Experimental evidence: These images illustrate the results of efforts by Weill Cornell radiologist Martin Prince (opposite) and Ramin Zabih, a computer scientist with a joint appointment in Ithaca's computer science department and the Medical College's Department of Radiology, to improve the diagnostic value of MRIs for patients with peripheral vascular disease. The images on the left were generated by a computer algorithm, while the images on the right were created by a radiologist using a manual method. In both cases, the automatic method produced a superior image, according to analysis by independent reviewers. The pair published their studies in *Radiology* and *Magnetic Resonance in Medicine*.

The Big Picture

Can an innovative computer program catch what the naked eye might miss?

by Alla Katsnelson

Sometimes, radiological diagnosis is easy—in the case of a compound fracture or a swallowed safety-pin, for example. But sometimes a clinician has to rely on intuition. "It's an Aunt Minnie," he'll say in those cases. Radiologists invoke Aunt Minnie's name to describe what happens when an overall Gestalt—rather than a single, distinct, quantifiable feature—leads to a specific diagnosis. Like a beloved and familiar relative, Aunt Minnie can't be defined by her component parts, but you know her when you see her. Yet as radiology evolves, Aunt Minnie may soon become a relic of the past, replaced by computer algorithms that

AMELIA PANICO

‘For a person, it’s easy to count the number of people in a room,’ says Zabih. ‘But for a computer, the exact opposite is true.’

NICOLA KOUNTOUPES / CORNELL UNIVERSITY PHOTO

Clear vision: Ramin Zabih collaborates with radiologists to replace intuition with evidence-based diagnosis.

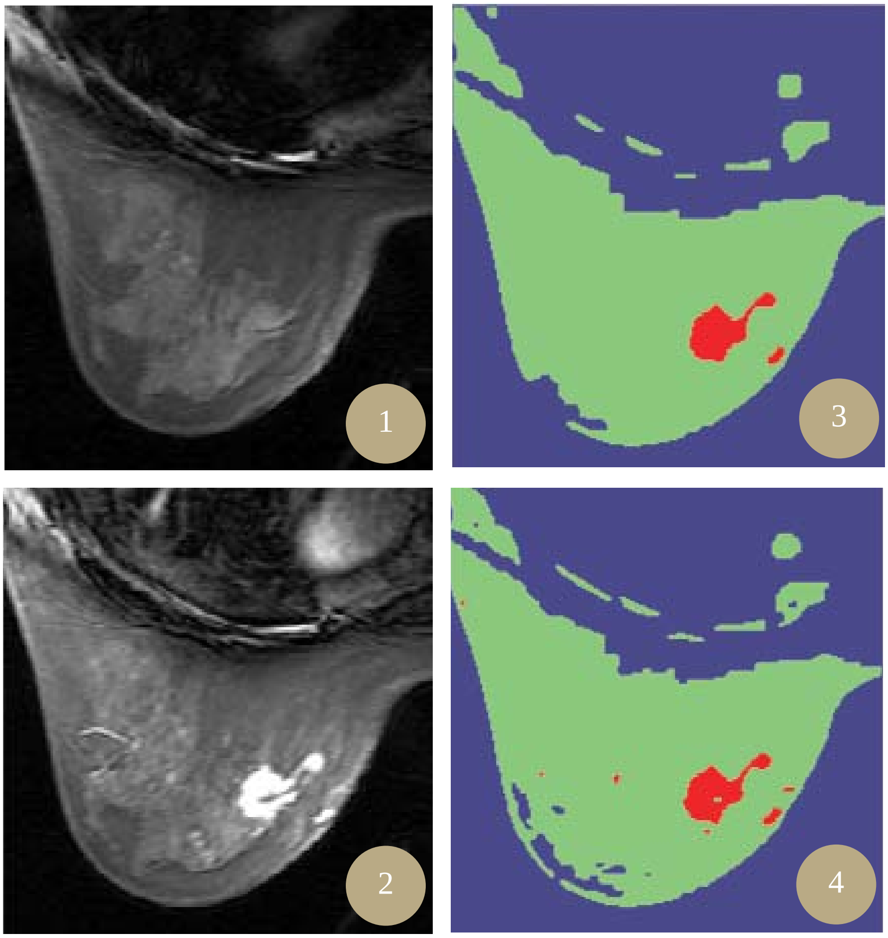
analyze millions of data points in a patient’s scans and guide radiologists toward an evidence-based diagnosis. And with image-guided, interventional techniques starting to replace conventional open surgery, the pace is quickening. At the moment, however, radiology—one of the most technology-driven and computer-oriented disciplines in the medical field—falls short on numerical measures. “Remember litmus tests in chemistry, the colored strips? Well, that is one step more advanced than radiology is now. We don’t even compare the image to a standardized chart,” says Weill Cornell radiology professor Dr. Martin Prince. “What if you sent your blood to the lab and the results came back as ‘oh, the sodium is lowish’? No. You get an exact number.”

Enter Ramin Zabih, a computer scientist with a joint appointment as an associate professor in Cornell’s computer science department in Ithaca and in Weill Cornell’s Department of Radiology. While radiology produces images for diagnosing and treating patients, Zabih studies images from an abstract mathematical perspective, with the aim of teaching computers to analyze them the way the human visual system does. Computer vision is deceptively complex; it involves figuring out what the human mind does instantly and intuitively, and translating the process into mathematical language. “If you ask a person is it easy or hard to do calculus, they say it’s hard. If you ask a person is it easy or hard to count the number of people in a room, they say it’s easy. But for a computer, the exact opposite is true,” says Zabih. “There is no computer that can detect even relatively trivial things about the difficult world of images.”

What perhaps makes Zabih unique as a theoretician is his deep interest in the clinical applications of his work. And with the focus on images, his research happened to be a made-in-heaven match for a joint venture in radiology. “If you’re simply doing mathematics,” he says, “there are so many possibly interesting problems, it’s hard to choose. It’s much better if you have an application in mind. Having an application like medicine, where your results actually matter, is really nice.” So in April 2000, the day after the computer science department voted to grant him tenure, Zabih phoned Weill Cornell’s Department of Radiology and requested the chance to spend his sabbatical year there, as he puts it, “hanging out.” A true academic convinced of the serendipity involved in innovative ideas, Zabih decided to go, he says, with no concrete project in mind. “I figured, I’ll visit for a year, and maybe at the end of the year they’ll be interested enough in what I’m doing to make some kind of collaboration out of it.” His biggest stroke of luck was meeting Martin Prince, director of Weill Cornell Medical Center’s Magnetic Resonance Imaging (MRI) services.

Prince, a pioneer in magnetic resonance angiography, is a wiry man with reddish hair and a warm chuckle. “MR has incredible, powerful advantages,” he says. “There’s no risk to patients, which means you can tinker and optimize, try this, try that, and it offers the opportunity to advance a diagnosis in a patient quickly. Say a patient comes in to do an X-ray, but it’s not optimal. Well, you live with it because you don’t want to expose them again to radiation. But with MR, you take the picture, it’s not optimal, you take it again. You can get it right.”

But getting it right is tricky. Despite MRI’s safety for the patient and spectacular image resolution, it is highly prone to motion artifacts, caused both by quirks in the imaging technology and the natural movements of a human body—even when the patient lies as still as possible. And getting a good image from a scan still requires coaxing. “Even though it’s been around for fifteen or twenty years as an imaging modality, the technology is still relatively new,” says Prince. “And the tools you need to figure out things haven’t become commercially available. So most centers



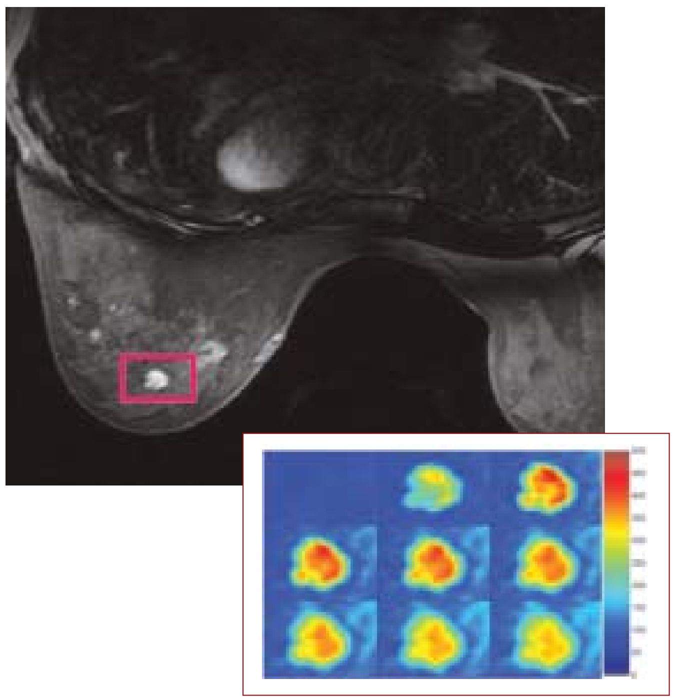
In living color: A breast tumor doesn't become visible in a scan of a patient's breast (1) until the contrast agent has reached it. Computer scientists combine the data from multiple scans taken in the minutes during which the contrast agent makes its way to the tumor (2) in an algorithm that highlights tissue differences. Red indicates tumors while green shows normal tissue. Altering the parameters of the program (3 and 4) allows the clinician to refine her analysis of the data, highlighting patterns which might not be obvious in the raw MRI, such as the additional red regions in image 4, indicating the possibility that smaller tumors have also begun to grow.

PROVIDED BY RAMIN ZABIH AND AMY GALE

just do simple picture-taking." Zabih's work with Prince, as well as a newer collaboration with Weill Cornell breast cancer specialist Dr. Ruth Rosenblatt, has focused on building a set of what the computer scientist calls "power tools" for increasing the quality of MRI images and for improving a radiologist's ability to analyze them. Each tool is built with the help of an algorithm, a mathematical insight about how to approach a problem. Essentially, these are formulas developed to analyze specific details in the image and plugged into the MRI software.

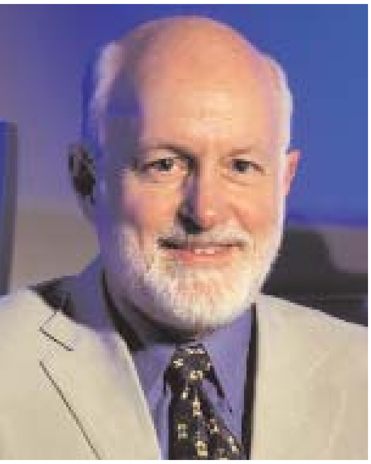
It's a Friday night in late November. In Weill Cornell's basement MRI Center, a technician behind a glass partition calls breathing instructions to a woman lying inside the MRI scanner. She's in her fifties and has an aneurysm; Prince is the radiologist on duty. The room reverberates with the machine's loud clunking and knocking. The woman's aorta pulses on a computer screen in the darkened control room, the valve opening and closing as her heart beats.

While he waits for the technician to finish, Prince turns to an adjacent computer to explain the potential of his research with Zabih. He clicks on an icon, launching a movie that shows a contrast agent flowing down a patient's leg to reveal the complex network of arteries. To transform the movie into data a radiologist can interpret, Prince explains, the consecutive frames must be combined into a single composite image that captures as much useful information as possible and filters out the irrelevant details.



Rate of change: An MRI of a patient's chest (above) shows a tumor, highighted in the fuschia box. The color enhanced data (inset) shows the diffusion of the contrast agent from injection, through the tumor, and finally into surrounding tissue.

JOHN ABBOTT



CHARLES HARRINGTON / CORNELL UNIVERSITY PHOTO

‘It’s like a spell-checker that recognizes patterns,’ says Rosenblatt of her work with Zabih. ‘You can build some science into what you do as a clinician.’

Lisa Staiano-Coico, above, and Robert Constable

The task can be accomplished manually, but “there’s a lot of skill involved in turning various knobs to see what you want to see,” says Zabih. “We built a program that turns those knobs automatically. And for a very specific task it’s actually as good as an expert radiologist.” The two published their work in the journal *Radiology* in February 2002 and in *Magnetic Resonance in Medicine* later that year, and are now looking into options for commercializing the application to make it widely available. Meanwhile, says Prince, they use the program regularly, on two or three patients a day.

The idea is not just to computerize but also to standardize the process of image-taking and analysis. In breast imaging, for example, the procedure for reading mammograms has been standardized throughout the nation, but similar guidelines haven’t been established yet for breast MRI. Consequently, “it takes sometimes up to an hour to look at one case,” says Rosenblatt, a professor of clinical radiology and director of the Women’s Imaging Center at Weill Cornell. “It’s not practical to do any significant number of cases in a busy schedule.” She and Zabih are in the early stages of assembling a computerized database of images with known pathologies. “It’s like a spell-checker that recognizes a certain pattern,” she says. “By building a database of experience and proven cases, you have the opportunity to build some science into what you do as a clinician.” In the future, they hope their database will allow them to accurately identify abnormalities in the scans of patients whose pathologies haven’t yet been diagnosed.

“When you look at an image, there are a tremendous number of details there,” says Prince. “That’s why you get Gestalt. But the computer doesn’t have to go for Gestalt. A computer can, in some mindless systematic way, figure out basic quantitative data about the patient.” Zabih, too, believes the numerical measures provided by computerization have the potential to revolutionize radiology. “The ability to measure something gives you a ton of leverage—for looking at patterns, doing diagnosis, following a patient’s progress year to year.” For example, Prince sees a lot of patients with peripheral vascular disease, a relatively common condition caused by a narrowing of the arteries in the legs. Currently, judging exactly how narrowed the arteries have become must be done by a radiologist looking at an image. “It’s fairly seat-of-the-pants,” says Zabih. “But if you could accurately characterize how narrowed the artery is, then you could do all sorts of cool things.” Physicians could, for example, change a patient’s diet, then quantify exactly how and to what degree such an intervention had affected the course of the disease. Another algorithm Zabih and Prince hope to develop would allow the MR scanning software to precisely measure individual organs. Clinical researchers could, for example, determine whether an enlarged prostate shrank after treatment with a particular drug.

Weill Cornell has a long history of collaborations with other institutions in New York City. The Tri-Institutional MD/PhD program makes it possible for students to conduct research at Weill Cornell, Memorial Sloan-Kettering, and the Rockefeller University. “There’s a growing interest in collaboration, not just between scientific disciplines but also between science and social sciences, between science and humanities, public health, and outreach,” says Lisa Staiano-Coico, who holds a joint appointment as vice provost of both the Medical College and Cornell University. “The more we highlight these collaborations, the more we can leverage our expertise and our strengths.” There are currently twenty-one active collaborations between Weill Cornell and Ithaca professors, involving seventy faculty members. A 1999 reorganization in the university’s computing faculty opened the door for stronger ties between biomedical sciences at the Medical College and Ithaca’s computer science department, considered one of the best in the country, but before Zabih, very few of these collaborations had been clinical in nature. “We’ve never had a scientist in the department with Ramin’s capability who is interested in working on these problems,” says Dr. H. Dirk Sostman, Weill Cornell’s chair of radiology, adding that the department looks forward to recruiting a second computer scientist in the near future.

For his part, Zabih is hooked. “If you’re a computer scientist and you see that some discipline is going to be turned upside-down by computers, it’s interesting,” he says. With a joint appointment between the university and Weill Cornell since July 2001, Zabih now focuses all of his research on problems that relate directly to medical imaging, and he shuttles regularly between the Ithaca and New York City campuses; in the fall he teaches in Ithaca, generally spending Monday through Thursday upstate and the rest of his time in New York, where he lives with his wife. “I’d be lying if I said she was really fond of the arrangement,” he says, “but it’s OK. We don’t have kids, and the cat doesn’t mind.”

Zabih doesn’t mince words on the topic of what he sees as the deepest challenge to bringing computer science to radiology, and to medicine in general—namely, that clinicians often have very

JOHN ABBOTT

Building a case: Dr. Ruth Rosenblatt teamed with computer scientist Ramin Zabih to create programs that help analyze MRIs.

little understanding of what computer scientists can offer. "There are a lot of people in medicine who think they want computer scientists but who actually just need computer programmers," he says. "They see someone like me walk by and their immediate reaction is, 'Great! You can fix my floppy drive.' " As a computer scientist, says Zabih, he grapples with theoretical questions about what kinds of problems computers can tackle. For example, when he and Prince began their research, it wasn't clear whether computers could be used to improve MRI scans. "Computer programmers are working on problems where a solution is clearly possible," he says. "Computer scientists are interested in expanding the horizons with our research."

For such cross-disciplinary projects to succeed requires both technical proficiency and highly developed communication skills, says Robert Constable, dean of Cornell's Faculty of Computing and Information Science. "The computer has to be given the problem in a way it can understand. For that to happen, first you need a physician who can explain the problem in a technical way. Then you need a computer scientist able to identify exactly what part of that problem a computer can solve. Basically, it involves recognizing when it is worth working on a problem."

Such collaborations really work, says Zabih, when problems are tackled from both ends. A researcher can design a solution, but a clinician has to test it. "They'll push back on you," says Zabih. "They'll say, 'Hmm, it does a pretty good job here, but in the following circumstance I notice that it doesn't work. Do you have any ideas?' Then you can say, 'Let me work on it.' That's the sort of loop that you want."

While Zabih's change in research focus since that first sabbatical may not have been a huge leap from a mathematical point of view, the change in environment was. "It's really different down here," he says. "It's hard to overstate. Down here they see patients; in Ithaca they teach." Clinicians, both he and Prince agree, tend not to be research-oriented, because expanding the frontiers of knowledge is simply not their job. Clinicians in the world of patients have a "highly conservative mindset," says Prince. "That sometimes precludes you from thinking of the key advances necessary. But the Ithaca campus doesn't concern themselves with our world of rules. Their number one rule is 'break the rules.' So it brings in fresh thinking on all the issues. Ramin can just come by, look around, and say, 'Why are you doing that?' Well, we always did that. We were told that's the way to do it." There are both advantages and drawbacks to such a difference in mindsets. Academics, Zabih says, like to impress other academics, but doctors don't care about how elegant the math is. "They care about what actually works." ■

ALLA KATSNELSON *is a science writer living in New York.*