LASER
BECKMAN LASER INSTITUTE

IN THE NEWS

Volume XI, Number 2, 1995

Institute Earns Two Program Renewals

The Beckman Laser Institute has received renewals for two of its National Institutes of Health (NIH) sponsored programs. More than $2.2 million in new funding will be available over the next four years for a variety of the Institute's most promising research and clinical studies.

The Institute's Laser Microbeam and Medical Program (LAMMP), now in its sixteenth year as an NIH-designated Biotechnology Resource, received a three-year endorsement from the NIH. LAMMP operates as a national user facility to foster the development of new instrumentation for biomedical applications and to promote close collaboration among academic, corporate, medical, and federal sectors. Currently, LAMMP sponsors research, service, and training projects in laser microsurgery, optical trapping, and other fields.

Dr. George M. Peavy (right) describes an innovative procedure to treat an endangered kit fox. (For the complete story, please see the Veterinary Update on page 6).

Among the reviewers' comments was praise for the program's newly added tissue interaction and optical diagnostics components. "The proposed extensions of the core research and development," wrote one member of the review section, "are of high technical merit."

Also renewed by the NIH was the Institute's long-standing study of Photodynamic Therapy (PDT) for the treatment of malignant tumors. The NIH praised the PDT project for its combination of clinical and pre-clinical studies and noted that "(the project) represents a thorough, innovative investigation of PDT mechanisms."

"The NIH renewal process has become increasingly competitive," comments Institute Director Michael W. Berns, Ph.D., "These competitive renewals demonstrate that the Institute continues to operate as one of the world's leaders in laser biomedicine." ■

Newsbriefs

LASER SKIN RESURFACING

Physicians at the Beckman Laser Institute are now performing laser assisted skin resurfacing. Conducted on an outpatient basis with local anesthesia, the cosmetic procedure can reduce the appearance of facial wrinkles and imperfections by as much as eighty percent.

According to Dr. Jay Applebaum, Assistant Clinical Professor of Dermatology, laser assisted skin resurfacing offers specific advantages over commonly employed chemical peels and dermabrasion techniques because the effect of the laser is uniform and highly selective. "In comparison to other techniques, laser resurfacing has the fewest risks," states Dr. Applebaum. "We have had exceptional results with wrinkles around the mouth and eyes, and even on non-elevated scars."

For more information on skin resurfacing, please call (714) 824-7997.

The Business of Science: Doing More With Less

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

"It was the best of times. It was the worst of times."
--A Tale of Two Cities (1859)

Charles Dickens' opening lines in *A Tale of Two Cities* could just have easily been written today. Surely Dickens' sentiment is just as poignant today as it was more than one hundred years ago. For those of us at the Beckman Laser Institute, these truly are the best of times. Our scientists are making new discoveries (see Research Update on page 4); our grants are being renewed through the most stringent peer-review system in memory (see Cover Story); and we are very fortunate to have a Board of Directors which continues to be very interested both in our long-term goals and our daily operations.

At the same time, however, these are the worst of times for major scientific research facilities such as ours. Competition for federal funds is tighter than ever before. We have been forced to write five times as many grants today as we did a few years ago in order to get the same number funded. In addition, the amount funded per grant is continually being reduced because of budget cuts and "the government is too big" attitudes which prevail both in Washington and around the country. Finally, the local Orange County bankruptcy has made it increasingly difficult for us to raise funds from the local philanthropic community. Clearly, we are facing new and unique challenges which require a well-planned and well-tailored strategy.

A Familiar Challenge

There is an old stratagem which can serve our present needs quite well, and unfortunately, few other options are open to us. In essence, we need "to do more with less." We need to be more frugal with the resources we have, and we must look critically at those programs and projects which may be lacking in vigor or are unable to sustain themselves. We need to be creative in seeking support through partnerships with the private sector as well as other high quality academic programs. Unless we cultivate productive liaisons to ensure that our research finds the most appropriate clinical applications, our mission will have failed. Even basic research must ultimately serve human ends if it is to withstand the pressures of the current economic climate, so we must find the most efficient avenues to ensure that our work serves the community at large.

Overcoming Obstacles

There are a great number of new challenges confronting us. By all indications from Washington, things are going to get worse for U.S. science before they get better. As the world around us continues to change, we must be prepared to devise new plans and to adopt new strategies so that the paths to our goals do not disappear. If we let adversity freeze us in our tracks, then we are doomed to failure.

I believe that something good can and must come of all this. We have an opportunity to take stock of what we have achieved since our doors opened almost a decade ago, and where we would like to be ten years from now. Through the foresight and wisdom of our founder, Arnold Beckman, Ph.D., we have a world class facility which is sustained by a healthy endowment and staffed by the best and brightest people.

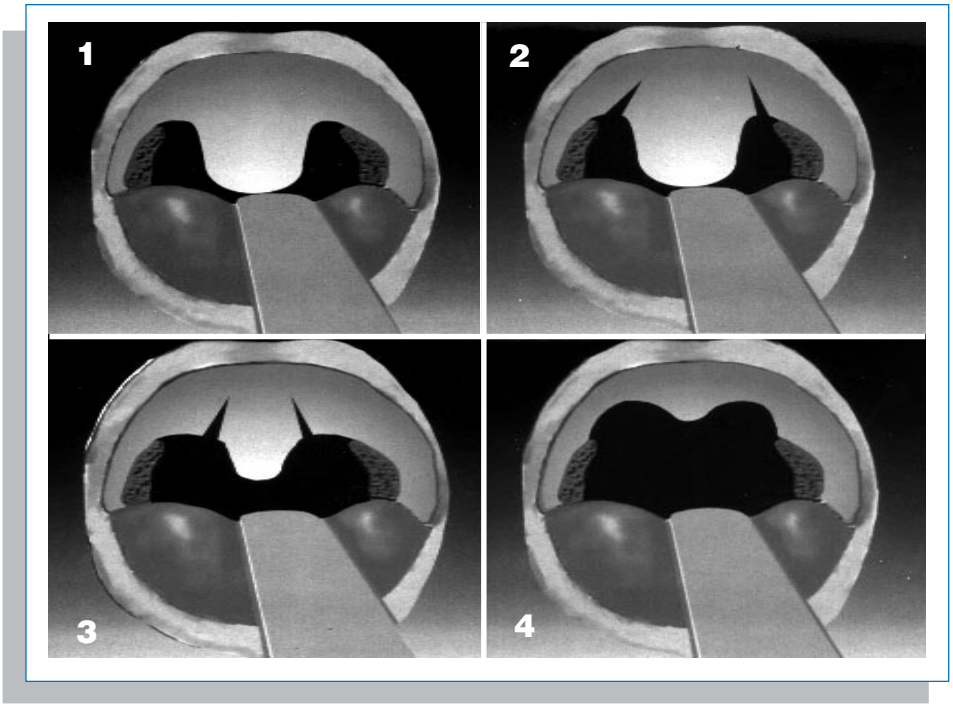
With that as our foundation, we can plan a course into the twenty-first century that will continue to keep the Beckman Laser Institute at the forefront of advances in Photomedicine. By focusing on that which is possible rather than that which is not, we can do more with less, and we can overcome the obstacles in front of us. ■

Laser Treatment for Snoring Yields Strong Results

Snoring affects more than 21 million Americans. The disorder can provoke marital discord, is often the subject of ridicule, and may be one of the presenting symptoms of sleep apnea, a potentially life-threatening respiratory disorder. Laser-Assisted Uvulopalatoplasty (LAUP) is a new outpatient, surgical treatment to alleviate snoring in patients with enlarged uvulas and elongated soft palates.

First practiced in the United States in 1993, LAUP was developed in France in 1989. The procedure is performed under local anesthesia in a series of incremental treatment sessions (1-5 office visits) and requires no hospitalization.

According to William Armstrong, M.D., Assistant Professor in the Department of Otolaryngology at UC Irvine, LAUP is far less traumatic to the airway than conventional surgical reshaping procedures. "LAUP is significantly less painful than conventional uvulopalatophyrngoplasty (UP3)," states Dr. Armstrong. "LAUP also averts the risks of general anesthesia. In most cases, this is a much safer, more practical procedure than the more radical UP3."



Schematic illustration of Laser-Assisted Uvulopalatoplasty (LAUP). The patient's uvula and soft palate are gradually resected in a series of incremental treaments.

Incremental Treatment

Unlike UP3 which requires hospitalization, LAUP is performed in a series of short office visits. In essence, LAUP utilizes the heat of the laser to shrink and tighten the tissues in the back of the patient's mouth (see accompanying figures). This process is undertaken gradually to guard against the risk of over-resection. As a result, LAUP eliminates the most extreme complications associated with UP3: regurgitation of food and drink and changes in speech.

Since 1993, more than 120 patients have been treated for snoring at the Beckman Laser Institute. Data obtained from these studies suggests that the procedure, generally performed with a CO_2 laser, is extremely effective for a significant number of patients.

The results of a recent patient survey indicate that LAUP rates extremely well for overall effectiveness as well as for patient comfort. Seventy-six percent of the Institute's LAUP patients indicated that the procedure alleviated 85% - 100% of their snoring. Of these patients, 72% reported that they obtained these results after only one or two treatment sessions.

Because LAUP achieves uvula and palate reshaping without significant impact to the airway, the laser-based procedure also substantially reduces pain and recovery time associated with UP3. In fact, 78% percent of LAUP patients reported no incapacitation, and most were able to return to their normal activities immediately after treatment. In contrast, UP3 patients typically require 1 - 3 weeks recovery time.

Future Studies

According to Dr. Armstrong, physicians may be able to hone the procedure further by testing different lasers. "LAUP used to require four to six treatment sessions. In some cases, we can now complete the treatment with half as many office visits," says Dr. Armstrong. "That is a step forward, but we may be able to offer even more rapid healing and better pain management. A thorough comparative laser study is definitely in order."

Dr. Yona Tadir, Institute Medical Director, also speaks of the laser procedure with great confidence and optimism. "We have already brought peace to many families," comments Dr. Tadir. "At the same time, I believe the procedure can be improved further. I think we are in an excellent position to initiate new studies."

For more information about LAUP, please call (714) 824-7997. ■

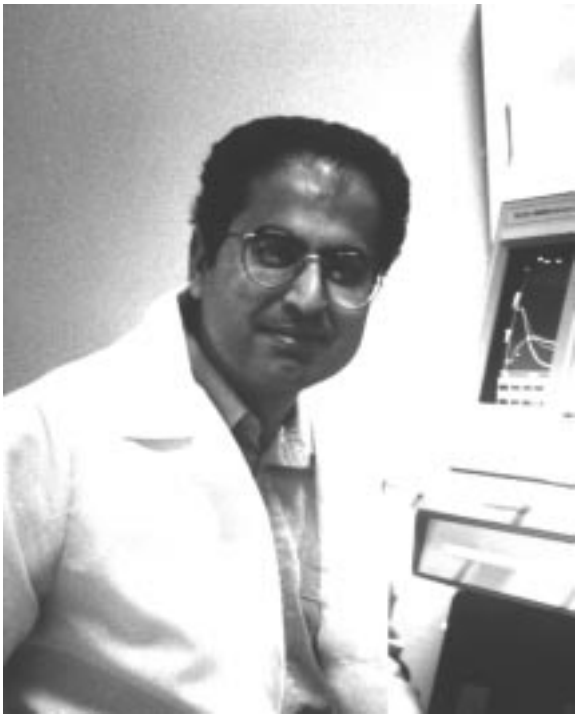
Bahman Anvari: Bringing Science to the People

Since coming to the Institute as the Packard Foundation Fellow in the summer of 1993, Bahman Anvari, Ph.D., has played an integral role in the development of a new technique to improve the laser treatment of dermatological disorders. A native of Tehran, Iran, Bahman completed his doctoral training in Bioengineering at Texas A&M University and has since been working to perfect "dynamic cooling" for application in the clinical management of patients with disfiguring birthmarks and other skin lesions

By applying small amounts of a cryogen compound to the skin surface during laser treatment, physicians can dramatically reduce thermal damage to the normal overlying skin layer. Since the cryogen reduces temperatures only in the upper skin layers, the technique does not diminish the therapeutic value of the laser in the abnormal blood vessels below.

Bahman recently presented the results of the first patient studies to an enthusiastic audience at the annual meeting of the American Society for Lasers in Surgery and Medicine. "People responded well," states Bahman. "In the past, we've been able to provide theoretical evidence to support the effectiveness of this technique, but now we have clinical evidence, too. That's the ultimate test."

According to Dr. Anvari, the Institute's multi-disciplinary environment has been a critical factor in the progress of his research. "I read quite a bit to keep up with my field," says Bahman, "but nothing compares to the conversations I've had with my colleagues. The pool of knowledge here has been crucial to the success of my research."



Postdoctoral Fellow Bahman Anvari, Ph.D., takes a moment out of his research schedule.

Bahman, who currently lives in Irvine with his wife, Soheyla, is also quick to emphasize the importance of communication skills for the advancement of science. "I try to use language which everyone can relate to, and I encourage my students to do likewise. After all, this work is for the benefit of patients, not specialists." ■

Industrial Associate Profile: DUSA Pharmaceuticals

Established to provide corporations with a window into the evolving world of biotechnology, the Beckman Laser Institute's corporate relations program offers companies a formal affiliation with the Institute which allows these firms to conduct joint research projects and tap into the Institute's expertise in laser biomedicine.

In response to inquiries by a number of smaller companies who expressed interest in establishing formal affiliations with the Institute, the Industrial Associates Program (IAP) was founded in 1992. The IAP permits start-up companies and highly-specialized divisions of larger companies the opportunity to collaborate formally with the Institute. The Institute currently has 13 Industrial Associates.

DUSA Pharmaceuticals, Inc., was one of the first companies to join this program. DUSA specializes in the development of photodynamic therapy (PDT) using 5-aminolevulinic acid (ALA) as the PDT agent. DUSA is primarily developing ALA PDT in the area of dermatology, for the indications of actinic keratoses, acne, hair removal, and psoriasis.

DUSA is working with Institute Medical Director, Dr. Yona Tadir, to develop ALA PDT for endometrial ablation (as a non-surgical alternative to hysterectomy for women with dysfunctional uterine bleeding). DUSA is also developing proprietary light sources and light delivery devices for its ALA PDT indications.

"We believe our working relationship with the researchers and staff at the Beckman Laser Institute has been mutually beneficial," states DUSA's Vice President for Scientific Affairs, Dr. Stuart L. Marcus. ■

Harnessing the FEL: Medical Studies Raise Questions

In the field of laser engineering, the Free Electron Laser (FEL) is often regarded as a clumsy giant. Costing tens of millions of dollars to build and operate, these huge machines, which were developed in the 1970's as part of the Star Wars defense project, occupy entire wings in the research laboratories where they are housed and require a staff of full-time engineers to keep them running. Yet, there are those who feel that, despite its high cost and large size, the FEL lends itself quite well to biomedical studies.

"The FEL certainly isn't one of the most practical lasers, but it has some very unique features which, nonetheless, make it a powerful research tool," says Institute researcher Curtis F. Chapman, Ph.D., who is currently conducting an FEL project at Stanford University, site of one of the nine operational FELs in the United States.

Dr. Chapman, a Hewitt Foundation Postdoctoral Fellow, makes monthly trips between the Beckman Laser Institute and the Stanford FEL laboratory to test the effects of infrared radiation on cell samples. The results of these studies will provide new insight into the mechanical and physical effects of laser microirradiation on biological samples and could help to improve the treatment parameters for many existing medical laser procedures.

Miniature Thermometers

According to Dr. Chapman, temperature increases during exposure to the FEL may significantly alter the biochemistry of cell samples. Even slight temperature changes (e.g., four degrees Celsius), for instance, when they are affected over very short time intervals, can be extremely damaging to living cells. The problem currently confronting researchers is how to determine the precise threshold at which the effects of laser microirradiation become irreversible or destructive.

In order to solve this problem, Dr. Chapman is conducting a study using temperature-sensitive, fluorescent dyes. By labeling cells with these fluorescent molecules prior to their exposure to the FEL, Dr. Chapman can make extremely accurate estimations of temperature increase. When stimulated by laser light, these special dyes begin to cast off energy in the form of fluorescent radiation. Since fluorescence intensity is related closely to temperature increase, these dyes are, in effect, miniature thermometers.

Dr. Chapman has recently completed a particularly informative series of thermal measurement studies. "We've recorded temperature increases in cells approaching six degrees Celsius," comments Chapman. "This may not seem significant. However, temperature increases of this magnitude are large enough to induce the production of an important class of stress proteins which actually protect cellular components from additional thermal and chemical damage."

Assistant Professor Bruce J. Tromberg, Ph.D., (right) and Curtis F. Chapman, Ph.D., prepare cell samples for experiments at Stanford's FEL laboratory.

Defending the FEL

Funding for medical and biomedical FEL studies is provided by grants administered by the Department of Defense's Office of Naval Research (ONR). These grants are made to academic institutions and biotechnology firms which promote the conversion of defense technologies into practical applications for human medicine. Recently, however, the FEL program has come under criticism.

In response to this criticism, Bruce J. Tromberg, Ph.D., Assistant Professor of Surgery and Physiology/Biophysics and leader of the UC Irvine-Stanford interdisciplinary team, argues that the FEL's wavelength tunability and short pulses allow researchers to address issues of broad biological importance. "For instance, we can examine structure-function relationships in single living cells which would ordinarily be totally obscured."

Dr. Tromberg credits the support facilities at UC Irvine and Stanford and the leadership of Dr. Alan Schwettman for much of the program's success. "We've constructed a very sophisticated microscope with the FEL which has become a model for important studies elsewhere," says Dr. Tromberg. ■

Innovative Treatment Helps Endangered Fox

The Beckman Laser Institute recently opened the doors of its Animal Operating Room to a group of journalists who came to observe an experimental surgery to remove a cancerous tumor from the ear of a rare and endangered Santa Catalina Island kit fox. The thirteen year-old fox, dubbed "Fauna" by its caretakers at the Catalina Island Conservancy, was brought to the Institute because her tumor proved to be resistant to conventional surgical techniques.

Reporters from local newspapers and televisions stations watched as Institute Veterinary Director, George M. Peavy, D.V.M., and Dr. Mike Wyatt, the veterinarian who treats Fauna at the Catalina Conservancy, performed photodynamic therapy (PDT), an experimental, light-based cancer treatment, to eradicate a golf ball-sized tumor growing in the fox's right ear.

The procedure, which lasted slightly less than one hour, was judged to be a success by Dr. Peavy, and Fauna's prognosis is good. While Dr. Peavy has performed PDT on cats, dogs, horses, and even a snake, this surgery marked the first time that an animal belonging to an endangered species has been treated at the Institute.

"Without PDT, this animal would have been put to sleep," states Dr. Peavy. "The growth of the tumor was extremely aggressive, and traditional surgical methods were ineffective. PDT gives this critter another chance at life, and the scientific community gets an important opportunity to put a relatively new technology into practice."

PDT typically involves the intravenous or topical administration of photoactive compounds known as photosensitizers. When light of sufficient energy and appropriate wavelength interacts with a sensitizer, highly reactive oxygen molecules are generated which irreversibly oxidize and destroy tissues in which the sensitizers have concentrated. These photosensitizers "localize" only in diseased tissues so that healthy tissues are not damaged.

After anesthetizing Fauna, Drs. Peavy and Wyatt used a CO_2 laser to remove the bulk of the tumor. A small, diode laser developed jointly by scientists at the Institute and Lawrence Livermore National Laboratory was then used to activate a photosensitive dye which had been injected into Fauna on the evening prior to surgery. Because the dye is activated only by light of a specific wavelength (i.e., color), it remained inert until Drs. Peavy and Wyatt applied the diode laser to the area.

After surgery, Fauna was transferred to Dr. Wyatt's veterinary clinic in Anaheim where she remained throughout her recovery. "She has made tremendous progress and has been returned to her habitat on Santa Catalina Island," states Dr. Peavy. ■

Beckman Laser Institute and Medical Clinic

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PRESENTATIONS

Institute Director **Michael Berns, Ph.D.,** spoke at the Biomedical Technology Opportunities workshop in Atlanta, GA, on "Laser Photonics for Biomedical Research: An Integrated Program." He also presented "Zap It, Trap It, Map It" at the Southern California Confocal Microscopy Users Group Acvanced Confocal Imaging Workshop. He lectured on "Laser Surgery: 21st Century Medicine" at the 100th Anniversary of UC Irivne's College of Medicine.

Yona Tadir, M.D., was an invited speaker at the 1995 World Congress of Gynecologic Endoscopy. He spoke on "The Future of Miinimally Invasive Surgery," "Photomedicine of the Female Genital Tract," and "Use and Abuse of Technology in Patient Selection of Endoscopic Surgery." Dr. Tadir also addressed the Biennial Meeting of the International Society for Gynecologoic Endoscopy on "Equipment Development and Applicaiton of New Technologies."

J. Stuart Nelson, M.D., Ph.D., was an invited speaker at the 15th annual meeting of th eAmerican Society for Laser Medicine and Surgery (ASLMS) in San Diego, CA, where he spoke on "Pulsed Photothermal Radiometry of Human SKin," "Topical 5-ALA for the PHotodynamic Therapy of Psoriasis and Actinic Keratoses," and "Pulsed Photo-thermall Radiometry of human Skin." He also presented "infrared Tomography for Diagnostic Imaging of Port WIne Stain Blood Vessels."

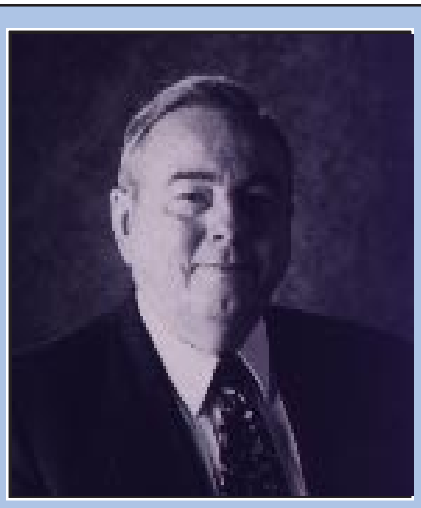
Bruce J. Tromberg, Ph.D., presented "Light and Drug Dosimetry During Photodynamic Therapy" at the 15th annual ASLMS meeting and "Two-Photon Processes in Laser Microbeams" at the Southern California Confocal Microscopy Users Group Advanced Confocal Imaging Workshop.

Yossi Neev, Ph.D., addressed the 15th annual ASLMS meeting on "The Effect of Ablation Spot Size on Surface Temperatures During IR and UV Laser Ablation of Dentin." He

PUBLICATIONS

NOTABLES

Richard A. Nesbit, Ph.D., has been elected to the Institute's Board of Directors. Dr. Nesbit, Vice President for Advanced Technology at Beckman Instruments, Inc. (Brea, CA), succeeds Beckman Instruments CEO, Louis T. Rosso, on the Institute's thirteen-member board. After joining Beckman Instruments as a senior engineer in 1964, Dr. Nesbit served thereafter in various positions, including Vice President of R&D, Quality Assurance, and Advanced Technology. Dr. Nesbit received his education at the University of California, Los Angeles.



NEWSBRIEFS

(continued from page 1)

RETRAINING THE SOUTHLAND

In collaboration with UC Irvine's Department of Electrical and Computer Engineering, the Beckman Laser Institute is currently participating in an outreach program sponsored by the Technology Reinvestment Program (TRP). The TRP was created to facilitate defense industry conversion and sponsors retraining efforts for individuals who have lost their jobs in the wake of cancelled defense contracts and defense spending cutbacks.

Participants in the UC Irvine program choose from three "hands-on" study tracks, including "Biomedical Systems and Applications" for which Institute Researcher, Gregory J. Sonek, Ph.D., serves as advisor. At present, one "trainee" is spending three months at the Institute studying biomedical applications of electronics and optics.

Richard McGrath, an electrical engineer who spent sixteen years working for a Southern California defense contractor before government contract cancellations and budget cuts forced the firm to lay him off, is working at the Institute under the direction of Dr. Sonek and Bruce J. Tromberg, Ph.D., Assistant Professor of Surgery and Physiology/ Biophysics.

Eric Anderson, Ph.D., (left) and Dick McGrath work in the Institute's laser spectroscopy laboratory. The two engineers, both former defense industry personnel, are working on a variety of collaborative projects with Institute researchers.

NEW SUBCONTRACT

EA Photonics, a Redondo Beach, California firm specializing in diode laser based instrumentation has subcontracted the Institute for a Small Business Innovation Research (SBIR) project titled "Photon Migration Spectroscopy Sensor (PMSS)." The six month project, sponsored by the United States Department of Agriculture, funds the design of a portable, non-invasive, optical monitoring unit which will be used to test the freshness and dietary content of perishable food items.

NEW OB/GYN HANDBOOK

Institute Medical Director Yona Tadir, M.D., has co-edited a newly revised handbook for clinicians in obstetrics and gynecology. Titled *Obstetrics, Gynecology, and Infertility*, the comprehensive reference book, co-edited by John D. Gordon, M.D., Jan T. Rydfors, M.D., and Maurice L. Druzin, M.D., is now in its fourth edition. This compact reference source is designed to fit in the pocket of a physician's jacket and has been issued to more than 10,000 OB/GYN fellows across the country. ■

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