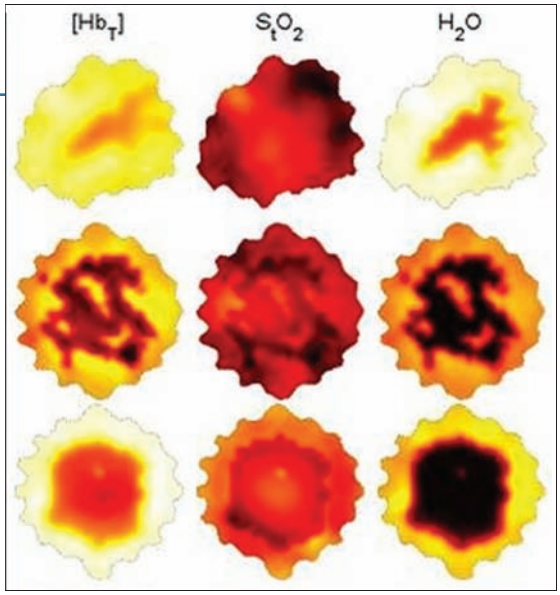

These experimental near-infrared images show (from the left) the hemoglobin concentration, oxygenated hemoglobin saturation, and percentage of water in the tissue of three breasts.

Could function prove better than form?

Looking at the *function* of a breast tumor—how it behaves at the cellular and molecular level—may increase the accuracy of standard methods of screening for breast cancer, which look for a tumor's *form*—a dense mass of tissue. That's the hope of an interdisciplinary team at Dartmouth.

Mammography remains the established way of detecting and diagnosing breast cancer, but there's growing recognition that the technology is showing its age. Dartmouth physicians and engineers have been collaborating to develop a new generation of imaging methods that examine how malignant tissue behaves rather than its structure.

New: "This is all new ground. We're looking beyond the usual anatomical thinking," says Steven Poplack, M.D., an associate professor of radiology and principal author of a paper to be published in a forthcoming issue of *Radiology*. The study examined the electromagnetic properties of abnormal and normal breast tissue and found that abnormal tissue (benign as well as malignant masses) showed an increase in image contrast of 150% to 200% over normal tissue.

The three methods in the study look at tissue's ability to scatter and absorb light, store electricity, and conduct current:

■ Microwave imaging spectroscopy (MIS) is sensitive to water content; it detects malignant tumors because they have more water and blood than normal tissue. The study found that in subjects whose lesions were larger than one centimeter, the predictive value of mammography doubled with the addition of MIS.

■ Near-infrared spectral tomography (NIR) measures hemoglobin and oxygen saturation in tissue. NIR was most effective in identifying abnormal tissue greater than six millimeters when looking at total hemoglobin concentration. Brian Pogue, Ph.D., an associate professor of engineering, is hopeful that a hybrid NIR-MRI technique could be used to monitor the effectiveness of chemotherapy. "That could make a difference in diagnosing whether a patient is responding to a particular therapy," he explains. Dartmouth is sharing its NIR data with a consortium of research institutions working on similar optical imaging technologies.

■ Electrical impedance spectroscopy (EIS) looks at how cells conduct and store electricity. It was able to distinguish between normal and abnormal tissue, though it's unclear yet if it can effectively differentiate between cancer and other abnormalities.

The three techniques were assessed individually as well as by combining the properties of all three. Results showed that the combined analysis was a better predictor than any individual method.

A fourth imaging technology is also being developed at Dartmouth, but it hasn't been investigated as thoroughly and so was not included in the *Radiology* paper. Called magnetic resonance elastography (MRE), it measures the stiffness of tissue; malignant tumors are harder and less elastic than normal breast tissue. "It's like being able to take your hand and feel locally where the stiffness is," says Keith Paulsen, Ph.D., a professor of engineering and principal investigator for the alternative breast imaging research.

Pluses: Additional pluses of the new techniques are that none of them use ionizing radiation or require compression of the breast. Instead, the subject lies prone on a special examination table that has an opening for the pendant breast, and a cross-section of the tissue is exposed to different wavelengths or frequencies of nonionizing radiation.

In addition to these four technologies prototyped at Dartmouth, an unrelated system being studied here has the potential to revolutionize imaging in the shorter term. "Tomosynthesis is probably much closer to commercialization," says Paulsen. "Many people think it will replace mammography."

Tomosynthesis is an enhancement of digital mammography; it involves taking multiple low-dose exposures of the breast from different angles. "The beauty of tomosynthesis is it gives you this slice-by-slice look," says Poplack. In a study of tomosynthesis as a diagnostic tool, he showed it was just as good as mammography at detecting cancer and had fewer false positives. In a new multi-institutional study, Dartmouth is now testing tomosynthesis as a screening tool. Poplack expects data analysis to begin in 2007.

Novel: Unlike tomosynthesis, Dartmouth's alternative imaging techniques are unlikely to replace mammography, but they do provide novel information with the potential to improve screening and diagnosis of breast cancer. "Radiologists and clinicians have never really looked at this kind of information in the way we're providing it," says Paulsen. The National Cancer Institute recently expressed its confidence in the work by awarding Paulsen's group $7.8 million in continuing funding for the next five years.

Even so, actual clinical application of any of the new methods is still in the distant future. "New technology development is a long row to hoe," says Poplack. LEE MCDAVID