CIMIT FORUM Agenda

Tuesday, June 5, 2001
2:00-4:00 PM (EST)

Wellman 1 Conference Room
Massachusetts General Hospital

2:00 - 2:55 PM	**Optical Techniques for Epithelial Cancer Detection**
Lev T. Perelman, PhD, *Assistant Professor, Harvard Medical School & Beth Israel Deaconess Medical Center*	Light scattering spectroscopy (LSS) has long been used to study great variety of materials ranging from isolated atoms to complex condensed matter systems. Biological tissue is yet another example of a complex system that can be studied with LSS. Light scattering can provide structural and functional information about the tissue. This information, in turn, can be used to diagnose and detect disease. One important biomedical application of optical imaging and spectroscopy is non-invasive/minimally invasive detection of pre-cancerous and early cancerous changes in human epithelium, such as dysplasia or carcinoma-in-situ. Detection of such conditions is particularly important because 85% of all cancers originate in the epithelium, and most such lesions are readily treated if diagnosed at an early stage. However, many forms of precancerous changes are difficult to detect and diagnose using conventional techniques, which require histological examination of biopsies obtained from visible lesions or random surveillance biopsies. Changes in the nuclei of the epithelial cells are amongst the most important indicators for dysplasia. The major diagnostic criteria include nuclear enlargement, increased variation in nuclear size and shape (pleomorphism), and darker staining of the nuclear material (hyperchromasia), the latter being due to increased concentration of chromatin. We have developed an LSS-based imaging method, which can provide quantitative, objective measurements of these parameters in real time without the need for tissue removal. The technique has been used successfully for non-invasive or minimally invasive imaging and detection of pre-cancerous changes in a variety of organs.
2:55 - 3:10 PM	**BREAK – REFRESHMENTS**
3:10 - 4:00 PM	**A Photochemical Method for Tissue Adhesion**
Robert W. Redmond, PhD, *Associate Professor, Wellman Laboratories of Photomedicine, Massachusetts General Hospital*	Lasers have been investigated for a variety of applications, such as surgical ablation, coagulation, skin resurfacing and hair and tattoo removal, all of which utilize the energy provided by the absorbed photons for thermal or mechanical effects. Reattachment of tissue by laser "welding" is an ongoing area of research that has met with mixed success. Thermal effects in the welding process cause denaturation of tissue that can complicate its use in some tissues where a loss of structural integrity cannot be tolerated. An alternative mechanism of laser activation is to induce photochemical reactions that can crosslink tissue surfaces to form a tight seal. This process does not require high temperature and thus, the denaturtion can be avoided and structural integrity retained. We are studying the application of Photochemical Tissue Bonding (PTB) to seal wounds in various collagenous tissues. Most of our experimental work has been focused on corneal repair where thermal denaturation cannot be tolerated due to the operation of the cornea as a major refractive component of the eye. Watertight sealing of incisional wounds has been achieved using laser irradiation of a few minutes' duration and modest powers. Wound healing studies show initial inflammation and neovascularization, which resolves in a few weeks. Following the promise shown in corneal applications, PTB is now being investigated as a non-mechanical method to attach skin and gingival tissue grafts and for tendon and ligament repair.

For more information about CIMIT, please visit: http://www.cimit.org
For directions to the MGH Campus, please visit: http://www.mgh.harvard.edu/depts/bigdig/homedir.htm

CIMIT MEETING SUMMARY 6/05/01

Lev Perelman, PhD, Beth Israel Deaconess Medical Center, described Optical Techniques for Epithelial Cancer Detection. The goal of the project is to detect both epithelial tumors and dysplasia using a noninvasive, large-area imaging technique which detects cellular scale features. In identifying dysplasia by the conventional technique of microscopy, the pathologist relies primarily on features of cell nuclei, namely enlargement, crowding and hyperchromicity. Conventional optical techniques used in cancer detection, fluorescence or absorption spectroscopy, are not applicable since the cell nuclei exhibit neither. The approach used, Light Scattering Spectroscopy (LSS), examines the spectral distribution of light scattered by the nuclei. Light from a broad-band source, a lamp, is delivered to the target via an optical fiber and the backscattered light collected and spectrally analyzed. Polarization techniques are used to eliminate the diffuse reflectance of the connective tissue beneath the epithelium. Mie scattering theory, which applies to scattering by objects much larger than the wavelength, can be applied to obtain the distribution of nuclei sizes. In-vitro experiments with cellular monolayers have been used to demonstrate that while normal colonic cells have typical nuclear diameters of about 5 microns, T84 colonic cells had nuclear diameters of about 10 microns. In addition, tumor cells show a broader distribution of nuclear diameters.

A number of in-vivo studies are now under way, involving sites such as the colon and esophagus, the oral cavity and the bladder. These studies use point measurements via a single fiber passed down an endoscope. The initial study of Barrett's esophagus showed a specificity of 97% and a sensitivity of 92 % using as discriminants the nuclear size and the number of nuclei under the probe, which is a measure of nuclear crowding. They are now performing in vitro imaging studies of LSS using a CCD-camera-based system.

Robert Redmond, PhD of the Wellman Laboratories, MGH described a photochemical method for tissue adhesion. The goal is to produce water-tight tissue bonds in a non invasive manner. The approach uses light to initiate a photochemical reaction involving the photosensitizer rose bengal, which leads to collagen cross links. Laser light at 514 nm is used, but the approach is different from more conventional laser tissue welding, which causes non-covalent bonding and can lead to tissue denaturation and tissue shrinkage. By contrast, the photochemical method produces covalent bonds.

Initial ex-vivo and in-vivo experiments have used a rabbit cornea model. The experiments involved determination of immediate wound strength by measurements of the maximum intraocular pressure the eye could sustain. Pressures in excess of 250 mm Hg could be sustained by the best welds. In-vivo experiments demonstrated similar high strength but required less total laser energy to obtain a weld. Good tissue approximation is needed for the technique to work well. Experiments applying the technique to the welding of corneal transplant grafts (keratoplasty), in animals and eventually in humans, are planned.   Other planned applications include skin grafts, gingival grafts and Achilles tendon repair.

Thomas Deutsch   6/11/01