In February 17, 2009, the Vietnam Vascular Anomalies Center (Vietnam VAC) opened in Ho Chi Minh City (formerly Saigon), Vietnam. With joint sponsorship from the Beckman Laser Institute (BLI), Massachusetts General Hospital/Harvard Medical School (Boston, MA), Baylor College of Medicine (Houston, TX), and Candela Laser Corporation, Vietnam VAC seeks to serve the medical needs of a large population of children and adults with vascular defects in Vietnam. The immediate goal is to provide free medical care to children under 6 years of age. The long-term goal is to provide free treatment to everyone who requires the assistance of Vietnam VAC in other parts of Vietnam and Southeast Asia. Although Vietnam’s economy is rapidly growing, the per capita annual income is about 400 U.S. dollars, and the country as a whole has limited resources for medical education and healthcare for the general population.

Dr. Thuy L. Phung (Baylor College of Medicine) and Dr. Thanh-Nga Tran (Massachusetts General Hospital and Harvard Medical School), two Vietnamese-American physicians who grew up in Vietnam before immigrating to the U.S., were aware first-hand of the tremendous medical needs in this country and had a strong desire to provide some medical assistance to children with vascular defects, such as infantile hemangiomatas, venous malformations and port wine stains. Their idea was enthusiastically supported by Dr. Martin C. Mihm, Departments of Dermatology and Pathology, Massachusetts General Hospital and Harvard Medical School, a well-known medical expert in vascular anomalies who has helped create vascular anomalies clinics in the U.S., Spain and Italy, and BLI Medical Director J. Stuart Nelson, M.D, Ph.D., who has extensive clinical experience in laser treatment of vascular lesions. The generous donation of a V-Beam Perfecta laser...
BLI Technology Transfer:  
A Long History of “Out-of-the-box” Thinking

by Michael W. Berns, Ph.D.  
Arnold and Mabel Beckman Professor  
Co-Founder, Beckman Laser Institute

Things are tough right now. The State of California budget is a mess. UC has to reduce expenditures. The Obama stimulus package of $13.4 billion for the National Institutes of Health (NIH) and the National Science Foundation (NSF) has engendered an enormous influx of grant applications so that the likelihood of any individual success for these applications is probably even lower than for regular grants, which was/is hovering around the 10-15% funding range – the lowest I can remember. So where are the dollars going to come from not only to keep a program viable, but to allow it to grow and flourish?

A tough question. But not necessarily one that the Beckman Laser Institute (BLI) isn’t in a good position to attack.

When Arnold Beckman and I founded the BLI in 1982, and the actual doors of our new facility opened in 1986, we had an “out-of-the-box” idea that the discoveries and technologies of the BLI could be translated into revenue-generating cash flow (a goal that was generally not embraced in academia at that time). That is why we designed a building (and eventually a program) that: (1) housed a combination of basic scientists (biologists), applied scientists (engineers and physicists), and clinicians; (2) actively pursued patenting the inventions made by this combination of talent; and (3) established a link with the private sector in the form of a corporate relations program which, at its peak, had a two-tier system of affiliation for about 30 companies. And in 1999, a new wing, the Photonic Incubator, was added on to the BLI for the purpose of providing actual space for the final stage development and testing of many of these technologies. The construction of this $3 million addition was funded by a remarkable combination of partners including the U.S. Department of Commerce (one of the first grants ever given out by that federal agency for the bricks and mortar construction of a facility on a university campus), community donors, and the university itself. Again, the “out-of-the-box” thinking of the BLI Founders had landed an unprecedented grant and, at the same time, brought us one step closer to the realization of some of our original goals.

How successful has this really been, and what can we do in the future? To answer the first question, all we need to do is look at the number of patents awarded (34), the number of license arrangements made (24), and the total revenue generated for the university, including the 15% “trickle-down” to the BLI program itself: the latter number being the crucial one for discretionary cash flow to the BLI director and which is directly tied to one of the University of California’s most successful patents, “Dynamic cooling of biological tissue during laser surgery,” invented by BLI Medical Director J. Stuart Nelson and his colleagues. And finally, the remarkable fact that the Photonic Incubator is now leasing space to two start-up companies, OCT Medical Imaging, Inc. (founded by BLI inventor, Prof. Zhongping Chen) and Modulated Imaging, Inc. (founded by BLI inventors, Profs. Bruce Tromberg and Tony Durkin and former BLI student, Dr. David Cuccia).

Given all of the above, BLI is in the...
Ph.D. candidates Christopher Raub, Eugene Huang and Sophie Chung walked through graduation ceremonies in June in anticipation of receiving their Ph.D. degrees.

Christopher Raub defended his thesis, "Linking optical and mechanical properties in models of fibrosis," on June 17. He worked in the lab of Biomedical Engineering Professor Steve George while collaborating very closely with BLI Director Bruce Tromberg’s lab through the LAMMP facility. He plans to begin a postdoctoral appointment in the Bioengineering Department of UC San Diego in the Cartilage Tissue Engineering laboratory headed by Dr. Robert Sah.

Eugene Huang, a Ph.D. candidate in the Department of Electrical Engineering and Computer Science, defended his thesis, "Noninvasive blood flow imaging for real-time feedback during laser therapy of port wine stain birthmarks," on August 19. After receiving his degree, Eugene will be an Assistant Specialist in Dr. Bernard Choi’s laboratory at BLI.

So Hyun “Sophie” Chung, who worked in BLI Director Bruce Tromberg’s lab, defended her thesis, “Characterization of water molecular state in in vivo thick tissues using diffuse optical spectroscopic imaging,” on August 14. Sophie will be joining Dr. Arjun Yodh at the Department of Physics and Astronomy, University of Pennsylvania, as a postdoctoral researcher.

Honors and Awards

So Hyun (Sophie) Chung
Biomedical Engineering Graduate Student Researcher Sophie Chung was designated as Chancellor’s Club Fund for Excellence Fellow for the academic year 2008-2009. As one of the oldest and largest support groups at the University of California, Irvine, the Chancellor’s Club was founded in 1972 and celebrates over 35 years of service to UC Irvine. Members include community leaders, alumni and parents of students. Funds raised though the Club are used to fund the prestigious Chancellor’s Fund for Excellence Fellowships. These fellowships are awarded to the brightest and the best graduate students at UCI who also show great promise as future leaders. Nominations of scholars are made by UCI Deans in their respective schools. Sophie’s research in Director Bruce Tromberg’s group at BLI involved breast cancer detection and treatment monitoring using a non-invasive optical imaging technology.

J. Stuart Nelson, M.D., Ph.D.
Medical Director J. Stuart Nelson received the Caroline and William Mark Memorial Award at the 29th annual meeting of the American Society for Lasers in Medicine and Surgery held on March 31-April 4, 2009. This award is the highest and most prestigious award that the society bestows. A previous recipient of this award in 1990 was BLI co-founder Michael W. Berns.

Kristen Kelly, M.D.
Associate Professor of Dermatology Kristen Kelly received the Dr. Horace Furumoto Innovations Professional Development Award at the 29th annual meeting of the American Society for Lasers in Medicine and Surgery held on March 31-April 4, 2009. The purpose of this award is to foster future technology innovators and leaders and to inspire their continued professional development through financial assistance.

Bruce Tromberg, Ph.D.
BLI Director Bruce Tromberg was named recipient of the 2009 SPIE Directors’ Award by the SPIE Board of Directors. The award is presented to an individual who, in the opinion of the Board, has rendered a significant service of outstanding benefit to the society. The Board made this selection based on Dr. Tromberg’s outstanding leadership as
When Only a Drop is Needed

When looking at a specimen on a slide under a microscope, the researcher will often first scan the specimen with an air immersion objective (10X magnification) and then wish to switch to a fluid immersion objective (100X magnification) to increase the optical resolution of what he/she is observing. At this higher magnification, the working distance between the slide and the objective lens is the shortest. It is necessary to apply some sort of fluid, i.e., immersion oil, to the gap between the objective lens and the slide. It is not feasible to navigate a traditional bottle of fluid to the tight space between the microscope objective turret, microscope stage and specimen. One risks overfill of the space thereby spilling immersion fluid onto other critical optics in the body of the microscope or onto other non-oil immersion objectives. So the researcher is required to remove the sample from the microscope stage to deposit a drop of immersion fluid onto the specimen or onto the objective. This takes extra time and is worsened by the fact that the specimen cannot be replaced exactly to its original position after the immersion fluid is delivered. Ideally, the immersion fluid should be delivered without moving the sample.

Assistant Professor in Biomedical Engineering Elliot Botvinick, along with Craig Rappaport, previously with McBain Instruments and now with Olympus America, and BLI co-founder Michael W. Berns, has invented an immersion fluid applicator which addresses the problem of delivering a drop of immersion fluid onto a specimen after the specimen is loaded onto the microscope stage. He calls the device the HummingBird.

The HummingBird takes the immersion fluid bottle out of the hands of the user and places it into one of the empty objective turret positions. With the HummingBird, the user only needs to rotate the objective turret to the position holding the HummingBird, raise the HummingBird tip to the specimen, lower the objective turret and rotate the immersion fluid objective into place. The immersion fluid delivery can be driven by pressure developed when the HummingBird is pressed against the specimen or by a pressurized gas or liquid which sits behind the immersion fluid, analogous to a ballpoint or gel type pen. In the case of an upright microscope, the immersion fluid can be delivered by gravity. For automated microscopes, the focus position of the turret at which the HummingBird will deliver a drop of immersion fluid can be programmed into the hardware, firmware or software controller, and immersion fluid delivery can be automated with the push of a button, the click of a mouse, or can be included within a macro or algorithm in which the immersion fluid delivery is done independent of any additional user input.

The HummingBird was recently patented by the USPTO (United States Patent and Trademark Office), and Dr. Botvinick envisions microscope manufacturers incorporating this product into their microscopes or microscope-part companies manufacturing a HummingBird compatible with each of the major microscope brands.

Founder’s Column (cont’d from p. 2)

perfect position to maintain and even increase a strong diversified cash flow (while other programs are severely strapped). This could be achieved by doing the following: (1) re-invention of a corporate affiliation program, (2) aggressive marketing of our patents/technology, and (3) facilitation of investment in the BLI company “spin-offs.” There are many ways that the last activity can have huge payoffs in the future, not the least of which being the charity of the spin-off company founders who are grateful to the organization (BLI) that contributed to their success by providing the environment for the conception and prototyping of their inventions. Two noteworthy examples of this type of philanthropy are Arnold O. Beckman who gave generously to his alma maters, Caltech and the University of Illinois, and David Packard who was just as generous to his alma mater, Stanford University. Both of these men were pillars of 20th century entrepreneurship and philanthropy. While giving generously to their alma maters, they also shared their wealth with many other institutions. Both played key roles in the success of the Beckman Laser Institute: Arnold O. Beckman as a co-founder, and David Packard as a member of the Board of Directors and a multimillion dollar donor. Both of these men were innovative and creative “doers.” I can think of no better role models for 21st century “out-of-the-box” thinking. Maybe some day, a “founder” of one of the BLI-spin-off companies will be able to become a 21st century philanthropist.
Detecting and Treating Dental Erosion Early

Dental Director Petra Wilder-Smith has just completed a clinical study using a novel non-invasive imaging approach to detect the effectiveness of medication against gastric reflux, especially in children. Dental erosion, the chemical dissolution of enamel without bacterial involvement, is an underreported yet rapidly increasing manifestation of gastroesophageal reflux disease (GERD) as well as recurrent vomiting and dietary habits. It leads to loss of tooth substance, hypersensitivity, functional impairment and even tooth fracture. To date, dental erosions have only been assessed using very basic visual methods, and no evidence-based guidelines or studies exist regarding the prevention or treatment of GERD-related dental erosions.

In a randomized, double-blind study, Dr. Wilder-Smith and her colleagues used optical coherence tomography (OCT) to quantify dental tissue demineralization and enamel loss before and after 3 weeks of acid-suppressive treatment with esomeprazole (a potent acid blocker) or placebo in 30 patients with advanced dental erosions and an abnormal acid exposure at the Bern (Switzerland) University Dental Clinic. OCT is a new high-resolution optical technique that permits minimally invasive imaging of near surface abnormalities in complex tissues and provides real time structural imaging. Enamel thickness, reflectivity and absorbance were measured by OCT pre- and post-therapy at identical localizations on teeth with the most severe visible erosions as well as multiple other predefined teeth.

After 3 weeks of double-blind treatment, significant differences in tooth enamel thickness and optical reflectance were seen in in vivo OCT imaging. Progressive enamel tissue loss and demineralization, as shown by optical reflectance changes, were seen in the placebo group. These changes were prevented to a significant degree in the other group by a twice daily dose of esomeprazole with evidence of remineralization and significantly slowed loss of enamel.

Dental erosions are permanent and potentially disfiguring. However, if enamel demineralization is detected sufficiently early, the enamel framework can be possibly remineralized using oral remineralization regimes, and preventative modifications in diet, behavior or medication can be instituted before symptoms occur and damage becomes irreversible.

The results of this initial study entitled “Quantification of dental erosions in patients with gastroesophageal reflux using optical coherence tomography before and after double-blind, randomized treatment with esomeprazole or placebo” has been accepted for publication in the American Journal of Gastroenterology.

Collaboration (cont’d from p. 1)

by the Candela Laser Corporation enabled the opening of the clinic on the main campus of the Nguyen Tri Phuong Hospital. In the first week alone, over 400 patients were seen. Dr. Nelson used this opportunity to teach the Vietnamese physicians, who have volunteered their time to work for VAC, how to perform laser treatment of vascular lesions using the Perfecta. Some patients treated by Dr. Nelson were children and adults with port wine stains and hemangiomas. Dr. Nelson returned to Vietnam VAC in August 2009 to continue the training.

The group of U.S. and Vietnamese physicians who are members of Vietnam VAC are striving to make VAC a sustainable and successful collaborative effort to provide humanitarian care to patients and to promote physician training and education in the field of vascular lesions.

Selected Recent Publications


Dr. Tromberg was honored at an Awards Banquet held in San Diego, CA, on August 5, 2009.

Zhongping Chen, Ph.D.
Associate Professor of Biomedical Engineering
Zhongping Chen was promoted to SPIE Fellow for recognition of his significant service to this society and to the greater science community. SPIE is an international society advancing an interdisciplinary approach to the science and application of light. Each year, SPIE promotes members as new Fellows of the Society. SPIE honored 59 new Fellows in 2009. More than 550 SPIE members have become Fellows since the Society’s inception in 1955. Dr. Chen was specifically recognized for achievements in biomedical photonics and optical coherence tomography.

Bernard Choi, Ph.D.
Assistant Professor of Biomedical Engineering
Bernard Choi was one of five professors across all engineering disciplines who was honored with a “Professor of the Year” award for exceptional contributions to teaching given by the UC Irvine Engineering Student Council at their annual awards banquet held on February 20, 2009, as part of the campus’ 36th celebration of National Engineers Week. Dr. Choi’s research interests include the development and application of in vivo optical imaging methods for novel therapy discovery with current collaborations in dermatology and neurobiology. He also leads research efforts on the use of chemical agents to reduce the optical scattering of biological tissue. Dr. Choi has also received a two-year grant from the National Institutes of Health (NIH) for “Noninvasive blood flow mapping for surgical guidance of vascular birthmarks.”

Eric Potma, Ph.D.
Assistant Professor of Chemistry
Eric Potma has received a National Science Foundation Career Award for “Super-resolution in coherent anti-Stokes Raman scattering microscopy.” The award is from the Experimental Physical Chemistry program to develop a coherent anti-Stokes Raman scattering (CARS) microscope with super-resolution. Development of this microscope will enable chemically selective imaging with a resolution down to the 50 nm length scale, opening up new areas in optical imaging of biological samples and engineered materials. The instrument will be used to study the nonlinear optical response of metallic nanowires and to examine the distribution of submicrometer sized lipids droplets in breast cancer cells.

Anthony Durkin, Ph.D.
BLI Assistant Professor
Anthony Durkin has been awarded two grants from the National Institutes of Health (NIH). The first, “Modulated imaging: a wide-field optical imaging platform for clinical research,” is a Jumbo Phase I SBIR (Small Business Initiated Research) grant. Dr. Durkin will be in charge of clinical application and David Cuccia of Modulated Imaging, Inc., will be in charge of technology fabrication. They will be developing a user-friendly Modulated Imaging platform capable of quantitative imaging of localized events at depths of several millimeters in thick tissues. This platform will enable quantitative insight into disease progression and therapeutic response in areas such as wound healing, dermatology, skin cancer and reconstructive surgery. In the second grant, “Impact of hypertonic-hypertonic saline solutions on ischemia-reperfusion injury in free flaps using Modulated Imaging,” Dr. Durkin along with Dr. G. R. Evans plans to test a new imaging device that will have the capability to guide reconstructive surgery and post-surgical recovery. The use of tissue transfer flaps is a method of moving tissue from a donor location to recipient location and re-attaching the arteries and veins to the blood vessels at the recipient site. This type of reconstructive surgery is subject to failure, however, which may include complications due to ischemia-reperfusion injury and vascular insufficiency. The imaging device can reduce post-surgery morbidity and reduce uncertainty in flap healing.

Samarendra Mohanty, Ph.D.
Postdoctoral researcher
Samarendra Mohanty received the AFER/Retina Research Foundation Travel Grant to provide travel support to attend the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting in Ft. Lauderdale, FL, on May 3-7, 2009. Dr. Mohanty, who works in BLI Co-founder Dr. Michael W. Berns’ lab and collaborated with Dr. Edward Wong of the Department of Ophthalmology, was selected from over 1,500 applicants based upon his abstract entitled “Targeted delivery of light-activated ion channels to retinal ganglion cells for restoring photosensitivity of photoreceptor-degenerated retina.”

Petra Wilder-Smith, D.D.S., Ph.D.
Dental Director
Petra Wilder-Smith was notified that her poster entitled “Quantification of dental erosions in GERD using optical coherence tomography (OCT): an interventional placebo-controlled study with esomeprazole” was

(Honors and Awards continued on p. 8)
**Arrivals and Departures**

**ARRIVALS**

**Eugene Chu, M.D.** will join Dr. Brian Wong as his Facial Plastic Surgery Fellow. Dr. Chu previously worked in Dr. Wong’s lab 10 years ago before spending 4 years at UC San Francisco and 6 years at Johns Hopkins.

**Chad Lieber, Ph.D.**, is a researcher from CHOC (Children’s Hospital of Orange County) who will be collaborating with several BLI faculty on biophotonics technologies in children’s health.

**Sucbei Moon, Ph.D.**, has joined BLI as a postdoctoral fellow in Dr. Zhongping Chen’s lab. Dr. Moon is working on the microendoscopic multiphoton microscope (mE-MPM) project. Dr. Moon is from Gwangju Institute of Science and Technology (GIST) in Korea.

**Darren Roblyer, Ph.D.**, is a postdoctoral fellow in BLI Director Bruce Tromberg’s lab. He will be working on diffuse optical spectroscopy imaging (DOSI) for monitoring breast cancer therapies. Dr. Roblyer’s Ph.D. thesis from Rice University was on multispectral optical imaging for oral cancer detection.

**Shigeto Ueda, M.D.**, Department of Surgery, Breast Oncology Service, National Defense Medical College, Japan, will be at BLI for the next two years working with Dr. Albert Cerussi on optical imaging of breast cancer. His wife, Kaoru Ueda, will be working in Dr. Cerussi’s lab helping with the clinical trials.

**Xiangqun Xu, Ph.D.**, joins BLI as a visiting scholar from Zhejiang Sci-Tech University in Hangzhou, China, where she is a professor. She is working at BLI with Dr. Zhongping Chen on non-invasive characterization of red blood cell aggregations using Doppler optical coherence tomography (OCT).

**DEPARTURES:**

**Byung Hoon Ahn**, Visiting Associate Project Scientist, has returned to Korea.

**Belinda Dao**, Junior Specialist, left on August 8 to attend medical school at UCI.

**Ken Lee**, Junior Specialist, who worked in Dental Director Petra Wilder-Smith’s lab, has been accepted into the one year Master’s dental program at UCLA.

**Thang Hoang Nguyen**, a Junior Specialist in Dr. J. Stuart Nelson’s lab, will be attending dental school at Cal Poly Pomona.

**Bin Rao** left BLI to take a postdoctoral position at Washington University in St. Louis, MO.

**Rogelio Sanchez**, who worked in the Biochemistry Lab, is leaving BLI to attend medical school at UCLA.

**Vaya (Wendy) Tanamai**, Junior Specialist, left BLI on July 31 to attend medical school at SUNY (State University of New York) at Buffalo.

**Allison Zemek**, who worked in Dr. Brian Wong’s lab, will be attending Stanford Medical School this fall.

**Newsbriefs (cont’d from p. 2)**

Dental University, one of the top dental schools in Japan.

During his two years at BLI from 1999-2001, Dr. Ebihara worked on two projects with Dr. Wilder-Smith using aminolevulinic acid (ALA) for ALA-based detection of oral cancer and using fluorescence to diagnose root canal decay and infection. Since that initial collaboration, Dr. Ebihara has sent a total of four students to BLI every other year during the summer to work on projects in optical diagnostics and laser techniques for root canals. Dr. Satoshi Watanabe will continue the collaboration by becoming a visiting researcher at BLI.

**PATENT DISCLOSURE**

Dental Director Petra Wilder-Smith, D.D.S., Ph.D., along with Drs. Zhongping Chen, Changsoo Kim and Young Jik Kwon, has filed a patent disclosure entitled “Photodynamic diagnosis and therapy in the oral cavity using toluidine blue (TBO).”
selected as a Poster of Distinction for Digestive Disease Week, held in Chicago, IL, on May 30-June 4, 2009. The study examined how to use dental erosion caused by gastroesophageal reflux (GERD) as a minimally invasive and cost efficient way to monitor GERD.

Jangwoen Lee, Ph.D.
Project Scientist Jangwoen Lee has been awarded a National Institutes of Health (NIH) supplemental grant entitled “Development of novel non-invasive optical diagnostic monitoring platform for mass casualty cyanide poisoning in clinical settings.” This grant is a supplement to the NIH CounterAct grant awarded to Professor of Pulmonary and Critical Medicine Matthew Brenner, M.D., “Rapid translation of novel cyanide treatment drugs to clinical practice using DOS.”

Brian J. F. Wong, M.D.
Professor and Vice-Chairman of UCIMC Department of Otolaryngology-Head and Neck Surgery Brian Wong has been awarded a grant from the Department of Defense for “Reconstruction of facial cartilage frameworks using electromechanical reshaping.” Extensive study of using lasers to generate heat led directly to a spin-off technology Dr. Wong refers to as electromechanical reshaping (EMR). EMR is a novel and patented tissue reshaping technique that may allow surgeons to bend cartilage into the shape they desire in a more elegant manner without having to crush, carve or suture.

Jae G. Kim, Ph.D.
BLI Postdoctoral Fellow Jae G. Kim, who works in the labs of Matthew Brenner, M.D., Professor of Pulmonary Medicine and Critical Care, and BLI Director Bruce Tromberg, was invited to present “Differential hemodynamic responses between brain and muscle tissue during novel cyanide antidote cobinamide treatments as observed by near infrared spectroscopy” at the 4th Asian and Pacific Rim Symposium on Biophotonics held on Jeju Island, South Korea, on May 27-29, 2009.

Veronica Gomez
Developmental and Cell Biology Graduate Student Veronica Gomez received a Teaching Award from the School of Biological Sciences. She received her award at the School of Biological Sciences Graduate Honors Convocation and Teaching and Faculty Awards Ceremony held on June 2, 2009. She was accompanied by her Faculty Advisor, BLI Co-founder Michael W. Berns.