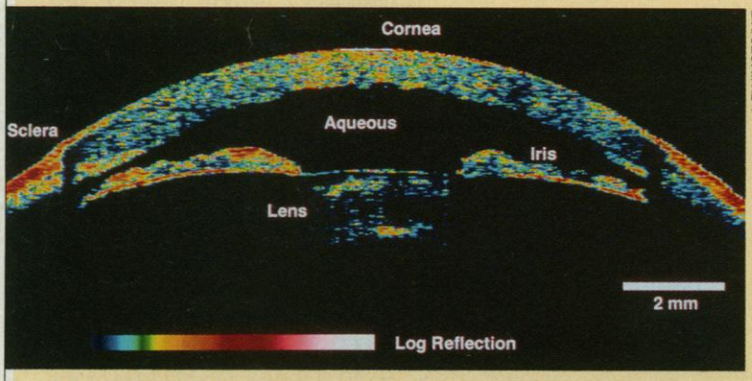
OCT: Images of Coherence

innovation IN IMAGING

Biomedical research and clinical medicine are always in search of fast, portable, inexpensive imaging techniques that do not require ionizing radiation, radioactive isotopes, or removal of tissue to detect early signs of illness. One intriguing possibility would be to convert safe, cheap optical technology into a means of getting those images. But existing optical techniques are not easy to use for imaging the body, since most tissues are at least partially opaque to most wavelengths of light.

Passing light through a tissue, however, is only one way of obtaining an image. Another is to exploit a branch of optics known as coherence interferometry to measure faint reflections of light off structures within the body. That's what James G. Fujimoto, an associate professor of electrical engineering at the Massachusetts Institute of Technology (MIT), and David Huang, formerly an M.D./Ph.D. student (now doing his residency), have been doing for the past 2 years. The result of their efforts, optical coherence tomography, or OCT, is a noninvasive, noncontact method using infrared radiation to provide cross-sectional images of biological tissues with the strikingly sharp resolution of between 10 and 20 microns.



J. FUJIMOTO/MIT

On further reflection. Optical coherence tomographic images like these, produced by reflections from the internal structures of the eye, could make it possible to pinpoint the earliest signs of ocular diseases.

Some of OCT's immediate applications will be in the eye, where the technique may make it possible to pinpoint noninvasively the earliest signs of glaucoma, macular degeneration, and other retinal diseases long before they are visible by any current means. That's a tempting payoff. But the reach of this new tomographic imager could extend far beyond the retina, providing images of the top few millimeters of almost any biological structure, including arteries and mucosal tissue. And though a couple of millimeters might not seem like much, a host of pathological conditions—including atherosclerosis and many cancers—begin in tissue surfaces.

The key to OCT is that coherent radiation (radiation in which all waves are aligned) exhibits interference when combined with radiation of the same phase. In the OCT scanner, infrared light from a superluminescent diode is split into two beams. One beam passes into the object to be imaged, the other travels to a moving reference mirror, and the two sources of reflected light are recombined in an interferometer that measures the interference. Coherent interference occurs only when the distance from a reflecting surface within the imaged object equals the distance from the reference mirror. Multiple scans across the object's surface are combined to produce a tomographic image. Image blurring caused by movement of the object during scanning is reduced by using computerized image processing techniques.

Using this method, Fujimoto and Huang, working with Eric Swanson at MIT Lincoln Laboratories, Carmen A. Puliafito, chair of the ophthalmology department at Tufts University School of Medicine, and other collaborators at the Massachusetts General Hospital and Harvard Medical School, have obtained images of transparent and opaque tissues with qualitative detail approaching that seen in stained histological samples, which have until now been the gold standard for understanding tissue structure. For example, in color-enhanced OCT images of the human retina and optic nerve, taken through a live subject's eye, the retinal nerve fiber layer and choroid are clearly visible as bright layers of reflected, or backscattered, light, while the subretinal fluid and pigmented layer show up as darker regions.

"The nerve fiber layer is the structure that degenerates in glaucoma, and the quantitative measure of its thickness provided by the OCT image could yield the first diagnostic technique capable of detecting the disease in its earliest stages and evaluating its progression," claims Fujimoto. Adds Puliafito, one of the developers of laser eye surgery: "We should finally be able to detect, and then treat, some of the leading causes of blindness before physical symptoms appear."

At the National Institutes of Health, Robert Bonner and Joseph Schmidt of the Biomedical Engineering and Instrumentation Program, and Alex Knuptel, a fellow at the Heart, Lung, and Blood Institute, are attempting to use OCT to image skin tumors, particularly melanoma. "We're testing different frequencies within the infrared to see if we can differentiate between melanoma and other kinds of tumors," said Bonner. He compares this effort with the search for a histological stain that will provide the greatest contrast between different tissue types.

In fact, OCT coupled with fiber optic technology may eventually provide a way of performing an in vivo optical biopsy. "We can imagine using coherence tomography in endoscopic procedures to look a few millimeters into tissues within the body," said Fujimoto, who has already obtained images of atherosclerotic plaque on human coronary arteries obtained at autopsy. Though the OCT images were not as finely resolved as histological sections, they did distinguish between fatty-calcified plaque, fibroatheramatous plaque, and healthy arterial surfaces. It currently takes tens of seconds to obtain such images, but Fujimoto is confident that further technological developments will reduce the time needed to acquire an image. If so, endoscopic OCT could provide real-time guidance during laser angioplasty procedures; the technique could also give researchers a way to diagnose the atherosclerotic process in vivo.

With the development of tunable diode lasers, it may also be feasible to conduct spectroscopic studies in vivo using OCT, and thus provide a new tool for both basic research and for clinical applications yet to be envisioned. Fujimoto expects it will be possible to measure tissue hydration, oxygenation of hemoglobin, and other physiological parameters in various microenvironments within the body. "OCT is only about a year and a half old, so we're just starting these investigations," said Fujimoto. "We really don't know where they will lead." But, if current indications hold, those destinations will be exciting ones.

–Joseph Alper