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**Nonlinear Interferometric Vibrational Imaging**

**Tissue-imaging Technique**

The long, anxious wait for biopsy results could soon be over, thanks to a tissue-imaging technique developed at the University of Illinois. The research team demonstrated the novel microscopy technique, called nonlinear interferometric vibrational imaging (NIVI), on rat breast-cancer cells and tissues. It produced easy-to-read, color-coded images of tissue, outlining clear tumor boundaries, with more than 99% confidence - in less than five minutes.

Led by professor and physician Stephen A. Boppart, who holds appointments in electrical and computer engineering, bioengineering and medicine, the Illinois researchers will publish their findings on the cover of the Dec. 1 issue of the journal *Cancer Research*.

In addition to taking a day or more for results, current diagnostic methods are subjective, based on visual interpretations of cell shape and structure. A small sample of suspect tissue is taken from a patient, and a stain is added to make certain features of the cells easier to see. A pathologist looks at the sample under a microscope to see if the cells look unusual, often consulting other pathologists to confirm a diagnosis. Rather than focus on cell and tissue structure, NIVI assesses and constructs images based on molecular composition. Normal cells have high concentrations of lipids, but cancerous cells produce more protein. By identifying cells with abnormally high protein concentrations, the researchers could accurately differentiate between tumors and healthy tissue - without waiting for stain to set in.

Each type of molecule has a unique vibrational state of energy in its bonds. When the resonance of that vibration is enhanced, it can produce a signal that can be used to identify cells with high concentrations of that molecule. NIVI uses two beams of light to excite molecules in a tissue sample. One of NIVI’s two beams of light acts as a reference, so that combining that beam with the signal produced by the excited sample cancels out background noise and isolates the molecular signal. Statistical analysis of the resulting spectrum produces a color-coded image at each point in the tissue: blue for normal cells, red for cancer.

Another advantage of the NIVI technique is more exact mapping of tumor boundaries, a murky area for many pathologists.
The margin of uncertainty in visual diagnosis can be a wide area of tissue as pathologists struggle to discern where a tumor ends and normal tissue begins. The red-blue color coding shows an uncertain boundary zone of about 100 microns - merely a cell or two. "Sometimes it's very hard to tell visually whether a cell is normal or abnormal," Boppart said. "But molecularly, there are fairly clear signatures."

The researchers are working to improve and broaden the application of their technique. By tuning the frequency of the laser beams, they could test for other types of molecules. They are working to make it faster, for real-time imaging, and exploring new laser sources to make NIVI more compact or even portable. They also are developing new light delivery systems, such as catheters, probes or needles that can test tissue without removing samples.

The National Cancer Institute of the National Institutes of Health sponsored the study. Other co-authors were Beckman Institute researchers Praveen Chowdary, Zhi Jiang, Eric Chaney, Wladimir Benalcazar and Daniel Marks, and professor of chemistry and physics Martin Gruebele.

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