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## A Better Breast Cancer Detector

By Robert F. Service  
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**CHICAGO, ILLINOIS**--Mammography is still the gold standard for the early detection of breast cancer, but it's far from perfect: The technique misses up to 20% of breast cancers. Soon, it may get a bit of help. Researchers reported here today at the annual meeting of the American Chemical Society that they've developed a pair of compounds that help spot the build up of tiny mineral deposits, a hallmark of breast cancer. If the compounds prove safe and effective in humans, they could prove a boon for combating a disease that afflicts 1 in 8 of women in the United States at some point in their lives.

### Target practice.

A new infrared imaging contrast agent highlights hydroxyapatite (purple), a mineral commonly associated with malignant breast cancer.

Credit: John V. Frangioni and Kumar R. Bhushan

With mammography, radiologists use x-rays to spot the dense tissue and tiny calcium deposits in breast tumors. These deposits, called microcalcifications, are common to

both benign and malignant tumors. While the mineral most commonly found in benign tumors is called calcium oxalate, another called hydroxyapatite is more common to malignant tumors. Mammography can't tell the two apart. But researchers have known for years that an osteoporosis drug called bisphosphonate can, as it binds to hydroxyapatite.

Several years ago, cancer researcher John Frangioni and his colleagues at Harvard Medical School in Boston, Massachusetts, began linking different imaging molecules called contrast agents to bisphosphonate in hopes that they could use the drug to target the contrast agents to the tumors. They hit upon one called PAM800 that's a combination of bisphosphonate and a fluorophore that emits near-infrared light. Early tests showed the compound worked to highlight microcalcifications of hydroxyapatite in mice. But the researchers couldn't produce enough of their compound to continue their studies.

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So for their current work, Kumar Bhushan, a postdoctoral assistant in Frangioni's lab, went back to the drawing board and came up with a new scheme for synthesizing large amounts of PAM800. That allowed the researchers to study the compound in pigs. And the animal studies reported today show that subcutaneous injections of PAM800 easily allowed them to highlight microcalcifications in the animals.

Frangioni's team also reported that they've created another set of hydroxyapatite-spotting compounds that not only gives off an infrared signal but also harbors a gadolinium-based chemical group that gives off a strong signal in MRI machines. Although the researchers have yet to test out this compound in animal studies, Bhushan says that they hope it will eventually give doctors a means for spotting tumors with the ultrahigh sensitivity of infrared imaging combined with MRI's ability to accurately pinpoint their 3-dimensional location.

"This looks like a good approach," says Bimal Banik, a medicinal chemist at the University of Texas Pan American, in Edinburg. Banik cautions that neither of the contrast agents has yet been tested on animals injected with breast cancer cell lines, which he calls an important step to take. But the early stage work is promising, he says, because it holds out hope that doctors will soon be able to image breast cancer with several techniques simultaneously, significantly increasing the chances of spotting the disease in its earliest stages.

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