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Citation: Conference on Lasers and Electro-Optics presentation, Friday, May 27, 2005, 10:45 a.m.

HIGHLIGHTS:

At a conference on optics and photonics, the director of the Biophotonics Research and Technology Development Laboratory of Cedars-Sinai's Department of Surgery will describe the development of an experimental fluorescence spectroscopy device that has been able to diagnose dangerous atherosclerotic plaques (vulnerable plaques) and aggressive brain tumors (gliomas). Laura Marcu, Ph.D., will present "Applications of Time-Resolved Fluorescence Spectroscopy to Atherosclerotic Cardiovascular Disease and Brain Tumors Diagnosis" at 10:45 a.m. on Friday, May 27.

FLUORESCENCE DEVICE TO DIAGNOSE ATHEROSCLEROSIS AND TUMORS DESCRIBED AT OPTICS CONFERENCE

LOS ANGELES (May 27, 2005) – In a presentation today at the Conference on Lasers and Electro-Optics (CLEO), researchers from Cedars-Sinai Medical Center's Biophotonics Research and Technology Development Laboratory described recent progress on a device that stimulates, collects and measures light emissions from body tissues to diagnose critical atherosclerotic plaques (vulnerable plaques) and aggressive brain tumors.

In both disease processes, early detection and precision can impact patient outcomes. Atherosclerotic plaque builds up quietly, usually causing no symptoms until reaching an advanced stage, and the results take more than 1 million American lives each year. Malignant brain tumors called gliomas grow and spread into neighboring tissues rapidly. When "image complete" resection is accomplished – meaning no tumor is visible on high-resolution scans – patients have a median survival of about 70 weeks. But when surgical removal is less than image complete, median survival drops to less than 19 weeks.

The technology to be described at CLEO is based on the fact that when molecules in cells are stimulated by light, they respond by becoming excited and re-emitting light of varying colors. Just as a prism splits white light into a full spectrum of color, laser light focused on tissues is re-emitted in colors that are determined by the properties of the molecules. When these emissions are collected and analyzed (fluorescence spectroscopy), they provide information about the molecular and biochemical status of the tissue.

"Time-resolved" spectroscopy adds a greater degree of specificity, measuring not only the wavelength of the emission but the time that molecules remain in the excited state before returning to the ground state. This information is valuable because some emissions overlap on the light spectrum but have different "decay" characteristics.

Currently, experiments are being conducted to confirm the ability of time-resolved laser-induced fluorescence spectroscopy (TR-LIFS) to differentiate brain tumor tissue from normal brain tissue and its ability to detect

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arterial plaque that is vulnerable to rupture, which often leads to heart attack or stroke.

Recent atherosclerosis research has found that the composition of plaque and its “vulnerability” to rupture may be more significant than the degree of arterial blockage as a precursor to heart attack and stroke. The lipid content of vulnerable plaque is different from that of stable plaque, and areas containing vulnerable plaque are infiltrated by immune system cells called macrophages. This inflammatory process weakens the plaque’s thin, fibrous cap, often leading to rupture and formation of blood clots that could plug the blood vessel. A variety of technologies are now being investigated for their potential to detect vulnerable plaque before rupture or to study how plaques develop and rupture.

This is believed to be the first documentation that the inflammatory cells, macrophages, can be detected in human atherosclerotic plaque using TR-LIFS. In a study of plaques collected from 34 patients undergoing surgical removal of carotid plaque, with 150 plaque areas analyzed, the TR-LIFS technique has been able to distinguish plaque found in inflamed areas from more stable plaque with a high degree of sensitivity and specificity.

Experiments are now being conducted on plaque that exists in patients’ blood vessels, both before and after it is removed during a surgical procedure called endarterectomy. Results found with the spectroscopic technique are then compared to those found when the specimens are later analyzed in the pathology laboratory.

“Right now, the goal of our research project is to define how well the TR-LIFS technique can detect the features of plaque vulnerability. But our objective is to develop a minimally invasive, intravascular probe that will monitor plaque over time or guide therapeutic interventions to prevent plaque rupture. It may be that our probe will be attached to an angioscope or to an intravascular ultrasound catheter to investigate the plaque,” said Laura Marcu, Ph.D., director of the Biophotonics Research and Technology Development Laboratory in Cedars-Sinai’s Department of Surgery.

“Results of spectroscopic examinations might be used to determine the most effective drug or treatment approach for a particular plaque. Physicians would be able to use this technology to determine whether plaque is stable or unstable, and they could use it to monitor the efficacy of a therapy. One of our next steps is to develop an intravascular catheter that will enable routine use of this technology *in vivo*, or in patients,” said Marcu, who will make the 10:45 a.m. presentation titled “Applications of Time-Resolved Fluorescence Spectroscopy to Atherosclerotic Cardiovascular Disease and Brain Tumors Diagnosis.”

In tests conducted on brain tumor tissue removed from 50 patients, TR-LIFS has been able to distinguish various types of brain tumor tissue from normal tissue. Furthermore, preliminary data collected from 17 patients during neurosurgery show that the technique can detect tumor cells left behind after tumor removal.

Neurosurgeon Keith L. Black, M.D., director of Cedars-Sinai’s Maxine Dunitz Neurosurgical Institute, said he is encouraged by the clarity that fluorescence technology may offer, especially because the most deadly tumors aggressively infiltrate neighboring tissue and are irregularly shaped with poorly defined borders. “Although our surgical goal is to remove as much tumor as possible without damaging healthy brain, distinguishing between the two can be extremely difficult, even with the sophisticated imaging techniques currently available,” he said.

The TR-LIFS apparatus consists of a laser, a two-way fiber-optic probe through which the laser light is delivered to the tissue and the fluorescence is collected, a spectrometer, a digital oscilloscope, and a computer workstation that provides user interface, coordination of components and interpretation software. While the components are now small enough to fit on a portable cart that can be taken into an operating room, additional studies on miniaturization of components and instruments are planned. In fact, the National Institutes of Health is providing funding for the development of microdevices.

While the basic hardware and software is the same whether brain tumors or blood vessels are being studied, the way the system operates is dependent on the unique characteristics of the tissue.

“Each biological system will be characterized by a distinct chemical composition, different molecules and different ways of identifying them,” said Marcu. “Therefore, to be sure the technology addresses particular questions and issues related to brain tumors, we must collect data from patients, analyze the data and define the spectral ranges of particular aspects related to the diagnosis of brain tumors. But those are very different from those related to atherosclerosis.”

The studies presented were supported by the National Institutes of Health, Grant #R01 HL 67377, and The Whitaker Foundation, Grant #RG-01-0346.

The studies on atherosclerotic plaques were conducted in collaboration with Michael C. Fishbein, M.D., and J. Dennis Baker, M.D., at UCLA Medical School and Julie A. Freischlag, M.D., at Johns Hopkins University. The studies on brain tumors were in collaboration with Keith L. Black, M.D., Brian K. Pikul, M.D., and William H. Yong, M.D., at Cedars-Sinai.

The Conference on Lasers and Electro-Optics (CLEO) is being held in conjunction with the Quantum Electronics and Laser Science (QELS) Conference at the Baltimore Convention Center from May 22 through 27. In addition to the May 27 presentation, Marcu was invited to preside over a series of sessions on Microfluidics, Flow Cytometry, and Biosensing.

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One of only five hospitals in California whose nurses have been honored with the prestigious Magnet designation, Cedars-Sinai Medical Center is one of the largest nonprofit academic medical centers in the Western United States. For 17 consecutive years, it has been named Los Angeles' most preferred hospital for all health needs in an independent survey of area residents. Cedars-Sinai is internationally renowned for its diagnostic and treatment capabilities and its broad spectrum of programs and services, as well as breakthroughs in biomedical research and superlative medical education. It ranks among the top 10 non-university hospitals in the nation for its research activities and was recently fully accredited by the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP). Additional information is available at www.cedars-sinai.edu.

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