Laser-Based Device Detects and Kills Melanoma Cells in the Blood

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Scientists have developed a noninvasive device that may not only detect melanoma cells traveling through the bloodstream, but also kill them.

The device, which the investigators call Cytophone, accurately detected cancer cells in 27 out of 28 people with melanoma. It also reduced the amount of cancer cells in participants' blood, suggesting that it may kill the cells.

The device uses laser beams and sound waves to scan circulating blood for melanoma cells. It does not require any needles or blood draws and can scan a person's entire volume of blood—about 5 liters—in a matter of hours.

The NCI-funded study demonstrated the feasibility of using the device to detect cancer cells in the blood of people with melanoma, said the study's senior investigator, Vladimir Zharov, PhD, DSc, director of the Arkansas Nanomedicine Center at the University of Arkansas for Medical Sciences.

"One problem with detecting circulating tumor cells is that they are found in very small amounts in blood," said Miguel Ossandon, PhD, of NCI's Division of Cancer Treatment and Diagnosis, who oversaw the study's funding.

According to the findings, published June 12 in Science Translational Medicine, the Cytophone device was able to detect a single cancer cell in a liter of blood, making it about a thousand times more sensitive than existing technologies that are used to search out circulating cancer cells.

Zharov and his team hope to build more devices so that they can conduct a larger study of more patients with melanoma.

And although this approach can only detect cells that have pigment, with some modifications it is also applicable to cancers other than melanoma, noted lead author Ekaterina Galanzha, MD, PhD, of the University of Arkansas for Medical Sciences. For example, by using nontoxic gold nanoparticles, the team used a similar approach to detect circulating breast cancer cells in mice and in blood samples from patients with breast cancer, she explained.

Finding Circulating Tumor Cells

Cancer cells are not always anchored to a tumor—some break away and float freely through the bloodstream and lymph system. Researchers have developed tests, called liquid biopsies, that detect and analyze circulating tumor cells with the goal of helping doctors care for people with cancer.

Most liquid biopsy tests involve collecting a vial of blood from a patient and then, in a laboratory, using sophisticated technologies to process and analyze the blood for the presence of cancer cells.

There are limitations to this kind of approach, the authors wrote. For example, taking cells out of the body and into a lab can alter them in ways that may affect the accuracy of analyses.

In contrast, Cytophone detects cancer cells while they're inside the patient's body. The device works by delivering short laser pulses to blood vessels under the skin of the person's hand while their hand is gently fixed in a customized holder. As circulating melanoma cells pass through the laser beams, the pigment inside them gets heated up, resulting in sound waves that are detectable by an ultrasound transducer.

Another advantage of the Cytophone approach is that it doesn't identify melanoma cells by specific molecular characteristics, which can vary greatly from patient to patient, said Kelly Nelson, MD, associate professor of dermatology at the University of Texas MD Anderson Cancer Center, who was not involved in the study. Cytophone "could potentially be applicable to a broader context of melanoma than more molecularly based approaches," she said.

Stopping Cancer in Its Tracks

After developing the device for many years and testing it in animals, Zharov's team obtained NCI funding to study it in a clinical setting.

First, the scientists used Cytophone on 18 volunteers who had melanoma and 10 who didn't to define baseline measures and train a computer algorithm to distinguish cancer cells from healthy cells.

No signals from cancer cells were detected in the healthy volunteers, although some signals of unknown origin were picked up. The researchers estimated that the device correctly identified those who did not have cancer (i.e., the specificity) 95% of the time. The participants reported no pain or skin changes.

Next, the team tested the approach on 10 additional people with melanoma to confirm that it could find circulating melanoma cells. Overall, the tool picked up cancer cells in all but one person with melanoma, demonstrating a high sensitivity (the ability to correctly identify those who have cancer).

For volunteers who had a concentration of circulating tumor cells that was high enough to be

detectable with conventional methods, the researchers also checked the number of circulating tumor cells in their blood samples using several different lab tests, verifying that the results from the Cytophone device were accurate.

As the scientists used the device on people with melanoma, they noticed an interesting and unexpected pattern: the signal from circulating tumor cells dropped over time. They wondered if Cytophone could be simultaneously detecting and destroying cancer cells.

“Although we had already demonstrated laser killing of circulating tumor cells in animals, this was not our initial goal in humans. We used relatively low laser energy for diagnostic purposes,” Zharov said.

When melanoma cells are heated by laser beams, tiny bubbles form around the pigment proteins inside the cells. As these bubbles rapidly expand, they can physically destroy the cells. Although laser beams can also heat pigment in red blood cells, bubbles do not form and so there is no danger of harming healthy cells.

In lab tests, the scientists found that one hour of laser beam exposure markedly reduced the amount of tumor cells in blood samples collected from patients, though the extent of the reduction varied from patient to patient. In one case, the device cut the number of cancer cells by 11-fold. The cell-killing feature may be dependent on the amount of pigment in melanoma cells, the researchers noted.

Because some circulating cancer cells have the ability to exit the bloodstream and form new tumors in other parts of the body (metastasis), destroying cells in the blood might reduce the risk of the cancer spreading, the scientists wrote.

Catching Melanoma Early

Although the Cytophone approach is far from being routinely used in a clinical setting, it could have several potential applications, the investigators said.

The team plans to focus on testing the device as a potential screening tool for early-stage melanoma, Zharov noted. Treatment is much more effective when melanoma is caught early than when it has spread to other places in the body, he explained. In the current study, the Cytophone device detected circulating tumor cells in all three participants who were known to have stage II melanoma.

Using the device as a screening tool could help identify people who should go on to receive a full body skin exam by a trained dermatologist, said Nelson. However, “obtaining the evidence that’s needed to support that approach requires a lot more research,” she added.

Monitoring for metastasis in people with early stage melanoma could be another potential application of the device, Nelson noted. People with early stage disease often worry that their cancer is spreading, she said, and the possibility of “having a noninvasive technique to detect

disease progression at its earlier stages is already giving patients a lot of hope.”

But further validation and testing are still needed before that even becomes a possibility, she stressed.

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