

Gary Tearney, PhD, presented a wide-ranging survey of optical diagnostic technologies. Laser-Induced Fluorescence (LIF) has been explored for many diagnostic applications. Fluorescence of exogenous or endogenous chromophores is excited by a light source, typically emitting in the ultraviolet or visible portion of the spectra, and results in emission of light at longer wavelengths. Characteristics of this fluorescence are used to detect diseased tissue. There are many variations on the general theme of LIF; either steady state or time-resolved spectra may be collected and analyzed. Sites studied by tissue autofluorescence (fluorescence due to endogenous chromophores) include colonic polyps and the urothelium of the bladder. Exogenous marker dyes or chromophores have also been used to study early cancer in the urothelium, as well as to determine the depth of burns. Recently, near infrared (NIR) emitting dyes whose emission is normally quenched have been used as markers. These dyes can be cleaved by enzymes associated with tumors to become fluorescent.

Reflectance spectroscopy involves the analysis of light backscattered from tissue; this light is affected by both absorption and tissue scattering. Signal processing of the spectra is often required; information about blood glucose and blood chemistry has been obtained. Blood oxygen saturation has also been measured with the goal of detecting necrotic tissue. A recent development is polarized reflectance spectroscopy, which has been applied to the detection of dysplastic tissue. Polarization techniques are used to reject multiply-scattered light from below the tissue surface; the weak modulation of the backscattered light from the tissue surface can be used to extract information about the distribution of nuclear sizes, which can reflect the presence of dysplasia. The approach has been used in vivo to study Barrett's esophagus.

Diffuse Optical Tomography (DOT) utilizes transillumination of tissue in either a transmission or reflection geometry to obtain the distribution of scattering and absorption sites in a volume of tissue. Computation, based on solving the radiative transport equation for the region of interest, is required to obtain the distribution. Blood is one of the absorbers that can be detected, leading to interest in the finding breast cancers by detecting angiogenesis. Other DOT applications have included the measurement of cerebral oxygenation in neonates, detection of brain injury or stroke and the assessment of neurological function.

Raman spectroscopy has been applied to the study of many tumors, such as breast, cervical and esophageal cancers. Raman spectroscopy analyzes the spectra of light scattered by tissue to obtain distinctive "signatures" characteristic of tissue components. Raman scattering is a weak process, leading to long data acquisition times. In addition, it is not well suited to fiber optic delivery because the fiber itself can contribute to the Raman signal.

Two-photon excitation of fluorescence allows deeper penetration into tissue, since the excitation wavelength now lies in the near-infrared spectral region, where absorption is weak. Used as an excitation source for confocal scanning fluorescence microscopy it

eliminates the need for the pinhole usually used to obtain optical sectioning. The technique can be combined confocal scanning reflectance microscopy, which uses scattering to obtain contrast, to obtain images with complementary sources of contrast.

An area of research now receiving increased attention is the development of new contrast agents. Such agents can be used to modulate the absorption or scattering of tissue; for example, aceto-whitening is used in-vivo to aid in the detection of cervical dysplasia. Quantum dots, fluorescent materials based on nanoparticles of semiconductors, have been used, together with delivery systems, to mark tissue.

The second part of the presentation focused on the detection of vulnerable plaque using spatial and temporal analysis. One means of detection uses speckle, a coherent interference of light remitted from a target. This interference pattern becomes time-dependent if a portion of the remitted light is modulated by Brownian motion of the lipid pool of a plaque. A feasibility experiment on cadaver aortas demonstrated such modulation, which can be quantified by measuring the temporal correlation of the speckle from the plaque as a function of position.

Plaque detection may also be possible using mini endoscopes. Conventional endoscopes using coherent fiber bundles are limited in size to about 1 mm by loss of resolution due to the decreasing number of fibers in the bundle and the 85% fill factor of the fibers. The result is that fibers become visible in the image. The OCT group at Wellman is modifying the spectral encoding scheme developed for confocal microscopy to construct mini endoscopes. A video of a feasibility experiment using a 0.6-mm-diameter fiber bundle showed impressive imaging. Mini endoscopes would find application in fetal and pediatric surgery as well as in angioscopy in adults.

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