

Bye-bye biopsy?

Emerging alternatives make it possible for doctors to get inside information on patients without cutting.

*By Marie McCullough
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The year after her 2005 heart transplant, the Hammonton, N.J., resident had to return to Hahnemann University Hospital every three or four weeks for a biopsy. A tube equipped with a cutting instrument was threaded through her neck and down her jugular vein to her heart, to remove tiny tissue samples. The cells were examined under a microscope to see whether she was rejecting the organ.

While the procedure wasn't painful, it was unnerving. Her heart beat erratically as pieces were plucked out.

"I knew they had to do it, but you have this wonderful gift of a new heart and you don't want to hurt it," said Sprague, whose own heart was ruined by chemotherapy for non-Hodgkin's lymphoma.

Sprague, 60, was "thrilled" when her doctor offered an alternative: Allomap, a gene expression test that can detect hints of heart rejection earlier than a biopsy - with nothing more invasive than a blood sample.

"It's exciting to be able to offer my patients a more comfortable and reliable diagnostic tool," says Drexel University cardiologist Howard J. Eisen, a leader of the pivotal four-year, multi-center study of Allomap published in 2006.

Allomap is part of a wave of innovations designed to reduce the need for surgical biopsy - if not replace it altogether.

Even though complications of modern biopsy such as infection and hemorrhage are infrequent - and deaths are very rare - the diagnostic approach is rather primitive, experts say. The process of cutting tissue, preserving it, and sending it to a lab for analysis is also time-consuming, expensive, and may miss the cells of interest.

What's more, some parts of the body are too inaccessible or delicate for routine sampling.

"In the eye, you don't want to cut," notes Craig Kelley, marketing director at Lightlab Imaging in Westford, Mass.

The firm is one of many that are capitalizing on advances in imaging technologies to cut out the cutting.

Lightlab's "optical coherence tomography," pioneered at Massachusetts Institute of Technology, uses an ultrathin fiber-optic cable to deliver infrared light within body structures, such as the eye. As the light waves bounce off tissues, measurements are taken and translated into high-resolution images - much like sound waves are converted into images with ultrasound technology.

Optical tomography is being used to diagnose macular degeneration and other eye diseases. It's also being used in Europe and Japan to assess coronary artery disease. (The Food and Drug Administration is considering approval in this country.) On the horizon are applications for diagnosing cancer and even dental problems.

"For cancers of the colon or lung, the standard now is to look at the organ with a lighted scope, then take a sample of tissue," says Joe Schmitt, Lightlab's chief technology officer. "With optical coherence tomography, you don't physically remove the cells, but you can see them at a microscopic level."

Here are other emerging alternatives to biopsy:

Vivascope combines laser scanning with microscope technology to produce cross-section images of layers of skin cells - without removing any tissue. The system is now being marketed by Lucid Inc., of Rochester, N.Y., for skin-cancer detection. It holds promise for diagnosing oral and cervical cancers and diabetic neuropathy, said Lucid chief executive officer Jay Eastman.

XDX Inc., of Brisbane, Calif., which makes Allomap, plans to develop similar gene expression tests to detect signs of lung transplant rejection and flare-ups of lupus, an autoimmune disease.

A number of companies have developed blood tests that can be used to measure and monitor liver damage in patients with various liver diseases. These tests, which analyze biochemical markers of liver injury, include Fibrosure, offered by LabCorp Services, and Hepascore, offered by Quest Diagnostics.

Many other substitutes for biopsy are in the pipeline.

At Drexel University College of Medicine, microbiologists Anand Mehta and Timothy Block have discovered a single antibody that is elevated in most - if not all - people with liver scarring, called fibrosis. They are working with the Hepatitis B Foundation, which Block cofounded, the National Cancer Institute, and a diagnostic lab company to develop a commercial test.

"Other noninvasive liver tests that are becoming available have undergone much larger studies," Block says. "Ours hasn't been tested in enough people, but so far, our marker seems better."

Competition is keen because the potential market is so vast. More than 10 million skin biopsies - by far the most common biopsy - are performed annually in the United States. About a million breast biopsies and 30,000 liver biopsies are done each year.

Nonsurgical tests won't necessarily be cheaper. XDX Inc. says Allomap costs about \$3,000, compared with \$3,000 to \$4,000 for a heart biopsy. A Vivascope skin test - which would be sent via the Internet to a pathologist trained to evaluate it - is expected to cost about \$350, the same as a skin biopsy, Eastman says.

But the new tests may save money by reducing the number of biopsies that turn out to be unnecessary. Currently, dermatologists do about 40 skin biopsies to detect a single case of melanoma, the most dangerous skin cancer, Eastman says.

Removing suspicious skin is also impractical in some situations, says Clifford Perlis, a dermatologic surgeon at Fox Chase Cancer Center, who is a paid medical consultant to Lucid.

"Currently, the definitive way to diagnose a funny mole is to cut it out," Perlis says, and do a microscopic analysis. "The problem comes when people have many moles or moles that are in cosmetically or functionally sensitive areas."

Despite all the research and development, noninvasive tests are catching on slowly among physicians. Allomap, for example, is available to patients at about 65 of the nation's 130 heart transplant centers, Eisen says.

"They were skeptical," Eisen says of his colleagues. "And some still are. Some said, 'Oh, people have been trying to do this for 20 years.' But the thing is, 20 years ago, the technology to do this didn't exist."

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