

Fall 1993

## Focal Spot, Fall/Winter 1993

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FALL/WINTER, 1993

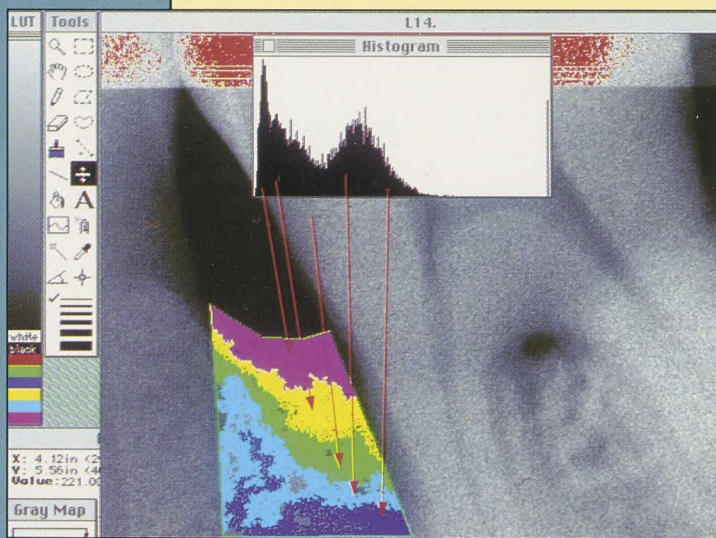
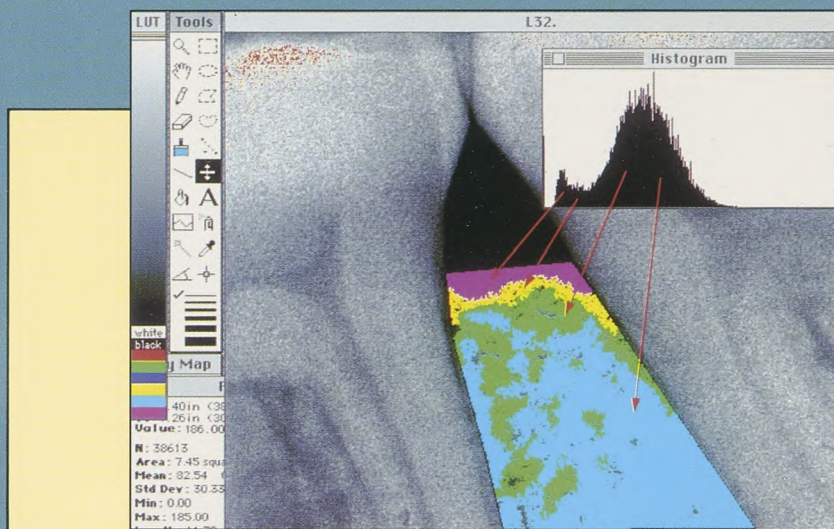
VOLUME 24, NUMBER 3

# FOCAL SPOT

ROCKRODT INSTITUTE OF RADIOLOGY

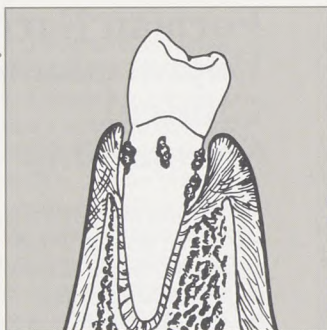


**A JEWEL  
IN THE  
MAKING**



A four-year study at the Institute will help to identify and treat patients who are at risk of bone loss in the upper and lower jaws. These histograms and color-enhanced images distinguish between healthy periodontal bone (depicted as a normal bell-shaped curve and a homogeneous distribution of color levels) and bone resorption (distortion in plot curve and extreme variance in brightness levels). For more information, turn to page 6.

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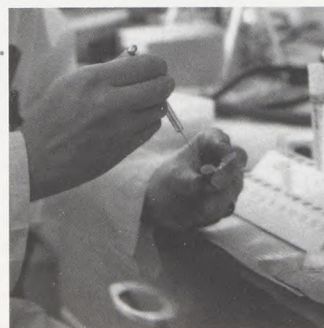


## A WOMAN'S HEALTH ISSUE

The combination of aerospace technology and digital imaging may help to establish a link between osteoporosis and periodontal bone loss in postmenopausal women.

## 12 A JEWEL IN THE MAKING

Positron emission tomography and a man-made version of one of the body's proteins offer a bright spot in the diagnosis and treatment of prostate cancer.



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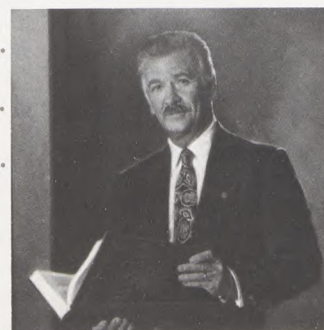
## IMAGING CENTER UPDATE

Construction of the Institute's research center moves steadily toward its scheduled mid-1994 completion date.

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### ON THE COVER:

Just as some breast cancer cells are receptive to the hormone estrogen, prostate cancer cells may carry receptors for somatostatin, a natural protein. In her lab at Mallinckrodt Institute, Dr. Carolyn Anderson hopes to synthesize somatostatin for use in prostate cancer research. Photograph by T. Mike Fletcher.

# SPOT NEWS



## Powers Delivers Probstein Lecture

After a 15-year absence from the Institute, William E. Powers, M.D., a recognized authority in treatment techniques for carcinoma of the uterine cervix and preoperative radiation therapy for head-and-neck tumors, presented the Probstein Oncology Lecture on September 10. Speaking on "Bone Metastases: Fallacies, Dogma, and Reason," Powers peppered his talk with witty observations (including a suggested list of little known punctuations and terms for use in scientific papers) while driving home the clinical facts about bone metastases.

Powers pointed out that bone metastases occur in 100,000 new patients each year. At least one-fifth of patients who die of cancer

William E. Powers, M.D.,

experience clinical bone metastases, and one-third of those patients develop fractures or cord compression that produce massive dysfunction. He believes that radiation therapy is the least expensive and most effective local chemotherapeutic agent known, and that any patient with clinical lesion metastases should be treated concurrently to systemic therapy with local high dose radiation therapy.

Powers, a 1993 recipient of the prestigious Gold Medal Award presented by the American College of Radiology, is a former director of the MIR Radiation Oncology Center. In the late 1960s, while on staff at the Institute, he recognized the necessity of shielding surrounding normal tissue from the high doses of radiation required to destroy tumors. His design for blocks made of an alloy called Cerrobend is used in radiation oncology centers nationwide. In 1965, working with Washington University computer scientists, Powers was instrumental in developing a computer system dedicated to radiation treatment planning. In 1978, he was appointed chairman of the Department of Radiation Oncology at Wayne State University School of Medicine in Detroit.

The Probstein Oncology Lecture was established in 1985 in honor of Carlos A. Perez, M.D., director of the MIR Radiation Oncology Center, and William Fair, M.D., former head of urology in Washington University's Department of Surgery.

## Forman Earns Unprecedented Clinical Scholarship

As the first MIR recipient of the Robert Wood Johnson Clinical Scholarship, Howard Forman, M.D., fourth-year resident in diagnostic radiology, will begin health services research in 1994 at the University of Pennsylvania's Wharton School of Business.

The scholarship is an unusual honor for a radiologist. During its 20-year history, past recipients have generally been clinicians, a number of whom have gone on to chair internal medicine departments at top U.S. medical centers. Many of the physicians who are members of First Lady Hillary Rodham Clinton's Task Force for Health Care Reform also received the award. The scholarship is sponsored by the Robert Wood Johnson Foundation, the United States' largest privately-funded health-care research foundation.

During his two-year program, Forman will focus his studies on the technology assessment and cost-effectiveness of health care. According to Forman, "In order to have an excellent health-care program, you not only need the technology and science but also the ability to deliver the health care."

## ACR/MIR: The Tradition Continues

At the American College of Radiology (ACR) Annual Meeting in September, three MIR faculty members stood among the 112 outstanding clinicians and scientists nationwide who were designated as ACR fellows: Venkata R. Devineni, M.D.; Joseph R. Simpson, Ph.D., M.D.; and Michael W. Vannier, M.D. The ACR annually recognizes those radiologists, radiation oncologists, and radiological physicists who make significant scientific or clinical research contributions or literary contributions in the field of radiology.

Devineni, an associate professor of radiology, Radiation Oncology Center, is clinical chief of radiation oncology at DePaul Hospital. He was chief resident during his training at Emory University and completed a fellowship at the Institute. Since joining the MIR faculty in 1980, Devineni's primary interest has been in clinical radiation oncology, specifically head-and-neck oncology.

Simpson, an associate professor of radiology, Radiation Oncology Center, joined the MIR faculty in 1978 after completing a residency in radiation oncology at the University of Wisconsin Hospital, Madison. During his training, he was chief resident, 1977 to 1978, and was named an American Cancer Society Clinical Fellow. At the Institute, Simpson has focused his research on treatment techniques of central nervous system tumors, including stereotactic external beam irradiation and 3-D treatment planning.

Vannier, professor of radiology, director of the Division of Radiology Research, is a pioneer in the clinical application of 3-D imaging. He works closely with surgical collaborators to identify and develop computer aids for diagnosis and treatment. After completing a residency in diagnostic radiology at MIR, Vannier joined the faculty in 1982.

An additional honor for the Institute is the renaming of MIR Director Ronald G. Evens, M.D., as secretary-treasurer of the ACR Board of Chancellors. Evens, a recognized authority in the socio-economics of medicine, was first named to the ACR Board in 1988. The 24-member Board is the governing body of the ACR, determining policy standards for this national organization of more than 28,000 radiologists.

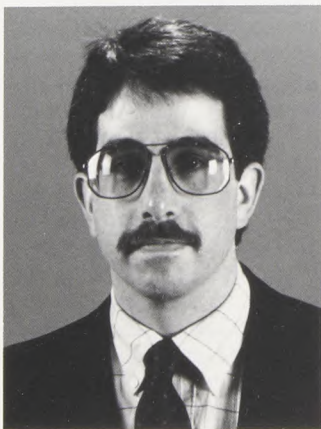
## Mirowitz Appointed Chief

In January of 1994, Scott A. Mirowitz, M.D., director of Jewish Hospital's magnetic resonance imaging section, will assume the responsibilities of radiologist-in-chief of the Institute's radiology department at Jewish Hospital. The appointment followed a six-month national search led by committee cochairs Ronald G. Evens, M.D., MIR director, and Wayne M. Lerner, DPH, president and senior executive officer of Jewish Hospital.

With this new alignment, the Institute will coordinate all radiologic services within Washington University Medical Center and at Barnes West in St. Louis County. According to Evens, Mirowitz will have an

excellent opportunity to develop a nationally recognized academic department while maintaining Jewish Hospital's long-standing tradition of providing excellent clinical service. Lerner believes the cooperative effort will further the roles of the Institute, Washington University, and Jewish Hospital as regional healthcare leaders and institutes for scientific inquiry.

Mirowitz has an outstanding reputation as a physician and a scientist. Under his leadership, Jewish Hospital's magnetic resonance imaging (MRI) section reported an 80 percent growth rate over the past three and one-half years while providing quality service to patients and physicians. An alumnus of Washington University School of Medicine, Mirowitz completed four years of training in diagnostic radiology through the MIR/Jewish Hospital-affiliated residency program and a one-year fellowship in magnetic resonance imaging.



Scott A. Mirowitz, M.D.



Barbara Monsees, M.D.

## Monsees Heads Breast Imaging Section

In recognition of the important role that mammography continues to play in women's health care, Barbara Monsees, M.D., was named chief of breast imaging, a new section under the Division of Diagnostic Radiology. As a member of the MIR team who, in 1986, brought the first mobile mammography van to the St. Louis region, Monsees is an effective advocate of the benefits of early detection of breast cancer through screening.

Monsees, who joined the MIR faculty in 1980, and a team of researchers hold the patent for a radiologically compatible filler for breast implants. She was instrumental in developing the new Mammography Screening Center at Barnes Hospital. The Center's location on the first floor of the hospital offers women convenient access to routine mammography screening.

## McClennan on Advisory Board

The Board of Directors of the Radiological Society of North America (RSNA) appointed Bruce L. McClennan, M.D., professor of radiology and chief of MIR's abdominal imaging section, to serve on the 1994 Public Information Advisory Board. As a board member, McClennan, an expert in the assessment of radioiodinated contrast agents and in genitourinary radiological research, will review abstracts and help select papers and scientific exhibits featured at the annual RSNA symposium.

Throughout the year, board members also serve as informational resources for the news media. Acknowledged as experts in scientific research, these physicians are often called upon by the American Medical Association (AMA) for clarification of data in reports issued by the AMA's Council on Scientific Affairs. This information is frequently published in specialty medical journals and quoted in news articles on health-related issues.

# SPOT NEWS



C. Douglas Maynard, M.D. (left); Mrs. Wendell Scott; and Ronald G. Evens, M.D.

## Important Issues in Radiology

"There are those who say that the golden age of radiology is past. Don't believe it. The future is brighter than ever before," admonished C. Douglas Maynard, M.D., invited speaker for the Twenty-second Annual Wendell G. Scott Memorial Lecture on October 11.

Maynard, president-elect of the American Board of Radiology, is a nationally recognized leader in the advancement of radiologic education and has introduced many innovative approaches to learning, such as television programming, research training for residents, and video-disk technology for board examinations.

He outlined the national issues facing medical professionals as a result of the Clinton administration's proposal for health-care reform:

- a perceived need to train more primary-care physicians,
- the debate on overspecialization,

- a requirement for demonstrated competence,
- turf issues between subspecialty groups,
- and the need for better defined quality.

According to Maynard, who is chairman of the Department of Radiology at the Bowman Gray School of Medicine, these topics are "causing gentle ripples and radiology is caught between the issues."

Accreditation is the subject of five congressional bills plus proposals by the Physician Payment Review Commission; the Association of American Medical Colleges; the Council on Graduate Medical Education, the parent organization for accreditation; and President Clinton. Common to all proposals is the recommendation to shift the balance from specialties to primary care, limit the number of postgraduate positions, establish national allocation, and fund only approved programs.

Nationwide, there are 204 accredited diagnostic radiology programs with 4,164 positions, and the Residency Review Commission is recognizing an increase in diagnostic radiology slots at the rate of 50 to 60 every six months. But Maynard predicts that as the U.S. health-care system is remodeled over the next five years, radiology faces the potential loss of a large number of funded slots.

Evidence of competence and continuing competence also is under review as there is a need in all specialties for a formal recertification program. The American College of Radiology's reorganized Task Force on Documenting Continuing Competence, chaired by MIR's Bruce L. McClennan, M.D., is investigating methods for documenting ability and skill of radiologists, radiation oncologists, and medical physicists.

## Slone Trained in Medical Journalism

As one of four recipients of the 1993 Melvin M. Figley Fellowship in Radiology Journalism, Richard M. Slone, M.D., recently learned from the masters the fundamentals of medical journalism. Sponsored by the American Roentgen Ray Society (ARRS), the fellowship encourages academic radiology careers and stimulates interest in high quality radiology journalism. The fellowship aims to improve the quality of radiology publications by teaching journalism skills early in the academician's career and providing training for manuscript reviewers and future editors. After completing the program, the fellowship recipients, as core teachers, can share their skills and knowledge of medical journalism with colleagues.

At the California-based editorial offices of the *American Journal of Roentgenology* (AJR), one of the nation's leading scientific publications, Slone received hands-on-experience in manuscript preparation and editing, the ethics of scientific journalism, and the peer review process. During the month-long fellowship, Slone, a clinical instructor and fellow in chest radiology, also travelled to the ARRS publication office in Virginia and to Waverly Press in Maryland to observe the mechanics of formatting and printing the journal.

He is now applying techniques learned from the fellowship program to research projects, including an analysis of coauthorship in radiology literature and the peer review process.

## ERL Helps Set Standard at RSNA

The Radiological Society of North America (RSNA) once again selected the MIR Electronic Radiology Laboratory (ERL) to develop software for a major demonstration of digital information management at the Society's 79th Annual Meeting, November 28 through December 3.

The Digital Imaging and Communication (DICOM) Standard, completed by the American College of Radiology (ACR) and the National Electrical Manufacturers Association (NEMA), defines universal storage and exchange of electronic images among the different types of imaging equipment. A successful demonstration of the DICOM Standard, involving 20 major manufacturers, was first featured at the 1992 RSNA Meeting, where MIR-developed software supplied the necessary bridge for transferring image data between central test nodes and each of the manufacturers' demonstration nodes.

Under contract with RSNA, the team of Stephen M. Moore, M.S.; David E. Beecher, M.S.; Sheldon Hoffman, M.S.; G. James Blaine III, D.Sc., director of the ERL; and R. Gilbert Jost, M.D., director of the Division of Diagnostic Radiology, developed software to support a much broader demonstration at RSNA '93 of image communication among various manufacturers using the DICOM Standard.

## Software Developed for Stereotactic Radiosurgery

Kanematsu Medical Systems awarded Principal Investigator Robert E. Drzymala, Ph.D., a one-year contract for \$93,500 to develop a special interactive software package for simulating and planning radiotherapy treatment of the brain and for directing brain biopsies. The user-friendly system will be available commercially by late 1994 and can be used with digital angiography, computed tomography (CT), magnetic resonance (MR), and positron emission tomography (PET).

During the scanning procedures, the patient's head will be immobilized by a stereotactic frame. The frame will show up as dots on the scans, indicating a definitive coordinate system. For 3-D treatment planning, the coordinate system will be used to target the radiation beam within one millimeter of the tumor. In neurosurgery, the system can provide better visualization for planning brain tissue biopsies; treating vascular abnormalities, such as arterial venous malformations (AVMs); and implanting devices that assist in chemically or physiologically manipulating brain tissue.

Coinvestigators for the project are Joseph R. Simpson, M.D., associate professor of radiology, and Keith M. Rich, M.D., associate professor of neurological surgery.



On September 29, friends and colleagues gathered in Scarpellino Auditorium for the unveiling of the official portrait of Carlos A. Perez, M.D., director of the Radiation Oncology Center. Perez's internationally acclaimed expertise in the field of radiation oncology earned him the prestigious Gold Medal Award, presented in 1992 by the American Society for Therapeutic Radiology and Oncology. On hand for the portrait presentation were (left to right) William H. Danforth, M.D., chancellor of Washington University; Ronald G. Evens, M.D., director of the Institute; Perez; and Todd H. Wasserman, M.D., clinical chief of radiation oncology at Jewish Hospital, who spearheaded the commissioning of the portrait.

## Moros Receives Grant

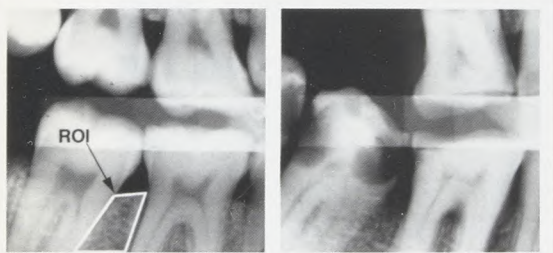
As principal investigator, Eduardo G. Moros, Ph.D., assistant professor of radiology and chief of hyperthermia physics service, received a three-year Biomedical Engineering Research Grant from The Whitaker Foundation to develop a system that will more effectively treat small and large superficial tumors.

Clinical studies have shown that hyperthermia (raising the temperature of tumor tissue to 42-45°C for an extended length of time) is an effective adjunct to radiation therapy, and the simultaneous delivery of these therapies provides a more beneficial method of treatment. Because of disparity between the therapies and the delivery systems, including length of treatment and equipment design, patients currently receive hyperthermia before or after radiation.

By integrating ultrasound technology with a scanning reflector, the MIR researchers propose to develop a new hyperthermia system, specifically designed for simultaneous use with external beam radiation machines.

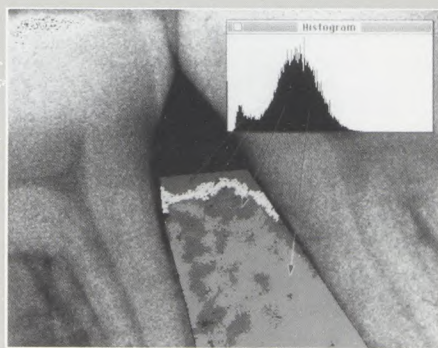
Coinvestigators for the \$178,640 grant, "An Ultrasound Array System for Simultaneous Hyperthermia and External Beam Radiation of Superficial Neoplasms," include William L. Straube, M.S., instructor in radiology; Robert J. Myerson, Ph.D., M.D., associate professor of radiology; Eric E. Klein, M.S., instructor in radiology; Daniel A. Low, Ph.D., instructor in radiology; and Bahman Emami, M.D., professor of radiology and associate director for research - Radiation Oncology Center.





**Normal**

**Diseased**



MIR researchers are using digital imaging to find a treatment that reduces the risk of periodontal bone loss in postmenopausal women.

# W/A Woman's HEALTH I • S • S • U • E

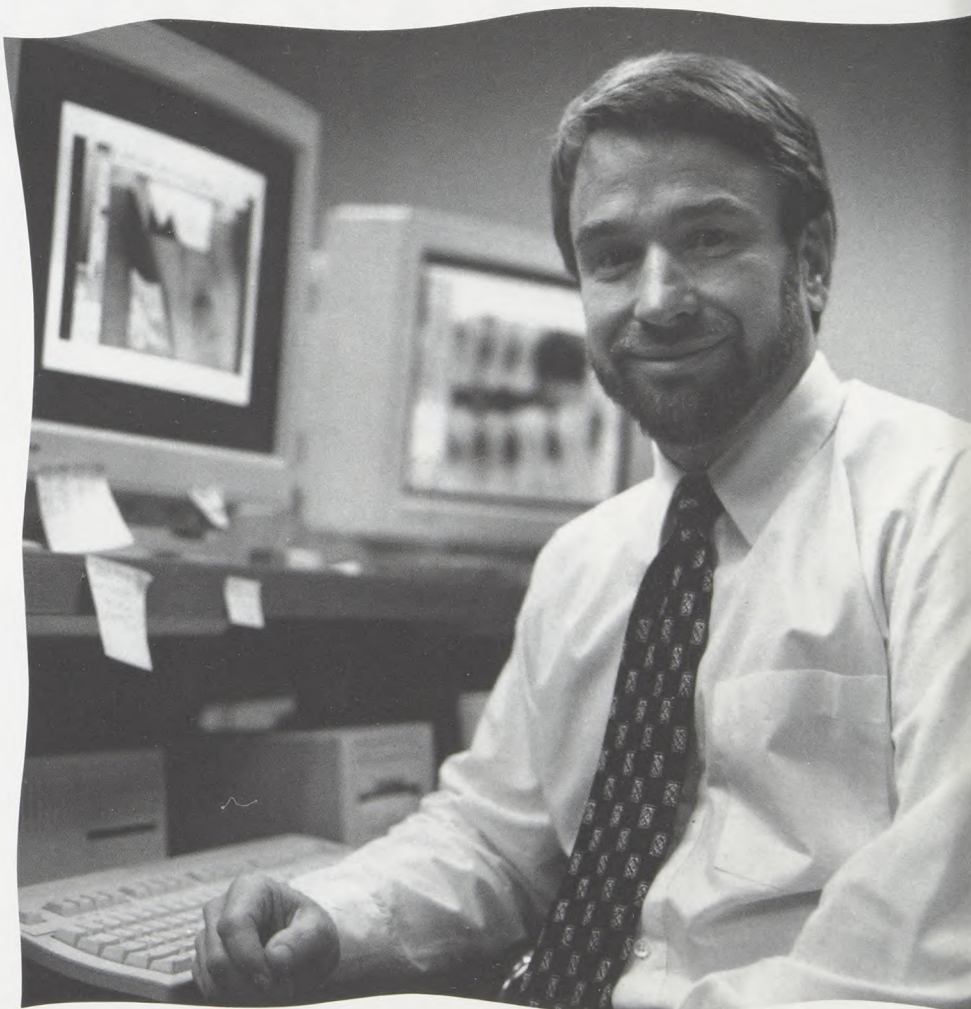
Digital imaging technology analyzes periodontal bone loss

**R**esearchers have known for some time that postcranial bone loss in women is one of the physiological changes that can accompany menopause. But little is known about the connection between periodontal bone loss and osteoporosis, or why some women lose bone more rapidly than others. Variations in periodontal bone loss patterns among patients first piqued the curiosity of Dr. Charles F. Hildebolt when he was practicing dentistry. During his nine years of private practice, Hildebolt saw certain patients who continued to lose their periodontal bone in spite of dental treatments and good oral hygiene. He also observed patients who continually had their dentures relined or remade because of the resorption of the alveolar processes (bony ridges in the upper and lower jaws in which the teeth are anchored). In some cases those patients underwent surgical ridge augmentation. Hildebolt wanted to find a method of identifying and treating those patients at risk. Now as a researcher at Mallinckrodt Institute of Radiology (MIR), he has received National Institute of Dental Research funding for a four-year study on the interrelationships between alveolar bone loss and postmenopausal osteoporosis.

“In dental school we were taught that alveolar bone loss could be caused by ill-fitting dentures, even though it appeared to be a bigger problem for women than men. It has also been suggested that both men and women lose the same amount of bone with age, but bone loss in women is easier to detect because they have less bone mass initially,” says Hildebolt, an MIR associate professor of radiology who carries both a dentistry degree and a Ph.D. in physical anthropology.

Clinicians and scientists generally agree that the periodontal alveolar bone resorbs with advancing age. However, it is not known how the estrogen therapy some postmenopausal women receive affects periodontal bone loss, or if the systemic mechanisms responsible for osteoporosis (bone deterioration in the postcranial skeleton) cause a simultaneous loss of periodontal bone. Hildebolt believes the causes of periodontal disease, a common precipitator of tooth loss and, consequently, also a contributor to ill-fitting dentures in older women, have not been firmly established, though bacteria in dental plaque has typically been named the culprit.

“By studying one hundred postmenopausal women, we are seeking to identify a group at high risk for periodontal bone loss, show how they can be identified early and inexpensively, and find a treatment that will reduce the risk for this group,” explains Hildebolt.



The combined disciplines of dentistry and anthropology provide Charles Hildebolt, D.D.S., Ph.D., with a unique multifaceted approach to research.

As principal investigator for the project, Hildebolt hypothesizes that the beneficial effects of estrogen therapy for osteoporosis may also be applied to periodontal bone loss. The study will quantify bone loss of the postcranial skeleton and periodontal bone, while comparing the rate of bone loss between women receiving estrogen and placebo therapies.

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*By applying NASA's Landsat technology, researchers will analyze digitally-enhanced radiographic images of the periodontal bones.*

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*"...the health of the periodontal bone may be shown to be a sensitive and specific marker of bone mass changes."*

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In order to study periodontal disease, Hildebolt had to come up with a way to quantify the rate of bone loss. That's where coinvestigator Michael Vannier, M.D., professor of radiology and director of the Institute's Division of Radiology Research, has provided a significant contribution. A former National Aeronautics and Space Administration (NASA) engineer, Vannier brings to radiology, through computer and programming support, the application of digital imaging used in space exploration.

**B**y applying the digital imaging process used by NASA's Landsat technology to study the topographical surfaces of other planets, researchers at MIR will analyze digitally-enhanced radiographic images of the periodontal bone of women participating in the study. The scanner-based imaging system provides an enhanced view of vertical bitewing radiographs, similar to conventional dental X rays. These films, which are held in place in the patient's mouth by custom-made positioning devices, go through a special exposure, processing, and digitization procedure. The end result is a more focused contrast and edge enhancement of teeth and bone surfaces than is found in routine dental radiographs. After the images are enhanced, precise geometric measurements of the periodontal bone can be made.

The digitized image improves visualization of the cemento-enamel junction (where the tooth enamel ends, often below the gumline) and the alveolar crest (the crest of the ridge in which the teeth are imbedded). Between these two points researchers will make six measurements (three on each side of the tooth - mesial, distal and mid-tooth), to be automatically stored in the computer data system and compared to other sets of measurements taken of the same teeth each year over a three-year period. In preliminary studies, the measuring technique using the digitally-enhanced images proved to be of submillimeter reproducibility, with less than .25 millimeter diversion.



Above: Michael Vannier, M.D., often collaborates with NASA in identifying down-to-earth applications for the space agency's research.



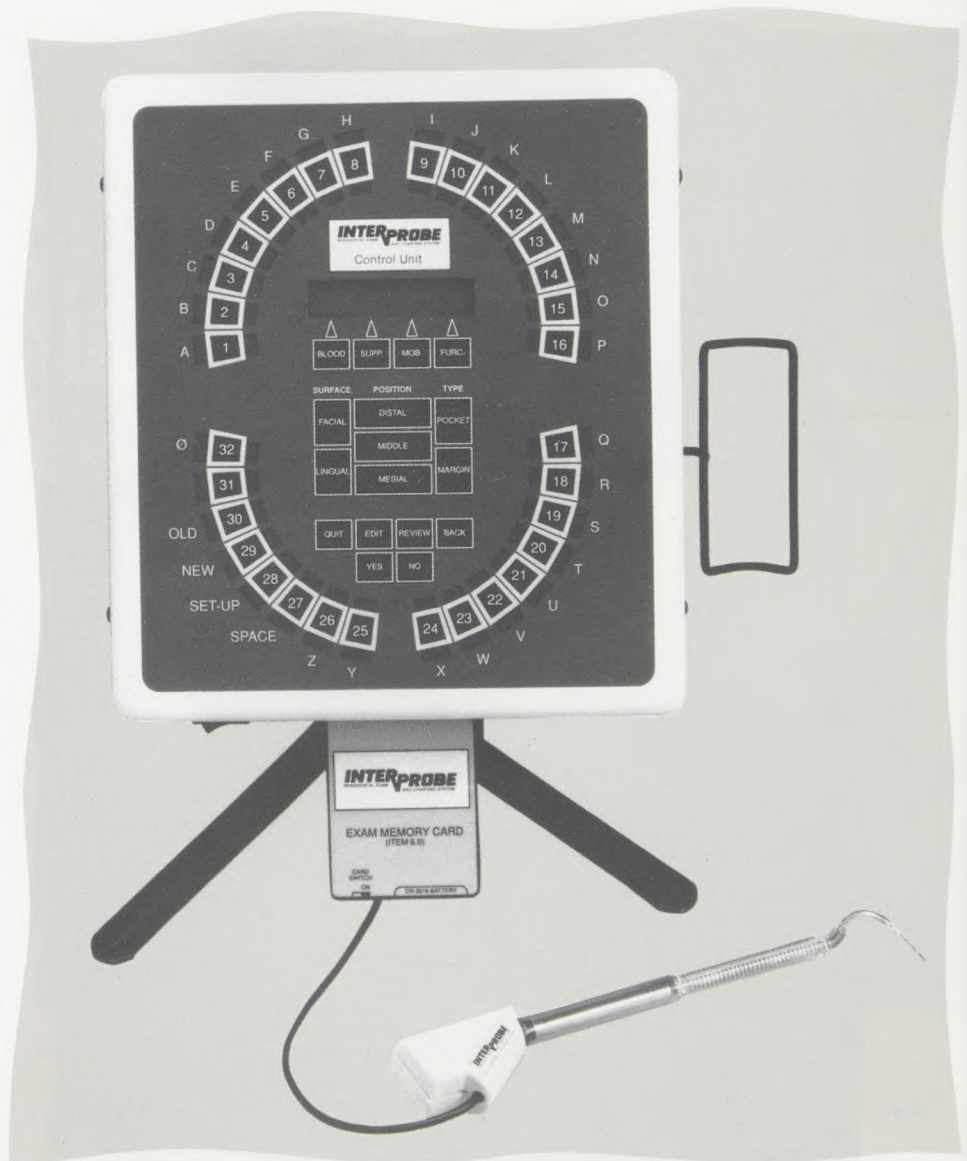
Left: Hildebolt and research team members Brent Rice, senior undergraduate student, and Naoko Yokoyama, data assistant.

"This kind of measurement technique is very time intensive," admits Hildebolt. "But it has a considerable advantage over traditional methodologies for measuring periodontal bone loss."

The accuracy in using this quantitative method is further augmented by taking measurements of both the facial (outer) and lingual (inner) crests of the alveolar ridge, eliminating any chance of under-measurement of bone loss by looking at only one surface.

In addition to the linear measurements to be analyzed, histograms from each radiograph will give researchers the opportunity to compare bone densities in the alveolar ridges. Using the specially designed computer software to select a region of interest (ROI) in a participant's radiographic image, a baseline of the plot of pixel frequencies or grey scales will be established for comparison of the three yearly radiographs. Comparing these histograms will allow researchers to detect the slightest change in bone density values.

Additional data will be provided through the use of INTERPROBE™, a pressure-sensitive electronic periodontal probe. Using this state-of-the-art computerized probe, a gingival-probing-depth measurement will be made at six locations per tooth. The distance from the margin of the gums (gingiva) to the depth of the probe penetration will be entered directly into the computer memory, with no manual entry required. The distance from the cemento-enamel junction to the depth of probe penetration also will be automatically entered.



This electronic probe manufactured by Bausch & Lomb Oral Care Division provides a computerized method for documenting periodontal disease.

*The beneficial effects of estrogen therapy for osteoporosis may also be applied to periodontal bone loss.*



The illustration depicts the progression of alveolar bone loss, (left to right) ranging from normal periodontal support to moderate bone loss to severe resorption.

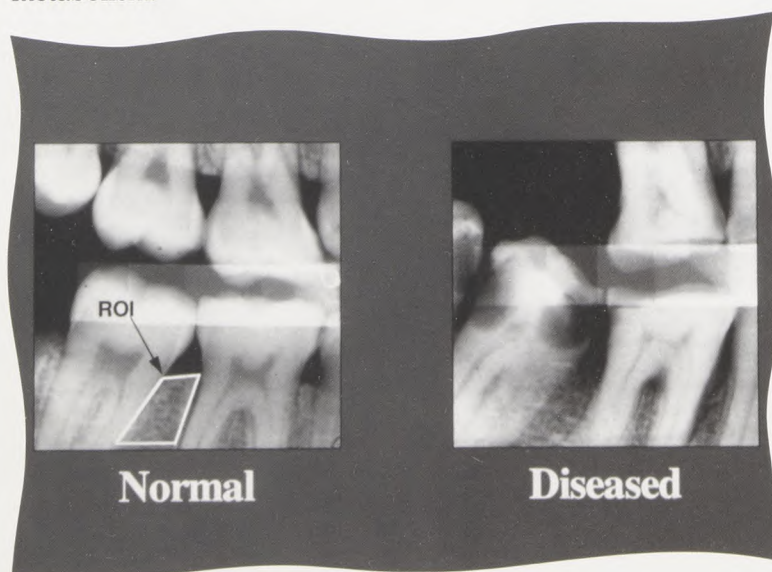
“If our hypothesis is correct, that alveolar bone densities are reduced by systemic processes in a specific group of women, it may be that alveolar bone loss caused by periodontal disease is exacerbated in these women,” Hildebolt suggests. “Even though a periodontal pocket does not necessarily indicate current disease activity, it is considered to be a characteristic of past periodontal disease. By comparing soft-tissue probing measurements with measurements of the alveolar bone, we may be able to establish if a specific group of postmenopausal women are at high risk of developing periodontal disease.”

To investigate how changes in periodontal bone mass relate to bone mass changes in other skeletal sites, changes in the height and density of the periodontal bone will be compared to changes in bone mineral content in the spine, forearm, and hip. A correlation matrix to assess these relationships will be computed for each yearly interval and for the overall data collected.

Patients for the research project will be recruited at the Washington University Medical Center and at the University of Cincinnati Medical Center. Criteria for inclusion in the study require that the women have at least 10 measurable teeth and have ceased menstruation for at least 24 months. They must also be in good health and taking no drug treatments (other than calcium) known to affect bone metabolism.

“Because of its unique association with the oral environment, the health of the periodontal bone may be shown to be a sensitive and specific marker of bone mass changes within an individual,” maintains Hildebolt. “Understanding the relationship between the bone mineral content of the postcranial skeleton and the periodontal bone in postmenopausal women will expand our knowledge of the menopausal influence on bone mass and may also provide an explanation for the nonperiodontal-disease-related alveolar bone loss in older females.” □

*Bridget McDonald is a free-lance writer, residing in the St. Louis-area.*



Plain film X rays show healthy alveolar bone (left) and bone loss (right).



In response to a call from the Society of Nuclear Medicine (SNM) for proposals on the use of unsealed sources for radiotherapy, MIR scientist Carolyn Anderson and a team of researchers received an SNM fellowship to compare copper-64 with copper-67.



# A JEWEL IN THE MAKING

It is said that every man, if he reaches a ripe old age, will have some stage of prostate cancer growing within him when he dies. That's because prostate cancer, which often causes no symptoms, can grow very slowly, confined to this gland for many years. If this cancer develops in a man in late life, death usually occurs from other causes, not the cancer.

But every year, growing numbers of men in their forties or fifties are being diagnosed with the disease. Unfortunately, when prostate cancer develops at this stage of life, it may turn lethal well before a man reaches old age. The cancer metastasizes to regions outside the prostate capsule before a middle-aged man is even aware he has it.

Within the last 10 years, diagnosing prostate cancer has become easier. Yet every year, nearly 40,000 men die from this disease; fatalities from prostate cancer are second only to lung cancer. One reason stems from the fact that conventional checks on the prostate's status — the digital rectal exam and a blood test known as the PSA (prostate-specific antigen) — are far from definitive.

If one of these tests suggests that something might be amiss, an ultrasound examination may be performed. Then, information from all these sources, considered as a whole, suggests whether a tumor is present. But many men shy away from having a digital rectal exam. What's more, the PSA test is not widely used. To add to the difficulty, results from a PSA are often imprecise; erroneous conclusions are drawn from about 30 percent of PSA tests.

Thus, the lethal statistics describing the fate of those who have prostate cancer are likely to persist for the foreseeable future. But at Mallinckrodt Institute of Radiology, there's a jewel in the making that may turn advanced prostate cancer into a less deadly disease.



# A JEWEL IN THE MAKING

This "jewel" is a tiny, metal-bearing protein. Once its gleam strikes the eye of a positron emission tomography (PET) scanner, which assesses biochemical processes and produces images of function rather than form, the protein should illuminate in unimaginable detail certain tumorous cells originating in the prostate. These cells that have spread to other regions of the body carry receptors for a hormone called somatostatin.

Using her background as an inorganic chemist and a radiochemist, Carolyn Anderson, Ph.D., and a team of scientists have synthesized what they hope is an exquisite sensor that signals, via a three-dimensional PET scanner, prostate cancer cells studded with somatostatin receptors. Once Anderson, an assistant professor in the Institute's Division of Radiation Sciences, and the other researchers find whether prostate cancer cells display receptors for somatostatin, they hope that oncologists will be able to exploit this vulnerability in diagnosing or treating prostate cancers with somatostatin-like compounds.

Somatostatin was once thought to be manufactured only in the brain, where it regulates the production of growth hormone. Now, it is known that many different types of cells throughout the body manufacture this tiny protein. What's more, many types of tumors can be treated with somatostatin — a field that's just beginning to be explored.

Since somatostatin's existence is cut short by the body's enzymes, the natural form of this protein cannot be used therapeutically. Sandoz Pharmaceuticals Corporation has manufactured a version of somatostatin, called octreotide (Sandostatin<sup>®</sup>), that resists biological degradation. Currently, the



Michael Welch, Ph.D., was one of the first researchers to apply modern organic chemistry to the preparation of radiopharmaceuticals used in medical imaging.

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*Tumorous cells in the prostate that have spread to other regions of the body carry receptors for a hormone called somatostatin.*

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FDA has licensed Sandostatin only for the treatment of symptoms of tumors arising in neuroendocrine tissue or pancreatic islets, says Joel Picus, M.D., a medical oncologist at Barnard Cancer Hospital. For prostate cancers that fail to respond to conventional treatments, Picus hopes to investigate whether Sandostatin is effective in pinpointing somatostatin receptors. If these receptors are present, what's the best way to spot them?

“The real technical problem,” says Michael Welch, Ph.D., director of the Division of Radiation Sciences, “has to do with the small number of receptors and the small quantities of octreotide they’ll bind.”

Imaging modalities like computed tomography (CT) and magnetic resonance imaging (MRI), which work well when visualizing milligram quantities of radiotracers, cannot detect substances like

*“It’s now thought that oncology research is the future of PET.”*



Barry Edwards, M.S.



Tammy Pajeau, M.S.

labeled octreotide, which are present in only one-millionth that concentration. Although the PET scanner is able to detect such small quantities, costs and chemistry have gotten in the way of starting this new line of research.

“Sandostatin is very expensive,” points out Anderson. “It costs about seven hundred dollars for ten milligrams. What we’re hoping to do is develop a new way of synthesizing octreotide so that we and other researchers who need to do solid-phase reactions can have an inexpensive, convenient source.”

## PROSTATE CANCER SYMPTOMS

Lying at the base of the penis, below the bladder and in front of the rectum, the prostate gland depends upon the male hormone testosterone to produce a fluid that is part of semen. The prostate surrounds the upper

portion of the urethra, the tube that empties urine from the bladder and carries semen through the penis.

The cause of prostate cancer is unknown, although some studies suggest that a low-fat diet may reduce the risk of developing prostate cancer. In its early stages, there are often no symptoms. When symptoms develop, they may include any of the following conditions:

- Blood in the urine
- Painful or burning urination
- Painful ejaculation
- Inability to urinate
- Difficulty in starting or stopping urination
- Frequent urination, especially at night
- Pain in lower back, pelvis, or upper thighs

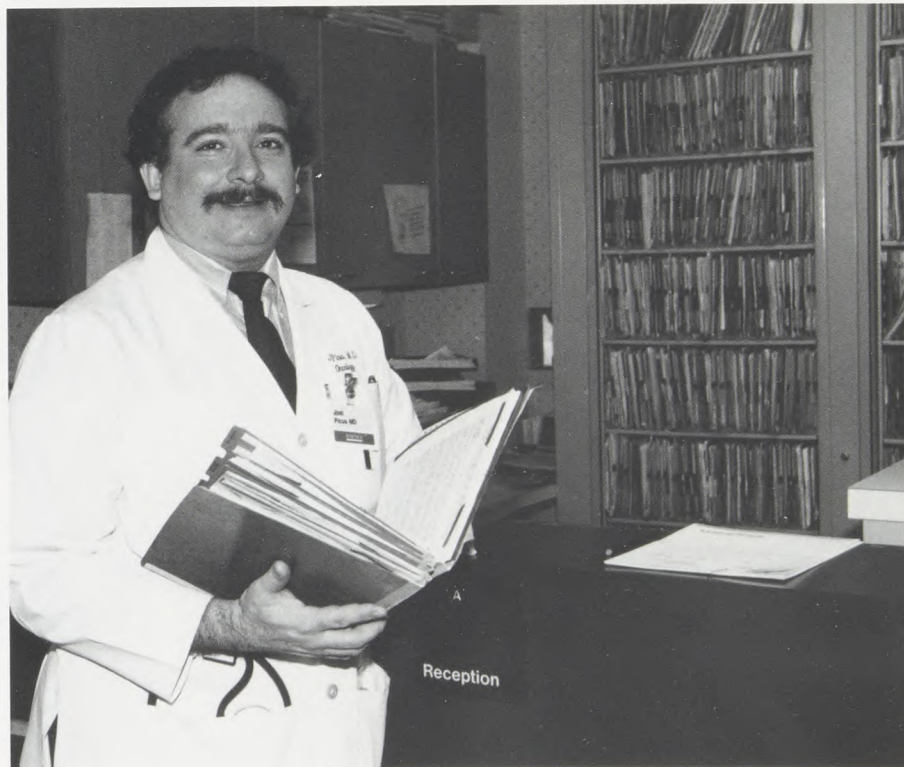
These symptoms do not always signal prostate cancer but should be checked by a physician.

# A JEWEL IN THE MAKING

Working with collaborators Gregg Fields and Cindy Fields at the University of Minnesota, Anderson and organic chemist Barry Edwards are developing a new and simpler version of octreotide. This synthesis is readily adaptable to preparing octreotide derivatives for PET imaging.

The Minnesota team sends a form of octreotide to the Mallinckrodt Institute researchers, who then take this unfinished "gem" through a series of steps. One of these steps involves attaching a positron-emitting metal, such as gallium-68 or copper-64, to octreotide. Tammy Pajeau, a senior research technician, then analyzes the radiolabeled compounds, determining their efficiency in binding to somatostatin receptors in various types of cells. If labeled octreotide binds to somatostatin receptors on prostate cancer cells, these sites will glow when viewed with either PET or single photon emission tomography (SPECT). Using a PET scanner that visualizes three dimensions, researchers can quantify the number of receptors.

"Ten years ago," says Welch, "no one used PET for oncology research. Now, nearly all the work being done on the current generation of PET scanners is oncology-related. It's now thought that oncology research is the future of PET."



Joel Picus, M.D., assistant professor of medicine, is director of the hematology lab, Division of Medical Oncology.

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*"This could be a home run, or we could strike out."*

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One of the beauties of using gallium-68 or copper-64, points out Welch, is that these isotopes need not be generated in an accelerator. For example, copper-64 comes from the University of Missouri's Research Reactor. Not using accelerator-generated isotopes brings down the overall costs.

Another advantage to using copper-64, says Anderson, is its rel-

atively long half-life (12 hours): "Researchers can image with copper-sixty-four up to twenty-four hours as compared to three or four hours with gallium-sixty-eight. This allows for better contrast between the tumor and the rest of the body."

“The other reason we’re interested in using copper-sixty-four is that it also has potential as a radiotherapeutic agent,” Anderson adds. “We’re doing some studies now with copper-sixty-four linked to monoclonal antibodies to study tumor shrinkage, but this approach could also be used with octreotide.”

As promising as this research is, there are still many unknowns, advises Picus: “This could be a home run, or we could strike out.”

No one knows whether some, or any, human prostate cancers display somatostatin receptors, of which there are more than one kind, or what kind of affinity they would have for octreotide. “Almost undoubtedly” there will be subtypes of these receptors, if there are any at all, on cancer cells, says Picus. “Our hope is that octreotide will be active on all subtypes.”

Octreotide’s usefulness in the treatment of prostatic cancer may be only as a staging tool, to discern information helpful to only 5 to 10 percent of patients. “But even if only a small percentage of patients are helped,” says Picus, “considering that that’s a group of about forty thousand every year, that’s quite a lot.” □

## IMAGING ILLUMINATES NEW WAYS TO TREAT CANCER

A few years ago, it was discovered that certain breast cancers grow more fiercely in the presence of estrogen if they have on their surface a receptor for the hormone. Estrogen that attaches to its receptor at a tumor cell surface kicks cell reproduction into high gear. If these estrogen receptors are missing, then something other than estrogen must be the impetus behind the tumor’s growth.

Through the use of radiolabeled estrogens, researchers, aided by the clinical work of Farrokh Dehdashti, M.D., assistant professor of radiology, are able to illuminate the hormone’s receptors. Once tumors that have estrogen receptors are differentiated from those that don’t, an oncologist can choose the most effective course of therapy. Breast cancer cells bearing estrogen receptors on the surface may be crippled by administering therapeutic substances like tamoxifen.

Tamoxifen mimics estrogen’s structure and latches onto the receptor. Once there, tamoxifen prevents natural estrogens from attaching. However, the bound tamoxifen — unlike its chemical cousin estrogen — does not jump-start the cell’s cycle of growth. Thus, the tumor’s growth slows or stops.

Using this radiolabeling scheme to pinpoint breast cancer cells carrying estrogen receptors has engaged Michael Welch, Ph.D., director of Mallinckrodt Institute’s Division of Radiation Sciences, for many years. Furthermore, in collaboration with a group at University of Illinois, led by John Katzenellenbogen, Ph.D., Welch reports that another application of this approach appears to be successful.

Prostatic cancers in animals can be differentiated according to the presence or absence of androgen receptors, which recognize testosterone. Now, says Welch, human trials are about to begin, to see if human prostatic tumors can be differentiated based on the presence or absence of androgen receptors. If so, then an oncologist can decide whether use of an anti-androgen will be appropriate therapy.

All of this work has been done using compounds labelled with non-metals, such as fluorine. But to pinpoint somatostatin receptors on breast cancer cells, a different approach was needed. New chemical syntheses and methods of protecting functional groups, as well as affixing metal isotopes, had to be devised. Carolyn Anderson, Ph.D., and a team of researchers, developed a way to illuminate these receptors in the PET scanner. “It wasn’t simple,” says Anderson. “We thought we’d be working with patients a year ago. Now, we hope to begin clinical trials in 1994.”

*Suzanne Hagan is a free-lance writer and editor, specializing in science and medicine.*

# IMAGING

UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE

**P**lans for the Institute's new imaging research center were announced in this year's spring issue of *Focal Spot*. Scheduled for completion in mid-1994, the facility will be one of the best equipped centers worldwide where research will focus on the development and application of advanced imaging systems.

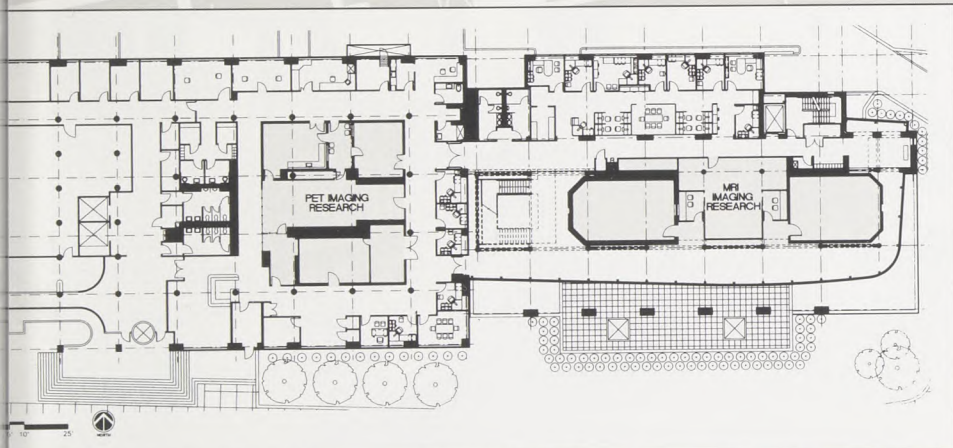
*The following is an update of building construction, equipment installation, and faculty and staff additions.*



**O**n May 25, the world's first prototype of a Tandem Cascade Accelerator (TCA) was rolled off a delivery truck and installed in the basement of MIR's East Building. The TCA offers a less complex alternative to the conventional cyclotron-produced radiopharmaceuticals used in PET studies. The collaboration of Michael J. Welch, Ph.D., director of the Institute's Division of Radiation Sciences, and scientists at an independent research and development company (Science Research Laboratory) transferred military-related technology developed under President Reagan's Star Wars program into a new cost-effective accelerator.

Since the accelerator's installation, MIR researchers have been checking the purity of TCA-produced isotopes. The TCA will support the imaging center's extensive PET research in addition to the clinical and research PET scanners at the Washington University Medical Center. In July, a successful test run pumped water and gases through a "rabbit line" to a PET scanner in the medical center.

# CENTER UPDATE



In August, a group of MR physicists, led by E. Mark Haacke, Ph.D., professor of radiology, moved into temporary offices on the third floor of the East Building, awaiting completion of the imaging center. These scientists have a broad range of research interests, including brain functional imaging, high resolution MR angiography, MR cardiopulmonary imaging, breast MR, fast imaging, general MR physics, and image reconstruction methods.

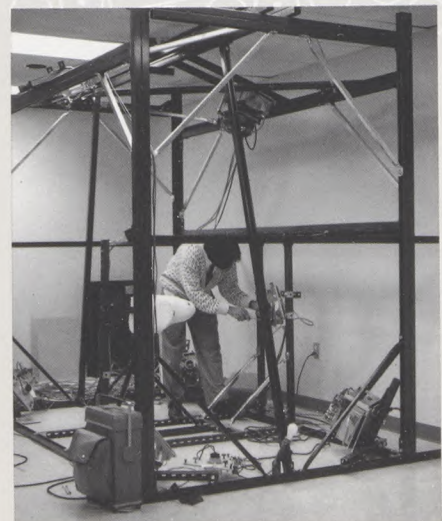
"The idea of working as a team at the imaging center matches my own philosophy of research," says Haacke, who was formerly at Case Western Reserve University in Cleveland. According to Haacke, he was drawn to the imaging center because of the top quality 3-D computer support available, the accessibility of contrast agent expertise, and the

Institute's clinical reputation. He predicts that in five years significant contributions will be made in brain functional imaging and particularly in MR cardiovascular imaging. Haacke believes these technologies will become extremely valuable tools in clinical application and in clinical research.

Other MR physicists are Debiao Li, Ph.D., assistant professor of radiology; Weili Lin, Ph.D., assistant professor of radiology; Dmitriy Yablonski, Ph.D., research associate; Shantanu Kaushikkar, M.S., programmer; James Goldfarb, M.S., research assistant; Ramesh Venkatesan, M.S., research assistant; and Song Lai, M.S., research assistant.

In early September, members of the Institute's Division of Radiology Research moved into offices on the third floor of the East Building, which were previously occupied by Washington University School of Medicine's Program of Physical Therapy. Under the leadership of Michael W. Vannier, M.D., professor of radiology, the Division serves as a focus and resource for multiple studies in technology assessment, clinical protocols, electronic imaging, and radiologic procedures. The establishment of the Division in 1990 indicated a major commitment to an expansion of clinical research projects at the Institute.

Below, Gulab Bhatia, M.S., instructor in radiology, checks on the housing construction for a 3-D body scanner that will improve procedures for fitting prostheses.



# IMAGING CENTER

UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE UPDATE

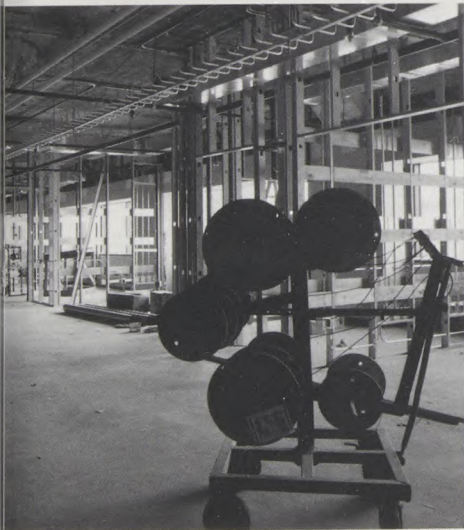
Looking like a monstrous steel stork carrying an overgrown bundle, a construction crane hoisted the 22,000-pound Siemens 1.5 Active Shielded Magnetom almost 60 feet into the air before depositing it onto a specially built ramp that led into the MIR's East Building. A portion of the East Building's wall on the first-floor level had been removed to accommodate the magnet's bulk, and workers guided the magnet through this opening and down the hall into the MR research area. The Institute received the magnet in mid-October as part of a new MR scanning system (Siemen's first and only one produced to date) that offers higher internal processing speeds, faster data acquisition, and larger memory banks than any other MR scanner now in use.



Offices and research areas are being constructed on the second floor of the East Building to house the neurological PET research faculty and staff, headed by Marcus E. Raichle, M.D., professor of radiology and neurology. Scheduled to move into their new facilities in early 1994, these PET scientists have focused their work on normal brain functions as well as major neurologic and psychiatric disorders. Of special interest is the functional mapping of the brain, especially the areas involved in sensory and language information processing.



The future home of Mallinckrodt Institute's imaging research center, at the corner of Scott and Taylor avenues, was once covered with asphalt and carried the sole distinction of "offering the closest parking to the East Building." Within the past four or five months, the site was excavated, foundations were laid, and steel support girders were set in place — all in preparation for the construction of a freestanding structure that will include four floors (counting the basement), cover 50,000 square feet, and house more than 100 faculty and staff members.





## THE DIRECTOR'S OFFICE REPORT

### NEW STAFF

**James W. Debnam, M.D.**, assistant professor of clinical radiology, Division of Diagnostic Radiology

**Menelaos N. Karamichalis, M.S.**, research assistant in radiology, Division of Diagnostic Radiology

**Peter E. Shile, M.D.**, assistant professor of radiology, Division of Diagnostic Radiology

**Robert A. Whitman, M.S.**, research associate in radiology, Division of Diagnostic Radiology

**Nathan C. Nelson, M.S.**, instructor in radiology, Division of Nuclear Medicine

**Rupak Kumar Das, Ph.D.**, research associate, Division of Radiation Oncology

**Weihua He, M.S.**, research assistant, Division of Radiation Oncology

**Assen S. Kirov, Ph.D.**, research associate, Division of Radiation Oncology

**David J. Scherer, M.S.**, instructor in radiology, Division of Radiology Research

**Lei Zheng, Ph.D.**, research associate, Division of Radiation Sciences

### PROMOTIONS

**Timothy J. McCarthy, Ph.D.**, was promoted to research instructor in radiology, Division of Radiation Sciences.

### OFF STAFF

**Clinton M. Anderson, M.D.**, instructor in radiology, completed a four-year residency and a one-year fellowship in magnetic resonance imaging, and has entered private practice with Colorado Imaging Association in Denver.

**Carlos F. Aquino-Aponte, M.D.**, instructor in radiology, completed a one-year fellowship in magnetic resonance imaging and has accepted a position with the Veterans Administration Hospital in San Juan, Puerto Rico.

**Gregg A. Baran, M.D.**, instructor in radiology, completed a two-year fellowship in neuroradiology and has entered private practice in St. Petersburg, Florida.

**Meredith W. Bell, M.D.**, instructor in radiology, completed a one-year fellowship in abdominal radiology and has accepted a position in the Department of Radiology, Duke University Medical Center.

**Richard L. Butler, M.D.**, completed one year of training in nuclear medicine and has entered private practice in Godfrey, Illinois.

**Leeanna Dick, M.D.**, instructor in radiology, completed a one-year fellowship in vascular and interventional radiology and has entered private practice with Durham Radiology Associates, Durham, North Carolina.

**Gerard M. Eagar, M.D.**, completed one year of training in diagnostic radiology and has accepted a position in the Department of Radiology, Taranaki Base Hospital, New Plymouth, New Zealand.

**Humberto M. Fagundes, M.D.**, instructor in radiology and chief resident, Division of Radiation Oncology, 1992-1993, completed a three-year residency and a one-year fellowship in radiation oncology. He has accepted the position of head of the GI/GU radiation section at Loyola University.

**Jeffrey E. Fischbein, M.D.**, instructor in radiology, completed a one-year fellowship in neuroradiology and has accepted a position with Good Samaritan Hospital, West Palm Beach, Florida.

**Robin Frank-Gerszberg, M.D.**, instructor in radiology, completed a one-year fellowship in pediatric radiology and has entered private practice with the Radiologic Group of North Jersey, Wayne, New Jersey.

**M. Gena Frederick, M.D.**, completed four years of training in diagnostic radiology and has received an abdominal fellowship at Bowman Gray Medical Center, Winston-Salem.

**Neal A. Frenkel, M.D.**, completed a four-year residency in diagnostic radiology and has received a cross-sectional imaging/body imaging fellowship at Jackson Memorial Hospital, Miami.

**Anastasios Georgiou, M.D.**, instructor in radiology, completed a three-year residency and a one-year fellowship in radiation oncology, and has entered private practice with Jackson/Madison General Hospital, Jackson, Tennessee.

**Patrick O. Gordon, M.D.**, instructor in radiology, completed a one-year fellowship in vascular and interventional radiology and has entered private practice in Jacksonville, Florida.

**Rosalie J. Hagge, M.D.**, completed one year of training in nuclear medicine and has received an appointment as resident physician in the Diagnostic Radiology Scholar's Program at Duke University Medical Center.

**Dale P. Harris, M.D.**, completed four years of training in diagnostic radiology and has received a body imaging fellowship at Stanford University.

**Paul S. Hsieh, M.D.**, completed four years of training in diagnostic radiology and has accepted a position in the Department of Radiology, Cedars-Sinai Medical Center, Los Angeles.

**Edith H. Kang, M.D.**, instructor in radiology and chief resident, Division of Diagnostic Radiology, 1991-1992, completed four years of training in diagnostic radiology and a one-year fellowship in magnetic resonance imaging. She has entered private practice with the Ramsey Clinic, St. Paul, Minnesota.

**Karl W. King, M.D.**, instructor in radiology, completed a three-year residency and a one-year fellowship in radiation oncology and has entered private practice with Radiology Inc., South Bend, Indiana.

**Mark D. Mayhle, M.D.**, instructor in radiology, completed four years of training in diagnostic radiology and a one-year fellowship in vascular and interventional radiology. He has entered private practice with Rock Hill Radiologists, Raytown, Missouri.

**Chun Ma, Ph.D.**, research associate, Division of Radiation Sciences

**Cynthia F. Morrison, M.D.**, instructor in radiology, Division of Diagnostic Radiology

**William A. Murphy, Jr., M.D.**, professor of radiology and cochief of the musculoskeletal section, has accepted the position of chairman of the Division of Diagnostic Imaging, M.D. Anderson Cancer Center, Houston.

**Kurt L. Openshaw, M.D.**, instructor in radiology, completed a one-year fellowship in vascular and interventional radiology and has entered private practice with St. Joseph Hospital, Orange, California.

**Nhan P. Truong, M.D.**, instructor in radiology, completed a one-year fellowship in musculoskeletal radiology and has accepted a position at St. Francis Hospital, Tulsa.

**John F. Walsh, M.D.**, completed a one-year fellowship in nuclear medicine and has returned to active duty with the United States Air Force, Wilford Hall, San Antonio.

**Jonathan White, M.D.**, completed six months of training in nuclear medicine and has entered private practice with the Maine Medical Center, Portland.

**Mark S. Zobel, M.D.**, completed four years of training in diagnostic radiology and has accepted a position at Seattle Children's Hospital, Seattle.

### FIRST-YEAR POSTGRADUATES

**Martin M. Anbari, M.D.**, received his Bachelor of Arts degree in natural science, medical degree, and law degree from the University of Pennsylvania.

**H. Scott Beasley, M.D.**, received his Bachelor of Science degree in optometry and his medical degree from Indiana University. He is a member of Alpha Omega Alpha.

**John A. Butman, M.D.**, received his Bachelor of Science degree in applied mathematics and biology from the California Institute of Technology and his medical degree from Washington University.

**Dayne D. Hassell, III, M.D.**, received his Bachelor of Arts degree in history and French from Tulane University and his medical degree from the University of Chicago - Pritzker.

**John J. Healey, II, M.D.**, received his Bachelor of Arts degree in biology from Emory University and his medical degree from the University of Texas Southwestern Medical School, Dallas. He is a member of Alpha Omega Alpha.

**Donald V. Heck, M.D.**, received his Bachelor of Science degree in mathematics from Wake Forest University and his medical degree from Duke University. He is a member of Alpha Omega Alpha.

**David A. Hillier, M.D.**, received his Bachelor of Arts degree in biology and Bachelor of Science degree in electrical engineering from Swarthmore College; Doctorate of Science in electrical engineering from Washington University, Sever Institute of Technology; and medical degree from Washington University School of Medicine. He has completed an internship in internal medicine at Barnes Hospital, St. Louis.

**William P. James, M.D.**, received his Bachelor of Arts degree in biology from Washington University and his medical degree from University of Missouri School of Medicine, Columbia.

**Debra M. Lau, M.D.**, received her Bachelor of Arts degree in biology from Barnard College at Columbia University and her medical degree from Albert Einstein College of Medicine, Yeshiva University. She is a member of Alpha Omega Alpha.

**Robert C. McKinstry, III, Ph.D., M.D.**, received his Bachelor of Science degree in electrical engineering from Boston University, masters degree in nuclear engineering and doctorate degree in radiological sciences from Massachusetts Institute of Technology, and medical degree from Harvard Medical School.

**Felix Song, M.D.**, received his Bachelor of Science degree in chemical engineering from the University of Illinois and his medical degree from Washington University.

**John E. Sunderland, M.D.**, received his Bachelor of Science degree in medical dietetics from The Ohio State University College of Medicine School of Allied Medical Professions, masters degree in nutritional biochemistry from Harvard University, and medical degree from The Ohio State University College of Medicine. He is a member of Alpha Omega Alpha.

**Scott A. Werden, M.D.**, received his bachelors degree in biologic sciences and his medical degree from the State University of New York at Stony Brook. He completed an internship in internal medicine at Duke University Medical Center and a residency in internal medicine at Boston City Hospital. Werden is a member of Alpha Omega Alpha.

### NEW FELLOWS

**Edward E. C. Angtuaco, M.D.**, instructor in radiology, is a fellow in neuroradiology. He received his Bachelor of Science degree in biology from Ateneo de Manila University, Philippines, and his medical degree from University of the East Ramon Magsaysay Memorial Medical Center, Philippines. Angtuaco completed an internship and a diagnostic radiology residency at the University of Arkansas for Medical Sciences, Little Rock. He has received American Board of Radiology certification.

## THE DIRECTOR'S OFFICE REPORT

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**Scott M. Baker, M.D.**, instructor in radiology and chief resident, Division of Diagnostic Radiology, 1992-1993, is a fellow in abdominal imaging. He completed four years of training in radiology at Mallinckrodt Institute of Radiology. Baker is a member of Alpha Omega Alpha.

**Clifford D. Barker, M.D.**, instructor in radiology, is a fellow in magnetic resonance imaging. He received his Bachelor of Science degree in mechanical engineering from Cornell University and his medical degree from New York Medical College. Barker completed an internship in internal medicine at Waterbury Hospital, Connecticut, and was chief resident, diagnostic radiology, 1991-1992, at New York University Medical Center. He is a member of Alpha Omega Alpha.

**Benjamin J. Bartnicke, M.D.**, instructor in radiology, is a fellow in abdominal imaging. He completed four years of training in radiology at Mallinckrodt Institute of Radiology.

**Harold F. Bennett, M.D., Ph.D.**, instructor in radiology, is a fellow in abdominal imaging. He received his Bachelor of Science degree in nuclear engineering from the University of Illinois, masters degree in nuclear engineering from the University of Florida, doctorate degree in nuclear engineering from the University of Illinois, and medical degree from the University of Illi-

nois College of Medicine. Bennett completed an internship at Methodist Hospital, Indianapolis, and a residency in diagnostic radiology at the University of California, San Francisco. He has received American Board of Radiology certification.

**Marc A. Borge, M.D.**, instructor in radiology, is a fellow in vascular and interventional radiology. He received his Bachelor of Arts degree in biology from Carleton College and his medical degree from the University of Chicago-Pritzker. Borge completed a residency in diagnostic radiology at the University of North Carolina Hospitals, Chapel Hill.

**Kun S. Chao, M.D.**, instructor in radiology, is a fellow in radiation oncology. He completed two years of residency in radiation oncology at Mallinckrodt Institute of Radiology.

**John J. Crowley, M.D.**, instructor in radiology, is a fellow in pediatric radiology. He received his undergraduate degree from Belvedere College, Dublin, Ireland, and his medical degree from Trinity College, Dublin. Crowley completed a residency in diagnostic radiology at Allegheny General Hospital, Pittsburgh.

**Patrick D. Datoc, M.D.**, instructor in radiology, is a fellow in magnetic resonance imaging. He received his Bachelor of Science degree in biology from Yale University and his medical degree from the Medical College of Virginia. Datoc com-

pleted a residency in radiology at the University of North Carolina Hospitals, Chapel Hill. He is a member of Alpha Omega Alpha and has received American Board of Radiology certification.

**Lane A. Deyoe, M.D.**, instructor in radiology, is a fellow in vascular and interventional radiology. He completed a one-year fellowship in abdominal imaging at Mallinckrodt Institute of Radiology.

**David S. Gierada, M.D.**, instructor in radiology, is a fellow in chest radiology. He received his Bachelor of Science degree in cell and molecular biology from the University of Michigan, Ann Arbor, and his medical degree from Wayne State University. Gierada completed an internship in internal medicine/pediatrics at Strong Memorial Hospital, Rochester, and a residency in diagnostic radiology at Milwaukee County Hospital. He is a member of Alpha Omega Alpha and has received American Board of Radiology certification.

**Carolyn A. Haerr, M.D.**, instructor in radiology, is a fellow in musculoskeletal radiology. She received her Bachelor of Science degree in Spanish from Creighton University and her medical degree from the University of Nebraska Medical Center. Haerr completed an internship and a residency in pediatrics at the University of Colorado Health Sciences Center, Denver, and a residency in radiology at Denver Presbyterian Hospital, Denver. She has received American Board of Radiology certification.

**Gregory A. Hatfield, M.D.**, instructor in radiology, is a fellow in neuroradiology. He received his B.E.E. degree in signal processing and biomedical engineering from the University of Minnesota, Institute of Technology; M.S. degree in engineering from the University of California, Los Angeles; and medical degree from the University of Minnesota Medical School, Minneapolis. He completed an internship at St. Mary's Hospital, San Francisco, and a residency in diagnostic radiology at the University of Michigan, Ann Arbor. Hatfield has received American Board of Radiology certification.

**Maurice L. King, M.D.**, instructor in radiology, is a fellow in radiation oncology. He completed two years of residency in radiation oncology at Mallinckrodt Institute of Radiology.

**Charles T. McConnell, M.D.**, instructor in radiology, is a fellow in neuroradiology. He received his Bachelor of Arts degree in chemistry and zoology from Miami University, Oxford, and his medical degree from Ohio State University, Columbus. He completed an internship in internal medicine and a residency in radiology at The Ohio State University Hospitals. McConnell has received American Board of Radiology certification.

**Timothy R. O'Leary, M.D.**, instructor in radiology, is a fellow in radiation oncology. He completed a three-year residency in radiation oncology at Mallinckrodt Institute of Radiology.

**Allen B. Oser, M.D.**, instructor in radiology and cochief resident, Division of Diagnostic Radiology, 1992-1993, is a fellow in neuroradiology. He completed a four-year residency at Mallinckrodt Institute of Radiology.

**James V. Piephoff, III, M.D.**, instructor in radiology and chief resident, Division of Radiation Oncology, 1993-1994, is a fellow in radiation oncology. He completed a three-year residency at Mallinckrodt Institute of Radiology.

**Gregory R. Saboeiro, M.D.**, instructor in radiology, is a fellow in vascular and interventional radiology. He received his Bachelor of Science degree in biology from Washington University and his medical degree from St. Louis University School of Medicine. Saboeiro completed a residency in diagnostic radiology at St. Louis University Medical Center. He is a member of Alpha Omega Alpha and has received American Board of Radiology certification.

**Maria E. Schmidt, M.D.**, instructor in radiology, is a fellow in breast imaging. She completed three years of training at Mallinckrodt Institute of Radiology.

**Joseph A. Schoenberger, M.D.**, instructor in radiology, is a fellow in vascular and interventional radiology. He received his Bachelor of Arts degree in chemistry and his medical degree from St. Louis University. Schoenberger completed a residency in diagnostic radiology at the Cleveland Clinic and has received American Board of Radiology certification.

**Kevin L. Shady, M.D.**, instructor in radiology, is a fellow in magnetic resonance imaging. He completed four years of training in diagnostic radiology at The Jewish Hospital of St. Louis.

**Richard M. Slone, M.D.**, instructor in radiology, is a fellow in chest radiology. He received his Bachelor of Science degree in physics from Stetson University, Deland, Florida, and his medical degree from the University of Florida, Gainesville. Slone completed a residency in radiology at Shands Hospital, University of Florida, and has received American Board of Radiology certification.

## DIAGNOSTIC RADIOLOGY RESIDENTS

**Steven M. Roth, M.D.**, received his undergraduate degree from the University of Pittsburgh School of Pharmacy and his medical degree from Temple University. He completed an internship in orthopedic surgery at the Hospital of University of Pennsylvania. Roth is a member of Alpha Omega Alpha.

**Thomas E. Vaughan, M.D.**, received his undergraduate and medical degrees from Washington University. He completed an internship in internal medicine at Portsmouth Naval Hospital. Vaughan is a member of Alpha Omega Alpha.

**Steven S. Winn, M.D.**, received his undergraduate degree from McGill University and his medical degree from Albany Medical College of Union University. He completed an internship in radiology at The Albany Medical Center. Winn is a member of Alpha Omega Alpha.

## NUCLEAR MEDICINE RESIDENTS

**Stephen J. Kennedy, M.D.**, received his Bachelor of Science degree in electrical engineering and his medical degree from Ohio State University. He was cochief resident, 1991-1992, diagnostic radiology, at Shands Hospital, University of Florida.

**James D. Matthews, M.D.**, received his Bachelor of Science degree in biology and music from the College of William and Mary and his medical degree from the Medical College of Virginia. He completed four years of training in diagnostic radiology at Mallinckrodt Institute. Matthews is a member of Alpha Omega Alpha.

**Thomas H. Vreeland, M.D.**, received his Bachelor of Science degree in biochemistry from Louisiana State University, Bachelor of Science degree in pharmacy from

Northeast Louisiana University, and medical degree from Louisiana State University Medical Center. He completed an internship in internal medicine at Louisiana State University Medical Center and a residency in radiology at the Medical Center of Virginia. Vreeland is a member of Alpha Omega Alpha.

## RADIATION ONCOLOGY RESIDENTS

**Bradley A. Kramer, M.D.**, received his Bachelor of Science degree in chemistry from Marquette University, Milwaukee, and his medical degree from The Medical College of Wisconsin.

**Alfred Tinger, M.D.**, received his undergraduate degree in physics from State University of New York at Binghamton and his medical degree from State University of New York - Health Center at Brooklyn. He is a member of Alpha Omega Alpha.

## VISITING PROFESSORS & INVITED LECTURERS

**Kyongtae Tyler Bae, M.D.**, second-year resident, spoke on "Automatic Detection of Pulmonary Nodules in CT Images" at the National Institutes of Health Research Festival, Bethesda, September 20-24.

**James A. Brink, M.D.**, assistant professor of radiology, spoke on "Intravenous Contrast Administration for Spiral Computed Body Tomography" at the William Beaumont Army Medical Center, El Paso, Texas, September 22.

**Carmen S. Dence, M.S.**, research instructor in radiology, presented "The Development of Positron Emitting Radiopharmaceuticals," Shanghai Medical University, China; "The Recent Developments in Low Energy Accelerators," Chinese Academy of Sciences, Nuclear Research Center, Shanghai; and "PET Research at Washington University," Beijing Normal University, China, October 30 - November 14.

**Bahman Emami, M.D.**, professor of radiology and associate director for research - Radiation Oncology Center, presented "3D Conformal Radiotherapy for Bronchogenic Carcinoma: A Review of State-of-the-Art" at the IASLC Workshop, Bruges, Belgium, August 29 - September 2.

**Louis A. Gilula, M.D.**, professor of radiology and director of the musculoskeletal section, presented refresher courses on "Ankle Tenosynovitis - Tenography and MRI" and "Dissociative

Patterns of the Wrist" at the 20th Annual International Skeletal Society Meeting, Toronto, August 15 - 20. He organized and directed the International Wrist Investigators' Workshop, September 28, Kansas City, Missouri. Gilula also displayed an exhibit on "Tailored Wrist Instability Series" (coauthored with **Nhan Truong, M.D.**, St. Francis Hospital, Tulsa; **Frederick Mann, M.D.**, University of Washington Medical Center, Seattle; and **Si-Won Kang, M.D.**, visiting physician, Taiwan) at the American Society for Surgery of the Hand, Kansas City, Missouri, September 29 - October 2.

**Harvey S. Glazer, M.D.**, associate professor of radiology, spoke on "CT of the Mediastinum - Differential Diagnosis," "Pitfalls in Radiologic Evaluation of Bronchogenic Carcinoma," and "CT of the Bronchi" at Chest Imaging - 1993, Harvard Medical School, Boston, October 18 - 21.

**Jay P. Heiken, M.D.**, professor of radiology and codirector of computed body tomography, lectured on "Spiral CT: Overview and Technical Considerations," "Spiral CT: Applications in the Abdomen," "Hepatic Masses: Detection and Characterization with CT and MRI," and "CT of the Peritoneal Spaces: Anatomy and Fluid Collections" at Summer Imaging and Interventional Techniques XI, sponsored by Emory University School of Medicine, Amelia Island, Florida, August 2 - 6. He also spoke

on "MR of the Kidneys and Adrenals," "MR Evaluation of Gynecologic Neoplasms," and "MR of the Liver: Lesion Detection and Characterization" at Magnetic Resonance Imaging 1993: Back to the Future, sponsored by the University of Cincinnati Department of Radiology, Cincinnati, October 13 - 16.

**Benjamin C. P. Lee, M.D.**, associate professor, as visiting professor, spoke on "New Techniques of MR Imaging" at the Neurological Institute, Lanzhou Medical Center, Gansu, China, September 13 - 16.

**Timothy J. McCarthy, Ph.D.**, research instructor in radiology, presented "Recent Developments in Radiopharmaceutical Production at Washington University" to the Faculty Pharmaceutical Services, Kyushu University, Fukuoka, Japan, October 18.

**Bruce L. McClellan, M.D.**, professor of radiology and chief of abdominal imaging, as chairman, organized "Health Care System Reform: Opportunities and Exigencies," the Summit Meeting, Aspen, August 6 - 8. He spoke on "Diagnostic Imaging Evaluation of Benign Prostatic Hypertrophy," "Imaging of Acute Renal Infections," "Reactions to Iodinated Contrast Media," "The Retroperitoneum," "Imaging of Renal and Adrenal Carcinoma," and "Laparoscopic Urologic Surgery: What Do Radiologists Need to Know?" at Radiology in Biarritz, France, September 26 - October 1.

**Ali Soleimani-Meigooni, Ph.D.**, assistant professor in radiology, Division of Radiation Oncology, as invited lecturer, spoke on "Quality Assurance and Clinical Implementation of Pulsed Dose

Rate Remote Afterloading System," Missouri Valley Chapter of the American Association of Physicists in Medicine Society, October 22 - 23.

**Stephen M. Moerlein, Ph.D.**, associate professor of radiology and biochemistry, as invited lecturer, presented "Development of Radioligands for PET Study of Brain Receptors" at the Technical University of Munich, Germany, July 29. As invited lecturer, he spoke on "Pharmacy Practice and PET" at the 206th National Meeting of the American Chemical Society, Chicago, August 22 - 27. Moerlein displayed a poster exhibit, "Comparison of [F-18] Benperidol and N-Methyl-[F-18] Benperidol as D-2 Receptor-Binding PET Ligands" (coauthored with **Joel S. Perlmutter, M.D.**, associate professor of neurology and radiology; **David Parkinson, Ph.D.**, WUMS assistant professor of cell biology and physiology; and **Michael J. Welch, Ph.D.**, professor of radiology and director of the Division of Radiation Sciences) at the 23rd Annual Meeting of the Society for Neuroscience, Washington, D.C., November 7 - 12.

**Eduardo G. Moros, Ph.D.**, assistant professor of radiology and chief of the hyperthermia physics service, as invited lecturer, presented "The Simultaneous Delivery of External Photon/Electron Beam Radiation and Superficial Microwave/Ultrasound Hyperthermia" to the Radiation Oncology Department, University of California, San Francisco, September 14.

**James A. Purdy, Ph.D.**, professor of radiology and associate director of the Radiation Oncology Center, presented "Volume and Dose Specifications: A Prerequisite for QA" at the 1993 American College of Radiology Symposium, "Quality Assurance of Radiation Therapy Treatment Planning Systems," Washington D.C., August 13.

**Joseph L. Roti Roti, Ph.D.**, professor of radiology, associate director of the Radiation Oncology Center, and chief of the cancer biology section, spoke on "DNA Supercoiling, The Nuclear Matrix and the Response of Mammalian Cells to Ionizing Radiation" at the Annual Meeting of the Japan Radiation Research Society, Hiroshima, October 28. He presented "Heat Modified Nuclear Proteins Associated with the Nuclear Matrix" at the Aichi Cancer Center Research Institute, Nagoya, Japan, November 1. Roti Roti lectured on "Role of the Nuclear Matrix in DNA Organization and Radiosensitivity" to the Department of Radiation Oncology Faculty of Medicine, University of Tokyo, November 2. He also spoke on "Involvement of Topoisomerase II in Radiation Induced G<sub>2</sub> Delay" at the Department of Radiation Research, Tokyo Metropolitan Institute of Medical Science, Tokyo, November 4.

**Henry D. Royal, M.D.**, professor of radiology and associate director of the Division of Nuclear Medicine, presented "Chernobyl: Perceptions and Realities," "Effects of Low Level Radiation: Scientific and Public Views," and "Risk Communication" at the Bethesda Naval Medical Center, Maryland, October 18. As visiting professor, he spoke on "The International Chernobyl Project" at the Joint Program in Nuclear Medicine, Harvard Medical School, Boston, October 21. Royal presented "Health Care Reform: Scientific Challenges" and "Chernobyl: Perceptions and Realities" at the 26th Annual Meeting of the New England Chapter, Society of Nuclear Medicine, Newport, Rhode Island, October 22 - 24.

**Stuart S. Sagel, M.D.**, professor of radiology, chief of chest radiology, and cochief of computed body tomography, spoke on "CT of the Pericardium," "High Resolution CT of the Pulmonary Parenchyma," and "CT of the Pleura" at the Third Summer Practicum of the Society of Computed Body Tomography and Magnetic Resonance Meeting, Keystone, Colorado, August 15 - 19. As visiting professor, he presented "Spiral CT in the Thorax" and "CT of Asbestos-related Thoracic Disease" at the University of Chicago, September 14. Also as visiting professor, Sagel presented "CT of Vascular Mediastinal Lesions;" "CT of the Thorax: Anatomy, Pitfalls;" and "Chest Radiology: Low Tech to High Tech" at Michigan State University, East Lansing, November 9.

**Barry A. Siegel, M.D.**, professor of radiology and medicine, and director of the Division of Nuclear Medicine, as guest lecturer, spoke on "Radiopharmaceuticals and the FDA" at the University of Texas, M.D. Anderson Cancer Center, Houston, September 28. He also spoke on "The Scintigraphic Evaluation of Pulmonary Embolism" at the Bethesda Nuclear Medicine Course, National Naval Medical Center, Bethesda, October 27.

**Marilyn J. Siegel, M.D.**, professor of radiology, presented "CT of Congenital Lung Malformations" and "CT of the Pediatric Pancreas" at the Third Summer Practicum of the Society of Computed Body Tomography and Magnetic Resonance Meeting, Keystone, Colorado, August 15 - 19. She lectured on "CT/MRI of the Pediatric Mediastinum" at the Houston Radiological Society, Houston, September 27. As visiting professor, Siegel presented "CT/MR of the Pediatric Mediastinum" at the University of Texas Health Science Center, Houston, and "Pediatric Retroperitoneum" at the Baylor University College of Medicine, Houston, September 28. She also presented "CT of the Pediatric Mediastinum," "Imaging of the Pediatric Kidney," and "Ultrasonography of the Acute Abdomen" at the Michigan Fall Radiology Conference, Birmingham, October 16. Siegel spoke on "Gynecologic and Testicular Sonography in Children" at the American Academy of Pediatrics 1993 Annual Meeting, Washington, D.C., October 29. As a visiting professor, she lectured on "Chest Applications of MRI in Children," "MRI of Abdominal and Pelvic

Masses in Children," and "Ultrasonography of Acute Abdominal Pain in Children" at the Technion-Israel Institute of Technology, Haifa, November 9.

**Richard M. Slone, M.D.**, clinical instructor in radiology, presented "Chest Radiology" at the University of California, San Diego, August 16.

**Michael W. Vannier, M.D.**, professor of radiology and director of the Division of Radiology Research, presented "Electronic Atlas of the Human Body" at the 1993 Society of Exploration Geophysicists Summer Research Workshop, Rancho Mirage, California, August 4. He spoke on "3D Biomedical Imaging" at Radiology Grand Rounds, Emory University Hospital, Atlanta, September 29.

**Michael J. Welch, Ph.D.**, professor of radiology and director of the Division of Radiation Sciences, as invited lecturer, presented the Special Lecture, "Recent Advances in Radiopharmaceutical Development and Applications," at the 33rd Annual Meeting of the Japanese Society of Nuclear Medicine, Miyazaki, October 29.

**Anthony J. Wilson, M.D.**, associate professor and director of emergency radiology, spoke on "Digital Musculoskeletal Imaging" at the Refresher Course, 20th Annual International Skeletal Society Meeting, Toronto, August 15 - 20.

## SYMPOSIA

### AMERICAN ASSOCIATION OF PHYSICISTS IN MEDICINE

*The following Mallinckrodt Institute staff members participated in the 35th Annual Meeting and Technical Exhibition of the American Association of Physicists in Medicine, Washington, D.C., August 8 - 12.*

#### PROFESSIONAL COUNCIL SYMPOSIUM

**James A. Purdy, Ph.D.**, "Standards for Radiation Oncology Physics"

#### YOUNG INVESTIGATORS' SYMPOSIUM

**Vivek Mishra, Ph.D.**; **Jeffrey F. Williamson, Ph.D.**; **Zuofeng Li, D.Sc.**; **Ali Soleimani-Meigooni, Ph.D.**; "RadioChromic Film Densitometry for High Dose Rate Ir-192 Dosimetry: Accuracy and Precision"

#### SCIENTIFIC PROGRAMS

**Program 2**  
**Eric E. Klein, M.S.**; **Daniel A. Low, Ph.D.**; **Christopher Durbin, Ph.D.**; **James A. Purdy, Ph.D.**, "Changes in Electron Beam Dosimetry with the New Scattering Foil-Applicator Systems on a C12100C"

**Eric E. Klein, M.S.**; **Daniel A. Low, Ph.D.**; **Christopher Durbin, Ph.D.**; **Ali Soleimani-Meigooni, Ph.D.**; **James A. Purdy, Ph.D.**, "Dosimetry for Clinical Implementation of Dynamic Wedge on a C12100C"

#### Program 3

**Ali Soleimani-Meigooni, Ph.D.**; **Harish Panth, Ph.D.\***; **Vivek Mishra, Ph.D.**; **Jeffrey F. Williamson, Ph.D.**, "Dependence of Linearity, Accuracy, and Low-Dose Limit of TLD Response on Nitrogen Flow in the TLD Reader." \*Best Medical International, Springfield, Virginia

**Ali Soleimani-Meigooni, Ph.D.**; **Eric E. Klein, M.S.**; **Christopher Durbin, Ph.D.**; **James A. Purdy, Ph.D.**, "Tissue Interface Measurements with GafChromic Film"

#### Program 4

**Ali Soleimani-Meigooni, Ph.D.**; **Eric E. Klein, M.S.**; **Vivek Mishra, Ph.D.**; **Daniel A. Low, Ph.D.**; **James A. Purdy, Ph.D.**, "GafChromic Film Dosimetry for Megavoltage X-ray Beams"

**Robert E. Drzymala, Ph.D.**; **Prithvi Narayan, M.S.\***; **Timothy R. O'Leary, M.D.**; **Keith M. Rich, M.D.\***; **Joseph R. Simpson, M.D.**; **Todd H. Wasserman, M.D.**; **William B. Harms, B.S.**; **John W. Matthews, D.Sc.**; **James A. Purdy, Ph.D.**, "A Computerized Treatment Planning System for Stereotactic Radiosurgery."

\*Department of Neurological Surgery, Washington University, St. Louis

#### Program 5

**Robert E. Drzymala, Ph.D.**; **Prithvi Narayan, M.S.\***; **Keith M. Rich, M.D.\***, "A Computerized System for Image-Based Planning of Stereotactic Brain Biopsies." \*Department of Neurological Surgery, Washington University, St. Louis

**Walter R. Bosch, D.Sc.**; **Daniel A. Low, Ph.D.**; **Russell L. Gerber, M.S.**; **Mary L. Vogelsang Graham, M.D.**; **Jeff M. Michalski, M.D.**; **Carlos A. Perez, M.D.**; **James A. Purdy, Ph.D.**, "An Electronic View Box Tool for Radiation Therapy Treatment Verification"

**Daniel A. Low, Ph.D.**; **Eric E. Klein, M.S.**; **Derek K. Maag, electronic technician**; **James A. Purdy, Ph.D.**, "The Commissioning of a Varian PortalVision™ Electronic Portal Imaging Device"

#### Program 6

**Zuofeng Li, D.Sc.**; **Ali Soleimani-Meigooni, Ph.D.**; **Vivek Mishra, Ph.D.**, "A Comparative Study of Dosimetric Properties of Solid Water and Plastic Water in Brachytherapy Applications"

**Zuofeng Li, D.Sc.**; **Jeffrey F. Williamson, Ph.D.**; **Harold Perera, Ph.D.**, "Monte Carlo Calculation of Kerma-to-a-Point Near Media Interfaces"

**Jeffrey F. Williamson, Ph.D.**; **Zuofeng Li, D.Sc.**; **Perry W. Grigsby, M.D.**; "Monte Carlo Aided Dosimetry of the MicroSelection PDR Source and Shielded Fletcher Colpostat"

**Jeffrey F. Williamson, Ph.D.**; **Ali Soleimani-Meigooni, Ph.D.**; **Perry W. Grigsby, M.D.**; **Steven Teague\***, "Acceptance Testing of a Novel Single-Stepping Source Remote Afterloader for Low Dose-Rate Brachytherapy: A Systematic Approach." \*Nucletron Corporation, Columbia, Maryland

#### Program 7

**Jeffrey F. Williamson, Ph.D.**, cochairman

**Eduardo G. Moros, Ph.D.**; **Eric E. Klein, M.S.**; **William Straube, M.S.**; **Robert J. Myerson, M.D.**, "Clinical Systems for Simultaneous Superficial Hyperthermia and External Beam Radiation"

#### Program 8

**Y. Abel Cheng, M.S.**; **William B. Harms, B.S.**; **Russell L. Gerber, M.S.**; **John W. Wong, Ph.D.\***; **James A. Purdy, Ph.D.**, "A Systematic Verification of a 3-D Electron Beam Dose Calculation Algorithm." \*Department of Radiation Oncology, William Beaumont Hospital, Royal Oak, Michigan

#### Program 9

**Eric E. Klein, M.S.**; **James A. Purdy, Ph.D.**, "A Comprehensive Dosimetric and Continuing Quality Improvement Program for a 50 kVp Endocavitary Unit"

#### SCIENTIFIC PAPER ABSTRACTS

**Nilesh L. Jain, M.S.**; **Michael G. Kahn, M.D.\***; **James A. Purdy, Ph.D.**; "A Decision-theoretic Model for the Objective Evaluation of 3D Radiation Treatment Plans." \*Department of Internal Medicine, Washington University, St. Louis

## INTERNATIONAL SYMPOSIUM ON RADIOPHARMACEUTICAL CHEMISTRY

*The following Mallinckrodt Institute staff members participated in the Tenth International Symposium on Radiopharmaceutical Chemistry, Kyoto, Japan, October 25 - 28.*

### SESSION II: TECHNETIUM RADIOPHARMACEUTICALS

#### Oral Presentation

Dal Y. Chi, Ph.D.\*; James P. O'Neil, Ph.D.\*; Carolyn J. Anderson, Ph.D.; Michael J. Welch, Ph.D.; John A. Katzenellenbogen, Ph.D.\*, "Novel Homodimeric Bis-bidentate (NS) Technetium(V) Complexes. An Approach to Metal Complexes that Mimic Steroid Hormones." \*Department of Chemistry, University of Illinois, Urbana

### SESSION III: POSITRONS

#### Oral Presentation

Timothy J. McCarthy, Ph.D.; Thomas A. Bonasera, M.S.; Michael J. Welch, Ph.D.; Shlomo Rozen, Ph.D.\*, "Application of Methyl Hypofluorite Chemistry: Synthesis of Novel Steroidal Substrates and Labeling with C-11." \*School of Chemistry, Tel-Aviv University, Israel

#### Poster Presentation

Carmen S. Dence, M.S.; Christy S. John, Ph.D.; Michael J. Welch, Ph.D., "The Combined Use of Microwave Heating and Photolysis in the Synthesis of [<sup>18</sup>F]-substituted Benzamides"

### SESSION V: RADIOISOTOPE PRODUCTION

#### Oral Presentation

Carmen S. Dence, M.S.; Michael J. Welch, Ph.D.; Barbara J. Hughey, Ph.D.\*; Robert E. Klinkowstein, Ph.D.\*; Ruth E. Shefer, Ph.D.\*, "A New Method of Nitrogen-13 Ammonia Production Applicable with Low Energy Accelerator." \*Science Research Laboratory, Somerville, Massachusetts

### SESSION VII: PEPTIDES, PROTEINS AND ANTIBODIES

Oral Presentation  
Michael J. Welch, Ph.D., chairman

Carolyn J. Anderson, Ph.D.; Buck E. Rogers, M.S.; Judith M. Connett, Ph.D.\*; Li W. Guo, Ph.D.; Sally W. Schwarz, R. Ph., M.S.; Kurt R. Zinn, D.V.M., Ph.D.\*\*; Michael J. Welch, Ph.D., "Comparison of Two Bifunctional Chelates for Labeling <sup>64</sup>Cu to Mab 1A3 and 1A3-F(ab')<sub>2</sub>: Chemistry and Animal Biodistribution." \*Department of Surgery, Washington University, St. Louis. \*\*Research Reactor, University of Missouri, Columbia

#### Poster Presentations

Wilson B. Edwards, M.S.; Carolyn J. Anderson, Ph.D.; Michael J. Welch, Ph.D.; Cynthia G. Fields, M.S.\*, "The Synthesis of DTPA-D-Phe<sup>1</sup>-octreotide by Solid-phase Synthesis." \*Department of Biomedical Engineering, University of Minnesota

Carolyn J. Anderson, Ph.D.; Wilson B. Edwards, M.S.; Tammy S. Pajeau, M.S.; Buck E. Rogers, M.S.; Kurt R. Zinn, D.V.M., Ph.D.\*; Henry V. Lee, B.A.; Michael J. Welch, Ph.D., "In vitro and in vivo Evaluation of [<sup>64</sup>Cu-CPTA-D-Phe<sup>1</sup>]-octreotide: An Agent for Quantitating Somatostatin Receptors with PET." \*Research Reactor, University of Missouri, Columbia

### SESSION VIII: RADIOPHARMACEUTICALS FOR NEUROTRANSMISSION

#### Poster Presentation

Stephen M. Moerlein, Ph.D.; Joel S. Perlmutter, M.D.; James L. Bockhorst, B.S.; David Parkinson, Ph.D.\*; Michael J. Welch, Ph.D., "N-Alkylated Analogues of [F-18]Benperidol as Dopaminergic D-2 Receptor Ligands." \*Department of Cell Biology and Physiology, Washington University, St. Louis

### SESSION IX: MISCELLANEOUS Oral Presentation

Timothy J. McCarthy, Ph.D.; Michael J. Welch, Ph.D.; Jian Zhang, M.S., "Nitric Oxide Synthase (NOS): Approaches to the Design and Synthesis of Inhibitors of this Enzyme Suitable for Radiolabeling and Measurement of in vivo Biodistribution"

#### Poster Presentations

Carolyn J. Anderson, Ph.D.; Christy S. John, Ph.D.\*; Robert K. Keast, CNMT; Henry V. Lee, B.A.; Michael J. Welch, Ph.D., "N,N'-Ethylene-di-L-cysteine: A Potential Ligand for Gallium and Indium Radiopharmaceuticals." \*Department of Radiology, George Washington University, Washington, D.C.

Sally W. Schwarz, R.Ph., M.S.; John O. Eichling, Ph.D.; Michael J. Welch, Ph.D., "Considerations Necessary for Determining Radiation Dosimetry of Positron Emitting Radiopharmaceuticals"

## HONORS/ AWARDS

Barry A. Siegel, M.D., professor of radiology and medicine, and director of the Division of Nuclear Medicine, is president of the Washington University Medical Center Alumni Association (WUMCAA). He earned both his undergraduate and medical degrees at Washington University and has been an MIR faculty member and director of the Division of Nuclear Medicine since 1973.



# FYI

## APPOINTMENTS/ ELECTIONS

**Jeffrey J. Brown, M.D.**, associate professor of radiology and chief of the magnetic resonance imaging section, was appointed director of the research residency at the Institute.

**Mary L. Vogelsang Graham, M.D.**, instructor in radiology, was appointed to the 1993-1994 Committee on Admissions, Washington University School of Medicine.

**Daniel A. Low, Ph.D.**, instructor in radiology, was appointed to full membership in the American Association of Physicists in Medicine.

**Bruce L. McClennan, M.D.**, professor of radiology and chief of the abdominal imaging section, will serve a two-

year term as the elected faculty representative to the Department of Radiology, Executive Committee.

**Ali Soleimani-Meigooni, Ph.D.**, assistant professor of radiology, was selected president-elect (1993-1994) of the Missouri Valley Chapter of the American Association of Physicists in Medicine.

**Michael W. Vannier, M.D.**, professor of radiology and director of the Division of Radiology Research, was named chairman of the Missouri State Medical Association's 1993-1994 Commission on Continuing Education and Health Manpower.



## ALUMNI NEWS

When Phyllis Isbell, R.T., retired after 38 years at the Washington University Medical Center, (left to right) doctors Jerry Palagallo, MIR '74; Art Bishop, '81; Tom Getz, '87; and Bill Berkman, '79, couldn't make it to the retirement party. So, the foursome from Methodist Medical Center of Illinois in Peoria donned fluoro gear and had this special photograph made for Phyllis' memory book.



Residents, trainees, and fellows for 1992-1993 were (front row, left to right) Doctors Neda Yagan; L. Santiago Medina; Colin P. Derdeyn; Scott M. Baker, chief resident; Ronald G. Evens, director of the Institute; Allen B. Oser, cochief resident; James R. Duncan; Neal A. Frenkel; Jeffrey A. Friedland; Andrew J. Fisher; Mary G. Alderman; (second row, left to right) Eric R. Weidman; Michele D. Semin; Kyongtae Tyler Bae; Valerie Christy Reichert; Lane A. Deyoe; Paul S. Hsieh; Maria E. Schmidt; Cynthia Karfias-Rigsby; Anthony M. Foti; Matthew J. Fleishman; Richard N. Edelstein; (third row, left to right) Michael C. Roarke; Eric S. Malden; Howard P. Forman; Meredith W. Bell; Robin Frank-Gerszberg; Spencer M. Smith; Benjamin J. Bartnicke; Hamid R. Latifi; Shawn P. Quillin; Farrel K. VanWagenen; (back row, left to right) Chi-Lai Ho; Rosalie J. Hagge; Francis J. Schlueter; Linda R. King; Dale P. Harris; James D. Matthews; Constance M. Courtois; Patrick O. Gordon; M. Gena Frederick; Mark S. Zobel; Gerard M. Eagar; Gary D. Luker.

# REFLECTIONS

by Henry D. Royal, M.D.

## COST CONTAINMENT AND TECHNOLOGY ASSESSMENT: SCIENTIFIC CHALLENGES

The cost of medical care has increased at a rate greater than the increase in the gross national product of the United States. Until now, medicine has been relatively immune to cost considerations. At some point, strenuous efforts to contain costs will necessarily be made and will be shaped by social, political and scientific forces. This review will discuss technology assessment and the scientific challenges that need to be addressed in an era of cost containment.

Concerns about costs have increased the demand for scientific evidence to show that a diagnostic test (as well as therapeutic interventions) benefits patients in some meaningful way. In the past, technology assessment focused on diagnostic accuracy. In the future, technology assessment will be focused on whether or not use of the technology improves patient outcome.

The Agency for Health Care Policy and Research (AHCPR) is a new federal agency created to encourage patient outcome research. The

AHCPR was instrumental in the development of "Practice Guidelines" that recommend how to best manage patients with various diseases.

## TECHNOLOGY ASSESSMENT

Technology assessment is one of many factors considered when developing a practice guideline and can focus on many different levels of efficacy (Table 1). These levels of efficacy have a natural hierarchy. Demonstration that a technology is "better" at a lower level of efficacy is a necessary but insufficient requirement to demonstrate that the technology is "better" at a higher level of efficacy.

The lowest level of efficacy measures the technical characteristics of the technology. For example, one type of computed tomography (CT) scanner may have better spatial resolution than another type of CT scanner. This technical advantage does not necessarily translate into better diagnostic accuracy, better patient management, or better patient outcome.

The next higher level of efficacy measures diagnostic accuracy. The most rudimentary study of diagnostic accuracy describes the findings in patients with a known disease as

compared to the findings of "normal" patients. This initial assessment simply determines whether or not further assessment of the technology should be pursued. Unfortunately, these preliminary assessments are often

misconstrued as indicating that the technology is clinically useful.

The accuracy of a test in differentiating normal from abnormal patients is expressed traditionally as the sensitivity and specificity. Unlike overall accuracy, these measures are independent of disease prevalence and, therefore, are a better measure of diagnostic accuracy. Despite their widespread use, sensitivity and specificity have a number of glaring deficiencies. First, the researcher is forced to reduce the results of a complex imaging test that displays many features to a binary result (normal or abnormal). This data reduction makes subsequent data analysis much simpler; however, the obvious drawback is that significant information from the test is ignored.

Second, the disease status of the patient also is reduced to a binary result. This oversimplification does not permit evaluation of test performance with disease severity. In addition, disease status is often determined by another imperfect test and does not necessarily represent the true disease status of the patient.

Third, sensitivity and specificity rarely are reported with 95 percent confidence intervals. This omission hides the fact that sensitivity and specificity measurements often are inexact simply due to the small number of subjects used to measure these two parameters.

Receiver operator characteristic (ROC) curves address some of the deficiencies of sensitivity and specificity. These curves traditionally classify the test result in one of five categories: definitely normal, probably normal, possibly abnormal, probably abnormal, and definitely abnormal. Four sensitivity, specificity pairs can be created by using a different threshold for distinguishing normal from abnormal test results. For example, a strict threshold would require that the test result be classified as "definitely abnormal" in order to be considered "abnormal,"

Table 1

### Levels of Efficacy

Level	Example
1. Technical Characteristics	Spatial Resolution
2. Diagnostic Accuracy	Findings in normals/abnormals
Descriptive	
Quantitative	Sensitivity/specificity ROC Curve Likelihood Ratio
3. Diagnostic Certainty	Post-test probability
4. Patient Management	Treatment changed because of test result
5. Patient Outcome	Patient outcome changed due to change in treatment
6. Societal Outcome	Cost/Benefit

# REFLECTIONS

continued from page 31

**Table 2**  
**Calculation of Likelihood Ratios**  
 Probability of a Test Feature  
 vs Disease Status

	D+	D-	LR
T <sup>1</sup>	.5	.005	100 (0.5/.005)
T <sup>2</sup>	.25	.025	10 (.25/.025)
T <sup>3</sup>	.1	.1	.1 (.1/.1)
T <sup>4</sup>	.01	.1	.1 (.01/.1)

T<sub>n</sub> = Individual Test Feature  
 D+ = Disease Population  
 D- = Nondisease Population  
 LR = Likelihood Ratio

resulting in the lowest sensitivity but the highest specificity. On the other hand, a lax threshold would classify all test results other than "definitely normal" as "abnormal," resulting in the highest sensitivity but the lowest specificity. Typically, the ROC curve is plotted as the sensitivity versus one minus the specificity. As test performance improves, the curve is shifted upward and to the left.

The final, and probably the best, way to express the diagnostic accuracy of a complex test is likelihood ratios. A detailed list of the potential features in an image is generated, e.g., the size of a lung nodule, whether its borders are smooth or ill defined, whether it is calcified, etc. How often these features are present in the disease of interest (e.g., malignant lung tumors) is compared to an appropriate "non-disease" group (patients with benign lung nodules) (Table 2). The likelihood ratio is calculated simply by dividing the probability of finding that particular test feature in patients with disease by the probability of finding that identical test feature in patients without the disease. If the likelihood ratio for a particular test feature is

■ much greater than 1.0 (the feature is much more common in patients with the disease than without the disease), the feature greatly increases the chances that the patient has the disease;

■ equal to one, that test feature does not help distinguish patients with and without the disease of interest;

■ much less than one, that test feature is useful for excluding the disease.

When test features are listed with their likelihood ratios, it becomes very apparent which features of an image

have the most diagnostic value. The likelihood ratios can be determined not only for the individual test features but also for combinations of test features.

## SCIENTIFIC CHALLENGES

In order to improve the cost-effective use of diagnostic tests, the emphasis of technology assessment must change. Multicenter studies to determine how a diagnostic test changes patient outcomes will be necessary. For example, patients may be randomized into one group of patients having the diagnostic test and another group not having the diagnostic test. Measures of morbidity, mortality, patient preferences and satisfaction would be obtained in each group to determine the impact of introducing the new test.

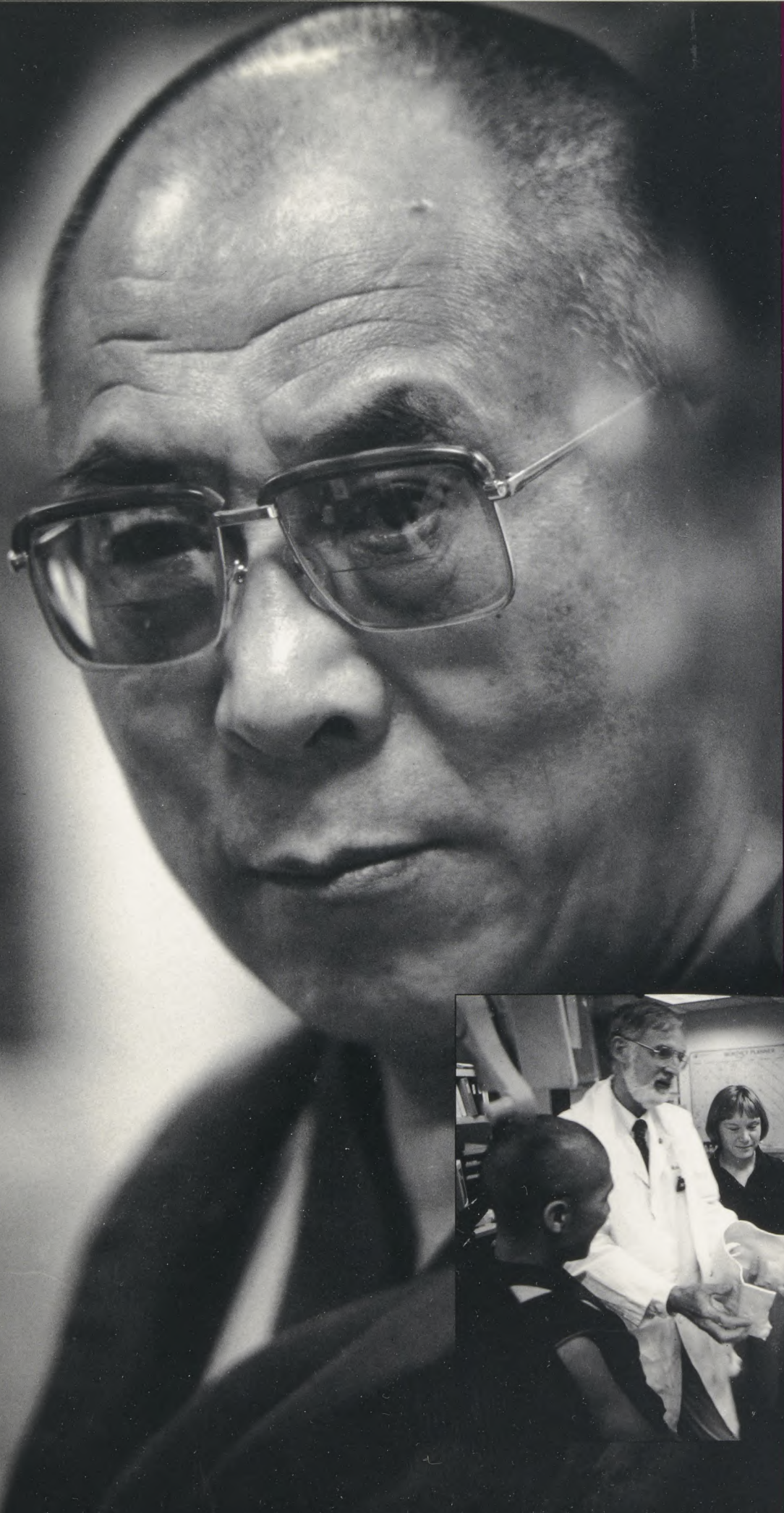
In the past we have measured the efficacy of a test, in the future we will measure the effectiveness of the test. Efficacy is measured by using a homogeneous well-defined patient population; the test is performed and interpreted in an ideal setting by experts in the field. Effectiveness would determine how well the test performs in a more realistic clinical setting. The impact of the test would

be determined in multiple medical centers to determine if the performance of the test is greatly reduced in a more realistic clinical setting.

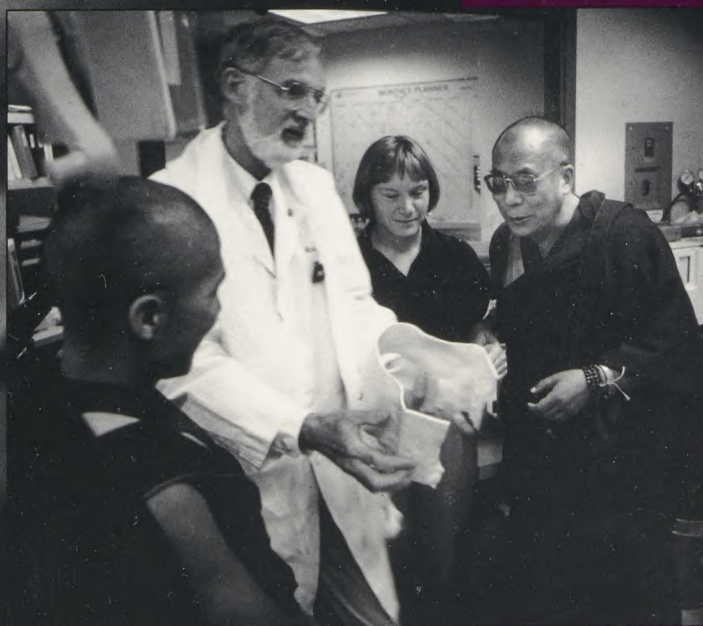
The development of more sensitive diagnostic tests may lead to some unexpected problems. First, the prognostic value of a test may decrease because everyone with the disease now has a positive test rather than just the most severely affected. Second, the apparent prevalence of disease increases. A good example of this problem is prostate cancer. Since clinically occult and insignificant disease is common, better diagnostic tests will increase the apparent prevalence of this disease. Third, the diagnosis of clinically insignificant disease will falsely increase our perceptions of the apparent efficacy of treatment. Patients whose disease would never have harmed them will now be regarded as cures.

The demand that medicine be more scientific and evidence-based is laudable. In the future, it will be a challenge to maintain the appropriate balance between the science and art of medicine. Scientists are better able to accumulate scientific evidence than are physicians. In order to understand pathophysiologic mechanisms, scientists can study inbred animals (in order to minimize confounding variables) and they can perform interventions that would be unethical in humans. Because of the limitations imposed when studying human disease, we must accept the fact that the science of medicine will always be flawed. If the demand for scientific evidence in medicine is too great, innovation will be greatly slowed and future patients will suffer. □

*Dr. Royal is professor of radiology and associate director of the Division of Nuclear Medicine. This article originally appeared in the September issue of MIR Update, a physician newsletter distributed quarterly by the Institute.*



As the guest of Washington University and Friends of Tibet, the 14th Dalai Lama of Tibet, His Holiness Tenzin Gyatso, was in St. Louis in September. His Holiness made a special visit to the Institute's seventh-floor positron emission tomography (PET) facility to learn more about the work of Marcus E. Raichle, M.D., professor of radiology and neurology and head of neurological PET research.



# FOCAL SPOT

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**Focal Spot** magazine is published three times a year by the Mallinckrodt Institute of Radiology at the Washington University Medical Center at 510 South Kingshighway, St. Louis, MO 63110.

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of Radiology  
510 South Kingshighway  
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