Institute Pursues New Med School Collaborations

Reseachers at the Beckman Laser Institute have initiated a new collaborative project with UCI’s Department of Neonatal Medicine, pushing to thirteen the total number of collaborations with departments and programs operating within the College of Medicine.

The new project, co-directed by Feizal Waffarn, M.D., Associate Professor in the Department of Neonatal Medicine, and Bruce Tromberg, Ph.D., Director of BLI’s Laser Microbeam and Medical Program, employs BLI’s near-infrared imaging system to improve endotracheal intubation in newborns with respiratory and other illnesses.

Conventional imaging methods for newborns rely on x-ray, which is limited by cost, time, and radiation exposure. By contrast, optical imaging can quickly and precisely locate the tip of an endotracheal intubation tube through an infant’s chest wall at low cost and without the use of ionizing radiation.

Institute Director Michael Berns, Ph.D., views interdepartmental collaborations as crucial to BLI’s success: “The neonatal collaboration and others like it prove that medicine can take big leaps forward on our own campus when the spirit of cooperation prevails.”

The Institute maintains strong collaborative ties with the Schools of Biological Sciences, Engineering, and Physical Sciences.

The award, disbursed under the auspices of the NOHR Foundation’s Year 2000 Research Program, will support Dr. Wong’s effort to develop an Optical Coherence Tomography (OCT) system with the high-resolution capabilities necessary to distinguish the miniature anatomical structures of the inner ear.

(Newsbriefs continued on p. 8)
Words of Wisdom: The Writing On My Wall

by Michael Berns, Ph.D.
Arnold and Mabel Beckman Professor
President and Director

Visitors to my office know that the white board in my conference is adorned by a set of aphorisms, witticisms and rules to live by which I have collected over the years.

The list grows monthly, and my daily experiences in life have forced me to shuffle and re-prioritize some of these “rules,” but the core remains the same. I want to share a few of these here in the hope that doing so will reinvigorate the mission which Dr. Beckman and I first undertook in 1982.

❖ Be mindful—integrity is perishable by success. As we become increasingly successful, the temptation to set aside integrity also increases, even if only on a subconscious level.
❖ Power corrupts! One really needs to be careful of this. With power comes responsibility.
❖ The bureaucratic mentality is the only constant in the universe! A favorite line of mine from Star Trek (the movie). It’s amazing how widespread this mentality is; maybe because it’s easier to be bureaucratic than it is to be creative and innovative.
❖ No “Bucks,” no Buck Rogers. It takes money (lots of it) to afford today’s “gadget” technologies. Some days I wish I had stayed a field biologist so that I could simply watch the animals play and the flowers grow.
❖ Don’t be a whiney excuse maker. Accept the consequences of what you do and don’t play the “blame game” (nobody ever wins). Put the facts on the table, and let the “chips fall as they may.”
❖ When I grow up, I want to be a little boy. I am fortunate to have been able to build my own toys and gadgets in a thirty-year quest for knowledge with meaningful applications.
❖ Failure teaches as much as success. Actually one can learn more from failures. Each failure educates us and provides us new chances for success.
❖ You need to communicate clearly to get the result you want. Often we don’t communicate effectively; sometimes we fail to communicate at all. Few of us are mind-readers so don’t expect someone to know what you want unless it is clearly articulated.
❖ Trapped by the trappings of success. We frequently believe ourselves to be as good as other people tell us we are. Worse yet, we may believe ourselves to be as good as we think we are.
❖ Life is a chess game; anticipate the moves of your opponent. Unfortunately, we often need to think in this manner in order to survive. It never ceases to amaze me how combative academia can be. It can become very unusual, even downright bizarre, inside the “ivory tower.”
❖ We are the architects of our own pain. Both in mind and body we often are the authors of our own fate. We create (continued on p. 7)
Physicians at the Beckman Laser Institute and Medical Clinic made history in January by launching one of the first patient studies on endometrial photodynamic therapy (PDT) for the treatment of dysfunctional uterine bleeding.

Researchers and physicians at BLI have dedicated eleven years to the endometrial PDT project, moving the technique from the “drawing board” to the clinic in a series of rigorous, step-by-step measures funded by the NIH and “incubated” as part of the Institute’s longstanding research on tumors. Pending the results of follow-up studies and continued approval from the Food and Drug Administration (FDA), endometrial PDT could be ready for second-phase clinical trials by the end of 2000.

A Medical Relay Race

“Endometrial PDT has been the culmination of intense institutional collaboration,” explains Yona Tadir, M.D., Professor of Obstetrics and Gynecology and principal investigator for the project. “You have to imagine this undertaking as a relay race with one researcher after another passing along the baton.”

The project began in 1989 when Dr. Tadir first arrived at BLI as a visiting researcher. “We started with elementary questions,” says Dr. Tadir. “For example, ‘Is the uterus a good target for PDT?’” From there, the questions became increasingly complex. Engineers, chemists, physicists, and physicians worked together to tackle each problem, one after the other. A steady stream of medical fellows from around the country and Europe has kept the project moving forward, and the stewardship of key UCI personnel, including Drs. Kristin Keefe and Philip DiSaia, has helped to keep the project on track. In order to document their progress, the BLI team has published over fifty articles detailing all phases of their work.

The goal, says Dr. Tadir, has remained fixed. “Our sights have always been set on one thing. We wanted to develop a user-friendly, minimally-invasive office procedure which could replace unpredictable drug therapies and costly, high-risk surgeries.”

In order to accomplish this, Dr. Tadir and the BLI team had to keep an eye on the competition. While other FDA-approved alternatives exist, none, says Dr. Tadir, offers the advantages of PDT.

Unlike the “balloon-type” devices currently under development, the proprietary Intrauterine Light Probe (IULP) developed at BLI requires no anesthetic for delivery and eliminates the risk of thermal damage which other devices can produce as they literally “cook” the endometrial lining.

The Promise of PDT

Photodynamic therapy (PDT) utilizes light-sensitive drugs in combination with laser light to selectively target and ablate (destroy) unhealthy tissues. When light of a specified wavelength and frequency interacts with these drugs, a chemical reaction begins which destroys abnormal cells where the photosensitizer has concentrated. Because these photosensitive compounds can be delivered directly to the diseased or abnormal tissue, PDT offers extraordinary selectivity. Healthy tissues are spared and remain viable while abnormal tissues are fully ablated.

Bruce Tromberg, Ph.D., Director of BLI’s Laser Microbeam and Medical Program, and Michael Berns, Ph.D., Institute Director, spearheaded many of the light and drug dosimetry studies which moved endometrial PDT from theory to practice. Both were also instrumental in the development (continued on p. 7)
Cuts, scrapes, burns, and incisions need not leave their mark on us, according to Vincent Wallace, Ph.D., a postdoctoral researcher at the Beckman Laser Institute. Together with Tatsuro Yomo, M.D., Chung-Ho Sun, Ph.D., and Mariah Coleno, a graduate student in Chemical and Biochemical Engineering and Material Sciences, Wallace is working on a wound healing project which combines the high-resolution, deep-tissue imaging capabilities of the two-photon microscope with the well documented principles of photodynamic therapy (PDT).

“Can we accelerate wound healing? Can we reduce scarring? I’m confident we can,” says Wallace, who joined the research staff at BLI in 1997 after completing his doctoral work at the University of London’s Institute of Cancer Research. “The trick will be to determine exactly what biological and chemical parameters affect the process. We’re looking at the healing process to see exactly how this works.”

A Biological Orchestra
The biology of wound healing is extraordinarily complex. Specialized cells known as monocytes and macrophages migrate through the extracellular matrix of damaged tissues, acting as tiny “conductors” which orchestrate the healing process. These cells release cytokines (i.e., growth factors) which are responsible for stimulating tissue contraction and regeneration. Too few cytokines result in poor or prolonged wound healing; too many cytokines produce inflammation and swelling.

Wallace uses two-photon microscopy to monitor collagen synthesis and regeneration in damaged tissues. Preliminary studies indicate that photodynamic therapy (PDT), a well known cancer treatment which employs laser light in combination with photosensitive drugs, inhibits the release of growth factors in damaged tissue and consequently slows down the process of tissue contraction. The significance of these results is two-fold, according to Wallace.

“We’re learning, first of all, that we can slow down the natural healing process. This is significant because it gives us increased control over scar formation. At the same time, it appears that PDT allows us to reduce inflammation which typically retards the healing process.”

Practical Applications
Wallace’s research will likely support a wide range of potential clinical applications. In the case of elective surgeries, low-dose PDT might be used to minimize the effects of scarring. In the event of trauma or emergency surgery, a slightly higher dose of PDT might be administered to control inflammation and promote more rapid healing.

“We’re really talking about tailoring the healing process to address the needs of individual patients,” says Wallace. “The body’s own chemistry gives us that flexibility.”

Current studies, funded by the Department of Defense, Office of Naval Research (DOD-ONR) monitor healing in artificial tissue cultures known as RAFT models. The next phase of Wallace’s research will target living tissue samples.
Sheryl Cherrison: Administrative Specialist

Sheryl Cherrison won’t back down from a challenge. Whether she’s on the tennis court volleying her way to victory or in the office wrestling with yet another administrative deadline, Sheryl has no trouble stretching herself to the limit.

“In my mind, that’s the unique aspect of working in a university setting,” Sheryl says. “You’re always confronted with opportunities for learning and personal growth.”

A native of Southern California, Sheryl arrived at BLI in 1996 after thirteen years in Redding, California, where she served in administration for the public schools. Along with husband, Larry, a respiratory therapist at UCI’s Medical Center and part-time pastor at the Mariners’ Church in Irvine, Sheryl has lived and developed her career in Washington, Texas, and Montana.

 Coming home to the Southland has given Sheryl a chance to enjoy family and to find her place in the BLI family as well. “For me, it’s important to be proud of the place where you work. I hold my colleagues in high regard, and I feel confident referring a friend.”

Sheryl and Larry have four children: Eric, 30; Cristian, 28; Charity, 22; and Shannan, 14. In addition to her passion for tennis, Sheryl enjoys a variety of church activities, walking on the beach, reading, and spending time with her kitten, Tucker, and her two “grand-dogs,” Madison and Creeper.

GOV’T AGENCIES AND FOUNDATIONS
Arnold and Mabel Beckman Fndn.
The David and Lucile Packard Fndn.
Department of Commerce
Department of Defense (ONR)
Department of Energy
The George E. Hewitt Fndn. for Medical Research
Hester Family Foundation
Hoag Foundation
National Institutes of Health
Whitaker Foundation

SUPPORTERS
Dr. and Mrs. Jay Applebaum
The Argyros Foundation
Dr. Arnold O. Beckman
Patricia Beckman
Dr. and Mrs. Michael W. Berns
Dr. and Mrs. Matthew Brenner
Mr. and Mrs. Nathaniel Brenner
Marilyn Burton
Cheng-Jen Chang, M.D.
The John Chao Family
Dr. and Mrs. W. Andrew Cies
Dr. Howard and Rita Conn
Mr. and Mrs. Duke Cooper
Mr. and Mrs. Brian Demsey
Dr. and Mrs. Norman Frankel
Mrs. Frederick Garry
Mr. and Mrs. Walter Gerken
Marilyn Hester Gianulas
Dr. and Mrs. Frederick Grazer
Mr. and Mrs. Gavin Herbert
Nora Hester
Mr. George Hewitt
Robert L. Jones, M.D.
Dr. and Mrs. Richard Kasper
Mr. and Mrs. Robert Kleist
Dr. and Mrs. Richard Kratz
Wallace Landholm, M.D.
Richard McCleary and Ileen Frankel
Frank and Linda Meyskens
Mrs. Warren S. Myers & Family
Tricia and Al Nichols
Richard and Hinda Rosenthal Foundation
Mrs. Audrey M. Schneiderman
Mr. and Mrs. Robert W. Scholler
Mr. and Mrs. John Stahr
Mr. and Mrs. Robert Sterman
Thomas T. and Elizabeth C. Tierney
D.E.L.T.A. Rescue
Orange Coast Rhodesian Ridgeback Club
Premier Laser Systems, Inc.

Shoreline Dog Fanciers Association
S. California Veterinary Medical Assoc., Orange County Chapter
S. California Veterinary Medical Assoc., Saddleback-Capistrano Valley Chapter

INCUBATOR CORPORATE PARTNERS
Candela Corporation
Newport Corporation
PhotoSense L.L.C.

CORPORATE AFFILIATES
Allergan, Inc.
Beckman Coulter, Inc.
Coherent, Inc.
ESC Sharplan Lasers, Inc.
SmithKline Beecham

INDUSTRIAL ASSOCIATES
Bio-Safe America
Candela
Carl Zeiss, Inc.
DUSA Pharmaceuticals, Inc.
Hewlett Packard
Medical Optics, Inc.
Olympus
Physical Optics Corporation
**Quincy’s Pride: Humans Helping Animals**

Quincy’s options were few when the seven-year-old mixed breed terrier arrived at the Beckman Laser Institute for treatment. A deep tissue lesion, known as a cutaneous angiomatosis, had intruded the right side of Quincy’s face, making normal activities a challenge.

“Routine surgery would have required removal of all of the affected skin on the right side of the face. That wasn’t an option,” says Dr. George Peavy, D.V.M., Director of the Institute’s Veterinary Outreach Program.

Instead, Peavy teamed with Stuart Nelson, M.D., Associate Professor of Surgery, to perform a laser procedure which Nelson has honed for the treatment of port wine stain (PWS) lesions in humans.

Peavy and Nelson used the Institute’s Nd:YAG laser during two treatment sessions to “photocoagulate” Quincy’s vascular malformation. “The absorption by hemoglobin circulating in the lesion results in thermal necrosis of the affected tissue,” explains Dr. Peavy. Following treatment, the lesion scabs and sloughs, leaving behind healthy, blanched skin.

“Quincy is the real winner here,” notes Dr. Peavy. “We took an established technology from human medicine and applied it to an animal that had no other options.”

Quincy poses for the camera before (inset) and after laser treatment for a vascular malformation affecting the skin over the right side of her face.

---

**AVON PLEDGES $2.2M FOR BREAST CANCER RESEARCH**

**Institute Receives New Diagnostics Funding Component**

The University of California, Irvine and the Beckman Laser Institute have received major funding from the Avon Breast Cancer Crusade to expand research on breast cancer diagnosis and treatment.

UCI will receive $2.2 million, a portion of the $14 million gift Avon is awarding to five breast cancer research facilities around the nation. A percentage of the UCI gift, administered by the Medical Center’s Chao Family Comprehensive Cancer Center, will go to support continuing work on a laser-based diagnostic device for the detection of early, pre-cancerous growths in the breast.

The laser diagnostic device, developed by Bruce Tromberg, Ph.D., Director of BLI’s Laser Microbeam and Medical Program, and John Butler, M.D., Professor of Surgical Oncology, measures the absorption and scattering of laser light as it propagates through breast tissue.

“We are proud to partner with UC Irvine and other beneficiaries to seek the possible causes, prevention, treatment, and cure of breast cancer,” said Patricia Sterling, Senior Manager, Avon Breast Cancer Crusade.

“It certainly provides us a boost when corporations like Avon take a leadership role,” adds Tromberg. 

---

**It’s Your Health**

- 1 in 8 women in the U.S. will be diagnosed with breast cancer.
- Breast cancer is the most common form of cancer among women.
- The incidence of breast cancer has been rising over the past two decades.
- Early detection improves chances for survival.

Source: National Cancer Institute
ENDOMETRIAL PDT: ‘RELAY’ SCIENCE

of Tadir’s IULP, the miniature (2.5 mm) fiber-optics-based device which delivers light into the uterine cavity.

“We’ve drawn on a huge pool of talent,” Tromberg says. “In some ways, this is the mother of all interdisciplinary projects at BLI. This is what happens when basic science and good pre-clinical models meet forward-thinking engineering and medical expertise.”

Oncologists have used PDT to treat tumors for more than fifteen years. Researchers at BLI are among the first to successfully apply the technique to gynecological medicine.

“More than 100,000 hysterectomies are performed each year to treat dysfunctional uterine bleeding,” states Dr. Tadir. “These are major procedures with long recovery periods and the possibility of severe complications. I am confident that a significant number of these surgeries can be avoided with the application of this new technique.”

The BLI team is currently working to recruit patients for additional testing. Assuming these studies go smoothly, Dr. Tadir sees a range of applications for endometrial PDT. Selective endometrial ablation prior to hormone replacement therapy (commonly prescribed to improve quality of life in post-menopausal women) might eliminate the heavy bleeding which frequently occurs as a side effect. Endometrial PDT could also play a role in the treatment of pre-cancerous lesions affecting the uterus.

Institute Director Michael Berns, Ph.D., gives the project high marks for innovation and collaboration. “When Dr. Beckman and I talked about the meaning of interdisciplinary science back in 1982, this is the kind of project we both had in mind. Our federal core support depends on our ability to take ideas like this from basic science to clinical trials.”

STUDENT RESEARCHER WINS UC ACCOLADES

Undergraduate Selected For “UC Day” Panel

Fourth year student, Ryan Lanning, a Biology/Chemistry double-major at UCI, traveled to Sacramento in March to present his work to University of California President Richard Atkinson and a group of California State legislators.

Selected as one of nineteen undergraduate stand-outs from eight UC campuses, Lanning participated on a panel of young researchers who were invited to the state capital for the annual “UC Day” events.

Lanning, a native of Escondido, California, presented the results of his research on breast cancer diagnostics, a project he has been working on for the past two years under the supervision of Bruce Tromberg, Ph.D., Director of BLI’s Laser Microbeam and Medical Program (LAMMP). The annual UC Day events highlight the educational and research advances that have contributed to the state’s economy and quality of life.

Research opportunities, once a rare thing for undergraduates, are becoming an increasingly important part of the university experience. “Research has been great,” Lanning says. “I’d rather be in the lab than buried in class. [The lab] is where [students] see how everything fits together.”

Words of Wisdom

situations and strive for achievements that consume our energies and eventually can subject us to pain and discontent. It is too easy, I think, to blame others for the unrealistic demands we often place on ourselves. When life starts to hurt, it is important that we take time for “soul-searching” and introspection.

❖ Pain is a teacher with a profound message. Each instance of pain is a lesson in life, a hint that something is wrong. We need to listen to these messages very carefully so as to avoid or ameliorate future pain. Listen to what hurts and adjust accordingly.

❖ Don’t take yourself too seriously (AOB’s Rule # 7). This is one of Dr. Arnold Beckman’s “rules of life.” Sometimes we get so caught up in our own self-importance or the importance of the task at hand that we lose sight of the really important things. Remember to make time for the little things. Stop to “smell the flowers.” Above all, make sure you spend time with your loved ones.

❖ Don’t embarrass yourself or others (Rule #2). This is another of Dr. Beckman’s profound messages. So often we do stupid and/or selfish things that not only tarnish our own image but also damage the reputations of friends, family, and mentors—the people who have placed their faith and trust in us.

❖ Put yourself in the other person’s shoes before reacting. We often react without thinking or considering how our responses will affect others. Take a good look before you leap. Ask yourself: what would you do if you were in the other person’s shoes? It may help you understand people better and, as a result, cause you to react less often (or at least more constructively).
(cont’d from page 1)

KEEPING AN EYE ON VISION

Johannes de Boer, Ph.D., Assistant Adjunct Professor of Surgery, has received new project funding from the National Eye Institute at the National Institutes of Health (NEI-NIH) to support continuing, multi-institutional research on diagnostic imaging of the human eye using polarization sensitive tomography.

The four-year project, directed by H. Grady Rylander, M.D. (University of Texas, Center for Biological and Medical Engineering), provides $1.7 million for the design and construction of new diagnostic instrumentation for retinal imaging as well as funds for pre-clinical and clinical trials for the new imaging device. Joining the BLI-Texas team in this collaborative endeavor are a core group of researchers at the Swiss Institute of Applied Optics (IAO).

“If fully successful,” one member of the NIH review committee comments, “[the proposed research] would provide a significant new methodology for bioengineering, and it would have a large impact on human health.” The project will run through January 2003.

Johannes de Boer, Ph.D., and Chris Saxer, Ph.D., take a break from their experiments. De Boer is working with researchers at the University of Texas, Austin to construct a retinal imaging device for the early detection of glaucoma. For more on imaging modalities for the eye, see “Keeping an Eye on Vision” at left.