LASER
BECKMAN LASER INSTITUTE

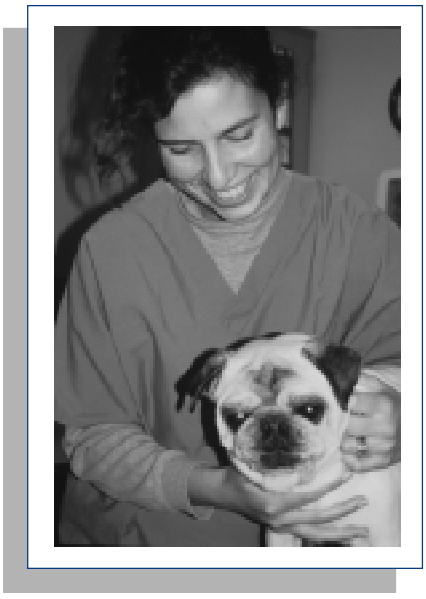
IN THE NEWS

Spring 1998

Grant Funds Women's Health Research

The Beckman Laser Institute is the recent recipient of a three-year grant from the National Institutes of Health. The $500,000 grant, awarded to Yona Tadir, M.D., director of medical research, will fund research into a new photodynamic therapy-based treatment for uterine bleeding. Photodynamic therapy (PDT) uses the interaction of a photosensitizing drug and laser light to selectively remove abnormal tissue, leaving normal tissue unaffected.

Dr. Tadir says that by targeting the endometrium—the inner lining of the uterus—for treatment, PDT could become a more reliable, less invasive alternative to endometrial ablation or hysterectomy, conventional remedies for uterine bleeding.



Veterinary Assistant Jill Monti-Frayne with laser surgery patient Sydney. (Please see the related article on pg. 5.)

"Endometrial ablation is an established therapy for uterine bleeding, but an imperfect one," explains Dr. Tadir. "Its results are highly variable and its risks range from perforation and bleeding to air embolism. We want to offer another option. We plan to build on our PDT expertise and fully develop treatment parameters to provide the medical community with a proper set of uterine PDT tools."

He adds, "If the experimental procedure is approved, it also may help many post-menopausal women who are undergoing hormone therapy and experiencing unwanted bleeding."

Besides the obvious benefit to patients, Dr. Tadir also sees an economic benefit to the research.

"Almost 600,000 hysterectomies are performed each year, making it one of the most common major operations in the U.S.," he says. "If PDT was made available to just one-third of those patients, the result could be millions of dollars in healthcare savings annually."

Director Michael Berns, Ph.D., also notes the significance of the research. "This potentially is an exciting non-cancer application of photodynamic therapy, an innovative technique originally developed for cancer treatment," he says.

The research will involve both animal and clinical trials. In addition to Dr. Tadir, researchers on the study include Bruce Tromberg, Ph.D., Kristen Keefe, M.D., Lars Svaasand, Ph.D., Lynn Bandurak, R.N., Lih-Huei Liaw, M.S., senior development engineer Jeff Andrews, and animal technician Laurie Newman. ■

Newsbriefs

LAMMP GRANT RENEWED

The Laser Microbeam and Medical Program (LAMMP), a biotechnology resource funded by the National Institutes of Health (NIH) since 1979, was rated "outstanding" following a recent NIH peer review. After a day-long site visit in November, the NIH has agreed to fund the LAMMP program at a total of approximately $4 million over the next five years.

"We're delighted to have earned such a terrific rating from NIH," says Bruce Tromberg, Ph.D., associate professor and LAMMP director.

Institute Director Michael Berns, Ph.D., notes, "This indicates the scientific community's high regard for our

(Continued on pg. 8)

The Institute's Unsung Heroes

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

This is the first in a series that I am going to write on the "unsung heroes of BLI." What do I mean by unsung heroes? Let me explain.

While the scientists and physicians often receive their recognition and gratification through publications, grant awards, or applause following their lectures, there are many people at BLI whose only recognition is through an occasional "lunch out" or a passing remark of thanks. Some don't even get that.

So I would like to focus attention on those people who do their jobs conscientiously, with dedication, and with the utmost of professionalism and high standards. One such group is the staff of the Surgery Laser Clinic.

Clinic Professionals

Our Nurse Director, Joyce Zeiler, R.N., B.S.N., has been with us for 12 years. Joyce, who was a nurse at her children's school before she came to BLI, has more experience with laser systems, laser procedures, and physicians and patients than almost any other medical professional I know.

Lynn Bandaruk, R.N., Lynda Schiebert, R.N., and Kathy Spagnola, R.N., have been with us a combined total of 22 years. (Please see a profile of Lynda on pg. 6.) These three nurses' experience with thousands of laser procedures also places them at the top of the list of most experienced and qualified nurses. They, along with Joyce, recently published their findings on pain management in the journal *Lasers in Surgery and Medicine*. The article, which focuses on pain after laser-assisted uvulopalatoplasty, highlights the duality of the nurses' role at BLI—nursing, as well as managing patient research protocols that are so important to BLI.

The addition in 1996 of Pam Aufhammer, R.N., to the full-time nursing staff, and the energetic assistance of Michelle Duran have rounded out that group of very dedicated and talented people.

You also will find in the clinic the hard-working reception and scheduling staff. Four-year veteran Barbara Bean manages the clinic's schedule along with her many other responsibilities. Manning the front desk are JoAnn Vandenberg and Juanita Garcia (a recent Mom—congratulations!). Things definitely would not run smoothly without their dedication and wisdom.

Then there is the "money person," Andrea Giancarli, whose persistence with third-party payers and precise management of the books keeps us solvent and competitive. And who could forget a true BLI "old-timer" and wisdom-giver, Elaine Kato. She started working with me in 1973 when the Institute was but an idea.

Last but not least is Ruth Bundy, who oversees the clinic's operations and serves as the crucial interface with other UCI clinical facilities.

Laser Experts

Of course, the clinic wouldn't run as well as it does without BLI's behind-the-scenes guys—the laser engineers. With 25 years of BLI experience between them, Jeff Andrews and Glen Profeta are unheralded assets and ones on whom the clinic and non-clinic staff rely.

Thank you to our unsung heroes, without whom the physicians could not work their "magic" and the Institute's reputation could not "sparkle." ■

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Beckman Laser Institute News
Nicole Knight, Editor

Treating Esophageal Cancer in Orange County

The Beckman Laser Institute recently hosted Kenneth Chang, M.D., the first Orange County physician to use photodynamic laser therapy to treat esophageal cancer.

The FDA-approved treatment, available through a collaboration between the Institute and UC Irvine's Chao Family Comprehensive Cancer Center, should help the 10,000 esophageal cancer patients diagnosed annually.

Photodynamic therapy (PDT) is a two-step process that uses a light-activated drug and a laser. The drug—Photofrin in this case—is injected and localizes, or concentrates, in cancerous tissue. When the laser light shines on the affected area, the drug triggers a chemical reaction that kills the cancer, leaving the surrounding healthy tissue relatively untouched.

During photodynamic therapy, Dr. Chang monitors color images of the esophagus on a television-like screen.

Esophageal PDT

During esophageal PDT, Dr. Chang, head of gastrointestinal oncology at UCI, and colleague Phuong Nguyen, M.D., use a hand-held probe called an endoscope. The endoscope contains specially-designed fibers that carry laser light to the site of the cancer. A tiny camera implanted in the instrument relays color images of the esophagus onto a television-like screen—images that Dr. Chang uses to position the laser.

Dr. Chang, an expert in endoscopic techniques with seven years of gastrointestinal oncology experience, says that PDT provides excellent results.

"Several days after PDT, the opening of the esophagus can be enlarged dramatically and patients once again can swallow without an operation or an esophageal prosthesis," he explains.

PDT also can help patients whose esophageal prostheses, or stents, have failed to stop cancer from invading their esophagus.

Dr. Chang explains. "I recently treated a 78-year-old woman with a history of esophageal cancer whose tumor was not responding to chemotherapy."

He notes that physicians at UCLA had implanted a metal mesh stent in the patient's esophagus twice, and that cancer grew through the stent both times.

"The tumor was obstructing her esophagus and limiting her ability to swallow," Dr. Chang says. "Now, four weeks after PDT, she is swallowing solids and liquids, and her weight has stabilized. She is very happy about the treatment."

Previous Treatment Methods

In the past, esophageal cancer has been treated by esophagectomy, surgically removing portions of the esophagus, a painful procedure with a high mortality rate.

In contrast, PDT is a scalpel-free outpatient procedure. The entire treatment takes less than two hours; general anesthesia is not required.

Although PDT is less invasive than esophagectomy, possible side effects include chest pain and pain during swallowing, both of which subside after several days. Patients also are advised to stay indoors for 30 days due to heightened sensitivity to sunlight.

Institute Director Michael Berns, Ph.D., says that he is pleased that the Institute now can offer esophageal cancer treatment.

"Developing and providing new laser-based applications like esophageal PDT is the Beckman Laser Institute's goal," Dr. Berns explains.

"Esophageal PDT is a promising new laser application that builds on the Institute's basic science and pre-clinical research which, thanks to National Cancer Institute funding, has taken place here over the past 15 years," he adds.

For more information about PDT to treat esophageal cancer, please call (714) 456-8440. ■

Illuminating Research on Oral Cancer Diagnosis

In 1998, over 30,000 Americans will contract oral cancer, a cancer that defies non-surgical early detection because it can look benign. Using light-induced fluorescence, Petra Wilder-Smith, Ph.D., D.D.S., hopes to create a diagnostic tool to help physicians and dentists determine easily—and without a scalpel—what *is* oral cancer and what isn't.

Cancer Detection Difficulties

"By looking, a dentist or physician can't tell whether a mouth lesion is cancerous or benign," says Wilder-Smith, assistant professor and director of the Institute's dental program.

"A white sore could be a harmless lesion that might remain benign for years—a physician doesn't know," she explains. "In this case, a physician has few options: either continually biopsy the lesion to monitor whether it has turned cancerous, or do nothing. If the lesion is on a person's lips or tongue, repeated biopsy—surgically removing a tissue sample—can be disfiguring and functionally disabling. On the other hand, doing nothing provides no information."

The problem is compounded, she adds, by the fact that 11 percent of dentists and 45 percent of physicians don't inspect for oral cancer because they don't feel adequately trained to do so.

Such obstacles, according to Wilder-Smith, help contribute to oral cancer's five-year, 50 percent survival rate. "It's unfortunate because if caught early, oral cancer has a better survival rate than most cancers," she says.

Which is why she and UCLA researcher Diana Messadi, D.M.Sc., are investigating whether laser light and fluorescence will illuminate cancerous changes. The research involves two approaches, Wilder-Smith explains.

Autofluorescence

Using a small, fiber optic instrument built with the help of Allan Wong, M.D., of Physical Optics Corporation, the team first will shine laser light—no stronger than that from a flashlight—into the mouths of hamsters. The study will determine how the light reacts in the mouths of healthy hamsters, and in those with precancerous and cancerous lesions. Wilder-Smith explains the rationale for using a laser.

(Left to right) UC Irvine student Young Yoon, Dr. Petra Wilder-Smith, Dr. Allan Wong, Laurie Newman, Peter Low, and student Linh Nguy next to the diagnostic instrument.

"When cancerous tissue is subjected to certain wavelengths of laser light, it may fluoresce," she notes. "Healthy tissue also fluoresces, but we're hoping it will do so in a different manner than unhealthy tissue."

During the year-long study, Wilder-Smith and Messadi will collect data on the fluorescent characteristics of healthy and diseased tissue.

"The goal is to identify relationships between tissue health and fluorescence with almost 100 percent accuracy," says Wilder-Smith.

Drug-induced Fluorescence

Building on the first approach, the two researchers also plan to use a light-activated drug, ALA, in conjunction with the fiber optic device.

According to Wilder-Smith, using ALA adds to the study for two reasons: it collects preferentially in cancerous tissue, and it chemically changes to another compound, Photoporphyrin IX, that fluoresces strongly.

"First, we'll treat the insides of the hamsters' mouths with the ALA," says Wilder-Smith. "Then we'll shine the laser light in their mouths and analyze how the cancerous and diseased areas fluoresce."

Because the photosensitizer collects mainly in diseased tissue, the researchers believe it will allow them to differentiate between healthy and unhealthy tissue.

"ALA provides a greater degree of diagnostic certainty," Wilder-Smith explains.

As with the first study, the scientists will gather measurements until they can discern with statistical certainty the fluorescent properties of healthy, precancerous, and cancerous tissue. Wilder-Smith anticipates that clinical trials could begin in a year.

"We hope our work will lead to the development of an inexpensive, non-invasive diagnostic instrument for dentists and physicians," she says. "While our current emphasis is on oral cancer, this technique also could be adapted to the diagnosis of gynecological and gastrointestinal cancers."

Director Michael Berns, Ph.D., agrees, noting, "This project complements the existing breast cancer diagnostic studies being conducted by BLI's Bruce Tromberg and by Dr. John Butler of the Chao Family Comprehensive Cancer Center." ■

Canine Corneal Therapy

The Institute recently hosted experimental laser surgery to treat canine blindness. The ground-breaking therapy may help dogs suffering from pigmentary keratitis, a pigmented corneal overgrowth common in dogs with prominent eyes and short noses.

Pet owner Anita Ridley said that she noticed a blackish film growing over the eyes of her pug, Sydney, in 1996. "He wasn't bumping into furniture, but I knew the overgrowth was a problem when Sydney couldn't jump onto the bed any longer," she explains.

Veterinary ophthalmologist Paul Jackson, D.V.M., initially prescribed anti-inflammatory drops to help control tissue growth and scarring on the pug's corneas. When Dr. Jackson realized the drops weren't helping, he proposed a laser alternative, phototherapeutic keratectomy (PTK).

"Using PTK to treat corneal scars in humans is widely accepted and highly successful," he explains. "My colleagues and I thought this excimer laser procedure also might help dogs with pigmentary keratitis." For the experimental treatment, Dr. Jackson teamed up with Art Giebel, M.D., a UC Irvine ophthalmic surgeon certified to use the VISX excimer laser.

Throughout PTK, the laser's pulses precisely remove corneal tissue. The surgery is relatively painless and, in humans, allows for rapid vision recovery.

During the treatment, the clinicians lased a six millimeter area of tissue to expose the underlying clear cornea. Afterwards, Sydney's eyelids were sutured shut to allow the epithelium, the thin protective layer over the cornea, to regrow. In humans, the epithelium grows back in three to seven days. Dr. Jackson says that canines may have a longer recovery period.

Drs. Jackson (left) and Giebel treat Sydney.

Although Sydney's owner knows that the surgery is experimental, she professes hope. "I felt we didn't have anything to lose," Anita says. "I remember the clarity his eyes had before the pigment grew over them. I'd give anything to have that clarity back."

Dr. Jackson notes that it's too soon to tell whether PTK will fully restore Sydney's sight, and for how long. "We hope the pigment won't grow back right away," says Dr. Jackson. He also intends to monitor what role such factors as dryness, exposure, irritation and inflammation play in pigmentary keratitis.

Veterinary Director George Peavy, D.V.M., is pleased that the Institute again has played a role in the development of a potential companion animal therapy.

"We hope that this therapy will work out for Sydney and other patients," he says. ■

Institute-Industry Endeavors Won't Wait

The Institute's Photonic Incubator, scheduled for completion in late 1998, is designed to foster collaborations between science and industry. But Institute scientists aren't waiting for that date to begin such projects. The following is a sampling of Institute-industry collaborations:

Associate Director J. Stuart Nelson, M.D., Ph.D., and Assistant Professor Zhongping Chen, Ph.D., have teamed up with IntraLuminal Therapeutics, Inc., a biomedical device maker. The collaborators are using optical Doppler tomography, an imaging technique, to distinguish plaque from normal tissue in vessels.

FDA studies on a new CO_2 laser have been the focus of a recent collaboration between Assistant Professor Petra Wilder-Smith, Ph.D., D.D.S., and the biomedical laser firm Clinicon. The laser, now FDA-approved, will be used during soft tissue surgery. Wilder-Smith continues to collaborate with Clinicon on other projects.

Director Michael Berns, Ph.D., Associate Professor Bruce Tromberg, Ph.D., and John Butler, M.D., of the Chao Family Comprehensive Cancer Center, plan to test the effectiveness of a new photosensitizer, lutetium texaphyrin. Working with Pharmacyclics Inc., the drug's manufacturer, the group will analyze the drug's efficacy during photodynamic therapy for breast cancer.

And BLI scientists, along with Nancy Allbritton, Ph.D., and her College of Medicine colleagues, recently filed a patent for the new laser micropipette technology. The technique, which rapidly ruptures a cell so that its biochemistry can be analyzed, has potential application in analytical chemistry. The researchers hope eventually to license the UCI technology.

"It's a positive sign," notes Dr. Berns, "to see so many Institute-industry collaborations before the Photonic Incubator has even opened its doors." ■

Lynda Schiebert: Clinical Laser Nurse Specialist

Lynda Schiebert, R.N., likes nursing because she enjoys helping people. But that's not all she likes about her job at the Institute's Surgery Laser Clinic. "Some of my favorite times are when I'm tormenting Dr. Stuart Nelson and my colleagues," she says with a laugh.

Not to say that she doesn't take her job seriously.

"I feel fortunate to work with someone of Lynda's caliber," says Associate Director J. Stuart Nelson, M.D., Ph.D. "She is skilled, experienced, highly professional, and a great nurse all around. She takes excellent care of our patients."

A native of Southern California, Schiebert has been a nurse at the clinic for six years.

"I assist physicians with laser treatments, provide patients with care and instructions and assess them postoperatively," she says of her job. Clinic nurses also educate physicians on laser usage and safety, establish treatment protocols, and conduct research.

"I like to establish a rapport with my patients," Schiebert explains, "gain their trust, and help them through their surgery emotionally and psychologically."

A skilled professional, her previous nursing experience includes 11 years as a critical care nurse at a medical center in Mission Viejo, Calif. She holds two certifications for emergency life support and is a VISX excimer laser technician. Recently, she and co-workers Joyce Zeiler, R.N., Lynn Bandaruk, R.N., and Kathy Spagnola, R.N., published a paper in the journal *Lasers in Surgery and Medicine* on pain management after laser-assisted uvulopalatoplasty.

Besides possessing technical skill, Nurse Director Zeiler says that Schiebert's gentle, personal care is exemplary. "Her greatest asset is her dedication to being an advocate for her patients," Zeiler notes.

When not busy nursing, Schiebert, who reports herself addicted to crossword puzzles, likes to read, visit her granddaughters, watch movies, and play with her pets.

Schiebert and her granddaughter.

"Laser nursing is unique, varied and challenging," says Schiebert. "I'm very proud to be a member of Beckman's excellent nursing staff." ■

Institute Contributors and Partners

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PRESENTATIONS

Michael Berns, Ph.D., presented "Laser Surgery: Organelles to Organs" at the meeting of the American Physical Society in Los Angeles, Calif.

J. Stuart Nelson, M.D., Ph.D., presented "New Directions in Minimally Invasive Lasers" at the Second Interdisciplinary Laser, Endoscopic and Medical Aesthetic Workshop in Los Angeles, Calif., and at the Advances in Laser and Cosmetic Surgery Conference at UC Davis. He also chaired the Photodynamic Therapy and Oncology session at the annual meeting of the American Society for Laser Medicine and Surgery (ASLMS) in San Diego, Calif.

Bruce Tromberg, Ph.D., presented "Frequency Domain Photon Migration for Tissue Diagnostics" and "Light and Photosensitizer Dosimetry in the Endometrium" at the First World Congress of Photomedicine in Gynecology in Zurich, Switzerland. He also presented a "Laser Microbeam and Medical Program" poster at the NIH Bioengineering Symposium in Bethesda, Md.

Petra Wilder-Smith, Ph.D., D.D.S., gave a keynote address on laser pulpotomy to the German Society for Laser Dentistry in Frankfurt, Germany.

Zhongping Chen, Ph.D., presented "Optical Doppler Tomography: Technology and Application" at the International Society for Optical Engineering's International Symposium on Biomedical Optics (SPIE) in San Jose, Calif.

Vickie LaMorte, Ph.D., presented "Using Laser Microbeams to Solve the Function of a Nuclear Body" at SPIE.

Tatiana B. Krasieva, Ph.D., presented "Cell Permeabilization and Molecular Transport by Laser Microirradiation in Functional Imaging and Optical Manipulation of Living Cells" at SPIE. She also presented "Fluorescence Microscopy for Pharmacokinetics" to the First World Congress of Photomedicine in Gynecology.

Johannes F. DeBoer, Ph.D., presented research on two-dimensional birefringence imaging in biological tissue at SPIE, ASLMS, and at the Optical Society of America's conference in Orlando, Fla.

Brian Wong, M.D., presented "Critical Temperature Transitions in Laser Mediated Cartilage Reshaping" at SPIE.

Xunbin Wei, Ph.D. candidate, presented "Mapping the Polarity for T cell Activation with an Optical Trap" at SPIE. He also presented the poster "T Lymphocyte Activation Studied with an Optical Trap" at the Biophysical Society's meeting in Kansas City, Mo.

Jill Monti-Frayne presented "Development of an Animal Emphysema Model of Lung Volume Reduction Surgery" to the Federation of Medical Research in Carmel, Calif.

PUBLICATIONS

Michael Berns, Ph.D., published "Laser Scissors and Tweezers" in *Scientific American*. He also published the chapters "Micromanipulation of Chromosomes Using Laser Microsurgery" in *Cell Biology*, and "Laser Scissors and Tweezers" in *Methods in Cell Biology*.

Petra Wilder-Smith, Ph.D., D.D.S., published "CO_2 Laser Treatment of Traumatic Pulpal Exposures in Dogs" in *Lasers in Surgery and Medicine*.

Zhongping Chen, Ph.D., published "Optical Doppler Tomography: Imaging *in vivo* Blood Flow Dynamics Following Pharmacological Intervention and Photodynamic Therapy" in *Photochemistry and Photobiology*.

Vickie LaMorte, Ph.D., published "Localization of Nascent RNA and CBP with the PML-containing Nuclear Body" in *Proceedings of the National Academy of Sciences*, and "Microinjection of Antibodies Neutralizing G Protein Function" in *G Proteins: Techniques of Analy*sis.

John C. Chen, M.D., published "Effect of Lung Volume Reduction Surgery on Pulmonary Diffusion Capacity in a Rabbit Model of Emphysema" in the *Journal of Surgical Research*.

Joseph Huh, M.D., published "Changes in Pulmonary Physiology after Lung Volume Reduction Surgery in a Rabbit Model of Obstructive Diffuse Emphysema" in the *Journal of Thoracic and Cardiovascular Surgery*.

Xunbin Wei, Ph.D. candidate, published "Mapping the Polarity for T cell Activation with an Optical Trap" in *Proceedings of the International Society of Photo-optical Engineers*.

ARRIVALS

Chi Quach has joined the Institute as an Assistant Accounting Analyst. She previously worked as an Administrative Assistant II at UCI's School of Engineering.

NOTABLES

J. Stuart Nelson, M.D., Ph.D., was elected to the Board of Directors of the American Society for Laser Medicine and Surgery.

Petra Wilder-Smith, Ph.D., D.D.S., was awarded a Culpeper Foundation grant.

Joshua Fishkin, Ph.D., was awarded a three-year postdoctoral traineeship by the U.S. Army for "Measurements of Breast Tissue Optical Properties."

Sarang Aranke, **Linh Nguy** and **Young Yoon** were awarded grants to fund dental research by UCI's Undergraduate Research Opportunities Program. The students, who have been working with Petra Wilder-Smith, Ph.D., D.D.S., will present their research at a UCI symposium in May.

NEWSBRIEFS

(continued from pg. 1)

program and is an endorsement of the LAMMP scientists' cutting-edge technological developments."

The LAMMP grant funds basic research on the interaction between light, cells, and tissue. One of the aims of the biotechnology resource is to provide state-of-the-art optical technologies to the biomedical research community for collaborative studies. Current areas of investigation include cancer detection, immune response, wound healing and genome / chromosome characterization.

JAPANESE DELEGATION VISITS

On January 23, 1998, medical engineering professionals from the Okayama Prefecture in Japan visited the Beckman Laser Institute as part of an international cooperation mission.

The delegation, comprised of Japanese physicians and businesspeople, toured the Institute with Director Michael Berns, Ph.D., who described the Institute's laser-based applications. Institute scientists Bruce Tromberg, Ph.D., Zhongping Chen, Ph.D., and Joshua Fishkin, Ph.D., also demonstrated such Institute technologies as frequency domain photon migration and optical Doppler tomography.

The visit, coordinated by Okayama's Department of Commerce, Industry & Labor, was designed to stimulate collaborative activities between California and Okayama scientists.

Drs. Tromberg (left) and Fishkin (right) explain photon migration to the Okayama delegation.

MBA GRADUATES CONSULT

As part of a post-M.B.A. project, four recent graduates of UCI's Healthcare Executive M.B.A. Program have formed a consulting team to tackle a "hairy" problem at the Institute. The consultants will analyze whether the Institute should incorporate a new hair-removal laser into its current spectrum of services.

Director Michael Berns, Ph.D., says that he looks forward to working with the healthcare professionals. "The consulting team will help us to determine whether this service is right for BLI and, if so, recommend how to implement it," he explains.

The consultants will present their findings in two months.

INSTITUTE PATIENTS PLEASED

Almost 100 percent of Institute patients surveyed rated the Surgery Laser Clinic's nursing staff "excellent" and would recommend the Clinic to a friend. Begun in 1997, the ongoing post-treatment survey is designed to assess patient satisfaction. ■

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