A patient receiving treatment on Lithostar, a new device for extracorporeal shock-wave lithotripsy (ESWL) treatment of kidney stones. The Lithostar unit at Mallinckrodt was the first in the nation. Inset: A uric-acid kidney stone being “blasted” by shock waves from the Lithostar unit. (Inset courtesy Siemens Medical Systems, Inc.) Story on page 22.
10 **UNLOCKING THE SECRET OF CELL KILLING**

Despite professional honors and the praise of his peers, Leonard Tolmach calls himself just an average, hard-working scientist. In the meantime, he's spent the better part of 30 years quietly advancing the field of cancer biology.

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Mallinckrodt's PET team searches for something that has fascinated philosophers for centuries—the link between the brain and the mind. Studies of language have already yielded significant clinical and research results.

22 **LITHOSTAR**

The technology involved in the treatment of painful kidney stones has grown tremendously in recent years, and Mallinckrodt is at the forefront with the first U.S. installation of this advanced, noninvasive lithotripsy system.

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**ON THE COVER:**
Peter T. Fox, M.D., research assistant professor of radiology and assistant professor of neurology, leads PET team efforts to map the functional anatomy of the normal brain. Photography by Mike DeFilippo.
**Murphy Assists Examiner In Heidnik Case**

The Philadelphia Medical Examiner’s Office was stumped, so it turned to Mallinckrodt’s William A. Murphy, Jr., M.D., professor of radiology and cochief of the Musculoskeletal Section.

The problem arose during investigation of the widely publicized Gary Heidnik murder-torture case. Philadelphia law-enforcement officials couldn’t link dismembered limbs found in Heidnik’s freezer with presumed victim Sandra Lindsay. The body’s face, skull and hands had been destroyed, making standard identification methods useless.

Philadelphia’s assistant medical examiner, Paul J. Hoyer, M.D., told the St. Louis Post-Dispatch in an April 19 article that members of his staff steered him to Murphy on the basis of forensic work Murphy had done as a student at Pennsylvania State Medical Center in Hershey, Pennsylvania.

Hoyer told the Post that Murphy had developed “a very special expertise” in matching unique bone characteristics in x-ray films.

“I’ve gotten to know human bones very well at Mallinckrodt and Barnes,” Murphy was quoted as saying, “and that’s extremely helpful in doing forensic studies. Each skeleton is unique—just like fingerprints.”

Murphy positively identified the bones brought from Philadelphia by matching x rays he took of them with films Hoyer had brought from Philadelphia, supplied by Lindsay’s parents.

**Tolmach Gives Schiffer Memorial Lecture**

Leonard J. Tolmach, Ph.D., professor of radiobiology in radiology, gave the Lewis M. Schiffer Memorial Lecture at the annual meeting of the Cell Kinetics Society March 26 in Vancouver, British Columbia, Canada.

Tolmach’s talk, “Temporal Aspects of the Interaction of HeLa Cells with X Rays and Other Toxic Agents,” related to his ongoing research studying the combined effect of irradiation and other agents, especially caffeine, on cell killing. (See related story on page 10.)

Sara Rockwell, Ph.D., professor of research in therapeutic radiology in the Department of Therapeutic Radiology at Yale University School of Medicine, New Haven, Connecticut, was on the five-member selection committee for the Schiffer Lecture Award, made up of past presidents of the society. Tolmach was chosen, she says, “not because of any one experiment but because of his entire career of outstanding, innovative and fundamental research examining the effects of radiation on mammalian cells and studying the cell cycle.”

**Evens Elected To Two Top Posts**

Ronald G. Evens, M.D., Elizabeth Mallinckrodt professor of radiology and director of Mallinckrodt, has been named president-elect of the Association of University Radiologists (AUR) and re-elected treasurer of the American Roentgen Ray Society (ARRS).

Evens was elected to the AUR post at its annual meeting, March 22-27, in Charleston, South Carolina. His term as president-elect runs until the AUR’s next meeting in April, 1988; he will then become president of the association. Evens’ duties for the AUR include chairing both the Scientific Program Committee for the 1988 annual meeting and the Selection Committee for the 1988 AUR Gold Medalists.
Evens was elected to his third term as treasurer of the ARRS at its annual meeting, April 27-May 4, in Miami Beach. He has served on the Executive Council of the society for 6 years. His current term as treasurer will run until the next ARRS annual meeting in April, 1988.

The Association of University Radiologists promotes excellence in laboratory and clinical investigation, teaching and clinical practice and seeks to stimulate interest in academic radiology as a career. Its goal is to advance radiology as a medical science and to provide a forum in which university-based radiologists can present and discuss the results of their research, teaching and administrative experience. The 1,500-member association was founded in 1953.

The American Roentgen Ray Society was founded in St. Louis in 1900, and it is the oldest of the American scientific radiological organizations. The national organization works to advance medical science through the study of radiology and gives particular emphasis to the significant teaching efforts of its members. More than 1,750 physicians belong to the society.

Yale’s Gottschalk Delivers First Biello Lecture

Alexander Gottschalk, M.D., professor of diagnostic radiology and vice-chairman of the Department of Diagnostic Radiology at Yale University School of Medicine, New Haven, Connecticut, delivered the First Daniel R. Biello Memorial Lecture April 20 in Mallinckrodt’s Scarpellino Auditorium. The lectureship is named for the late, respected Mallinckrodt physician who died in June, 1986, after a long struggle with Hodgkin’s disease.

Gottschalk is a distinguished alumnus of Washington University Medical School. He has won numerous honors for his important research contributions to radiology and nuclear medicine, among them the 1987 Gold Medal of the Association of University Radiologists.

Gottschalk’s talk, “Pulmonary Embolism: Past, Present and Future,” addressed one of Biello’s long-standing scientific interests.

At the time of his death, Biello was professor of radiology and associate director of the Division of Nuclear Medicine. He was a highly productive scientist, with more than 50 journal articles and book chapters to his credit. Through a series of studies, performed in collaboration with investigators at other institutions—including Gottschalk at Yale—he developed new criteria for interpreting ventilation-perfusion lung scans. His approach, known as the Biello Criteria, has been adopted into general use by the nuclear medicine community.

The Biello Lectureship serves as a lasting testimonial to the respect Biello’s Mallinckrodt colleagues have for this unique man.

Two Students Honored With Wilson Award

Graduating medical students Brent T. Layton, M.D., and Justin Starren, M.D., were jointly honored as winners of the 1987 Hugh M. Wilson Award. Presented annually since 1968, the award recognizes meritorious work in the basic or clinical radiological sciences.

In recommending Layton and Starren as co-winners, Ronald G. Evens, M.D., Elizabeth Mallinckrodt professor of radiology and director of Mallinckrodt, noted that “it is a special time when we have two such outstanding candidates for the Hugh Wilson Award.”

Layton was nominated by Michael W. Vannier, M.D., associate professor of radiology, for his work in refining techniques for surface extraction of soft-tissue structures intracranially. “Brent Layton is an outstanding candidate,” wrote Vannier in his letter of recommendation. “He is articulate, intelligent and a very hard worker. I have found him to be remarkably innovative, very reliable and conscientious about his research.”

Tom R. Miller, M.D., Ph.D., associate professor of radiology, was similarly enthusiastic in his recommendation of Starren. “Justin has developed computer software for three-dimensional display of cardiac PET data,” noted Miller. “He is unusually energetic and self-motivated, working many extra hours and often being at least one or two steps ahead of me in carrying out each phase of the project.”

Layton and Starren received their prize at the Annual Senior Awards Night in May.
CIC Celebrates 10th Anniversary

The Cancer Information Center (CIC) celebrated its first decade July 16, with an afternoon open house for the public and an early evening gathering for invited guests.

The CIC was founded in 1977 by Carlos A. Perez, M.D., professor and director of the Radiation Oncology Center. "Dr. Perez was motivated to start a cancer center," says Lois Howland, R.N., CIC managing director, "because he felt his patients would respond better to treatment if they were well informed."

Designed to serve three primary needs—offering information, resources (e.g., free wigs and breast prostheses) and emotional support—the CIC was the first such institution in the United States.

Originally situated down the hall from its present location in the busy Barnard Free Skin and Cancer Hospital corridor, the CIC began as a small office run principally by volunteers with help from the Radiation Oncology staff. Sally Hermann played an instrumental role in starting and expanding the CIC, serving as the center's long time volunteer chairman. "Sally was one of the founding volunteers," says Howland, "and she's the only volunteer who's still here 10 years later." The CIC remains heavily dependent on its 14 volunteers for their helping hands and sympathetic ears.

Howland assumed the center's reins in 1984, when Barnard joined the Radiation Oncology Center as a cosponsor and the CIC moved to its current, expanded quarters. The new space enabled the center to help a larger patient population. In its first year of operation, the CIC saw 800 patients; last year, 9,000 people were aided by the center's services. "Every year, it seems we grow a little more," states Howland.

The CIC's continued growth pleases its managing director, but Howland would like to do still more to help cancer patients and their families. "I would like the physicians to use us more as a resource center. We look to them to send their patients here, because we want to reach out to people. "We're not just a resource center for Barnes Hospital," Howland concludes. "We want to be a community resource center, too."

Public Relations Wins Bronze Quill

Mallinckrodt's Public Relations Department was recently honored with a 1987 Bronze Quill Award of Excellence for its marketing and publicity efforts supporting the Mallinckrodt Mammography Mobile. Michaela Gold, director of Public Relations, accepted the award—in the category of Total Communications Programs—on May 19.

Sponsored by the St. Louis chapter of the International Association of Business Communicators (IABC), the Bronze Quill recognizes outstanding work in the public relations and advertising fields. The award states that Mallinckrodt "has achieved the highest standards in professional communications in competition with fellow St. Louis area business communicators."

Receiving citations of merit in the Total Communications Programs category were Shell Oil Company and Fleishman-Hillard for Union Electric. Winners in other categories included such prestigious firms as McDonnell Douglas, Ralston Purina, Maritz Motivation and Anheuser-Busch.

Glazer Elected To CT Society

Harvey S. Glazer, M.D., assistant professor of radiology, was one of two physicians recently elected to membership in the Society of Computed Body Tomography, the members of which comprise the acknowledged clinical and research authorities in the modality worldwide. Prior to the election, the society had only 49 members. Other MIR physicians belonging to the organization include Dennis M. Balfe, M.D., associate professor of radiology; the institute's director, Ronald G. Evens, M.D., Elizabeth Mallinckrodt professor of radiology; Joseph K.T. Lee, M.D., professor of radiology; Stuart S. Sagel, M.D., professor of radiology, and Marilyn J. Siegel, M.D., associate professor of radiology.

Former MIR radiologist Robert G. Stanley, M.D., now chairman of radiology at the University of Alabama at Birmingham, is also a member of the society. The other new member, Richard L. Baron, M.D., now on the staff at the University of Washington, received his residency and fellowship training at Mallinckrodt.
Wong Awarded Research Grant

John W. Wong, Ph.D., assistant professor of radiation physics in radiology in the Physics Section of the Radiation Oncology Center, has been awarded a $180,000, 2-year grant by the National Cancer Institute.

With W. Robert Binns, Ph.D., senior research scientist in the Department of Physics at Washington University, Wong is developing a practical dosimeter system for precise areal measurements of radiation using a plastic scintillator.

Water-tank dosimeter systems currently used in radiation therapy require large amounts of data-acquisition time, limiting the number of measurements that can be taken. The plastic-scintillator system Wong proposes would enable more exhaustive measurements by dramatically reducing the time needed to acquire dosimetric information. "We're talking about reducing a 10-minute measurement to 10 seconds," says Wong.

An added benefit of the plastic-scintillator system, now in a prototype form, is its relatively low cost. "A typical scanning tank ranges from $45,000 to $80,000," says Wong. "We put together this system for about $6,000."

Because of its potential, Wong has already received inquiries about the device from several universities. He notes, however, that the system is still in the early stages of development.

Institute Of Medicine Elects Ter-Pogossian

Michel M. Ter-Pogossian, Ph.D., professor and director of the Division of Radiation Sciences, has been elected to the prestigious Institute of Medicine of the National Academy of Sciences.

New members of the Institute of Medicine, which has a total active membership of 468, are elected by present active members from among candidates chosen for major contributions to health and medicine. Ter-Pogossian's pioneering role in developing the use of cyclotron-produced radionuclides in biomedical research stands as one of his principal achievements. In 1974, with his colleagues at Mallinckrodt, Ter-Pogossian helped develop positron emission tomography (PET), the first method for meaningfully assessing biochemical changes in the living subject.

As a new member of the Institute of Medicine, Ter-Pogossian makes a commitment to devote a significant amount of volunteer time on committees engaged in a broad range of studies on health policy issues. Election to the institute is both an honor and an obligation to work on behalf of the organization and its studies.

Chartered in 1970 by the National Academy of Sciences, the Institute of Medicine enlists distinguished members of medical and other professions for the examination of policy matters pertaining to the health of the public. Current projects include investigations of how homeless people might get treatment for injuries and illness and how enough physicians can be trained to cope with the ills of an increasing population of elderly.

PET Team Receives $7 Million Grant

Mallinckrodt's PET research team has received a nearly $7 million, 5-year grant from the National Heart, Lung and Blood Institute to support the continuing cyclotron production of radioactive nuclides and their use in imaging metabolism in various organs of the body.

Headed by physicist Michel M. Ter-Pogossian, Ph.D., the Washington University Medical Center
interdisciplinary PET team includes neurologist Marcus E. Raichle, M.D., pulmonary specialist Daniel P. Schuster, M.D., cardiologist Burton E. Sobel, M.D., and chemist Michael J. Welch, Ph.D.

The $6,920,838 grant extends support for the cyclotron project through its 29th year, making the grant one of the longest running at Washington University. The two cyclotrons funded by the grant produce the radionuclides used in positron emission tomography (PET) studies. The original cyclotron, now entering its 25th year of use, was the first in the nation to be located in a medical setting. Mallinckrodt is the only institution to house two cyclotrons.

Ter-Pogossian, professor and director of the Division of Radiation Sciences, helped develop PET in the early 1970s. Because of his key contributions, Ter-Pogossian is often acknowledged as the “father” of PET, but he emphasizes the importance of the PET research team, which includes clinicians, physiologists, chemists, physicists, mathematicians, engineers and computer scientists.

Evens Speaks At WHO Conference

Ronald G. Evens, M.D., Elizabeth Mallinckrodt professor of radiology and director of the Mallinckrodt Institute of Radiology, served as an invited expert witness to the World Health Organization’s (WHO) Consensus Conference on PET/MRI Imaging, April 2-3, in Tel Aviv, Israel.

Evens’ presentation, “The Modern Imaging Department—Clinical, Research and Economic Considerations,” focused on the resources, economic requirements and human skills necessary in organizing the contemporary imaging center.

The conference, sponsored by WHO and the Israeli Minister of Health, served to advise the government of Israel on the current and potential impact of magnetic resonance imaging (MRI) and positron emission tomography (PET) on clinical practice and research. The other invited U.S. experts were David Kuhl, M.D., professor of radiology, University of Michigan, and Stanley Baum, M.D., professor and chairman of radiology, University of Pennsylvania.

Hodges Honored At ASNR’s 25th Annual Meeting

Fred J. Hodges III, M.D.

Fred J. Hodges III, M.D., professor of radiology, was among 25 persons honored at the silver anniversary meeting of the American Society of Neuroradiology (ASNR), May 10-15, in New York. Founding members and past presidents of the society (Hodges is both) were presented with Tiffany crystal obelisks.

“This was the 25th meeting, and therefore an anniversary. They decided to make an issue out of it, because they felt that a lot of the founding people would not be there for the 50th,” Hodges says, half-jokingly. “If they had it now, they could have it for the majority of the people who founded the society.”

The ASNR has grown in the last quarter century from its original dozen founders to more than 1,200 members nationwide. Hodges’ accomplishments won’t be lost on his family—his uncle, brother and nephew are all radiologists, as was his late father.

Grigsby Receives ACS Career Development Award

Perry W. Grigsby, M.D., assistant professor of radiology, has been awarded the American Cancer Society’s Clinical Oncology Career Development Award for the years 1987-1990.

Grigsby, who joined the Mallinckrodt staff last July after 4 years as a resident here, including a year as chief resident, received the award for clinical research in the treatment of gynecological malignancies and for laboratory research in hyperthermia.

The award, Grigsby says, “allows me to have time to be able to do research—to have time away from my clinical responsibilities.” That extra time will be especially useful to Grigsby, since he’s currently enrolled in Washington University’s MBA program—“a student once again,” he says. “There’s a lot of business in medicine, a tremendous amount. A lot of business people don’t have the medical background, and we physicians don’t have the business background.”

Graduate business degrees for physicians, Grigsby says, “will be beneficial to the profession, as well as personally, and beneficial to the patients.”
Radiation Oncology Issues Report

The Radiation Oncology Center in May published its 1985-1986 Scientific Report. First issued in 1972, the biennial report provides a timely compilation of the center's research papers before their publication in scientific journals.

Distributed worldwide to members of the radiation oncology community, the book also serves to publicize the center itself, reviewing its organization, activities, projects, capabilities and facilities.

Included in the volume are papers from all areas of the center—Clinical, Physics, Cancer Biology and Oncology Data—with a special section devoted to the Hyperthermia Program.

Perez And Pilepich Attend NIH Conference

Carlos A. Perez, M.D., professor and director of the Radiation Oncology Center, and Miljenko V. Pilepich, M.D., associate professor of radiology, participated in the Consensus Development Conference on the Management of Clinically Localized Prostate Cancer on June 15-17 at the National Institutes of Health (NIH) in Bethesda, Maryland.

NIH's consensus development program brings together biomedical investigators, practicing physicians, consumers and others to evaluate and review the scientific soundness of health-related technologies. A primary objective of the program is to provide physicians and consumers with information on the safety and effectiveness of drugs, devices and procedures.

Perez was pleased with the success of the prostate cancer consensus conference. It produced, he says, "a very important document. We tried to outline guidelines for the evaluation and treatment of patients with carcinoma of the prostate and to point out areas that need research. I think there are a lot of controversial areas in the workup and more in the therapy of patients. I think the document will be very helpful in outlining the existing differences of opinion between urologists and radiation oncologists as to the best way to treat those patients."

Perez noted that he and Pilepich were accompanied by Herbert Lepor, M.D., Jewish Hospital's chief of urology.

Perez Radiation Oncology Text Published

Principles and Practice of Radiation Oncology, a major new text edited by Carlos A. Perez, M.D., professor and director of Mallinckrodt’s Radiation Oncology Center, and Luther W. Brady, M.D., professor and chairman of the Department of Radiation Oncology and Nuclear Medicine, Hahnemann University, Philadelphia, was published in April by Lippincott.

Already slated for a second printing, the book has sold briskly. "The initial reaction is quite favorable," says Perez. "There hasn't been a comprehensive work on radiation oncology since 1980, so the book fills a real need."

A detailed, practical text covering every aspect of radiation oncology, the book contains current, state-of-the-art treatment regimens for all cancer sites.


Vannier Participates In National Videoconference

Michael W. Vannier, M.D., associate professor of radiology, appeared as a featured panelist on the April 2 broadcast of the Computerized Medical Imaging Videoconference. Produced by the Milwaukee Area Technical College (MATC) in Wisconsin, the conference was sent by satellite to 94 sites throughout the country. Vannier's portion of the program, which consisted of a prerecorded demonstration of his three-dimensional reconstruction work and a live question-and-answer discussion, concerned medical computer graphics and image processing. Conference participants, from left, were Ralph Smathers, M.D., Stanford University Medical Center; Robert E. Alvarez, Ph.D., Digidrad Corporation; Samuel J. Dwyer III, Ph.D., University of Kansas Medical Center; Vannier; David L. Yuille, M.D., St. Luke's Hospital, Milwaukee; John A. Giunta, AT&T Bell Laboratories; Anthony Lando, Philips Medical Systems; and Joe Marion, General Electric.

FOCAL SPOT, SUMMER 1987
MEDIA FOCUS

The Cancer Information Center, cosponsored by Mallinckrodt's Radiation Oncology Center and the Barnard Free Skin and Cancer Hospital, celebrated its Second Annual Flower Day April 28, and it made for an upbeat human interest story. KMOV-TV's Al Wiman aired a brief report on the 5 p.m. newscast, as did KTVI-TV at 6 p.m., with a voice-over by anchor Kim Hindrew. Flower Day commemorates April as Cancer Control Month, and the CIC emphasizes its services to cancer patients and their families. Coping, a national magazine devoted to cancer issues, also featured a photo of the event in the "Upfront" section of its June issue. All reports featured CIC's managing director, Lois Howland, R.N.

The Wall Street Journal's Eastern Edition took note of Mallinckrodt's participation in Philips Medical Systems' "Pegasus Project," which involves research in enhancing three-dimensional images with the Pixar Image Computer. The March 20 dispatch listed Mallinckrodt in the company of Duke University Medical Center in Durham, North Carolina; Emory University in Atlanta; Johns Hopkins Medical Institutions in Baltimore; and the Mayo Clinic in Rochester, Minnesota.

Lisa Borders, staff writer for the Standard-Times of New Bedford, Massachusetts, quoted from an article by Bruce L. McClennan, M.D., professor of radiology, in a piece about one of his scientific interests, the new, nonionic contrast media. In the January 1987 issue of Radiology, the journal of the Radiological Society of North America, McClennan had written that the greater safety and patient tolerance of the nonionic contrast media "is no longer speculation, but has been proved by scientific study and clinical use."

The importance of mammography to women's health—and the central role Mallinckrodt plays—remains strongly in the public eye. Judy M. Destouet, M.D., associate professor of radiology and head of Mammography at Mallinckrodt, is highly regarded by the local television media as an articulate on-camera spokesperson for Mallinckrodt.

Destouet appeared February 19 in a KMOV-TV segment with reporter Al Wiman and patient Diane Sheehan, discussing radiation doses associated with different methods of mammography. Destouet advocated the use of the most up-to-date, dedicated mammography systems and encouraged women to ask questions of doctors and technologists.

The American College of Radiology announced its 1986 Radiology News Awards last April. KMOV Radio's Margie Manning took second place in the broadcast media category for "Stalking the Silent Killer," a four-part series that focused on mammography and breast conservation treatment. Manning's report featured MIR's Destouet; Gary Brink, R.T., B.S., FASRT, Mammography Outreach Program administrator; and Robert R. Kuske, M.D., assistant professor of radiology.
The appearance of Ronald G. Evens, M.D., Elizabeth Mallinkrodt professor of radiology and head of MIR, and Jerome R. Cox, Jr., Sc.D., chairman of Washington University's Department of Computer Science, in Digital Equipment Corporation's national advertising campaign drew the attention of the St. Louis Business Journal. Reporter Patricia Miller, in the Business Journal's April 27 issue, quoted R. Gilbert Jost, M.D., professor and chief of Diagnostic Radiology and cochief of the Computer Section. "As the largest radiology department in the country," said Jost, "we are a major contributor to research" in experimental networking systems for complex diagnostic images.

The Kennedy Space Center's (KSC) Spaceport News credited Michael W. Vannier, M.D., associate professor of radiology, with helping NASA project manager John Larson develop the computerized industrial tomographic analyzer (CITA) unit at KSC. It functions much like a typical medical CT scanner and can image items as small as a wristwatch or as large as 5-feet wide or 6-feet tall and as heavy as 2,000 pounds.

The arrival of this country's first Siemens Lithostar extracorporeal shock-wave lithotripsy (ESWL) machine (see related story on page 22) generated much attention among the national and local press. Medstar Productions, the Allentown, Pennsylvania-based medical-news production company, visited MIR April 9 to tape a procedure and to interview coinvestigators Bruce L. McClennan, M.D., professor of radiology, and Ralph V. Clayman, M.D., associate professor of urologic surgery and radiology. The report, by Medstar's Dave Lucas, was released May 1. Medstar supplies medical news to 47 client television stations nationwide through Lorimar Telepictures.

Marjorie Mandel of the St. Louis Post-Dispatch was first in the city to break the story in the Post's March 3 edition, in which McClennan compared the physical and economic effects of conventional lithotripters to Lithostar. He was quoted as saying, "It has performed to our satisfaction and expectations."

Science and medicine writer Roger Schluter covered Lithostar on the front page of the "Lifestyle" section of the Belleville News-Democrat on March 24. The feature, which included a lengthy interview with McClennan and a diagram illustrating Lithostar's functions, ended with a paragraph inviting kidney-stone patients to call Mallinkrodt for referral information.

Local television reporters were equally eager to report the news about this new kidney-stone treatment. KMOV-TV medical reporter Al Wiman, in a March 10 broadcast, interviewed Lithostar coinvestigators McClennan and Clayman. KSDK-TV, in a "Today in St. Louis" segment on March 13, featured Lithostar, McClennan and Clayman in a report by Kathy Leonard. Lisa Allen, KTVI medical reporter, spent several hours observing a Lithostar treatment, and aired an in-depth piece on March 26 at 5 and 10 p.m.

Steve Kraushaar of Washington University Broadcast Services produced an excellent TV/radio package on Lithostar and its first U.S. clinical trials. Among the electronic media outlets using Kraushaar's tape were KMOX-AM in St. Louis; KCNC-TV, Denver; WTVC-TV, Chattanooga; KRCG-TV, Jefferson City; KPRC-TV, Houston; and WDFV-TV, New Orleans.

A presentation and subsequent press conference on Lithostar at the American Roentgen Ray Society meeting May 1 in Miami Beach generated still more media interest in Lithostar. Thomas Hill, regional correspondent for the Medical Post, reported on McClennan's presentation, as did the International Medical News Group's David Branch. Miami's WPLG-TV and WTVJ-TV broadcast reports on McClennan's press conference.

MIR's Lithostar investigation also received mention in the "News Scan" section of the May issue of Applied Radiology.
UNLOCKING THE SECRET OF CELL KILLING
Leonard Tolmach has spent the better part of 30 years quietly advancing the field of cancer biology.

by Charlie Leonard
“One of our foreign colleagues kept addressing me as Dr. Phillips,” Leonard J. Tolmach, Ph.D., said in the Radiation Research Society’s Failla Memorial Lecture in April of last year. “Ever since, I’ve been a bit vague as to who I really am.”

The society wasn't vague at all, and Tolmach, professor of radiobiology in radiology at Mallinckrodt, thus received one of radiation research's highest honors. This year, in addition, he received the Cell Kinetics Society’s Lewis M. Schiffer Memorial Lecture Award, yet the scientist scoffs at the notion that he's anything special. Rather, he says, he's “just an average, hard-working scientist. There are thousands of them; every university’s full of them.”

But the average, hard-working scientist doesn’t garner such awards, nor the kind of admiration Tolmach’s colleagues and peers have for him. “He’s recognized worldwide for his scientific contributions to the field of radiation research,” states Joseph L. Roti Roti, Ph.D., professor and chief of the Cancer Biology Section in the Radiation Oncology Center.

In his nearly 30 years at Mallinckrodt, Tolmach has tried to unlock the secret of cancer cells’ sensitivity to radiation and other toxic agents. “The general statement,” Tolmach says, “is that we are interested in the mechanism by which radiation kills cells. This process is, after all, the one that the radiation oncologist is making use of when he treats cancer with radiation. The hope is that as more and more details are learned about the mechanism by which cell killing occurs, the oncologist will be in a position to improve treatment so as to maximize the killing of cancer cells and minimize the killing of the normal tissue cells.”

This line of research has led Tolmach to several discoveries that have had a lasting impact on radiation research in particular and cell biology in general.

In 1963, Tolmach and Japanese postdoctoral fellow Toyozo Terasima devised a method for collecting synchronous mammalian cells for study. Tolmach noticed that cells in mitosis, just before dividing, rounded and loosened their attachment to the glass Petri dish. He suggested to Terasima that he try to wash off the cells, and Terasima took it from there, rinsing them from the dish with a stream of growth medium. Terasima’s and Tolmach’s mitotic collection method made a major impact on the study of the cell cycle. Previously, researchers couldn’t easily study cells in discrete stages of the cycle. Earlier efforts at synchronizing cells disturbed cell metabolism, and very few types of cells—such as certain slime molds—grow in synchrony naturally.

“It has resulted in a tremendous amount of follow-up,” says George Hahn, Ph.D., professor of therapeutic radiology at Stanford University and president-elect of the Radiation Research Society. “He and Dr. Terasima applied it to radiation, but a lot of people have applied it to all kinds of other things since then. It must be one of the most widely cited papers of that period.”

Tolmach characteristically downplays the discovery (“People who have good sense use it,” he chuckles) and just as typically, one learns, finds a way to make it seem, well, fun. The following is from Tolmach’s Failla Lecture presentation:
Unlocking the Secret of Cell Killing

Mitotic Selection
(should be chanted nasally, to a guitar accompaniment)

When HeLa cells, growing stuck to a flask,
get close to mitosis, they prepare
for the task:
you tend to come loose. If you persevere
you can pull them free with a little shear
from a stream of medium,
or a spin,
or a shake.

Now you plant them again in a Petri plate
and they start off together; they seem to relate:
for the first 7 hours they’re all in G1,
and S, in each cell, has for sure begun
by 12 hours
(you can pulse with thymidine).

Well, away they go across G2,
and by 15 hours the fastest are through
and enter mitosis. Now, we have found
that by 22 hours all have been around
the cycle
in synchrony
more or less.

Tolmach's work with HeLa cells, radiation and caffeine
has been published, so far, as an eight-part series in the journal Radiation Research. Earlier work in the late 1960s resulted
in the elucidation of the concept of potentially lethal damage
(PLD) inflicted by radiation on cancer cells. When a cell receives
the initial radiation insult, it sustains a tremendous amount of
damage, but it is able to repair much of the damage by itself if
left untreated further. Tolmach and then-graduate student Robert A. Phillips found that the amount of cell killing can be modified by
altering the incubation conditions under which an irradiated
culture is maintained. Caffeine is one of the agents Tolmach and
his colleagues have used to enhance the expression of PLD
in cancer cells.

AUDRI is so important
to Beetham’s and
Tolmach’s work that
she has her own
nameplate on the
door:

The PLD concept “has had quite a number of implications in
terms of the genetic makeup of cells,” Hahn says. “I think it can be quite important. Dr. Tolmach has been at it for several years, and he is, without a doubt, the authority in the world on it.”

Carlos A. Perez, M.D., professor and director of Mallinckrodt’s Radiation Oncology Center, says Tolmach’s studies have added to the working knowledge of oncologists. “Also in collaboration with Dr. Terasima,” Perez says, “he showed that mammalian cells have a different response to radiation according to their position in the reproductive cycle. That is a very important concept in trying to understand problems with fractionated radiotherapy,” which involves dividing a dose of radiation into increments administered at intervals over time. Potentially lethal damage, Perez continues, “is another very important concept in our understanding of fractionation and of the potentially increased effectiveness of radiotherapy combined with chemotherapy.”
Although one doesn't often think of the study of cell biology as a roaring good time, working in Tolmach's lab "is always interesting and unusual," says Karen L. Beetham, Ph.D., instructor in cancer biology in radiology and Tolmach's collaborator since 1979. Their lab, she says, is characterized by "a steady stream of gadgetry." Tolmach's gadgets allow him and Beetham to include a tremendous amount of detail in their studies—detail that otherwise might be missed.

The first of the Tolmach lab gadgets was produced in the late 1950s with technologist Allan Rossel: a foot-pedal-operated Bunsen burner. An equipment manufacturer agreed to produce it commercialiy, and Tolmach still gets an occasional, rather modest royalty check. "Enough to buy a ham sandwich," he deadpans.

Other, more important devices followed: a multiplexed time-lapse photomicrography system, developed in Tolmach's lab, which allows for several separate time-lapse films to be taken simultaneously of multiple cell cultures with a single camera and microscope; an automated device for continuous labeling of cultured cells, also developed here at the university in Tolmach's lab; and an automatic pipette washer, developed with a professor of molecular biology then at Vanderbilt University.

Tolmach's favorite brainchild, though, is AUDRI.

AUDRI is so important to the work Beetham and Tolmach are carrying out that she has her own nameplate on the laboratory door. "AUDRI is a way of life," Tolmach says.

AUDRI developed more than 15 years ago, is an "AUtomatic DRug Injector," a robot that carries out some of the more tedious tasks the lab's research requires. "The problem," Tolmach explains, "is that if one wants to explore what happens over a protracted period of time, by which I mean more than a working day, one has to come in and do the manipulations by hand. To do this after working hours requires a devotion beyond the call of duty that is not easily obtained. So we decided we needed a robot to work all night long. The product is AUDRI. Many individuals contributed to her development," Tolmach is quick to point out, "especially several who were associated with the Biomedical Computer Lab at Washington University."

AUDRI consists of a cell incubator containing a helical shelf that holds 48 pairs of culture dishes; a workstation comprising suction cups, for raising and replacing dish lids, and manifolds of tubing, for removing and replacing small volumes of drug-containing growth medium; and, in its other section, a chamber housing pumps, tubing and up to four different treatment solutions to be injected into the cultures in the incubator.

AUDRI was initially controlled by a crude, paper-tape-driven computer known as HERO (HElix ROTator), and in fine Tolmach style, AUDRI and HERO were married in a ceremony marked by formal invitations and a champagne reception. HERO, however, was a victim of advancing computer technology and was replaced by an Apple microcomputer. A divorce ensued.

"AUDRI indeed is useful," Tolmach says. "We would not be able to generate the kind of data we do generate without her."

"It's quite a lot of fun," says Sara Rockwell, Ph.D., of AUDRI. Rockwell is professor of research in therapeutic radiology at Yale University School of Medicine, a past president of the Cell Kinetics Society and a longtime admirer of Tolmach's work. "When you think about the day in which that was built, and the way they put it together, it really was quite an inventive little piece of machinery. It predates much of the automated biological equipment in the laboratories now."

One might notice that Tolmach's name often appears last on his papers—behind those of his coauthors and students. "He's very modest that way," says Beetham. "Not too many people would do that; it's very rare."

Rockwell agrees. "It's not only modesty," she says. "I think he also views himself as a teacher, which is something that many of us in science forget. And he takes a great interest in the people coming out of his lab—what he's giving them in the way of a springboard for their future success."

"When I was a postdoc, which is now 20 years or so ago," Rockwell recalls, "he was already a very highly acclaimed scientist. And yet he took time at conferences to talk to the students and to answer questions, even though they were sometimes stupid questions. He never made you feel as though they were stupid."

"He's a very human person," Stanford's Hahn adds. "He's fun, he's full of ideas. He's a skeptic, which is really what a scientist should be."
PET researchers establish new connections between the mind’s activity and the brain’s anatomy.

by Cliff Froehlich

Explorers, civilization’s point men, have long catalogued the visible world—defining boundaries, tracing sources, lifting mystery’s veil. However remote or inaccessible, the near and far reaches of the earth’s exterior landscape have been surveyed, pictured and permanently recorded with T-square-and-protractor precision.

Ironically, man’s closer-to-home interior topography—the unseen lay of the mind’s land—remains less well charted. The neuronal pathways on which thought travels when people speak, attend or remember are marked only in light pencil, a rough sketch with minimal detail.

In Mallinckrodt’s Division of Radiation Sciences, cartographers of the human brain are now beginning to erase those tentative lines, using positron emission tomography (PET) to map with startling exactitude the centers and connections of higher function in man.

Discoveries already made promise to challenge the researcher’s age-old models of language production and to meet the clinician’s immediate and future needs for assessing brain organization.

Peter T. Fox, M.D., research assistant professor of radiology and assistant professor of neurology, prepares to insert an IV line before starting a mapping study on PET VI.
MAPPING THE BRAIN

Peter T. Fox, M.D., group leader of these initial expeditions into unknown cognitive territory, describes the project's long-term end as "mapping the functional anatomy of the normal brain," providing a full and objective representation delineating the specific areas of the brain that control human behavior, from its simplest manifestation to its most complex.

A research assistant professor of radiology and assistant professor of neurology, Fox has pursued this goal since arriving at Washington University Medical Center as a neurology resident in 1980. "My interest through all that time has been in developing ways we can map the brain, starting first with applications in normals and then moving to applications in disease. As far as I can see, PET is the most powerful means of accomplishing that."

When Fox began his first experiments in Radiation Sciences as a resident, however, he quickly discovered that tapping PET's apparent potential as a mapping tool would require considerable preliminary work. Simply forcing the brain to work long and hard enough during the 40-second PET scan proved difficult.

"A fair amount of time went into the early studies here for developing paradigms to continuously stimulate the brain over a period of time," states Marcus E. Raichle, M.D., professor of radiology and neurology and supervisor of neurological PET research at Mallinckrodt. "How much information does the brain have to receive to produce a response that the PET can measure?"

As the researchers gained experience in answering such questions, new—and singular—techniques began to emerge (see sidebar). These sophisticated methods—developed specifically for mapping purposes—give Mallinckrodt unique capabilities. "Our mapping data consist of averaged, subtracted images," says Fox. "In that sense, they're going to be totally unfamiliar to anybody in the world doing PET unless they're here."

While the means of obtaining, interpreting and manipulating the PET data were being refined, the groundwork for mapping higher cognitive functions in man was also being laid.

"We've mapped motor areas in the brain involved with hand movement, eye movement and speech and sensory areas involved with vision and tactility," states Fox. "That's helped us get the landscape laid out of what areas are involved in just the sensation and the raw motor tasking. Having gotten a feel for the basics, we're going on to more complicated functions, drawing on what we've learned in the primary neural systems."

The first of these more complex studies—language mapping experiments begun less than 2 years ago in conjunction with the McDonnell Center for Studies of Higher Brain Function—has moved forward with unexpected speed. The experiments—even at this early juncture—have yielded significant results, providing both new theoretical models of brain function and useful clinical tools.

Michael I. Posner, Ph.D., professor and director of the Division of Neuropsychology, and Steven E. Petersen, Ph.D., research assistant professor of neuropsychology, both of the Department of Neurology and Neurological Surgery, serve as

PET Methodology

Developed at Mallinckrodt in the early 1970s—under the direction of Michel M. Ter-Pogossian, Ph.D., professor and director of the Division of Radiation Sciences—positron emission tomography (PET) assesses biochemical processes in the living subject, producing an image of function rather than form.

In PET studies, biologically important elements, such as oxygen, are labeled with short-lived, cyclotron-produced radioactive nuclides. These nuclides, after inhalation or infusion, travel through the bloodstream in routine fashion, serving as tracers of normal physiological activity. As the nuclides decay, they emit positively charged electrons, or positrons, which in turn strike electrons, producing an annihilation reaction and releasing energy in the form of photons. A circular array of detectors measures this energy, localizes the source of each annihilation detected and ultimately yields a picture of circulation or metabolism. Seven cross-sectional slices—akin to computed tomography (CT) images—result, with areas of activity glowing bright.

Simply put, because blood flow and metabolism increase during activity, PET enables the mind's explorers to identify those areas of the brain working harder during a specific assigned task. Using PET as surveying instrument, a functional brain map can be rendered. Useful maps, however, require the measurement, anatomical localization and consistent replication of often subtle regional changes in brain activation.
levels. In practical terms, several problems need solution before successful mapping can occur.

Mark A. Mintun, M.D., assistant professor of radiology in the Division of Nuclear Medicine, has played a key role in developing the various statistical approaches necessary to overcome these difficulties. “Lots of people talk about PET being able to map the brain,” says Mintun. “They take a single picture of the brain at rest or doing something, and they say, ‘You see this area over here? This is what I think is going on.’ The science is very weak. It’s nice for pictures, but the real bottom line is it’s guesswork.”

“We’re in a new world here. We’re looking at responses purely and precisely, and that gives a new dimension to our mapping.”

To eliminate that element of subjectivity—eyeballing a PET scan to discern the area of activation—the researchers developed a means of directly subtracting images. Peter T. Fox, M.D., research assistant professor of radiology and assistant professor of neurology, explains: “Instead of getting one image at rest and another image during stimulation and then looking at them side-by-side, we overlay and subtract them to get at a new type of image—just of the difference.”

“We do two rapid experiments and subtract the images, and now you see only the change,” Mintun states. “This is dramatically different. There’s no question whether you see it or whether the person responded. It’s just not guesswork anymore.”

Subtraction also enables a far more precise localization of the response. The PET VI scanner currently used in mapping experiments has a resolution of only 18 mm. Using the subtraction strategy, however, the researchers are able to localize the area activated with vastly improved precision, to between 1 and 1.5 mm. Mallinckrodt’s newest instrument—Super PET III—will have an operational resolution of around 7 mm, but its ability to localize a response may be as low as 300 microns, nearing the size of the cortex’s primary functional unit.

“We’re in a new world here,” Fox asserts. “We’re looking at responses purely and precisely, and that gives a new dimension to our mapping.”

The subtraction images provided a powerful aid for identifying responses, but a technique for pinpointing the exact anatomical location of the activity was still required. “We needed ways of describing where responses took place in clean, precise terms,” says Fox. “We wanted to have a coordinate system, so we could say whether two responses were in the same location and give that statistical significance.”

The approach eventually devised is based on neurosurgical stereotaxy, a well-accepted method that uses fixed landmarks in the brain or in the skull as anatomical guides. By placing the PET data into stereotactic three-dimensional space, the researchers are able to assign x, y and z coordinates to a response—its latitude and longitude, in a sense—relating it to an exact anatomical location in a reference atlas.

This conversion of PET data into a stereotactic framework provides an important springboard for clearing another mapping hurdle—sensitivity. “When we look at relatively subtle activations,” says Fox, “the noise level of the image gets very close to the response magnitude. If we’re trying to map language, for example—in which neuronal activity is less robust—we need some way to suppress noise. A very simple way is signal averaging: You make the measurement any number of times and then average them.

“Because we put everybody into the same stereotactic coordinate space—each brain, in essence, is normalized—we can thus average across subjects. The random background noise cancels, whereas task-related focal responses are spatially consistent and sum. Noise goes down, and we’re left with the response standing out clearly against the noise. Things we never possibly could have detected, we now detect easily.” □
MAPPING THE BRAIN

Left: Serial model. Speaking a written word follows a path from the primary visual area to the angular gyrus, where a sound is associated with the visual word form. The word then moves to Wernicke’s area, where meaning is attached. The word is next relayed to Broca’s area, where it is programmed for articulation, before finally moving to motor cortex. (After Geschwind, Scientific American, September, 1979.)

Right: Dual-route model. Speaking a heard word involves areas similar to those suggested by the accepted neurological model; however, the roles those areas play in the two models are not the same. For example, the supramarginal gyrus, near Wernicke’s area, serves as the area for activation of a stored word form in the dual-route model, but it does not have the semantic, meaning-association function ascribed to Wernicke’s area by the serial model. Speaking a written word is distinctly different. After a word enters the brain by the visual cortex, visual word forms are activated in the nearby lateral visual cortex, without the involvement of the angular gyrus or Wernicke’s area. Broca’s area is still involved, but it is considered primarily a movement-programming area. The semantic function served by Wernicke’s area in the serial model is filled here by Area “45” of the frontal cortex, whether the word is heard or seen. This is the area active when a verb is generated by the subject in the initial PET language experiments.

important collaborators on the language project.

“As the mapping studies evolved,” says Raichle, “we began to attract the attention of people who had a much more sophisticated idea of what is worth looking at in the human brain. We’ve established this wonderful interface with people such as Posner in cognitive psychology.”

“We’d been dabbling with language a little bit,” Fox explains, “and we decided this would be a good pilot study for us to work on together. When Posner joined the group, the language experiments really took on a new character. His background in analyzing the mental subcomponents of human cognitive tasking added a new level of expertise to what we were doing.”

Petersen, a neurobiologist, provided the bridge between the somewhat separate worlds of the cognitive psychologist and the neurologist. In Petersen’s view, this gathering of researchers from different fields is the key to the laboratory’s success. “The idea here is that one person can’t know it all,” says Petersen. “We’re able to ask much more precise questions because of the interlocking expertise of the people involved.”

The cognitive inquiries the research group is now making involve activities that Raichle cites as “uniquely human.” Petersen describes these higher-level mapping studies as a search for “the things that take place between sensation and motor output, things related to thinking, not simply to moving your hands or eyes. We’re looking at an area philosophers have been examining for a long time—the relationship between the mind and the brain.”

When Posner and Petersen formulated their initial PET experiments with Fox, two trials were started in parallel: The first—believed to be the simpler and more viable—was a study of attention using rapid, ballistic eye movements, and the second—“the more ethereal,” in Petersen’s words—was a study of language.

Surprisingly, says Posner, “the language work has gone the fastest, even though everyone would think that’s by far the more difficult problem.” Work with attention continues—it remains Posner’s primary interest—but the language experiment has thus far been pursued with more vigor.
because of its positive early results and unique nature. “It has a lot of romance to it,” Petersen states. “We’re able to look at something only humans can do and get a real handle on the neural mechanisms of how language processing is organized in ways that I don’t think have been done before.”

In designing the language experiment, the researchers took a much more circumscribed approach than such a broad description indicates. “It’s a little presumptuous to say it’s language, because it’s not the whole problem,” says Posner. “What we’ve tried to do is isolate a part of language that is fairly well understood from some points of view. By doing that, we hope to understand the neurosystems that support lexical access, the taking in and understanding of individual words.”

“We aren’t studying language in its full-blown syntactic and emotional context,” Petersen confirms. “We’ve tried to simplify the really complex issues in language down to a set of problems that can be attacked experimentally using PET.”

The experimental paradigm that eventually resulted from early trials consists of four hierarchical stages, proceeding from a simple task to tasks of steadily higher levels of complexity. During the first task, the subject simply stares at a fixation point on a video monitor. In the second task, the subject watches as a list of nouns passes by on the screen. The third task requires the subject to repeat those nouns aloud. In the fourth and final task, the subject generates verbs, or uses, associated with the nouns flashing by (“drive” would be the use for “car,” for example).

Once the data are acquired, the researchers subtract each image from the image following. By subtracting the first task from the second, areas involved with passive word processing are identified. In subtracting the second from the third, areas of motor output and active word processing are pinpointed. The last subtraction—the third from the fourth—yields those areas used for a strictly mental event.

“What we’re left with at that final stage,” says Petersen, “are areas activated by cognition, by what went into generating the verb, or semantic associate.

“This has a lot of romance to it. We’re able to look at something only humans can do.”

When we first did that, I think Peter Fox and I were both sitting there saying the PET isn’t going to be sensitive enough to see this. But we get clear activation at that stage.”

After a complete series of subjects underwent the language experiment using visual stimuli, the researchers repeated the study with auditory input—nouns were heard rather than seen—to further cross-reference the data.

“At the sensory stage,” explains Petersen, “the results should be different, but the same operations should go on at the highest stage. That appears to be what we have: At the generate-verb stage, we get very similar areas activated for both auditory and visual input. The data give us a lot of confidence, because the activation is replicable not just across a bunch of people but across sensory modalities.

“That is very, very pleasing. At the generate stage, we really think we have areas that are related to cognition itself.”

The results of the language mapping were as unforeseen as they were impressive. “We found areas similar to those identified by studies of brain lesions and behavioral techniques,” explains Petersen, “but the tasks with which we find the areas don’t seem exactly appropriate to some of the accepted models.”

The standard neurological model of language processing—the taking in, understanding and speaking of a word—was summarized by Geschwind in 1979 (see illustration). “His approach to speaking the written word is very serial,” Petersen says. “Information goes from A to B to C to D in one straight line. Seeing a word starts in the primary visual cortex and moves forward to the angular gyrus, where it’s phonologically encoded—a sound is associated with it. Information is then shipped forward to Wernicke’s area, where a meaning is added on. That is piped forward to Broca’s area, where it is programmed for production and output. Finally, that goes to motor cortex and out.

“The areas that we see light up don’t fit with this model perfectly. When we did our original studies, which were all vision and very meaning based, we never found any activation in Wernicke’s area or the angular gyrus. When that first occurred, we were all horrified that these areas weren’t lighting up. Mike Posner, however, took a step back and said, ‘Well, this fits
with what I know."

"In cognitive psychology, there is another picture about reading words," Posner continues. "It's the idea that visual print can be translated in two ways. You can sound a word out, or if you're quite familiar with reading, you might have an ability to take that print and translate it into semantic descriptions without sounding it out."

"It seems possible," summarizes Petersen, "for a word to come in and have 'wordness' associated with it very early. That information then has access to parallel routes—one for phonology and one for meaning. So you can access meaning without having to translate the word into a sound."

The researchers initially were concerned that the absence of activation in the expected areas was caused by a lack of sensitivity in the PET itself. The auditory experiments that followed, however, quickly disproved that hypothesis, producing clear activation near the angular gyrus and Wernicke's area.

Two related discrepancies with the classic model of speech production were thus immediately evident:

■ The processing of words is distributed—that is, there is no single pathway for language comprehension.

■ The decoding process is activated very early and is virtually involuntary, taking place in the immediate environs of the sensory system through which the input is received.

The findings' third and final variance with accepted teaching involves Broca's area, long thought to be a language-specific area for speech production. "During our generate-verb task," says Fox, "we get a nice, clean response in front of Broca's area by about 2 cm [Area "45" in illustration]. If you speak, Broca's area is certainly active, but if you just wriggle your tongue, it's also active. If you wriggle your fingers, it's active. If you think about wriggling your fingers, it's active. So it's not Broca's area that's involved in semantic linking—it's this anterior area—but most lesions in the vicinity cover both."

As the PET data mount, it is becoming increasingly clear that standard neurological thought about the processing of words is, in Fox's blunt assessment, "just fundamentally wrong."

"The results are, I think, going to be very interesting," agrees Posner. "They'll require a reevaluation of what in clinical neurology is an accepted view of the anatomy of word processing—a view that comes from studies of 100 years ago."

"A big question people have had about PET," Petersen believes, "is whether it can tell us something new. I think the language work gives us a positive answer. We appear to be able to arbitrate between two competing theories—the dual-route and the serial models—and say it looks very much like the dual-route is correct."

In addition to providing new perspectives on language function, the mapping experiments have pointed the researchers in several promising directions. An immediate—and highly practical—result of the language study is its apparent usefulness in the clinical arena as a preoperative test for locating language function in the brain. Because language is generally housed, or lateralized, on a single side of the brain—the dominant hemisphere, usually the left—it becomes important for the neurosurgeon to identify that side before operating.

"A test to determine language dominance is usually done in patients for whom surgery is contemplated for the control of epilepsy," says Raichle, "because the area in which the seizures originate might be on the side of the brain where language is housed. You've accomplished nothing if you've taken out a damaged part of brain and encroached a bit on normal brain."

At present, a Wada test is performed to provide the neurosurgeon with this key language-location information. The examination requires threading a catheter through the groin into the left internal carotid artery. A dye is given and x-ray taken to verify the catheter's position in
the patient is instructed to speak, and a short-lived barbiturate is then injected. If language is located on the left, the patient will become mute for approximately a minute. After the subject recovers, the catheter is redirected into the right internal carotid artery, and the procedure is repeated. In this instance—given left-hemisphere dominance—speech should not be impaired.

"That has been the traditional way of determining language function," states Sidney Goldring, M.D., professor and head of the Department of Neurological Surgery. "Although the Wada test has been and is a very valuable examination, it does carry a risk with it since it's an invasive procedure. There's a chance of stroke—that happens infrequently, but it can occur."

"This is not a zero-risk procedure," echoes Raichle, "and the best it can do is tell you that language is in one hemisphere or the other. But it isn't the whole hemisphere that's involved—there are some very discrete areas that relate to language."

During the PET mapping experiments, many of these language-specific areas were precisely localized, with the generate-verb task providing a strong indication of the dominant hemisphere. Tests are now under way comparing results from the two procedures in the same patients. "So far, it's highly encouraging," says Raichle.

"We're as good as the Wada test and much more specific in pinpointing language areas."

"The beauty of the PET examination," Goldring states, "is its great potential relief to the patient. The test is a noninvasive procedure with little risk. The probability that it will become a very useful clinical tool is pretty high."

Once the researchers satisfactorily demonstrate the clinical utility of PET language-location studies—a more comprehensive sample is still needed—it's expected that the Division of Nuclear Medicine will assume responsibility for the test's implementation as a routine clinical examination.

Nuclear Medicine's clinical PET facility on the seventh floor is now under construction. "I wouldn't be surprised that within a year this test is a major part of a workup for patients undergoing surgery for these sorts of problems," says Raichle.

Peering somewhat into the future, Fox envisions further clinical uses for PET mapping. "We may be able to offer neurosurgeons the ability to do preoperative functional mapping on patients to guide their intervention. What the surgeons do now is electrically stimulate the brain to establish landmarks. What we should be able to do is give the neurosurgeons a map on a skull x ray or CT scan indicating the specific spots where functions are. So the surgeons would know beforehand whether the tumor to be resected lies in front, behind, left or right of a function they want to avoid disturbing."

Although Goldring is intrigued by the possibilities such a functional brain map would offer—"That kind of information would be extremely important"—he is careful to sound a note of caution. "You're dealing with research here—if you hit a snag, it may take a good deal longer than you anticipated. But this isn't just science fiction or speculation. It has the potential of being worked out."

The mapping researchers also exercise self-restraint in discussing their early results, but as Petersen admits, "It's hard not to be excited about the project. PET offers a way to do real human neurobiology that wasn't open before. As we learn, the scientific applications are really boundless: They're limited only by the experimenter's imagination."

"The work toward mapping the human brain isn't something that I can ever see an end to," concludes Fox. "I keep seeing new ways of using PET to piece apart normal function and to understand psychiatric, neurological and vascular disorders. "It's an area in which exploration is just beginning."
As Ray Dolan lay on the table last March waiting to receive a revolutionary treatment for kidney stones, he wasn’t worried about pain or discomfort. Instead, Dolan says, “My curiosity was piqued. I was more interested in the technology and the procedure than I was in what it would feel like.”

The 64-year-old retired head of national sales for The Equitable in New York had traveled to Washington University’s Mallinckrodt Institute of Radiology from his home in New Canaan, Connecticut.

He had come for treatment on a new machine called Lithostar, the latest U.S. arrival in the fast-changing world of extracorporeal shock-wave lithotripsy (ESWL) technology. The Lithostar at Mallinckrodt was the first in the nation, and Ray Dolan was one of the first 25 patients in the United States to receive the new treatment.

The medical staff had demonstrated to Dolan how the simple procedure would work. It promised great relief to Dolan and patients who, like him, are afflicted with this extremely painful and fairly common malady. Roughly one person in ten will develop some
type of urinary tract stone in a lifetime; men are affected three times more often than women. In six of ten of these patients, the stone will pass spontaneously, but for the remainder, surgery had been the only answer until very recently.

Bruce L. McClennan, M.D., professor of radiology and head of the Abdominal Imaging and Genitourinary Sections at Mallinckrodt, says Ray Dolan was the perfect Lithostar candidate. “He had a solitary stone in the left renal pelvis of a nonobstructed kidney, which is a perfect position for treatment. And the stone was dense enough to focus on easily.” Dolan came to St. Louis because his heart condition precluded the use of the general anesthetic often associated with treatment on conventional water-bath ESWL machines.

McClennan, who presented the nation's first report on Lithostar at the American Roentgen Ray Society meeting in Miami Beach last May, is coinvestigator in the U.S. Food and Drug Administration (FDA) clinical trials with Ralph V. Clayman, M.D., associate professor of urologic surgery and radiology at Washington University School of Medicine.

Clayman has seen kidney-stone treatment advance with remarkable speed in the relatively recent past. The first nephrectomy, or surgical removal of a kidney, occurred in 1869. “In the first 100 years,” Clayman says, “the only treatment for kidney stones was open surgery. Between 1976 and 1982, the entire field of surgical therapy for renal stones changed from open surgery to percutaneous techniques, a relatively simple procedure performed through a small incision in the skin. Between 1982 and 1987, the treatment became largely one that can be done extra-corporeally with ESWL.”

ESWL “blasts” the kidney stone with shock waves until the stone is broken up into small fragments that can be passed with the urine. Clinical trials on the first lithotripters began in Europe in 1980. Developed in Germany and still in use nationwide, these units required the patient to be placed into a bathtub containing ionized, degassed water through which the shock wave passes. The wave itself, generated by an electrode analogous to a spark plug, is focused by an ellipsoid lens to attain a focal area small enough to hit the stone. The shock wave, “aimed” with the aid of fluoroscopy, is triggered by the patient’s electrocardiogram (ECG) in the water-bath system.

The water-bath lithotripter provided the first breakthrough into noninvasive treatment of kidney stones—a major feat. Nevertheless, some problems remain with this early form of lithotripsy. “One problem with the original ESWL that Lithostar overcomes,” explains McClennan, “is the need for general or epidural anesthetic and thus the need for a stay in the hospital.” With the Lithostar, patients normally require only a local anesthetic and can be treated as outpatients.

Gallstones are the next step for lithotripsy. Tests have already begun at Mallinckrodt.

The water bath, an integral part of traditional lithotripters, presents other problems as well. The bath itself puts limits on the height, weight and girth of patients who can fit in the bath. Lithostar, because it involves only a tabletop and no bath, can treat many patients who otherwise would be ill-suited for water-bath lithotripsy.

The electrode that generates the shock wave in a water-bath lithotripter is a consumable product that must be replaced after 800 to 1,000 shocks—often during treatment, adding to its expense and complexity. Lithostar’s shock wave, on the other hand, is developed within a self-contained shock tube (there are two tubes in the table) filled with degassed water, eliminating the need for the bathtub.

The Lithostar system generates the shock wave by electromagnetic displacement of a steel membrane, often compared to the functioning of a loudspeaker, bypassing the need for consumable electrodes. The shock wave itself is less forceful in the Lithostar than in the water-bath system, and it dissipates immediately on hitting the stone—no pain results from the wave exiting the body as it does in the water bath—thus helping to do away with the more complicated epidural or general anesthetic procedures. In Lithostar treatment, the patient’s flank is simply infiltrated with a local anesthetic.

Other Lithostar design improvements include the housing of the fluoroscope and hard-film x-ray system within the table, for immediate localization of the stone and evaluation of treatment. More importantly, respiratory gating of the shock wave allows it to enter the body when the stone is precisely in...
Ray Dolan noticed Lithostar's gating feature right away. "I was conscious at first of the number of shocks that came when I was exhaling and that none came while I was inhaling. I started playing a game with how long I could exhale and how many 'tappings' could take place. I got it up to 12, I think."

Dolan's stone formation was timely, considering the speed with which stone treatment is moving. "In 1977, he would have had open surgery. In 1982, he would have had percutaneous stone removal. The stone machine didn't really become available in this country until late in 1984," says Clayman.

But the ESWL system available in recent years would not have suited Ray Dolan. Bernard Lytton, M.D., chief of urology at Yale University Medical Center, sent Dolan to Mallinckrodt because his heart condition restricted the treatment options available to him back East.

A myocardial infarction Dolan suffered in 1972 and his reliance on heart medication made his doctors wary of even relatively simple percutaneous surgery or water-bath lithotripsy, because of the risks of anesthesia. Dolan's doctors determined that since his stone was so large ("If I'd passed it, I'd be in the Guinness Book of World Records," Dolan jokes) and since a Lithostar would not be available nearby for quite some time, he should travel to St. Louis for the treatment.

"Once the procedure began," he says, "the tapping was of no consequence. The whole atmosphere made it very comfortable for me. I was not apprehensive at all. And with the heart disease I have, I was feeling very good, because both my ECG and breathing were on monitors. I felt very secure."

Dolan and other Lithostar patients (and their insurance companies) will also feel comforted by the cost of Lithostar treatment, which, once it is approved and in relatively widespread use, should be less than the cost of treatment on water-bath lithotripters, McClennan says. Patients will save the cost of anesthesia and, since it's an outpatient procedure, the cost of a hospital room.

McClennan stresses the versatility of the system. At Mallinckrodt, he says, Lithostar is "proving that it is an all-purpose, do-it-all-on-the-same-spot table." One successful percutaneous nephrostomy has already been performed on the Lithostar table here, as have stent placements, endoscopy and stone manipulations. "With Lithostar, you don't need to buy a dedicated lithotripsy system,"

McClennan says. "Instead, you can buy a room that can be used for surgery, radiology and all forms of kidney-stone treatment.

"This flexibility will make Lithostar affordable for a large community hospital with a large patient-capture area," McClennan says. "The concept of ESWL will eventually become widely disseminated." Thus out-state kidney-stone patients, in the near future, won't need to travel to large metropolitan areas for treatment.

Lithostar's adaptability promises to provide a cost-efficient hedge against the ever-quickening advancements in stone-treatment technology. McClennan and Clayman agree that the next generation of ESWL will take a truly tremendous step forward. "Future technology will use ultrasound focusing and a shock wave gen-

The versatile Lithostar system allows localization of kidney stones and evaluation of treatment to be done on the same table, with the patient remaining in the same position. The table is also useful for a variety of other radiological and urological functions.
Coinvestigators Clayman and McClennan explain the advantages of the new ESWL system to a group of visiting Texas physicians.

erated by a piezoelectric source,” Clayman says. “This procedure can be performed with no anesthesia. And it’s extremely inexpensive—perhaps as low, from the standpoint of consumables, as $10 per treatment. These machines are already being tested in Europe and are expected in the United States within a year for testing.”

Gallstones are the next step for lithotripsy, McClennan says. Lithostar and water-bath machines have been used to break up gallstones in Germany, and gallstone tests with Lithostar have already begun here at Mallinckrodt.

Extracorporeal treatment of gallstones, which are more common than kidney stones, could represent a major leap away from surgery and toward noninvasive treatment.

“The real story,” McClennan says, “is that the technology is leading the science. We’re out rushing to do the research—to substantiate scientifically the usefulness of the new technology.”

It remains for McClennan and Clayman to improve Lithostar’s performance and to add to the relatively small pool of scientific data on this latest ESWL technique. McClennan is enthusiastic about both, 6 months after Lithostar’s installation.

“During the entire month of May, we didn’t have a single failure,” he says. “We can treat almost any stone we can visualize. I’m quite confident about that.”

Continuing to improve patient tolerance is paramount in this early Lithostar research, McClennan says. “Down the road, improvements will make the shock more powerful at a still-lower energy. That means even less anesthetic would be required, and it would make the treatment of larger patients possible by focusing even deeper in the body. We’ll continue to modify the system.”

However, McClennan cautions, “There are still some unanswered questions about the long-term success of ESWL. We’re just now beginning to follow patients treated 2 years ago with water-bath ESWL. It takes several years to evaluate precisely any new technology.’’

More immediately, for Ray Dolan, his treatment with Lithostar means he has beaten surgery for the second time in his life. The active, energetic executive refused recommended bypass surgery after his myocardial infarction in 1972. “I said, ‘Well, surgery is plan A. What’s plan B?’ The doctors were a little upset with me, but they said I’d have to lose 50 pounds and run 5 miles a day. I did, and I’ve been doing it for 15 years now.”

By getting this quick, noninvasive, simple treatment, Dolan not only avoided surgery, anesthesia and their risks, he was barely even thrown off his pleasant new routine of semi-retirement. He still runs daily, and he serves on the boards of directors of several companies. “I advise rather than command,” Ray Dolan says. “And I’m enjoying the devil out of it.”

McClennan derives a different sort of satisfaction from Lithostar’s success. “When the urologist calls you and says the patient’s doing great, the treatment didn’t bother him a bit and, by the way, his stones are all gone—that’s it. That’s what we want to do.”

“The ability to effectively treat patients with kidney stones in a noninvasive, nonpainful manner,” adds Clayman, “brings the greatest sense of accomplishment. To cure and not harm is really the goal of each technological advance; to this extent, the current studies of the capabilities of the Lithostar have been most rewarding.”
NEW STAFF
Arthur F. Bishop, M.D., instructor in clinical radiology, Diagnostic Radiology

NEW BUSINESS OFFICE EMPLOYEES
Linda Davidson, assistant business manager-patient accounts
Mary Gerould, administrative assistant-personnel and payroll

SYMPOSIA

Jay P. Heiken, M.D., assistant professor of radiology, presided over the scientific session on “Technical Developments” at the Fifth Annual Meeting of the Society for Magnetic Resonance Imaging, San Antonio, Texas, March 3. He acted as a consultant in magnetic resonance imaging at the Royal Marsden Hospital, Surrey, England, March 11-13. Heiken presented the lectures “CT of the Pancreas” and “CT of the Peritoneal Spaces” and a workshop on “CT of Pelvic Tumors” at the “London Course in Whole Body Computed Tomography,” Auchterarder, Perthshire, Scotland, March 15-19.

Todd H. Wasserman, M.D., professor of radiology, chaired the Committee on Chemical Modifiers of Radiation Treatments and participated in other committee functions at the semiannual meeting of the Radiation Therapy Oncology Group, Baltimore, January 18-20. He served as an advisor concerning the potential development of a new drug, SR-2508, as a chemical modifier of radiation effects at a Food and Drug Administration meeting, Bethesda, Maryland, February 5. Wasserman was an invited reviewer for the development of a national program on radioactive antibodies in the diagnosis and treatment of cancer at a National Cancer Institute meeting, Bethesda, Maryland, February 11-13. Wasserman’s sabbatical research on a new assay for tumor cells was presented and discussed at the International Conference on Tumor Response Endpoints, Banff, Canada, April 21-24, and at the Radiation Research Society Annual Meeting, Atlanta, February 24-26. The assay is designed to be inexpensive, semiautomated and quick, and it has potential benefit in screening the responsiveness of tumors to chemotherapy and radiotherapy. As an invited participant, Wasserman attended a combined National Cancer Institute/Armed Forces Radiobiology Institute Symposium on Radiation Protection and the Use of Chemical Agents as Radioprotectors in Bethesda, Maryland, March 13-14. He attended and participated in meetings of the Cancer and Acute Leukemia Group B Lympoma Committee in Salt Lake City, February 13-14, and the Cancer and Acute Leukemia Group B Semiannual Meeting in Cambridge, Massachusetts, April 29-May 2. Several protocols of this group are being used at Washington University Medical Center. Wasserman presented an abstract on his work with the radiosensitizers SR-2508 and Ro-03-8799 at the Eighth International Congress of Radiation Research, Edinburgh, Scotland, July 20-24. He received a travel grant from the Radiation Research Society to attend the meeting. As chairman of the Chemical Modifiers Working Group, Wasserman attended the Radiation Therapy Oncology Group Meeting in Philadelphia, July 8-10. He spoke at the Intraoperative Radiation Therapy Meeting in Philadelphia, July 10-11.

Stuart S. Sagel, M.D., professor of radiology, presented four talks on “Thoracic CT with MRI Correlation” at the Winter Imaging Seminar, Vail, Colorado, February 21-28. He also lectured on various topics relating to thoracic and abdominal CT at the Computed Body Tomography Workshops, Vail, Colorado, March 23-28.

SYMPOSIA

Marilyn J. Siegel, M.D., associate professor of radiology, presented "CT of the Pediatric Mediastinum: Normal Anatomy and Pathology," "CT of Pediatric Retroperitoneal Tumors" and "CT of Pelvic Masses in the Pediatric Patient" and gave a workshop on "CT Evaluation of the Pediatric Patient" at the symposium "Computed Body Tomography 1987: The Cutting Edge," Orlando, Florida, March 5-8. Siegel spoke on "CT of the Pediatric Pelvis" and presented workshops on "CT of the Pediatric Chest" and "CT of the Pediatric Abdomen" at the 10th Annual Meeting of the Society of Computed Body Tomography, San Diego, March 20-24.


Michel M. Ter-Pogossian, Ph.D., professor and director of the Division of Radiation Sciences, presented "Recent Developments in Medical Imaging" at the American Association for the Advancement of Science Annual Meeting, Chicago, February 14-18.


Judy M. Destouet, M.D., associate professor of radiology, presented "Effect of Community Interventions on Screening Mammograms," coauthored by Barbara Monsees, M.D., and Michael W. Vannier, M.D., at the 87th Annual Meeting of the American Roentgen Ray Society, Miami Beach, April 26-May 1.

Bahman Emami, M.D., professor of radiology, presented "Current Status of Clinical Hyperthermia in Oncology" to the Upstate New York Society for Therapeutic Radiology and Oncology, Syracuse, New York, May 16.

Harvey S. Glazer, M.D., assistant professor of radiology, presented "MRI of the Thorax" and "Historical Casts of Mediastinal CT" to the Kansas Radiological Society, Kansas City, April 11.


Klaus Sartor, M.D., associate professor of radiology, was coauthor of "Possibilities and Limitations of MRT in the Diagnosis of Intracranial Vascular Malformations," presented at the German Roentgen Society Annual Meeting, Hamburg, West Germany, April 30, and at the German Society of Neurosurgery Annual Meeting, Muenster, West Germany, May 4. He presented "Dystonia, Myoclonus, Choreo and Athetosis: CT and MR Findings" at the American Society of Neuroradiology Annual Meeting, New York, May 11.


Bruce L. McClennan, M.D., professor of radiology, attended the meeting of the Missouri State Medical Association, as a delegate, and the Missouri Radiology Society, as a board member, Lake of the Ozarks, Missouri, April 2-5. He moderated a session, presented a paper on “Costs and Economics of MRI” at the Southwestern Medical School, Parkland Hospital, Dallas, May 16-19. He presented “Radiology of Bone Tumors,” “Cervical Spine Trauma,” “Percutaneous Bone Biopsy” and “Roentgenographic Approach to Hand Problems” at the Ospedale Civile Di Padova, Padova, Italy, June 15-19.

Robert R. Kuske, M.D., assistant professor of radiology, presented “Treatment of Breast Cancer with Hyperthermia and Irradiation” at the University of Sao Paulo, Brazil, March 2-4.

Elections

Don C. Arwood, M.D., resident in radiation oncology, was recently elected to the Executive Board of the Association of Residents in Radiation Oncology.

Alumni News

Jeannie Kinzie, M.D., former resident and staff physician (1971-73), has been appointed a consultant to the Food and Drug Administration to serve in the Center for Devices and Radiological Health, Radiologic Devices Panel, and has become a U.S. associate editor of the International Journal of Radiation Oncology, Biology and Physics.

The Public Relations Department requests that alumni keep the office informed—by either phone or mail—of activities meriting attention in Focal Spot.

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FYI

VISITING PROFESSORS & GUEST LECTURERS

Joseph L. Roti Roti, Ph.D., professor of cancer biology in radiology, spoke on “Flow Cytometric Methods to Study Nuclear Structure” at Northwestern University, Evanston, Illinois, March 11. He presented “Effects of Heat and Radiation on DNA Supercoiling” at the University of Chicago, March 10, and “Effects of Hyperthermia and Radiation on Nuclear Structure” at Case Western Reserve University, Cleveland, April 29-30.

Harvey S. Glazer, M.D., assistant professor of radiology, presented “CT vs. MRI Applications in the Thorax” at Georgetown University Hospital, Washington, D.C., April 2.

Joseph K.T. Lee, M.D., professor of radiology, presented several lectures and workshops at the “MRI Seminar” at the University of Michigan, Ann Arbor, Michigan, May 21-22.

APPOINTMENTS

Joseph L. Roti Roti, Ph.D., professor of cancer biology in radiology, was reappointed associate editor of the Cancer Research Journal for a 3-year term.

Gary Ratkin, M.D., F.A.C.P., clinical instructor of radiology, has been reappointed chairman of the Clinical Practice Committee of the American Society of Clinical Oncology (ASCO) for the third year. He chaired the Annual Clinical Practice Forum at the annual session of the ASCO on the topic “Are Response Modifiers Ready for the Practicing Oncologist?”

Stuart S. Sagel, M.D., professor of radiology, served as visiting professor at the University of Maryland, Baltimore, and guest lecturer for the monthly Maryland Radiological Society meeting, May 18-19.

Michael W. Vanner, M.D., associate professor of radiology, presented “Optimal Imaging of Ceramics Using a Medical CT Scanner” at the Argonne National Laboratory, Division of Materials and Components Technology, Argonne, Illinois, March 4.

Carlos A. Perez, M.D., professor and director of the Radiation Oncology Center, spoke on “Carcinoma of the Cervix” and “Carcinoma of the Endometrium” at the University of California, Los Angeles, May 4-5.

Michael Kleinhoffer and Paul Becker, MIR students, participated in a meeting of the Fourth District of the Missouri Society of Radiologic Technologists (MSRT) at St. Louis Community College at Forest Park, February 19.

Becker received the Mallinckrodt Fellowship Award for Continuing Education from the Fourth District.

Gary S. Brink, R.T., B.S., FASRT, administrator of the Mammography Outreach Program, spoke on “Current Health Trends and Their Effect on Radiologic Technologists” to the Missouri Society of Radiologists, Omaha, Nebraska, March 25-27.

Norman L. Hente, R.T., B.S., technical supervisor in charge of photography and television, presented “Current Health Trends and Their Effect on Radiologic Technologists” to the Midwest Gateway Parliamentarians, St. Louis, May 18-19. He lectured on “Bystaws—Meaning and Modification” at the Spring Into Fashion with Successful Meetings Seminar, sponsored by the Midwest-Gateway Parliamentarians, Scarrellino Auditorium, April 4. Hente spoke on “The Mallinckrodt Experience” to the Nebraska Society of Radiologic Technologists, Omaha, Nebraska, April 25. He was elected lieutenant governor of Region 2 of the American Institute of Parliamentarians at the 1987 Region 2 Conference, Des Moines, Iowa, May 3.

In this capacity, Hente will be responsible for the 1988 Region 2 Conference. He presented “Williamsburg Practicum: Parliamentary Education” to the Midwest-Gateway Parliamentarians, June 17.

The 55th Annual Conference of the MSRT will be held at the Holiday Inn-Westport, St. Louis, October 7-10.

Charles Schaab, R.T., has recently been promoted to assistant supervisor of special procedures.

Emilee Murray, B.S., R.T., helped present the symposium on “Radiology and Early Colon Cancer” with Jay P. Heiken, M.D., and Dennis Balfe, M.D., both of Mallinckrodt, and Igor Laufer, M.D., University of Pennsylvania, St. Louis, November 8.

Robert H. Knapp, R.T., B.M., lectured on “Computer Applications in Medical Imaging Systems—CT, DVI and MRI” at the First Annual Spring Seminar of the MSRT Fourth District, St. Louis, May 16. At the seminar, Hente presented “Current Health Trends and Their Effect on Radiologic Technologists,” and Brink spoke on “Imaging Modalities in Radiology Today.”

Don Bernier, C.N.M.T., technical supervisor in the Division of Nuclear Medicine, has coauthored the second edition of Nuclear Medicine Technology and Techniques, to be published soon by The C.V. Mosby Company.

The Public Relations Department requests that the technology staff keep the office informed of activities meriting attention in Focal Spot.
The May 1987 issue of *Investigative Radiology* includes a report entitled “Advancement of Women in Academic Radiology.” Nancy O. Whitley, M.D., and colleagues (two women and four men representing five universities) studied women and men in academic radiology departments throughout the United States, focusing on academic faculty rank and promotion history. This report, encouraged by the Association of University Radiologists, recognizes the increasing importance of women in our specialty, both in community and academic practices.

Since the late 1960s, increasing numbers of women have matriculated in medical schools, and this report documents the increasing number of women who are now or will be radiologists. For example, only 9% of the U.S. medical students in 1969 were women, compared with more than 30% in 1985. Currently 21% of radiology residents in training are women, and this percentage undoubtedly will increase.

The source of data for the report consists of responses to a questionnaire sent to 129 university diagnostic radiology departments in the United States. A total of 1,199 faculty member replies were received from 89 of the departments and were used to evaluate the academic progress of women and men currently on university radiology faculties. The replies were from 200 women and 999 men, representing 66% of the women and 59% of the men in the 89 departments—a very good response for any questionnaire.

The results of the survey showed that women were more likely to be in the lower academic ranks than men (60% of men were associate or full professors, while only 29% of women held these higher ranks) and that women stayed longer in the lower ranks than men. However, there were reasons for the slower promotion pattern, as can be inferred from some of the survey results summarized as follows:

1. Women published less than men. On the average, men had published 36 academic papers, compared with 14 published by women.
2. Similar differences in publishing numbers were found when the profiles of those who had published in three major radiology journals (*Radiology, American Journal of Roentgenology, and Investigative Radiology*) were compared: On the average, men had published 11 articles while women had published five.
3. Considering other academic publication data, men had 21 original publications compared with nine for women, and men had 13 first-author papers compared with six for women.
4. Women had fewer research grants: 19% of men had funding from their universities, National Institutes of Health, or other sources, compared with 12% of women.
5. There were no differences in several other factors relating to academic appointment. A similar percentage of women and men were board certified, both were similar in age at the end of residency training, and both spent approximately the same amount of hours each week teaching medical students, residents, or practicing radiologists.

Because it was possible that important differences in data were related to the fact that the women were relatively younger than the men, Whitley et al. matched the 200 women with 200 of the men of similar age. The findings were basically the same as those described above, although the differences were sometimes not as noticeable.

More men than women were in the higher academic ranks (44% vs. 29%). More men than women had extramural grants (19% vs. 7%), and the men had published more total papers than had the women (28 vs. 14).

Although the survey showed that women are overrepresented in the lower academic ranks and underrepresented in the higher ranks, there are appropriate reasons if one considers current academic standards. The women had published less and had fewer grants. While the commonly used phrase “publish or perish” is a little strong, it is based on reality. Universities have standards for promotion that emphasize academic contributions as documented by papers and research projects supported by grants.

There are important requirements for each individual before he or she can be advanced to the
next rank. Although there is a broad range of promotion criteria, including teaching and community service, a most important academic requirement, and the easiest one to evaluate with some degree of objectivity, is publishing. The results of Whitley et al. (the publication of which, for example, will help in the promotion of only one or two of the six authors since the others are already full professors) indicate that there is no apparent discrimination in evaluating academic promotions between men and women. If anything, the data suggest that women are promoted to full professorship with fewer publications than men. Male professors had written a total of 70 articles, while the female professors had only published 40. This discrepancy was not related to the age differences because the age-matched data showed essentially similar numbers (67 articles for the men and 40 for the women).

My fellow chairpersons (essentially all men) and others with responsibility for academic promotions can be pleased that no discrimination was identified. However, the report does identify a serious problem: Women in academic medicine are apparently not as productive as their male colleagues. Because women are an increasingly important part of our specialty, radiology chairpersons must identify those factors that prevent women from achieving a similar level of productivity. My own experience suggests at least three factors.

In our society women often have important family responsibilities that are not shared equally by men. These responsibilities usually focus on children, but may include parents, grandparents, and other individuals related by birth or marriage. These responsibilities take considerable time and personal effort and are likely to occur at the same time in life (age 25-45 years) that is so critical to the development of a professional career. To be a full-time mother, wife, and radiologist must create a situation with conflicting priorities. Of course, having no children is one alternative that may alleviate some of the conflicts; this may be satisfactory to some women, but not to all.

A second reason is emphasized in the article by Whitley et al., who refer to it as “professional socialization.” The phrase refers to difficulties brought about by the relatively recent acceptance of women in the medical profession, including academic radiology, and describes the problems women face because of the paucity of female role models and leaders in our specialty. This possibility suggests discrimination at a subtle level, as suggested by such phrases as “the old boys’ club.”

A third possible factor is that women in academic radiology are less aggressive in their pursuit of rapid promotion. The individual who gets promoted from assistant to associate professor in 3 or 4 years at the Mallinckrodt Institute (compared with a more typical interval of 5 or more years) has not only written many articles but has been “academically active” in other ways. He or she has usually spent considerable time on the national lecture circuit, has been active in several professional societies, and has participated in multiple collaborative research projects. These activities require hours, days, and nights away from home, usually in addition to assigned clinical and teaching responsibilities.

Some women will be satisfied to maintain a more regular schedule and wait longer for promotions.

For the benefit of our specialty, as well as women radiologists, we must have a better understanding of why there is an apparent reduced academic productivity. I predict there will be no single or simple answer, but, without a better understanding of the problem or problems, we cannot develop effective solutions. We need to encourage and find support for future research on these social and professional issues.

While waiting for more information, the radiologic community should do its best to welcome women into its ranks and to provide them with the environment and resources to become equal colleagues, whether in academic or clinical practice. Chairpersons can be supportive in many ways, including adjusting schedules when possible to help women colleagues. Even with such support, both women and men should recognize that, appropriately, it may take more time for some women to be promoted because of family responsibilities that delay the development of academic credentials and subsequent promotions.

Ronald G. Evens, M.D., is Elizabeth Mallinckrodt professor of radiology and director of Mallinckrodt.

These positron emission tomography (PET) images are part of a mapping study to determine language dominance. The images were obtained from a right-handed epileptic man who was being considered for surgical resection of a seizure focus. It was not known on which side the seizure focus would be found or which hemisphere controlled his language. First row. The top row contains resting-state blood flow images. The area of decreased blood flow associated with an epileptic focus can be seen on the left of slices 5, 6 and 7. Second row. The second row of images was obtained while the subject repeated aloud words presented on a video monitor. The area of decreased flow associated with the epileptic focus is again seen. Task-related blood flow changes, however, are very difficult to perceive in this format. Third row. The third row of images shows a subtraction of resting-state images from task-state images. These images clearly show the areas of increased blood flow associated with the task of reading aloud. Fourth row. To obtain the images in the final row, the subject was asked to generate verbs associated with the nouns previously read aloud. The images obtained when the subject read the nouns aloud were then subtracted from those obtained when the verbs were generated. The visual input, the processing of the visual word form and the motor output are identical in the two tasks—and so fall out of the subtraction—leaving visible only those areas related to the purely cognitive act of searching for and recognizing a semantically related word. Story on page 14.
Three-dimensional reconstructions of magnetic resonance images of the heart, like the one above, are improving diagnosis, surgery planning and treatment for pediatric cardiac patients. The next Focal Spot cover story explains the breakthrough and introduces you to the scientists behind it.