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Medical Solutions

The Magazine for Healthcare Leadership

Zooming into the Brain

Cognitive neuroscientist Rainer Goebel hopes to crack our mind's code

Tackling Stroke Worldwide

Experts share their knowledge and visions

Modern Healthcare for All

A Chinese county-level hospital in times of change

There are **17 million new stroke cases** each year, of which about **6 million** result in death.

Around **100,000 newly diagnosed diabetes patients** in Germany each year **have peripheral nerve damage** and are also at risk of stroke.

An estimated **44.4 million people** worldwide are suffering from dementia.

Total costs of care for Americans aged 65 and older with Alzheimer's disease are set to **rise five-fold between 2010 and 2050.**

Survival rates only increase significantly with brain tumor removal of **98 percent** or more.

Hermann Requardt,
Member of the
Managing Board of
Siemens AG and CEO
of Siemens Healthcare

Dear Reader,

Until 20 years ago, no adequate clinical treatment was available for patients suffering from stroke – and so there was no means of influencing the outcome of their disease, which could range from severe neurological deficits to death.

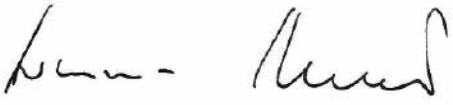
Thanks to modern medical imaging, neurologists can gain deeper insights into our central and peripheral nervous system. Today, imaging enables accurate diagnosis, appropriate treatment decisions, and monitoring of many neurological diseases. Stroke can be diagnosed and treated shortly after the occurrence of the incident – with a tremendous impact on the patient's survival and quality of live – and on the costs saved, e.g., for institutional care. In neuro-oncology, detailed knowledge on the location of functional areas in the brain allows a much more targeted tumor resection, which results in increased patient survival rates.

Neurological diseases continue to present challenges. Patient selection for different types of interventional stroke treatment still requires optimization. For patients suffering from the various types of dementia, imaging has become a prerequisite for research into treatment options. Low- and middle-income countries have to deal with the growing prevalence and awareness of neurological disorders, such as stroke. They need professionals, tools, and workflows for timely diagnosis and therapy – tailored to their local needs.

Siemens Healthcare's technology supports neurology experts in a variety of healthcare settings. Working with these experts, we invest in advancing the diagnosis of neurological diseases and in developing novel strategies for more individualized, more effective, and less invasive therapies.

In this issue, healthcare professionals from different neurological specialties share their experiences, insights, and best practices.

I hope you enjoy reading our magazine



Hermann Requardt
Member of the Managing Board of Siemens AG
CEO of Siemens Healthcare

Contents

Enhancing our understanding of neurological diseases

MR-PET imaging for dementia patients

Focus Topic: Neurology

Intelligent care concept for young diabetes patients in the Netherlands

New healthcare delivery models for China's growing population

Features

The Maastricht Brain Imaging Center is located on the Southern campus of the city's university.

"We Will Increasingly Come to Understand the Mind in Biological Terms"

Using ultra-high field magnetic resonance imaging systems, which are currently under investigation at just a few centers in the world, cognitive neuroscientist Professor Rainer Goebel examines the functional microstructure of the cerebral cortex at Maastricht University – and hopes to decode essential mental processes. Professor Goebel explains how the image of the healthy human brain as well as the knowledge, diagnosis, and treatment of many neuropsychiatric illnesses could change in the next few years.

Text: **Martin Lindner**
Photos: **Thomas Steuer**

Professor Goebel, you began your scientific career studying psychology. How does a psychologist end up doing brain research with an MRI scanner?

Professor Goebel: I have always wanted to understand how our minds and our brains are interrelated. How do emotions, memories, and perceptions develop? These are the basic questions of psychology, but no one could offer me any good answers when I was in school. It was only since the 1990s, with the development of functional magnetic resonance imaging (fMRI), that we've been able to measure brain activity and study mental processes with a live and ▸

Right: Neurocognitive reserach is one pillar of Prof. Goebel's work – passing his knowledge onto his students is the other.

About Rainer Goebel

Rainer Goebel, PhD, is a German-born professor for Cognitive Neuroscience at Maastricht University in the Netherlands and is the founding director of the Maastricht Brain Imaging Center. After his studies in Psychology and Computer Science, he became a fellow at the Max Planck Institute for Brain Research in Frankfurt, Germany. Since the mid 1990s, he has continued to develop "BrainVoyager," an internationally esteemed software tool for the analysis and visualization of functional neuroimaging data. Besides his position at Maastricht University, Dr. Goebel is team leader of the "Neuroimaging and Neuromodeling" group at the Netherlands Institute for Neuroscience in Amsterdam. In 2014, he was selected as a member of the Royal Netherlands Academy of Arts and Sciences.

completely non-invasive method using the scanner. And, it's something that has fascinated me ever since.

Have you ever gone through the scanner yourself?

Professor Goebel: Hundreds of times.

What is it like to look inside your own skull?

Professor Goebel: I was nervous the very first time. Would they discover a small tumor? Was something not right? Now that I know everything is normal, I enjoy looking at my brain.

Do the images arouse a feeling of grandeur?

Professor Goebel: Absolutely, I have a great deal of respect – along with the desire to see even more detail, because, initially, the fMRI scans were somewhat disappointing. For example, you want to know how feelings are represented in the brain – and then you see a few colored spots in the images that merely show that the emotional centers are active, but not whether I am sad or happy. Or you see that the language center is active, but not what words are being spoken.

And those are the kind of details you now want to identify?

Professor Goebel: That is one of the main objectives. The current MRI scanners that work with magnetic-field strengths of 1.5-tesla or-3 tesla have achieved a spatial resolution of two to three millimeters. In our Brain Imaging Center, we now also have two ultra high-field scanners with magnetic-field strengths of 7[1] and 9.4[1] tesla. Simply put, you get a strong image signal with higher field strengths. You can zoom deep into the brain and measure activity in areas that are tiny. Only few have ever seen brain images like the ones we're getting with our ultra-high field scanners.

Do you expect a qualitative leap in research?

Professor Goebel: Yes, we are profiting from a lucky fluke of nature. The cerebral cortex has characteristic functional units called the cortical columns. These modules contain approximately 10,000 nerve cells that all do the same thing – for instance, they react the same way to a certain sensory input. This represents a kind of redundancy principle in the brain. We are familiar with the column architecture, particularly in the perceptive areas of the cortex[2], but there are probably comparable functional modules in most – if not all – areas of the brain. The main point is now that with the new ultra high-field scanners we may not be able to detect the activity of individual neurons, but we can detect individual functional modules since they are in a detectable range of the scanner. This means, for the first time, we might be able to improve our understanding ▸

Train your Brain

Patients can learn to control their own brain activity using real-time signals from a 3-tesla brain scanner. This neuro feedback opens up new ways of treating, for example, chronic pain, Parkinson's, strokes, or depression.

When around 150 internationally recognized experts in neuronal imaging met in Zurich, Switzerland, in February 2012, it marked a milestone in the development of an emerging therapeutic discipline: brain-scan-based neuro feedback. Back then, the scientists discussed – at the first-ever international conference on the subject – the state and prospects of the methods in which patients learn to control their brain activity.[3]

The principle involved is simple: While lying in a magnetic resonance imaging (MRI) scanner, the patient views a monitor that shows in real time how active a certain area of the brain is, for example, an activity "thermometer." Just as it is possible in other forms of bio feedback to control one's heartbeat and blood pressure, the patient learns to decrease or increase brain activity in the respective region using various mental tasks and imagery – and can immediately see the success of their efforts in the scanner signals. Special software analyzes and visualizes the scanner data.

The idea of neuro feedback is not new. Neuro feedback based on electrical brain activity measurements (EEG) has been used for a long time, for example, to train people with epilepsy to suppress their seizures or to mitigate an attention deficit hyperactivity disorder (ADHD). However, the scanner-based process permits a deeper look into the brain and a much more precise analysis of activity patterns, which expands the spectrum of potentially treatable illnesses. Neuro feedback training is typically performed in several sessions in MRI machines with a field strength of 3-tesla.

The innovative approach has been developed over the past decade by a relatively small number of international specialists – including Rainer Goebel, who conducted basic research on scanner-based neuro feedback in close cooperation with German neuro researchers Niels Birbaumer and Nikolaus Weiskopf. Interest in the method has since grown considerably. Pilot studies by various teams show that self-regulation of brain activity can alleviate chronic pain, reduce motor deficits in Parkinson's disease, or even improve rehabilitation after a stroke.[4]

The results in patients with depression are especially promising. A Phase I randomized clinical trial, which examines the benefits of scanner-based neuro feedback in regulating the emotional centers of the brain, is almost finished.[5] There are more clinical trials on other diseases to follow as part of "BrainTrain," an international collaborative research project supported by the European Commission.[6]

[3] Sulzer J, Haller S, Scharnowski F, Weiskopf N, Birbaumer N, et al. (2013). Real-time fMRI neurofeedback: progress and challenges. Neuroimage 76:386-99
[4] Weiskopf N (2012). Real-time fMRI and its application to neurofeedback. Neuroimage 62:682-692
[5] http://clinicaltrials.gov/show/NCT01544205 (accessed 19/10/2014)
[6] www.braintrainproject.eu (accessed 19/10/2014)

of the code with which a sensory input is represented in the cortex.

Can you give us an example?

Professor Goebel: Take facial recognition. What we already suspect from current experiments is that specific facial features – such as the distance between the eyes, the hairline or the position of the eyes in relation to the mouth – are coded by the activity of individual cortical columns. The brain breaks down (so to speak) the sensory input at the columnar level into different aspects, into a distributed code. Based on a specific column pattern, it might be possible that the scanner has the ability to – in principle – discern whether you are looking at your partner's face or the German Chancellor's face. It makes a detailed reading of the brain activity possible. Cortical column patterns probably also explain how the brain registers new faces and recognizes them again later.

Part of your research focuses on not just measuring these processes in the scanner, but also modeling them with a computer.

Professor Goebel: That's right. The models help us generate and test new hypotheses. We can simulate which macroscopic areas of the brain and neuronal networks would have to be active during a cognitive process, all the way to the level of the cortical columns. In the process, we also make up new, hypothetical ▸

Risks and Limitations of Ultra High-Field MRI

There are safety limitations when using ultra high-field MRI. These include higher power radiofrequency pulses and the potential for tissue heating or coil burns, stimulation effects from stronger, faster-switching gradients and moving within a higher magnetic field and, most prominently, the potential dangers associated with the main magnetic field, such as ferromagnetic projectiles in the scan room and effects on implanted medical devices. As of 2003, the U.S. Food and Drug Administration specified the criteria for significant risk in humans from the main field to be 8-tesla for adults and infants older than one month and 4-tesla for neonates.

7T MRI is labeled as an investigative device and cannot be used for clinical diagnosis. Instead it can be used for clinical research under the approval of an institutional review board and with informed consent.[1]

"The great hope is to achieve individualized treatments."

Rainer Goebel, PhD,
Professor of Cognitive Neuroscience,
Maastricht University, The Netherlands

columns, for example, because we assume that the brain interprets two vertically stacked lines coded in V1 as the letter "T" in a higher visual area and this is coded in its own cortex column. We then have to compare these models with actual data measured in the scanner in order to correct and further develop them. This is a lengthy process that will take years, but could further the field of neuroscience and eventually medicine enormously.

Are there already tangible effects?

Professor Goebel: One example we're currently working on is reading disabilities in children, also known as dyslexia. Thanks to the improved scanner resolutions, we hope to determine why and where letters are mixed up in the cortex through incorrectly coded column patterns and what kind of training can best influence this – in other words, how the brain's plasticity can be used for treatment. But we also expect significant advances in our understanding of depression or schizophrenia.

In what way?

Professor Goebel: Today it is really clear that there is not just one form of schizophrenia or one form of depression. Using genetic data, for example from population studies, as well as using brain scan data, we hope to be able to define new subtypes within the next few years – in other words, get away from simply relegating them to one drawer and develop more refined disease concepts. We need to learn how to understand individual brains. For example, it is possible that different forms of depression can be clearly differentiated from a neurobiological standpoint. The great hope is to make disease diagnoses more multifaceted and to achieve better adapted, more individualized treatments through more detailed imaging.

Are there similar perspectives for neurodegenerative diseases such as Alzheimer's?

Professor Goebel: With Alzheimer's, we believe that it will at least be possible to make an impactful assessment – because the ultra-high field scanners will probably be able to detect signs of degeneration in the fiber connections of the brain. The high scanner resolution can also help with Parkinson's when, for example, a patient is supposed to receive what's called a "brain pacemaker" and precise neurosurgical planning is required for the surgery. However, the advantages of imaging

Left: At the Faculty of Psychology and Neuroscience, international research teams are working together to better understand the human brain.

for treatment do not depend only on a maximum image resolution, but also on the possibility of having scanners that are integrated into new treatment concepts. For instance, for many years we have been examining the possibility of targeted neuro feedback with a 3-tesla scanner in which patients can learn to control the activity levels of individual areas in the brain using signals from the scanner (see box on page 9 entitled "Train your Brain"). This opens up completely new treatment paths for a wide range of illnesses, such as phobias or depression.

Do the modern images of the brain also change how we see ourselves?

Professor Goebel: We hope, in ten years, people may say: "Doctors determined in a brain scan that my left amygdala in the limbic system is overstimulated. That's why I am going to neuro feedback therapy to be less afraid of spiders." Overall, how mental processes work in detail may be much better understood and might even be included in textbooks. We may learn to talk much more concretely and realistically about our brain and ourselves. We will increasingly come to understand the mind in biological terms.

Are we losing our mystique due to fMRI?

Professor Goebel: No, because the images do not provide information about the subjective experience, the experience of our own consciousness. The I-perspective remains a mystery, even for us. ■

Dr. Martin Lindner is an award-winning science writer based in Berlin, Germany. After his medical studies and a doctoral thesis in the history of medicine, he went into journalism. His articles have appeared in many major German and Swiss newspapers and magazines.

[1] MAGNETOM 7T and 9.4 T are ongoing research. All data shown are acquired using a non-commercial system under institutional review board permission. MAGNETOM 7T and 9.4T are still under development and not commercially available yet. Their future availability cannot be ensured.

[2] http://www.nobelprize.org/nobel_prizes/medicine/laureates/1981/press.html

Brains Unlimited

An interdisciplinary platform for neuro researchers, clinicians, and entrepreneurs

Brains Unlimited is housed in a brand-new building complex close to Maastricht University Medical Center, near the historical center of the Dutch city. It is a center for the interdisciplinary exchange of ideas for neuro researchers, clinicians, and entrepreneurs. The platform, which was officially opened by the Dutch king in 2013 and is supported by Maastricht University and financed by the European Union, among others, will help scientists and companies discover fundamentally new insights into diseases such as Alzheimer's, Parkinson's, or multiple sclerosis to hopefully make them clinically and commercially viable.

The key to the project is an ultramodern scanner lab that is equipped with three Siemens MRI scanners with high and ultra-high magnetic field strengths. Only a few centers around the world currently have such powerful equipment. Scientists from the Department of Psychology and Neuroscience at Maastricht University work closely with the imaging unit. *Brains Unlimited* also has a business start-up center that helps companies develop scientific business models.

Brains Unlimited originated from an initiative of the Maastricht Brain Imaging Center under the leadership of Professor Rainer Goebel, PhD. Since then, the project team, who works closeley with the Center of Magnetic Resonance Research in Minneapolis, USA, the Jülich Research Center in Germany, and Siemens Healthcare, has built up a network with many national and international research groups. For more information, please visit www.brains-unlimited.nl.

A phantom head helps simulate brain tissue for testing new methods and tools in neuroradiology.

The Right Mind at the Right Time

As a stroke expert, Dr. Charles Strother has treated countless patients. As a researcher, however, he helps develop methods and technologies that may enable thousands of his colleagues to treat their patients faster and more effectively in the future.

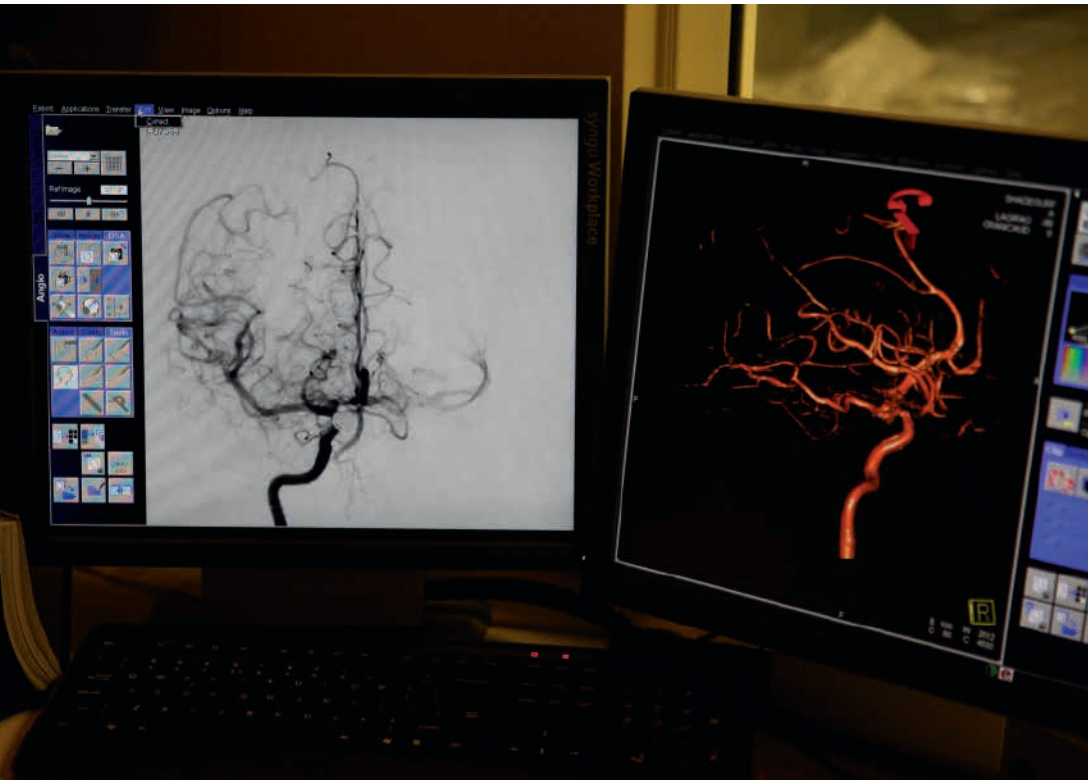
Text: **Jürgen Schönstein** Photos: **Steffen Thalemann**

No one knows the field of neuroradiology better than Dr. Charles Strother, Professor Emeritus of the University of Wisconsin School of Medicine and Public Health in Madison, Wisconsin. When Dr. Strother is asked about the history of this relatively young discipline, he can think of a dozen names – such as Per Amundsen from Norway, a pioneer of minimally invasive catheter technology, or Guido Guglielmi, the inventor of the eponymous Guglielmi Detachable Coil (GDC), still a standard tool for neuroradiologists, Dr. Thomas Hans Newton, former Professor of Radiology and Head of Neuroradiology at the University of California in San Francisco, Russian neurologist Fedor Serbinenko, and Dr. Strother's co-workers Charles Mistretta and Guang-Hong Chen. But there's one name he never mentions: his own. The 73-year-old neuroradiologist tells us, without any sign of false modesty, that he is only "along for the ride." This, however, is one of the most ridiculous understatements imaginable. There is a reason why Dr. Strother was the recipient of the ASNR Foundation Outstanding Contributions in Research Award at this year's annual meeting of the American Society of Neuroradiology, and why he is one of the most frequently quoted neuroradiology authors in the world.

Helping Doctors Help Patients

Dr. Strother, who has treated countless patients in a clinical career spanning more than 45 years, is one of the world's leading stroke experts. He has also researched and developed numerous successful treatment methods and technologies. In short, Dr. Strother has not just helped patients directly, but during the last four and a half decades has played a decisive role in helping his colleagues treat their patients more effectively.

At the beginning of his career, however, even Dr. Strother himself could not have predicted that he would become one of the top experts in his field. "My father enjoyed mocking me that I had managed to 'squeeze' the workload of eight semesters into ▸



Dr. Strother is currently working with Siemens on further developing biplane 3D options in angiography for stroke patients.

"Outstanding medical physicists are the key to every success I've ever had."

Dr. Charles Strother, Professor Emeritus of the University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA

five years," he explains. Academic work was simply not his thing back then. "I was anything but an outstanding student. I was more interested in sports, especially football and baseball." And more than once, he even had to transfer schools after falling hopelessly behind in his studies.

Medical school would not have even occurred to Dr. Strother if he hadn't – by pure chance – taken a work-study job in a hospital in Fort Worth, Texas. The job was washing laboratory glassware, and as menial as the task was, it awakened his interest in medicine. At the age of 22, in 1963, he enrolled at the University of Texas in Galveston. Four years later, he graduated with high honors and began his clinical training in internal medicine at the University of Wisconsin in Madison.

In another typical, yet decisive, coincidence, Dr. Strother was again in the right place at the right time to meet his future wife, Elizabeth, whose brother happened to be a neurosurgery resident at Stanford University in California. After completing his military service, during which he served as a physician in the Special Forces in Panama, Dr. Strother moved to Stanford to begin his residency as a neurologist. During his residency training, he also had a rotation in radiology, which he felt was a rather boring department. "We couldn't really treat anything in the brain," Dr. Strother says. "There was diagnostic angiography, but no therapeutic interventions."

Learning to Be Minimally Invasive

It was then, however, that he met Norwegian visiting professor Per Amundsen, who had developed a minimally invasive catheter method as an alternative to the then-commonplace practice of injecting contrast medium directly into the artery. "I saw these small incisions in the groin, saw that the patient was conscious – and I thought to myself: 'This is exciting. This could change everything.'" He decided to become an interventional neuroradiologist.

The idea that doctors can use radiology methods not just for diagnoses, but also for minimally invasive procedures was

The next big challenge for Dr. Strother and his colleagues: Trying to intervene before aneurysms develop.

put into practice during Dr. Strother's fellowship at the University of California in San Francisco. "We had several patients with recurrent nosebleeds," he explains. "My colleagues and I got the idea to use a catheter to block the bleeding vessels with small particles."

With far-reaching success: the journal article about this embolization, published by Dr. Strother and the former chairman of Radiology at UCSF, Hans Newton, in 1976, triggered a chain reaction. It inspired Russian neurosurgeon Fedor Serbinenko, for example, to develop a detachable balloon catheter that allows doctors to treat vascular malfunctions, such as carotid cavernous fistulas, which until then had been virtually untreatable.

"It was a terrible situation, and the surgical procedure was gruesome – only a few patients survived it," Dr. Strother says. "But the balloon catheter worked great." It was the first neuroradiological instrument that had a significant clinical benefit and was far superior to every other method.

In general, Dr. Strother seems to have been present whenever there was a new breakthrough in neuroradiology. In the early 1990s, Italian neurosurgeon Dr. Guido Guglielmi experimented with electroembolization methods at the University of California in Los Angeles (UCLA) and, in the process, (accidentally) developed a detachable platinum coil that is used to occlude brain aneurysms. Dr. Strother came into contact with this technology very early on through a friend from his studies at Stanford whose company had started devel- ▸

About Dr. Charles Strother

Born in McKinney, Texas in 1941, Dr. Charles Strother is an Emeritus Professor at the University of Wisconsin School of Medicine and Public Health in Madison. Since 2012, he has devoted himself to medical and technical research at the Clinical Science Center in Madison, with financial support from Siemens Healthcare and the National Institutes of Health. He began his medical career at the University of Texas in Galveston; he discovered neurology (especially neuroradiology, which has been decisively shaped by him) during his time as a resident at Stanford University in California, where he recognized the possibilities of endovascular catheter technology.
Dr. Strother has spent the majority of his career at the University Hospital in Madison, with brief stays in Paris, Oslo, and Baylor University in Houston, Texas. He was elected to a one-year term as president of the American Society of Neuroradiology in 2003, which honored him with the ASNR Foundation Outstanding Contributions in Research Award in 2014. As stroke expert, he is the author of four books and more than 150 scientific publications, including some of the most frequently cited publications in this discipline.
When he is not researching new technologies, such as 4D angiography[1], Dr. Strother enjoys traveling to exotic destinations with his wife, Elizabeth, or jogging around the lakes of Madison to stay in shape.

Management Summary

Challenge:
Development of practical treatment methods and technologies in interventional neuroradiology.

Solution:
Combining more or less random discoveries and ideas in daily hospital routine with inventive spirit and technical expertise.

Result:
The development of, among other things, the life-saving detachable balloon catheter or the Guglielmi Detachable Coil (GDC) into a clinically usable product.

oping the coil into a clinically usable product. Today, it is referred to as the Guglielmi Detachable Coil – or GDC Coil – and Dr. Strother, who had since returned to the University of Wisconsin, was involved. "We put a lot of work into our lab," he says. "The University of Wisconsin was the second clinic in the world (after University of California, Los Angeles) to use these coils to treat aneurysms."

The Key to Success: Collaboration

Dr. Strother was hired by the University of Wisconsin in 1976 to help build a growing section of neuroradiology. It was the close proximity to the colleagues in medical physics here that, in his own opinion, helped him the most: "These outstanding medical physicists are the key to every success I've ever had," he insists. His colleague Charles "Chuck" Mistretta, for example, developed Digital Subtraction Angiography (DSA) here.

Imaging is crucial to everything that specialists in this field do. As Dr. Strother explains: "Anything we can see, we can generally also repair. Imaging is a fundamental component that makes all of this possible." There is no comparison to the film-based methods he had to work with at the beginning of his career. Every minute counts, especially with ischemic strokes: "As we say, 'time is brain' – or rather 'time is neurons.' It is estimated that for every minute of ischemia, you lose about two million neurons." The less damage there is, the more quality of life remains for the patient, which also translates into dramatically fewer follow-up and long-term care costs – an important argument especially in light of the current healthcare cost reform in the United States.

That being said, however, rushed treatment can sometimes be more harmful than helpful. "First of all, in a patient with an acute ischemic stroke, we have to determine what damage has already occurred and then decide if intervention will only make the situ-

ation worse," Dr. Strother says. He is currently working with Siemens on further developing biplane 3D options in angiography that would allow doctors to bring stroke patients directly into the angio suite and do all the diagnostic imaging there, which would spare them the long stays in CT or MR, as well as transfers to and from those modalities. "We are talking about the angio suite as the stroke unit of the future, and that's catching on, from Germany to China."

Looking at Time

One essential element for this is the flat detector, which can image soft tissue in CT quality and visualize high-contrast blood vessels in better spatial resolution than with a conventional CT. Dr. Strother, however, who has concentrated fully on research in this area since his retirement to emeritus status in 2011, is no longer satisfied with these high-resolution 3D images. "I always realized that the 3D modeling with the contrast medium flowing through the vessel should also include temporal information in the dataset," he explains. "But I didn't know how to get it."

He went to Dr. Mistretta, whose office is next to his and who had already developed 3D DSA, and asked him: "Chuck, there has to be a way." And the more Mistretta insisted it was impossible, the more Dr. Strother urged him to try. "At some point he gave in – probably, just to finally get rid of me," Dr. Strother says. "Three days later, he had found a solution." 4D DSA[1] is currently being developed in cooperation with Siemens, and it is hoped that this technology will translate into fewer X-rays and therefore less radiation exposure for patients, but also into lower costs.

This story demonstrates that Dr. Strother is not just "along for the ride" when it comes to research, as he himself claims. If anything, he is a scout with a refined sense of what the future holds. And what does his sense tell him about his own future as a researcher? "I hope it will tell me when I should stop – before other people do." ■

"We Try the Best We Can All the Time"

Neuroradiology was decisively shaped by Dr. Strother. In this film, he looks back at his impressive career.

To watch the video, scan the QR code using the reader app on your smartphone or enter the URL into your browser.

www.siemens.com/charles-strother

At the University of Wisconsin, Dr. Strother helped build the section of neuroradiology.

Jürgen Schönstein, who has a graduate degree in Geography (Diplom-Geograph), has been a journalist since 1985. He has worked for *DIE WELT*, *Springer Foreign News Service* (New York Correspondent) and *FOCUS* (U.S. Correspondent from 2001 to 2010), to name just a few. He has been the editor-in-chief of the German science portal ScienceBlogs.de since the beginning of 2011 and teaches academic writing at the Massachusetts Institute of Technology. Jürgen Schönstein is also a freelance writer for the German economic journal *BILANZ* and lives in Cambridge, Massachusetts.

[1] Under FDA review. Not available for sale in the U.S.

On the Cutting Edge of Neurosurgery

Huashan Hospital, located in the heart of Shanghai, is home to one of the finest neurosurgery facilities. The department stands out for groundbreaking research it has conducted on intraoperative MRI as well as its intelligent use.

Text: **Rebecca Kanthor**
Photos: **Tang Ting**

Shanghai is a bustling city of 24 million people and the largest in China. Huashan Hospital is located right at the center. Hundreds of patients pass through the gates at all hours of the day. It's a typical scene for a public hospital here. But just a short walk from the main building, a vastly different sight awaits in the hospital's award-winning Neurosurgery Department. Past the doors and inside the operating suite, the atmosphere is quiet, but there is an air of excitement and purpose. The only sounds are the buzz of computers and the hushed whispers of doctors in blue-green scrubs discussing cases.

We are standing in one of the finest neurosurgery departments in China. With 600 beds, 110 staff and 15 full professors, the department is part of Fudan University's Medical School, ranked among the top three in this country. This is more than just a clinic, says Neurosurgery Department Chair Dr. Liang-fu Zhou. In fact it is one of the longest established neurosurgery departments in the country, and attracts a large number of patients, both Chinese and foreign. It also attracts cooperation with industry, including with Siemens and IMRIS, whose intraoperative magnetic resonance imaging (ioMRI) technology the hospital uses.

Last year, the department completed almost 16,000 surgeries, among them more than 10,000 craniotomies, making it one of the busiest neurosurgery departments in the world. The department is also ideally suited to conduct research. Roughly 15 percent of last year's craniotomies were glioma cases, and a team from the department recently won the Journal of *Neuro-Oncology* Award at the Congress of Neurological Surgeons (CNS) Annual Meeting for the study it did on ioMRI's impact on patients with glioma.

Brain surgery relies on a tricky balance of cautious and aggressive measures. The doctors must remove as much of the tumor as possible; unfortunately, many tumors lie close to functional brain tissue that controls important functions such as speech and motor skills. Surgeons must be very careful not to remove healthy tissue around those areas but to resect as much tumor as possible without affecting function. That's where ioMRI, an image-guided neurosurgery technology, has proven to be extremely useful. ioMRI is used in conjunction with neuronavigation – together they help create accurate images of the brain during surgery, leading to impressive results.

Insight into the Surgeon's Work

Through the gallery window, we can look into the operating room as Dr. Zhou performs brain surgery on a patient. This is the department's 1,017th operation with ioMRI. Today's patient is a 27-year-old-man who suffered from a seizure a month before and has been diagnosed with a right frontal low-grade glioma. A team of five doctors and nurses works together on the surgery, which can last from five hours to up to eight hours. The scanning procedure itself takes about a half hour in all. Giant screens on the walls of the operating room show the patient's MRI brain scan.

Several other doctors are monitoring a bank of computer screens out in the gallery. One of them points out a distinct mass on the left side of the brain. "There's residual tumor," he says. That clear brain map is possible due to the intraoperative MRI scanner system that is used once or, in some patients, twice during the surgery to give the surgeon a precise update on the progress of resecting the tumor. This is just one of the many maps MRI is able to produce to support brain ▸

Neurosurgery Department Chair Dr. Liang-fu Zhou (above); a patient's brain scan (below)

Portrait painting of Dr. Liang-fu Zhou hanging on the wall of Huashan hospital's lobby.

surgery. Other computer screens show a bright rainbow of colored nerve tracts intersecting each other like the traffic on Shanghai's busy highways. This so-called tractography, as well as other techniques, such as Intraoperative Neurophysiological Monitoring (IONM), electroencephalograms (EEG), blood oxygen level dependent signal (BOLD), or functional MRI, help the surgeons resect enough tissue to remove the tumor while avoiding damage to neuronal tracts that are part of the control system of important body functions like speech and motor skills. This is what surgeons want: to resect as much non-functional tumor tissue as possible while leaving as much functional, healthy tissue as possible. This is crucial for a patient's fast recovery with minimal rehabilitation. But making those detailed cuts is particularly hard in the brain. The ioMRI helps surgeons to identify residual tumorous tissue and tells them whether they have resected enough or could resect further.

Benefits of ioMRI

Dr. Bernd Hofmann, Neurosurgeon and Head of the Clinical Competence Center Neuroscience at Siemens says, "The most important thing is that you get immediate feedback about the extent of removal, the success of your procedure, and the prognosis of the patient." According to Dr. Zhou, 3T ioMRI has been an amazing tool benefiting both the hospital's patients and doctors. "This is more accurate than conventional neurosurgery with or without neuronavigation," says 72-year old Zhou, who has been leading the department for more than 30 years and remembers each new radical development in image-guided neurosurgery that the department has adopted. Of course, he adds, a surgeon's experience is crucial and irreplaceable. He quotes Dr. Lars Leksell, the founding father of radiosurgery: "A fool with a tool is still a fool" and adds, "a surgeon should be a master rather than a slave of a tool."

Removing as much tumor as possible is key, Dr. Hofmann from Siemens agrees, "We can't cure the patients, but [we can] prolong their survival. We know from the scientific evidence that the patient can survive longer if you take out more tumor." Studies[1] show that only from a 98% tumor removal upwards, survival rates are increased significantly.

One advantage of ioMRI is that it can alert the surgeon to brain shift, which conventional neurosurgery with or without neuronavigation cannot. Brain shift is the tissue deformation and shift that occurs during neurosurgery when the removal of a tumor results in a loss of the spatial relation established between the patient (brain) and the MR/CT image volumes acquired prior to surgery. It can have a major impact on the safety and accuracy of the surgery, Dr. Zhou says, but updated brain images from an ioMRI scan combined with neuronavigation can help the surgeon compensate for brain shift and modify surgical strategy. "Intraoperative MRI is the most useful and preferable tool right now because it can detect the brain shift during surgery, so the surgeon can correct the strategy. Then the surgeon can remove more of the tumor." He calls the method "maximum safe tumor resection" and says it is showing to be useful in real-time tumor resection control and accurate functional preservation.

Solutions for an Intraoperative Neurosurgery Setting

There are a variety of different solutions for hospitals wanting to incorporate an ioMRI system. Siemens offers two alternatives for providing patients with MRI for intraoperative neurosurgical imaging method during surgery.

Shanghai's Huashan Hospital is one of five IMRIS VISIUS Surgical Theatre installations in China, where a Siemens MRI on a ceiling rail is moved between the OR and an adjoining diagnostic imaging room. This has the benefit of ensuring that the patient does not suffer from unnecessary movement, limits the risk of brain shift in the imaging, and also optimizes the use of the scanner, since it allows the equipment to be used for other patients while surgery is in progress next door.

Another solution for neurosurgery from Siemens, is the MAGNETOM® Combi Suite Neurosurgery[4], specially designed to combine state-of-the-art MRI imaging technology with safe and efficient transfer of the patient between the operating table and the MRI. The facilitator of this transfer is the Combi Dockable Table, enabling single patient transfers each way with direct docking of the table with the MRI system. This flexible solution is compatible with selected OR tables from MAQUET and TRUMPF and enables cost- efficient use of the MRI for standard diagnostic as well as intraoperative imaging supporting one or more operating theatres.

Within the surgical setting, the surgeons can perform an MRI of the brain to keep track of their progress and additional resection may take place if needed within the same surgical procedure. At Huashan Hospital, each patient is intraoperatively scanned an average of 1.88 times within the intraoperative setting. When clinically feasible, additional resection may occur based on the MRI results. The patient operated on today was only intraoperatively scanned once, because the scan showed that the tumor had been totally removed on the first attempt.

Groundbreaking Research

The department integrated intraoperative MRI into their surgical setting in 2010. Currently, Huashan is the only department with an ioMRI suite in Shanghai and one of only ten throughout China. Dr. Xiaodong Zhuang, an associate professor in the department, is part of the team of doctors working on this surgery. "It costs more money, it takes more time initially, but it benefits the patients," he says. It might take a bit more time initially, but both Dr. Zhuang and Dr. Zhou agree that it saves the patient from early relapses and second surgeries due to residual tumor tissue. Dr. Zhou adds, "Using ioMRI benefits the patients because it means that more of the tumor is resected the first time around. And this is good for the hospital too, because patients don't come for return surgeries." The hospital has seen another benefit in that it can use the ioMRI system for other non-surgical scanning purposes as well.

But the impact of Huashan's Neurosurgical Department's work extends beyond the individual patients' prognosis. The Neurosurgical Department stands out for the groundbreaking research they have conducted on the role of ioMRI combined with neuronavigation in improving extent of resection of gliomas. From 2010 to 2012, a 15-member team led by Dr. Jin-Song Wu began a clinical study on the use of 3T ioMRI with neuronavigation on 373 patients. The research team measured results and followed up with patients for three months after surgery. The preliminary results released last year in an article in Chinese Medical Journal show a marked improvement for 161 patients with cerebral gliomas who underwent surgery using the intraoperative ▸

Hospital visitor in front of the wall with photo portraits of young doctors and specialists of Huashan Hospital (above); Entrance area of the hospital (below).

MRI method. Before intraoperative MRI surgeries, there was 55.90 percent gross total resection rate. With use of ioMRI, the gross total resection rate was 87.58 percent, a marked improvement. The ratio of benefit in extent of resection was 39.13 percent. 158 of the 161 glioma patients accomplished follow-up at 3 months postoperatively. 12.42 percent suffered from early motor deficit after surgery; late motor deficit was, however, observed in 3.16 percent. 13.04 percent had early speech deficit and only 3.80 percent displayed late speech deficit. In the article, the doctors wrote, "We believe that 3T ioMRI provides neurosurgeons with dynamic functional and anatomical maps of brain structures, which improves the overall accuracy and safety of surgery, and helps decrease permanent surgical morbidity."

Management Summary

Challenge:
To maximize extent of tumor resection within the intraoperative setting while minimizing the impact on functional brain tissue.

Solution:
The 3T ioMRI Integrated Neurosurgical Suite at Huashan Hospital reveals residual tumors in the intraoperative setting and helps compensate for brain shift, enabling the neurosurgeons to achieve a higher extent of resection while minimizing impact on the patient.

Result:
Better treatment for the patient that leads to higher success rate and better hospital workflow. This means better management of brain tumor patients. The research results confirm the improved success of ioMRI for patients and could be the evidence needed to allow the technology to become more widespread.

Award-Winning Value for Patients

Last autumn, when the team received the *Journal of Neuro-Oncology Award*[3], Dr. Wu was quoted in a press release as saying of ioMRI, "This leads to more improved progression-free survival and quality of life than using conventional neuronavigation. Although these are early results we believe they are showing trends to statistical significance and will be the highest level of ioMRI evidence for glioma surgery to date." According to Dr. Ignacio Vallines, Head of MR collaborations for North East Asia at Siemens, "innovative approaches to combine imaging and therapy in an effective way are at the core of our R&D collaborative efforts with clinical research partners across the globe. We are proud to actively contribute to further develop the clinical and operational value of intraoperative MRI imaging together with Huashan Hospital."

Although ioMRI requires a substantial initial investment and hasn't yet been universally adopted, the team's research is likely to have a strong

Huashan Hospital's ioMRI solution is mounted on a ceiling rail (above) and can be moved in and out of the OR (left) from an adjoining room.

impact on the spread of ioMRI use throughout the medical world. "Shanghai is the first site performing a prospective trial on a large number of patients which may fulfill all requirements to generate the evidence needed to successfully apply for reimbursement in countries granting reimbursement based on clinical evidence only," says Dr. Hofmann. He adds, "They are doing what should have been done a long time ago but in early times of ioMRI we didn't think about it."

The story of how Huashan Hospital acquired their ioMRI suite is different from private hospitals around the world that have invested in the technology. While private hospitals may see a financial benefit of investing in an intraoperative MRI system, Zhou says that financial payoff was not a factor for his department: "This is a government hospital so we don't consider profit. We're one of the largest neurosurgical centers in mainland China. A lot of patients are coming here, not just VIPs, so the government has seen the benefit in providing this technology."

Not just any hospital in China can invest in one of these systems, because import licenses are hard to qualify for and can take a long time to process. Instead, the Ministry of Health selects leading hospitals to test out experimental technology in order to evaluate its usefulness as a tool. With such favorable results from the Huashan study, the government may issue more import licenses or even prioritize usage of the technology in the government's next five-year plan.

Wide-reaching Ripple Effects

Looking at surgery success rate and benefit to patients, doctors, and hospitals is important to assess an experimental method. Taking these factors into account, incorporating intraoperative MRI might just trigger the start of a wide reaching ripple effect. Better treatment for the patient can mean a better hospital workflow, fewer follow-up surgeries and lower mortality rates. The farthest reaching ripple is the cost to society. When tumors are resected as precisely as possible the first time around, this will not only benefit the patient, it will also likely benefit the health system, as long-term cost will drop.

In the end, that may be another impact of Huashan Hospital's work. The research results confirm the improved success of the ioMRI method for patients and could be the evidence needed to allow the technology to become more widespread. And that will have an immeasurable impact on global society as patients benefit from higher total resection rates and both the emotional and financial cost of taking care of patients is reduced. ■

Rebecca Kanthor is an independent journalist based in Shanghai. Her work has appeared in *Nature, Scientific American*, and on Public Radio International, CBC Radio, and the BBC.

→ www.siemens.com/Intraoperative-MRI

[1] Lacroix M et al, JNS 2001
[2] Chin Med J 2012;125(24):4328-4333
[3] Clinical Neurosurgery, Vol 61, No. 1, Aug. 2014
[4] The products/features (here mentioned) are not yet commercially available in the US and some other countries. Due to regulatory reasons their future availability cannot be guaranteed. Please contact your local Siemens organization for further details.

Tackling Stroke Worldwide

Professor Stephen Davis of the University of Melbourne is the president of the World Stroke Organization (WSO), the international non-governmental organization working to reduce the global burden of stroke with a unified voice. Professor Davis talks to *Medical Solutions* about the increasing threat and burden of stroke in the third world.

Interview: **Alysia Battersby**

About Professor Stephen Davis

Professor Stephen Davis is professor of Translational Neuroscience at the University of Melbourne, Australia. His research interests are centered on clinical trials and brain imaging research for improved acute stroke management and secondary stroke prevention. Professor Davis is the Director of Neurosciences and Continuing Care, Director of Neurology and Director of the Melbourne Brain Centre at the Royal Melbourne Hospital, and has been the president of the World Stroke Organization since October 2012.
Siemens Healthcare has just entered a two-year relationship with the WSO to help improve stroke services in developing and emerging countries. These activities underline the already existing expertise at Siemens Healthcare in optimizing processes in stroke care and will influence the development and further improvement of customized Siemens solutions, consisting of consulting services and modalities, for existing and newly to be founded stroke centers.

Professor Davis, why is the fight against stroke a global challenge?

Davis: We know that every year there are 17 million new strokes and six million deaths from stroke, making stroke the second biggest killer in the world. The challenge of stroke is enormous because not only is it a condition with a high mortality rate, but there is often substantial disability in survivors. We know that there are well over 30 million stroke survivors in the world with varying levels of disability.

Why is the fight against stroke particularly important in the third world?

Davis: We know that the rates of stroke are increasing in the developing world and middle income countries. With the increased lifespan of the world's population the burden of stroke is even greater. Stroke is a massive challenge around the world and we need global strategies to reduce the burden of stroke.

What are the WSO's strategies to tackle this challenge?

Davis: We will be launching our global action plan for quality stroke services around the world at the World Stroke Congress in Istanbul this year in October. The WSO is focused on three major planks of stroke care: prevention, acute stroke care, and rehabilitation combined with post-stroke care. We think we can impact globally on stroke, particularly in the areas which need it most, which is the developing world.

Why does the WSO promote the development of stroke units in low and middle income settings?

Davis: Stroke units have been proven to improve outcomes of stroke in low and middle income settings, not just in high income settings. So we've got the formula, we know that it works and we now have to work with governments, with health organizations through education and advocacy, working with our lay supporters to ensure that there are adequate health services in every region of the world.

How can stroke units be employed cost-effectively in the developing world?

Davis: Unfortunately, even the 'essential stroke care' service is grossly deficient in many parts of the world. However, we believe that some principles we use will improve outcome for patients even in the most disadvantaged settings. But we still believe that there are elements of care that can make a difference. Even without resources, we can purport to give patients the standard principles of care,

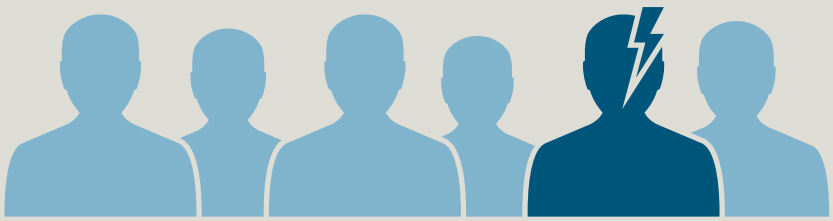
Facts and Figures

There are 17 million new strokes each year, about 6 million of which result in death[1].

Today,

70%

of all strokes occur in low and middle income countries where the incidence of stroke is rapidly increasing[1].



1 in 6 people will have a stroke in their lifetime[2].

[1] Feigin, V.L., Forouzanfar, M.H., Krishnamurthi, R., Mensah, G.A., Connor, M., Bennett, D.A., Moran, A.E., Sacco, R.L., Anderson, L., Truelsen, T., et al. (2014). Global and regional burden of stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. Lancet 383, 245-254

[2] World Health Organization (2004). Atlas of Heart Disease and Stroke. [Online]. Available from: http://www.who.int/cardiovascular_diseases/resources/atlas/en/. Accessed 05/09/2014

for example, by paying attention to the swallowing capability of the patient, treating fever, preventing pneumonia, preventing infections, mobilizing people as quickly as possible, screening patients for urinary incontinence, assessing their hydration status, and involving the family in discharge planning. And we can provide some basic elements of rehabilitation and prevention. So even in the most disadvantaged settings, we believe that some principles that we use will improve outcome and reduce the mortality rate – and improve the functional outcome for the patients.

Can you give me an example of how the WSO is promoting public awareness of stroke?

Davis: One of the great examples of how we get change is through our annual World Stroke Day award for countries that have the best campaigns. For example, last year the winners were Sweden, the United States, and Peru. A special mention also went to Mongolia. In these countries, they have everything from internet-based activities, social media, street marches, promotion of football games, and buses that travel around with stroke messages on them. So we use a lot of innovative outreach techniques to educate the public and to promote the principles of stroke care with politicians and decision-makers.

What would you describe as the WSO's achievements so far?

Davis: I think the success of WSO has been to partner with other likeminded organizations and to get the stroke support bodies around the world to work together with common aims. Very importantly, we've been accepted by the World Health Organization as the lead international body of stroke and we're members of the United Nations Economic and Social Council. We're closely involved with the Non-Communicable Diseases Alliance because we believe about 80 percent of stroke can be prevented by treating elevated blood pressure, tackling obesity, quitting smoking, increasing physical activity, reducing salt and excessive alcohol intake, detecting and treating atrial fibrillation, diabetes and others. The biggest way we can effect change is through our partner organizations around the world. It's the big picture activities that we're involved in with these organizations that are important. ■

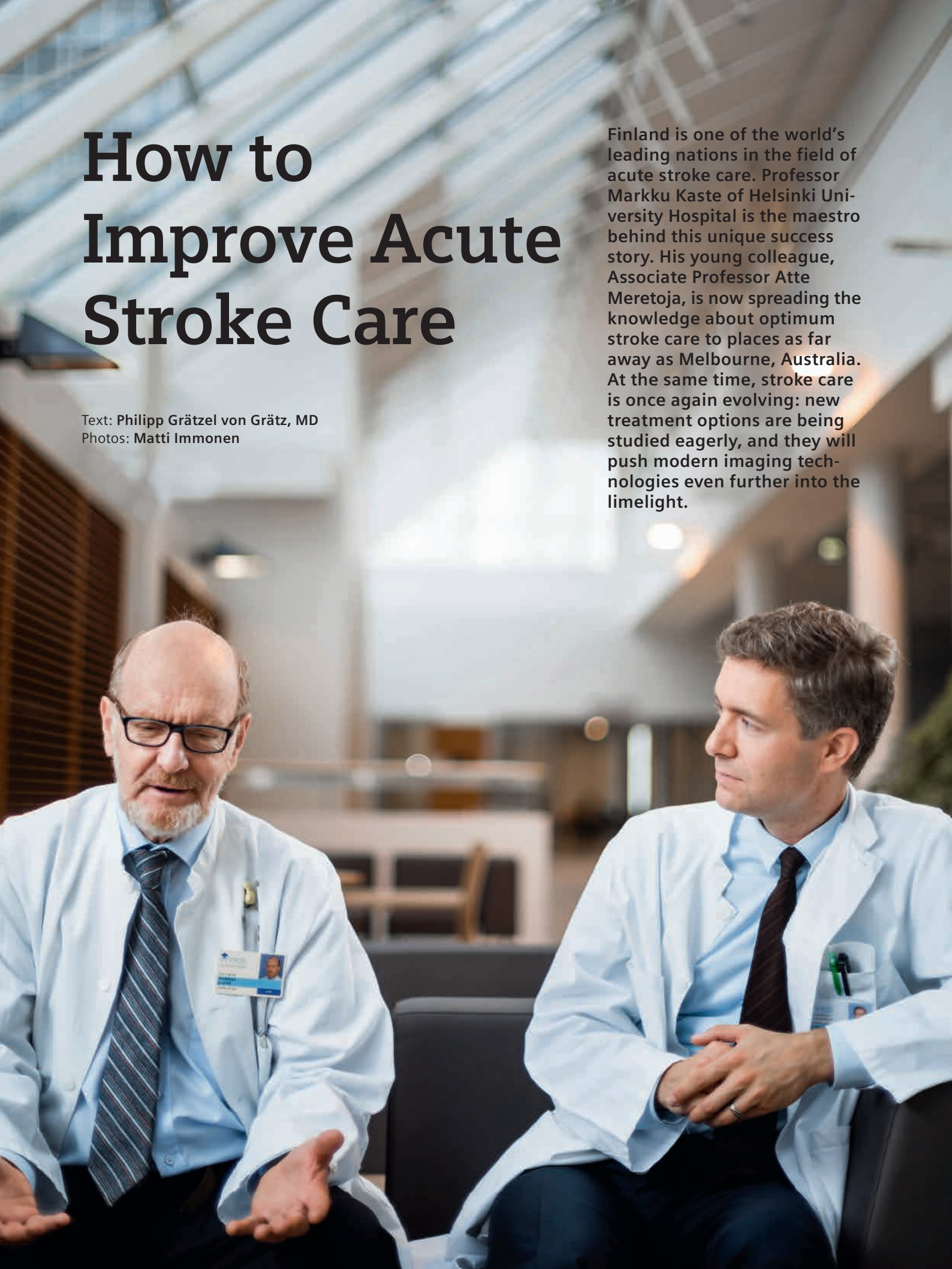
Dr. Alysia Battersby, PhD, director of BioMedWord Ltd., is a medical and scientific writer with over 10 years of scientific research experience. She has written and edited manuscripts published in peer-reviewed journals and has communicated topics in life sciences to specialized audiences and to the general public.

➔ **www.siemens.com/stroke**

How to Improve Acute Stroke Care

Text: **Philipp Grätzel von Grätz, MD**
Photos: **Matti Immonen**

Finland is one of the world's leading nations in the field of acute stroke care. Professor Markku Kaste of Helsinki University Hospital is the maestro behind this unique success story. His young colleague, Associate Professor Atte Meretoja, is now spreading the knowledge about optimum stroke care to places as far away as Melbourne, Australia. At the same time, stroke care is once again evolving: new treatment options are being studied eagerly, and they will push modern imaging technologies even further into the limelight.



How Times are Changing

When Markku Kaste began working in stroke care four decades ago, there was no computed tomography (CT) or magnetic resonance imaging. Stroke patients with intracerebral bleeding survived for three days on average. There was no causal therapy for patients with ischemic stroke. And specialized stroke units were a pipe dream.

Markku Kaste: There was nothing. Many neurologists didn't actually want to treat or see these patients, especially elderly patients, since there was so little that we could do for them. This has changed massively during the last decades. Thanks to modern imaging, we now know exactly what is going on in the brain. Several randomized controlled trials from the 1980s onward made us aware that treating patients in specialized stroke units makes a huge difference: more patients now survive, and the likelihood of long-term disability has fallen considerably. Then intravenous thrombolysis came. We are getting quicker and quicker at administering it, and this means that we are able to rescue brain tissue that would otherwise be lost forever. All this has led to a steady increase in survival rates. There are more and more stroke survivors in Finland these days, and the number will increase further.

Atte Meretoja: We are in the fortunate position of having access to data on how exactly stroke care in Finland has evolved. The national Finnish PERFECT registry shows that, over the last ten years, we were able to reduce stroke mortality from 30 to 25 percent, and this trend is ongoing. Patients with intracerebral hemorrhages are also better off these days. They now survive on average for five years after the bleeding. Stroke incidence, by the way, is interesting to study as well. Finland has the most rapidly aging population in Europe. In spite of this, the overall stroke incidence is pretty steady. In other words: for a given age group, the risk of suffering a stroke is actually falling. This is thanks to better risk factor control. The PERFECT data suggests that we have not only improved stroke care, but also stroke prevention.

Today's Stroke Care in Finland and Beyond

Improvements in stroke care in Finland are not restricted to the Helsinki area: The success story started there, but quickly spread throughout the country. The number of patients who are treated in specialized stroke centers has steadily increased in Tampere and Turku, in Oulu and Joensuu. Overall, 70 percent of all Finnish stroke patients ▸

Professor Markku Kaste (left) and Associate Professor Atte Meretoja (right) are active in spreading the word on optimum stroke care.

are now treated in stroke units. The remaining 30 percent are largely patients in the remote and sparsely populated northern parts of the country. But even then, at least indirect access to stroke specialists is available in most places. Helsinki University offers telestroke services to remote hospitals several hundred times a year, in addition to the 2,000 or so stroke patients treated on-site by the Helsinki neurologists. In fact, stroke patients in remote parts of Finland probably have a better chance of receiving the best care than patients in many other parts of Europe.

Markku Kaste: The European Stroke Initiative carried out a large study with more than 300,000 patients from all the major countries in Europe. It emerged that Europe-wide, only one out of seven stroke patients is admitted to a stroke unit. 42 percent are treated at hospitals with less than 50 stroke patients per year. Such a hospital will not and cannot have the necessary infrastructure for optimum stroke care.

Atte Meretoja: The most interesting figure in this context is the number of patients who get intravenous thrombolysis. In Helsinki, 16 percent of all ischemic stroke patients get intravenous thrombolysis. This is the population-based rate, and it is by far the highest in the world. The second-highest population-based rates are from Germany at 12 percent. In the US, the population-based intravenous thrombolysis rate in ischemic stroke is 4 percent. In Australia and in most European countries, it is probably around 6 percent. Individual hospitals achieve higher rates, for example, the Helsinki University Hospital at 31 percent of all ischemic stroke admissions.

When Speed is King

Using intravenous thrombolysis is one thing, but it is not enough simply to administer it. To be as effective as possible, it has to be used quickly. The neurologists in Helsinki have been working on an optimum protocol for intravenous thrombolysis administration for more than a decade. The target parameter was a reduction in what is called the door-to-needle time. This is the time that passes from the moment the paramedics carry the patient through the entrance door of the hospital until the life-saving thrombolysis is finally administered. Door-to-needle time is of the utmost importance in patients with ischemic stroke, not only for survival but also in terms of quality of life.

Markku Kaste: We have all these calculations that tell us how many neurons we can save by treating the patient quicker. But it is not only neurons. Being quick when a stroke patient comes to the hospital directly translates into quality of life for the patient. We have shown that saving 15 minutes in door-to-needle time means on average one month more of high-quality life for the stroke patient.

Atte Meretoja: In Helsinki, we managed to reduce average door-to-needle time to 18 minutes. This means that we are more than one hour quicker than, for example, our colleagues in the US or indeed in many parts of Europe. This difference adds up to a plus of four months of disability-

“The improvement in stroke care at Helsinki University is absolutely cost-effective”.

Professor Markku Kaste, Head of the Department of Neurology, Helsinki University Hospital

free life. That's a lot. It really makes a difference, not only for the statistics, but for every individual patient.

Step-by-Step Improvements

The massive reduction in door-to-needle time at Helsinki University was a result of several measures that the neurologists introduced step by step over the period of a decade. Kaste, Meretoja, and their colleagues have recently published these steps in the form of a twelve-point priority list. One very important aspect on that list is a better involvement of the emergency medical services. The hospital is pre-notified that a stroke patient will arrive. This makes it possible to pre-order certain tests, to communicate with relatives, to obtain information on the individual medical history, and to take care of some of the usual admission bureaucracy in advance. Another important factor is the relocation of a CT scanner right into the emergency department (ED).

Atte Meretoja: The relocation of the CT scanner in 2004 was a crucial step. It didn't immediately lead to a reduction in door-to-needle time, but it helped us to identify other bottlenecks that we could eliminate once the CT was available. Because we no longer had to wait for the CT, we realized how important it was to have proper pre-notification. Another example: we learned that, for our stroke patients, it is not necessary to go through the ED cubicle. We transport stroke patients directly into the CT room. We do a brief neurological examination and some point-of-care lab tests and perform the CT examination immediately afterward. The lab results are available as soon as the CT is done. These refinements of the admission processes save us an awful lot of time.

Markku Kaste: Another important aspect is that we have stroke specialists available at the emergency department all the time. We have 40 neurologists in total in our department. This makes it possible to offer a 24/7 service. The interesting thing is that the improvement in stroke care at Helsinki University is absolutely cost-effective. We carried out a monetary analysis for the year 2007, which revealed that we paid 11.3 million euros for 2,000 stroke patients who were treated in our hospital plus 3.2 million euros for the neurological emergency room with its 6000 admissions. The successful treatments with stroke unit care and thrombolysis saved us 14.4 million euros in costs for chronic care. This means that the neurological ER is actually cost-neutral, and the hospital not only gets better stroke care, but also better care for other neurological emergencies like acute seizures. It's like buying a Mercedes and getting a BMW or two on top.

Helsinki University Hospital has 40 neurologists on-site and offers telestroke services to remote hospitals several hundred times a year.

A Blueprint for Other Countries

Finland is only one country. So can the Finnish success story be transplanted to other territories? Atte Meretoja has recently proven that it can be. He left for a fellowship to Australia's University of Melbourne for 18 months to test the applicability of the Helsinki protocol in a totally different healthcare setting. The results were impressive. ▸

Management Summary

According to the experience of Professor Kaste of Helsinki University Hospital, acute stroke care can be optimized substantially by reorganizing processes in the ED. Due to improved communication between emergency service together with hospital and CT imaging made available right in the ED, Helsinki University Hospital was able to get door-to-needle time down to as little as 18 minutes on average. This will substantially increase the likelihood of good patient outcome and reduce the risk of permanent disability after stroke. Arming the ED with neurological expertise will also benefit patients with other neurological emergencies, for example, seizures. In the future, the integration of neuroradiological angiography suites into the acute care setting might make stroke care even more of an interdisciplinary endeavor.

Atte Meretoja: Within a year, the Helsinki result could be duplicated. Measures for process improvement similar to those mentioned above drove door-to-needle time down from 45 to 21 minutes. What was not possible was copying the 24/7 service since the neurological department at the Royal Melbourne Hospital was far smaller than the one in Helsinki. But still, a lot was achieved through relatively simple measures.

Joining Forces

Industry, too, can help to spread the message of better stroke care through process optimization. The Act on Stroke initiative that was launched by Siemens Healthcare Consulting in 2010 specifically aims to improve processes in stroke treatment. Based on a systematic model encompassing care guidelines and clinical expertise, it allows the level of maturity of complex clinical processes to be rated for an individual hospital.

Markku Kaste: We are all in one boat that is heading in the same direction. We will achieve the best results if we join forces. Industry has considerable experience in how to effectively distribute information. It is far better at it than we are. Why not help to distribute printed guidelines, for example? Why not support training projects of the European Stroke Organization? We have to tell our colleagues all over the world in as many face-to-face meetings as possible about how optimum stroke care can and should be organized. That is our duty.

Not Yet Over the Finish Line

What optimum stroke care looks like in the year 2013 can be seen at Helsinki University. But stroke care as it is today is certainly not carved in stone. Stroke therapy could well change considerably in the years to come: intra-arterial clot retrieval devices that can be used to manually extract

Modern stroke care would be inconceivable without rapid brain imaging. At Helsinki University Hospital, reallocating a CT to the emergency department enables thrombolytic therapy to be administered to stroke patients in only 20 minutes.

More Insights into the Finnish Approach

Markku Kaste and Atte Meretoja explain how they improved workflows in the stroke unit of Helsinki University Hospital and how that affected the outcome for the patient.

To watch the video, scan the QR code using the reader app on your smartphone or enter the URL into your browser.

www.siemens.com/acute-stroke-care

blood clots and open obstructed cerebral arteries are already being tested in numerous clinical studies. The challenge is to select stroke patients who benefit from these therapies as effectively and – again – as quickly as possible. This will necessitate modern imaging technologies that go well beyond the plain CT imaging that is still, in many places, the standard of care in CT diagnostics.

Atte Meretoja: Intra-arterial therapies are heavily researched in the stroke community worldwide. At our institution, we perform around 50 to 100 recanalizations with intra-arterial devices per year. The global stroke community hasn't nailed the selection criteria for these interventions yet, but I am pretty sure that we will get there over the next couple of years. Imaging will definitely play a role here. At the moment, we supplement the plain CT scan with a CT angiography and a CT perfusion scan in patients who might benefit from interventions in addition to intravenous thrombolysis. It could well be that, in the future, we will use the CT to directly image collaterals or to measure the lengths or even the composition of a clot.

What the Future Holds

Parameters like clot length or the degree of collateralization might help to allocate patients to the best therapies. But they have to be tested rigorously in clinical trials, and indeed they are already being tested.

Markku Kaste: These are exciting times in stroke care. We will see a lot of interesting results from ongoing trials in the years to come. One thing that won't change is that emergency imaging will remain the cornerstone of stroke care. The other thing that will always be true is that good stroke care is about teamwork. Today, paramedics and hospital staff have to cooperate closely to achieve the shortest possible door-to-needle times. And in future, neurologists, interventional neuroradiologists, and neurosurgeons might have to cooperate far more closely than they do today to provide optimum interdisciplinary treatment for our stroke patients. Maybe we will have a common emergency room for diagnosis and treatment of acute stroke patients one day, similar to the cath labs of cardiologists. Who knows? ■

Philipp Grätzel von Grätz is a medical doctor turned freelance writer and book author based in Berlin, Germany. His focus is on biomedicine, medical technology, health IT, and health policy.

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The Neuro Navigators

Heidelberg University Hospital in Germany offers not only world-class medical care; when necessary, the physicians are willing to question medical paradigms. Here, neuroradiologists use magnetic resonance neurography to visualize peripheral nerves. The examinations of the tiny nerve bundles have yielded a somewhat surprising result. Some patients with neurological diseases need different treatment than previously believed.

Text: **Dr. Thomas Meissner** Photos: **Uwe Mühlhäusser**

If the lights suddenly go out in a single house in Heidelberg's historic *Altstadt* (old town), one might assume the cause of the power failure is within the house itself. It has to be possible to repair the damage somewhere in the house – and not, say, on the Königstuhl, a nearby mountain where one would think that a power distribution station might be located. No, everything must be fine up there! Otherwise, at least half if not the entire city would be dark.

If we were talking about nerves instead of power lines, this assumption might be false. The cause of the "power outage" when it comes to paralysis of the top joint of the thumb, for example, is surprisingly often "at the top of the hill" – in other words, close to the trunk and the nerve roots, explains Mirko Pham, MD, Associate Professor and Managing Senior Physician of the Department of Neuroradiology at Heidelberg University Hospital. Doctors have suspected this for a while, but now it has been finally proved with magnetic resonance neurography (MRN). This

Experts in imaging peripheral nerves: Mirko Pham, MD, Associate Professor and Managing Senior Physician, and Philipp Bäumer, MD, MSc, both of the Department of Neuroradiology at Heidelberg University Hospital.

changes a lot – for the understanding of several peripheral nerve disorders, for physicians in search of a diagnosis and, most of all, for the patients and their treatment.

Revolutionizing Diagnostic Testing

With MRN, Dr. Pham and his colleague Philipp Bäumer, MD, MSc, from the Department of Neuroradiology led by Professor Martin Bendszus, MD, provided the first direct evidence that, in certain circumstances, peripheral nerve damage could be at a completely different location than often previously suspected. The Heidelberg neuroradiologists are the first specialists in Germany to take advantage of this new technology, using the MAGNETOM® Verio, a 3 Tesla (T) magnetic resonance imaging (MRI) system from Siemens and a number of special coils*. There are fewer than 10 comparable sites worldwide. "Magnetic resonance neurography may revolutionize the diagnosis of peripheral neuropathies," claims Dr. Pham. Because, for the first time in medical history, it allows doctors to visualize miniscule nerve damage that sometimes has a substantial impact.

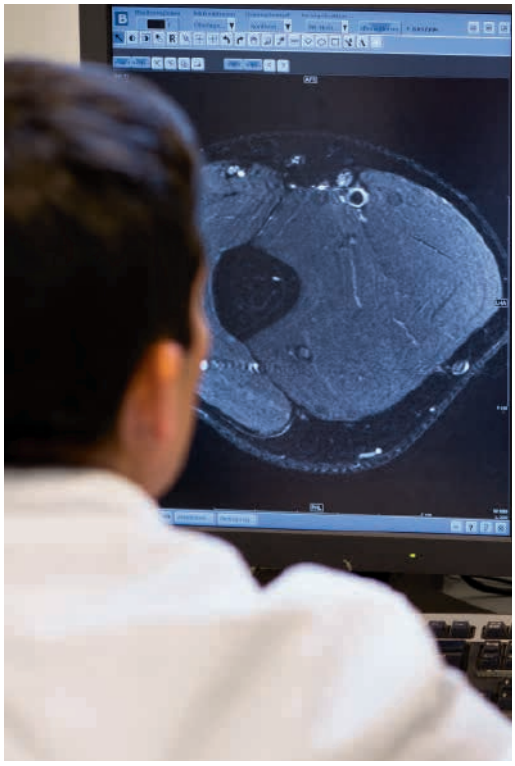
Peripheral nerve damage can develop in the course of various diseases. In many cases, the cause and location of the damage are hard to find. In approximately one out of every four patients, no definitive diagnosis can be made[1]. For example, nearly 50 percent of all diabetes patients experience sensory alterations in their fingers or toes at some point during the course of their disease. In Germany, that adds up to approximately 100,000 new diabetes patients with peripheral nerve damage each year[2]. Other problems involving peripheral nerve damage include impaired nerve functions due to inherited metabolic disorders, genetic preconditions, as a side effect of chemotherapy, the result of alcohol abuse, or damage that occurs spontaneously. Burning pain, neurosensory disorders, skin alterations, or muscle weakness are just a few symptoms of peripheral nerve lesions. To reach a diagnosis, doctors have primarily had to rely on information from the patient as well as clinical and electrophysiological examination methods. The causes and locations of the damage can be very challenging to determine correctly, and common errors are possible using conventional methods. To see exactly by electrical nerve conduction examination where the ▸

Management Summary

Challenge:
Peripheral nerve disorders are quite common. The causes and locations of the damage can be challenging to determine correctly if only conventional diagnostic methods are used, leaving possible errors of localization.

Solution:
Magnetic resonance neurography (MRN) based on the MAGNETOM Verio 3T MRI system makes it possible to locate lesions of the peripheral nerves.

Result:
Magnetic resonance neurography has fundamentally changed the diagnostic investigation of peripheral nerve lesions. It contributes to a new understanding of some symptoms that are accompanied by peripheral neuropathies. It increases the accuracy of medical diagnoses and has an impact on doctors' therapy strategies.[1]



nerve is hurt, in analogy is somewhat comparable to an electrical engineer who is trying to see in thick fog where an above-the-ground electrical line is hit. The engineer could only indirectly assume which area of the cable was damaged based on his observation of electrical failure.

However, knowing the location of the nerve damage means that neurologists can give the disease a name. With the name, they have an idea at least of what is causing the disease and can therefore come up with a strategy for treatment. If the location is not correct, this may result in diagnostic collapse. Dr. Bäumer and Dr. Pham have confirmed the suspicion that conventional methods of locating nerve damage may fall to misconceptions about true lesion locations. This has led and continues to lead to potentially unnecessary and unsuitable treatment. Conversely, identification of the location of the lesion or several lesions on the nerve offers evidence of the mechanism behind their development and therefore enough information to determine surgical or drug-based treatment options.

A Visit to the MRI Suite

Philipp Bäumer and Mirko Pham lead the reporter into the heart of the Neuroradiology Department, where the green-and-white MRI unit stands in a brightly lit room. The 70-centimeter opening of the short 3 Tesla MRI system is almost inviting. Even children are able to lie still here for several minutes. A motorcyclist was recently lying on the system's examination table, his left arm paralyzed

A high magnetic field strength of 3 Tesla, together with dedicated coils, allows high-resolution microstructural imaging of the nerves. Specific examination protocols in addition give even greater detail.

after an accident. Sitting in front of the monitors, Dr. Bäumer and Dr. Pham explain his injuries. With the help of various special coils for the shoulder and arm, they were able to provide the neurosurgeon with crucial information for his operation: in addition to a nerve root centrally torn out from the spinal cord, the axillary nerve had become completely detached.

The neurologists were able to create a 3D data set that improved the precise localization of the damage and showed the surgeon the proper path of entry. But MRN can do even more. A high magnetic field strength of 3 Tesla, together with dedicated coils, it allows high-resolution microstructural imaging. Together with specific examination protocols, it is possible to visualize not only the "thick power cable," but all of the small wires in the cable. "The move from 1.5 to 3 Tesla was a quantum leap," explains Dr. Bäumer. "It does not just allow us to assess the nerve as a whole, but also its substructures, the very tiny nerve fiber bundles." This is important as the nerve is often not completely damaged, but rather, only these small substructures are selectively affected. The individual nerve fiber bundles (nerve fascicles) and their nerve fibers have different functions, as Dr. Bäumer and Dr. Pham have proven. And malfunctions of individual fascicles lead to unpredictable and unexpected, sometimes very confusing symptom patterns.

Where the Nerve Damage Really is

Patients with Kiloh-Nevin Syndrome (or Anterior Interosseous Nerve Syndrome – AINS), for example, can no longer bend the tips of their thumb and index finger – the severe impairment to everyday activities that results from this is easy to imagine. For decades, doctors thought that it was primarily due to nerve damage resulting from compression of the nerve in the forearm, and attempts have been made to decompress the apparent damage to the compressed AIN in the forearm through surgery. Dr. Pham, Dr. Bäumer, and their colleagues recently examined 20 AINS patients using MRN and compared them with 20 healthy individuals. They found that all patients had lesions of the small nerve fascicle in the upper arm, especially in a certain section of the nerve and always in the same region of the nerve cross-section[3].

Dr. Pham and Dr. Bäumer have thus confirmed, using a rare but prototypical disorder, that individual nerve fascicles perform selectively assigned functions and that these functions are determined "up on the hill" (in other words, closer to the trunk). Furthermore, the symptoms of Kiloh-Nevin Syndrome frequently don't have a mechanical origin, but are probably autoimmune and inflammatory in nature. Consequently, these patients do not need surgery, but should be treated with anti-inflammatories. "The diagnosis can only be accurately established with magnetic resonance neurography," states Dr. Pham.

And Dr. Bäumer adds: "We have since had similar findings for other nerves, such as paralysis of the extensor muscle in the finger – called drop finger." When the fingers and/or ▸

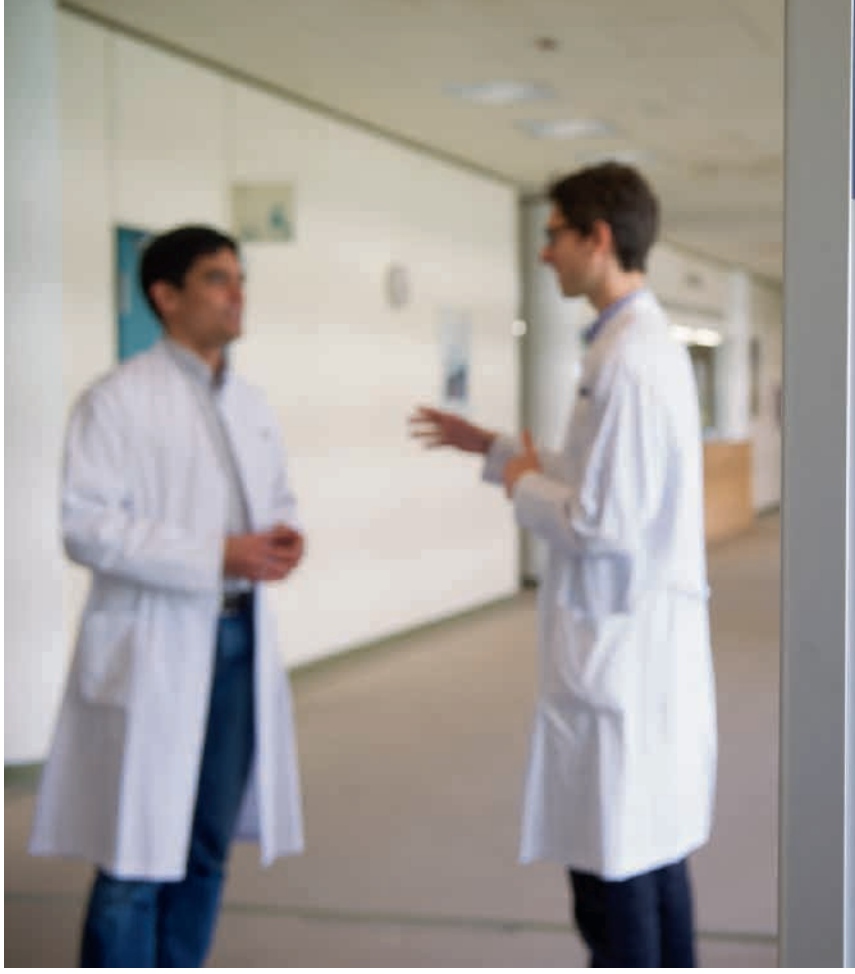
the wrist can no longer be extended, doctors assumed it was due to compression of a radial nerve branch in the elbow that should be treated with surgery, explained Dr. Bäumer. However, the neuroradiologists have determined that in certain cases, this may also be caused by damage "on the hill." Up to now, this has scarcely played a role in the patient's treatment.

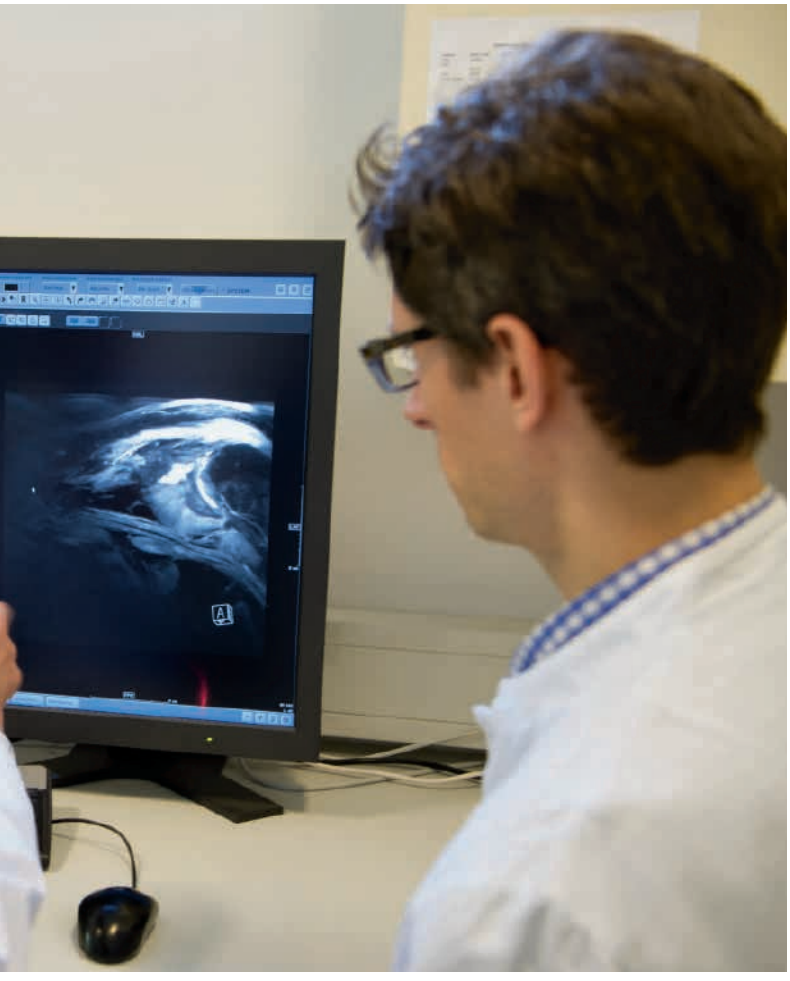
In the case of diabetic polyneuropathy due to poor control of the blood sugar, the nerve damage initially manifests itself as a loss of vibration sensitivity in the feet; later on, the patients no longer feel pain, temperature, or even significant injuries to their feet. The result of the nerve and vascular damage are strong infections, large ulcers, which in some cases can even lead to amputation of the foot. "Until recently, doctors thought that the nerves were 'singed' from the bottom up," says Dr. Pham. "However, magnetic resonance neurography has shown us that metabolic disorders can lead to damage in several locations of the peripheral nerves, and mainly where the nerves are particularly large-caliber – in the thigh."

Early Diagnosis is Possible

This changes the fundamental assumptions regarding the symptoms described here. In the future, doctors will likely be able to diagnose nerve damage earlier and more precisely than they can now using MRN, and in some nerve diseases, probably even before the first symptoms appear. Doctors can try to prevent, delay, or even reverse the damage with medication. Some important further developments in MRN are perfusion measurements of the nerve's blood supply with perfusion magnetic resonance imaging and diffusion tensor imaging (DTI). With these techniques, doctors can detect perfusion alterations in risk areas that are characteristic of certain diseases and quantify the function and integrity of a nerve.

Dr. Pham received a €200,000 (US$ 259,000) research stipend from the Else-Kröner-Memorial Foundation in March 2014 to fund their further development of MR Neurography. The methods have long since become clinical routine at Heidelberg University Hospital – a unique selling point that attracts referrals from all over Germany. The radiologists point out, however, that MRN does not replace the neurologist's conventional diagnostic tools, but refines them. Conventional diagnostic methods such as screening and diagnostic phases are still necessary. "We provide additional criteria that tell the neurologists whether their suspected clinical and electrophysiological diagnosis was correct," says Dr. Bäumer. And Dr. Pham explains: "We have the good fortune to be able to use this advanced technology and the responsibility to do so sensibly." ■





Magnetic resonance neurography has become clinical routine at Heidelberg University Hospital – a unique selling point that attracts referrals from all over Germany.

Thomas Meissner, MD, is a medical journalist in Germany. He worked as a doctor in Germany and the UK before completing training as a journalist with the German periodical *Ärzte Zeitung*, where he worked as an editor. He has been a freelance medical journalist for trade and consumer media publications for the last 13 years and has an office in Erfurt, Germany.

→ www.siemens.com/MR-Neurography

[1] Pham M. *Der Nervenarzt* 2014; 85: 221-237
[2] Press release, "Kleinste Nervenschäden erstmals sichtbar gemacht," Universitätsklinikum Heidelberg, 18.03.2014
[3] Pham M. et al. *Neurology* 2014; 82: 1-9

* The statements by Siemens' customers described herein are based on results that were achieved in the customer's unique setting. Since there is no "typical" setting and many variables exist there can be no guarantee that other customers will achieve the same results.

Trying to Exclude Alzheimer's Disease with MR-PET Imaging

The Mallinckrodt Institute of Radiology, part of the Washington University School of Medicine in St. Louis, Missouri, USA, is the first institution in the world to use a new tracer for amyloid plaque imaging with a scanner that combines magnetic resonance imaging (MRI) and positron emission tomography (PET). Prof. Robert McKinstry, Radiology Research Facilities, is working intensively on the detection of Alzheimer's disease and other neurodegenerative diseases. On a visit to the state-of-the art Center for Clinical Imaging Research, he describes why combined MR-PET is a valueable imaging device for dementia patients.

Text: **Kathleen Raven** Photos: **Thomas Steuer**

The Greek physician Galen knew doctors could not treat the brain without intimately knowing its contours and connections[1]. Yet even as medical imaging advanced over the centuries, the human brain remained out of focus. Now, as the world population ages faster than ever, physicians and researchers have an excellent tool for studying neurodegenerative diseases like Alzheimer's, Parkinson's, or Huntington's disease: Siemens' Biograph mMR system. This medical device combines anatomical details from MRI with molecular activity gained through PET and welds both in a single, information-rich image. As a result, doctors at Washington University's Mallinckrodt Institute of Radiology in St. Louis, Missouri, obtain stunning images beyond Galen's wildest imagination.

Visualizing a Path Toward Treatment

One afternoon recently, a group of physicians huddled inside a conference room on the Barnes-Jewish Hospital campus in St. Louis. A projector flashed brain images obtained from the Biograph mMR system onto a white screen. In the top row of images, the brain's white matter is nestled near the organ's edge. In the bottom row, this white area appears smaller and further away from the edges. One doctor taps a few keys on the computer to show PET images superimposed on the MRI scans. Suddenly beta amyloid – the telltale protein of Alzheimer's disease (AD) –

The Mallinckrodt Institute of Radiology is prepared for the future challenge: detecting Alzheimer's and other neuro-degenerative diseases.

glows menacingly in the lower row of images. The buildup of amyloid plaques is one of the key pathological indicators for AD. Both images "help us to understand what's going on and make a better diagnosis," said Jonathan McConathy, MD, PhD, assistant professor of radiology at the university.

Improved evaluations are crucial as physicians and researchers race to understand AD and other forms of dementia. In the EU, about five million older adults, nearly one percent of the population, suffer from AD. The same proportion of U.S. adults is affected by the disease[2]. AD is the leading cause of dementia among older adults, but severe cognitive impairment can also come from frontotemporal or vascular dementia, as well as Huntington's or Creutzfeldt-Jakob disease. The Washington University physician researchers noted that the mMR scanner can help distinguish among these other forms of dementia. Although no therapeutic agents have been approved for AD, McConathy and his colleagues believe technology like the Biograph mMR system might contribute directly to drug development. For one thing, better evaluation could lead to more accurate clinical trial patient populations.

In addition to amyloid plaques visible in PET images after injection of tracers or radiopharmaceuticals, research suggests an overabundance of a different protein in the brain, called ▸

Neurogradiologist Prof. Robert McKinstry aims to distinguish AD from other dementia forms in his patients.

tau, might indicate advanced-stage AD. "Ideally, you'll want to enroll patients who are amyloid-positive, but tau-negative," explained neuroradiologist McKinstry. Some of the larger U.S. clinical trials in AD could be recruiting patients with irreversible neuronal damage, which might explain why therapeutic trials have struggled, he explained. Thus, the Biograph mMR system could be used to properly identify the ideal study participants. The system can be used in conjunction with amyloid imaging biomarkers. Amyloid imaging helps visualize amyloid plaque in the brain associated not only with AD, but also with other causes of cognitive decline. PET imaging using amyloid biomarkers can provide valuable data on neuritic plaque density. If AD can be excluded, then in some cases it may be possible to find treatable causes for cognitive impairment. For this reason, simultaneous MR and PET imaging is also therapy-relevant.

Molecular Imaging

Future dementia studies will continue to grow in sophistication, and since the Biograph mMR system can be used with a wide range of PET tracers, including the more commonly used carbon 11 Pittsburgh compound B (C-11 PIB), it shows potential to adapt to new clinical trial protocols and approaches. These imaging biomarkers can visualize accumulations of beta amyloid in the living brain.

While no imaging test by itself will provide absolute evidence of AD or another type of dementia, researchers use the Biograph mMR system to obtain critical diagnostic information that would not have been possible just a few years ago. Currently, physicians check off three criteria in order to help distinguish AD from other dementia forms, McKinstry said. First, the amount of amyloid plaque present in the brain is measured. Next, researchers use volumetric MRI information for signs of atrophy or shrinking within the brain. Finally, and this item requires more clinical study, physicians attempt to observe the brain's circuitry, or how different parts of the organ "talk" to each other, through hybrid MR and PET. The combination of these imaging features along with the clinical presentation can place the patient on the spectrum of AD, the physicians said, adding that none of the above measurements are standardized yet.

Improving the Patient Experience

More than just a tool, the Biograph mMR system can add convenience for study participants. Finding one's way through a large hospital can be confusing for patients at the best times, and this is exacerbated in patients struggling with cognitive impairment and impaired mobility. Since the scanner simultaneously gathers MRI and PET information, men and women involved in neurodegenerative-related studies at Washington University do not have to give as much personal time. In a typical "washer/dryer" technique, where the patient stays in one place and is shuttled between the two system types, the PET and MRI imaging may take one hour each. But that time sacrifice does not include traveling to and from the clinic, noted Tammie Benzinger, MD, PhD, assistant professor of radiology. When

Management Summary

Challenge:
Neurodegenerative diseases like Alzheimer's are increasing worldwide. Delayed detection of dementia or missed diagnosis deprives affected people of numerous potential benefits and imposes unnecessary physical and emotional burdens on their caregivers.

Solution:
The Washington University School of Medicine (WashU) in St. Louis tackles these challenges: Mallinckrodt Institute of Radiology is the first institution in the world to use a new tracer for amyloid plaque PET imaging with Biograph mMR.

Result:
A Biograph mMR amyloid plaque PET scan can rule out the presence of AD pathology in the brain, and is expected to decrease the frequency of false-positive evaluations. If the scan result is negative, it is very unlikely that a patient has AD. If AD can be excluded, it will prompt investigation for other causes of cognitive impairment.

she sees her patients, they give "half a day of their life to drive up here," Benzinger said, adding that "it's a lot to ask patients when they are sick or disoriented." Shorter scanning times can add up. In a study of cerebral metabolism at the university, researchers recorded a 40 percent time saving with the Biograph mMR system, McKinstry said. Researchers recently convinced a patient with mild cognitive impairment and claustrophobia to participate in a study that utilized the single systems, Benzinger explained. Past research also relied heavily on the presence of dementia-related biomarkers in cerebrospinal fluid (CSF) drawn from commonly executed lumbar punctures. However, some patients view lumbar puncture as a risky method and up to 40 percent of patients experience post-lumbar puncture headaches[3].

Jonathan McConathy, MD, PhD, and his colleagues believe technology like the Biograph mMR system (right) might contribute directly to drug development for neurodegenerative diseases.

Upfront Investment, Downstream Savings

All of the physicians acknowledged that even though the Biograph mMR system is FDA approved, combined PET-MR is not recognized as a single modality in most insurance plans, nor by Centers for Medicaid and Medicare. "PET faced a similar situation by itself," McConathy said. To illustrate this point, he explained that he keeps on hand an abstract published in the early 2000s. The paper discusses the merits of using combined PET and computed tomography (CT) scans – considered a new technology at the time. "I just substitute PET-MR (in the abstract) and the conversation is very similar," McConathy said. He added that the argument to use the Biograph mMR system will become "compelling" later on, as drug companies starting on dementia clinical trials strive to know as much as possible about a potential patient population before administering an interventional drug.

The field's understanding of AD and other forms of dementia has changed tremendously in the past few years, Benzinger explained. Now AD can be compared to a condition like heart disease, where cholesterol plaque might accumulate inside arteries long before a person suffers a stroke or heart attack. By the time a patient has amyloid deposits in the brain, the organ "has already started to dissolve," and the therapeutic agents currently being tested cannot reverse this damage, Benzinger said. The future of AD will be rooted in prevention, the physicians agreed. And the prevention will wholly depend on the imaging. ■

Kathleen Raven lives in New York City and specializes in medical reporting. Her science writing has been published in *Nature Medicine*, *Nature*, and *Scientific American*. She holds two volunteer positions within the U.S.-based National Association of Science Writers (NASW).

➔ www.siemens.com/mMR

1 http://www.medscape.com/viewarticle/769263_8
2 https://www.alz.org/alzheimers_disease_facts_and_figures.asp
3 http://www.ncbi.nlm.nih.gov/pubmed/24726041

A New Era in the Public Healthcare Sector

At the new Centro de Especialidades Médicas Ambulatorias (CEMA), the Argentine city of Mar del Plata is linking its outpatient facilities and medical centers together. One major partner in the model project is Siemens – in both the in vitro and in vivo areas.

Text: **Andreas Fink** Photos: **Javier Pierini**

Germán Giles, Healthcare Technology Director of the municipality of General Pueyrredón, Argentina (left); CEMA's modern organization is reflected in its modern design (opposite).

Beaches, fishing, and sweet pastries filled with dulce de leche have been the hallmarks of Mar del Plata in the past. But now, the city – located on the Atlantic coast, about 400 kilometers south of the Argentine megacity of Buenos Aires – has a new trademark: the Centro de Especialidades Médicas Ambulatorias (CEMA), which opened in November 2012, is a model project for the public healthcare sector in Argentina, a country of 40 million, and throughout the region. CEMA is an institution with a modern design and organization, equipped with high-performance, state-of-the-art medical technology. It is the new public healthcare center for the Municipality of General Pueyrredón, which encompasses the city of Mar del Plata and the surrounding area in a radius of more than 30 kilometers. It also marks a huge step forward in delivering healthcare to the uninsured. The location itself says it all: the new three-story building was constructed on open land near the soccer stadium, which was built for the 1978 World Cup. But what might seem like an outlying area of the city is the geographic center of the municipality, excellently accessible thanks to the two main *avenidas,* and not far from the main public hospital.

Upgrading Healthcare Centers

"The choice of location was a strategic decision," says Germán Giles, the Healthcare Technology Director of the municipality, which has been positioned between the two traditional levels of the Argentine public healthcare system. The system previously consisted of 33 healthcare centers scattered across the municipality, with some of them more than 30 kilometers away from the city center. There were also two hospitals: a general hospital and a mother and child center. "We were faced with the situation that our healthcare centers were very poorly equipped. That meant that many patients, even those suffering from less complex problems, went straight to the hospitals, which were unable to cope with the huge patient load. In light of our city's steady growth, we realized that we had ▸

"As politicians, we have a duty to ensure first-class healthcare, including for poorer segments of the population."

Gustavo Pulti, Mayor of Mar del Plata, Argentina

Mayor Gustavo Pulti (above); Dr. Alejandro Cristaldi, General Manager of the CEMA outpatient center in Mar del Plata, Argentina (right); Dr. Alejandro Ferro, the city Secretary of Health (far right).

to upgrade the healthcare centers to take some of the strain off the hospital facilities. But we also had to do it as efficiently and cost-consciously as possible."

In 2008, the idea of building an outpatient center serving a dual function was born. The new center would act first as a coordination unit and central lab for all healthcare centers, and second, it would to provide diagnostic and treatment options for patients who cannot receive adequate care at external facilities but do not need inpatient treatment.

CEMA as a Flagship

"The ground was broken on January 18, 2010, and by August 2013, CEMA had already helped more than 60,000 patients," says CEMA General Director Dr. Alejandro Cristaldi proudly. Cristaldi, a clinician born in Mar del Plata, is among those who wished to modernize the established healthcare system – with CEMA as a flagship, both medically and aesthetically.

The first floor of the building's façade is covered by perforated metal panels. As soon as they pass through the glass doors, patients and visitors reach the reception area, where employees record personal information and check referrals. This is an essential step, since CEMA only treats patients who have been referred there by one of the healthcare centers. Color-coded information signs throughout the 6,200-square-meter building point the way to the treatment departments. The lab area is coded orange, pediatrics is green, and dentistry takes place in treatment rooms painted a sunny yellow.

Glass, white pillars, and light-colored stone flooring create a friendly atmosphere that stands in stark contrast to the stuffy, poorly lit hospital corridors and foyers where patients used to

Investing in a Healthy City

The Centro de Especialidades Médicas Ambulatorias (CEMA) is the new hub of the public healthcare system in the Argentine city of Mar del Plata. Located in the geographic heart of the coastal city, it links together the 33 healthcare centers throughout the municipality and the two provincial public hospitals.

CEMA acts both as an outpatient facility and a diagnostic center. The facility treats patients – only by referral from healthcare centers – who need care beyond what the external facilities can offer, but do not need to be admitted to a hospital as inpatients. CEMA is also home to the central lab where samples from all outpatient facilities in the city are analyzed.

The center, which opened in November 2012 and occupies about 6,200 square meters, currently treats about 600 patients per day. Working at full capacity, it should be able to treat 1,500 people a day at no charge. About 38 percent of Mar del Plata's 636,000 inhabitants do not have health insurance, so they have to rely on the public healthcare system.

Building CEMA cost about US$ 11 million, which was divided between the Argentine Federal Government, the Province of Buenos Aires, and the Municipality of General Pueyrredón, which encompasses Mar del Plata and the surrounding area. Ongoing maintenance is financed by the municipality, which has instituted a new healthcare contribution paid by wealthier real estate owners.

spend hours waiting. "We're happy about the structural design of CEMA," Cristaldi says, "but I'm even prouder of the IT solutions. The center has been digital right from day one."

The Digital Shift

A new era is dawning in Argentina's public healthcare sector. Before CEMA began operating, all medical records in the entire municipality were taken down and filed on paper. "Our stated goal must be to fully digitize all the healthcare centers as well, in order to keep records on all our patients and accelerate our processes. We also hope to do without any printed requisitions and X-ray images in the future. That will substantially cut costs," Cristaldi explains.

Another step that should help boost efficiency in the future is digital recording of information on lab samples at the healthcare centers. Today, when a blood sample is taken at one of the centers, the patient's data still has to be recorded manually on paper. These documents then accompany the blood or urine specimen tubes, which travel by delivery vehicle to CEMA, where employees transfer the information and the tests that have been ordered into the digital laboratory information system (LIS). Once data entry is complete, the computer system generates an adhesive label with a barcode, which is then attached to the specimen tubes. From then on, the patient's record is digitized.

What follows after that is a trip to the heart of Mar del Plata's new healthcare network: the lab, which occupies 320 square meters. The lab began operating in late July 2012. "We ▶

CEMA is an example of successful healthcare consolidation, unifying the first and third level of public healthcare.

had 120 patients a day at the start," says technical director Giles. "Nowadays we examine samples from 300 patients a day, but we plan to grow much more." The system can be easily expanded with additional diagnostic machines to manage a higher throughput. CEMA is supposed to examine 1,500 samples per day, with about another 500 samples coming from the healthcare centers.

Efficient and Powerful

Siemens was awarded the contract for all of the lab equipment. The centerpiece is a laboratory automation system with a robotic arm that grasps the blood sample tubes and an optical lens that reads out the test requirements encoded in the bar code before the arm lifts the samples into one of the machines connected to the system. "The system is a huge help to us in managing the samples," Giles says. "It significantly reduces the amount of time spent on lab analysis," the CEMA technology head says.

"Thanks to the Siemens solution, we can perform many more different tests," says center director Cristaldi, adding, "and we can do it in much less time, too!" Cristaldi points out that where the former lab capacity was limited to 350 analyses per day, the Siemens system can now handle 800 samples per hour. Outstanding performance, speed, and ruggedness were also among the decisive factors in favor of installing further Siemens analysis equipment at the CEMA lab. The other equipment includes a hematology system, which CEMA says is the fastest in the whole city. "Siemens offered us technology with very high

A Model for the Future

Watch CEMA's experts explain how the center became a reference model for public health in Latin America.

To watch the video, scan the QR code using the reader app on your smartphone or enter the URL into your browser.

www.siemens.com/cema-argentina

The laboratory's centerpiece is an automation system, which reduces the time spent on lab analysis.

quality and performance at a very attractive price," Cristaldi says. Technology head Giles adds: "All of these units were launched on the market years ago and are known for their reliability."

Still, it is very important to the responsible parties at CEMA for there to be local technical support, with phone support where it is needed. "The fact that all of the equipment in the lab is from the same manufacturer is a big advantage," says Cristaldi, "since it means we always have the same dependable contact people." The commodity contract between CEMA and Siemens stipulates that the Siemens group of companies will handle the service, maintenance, and updating of the equipment. "That's extremely important to us, since technological change is extremely fast paced. Beyond that, here in relatively remote Argentina, there are traditionally issues with replacement parts getting held up in customs," Cristaldi says.

Alongside its lab equipment, CEMA also decided on medical imaging equipment from Siemens. The equipment includes a 16-slice computed tomography (CT) scanner plus post-processing workstation with special software for two-dimensional and three-dimensional visualization. "We chose this unit because it meets the requirements of our RFP better than all the others," says Giles. The CEMA tomograph needed to be fast, while also emitting as little radiation as possible. "In fact, the SOMATOM® Emotion has one of the lowest levels of radiation in the entire city. That's eminently important because it means we can also use it in pediatrics. The scanner completes a full thorax/abdomen imaging scan in just a few minutes. Besides that, this tomograph also has another important asset: the table is suitable for people who weigh as much as 200 kilograms. This feature has already been a big help to us several times."

The CEMA director says that there are two advantages in the fact that both the in vitro technology used in the lab and the center's in vivo technology, in the form of the CT scanner and connected workstation, are from Siemens: "First, all of the equipment is top-of-the-line technology, and second, the fact that Siemens technology is used in two areas results in ongoing, highly engaged communication with the company's representatives." Technology head Giles thinks that the combination of the in vitro and in vivo equipment is outstanding. He adds, "Receiving the first VersaCell® solution in the entire country as part of our laboratory automation was a big challenge for our employees. Our close cooperation with Siemens has allowed us to learn about many test options that weren't possible before, and the software for the tomograph workstation gives us analysis options we never had before." ▸

The CT scanner is a good example of the financing that the system made possible for CEMA, financing that is unusual for Argentina: construction of the building was financed by the Argentine Federal Government, the unit itself was purchased by the Government of the Province of Buenos Aires, and the costs of the workstation, service and maintenance, and operation are borne by the municipality.

Building and equipping CEMA cost the equivalent of US$ 11 million, and annual maintenance will cost about half that. To finance that amount, the Municipality of General Pueyrredón introduced an earmarked contribution for healthcare that is collected together with the fees for lighting and street cleaning. The amount of the contribution depends on the size of the property; 35 percent of the 350,000 homeowners in the area pay nothing, while 45 percent pay the equivalent of between one and five US-dollars monthly. Owners of larger houses have to pay around 12 US-dollars a month.

Increased Share of Budget

"In fact, there have been no protests against the charges," says Mayor Gustavo Pulti, pleased. This additional income has allowed him to increase the share of the municipal budget that goes toward healthcare expenditures from just one percent to eleven. "Argentina has a great tradition in public healthcare," Pulti says, referring to the 1940s and 1950s, when most of the public clinics still in operation today were built under the Juan Domingo Perón government. "But unfortunately, the present day is very dismal. As politicians, we have a duty to ensure first-class healthcare, including for poorer segments of the population. Here in Argentina, health is a basic right enshrined in the constitution."

About 39 percent of the 636,000 people living in the Municipality of General Pueyrredón do not have health insurance, so they have to rely on the free public healthcare system. The prospect of work in agriculture and in the major tourist destination, which draws three million people in the summer, have brought a steady

The multislice SOMATOM Emotion 16 CT reduces patient radiation exposure and saves time.

The Healthcare System in Argentina

From the Argentine viewpoint, health is a human right, and it is protected as such by the country's constitution. This means that the government has to provide free medical care to all patients, including foreign nationals. During the country's economic boom in the mid-20th century, this kind of general healthcare was still possible, albeit with the forms of treatment available at the time. But recurring economic crisis and sharp increases in the costs of both personnel and technology have severely curtailed the government-run options. Economically liberal governments pushed private healthcare in the last third of the 20th century. The social crisis that followed the Argentine government's 2001 bankruptcy, however, meant that the neglected public outpatient facilities and hospitals were faced with an increasing number of patients needing treatment.

Since then, the Argentine economy has seen strong growth, but 36 percent of the population still lacks health insurance, as the national statistics bureau, INDEC, reported in 2011. Fifty-seven percent of Argentinians receive services from one of the country's more than 300 *obras sociales*. These social organizations, financed through contributions from insured beneficiaries and their employers, are open primarily to workers (white or blue collar). About five percent are members of one of the more than 500 private insurance plans, and two percent receive government-sponsored care[1].

There are 18,000 healthcare facilities in Argentina. Half of them are private and half are public. Of the government-run institutions, 1,373 are hospitals that admit patients for inpatient treatment. Most of the public healthcare facilities are financed by the country's 24 provinces, and municipalities are also in charge of a number of hospitals and outpatient facilities[2].

CEMA's staff examines samples from 300 patients a day, but the numbers are intended to grow.

Distribution formulas vary by province. About 83 percent of funds in the public sector come from taxes, and the rest comes from the obras sociales. But most of these organizations have their patients treated at private hospitals; only a few of them maintain facilities of their own. Those who wish to take out private insurance can choose between a private health insurance plan and membership in a private hospital.

According to data supplied by the World Bank, Argentina – the government and private individuals – spent about 8.1 percent of GDP on healthcare in 2011[3]. Private studies put the figure even higher, some at nearly ten percent of GDP. These figures are about on par with what European countries spend. But when it comes to indicators such as child mortality, Argentina does worse than comparable countries with lower healthcare expenditures, such as Chile and Uruguay[4]. Most experts agree that the system's inefficiency is rooted in two factors: the complex tangle of responsibilities spread across the federal government, provinces, and municipalities, and a serious lack of transparency among the *obras sociales*, most of which are dependent on unions or provincial governments[5].

[1] Federico Tobar, Sofía Olaviaga, Romina Solano: Complejidad y fragmentación: las mayores enfermedades del sistema sanitario argentino. Centro de Implementación de Políticas Públicas para la Equidad y el Crecimiento CIPPEC, Buenos Aires 2012, S. 2 http://www.fmed.uba.ar/depto/saludpublica/108 DPP Salud, Complejidad y fragmentacion, Tobar, Olaviaga y Solano, 2012 [1].pdf, last consulted 10-24-2013

[2] Pan-American Health Organisation: Health in the Americas: Argentina. Retrieved on: http://www.paho.org/saludenlasamericas/index.php?id=18&option=com_content&Itemid=&lang=en, last consulted 10-24-2013

[3] http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS, last consulted 10-24-2013

[4] http://www.indexmundi.com/g/g.aspx?v=29&c=uy&l=es, last consulted 10-24-2013

[5] Federico Tobar, Sofía Olaviaga, Romina Solano: Complejidad y fragmentación: las mayores enfermedades del sistema sanitario argentino. Centro de Implementación de Políticas Públicas para la Equidad y el Crecimiento CIPPEC, Buenos Aires 2012, S. 2 http://www.fmed.uba.ar/depto/saludpublica/108 DPP Salud, Complejidad y fragmentacion, Tobar, Olaviaga y Solano, 2012 [1].pdf, last consulted 10-24-2013

flow of newcomers, including from the neighboring countries of Paraguay and Bolivia. But many of the new arrivals are penniless when they get there, and they have to deal with the harsh seaside climate and its abrupt temperature changes. "We can't leave these people defenseless," says Dr. Alejandro Ferro, the city's Secretary of Health, who practiced medicine in Canada for many years. From there, he brought many of the principles that are now being implemented at CEMA and the healthcare centers associated with it: top-of-the-line technology, cost consciousness, efficiency, and networking.

The good relationship between the city's leading officials and both the provincial and national goverments helped to ensure that, in an arrangement seldom seen before, three public financing bodies worked together to bring about the pioneering project. For those responsible in the city government and the CEMA management, there's no question about it: the new center and the modernized external facilities will bring significant gains not only in terms of treatment options, but also, and above all, in terms of prevention.

City officials Pulti and Ferro know that their healthcare system can serve as an example to many other municipalities – in Argentina, throughout the region, and even in other areas around the globe. "We would be happy to share our experiences", says Mayor Pulti. ■

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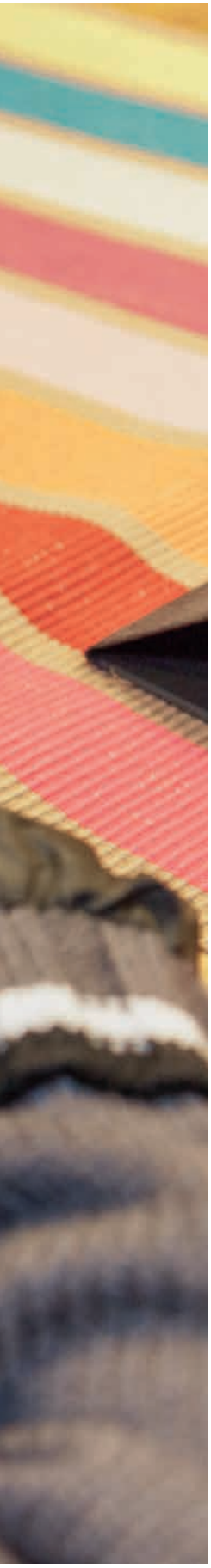
The outcomes achieved by the Siemens customers described herein were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption), there can be no guarantee that others will achieve the same results.



The risk of the disease's life-threatening long-term effects in diabetes patients can be minimized when they regularly determine their HbA1c levels.

24/7 Service for Young Diabetes Patients

In the Netherlands, pediatrician Henk-Jan Aanstoot has implemented an innovative concept for treating children and adolescents with diabetes. A 24/7 service, cutting-edge lab technology, and the Internet as a medical information channel are all part of the successful approach of the treatment center Diabeter.

Text: **Kerstin Schweighöfer** Photos: **Thomas Steuer**

The shock is written on Marianne Tijhuis' face. "What? 74 mmol/mol? That can't be!" she exclaims when she hears the test results. The graceful young woman glances at the play corner where her son Hugo is lying on his stomach and playing with a wooden train. "That isn't lower, that's much higher than last time!" Henk-Jan Aanstoot is used to this reaction. "Now, don't drive yourself crazy!" he says as he gently puts his arm around her shoulder. "We've just started treating him. It will go down again. We can do this!"

It – the HbA1c level – should be under 52 mmol/mol. HbA1c is an indicator of the blood glucose levels over the previous eight to 12 weeks, which is why it is also referred to as the long-term glucose control, says Aanstoot. Nine-year-old Hugo is one of the 1,000 children with diabetes who are being treated by Dr. Aanstoot and his team at Diabeter in Rotterdam, the Netherland's national center for diabetes in children and adolescents. The 57-year-old pediatrician specializes in diabetes mellitus, the chronic and as yet incurable metabolic disease, and his treatment method is unique. Diabeter's patients can be assured of receiving 100 percent attention, are intensively treated and cared for seven days a week, 24 hours a day – by four doctors, two psychologists, four dietitians, one social worker, and 13 nursing staff members.

This allows them to get their blood glucose level under control and ▶

Thanks to Diabeter's concept, children learn to interpret their blood sugar data themselves, saving them frequent hospital visits.

stabilize it better, faster, and more sustainably. They learn to live with the disease and can delay or even completely prevent the development of complications and long-term damage. "We concentrate fully on the disease. It's our strength; we don't do anything else," explains Aanstoot after he has spoken some more encouraging words to Hugo's mother and is heading toward his office. "When there are complications, parents can call us even in the middle of the night – and immediately have a doctor at the other end of the line!"

Focusing on Treating the Disease

Aanstoot used to work as a pediatrician in a hospital, where this kind of comprehensive and focused care was never possible. He had to deal with all kinds of diseases, rushed between asthma and leukemia patients and the occasional birth. This big, powerfully built man, who always has a friendly smile on his face, founded the treatment center in 2006 with his colleague, Dr. Henk Veeze. In addition to the one in Rotterdam, there are now also centers in Veldhoven and Deventer. "A fourth center is supposed to open this year in Amsterdam," states Aanstoot as he sits at his cluttered desk in front of a wall of pictures of himself with prominent scientists and politicians, such as former U.S. President Bill Clinton. Hearing the dedication and passion with which Anstoot talks about diabetes, it is obvious that diabetes research is his life and that the treatment of children with diabetes is his calling.

Diabetes mellitus has become an epidemic. It now accounts for 11.6 percent of all healthcare costs in the Western world.[1] "There are currently 300 million people with diabetes worldwide," says Aanstoot. "It has a lot to do with our lifestyle. We keep getting heavier and exercise less and less," he says while explaining the connection between the global obesity epidemic and diabetes. And the number of people with diabetes is growing. Drastically. By 2025, almost 552 million people could be affected by it.[1] The vast majority of diabetes patients have type 2 diabetes, says Aanstoot. The cells in their body develop a resistance to insulin, which means this hormone can no longer move glucose from the blood into the cells. Type 2 diabetes is not just genetic; it is favored by factors such as obesity and physical inactivity. The number of newly diagnosed patients increases 15 percent per year. The disease is also

referred to as adult-onset diabetes, because until recently it was primarily the 50+ generation who developed it. However, it is now not just people in their 40s, 30s, or even 20s who are developing type 2 diabetes; more and more children are developing it as well.

The number of patients with type 1 diabetes is also growing. With this autoimmune disease, the body's defense system attacks the insulin-producing cells in the pancreas, Aanstoot explains. "It's like a civil war; the soldiers are killing their own people," explains the doctor. Children have always developed type 1 diabetes, but they are now getting younger and younger. As Aanstoot states: "We treat babies with type 1 diabetes here!" The number of children under the age of five who have developed type 1 diabetes has doubled in the last five years and grows five percent every year. "It can't be genetic. Genes don't change that fast!" Diabeter builds awareness of the global epidemic of diabetes in a partnership with the International Diabetes Federation (IDF). Diabeter supports the IDF's Life for a Child program. With help from different groups and companies, including support from Siemens, they helped to establish dedicated pediatric diabetes clinics in Nepal both by direct support or with education projects.

Infant Patients

Aanstoot's patients are between zero and 25 years old, and almost all of them have type 1 diabetes. "When we started here in Rotterdam, we had 200 patients and estimated it would grow to 400 at the very most," he reflects. "In Rotterdam, Deventer, and Veldhoven we now have a total of 1,500 patients." It is not just because the number of children with diabetes is growing. More and more parents are hearing about Diabeter and prefer to have their children treated there than in a hospital. "We feel like we're in good hands here," says Marianne Tijhuis, who before heading home is savoring another cup of coffee in the cozy sitting area and watching her son play. Hugo, who was diagnosed with diabetes when he was 18 months old, began treatment at Diabeter just a few months ago. "I can already see that he feels much better, that he has become more stable."

Annemiek van Leeuwen, who has just come in and is standing at the counter with her husband and daughter, confirms that fast help ▸

E-health for Diabetes Patients

Diabeter uses software that has been developed especially for diabetes patients. It makes it possible to create a digital file to store not only information like age, weight, blood pressure, height, and HbA1c levels, but also all of the blood glucose measurements the patient performs – up to seven per day. To transfer the data, the patient simply connects the glucose sensor to a computer via the USB port. All of the measurements for that month are displayed automatically on the screen as colorful rectangles. Green is good, because then the (fasting) glucose level is hovering around 100 milligrams/deciliter (mg/dl). Blue is too low, and red is too high. Most parents and children quickly learn to interpret the measurements. The Diabeter staff can also view the file through the Internet. If a single reading is too high, there is no need for concern. However, if two consecutive readings are too high, the patient's parents will need to contact the treatment center, or the experts at Diabeter get in touch themselves because they've noticed the change when checking the file on the web. The same applies for readings that are too low.

If the graphic predominantly contains green rectangles, the file will simply need to be e-mailed to Diabeter once a month so it can be noted. If the patient's parents are unsure, they can request a response. If they have missed something, Diabeter will respond on its own.

In this way, diabetes care can be very comprehensive and focused without requiring the patients to travel to the treatment center. E-health allows patients to stay in close contact without a physical presence. One patient reports in regularly via Skype – the patient's father works for an oil company and the family lives in Qatar.

is often necessary, especially with diabetes. "The speed with which they respond here is amazing!" Her 11-year-old daughter, Isabelle, has had diabetes for the last two years and has an appointment today to measure her HbAc1 level. "The first year, she was treated in the local hospital, but then we heard about Rotterdam and wanted to come here." Van Leeuwen says there is no better place: "She doesn't get such comprehensive and focused care anywhere else."

Regular checks are a must for diabetes patients. An artificial pancreas, which would automatically solve all of the problems, is not yet available. Sensors have now been developed that continuously measure the blood glucose level, but there are no intelligent insulin pumps. Fluctuations have to be balanced out manually, with insulin injections. The care at Diabeter is so intensive that frequent hospital visits are not necessary. Thanks to e-health (see sidebar), 90 percent of the information exchange between doctor and patient happens via e-mail. In the early stages, when the children and parents are still unsure, they can schedule appointments or call the center. Once they become more familiar with the disease and the treatment, contact can then take place via the Internet. It is not just cost-effective, but also practical. "It's simply ideal," says Annemiek van Leeuwen, who lives near the town of Leiden, approximately 40 kilometers from the center of Rotterdam. "We only have to travel to Rotterdam every three months to determine her HbA1c level."

Discipline Pays Off

The appointment is like a moment of truth, like an exam, because this is when it becomes clear whether or not the patients have done their best to manage their diabetes in the last three months. The long-term blood glucose, the HbA1c level, shows how many hemoglobin molecules have glucose attached to them. In healthy people, the number is between 31 and 42 mmol/molpercent. In diabetes patients, it can increase to over 96 mmol/molpercent but should be kept below seven – otherwise the risk of long-term damage from diabetes (such as a stroke, heart attack, blindness, kidney failure, or the amputation of limbs) increases dramatically after around 15 years. And the risk of something like that actually happening does not increase linearly with each HbA1c percentage point, but rather exponentially, says Aanstoot. That explains why Marianne Tijhuis was so upset about Hugo's reading, which had climbed to over nine percent.

But as Aanstoot says: "We don't view this number as a threat, but as a challenge!" And his team deals with this challenge successfully. Thanks to Diabeter's comprehensive care approach, patients' HbAc1 levels decrease on average from 8.5 to 7.5 percent within a year. And as recent research has shown, the risk of complications decreases – significantly – with each lower percent point. "It's not exponential, but it's at least halved," states Aanstoot. "That is more than we thought."

The precise measurement of the HbA1c level is performed at Diabeter using DCA Vantage® analyzers. In just six minutes the machines analyze the blood and print out the test results, and the patients immediately know where they stand. "Perfect!" exclaims Aanstoot. Another big advantage is that the doctors just need one small drop of blood from the patient's fingertip for the HbA1c measurement – and children no longer have to go to the hospital to get their blood drawn from a vein. The Siemens devices are small, compact, and mobile and can be used everywhere, including general practitioners' offices. And since lab technicians are not required to analyze the blood, the results are available faster

Management Summary

Challenge:
More and more children and adolescents are developing diabetes. According to the WHO, it has become a global epidemic. Diabeter builds awareness of the global epidemic of diabetes; including a partnership with the International Diabetes Federation in the celebration of World Diabetes Day (14 November), and conducts surveillance of diabetes and its risk factors in children and adolescents.

Solution:
A very consistent lifestyle and medical care are needed to minimize the risk of life-threatening long-term effects. Regular determination of HbA1c levels using DCA Vantage analyzers plays an important role in this.

Result:
Thanks to its very comprehensive and focused care approach, the Diabeter treatment center is able to help protect children and adolescents from the long-term effects of chronic diabetes. Patient care is also more cost-effective than in a normal hospital, states Henk-Jan Aanstoot, the co-founder of Diabeter.

"It is not just practical; it is also cost-effective."

Dr. Henk-Jan Aanstoot, pediatrician, co-founder of Diabeter, Rotterdam, Netherlands

and are more cost effective than if they came from an external lab.

Cost Savings Thanks to Shorter Hospital Stays

The third and most significant cost-saving factor, besides e-health and the innovative diagnostic and lab technology, is the duration of hospital stays at Diabeter. "Hospitals are the most expensive hotels in the world," states Aanstoot.

"And that doesn't include the treatment costs, mind you!" Only three percent of all Diabeter patients per year have to be admitted to hospital due to complications. According to Aanstoot, for diabetes patients who are treated by a pediatrician in a hospital, the number is 20 to 50 percent – in other words almost ten times more. This is due to the comprehensive, focused care approach, which ensures that the situation does not escalate – if, for example, a child has diarrhea or a fever. Someone is available at Diabeter day and night.

In addition, once a child has been diagnosed with diabetes he or she normally has to be admitted to a hospital for a week for observation, and another week or even two once the child begins treatment with a sensor and insulin pump. However, at Diabeter, one of the 13 members of the nursing staff comes to the patient's house in the early stages of treatment. All in all, the medical care of a Diabeter patient costs the insurance companies only €3,000 a year – approximately €1,000 less than the conventional treatment by a general practitioner and a specialized hospital, estimates Aanstoot. The insurance companies have not given him any concrete numbers so far, "but they have already confirmed that our costs are lower," states the doctor proudly. ■

Kerstin Schweighöfer graduated from the Henri Nannen School of Journalism in Hamburg and has an M.A. in Roman Philology, Political Science and Art History from the Ludwig Maximilian University in Munich. She has been working as a freelance foreign correspondent in the Netherlands since 1990, and works predominantly for ARD radio stations, *Deutschlandfunk*, *Focus* news magazine and *Art* magazine.

→ www.siemens.com/diabetes

[1] www.idf.org
[2] WHO: http://www.who.int/mediacentre/factsheets/fs312/en/

The statements by Siemens' customers described herein are based on results that were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption) there can be no guarantee that other customers will achieve the same results.

Maximum Accuracy for the Smallest Cancer Patients

The University Hospital in Leipzig is one of the few medical centers in Germany to have a device that combines magnetic resonance imaging (MRI) and positron emission tomography (PET). The Biograph mMR system meets and even exceeds the center's already high expectations for use of equipment to help physicians in diagnosis and follow-up care of pediatric cancer patients.

Text: **Martina Lenzen-Schulte, MD**
Photos: **Christoph Busse**

The Pediatric Radiology and Nuclear Medicine departments at the Leipzig University Medical Center can be pleased to have achieved not one, but two superlatives. First, they are part of the first hospital worldwide whose combined MR and PET imaging has been certified and approved for regular use in patients. That means this diagnostic method can be used beyond the scope of studies, where a time-consuming process of approval by an ethics committee is needed. At the same time, the certification also marks a show of confidence for the Leipzig center: Wherever the radiologists or nuclear medicine specialists involved believe

hybrid imaging is necessary to investigate clinical questions, they can order the scan.

And that is not the only pioneering role in terms of simultaneous MR and PET imaging. The Leipzig doctors can also proudly say that their hospital is the birthplace of the world's first scientific publication that reports primarily on experiences with using the Biograph mMR system in pediatrics[1], and specifically pediatric oncology.

"The Biograph mMR is practically made for children," says Professor Franz Wolfgang Hirsch, MD, Head of the Pediatric Radiology Department, summarizing the system's many advantages by citing one common denominator involved in this kind of combination for his youthful patients. What he means by that, first, is the precision of the imaging process. "We have known for a long time that MRI shows us anatomical structures with excellent image quality. This form of imaging is unbeatable in terms of anatomical contrast, especially in dealing with soft tissue," Hirsch says. "But what we find especially impressive is that this is possible with a 3 Tesla unit on these small bodies, even without disruptive artifacts. That wasn't always possible with the larger diameter of an adult body," Hirsch says. To this positive point, he adds, "I'm pretty surprised by the excellent image quality."

Better Detection Sensitivity than Usual

Professor Henryk Barthel, MD, Assistant Medical Director at the Leipzig University Medical Center Nuclear Medicine Department, confirms his colleague's judgment with regard to measurement accuracy: "That's definitely also true of the PET component. We see that the detection sensitivity is higher than with conventional measurements. The system truly offers the best of both worlds." This directly affects the quality of diagnostic services, since quantitative registration of tracers is one measure of the metabolic activity of cells, including those in tumor tissue. "For example, we use a glucose analog that has been radioactively marked with fluorine-18, which gives us valuable information on metabolic rates in the cells," Barthel explains. "In my opinion it has been very clearly shown that this is also the most reliable criterion for responding to tumor therapy," he says. The importance of the new method quickly becomes apparent when one considers what quantification means: "That means we can also quantify the response to the treatment."

The value that the true combination of PET and MRI in Biograph mMR adds has even more facets than that. "In pediatric oncology in particular, we are faced with more than just the task of using imaging to support diagnosis. We also play a major role in providing follow-up care for these patients, for example, those with common pediatric forms of cancer, such as lymphoma – cancer of the lymph nodes – or various types of blood cancer, like leukemia," the Leipzig-based radiologist explains, citing further challenges in his discipline.

"So in a patient with lymphoma, if we need whole-body staging, we can now use the Biograph mMR system to achieve it, to a level of accuracy we have never known before, with low radiation exposure," Hirsch points out. "Even more than for initial classification of the tumor, this plays a major role in the further course of treatment. A malignant lymph node tumor shrinks during treatment, but some residual tissue or stroma remains," Hirsch explains.

Great Strides in the Quality of Follow-up Care

Especially in the case of follow-up, hybrid MR and PET can provide valuable information: "In evaluating the tumor residue, the MRI alone left us in some cases with a number of unanswered questions. Merely based on the anatomy of the structures, it is not possible to say with certainty how biologically active the remaining tissue still is," Hirsch says, touching a nerve in pointing to previous deficiencies. Now, simultaneous functional evaluation by means of PET can supply exactly that information. And that, Barthel concludes, "is a truly great stride in the quality of follow-up care." ▶

Professor Franz Wolfgang Hirsch, MD

He studied medicine at the University of Halle and went on to work at locations including the University Medical Center in Halle and Royal Marsden Hospital in London. In 2002, he was appointed Professor of Pediatric Radiology at the University of Leipzig, where he heads the pediatric radiology unit within the Department of Imaging and Radiation Medicine. Hirsch chaired the Deutsche Röntgengesellschaft's (German Radiology Society, DRG) pediatric radiology task force and served as a member of the board of the Gesellschaft für Pädiatrische Radiologie (Pediatric Radiology Society). He is a member of the Board of Directors for the DRG's Academy for Continuing and Professional Radiology Education. His main scientific interest is the use of simultaneous MR and PET in pediatric diagnostics and fetal MRI.

Professor Henryk Barthel, MD

He studied medicine at the universities of Greifswald and Leipzig from 1988 to 1994. After stints practicing medicine and as a researcher in Heidelberg, Leipzig, and London, he has been an Assistant Medical Director at the Department of Nuclear Medicine, headed by Professor Osama Sabri, MD, at the University Medical Center in Leipzig since 2003. His duties in this position encompass neuro PET and simultaneous PET/MR imaging. His scientific work focuses particularly on PET and simultaneous PET/MR imaging in dementia and stroke and to visualize stem cells. He is a member of the neuronuclear medicine task force of the Deutsche Gesellschaft für Nuklearmedizin (German Nuclear Medicine Society) and Vice President Elect of the Brain Imaging Council of the U.S.-based Society of Nuclear Medicine and Molecular Imaging.

The Pediatric Radiology and Nuclear Medicine department at the Leipzig University Medical Center is one of the few locations in Germany to own an MR-PET.

This has tangible clinical consequences, as Barthel adds: "We deliberately analyzed once what kind of tumor classification emerges if we use one of the two methods – PET or MRI – alone, and what the outcome is when we combine the information." There are differences, as one might already suspect based on other studies. For example, when used alone, MRI can result in a false positive that makes the remnants of a tumor seem more dangerous than they actually are. "But we nuclear medicine specialists can then see via PET that the tumor is no longer vital. That means it definitely responded well to treatment, and we can confirm that the cancer is in full remission," Barthel says.

This spares the patient further or more aggressive rounds of treatment. And that is the goal in pediatric oncology. Hirsch points out one thing: "We can now achieve success rates of 95 percent in terms of lymphomas such as Hodgkin's disease; there's hardly any room for improvement. Our focus now is on reducing the side effects associated with treatment and preventing possible long-term harm due to factors such as unnecessary chemotherapy."

Physicians treating these forms of cancer in children are now moving forward cautiously, with one motto: "As little as possible, as much as necessary." With that in mind, Hirsch says, "The new options in hybrid imaging are an invaluable help with regard to this method of titration, providing just the right amount of treatment and no more than that." Hirsch assumes that in the long run, this will result in new standards in follow-up care: "I think that in the future, this kind of monitoring of the course of the disease should replace the X-ray scans that are still required in study protocols today."

Barthel points out that there could also be economic advantages associated with this: "Advanced cancer treatment is extremely costly. If simultaneous MR and PET examinations show that the patient will not respond to a treatment, the patient does not have to undergo a useless treatment that would only be a strain on him or her, and the plan can shift to a different treatment instead."

Guidance for Biopsies

Simultaneous MR and PET imaging offers advantages in guiding biopsies as well: "Especially when it is necessary to take a tissue sample to confirm a brain tumor diagnosis, the exact location of the sample isn't arbitrary. In a procedure as invasive as a biopsy, the person who inserts the needle needs a reliable guide," Barthel explains. Hirsch uses an example to illustrate the advantages of this method: "In one case, we wanted to use a biopsy to clarify how aggressive an astrocytoma – a certain kind of brain tumor – was. The simultaneous acquisition of the MR and PET data showed that, unlike most cases, the simple access route via the base of the skull would not have been the best one, since the tumor's main metabolic activity was located elsewhere. If we hadn't had this information, we would have performed the biopsy on that tumor in the wrong place, misjudging the tumor."

In cases like these, there is a risk that a grade III astrocytoma might be biopsied at a site that leads to its being diagnosed as a less-aggressive grade I tumor, with the patient then receiving less than adequate treatment. "Of course, that's just one example. But it does illustrate the potential that more accurate guidance of a biopsy can offer," Barthel points out.

Minimizing Adverse Effects of Scanning

Another argument in terms of the strain on young patients is that the patient needs only one scan, not multiple scans. "This means not only that the child and parents only have to come to the hospital for one scan," Hirsch explains, "but also that we only have to anesthetize those patients who need it for the examination once."

This is due to the fact that the accuracy of imaging depends on various factors, including on how well it can be correlated with breathing movements. "To do this, the device uses a breathing sensor attached to a belt to trigger the image to start at the end of inhalation," Barthel says. "But not all children can breathe as calmly as necessary to achieve the most accurate measurement possible, and that means anesthesia is necessary," he adds.

Estimated scanning time is about one and a half hours, but due to the high quality of the images, the time needed is now much shorter: "We can manage with 40 to 50 minutes per exam. The unexpectedly good quality of the images makes that possible for us. We don't use this to depict the anatomy perfectly," Hirsch says, explaining the strategy, "but instead, we translate it into time gained in order to minimize the strain on the children wherever possible."

As Barthel explains, there are currently seven scientific partners in Leipzig involved in research using the Biograph mMR. The spokesman for this consortium is the Director and Chairman of the Leipzig University Medical Center Nuclear Medicine Department, Professor Osama Sabri, MD. Along with Pediatric Radiology and Nuclear Medicine, participants include the Neuroradiology and Radiology departments, the Herzzentrum Leipzig (Leipzig Cardiac Center), the Max Planck Institute for Human Cognitive and Brain Sciences, and the Fraunhofer Institute for Cell Therapy and Immunology. ■

Martina Lenzen-Schulte, MD, is a physician, medical journalist, and author of nonfiction books. She works as an editor for Medscape Germany.

Challenge: Pediatric Cancer

- Biograph mMR, which is based on a 3 Tesla MRI system, is ideal for use with children in terms of image quality.
- Biograph mMR represents an excellent device for pediatric oncology that combines all of the requirements for morphological resolution and detection of metabolic activity with minimal radiation exposure.
- The question of whether a patient will respond to a treatment can be answered reliably, and better than with single modalities, for pediatric tumors. The Leipzig studies recommend that the Biograph mMR system be integrated into follow-up care protocols. The risk of excessive or insufficient treatment is reduced.
- The extremely important step of localizing elevated metabolic activity at the tumor site is crucial in achieving the correct biopsy, and hybrid imaging delivers great success in this process. The biopsy, in turn, is the basis for assessing how aggressive the tumor is and what the correct treatment is.
- Since the scan takes place only once, children do not need to undergo anesthesia repeatedly. The workflow is simplified as parents and children only have to go to the hospital for a single exam. At 40 to 50 minutes, the scanning time is significantly lower than previously assumed.

→ www.siemens.com/mMR

[1] Hirsch FW, et al.: PET/MR in children. Initial clinical experience in paediatric oncology using an integrated PET/MR scanner. Paediatric Radiology 2013;43(7):860-875. http://dx.doi.org/10.1007/s00247-012-2570-4

Xianfeng in the Hubei province is not easy to reach. After a two-and-a-half-hour flight from Shanghai to Enshi, we spend another two hours driving southwest through rolling hills covered with the lush vegetation of humid climates. Granted, a highway is under construction, but for now the only alternative to this bumpy gravel road is to take the train.

With a population of 360,000, Xianfeng is a small town by local standards, and, as our hosts remark with pride, it sits in an area almost entirely covered by forests: it is the green lung of central China – or, in the colorful words of Dr. Wu Bi Sheng, Vice President of Xianfeng hospital, it is a "natural oxygen bar."

Founded in 1950, Xianfeng hospital's newly built U-shaped complex with two high-rises sits on top of a hill overlooking the town. By Chinese standards it is not a large hospital: its staff of almost 500 tends to about as many beds. There are 139 doctors, according to Dr. Wu, and 245 nurses and healthcare professionals.

The Doctors

Dr. Wu is a wiry man, and you wouldn't call him tall. He has the quiet demeanor of a man who has weathered many storms in his life. His hands are in perpetual motion. Dr. Wu is originally from Xianfeng, and after a stint in a neighboring province he came back to his hometown to work.

Dr. Yang Wan Fa, a man of jovial appearance, is the radiologist on duty on the day of our visit. He is from Xianfeng as well and was attracted to the nobler side of medicine from an early age. Growing up in the countryside, he had to work harder than average to succeed but managed to graduate in 1984. At the time, in China people were assigned where they were needed. Although Dr. Yang initially wanted to work in the city, now he is happy to have been working for Xianfeng Hospital for almost 30 years.

The Patients

We met a woman whose 72-year-old mother is suffering from pancreatitis. Her exams and therapies were billed at approximately RMB 50,000 (approxi-

Modern Healthcare For All

The rampant economic growth and the shiny skyscrapers of China's coastal cities are a distant reality for the people in the rural parts of this vast country, and the challenges of providing healthcare to them are of a singular scale. *Medical Solutions* visited a county-level hospital in the central Chinese province of Hubei.

Text: **Michele Travierso** Photos: **Tang Ting Ting**

Challenges and Hope

As China experiences the effects of the healthcare reforms of 2009 and the policies outlined by the 12th five-year plan (2011 to 2015), the challenges the government faces are unprecedented. The divide between urban and rural is growing wider and there are demographic and developmental issues at play that could disrupt the growth of the past decades. But there is cause for hope as well, as investments in infrastructure and more widespread insurance coverage have ripple effects across the country.

mately US$ 8,000). She said 80 percent of that amount was covered by her health insurance, which still left her a bill of circa 8,000 RMB to pay. Despite the relief provided by her plan, that is still a significant sum. Many of this woman's fellow patients – some coming from as far as 100 kilometers away – are of modest means and spend their lives tending fields surrounding the town. They have little exchange with other residents of this huge nation, let alone with foreigners.

The Challenges

Dr. Wu explains one of the many hurdles rural hospitals face: they have a hard time attracting and retaining medical talent. "Most young professionals would prefer working at city-level and not county-level hospitals, where they would have a higher salary, better training, advanced machines, and a more promising career ahead of them," he explains. And looking around, many of the doctors are indeed middle-aged. On the other hand, adds Dr. Wu, doctors in smaller hospitals get to see a larger variety of cases than they would in a city-level hospital, with more rigid hierarchies and politics.

But how does the Xianfeng experience relate to China at large? Industry experts recognize the genuine efforts of the central authorities, but the challenges are of a scale rarely encountered elsewhere: imagine ▸

With 360,000 people living in Xianfeng, the rather small Chinese city is facing numerous challenges in healthcare. Its local hospital has found ways to resolve them.

Healthcare in Rural China: A Shortage of Funds and Talent[1]

The guidelines of the 12th five-year plan make a strong case for the county-level hospitals to become the backbone of China's national healthcare system. Officials aim for 90 percent of conditions, both common and serious, to be treated locally. This should reduce the pressure on major city and university hospitals, which, on top of providing for the surrounding population, have to tend to rural residents in search of better doctors and newer medical equipment.

The main hurdle to the realization of this vision is an economic one: hospitals across the country are starved of funds, and smaller ones even more so. The recent reform didn't address a system of incentives that sees doctors remunerated on the basis of the amount of people they see and, at the same time, makes examinations and drug sales the main source of income for hospitals. Compounding the problem, there are caps on the amount of money they can reclaim from government-run health insurance funds, discouraging hospitals to take in gravely ill patients.

There's a shortage of talent as well. Because of the different working conditions in cities and rural areas, young doctors don't want to work in the countryside, where they see their career options and earning potential curtailed. To address this, the government recently called for more than 150,000 new primary care physicians to join the medical ranks by 2015.

As the trite Chinese saying goes, where there are challenges, opportunities abound: a more relaxed investment landscape makes it more attractive for foreign healthcare companies to tap the need of an increasingly wealthier population. There's also a growing demand for well-engineered medical equipment that helps cash and talent strapped rural hospitals keep their rising costs under control as well as increase the quality and speed of their services. It's a challenge worthy of the best minds in the field.

[1] World Health Organization, http://bit.ly/1orr5vk (last accessed on 14/11/07)

providing services for a population the size of the United States, with a relatively high standard of living, only marginally lower than in Europe, for example, living in the developed coastal areas. On top of this, the state has to provide basic healthcare for another billion people of much lower income. It is hard to come up with a sensible national healthcare plan that accommodates the needs, and works within the contraints, of two very different sets of people.

The Numbers

China has made undeniable progress from the era of the "barefoot doctors" of the late 1960s, according to a McKinsey report on the state of Chinese healthcare. Life expectancy has risen fast in the past 30 years. It now ranks 49th, with an average lifespan of 76, on par with Poland, Argentina, and Turkey. For comparison, the United States ranks in the mid-thirties, at 79 years, but China still does better than countries like Mexico (75) or Brazil, and Russia (69).

These great strides however should not make us forget the main challenges. Despite swift reforms aimed at improving the share of the private sector, the government still provides most of the healthcare services: at the time of the 2009 reforms, only 12 percent of beds were tended by the private sector. Other numbers give an idea of the amount of progress achieved in the span of a few but momentous years: from 2006 to 2011 the total healthcare expenditure more than doubled, increasing from US$156 to 357 billion, almost 5 percent of GDP. It is now projected to hit the 7 percent mark by 2020, according to a McKinsey report. Coincidentally, the number of people with at least some form of medical insurance increased from less than half the population to almost 95 percent. In rural areas, the out-of-pocket rate is still 50 percent.

The Reform

In 2009, the government announced the blueprints for a major healthcare reform that came into effect with the 12th five-year plan (2011 to 2015). According to the guidelines, the large majority of conditions should be treated at county-level hospitals. Also, poorer patients with severe conditions should be reimbursed of at least 90 percent of their medical costs under the New Rural Cooperative program, the insurance system designed to cover rural citizens. Under the plan, the vast majority of Chinese should experience more affordable cures closer to their homes. Hence the emphasis on and support of hospitals like Xianfeng, which are fighting the battle to provide both essential and more advanced services to the local population at a reasonable cost.

There are limits to the reform that have not been addressed by the authorities though. The main con- ▶

Times of Change for China's County-Level Hospitals

In this film, Dr. Wu explains how Xianfeng County People's Hospital managed to become a leading institution among county-level general hospitals in its area.

To watch the video, scan the QR code using the reader app on your smartphone or enter the URL into your browser.

www.siemens.com/healthcare-in-rural-china

straint that doctors of Xianfeng hospital face, just like their colleagues across China, is an economical one. The reform cuts at the hospital's main source of funding without providing real alternatives. Additionally, costs are rising across the country, just as people's expectations of what constitutes a dignified healthcare experience. How to match these factors in the most efficient way is what keeps health professionals awake at night. Dr. Wu is no exception. "We are currently confronting the contradiction between people's increasing health demands and the development of medical science itself," he says. He makes the example of a hypothetical rural patient diagnosed with a grave disease – a cancer, say – whose odds of survival depend not only on the course of the illness but also on the size of his or her pocket: "The early diagnostics and effective treatments he or she might need most is what we currently cannot afford."

Doctors in China are paid by the number of patients they see, so they need reliable equipment like their CT scanner, purchased in 2002. The SOMATOM Esprit provided a great service over the years, and had an excellent uptime record. In Xianfeng it supports around 80 patient examinations per day. Having this equipment available in rural areas like the province of Hubei has a huge impact on access to this kind of healthcare. Otherwise they would have to visit overcrowded hospitals in bigger cities far away and spend more money on travel, which not everyone can afford. But working with more modern equipment would help doctors as well as patients, who would not have to wait so long. That's why the hospital is on the lookout for a new, faster CT scanner.

The Push for Equality

China is currently laboring to avoid the infamous "middle income trap" – that developmental situation in which a country loses its low-cost manufacturing competitiveness before becoming a consumer economy. On top of this, a demographic issue is arising: a rapidly aging population, coming to terms with the consequences of the single-child policy, and a general population that has increased its consumption of red meat and sugar only in the last few years. The average Chinese person of working age supports two parents and four grandparents. When it comes to the decisions facing China, few countries have been dealt such a difficult hand.

Dr. Wu Bi Sheng, Vice President of Xianfeng hospital, Hubei province, China

At the end of our visit in Xianfeng, dense as it was with facts about an issue affecting millions of people, I get a minute alone with Dr. Wu. I ask him what he would wish for if he had a magic wand. Quietly, with a warm smile, he says: "I wish I had a button that I could press to make the pain of patients go away." ■

Michele Travierso is a writer based in Shanghai. He covers science, technology, and aerospace for a variety of titles, including *The Economist, The New York Times, Wired,* and *Time*.

Accurately and Selectively Targeting the Tumor

Dr. Michael J. Wallace is considered to be an innovative interventional radiologist. He uses the latest imaging techniques such as the advanced cone beam computed tomography in minimally invasive transarterial chemoembolization (TACE) procedures, and believes it positively impacts the survival rate of some types of liver cancer patients at the University of Texas MD Anderson Cancer Center.

Text: **Jürgen Schönstein** Photos: **Thomas Steuer**

Procedures such as TACE require experience to gain a certain level of competence and expertise – and lead aprons to protect those experts from radiation.

Dr. Wallace, you are one of the leading interventional radiologists in the world. What exactly is "interventional" about your work?

Dr. Wallace: Interventional oncologists and interventional radiologists use modern imaging techniques such as fluoroscopy, angiography, C-arm cone-beam computed tomography (CT), CT scans, magnetic resonance imaging or ultrasound to guide an invasive procedure. This imaging is used to treat tumors directly or to sample tumor tissue that can then be characterized. Also, part of the scope of practice of the interventional radiologist is the broad array of palliative treatments for patients suffering from complications of cancer or its therapy, by trying to alleviate pain, manage infection, improve nutrition, or stop bleeding.

Where do you see the advantages of interventional radiology here?

Dr. Wallace: It depends. If you talk about conventional cancer therapy, most cancer therapies take a big, broad, "elephant gun" approach. But as we evolve, medical knowledge is getting to the point where we can be smarter about these therapies. They are specifically targeted to the tumor, and as we move forward, their targets are tumors with known genetic abnormalities. I think in the next five to 10 years, we are going to see a smarter and more individualized approach to general cancer treatment become part of the routine practice.

You deliberately talk about "treating," not "healing"?

Dr. Wallace: Take the example of liver cancer. Often, patients with liver cancer are also suffering from an underlying liver disease. In other words, they are battling two different kinds of diseases. The oncologic therapies that we offer do not really address the underlying liver disease. The issue for these patients is tumor control.

What is the purpose of interventional radiology? That it targets the tumor, but not the blood stream or healthy tissue and therefore not the entire body?

Dr. Wallace: Correct! We use regional or local therapies. Even when the tumor has metastasized, we can still take care of a range of metastases, as long as they are limited in number and distribution – these are areas we can impact.

Which realistic goal can be achieved in this way?

Dr. Wallace: There are definitely things we can do to prolong survival. While we may not be able to cure a patient, we can effectively lengthen their survival, and hopefully still maintain their quality of life in the process.

Are you saying that cancer could become more like a chronic disease that does not go away, but can be managed?

Dr. Wallace: That is exactly what we are trying to do. But we have to be realistic and define what "chronic" means here – it may not necessarily be a period of 20 years, because maybe we can increase survival by two years. Obviously, we would like to cure cancer, but until that is possible, it would be nice to maintain control.

What are the survival rates?

Dr. Wallace: There are so many different forms and stages of cancer, and they all have their own survival rates. If we look at liver cancer as an example, it depends on how aggressive the tumor(s) is/are, what stage they are at and when we find them. The survival rate can be 18 months to two years, and up to three or four years when we treat them with the transarterial chemoembolization (TACE) procedure. For small tumors that are limited in number, other local therapies like percutaneous ablation can be used with curative intent. TACE is typically used when local ablation is not feasible. While TACE has been around for decades, the recent improvements in intra-procedural imaging afforded by C-arm cone-beam CT has given us the necessary anatomic information to be more targeted and therefore more aggressive with treating these liver cancers. With TACE, small particles that are loaded with chemotherapeutic agents are injected so precisely into the artery feeding the tumor that they restrict the blood supply while cytotoxically targeting the tumor. Of course, the best therapy would be liver transplantation or resection, where the tumors are surgically removed. But not all patients are ideal candidates for this, and we can then offer them the next-best options.

Do your patients generally respond better and feel better with interventional radiology than they would with standard chemotherapy?

Dr. Wallace: One of the benefits of using minimally invasive image guided local or regional therapies delivered by an interventional radiologist is that you don't get the same side effects as you would with systemic chemotherapy in which the entire body is exposed to the drug. When treating some metastatic tumors to the liver however, it does not replace systemic chemotherapy: With metastases, we know that it is not enough to treat just one or two specific regions of the body, because this does not take care of unseen metastases that haven't shown themselves.

Can patients also manage with lower chemo doses thanks to the TACE method?

Dr. Wallace: Typically, we can give a higher concentration of the chemotherapeutic drugs or other transarterial regimens, because with modern imaging they are selectively administered to the region of interest through the blood stream. And because it is bound to a particle and lodges into the vessels of the tumor – the drug does not leach into the entire blood system to the same degree as if you simply administered the drug alone – the side effects are not typically seen in the whole body. The effects are mainly within the liver, and that is better tolerated.

Are the therapeutic agents in TACE the same as in systemic chemotherapy?

Dr. Wallace: The drugs used for TACE depend on the type of malignancy being treated. On occasion, drugs that have stopped being effective when given systemically through the vein might still be effective if given directly in the artery leading to the tumor.

Management Summary

Challenge:
Liver tumors are considered to be extremely dangerous, with a very poor long-term prognosis for patients.

Solution:
By precisely guiding the catheter using *syngo* DynaCT, liver tumors can be treated accurately and safely with transarterial chemoembolization (TACE).

Result:
Wallace was able to show that treating tumors with this technology (*syngo*® DynaCT) can contribute to the improvement of the survival of his patients on average by approximately 10 months or more depending on the extent and characteristics of the tumor.

How frequently do your patients have to come in for treatment?

Dr. Wallace: Usually we will do a session, let them convalesce and then repeat the CT scan after a month. We usually repeat that about once a month until we get to the point where we say we are finished or where we believe that further improvement is no longer possible. That usually ranges from one to three sessions, and each session takes about two to three hours, depending on the number and the size of the tumors and the complexity of the vascular system supplying these tumors. Our goal is to get as close to each tumor as possible.

What progress has been made in the field of interventional oncology in the last 10 years?

Dr. Wallace: A tremendous amount has happened in the field of interventional radiology over the last one to two decades for cancer therapies. The term interventional radiologist is often used interchangeably with interventional oncologist as their scope of work in some centers has focused to a greater degree on cancer. Percutaneous ablation therapy is one example of a significant step forward for image-guided therapies. First came radio-frequency ablation and subsequently cryoablation technologies and now we have devices that use microwave technology and non-thermal technologies. The tumors are killed using these technologies by directly inserting probe-based devices into the desired target. We have devices that cause a heating effect, we have devices that cause a freezing effect, and we now have a device that creates an electrical current that damages the cell membrane. Each type of therapy has advantages and limitations and we must apply the best therapy for the particular patient. A lot has happened in the past decade for percutaneous intervention, which has really advanced our ability to take care of small volumes, small lesions, small numbers, reasonably effectively. Using these ablative technologies we can treat the liver, kidneys, lungs, and even bone. With bones it is more often used for pain palliation rather than tumor control. But that is one area we definitely impact. With regard to the angiography advances, of which TACE is part, I think that the biggest advantage has been in the imaging that is available to us while we are doing a vascular procedure. Digital subtraction angiography (DSA) was the basic two-dimensional imaging used to guide TACE procedures and other vascular procedures. The imaging information was limited to seeing the vascular anatomy and tumors that tend to have increased or normal vascular density. In 2005, C-arm cone-beam CT was introduced clinically and has dramatically improved the imaging information during TACE and other similar procedures. C-arm cone-beam CT allows the same angiography unit that produces DSA imaging to now acquire a "CT-like" image and so we can better define the target lesions within the liver and the arteries supplying them. This allows us to be more selective to the tumor, thus delivering a higher dose of the drug to the tumor and reducing the amount of collateral damage to the surrounding healthy liver tissue. It is believed that this more selective and aggressive approach improves the efficacy and safety of this complex therapy. ▸

Outside view of the world-renowned University of Texas MD Anderson Cancer Center in Houston, Texas.

The Experience of Over 10,000 Procedures

For Dr. Michael J. Wallace, 47, his work as the Section Chair ad interim of Interventional Radiology at The University of Texas MD Anderson Cancer Center in Houston is more than just a job. Not simply because he is a respected interventional radiologist specializing in liver cancer treatment at a world-renowned cancer center and has published more than a hundred articles in peer-reviewed journals. Nor is it because the task he has set himself is constantly growing: Liver cancer is one of the most deadly forms of cancer. If left untreated, it can often lead to death in just a few months, and its frequency has almost quadrupled in Europe, for example, since the late 1970s.

This job is, as he says, extremely special to him because his father, Dr. Sidney Wallace, Professor Emeritus at The University of Texas MD Anderson Cancer Center, was one of the founders of interventional radiology and built the program at MD Anderson Cancer Center in Houston from 1966 to the mid-1990s. Dr. Sidney Wallace died of cancer in May 2013 at the age of 84. "It is therefore not just a special place, but also a special 'specialty' for me," explains Wallace, who, according to his own estimates, has already performed over 10,000 of these procedures in his career.

One of the main components of his research focuses on the technological improvement of the equipment that he uses as an interventional radiologist; Wallace therefore works very closely with manufacturers such as Siemens. A significant contribution of such collaboration was the early adoption of C-arm cone-beam 3D imaging in the angiography suite to improve selective targeting of tumors in the liver. Wallace was able to show that treating tumors with this technology (*syngo*® DynaCT) can contribute to the improvement of the survival of his patients on average by approximately 10 months or more, depending on the extent and characteristics of the tumor.

Which innovation do you wish for the most?

Dr. Wallace: Now that the imaging is so good, our other tools, our catheters for example, need to get more nimble. It used to be that we could not get closer to the tumor because we couldn't easily match the blood vessel to the target tumor due to an abundance of overlapping vessels. Now, we need smaller and more responsive microcatheters to get as close to the tumor as possible. These tiny microcatheters are about one millimeter in diameter and are directed by maneuvering a shaped guidewire through the catheter into the desired vessel. We need improvements in the size and flexibility of the catheters in order to access the smaller and more tortuous targeted vessels that are visible with today's imaging technology.

And what is the best possible outcome that a patient could expect?

Dr. Wallace: The first thing I say when I talk with patients is: my goal is not to set them back. I have to balance the risk of an intervention and the likelihood of success, whatever that is meant to be: tumor ablation, stopping the bleeding or what have you – there is always a balance between risk and benefit.

What is your biggest personal success story?

Dr. Wallace: There are plenty. I had one liver patient who was not considered a candidate for a transplant, because of the size and the numbers of his tumors. After we treated him, some of the tumors shrunk to an acceptable size and some went away completely, and he subsequently received a liver transplant, which is the best possible situation for long-term survival. So he went from potentially having maybe less than three years of survival to his best option, and that means longer-term survival. The five-year survival rate for liver transplants is around 60 to 70 percent. That is a big deal. That is a survival success. But I can tell you another story: I had a very close colleague and teacher of mine who had very advanced-stage cancer with

3D angiographic imaging supports more targeted liver cancer treatment.

a tumor invading the portal vein. And even though we knew that long-term survival was not feasible, we pushed on for a rather aggressive therapy. We performed TACE and focused attention to the portal vein tumor thrombus in addition to the large left lobe liver lesion. The effects of the treatment to the tumor thrombus allowed a surgeon to resect and thrombectomize the tumor in the portal vein. My colleague ultimately lived two years from the time of TACE, whereas these types of patients usually only live around 12 months or less.

Is interventional radiology available for most cancer patients?

Dr. Wallace: Many small hospitals may not necessarily have the depth of experience in their physician group to provide it, but there are many moderate to large hospitals across the country that provide really good cancer care.

What role does the duration of the interventional procedure play?

Dr. Wallace: As interventional radiologists, we want to work efficiently, and we don't want to prolong the procedure because there are always risks. Catheters in blood vessels can lead to thromboses – you want to work continuously, without having to wait. When cone-beam imaging was first introduced, it took five or six minutes to set up, and another 11 minutes to acquire and reconstruct the 3D images. That was 16 to 17 minutes of "dead" time when nothing happened. Now the reconstruction times are less than 30 seconds, so it has really substantially improved.

Where do you see other areas of improvement?

Dr. Wallace: Integration of imaging and guidance information is a necessary improvement that is being worked on. For example, leveraging all the important imaging that is done either before or during an intervention and overlapping the current instrument position and treatment step would maximize real-time decision making potential and thus help make our job easier. Some of this technology may allow for projecting the target vessels or tumor over a live fluoroscopic image and some may allow for optimizing the treatment approach. Right now, I do this in my head, based on my experience. If this processing of imaging information were automated, it would allow more doctors to work more effectively instead of having to spend years becoming really experienced in the art. The goal of this technology is to bring everybody up to using it effectively and to get value out of it. ■

Jürgen Schönstein, who has a graduate degree in Geography (Diplom-Geograph), has been a journalist since 1985. He has worked for *DIE WELT*, Springer Foreign News Service (New York Correspondent) and *FOCUS* (U.S. Correspondent from 2001 to 2010), to name just a few. He has been the editor-in-chief of the German science portal ScienceBlogs.de since the beginning of 2011 and teaches academic writing at the Massachusetts Institute of Technology. He is also a freelance writer for the German edition of *WIRED* and lives in Cambridge, Massachusetts.

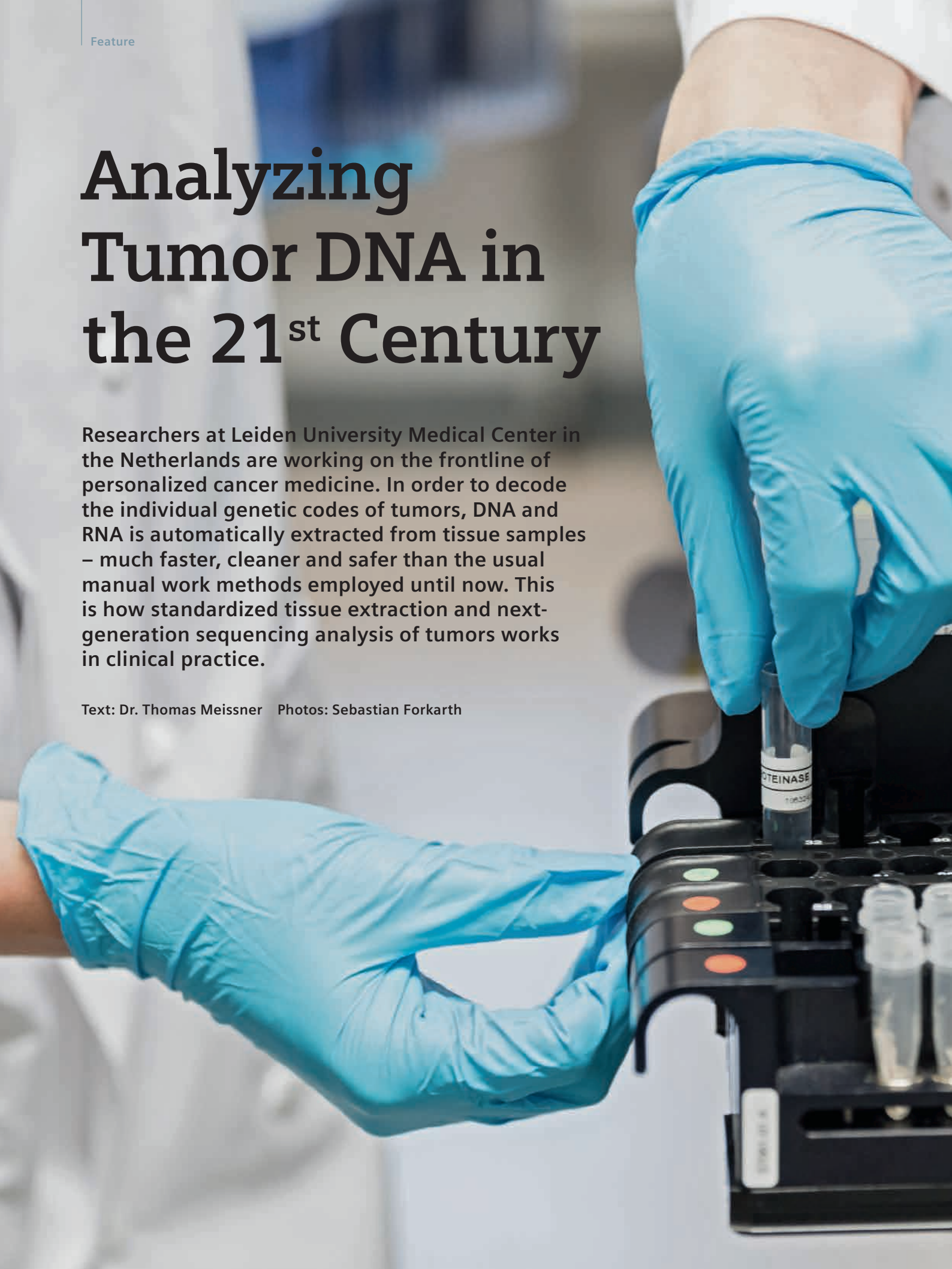
➔ www.siemens.com/interventional-oncology

The statements by Siemens' customers described herein are based on results that were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption) there can be no guarantee that other customers will achieve the same results.

Analyzing Tumor DNA in the 21st Century

Researchers at Leiden University Medical Center in the Netherlands are working on the frontline of personalized cancer medicine. In order to decode the individual genetic codes of tumors, DNA and RNA is automatically extracted from tissue samples – much faster, cleaner and safer than the usual manual work methods employed until now. This is how standardized tissue extraction and next-generation sequencing analysis of tumors works in clinical practice.

Text: Dr. Thomas Meissner Photos: Sebastian Forkarth



Barely a stone's throw from Leiden's main train station, the Leiden University Medical Center (LUMC) is a functional building that is wider than it is tall. Inside there is a labyrinth of winding hallways, low ceilings, and signs that point in all directions. When asked where the Department of Pathology is, two young men with name badges hooked to their jeans spontaneously escort the reporter and photographer two floors up. We walk around a few corners and find ourselves in the small office of Ronald van Eijk, PhD, molecular biologist and in the department for 12 years.

Even if there are no signs of autopsy tables or refrigerated rooms in which corpses are stored before examination, we are in the Department of Pathology. Instead, there are two understated desks, two computers, books, paperwork, and not much room. Ronald van Eijk and his colleague, molecular biologist Tom van Wezel, PhD, have the future of molecular pathology in their sights, because it is the prerequisite for personalized medicine of the future.

"My job lies somewhere between diagnostics and research. We are developing new tests, validating new equipment, and discussing and evaluating new developments and innovations," explains van Eijk. "You might call it research-driven technological development that will be implemented and change diagnostics in the future."

The era of personalized medicine began more than a decade ago when the breast cancer drug Herceptin, which targeted a specific receptor of tumor cells, came on the market. More and more targeted therapies against specific characteristics of cancer cells are being developed now, and the treatment strategies are becoming more and more varied.

Ronald van Eijk and Tom van Wezel at work in the Department of Pathology of the Leiden University Medical Center.

This requires much more intensive diagnostics than ever before. "The number of our analyses has increased tenfold in the past ten years," says van Wezel.

Van Eijk's and van Wezel's work is targeted at the genetic make-up of the cancer cells. The cancer cells have to be enriched and dissected from minuscule tissue samples which are, in most cases, both formalin-fixed and paraffin-embedded (FFPE) tissue samples. In a next critical step, the nucleic acids have to be extracted from the cancer cells' nuclei, and their genetic information removed with as little damage to them as possible. The recovered isolated nucleic acids contain data that give the cancer specialists information about which therapy is best for the respective patient, because there are significant differences in the genetic patterns of tumors, even between patients who have the same type of tumor. This is why the development of diseases can be so different. In order to treat the cancer subtypes more effectively, oncologists need a lot more details about the tissue than the standard information that is currently being provided. Only then can specifically effective drugs be developed. Because tumor tissue changes during therapy, the information has to be constantly checked over the course of the disease, so that the treatment can be properly adapted at the right time.

This is an enormous challenge for molecular pathology because the analysis of a patient's genome sequence in cancer cells should become part of routine diagnostics. Today, this complex gene analysis can be accomplished within a few days using next-generation sequencing (NGS). With NGS, the individual and most relevant pattern of genetic changes in tumor tissue can be analyzed simultaneously to determine the effective treatment. However, the genetic material has to be extracted from the cells first. This is a process that, until now, has been extremely time-consuming, requiring a great deal of human resources, according to van Eijk. Until recently, it has ▸

been performed manually and with varying quality, has not been standardized, and has involved the use of toxic chemicals such as xylene and ethanol. The DNA yield has, therefore, often been low and of poor quality for downstream genetic analysis.

Getting to the Nucleus Faster and Cleaner

With the Tissue Preparation Solution (TPS), Siemens Healthcare Diagnostics now offers the only fully automated IVD (in vitro diagnostics) system for the isolation of nucleic acids from solid histopathological samples. It can extract DNA and RNA molecules simultaneously from a single clinical fresh-frozen (FF) or formalin-fixed and paraffin-embedded (FFPE) tissue sample – a xylene-free method without any manual deparaffinization or lysis steps in between. In the past few years, van Eijk and his colleagues have integrated the system into the operations of the molecular pathology lab at LUMC, leveraging productivity and accuracy of reported clinical results.

Researchers would prefer fresh-frozen tissue samples, but only a few hospitals have the ability to freeze tissue at -80° C. That is why most samples are FFPE samples, which can be stored at room temperature for decades – hundreds of millions of samples are currently stored in global tissue banks around the world. However, this scientific treasure trove cannot be used that easily. The problem: "The DNA and RNA from the FFPE samples is already damaged because the tissue has been fixed with formalin and embedded in paraffin," explains van Eijk. The paraffin has to be laboriously removed using toxic chemicals like xylene in order to access the nucleic acid, losing yet more DNA and RNA in the process.

Van Eijk shows us the processes, explains the equipment, and describes the lab technicians' tasks. "There's a need for a quicker, safer and more standardized way to obtain cleaner DNA and RNA with fewer variations from technician to technician. Automated technology like this offers big advantages," states Van Eijk. This high-throughput automated system can save up to 24 hours compared with tedious manual extraction methods, enabling treatments to begin much earlier than before.

Van Eijk and van Wezel have also determined that they get a higher DNA yield and better DNA quality than with manual extraction. As van Wezel explains: "The higher DNA quality means that we have fewer failures in the analysis of the DNA." Doctors have to be told less often than before that the time-consuming DNA analyses have not yielded results. This is also important in light of the increasing cost pressure in hospitals. If the patient gets the right therapy at the right time, this can positively influence the patient's prognosis while the costs of treatment stay under control.

Automated DNA and RNA isolation is a major step forward, particularly for cancer research projects. "We were able to show in a colon cancer research study that we're capable of isolating DNA from 600 to 800 tumors and

Lab automation proved to be a success for analyzing tumor tissue samples in Leiden.

Management Summary

Challenge:
Hundreds of millions of samples worldwide lie dormant in tissue banks that, up to now, could only be analyzed by the manual extraction of genetic material. Researchers consider these archived samples to be a treasure trove of data that would enrich molecular pathology and personalized cancer therapy enormously.

Solution:
The Tissue Preparation Solution, a fully automated system for the isolation and purification of nucleic acids from solid tumor samples, improves and expedites diagnostic testing for cancer patients. These patients could benefit from next-generation sequencing (NGS) analysis and personalized oncology treatment decisions, one of the most significant medical innovation projects.

Result:
Molecular tumor diagnostics is already clinical routine at the Leiden University Medical Center. With the help of fully automated tumor diagnostic workflow, samples can now be processed twice as fast as before and determined with 99 percent accuracy. As lab director Ronald van Eijk explains, "We are now on track toward more automated and digital pathology."

conducting mutation analysis within three months," explains van Wezel. "In these specific experiments, automation saved us approximately six to eight months by the end of the project." Since the Siemens TPS can extract DNA and RNA from FFPE samples that have been stored for up to 21 years with a success rate of 99 percent, research projects such as this one could help uncover the nature of diseases in the hundreds of millions of FFPE blocks stored in pathological archives[1].

More Tests for Better Patient Care

We are now standing in front of the Siemens TPS in the lab for molecular tumor diagnostics. Two lab technicians are loading the equipment with 48 tissue samples from which the DNA and RNA will be extracted simultaneously. The cancer cells in the tissue sections have already been previously identified, marked under a microscope, and dissected into a collection tube for extraction. After the system is started, it proceeds with full automation and completes the isolation of RNA and DNA from 48 samples within four hours. Afterwards, the technicians can perform expression analyses, genotyping, or mutation analysis. While two lab technicians used to spend at least half a day manually extracting the DNA, they can now devote themselves to other tasks after starting the automated nucleic acid isolation.

"The number of tests per patient is dramatically increasing," explains van Eijk. "We have about 50 patients per week for which we do FISH[2], PCR (polymerase chain reaction), or other analyses. A few years ago, it was maybe half that." Per sample, less collected micro-dissected tissue is needed now for the DNA analyses than before, explains van Eijk. "We used to measure the DNA concentration before continuing with the other analyses, because with manual extraction methods we had to work with large differences in concentration between the different isolates. Now, for many applications, we are pretty sure that we can dilute the isolate in a standardized way and then immediately have our downstream results. So for these, we skip one step in the process: the DNA concentration measurement."

It is noon now. Ronald van Eijk leads us into the awe-inspiring *Curatorenkamer* (Curator's Room) in the *Acedemiegebouw* (Academy Building) – an ideal interview location. We are surrounded by large oil paintings by the Dutch painter Theodoor van der Schuer (1634-1707), created centuries before medicine and pathology were characterized by computers and machines.

Van Eijk explains the significance of his research: "We are now on track toward digital pathology." Classic pathology with a scalpel and microscope is being replaced more and more by computer-assisted diagnostic methods and automated processes. At such a historic location, where modern medicine and tradition are intertwined, researchers also want to preserve things that have been tried and tested for many years. *Omnia probate. Quod bonum est tenete* is written above the door of one of the former Leiden pathology buildings – "Test everything. Hold on to the good." Ronald van Eijk used this quotation as the preface for his dissertation, *Technological Advances in Molecular Pathology*. When asked what he would preserve from the past despite digitalization and automation, his answer is perhaps also somewhat patriotic: "The microscope!" ■

After graduating from medical school, passing the state board exams, and earning a doctorate in medicine, **Dr. Thomas Meissner** worked as a doctor in the UK and Germany. He has worked in the internal medicine, orthopedics, general and trauma surgery, anesthesiology, and intensive care departments. In 2000, he completed training as a medical journalist with the German periodical *Ärzte Zeitung* and was employed as an editor. Dr. Thomas Meissner has been working as a freelance medical journalist for trade and public media publications since 2001.

➔ www.siemens.com/laboratory-diagnostics

[1] Siemens Healthcare Diagnostics, data on file
[2] fluorescence in situ hybridization sequencing

Siemens Tissue Preparation Solution for therapy and research

The Tissue Preparation Solution (TPS) from Siemens Healthcare Diagnostics is a fully automated system for the isolation and purification of nucleic acids from formalin-fixed, paraffin-embedded (FFPE), and fresh frozen tumor samples. It improves, standardizes, and expedites diagnostic testing for cancer patients, especially in connection with the developments regarding next-generation sequencing (NGS) and personalized medicine in oncology. The TPS replaces non-standardized manual extraction methods, which are more time-consuming, of varying quality, and require a lot of human resources as well as the use of toxic chemicals.

Tissue samples from tumor patients are primarily available as formalin-fixed, paraffin-embedded (FFPE) samples. The Siemens TPS can extract DNA and RNA molecules from up to 48 FFPE samples in less than four hours. The xylene-free deparaffinization and optional automatic DNase I digestion step are fully integrated. The silica-coated paramagnetic nanoparticles developed by Siemens simplify the automatic isolation of nucleic acids and contribute to the quality and purity of extracted nucleic acids.

TPS enables isolation of DNA and RNA with higher quality and purity. Using PCR (polymerase chain reaction), measurable RNA or DNA can be extracted from several thousand FFPE samples that are up to 21 years old with a success rate of around 99 percent. The Siemens TPS paves the way for standardized routine biomarker diagnostics in personalized medicine, and is used in numerous retrospective biomarker studies with archived FFPE material.

Source: Hennig, G. Forum Aktuell 2011; 4: 6-7

Creating a Living Laboratory Together

Salvato Trigo, 65, a well-known professor of literature, is founder, owner and rector of the University Fernando Pessoa in Oporto, Portugal. His latest visionary project: to create the first private teaching hospital in Portugal to promote quality and up-to-date education while ensuring access to healthcare services for those who need it most. Through a partnership with Siemens, a comprehensive range of high-value clinical and operational solutions will be ensured for the next 15 years.

Text: **Patrícia Fonseca** Photos: **Walther Appelt**

The teaching hospital's doctors don't see patients as customers, but as partners in their medical training.

Born into a family of blacksmiths in the northern region of Portugal, Salvato Trigo began his teaching career in high school before moving into the private higher education sector, creating in 1983 the Oporto School of Journalism. Five years later, he decided to establish the "Foundation for Education and Culture Fernando Pessoa," named after the famous poet. This non-profit organization wants to play a "key role in the scientific, cultural, social, and economic development of society." The University Fernando Pessoa was officially recognized in 1996 when it received the status of a public interest organization. When the Fernando Pessoa's Foundation started the healthcare project in 2008, the challenge was to create a teaching hospital in a state-of-the-art, hands-on environment, while systematically providing and improving the quality of care for the community at affordable prices. One year after the inauguration, we find an imposing structure, a monument of philanthropy and health that does not follow the logic of profit. Professor Salvato Trigo wanted to create a hospital that could also serve as an "in vivo" laboratory – and he managed to do it.

In January 2014, the teaching hospital Fernando Pessoa celebrated its first year. Was this the start of a healthcare revolution?

Salvato Trigo: The basis of our philosophy in healthcare is in Plato's dialogues. Health is the balance between the physical dimension and the spiritual dimension of mankind. When we organize a healthcare system, we have to decide whether to invest in health or to spend on disease. In our hospital, we created a health environment for our patients – this was the beginning of our healthcare revolution. We aren't primarily interested in the so-called "disease market," but more in the "health market." This means that we want people to come here and consult with our doctors while healthy, and not just when they're suffering. We want to contribute to the prevention of disease, first and foremost. And when people are actually sick, we do not look at patients strictly as customers, but as partners who help us fulfill our mission: to train future health professionals well. Our hospital has emerged to respond to an intrinsic need of the university itself. University Fernando Pessoa has three colleges, the most important of which, in terms of the number of students, is Health Sciences, where it is offered a wide range of Health degrees, most of them dependent on the National Health System, through its network of public hospitals, to host our students for internships and clinical training. With our teaching-hospital at Gondomar, a town of the Metropolitan area of Oporto, we can offer the best possible clinical training to our students.

What's your economic assessment so far?

Trigo: The balance is positive. Possibly it could have been better if the country context were different, if we weren't going through a serious financial crisis. In the health sector, we feel that a lot. Our decision was not to invest in just another private ▸

Management Summary

Challenge:
To create a teaching hospital in a state-of-the-art hands-on environment, while systematically providing and improving the humanity, safety and quality of care for the community at affordable prices.

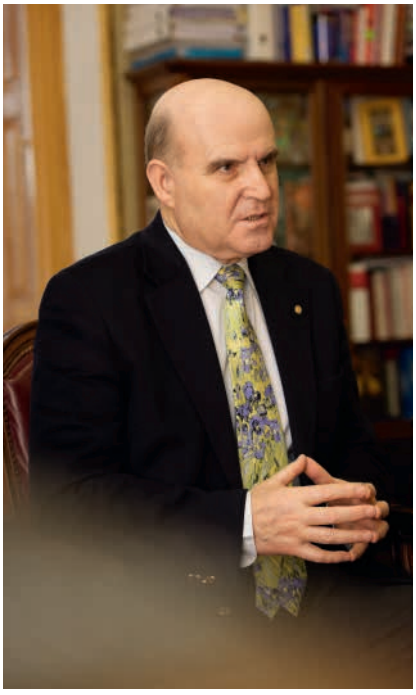
Solution:
Through a partnership with Siemens, a comprehensive range of high-value clinical and operational solutions for the next 15 years will be ensured.

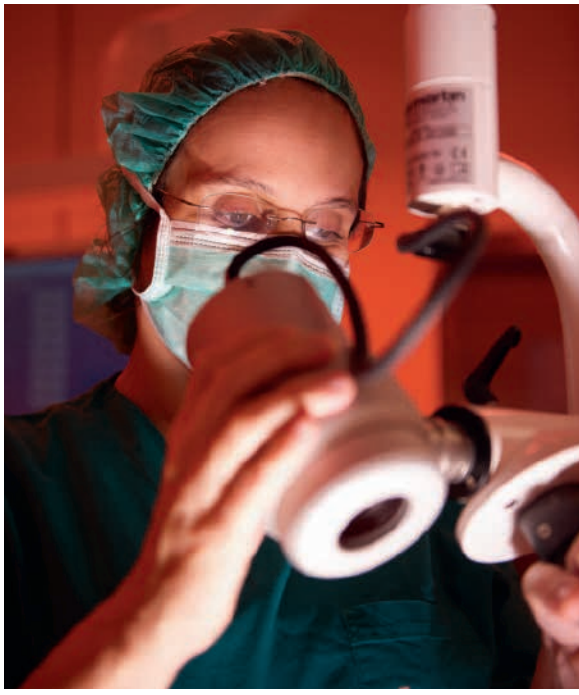
Result:
One year after its inauguration, Fernando Pessoa is a thriving hospital that does not follow the logic of profit, attracting thousands of patients and offering the best possible clinical training to its students.

hospital – replicating existing models would have been a waste. Nevertheless, I am sure that we will reach breakeven in three years if the National Health System (NHS) signs the agreements with the hospital. Without patients from the NHS, we will achieve breakeven in five years' time.

What else distinguishes this project?

Trigo: We want to distinguish ourselves from other private hospitals through humanity, safety and quality. This means an extreme concern for the safety of patients while they are in the hospital setting. It also means that we look for the best quality in treating the patients in a kindly human way as our teaching-learning partners. So we can improve our clinical research and develop professional skills. This means we pay attention to people, listening to their stories, explaining their condition in a simple way, reassuring them and conducting more adjusted care.





A man and his mission: Salvato Trigo could make health services more affordable while enabling students to improve their skills hands-on.

Can you describe this patient-doctor relationship?

Trigo: We want every patient to feel special here, and be aware that we are not an industry where the main objective is to respond quickly so profits can grow, but a place where they themselves are the priority. We understand that the most important thing in healthcare is time. We need time to listen, to learn, and then advise. The relationship we build with our patients, we believe, will mean that they become our main disseminators, as they will advise their family, friends, and neighbors to come to our hospital, where they felt welcomed, receiving the attention and care they needed.

Is that happening already?

Trigo: Yes, it is. Many of our patients were referred to us by someone close to them. If we look at the data of the development of this first year, we are a bit below what we anticipated – but we are not far below. There were small deviations in certain areas, while in others we even went beyond the objectives we had set ourselves. That is true for specialties such as dentistry, ophthalmology, gynecology, orthopedics, physical medicine, and rehabilitation. But our concern, knowing that projects like these are not built from one day to the next, is to fulfill our function, which also has a social aspect. The hospital is owned by the Fernando Pessoa's Foundation, which changes everything. We pay for work; we do not pay for capital. Our primary concern is not to arrive at the end of the year and have dividends to make our shareholders happy, because there are no shareholders.

Is this a philanthropic business model?

Trigo: Our main concern is to have a fair price for the provision of services. Our price list is 30-40 percent lower, on average, than in other private hospitals because we work not only with physicians with PhDs and a strong clinical reputation, but also with our medical students with lower salaries, achieving quality of care and pursuing our teaching mission. As a teaching hospital, we do not want to be a hospital for elites; we want to be a hospital for everyone. And when we began this project, we had already tested our capacities in this area,

One year in numbers

Patients treated (in- and outpatients)
15,500

Exams
7,380

Surgeries
322

Health Card D'Ouro subscribers
27,500

Emergency patients (adult and pediatric)
4,000

because we had our own educational clinics at the university. The difference is that, at the university, the 'doctors' are students, while at the hospital, healthcare professionals provide the services and the students just observe and learn. Our teaching clinics are a huge success precisely because they attract people who, due to their economic difficulties, have no access to private practices, such as those for dentistry, physiotherapy, speech therapy, psychology, etc. Our purpose, right from the start, was to serve the most vulnerable sections of the population.

Another innovation at this hospital is the healthcare card that offers discounts for patients. How well has it been received so far?

Trigo: It has been very well received by the population, we have about 27,500 members. Our goal for the first year was 6,000, so we more than quadrupled this goal. The card offers discounts on any service provided at the hospital and costs only 12 euros per year. The card has already paid for itself with the first appointment at the hospital. Its users get a 30 percent discount on a consultation, which usually costs 50 euros, or 35 euros with the discount. The idea of the card is to promote loyalty to the hospital. And we also offer a card to all students at the University Fernando Pessoa, with a credit of 50 euros, which can be used by them or by their immediate families.

What role does Siemens play in this project?

Trigo: I went to Germany in 2009 to meet with the Siemens International Vice President, to whom I explained the project. We talked for an hour and at the end of the meeting the Vice President told me that Siemens was on board. What we proposed was a little different than usual because we wanted not only to have a supplier, but to create a partnership through which we could also contribute something to the development of Siemens. In this way, we can learn from each other in order to achieve our primary dream: to create a living laboratory together, merging the technical project design and management of Siemens with the skills and abilities of a young team of undergraduate and graduate systems and computer science engineers, architects, managers, information and communication professionals, all of them trained by our university.

What more do you hope to accomplish in the near future?

Trigo: Our main goal for the future is always try to do things differently, to make things better. We are already preparing internationalization, both in the provision of healthcare and in the teaching and clinical research associated with it, focusing on medical training, national and international postgraduate studies, and taking advantage of our excellent center of anatomy and experimental surgery, which is attracting international patients as part of qualified health tourism. We are luring some foreign doctors, especially surgeons, who wish to bring their own customers to our hospital to undergo surgeries or other treatments at a very competitive cost. For example, we have just signed an agreement with French esthetic surgeons, which will bring some of their patients to Portugal. These surgeons are highly specialized so we are asking them to extend their visits so they can train our students and young surgeons. I also believe that this model of conceiving, building, and managing a teaching hospital has the potential to be replicated and exported to other countries, especially to Portuguese-speaking countries in Africa, which still face a period of reconstruction and where much remains to be done. We can present a distinctive offer to these markets, which could also include the training of the healthcare professionals. As we know, it's easy to construct a building. But a hospital is much more than a building. ■

Patricia Fonseca has been a senior writer/editor at Visão newsmagazine Portugal since 2003. She studied journalism at Washington University. Her latest awards: EU Health Prize finalist with a report about experimental cancer treatments (2012), Novartis Oncology Press Prize (2012)

The statements by Siemens' customers described herein are based on results that were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption) there can be no guarantee that other customers will achieve the same results.

Medical Education for Better Access to Affordable Healthcare

In this film, Salvator Trigo explains how both medical students and patients can benefit from a private teaching hospital.

To watch the video, scan the QR code using the reader app on your smartphone or enter the URL into your browser.

www.siemens.com/patients-as-partners

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Healthcare Experts Fighting against Breast Cancer

October was worldwide Breast Cancer Awareness Month. To mark this occasion, *Medical Solutions* Online featured stories of healthcare professionals around the world who are committed to the battle against this disease.

→ **www.siemens.com/Breast-Cancer-Series**

Inching Closer to a Future Without Multiple Sclerosis

In New York, Dr. Saud A. Sadiq and his team work round the clock to find first the cause of and, then, hopefully a cure for multiple sclerosis (MS). A renowned expert in treating MS, Dr. Sadiq explains how MRI technology improved the way he practices.

→ www.siemens.com/Multiple-Sclerosis

Cancer Treatment for the Poor

Egyptian cancer specialist Dr. Assem Rostom returned to his birthplace to treat the poor for free after 35 years of work in the United Kingdom. With support from local businessmen, he built the "Ayadi Al-Mostakbal" oncology center in Alexandria. Read how the oncologist managed to offer cancer treatment free of charge to those who cannot usually afford it.

→ www.siemens.com/AAOC-Egypt

Surgery 2.0

Revolution in the operating room: A combination of novel surgical navigation and positioning, using infrared light instead of x-radiation, offers a high degree of minimal invasiveness. The benefits for hospitals and patients can be striking. Find out more in our business case from University Clinic in Ulm.

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A Ferrari in the Lab

The Santa Casa Hospital in Porto Alegre, Brazil, is one of South America's leading hospitals. Lab director Dr. Carlos Franco Voegeli uses innovative technology to increase significantly the lab's speed, performance, and precision.

→ www.siemens.com/Lab-Automation-Brazil

Complying with the Affordable Care Act

Healthcare reform in the U.S. is forcing hospitals to reassess their protocols and engineer their clinical workflow processes differently than before. How the center reduced costs while decreasing readmission rates and improving patient satisfaction is featured in this article.

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Treating the Hardest Kidney Stones

Ahmedabad in India has among the world's highest number of urologists, and their patients have extremely tough kidney stones. State-of-the-art lithotripters are an effective and affordable way to treat these patients.

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At the Forefront of Cardiac CT

To improve cardiac diagnosis and follow-up after stent placement, the private Jessenius diagnostic center in Nitra, Slovakia, upgraded their existing computed tomography system with two new detectors – and with striking results. In an interview, the responsible decision-makers talk about the reasons for their choice.

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Real-time Volume ICE Improves Cardiac Interventions

Intracardiac echocardiography (ICE) plays an essential role in guiding complex cardiovascular interventions. Real-time volume ICE was used in clinical application for the first time at the Centro Hospitalar Vila Nova de Gaia/Espinho in Portugal. The article describes the essential benefits of this procedure.

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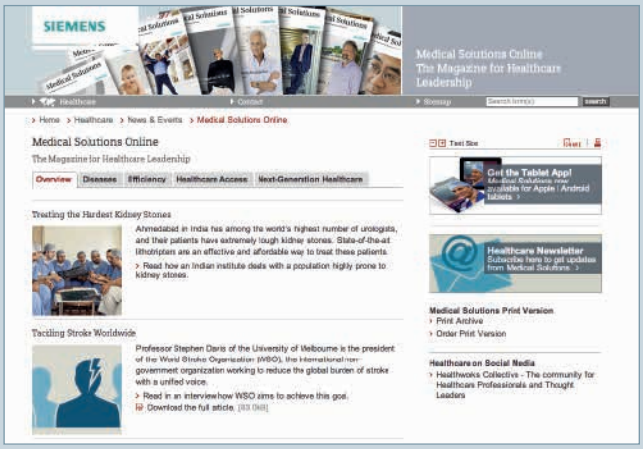

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