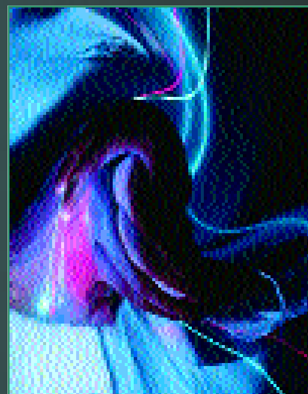
MEDICINE



Americans are concerned about improving the quality and efficiency of health care in the United States. Innovations in medical technology can address this concern, revolutionizing many medical procedures and enhancing the quality of medical products and services. For example, newly developed laser techniques are being used to selectively kill viruses or cancers, replacing traditional radiation and chemical treatments that are toxic to the human body. Sophisticated technology will offer physicians better, more accurate diagnostic and surgical tools, potentially saving lives and improving patient care. Also, such technologies often reduce or eliminate the need for hospital care, thereby reducing associated costs.

Today's Market

The United States produces more than half the world's medical technology, employing about 301,000 people and exporting about $11.4 billion in products. In 1995, the United States produced $56.7 billion in medical devices and diagnostic products; production is projected to grow to $70.9 billion by 1998.[1] Innovative medical technologies are needed to help reduce the rising costs associated with today's health care. According to a recent report by the U.S. Department of Health and Human Services, the Nation's total spending for health care in 1995 increased 5.5 percent to nearly $1 trillion, an estimated average of $3,621 per person.[2]

Tomorrow's Opportunity

The technical expertise used to solve the complex needs of ballistic missile defense has a fortunate spillover. It has resulted in new medical technologies some 10 years ahead of the medical curve that are beginning to make diseases easier to detect and simpler to manage. Many organizations are applying these technologies, making new breakthroughs in treating breast, cervical, and esophageal cancer, among other ailments. The following section describes eight of these innovations.

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[1] Industry figures are cited from the Health Industry Manufacturers Association's U.S. Medical Technology Industry Fact Sheet.

[2] U.S. Department of Health and Human Services. 1997. National health expenditures for 1995. Press release, 27 January. World Wide Web at http://www.os.dhhs.gov/news/press.

. . . breakthroughs in laser medicine that help specialists provide better care to skin, kidney, and burn patients.

LASER R&D PROMISES NEW MEDICAL THERAPIES

In the early years of medical laser research, doctors used single-wavelength lasers with limited dynamic properties. When the free-electron laser (FEL) was developed, it offered short pulses, high peak power, and a greater range of wavelengths. Not surprisingly, this innovation yielded a host of insights in the medical field; the Wellman Laboratories of Photomedicine (Boston, MA) is a nexus of these advances.

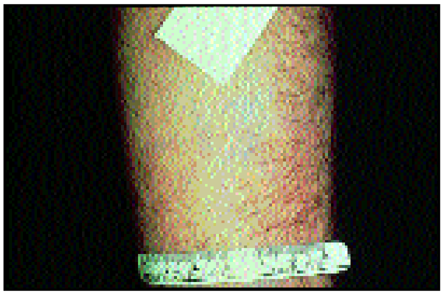
From 1986 to 1991, BMDO provided support to the Wellman Laboratories of Photomedicine at Massachusetts General Hospital (MGH) through the Medical Free-Electron Laser (MFEL) program. The U.S. Congress conceived the MFEL program as a means to transfer technology from military laser research to medicine. Now part of the MGH's Laser Center, Wellman Laboratories built a stellar reputation and a long list of successes in laser medicine. Their laser-related successes follow.

THROUGH ITS MFEL PROGRAM, WELLMAN LABORATORIES' RESEARCH AND TECHNOLOGY TRANSFER RESULTED IN OVER $250 MILLION IN SALES OF LASER EQUIPMENT, BOTH DOMESTICALLY AND INTERNATIONALLY.

- **Assessing and treating burns.** In burn therapy, an infrared laser system optically determines the depth of the burn and uses a carbon dioxide laser to remove the injured tissue quickly and precisely in preparation for skin grafts. This method reduces blood loss and the imprecision of physical debridement (cutting or scraping away the tissue with surgical instruments). Wellman patented the optical diagnostic component of this technology; Sandia National Laboratories (Albuquerque, NM) and MGH are developing a therapeutic device through a Cooperative Research and Development Agreement (CRADA).

- **Eliminating kidney stones.** The laboratory developed a laser-based lithotripsy method to eliminate kidney stones nonsurgically. Kidney stones afflict 400,000 people each year. Instead of sound waves, this method uses an intense light beam to create a shock wave in the fluid medium surrounding the stones, causing the stones to shatter. Excretion of the fragments takes place with little or no pain. Wellman Laboratories holds three patents that arose from a collaboration with a major laser company that licensed the invention, generating over $100 million in revenues.

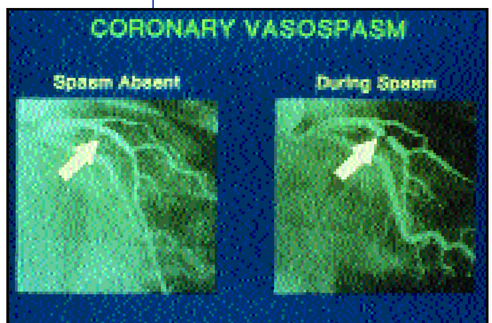
- **Removing undesirable skin features.** Wellman Laboratories introduced laser treatments for nonscarring removal of tattoos, portwine stain birthmarks, pigmented moles, and vascular lesions of the skin. Before this type of laser therapy, there was no effective way to achieve satisfactory outcomes with these conditions. Wellman Laboratories continues to work on the system, optimizing and reducing costs of laser delivery systems and applying selective treatments to other organs besides the skin. A Wellman Laboratories' report estimates that 300,000 patients have been treated with this therapy, generating $250 million in business revenues. In cosmetic surgery, for example, laser removal of "spider veins" on the face and legs is growing in popularity. MGH filed a patent application in 1991 for laser removal of skin lesions and tattoos and licensed the technology. Laser products for dermatologic use are on the market and MGH receives royalties.



Laser treatment selectively and safely removes pigment from tattoos, revealing normal skin color.

- **Shining new light on cancer and arthritis.** Wellman Laboratories also studied and advanced photodynamic therapy (PDT) of various cancers. Rheumatoid arthritis (RA) may also be amenable to treatment by PDT. Degenerative changes associated with RA are treated by injecting photoactive drugs into the synovial fluid that surrounds an RA-affected joint, then irradiating it with a low-powered laser source. For PDT of cancers, MGH filed a total of eight patent applications. A CRADA with Lawrence Livermore National Laboratory (Livermore, CA) resulted from these studies. Two patents that cover the device and method of use have been awarded for PDT of dysfunctional uterine bleeding. Wellman Laboratories licensed the inventions to a medical start-up company. Wellman Laboratories is collaborating with two companies to establish research programs for drug development for this application. These treatments are in development, and Wellman Laboratories is also working with a recent FDA-approved compound for the treatment of late-stage esophageal cancer.

■ **Reducing brain damage.** In hemorrhagic stroke or head injuries, arteries in the brain respond to bleeding by contracting (vasospasm), thereby shutting off the blood supply to areas in the brain. This protective mechanism causes even more damage by depriving the injured brain of needed oxygen. A short-lived, low-powered laser pulse instantly reverses vasospasm, re-establishing blood flow to the stroke-affected area and possibly reducing brain damage. Wellman Laboratories estimates that 800,000 persons each year are impaired by head trauma and brain hemorrhage. Wellman Laboratories designed a laser catheter system that threads into cerebral arteries to deliver laser light. Undergoing testing, this system may be in clinical use within the next one to two years. A Wellman Laboratories' report estimates the cost benefit of early intervention and effective therapy of early stroke at about $3 billion, in terms of lifetime dependency.



■ A short pulse of laser light can instantly reverse arterial spasm, restoring critical blood flow to the heart muscle.

For laser-induced vasodilation of cerebral arteries, MGH filed two patents and is in licensing negotiations. For preventing coronary artery narrowing with a PDT agent (such as chloroaluminum phthalocyanine) MGH filed two additional patents and is negotiating a license. This treatment is not yet clinically available.

According to Lynn Osborn at MGH and market analysis by Arthur D. Little and Co. in Cambridge, Massachusetts, the MFEL program's research and technology transfer resulted in over $250 million in sales of laser equipment, both domestically and internationally. This figure does not include the cost savings resulting from decreased hospital stays or from more rapid patient recovery and return to work.

ABOUT THE TECHNOLOGY

The FEL employs high-frequency electromagnetic fields to control and accelerate bursts of electrons, causing the particles to emit coherent light. Because the characteristic wavelength of the emitted light depends on the properties of the excitation fields, rather than on the intrinsic properties of the medium being excited, FEL emissions are continuously tunable over some range of operation. This behavior contrasts with other lasing mechanisms, which produce one of several discrete wavelengths available for that particular laser material. The continuously variable wavelength feature makes the FEL extremely valuable as a research tool to explore the effect of wavelength on any laser-based process or effect.

During BMDO development of FELs for high-power applications, interest arose in applying these advancements to the then-new field of photonics in medicine. Laser treatments had already shown promise for several skin therapies, surgical cutting, and selective tumor ablation. BMDO established the MFEL program to research and refine these processes and to explore new medical applications, such as PDT. The program's intent was not to develop FELs for medical uses, but to find the best laser operating conditions (wavelength, pulse shape, intensity) for a given therapeutic outcome, and then to use that knowledge to determine the best laser source for the application.

Can You Imagine . . .

. . . 3-D imaging equipment that makes delicate surgery safer and helps train new doctors.

REAL IMAGES OFFER REAL BENEFITS TO MEDICINE

Performing surgery through the eye of a lens, whether endoscopically or microscopically, takes time and training to perfect. As difficult as hand-eye coordination is in procedures like laparoscopic abdominal surgery and microvessel suturing, adding cameras and specialized tools makes it even more complicated. Surgical tools that function as naturally as possible can minimize the impact these tools have on hand-eye coordination.

To this end, VRex, Inc., a marketing arm of Reveo, Inc. (Hawthorne, NY), now offers real-time 3-D imaging equipment for medical education and surgeries. The company's µPol™ system works with microscopes and endoscopes to give physicians an accurate 3-D view of the surgical field. The surgeon looks through normal eyepieces, manipulates tools, and performs procedures, while observers use passive glasses to view the procedure on an output display. Students at remote sites could also view the operation on a display.

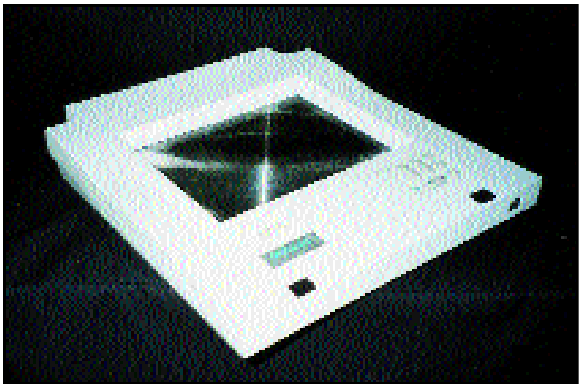
VREX DEMONSTRATED STEREO ENDOSCOPY WITH THE µPOL™ SYSTEM AT NUMEROUS MEDICAL CONVENTIONS.

In demonstrations of stereo endoscopy with the VRex system at numerous medical conventions, surgeons acknowledged the advantages of the 3-D capability. It restores depth perception, reduces operating time, and allows surgical execution to a precise depth. These advantages are crucial in such procedures as nasal sinus endoscopy, which poses a risk of damage to the brain, optic nerve, and carotid arteries.

The company's award-winning 3-D stereoscopic notebook computer—CyberBook™—also uses the µPol system. Along with CyberBook, VRex introduced a Microsoft Windows™ and Apple Macintosh™ compatible SMUX™ software program. SMUX enables users to create 3-D stereoscopic images and display them on the CyberBook. CyberBook sells for as little as $3,500 and SMUX costs between $300 and $400.

Other 3-D stereoscopic products include the VR-1000™ and CAM-3000™. VR-1000, a compact liquid crystal display projection panel, displays flickerless video and computer graphics on large screens from a conventional overhead projector; CAM-3000 is a compact 3-D stereoscopic video camera.

Reveo received BMDO SBIR contracts to build a stereo printer, display, and camera for viewing missiles, decoys, and other battlefield situations in 3-D. The company developed micropolarized viewing hardware, a polarization encoding system, and spatial multiplexing methods to enhance its displays.



■ Reveo has recently introduced the world's first 3-D stereoscopic overhead projection system, pictured above, which uses polarization encoding to project two digital images simultaneously.

ABOUT THE TECHNOLOGY

The system's µPol array uses polarization encoding to project two digital images simultaneously. The system uses spatially multiplexed imaging (SMI) to arrange the left and right images of a stereo pair by position in space instead of by time. It transforms incoming unpolarized light into two perpendicular polarized states, each of which passes one of the stereo pairs of images. Passive polarized glasses decode the polarized (or encoded) images, passing the appropriate image from the stereo pair to the appropriate eye. Processing the images spatially eliminates flicker, so SMI can be used for video and television. In addition to producing 3-D images for all VRex display devices, SMI can generate 3-D transparencies.

RIGID TUBING FINDS MEDICAL MARKET IN OPERATING ROOMS

Can You Imagine . . .

. . . a strong, lightweight surgical tubing that offers low-cost advantages to physicians and hospitals.

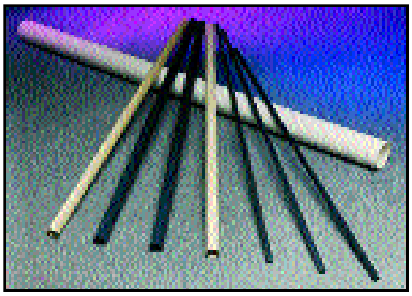
Using surgical equipment presents risks. The most obvious ones concern the patient, but the surgeon must also be wary. For example, the high-voltage surgical cautery knife minimizes bleeding during incision-making, yet poses both an electrical hazard and a source of sparking. Metal-to-metal contacts, such as when the knife grazes a surgical clamp, can cause unpleasant shocks; they also can produce sparks that, in the presence of volatile anesthetic gases and high-concentration oxygen in the operating room, may ignite small fires and, rarely, explosions.

Foster-Miller, Inc. (Waltham, MA), developed strong, lightweight medical tubing that electrically shields devices for endoscopic and laparoscopic procedures, minimally invasive techniques that help to reduce both the length of hospital stays and risks associated with major surgery. Made from an innovative polymer developed for BMDO satellite applications, the surgical tubing minimizes electrical hazards through superior insulation properties. The material costs 30 percent less than fiber-reinforced composite tubing, and it resists delamination under the high pressures and temperatures required for medical sterilization.

FOSTER-MILLER'S SUBSIDIARY, SUPEREX POLYMER, HAS FORMED AN AGREEMENT WITH ACT MEDICAL, WHICH WILL PRODUCE AND SELL LCP TO MEDICAL DEVICE MANUFACTURERS.

The company formed a subsidiary called Superex Polymer, Inc. (Waltham, MA), to commercialize this tubing. Superex Polymer then entered into an agreement with ACT Medical, Inc. (Waltham, MA), a manufacturer and vendor of specialized materials, to produce and sell its liquid crystal polymer (LCP) to medical device manufacturers. For example, ACT uses the LCP tubing for cannulae, the tubes through which doctors insert cameras and surgical instruments into the body. LCP tubing could find a substantial market in the field of minimally invasive surgery; the industry projects nearly 4 million such procedures in the United States in 1996.[1]

Pursuing other R&D efforts that may bring LCP technology to the market, Superex is developing LCP thin films for printed circuit boards (PCBs). Manufacturers of PCBs use epoxy to laminate copper on layers of fiberglass, a high-cost, time-consuming, multistage process. However, most polymer alternatives expand and contract with temperature fluctuations, limiting their application. Superex's thin films will tolerate temperature differences, leading to lower production costs. The company is building a thin-film process facility and expects production to begin in late 1996. Superex teamed with Brampton Engineering, a Canadian company, to market LCP films and laminates to electronics manufacturers.



■ Among other applications, Superex's LCP tubing is used as cannulae, tubes through which doctors insert cameras and surgical instruments into the body.

LCP technology could also solve the flatness and contamination problems that have caused the beer industry to shun plastic bottles until now. Superex is working with five companies from Europe, Japan, and the United States to develop a multilayered LCP bottle for beer. Superex expects to license its technology, slated for completion by July 1997, to these five companies.

ABOUT THE TECHNOLOGY

Superex's material property improvements turn on advanced die technology. The die simultaneously orients polymer molecules perpendicular to each other and at an angle to the length of the tubing. This orientation solves the problem of poor transverse strength that, until now, made LCP virtually useless in many applications because of its tendency to split or thin unevenly when stressed in the nonmachine direction. In 1995, Foster-Miller's LCP extrusion process won an R&D 100 award from *R&D Magazine* as one of the year's 100 most significant innovations.

[1]Global Industry Analysts, Inc. 1995. Medical industry market research reports: Endoscopy equipment. World Wide Web at http://www.globind.com/315.htm.

Can You Imagine . . .

. . . a neural network technology that helps doctors double-check Pap smears for suspicious cells, increasing the reliability of tests for cervical cancer.

IN ADDITION TO DETECTING CERVICAL CANCER, HNC MAY APPLY ITS NEURAL NETWORK TECHNOLOGY TO SCREEN FOR LUNG CANCER.

PAPNET IMPROVES SCREENING EFFICACY FOR CERVICAL CANCER

Cervical cancer strikes about 65,000 U.S. women per year, accounting for 5,000 deaths annually.[1] However, during the past 30 years a screening test called the Pap smear accounted for a 63 percent decrease in the death rate from this disease.[2] Curable if caught early enough, cervical cancer is one of the few human malignancies strongly associated with the human papilloma virus (HPV). A Pap smear helps reveal the presence of HPV and helps a patient discover her risk factor for cervical cancer.

Laboratories perform over 50 million Pap tests in the United States every year.[2] Due to the large volume and fast turnover of test slides in a typical histology laboratory, positive test results are sometimes overlooked. When this occurs, a potentially curable carcinoma-in-situ can progress to an invasive cancer. In late 1995, Neuromedical Systems, Inc., received FDA approval for a neural net–based screening method that greatly increases the odds of detecting a suspicious Pap smear, helping to save women's lives. This computerized system owes part of its existence to BMDO funding through HNC Software Inc. (San Diego, CA).

HNC developed avalanche neural network computer architectures and systems for BMDO to detect ballistic missiles. HNC's network technology now forms the basis of Neuromedical Systems' PAPNET® Testing System. This system uses fast, powerful neural network algorithms to quickly identify the signs of malignancy in cell clusters. With the PAPNET test, cytology labs increase the total detection of abnormalities up to 30 percent. The FDA approved the system in November 1995, and more than 40 U.S. clinics and 15 countries now use it.

Neuromedical Systems, which acquired its software development tool for neural networks from HNC, holds a patent for applying neural networks to cell analysis. The company may apply the technology to develop automated systems for lung cancer screening, urinalysis, and other cell analyses.

■ PAPNET® uses HNC's neural network technology to detect potentially missed abnormal cells on a woman's Pap smear.

ABOUT THE TECHNOLOGY

Showing the system a variety of images representing both benign and malignant cervical cells trains the computer to read Pap smears. The computer examines the images and learns the most salient characteristics of each type of cell or cell cluster. For example, large and misshapen nuclei can signify cancer. After the network is trained, it can be used in an automated system to quickly scan slides and flag abnormalities.

PAPNET uses two separate neural networks, one trained to recognize suspicious single cells, and the other trained to recognize abnormal cell clusters. The system selects and records color images of the 128 most suspicious cell images on a smear, and allows the cytologist to scrutinize them. In unassisted visual screening, the error rate (classifying abnormal smears as normal) can be as high as one in three. In a test of 1,247 Pap smears, the PAPNET system identified 517 of 534 abnormal smears, for a 97 percent accuracy rate. Note, however, that PAPNET is a supplemental screening method: A qualified pathologist makes the final diagnosis.

[1]University of Pennsylvania Cancer Center. 1996. Clinical trials news: New treatment options for cervical cancer. World Wide Web at http://oncolink.upenn.edu/upcc/clin_trials/fall94/RUBIN.html.

[2]U.S. News Online. 1995. Health: Digital help to spot cervical cancer. World Wide Web at http://www.usnews.com/usnews/nycu/cervical.htm.

DRUG-SCREENING SOFTWARE GOES COMMERCIAL

Can You Imagine . . .

. . . an algorithm that promises to transform new drug research by rapidly suggesting candidate molecules.

Advances in the pharmaceutical industry can be painfully slow and costly. Typically, it takes an average of 15 years and nearly $500 million to bring just one new drug from the laboratory bench to the pharmacy shelf.[1]

In an effort to expedite drug development, researchers have turned to computational chemistry, a branch of theoretical science that uses digital computers to model systems of chemical interest. But even this computerized technique is time consuming. For example, a full all-atom simulation of just two interlocking molecules can consume hundreds of hours of computer time, even on supercomputers.

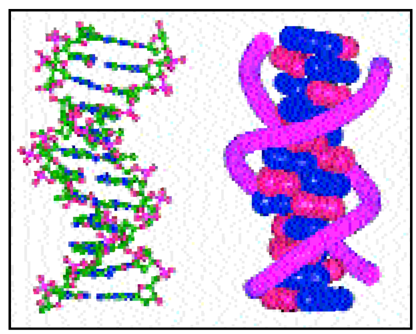
Moldyn, Inc. (Arlington, VA), developed a computer algorithm that reduces the time needed to model the dynamics of large molecular systems. The company's algorithm, MBO(N)D[2], promises to transform new drug research, helping find new cures faster. Moldyn, a subsidiary of Photon Research Associates, Inc. (San Diego, CA), developed this technology using BMDO-funded modeling methods designed to simulate the dynamics of large space-based structures.

MOLDYN'S COMMERCIAL PLANS FOR ITS COMPUTER ALGORITHM INCLUDE PARTERNERING WITH LEADING PHARMACEUTICAL COMPANIES AND A COMPUTATIONAL CHEMISTRY SOFTWARE FIRM.

Because it increases computational speed, MBO(N)D will make the discovery of new drugs and the development of new materials through computational techniques more practical. Tests of the algorithm show that it simulates the dynamics of large molecules (10,000 atoms) up to 50 times faster than conventional all-atom modeling techniques. With further refinements, the algorithm could even be applied to even larger molecules (10,000 to 100,000 atoms) at speeds 100 to 1,000 times faster than all-atom approaches.

Moldyn received an Advanced Technology Program award from the National Institute of Standards and Technology to help bring this technology to the pharmaceutical industry. In this project, the company and its partners will refine the algorithm for commercial use. Moldyn's partners in the project include leading pharmaceutical companies, a computational chemistry software firm, and leading academics in the field of computational chemistry.

The company plans to market the MBO(N)D algorithm as a stand-alone software package and as an interface module link to software already on the market. The stand-alone package targets developers of new drugs and materials, while the interface module targets software firms.



■ Moldyn's algorithm can simulate DNA (pictured above right) 50 times faster than all-atom modeling techniques (pictured above left).

ABOUT THE TECHNOLOGY

MBO(N)D accelerates computational speed without affecting chemical and physical realism through a technique known as substructuring, which combines atoms into interacting groups of rigid and flexible bodies. The algorithm also filters out small-scale motions that do not affect the overall behavior of the molecule. These two innovations reduce the number of system variables and allow the simulation to be computed over a smaller number of time steps.

[1]Pharmaceutical Research and Manufacturers Association. 1996. The drug development and approval process. World Wide Web at http://www. phrma.org/charts/approval.html.

[2]MBO(N)D stands for multibody order(n) dynamics. Multibody refers to the method of combining the molecules in a series of substructures; order(n) refers to the number of variables in the model. In conventional simulations, the number of variables equals the number of objects squared (n^2). MBO(N)D reduces the number of variables to the number of objects (n).

Can You Imagine . . .

. . . a breast ultrasound instrument that could examine breast abnormalities not readily apparent with x-ray mammography.

BREAST ULTRASOUND MAY SAVE WOMEN'S LIVES

An important addition to mammographic screening in recent years, breast ultrasound helps doctors decide whether a suspicious area on a mammogram is a benign cyst or a malignant tumor. Investigators found new ways to use hand-held ultrasound wands for this task. Manufacturers of ultrasound equipment also responded to the needs of clinicians, developing specialized units for breast ultrasound.

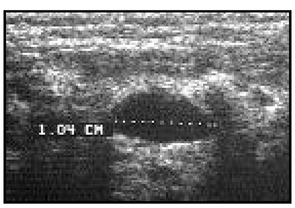
Demonstrating its proactive corporate strategy of continual innovations in breast imaging, ThermoTrex Corporation (San Diego, CA) transferred some of its BMDO-funded advanced imaging technology into the growing field of breast ultrasound. ThermoTrex is also developing digital mammography techniques.

SONIC CT™ IS UNDERGOING LIMITED TRIALS AT THE HILLCREST CENTER FOR WOMEN'S HEALTH IN SAN DIEGO, CALIFORNIA.

In its unique approach, ThermoTrex incorporated computed tomography (CT) techniques into breast imaging with ultrasound. Sonic CT™ images the breast in a slice-like fashion using high-frequency sound waves. This method yields an image relatively free from overlying tissue interference, helping doctors to see features not always apparent with x-ray mammography. Radiation exposure is not a concern with this method, because Sonic CT uses ultrasound instead of x-rays to form a breast image. Also, this technology does not require painful compression of the breast.

Sonic CT can spot breast abnormalities not associated with microcalcifications. Thus, it could assess such conditions as fibrocystic breast disease (also called "lumpy" breast disease). It also could help reduce the number of breast biopsies, 80 percent of which turn out negative. Currently, Sonic CT is undergoing limited trials at the Hillcrest Center for Women's Health in San Diego, California.

ThermoTrex is developing Doppler CT, an imaging technology related to Sonic CT. This device uses ultrasound to assess blood vessels for blockages. Specifically, it will detect blood flow speed and image vessels in three dimensions, providing useful information for examining coronary and carotid arteries to assess the risk of heart attack and stroke, respectively. Doppler CT also can image the peripheral blood vessels of the legs, an important capability for detecting blood clots in elderly patients after surgery and during prolonged periods of bed rest.



Courtesy of New South Wales Breast Cancer Institute.

■ Ultrasound can help confirm the presence of a malignant lesion, as pictured above.

ABOUT THE TECHNOLOGY

Both Sonic and Doppler CT devices convert ultrasound signals into digital images of anatomical features and electronically process and store them, just as x-ray images are manipulated in "conventional" CT. Sonic CT uses low-frequency ultrasound to produce cross-sectional slices of the breast, acquiring images in near-real time. Doppler CT will measure the velocity of blood coursing through vessels. Blood flows at a higher speed through a passage narrowed by plaque or scar tissue than through an unobstructed blood vessel with a wider diameter. Therefore, comparing the speed of blood flow in adjoining areas of an artery allows detection of blockages in that artery.

PHOTODYNAMIC THERAPY EMERGES IN WAR ON CANCER

Esophageal cancer leaves many of its victims unable to swallow, and nearly always results in death. The American Cancer Society projects diagnosis of 12,300 people in the United States with esophageal cancer in 1996 and 11,200 deaths from it.[1] Doctors have limited treatment options.

Now there is a new treatment for esophageal cancer, based on a method that holds great promise for other cancers, as well as for noncancerous conditions. The FDA-approved Photofrin® captures light energy and uses it to selectively destroy diseased cells. It is the first drug ever approved for the photodynamic therapy (PDT) of cancer.

Photofrin was originally developed by Dr. Thomas Dougherty as an anticancer agent at the Roswell Park Cancer Institute (Buffalo, NY). The Medical Free Electron Laser (MFEL) program at Baylor Research Institute (Dallas, TX) studied it as a blood purifier. BMDO's MFEL program, established by Congress to transfer BMDO-sponsored free-electron laser (FEL) technology to medical and other spinoff applications, initially funded some of this laser research.

Using laser light of a specific wavelength, Photofrin produces an oxygen radical that kills cells in its immediate vicinity. Abnormal tissues selectively absorb the drug, which laser light then activates, making it a well-controlled therapy that avoids harm to normal cells. In late-stage esophageal cancers that obstruct breathing and swallowing, PDT is a kinder alternative to surgery, which causes pain and forms scar tissue.

Baylor eventually licensed Photofrin to QLT Phototherapeutics, Inc., which submitted the drug for FDA approval. QLT awaits FDA approval to use Photofrin in the treatment of bladder and some lung cancers. The company is conducting extensive research in PDT for treatment of a wide variety of cancers and for noncancerous disorders such as psoriasis, rheumatoid arthritis, and cardiovascular disease.

Many exciting clinical advances resulted from Baylor's MFEL-related research, including unique photoactive drugs for collagen repair in the knee joint and improved methods for treating eye disease. Baylor has developed a photochemical to isolate stem cells from blood in order to restore the marrow of chemotherapy patients and other immunocompromised individuals. Baylor also developed a photochemical, now available in Taiwan and Egypt, that can reverse drug resistance in malaria sufferers.

ABOUT THE TECHNOLOGY

PDT involves techniques in which photoactive dyes kill viruses or cancers when irradiated with laser light. The dyes selectively attach to a number of enveloped viruses, such as HIV, hepatitis, Epstein-Barr, cytomegalovirus, and herpes, as well as many cancerous cells. When light of a specific wavelength and intensity shines on the dye, a chemical reaction begins that gives off a toxic oxygen radical, called singlet oxygen, that exists for a short distance and for a fraction of a second. The oxygen radical breaks down the viral sheath and kills the virus.

Because these dyes produce this radical when they absorb laser light of a specific wavelength, Baylor used an FEL and other lasers to deliver the correct wavelength. Before FELs, doctors used continuous-wave lasers, which could not produce the variety of wavelengths and very short pulses of FELs. The FELs produce more precise and varied wavelengths, enabling researchers to study discrete interactions of light and matter.

[1]Cancer facts and figures. 1996. American Cancer Society. 1-800-4-CANCER.

Can You Imagine . . .

. . . techniques in which photoactive dyes kill viruses or cancers when irradiated with laser light.

QLT PHOTOTHERAPEUTICS, INC., HAS ACQUIRED A LICENSE FOR PHOTORIN, WHICH AWAITS FDA APPROVAL FOR USE IN THE TREATMENT OF BLADDER AND SOME LUNG CANCERS.

Courtesy of Beckman Laser Institute.

■ Fiber optics can deliver light energy through endoscopes and catheters in PDT for cancer.

Can You Imagine . . .

. . . an imaging technology that offers medical researchers a less destructive way to look at samples under a microscope.

ESSEX'S TECHNOLOGY HAS SUCCESSFULLY IMAGED A VARIETY OF BIOLOGICAL SPECIMENS AND SEMICONDUCTOR MATERIALS.

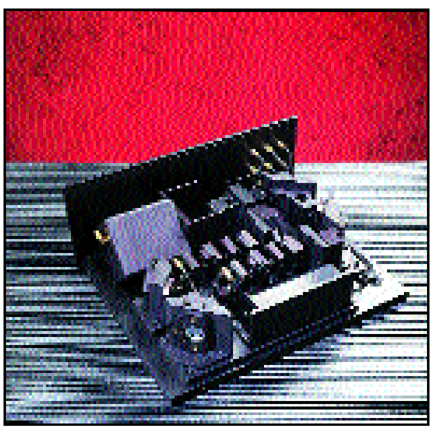
NEW METHOD ELIMINATES FIXING IN BIOLOGICAL ANALYSES

To look at some of life's smallest building blocks, many light-based imaging methods require physical alteration of the biological material before viewing. Preparing a sample for viewing often means stabilizing the cell with special chemicals and removing all the water, potentially distorting the image of the cell and its contents. Newer techniques can eliminate some fixative steps, but may also cause photo-bleaching, a phenomenon that can ruin parts of the image.

A new imaging method offers a less destructive means of biological analysis and of examining industrial and semiconductor materials. Essex Corporation (Columbia, MD) developed a synthetic aperture microscope (SAM), based on synthetic aperture radar. The device produces high-resolution, 3-D, complex-valued representations in a few seconds, with reduced alteration of the specimen. It also allows specimen viewing from a greater distance than many light-based imaging methods. Applications of the SAM include both macroscopic and microscopic imaging.

The SAM, a coherent-light microscope, can resolve images as small as one-quarter the device's operating wavelength. Thus, using ultraviolet light (280 nanometers) allows visualization of sample features as small as 70 nanometers. Working with Dr. Lee Peachey, a biology professor at the University of Pennsylvania, Essex discovered that this resolution gives a sharp view of the complex eyes of fruit flies and the intricate exoskeletons of diatoms (microscopic algae). It also produces detailed images of carbon fibers and diffraction gratings.

Essex's device can operate at wavelengths from ultraviolet to visible and infrared. Independent of working distance, the device resolves very small features from several inches away. By changing the focal lens of the SAM, Essex expects to increase this distance to four to six inches or even more.



■ Essex's microscope works in tandem with ImSyn™ (pictured above), Essex's high-speed optical processor which forms images from a wide range of sensor inputs.

The SAM works in tandem with ImSyn™, Essex's high-speed optical processor which is capable of forming images from a wide range of sensor inputs. An outgrowth of BMDO-sponsored research in rapid optoelectronic processing of radar signals, the ImSyn processor significantly cuts data processing time in magnetic resonance imaging (MRI), ultrasound, and other diagnostic examinations. For example, the optoelectronic processor allows physicians to see a target tumor or other anatomical feature in real time, and its high speed increases the resolution of images and prevents blurring.

Dr. Peachey notes that when used to collect data digitally, the SAM may mimic different types of microscopes. Thus, a biological sample would be subjected to only one data collection event because the digital data could continually be rearranged to produce images in different formats. The SAM also could generate full phase and amplitude information for 3-D holographic imaging, allowing the viewing of images from different angles. Today's microscopes that use film or charge-coupled devices record only amplitude information.

ABOUT THE TECHNOLOGY

SAM's key, the ImSyn processor, takes data directly from any sensor, such as an MRI coil, and sends real-time imaging to the workstation for display. Standard workstation software performs image enhancement and manipulation, if desired. The system, a 2-D real-time Fourier transform processor with high-speed input and output, uses optoelectronic technology for speed and flexibility. The processor transforms the received data into images and then forwards those images to the image analysis workstation. The complex correlation with an appropriate pattern in a database forms the pattern recognition option.