Listening to the sound of skin cancer

October 16 2006

Researchers at the University of Missouri-Columbia can now detect the spread of skin cancer cells through the blood by literally listening to their sound. The unprecedented, minimally invasive technique causes melanoma cells to emit noise, and could let oncologists spot early signs of metastases -- as few as 10 cancer cells in a blood sample -- before they even settle in other organs. The results of the successful experimental tests appear in the Oct. 15 issue of the journal *Optics Letters*, published by the Optical Society of America.

The team's method, called photoacoustic detection, combines laser techniques from optics and ultrasound techniques from acoustics, using a laser to make cells vibrate and then picking up the characteristic sound of melanoma cells. In a clinical test, doctors would take a patient's blood sample and separate the red blood cells and the plasma. In a healthy person, the remaining cells would be white blood cells, but in a melanoma patient the sample may contain cancer cells. To find out, doctors would put the sample in saline solution and expose it to rapid-fire sequences of brief but intense blue-laser pulses, each lasting just five billionths of a second.

In lab tests, the Missouri-Columbia team was able to detect melanoma cells obtained from actual patients, showing that the method can spot as few as 10 cells in saline solution. The dark, microscopic granules of melanin contained in the cancer cells absorb the energy bursts from the blue-laser light, going through rapid cycles of expanding as they heat up and shrinking as they cool down. These sudden changes generate loud cracks -- relative to the granules' size -- which propagate in the solution

like tiny tsunamis.

The sound waves produced by melanin are high-frequency ultrasounds, meaning that they cannot be heard by the human ear, even if amplified. However, researchers can pick them up with special microphones and analyze them with a computer. Other human cells do not contain pigments with the same color as melanin, so the melanin signature is easy to tell apart from other noises, said John Viator, a biomedical engineer at Missouri-Columbia and a coauthor of the Optics Letters paper. And the presence of melanin granules in the blood is an unmistakable sign. "The only reason there could be melanin in the human blood is that there would be melanoma cells," he said.

This new blood test would allow for a much more timely diagnosis of metastasis and with early diagnosis comes early treatment and increased likelihood for survival. As one of the most aggressive forms of cancer, if a melanoma is not removed at its earliest stages, it will penetrate into the deep layers of the skin. From there its cells can break off and pass into the circulatory and lymphatic systems, spreading to other organs and creating metastases even after the original melanoma has been surgically removed.

An earlier metastasis warning, as this blood test provides, could alert oncologists to the cancer when it's at its earliest stages in other parts of the body and help them to begin a quicker counterattack, for example by administering chemotherapy, said Viator. "Our method can help doctors plan treatment to battle the spread of the disease," he said.

Current techniques to monitor the disease spread and recurrence have proven to be inaccurate, time-consuming and painful, according to the researchers. This new blood test would enable physicians to have a more accurate method of monitoring for metastasis.

In fact, the blood-test procedure could be performed regularly such as in screenings for high-risk patients, requiring just a small sample of blood, and its results would be almost immediate. "It could take just 30 minutes to find out if there are any circulating cancer cells," Viator said.

Other labs have used photoacoustic detection for scanning mouse brains and for mapping port-wine stains (birthmarks), but this would be its first application to oncology, Viator said. The team is now planning a pilot study on actual blood samples from patients, and larger clinical studies will need to be done, but the test shows great promise for early detection of the spread of this disease, according to Viator.

The team is also working with other Missouri-Columbia scientists in the veterinary college and the department of surgery to extend the reach of its technique to other types of cancer. Because of melanin, melanoma is the only type of cancer whose cells will strongly absorb all wavelengths of light, emitting ultrasounds that stand out from those of other cells. But artificial materials could also be introduced, to act as light absorbers -- and as noise makers. "We're looking for methods to attach other kinds of absorbers to cancer cells," Viator said. For example, he said, gold nanoparticles -- particles only a few millionths of a millimeter wide -- could be attached to the cells using proteins that bind to special receptors on the cells' membranes. With their own photoacoustic signature, the gold particles would then signal the presence of cancer cells.

Citation: "Photoacoustic detection of metastatic melanoma cells in the human circulatory system," by Ryan M. Weight, John A. Viator, Paul S. Dale, Charles W. Caldwell, and Allison E. Lisle, *Optics Letters*, Vol. 31, Issue 20, pp. 2998-3000.

Source: Optical Society of America