio. Gouma plans to seek FDA emergency-use authorization for the breathalyzer—which, during public health emergencies, permits use and distribution of certain medical products without full approval.

Earlier this year, Nian Sun, a Northeastern University engineering professor, made the switch from studying gas sensors that detect lung cancer biomarkers to sensors targeting the novel coronavirus. With an NSF grant received in June, Sun and his colleagues have developed a handheld breathalyzer outfitted with electrochemical sensors made to catch viral particles from the air, including from exhaled breath.

The sensors contain tiny imprinted cavities that exactly match the shape and size of the spike proteins protruding from the surface of the SARS-CoV-2 virus. "We make a mold for the specific virus," Sun says. Like a key going into a lock, the virus' spike proteins, and only those proteins, fit within the sensors' cavities. Hydrogen bonds provide electromagnetic force that binds the airborne viral particles to the sensors' imprints, triggering an increase in measurable electrical resistance. The more particles there are, the higher the resistance.

The breathalyzer designed by Nian Sun's lab uses electrochemical sensors made to catch viral particles from the air, including from exhaled breath. PHOTOGRAPH: RUBY WALLAU/NORTHEASTERN UNIVERSITY

The user blows into a one-way airflow disposable tube, and LEDs on the device indicate results. A red light means the virus has been detected, green indicates a negative reading, and yellow is borderline, possibly requiring another exhale or further testing, Sun says. Sun says false positives would be unlikely, since the sensors won't engage any other type of virus. "This kind of sensor has extremely high specificity," he says. "We can even differentiate different [SARS-CoV-2] strains."

The prototype, which measures only a few inches in length and width, produces results in just one or two seconds, which can then be wirelessly transmitted. "This device doesn't need any special training [to operate] and does not need any special reagents, so it's pretty straightforward," Sun says.

Testing the sensors in the lab has involved using frozen, inactivated SARS-CoV-2 viruses. Now, pending approval from the institutional review boards at potential testing sites—a requirement for research involving people—Sun and his colleagues hope to soon test the breathalyzer among patients from Massachusetts General Hospital and Northeastern student, faculty, and staff volunteers. Part of the testing will involve comparing breathalyzer results against results from nasal swab tests, Sun says. He, too, plans to apply for FDA emergency-use authorization for his device.

But breath analysis can be complex. Our every exhale swirls with hundreds of compounds originating from the mouth, gut bacteria, food, and ingested medications, says Raed Dweik, chair of the Cleveland Clinic Respiratory Institute. Even our environment comes out in the breath. “When patients come to me [after] driving on the highway, I can detect diesel exhaust on their breath,” he says. In other words, he continues, “there are challenges for breath analysis, because the breath does not only have what you’re looking for, it has a lot more.”

For example, says Dweik, once while he was conducting a study, he detected a certain compound in 100 percent of the hospital patients’ breath samples that was absent from the breath of all the healthy participants in the control group. That might look like the compound was a signifier of a disease, but after digging deeper, the researchers traced it to a hospital cleaning solution not used in the clinic where controls were evaluated. “So you have to be really careful when you do breath,” Dweik says. “You see a lot of people publishing papers or making claims about how breath is great, but if you look deeper into their data you realize they have not controlled for the environment.”

Dweik, who has studied breath-based diagnosis of liver disease, kidney failure, and other diseases, hasn't specifically reviewed either Gouma's or Sun's breathalyzers. But he says he’s cautiously optimistic about Covid-19 breathalyzers but enthusiastic about their potential. “The potential is huge,” Dweik says, but he emphasizes that “breath testing, or any test, has to be done accurately.”

Beyond detecting Covid-19, Cristina Davis, a UC Davis engineering professor and chair, thinks analyzing breath could also help determine if a Covid patient’s immune system will overreact to the infection, leading the body’s own defenses to damage itself, potentially fatally. “Some even seemingly healthy people have [this] issue come up,” says Davis. “So why is that? And can we see something in their breath that would allow us to predict that this patient is going to have more problems than another patient?”

Davis and her collaborators are collecting and analyzing breath aerosols from people who have Covid-19 using previously developed palm-sized devices that capture breath condensates. Larger molecules such as cytokines and eicosanoids—signaling molecules linked to inflammation and other processes—can also be found in breath aerosols, Davis says. By analyzing the condensates using mass spectrometry, Davis hopes to pinpoint which concentrations of these molecules could indicate a likely immune system overreaction. To correlate, she’ll compare these levels against study participants’ pulmonary function testing, which determines how well the lungs are working, and eventual outcomes—including how ill people become. Should she find a correlation between these molecules and people who wind up with severe immune reactions, Davis says, this technology could help predict which future Covid-19 patients should be closely monitored for inflammation problems.

To participate in the test, patients exhale into a disposable mouthpiece connected to the device, and their breath condenses into a liquid that can then be poured into a vial and stored in the freezer until it’s collected for analysis. Participants in her team’s study, being conducted by the UC Davis School of Medicine and the VA Northern California Health Care System, can provide breath samples at Covid-19 testing sites or if they’re admitted to the hospital. The collection devices can also be sent home with people who don’t require hospitalization.

Yet even though these new devices offer some intriguing possibilities, PCR probably isn’t going anywhere soon. “PCR and other traditional detection assays, they’re pretty good,” notes Davis. “I think that breath analysis can play a role. In my mind I don’t see it replacing those traditional measures; I see it as being something that can augment.”

Other experts even think that Covid-19 detection technologies might be used in combination. "I think it's really good to have complementary tests that work in different environments," says Heather Walker, facility manager of the University of Sheffield's Biological Mass Spectrometry Facility. She says that PCR is reliable but slow and that a rapid, nimble testing method, like a breathalyzer, could be great for, say, testing passengers before they board an airplane.

Different types of Covid-19 tests can also reveal different kinds of information. "Certainly with breath analysis you would expect a change in metabolism if you had the virus," Walker says, which would correspond to a change in the compounds expelled in breath. "But you wouldn't necessarily be looking for antibodies to see if somebody had had the virus already and had recovered." (Antibody tests are usually done using a blood draw.)

So, when could Covid breathalyzers be available? That could depend on FDA approvals and on manufacturing capabilities for large-scale production, among other factors. Should she receive an emergency-use authorization, Ohio State's Gouma hopes to begin deploying the devices as soon as this fall. At Northeastern, Sun says he and his colleagues are working to obtain a manufacturing partner for the device, and they'll also still need FDA approval.

Perhaps our breath, a culprit in spreading Covid-19, will ultimately be used to our advantage. "I think that the time is now when breath analysis and minimally invasive diagnostics and monitoring can really help the world," Davis says.

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