Expanding Sound: Pushing the limits of imaging technology
Volunteers are needed for a National Lung Screening Trial to compare the effectiveness of spiral computed tomography (CT) scans and chest X rays in detecting lung cancer. David Gierada, MD, assistant professor of radiology, is principal investigator for this two-year clinical trial, which is sponsored by the National Cancer Institute and Washington University School of Medicine.

If you meet the following criteria, you may be one of the 6,000 patients eligible to participate in this important study.

- Man or woman between the ages of 55 and 74.
- Have a history of longtime and/or heavy cigarette smoking, for example:
  - At least 1 pack/day for at least 30 years
  - 1 ½ packs/day for at least 20 years
  - 2 packs/day for at least 15 years
  - 2 ½ packs/day for at least 12 years
  - 3 packs/day for at least 10 years.
- Currently a smoker or have quit smoking within the last 10 years.
- Have NOT been diagnosed with lung cancer.
- NOT undergoing treatment for any cancer other than non-melanoma skin cancer.
- Have NOT had any portion of your lung removed.
- Not participating in a cancer prevention trial, other than a smoking cessation program.
- Not participating in another cancer screening trial, including PLCO.

Participants will receive 3 annual screening exams (either spiral CT or chest X ray). There is no charge for the exams. Validated parking is available for each visit.

Call the Volunteer for Health Office at (314) 362-1000 to see if you are eligible to participate.
Cochlear implants have restored hearing for thousands of patients, but no technology has been available to image the implant’s insertion depth—which determines the extent of hearing gained. Researchers at MIR and in the Department of Otolaryngology now are using computed tomography and new imaging techniques to expand sound.

Hyperthermia is a decades-old treatment for many types of malignant tumors. Clinicians and physicists in the Department of Radiation Oncology are now investigating the benefits of using hyperthermia and radiation simultaneously to treat patients with recurrent breast cancer.

In the postgenomic future, most anatomic disease may no longer exist as a result of early detection at the molecular level. And Mallinckrodt Institute will be in the forefront of this future medical care thanks to its Molecular Imaging Center now being established at MIR.

With more than 2,500 participating athletes, the 2002 Winter Olympics in Salt Lake City was the largest of the winter games ever held. A Mallinckrodt Institute radiologist was on staff at the Olympic Polyclinic, providing health care for athletes from 77 countries.

More than 80,000 patients annually receive emergency or trauma care at Washington University Medical Center. The new Charles F. Knight Emergency and Trauma Center can provide urgent, emergent, and trauma/critical care as well as observation in one convenient location.

Researchers Bruce Whiting, PhD, and Margaret Skinner, PhD, are using the Somatom Plus 4 Volume Zoom computed tomography (CT) scanner in their cochlear implant study. This machine has multirow detectors that help produce high-resolution scans. Photograph by Tim Parker.
**Spot News**

**Picus elected to FPP Board**

Daniel Picus, MD, professor of radiology and of surgery and director of the Division of Diagnostic Radiology, was elected in January to a three-year term on the Washington University School of Medicine (WUSM) Faculty Practice Plan (FPP) Board of Directors. He is one of six faculty-at-large representatives on the Board, all of whom are selected based on ballots submitted by the WUSM full-time clinical faculty.

The FPP was established in 1997 to manage the medical school’s clinical operations, with responsibility in the areas of clinical oversight, administration, fiscal management, and clinical planning. Marilyn Siegel, MD, professor of radiology and of pediatrics, was one of the first faculty representatives on a then-13 member Board. She was appointed to an initial two-year term and asked to remain for an additional three-year term, which was completed in January 2002. The FPP Board is now comprised of 30 members and includes the heads of WUSM’s clinical departments. Gilbert Jost, MD, professor of radiology and head of Mallinckrodt Institute, represents the Department of Radiology.

**Middleton authors second sonography reference**

Case Review: General and Vascular Ultrasound, written by William Middleton, MD, professor of radiology, is one of 14 volumes included in the Case Review series published by Mosby Inc. The 242-page book includes 211 cases that are divided according to complexity and range from gallbladder sludge to intrahepatic biliary ductal dilation, from tumor thrombus of the renal vein and inferior vena cava to muscle tear and hematoma. The book contains 440 general and vascular ultrasound images, including 84 color plates.

Middleton selected and scanned cases representative of material typically used for board examinations. Cases are presented in a question-and-answer format that allows readers to assess their proficiency in each subspecialty. According to Middleton, his goal is “to provide an affordable, useful, and enjoyable learning tool for sonographers, residents, and practicing physicians.”

The Case Review series cross-references Mosby’s The Requisites™ series, for which Middleton coauthored a volume titled Ultrasound: The Requisites.

**Gado named outstanding educator**

Washington University School of Medicine students annually honor those faculty members who possess the attributes of an outstanding teacher: creativity, organization, knowledge, compassion, energy, and dedication. Mokhtar Gado, MD, professor of radiology, was among those honored at the Distinguished Service Teaching Awards ceremony held in January at the Eric P. Newman Education Center on the Washington University Medical Center campus.

Mokhtar Gado, MD, professor of radiology, was among those honored at the Distinguished Service Teaching Awards ceremony held in January at the Eric P. Newman Education Center on the Washington University Medical Center campus.

Gado came to Mallinckrodt Institute in 1970 as an instructor in radiology and was appointed chief of neuroradiology in 1971. He was named professor of radiology in 1976. Gado stepped down as neuroradiology chief in 1991 to devote more time to clinical and research activities. He is internationally known for his studies of Alzheimer’s disease, cerebrovascular disease, and depression.

Gado directed the neuroradiology fellowship training program at the Institute from 1971 to 1998, and in 1996, he was elected by the diagnostic radiology residents as Mallinckrodt Institute’s Teacher of the Year. He is a fellow of the American College of Radiology and past vice-president of the American Society of Neuroradiology. Gado has served as a reviewer or as an editorial board member for several medical journals.
ACS honors Monsees

Barbara Monsees, MD, professor of radiology and chief of breast imaging, was recognized by the American Cancer Society (ACS) as a national leader in the field of breast imaging. In March, Monsees was one of the recipients of the St. Louis Spirit of Health Recognition award, which is sponsored by the ACS Heritage League Founders and Ortho Biotech.

Monsees is a nationally known advocate of the early detection of breast cancer through mammography and of affordable, accessible, high-quality breast imaging services. She recently completed a four-year term as chair of the FDA’s Quality Assurance Advisory Committee for the National Mammography Quality Standards Act and is the current president of the Society of Breast Imaging.

WUSM ranked third in nation

The fifteenth annual survey of graduate and professional programs conducted by U.S. News & World Report magazine lists Washington University School of Medicine in St. Louis as the third top-ranked medical school in the nation, following Harvard University and Johns Hopkins University. In 2001, WUSM tied with the University of Pennsylvania for fourth place. WUSM’s physical therapy program retained its perennial first-place ranking. Other WUSM specialties and programs in the top-ten list are the AIDS program, occupational therapy, internal medicine, cell biology, the drug/alcohol abuse program, genetics, microbiology, molecular biology, neurosciences, pediatrics, women’s health program, and pharmacology/toxicology.

The magazine’s survey of Honor Roll hospitals ranked Barnes-Jewish Hospital in a tie for seventh place with the University of Michigan Medical Center.

WUSM diagnostic radiology chief residents: (left to right) Scott Andersen, MD; Naveen Parti, MD; and Robert Kadner, MD.
Collaborative research between the departments of Radiology and Otolaryngology is helping to create sounds from silence for patients with hearing loss.

Thousands of profoundly deaf men, women, and children have received an implanted device that permits them to hear carefully spoken speech, a honking car horn, and sounds such as a baby’s wail. Now, Bruce Whiting, PhD, research assistant professor of radiology, and his colleagues at Mallinckrodt Institute of Radiology (MIR) and the Department of Otolaryngology at Washington University School of Medicine want to expand the sound experience of cochlear implant recipients even further.

by BARBRA RODRIGUEZ
More than 40,000 people worldwide, some as young as one year, have received a cochlear implant: a sound-receiving device and a series of electrodes implanted into the head that transfers sounds processed by a portable device as an electrical signal to the auditory nerve of the inner ear. Some patients have received a cochlear implant because of trauma to ear structures, such as delicate hair cells that transmit sound information or because of complications from diabetes, Meniere's disease, or otosclerosis (the development of bony growths in the inner ear). And other patients, as they age, simply no longer benefit from the most powerful hearing aids.

Using the implants, more than half of the patients can hear about 80 percent of the words in recordings of well-articulated, easy sentences, such as the test developed at Central Institute for the Deaf at Washington University Medical Center. Phone conversations or other sounds may still be difficult though, be it a whispered aside between friends, the comments of a loved one watching television in the next room, or a hushed passage of a Beethoven symphony.

Imaging roadblocks

How deeply a hearing implant’s thin strand of electrodes is placed into a patient’s inner ear was thought to influence the extent of hearing ability gained. But no one knew for certain where each electrode was in the cochlea after surgery because no adequate diagnostic imaging techniques existed. Conventional radiographs did not provide enough three-dimensional information about anatomy, while cross-section modalities (CT, MRI) blurred individual array elements.

“The electrode insertion is done blind,” says Margaret Skinner, PhD, professor of otolaryngology and director of the School of Medicine’s cochlear implant program.

In the 1990s, Skinner teamed up with Mallinckrodt Institute imaging specialists and researchers across the country to improve imaging of cochlear implants in the inner ear. Whiting began directing the current imaging project soon after coming to Mallinckrodt Institute in 1997 from industrial positions where he had worked on computed radiography and other medical imaging technology. “With Bruce’s input, we’re trying to push the limits of imaging technology to the max,” Skinner says.

The bionic ear

Components of the ear normally turn sound waves into vibrations within fluid-filled channels of the spiraling, snail-shaped cochlea. Jutting into one channel are cells whose surface is dotted with hairs. Just as seaweed bends in response to a passing wave, the hairs are indirectly bent by the passing vibrational waves, which stimulates the cells to activate nearby auditory neurons.
A cochlear-implant user wears an external microphone and a battery-powered speech processor, which groups incoming sounds of similar pitches together. The packets of electrical sound information, or filter bands, are sent to a receiver implanted under the skin of the patient's skull. The receiver relays the signals to the electrodes threaded into one of the cochlea's channels, which excite auditory neurons lying beneath the channel wall.

Selected pitches, or frequencies, of sound are sent to different electrodes because neurons along the cochlea's length usually respond to different pitches. For example, the vowel in the word "caught" is loaded with lower-pitched sounds that normally create vibrational waves further into the cochlea. An implant recipient whose electrodes only extend halfway into the cochlea may thus receive this lower-pitched information at the wrong neurons.

**MIR research**

To determine if insertion depth influences hearing ability, Whiting joined an imaging project initially begun by Kyongtae Bae, MD, PhD, assistant professor of radiology. The study involved patients who had a 22-electrode array implant, manufactured by Cochlear Corporation, that could deliver digital speech information to 22 areas within the cochlea.

Bae was testing the possibility of visualizing the implants by combining the high spatial resolution information of computed radiography (CR) with the improved 3-D positional information of computed tomography (CT). This combination required precise positioning of a patient's head so the central ray in the radiograph was aligned to the long axis of the spiral cochlea—which was accomplished under the guidance of Franz Wippold, MD, associate professor of radiology and chief of MIR's neuroradiology section, and with expert assistance from radiology technologists. CT scans were performed with a patient's head positioned so image slices were orthogonal to the cochlear axis. To align the images, Bae attached six metal spheres to each volunteer's face to identify the same positions on each image.

Whiting modeled this approach using computer algorithms and revealed that any movement of the reference spheres between scans would throw off the alignment process. "If the alignment was off by just fractions of a millimeter," Whiting says, "then the alignment could be off by centimeters when we mapped back to the head."

He suggested using the irregularly shaped implant receiver and electrode wires as reference objects to provide about 50,000 comparative points between the images. An algorithm to determine alignment transformation was developed, and more than a year's effort permitted the relative position of implants in the cochlear channel to be determined for a dozen patients, as reported in the November 2001 issue of the journal *Radiology.* "We were able to take these three-dimensional structures that were visible on the CT scan but not on the X ray and superimpose them," Whiting says.

The coregistered CR and CT information helped Skinner determine that insertion depth mattered. When some electrodes could not be inserted into a patient's cochlea, the speech processor was programmed so no sound information was delivered on those electrodes. Meanwhile, the processor sent the remaining, inserted electrodes mismatched pitch information, or frequency bands.

"As it turns out, frequency band assignment is a very important factor in a patient's speech recognition," Skinner says. "The better the match between the characteristic frequencies for the neurons and the bands they set, the faster a patient is going to learn and understand speech."
Those patients who had the full array inserted, for example, often achieved close to 100 percent word recognition of pre-recorded sentences. But a woman with a narrow cochlear canal, or other patients who had less than half an array inserted because of a short cochlea or disease-related channel damage, fared much worse.

Other implant recipients eventually achieved the 80 percent word recognition despite having as little as half of an electrode array inserted, suggesting, as Skinner notes, that mentally astute people with few factors to hinder sound recognition can mentally adapt to a moderate extent of pitch mismatch.

The image coregistration process also allowed the investigators to visualize when an electrode strand was kinked or constricted, which disrupted the affected electrode’s function. Such information should allow audiologists in the future to improve an implant user’s hearing by parceling out sound information to the remaining electrodes.

In 2000, Barnes-Jewish Hospital purchased a Somatom Plus 4 Volume Zoom scanner, based on new, multirow CT technology. The CT scanner, manufactured by Siemens, has four rows of X-ray detectors, which permit scans to cover about four times more volume in a given time. The device also has a high-resolution mode, with upwards of twice the resolving power of previous helical scanners. Evaluations indicated the hearing researchers can locate individual electrodes that previously were a blur on CT scans.

Further research

About 20 patients who have newer versions of cochlear implants have been scanned this past year on the Volume Zoom scanner with great success. But Whiting, Skinner, and their colleagues are not satisfied that everything has been done to improve the benefit of implants. Whiting is in the third year of a grant from The Whitaker Foundation to enhance the Volume Zoom imaging information even further. In part, the work involves constructing mathematical models that predict the physics of CT data acquisition. The goal: removing imaging artifacts created by radiodense electrodes and other metal implant components.

These components produce stark white regions on CT images that obliterate underlying details in the same way that sunlight reflected into a rearview mirror masks part of the image. Whiting is addressing the issue, using statistical reconstruction algorithms developed by Washington University colleagues Joseph O’Sullivan, PhD, professor of electrical engineering and of radiology; Donald Snyder, PhD, professor of electrical engineering and of radiology; and David Politte, PhD, research instructor in radiology.

Events leading to the widespread use of cochlear implants

Early 1800s
Count Alessandro Volta, a pioneer in electrochemistry, developed the electrolytic cell and attempted to determine what effect electric current had on sensory systems.

1930s
Organized studies are conducted to determine whether stimulation of the auditory nerve could result in the sensation of hearing in humans.

1957
Researchers observed that activation of the auditory nerve with an electrical device provided auditory stimulation in humans. This observation paved the way for cochlear implants.

1970s
Cochlear implant was developed and tested in labs in Australia.

1970s/1980s
Cochlear implant was developed and tested in the United States.

1984
U.S. Food and Drug Administration approved the 3M/House single-channel cochlear implant as first device to replace a human sense.

1990
FDA approved the 22-channel Nucleus cochlear implant for use in children between the ages of 2 and 17.
Specifically, Whiting has created a 3-D model of the ideal CT acquisition process—how X rays would pass through an implant and reach the Volume Zoom detectors with attendant distortions. He then compares the implant’s estimated signal and actual signal and corrects for inconsistencies on the reconstructed image.

The process works well, although Whiting has a few remaining distortions to remove. He also intends to shorten the hour-long computational process to make the approach more clinically relevant.

The improved images from this 3-D modeling effort also have allowed the implant researchers to better visualize the exact position of each 0.5-mm wide electrode within the cochlear channel. Using image registration algorithms developed by Barry Bruns- den, research engineer in MIR’s electronic radiology laboratory, surgeons can now do preimplant and postimplant imaging and learn about bone damage that can affect surgical implantation.

The sharper images also have given the hearing researchers a better understanding of where implanted electrodes rest within the cochlear channel, which will aid in enhancing the implant’s benefits. An electrode’s position within the scala tympani channel of the cochlea influences hearing. An electrode resting far from the neurons requires more current, whereas a closer electrode requires less current to cause a sensation of hearing. A patient needs just the right amount of current to each electrode to hear sound with the least distortion.

Skinner and Whiting have begun sending the electrode positional information to Charles Finley, PhD, associate professor of otolaryngology, at the University of North Carolina School of Medicine. Finley’s estimates of the electrical field produced around each electrode will be used to model the anticipated effect on nearby auditory and other neurons. That knowledge will be combined with additional information about the functional status of a patient’s auditory neurons.

Altogether, the imaging information, electrical field monitoring, hearing tests, and other efforts of the clinicians, scientists, and engineers should permit more effective programming of a patient’s sound processors. The efforts may also provide the informational impetus to convince cochlear implant manufacturers to develop more tailored models for patients with different circumstances. “The imaging effort is just a piece of the picture,” Whiting says. “It’s an important part of the research, but I believe there’s a wealth of other activities that are going to be based on the imaging, which eventually will lead to better patient outcomes.”

Applying his computational background to a project that links technology to patient care already has been rewarding, Whiting adds. “It’s very satisfying to translate these new technical ideas into something that has real life benefits,” he says.
When breast cancer recurs...

RADIATION
ONCOLOGY
CLINICIANS
AND PHYSICISTS
ARE INVESTIGATING
THE BENEFITS
OF USING HEAT
AND RADIATION
SIMULTANEOUSLY
TO DESTROY
CANCER CELLS.

BY CHRIS WAYLAND
FOR A WOMAN WHO HAS HAD A MASTECTOMY FOLLOWING A DIAGNOSIS OF BREAST CANCER, THE TUMOR IS GONE BUT THE RISK OF RECURRENCE REMAINS IF CANCEROUS CELLS ARE PRESENT IN THE CHEST WALL. HEAT-INDUCED RADIOSENSITIZATION IS KEY TO ATTACKING THIS NONVISIBLE CANCER, SAYS ROBERT MYERSON, PHD, MD, CLINICAL CHIEF OF HYPERThERMIA AT MALLINCKRODT INSTITUTE'S DEPARTMENT OF RADIATION ONCOLOGY. MYERSON IS THE PRINCIPAL INVESTIGATOR FOR A NATIONAL INSTITUTES OF HEALTH/NATIONAL INSTITUTE OF CANCER-FUNDED CLINICAL STUDY OF THE LONG-TERM EFFECTS OF SIMULTANEOUSLY TREATING RECURRENT BREAST CANCER WITH HEAT TREATMENTS, KNOWN AS HYPERThERMIA, AND RADIATION THERAPY. ULTRASOUND DELIVERS THE HEAT, BRINGING THE CANCER CELLS TO A TEMPERATURE OF 41°C (JUST BELOW 106°F) AND MAKING THE CELLS MORE RECEPTIVE TO RADIATION. THE RESULT? MORE CANCEROUS CELLS ARE DESTROYED BY THIS DUAL THERAPY THAN WHEN RADIATION IS USED ALONE. THE NUMBER OF TREATMENTS GIVEN, THE TIMING OF THE HYPERThERMIA, AND THE TECHNOLOGY USED TO DELIVER THE TREATMENTS PLAY KEY ROLES IN THIS FIVE-YEAR STUDY.

W e know that mild temperatures of heat given at the same time as radiation can markedly enhance the ability of radiation to kill cancer cells. It's very important that the radiation and the heat be given at the same time,” says Myerson. “If a patient receives the heat and then ten minutes elapse before she is given the radiation treatment, the radiation enhancement is much, much less.” By itself, 41°C would not kill any cancer cells or normal cells unless the temperature was maintained for an extremely long time, Myerson says, adding that hyperthermia would only be given for an hour. But an hour is long enough to interfere with the ability of the cells to repair themselves from the effects of radiation.

Since hyperthermia is delivered at either 41°C or 42°C, heating the entire target area consistently makes the synergistic effect with the radiation work best. Temperature monitors track the heat at eight to 12 points on the skin of the chest wall, and the heat can be redirected through a sophisticated grid pattern that allows the heat to be turned on and off.

“We have a huge amount of flexibility in the distribution of the heating pattern to the chest walls. If the patient does have discomfort in one part of the chest wall, we can selectively reduce the heating in that area,” Myerson says.
The clinical study

Each woman participating in the study will receive four hyperthermia treatments. One area of her chest wall, either the lateral or middle portion, will be heated and compared to the nonheated site. Radiation will be applied to the whole targeted area. Researchers will look at long-term effects such as tissue discoloration or scar tissue.

“The first group of patients will receive four hyperthermia treatments,” Myerson says. “If the late effects in the heated portion of the chest wall are not different than those in the nonheated portion or if the changes in the heated portion are smaller than the benefits in terms of attacking cancer cells, then we will open the second ‘arm’ of the study, and in the second arm the patients will receive eight hyperthermia treatments.”

To be eligible for this study, a woman must have had a tumor that originally was larger than two and one-half inches but either has been removed or shrunk with chemotherapy to an inch or less, or she must have four or more lymph nodes with cancer cells. Other criteria include a recurring cancer on the chest wall that has not been previously treated with radiation, and a woman must be 18 years or older. The study consists of two “arms,” and each arm will include 37 patients. To date, 11 women have been accepted into the study.

In two previous studies, Myerson and co-investigators looked at the short-term effects of using hyperthermia and radiation therapy for women with high-risk breast cancer and found that the patients tolerated the treatments well. These patients’ tumors were larger than the tumors of the women in the current study, so these first groups of women (72 total) received four, six, or eight hyperthermia treatments. Results of these previous studies showed that the benefits of treatment with hyperthermia outweighed any adverse effects. This finding led to the current five-year study.

Hyperthermia

Hyperthermia was first used in the Radiation Oncology Center at Mallinckrodt Institute in the late 1970s, where doctors found the treatment to be effective in reducing large tumors. Treatments of 30 minutes to 60 minutes duration had a palpable benefit in decreasing the tumors and killing cancer cells, according to Eduardo Moros, PhD, a physicist in the Department of Radiation Oncology.

Grants

This important research is supported by these NIH/NCI grants.

“Simultaneous thermoradiotherapy for breast carcinoma”
Principal Investigator Robert Myerson, PhD, MD, professor of radiation oncology
Carlos Perez, MD, professor of radiation oncology

“Ultrasonic systems for simultaneous thermoradiotherapy”
Principal Investigator Eduardo Moros, PhD, associate professor of radiation oncology
Marie Taylor, MD, instructor in radiation oncology
William Straube, MS, instructor in radiation oncology

Eduardo Moros, PhD, associate professor of radiation oncology
William Straube, MS, instructor in radiation oncology

Joanne Mortimer, MD, associate professor of medicine
David Mansur, MD, assistant professor of radiation oncology
Imran Zoberi, MD, instructor in radiation oncology
“During the early eighties, hyperthermia became the new weapon against cancer, and its use became very widespread in the radiation oncology community,” Moros says.

Companies began manufacturing devices specifically for different applications of hyperthermia. Radiation oncologists started clinical trials, and hyperthermia studies began under the auspices of the Radiation Therapy Oncology Group, a multi-institutional cooperative organization comprised of major research institutions in the United States and Canada. But as more clinical studies were done, investigators discovered the benefits of hyperthermia were not as good as those reported in earlier findings. Researchers questioned the disparity and in the late 1980s began to reassess the treatment.

They concluded that “it was more difficult to heat tumors than was originally expected,” says Moros. Only tumors less than three centimeters were responding positively to hyperthermia. According to Moros, researchers looked at thermometry and the devices used for delivering the treatment, and changes were made in 1991. “Basically we scratched ninety percent of the clinical equipment we had and started over,” he says.

Simultaneous therapy

Around 1993, researchers and clinicians decided that one avenue to pursue was delivering the hyperthermia and radiation at the same time. In the past, some patients with recurring breast cancer appeared to need more radiation than their bodies could safely handle. “There is, of course, a limit to the amount of radiation that can be given to a patient or to a particular volume of tissue,” Moros explains.

But radiation dosage could be maximized when used in tandem with hyperthermia, and this synergism resulted in more cancer cells being killed with each dose and with little or no adverse effects. According to Moros, the most common adverse effect of hyperthermia is blistering; burns rarely occur.

Myerson realizes that 41°C sounds like a high temperature, but he reminds patients that hot tubs are usually set at the same temperature. Also the patient’s whole body does not reach 41°C, just a small area of skin about six inches wide on the chest wall. “Most patients tolerate the heat treatment extremely well,” he says.
Research and development

In the Department of Radiation Oncology, the ultrasound-delivered heat is given before and after the radiation therapy, with patients receiving both heat and radiation treatments in the same room from two separate pieces of equipment. Moros is principal investigator of a National Institutes of Health/National Cancer Institute grant to design a new ultrasound system. He and Petr Novak, a research associate, are designing portable equipment that can be integrated into the stationary radiation-delivery system. A lightweight model of the equipment is about the size of a laptop computer. The new equipment uses ultrasonic rays, which are aimed at two mirrors that move and direct the rays to the targeted area. By bouncing the rays off the moving mirrors, a large area can be covered without having to move the ultrasound source. Current equipment operates at frequencies of 1 MHz and 3.5 MHz, allows penetration at 8 centimeters or 3 centimeters respectively, and has no mechanism adjustments to the penetration area. The new equipment will operate at 1 MHz and 5 MHz and will allow for adjustments by having one ray firing at 5 MHz and one at 1 MHz.

“The new system is like mixing two colors to get a color in between,” Moros explains. He and Novak plan to have the new device completed within the next two years, Moros says, adding that commercial equipment has already been modified to achieve some of the elements available in the new equipment. Three-dimensional capabilities, portability, and ability to deliver heat simultaneously are all elements that previously have not been available in one machine.

“Hyperthermia in conjunction with radiation therapy was always considered a last resort for recurring breast cancer,” Moros says. “But with recent advances in technology, patients are now being treated with simultaneous therapy before receiving standard radiation.”

Editor’s note: If you are interested in participating in the Department of Radiation Oncology’s simultaneous hyperthermia and radiotherapy study, call 314-454-7226 for more information.

SURLAS (Scanning Ultrasound Reflector Linear Arrays System). External beam radiotherapy and ultrasound hyperthermia can be delivered simultaneously to a superficial target. The applicator’s dimensions (especially the height, ~2.6 cm) and construction materials were selected to assure acceptable attenuation of the photon/electron beam.
Today, the field of radiology is focused on using sophisticated imaging tools—positron emission tomography (PET), computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, and even digital radiography—to detect anatomic changes that indicate disease. In a case of suspected breast cancer, for example, the radiologist draws from an arsenal of diagnostic imaging tools to determine whether the mass is malignant, based on its density, margins, bulk, and blood flow.

But in David Piwnica-Worms' vision of the postgenomic future, molecular imaging will change this picture, shifting the emphasis away from anatomy to specific receptors, enzymes, or genes and how they are expressed. To evaluate that breast mass, the physician might ask these kinds of questions: Is there a mutant P53 transcription factor present? Is a transporter such as MDR1 P-glycoprotein expressed on its surface? And what do those things reveal about its characteristics?
"As researchers, we can envision that twenty-five or thirty years from now medical practice will occur mainly at a genetic and molecular level, where there are certain biochemical signs that will be treated systemically with highly targeted, specific drugs," says Piwnica-Worms, professor of radiology and of molecular biology and pharmacology. "That means a large swath of anatomic disease may no longer exist because it is treated as a molecular, biochemical abnormality long before there is any anatomic change."

Piwnica-Worms and Mallinckrodt Institute of Radiology (MIR) have just taken a giant step toward that future by receiving a major five-year, $10.5 million grant from the National Cancer Institute (NCI) to establish a molecular imaging center at Washington University. Its goal is to bring together Washington University investigators from different disciplines to apply molecular imaging approaches to various cancer-related questions.

The earlier phase of the grant application process also attests to MIR's reputation. When the NCI announced this new program in 1999, Piwnica-Worms applied for one of the nine initial P20 planning grants to lay the groundwork for the MIC. The resulting three-year, $1.2 million grant allowed him and his colleagues to begin several pilot projects. One involved Jeffrey Milbrandt, MD, PhD, of the Department of Pathology, who was looking at patterns of gene expression in prostate cancer models; another had Paul Allen, PhD, also of the Department of Pathology, studying T-cell trafficking in vivo in a tumor ablation model. This year, they were among the first group of centers to convert from a planning grant to a full center grant.

Today, the MIC is composed of several parts. There are four major RO-1 research projects—running the gamut from basic cell biology to translational research to a molecular imaging clinical trial in humans—all designed to be multidisciplinary, with molecular biologists, biochemists, and imaging scientists working together. There are also four multidisciplinary pilot projects, which may eventually develop into RO-1 projects. Then there is the education and training piece, in which lectures and seminars train people in molecular imaging techniques.
THE GROWTH OF MOLECULAR IMAGING

The impetus behind the MIC came from Piwnica-Worms, who has been interested for some time in exploring a multidisciplinary approach to imaging questions. Piwnica-Worms, whose doctoral work was in cell physiology, completed a diagnostic radiology residency at Brigham and Women's Hospital in Boston, where his group developed diagnostic radiopharmaceuticals used in animal studies. In one study, a contrast agent was injected into a lab rat, and images were taken as the agent entered the animal's heart.

"But no one was asking where the radiopharmaceuticals went in the heart cell or what the biochemical pathways of localization were," he says. "The chairman of the radiology department supported my interest in these areas, using new agents. These radiopharmaceuticals ended up having some very interesting biochemical mechanisms, which led me to look at imaging problems from a biochemical perspective."

Piwnica-Worms came to MIR in 1994 and set up his own lab along these same lines, with chemists, molecular biologists, and imaging scientists involved. At times, that cross-pollination has created a remarkable synergy. "Researchers have gained insight into a biological problem because of the chemistry. Or they have planned the chemistry because they have biology in mind while addressing certain questions or directing the synthesis," he says.

Meanwhile, molecular imaging took off as a field around 1998, when groups began describing the new research approach as "characterizing and measuring biological processes in animals and humans at the cellular and molecular level, using remote imaging detectors."

So many researchers have since become interested in the field that they have formed the Society for Molecular Imaging, which has already established links with older groups such as the American Association of Cancer Research. But this approach, though new, is actually a way to broaden the scope of an existing field: nuclear medicine. For instance, a critical nuclear medicine tool—fluoro-2-deoxy-D-glucose (FDG) PET imaging—already involves the molecular probing of a transporter and a specific enzyme. Another important tool, octreoscan receptor imaging, has long used a peptide-based radiopharmaceutical to study the expression of somatostatin receptors type 2 (SSR-2) in tumors.

And some of the researchers taking part in the Molecular Imaging Center have been working in nuclear medicine for some time. Michael Welch, who also codirects MIR's Division of Radiological Sciences, was one of the first researchers to apply modern organic chemistry to the preparation of radiopharmaceuticals used in medical imaging and has long developed radiopharmaceuticals that target enzymes and receptors. For the past decade, Piwnica-Worms himself has been doing functional imaging of the multidrug resistance (MDR1) P-glycoprotein transporter, expressed in many cancers.

But for a major cohort of the investigators, the MIC represents an entirely new source of funding and collaboration that would not have existed except for this initiative," says Piwnica-Worms. "And now that the MIC is here, a dozen other relationships are forming because of the infrastructure that has been built and the expertise that has been developed. So, in a major way, the Molecular Imaging Center has generated brand-new collaborations, new types of research."

A PARADIGM SHIFT

While it can still be used to make diagnoses, assist in therapeutic planning, and predict prognosis, molecular imaging represents a number of distinct differences over traditional imaging. Conventional radiology aligns researchers and even clinicians by their expertise in different kinds of technology, such as MRI or CT, but molecular imaging does not. Instead, it addresses basic biological questions and matches those questions to the tools that best answer them.
It also allows researchers to look at molecular events, but not just in a tissue culture or as an isolated specimen under a microscope. Rather, molecular imaging lets scientists study biochemical abnormalities in living organisms, such as transgenic or gene-deleted mice, at the cellular and molecular level. To do this, the scientists need imaging tools (PET, SPECT or micro-PET) as well as the rigor of molecular cell biology and biochemistry to validate their findings.

"So molecular imaging takes the power of molecular biology and marries it with the technologies of the imaging department and begins to look at biochemistry and physiology in a new way," says Piwnica-Worms.

Another change is the shift away from the slow-moving process of developing radiopharmaceuticals that target a specific tumor receptor. Molecular imaging also uses "reporter genes"—enzymes, added to the cell, which are imageable reporters of underlying gene regulation. In a matter of months, these reporter genes can be added to an entire cellular system and then used to study many different biological questions in vivo.

And this approach also has the potential to move medicine away from what Piwnica-Worms calls "group therapy," or the idea of "treating all patients the same with the same drug and the same dose and hoping that twenty-five percent of them respond," he says. In the future, physicians will be able to tailor therapy to the individual. "Clinicians will be able to get a molecular signature of each person and then manage therapy, diagnose, and guide patient management on an individual basis."

THE MIC'S FUTURE

Along with his hopes for molecular imaging, Piwnica-Worms also has goals for the MIC. Currently, the imaging center is a collaborative research network, not a physical space. Eventually, he would like to see it become a large, centralized laboratory facility where researchers could work near collaborators in other departments. He would also like to see the MIC expand the scope of its inquiry beyond cancer to areas such as infectious, cardiovascular, and neurologic disease.

For now, Piwnica-Worms is pleased with the progress made, and he remains intrigued by the concept of molecular imaging, including its aesthetic qualities. "For seasoned investigators," he says, "science is like art. There is beauty and creativity in a well-conceived experiment or a beautifully done series of studies."

One of the recent research papers from Piwnica-Worms' lab contains an image of a mouse with two tiny tumors in its axilla. Proteins on these tumors must interact to turn on a PET reporter gene, which makes it possible for scientists to image them. "These proteins interact and dance," says Piwnica-Worms, "so that we are able to look at them from outside the body. That is really exciting for me. I find great satisfaction in the rigor, the vision, and seeing it all happen."

Imaging protein-protein interactions in vivo using microPET and reporter genes. The binding of one protein to another protein within cells regulates how cells divide, sends signals from the cell exterior to the cell interior, and mediates when and how cells move, grow, and die. Molecular imaging of these protein-protein interactions in vivo will provide a broad-based tool for researchers to integrate existing knowledge of protein interactions within the complex physiological context of living animals. Here, a tumor suppressor protein known as p53 and a viral transforming protein known as large T antigen (TAg), two interacting proteins known to be involved in turning a normal cell into cancer, are each fused to different portions of a transcription factor. Both portions of the transcription factor are required to activate a PET reporter gene known as HSV1 thymidine kinase, but only one portion can bind on its own to specific DNA sequences that regulate activation of the reporter. However, when p53 and TAg proteins interact, the second factor is now properly assembled, thereby switching on the reporter gene. The activated reporter can be detected by microPET imaging of living mice using the positron-emitting radiopharmaceutical 18F-FHBG. (Left) Photograph of the anterior thorax of a mouse with axillary xenograft tumors containing non-interacting proteins (small arrow) and interacting p53-TAg proteins (large arrow). (Right) Coronal microPET image of the same mouse showing accumulation of 18F-FHBG only in the tumor expressing the interacting p53-TAg proteins (large arrow). Asterisk denotes radiotracer in the gallbladder. Intestinal activity from normal hepatobiliary clearance of the radiotracer is observed in the lower portion of the image.
Bioluminescence of tumor xenografts in a living mouse: Firefly luciferase, the same gene that makes fireflies glow, has been transduced into human HeLa cervical carcinoma cells and tumors grown in an immunocompromised mouse. Substrate for the luciferase enzyme was injected into the mouse causing only the four transduced tumors to glow. The images are obtained in a special light-tight box with a sensitive CCD camera. Regions-of-interest can be demarcated on the images to quantify the areas of gene expression.

RESEARCH PROJECTS

The Molecular Imaging Center includes four major RO-1 grants, which are directed by researchers from a wide range of disciplines. “The Center provides a vehicle for researchers with diverse expertise to come together to design novel, multidisciplinary strategies that answer important biological questions,” says Jeffrey Milbrandt, MD, PhD, professor of pathology and medicine.

He and Gary Luker, MD, instructor in radiology, are developing a system to detect the activity of a specific pathway in living animals. Eventually, this may let physicians monitor the growth of tumor cells in vivo, along with the human response to chemotherapeutic agents. Molecular imaging is exciting, says Milbrandt, because it enables him to track the activity of a single gene in order to determine how tumor progression is affected by the integrated biology of a living system. “This will hopefully enable me to understand how molecular changes result in malignant transformation,” he says.

In his project, Paul Allen, MD, professor of pathology, is continuing his pilot project research into T-cell trafficking in an immunotherapy tumor ablation model. And Lee Ratner, MD, PhD, professor of medicine and of molecular microbiology, is focusing on two human pathogens associated with tumors—human immunodeficiency virus (HIV) and human T-cell lymphoma/leukemia virus (HTLV)—with a goal of imaging virus-infected cells in vivo. “Our research group’s interest is in examining the efficacy of antiviral therapies in many different tissues of infected individuals,” he says.

Finally, David Piwnica-Worms, MD, PhD, is collaborating with medical oncologist Ramaswamy Govindan, MD, instructor in medicine; radiologist Farrokh Dehdashti, MD, associate professor of radiology; and chemist Michael Welch, PhD, professor of radiology and of chemistry, in a clinical trial of molecular imaging. Patients with advanced, small-cell lung cancer will have a technetium-94m-sestamibi scan shortly before therapy, then the researchers will observe the patients over time to see how the imaging predicts their outcome and the occurrence of multidrug resistance (MDR), a much-feared cause of chemotherapy failure in several forms of cancer.

“Our goal is to know early on that a patient is likely to become multidrug resistant,” says Piwnica-Worms. “With this information, a physician could alter the patient’s therapy; and, since patients who present with MDR tend to have a more aggressive course of disease, the physician could also have some prognostic information.”

Editor’s note: A listing of key faculty for the Molecular Imaging Center was announced in the “Spot News” section of the fall/winter 2001 Focal Spot magazine.
2002

RADIOLOGY AT THE
Winter Olympics

BY VICKI KUNKLER
The nineteenth Winter Olympics had all the ingredients of a sports fan’s dream: drama (accusations of rules violations, unfair judging, and drug use), memorable performances (from dark-horse Sarah Hughes’ spectacular figure-skating performance to Jim Shea’s bittersweet victory in the skeleton event), wins (more gold medals won by the United States in 2002 than in any other Winter Olympics), and a rousing flourish of Americana in the closing ceremony (including singers Bon Jovi, Willie Nelson, and Gloria Estefan).

William Middleton, MD, professor of radiology, was among those fans attending the 2002 Winter Olympics in Salt Lake City, Utah, in February. He was not there as a spectator but as an official member of the Olympics medical team. Nationally known for his expertise in musculoskeletal ultrasound, Middleton was one of eight radiologists from the United States’ top medical centers invited to staff the Olympic Polyclinic and provide health care for the athletes, coaches, and trainers.

“It was personally very gratifying to be invited, but I was especially pleased that the organizing committee responsible for the Polyclinic recognized the contribution ultrasound could make to these athletes,” says Middleton.

For an athlete, a quick diagnosis of an injury could mean the difference between returning to competition or being forced to withdraw. The Polyclinic staff diagnosed and treated common, sports-related injuries as well as more chronic injuries for the 2,500-plus athletes representing 77 countries. Cases ranged from a German bob-sledder’s torn plantar fascia (the fibrous sheet of tissue on the sole of the foot) to a Canadian skier’s patellar tendonitis to a Caribbean bobsledder’s scrapes and cuts. Middleton also saw cases of existing medical problems such as kidney stones and gallstones.

For the injured athlete, radiology was the nerve center of the Polyclinic. Everyone, including the athlete, the trainer, the doctor, and sometimes teammates, congregated in our reading room to see how serious the injury was,” says Middleton. “The athletes’ decision whether or not to return to competition frequently hinged on the results of their scans.”

The clinic was open from 8 in the morning until 11 in the evening each day and was always staffed by one or two radiologists. The facility was equipped with digital health-imaging equipment, including a mobile magnetic resonance scanner, an ultrasound machine, and X-ray equipment. Patients who needed computed tomography scans were sent to nearby University of Utah Health Sciences Center.

Hockey player with shoulder pain. The ultrasound shows a defect (cursors) in the surface of the humeral head typical of a compression fracture (called a Hill Sachs deformity) that occurs with shoulder dislocation. This could not be seen on X-rays.

Downhill skier with right knee pain. The ultrasound shows thickening and distortion of the right (RT) patellar tendon (cursors) typical of patellar tendinosis. The normal left (LT) patellar tendon is seen for comparison.
Above: From the ultrasound, Middleton could determine that this member of the Canadian ski team had patellar tendonitis.

Middleton’s tour of duty was the last week of the Olympics. A standard shift was eight hours, but Middleton says he liked to extend his shift to take full advantage of the once-in-a-lifetime experience. “In radiology we saw, on average, one patient every thirty minutes,” he says. “Performing and interpreting the scans was the easiest part. Dealing with a new dictating system, new PACS system, new ordering system, and an unfamiliar support staff was the tough part. Getting the films and reports to the athletes so they could take the records to their hometown physicians was, perhaps, the most difficult part of all my medical responsibilities.”

This year was the first time Middleton was involved in the Olympics, and he says he would enjoy being on the medical staff for future games. The Winter Games in Turin, Italy, are only four years away.

OLYMPICS TRIVIA

- The Olympics were held in St. Louis in 1904, occurring simultaneously with the Louisiana Purchase Exhibition (or World’s Fair). Boxing was added as an Olympic sport during the 1904 games.
- The flag flown at all Olympic games was introduced during the 1920 games in Antwerp, Belgium. It contained 5 interlocked rings representing the five significant continents. At least one of the colors in the flag—blue, yellow, black, green, and red—appears on the flag of every country in the world.
- The first Winter Olympics were held in 1924.
- An estimated 3.5 billion people worldwide watched the 2002 televised games.
- There were more than 55,000 spectators in the Rice-Eccles Olympic Stadium during the 2002 Winter Olympics closing ceremony.
- 15,000 police troops and security volunteers made this year’s games one of the safest in Olympic history.
- The United States won 34 medals (10 gold, 13 silver, 11 bronze) in the 2002 games. Germany was in first place with 35 medals; Norway was third with 24 medals; Russia and Canada tied for fourth place with 17 medals each.
- Women’s bobsled was introduced at the 2002 Winter Games. The U.S. team won a gold medal, and Vonetta Flowers, the team’s pusher, was the first black athlete ever to win a gold medal in the Winter Games.
- Freestyle skier Shannon Bahrke won the United States’ first medal (a silver) the first day of competition.
- Snowboarder Chris Klug won a bronze medal in the parallel giant slalom—just 19 months after undergoing a liver transplant.
- This was Brian Shimer’s fifth, and last, Winter Olympics competition. Shimer won his first medal—a bronze medal in men’s bobsled.
- Jimmy Shea’s father and grandfather were Olympic athletes. Shea won a gold medal this year in skeleton.
- At the opening ceremony, U.S. athletes carried the tattered American flag from the World Trade Center.
February 5 not only marked the grand opening of The Charles F. Knight Emergency and Trauma Center but also the finalization of the Washington University Medical Center campus integration project begun in 1996. The emergency facility, housed in the new southwest tower at 400 South Kingshighway Boulevard, serves patients previously seen at three medical center emergency care units: Barnes-Jewish Hospital (BJH) south, the Schukar unit, and BJH north.

The facility is divided into areas for urgent care, emergent care, trauma/critical care, and observation—each with its own waiting areas and nursing stations. The center has a convenient, patient/visitor parking garage; a covered ambulance bay; a dedicated elevator for the roof-top helipad; a work room for police, EMS personnel, and firefighters; and a state-of-the-art radiology section.

**FOR THE RECORD**

- More than 80,000 patients annually receive emergency or trauma care at Washington University Medical Center.
- The Emergency and Trauma Center was built to exceed earthquake safety standards.
- Biological or decontamination needs are served by inside and outside decontamination units with separate septic systems.
- The new center covers 52,000 square feet and has 61 beds.
- The facility has computerized triage, tracking, order entry, and documentation systems.
- Washington University Medical Center has the only academic emergency medicine residency program in the St. Louis area.
- BJH is the only St. Louis hospital to be accredited by the American College of Surgeons as a Level I Trauma Center.

**Below left:** Christine Peterson, MD, second-year diagnostic radiology resident, and David Rubin, MD, assistant professor of radiology and chief of musculoskeletal radiology, are shown in the reading room.

**Below middle:** A spacious lobby — and friendly faces — welcome patients to the Emergency and Trauma Center.

**Below right:** Christine Menias, MD, instructor in radiology, and Chris Tincher, RT(R), in the control room for the new Volume Zoom CT scanner.
Promotions

Walter Bosch, DSc, instructor in radiation oncology, was promoted to research assistant professor of radiation oncology, Physics Division, Department of Radiation Oncology.

Clifford Chao, MD, assistant professor of radiation oncology, was promoted to associate professor of radiation oncology, Clinical Division, Department of Radiation Oncology.

Robert Drzymala, PhD, assistant professor of radiation oncology, was promoted to associate professor of radiation oncology, Physics Division, Department of Radiation Oncology.

William Straube, MS, instructor in radiation oncology, was promoted to research assistant professor of radiation oncology, Physics Division, Department of Radiation Oncology.

New Faculty

Bhargavi Patel, MD, visiting instructor in radiology, Division of Diagnostic Radiology, Department of Radiology.

Alan Williams, MD, instructor in radiology, neuroradiology section, Division of Diagnostic Radiology, Department of Radiology.

First-Year Diagnostic Radiology Resident

Humberto Rosas, MD, assistant in radiology, received a medical degree from Duke University School of Medicine. He completed a two-year surgery internship at Barnes-Jewish Hospital, St. Louis.

Grants

Carolyn Anderson, PhD, associate professor of radiology and of molecular biology and pharmacology, received a $1.6 million grant from the National Cancer Institute to study “Radiopharmaceuticals based on cross-bridged ligands.” Anderson and Edward Wong, PhD, University of New Hampshire, are principal investigators for the five-year grant. Mallinckrodt Institute coinvestigators

Senturia Lecture

The Eighth Annual Hyman R. Senturia Lecture was presented on February 22. Rosemary Stevens, PhD, MPH, professor of history and sociology of science at the University of Pennsylvania, spoke on “The formal structure of specialization in medicine.” William Reinus, MD, associate professor of radiology and coordinator of the Senturia Lecture, presented Stevens with a commemorative plaque.
are Xiankai Sun, PhD, research associate, and Mu Wang, MD, staff scientist. Consultant is Michael Welch, PhD, professor of radiology and of chemistry and codirector of the Division of Radiological Sciences.

Robert Gropler, MD, associate professor of radiology, of medicine, and of biomedical engineering, as principal investigator, received a $1.5 million grant from the National Institutes of Health for “PET quantification of myocardial substrate metabolism.” Coinvestigators are Pilar Herrero, MS, research scientist of radiology; Gary Hoffman, research associate; Terry Sharp, technical supervisor; Zulfia Kisrieva-Ware, MD, PhD, data analyst; Matthew Marison, research technician, Department of Internal Medicine; Jun Young Kwon; John Holloszy, MD, professor of medicine; Michael Welch, PhD, professor of radiology and of chemistry; and Samuel Klein, MD, professor of medicine.

Jacob Locke, MD, instructor in radiation oncology, as principal investigator, received a five-year National Institutes of Health Mentored Physician-Scientist Grant to study “Indomethacin and P38 regulating AP-1 in heat shock.” Locke’s mentors for the $618,000 grant are Joseph Roti Roti, PhD, professor of radiation oncology and director of the Division of Radiation and Cancer Biology, and David Piwnica-Worms, MD, PhD, professor of radiology and of molecular biology and pharmacology.

Dmitriy Yablonskiy, PhD, assistant professor of radiology and professor of physics, as principal investigator, received a $1.4 million grant from the National Institutes of Health/National Institute of Neurological Disorders and Stroke to study “Brain temperature control during functional activation.” Coinvestigators for the four-year grant are Marcus Raichle, MD, professor of radiology and of neurology and neurobiology and codirector of the Division of Radiological Sciences; Joseph Ackerman, PhD, professor of chemistry, of medicine, and of radiology; Larry Breitthorst, PhD, research associate; and Charles Hildebolt, DDS, PhD, associate professor of radiology and adjunct associate professor of anthropology.

Jie Zheng, PhD, research assistant professor in radiology, as principal investigator, received the Charles E. Culpeper Biomedical Pilot Initiative, a one-year grant sponsored by the Rockefeller Brothers Fund, to study “Identification of rupture-prone coronary artery plaques with magnetic resonance imaging.” Coinvestigators for the $25,000 grant are Ruth Okamoto, PhD, Department of Mechanical Engineering; Haodong Xu, MD, Department of Pathology; Jeffrey Saffitz, MD, Department of Pathology; and Robert Gropler, MD, associate professor of radiology, of medicine, and of biomedical engineering.

Caroline Anderson, PhD, associate professor of radiology and of molecular biology and pharmacology, was appointed to the Washington University Medical Center’s Continuing Review Committee for the Human Studies Committee.

Thomas Conturo, MD, PhD, associate professor of radiology and adjunct professor of physics and of biomedical engineering, was appointed as an ad-hoc referee of National Institutes of Health/National Institute of Mental Health grants for Studies to Advance Autism Research and Treatment Program (STAART) Centers.

Maurizio Corbetta, MD, associate professor of neurology and of radiology, was appointed to the editorial board of the journal Cortex.

Dione Farria, MD, MPH, assistant professor of radiology, was appointed to the American Cancer Society’s Reach to Recovery Advisory Board, Heartland Division.
Jacob Locke, MD, instructor in radiation oncology, was appointed as the Department of Radiation Oncology representative to the Washington University Disclosure Review Committee.

Robert McKinstry, MD, PhD, assistant professor of radiology, was appointed to the National Institutes of Health Ad Hoc Study Section, Center for Scientific Review, High End Instrumentation Program.

Eduardo Moros, PhD, associate professor of radiation oncology, was appointed to a three-year term as a grant reviewer for the National Institutes of Health Center for Scientific Review, Radiation Study Section.

Joel Perlmutter, MD, professor of neurology and of radiology, was appointed by the American Academy of Neurology as the 2002 Topic Chairman for Neuroimaging.

William Powers, MD, professor of neurology and of radiology, was appointed to the Oversight Committee for the National Institute of Neurological Disorders and Stroke Multicenter Trial of Neuroprotection in Parkinson Disease. He was appointed to the editorial board of The Journal of Cerebral Blood Flow and Metabolism.

Marcus Raichle, MD, professor of radiology and of neurology and neurobiology and codirector of the Division of Radiological Sciences, is chairman-elect of the American Association for the Advancement of Science Section on Neuroscience.

Marilyn Siegel, MD, professor of radiology and of pediatrics, was appointed chairwoman of the Refresher Course Committee, Pediatrics Subsection for the 102nd Annual Meeting of the American Roentgen Ray Society, to be held April 28 through May 3 in Atlanta, Georgia.

Anurag Singh, MD, assistant in radiation oncology, was elected to a two-year term on the Executive Board of the Association of Residents in Radiation Oncology.

Jeffrey Bradley, MD, instructor in radiation oncology, served as an instructor for the 3D Practicum at the American Society for Therapeutic Radiology and Oncology Meeting in St. Petersburg, Florida.

Clifford Chao, MD, associate professor of radiation oncology, was a panel member for Operations Research Applied to Radiation Therapy, a National Institutes of Health/National Science Foundation Workshop held in Washington, DC.

Eric Klein, MS, associate professor of radiation oncology, was named course director for the American College of Medical Physicists Radiation Oncology Refresher Course, held in Orlando, Florida.

Joel Perlmutter, MD, professor of neurology and of radiology, was selected by The Hereditary Disease Foundation as a participant in the Venezuela Huntington Disease Research Project. He was named the external advisor for the Molecular Genetics of Early Onset Torsion Dystonia Program, directed by Xandra O. Breakefield, PhD, of the Molecular Neurogenetics Unit at Massachusetts General Hospital in Boston.

David Piwnica-Worms, MD, PhD, professor of radiology and of molecular biology and pharmacology, was named chairman of the American Association for Cancer Research Conference on Molecular Imaging in Cancer: Linking Biology, Function and Clinical Applications In Vivo, held in Orlando, Florida.
Lectures/ Presentations


Maurizio Corbetta, MD, associate professor of neurology and of radiology, presented “Goal-directed and stimulus-driven attention in the human brain” at the Psychology Colloquium, University of Pittsburgh, Pennsylvania, March 16.

Steven Crawford, MD, clinical fellow, presented “Validation of an angiographic method for estimating flow to distal tissue beds” at the 27th Annual Scientific Meeting of the Society of Cardiovascular and Interventional Radiology, Baltimore, Maryland, April 7.

Colin Derdeyn, MD, associate professor of radiology, as keynote lecturer, presented “Pathophysiology of acute and chronic cerebrovascular disease” at the 2nd Annual International Meeting of CT/MR Brain Perfusion, San Francisco, California, March 29.

Biello Lecture

On March 11, Steven Larson, MD, chief of nuclear medicine service at Memorial Sloan-Kettering Cancer Center in New York City, presented The Sixteenth Annual Daniel R. Biello Memorial Lecture, “Measuring tumor response with PET.” Shown with Dr. Larson (right) is Barry Siegel, MD, professor of radiology and of medicine and director of the Division of Nuclear Medicine, and coordinator of the Biello Lecture.
Louis Gilula, MD, professor of radiology and of surgery, spoke on “Vertebroplasty and metastatic disease” at Missouri Baptist Hospital, St. Louis, Missouri, January 17. He presented “Imaging of distal radius fractures” at the Wrist Workshop, sponsored by the Hand Therapists and Trainers Association, St. Louis, Missouri, March 5. Gilula spoke on “Introduction to vertebroplasty,” “Lumbar and sacral nerve blocks,” and “Discography—lumbar” at the 25th Annual Winter Skeletal Symposium sponsored by the University of Pennsylvania, Lake Louise, Alberta, Canada, February 3-8.


Eric Klein, MS, associate professor of radiation oncology, spoke on “Clinical IMRT at Mallinckrodt Institute;” “Technology assessment of MLC, EDW, and IMRT;” and “Heterogeneity corrections and lung prescriptions” at the John Wayne Cancer Institute, Santa Monica, California, March 6. He presented “Heterogeneity corrections and lung prescriptions in radiation oncology” at the Florida American Association of Physicists in Medicine Meeting, Orlando, Florida, March 15. Klein presented “Acceptance, testing, and commissioning of Linacs;” “Facility shielding, design, and general radiation safety;” and “Special procedures: total body irradiation, stereotactic radiosurgery, IMRT” at the American College of Medical Physicists Radiation Oncology Refresher Course, Orlando, Florida, March 24 and 25.

Jay Heiken, MD, professor of radiology, chief of abdominal radiology, and cochief of body computed tomography, presented “A practical approach to small bowel obstruction” at Twentieth Annual Practical Radiology at Whistler, sponsored by the University of British Columbia, Whistler, British Columbia, Canada, February 3-8.

Carlos Perez, MD, professor of radiation oncology and chairman of the Department of Radiation Oncology, presented "Radiation therapy in postradical prostatectomy rising PSA" to the Greater St. Louis Society of Radiologists, St. Louis, Missouri, February 19. He spoke on "Cytoprotective agents in combined modality therapy in head and neck cancer" and "Advances in radiation oncology" at the 4th Annual Palm Beach Cancer Symposium, Delray Beach, Florida, March 22 and 23.

Mehdi Poustchi-Amin, MD, clinical fellow, presented the scientific exhibit "Principles, applications and protocols of the practical MRI of the body" at the 13th Annual Meeting of the American Society of Emergency Radiology, Orlando, Florida, March 16-20.

Barry Siegel, MD, professor of radiology and of medicine and director of the Division of Nuclear Medicine, as visiting professor, spoke on "Oncologic FDG-PET: artifacts, variants, and benign lesions simulating cancer" and "Current status of PET in clinical practice" at Brown University School of Medicine and Rhode Island Hospital, Providence, Rhode Island, January 7. He presented "FDG-PET: artifacts and variants" and "Applications of PET in oncology" at the 19th Annual Conference of the Society of Nuclear Medicine, Hawaii Chapter, Honolulu, Hawaii, February 16 and 17. Siegel presented "FDG PET: artifacts and variants" at the 2002 Mid-Winter Educational Symposium of the Society of Nuclear Medicine, Scottsdale, Arizona, February 9 and 10.


Yuan-Chuan Tai, PhD, assistant professor of radiology, spoke on "MicroPET—positron emission tomography in molecular imaging" at the American Association for Cancer Research Special Conference in Cancer Research: Molecular Imaging in Cancer, Orlando, Florida, January 26.


Franz Wippold, MD, associate professor of radiology and chief of neuroradiology, as visiting professor, spoke on "Anatomy of the temporal bone" and "Lesions of the cerebellopontine angle" at Michigan State University, East Lansing, Michigan, March 11 and 12.
SYMPOSIA

In this section of FYI, only those faculty and staff who have Department of Radiology or Department of Radiation Oncology appointments are listed.

THE AMERICAN ASSOCIATION OF NEUROLOGICAL SURGEONS/CONGRESS OF NEUROLOGICAL SURGEONS SECTION ON CEREBROVASCULAR SURGERY AND THE AMERICAN SOCIETY OF INTERVENTIONAL AND THERAPEUTIC NEURORADIOLOGY

The Fifth Joint Annual Meeting
Dallas, Texas
February 3-6, 2002

DeWitte Cross, MD, member, Abstract Committee; moderator, Oral Presentations 11-20.

Colin Dereyn, MD, codirector, Special Course: Technical and Pharmacologic Considerations in Acute Stroke Therapy and Intracranial Angioplasty/Stenting.

ORAL PRESENTATIONS

Colin Derdeyn, MD; Christopher Moran, MD; DeWitte Cross, MD; David Jeck, MD; Thomas Pilgram, PhD; Keith Rich, MD; Robert Grubb, MD, "Procedural thrombus and postprocedural ischemic events after treatment of intracranial aneurysms with GDC."

Colin Derdeyn, MD; David Jeck, MD; Christopher Moran, MD; DeWitte Cross, MD; Keith Rich, MD; Robert Grubb, MD, "Long-term outcome after angioplasty for symptomatic carotid stenosis."

SPECIAL COURSE

Intracranial Atherosclerotic Disease and Revascularization

Colin Derdeyn, MD, "EC-IC bypass study results, controversies, new trials."

POSTER PRESENTATION

David Jeck, MD; DeWitte Cross, MD; Colin Derdeyn, MD; Christopher Moran, MD, "Carotid stenting for treatment of carotid dissection."

INTERNATIONAL SOCIETY FOR MAGNETIC RESONANCE IN MEDICINE

Diffusion MRI: Biophysical Issues (What Can We Measure?) Workshop
Saint-Malo, France
March 10-12, 2002

Thomas Conturo, MD, PhD, chairman, "Diffusion and Pathophysiology" scientific session.

ORAL PRESENTATIONS

Nicolas Lori, graduate research assistant in radiology; Erbil Akbudak, PhD; Joshua Shimony, MD, PhD; Abraham Snyder, PhD, MD; Thomas Conturo, MD, PhD, "Identifying the white matter pathways involved in lesions and MRI contrast patterns using diffusion tensor tracking."

Nicolas Lori, graduate research assistant in radiology; Erbil Akbudak, PhD; Joshua Shimony, MD, PhD; Abraham Snyder, PhD, MD; Thomas Conturo, MD, PhD, "Diffusion time assignment and q-space formalism for finite-duration diffusion-encoding gradients: simulation of 3D random walks."

Jeffrey Neil, MD, PhD, "Diffusion anisotropy in the developing human brain."

POSTER PRESENTATION

Sanjeev Bhalla, MD; Elizabeth McFarland, MD; Ronan McDermott, MD; Christine Menias, MD; Amy Hara, MD; Adolf Huette, MD; Thomas Pilgram, PhD, "Prospective MDCT study of CT colonography compared to colonoscopy: diagnostic performance of experienced and recently trained readers."

POSTER PRESENTATION

Joshua Shimony, MD, PhD; Abraham Snyder, PhD, MD; Nicolas Lori, graduate research assistant in radiology; Thomas Conturo, MD, PhD, "Automated clustering of diffusion tensor track data into neuronal pathways."

SOCIETY OF COMPUTED BODY TOMOGRAPHY AND MAGNETIC RESONANCE

Twenty-fifth Annual Course
Charleston, South Carolina
March 18-22, 2002

Stuart Sagel, MD, moderator, Thoracic Imaging.

Marilyn Siegel, MD, moderator, Pediatric Imaging.

CUM LAUDE SCIENTIFIC PRESENTATION AWARDS

Kyongtae Bae, MD, PhD; Jay Heiken, MD; Huy Tran, MD, "Uniform vascular contrast enhancement and reduced contrast volume achieved by multiphasic injection method: clinical validation."

Sanjeev Bhalla, MD; Elizabeth McFarland, MD; Ronan McDermott, MD; Christine Menias, MD; Amy Hara, MD; Adolf Huette, MD; Thomas Pilgram, PhD, "Prospective MDCT study of CT colonography compared to colonoscopy: diagnostic performance of experienced and recently trained readers."
IN MEMORIAM

It is with profound sadness that we report the death of Juan M. Taveras, MD, the third director of Mallinckrodt Institute of Radiology. Taveras, 82, died in his native Dominican Republic on March 28 from leukemia.

Taveras was one of the world’s leading neuroradiologists, and under his leadership the Institute became a major center for neuroradiological research and clinical studies. During his directorship, the Institute underwent a tremendous expansion in organization and the physical plant, including further organization of the subspecialty system (begun by Hugh Wilson, MD, second director of MIR), funding for the addition of four new laboratories and five shell floors, and construction of Scarpellino Auditorium.

Taveras came to MIR in 1964 from the Neuroradiological Institute, Columbia Presbyterian Medical Center, in New York. After his departure from Mallinckrodt Institute in 1971, he was named radiologist-in-chief at Massachusetts General Hospital in Boston and professor of radiology at Harvard University. He became professor of radiology emeritus in 1988 and, in 1989, Harvard created the Juan M. Taveras Professorship.

He returned to the Dominican Republic to establish and direct the Centro de Diagnostico, Medicina Avanzada, Laboratorio y Telemedicina, at the Plaza de la Salud in Santo Domingo. According to The Santo Domingo News, “it is likely the Plaza de la Salud will be renamed in his honor.”

Taveras was often honored for his medical expertise and received a Gold Medal Award from the Radiological Society of North America (1980), the Association of University Radiologists (1985), the American Society of Neuroradiology (1995). He was a fellow of the American Heart Association (Stroke Council) and of the American College of Radiology and was the founding editor of the American Journal of Neuroradiology.

He is survived by his wife Mariana and his sons, and stepsons. Memorial donations may be sent to the Centro de Diagnostico in Santo Domingo.
IN MEMORIAM

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We sadly report the death of William Powers, MD, former director of MIR’s Radiation Oncology Center, who died in Sarasota, Florida, on November 17, 2001, from cancer. He was 79.

Powers was a recognized authority in treatment techniques for carcinoma of the uterine cervix and in preoperative radiation therapy for head and neck tumors. During his tenure at MIR, Powers played a key role in radiation oncology breakthroughs, including the development of the Cerrobend blocking system to protect healthy tissue while high doses of irradiation are delivered to tumors and the design and development of high-energy linear accelerators. He and MIR cancer biologist Leonard Tolmach, PhD, first proved the existence of hypoxic cells in tumors.

Powers came to Mallinckrodt Institute in 1952 as a diagnostic radiology resident and joined the faculty in 1955 as an instructor in radiology. He served as director of the Radiation Oncology Center from 1965 to 1975, taking a one-year sabbatical (September 1969 through August 1970) to work with the National Cancer Institute, as chief of Radiation Oncology, Extramural Branch, on developing radiation therapy centers in the United States. He left MIR in 1975 and was a visiting professor at the University of Missouri, Columbia, and at the Thomas Jefferson College of Medicine in Philadelphia.

In 1978 he once again yielded to the lure of academic administration and accepted the dual position of chairman of the Department of Radiation Oncology at Wayne State University and chief of radiation oncology at Harper Hospital in Detroit, Michigan, where he remained until his retirement in 1997.

Powers received Gold Medal awards from the American College of Radiology and from the American Society of Therapeutic Radiology and Oncology. He was a member of the President’s National Cancer Advisory Board.

He is survived by his wife Linnea and five children. Memorial donations may be sent to the Department of Radiation Oncology at Washington University School of Medicine in St. Louis.
To Our Physician Colleagues

The Clinical Positron Emission Tomography (PET) Center on the seventh floor of Mallinckrodt Institute of Radiology at Washington University Medical Center is one of the Midwest’s leading PET imaging centers, offering comprehensive diagnostic testing for patient care. The center has two PET scanners and is staffed by Mallinckrodt Institute nuclear medicine physicians, who collectively have more than 145 years of experience in nuclear medicine and PET.

Opened in 1988, the Clinical PET Center was one of the first facilities worldwide to make the transition from research to medical practice and now performs more than 20,000 nuclear medicine exams and over 2,100 PET procedures annually. Our PET specialists are full-time clinical physicians of the Washington University School of Medicine and are on staff at Barnes-Jewish and St. Louis Children’s hospitals.

More information about PET imaging and scheduling can be accessed online at http://gamma.wustl.edu/division/clinical-information.html

Call (314) 362-7418 to schedule PET examinations for your patients.

Washington University in St. Louis
School of Medicine
Mallinckrodt Institute of Radiology