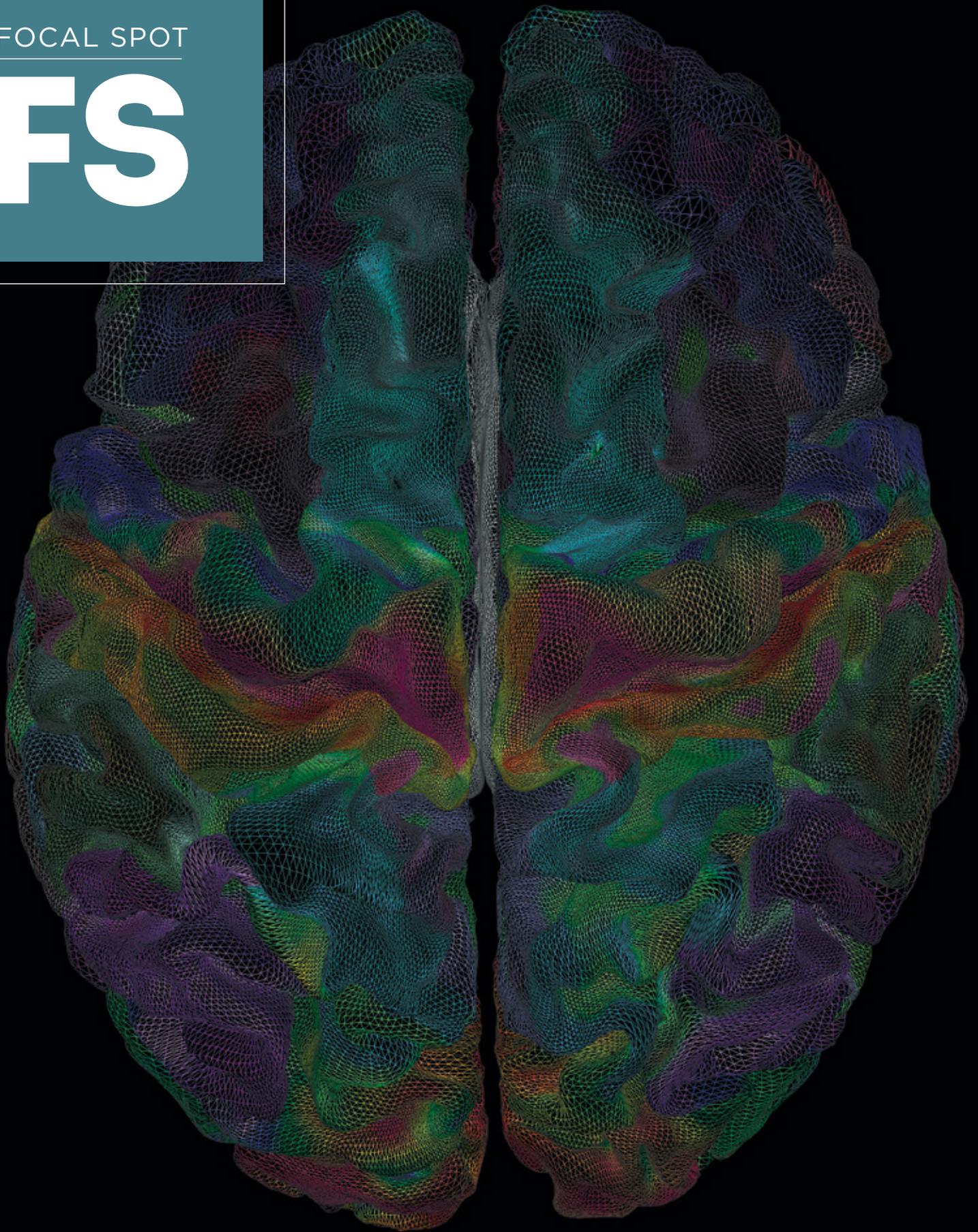


FOCAL SPOT

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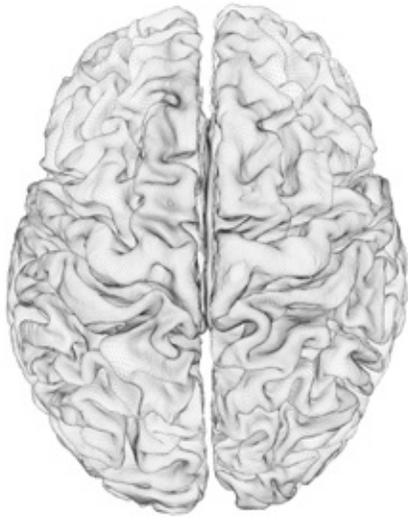
**SPRING 2014** The Human Connectome Project

MALLINCKRODT INSTITUTE OF RADIOLOGY // WASHINGTON UNIVERSITY // ST. LOUIS



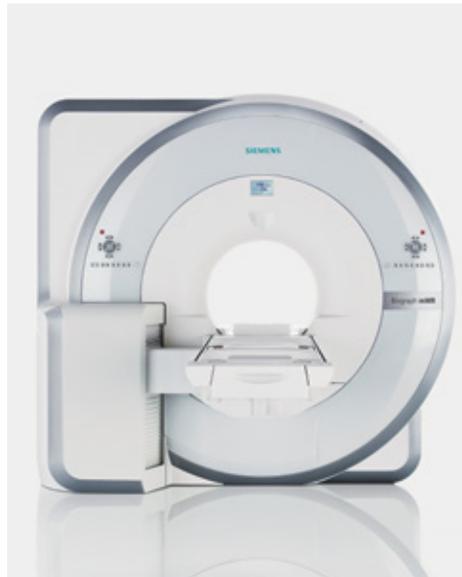
# 6 SEEING IS BELIEVING

High-tech goggles developed by Mallinckrodt researchers provide a clearer view of cancer



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Mallinckrodt radiologists play an integral role in the Human Connectome Project, using the latest imaging technologies to detail the brain's intricate networks.



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Combining two imaging procedures — PET and MRI — allows researchers and clinicians to produce more detailed images than either technique alone.



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Multidisciplinary investigators from across Washington University have access to a “supercomputer” run by Mallinckrodt and the university’s School of Engineering.

### ON THE COVER

A colorful image of the brain from the National Institutes of Health (NIH) Human Connectome Project, the first large-scale attempt to collect data about the healthy adult human brain. Washington University plays a leading role in the effort, which makes the data it gathers available to the scientific community to promote further discoveries linking brain connectivity to human behavior.



## 2 SPOT NEWS



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### FOCAL SPOT MAGAZINE SPRING 2014

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## 28 FYI

# Focal Spot: Then and Now

Forty-three years ago, *Focal Spot* began as a one-color, single-sheet newsletter printing news about life at Mallinckrodt Institute of Radiology. Its editor, public relations maven Virginia Trent, made sure it was upbeat, newsy and helpful. It offered discount coupons for flights to the International Congress of Radiology and the like.

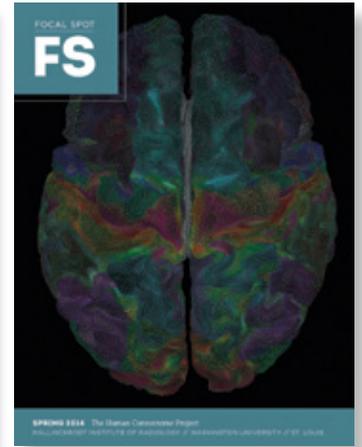
For the next four decades, the publication evolved alongside the institute it covered, growing eventually into a full-color, glossy magazine that focused on the pioneering work

of faculty members, but always retaining its attention to the real-life stories of Mallinckrodt's people. Editors Michael Gold, Steve Kohler and most recently Vicki Kunkler worked to preserve the written record and loving attention that few academic medical departments anywhere enjoy.



**Above:** Vicki Kunkler

For more than 20 years, Kunkler made the magazine the best she could. Her persistent good nature saw to it that many of Mallinckrodt's characters became her friends, and even some of those who shun the spotlight happily agreed to be featured in its pages; it was an honor. Then, about five years ago, Kunkler fell ill. For two years, she nonetheless managed to shepherd



the magazine through the thousands of decisions each edition demands. More than two years ago, Mallinckrodt lost its good friend, unofficial historian and passionate publisher to cancer. If it's true that no one is irreplaceable, Kunkler challenged the rule. But, better than anyone else, she knew the magazine existed for a big purpose.

And so, after some deliberation, *Focal Spot* is back — reincarnated with a more modern look and approach, tied to electronic communications but still printed to carry the weight that only ink on paper can produce. The new editor, Holly Edmiston, comes to Mallinckrodt from Washington University School of Medicine public affairs, where she edited *Outlook* magazine. *Focal Spot* will publish three times a year, telling the stories and recording the life of a place known as the world's premier radiology department.

# Residency program takes top honors in 2013

For the fourth time in seven years, Mallinckrodt Institute of Radiology was named the Best Radiologist Training Program by radiology community website auntminnie.com.

"The secret to our success is our commitment to resident education, even as we maintain a strong research program," says Jennifer E. Gould, MD, assistant professor of radiology and director of Mallinckrodt's residency program. "People know Mallinckrodt for its research, but the clinical staff is with residents all day, every day, reading at viewboxes. We try to ensure that residents receive immediate feedback on the cases they read, because that's how they really learn."



Since its inception in 1999, auntminnie.com has grown into a leading website for residents, fellows, radiologists, and other medical imaging professionals. The site features news and information related to medical imaging, cases to review, career information, hosting forums, and more.

Founded by Phillip Berman, MD, the name auntminnie.com refers to an "Aunt Minnie," a term coined in the 1940s by University of Cincinnati radiologist Ben Felson, MD, to describe cases that "have findings so specific and compelling that no realistic differential diagnosis exists: 'If it looks like your Aunt Minnie, then it's your Aunt Minnie.'"

# 100 years of radiology at Washington University

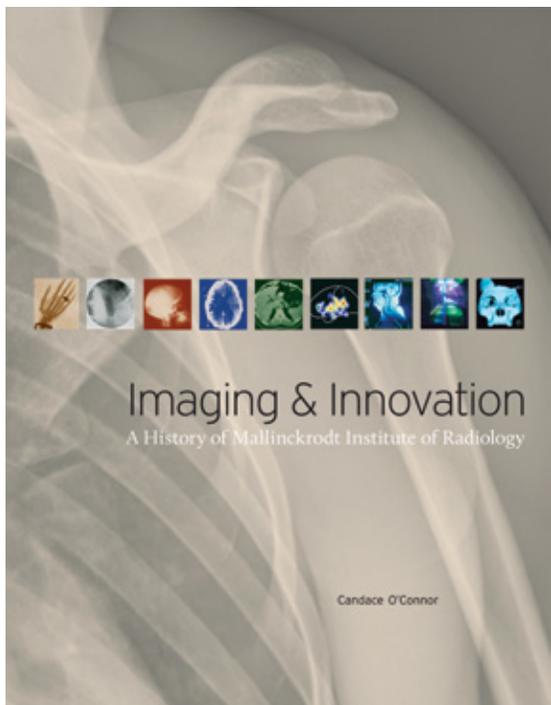
“The dinner for faculty and friends gave us a chance to think back,” says R. Gilbert Jost, MD, the Elizabeth E. Mallinckrodt Professor and head of the Department of Radiology, speaking at a gala event held to celebrate the first 100 years of radiology at Washington University.

The reception and dinner, held at the Ritz-Carlton in St. Louis in 2013, included Jost’s comments about radiology and the many changes seen in the field over the decades. Also speaking were chancellor Mark S. Wrighton, PhD, School of Medicine dean Larry J. Shapiro, MD, and former medical school dean and chancellor William H. Danforth, MD. Radiologists Marcus E. Raichle, MD, and Barry A. Siegel, MD, shared recollections from their tenures with an audience of current and former Mallinckrodt faculty and other School of Medicine department chairs and their guests.

A video shown at the event summarized the entirety of Mallinckrodt’s storied history to date — from its earliest days when the medical school acquired its first X-ray machine

to today’s environment of translational research and multi-disciplinary collaboration.

Jost, who joined the School of Medicine faculty in 1975 and assumed the role of department chair in 1999, noted that in the early 1970s alone, the university had a new chancellor and a new head of radiology just as the invention of the PET scanner was underway at Washington University and the first CT scanners were appearing on the scene.



**Above Right:** Mallinckrodt’s guests mingle before the event. **Left:** A copy of Candace O’Connor’s new book, *Imaging & Innovation — A History of Mallinckrodt Institute of Radiology*, was distributed to attendees.

**Right:** Dr. and Mrs. R. Gilbert Jost (Peggy) accept a replica of Jost’s official portrait from Ronald G. Evens, MD.

## SPOT NEWS

# Evens chairs National Library of Medicine Board

Ronald G. Evens, MD, professor of radiology and of medical economics, has been appointed chairman of the Board of Regents for the National Library of Medicine (NLM). The NLM is a division of the National Institutes of Health (NIH), and its Board of Regents helps advise and guide the library as it manages the worldwide flow of medical information.

Located in Bethesda, Md., the NLM is the world's largest medical library, housing not only historic medical manuscripts dating back more than 1,000 years, but also vast computer records of the latest research and discoveries in everything from the Human Genome Project to information on toxins in the environment.



Above: Ronald G. Evens, MD

Many of the library's services, such as PubMed, a searchable database of millions of medical studies, and TOXNET, an integrated database of hazardous chemicals, toxic releases and environmental health, are available free online.

Evens was the director of Mallinckrodt Institute of Radiology from 1971 to 1999. During his long tenure at Washington University Medical Center, he also served as president of St. Louis Children's Hospital, vice chancellor for finance and administration for the university, and president of Barnes-Jewish Hospital.

# Mallinckrodt expands its hospital presence

St. Charles County residents now have access to the same high-quality, exceptional radiology services provided by Mallinckrodt Institute of Radiology at Washington University Medical Center.

In December 2013, Mallinckrodt joined forces with Progress West Hospital in O'Fallon, Mo. Located just north of I-64/40 in O'Fallon, Progress West, part of BJC HealthCare, opened its doors in 2007 as a full-service hospital serving St. Charles County and environs.

"Our goal is to provide world-class radiology services to residents of St. Charles County," says Michael W. Penney, MD,

assistant professor of radiology and chief, Barnes-Jewish St. Peters Hospital and Progress West Hospital. "We offer a broad range of radiology options, including interventional radiology, at Progress West, and I firmly believe that our practice there will grow rapidly as patients and referring physicians are exposed to our compassionate and comprehensive care."



Above: Michael W. Penney, MD

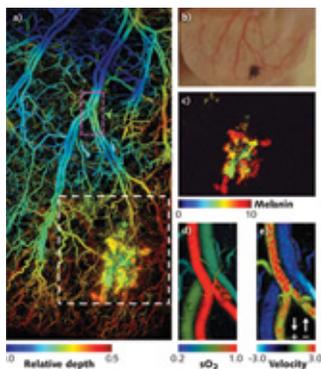
Procedures that are only available at the medical school may see some increase as patients from O'Fallon will now be better connected to the downtown facility and able to take advantage of those resources.

The addition of radiology services at Progress West marks Mallinckrodt's first hospital expansion since aligning with Barnes-Jewish St. Peters Hospital 15 years ago. Mallinckrodt Institute of Radiology faculty continue to serve patients there and at Barnes-Jewish Hospital, Barnes-Jewish West County Hospital, St. Louis Children's Hospital and other locations.



Above: Progress West Healthcare Center

## NIH honors Wang with highly competitive award



**Above:** Lihong Wang, PhD, and images from his research

Cancer researchers have been limited by current imaging technology in their ability to detect not only the structure and function of tumors, but also tumor cell circulation. A technology proposed by Lihong Wang, PhD, may hold the key to reaching these goals.

Wang, the Gene K. Beare Distinguished Professor of Biomedical Engineering and a professor of radiology at the School of Medicine, has received a 2013 Transformative Research Award from the National Institutes of Health (NIH). He was one of only 10 recipients of the award, given to scientists proposing highly innovative approaches to major contemporary challenges in biomedical research. The award promotes interdisciplinary approaches by investigators who propose research that has the potential to create or overturn fundamental paradigms.

The award was one of 78, totaling \$123 million made by the NIH in its High Risk-High Reward program, supported by the NIH Common Fund.

The goal of the five-year, \$3.5 million grant is to translate this technology, called single-cell label-free photoacoustic microscopy (PAM), immediately into the clinic for cancer screening, detection, prognosis, and monitoring.

Specifically, PAM will be used for imaging circulating single red blood and tumor cells, as well as single circulating tumor cells. The proposed single-cell label-free imaging in living humans has the potential to facilitate translation of basic research to the clinic, detect metastases at an early stage, and to produce tumor response to the therapy. As a result, it may enable earlier therapeutic interventions and curative surgical treatment and improve survival of patients with cancer.

## New cyclotron brings increased capacity

More than 70 years ago, Washington University built the first cyclotron dedicated to producing isotopes for medical and biological research. Recently, Mallinckrodt Institute of Radiology installed the latest iteration of what has been a long progression of cyclotron technology.

The new Advance Cyclotron Systems Inc. TR-19 cyclotron was lowered by crane into its vault at Mallinckrodt's East Building in February. The unit, part of a project in the works for more than a decade, is a particle accelerator that will produce radioactive isotopes, many of which are used with positron emission tomography (PET) scanners to image biological processes and disease states in oncology, neurology, and cardiology. After a transition period, the new cyclotron will replace two others on campus that make these compounds.

"The new cyclotron will have higher energy and increased capacity to produce the PET drugs we need," says Sally J. Schwarz, RPh, MS, research associate professor of radiology and co-director of the Cyclotron Facility. Also under construction next to the vault is a Good Manufacturing Practice facility, a strictly controlled sterile environment to prepare radiopharmaceuticals for use in patients.

"If everything goes well with the installation processes, we hope to have the new cyclotron producing radiopharmaceuticals in the next two to three months," says cyclotron co-director Gregory Gaehle, MS. "The GMP facility still has some construction and certification to complete, so it will take longer to bring that facility online."

The facility's mission is to provide PET isotopes, radiochemicals, radiotracers, and radiopharmaceuticals to the research and medical community for use in research and clinical practice. //



**Above:** An artful installation



# SEEING IS BELIEVING

by Tony Fitzpatrick

# A NEW OPTICAL IMAGING TECHNIQUE MAY CUT RISK FOR CANCER RECURRENCE

The goal of any cancer treatment is to eliminate cancerous cells without inflicting unnecessary collateral damage. Often this is accomplished by surgery, but the propensity of cancers to invade adjacent tissue or metastasize to other parts of the body can limit its effectiveness. Single cancer cells are invisible to the naked eye and can regrow into new tumors.

For this reason, cancerous tissue is examined once removed to determine if a margin of healthy tissue is present. Still, until now surgeons have had to rely on the hope that all cancerous cells have been removed successfully. A new technology developed by researchers at Mallinckrodt Institute of Radiology may change that hope to a certainty, benefitting both physicians and the patients they serve.

“Surgeons won’t have to worry about what they can’t see if they can be reassured that optical imaging has shown them all that needs to be addressed,” says Samuel I. Achilefu, PhD, professor of radiology and director of Mallinckrodt’s Optical Radiology Laboratory (ORL).

Achilefu, professor of biochemistry and molecular biophysics and of biomedical engineering, explains that most patients die from elusive and deadly metastatic tumors that take off from the primary base of the cancer.

With optical imaging, a surgeon can find the margins of tumors — which can metastasize if not removed — on the spot because of the optical techniques that Achilefu and his ORL staff have developed and refined over a decade.

“Optical imaging is enabling us to find diseased tissue such as cancer and kill it,” says Achilefu. “It provides us the weapons to enforce the philosophy of ‘seek and treat,’ and it does so in real time and at markedly lower cost than traditional radiology technologies.”

Optical imaging makes use of lasers, sensors, computation, cameras, hemoglobin ratios in the blood, and molecular contrast agents to harness visible, ultraviolet, and near-infrared light for a growing variety of medical applications, from cancer detection to brain activity monitoring. Achilefu and his group work in near-infrared light (NIR) to ply their experiments.

Among the most exciting recent ORL developments is the discovery of what appears to be a universal cancer agent, or marker, and the nearly simultaneous development of a novel vision tool — a “new-age” pair of goggles — that can find these markers anywhere in the body.

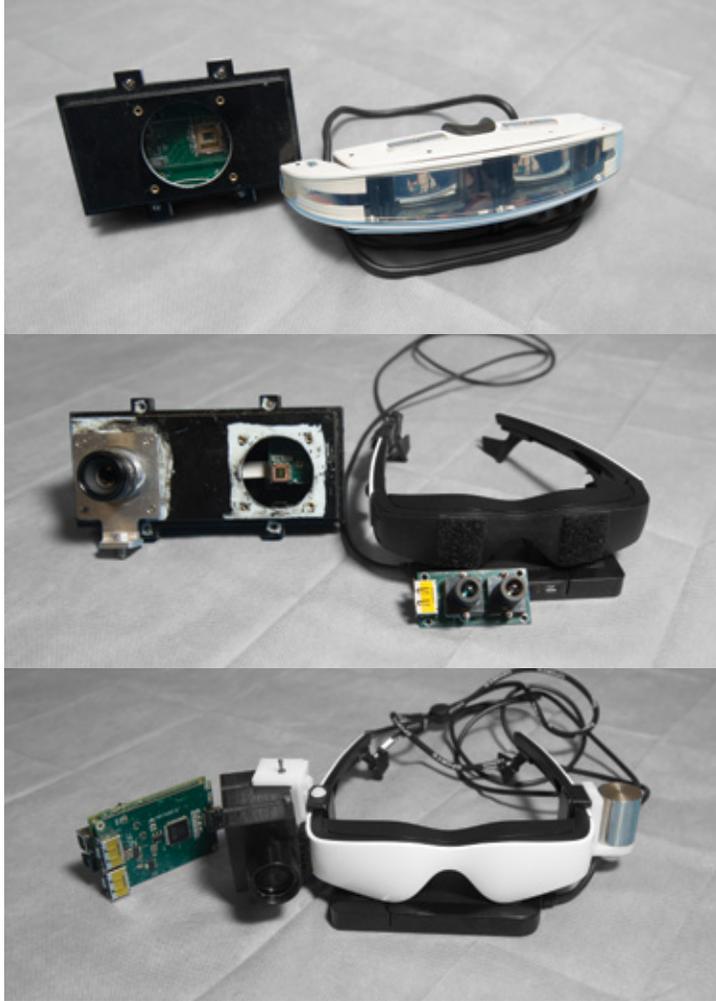
Achilefu has discovered a molecular marker, LS301, which, when injected, circulates through the body and gets trapped in cancer cells. “LS301 could accelerate cancer diagnosis, determination of treatment response, and surgical margin assessment,” he says. “It’s a huge discovery, and we’re really excited about it.”

Currently, the U.S. Food and Drug Administration (FDA) has not approved the use of LS301 on humans or large animals, but Achilefu is cautiously optimistic that human clinical trials will begin in the near future.

In tandem with this breakthrough is the development of a pair of head-mounted, superhero-like goggles that enable a surgeon to see, in near-infrared light, tumors that fluoresce because of LS301 or other cancer-targeted fluorescent drugs. The goggles are now in their fourth generation of development, with miniature cameras and sensors and a tiny computer on the nose bridge that can detect NIR as well as visible light, “important because we do not want to compromise the surgeon’s natural, visual perception of the surgical environment,” says Achilefu. “Basically, we encoded instructions into the goggles so you can see what lights up. It’s like watching a 3D movie in real time.”

As the Achilefu team awaits FDA approval of LS301 for human use, an alternative non-cancer-specific, near-infrared dye used in humans, indocyanine, has been used to demonstrate feasibility of the technology in imaging human liver cancer. In collaboration with oncologic surgeons at Washington University and the University of Missouri School of Veterinary Medicine, clinical studies in human and canine cancer patients are planned for 2014.

Left: Fourth-generation goggles going into clinical trials // Tim Parker



**Above:** Generations of goggles // *Tim Parker*

The conception and development of the medical imaging goggles represent multidisciplinary efforts involving many graduate students, postdoctoral fellows, and faculty. Currently, Washington University computer scientist Viktor Gruev, PhD, and optical engineer Ron Liang, PhD, a collaborator at the University of Arizona, have jointly made major contributions in the development and miniaturization of the optics, sensors, and head-mounted design of the goggle system. Graduate students Suman Mondal and Shengkui Gao, as well as postdoctoral fellow Nan Zhu, have anchored the newer generations of the technology. Seminal contributions by Yang Liu, PhD, assistant professor at the University of Akron in Ohio, who first worked on the project as a graduate student, Adam Bauer, PhD, and Joseph P. Culver, PhD, associate professor of radiology, made the goggle vision a reality. A \$2 million grant from the National Cancer Institute supports the project.

Achilefu's vision for the newly created ORL in 2002 was to build an interdisciplinary research program consisting of independent investigators with common goals. Today, that vision has been realized; about

40 members — from graduate students and postdocs to full-time faculty — now work at the ORL.

Joseph P. Culver, PhD, associate professor of radiology, works in human and mouse neuroimaging and with Achilefu on more generalized molecular imaging topics. Enticed to join the ORL in its early days from Massachusetts General Hospital, Culver has expertise in ultra-fast lasers, physics, engineering, and what is called diffuse optical tomography (DOT), a near-infrared technique for three-dimensional imaging of tissues. One system he created uses fiber optics to provide valuable information about brain function by observing how light is absorbed when the brain “blushes” (blood flow during tasks).

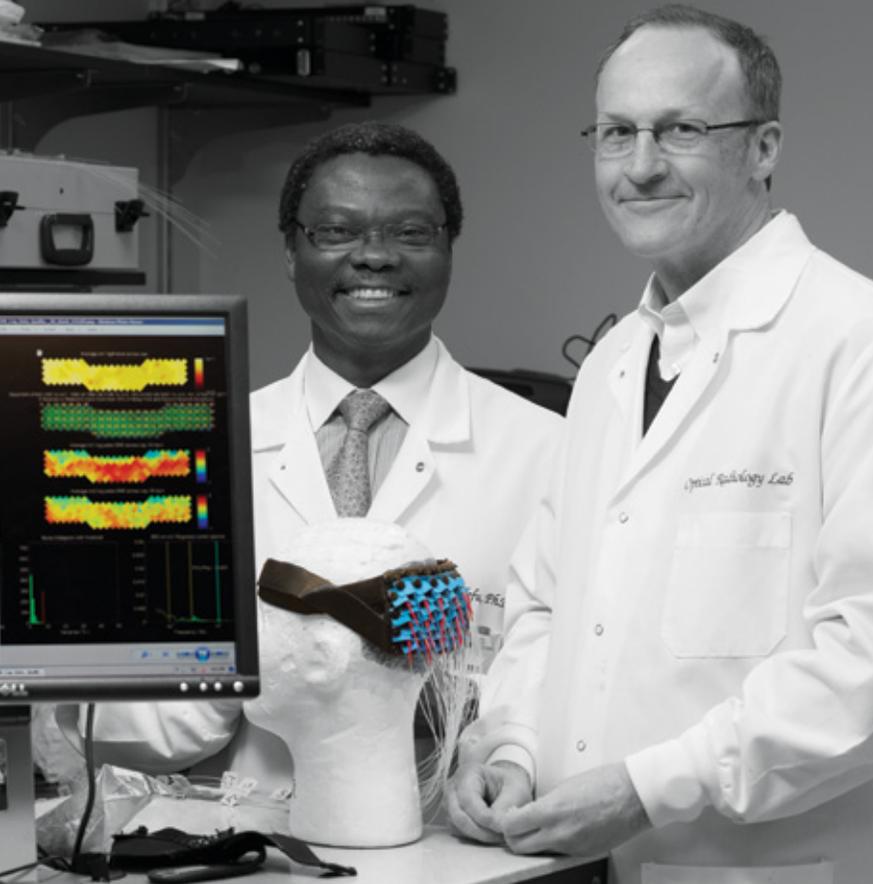
“We try to embed ourselves within the medical school’s neuroimaging community, which is world-leading in both positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), and match up with them in places where optics can help out,” Culver says. “Overall, we are focusing on providing imaging that is similar to fMRI but capable of being used in situations that fMRI cannot address.”

For example, Culver’s group is developing a portable optical brain-imaging system that can measure what is going on inside the human cerebral cortex with the use of what will eventually resemble a scuba cap. Right now, the system resembles a dreadlocks wig of optical fibers, with half of the fibers sending light into the brain and the other half receiving light coming back out.

“You just slip the cap on and the system can start imaging your brain,” Culver says. “We can’t image deep in the head but can image the cortex, and we can get data about blood dynamics that is very similar to fMRI. We’re working on ways to make the imaging as analogous to fMRI as possible, particularly the image quality, and then take it into places like critical care units, where it’s necessary to bring the imaging system to the patient rather than bring the patient to a fixed imaging scanner.”

Another of Culver’s research interests is in imaging subjects with metal implants such as cochlear implants, pacemakers and deep-brain stimulators, which “drifts into some really interesting neuroscience topics,” he says. “If you’re doing things like turning on deep-brain stimulators, how does that affect neural circuits and networks? If you get someone with a cochlear implant who hasn’t been hearing before, how does the brain respond to that new sensory input?”

Yet another area of interest is the exploration of juvenile brain activity. When the cap eventually gets smaller, “we’ll be able to put a kid on his mom’s lap and



**Clockwise:** Sameul I. Achilefu, PhD, and Joseph P. Culver, PhD, in the lab; server room for data output; test subject wearing the current optical brain imaging system // *Tim Parker*

image his brain function during normal situations,” says Culver. Such capability may lead to a better understanding of spectrum diseases like autism and ADHD by providing a baseline of normal brain development and function.

Achilefu currently is working with colleagues in the medical school’s Division of Dermatology on a hand-held device, a fairly simple pad placed around tissue of interest, that will record contrast agents in search of disease. Another tool under development may make it possible for gastroenterologists to easily identify cancerous and pre-cancerous lesions in the colon that are not raised like the more easily detected polyps. He also is exploring multimodal systems that combine an optical imaging feature with another imaging method such as PET or MRI to probe a particular area of interest, such as proteases, enzymes that are the targets of many drugs.

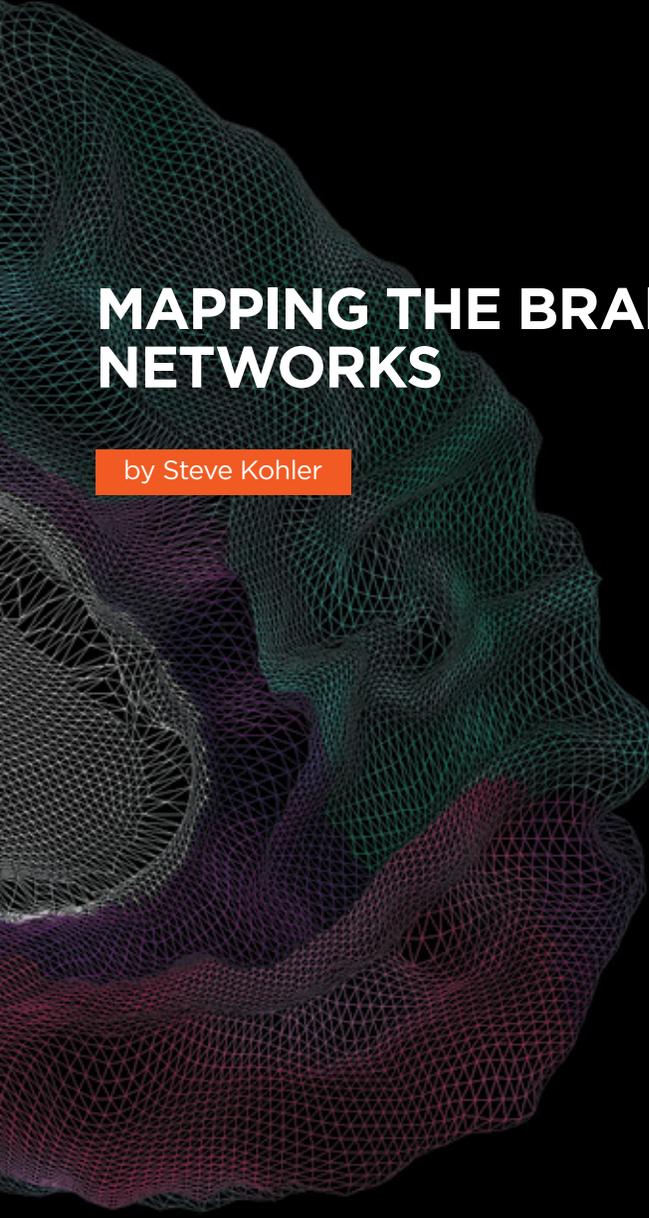
The collaborative nature of the ORL’s work has exceed Achilefu’s early hopes for the laboratory and what it can achieve.

“It’s wonderful to work with ORL personnel,” Achilefu says. “We are all eager to find the next breakthrough in biomedical research through molecular and physiologic imaging and image-guided therapeutic interventions.”





WELL  
CONNECTED

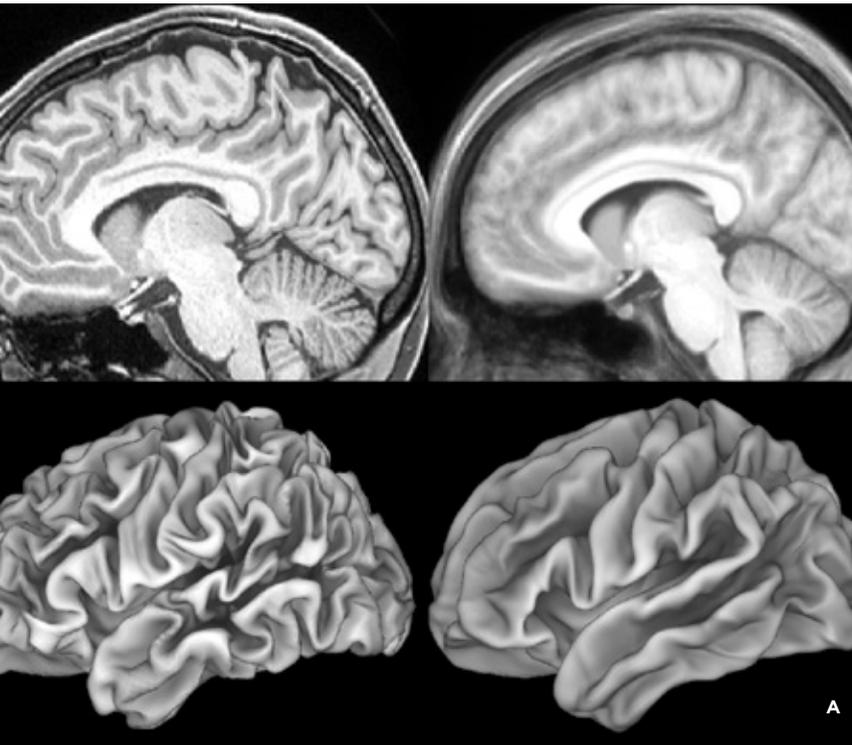


# MAPPING THE BRAIN'S NETWORKS

by Steve Kohler

At roughly three pounds, a human brain accounts for only about two percent of total body weight, but whether it's concentrating hard or daydreaming, it consumes roughly 20 percent of the body's basal energy. Just how the brain converts that energy to the staggering variability of thought, personality, emotion, interest and perception that humans exhibit has been one of science's obstinate mysteries.

It's known, however, that much of the brain's work occurs in orchestrating the intricate networks that connect its processing units. In fact, "Individual variability in brain connections underlies the diversity of our thinking, perception and motor skills . . . the connections are most of what makes us who we are," says neuroscientist David C. Van Essen, PhD.



Now in its fourth of five years, the Human Connectome Project (HCP) is mapping those connections and revealing the brain's interconnectedness in all of its detail. The project's broadest goal, according to Van Essen: "describe the full pattern of long-distance connections between each brain region and every other brain region."

The HCP is a consortium of more than 100 scientists and staff at 10 institutions in the United States and Europe — including a large contingent of Mallinckrodt researchers and clinicians — that is scanning the brains of 1,200 normal subjects, analyzing the imaging data and publishing it on the Internet for interested parties to use at no cost. As the project proceeds, the team works to improve every aspect of brain imaging.

Van Essen, Alumni Endowed Professor and head of the Department of Anatomy and Neurobiology at

Washington University School of Medicine, is joined by Kamil Ugurbil, PhD, director of the Center for Magnetic Resonance Research and the McKnight Presidential Endowed Chair Professor at the University of Minnesota, as co-principal investigators of the \$30-million-plus project. Funding comes from 16 National Institutes of Health (NIH) institutes and centers and the McDonnell Center for Systems Neuroscience at Washington University.

## NEW THINKING

Conventional wisdom about brain function held that discrete regions, 150 to 200 in each hemisphere, were dedicated to particular tasks such as math or language. It was believed that they did their jobs and sent their answers on for further processing, Van Essen explains.

The revamped thinking is that networks of those same regions — collections of cortical areas — form and communicate to do the brain's work. "It's exquisitely coordinated, with some elements more active at any moment," says Van Essen. Imagine the globe with its political subdivisions, each with its individual interest. Where the significance occurs and the work gets done is in their various and changing interactions.

So, how to sort out the daunting complexity of the brain's connecting cables, those tens of billions of axons that link many of its 90 billion nerve cells? Enter imaging technology with several sophisticated, noninvasive approaches: diffusion imaging (dMRI), functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG).

## DMRI

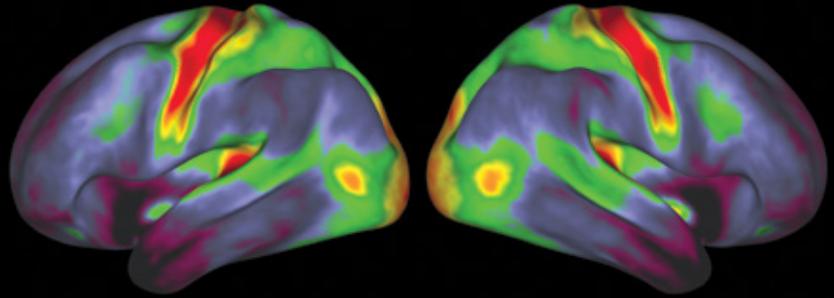
Like most magnetic resonance imaging, dMRI reveals the activity of water molecules. Unconstrained, those molecules bounce around randomly in tissue. But confined within the walls of an axon, they assume directionality, somewhat like water in a hose, explains Joshua S. Shimony, PhD, MD, associate professor of radiology. By recording that movement, images of the axons' paths through the brain's white matter (so named because of the white myelin that ensheathes the axons) can be generated, and long-distance connections can be mapped.

Among the imperfections of dMRI is its resolution: In this application, the technique resolves down to about

**A Individual vs. Group Average — Anatomical**

A comparison of an individual MRI volume and brain surface (left) and a group average volume and surface from 12 subjects (right) collected by the Human Connectome Project.

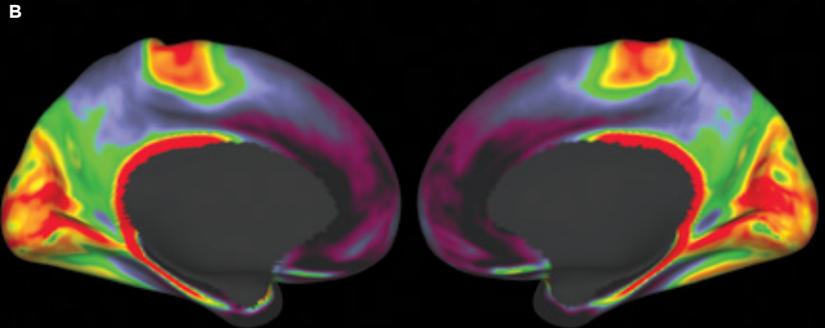
*Image courtesy of the WU-Minn HCP consortium*



**B Myelin Map — Montage**

A map of myelin content in human cerebral cortex. Regions in red and yellow have high myelin content, whereas regions in blue, indigo, and black have low myelin content. These “myelin maps” provide useful markers for functionally distinct subdivisions of human cerebral cortex.

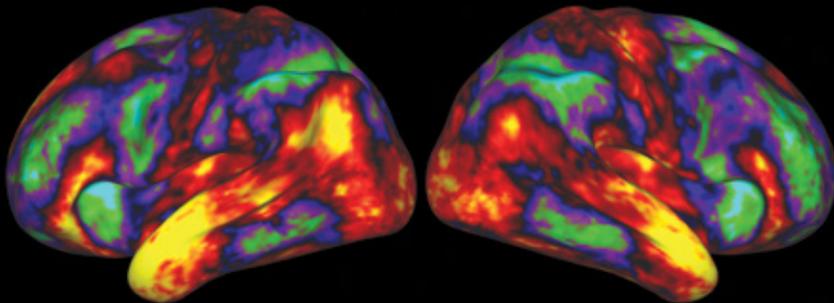
*Image courtesy of M. F. Glasser and D. C. Van Essen for the WU-Minn HCP consortium*



**C Story vs. Math — Task-fMRI**

A map of brain regions associated with language processing in human cerebral cortex. Yellow and red regions are activated by a task involving listening to stories, whereas green and blue regions are more strongly activated by a task involving arithmetic calculations.

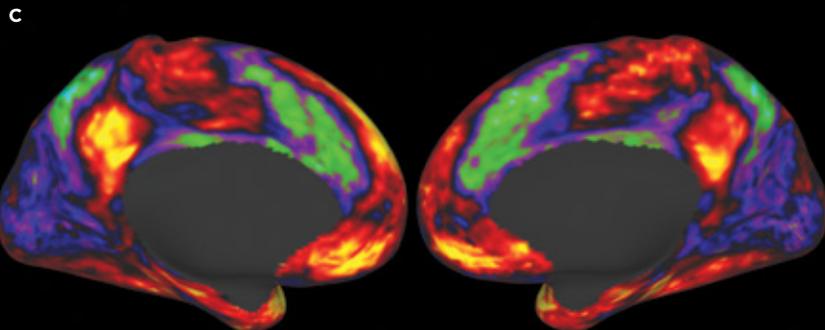
*Image courtesy of D. Barch, M. Harms, and G. Burgess for the WU-Minn HCP consortium*



**D Functional Connectivity Right Hemisphere — Parietal**

A map of average “functional connectivity” in human cerebral cortex (including subcortical gray matter) collected on subjects while “at rest” in the MRI scanner. Regions in yellow are functionally connected to a “seed” location in the parietal lobe of the right hemisphere, whereas regions in red and orange are weakly connected or not connected at all.

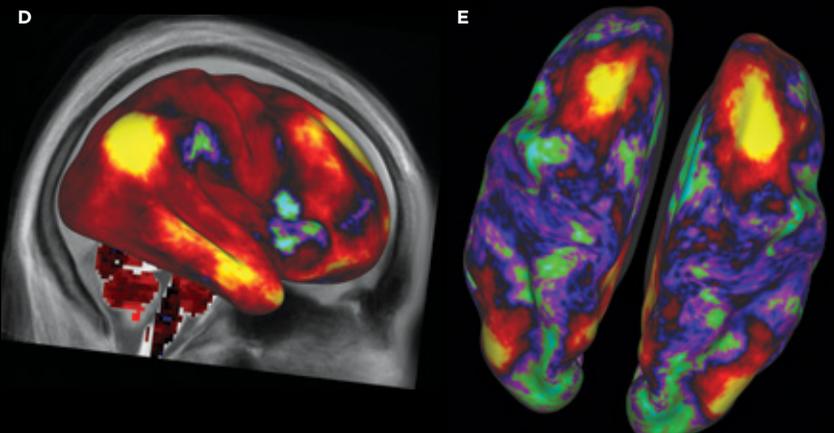
*Image courtesy of M. F. Glasser and S. M. Smith for the WU-Minn HCP consortium*



**E Functional Connectivity Both Hemispheres — Frontal Seed**

A map of the average “functional connectivity” in the human cerebral cortex collected on healthy subjects while “at rest” in the MRI scanner. Regions in yellow and red are functionally connected to the “seed” location in the right frontal cortex, whereas regions in green and blue are weakly connected or not connected at all.

*Image courtesy of M. F. Glasser and S. M. Smith for the WU-Minn HCP consortium*





2 millimeters, roughly 8/100 of an inch. A single axon is less than one percent of that size, though they vary dramatically in caliber. So dMRI is capable of seeing only groups of axons, and some information is lost. Fortunately, axons bundle together as they connect nerve cells in one region to those in another, says Shimony.

Also difficult is deciphering the path where bundles of axons cross one another. Did all of the axons go straight, or did some turn left to join a crossing bundle? Van Essen says one bundle looks like another and that the team is working to improve these analyses as it builds the connectome.

Much of the dMRI analysis is being done at England's Oxford University, by a group recruited for its experience and expertise in the evaluation of neuroimaging data.

## FMRI

Focused on the processing units in the gray matter of the brain where higher functioning occurs, fMRI plots those regions that are turned on and those where activity is dialed back. Busy regions of the brain require more glucose and bloodflow, Shimony says, and fMRI generates what is called the BOLD signal — for Blood Oxygen Level Dependent — to illuminate relative activity.

The technique does not reveal the axons that connect areas of high activity but rather the active areas themselves. Because particular parcels are working together, the long-distance connections are inferred. By combining this data with data from the dMRI images, the connectome map becomes more complete.

Working together, the Washington University and University of Minnesota groups have reduced the time needed to acquire a single brain image from several seconds to just seven-tenths of a second, one of the consortium's valuable advances to brain studies.

## MEG

Consortium members at Saint Louis University and institutions in Europe contribute to the effort via their expertise with magnetoencephalography (MEG), a technique that records magnetic fields produced in areas where high levels of electrical activity correspond to increased brain function. The resulting images provide high-speed, detailed data about activity, but spatial resolution — precisely where the activity is occurring — is more difficult to interpret. Overlaying the MEG and MRI data increases the map's information density.

## TASKING & TESTING

To obtain data about particular brain functions, much of the fMRI data is collected as subjects perform tasks in the scanner. Deanna Barch, PhD, professor of psychology in Arts & Sciences and professor of radiology, leads the work developing quantifiable tasks that require the collaboration of specific brain regions.

"We've developed seven domains," she says, "more than most previous brain studies." Included are sensory motor tasks (finger tapping, for example), emotional tasks (recognizing and responding to faces expressing emotion), working- and long-term memory tasks and language tasks, among others. Comparing the brain activity of all subjects to the tasks being performed will help answer the question: "Are there differences in behavior related to differences in patterns of connectivity and/or activity?" asks Barch.

And to get yet another angle on brain activity, investigators record images of the brain in a resting state. About 20 years ago, it was learned that even while relaxing, wildly different and distant parts of the brain busily operate in synchrony and that networks clearly link them. By analyzing resting state data, Van Essen says the team gets "one more way to inspect the elephant in the dark room."

Barch also has provided behavioral tests that subjects undertake prior to scanning: personality evaluations, cognitive performance exams, gauges of vision, hearing, smell, and taste, grip strength measurement, and many others. All of the data on individual performance are analyzed to relate it to brain connectivity.

## DATA

The scans and attendant information produce huge amounts of data to be processed, analyzed and published. When complete, the human connectome will comprise as much as 1 petabyte of digital information, equivalent to about 1 million gigabytes. Just to accommodate digital storage, the project has invested \$1 million. According to Daniel S. Marcus, PhD, assistant professor of radiology and director of the Neuroinformatics Research Group at Washington University School of Medicine, results on 500 subjects will be available in the spring of 2014.

Among the many processing tasks, including eliminating noise from the raw data, one of the team's biggest challenges has been the creation of an atlas, a sort of average of the scans to which any new scan can be compared. The atlas requires spatial registration of the brains' parcels for every subject. "Everyone's

head is different, and they may be in the scanner in a slightly different position, so the raw data doesn't align perfectly," Marcus says in describing the job. When processing is complete, the resulting atlas is a matrix of every point's connection strength with every other point in the normal brain.

Marcus also oversees publication of HCP findings. De-identified results are available to everyone — no advanced degree required — at the project's website: [humanconnectome.org](http://humanconnectome.org). There, a visitor will find:

> **ConnectomeDB** — a data management platform that allows users to identify groups of subjects (left-handers, for example) and download data for these groups. The HCP informatics team is currently developing data mining tools to allow users to analyze data and test hypotheses online.

> **Connectome Workbench** — a downloadable, interactive tool for visualizing maps of connectivity that talks to the database.

> **Connectome in a Box** — the huge package of all of the lightly processed data.

Says Marcus, "The Human Connectome Project represents a major advance in sharing brain imaging data in ways that will accelerate the pace of discovery about the human brain in health and disease."

## PARTICIPANTS

Barch, who also contributes to subject recruitment and selection, says that more than 500 volunteers have been scanned to date, and the project is on track to finish on schedule.

Ideally, each volunteer family includes a set of identical or fraternal twins and at least one other sibling, all ages 22 to 35. "This gives us the most powerful design for determining genetic effects on quantitative traits," she explains. Already, the model has confirmed that even identical twins have measurably different brain connections and that brain circuits are heritable, some more than others.

Subjects travel to St. Louis to spend two intense days in testing and four scanning sessions. "These individuals make a huge contribution to science," says Barch. Their efforts make it possible to understand the healthy human brain and also "enable future projects that probe the changes in brain circuits that underlie a wide variety of brain disorders affecting humankind, including autism and schizophrenia," says Van Essen.

As the HCP expands to include younger and older subjects and its data reaches more users and they imagine more applications for it, the impact on understanding and health made by the generous volunteers will continue to grow. 🍌

**Below:** Connectome Workbench interface



# COMBINING TECHNOLOGIES CREATES AN IMPORTANT DIAGNOSTIC TOOL

by Judy H. Watts



“It’s the hottest thing in radiology,” says Barry A. Siegel, MD, professor of radiology and chief of the Division of Nuclear Medicine at Mallinckrodt Institute of Radiology. The always plainspoken nuclear radiologist — who was instrumental in development of the clinical PET service at Mallinckrodt and foresaw the ensuing PET/CT technology — is referring to Mallinckrodt’s newest multimodal imaging machine, the PET/MRI scanner.



Following FDA approval in 2011, the device was installed in the department’s Center for Clinical Imaging Research (CCIR), located at Barnes-Jewish Hospital. It was the third PET/MRI acquired in the United States — following Massachusetts General Hospital and the National Institutes of Health — in keeping with the research institutions’ role in evaluating new technologies.

Called the Siemens Biograph mMR, the PET/MRI represents a feat of engineering that effectively melds two long-established — but very distinct — technologies, positron emission tomography (PET) and magnetic resonance imaging (MRI). A PET scan uses a radioactive compound, usually injected, to visualize biology at the molecular level. Common uses of PET include tracing metabolic activity and discovering malignant tissue. PET is clinically helpful for staging cancers and for neurological applications such as detecting the effects of Alzheimer’s disease and pinpointing the locations of seizures. An MRI machine produces a magnetic field and radio waves to create detailed images of tissues, organs and bones based on water concentrations in the body. The PET/MRI simultaneously performs both scans, producing more detailed images than either technique alone.

## CLINICAL POSSIBILITIES

Perhaps the most obvious benefits of the new system, according to Siegel, are its superior soft-tissue contrast and PET/MRI’s ability to probe specific tissue functions to provide information the PET/CT cannot. (In CT, or computed tomography, X-rays are used to image cross-sections of the body; when stacked, these slices provide three-dimensional views of a particular area.)

Further, radiation exposure is reduced in adults by 50 percent when PET/MRI is used, delivering a notable benefit for children and young adults who have lymphoma or other conditions requiring multiple scans to monitor treatment. In fact, Kathryn Fowler, MD, assistant professor of radiology in the department’s abdominal imaging section, says research shows the effective dose of a PET/MRI scan for children can be reduced to as little as 20 percent that of an equivalent PET/CT examination. Gheetika Khanna, MD, an associate professor of radiology who specializes in pediatric radiology, notes the PET/MRI is particularly helpful for younger patients who require sedation for imaging. The PET and MRI studies can be performed in the same setting, avoiding the need for multiple sedations.

Since its installation, the new technology has generated excitement and hard work. “Acceptance testing and optimization of protocols needed to be done, post-processing of two imaging types had to be worked out, and since we’re an extremely active research center, we were really pushing the PET/MRI to its limits,” says Pamela K. Woodard, MD, professor of radiology and biomedical engineering, and director of the CCIR, where the system is housed.

Just as research using the PET/MRI has flourished in Mallinckrodt’s already rigorous investigative environment, so too have discussions and energetic debate, in weekly PET/MRI steering committee meetings, in radiology laboratories and at national and international conferences — amid multiplying signs of promise for diagnosis, treatment, and care. Because definitive statements about this infant technology’s capabilities can only rest upon exhaustive evidence-based research, many such critical findings will emerge over time — and following PET/MRI’s clinical implementation, in 2014, at CCIR’s hospital home.

Tammie S. Benzinger, MD, PhD, assistant professor of radiology and neurosurgery, states that although the system provides much opportunity for research, the PET/MRI’s usefulness for oncologic and whole-body imaging also has been validated. Its combination of PET and MRI techniques can help to distinguish between tumors and soft-tissue scarring following treatment in both neurological and whole-body oncologic diagnosis, she says. Referring clinicians agree. Perry W. Grigsby, MD, professor of radiation oncology, chief of the gynecologic radiation oncology service, and director of the brachytherapy center, says the PET/MRI will be “absolutely advantageous” to his specialty. “The machine allows us to ask and answer questions about both PET and MRI characteristics that we really weren’t aware existed before,” says Grigsby. “It’s allowed us to acquire much more information.”

To illustrate, Grigsby notes that, “With the PET portion of the PET/MRI, we can see which part of large cervical tumors respond to therapy by way of looking at the different areas of glucose metabolism highlighted with tracers that accumulate in cancer cells, which are highly active. With the MRI portion, we can see which parts of the tumor respond to treatment — and in some cases, both [modalities] show us that the same area of the tumor is responding and in another case, different areas seemed to be responding in different ways. Among all the patients I see with cervical cancer, I would stop doing PET/CT and do PET/MRI.”

Farrokh Dehdashti, MD, professor of radiology and co-leader of the Oncologic Imaging Program at the Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine, says: “Some patients — for example, individuals with rectal or gynecological cancers — need both PET and MRI studies, and it will be convenient for the patient to have both tests done at the same time. The MR images will be co-registered with PET images without or with minimal motion artifact. This makes interpretation easier and probably more accurate. Thus, there are patients who would benefit from this modality.”

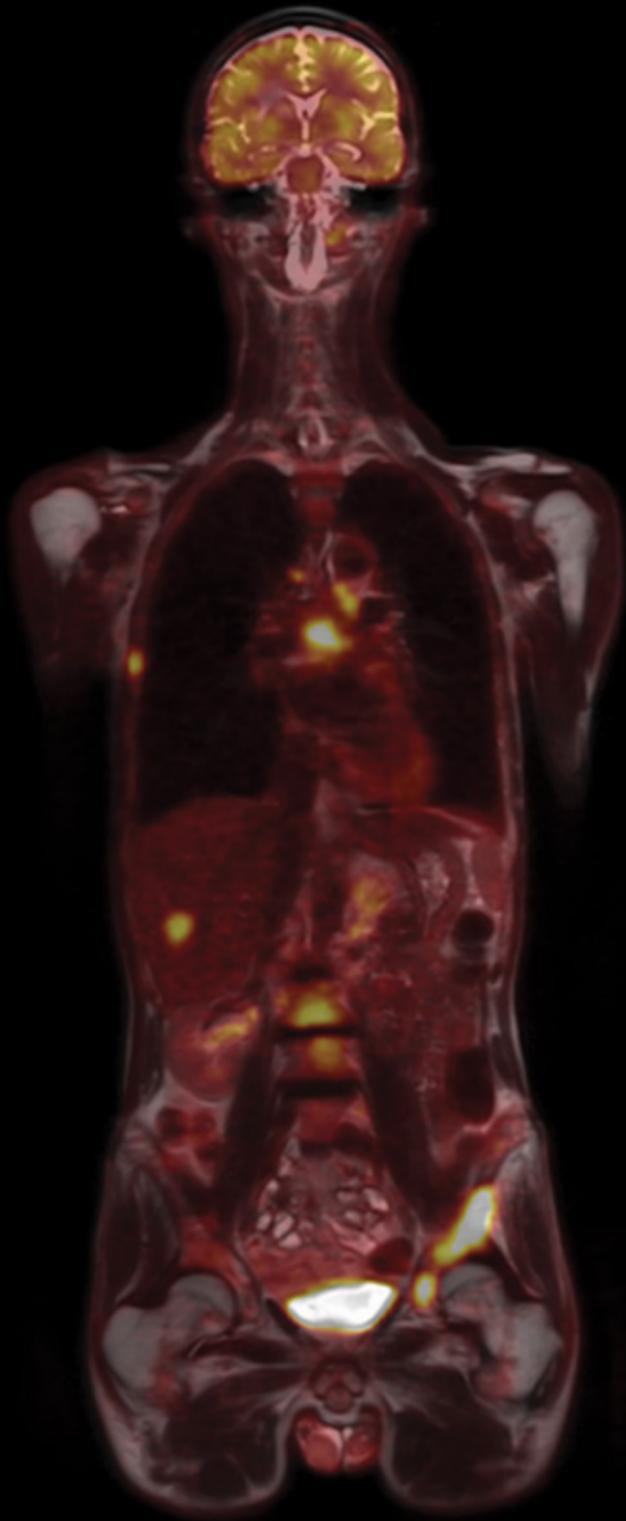
All in all, the action — and the buzz — is likely to intensify. Jonathan E. McConathy, PhD, MD, assistant professor of radiology, works with adults and children and is enthusiastic about the technology’s use in suitable cases. Both McConathy and Parag J. Parikh, MD, assistant professor of radiation oncology and of biomedical engineering, expect that when clinical use begins, the machine will be a boon to translational research, the results of which will reach the community, in part, because PET/MRI’s “one-stop shop” will help attract participants. “Recruiting patients for a recent trial — during which the PET/MRI yielded new information — was very easy,” says Parikh, who leads Washington University’s gastrointestinal radiation oncology service. “The PET/MRI’s capabilities really resonated with the patients, and they understood the importance of the research.”

“We’re primed and ready, just waiting for the go-ahead,” says Fowler. To prepare, she and McConathy spent a week at Munich’s Technische Universität München (TUM) one of Europe’s leading research institutions, studying effective PET/MRI protocols and sequences. Now, she says, “we have our own PET/MRI protocols in place for virtually every clinical question that might arise.”

## TRANSLATIONAL RESEARCH

In addition to notable findings and preliminary results, the research using PET/MRI at the CCIR has built upon the Mallinckrodt tradition of research teamwork and regular intensive communication. As Dehdashti puts it: “Now, the MRI experts and nuclear medicine experts are talking with each other, trying to learn from each other and collaborating on group projects.”

The formidable amount of research underway at Mallinckrodt benefits immensely from the PET/MRI’s



#### **PET/MRI fusion**

New promise for diagnosis, treatment and care

*Image courtesy of Pamela K. Woodard  
Mallinckrodt Institute of Radiology*

“ability to put so many types of information together simultaneously,” Siegel says, such as assessing MRI signals showing which brain regions are activated during a particular task or while observing glucose metabolism. “Previously, you had to do two separate exams, register the data, make a decision, get the data simultaneously and nail down your hypothesis in the same location. There are many opportunities,” he says, “to ask some very interesting research questions that would be difficult to answer if tests were done at different points in time. So simultaneous data are always better.”

Marcus E. Raichle, MD, professor of radiology, neurology, neurobiology and of biomedical engineering and a member of the National Academy of Sciences’ Institute of Medicine, has received a National Institutes of Health (NIH) Program Project Grant to use PET/MRI to investigate Alzheimer’s disease in diabetic patients and the various mechanisms of anaerobic glycolysis. Other research utilizing PET/MRI includes two international studies assessing novel radiopharmaceuticals to target abnormal plaque development and proteins increased in Alzheimer’s disease, on which Benzinger is site principal investigator and leads the imaging core. Dehdashti and Grigsby are leading an NIH study that assesses a novel hypoxia-targeting agent to show which pelvic tumors respond best to therapy, and Woodard and others have funding to use PET/MRI to investigate novel copper PET imaging agents, one developed by their team to assess atherosclerosis.

As continuing interdepartmental collaborations at Mallinckrodt draw upon what Washington University Danforth Campus creativity expert R. Keith Sawyer, PhD, professor of education and of psychology, calls group genius — will innovations appear and new applications arise to serve both bench and bedside?

“Absolutely,” says Benzinger. “A lot of thinking about new projects is coming along. In just one example, in the spring we’re going to image the protein tau in the brain — its accumulation is a hallmark of neurodegeneration — by using a PET imaging agent, and we’re already thinking about combining that with brain functional mapping using resting-state MRI.”

Many observers — and PET/MRI users — believe that the new technology will be of vastly increasing benefit to research and clinical practice in areas ranging from neuro-oncology and neurology to cardiology and pulmonology, gastroenterology, rheumatology, neonatology, and pediatrics. All of the research has the potential to improve the health and well-being of patients. 



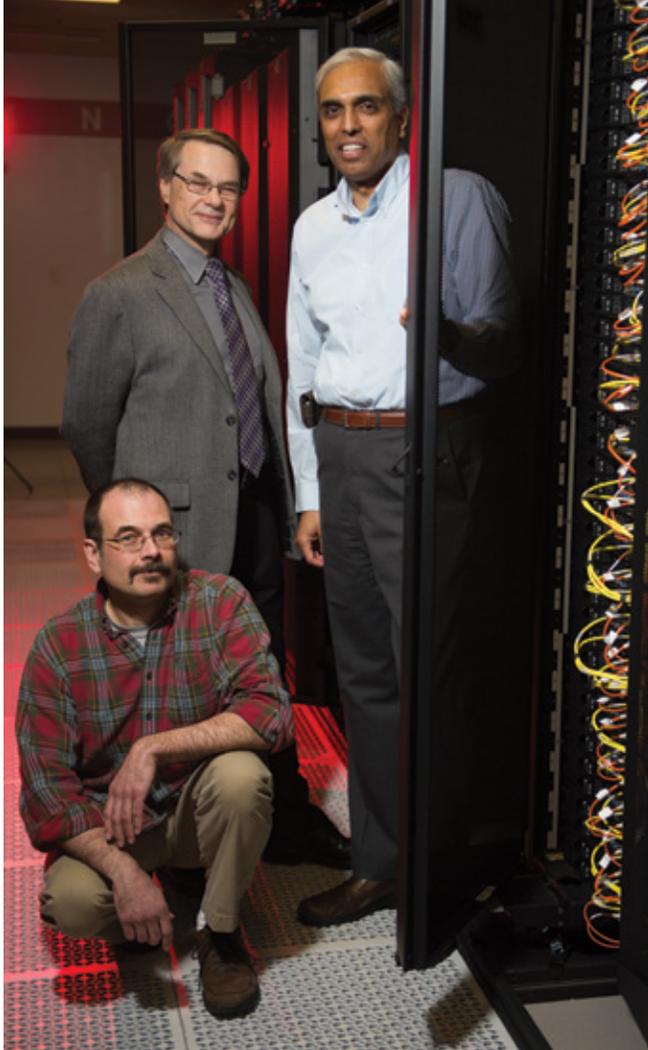


# COMPUTING IN CONCERT

## HIGH-PERFORMANCE PROCESSING ENABLES INNOVATION

by Mary Ellen Benson

When the problem is a monstrously intensive computational task—describing a whole system like the brain or the entire human genome or reconstructing highly detailed images, for example—a single computer is a clumsy and slow tool. More elegant and speedier is the “supercomputer,” actually many dedicated processors working together in close proximity to save time moving data around. Not one giant bee, but a hive of many workers all dedicated to the same problem.



**Top, pictured left to right:** Malcolm Tobias, PhD, Fred W. Prior, PhD, and Rohit V. Pappu, PhD  
**Bottom:** Supercomputer — *Human Connectome Project sector* // TIm Parker

Fred W. Prior, PhD, professor of radiology and director of Mallinckrodt's Electronic Radiology Laboratory, recalls receiving an email from department director R. Gilbert Jost, MD, about five years ago saying, "There's this NIH (National Institutes of Health) grant, and one of the things you can buy is a supercomputer. Why don't you see if anybody's interested?"

Prior, who directs the Center for High Performance Computing (CHPC), says he was skeptical but called a meeting of people he thought might be interested, assuming a small turnout. "Everybody I invited came," he says, "and they brought their friends. There was tremendous interest." He attributes it to a "pent-up demand for high-performance computing" since an earlier center in the Department of Physics had closed.

So Prior wrote the grant, which was accepted, but, he says, "The government didn't get a budget that year, so there wasn't any funding." He notes that reviewers asked them "to prove that the algorithms you're talking about actually would be improved if you had this computer." To resubmit the grant, he partnered with IBM, which ran the simulations and gave him the results.

When the system eventually was funded, it was purchased from IBM and housed in the Genome Institute's data center. For the first couple of years, they ran it in what Prior calls "family and friends" mode. He says, "If you were in radiology, were collaborating with radiology, had some link, however tenuous, we'd give you an account and it was free."

When the CHPC wanted to expand access to the rest of the university, two issues needed to be addressed. One was to develop a funding model that would be sustainable, and the other was to assure there was high enough network bandwidth to move large data sets between the medical and Danforth campuses.

"We put our high-performance computer on the highest bandwidth network at Washington University," Prior says. "And now there's a high-speed link dedicated for research between the campuses, and we're hoping to maintain and grow that."

Today, researchers across the university — from medicine to engineering to economics to music — are taking advantage of the supercomputer to advance their research, which in many cases helps them attract grant money to support it. To date, the CHPC has processed more than 3.4 million jobs that have consumed a total of 19.8 million processor hours. To do that much computing on a single processing core would require approximately 2,260 years. The system earns its "super" appellation.

The funding model was developed “with a lot of help from the dean’s office” at the School of Medicine. Prior says, “We convinced the school’s executive faculty and the deans on the other campus that this should be a fee levied against departments so that all of their faculty could have free access to the system.”

Another important step was when the School of Engineering & Applied Science “made us a deal we couldn’t refuse” and became co-operators of the center. Prior remains the director in charge of day-to-day operations, and his co-director is Rohit V. Pappu, PhD, professor of biomedical engineering and a member of CHPC’s executive committee.

In place of having each engineering school department pay a fee to use the supercomputer, the school upgraded the computer with Graphics Processing Units (GPUs). GPU-accelerated computing offloads computer-intensive portions of an application to the GPU, while the remainder of the code runs on the CPU. The result? Applications run significantly faster.

For investigators like Pappu, access to the supercomputer has solved the issue of trying to find money for annual purchases of computer hardware.

“keeping the users happy,” and as “a wizard at adjusting how the scheduling system works.”

Tobias also works closely with what Prior calls the “invisible network” — graduate students and postdocs. Prior says they are “the people who actually figure out how to use this thing, and then they talk to each other.”

Key too, Prior says, is an executive committee of leaders from both campuses. According to Pappu, a primary role of the executive committee is to determine how to fund the CHPC and how to sustain it, particularly when a dynamic at play is Moore’s Law (from Intel co-founder Gordon Moore), which says that the speed of processors basically doubles every 18 months.

That, of course, requires ongoing investment. The CHPC leaders are looking at the kind of analysis that’s being done on the supercomputer by the Human Connectome Project, and then projecting what will happen. They are seeking funding to add higher performance components with a focus on leading-edge GPU computing elements. They also plan to hire a GPU programmer.

“Lots of applications do well on GPU hardware,” Pappu says, “but converting what is designed to work

## “Funding agencies are extremely happy giving you money for your work if you tell them you have access to a supercomputing resource.”

He explains that funding agencies will not fund a grant for computing equipment and will take out any line item on computing infrastructure, which posed a “significant limitation” to his laboratory’s research.

The paradox, he says, is that “funding agencies are extremely happy giving you money for your work if you tell them you have access to a supercomputing resource.”

This was one thing that led Ralph S. Quatrano, PhD, dean of the School of Engineering and the Spencer T. Olin Professor, to invest in the GPUs. “The idea, then, was it would enable more grants to come through and provide greater collaboration,” Pappu says. It would also give the engineering school “a fertile playground” in the area of GPU computing.

But the GPUs have benefited much more. They have been integral to the Human Connectome Project, which is one of the biggest users of the supercomputer, as well as to investigators in the Department of Radiology, which is the other superuser of the system.

Overseeing the work of the CHPC and keeping it running is Malcolm Tobias, PhD, senior system administrator. Prior describes him as having a “tremendous knowledge of high-performance computing,” as

on a CPU to work on a GPU takes a lot of know-how and technical skill.” He envisions that “as this enterprise grows, we hope to have about half a dozen people between the two campuses who will enable the work of about 30, 40, 50 — maybe even 100 — scientists who are all using high-performance computing to advance their particular areas of research.”

Pappu believes two things are needed to advance researchers’ work. “There’s innovation that we bring to the table in terms of state-of-the-art models that enable computations in ways that are unique. But all that would add up to naught if we didn’t have the Center for High Performance Computing. You need both. You need the innovation, but you also need the resources.”

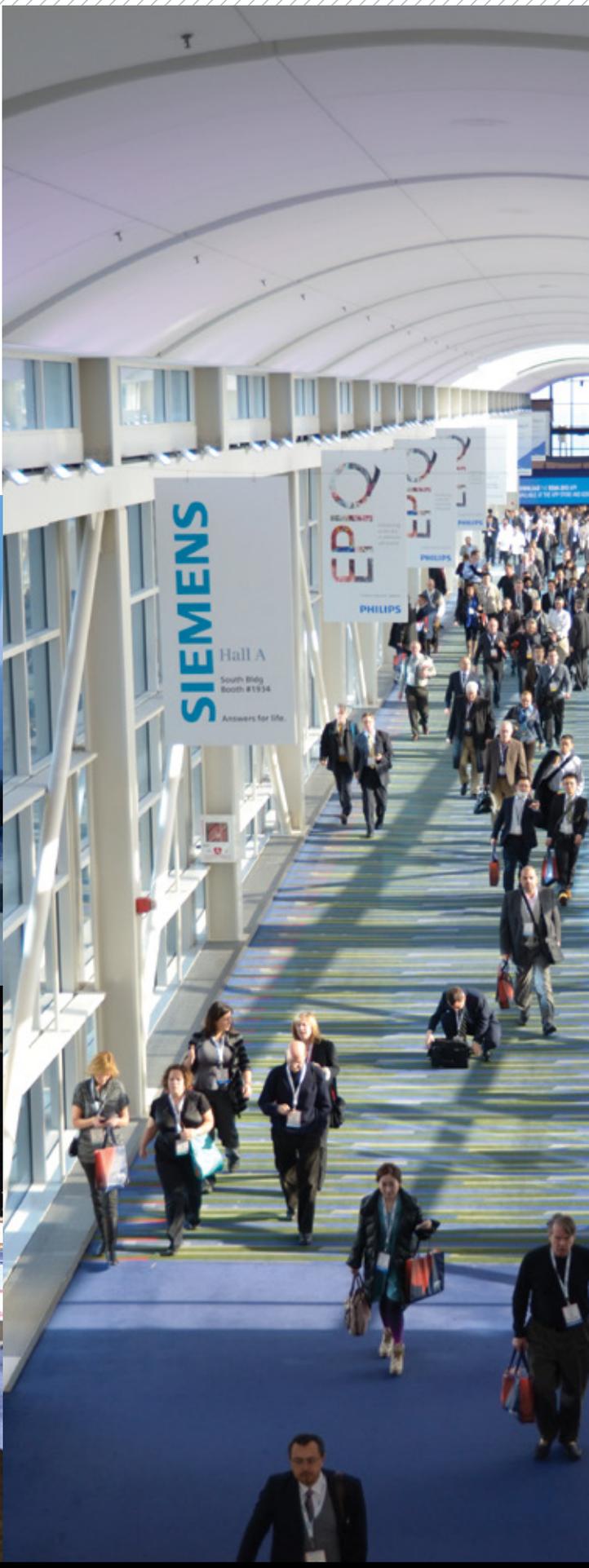
He praises Jost, director of Mallinckrodt Institute of Radiology, as being “genuinely instrumental in the early days, in recognizing the importance of high-performance computing, and then putting his support behind the venture,” with further support from Larry J. Shapiro, MD, dean of the School of Medicine.

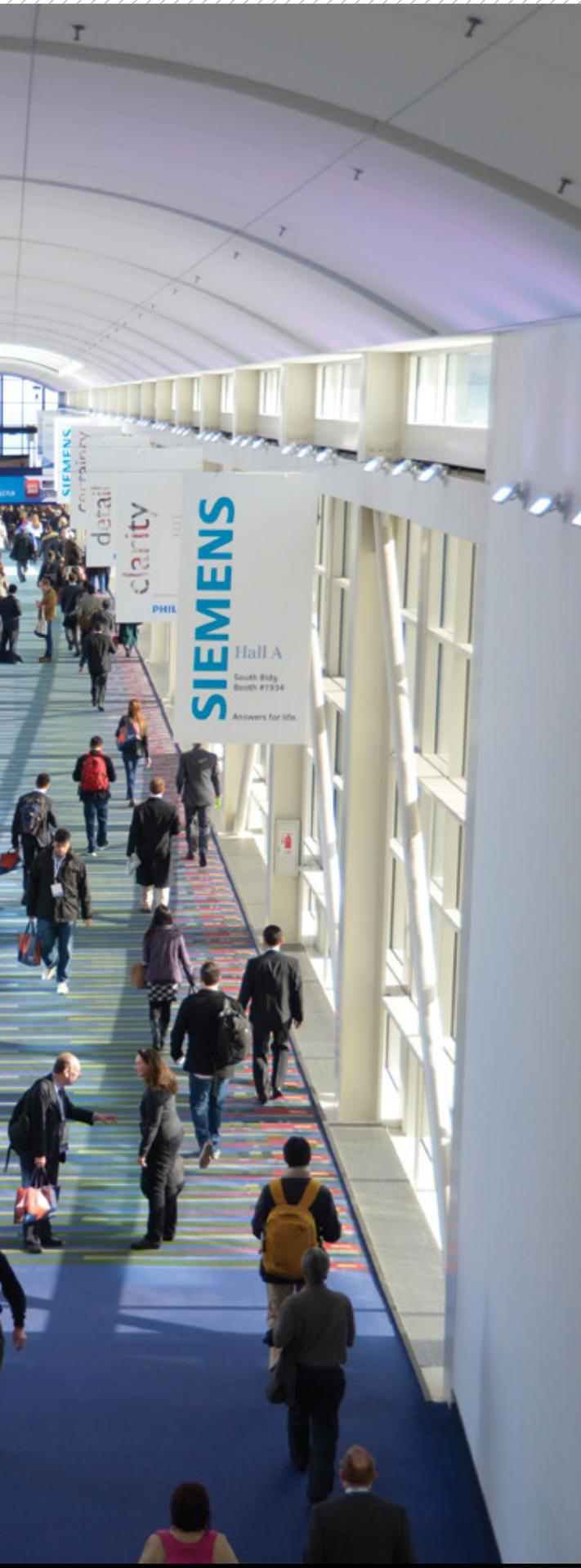
Without them, he says, “I don’t think any of this would have happened. For me, at least, it has been a transformative entity.” 🌟

# RSNA 2013

## THE POWER OF PARTNERSHIP

Radiology professionals from around the world gathered in Chicago December 1–6 at the Radiological Society of North America's 99th scientific assembly and national meeting. The event, held at McCormick Place Convention Center, focused on the profession's need for teamwork — within radiology, between departments outside of radiology, with patients, and with international partners. The week's keynote speaker was former U.S. Secretary of State Condoleezza Rice, who advocated using education and leadership to tackle current health care challenges. More than 54,000 people attended RSNA. //





**Current and former residents and faculty renewed acquaintances at RSNA and at the Mallinckrodt reception held at the Hyatt Regency of Chicago's Crystal Ballroom.**

- A** Delphine Chen, Ron Evens, Evan Unger    **B** Peggy and Gil Jost
- C** Pamela Woodard, Cylon Javidan-Nejad, Andy Bierhals
- D** Parinaz Massoumzadeh    **E** Sabrina Ward, Iris Gibbs, Cooky Menias
- F** Clint Jokerst, Luke and Carrie Linscott    **G** Hilary Purdy, Yaseen Oweis, Anup Shetty, Ron Loch, Jim Raptis, Chris Smith
- H** David Rubin    **I** Jay Heiken, Katie Fowler

*All RSNA images photographed by Mickey Wynn, MIR Visual Media Center*



**RICHARD E. HELLER III, MD, MBA**, is a pediatric radiologist in private practice with Radiology Imaging Consultants in Oak Lawn, Ill., and the newly named chair of radiology for Advocate Children's Hospital, part of Advocate Health Care, the largest health care provider in Illinois. He and his wife, Beth, vice president of Harry Caray's Restaurant Group, are passionate about children's charities (they have two boys: Richard IV, 8, and Julian, 5) and art, and they have found unique ways to express those passions in both their personal and professional lives.



**Above:** Heller with world-renowned pop artist Jeff Koons in front of the Koons-designed CT scanner at Advocate Children's Hospital in Chicago

## How did you become interested in pediatric radiology?

My grandfather was a surgeon, and my father is a pediatric radiologist. I was interested in both fields, and although my original intent was to become a surgeon, I was a little surprised to learn that I wasn't that coordinated and was therefore advised to seek vocation elsewhere!

## Once you decided to specialize in radiology, why did you choose Mallinckrodt for residency training?

There is no place better. You can get a great education at other institutions, but Mallinckrodt is second to none in terms of education, training, and research. And it's only grown stronger in the years since I moved on. It's a huge credit to the Mallinckrodt leadership that there's not a lot of turnover; people stay for years and years.

## Who were some of the people at Mallinckrodt who left the greatest impression upon you?

Bill McAlister, a friend of my father's, was a huge influence during my initial interview and residency; a fountain of knowledge, he remains a friend and mentor. Gary Shackelford, who is now retired, was a big name in the field and a real pleasure to work with. Tom Hermann is one of the brightest men I've met in life — medicine or otherwise. And Marilyn Siegel — well, you're not going to do better anywhere. It truly was a pleasure to train with everyone in the pediatric radiology section.

## Do you feel your training at Mallinckrodt gave you an advantage as you began and now continue in your career?

Absolutely. Mallinckrodt opened doors for me in two ways. First, because it is such a large program, the Mallinckrodt network extends throughout the country. This means that I can find a Mallinckrodt radiologist in any region of the country when I need to reach out. Second, the Mallinckrodt brand is so respected that it practically opens doors by itself. When someone hears you trained at Mallinckrodt, the expectation is that you will perform at a very high level.

## Does your association with Mallinckrodt continue to play a role in your professional life today?

Yes. Bob McKinstry has become a close contact; we have different approaches and that is helpful when dealing with issues such as the changing dynamic of radiology and the shifting health care marketplace. Sanjeev Bhalla and Cooky Menias were both senior to me and very influential — a dynamic duo. We remain friends and I don't hesitate to reach out for their help. I've also stayed close with fellow residents, such as Howard Harvin and Naveen Parti, who are both wonderful radiologists.

## CAREER PROFILE

**RICHARD E. HELLER III, MD, MBA**

**2012 // MBA**

Kellogg School of Management,  
Northwestern University

**2005 // Pediatric Radiology Fellow**

Harvard Medical School,  
Boston Children's Hospital

**2004 // Diagnostic Radiology Resident**

**Mallinckrodt Institute of Radiology,  
Washington University  
School of Medicine**

**2000 // Medical Intern**

Feinberg School of Medicine,  
Northwestern Memorial Hospital

**1999 // MD**

Feinberg School of Medicine,  
Northwestern University

**1995 // BA**

Colgate University

### In which are you more invested — the business of medicine or clinical practice?

I enjoy both. Being a practicing radiologist who reads exams every day helps me to remain creative and gives me credibility and insight into the business aspects of health care. One of my non-clinical activities is consulting on investment and growth strategies in the health care industry, and I have a special interest in the medical imaging services market and in health information technology. I will be speaking on value creation in radiology at RSNA 2014.

### What are your interests beyond radiology?

My biggest passion outside of medicine is art, particularly the importance of art for the community and for children. My wife and I have a contemporary art collection featuring works by Andy Warhol, Jenny Holzer, and Glenn Ligon, among others. I currently serve as acquisition chairman of Emerge, the emerging artist acquisition council for the Museum of Contemporary Art in Chicago. Recently, through my wife, I've also become involved in imaging sports memorabilia.

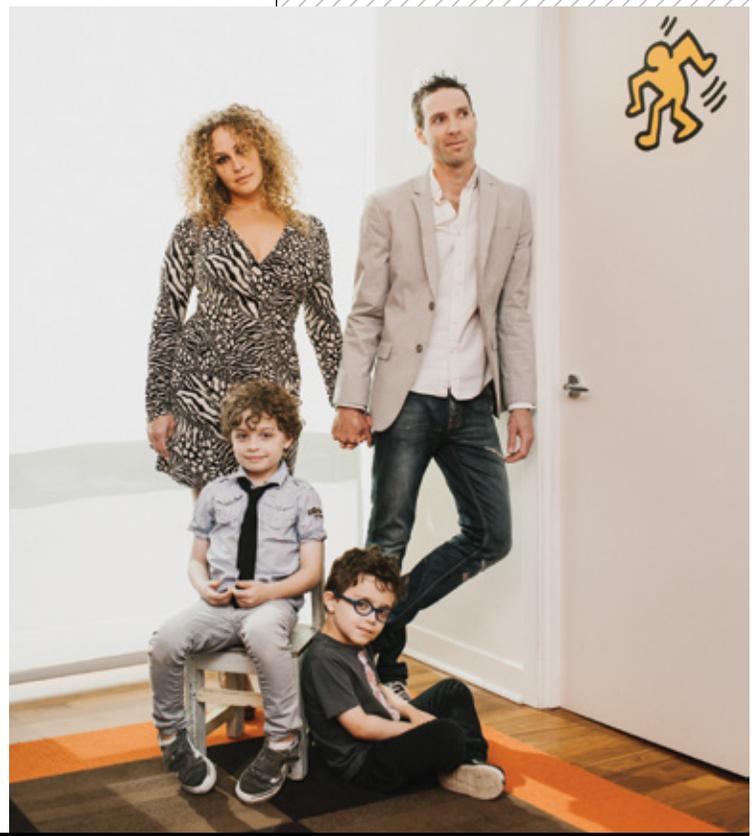
### How did you first become interested in art?

My love of art really started to blossom while I was at Mallinckrodt; I found art to be a very useful and important hobby to focus my mind and relax during the intensity of residency training. In fact, I purchased my first "significant" piece while still a resident, paying monthly installments on it until we sold our home in St. Louis to move to Chicago.

### How have you managed to blend your passion for contemporary art with your professional life?

After we relocated, my wife and I were looking for a local charity to support. We found RxArt, a non-profit organization that installs art in pediatric hospitals to stimulate healing. Working with RxArt founder and president Diane Brown, we were very blessed and lucky to bring Jeff Koons to my facility, Advocate Children's Hospital in Chicago, where he and his studio designed an entire CT scan room, including the machine itself. 🌀

**Right:** Heller with his wife, Beth, and sons Richard, left, and Julian at their Chicago home // *Daniel Shea*



## IN MEMORY



**Above:** Michael J. Welch, PhD

Family and friends of Michael J. Welch, PhD, gathered in Spring 2013 to honor him with the dedication of the Michael J. Welch conference room. Located in the Clinical Sciences Research Building at Washington University School of Medicine, the renovated and refurbished space displays a collection of Welch's many awards and achievements.

Welch was a pioneering radiochemist and the author of more than 550 papers on the use of radioactive drugs in the diagnosis and treatment of disease. He died May 6, 2012, at age 72.

"Dr. Welch was widely regarded as the world's leader in his specialty, which was radiopharmaceutical chemistry," says R. Gilbert Jost, MD, the Elizabeth E. Mallinckrodt Professor and director of Mallinckrodt Institute of Radiology. "He was largely responsible for the development and widespread use of radioactive pharmaceutical agents in medical research and practice."

Welch's many accomplishments include contributions to the compounds that allow imaging of brain blood flow and creation of imaging agents for the study of many types of cancer. He also worked to ensure that an adequate

supply of radiopharmaceuticals was available for medical treatment.

Welch was a professor of radiology, chemistry, biomedical engineering and of developmental biology. He was the founding leader of the Oncologic Imaging Research Program at the Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine and a member of the cancer center's senior leadership.

"We are blessed with quite a few spectacular scientists here at Washington University, but Michael Welch was truly one of the giants," says Robert J. Gropler, MD, professor of radiology, chief of the Division of Radiological Sciences, and a frequent collaborator with Welch. "We've lost someone very special."

Born and raised in England, Welch earned bachelor's and master's degrees in natural sciences at Cambridge University. He earned a doctorate in chemistry at the University of London in 1965.

Welch joined the Washington University faculty in 1967. Through mentor Michel M. Ter-Pogossian, PhD, he contributed to the development of positron emission tomography (PET) at the university in the early 1970s.

"Michael Welch was the most amazingly plugged-in scientist in terms of the interfaces between many different disciplines of biomedicine and other sciences," says longtime collaborator and friend Barry A. Siegel, MD, professor of radiology and chief of the Division of Nuclear Medicine.

Welch was elected to the Institute of Medicine and received many of his field's highest honors, including the Benedict Cassen Award from the Society of Nuclear Medicine. In 2008, the society named its award for outstanding contributions to radiopharmaceutical research after Welch. Washington University's recognitions of Welch have included its Distinguished Faculty Award and its 2nd Century Award.



**Above:** Michael Welch's family has established a foundation in his honor to support research in nuclear medicine. Memorial contributions may be made to the Dr. Michael J. Welch Foundation, 55 Walls Drive, Fairfield, Conn., 06824. To learn more, please visit: [mjwelchfoundation.org](http://mjwelchfoundation.org).

## APPOINTMENTS

### **Beau M. Ances, MD, PhD**

Associate Professor of Radiology  
(primary appointment in the  
Department of Neurology)

### **Andrew R. Coggan, PhD**

Research Assistant Professor of Radiology

### **Konstantin Maslov, PhD**

Research Associate Professor of Radiology  
(primary appointment in the Department  
of Biomedical Engineering)

## PROMOTIONS

### **Paul K. Commean, BEE**

Research Assistant Professor of Radiology

### **Joel R. Garbow, PhD**

Research Professor of Radiology

### **Michelle Lee, MD**

Assistant Professor of Radiology

### **Daniel S. Marcus, PhD**

Associate Professor of Radiology

### **Vincent M. Mellnick, MD**

Assistant Professor of Radiology

### **David G. Politte, DSc**

Research Assistant Professor of Radiology

### **Fred W. Prior, PhD**

Research Professor of Radiology

### **Joshua S. Shimony, MD, PhD**

Associate Professor of Radiology

### **William M. Spees, PhD**

Research Assistant Professor of Radiology

### **Zhude Tu, PhD**

Associate Professor of Radiology

## GRANTS

**Delphine L. Chen, MD**, assistant professor of radiology, and **Andrew E. Gelman, PhD**, associate professor of surgery, received a four-year, \$2,738,293 grant from the National Heart, Lung, and Blood Institute for research titled “Positron Emission Tomographic Imaging of Lung Transplant.”

**Colin P. Derdeyn, MD**, professor of radiology, neurology, and of neurological surgery, received an \$80,720 subcontract (total award is \$7,186,649 to the University of Cincinnati) for the NIH StrokeNet National Coordinating Center. The aim of the grant is to coordinate and provide central infrastructure for stroke clinical trials involving prevention, treatment, and recovery. Derdeyn is the co-chair of the Imaging Core and the chair of the Interventional Working Group.

**Monica Shokeen, PhD**, instructor in radiology, received a \$955,889 grant from the National Institutes of Health (NIH)/National Cancer Institute (NCI) for “Receptor Targeted Molecular Imaging of Multiple Myeloma,” on which she will serve as principal investigator. The goal of the four-year grant is to evaluate a novel multiple myeloma molecular imaging approach to image early stage disease using a VLA-4 targeted PET probe in mouse models which closely emulate human myeloma bone disease and progression. The described studies will directly compare this innovative imaging methodology in pre-clinical models with FDG/PET, the current imaging standard, and will lay the groundwork for first-in-man clinical trials.

**Pamela K. Woodard, MD**, professor of radiology, and co-investigators **Suzanne E. Lapi, PhD**, assistant professor of radiology, **Jie Zheng, PhD**, associate professor of radiology, **Farrokh Dehdashti, MD**, professor of radiology, **Robert J. Gropler, MD**, professor of radiology and associate professor of biomedical engineering and of medicine, **Gwendalyn J. Randolph, PhD**, professor of pathology and immunology and of medicine, **Robert W. Thompson, MD**, professor of surgery, radiology, and of cell biology and physiology, and **Ling Cheng, PhD**, received a one-year, \$50,000 BJHF/ICTS Award for “Non-Invasive Detection of Hypoxia in Atherosclerotic Plaque with Cu [64]-ATSM PET-MRI.”

## TRANSITIONS

**Jay P. Heiken, MD**, will be stepping down as co-director of Body CT after more than 18 years to devote his time to mentoring fellows and residents.

**Vincent M. Mellnick, MD**, has joined **Sanjeev Bhalla, MD**, as new co-director.

**Michael F.Y. Lin, MD**, has been appointed to head the quality and safety office for Abdominal Imaging.

**Kathryn A. Robinson, MD**, and **William D. Middleton, MD**, have been appointed as co-directors for the ultrasound service.

**Motoyo Yano, MD, PhD**, has been appointed director for the 3D imaging service for Abdominal Imaging.

## LECTURES

**Delphine L. Chen, MD**, assistant professor of radiology and of medicine, presented “Imaging Lung Inflammation with Positron Emission Tomography” at Cedars-Sinai Hospital, Department of Internal Medicine, in Los Angeles, Calif., on September 26, 2013. She spoke on the same subject as a radiology visiting professor at Cincinnati Children’s Hospital on October 23, 2013, an invited lecturer at the University of Wisconsin, Department of Radiology, in Madison, Wis., on October 31, 2013, and as an invited speaker for the Asthma and Airway Diseases Conference held at Washington University School of Medicine on January 9, 2014. Chen also served as session moderator for “Emerging Pulmonary Functional Imaging Techniques: What the Clinician Should Know” at the CHEST 2013 Annual Conference in Chicago, Ill., on October 26-31, 2013, and presented a lecture titled “Overview of Functional Lung Imaging Techniques.” Chen, a recipient of the American Thoracic Society Young Investigator Award, presented “PET Imaging with [11C]PBR28 and [18F]FDG Distinguishes Macrophage from Neutrophil Lung Inflammation” at the Young Investigators Session of the Asian Pacific Society of Respiriology 2013 Annual Congress in Yokohama, Japan, on Nov 11-14, 2013.

**Carmen S. Dence, Pharm Sci, MS**, associate professor of radiology, recently returned from her sixth trip to South America as a mission expert of the International Atomic Energy Agency (IAEA). On this trip, Dence presented lectures and practica in Brazil at the country’s leading institutions in Porto Alegre and Sao Paulo, and she also spoke at two symposia in Sao Paulo.

**Colin P. Derdeyn, MD**, professor of radiology, neurology, and of neurological surgery, presented “Final Results of the SAMMPRIS Trial” at the 6th International Conference on Intracranial Atherosclerotic Disease/Society of Vascular Interventional Neurology Annual Meeting in Houston, Texas, on October 26, 2013. He also spoke on “Perfusion Parameters that Matter Most for Acute Stroke Outcomes and Triage” and “Acute Stroke Intervention: Is it Stentrievors, or the Next Generation Device, or is it Treating 0-3 hours that Matters Most?” at the Advanced Interventional Management Symposium in New York, N.Y., on November 19, 2013.

**Suzanne E. Lapi, PhD**, assistant professor of radiology and of biomedical engineering, gave a lecture titled “Production of PET Radiometals: 64Cu and 89Zr” at the North American Particle Accelerator Conference held in Pasadena, Calif., on October 3, 2013.

**Jonathan E. McConathy, MD, PhD**, assistant professor of radiology, presented “Biograph mMR Applications in Pediatric Neuroimaging” at the Siemens Biograph mMR Users Group Meeting in London, Ontario, on September 28, 2013. He also spoke on “Targeting Amino Acid Transporters for Oncologic Imaging” at the Cancer Center Retreat at the University of Alabama, Birmingham, on November 5, 2013.

**Robert C. McKinstry III, MD, PhD**, professor of radiology and of pediatrics, presented “Simultaneous PET/MR: Neurological Applications and Clinical Performance” at the 2nd PET/MR Workshop: What You Need to Know held at Case Western Reserve University in Cleveland, Ohio, on September 13, 2013.

**Barry A. Siegel, MD**, professor of radiology and of medicine, and vice chair for nuclear medicine in radiology, presented the First Annual R. Edward Coleman, MD Memorial Lecture, “Impact of PET on the Management of Patients with Cancer: What We Have Learned From NOPR,” at the Southeastern Chapter, Society of Nuclear Medicine and Molecular Imaging Annual Meeting in Charlotte, N.C., on October 12, 2013; he spoke on the same topic at the Western Regional Society of Nuclear Medicine Annual Meeting, George V. Taplin, MD Lecture in Pasadena, Calif., on October 26, 2013. Siegel presented “Impact of PET and PET/CT on Management of Patients with Cancer,” “PET in Oncology: Monitoring and Predicting Response to Treatment,” “PET in Oncology: Beyond FDG,” and “Current Status of PET/MRI” at the Macquarie University 10th Annual Integrative Imaging Symposium held in North Ryde, New South Wales, Australia, on November 2, 2013. He also spoke on “What Have We Learned from the National Oncologic PET Registry?” at the University of California-Los Angeles’ Cardiovascular Molecular Imaging Symposium in Santa Monica, Calif., on November 14, 2013.

## ELECTIONS

**Keith C. Fischer, MD**, associate professor of radiology, is serving a one-year term as president of the Missouri Radiological Society.

**James E. Kelly, MD, MA**, instructor in radiology, was elected as a member-at-large of the medical executive committee at Barnes-Jewish St. Peters Hospital for 2014.

**Geetika Khanna, MD**, associate professor of radiology, has been named assistant editor of *Pediatric Radiology*.

**Robert C. McKinstry III, MD, PhD**, professor of radiology and of pediatrics, is serving a two-year term as president of the Society of Chairs of Pediatric Radiology Departments at Children's Hospitals (SCORCH). He also is chair (2014-16) of the Children's Medical Executive Committee at St. Louis Children's Hospital.

**Sharlene A. Teefey, MD**, professor of radiology, was elected to the board of Microfinancing Partners in Africa, a St. Louis funding organization that empowers women in four African countries to lift themselves out of poverty. She also serves as head of the group's research and education committee.

## IN FOCUS



**Above:** Joseph E. Ippolito, MD, PhD

Every living entity — whether it's a human being, a bacterium, or a cancer cell — needs energy to survive. Joseph E. Ippolito, MD, PhD, instructor in radiology, believes that by identifying specific metabolic — or energy-related — features of a cancer cell that allow it to survive, researchers may be able to selectively kill cancer cells in patients.

Ippolito has discovered a new metabolic pathway in cancer cells that is activated by stress and directly correlates with poor outcomes in multiple cancers. The pathway involves the synthesis of the neurotransmitter gamma-aminobutyric acid (GABA).

According to Ippolito, metabolism can change if a cancer cell becomes “stressed.” For example, in a large tumor where cancer cells are constantly dividing, they need a steady supply of oxygen and nutrients to survive. “Crowded” cells in the center of the tumor may not have access to these critical elements and become “stressed” to the point that their metabolism changes to adapt to these new conditions. As a result, chemotherapy and radiation therapy may not have as significant an effect on these tumor cells. In addition, the cells have a higher propensity for metastasis.

Ippolito's interest in the metabolic features of aggressive cancers is nothing new. He earned his undergraduate degree

in biochemistry from Cornell University and graduated from Washington University School of Medicine's MD/PhD program with a PhD in molecular biophysics in 2007. As a graduate student, he worked on several cancer metabolism-based projects and continues that research today.

In 2013, Ippolito received a one-year, \$40,000 Seed Grant from the Radiological Society of North America (RSNA) to study “Metabolic Characterization of the Neuroendocrine Cancer GABA shunt.” Data from the project will indicate the feasibility of the research prior to applying for funds from other agencies.

After receiving his MD/PhD, Ippolito completed residency training and a fellowship in body MRI at Mallinckrodt Institute of Radiology. Today, he spends about 80 percent of his time conducting research and the balance on clinical service doing predominantly MR and CT imaging. His focus is on oncologic imaging, with an interest in prostate MRI.

The blending of his expertise in biology, chemistry, and imaging has proved beneficial. To understand how the pathway he discovered allows cancer cells to survive, Ippolito is using a combination of optical, MR, and nuclear imaging in conjunction with advanced chemical and genetic techniques. He also uses this information to develop novel approaches to treating aggressive cancers, such as with off-label FDA-approved pharmaceuticals.

“My goal is to make advancements in cancer metabolism at the bench and to take those discoveries to the clinical setting,” says Ippolito. “We can do that by developing new imaging techniques that will allow physicians to detect aggressive disease, stratify patients based upon severity of their disease, and identify molecular details about the cancer that can be used for therapeutic purposes.”

— Holly Edmiston 

# A LOOK BACK

## PET/MRI HISTORY

Mallinckrodt Institute of Radiology physicians began building a PET (positron emission tomography) prototype in the early 1970s; the technology proved beneficial for research and, in later iterations, clinical imaging. A decade later, MRI (magnetic resonance imaging) became available for clinical use. Today, PET/MRI simultaneously performs both scans, with two main benefits: It reduces radiation exposure for patients, and it produces more detailed images than either technique alone. To learn more about this important new diagnostic tool and its implications for translational research, please turn to page 16. ▒

### A First human scanner, 1974

*Image courtesy of William Margenau*

### B PET V illustration

*Mallinckrodt Institute of Radiology Archives*

### C Magnetic Resonance Imaging (MRI)

Ronald G. Evens, MD, left, and William A. Murphy, MD, prepare a patient for an MRI scan.

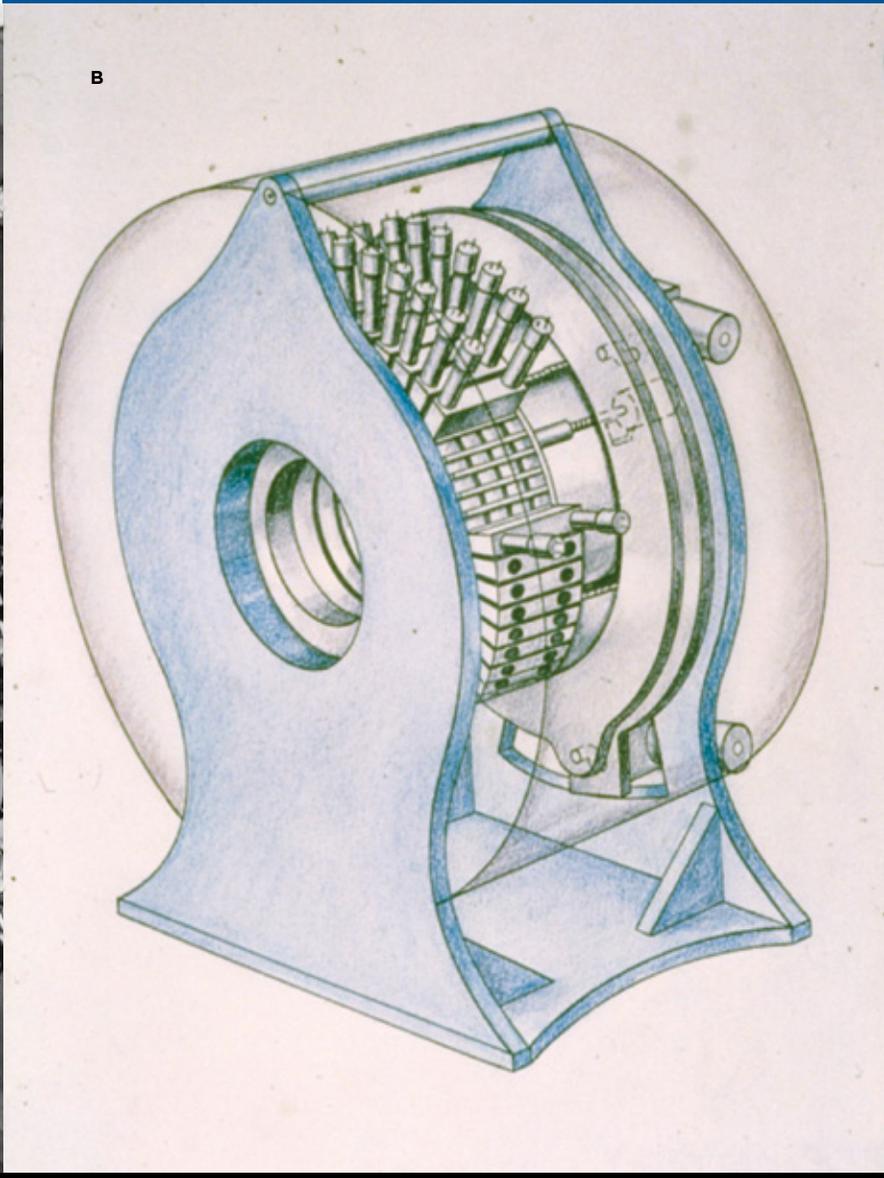
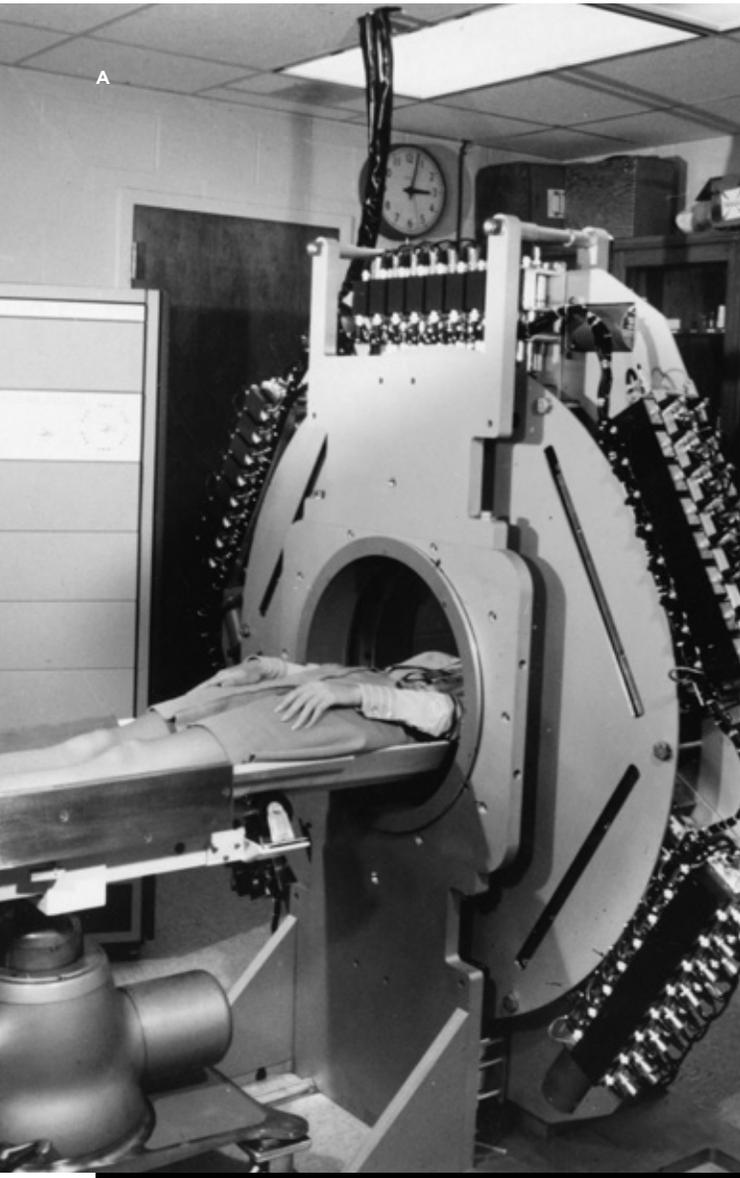
*Image courtesy of William A. Murphy*

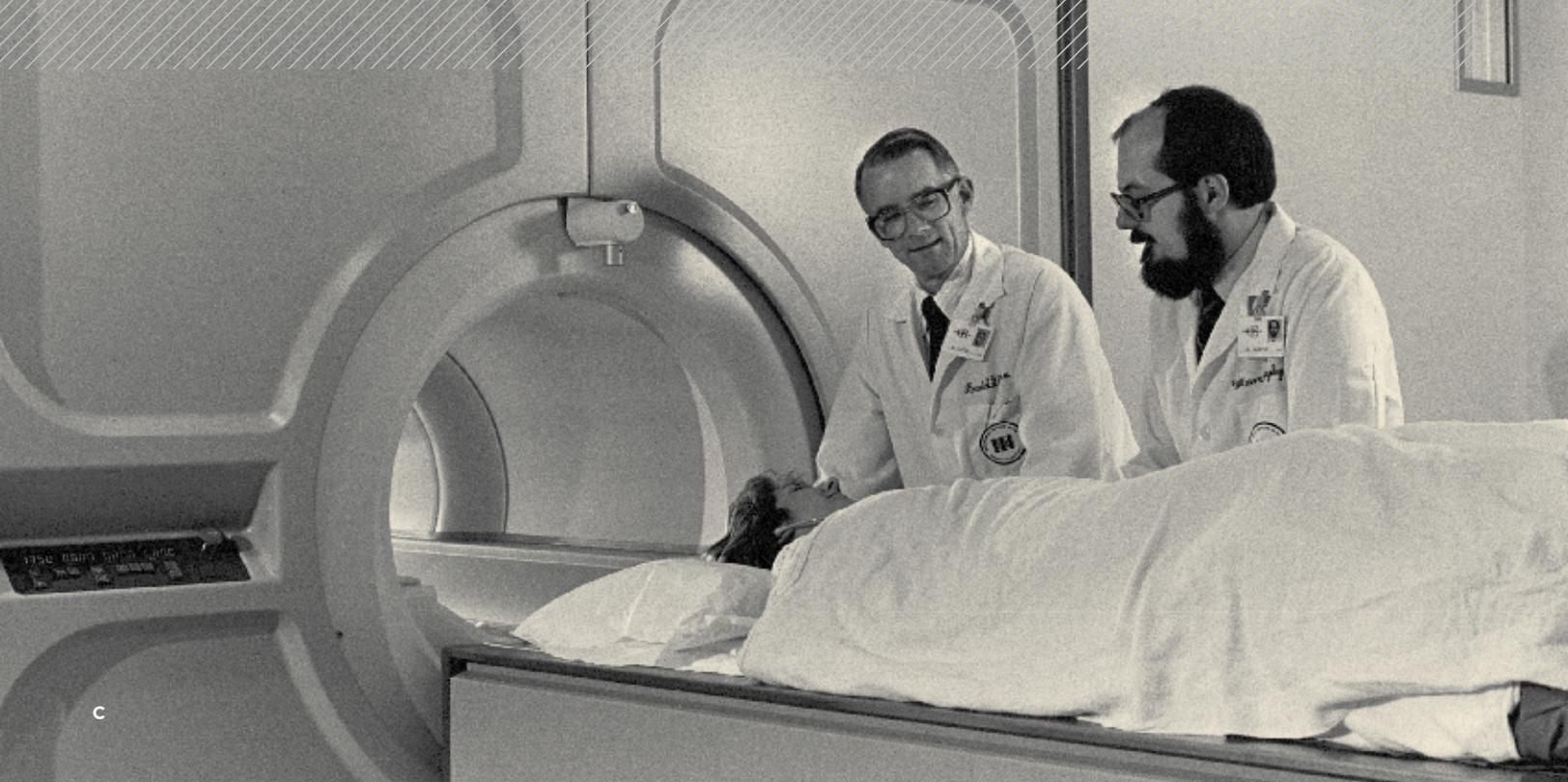
### D PET diagram showing rotation of detectors, 1960-70s

*Image courtesy of Marcus E. Raichle*

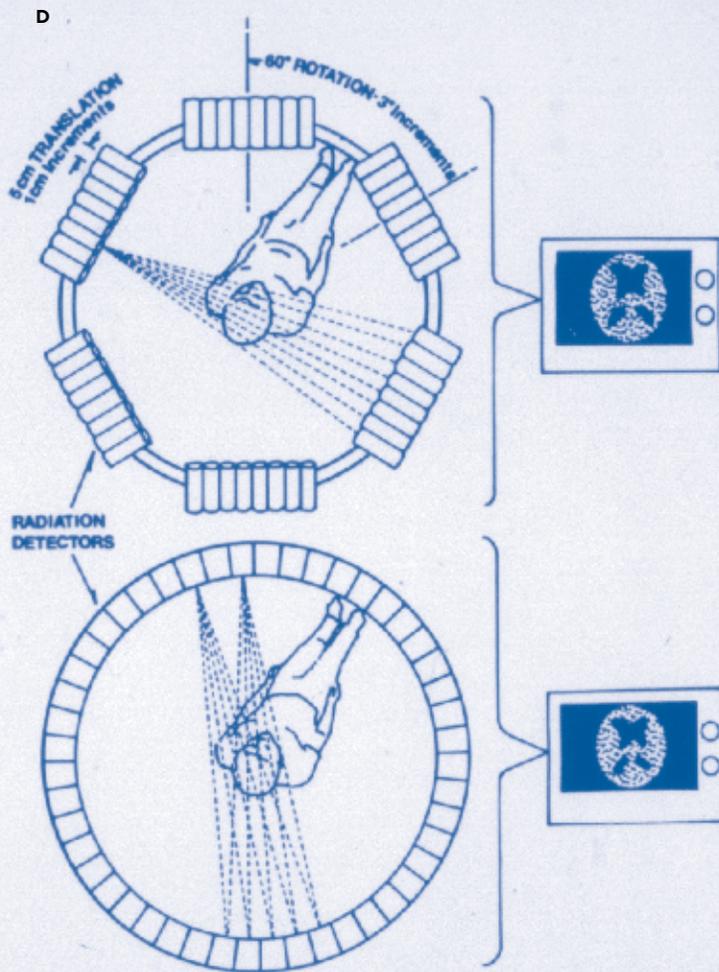
### E-F Diagrams of the 26-probe PET scanner, known as the "Lead Chicken," early 1970s

*Image courtesy of Marcus E. Raichle*

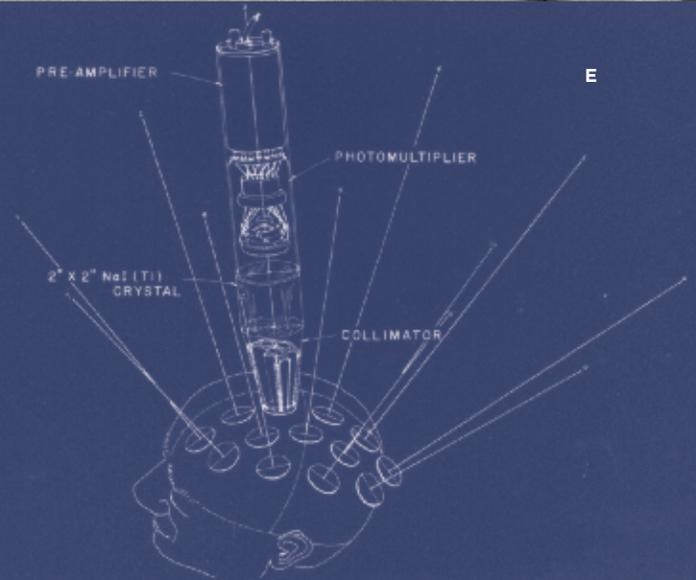




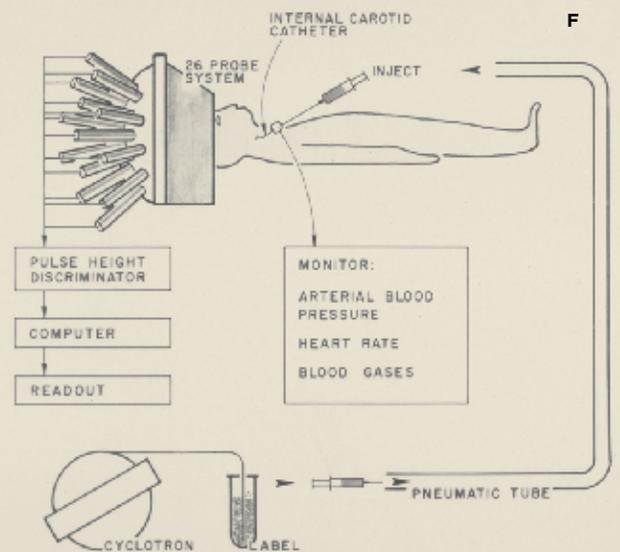
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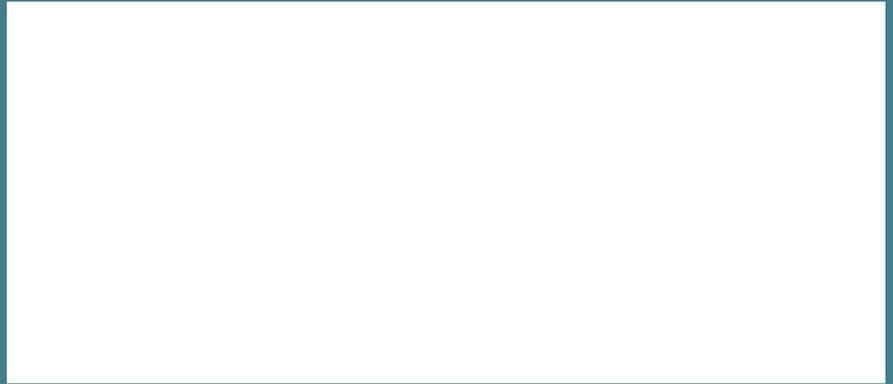
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**Below:** This photoacoustic microscopy image shows a melanoma tumor. Lihong Wang, PhD, and members of his laboratory developed photoacoustic tomography, a technique that relies on light and sound, to create detailed, color pictures of tumors deep inside the body. The procedure may eventually help doctors to diagnose cancer earlier than is now possible and to more precisely monitor the effects of cancer treatment.

To learn more about Wang and his research, please turn to page 5.

