Medical Xpress

Catching cancer's spread by watching hemoglobin

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In an advance that can potentially assist cancer diagnosis, a new optical technique provides high-resolution, three-dimensional images of blood vessels by taking advantage of the natural multiple-photon-absorbing properties of hemoglobin, the red-blood-cell molecule that carries oxygen throughout the bloodstream. The research will be presented in Baltimore at CLEO/QELS, May 6 – May 11.

The new laser-based method, developed at Duke University, should provide 3-D images of blood vessels in relatively deep tissue (up to 1 mm, much better than conventional microscopes) with a resolution at the micron scale (at the level of blood cells, which is better than MRI resolution) and does not require any contrast agents or fluorescent markers (unlike most other high-resolution vessel-imaging techniques).

Clinically, the imaging technique can potentially be used to detect the spread of cancer, since angiogenesis—the growth of new blood vessels from existing ones—often signals the proliferation of tumors. This may make the technique convenient and powerful for helping to diagnose diseases such as melanoma, the deadliest form of skin cancer. The technique can image blood vessels up to a millimeter below the surface. Looking at blood vessels just below skin growths would be very useful for distinguishing between malignant and benign skin tumors, and would remove the critical need for skin biopsies, which is especially helpful if there are multiple suspicious areas that need to be investigated.

Since hemoglobin is highly concentrated in red blood cells, imaging the

locations where this molecule occurs can map out the distribution of red blood cells and reveal the vessels themselves. If the imaging is fast enough, researchers can capture snapshots of blood flow in individual vessels. Moving beyond mere imaging, the technique can detect the difference between oxygen-carrying hemoglobin (oxyhemoglobin) and oxygen-lacking hemoglobin (deoxyhemoglobin). This is important for monitoring tumors, because the oxygenation state around cancerous tissue and the size and density of blood vessels around the tumor can provide a lot of information about the progression of a tumor and its response to anti-cancer drugs.

In the technique, two lasers at different wavelengths (colors) send ultra-short pulses (lasting only a femtosecond, or a quadrillionth of a second) on a blood vessel. The hemoglobin absorbs light from both of these lasers at the same time, in a process known as "two-photon absorption," and then gives off signals that can be detected to build up an image. One "pump" laser boosts (excites) hemoglobin molecules to a higher energy state. The other "probe" laser monitors the hemoglobin after the excitation. Sometimes the pump laser is off and there is no two-photon absorption. By subtracting the signal from the "off" state from the "on" state (when two-photon absorption occurs), the researchers remove unwanted scattered light from the data and can get high-quality signals from hemoglobin molecules.

To map out the hemoglobin distribution, the researchers scan laser beams across the sample, a process that then reveals the outlines and contours of blood vessels. By taking images at different depths and stacking these images layer by layer, the researchers can reconstruct 3-D images of blood vessels.

A major advantage of the technique is that it is "label-free," meaning it does not require the addition of fluorescing molecules but rather relies on the inherent light-absorbing properties of hemoglobin. While the

technique has been demonstrated in vitro (by excising tissue samples and imaging the vessels on a glass dish), imaging in the living body is possible either for vessels up to a millimeter below the surface or through the use of minimally invasive probes, being developed in various labs, that can be inserted in the body.

Source: Optical Society of America