Medical Solutions

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SIEMENS

Next-Generation Healthcare

Dennis A. Ausiello sees profound changes ahead in medicine.

"We have an ethical obligation to transition from experience-based to knowledge-based medicine."

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

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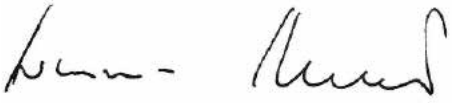
Dear Reader,

Today's healthcare providers face growing political and economic pressure and rapid increases in medical knowledge and clinical and technological developments. At the same time, the initial question physicians used to ask – "What is wrong with the patient?" – is being replaced by the outcome-oriented question, "What is going to help the patient?"
This approach follows the thinking of Dennis A. Ausiello, MD, an eminent clinician and pioneering research scientist. He sees the role of scientists as collecting and critically assessing massive amounts of data on our health that may reveal what takes individuals from wellness to illness, and back again (page 26).
Understanding the patient's disease with imaging and lab diagnostics is a first step in that direction. In the case of Alzheimer's, researchers at the Banner Alzheimer's Institute make use of our innovative combination of imaging IT, PET·CT, and PET imaging biomarker production to help diagnose and differentiate Alzheimer's from other forms of cognitive decline that are already treatable today (page 14).
Understanding the patient's biology through molecular diagnostics is the second step in discovering what will help the patient. At university hospitals in Kiel and Heidelberg, next-generation sequencing helps analyze genes relevant for particular diseases, such as chronic myocardial dysfunction or inflammatory bowel disease. This can be done faster and more cheaply than ever before. Together with filtering algorithms for the processing and interpretation of large amounts of resulting data, the researchers have tailored risk estimates to help derive therapeutic options based on each patient's individual genetic background (pages 6 and 10).
However, these two steps require the support of state-of-the-art databases to help clinicians answer our question, "What is going to help the patient?" These databases contain essential assessments of similar cases and provide structured outcome analysis and decision support based on standards of care. The THESEUS MEDICO research project lays the groundwork for a semantic technology that combines knowledge-based information processing with semantic machine learning. This software analyzes and structures medical data and links it to other relevant information, helping physicians derive clinical decisions right at the point of care (page 20).
In the end, we may know what is going to help the patient, but still not be in a position to do so. Here, we have an ethical obligation to transition from experience-based to knowledge-based medicine, that is, to apply the best available scientific knowledge to clinical decision-making. Imagine the lives that could be saved by applying new treatments sooner and on a more targeted basis, rather than after 10 years of double-blind studies without patient pre-selection to verify every effect and side effect. Instead, biological models could help predict the effectiveness of new therapies, which, naturally, need critical evaluation in clinical practice but could be applied until empirically falsified.
I hope you find these articles helpful in planning the future of your institution.



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Features

A Pink Year

In order to support experts and healthcare professionals in detecting breast cancer as early as possible, Siemens raised awareness with its global campaign "Turn your city pink!" From October 2011 until October 2012, participants were able to submit pictures and videos of their "pink actions" to the campaign's website and join the Facebook page – also via a "PinkCity" App for mobile users. For each submission, Siemens donated five US Dollars to breast cancer organizations. Throughout the year, online users could vote for their favorite submission and choose a monthly winner who received a pink Apple iPad.[1]

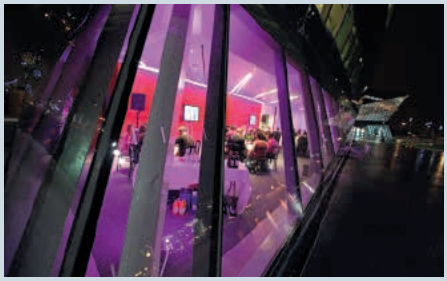
However, the campaign's website not only saw submissions from online users. Siemens also sent out the 27-year-old media designer Tina Kirner as a "Pink Ambassador" to the streets of the world's cities to help turn them pink. Tina traveled to ten countries in only four months. Equipped with a pink backpack full of pink accessories and a digital camera, she took more than 10,000 pictures of volunteers during her trip to the Netherlands, Denmark, Spain, Singapore, South Africa, Australia, USA, Colombia, Chile, and Brazil. While convincing passers-by to contribute to the campaign, Tina also used the opportunity to inform them about the risk factors of breast cancer and the need for early detection. After her trip, Tina was present at a final celebratory event in London in October. During a "pink dinner", she had the chance to meet the ten lucky monthly winners, of which four were themselves breast cancer survivors. Siemens also used the ceremony to hand over the donation to four international breast cancer organizations. With 18,230 photos and videos submitted, the campaign managed to raise 91,150 US Dollars to support breast cancer organizations to inform people about the disease and the importance of early detection. As a special event during the closing ceremony, a blogger "Get Together" provided the opportunity to discuss the needs and challenges of patient communication on social media. Eight bloggers and platform owners from the U.S. and Europe swapped experiences and discussed improvements in patient communication. The campaign's Facebook page had more than 130,000 fans, proving that social media is a successful channel to encourage the public to take action. The page will be live for one more year, featuring updates on breast cancer and links to blogs on breast cancer. All in all, the breast cancer awareness campaign reached an estimated half a million people worldwide through different media and reminded them of the importance of early detection. For more insights into Tina's world tour, the "pink dinner" and the blogger event, please access the link below.

[1] iPad is a trademark of Apple Inc., registered in the U.S. and other countries.

www.siemens.com/pink-news

"Pink Ambassador" Tina Kirner traveled the continents to turn their cities pink.

Pink bras pointed the way to the breast cancer event at "The Crystal".



The campaign ended with a dinner in pink.

Medical Solutions Goes Online

The Medical Solutions magazine that you are currently holding in your hands now has an online sibling. Just as you are used to in the print version, Medical Solutions Online focuses on the experiences and best practice sharing of healthcare decision makers and thought leaders. The new online magazine will be updated continuously and will feature stories from the print version enriched with multimedia content, additional expert interviews, facts and figures, and more. For example, you can watch a video of the interview with our cover hero David A. Ausiello and gain greater insight into this issue's stories from Heidelberg and Kiel, Germany, where doctors are taking healthcare diagnostics a significant step further with next-generation sequencing.
Medical Solutions Online can also be browsed via mobile devices such as smart phones and tablets.
Feel free to take a look and bookmark our new online magazine!

www.siemens.com/
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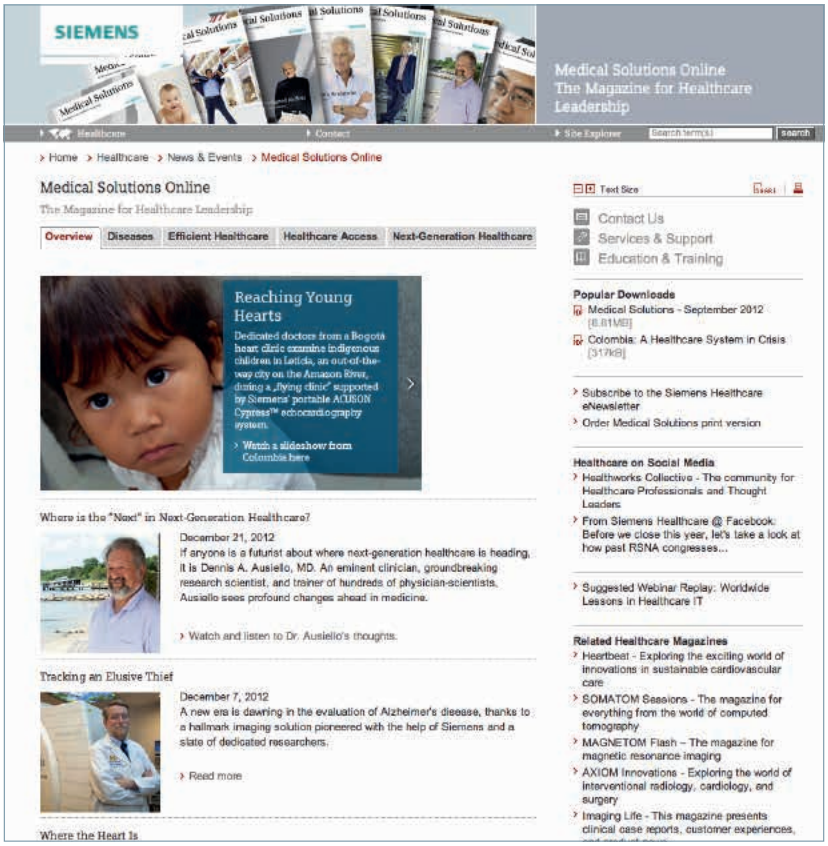
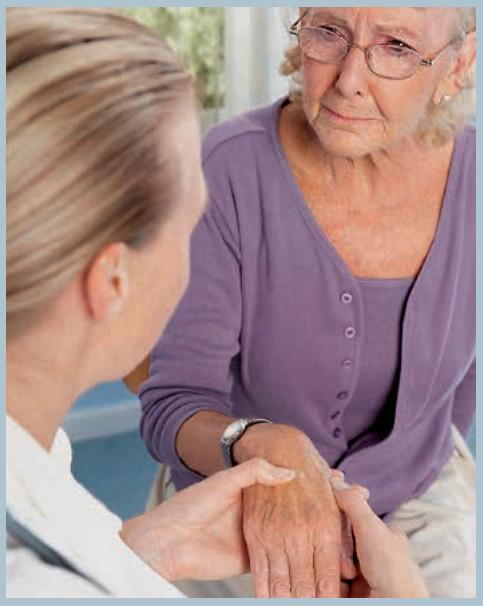




www.siemens.com/diagnostics

Early Rheumatoid Arthritis Detection Made Easier

Siemens' new Anti-Cyclic Citrullinated Peptide (anti-CCP) IgG assay, a blood test for the diagnosis of Rheumatoid Arthritis (RA), is now available outside the U.S. on IMMULITE® 2000/2000 XPi systems. RA is a disease that affects one percent of the population worldwide.[1] High levels of the anti-CCP antibody indicate a more aggressive RA and a higher risk of joint damage as compared to patients with low levels. In the past, the Rheumatoid factor (RF) test along with physical assessment of the patient was used as a criteria for RA diagnosis. However, clinicians agreed that these criteria were not sufficient for the diagnosis of early RA. With a specificity of 99 percent, the anti-CCP assay from Siemens is an accurate marker for RA diagnosis and RA differentiation from other arthritic conditions. Anti-CCP antibodies pre-date the diagnosis of RA and may be found years before symptoms of RA develop. Furthermore, the specificity is higher compared to the RF test: 96 to 100 percent compared to 74 to 87 percent respectively. Anti-CCP can also differentiate RA from other inflammatory arthritic conditions.

[1] Yelin E, Callahan LF. The economic cost and social and psychological impact of musculoskeletal conditions. Arthritis Rheum. 1995;38:1351-62.

An Ecosystem for More Efficiency

Point-of-care (POC) testing continues to grow and as POC testing programs expand, so do the challenges of managing the increasing activities and responsibilities.

Siemens POC Ecosystem™ solutions aim to improve a point-of-care (POC) coordinators' ability to meet challenges in effectively managing their POC testing program focusing on eight core components: device management, operator management, quality control, compliance reporting, competency management, inventory management, remote monitoring, and mobile access. For example, the RAPIDComm® Data Management System is one of the key solutions of Siemens POC Ecosystem. The RAPIDComm system makes it possible to manage the instrumentation and consumables for hundreds of testing devices used throughout the hospital by non-laboratory personnel, the development and administration of point-of-care training programs, and helps ensuring internal and external compliance requirements are satisfied all while striving to reduce cost and improve efficiencies.

Although solutions for each of the components exist today, efficiently managing all aspects of a POC program requires close collaboration among healthcare institutions, device manufacturers, and information technology vendors in the future. Siemens POC Ecosytem™ solutions help to address those challenges.

www.siemens.com/poc

Developing New Graves' Disease Assay

Siemens signed an agreement with KreLo GmbH Medical Diagnostics for the rights to develop an automated thyroid-stimulating antibody (TSI) assay used in the differential diagnosis of Graves' disease (GD). With this agreement, Siemens Healthcare Diagnostics expects to be the first in vitro diagnostics distributor of an automated TSI assay featuring stimulating TSH receptor antibodies that are specific to the diagnosis of GD.

Thyroid stimulating immunoglobulins (TSIs) are auto-antibodies that bind to the TSH receptor on thyroid cells, resulting in GD, the most common cause of hyperthyroidism. GD is an autoimmune disease affecting approximately 3.45 million people in the United States alone. Accurate diagnosis and treatment of GD early in the disease process improves patient quality of life by limiting many of the manifestations of GD, including heart palpitations, irritability, anxiety, fatigue, and insomnia. Although there are a few other automated assays for a similar thyroid marker, TRAb, or TSH receptor, auto antibody, these assays cannot differentiate between blocking and stimulating activity of TRAb, which is important in certain thyroid dysfunctions. The stimulating antibodies directed against the TSH receptor cause GD. The design of the Siemens TSI assay is specific to the measurement of stimulating TSH receptor antibodies and is expected to differentiate the diagnosis of GD. For information on Siemens' thyroid solutions, visit the website below.

www.siemens.com/thyroid

Siemens Introduces New Portable Ultrasound System

Siemens expands its ultrasound portfolio with the ACUSON P300™ ultrasound system, a compact portable device for a variety of clinical settings.

The new system is designed to meet the diverse imaging needs for a wide spectrum of patients, body types, and clinical disciplines – from radiology and general imaging to cardiovascular imaging, from obstetrics and gynecology (OB/GYN) to specialty imaging including muscoloskeletal, breast, and small parts. It encompasses advanced ultrasound technology and excellent imaging performance in one portable package, thus enabling comprehensive patient care everywhere and anytime.

The ACUSON P300 system is ideal when a physician needs to obtain a fast diagnosis under difficult conditions – for instance, where space is limited or a mobile solution is needed. The high image quality and broad spectrum of applications of the new portable unit is designed to meet the expectations of today's healthcare environments in mobile ultrasound systems.

www.siemens.com/p300

All in the Family

And then they were two: One year after Siemens unveiled its 128-slice SOMATOM® Perspective computed tomography (CT) scanner, it launched a second model at the 2012 Radiological Society of North America (RSNA) conference. The new family member comes in a 64-slice configuration and is ideally suited for major clinical fields in medical imaging.
"Scanner requirements vary from practice to practice," says Florian Belohlavek, Siemens Global Product Marketing Manager CT, when asked about the need for building a SOMATOM Perspective family. "So we offer various configurations."
The 64-slice scanner is aimed at larger private practices and smaller hospitals, offering them a first step toward the upper-end of CT. It also makes it easier to take the second step: customers using the 64-slice configuration can upgrade to 128-slice. Both SOMATOM Perspective family members offer a host of upgraded components.
But no matter which configuration is chosen, one aspect of the SOMATOM Perspective remains the same: it is one of the most economical CT of its class. Installation is fast and easy and power consumption as well as cooling requirements are lower. Furthermore, the eMode enables a patient-friendly and financially efficient use of the SOMATOM Perspective family.

www.siemens.com/
SOMATOM-Perspective

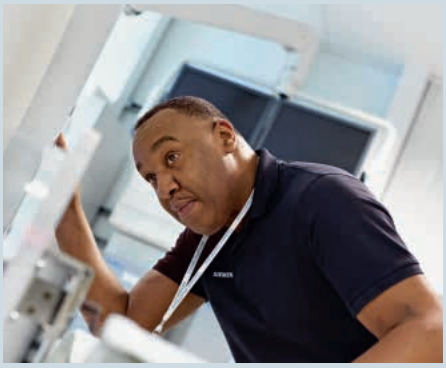
Combining Products – Improving Efficiency

syngo®.via and *syngo*® Dynamics are now accessible from one workstation. The results of a study conducted in 2012 by Siemens Healthcare with six customers in Germany, Austria, and Spain illustrated that *syngo*.via can help save significant time when reading medical images without compromising accuracy. For example, the software automatically loads images into the appropriate application and sorts them into the corresponding layout – pre-processed according to the disease-specific requirements. This eliminates the need to manually choose the application, load data, and select corresponding layouts. Combined with *syngo* Dynamics, workflow efficiency can be improved even further. *syngo* Dynamics is a multi-modality, dynamic image review and archiving system using knowledge-based reporting. Optional interfaces to clinical or hospital information systems allow the distribution of results in a variety of formats. This helps facilities to create a filmless and paperless environment. *syngo*.via and *syngo* Dynamics help in delivering high-quality cardiovascular care by providing unique reading and reporting.

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.

Customer Service Redefined

Siemens Healthcare customers can now benefit from a new range of services, which focus not only on product performance but also on helping users to get the best results with education and consulting services.
The application team at RSNA showcased real-time optimization and workflow enhancements by connecting a workstation via Siemens Remote Services. By focusing on the outcomes of this portfolio of services, we are closer to meeting all of our customers' needs in today's Healthcare environment.



Latest Ultrasound Make-Up

Siemens is expanding its ultrasound portfolio by launching the ACUSON X700™ system. The new ultrasound device provides advanced signal processing technology as well as improved contrast and detail resolution enabled by algorithms migrated from premium performance platforms. It also offers workflow-enhancing applications that automate routine tasks for faster results, for example, *syngo*® Arterial Health package for semi-automated intima-media thickness measurements, and Auto Left Heart measurements.
The 20-inch flat panel display with integrated handle offers easy visibility in any scanning position. The system's swiveling, height-adjustable control panel accommodates any user height in both sitting and standing positions. Its small footprint makes the ACUSON X700 system ideal to transport and use in tight spaces. Siemens further expanded its ultrasound portfolio with the aqusition of Penrith Corporation, a manufacturer of integrated ultrasound imaging systems, especially in the portable ultrasound segment. The acquisition aims to strengthen Siemens' competitive position in a market that continues to show double-digit growth such as point-of-care and ultrasound image-guided interventional procedures.

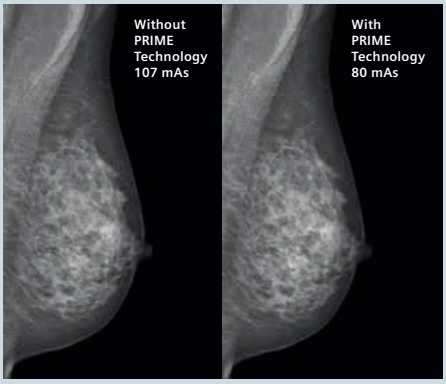
www.siemens.com/x700

New mammography system can lower radiation dose up to 30 percent

Siemens Healthcare is launching the MAMMOMAT® Inspiration PRIME Edition[1], the first mammography device that can lower dose up to 30 percent without compromising image quality. In the MAMMOMAT Inspiration PRIME, the scatter radiation grid , which has been commonplace up to now, is replaced by a new algorithm for progressive image reconstruction. The conventional scatter radiation grid absorbs scattered radiation to ensure image quality. Since it also, however, absorbs part of the primary radiation, a higher dose is needed to obtain images of the desired quality. The new algorithm can identify the scatter-causing structures and calculate a corrected image. Thus, the primary radiation can be completely used and high-quality images can be achieved with less dose.

[1] Pending 510(k). Under FDA Review. Not available for sale in the U.S.

www.siemens.com/inspiration



25-percent dose reduction with PRIME technology

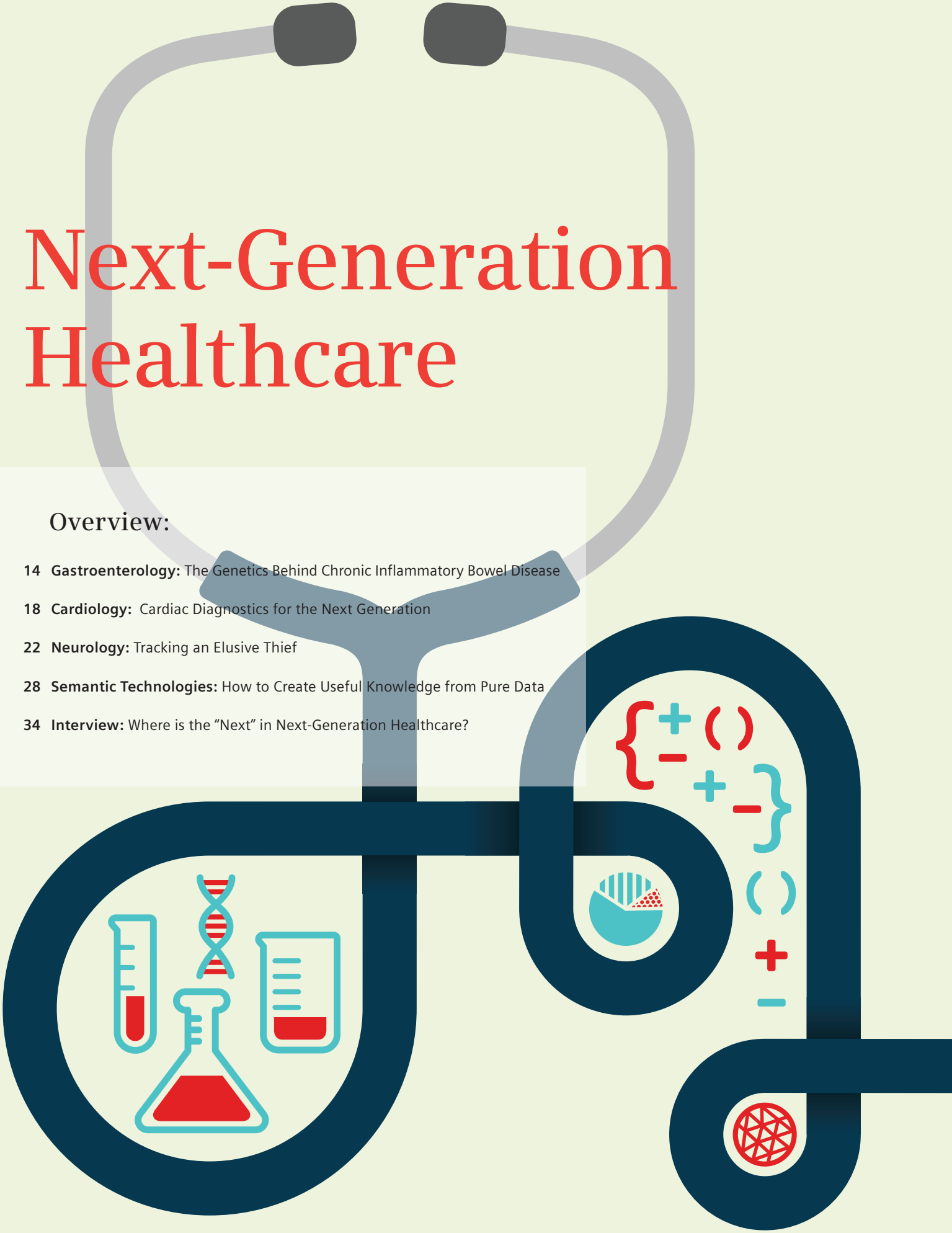
Empowering Preclinical Research

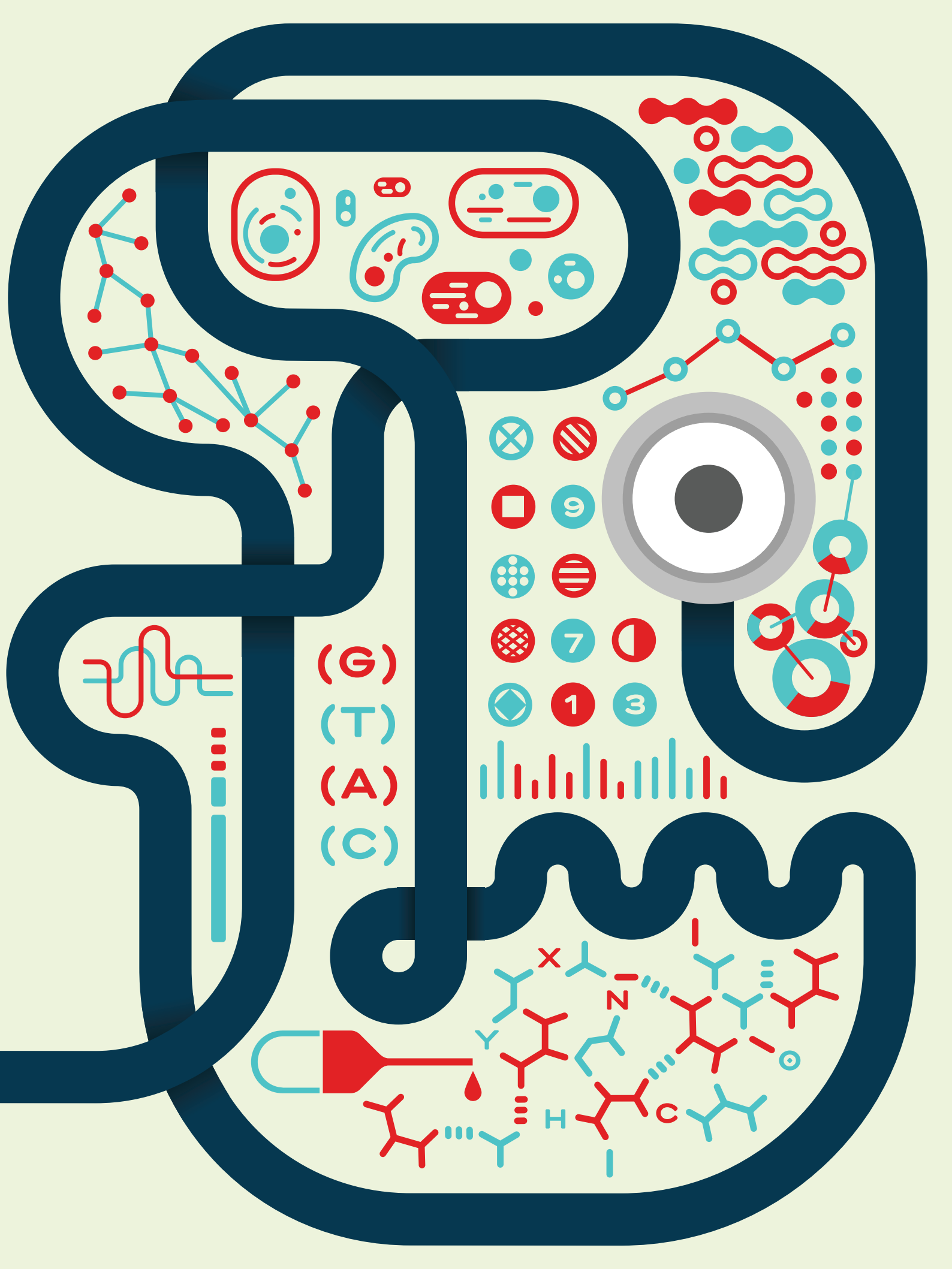
Siemens Molecular Imaging recently launched several solutions for preclinical molecular imaging.
One of them is the latest version of the image visualization and analysis software package, Inveon™ Research Workplace (IRW) 4.1. Building upon the 4.0 version of Siemens IRW software, IRW 4.1 contains enhanced features and capabilities for improved workflow, synchronized quantification, and persistent image visualization settings. Furthermore, a low dose technology is now available for the Inveon CT. In preclinical imaging research, repeated exposure to ionizing radiation may cause unintended biological effects such as inhibited tumor growth or tissue damage, which could affect the overall results and hence the conclusions of the study. The Inveon low dose CT option tackles the challenge of CT dose in preclinical imaging research, providing a solution that enables reliable longitudinal CT imaging studies. Innovations like these can empower customers in their research and inspire them to make breakthrough discoveries in molecular diagnosis and therapy.

www.siemens.com/preclinical

Next-Generation Healthcare

Overview:

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The Genetics behind Chronic Inflammatory Bowel Disease

Chronic inflammatory bowel disease is on the rise in industrialized countries and it poses a diagnostic and therapeutic challenge to physicians. Researchers from the Institute for Clinical Molecular Biology in Kiel, Germany, believe that learning more about the genetic basis through next-generation sequencing might lead to more specific approaches.

Text: **Wiebke Kathmann** Photos: **Andreas Lang**

The answer lies in the genes and in the adequate analysis of a patient's blood.

Chronic inflammatory bowel disease (IBD) – especially Crohn's disease and ulcerative colitis – are affecting an increasing number of people in industrialized countries. This may be due to the immune system not being sufficiently activated during childhood. Even hygiene has its downside.

Professor Andre Franke, PhD, is a geneticist at the Institute for Clinical Molecular Biology (IKMB). Earlier this year[1], he and his team of researchers were able to show how a lack of contact with ubiquitous microorganisms during early childhood increased the likelihood of developing chronic inflammatory diseases in later life – be they of the intestine, skin, lung, or joints. When insufficiently challenged, the immune system seems to get bored and initiate inflammatory reactions. Therefore, IBD may be considered a paradigm of a disease resulting from civilization, as Stefan Schreiber, MD, Director of the IKMB, puts it.

Patients affected by IBD must not only deal with bloody diarrhea of differing intensity, but also with life-threatening complications like fistulae, rupture, or cancer of the colon. Their quality of life is severely impaired; their life expectancy shortened.

Despite advances in IBD therapy over recent years, more specific and individualized therapies are needed. Beyond that, an altogether different approach is required, as Schreiber – who is also Director of the Clinic for Internal Medicine at the University Hospital of Schleswig-Holstein (UKSH) and Dean of the Medical Faculty at the Christian Albrechts University in Kiel – explains: "Today, we are treating illnesses like Crohn's disease at a stage were macroscopic damage to the intestinum has already taken place. Controlling the disease at this stage is no longer possible. We need to advance the diagnosis to earlier stages of the disease process, before the immune system

Stefan Schreiber, MD, Director of the IKMB, aims to detect IBD at a much earlier stage than it is now, by using information on gene mutuations.

DNA data is semi-automatically transferred to a server for analysis.

has run amok." Schreiber expects that a more comprehensive risk assessment, including information on gene mutations, will help to detect diseases at a much earlier stage when true healing is still possible.

At the Forefront

Physicians, geneticists, biologists, and bio-information specialists work together at the IKMB, studying the complex interaction of genes, epigenetics, and environmental factors in the pathogenesis of IBD. The IKMB and the Clinic for Internal Medicine are world-renowned centers of excellence for the diagnosis and treatment of IBD. They have made great contributions to the understanding of the underlying processes of IBD. By bringing together high-level patient care and basic research, they are also providing an opportunity for the transfer of research results to the clinic.

Impact of Mutations

As with many diseases, IBD cannot simply be blamed on one mutant gene. There is more to the puzzle. Genetic research has shown that several genes are involved. Besides, even though the phenotype of affected patients in Asia and Europe is the same, the genetics are not. To determine the clinical relevance of each mutation found, the mutant genes must be matched up to a representative pool of genetic information from the population. To find and understand disease-associated alterations in DNA requires the comparison of huge amounts of data from genome sequencing and the need for algorithms to help annotate it.

High-throughput Sequencing: An Important Tool

Today, a patient's genome can be sequenced within six weeks, thanks to next-generation sequencing. As Franke explains, the first step is taking blood from the patient. Then lymphocytes are purified; their DNA is enriched and prepared for sequencing. Afterwards, the data is semi-automatically transferred to a server for analysis.
Thanks to the targeted re-sequencing approach developed in Kiel, which selectively enriches coding regions of the genome – the so-called exome – the process can be sped up. Exome sequencing involves about one percent of the genome, and it is therefore not only faster, but also cheaper and more likely to make it into clinical practice.
According to Schreiber, the possibilities for exploring the sequence of the human genome have expanded tremendously over recent years, much like they did for personal computers about 15 years ago. "Nobody could have imagined that we would be able to do such complex things on a computer as we can nowadays on an iPhone[2] ," Schreiber explains. "It is similar with genetics. The technical revolution in creating sequencing data has opened new doors. It is no longer the privilege of human geneticists to analyze genetic data and then announce the connection to symptomatic diseases in a black-and-white manner. Today, research-

From Bench to Bedside

In Kiel, one successful example of the effect that high-throughput sequencing can have on treatment choices comes from a 3-year-old boy with transmural, discontinous colonic inflammation resembling Crohn's disease. The intestinal inflammation was resistant to both immunosuppressive treatment and modern treatment approaches using antibodies against the cytokine Tumor Necrosis Factor alpha. Even a protective ileostomy couldn't stop the inflammation. It only reduced the severity of the colitis. It is known that, especially in young patients, the genetic impact on disease manifestation is very strong: the more severe the disease, the more likely a genetic contribution.
"We performed whole exome capture and sequencing on the affected child and his parents," Franke explained. The exome of child and parents was enriched and sequenced, with the base sequences read automatically. Thereafter, the sequences of all three were compared to the human reference genome and among each other. The final step of the annotation of variants was performed using an alogrithm developed in Kiel (snpActs) and a commercially available algorithm (ANNOVAR). "For the identification of de novo mutations in the child, we used Varscan's somatic mutation detection command together with our own in-house scripts," says Franke.
With this procedure, the Kiel researchers identified a novel, hemizygous nonsense de novo mutation in an exon of a gene that had recently been shown to cause a Crohn's disease-like illness[1]. For Franke, this demonstrates that exome sequencing allows an unbiased detection of the genetic alterations associated with rare clinical phenotypes and provides significant insights into the pathophysiological mechanisms of IBD.

[1] Worthey EA et al.: Making a definitive diagnosis: successful clinical application of whole exome sequencing in a child with intractable inflammatory bowel disease. Genetics in Medicine (2011) 13, 255–262; doi:10.1097/GIM.0b013e31820881582011.

> "Today's challenge lies in finding the few mutations within the set of the hundreds of thousands of letters of the genome that contribute to the clinical phenotype."
>
> Professor Andre Franke, PhD, Geneticist, Institute for Clinical Molecular Biology (IKMB), Kiel, Germany

ers and physicians from different fields can explore the data and relate mutations to human phenotypes."

Managing the Flood of Data

Sequencing is no longer the challenge. "Today's challenge lies in finding the few mutations within the set of the hundreds of thousands of letters of the genome that contribute to the clinical phenotype; especially, the high-penetration phenotypes of children affected by IBD, where genetics play a major part in the disease's development," Franke states.
Therefore, bio-information algorithms that automatically separate meaningful data from that which is unimportant are needed to improve clinical usability of high-throughput sequencing. "This is where we need an industry partner like Siemens, who has experience in dealing with huge volumes of data," says Franke. The intellectual contribution for developing these algorithms comes in part from a large technological platform, the popgen biobank. This was developed in Kiel within the Deutsche Forschungsgemeinschaft (German Research Foundation)-sponsored Excellence cluster, 'Inflammation'. It allows the Kiel researchers to systematically compare the genetic make-up of large populations and to generate new insights into the relationship between variants and specific human phenotypes. This work builds the intellectual context in which data from high-throughput sequencing is interpreted. Until recently, this information was distributed by a number of sources, including the Internet, yet it wasn't freely accessible. Now, it all flows into the system supporting the annotation algorithm. To fully understand how and where genetic information plays a role in diseases – and not just those like IBD – Franke believes that it will take another ten years.

Hopes for the Future

In the long run, identifying genetic make-up might lead to approaches like gene therapy or stem cell therapy – especially in those young patients with a really bad prognosis – "but," Schreiber cautions, "it is not just the genes. It's the whole risk profile, including nutrition, body type, and exercise habits that will have to be included in patient management choices in the future. I see the physician of the future as a guide for the patient, helping him or her balance genetic risks against lifestyle choices."

*Medical writer **Wiebke Kathmann** is a frequent contributor to medical magazines aimed at German-speaking physicians. She holds a Master's Degree in Biology and a PhD in theoretical medicine. She worked as an editor for many years, before becoming a freelancer in 1999. She is based in Munich and Karlsruhe, Germany.*

[1] Olszak T. et al. http://www.sciencemag.org/content/early/recent, 22 March 2012/Page 1/10.1126/science.1219328.
[2] The iPhone is a registered trademark of Apple Inc., registered in the U.S. and other countries.

Further Information

healthcare.siemens.com/hospital-it/thought-leadership-and-industry-initiatives

Management Summary

Challenge:
- Increasing numbers of patients in industrialized countries suffer from chronic inflammatory bowel disease (IBD)
- Improving the specificity of diagnosis and therapy in IBD
- Identifying the genetic make-up of the individual IBD patient
- Mastering the huge amount of data derived from genome or exome sequencing

Solution:
- Next-generation sequencing as a means of saving money and time
- Biobanks providing the necessary data on the genome of healthy individuals
- Algorithms helping to distinguish functional from ineffective mutations: in other words, detecting clinically relevant mutations
- An interdisciplinary approach: integrating insights from molecular biological approaches with clinical experience

Result:
- Greater understanding of the individual risk profile of patients as the basis for individualized medicine
- Better understanding of the genetic basis of diseases like IBD, thanks to a targeted resequencing approach
- Improved clinical usability of high-throughput sequencing results

Cardiac Diagnostics for the Next Generation

The man who revolutionized emergency diagnostics in myocardial infarction during the 1980s and early 1990s by introducing troponin biomarkers has accepted a new challenge. Hugo A. Katus, Head of Cardiology at Heidelberg University, and Benjamin Meder plan to add state-of-the-art genetic sequencing to the diagnostic routines of myocardial disease patients. Will he also succeed this time?

Text: **Philipp Grätzel von Grätz** Photos: **Andreas Teichmann**

It is a scene typical of research during the 21st Century: Three people are gathered around a huge computer screen in a dimly lit room, watching something colorful as it repeatedly expands and contracts: the heart of a zebrafish larva. Three days earlier, the same researchers introduced a gene to the larva. It was the same gene that causes chronic myocardial disease in humans. The fish will help them to understand how this gene works. On the screen and clearly noticeable, the zebrafish heart is beating – but not properly. There is something wrong with the dynamics of its contractions. The researchers hope to figure out what exactly is happening on a molecular level within the next two or three months.

All in the Genes

"Genetic research has evolved considerably in recent years," says Professor Hugo A. Katus, MD, Head of the Department of Cardiology, Angiology, and Pneumology at Heidelberg University, Germany. "It has become a clear focus in all life sciences. In cardiovascular research, genetics helps us to understand what the risk of cardiac disease actually means. We are increasingly able to identify patients at high risk of disastrous cardiovascular events by analyzing their genome. And with this genetic knowledge, we can prevent events because it helps us to choose proper therapies. It is all about making a correct diagnosis in the first place. Without accurate diagnosis, there is no such thing as a tailored treatment."

Katus has an impressive track record of developing tools that improve diagnostics in cardiology. During the 1980s and early 1990s, he spearheaded the introduction of the biomarker troponin as a tool for earlier diagnosis of myocardial infarction. Today, more or less every major clinic in the world uses various forms of troponins to recognize or rule out infarction in patients with acute chest pain. Few other newly developed diagnostic tests have had such an impact.

More than a Research Tool

But is possible to repeat such success? The cardiologists in Heidelberg certainly hope so. Their vision is to develop an easy-to-use genetic test that provides a comprehensive overview of the genetic background of patients with chronic heart failure. This test would not be a research tool, but one that can be used in daily clinical practice. And unlike troponins, it would not be a test for the emergency room, rather, one for chronically ill patients: a test that could be ordered and interpreted by clinical cardiologists – or even by a doctor at a private practice.

"The prevalence of chronic heart failure is growing faster than any other cardiac disease at the moment," says Katus. "We are expecting an increase of 30 percent over the next decade, for two reasons: first, people are generally getting older. And second, our treatments in cardiology have become quite successful; enabling today's cardiac patients to live longer than they did in the past."

With the growing number of heart failure patients, there is an increasing need to stratify patients properly and to tailor therapies according to the individual genetic background. Benjamin Meder, MD, the Head of Genetic Research in Katus' department, explains how this approach is already practiced today: "We know from studies that chronic cardiomyopathy patients with a mutated variant

Professor Hugo A. Katus, MD, is Head of Cardiology at Heidelberg University and piloting a new approach to identifying genes in a patient's blood sample: "next-generation sequencing."

of the gene Lamin A have a far higher risk of developing life-threatening cardiac arrhythmias. For this reason, we often recommend implanting a defibrillator in these patients at an early stage."

Diagnostic Challenges

Unfortunately, it is not always so straightforward. "Today, we are aware of more than 50 genes that are of relevance to cardiomyopathies. And the number is constantly growing. This is increasingly becoming a diagnostic nightmare," says Meder. To date, genes in cardiac patients were analyzed using a method called Sanger Sequencing. It was originally developed during the 1970s. Theoretically, all of the 50 or more genes relevant to chronic cardiomyopathies could be analyzed in this way. However, according to Meder, this is not an option: "It would take ages, and it is extremely expensive."

To address this challenge, Katus and Meder are piloting a new approach to identifying genes in a patient's blood sample: a nano-scale method, called "next-generation sequencing." It is a complex technique, but the advantage is that all the relevant genes can be analyzed in one go. "We take the blood samples, isolate the DNA and break it up with ultrasound," Meder explains.

"Without accurate diagnosis, there is no such thing as a tailored treatment."

Hugo A. Katus, MD, Head of Cardiology, Heidelberg University, Germany

"Afterwards, the fragments that are interesting to us are separated with the help of magnetic beads, before they are fed into the next-generation sequencing machine." This machine – a highly sophisticated lab robot – "reads" the gene fragments step-by-step, nucleotide-by-nucleotide. Ten days later, the results are ready. Up to 100 patients can be analyzed in parallel," explains Jan Haas, Biologist in the team of Meder.

Finding the Needle in the Haystack

However, one problem remains: Next-generation sequencing machines produce vast amounts of data that is practically impossible for the human brain to analyze. This is why Katus and Meder are collaborating with researchers from Princeton University and with software experts from Siemens. They are developing a software tool that will use scientific and medical knowledge databases to analyze the huge volumes of data generated by the sequencing machines. The ultimate goal is to create a diagnostic test that will generate a report, which can then be read and understood not only by professional geneticists, but also by resident doctors in routine patient care. "Complex analytics like this can never be done without innovative IT solutions," says Katus.

The number of genes is not the only factor that makes genetic data difficult to interpret. There is also the need to determine whether genes are interacting with each other in a way that might be clinically relevant. In other words: In contrast to a troponin test, a genetic analysis of a complex disease is not about measuring a single biomarker and defining a proper threshold. Rather, it is about pattern analysis.

The software for the next-generation sequencing project will be deployed in Heidelberg during late 2012. Meder is already looking forward to it. "We will test it rigorously; for example, in the context of the Europe-wide INHERITANCE study that involves more than 1,000 dilated cardiomyopathy patients from eight European centers." All genetic diagnostics for this study are being done in Heidelberg. "We are very proud to be part of such an endeavor. One that brings together the crème-de-la-crème of European research into this particular disease," he continues. Initially, the software will provide a report summarizing the results of the genetic analysis; providing information about quality issues concerning the sequencing

"More than 50 genes are relevant to cardiomyopathies; the number is constantly growing."

Benjamin Meder, MD, Head of Genetic Research, Department of Cardiology, Heidelberg University, Germany

Blood samples' DNAs are isolated and broken up with ultrasound before the interesting fragments are separated with magnetic beads and fed into the next-generation sequencing machine.

Management Summary

Challenge:

- Learn more about the links between genes and the clinical consequences for heart patients
- Predict the risk of dangerous events in patients with chronic heart failure, based on their individual genetic background

Solution:

- Use next-generation sequencing to analyze disease-relevant genes faster and cheaper than before
- Apply an IT solution to the processing and interpretation of the large amount of sequencing data

Result:

- A clinical report providing information about the genetic profile of an individual heart failure patient in a way that is meaningful to clinicians in their daily routines
- Tailored risk estimates that help to personalize treatments according to the individual genetic background

process. Later, the report will also include clinical information about the risk of life-threatening arrhythmias, or on the risk of a particularly rapid loss of left ventricular function. "Depending on the risk profile, we might order additional diagnostics like an MRI examination in the future. Or we might recommend specific pharmaceutical therapies earlier than we normally would," Meder adds.
Linking next-generation sequencing results with therapeutic interventions will require many clinical trials and a lot of additional research. However, this is equally true of any new diagnostic test. Katus knows this from experience: "When we introduced troponin, it took us ten years to develop the test, and another five to convince the community of its usefulness."

The Benefits of Cooperation

The success of the next-generation sequencing project will depend on whether the combination of sequencing and IT-based analytics will be able to provide meaningful data. It will also depend on the ability of software architects to summarize and present the data in a way that is useful for clinicians. "It has to be easy," Katus notes. "Every doctor should be able to use it. Our goal is that five years from now, every cardiologist will use genetic tests as naturally as he uses the ECG today."
According to Katus, integrated research of this kind is only possible when academia and industry collaborate closely: "Processing genetic data is not something we can do on our own. We need innovative IT companies to help us. I am deeply convinced that real progress is only possible when experts from different fields come together and create a new perspective."
Meder points out that this "integrated environment" – where clinicians, genetic researchers, and IT experts work closely together – is part of what makes working in cardiovascular research at Heidelberg so attractive to young scientists and engineers. "Research that aims to bring something into the market always needs industry at a certain point," he says. And this is exciting for younger colleagues because they learn to ask clinically relevant questions."
Next-generation research for next-generation researchers: In Heidelberg, it has become reality.

Philipp Grätzel von Grätz *is a practitioner of internal medicine turned freelance writer and author, based in Berlin, Germany. His specialties are biomedicine, medical technology, health IT, and health policy. He also holds a Master of Science in Communication (Imperial College, London).*

Further Information

http://healthcare.siemens.com/hospital-it/thought-leadership-and-industry-initiatives

Thanks to Siemens' Biograph mCT PET·CT technology, researchers like Kirk A. Frey, MD, PhD, will be able to gain more insights into Alzheimer's disease.

Tracking an Elusive Thief

A new era is dawning in the evaluation of Alzheimer's disease, thanks to a hallmark imaging solution pioneered with the help of Siemens and a slate of dedicated researchers.

Text: **Diana Smith** Photos: **Dwight Cendrowski (Michigan), Jason Millstein (Arizona)**

Alzheimer's disease is truly one of the cruelest diseases that strikes the elderly, at the height of years that are supposed to be "golden." Instead, the neuro-degenerative disorder snarls the body's command center, slowly eroding brain function. It robs victims of their memory, steals the most basic of bodily functions and finally life, over a course that can last a decade or more.

There is no known cure. Further, today's most effective drug therapies for Alzheimer's only assuage symptoms, doing very little to slow progression of the disease.

Progressive mental decline and aging have been noted in history for hundreds of years. But it wasn't until 1906 that a German physician, Alois Alzheimer, put together pieces of the puzzle, identifying a collection of brain cell abnormalities as a specific disease. When Alzheimer performed an autopsy on one of his patients who died after suffering for years with severe memory problems and confusion, he discovered dense deposits surrounding the nerve cells, and inside the cells, he observed twisted bands of fibers. Today, this degenerative brain disorder is named after him, and when found during an autopsy, these plaques and tangles mean a definitive diagnosis of Alzheimer's disease.

The brain lesions between cells are abnormal, insoluble protein deposits called amyloid plaques. Amyloid plaque is widely believed to be a precursor to another kind of abnormal protein, the neurofibrillary tangles (NFTs), or hair-like threads that exist within nerve cells of Alzheimer's patients. Over time, amyloid plaque and neurofibrillary tangles clump into a convoluted mess of blockages in the brain, halting normal nerve cell transmission.

Research and Clinical Challenges

Amyloid plaques are of great interest to researchers, including Kirk A. Frey, MD, PhD, of the University of Michigan Alzheimer's Disease Center in Ann Arbor, Michigan, USA, and Adam S. Fleisher, MD, of the Banner Alzheimer's Institute in Phoenix, Arizona, USA. "The interplay of what goes wrong in the brain in the processing of proteins is very important," says Frey.

For researchers and clinicians, the challenge was that amyloids in the brain

Study uses New PET Imaging Agent to Identify Tau Proteins

Across the globe, the number of Alzheimer's cases is growing at epidemic levels due to aging populations and extended life expectancies. With no known cure, there is great demand for research and eventual treatments to halt this merciless disease.

A research team led by Hartmuth C. Kolb, Vice President of Molecular Imaging Biomarker Research at Siemens, recently performed preclinical studies using [18F]-T807 compound in positron emission tomography (PET) imaging that selectively targets neurofibrillary tangles (NFTs) of tau protein, a key abnormality that is present in Alzheimer's disease.

Two critical protein abnormalities are associated with Alzheimer's disease: 1) NFTs of hyperphosphorylated tau protein and 2) senile plaques consisting of beta-amyloid peptides. Both protein abnormalities are considered to be targets for therapeutic intervention, in addition to being biomarkers for targeted in vivo imaging agents.

Researchers report that the severity of tau abnormalities and NFT burden consistently correlates with the degree of cognitive impairment and neuronal circuitry deterioration associated with Alzheimer's disease dementia, but the presence of beta-amyloid brain plaques lack that correlation. For this reason, NFT can potentially be an additional imaging biomarker for Alzheimer's-related dementia.

According to information released by Siemens, "the research team designed, synthesized, and tested more than 900 compounds in an effort to identify [18F]-PET tracers that possess strong binding affinity and selectivity toward tau protein tangles. Researchers created a competitive autoradiography assay to test compounds that would bind to native tau tangles and beta-amyloid plaques on sections of postmortem human brain tissue. In in vitro assays, the compound [18F]-T807 displayed a high level of binding affinity and good selectivity for tau aggregates over beta-amyloid plaques. The researchers' in vivo and in vitro studies suggest that "[18F]-T807 possesses suitable properties and characteristics to be a specific and selective PET tracer for the imaging of paired helical filament tau in human brains."

A major issue with Alzheimer's disease is identifying an imaging biomarker that can accurately identify the progression of clinical symptoms and allow extrapolation back to early preclinical stages. Based on the study, tau deposits may allow this to happen. Authors of the study plan to test the [18F]-T807 tracer clinically in Alzheimer's disease patients to determine its usefulness as an early diagnostic tool of the disease.

Siemens supported the research study, "A Highly Selective and Specific PET Tracer for Imaging Tau Pathologies," and is developing the [18F]-labeled compound as a potential PET imaging agent. Research data was published in the August 2012 issue of *The Journal of Alzheimer's Disease*.

Amyloid plaques in the brain are of great interest to Kirk A. Frey, MD, PhD, of the University of Michigan Alzheimer's Disease Center.

could previously only be detected during an autopsy. Clinicians do not have reliable tools to accurately assess the cause of cognitive decline, but rather make "probable" diagnoses based on mental and cognitive examinations.

"In research clinics, such as the one here at the University of Michigan and other universities and academic centers worldwide, the accuracy of that clinical designation has probably been no better than 80 percent," explains Frey. "We could not be completely confident until the pathol-

ogist told us. Despite our best efforts, we would be wrong in evaluating one in five patients."
He adds, "You can imagine what kind of problem this poses. For clinical trials, a pharmaceutical firm has an idea about possible pathological processes and wants to target that as being specific to Alzheimer's disease. You mount a trial where, at best, one in five patients does not have the problem that you're targeting, and therefore, of the patients in treatment, one in five will not benefit."

The Next Frontier

That scenario now has changed, thanks to an innovative imaging solution unveiled earlier this year by Siemens: The first-of-its-kind comprehensive amyloid imaging solution[1] designed to detect beta-amyloid in the living brain. The new imaging solution is multi-pronged, encompassing four unique elements – the manufacturing and distribution of a PET imaging biomarker, the Biograph® mCT PET·CT scanner, *syngo*®.PET Amyloid Plaque[1] neurology quantification software, and the support network an imaging institution needs to plan, implement, and successfully operate amyloid imaging services.
According to Fleisher, the new solution may play a critical role in future Alzheimer's research. "It's a game-changer," he says. The PET scan utilizes imaging biomarkers – small molecular tracers that monitor biological processes – to detect amyloid in the brain. "If amyloid is not present, even with dementia, it is not Alzheimer's."
Dementia is a late stage of Alzheimer's disease, explains Fleisher. "Amyloid plaque starts in the brain 10 to 20 years before symptoms are exhibited. Research is being done to see if, through the detection of amyloid plaque, it may be possible to predict the onset of Alzheimer's disease years before symptoms appear," he says. "This would not only allow earlier treatment, but also, hopefully, enable the development of better drugs that effectively block, or even reverse, the progression of the disease."
A key component of the Siemens imaging solution is the software, *syngo*.PET Amyloid Plaque, which takes a patient's PET amyloid exam and automatically registers it against a reference model of a PET amyloid brain. When combined with visual assessment, these capabilities assist physicians in making an interpretation of the PET image. The new software's algorithm strongly correlates with the reference model (Fleisher method) developed by Dr. Fleisher and his research colleagues. Fleisher utilized six emperically derived regions of amyloid plaque formation for the analysis of the data and established a threshold value to distinguish between a healthy brain and one afflicted with Alzheimer's.

Adam S. Fleisher of Banner Alzheimer's Institute hopes to find ways to block, or even reverse, the progression of Alzheimer's disease.

> "Research is being done to see if, through the detection of amyloid plaque, it may be possible to predict the onset of Alzheimer's disease years before symptoms appear."
>
> Adam S. Fleisher, MD, Banner Alzheimer's Institute, Phoenix, Arizona, USA

During a scan, some amyloid tracer is naturally retained in the normal brain, so it is important to differentiate between white matter tracer uptake and gray matter amyloid plaque deposits. Amyloid within the brain's white matter is considered normal in most cases, but tracer uptake in the gray matter may indicate abnormal activity. However, white and gray matter are integrally interlaced in a compact manner, making differentiation a challenge. Siemens new Biograph mCT offers the highest image quality[2] at the industry's finest volumetric resolution of 87 cubic-millimeter and accurate, quantifiable results.
After imaging the brain, the *syngo*.PET Amyloid Plaque software automatically compares a patient's scan with a reference model PET scan, which identifies six zones to evaluate pathological levels of amyloid plaque burden. "This information gives radiologists an additional tool when they conduct visual assessments and make evaluations," says Fleisher. "The images support other clinical findings, giving clinicians added confidence for their evaluation."
The third element of the solution is the PET imaging biomarker manufacturing

Siemens' Biograph mCT significantly contributes to Alzheimer's research due to its finest volumetric resolution.

and distribution expertise of PETNET Solutions, a Siemens company. Siemens' PETNET Solutions employs a dedicated staff and a fully integrated operational support infrastructure for the production of amyloid imaging biomarkers, which enables it to offer imaging centers and hospitals a high level of delivery reliability of up to 96 percent.

"For clinical use, as well as for research use, reliability in obtaining radiotracers is critically important," says Fleisher. "For patients, it has to do with scheduling and fitting into busy scanner schedules, and when you have tracers that can be produced and delivered reliably, it translates into time, it translates into convenience for patients, and ultimately, it translates into cost savings for our center."

Beyond the Foundation

For imaging centers and departments, implementing and expanding these amyloid imaging services can be challenging. In the planning stage, if customers create a flawed business plan it could lead to revenue loss. An incomplete implementation plan can cause delays in starting up this new clinical service. In the growth stage, a limited referral base and unawareness of offerings can restrict patient access and business growth. Finally, during the operational stage, inconclusive or wrong interpretation of amyloid imaging cases can lead to unsatisfied referring physicians, which can limit demand for amyloid imaging services. Siemens' PETNET Solutions leverages the expertise of its field staff who average over 10 years of experience in PET imaging to help customers ensure successful implementation of amyloid imaging services. There are two key areas where they help customers: The first is with a personalized plan that involves a walk-through to identify site requirements to help ensure no step is missed to enable customers' success when they go live with offering amyloid imaging. The second is the large network of expertise ranging from workflow and marketing support, to scanner protocols, clinical training, and business plan support, which enables customers to have access to resources essential for a successful implementation of amyloid imaging.

An Unmerciful Disease on the Rise

In North America, Alzheimer's disease holds 5.4 million people hostage – most of them over age 65. Every 68 seconds, a person in the United States develops Alzheimer's. Also in the USA, deaths from Alzheimer's disease have increased 66 percent between 2000 and 2008, while deaths from other major diseases, including the nation's number-one killer, heart disease, have all decreased during

the same period.[3] And, Alzheimer's is the only disease in the top ten with no cure.

Worldwide, there are an estimated 36 million people who are victims of the devastating illness.[4] This number is expected to nearly double every 20 years to an estimated 65.7 million in 2030 and 115.4 million in 2050.[4] Many experts predict that with the rise in the aging population, Alzheimer's disease may well be the next global health epidemic.

"Alzheimer's disease is a very significant global healthcare problem," concurs Frey. "It's an exceedingly common medical problem, and it's also exceedingly expensive, not only in terms of family and caregivers, but also in terms of healthcare resources. Medications that are regularly prescribed and used for symptomatic treatment of Alzheimer's have some effectiveness, but they are not as effective as we would want or need, and they are relatively expensive," Frey reports. "In the United States, expenditures of US$2,000 to US$3,000 per year just for prescription medications are not uncommon."

Yet, that expense is miniscule compared to someone who requires 24/7 supervision for their care. According to Frey, the family almost always bears the burden of care at first, but eventually, virtually all demented patients require an institutional setting to medically manage their safety as well as to supervise their daily care and daily activities. Those expenses are very substantial.

Currently, Alzheimer's is one of the most expensive illnesses society must bear, with global costs reaching US$604 billion in 2010.[4] And, that number is expected to skyrocket as the population around the globe ages. Siemens is working to help provide solutions. The first step is Siemens' comprehensive imaging solution to detect amyloid plaques, one of the key pathological features of Alzheimer's disease, in a living person. With this new solution, the only one currently available, researchers now have a new way to evaluate Alzheimer's and other causes of cognitive decline. Most importantly, the solution provides clues to help track down this elusive and silent thief – and killer.

Diana Smith *is a freelance writer specializing in health and medical topics. She is based outside of Austin, Texas, USA.*

[1] *syngo*.PET Amyloid Plaque quantification software is intended for use only with approved amyloid radiopharmaceuticals in the country of use. Users should review the drug labeling for approved uses.
[2] Based on competitive information available at time of publication. Data on file.
[3] Alzheimer's Association Fact Sheet, "2012 Alzheimer's Disease Facts and Figures," March 2012.
[4] Alzheimer's Disease International, "Dementia Statistics," www.alz.co.uk/research/statistics.

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.

Further Information

www.siemens.com/alzheimers

Management Summary

Challenge:

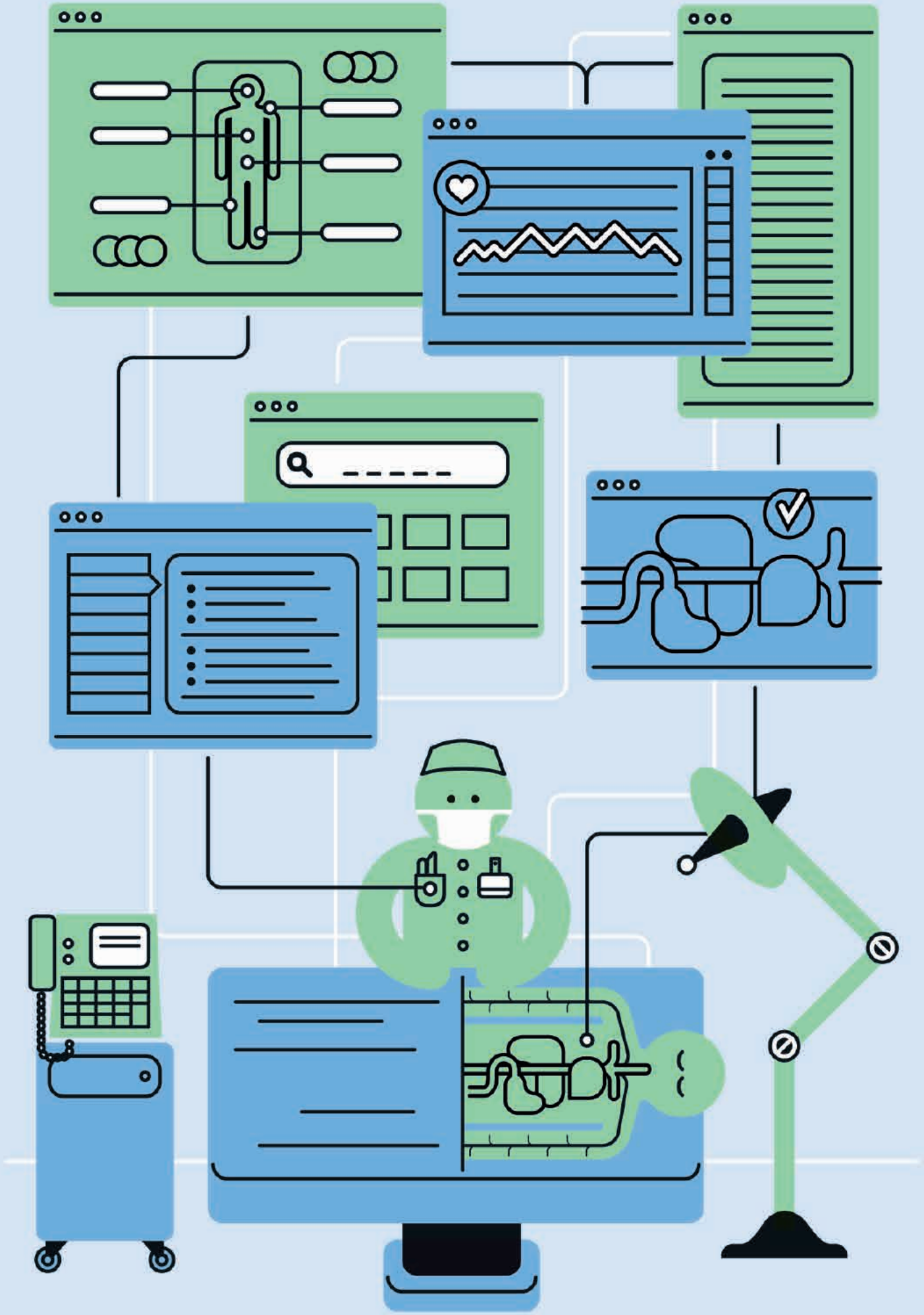
- Visualizing amyloid proteins in the brain, believed to be a primary abnormality in Alzheimer's disease, previously inaccessible until autopsy
- Discovering how to image amyloid plaques to aid in assessment and research
- Utilizing a PET imaging solution to help doctors determine whether potential drugs or treatments in clinical trials are improving condition or not

Solution:

- An innovative, one-of-a-kind comprehensive amyloid imaging solution, combining Siemens new Biograph mCT, *syngo*.PET Amyloid Plaque quantification software, and PET imaging biomarker production and distribution, which allows physicians and researchers to identify beta-amyloid neuritic plaques in the living brain

Result:

- A new imaging solution that allows physicians to readily identify brain amyloid plaques that are primary factors in Alzheimer's disease in living patients, leading to more accurate evaluation
- Possibility that researchers may be able to predict onset of disease at a much earlier stage, since brain amyloid plaques are present years before dementia symptoms develop
- Potential for a PET imaging modality like the Biograph mCT to play a critical role in research and treatment, showing clinicians whether treatments are effective at reducing or stabilizing amyloid plaques
- Optimism to find new treatments to manage this devastating disease



How to Create Useful Knowledge from Pure Data

Imagine a hospital where patient data from numerous sources is made accessible to ward physicians with the help of hyperlinks and intelligent indexing. Imagine a healthcare system that hands its patients – not an envelope or a CD-ROM – but an integrated data set that allows them to truly understand their illness, and even use the Internet to obtain additional information. Imagine a radiologist who uses semantic technologies to navigate smoothly through the myriad imaging data. Welcome to the future of semantic technologies in health information retrieval.

Text: **Philipp Grätzel von Grätz** Photos: **Detlef Schneider** Illustration: **Alberto Antoniazzi**

Professor Alexander Cavallaro's vision of the educated lymphoma patient of the future is very different from today's patient, who carries the computed tomography (CT) images of his lungs and abdomen home on a CD or DVD after a routine radiological examination. In Cavallaro's vision of the future, the lymphoma patient would open his radiological report on a tablet-PC to find a document with relevant hyperlinks – much like an Internet page. The patient would learn that, for example, his spleen is enlarged. After clicking on "spleen," the corresponding radiological image would appear. It would show exactly where the spleen is located and what it looks like.

The patient would also learn that, while his spleen is still larger than normal, it is in fact considerably smaller than it was at his last radiological examination: a sign that the chosen cancer therapy is working. Another click would open a window listing hyperlinks to additional, context-specific patient information; for example, to the lymphoma pages of the Internet encyclopedia Wikipedia, to a patient self-help website or a drug database with patient information on side effects and the importance of drug adherence.

Not Only a Benefit for Patients

Cavallaro is Senior Radiologist of the Imaging Science Institute (ISI) at Erlangen University Hospital, Germany. As such, not only does he have a vision for patients,

Cavallaro envisions a future where patients would open their radiological reports on a tablet-PC to find a document with relevant hyperlinks – much like an Internet page.

The THESEUS MEDICO research project brought together radiologists from the University of Erlangen and experts from the German Research Center on Artificial Intelligence (DFKI), as well as researchers from Siemens, the Fraunhofer Society, and Munich University.

but also for the physicians responsible for their care. These doctors do not necessarily need hyperlinks to patient websites, but they do need links to previous images to make comparisons and assess the effectiveness of the treatment. They also need to integrate imaging and laboratory data, as well as information on clinical signs and symptoms, in order to make a diagnosis or modify a treatment plan. Equipping a medical report with this kind of context-specific and target group-specific information is not easy. It can only be done with the help of the semantic technologies that come from artificial intelligence research. Semantic technologies structure information from different data sources with the help of an ontology: a structured dictionary. Thanks to semantic technologies, information from the Internet or another data collection can be filtered by content, so that a document search reveals only the most relevant and appropriate documents in a given context. "Standard Internet searches provide millions of documents, most of which are useless," Cavallaro explains. "Semantic searches really stick to the point. This is what makes them so suitable for a highly specialized field like medicine."

Research: A Team Effort

Just how semantic technologies can be applied to medicine was illustrated by the THESEUS MEDICO research project, which brought together radiologists from the University of Erlangen, experts from the German Research Center on Artificial Intelligence (DFKI), as well as researchers from Siemens, the Fraunhofer Society, and Munich University. "MEDICO" was one of several cases put forward for the use of the THESEUS research program, which was initiated by the German Federal Ministry of Economics and Technology in 2007, in order to support technologies for an "Internet of services."

"When we discussed how medicine might benefit from semantic technologies, we soon realized that we really needed software solutions that could search and – to a certain degree – interpret images," Cavallaro recalls. Since images, and in particular radiological images, are an indispensable part of modern medicine, it simply did not make sense to talk about applying semantic technologies to medicine without considering images. The consequence was that, although THESEUS MEDICO was not fundamentally about computer-aided detection, it involved a considerable amount of computer-aided research. This led, among other results, to new algorithms for image analysis about which the Erlangen scientists reported in prestigious scientific journals.

An Anatomical Algorithm

The case chosen for the THESEUS MEDICO project was that of a lymphoma patient. "We chose lymphoma because we wanted

> "Semantic searches are suitable for a highly specialized field like medicine."
>
> Prof. Alexander Cavallaro,
> Senior Radiologist,
> Imaging Science Institute (ISI),
> Erlangen, Germany

THESEUS MEDICO can greatly aid clinicians like Cavallaro in decision support by learning, adjusting, and trying to understand medical data via semantic technologies.

"Our prototype solution can identify and visualize most relevant organs correctly, within two minutes."

Prof. Alexander Cavallaro,
Senior Radiologist,
Imaging Science Institute (ISI),
Erlangen, Germany

to analyze the whole body, and we needed a disease with a certain radiological dynamic over time; so we could analyze, for example, treatment effects," Cavallaro explains. One of the first steps was to develop an algorithm that could identify various abdominal and thoracic organs on CT scans of the chest and abdomen automatically, within a reasonable time. It was a considerable success: "Our prototype solution can identify and visualize most relevant organs correctly, within two minutes. This includes the esophagus and the pancreas: two organs that no other IT system seems to have ever been able to identify in such a short period of time," says Cavallaro.

Bone metastases, pathological lymph nodes, and alterations of blood vessels can also be detected automatically. This image information allows the automatic creation of hyperlinks between words in text documents, like a radiological report, that were beforehand semantically analyzed by the system, and corresponding areas in the imaging data set – provided that proper ontologies are used: in this case, the radiological ontology RadLex and the anatomical ontology Foundational Model of Anatomy (FMA).
The ability to automatically analyze imaging data sets and to provide detailed links between radiological reports and radiological images is certainly impres-

sive. But does it help in day-to-day medical scenarios? Cavallaro is convinced that it will do: "There are many, many ways in which the results of THESEUS MEDICO could become part of actual products in the future."
For example, applying semantic technologies to radiological images could help physicians in the wards to better understand radiological images and reports. This might also improve workflows, says Cavallaro: "Many radiological images are not self-explanatory. And the result is that we need many phone calls to explain images to our colleagues." By linking images with the pathological findings in reports, and by providing meaningful hyperlinks, the number of these explanatory phone calls could be reduced considerably.

Helping the Physicians

Medical education, too, can benefit from a more semantic approach. Semantic technologies can be used to map anatomic drawings with radiological images of real patients, and at the same time, offer context-specific links to textbooks or scientific publications. "We have done this with three cases so far. They will be part of the anatomy course at Erlangen Medical School in the future," Cavallaro adds.
One problem remains, though: Even if the necessary meta-information is mainly accomplished by the system, the radiologist still has to validate or complement. A fact of which Cavallaro is very aware: "It is true that, in the beginning, it is more work for the radiologist, even though he is assisted by computer-aided capabilities. However, image analysis methods get constantly better and one has to also look at the whole package. There are so many benefits from a more semantic approach to radiology. I am convinced that, in total, it will even out."
One of these benefits became apparent in the very early phase of THESEUS MEDICO. It had to do with the automatic analyses of organs and their locations. Once, for example, a pathological lymph node is described semantically, the system is able to "jump" to exactly that location in a follow-up examination. The radiologist no longer has to go through all the CT slices. With the help of semantic technologies, he is directed to the point of interest immediately. "This helps during the creation of a report. But it also makes radiological demonstrations far easier," Cavallaro explains. Time-consuming searches for follow-up images, while the rest of the department waits in the demonstration room, are eliminated. Each pathology that the radiologist wants to show and discuss with his colleagues is available instantly.

A Step into the Future

THESEUS MEDICO was a research project. It is not an off-the-shelf product at the moment. "But it certainly paves the way for the further development of the many IT solutions we use today – especially in the fields of radiologic reporting and data integration," says Cavallaro. The radiologist is convinced that semantic technologies are the way forward – for moving from the age of complex data collection toward the age of knowledge and interpretation of data. Using semantic technologies, it might be possible to conduct image-based searches of a patient database in order to identify patients with similar conditions. This could be of great help to a doctor who is confronted with a difficult or unusual case. "That is just one example. THESEUS MEDCIO has opened many windows," says Cavallaro. "At the Imaging Science institute, we are definitely planning to go on with this kind of research."

Philipp Grätzel von Grätz *is an Internal Medicine physician turned freelance writer and author, based in Berlin, Germany. His specialties are biomedicine, medical technology, health IT, and health policy. He also holds a Master of Science in Communication (Imperial College, London).*

The displayed solution is a prototype and under development. Not available for sale. Its future availability cannot be ensured.

Further Information

http://www.theseus-programm.de/en/920.php

Management Summary

Challenge:
- Link radiological image data to textual documents in a way that is useful for clinicians and patients
- Find ways to automatically interpret radiological images

Solution:
- Work with computer-aided detection tools to automatically describe the location of organs and pathologies
- Use semantic technologies from artificial intelligence research to create meaningful links between images, other sources of clinical information, and Internet resources of all kinds

Result:
- Patients would receive a radiological report with hyperlinks to radiological images, as well as context-specific hints for further reading on the Internet
- Ward physicians could seamlessly integrate radiological images with laboratory data and patient symptoms. They can also access professional information sources online
- Radiologists would benefit from workflow improvements in reporting and image retrieval

Where is the "Next" in Next-Generation Healthcare?

If anyone is a futurist about where next-generation healthcare is heading, it is Dennis A. Ausiello, MD. An eminent clinician, groundbreaking research scientist, and trainer of hundreds of physician-scientists, Ausiello sees profound changes ahead in medicine.

Interview: **Louisa Kasdon** Photos: **Jeff Frits**

According to Dennis Ausiello, medicine will evolve toward patient-centered continuous care and away from episodic hospital-based care, enabled by a full-throated multidisciplinary effort to stratify human sub-populations by studying the human phenotype. He sees teams of scientists coming together, collecting and critically assessing massive amounts of data about our health that may unravel what leads us from wellness to illness, and back again. We caught up with Ausiello at his vacation home on Cape Cod, a place where he has an unobstructed view of the Atlantic Ocean – and, quite possibly, the horizon of next-generation healthcare.

What does next-generation healthcare mean to you?
AUSIELLO: Next-generation healthcare is a basic sea change in medicine. The next generation of physicians will not be encumbered by the four walls of a hospital. Traditionally, you go to the doctor when you have a headache, a backache, or chest pain. We take a snapshot of your problem, assess it over a very narrow period of time, and then we send even our sickest patients out into a black hole and don't see them for six, eight, or nine weeks. Next-generation healthcare will move us to pre-symptomatic continuous care. To get there, we need to develop a robust assessment of human phenotype – a continuous read-out of our human body. Everything we do minute by minute, day by day, is part of our phenotype. The obvious things, like our blood pressure, our temperature, our respiration, but also our behaviors, our dietary habits – the whole variety of activities that influence the way our body responds to our own genetic makeup and to our environment. We are going to quantitate the human phenotype with four 'P's.

What are the four 'P's?
AUSIELLO: The first is Precision. The second is Perpetual, much more continuous. The third is Perturbable – we need to understand what happens when you

Dr. Dennis A. Ausiello sees next-generation healthcare as a basic sea change in medicine.

get up, when you sleep, when you're angry, when you're sad, when you're eating, when you're not eating, when you're swimming, and so on. The fourth P is for Performance, which means that measurement needs to create data that leads to knowledge that's actionable.

What is the relationship between translational medicine and next-generation healthcare?
AUSIELLO: Most people understand that a discovery pathway occurs in all areas of science – whether it is chemistry, physics, mathematics, or biology. Translating physics into the transistor or translating power into rocket ships, that's translation. But the human organism is enormously more complex than a rocket ship and much more than an engineering problem. Translational medicine means fundamentally understanding complex science that allows us to elucidate pathways in the human organism. These pathways can lead to either our well-being, or our disease, and allow us to say, 'Here's something wrong.' How do we influence what's wrong? It could be a drug, it could be a device, it could be a change in behavior, it could be a change in diet or exercise. That's translational medicine – understanding the science in such a profound way that we can vastly move to doing something about it rather than simply saying these pathways are involved in cancer, multiple sclerosis, or diabetes, but we have no capacity to change human well-being.

How close are we to making leaps from the lab to patient care?
AUSIELLO: Profound changes will occur in this arena in the next twenty-five years. The blue print for understanding is there. The human genome project will influence almost everything we do going forward. On the other hand, without a nuanced understanding of human phenotype, we can't align the understanding that we're garnering from the genotype in ways to make a translational difference. We are striving now with the enormity of the information that we've obtained from the human genome and will use that information to prioritize how we develop drugs and devices that will alter the course of human wellness and disease.

How can we manage the vast amount of data being generated and collected by current research?
AUSIELLO: It becomes absolutely essential that we don't simply accumulate data, but we accumulate data to create knowledge that's actionable. That requires more than just the typical biological approach to understanding problems and involves mathematicians and computational scientists. How we acquire the data, how we store the data, how much we store – these are all very real problems because they are very real costs. At the end of the day, the data needs to be interrogated to provide meaningful, actionable knowledge.

Can phenotypic stratification make clinical trials more efficient and cost-effective? Can it streamline the process of bringing a drug to market?
AUSIELLO: Yes. Discovery pathways for new drugs are costly, and the majority

Dennis Ausiello, MD

Since 1996, Dennis A. Ausiello has been the Chief of Medicine at Massachusetts General Hospital (MGH) and Chief Scientific Officer of Partners HealthCare. He has made a substantial contribution to the knowledge of epithelial biology in the areas of membrane protein trafficking, ion channel regulation, and signal transduction, and published numerous articles, book chapters, and textbooks.
Dr. Ausiello manages a clinical, research, and education budget exceeding US$600 million annually and oversees the training of more than 170 house officers, 500 graduate students and post-doctoral fellows, and medical students. He was also Director of the MD/PhD Program at Harvard Medical School and the Massachusetts Institute of Technology.
Dr. Ausiello was on the Board of Directors of the Broad Institute, an independent partnership of Harvard and MIT faculty working in human genetics, and on the Board of Directors for the nonprofit organization Research!America, the leading advocate group for investment in biomedical research in the United States.

of the cost is in Phase III clinical trials before a drug is approved. In earlier cancer trials, we were only getting fifteen or twenty percent response to a new drug regimen, and then discovered that by working with genetic mutations we could stratify the sub-population and get a ninety percent response. If diabetes falls into five groups and I have a drug that affects only Group One, it becomes obvious that if I populate Group One with those patients I have a much higher chance of understanding whether that drug is successful or not. We're not there yet, but the movement to stratify phenotype and genotype can make drug discovery process less risky – which is important, since today the business model for drug discovery is overwhelmingly against success.

How do cost pressures influence innovation in healthcare?
AUSIELLO: Innovation is always responsive to the environment in which it exists. Nobody wants a drug that is no better than five other drugs that are already on the market, so there is a growing initiative for pharmaceutical companies to be sure that they're first in class, or best in class, and that becomes an even higher and more difficult standard to achieve.

How should industry and academia best work together to fast-track next-generation healthcare?
AUSIELLO: Today, there is more transparency and a growing understanding of the role of collaboration between academy and industry. Unfortunately, we had a generation in which the understanding of the complexity of drug discovery or device discovery was relatively unknown in the academy. Therefore, the pharmaceutical companies or the medical device companies were viewed simply as marketing enterprises – taking 'our' ideas and simply marketing them. Eighty-five percent of the ideas for a drug or device do emanate in the academy out of the work that is funded by the National Institutes of Health and research foundations. But, largely, the translation of ideas developed in the academy is done by the pharmaceutical companies or the device companies, not by the academic research institutions. It is a very complex, very high-risk business. Only one in two hundred of those initiatives are ever successful.

Cost reduction through next-generation healthcare?
AUSIELLO: I'm very cynical about predicting that we can decrease costs with this vision. The proof ultimately will be in the pudding. I truly believe that moving medicine to pre-symptomatic continuous care will allow for transforming our ability to create wellness rather than disease, to prolong wellness rather than cure disease and to prolong the timeframe until you might develop the disease. Controlling costs will not be about the magnetic resonance exam in the last year of life, but the sensor or the diagnostic or the phenotypic analysis earlier in life, about preventing the onset of illness instead of treating the illness. To really improve not just the quality of care but the efficiency and effectiveness of care, we need to build a culture around the physicians and patients as partners in a healthcare plan.

> "Controlling costs will be about preventing the onset of illness instead of treating it."

Dennis A. Ausiello, MD, Chief of Medicine, Massachusetts General Hospital (MGH), Chief Scientific Officer, Partners HealthCare, Boston, Massachusetts, USA

Dr. Ausiello calls for a robust assessment of the human phenotype to create knowledge that is able to change human well-being.

How do you change the culture of medicine to become more patient-centered?
AUSIELLO: My generation has done a very good job of telling patients what we know about a problem and we have done a terrible job of telling what we don't know about a problem – and how patients can help. We need our patients foremost to understand that what they do, what their family does, what their environmental influences are, will be a factor in influencing how we stratify the degree of wellness and disease in patients and in populations of patients.

In the future, do you see patients remotely connected to the healthcare system, putting in data from their homes as they go?
AUSIELLO: I don't see that as a future, I see it happening now. It's not well organized and it is not yet well prioritized. But what information do we really want to know, how do we orchestrate it, how do we accumulate it, and how do we assess this very large amount of data that will now be accumulated? It's a global experiment in the sense that it requires active and passive assessment of information in a much broader scale, in a much more diverse geography than we ever contemplated in medicine before.

How can next-generation healthcare narrow the gap between the Haves and the Have-nots?
AUSIELLO: There is great poverty in the world, yet everyone has a cell phone. In the digitized world we live in today, there are tremendous opportunities to develop better access, better information, and ultimately better quality of care. That kind of intervention will only get more profound as the technology improves. For example, if you walk into a hospital

in rural India, you see one obstetrician observing a hundred to a hundred and fifty women in labor. In nations like the United States, we have exquisite sensitive monitoring systems that can pick out the one in 100 or one in 200 women that is in fetal distress during delivery. We have bands that can monitor fetal heart rate on the computer screen and even one physician can now pick out the one in 100 patients that is in difficulty – working either locally or potentially remotely.

How is the concept of "wellness" evolving?
AUSIELLO: The scientific revolution has allowed us to better understand the qualities of wellness in a more nuanced way, even in a molecular way. We will understand what our genetics contribute to our environment and which behaviors might contribute to making us healthy and well, rather than making us obese, diabetic, or hypertensive. In medicine, we have to change our mandate from talking only about curing a disease to talking about how we move from wellness to disease, how we prevent the movement to illness, or figuring out how we can move back into the wellness column. That becomes an important scientific problem.

Can you speak a little about the CATCH program, the Center for Assessment Technology and Continuous Health that you've developed with the Massachusetts Institute of Technology (MIT) and the Massachusetts General Hospital (MGH) and partnered with Siemens Healthcare?
AUSIELLO: I truly believe that the next great frontier is the quantification of human phenotype. At MIT and MGH, we are building an academic program and partnering with a variety of industry partners because we believe that there is an enormous entrepreneurial opportunity in data acquisition, data analysis, and data interpretation. One of those partners is Siemens. We are building an academic program that can perform in this space of quantified human phenotype. Our pilot project will assess 100,000 diabetics from a genetic point of view and a phenotypic point of view. This research will enable us to learn whether there are sub-populations that will allow for better understanding and management of the disease within those populations. We hope to provide a dashboard for clinicians that will fundamentally change the way we interpret the problems of the disease, the segmentation of the disease, the use of current medications – or the discovery of new medications.

> "In medicine, we have to change our mandate from talking only about curing a disease to talking about how we move from wellness to disease, how we prevent the movement to illness, or how we can move back into the wellness column."
>
> Dennis A. Ausiello, MD, , Chief of Medicine, Massachusetts General Hospital (MGH), Chief Scientific Officer, Partners HealthCare, Boston, Massachusetts, USA

If you had to single out one major change that could improve the quality of healthcare, what would it be?
AUSIELLO: If we can move medicine from episodic symptomatic care – a reactive approach to medicine – to pre-symptomatic continuous care, we will be able to both understand and intervene much earlier, presumably to either prolong the onset of a particular illness or prevent it all together.

Louisa Kasdon *is a Boston-based journalist with more than 500 published articles and books on food, health, science, and business. She is a graduate of Wellesley College, MIT, and the winner of the M.F.K. Prize for Excellence in Culinary Writing.*

Six-year-old Kirill recently underwent surgery to close a ventricular septal defect.

Oleg Pawlowitsch Lukin, MD, and his collegues have their hands full: the facility's 167 beds are always fully occupied.

Matters of the Heart in the Ural Mountains

South of the Ural Mountains, in Chelyabinsk, Russia, a dedicated cardiovascular center opened its doors in early 2011. More than 5,000 surgeries will be performed at the hospital this year. All treatment is free of charge to the patients, who travel great distances – sometimes more than 500 kilometers – to have surgery in Chelyabinsk.

Text: **Diana Laarz** Photos: **Jan Lieske**

Last year, doctors at the Chelyabinsk facility performed heart surgeries on about 80 infants and are willing to handle even more cases if the neonatal intensive care unit is expanded.

Mikhail Affanassyevitch Pavlov's 71-year-old heart is about to fail. The coronary arteries that supply the heart muscle with blood are severly stenosed. A computer screen on the desk shows a black-and-white image of Pavlov's heart; the blood vessels look like a river delta. "Here," says the cardiologist, Andrei Selivyorstov, MD, pointing to a spot where the blood flow is reduced to a minimum. "Here, too. And here." Pavlov needs three bypasses – at least. Selivyorstov explains to him how his ribcage will be opened and his ribs will be bowed apart. Cardiac surgeons will then place bypasses. Pavlov's arms lie calmly on his chair's armrests and his wrinkled, grandfatherly face stays completely motionless. When the doctor finishes his 20-minute explanation, Pavlov says just one sentence, "Well, then, let's get started."

Pavlov is a lucky man, and he knows it. "With his heart in this condition, he would have been in bad shape just a year-and-a-half ago – when patients in Pavlov's home city of Chelyabinsk still had to wait a year or more for a bypass operation. Some of them did not survive the waiting time," says Selivyorstov. But now, Pavlov sits in a treatment room in the newly constructed Clinical Center for Cardiovascular Diseases. "When should I come back?" Pavlov asks. "We'll start in a week," Selivyorstov answers.

A Modern-Day Oasis

Chelyabinsk, south of the Ural Mountains, straddles the boundary between Europe and Asia. The city has a population of just over a million and boasts few tourist attractions, teeming instead with the smoking chimneys of its sprawling industrial areas. Viewed from the air, the landscape of Chelyabinsk is made up of housing complexes in varying shades of gray. But on the western outskirts of the city, behind a grove of birch trees and right on Heroes' Prospect, a major traffic artery, lie the blocky beige buildings of the Chelyabinsk Cardiac Center, like dice thrown down on a green field. It looks like a modern-day oasis.

As part of its National Priority Health Project, the Russian government has installed eleven specialty clinics in recent years in regions of the country that lie far from its major centers of Moscow and Saint Petersburg, one of them in Chelyabinsk. Construction got under way in 2007, and the first cardiac surgery was performed in late January 2011. This year, doctors estimate that they will perform more than 5,000 operations at the center. Its 167 beds are always fully occupied. Treatment at these regional specialty clinics is free – the government in Moscow transfers more than 30 million euros to Chelyabinsk alone each year to ensure it. "Up until a few years ago, we could only dream of having a clinic like this," says Oleg Pavlovich Lukin, MD, the facility's Medical Director, as he sits at his office desk. A carved wooden icon hangs on the wall in the corner, and the computer screen on his desk shows a live close-up from one of the three operating rooms. Lukin is in constant radio contact with the doctors performing the surgery.

Born and raised in Chelyabinsk, Lukin is a man of measured movements with a soothing storyteller's voice. Before being

64-year-old Alexandra Braskina (left) had a bypass surgery six weeks ago and is now planning her future. Magnetic resonance technology from Siemens (right) helped the surgeons to plan the procedure.

offered his current position at the new center, he worked at the district hospital. He is too polite to speak poorly of the conditions at his old job, but his words make one thing very clear: The cardiac center, equipped with state-of-the-art technology, has catapulted the doctors in Chelyabinsk into a new era in medical care. Patients are traveling to the center from the surrounding regions of Siberia, going distances of more than 500 kilometers to receive treatment in Chelyabinsk. "Just a few years ago, many Russian men didn't live to see their 60th birthday," Lukin says. "Now, we are seeing more and more patients who are 70 or older."

Relatively Low Life Expectancy

Demographic change is a fact of life in Russia. The population of about 140 million is shrinking. Researchers expect the figure to decline from the current 141.9 million to fewer than 130 million by the year 2025. Two main factors have contributed to this development. First, after the upheaval of the 1990s, Russian women are having fewer children. Second, life

The National Priority Health Project

Russian President Vladimir Putin initiated the National Priority Health Project in early 2006. The goal of the project is to improve medical care in Russia. Alongside pay raises for doctors and nurses and continuing professional education opportunities for healthcare workers, the project's main area of focus is building state-of-the-art specialty clinics in 15 regions across Russia. The new clinics specialize in cardiac surgery, trauma, orthopedics, or neurosurgery. The first of them was built in Khabarovsk, in the Russian Far East, near the Chinese border. Ten other healthcare centers have been built in the meantime, including the one in Chelyabinsk. The government hopes the cardiac clinics will help reduce mortality due to cardiovascular disease in Russia from 325 cases per 100,000 people to 250. The Russian government has invested more than ten billion euros in the health project to date.

expectancy in Russia is still relatively low, especially among men. At the end of the last millennium, life expectancy was 58.9 years. Now, Russian men live, on average, 64.3 years.
In fact, specialty clinics like the one in Chelyabinsk are designed to improve healthcare and thereby increase life expectancy. Nearly 57 percent of people in Russia die of heart attacks or other cardiovascular diseases, which makes state-of-the-art medical care especially important in remote areas and in industrial cities like Chelyabinsk. The Urals are widely considered an idyllic natural landscape, but in Chelyabinsk itself, factories constantly belch exhaust into the air. The city's metal combines are among the largest in Europe, producing iron alloys, stainless steel, pipes, cranes, tractors, and crawler tractors. The city leaves a gritty coat on the skin, tongue, and eyes in just a short time.

Neonatal Intensive Care Unit

When Lukin strides down the hallways in his hospital, he stops about every five meters to pat a doctor on the shoulder, shake hands with a nurse, and share a few friendly words. Most of the clinic's 700 employees had previously worked at the district hospital, so they have known each other for a long time. They all received extensive cardiology training. The district hospital is now staffed with new employees. Later, Lukin stops in the room leading to the magnetic resonance imaging (MRI) unit to discuss with three other colleagues cardiac MR images of a six-month-old child the clinic has received from a hospital in Orenburg, about 500 kilometers to the southwest. The cardiologists can see from the images that the right ventricle is two to three times larger than the left. But they can't tell the cause from the images sent by the referring institution. The infant has an appointment in Chelyabinsk the next day. The doctors hope that the Siemens MRI unit in the next room will provide more detailed pictures. "The child is near death, and we are the parents' last hope for help," Lukin says. Previously, 90 percent of newborns who had severe congenital heart disease and were too weak to travel to Moscow died. Last year, though, the Chelyabinsk facility successfully performed cardiac surgery in about 80 infants. Lukin hopes to expand the neonatal intensive care unit to handle more cases in the future.

Future Plans: Heart Transplants

As with its neonatal treatment activities, the clinic's other successes are obvious, even just a year-and-a-half after opening. In Chelyabinsk and the surrounding area now, no one has to suffer months of chest pain waiting for a bypass operation or for interventional coronary therapies. The waiting list for cardiac pacemakers is getting shorter, and Lukin believes it will only take another year to get through this massive workload. In a couple of years, he hopes his clinic will also be able to handle heart transplants. "And in as little as one or two years," he says confidently, "the results of our work will be evident in the population statistics for the Ural area." By then, more infants will survive the difficult first few weeks, and people

"Patients had to wait a year or more for a bypass operation. Some of them did not survive the waiting time."

Andrei Selivyorstov, MD,
Clinical Center for Cardiovascular Diseases,
Chelyabinsk, Russia

The Urals are widely considered an idyllic natural landscape, but in the city of Chelyabinsk factories constantly belch exhaust into the air.

Management Summary

Challenge:

- Inadequate medical care for patients with cardiovascular diseases in a sparsely populated region of Russia
- Wait times of up to two years for cardiac surgery
- Medical technology below current standards
- Low life expectancy, especially among men

Solution:

- Construction of a regional clinic and medical center for cardiovascular disease
- Center equipped with medical technology from Siemens
- Treatment offered free of charge to all Russian citizens
- Cooperation with hospitals in surrounding areas

Result:

- More than 5,000 operations each year
- Wait times for bypass and coronary interventions eliminated
- Wait time for placement of cardiac pacemakers shortened to a few months
- About 80 life-saving cardiac surgeries performed on infants with severe congenital heart disease each year
- Higher life expectancy in the Ural region

will get older thanks to a bypass, stent, or pacemaker from Chelyabinsk.

No patient ever looks forward to going to the hospital. But the people in the hallways of the cardiac clinic here on the outskirts of Chelyabinsk truly value this center, especially because it is so different from many public clinics in Russia. The corridors are painted bright, cheerful shades of yellow, there are comfortable sofas in waiting areas, and the overall mood is calm, focused, and yet also relaxed.

Take, for example, 64-year-old Alexandra Braskina, who sits on the bed in her room, six weeks after her bypass surgery, cheeks rouged, and smiles as she talks about her plans to grow tomatoes in her garden again soon. Or six-year-old Kirill, who underwent surgery to close a tiny hole in the wall of his heart. When his doctor comes to the door, he shouts happily and flings himself at her with open arms. Vladimir Feoktistov, 61 and also a bypass patient, waits for the car that is coming to pick him up and drive him home. His grandchildren are waiting for him, and Feoktistov wants to play with them again. Every one of these patients has already benefited from the cardiac center in Chelyabinsk. For Mikhail Affanassyevitch Pavlov, who just learned today that he will have surgery soon, the hardest part still lies ahead. But from the way he leans casually against the reception counter, waiting for his papers, he doesn't look overcome by fear. "No point," he says. "I just have to get through this, and then everything will be fine."

It is already evening when Lukin hears of the arrival of two new patients. Both are slightly over 50. Both are right on the verge of a heart attack. Should they wait until the next day? A brief word with the head of the radiology unit and Lukin has made his decision. The catheter labs are prepared again. That night, the doctors at the cardiac center in Chelyabinsk work until three o'clock in the morning.

Diana Laarz *is a correspondent in Moscow. She has been a journalist since 2006, writing reports for various German-language magazines and journals.*

Further Information

www.siemens.com/cardiology

An Ambitious Project in a Difficult Setting

State-of-the-art equipment, highly qualified staff, a pleasant environment, and efficient cost control – that's the recipe the brand new private hospital Sofiamed is using to successfully establish itself on the market in the Bulgarian capital. It's a tough environment. Patients with supplementary insurance or self-payers are very limited, so the majority of financing has to come from general health insurance.

Text: **Rudolf Hermann** Photos: **Eugenia Maximova**

Boyko Penkov, MD, MBA, reaches for a pen and paper, and with a sweeping gesture, he sketches three concentric circles on the page. "The big circle represents what we would all like to get, ideally, from our healthcare," he explains. "The smallest circle shows what we can realistically expect in fact at a given time. And the middle circle is what would be possible if the available money circulating in our healthcare system were truly disbursed on target and sensibly."

Penkov sits in the sober, but state-of-the-art office of the Medical Director at the Sofiamed hospital. The brand new building is located on Georgy M. Dimitrov Boulevard, a short distance outside the city center of the Bulgarian capital, Sofia. The shelves in his office seem to be filling hesitantly, a sign that Penkov – who is not only the hospital's Medical Director, but also its Managing Director – has not been here long. And in fact, the hospital has only been operating for a few months.

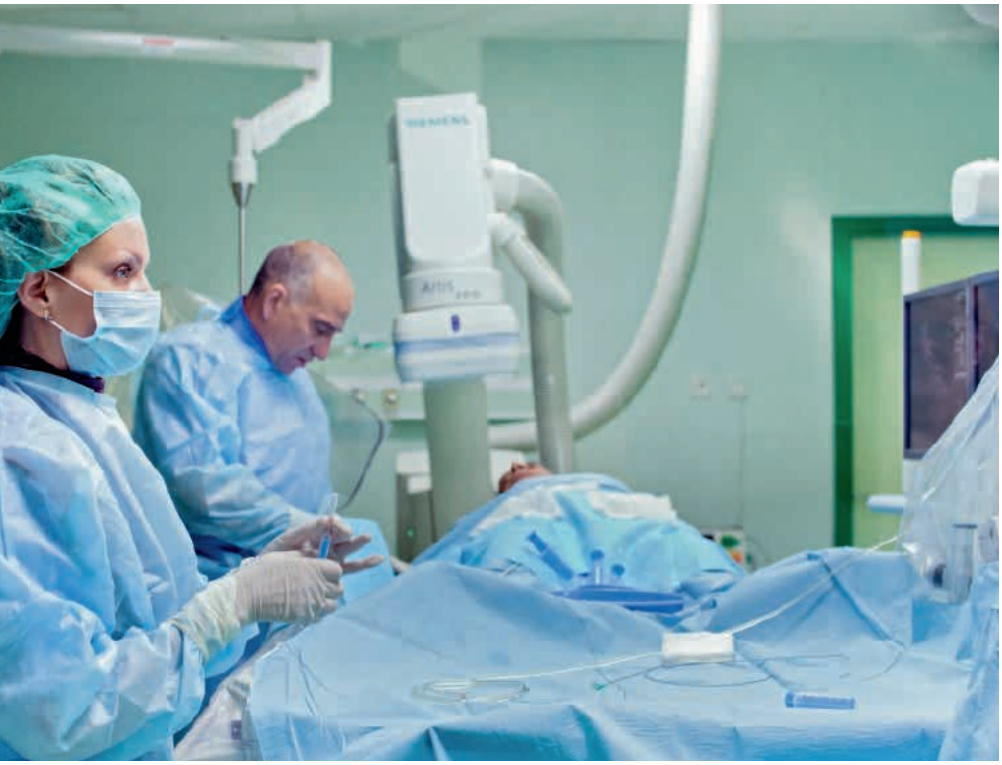
With its 440 beds, the Sofiamed hospital is one of the largest private investments ever made in the Bulgarian healthcare sector. Its sponsor, the pharmaceutical company Bulpharma, which already operates smaller hospitals in the city of Pazardjik and other small towns on the

Dr. Boyko Penkov sketches a healthcare system where the available money is truly disbursed on target and sensibly.

Thracian Plain, was thus able to make the leap into the capital city. Health Minister Desislava Atanasova, the head of the country's National Health Insurance Fund, Plamen Tsekov, and other prominent figures from the fields of healthcare and healthcare policy attended the festivities to celebrate the hospital's opening. According to a notice published by the agency InvestBulgaria, the hospital required an investment of about 35 million leva (17.5 million euros). Sofiamed's 14 units are state-of-the-art in terms of equipment. Siemens Healthcare played a major role in supplying the medical equipment, providing ten systems to four departments. The flagships in radiology are a MAGNETOM® ESSENZA magnetic resonance imaging (MRI) unit and a SOMATOM® Emotion computed tomography system. The cardiology department is home to an Artis zee®, an angiography system used for cardiac examinations and percutaneous coronary interventions (PCI). CARE dose saving technology features a broad range of applications helping to reduce radiation dose to staff and patients while CLEAR image processing software takes care of optimizing image quality. And, two mobile X-ray stations, a SIREMOBIL Compact L C-arm system for the orthopedics department, radiography and fluoroscopy equipment, and an ACUSON® X300™ ultrasound system complete the range of Sofiamed's Siemens equipment. "Recently, we have been seeing a tendency for hospitals to buy high-end new equipment," says Todor Vodenicharov of Siemens Bulgaria. "That's a change from just a couple of years ago, when it was more common for hospitals to look for equipment secondhand."

The Pull of the West

So what was the main factor in Sofiamed's decision to purchase its imaging equipment mainly from Siemens? The team



Sofiamed's cardiology department features an Artis zee angiography system.

> "Ninety percent of our income comes from the public health insurance fund."
>
> Boyko Penkov, MD, MBA,
> Medical Director and Managing Director,
> Sofiamed, Sofia, Bulgaria

sought advice from radiology experts at the military hospital in Sofia, a leading government-run healthcare institution, explains Medical Director Penkov, and they recommended Siemens. Various people have been happy about the choice, including Plamen Chupetlovski, MD, who is working at the Diagnostic Imaging department at Sofiamed. He worked with systems from Siemens at his previous job, he says, so he is very familiar with them. As reasons for the shift to Sofiamed, Chupetlovski cites the hospital's excellent equipment and the prospects it offers. At the same time, though, he points out that these days, it is easier to bring in high-quality equipment than well-trained staff members who are also able to operate the modern units properly. Young specialists in particular tend to leave the country for the West if they have learned Western foreign languages in school, but hospitals like Sofiamed are changing this negative trend. Besides, Chupetlovski himself is part of the generation that had to learn Russian; moving away is out of the question for him. He did, however, take the opportunity to move, after years as a military emergency physician, to a position with less exposure to stress and more pleasant working conditions.

The equipment at the Sofiamed hospital is state-of-the-art, the atmosphere is friendly, the building spick and span, and staff members praise their above-average pay and other conditions. Nevertheless, patients look just the same as in government-run hospitals. And with good reason: The private healthcare sector in Bulgaria is rudimentary at best. The vast majority of patients get their insurance through the government health insurance fund, with which Sofiamed, like other institutions, has a contract. "Ninety percent of our income comes from the public health insurance fund," Penkov says. "The other ten percent is divided between services that are covered by private supplementary insurance plans or that patients pay for themselves."

Free healthcare illusory

As in most former socialist countries in Eastern and Central Europe, the people of Bulgaria still tend to take the stance that the state is obligated to offer its citizens comprehensive healthcare free of charge. This is becoming appreciably more difficult today. Treatment methods, medications, and equipment are increasingly better, but also increasingly more expensive, making free healthcare an illusion. During the transition period from socialism to democracy, to receive not only basic care but also more specialized care, patients often paid under the table for services. This distasteful practice is still present in healthcare today. Experts estimate that "informal" payments make up a significant minority share of the money circulating in the healthcare system. But politicians of all stripes consider it daring to question the mythos of the egalitarian, free healthcare system and to offer the Bulgarian people more freedom to choose through optional supplementary insurance plans, since it would mean a step toward inequality.

A Practical Test

In this environment, Penkov considers himself and Sofiamed to be facing a major challenge: lead a privately financed

hospital with top-quality equipment in a healthcare system where those with supplementary insurance and self-payers make up only a tiny segment, thus offering few opportunities to generate revenue that could be used to finance higher standards. It's not an easy job. In fact, Penkov says Sofiamed has to generate its income primarily through patient figures and capacity utilization. One might think that people would be happy to go to a friendly, new, well-equipped private hospital if their health plan handles the payment. But Penkov notes that Bulgarians in general are not very willing to shift medical environments, if in fact they go to the doctor at all.

This is where Michaela Yurieva comes in, as the person responsible for the hospital's marketing department. "I'm not a fan of aggressive advertising methods," she says. "Hospitals should be discreet in their public image." To Yurieva, the best form of advertising is a satisfied patient: "Someone who has been treated well and felt comfortable will tell others about it." The hospital holds open house events and special promotions offering free check-ups to help potential patients overcome their misgivings about the new facility. It's a reasonable approach that was spectacularly successful for one patient in particular. One day, when the cardiology unit at Sofiamed was offering its services free of charge, a patient interested in preventive care had to be taken right from the doctor's office to the cath lab because he suffered from a sudden heart attack.

Patient Loyalty and Cost Control

To secure its business success, Sofiamed has to be able to win patients' long-term loyalty. It is a challenging task, exacerbated by the fact that, according to experts, there is a surplus of available hospital beds in the Bulgarian capital, so patients are free to choose their hospital. Penkov believes the most fruitful approach will involve not only highly qualified medical staff and state-of-the-art equipment, but also efficient cost controls. "A public hospital of a similar size would probably have an administrative staff of around 100, but we get by with 15," he says with some pride.

What Penkov would like to see from the government and politicians is equality between private and public hospitals. The privately financed sector, he says, still has to face a certain level of mistrust in some segments of the population and in the political sphere. But what the country's healthcare system needs is the development of a national priority strategy, not political trench warfare. "If we can manage that," he says, picking the sketch of the three circles up again, "then we will be able to leave the smallest circle behind and offer our patients a better healthcare system."

Rudolf Hermann *is a journalist based in Prague with years of experience regarding political and economic developments in Central and Eastern Europe.*

Management Summary

Challenge:

- Establish a top-quality private hospital in a healthcare market financed largely through the public healthcare fund, with only a very small sector of self-payers and those with supplementary insurance

Solution:

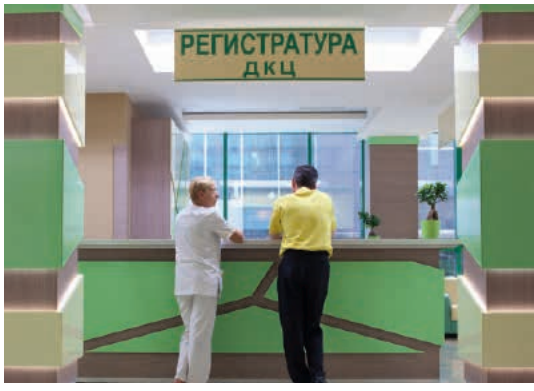
- Top quality in terms of equipment, medical services, and overall service to distinguish the facility from competitors
- Efficient cost controls so that better services can be offered at lower cost
- Create an appealing working environment to attract top staff members

Result:

- General hospital with a broad range of services offered at a high level, but one that still has to achieve success on the market

Further Information

www.siemens.com/healthcare



State-of-the-art equipment, a pleasant environment and friendly, highly qualified staff are key elements of Sofiamed's business strategy.

Heart Nirvana

Where is the best cardiac care in the world? A major academic or research center? The home of the first heart transplant? Excellent guesses, but when it comes to diagnosing acute coronary syndrome, the honor just may belong to a not-for-profit community hospital in a small urban area in the U.S. heartland.

By Diana Smith

At the regional Mercy Medical Center, 90 percent of STEMI patients receive catheterization in less than 90 minutes.

> "When we started the Emergency Chest Pain Center, we looked at the data and the research and decided on Troponin-I."
>
> Frank J. Kaeberlein, MD,
> Medical Director, Emergency Department,
> Co-Director, Emergency Chest Pain Center,
> Mercy Medical Center, Canton, Ohio, USA

Mercy Medical Center, a 476-bed regional facility in Canton, Ohio, USA, has been at the forefront of door-to-reperfusion time in ST-elevation myocardial infarction (STEMI) patients for ten years and currently has its fastest door-to-balloon time ever – a blazing seven minutes. According to Mercy's internal studies, ninety percent of patients receive catheterization in less than 90 minutes, with nearly 10 percent in 15 minutes or less.

A 114-Year Legacy

With about 75,000 residents, Canton may seem an unlikely location for a world-class cardiac care facility. The city is the birthplace of American professional football and the National Football League (NFL) Pro Football Hall of Fame and the National First Ladies Library and Research Center. The William McKinley Presidential Library/National Monument is also located in Canton.

But Canton also has a long legacy of compassionate, quality healthcare. The original Mercy Hospital, which was located in President McKinley's former home, opened in 1908 with 18 beds. In 1952, a new 68-bed facility was built on 30 acres of donated land. Since then, it has undergone building additions three times.

Mercy Hospital became Mercy Medical Center in 1979, and today Mercy continues its mission, serving five counties in Northern Ohio with 620 medical staff members and 2,500 employees.

Cardiac services have long been an important focus at Mercy. According to HealthGrades, an independent healthcare rating organization, Mercy Medical Center ranks in the top five percent of hospitals nationally for overall cardiac care, cardiology services, and coronary interventional procedures, and first in the state of Ohio, an ultra-competitive environment with the greatest percentage of best-performing hospitals of all states.

Recognized among the top 50 heart hospitals in the country for five years in a row by Thomson Reuters, Mercy has pioneered a number of innovative, life-saving protocols in coronary interventional procedures. It installed the country's first and only fixed catheterization laboratory in an emergency department, mere steps away from the ambulance bay and emergency room (ER) entrance.

Additionally, the hospital, operated by the Catholic Sisters of Charity Health System, implemented the country's first-ever accredited Chest Pain Center relying on Troponin-I as the biomarker of choice. Remarkably, the hospital did it in 1998 – years before Troponin was recognized as the preferred biomarker in acute myocardial infarction. Now, three Siemens Stratus® CS Acute Care™ Diagnostic Systems analyze high-sensitivity[1] Troponin-I for approximately 1,800 patients per month in the ER.

Time is Muscle

"Nowhere is time more essential than when a patient enters an emergency department with a myocardial infarction

[1] High-sensitivity as defined by the joint ESC/ACC committee as an imprecision level of 10% at the 99th percentile of a normal population.

Cardiovascular Disease in the U.S.

How many people in the U.S. have cardiovascular disease?
Almost 50 percent (49.7 percent) of U.S. adults aged 20 or older (an estimated 107.3 million persons) have at least one of three risk factors for CVD – uncontrolled hypertension, high cholesterol level (LDL), and current smoking.[1] An estimated 1 in 3 American adults (83 million) live with some type of cardiovascular disease.[2] One in three (approx. 800,000) deaths reported each year in the U.S. are the result of cardiovascular disease. And in the U.S., heart disease is the leading cause of death for most ethnicities.

What is the most common cardiovascular disease?
Coronary heart disease is the most common type of heart disease. In 2008, more than 400,000 people died from coronary heart disease.[3]

What proportion of health expenditure goes toward cardiovascular diseases?
In 2010, total cost of cardiovascular disease was estimated at USD $444 billion. Treatment accounted for about USD $1 of every USD $6 spent in the U.S.[4]

[1] http://www.cdc.gov/mmwr. Million Hearts: Strategies to Reduce the Prevalence of Leading Cardiovascular Disease Risk Factors – United States, 2011. Last accessed May 22, 2012.
[2] http://www.cdc.gov/chronicdisease/resources/publications/AAG/dhdsp.htm. Last accessed May 22, 2012.
[3] http://www.cdc.gov/HeartDisease/facts.htm. Last accessed May 22, 2012.
[4] http://www.cdc.gov/chronicdisease/resources/publications/AAG/dhdsp.htm. Last accessed May 22, 2012.

Global Challenge: Better Outcomes, Cost-Efficient Care

Sandra Sieck, one of the USA's top experts on healthcare business reform and Chief Operating Officer of the Society of Chest Pain Centers, has worked with thousands of hospitals to optimize clinical and financial outcomes. She says, "In the 21st century, health is a shared responsibility, involving equitable access to essential care and collective defense against the evolution of chronic conditions."

According to Sieck, all stakeholders must take responsibility, with a focus on three endpoints:

- Increase quality
- Decrease cost
- Increase patient satisfaction

To achieve these goals, many hospitals are focusing on internationally accepted medical guidelines and key technology. "Delivering quality care while lowering costs exists both within the USA and other healthcare markets," Sieck says. "Governments are seeking care processes based upon proven outcomes and are pursuing improvement initiatives based upon science and best practice." France, Italy, and Spain rank first, second, and seventh for quality of care, access, equity, healthy lives, and health expenditure per capita. Japan is 10th, Switzerland is 20th and Germany is ranked 25th. The USA is listed 37th.

Sieck adds that several other countries have emerged as adopters of good clinical practices. "China, for example, is experiencing an aging population and is addressing the development of a better delivery of healthcare services in its Five-Year Plan. In India, healthcare is one of the nation's largest sectors in terms of both revenue and employment due to its increasing population and expanding middle class. The growing elderly population is placing an enormous burden on India's healthcare infrastructure." However, she says, "An aging population is a global challenge."

All countries are reviewing the business of healthcare for a greater value proposition for the dollar, explains Sieck. But in the U.S., value-based purchasing, implemented under the Patient Protection and Affordable Care Act, is expected to be a major driver of fundamental, widespread change. Value-based purchasing demands that identified patient populations receive specific medical and clinical tests and treatment in accordance with professionally recognized standards of healthcare to assure reimbursement. Through this program, the Centers for Medicare and Medicaid (CMS) will reward hospitals that provide high-quality care and deliver standardized, comparative, and transparent information on patient outcomes, healthcare status, patient satisfaction, and costs of services provided.

To be successful under value-based purchasing, hospitals must make operational improvements, which will affect quality, care, and economic outcomes, including:

- Faster time to decision – turning results quicker from diagnostic order to treatment decision
- Improved asset and resource utilization
- Reduced length of stay without incurring compliance issues or negative patient outcomes
- Fewer admissions for unnecessary chest pain rule-out

or heart attack," says Frank J. Kaeberlein, MD, Medical Director of the Mercy Emergency Department and Co-Director of Mercy's Emergency Chest Pain Center. It's a race against the clock to perform the right intervention, as an estimated 85 percent of heart damage occurs within the first two hours of a heart attack, and even minutes without intervention can trigger irreparable heart damage. That was the driving force to create a Chest Pain Center, Kaeberlein explains. "The old adage 'time is muscle' is really true. Our goals were to rapidly treat heart attack patients when they came in and to rapidly, efficiently, and safely evaluate all the other patients with chest pain to provide the best, fastest care we could for our patients."

The majority of cardiac patients who arrive at the hospital's busy emergency department are not classified as full-blown STEMI from an electrocardiogram. Yet, for these patients, time is just as critical. In these non-STEMI cases, standard protocol calls for cardiac biochemical marker testing, which requires that blood be drawn and evaluated for chemical indicators that show if a heart attack has occurred. At Mercy, this means a high-sensitivity Troponin-I test. "When heart cells die, they release Troponin into the bloodstream," explains Kaeberlein, "so elevated Troponin is a good indicator of heart attack. When we started the Emergency Chest Pain Center, we looked at the data and the research and decided on Troponin-I. We also decided on point-of-care testing. We realized early on that to identify heart attack, obviously you have to do the tests for that up-front," comments Kaeberlein. "In terms of walk-in patients, we've done EKGs at triage for many years. We also started doing Troponin at cardiac triage."

Fast, Seamless Results

The benefits for patients are many, according to Mary Ann Burich-Boccia, MBA, MT (ASCP) SBB, Administrative Director, Pathol-

ogy and Laboratory Medicine at Mercy Medical Center. "Having the Stratus analyzers in the ER cuts down the time factor for results significantly," she says. "A trained phlebotomist or nurse can draw the blood for testing, label the sample, walk over, and put it on the instrument – all in the ER." Results are usually back in 14 to 17 minutes. Doing all of this in one place also means fewer handoffs, minimizing errors and increasing efficiency and cost-effectiveness, adds Burich-Boccia.

Claudia Wilkins, MT (ASC), a 35-year laboratory veteran, has responsibility for training operators at Mercy Medical Center on the Stratus system. "There are about 100 people – phlebotomists and nurses – who can use the system," she says. "There is no pipetting, and the ease of use and the consistency are big factors why we chose the Stratus. The volume and pace of work have significantly increased in the ER and elsewhere in the hospital, so it is crucial to have a system that is efficient, and located where you need it."

Kaeberlein says that Mercy's lab deserves a lot of credit. "Labs are concerned about compliance issues and CLIA [Clinical Laboratory Improvement Amendments] regulations and those kinds of things," he notes. "The people in our lab here, to their credit, were willing to try point-of-care testing along with us."

Twenty years ago, Mercy's ER was seeing 35,000 patients a year, reports Kaeberlein, adding, "This past year, we saw 65,000. In addition, patients are older and sicker and have multiple problems and multiple medications. We are seeing many more complex cases than we did two decades ago. So it is really important to be efficient in evaluating patients. That has always been a priority for us. You have to get patients through quickly, but also safely."

Thanks to its innovative, dedicated ER cath lab, groundbreaking protocols and cutting-edge equipment, Mercy Medical Center has catapulted itself into the position of being a global leader in diagnosing acute coronary syndrome. "It's obviously nice to work in a place where we provide state-of-the-art care," says Kaeberlein. "When I hire doctors, I say my emergency department is not nirvana, but for treating heart attacks and chest pain, it kind of is."

***Diana Smith** is a freelance medical writer based in Liberty Hill, Texas, USA.*

Three Stratus CS Acute Care Diagnostic Systems analyze Troponin-I for approximately 1,800 patients per month in Mercy's ER.

"Having the Stratus analyzers in the ER cuts down the time factor for results significantly."

Mary Ann Burich-Boccia, MBA, MT (ASCP) SBB, Administrative Director, Pathology and Laboratory Medicine, Mercy Medical Center, Canton, Ohio, USA

Management Summary

Challenge:

- Optimize solutions for patients with chest pain or atypical MI symptoms
- Obtain fast, precise Troponin-I biomarker measurements to supplement ECG and other findings
- Allow for better risk stratification of patients who present with chest pain in the emergency department

Solution:

- Installing point-of-care Stratus CS analyzers with high-sensitivity Troponin-I in the emergency department
- Cross-train nurses and lab personnel to use equipment
- Establish protocol for use of the systems that support best patient care and clinical workflow

Result:

- Troponin-I analyzed by Stratus CS systems right in the ER
- Accurate diagnoses and fast intervention
- State-of-the art care in Emergency Chest Pain Center
- Outstanding experience in cardiac management provided as standard for physicians and hospitals worldwide

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.

Further Information

www.siemens.com/stratus

Searching the Brain's Pathways for Autism Clues

Years of research are beginning to pay off at The Children's Hospital of Philadelphia, where scientists are unlocking the secrets of a global autism epidemic.

Article by: **Ron French** Photos by: **Scott Lewis**

The Children's Hospital of Philadelphia uses MRI techniques to reveal the connections in the brain's wiring.

Timothy Roberts, PhD, works in the middle of an epidemic. In the 20 years the researcher has studied autism, the diagnosis rate among children in the United States has risen from one in 1,000 to one in 88. No one is sure of the cause, how to prevent it, or how to treat it.
Some of the answers may come at The Children's Hospital of Philadelphia (CHOP), where Roberts and his peers are conducting cutting-edge research on the often debilitating spectrum of brain disorders, aided by Siemens scanning technology. There, leaders in the field of autism research are looking for clues in the wiring of the brain that they hope will shed light on one of modern medicine's darkest secrets: the cause of – and possible cure for – autism.

Many Disorders, Few Answers

Autism, a set of brain disorders that affect a child's social and behavioral development, is typically diagnosed when a child is between two and five years old. Symptoms range across a wide spectrum, from severe communication disabilities and repetitive movements, to social awkwardness. Boys are about five times more likely to be diagnosed with autism than girls, according to a study by the Centers for Disease Control and Prevention. That same study found that white children are slightly more likely to develop autism than black and Hispanic children.

Children in other developed countries have rates similar to that of the USA, with some variation for cultural differences in what behaviors are within the autism spectrum, says Roberts, who is Vice Chair of Research in the Department of Radiology and part of the Center for Autism Research at CHOP. "These children and young adults have difficulty maintaining social interactions," Roberts says. "Sometimes they don't get social cues; sometimes they don't feel comfortable in social situations. That's probably the most devastating area."
Also devastating is the rising number of diagnoses. "It does seem like an epidemic," Roberts says. "In fairness, awareness in 2012 is much greater than it was five years ago, and certainly greater than 10 years ago. Many cases were being missed in the past. Today, parents are more informed, and primary physicians are more informed."
In addition, the diagnostic category has been broadened beyond the "classic autism" of repetitive movements and severe communication problems. "It's likely you're going to get more cases, just because you have a broader definition," Roberts says. "And yet, those two factors alone cannot account for the prevalence figure of one in 88 [when it used to be one in 1,000]," Roberts says. "There is a real biological basis to the growth as well."

Timothy Roberts, PhD, is conducting research on the cause and possible cure for autism, aided by Siemens scanning technology.

The nature of that biological basis continues to be a daunting challenge for researchers. What we know is that autism results from a complex interaction of genetics and environment. "It's not a single gene," Roberts explained. "There maybe 10 or more genes that have to interact, and even then, they may require an environmental trigger. So you need the genetic predisposition and the environmental trigger."

Complicating the research is the fact that autism is an umbrella term covering various disorders with different behavioral manifestations and, likely, causes. In some rare cases, autistic children are able to accomplish mental feats that few "normal" people can. "It's not inconceivable that some will function better, in some niche way," Roberts says. "They may have [brain] connections that may be absolutely optimal for remembering 24-digit numbers, something the rest of us can't do."

A recent study published in *Intelligence* magazine found that eight prodigies in music, art, and math scored high in autistic traits, most notably a stunning attention to detail. "It's all a question of degree," Roberts says. "Autism is a big mystery. It's a very heterogeneous disorder."

Searching for Commonalities

While the behaviors of autistic children are different, Roberts theorizes that there are commonalities deep in the brain. "There might be a fundamental enough level of abnormal conductivity that there will be common features that unite these children," he explains. Find that commonality, and doctors can begin the search for treatments that go beyond the behavioral treatment of today.

Roberts' research looks for those commonalities in the wiring of the brain, particularly the pathways for sound. He says the brains of eight of every 10 autistic children respond to sound about one-hundredth of a second later than the brains of non-autistic children. In a casual conversation, autistic children's brains may be ten words behind. "These delays add up and cascade," Roberts says. "Suddenly, conversations become complex."

Not only does the research indicate a possible reason for the communication problems of many autistic children, but it could be used as a biomarker to diagnose autism at an earlier age. That's important, because behavioral therapies for autism are more effective the earlier they begin, Roberts says.

To help with diagnosis, researchers at CHOP use diffusion magnetic resonance imaging (MRI) to map the white matter of the brain, and magnetoencephalography (MEG) technology to map the electrical activity in the brain.

"This is a very difficult problem that warrants a multimodal approach," Roberts says. "No single modality will have the answer here. We know the delay is coming from the auditory cortex, and that's where the MRI helps out. The source of the magnetic field can be identified in an anatomic context, so that's the way that MRI and MEG get fused."

Roberts uses a Siemens MAGNETOM® Verio, a 3T system he credits with giving him the ability to reveal the quality of connections in the brain's wiring. "The MRI is very good at various types of diffusion imaging," he says. "MRI is an awesome technique."

The second piece of technology, the MEG, allows researchers to record brain activity in real-time, in millisecond time scale. Looking something like a 1950s hair dryer, the MEG essentially measures the electrical current given off by nerve cells with every thought and feeling. "We have a helmet full of these magnetic field detectors, able to pick up spatial and temporal representation of brain function," Roberts explains.

The Ideal Combination: Therapy and Imaging

It's a slow process, frustratingly so for parents looking for help for their kids. But work like that being done in Philadelphia is offering glimmers of hope. And much of that hope is predicated on scanning technology.

Beyond using imaging equipment to diagnose autism earlier, systems such as MAGNETOM Verio could be used to help determine the effectiveness of behavioral and pharmaceutical therapies.

Behavioral therapy "probably needs to be done hand-in-hand with imaging so we can watch brain reorganization and teach the teachers, in a sense," Roberts

"Autism is a big mystery. It's a very heterogeneous disorder."

Timothy Roberts, PhD,
Department of Radiology and Center for Autism Research,
The Children's Hospital of Philadelphia,
Philadelphia, U.S.

Roberts and his collegaues at CHOP use diffusion MRI to map the white matter of the brain, and magnetoencephalography (MEG) technology to map the electrical activity in the brain of autism patients.

says. "There are wonderful practitioners who are doing wonderful things with these children, but there's no way to determine what is going on inside the brain, so there's no way to tell whether what you're doing is having an impact inside the brain or whether what you're doing is a waste of time." In the same way, imaging will likely play an important role in clinical trials of autism drugs, both determining their effectiveness more quickly, and screening patients to find those who are most likely to benefit. Roberts predicts that several kinds of drug treatments for autism will be available in the next 10 to 15 years, and imaging likely will be used to help determine which drugs will help which patients. For now, he says, "Parents need to recognize signs of atypical behavior earlier. There are signs that could be picked up as early as nine to 12 months." One common trait is a child not turning his head when a parent calls his name. "Most children respond to their name being called," Roberts says, adding that oftentimes, parents can tell from videos of one-year birthday parties if the child isn't interacting with other children. "If you have an early suspicion, then you should have more thorough testing and have the diagnosis confirmed," Roberts urges, "while the brain is still more able to adapt."

***Ron French** is senior writer at* Bridge *magazine, where he writes extensively on healthcare. He lives in Okemos, Michigan, USA.*

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.

Further Information

www.siemens.com/verio

Management Summary

Challenge:

- Diagnosis of autism spectrum disorder reaching epidemic scale with little understanding of cause or treatment
- Difficulty finding common abnormalities in the brain tying autism patients together

Solution:

- Use of MAGNETOM Verio to give researchers the best views yet of white matter connections in the brain through diffusion MRI
- Using MRI images merged with MEG to show whether patients have a delay in processing sound

Result:

- Hope for the first autism biomarker, which could be used for early detection of the brain disorder
- Potential use in development of behavioral and pharmaceutical therapies for autism

Evolution in Medical Technology: From the Lab to the Patient Bed

The RAPIDPoint 500 system from Siemens expands opportunities for rapid analysis of critical blood values right where the patient is – providing an advance in point-of-care testing in emergency and intensive medicine.

Text: **Frank A. Miltner** Photos: **Detlef Schneider**

A whopping ten million dollars is supposed to go to the first person who develops a mobile device that can diagnose patients with the same accuracy as a panel of doctors. Visionary Peter Diamandis, head of the X PRIZE Foundation, considers the miniaturization of portable medical analysis to be one of the most important technological development goals of the present day. This little wonder device takes its example from the screen: the "medical tricorder" from Star Trek, used in the hit series by the chief medical officer of the USS Enterprise, Dr. Leonard McCoy. The futuristic diagnostic tool, about the size of a portable CD player and equipped with a vigorously blinking light, gained a cult following among fans of science fiction. In fact, this futuristic idea born in the 1960s, like so many others, offers a fascinating vision for medicine: A miniaturized sensor system that takes just seconds to analyze all of a person's vital parameters, including health status and medical issues, noninvasively.

A Simple Principle: Point-of-Care Testing

The X PRIZE Foundation plans to decide about the prize in 2015. "There definitely won't be a tricorder by then, but evolution is moving in that direction," says Professor Peter B. Luppa, MD, from Munich, Germany. He is one of the world's foremost experts on point-of-care testing (POCT). The principle behind it is simple: Analyses no longer take place in the traditional manner, in a lab only, but as close as possible to where the patient actually is, whether that is in a hospital ward, at the bedside, at the scene of an accident, or even at home, as with home pregnancy and blood glucose tests that are now widely available. POCT is especially complex, and relevant, in intensive care units, where medical professionals deal with patients in emergency situations and critical, life-threatening conditions. The crucial advantage: saving valuable time – time that can make the difference between life and death.

The Next Generation

POCT technology continues to evolve. Dr. Luppa has listened to fellow experts discussing this field and noted a few trends:

- **Accessibility:** POCT technology is destined for use in countries with less highly developed healthcare systems. Blood gas measurement, in particular, is an important tool for doctors dealing with infectious tropical diseases. Here too, systems with zero maintenance requirements are ideal. The devices should, however, also be capable of operation independent of the electrical supply; battery operation should be an option.
- **Measurement parameters:** Doctors analyzing blood gases in intensive medicine also want albumin, phosphate, and magnesium measurements as parameters at the point of care. That would make it possible to measure the strong ion gap, which defines more complex disruptions of the acid-base balance.
- **Online training:** Siemens has just launched an e-learning system to enable automated online staff re-certification. This would be a helpful tool for the POCT coordinator.
- **Specific devices and miniaturization:** In blood gas measurement, there is a trend toward differentiation between a single, large, all-in-one device capable of reading an increasing number of parameters, and multiple additional small devices tailored specifically to certain areas of use. This will also enable miniaturization.

"Every analysis performed at the point of care frees up time the staff would have to spend on the logistics of getting a sample to the central lab and back."

Professor Peter B. Luppa, MD, Head of the Central Lab,
Technische Universität München (TUM), Germany

A Clear Clinical Advantage: Lactate Measurement at the Point of Care

To Professor Manfred Blobner, MD, lactate testing is an important task for patient admission.

Interview with Professor Manfred Blobner, MD, senior physician of the Anesthesiology Clinic at the Klinikum rechts der Isar, TUM, Germany. He works primarily with patients in anesthesia and intensive care.

Professor Blobner, how important is fast lactate measurement in intensive medicine, right at the point of care?
BLOBNER: For us, it is a critical parameter that we regularly apply when admitting patients, especially those with critical conditions. Depending on how the initial results turn out and how sick the patient is, you might have to take follow-up measurements frequently.

Is lactate measurement at the point of care standard today?
BLOBNER: No, unfortunately not. There are still many hospitals where lactate measurement at the point of care is not possible.

Who performs the blood analyses?
BLOBNER: Usually the nursing staff, sometimes the doctor. In general, doctors only order the test, and practically two minutes later they have the results printed out in their hands. That also saves time for the caregiver, who otherwise would have to fill out a lab request form and put it in our pneumatic tube system or order transportation service to the central lab. Now, the patient's ID data is just scanned with a bar code, the patient's data is accessible, and after the rapid blood gas analysis, the measurement values are put into the electronic information system right away. It's definitely very convenient.

What can you tell from the lactate value?
BLOBNER: The value is not very specific, by which a high lactate plasma concentration indicates a problem with the patient's microcirculation, but the reverse is not the case. A low-to-normal lactate value does not, of course, indicate that the patient is healthy. Still, it is essential, since the lactate value helps us identify which of our patients require further treatment. You might say it draws our focus to certain patients. Lactate clearance, meaning how quickly a patient clears lactate from his body, is also becoming increasingly important. In this case, repeat measurements are crucial.

How does clearance take place?
BLOBNER: It occurs when we clear up the patient's underlying medical condition, which means the lactate plasma concentration is a good parameter for assessing the patient's overall condition.

Can you rely on the measurements?
BLOBNER: Yes, completely. Although we are physically moving further and further away from the central lab, point-of-care measurement has never been as accurate as it is today. And that, by the way, is also a fundamental quality requirement set by the German Medical Association ("RiliBÄK"). The effect is highly desirable: Because the system is connected online and offers remote control by the POCT coordinator in the central lab, we can rely on the devices – and focus our attention on the critically ill patients.

Dr. Luppa is responsible for the central lab of the Klinikum rechts der Isar, Technische Universität München (TUM) in the Bavarian capital city. The University Medical Center has 1,050 beds and treats about 58,000 in-patients and 220,000 out-patients each year. With his 130 staff members, Dr. Luppa performs in the routine lab four million analyses each year, including those conducted using the approximately 150 POCT devices present throughout the hospital's units. He considers POCT an extension of the central lab, like a network of small satellite labs. Twenty POCT units are specially equipped for blood gas analysis and also closely connected to a POCT quality control center. Traditionally, blood gas analysis is geared primarily toward the partial pressure values of oxygen and carbon dioxide. Today, the term also includes analysis of the pH value, several ions, and additional parameters such as glucose that can be seen from the blood (see sidebar). "POCT has spread rapidly in many countries around the world in recent years as a modern form of laboratory diagnostics, including in the United States, Germany, the UK – and, to a lesser extent, in others, such as France and Japan," Dr. Luppa says. In Germany, the POCT market now encompasses about a billion euros each year. Dr. Luppa points out that there are various factors involved in the spread of the technology, such as the interconnectivity of POCT devices and the link to the central laboratory. For the outpatient sector, there are a few large central labs in Germany, for example, but France has a dense network of smaller labs – so the distances to travel back and forth are shorter. As always, country-specific reimbursement is also a factor for the implementation of POCT. In Germany, like in the United States, medical centers have been working with diagnosis-related groups (DRGs) for some years now, and health insurance companies pay for each analysis performed in private practices.

RAPIDPoint 500 System

The TUM Medical Center in Munich, like many others, adopted POCT years ago. But the evolution of the devices did not stop there and, in fact, is ongoing at the facility. For several months now, Dr. Luppa has also been working with RAPIDPoint® 500 from Siemens, putting this new instrument to the test. The final verdict: "With its compact nature and outstanding maintenance friendliness, the RAPIDPoint 500 analyzer represents another step forward from its predecessors." The innovation: Now, the unit can determine a patient's lactate blood concentration in approximately 60 seconds on a cartridge-based instrument.

The RAPIDPoint 500 blood gas system determines a patient's full parameter panel, including lactate, in approximately 60 seconds.

Management Summary

Challenge:

- Point-of-care testing (POCT) – shifting biochemical analysis from the central lab to hospital wards to save time and improve treatment quality for patients in emergency rooms and intensive care units, who are often in life-threatening situations
- POCT device utilization to measure lactate in the blood of emergency patients. In patients who have just been brought in and whose pathologies are unclear, the lactate concentration supplies important information regarding the cause of the patient's medical problem, such as the progress of circulatory shock, an inadequate supply of oxygen to the organs ("hypoxaemia"), or sepsis – all critical conditions

Solution:

- A POCT device should be easy to use and maintain so that even clinical personnel without training in laboratory diagnostics are able to handle it and high analytical quality is ensured
- POCT devices should ideally be connected to a POCT coordination center, e.g., the central lab of a medical center, where trained staff members monitor quality remotely

Result:

- RAPIDPoint 500 Blood Gas System represents the next stage in the evolution of the Siemens RAPIDPoint POCT family and combines these requirements in a single device. Now, lactate values can be provided within approximately 60 seconds on a cartridge-based instrument, the system does not require staff with training in laboratory medicine, and it supplies full connectivity with the medical center's laboratory information systems
- With its replaceable cartridge and automatic quality assurance and calibration, the RAPIDPoint 500 system is practically maintenance free. The measurement cartridge houses all of the analytical systems, including sensors and reagents. All the staff has to do is replace the cartridge – which is about as easy as replacing the toner cartridge in a printer
- Clinical staff members can focus more of their attention to patients, with less time spent on operating the device, or dealing with quality assurance or maintenance

This shows whether the blood is too acidic, thus indicating the patient's critical condition. The RAPIDPoint 500 analyzer is suitable for all facility sizes and for specialists in private practice, e.g., pulmonologists.

Dr. Luppa's field of research is biosensorics. He knows how difficult it is to optimize an enzymatic reaction that is, in itself, so simple that it proceeds independently without maintenance.

Siemens has been able to improve its electrochemical lactate sensor technology in such a way that it is now comparable in analytical quality to the central lab measurements. It does so even in whole blood, which contains a lot of disruptive factors.

A recently published study conducted by Dr. Luppa and Dr. Blobner on more than 1,500 patients in an intensive care unit has even shown that the initially measured glucose and lactate plasma concentrations are suitable for use in predicting patient mortality.[1]

The sensor's lifespan has also been improved. It now runs for at least 28 days without requiring maintenance, so it can be integrated into the automatic measurement cartridge. And that measurement cartridge itself is another big advantage of the RAPIDPoint 500 instrument. It contains the system's full miniature lab, complete with all the diagnostic sensors and reagents. "It's like an automatic transmission – everything regulates itself independently," Dr. Luppa says. The self-contained measurement cartridge works independently for nearly a month, and can then be replaced as easily as a printer's toner cartridge. The RAPIDPoint 500 system may not be as small as a tricorder – a RAPIDPoint 500 system is closer to the size of a personal computer – but it is almost as compact in its work.

Is it worthwhile as a purchase? "It's absolutely reasonable from an economic point of view," Dr. Luppa points out, "since every analysis performed at the point of care frees up time the staff would otherwise have to spend on the logistics of getting the sample to the central lab and back. And it's definitely worthwhile from the medical perspective. Medical guide-

Professor Manfred Blobner, MD, and Professor Peter B. Luppa, MD, work together to make POC testing more efficient.

lines list blood gas measurement at the point of care as a best practice, including lactate measurement. By making this purchase, we are only doing what we have to as doctors."

Increased reliability of POCT measurements

But does the trend to move partly away from the lab and toward POCT generally lead to diminishing analysis quality? "Quite the opposite," Dr. Luppa says. "We have about 20 POCT units, and all of them are bidirectionally connected to our POCT server online. Laboratory technicians monitor the quality of all of our devices, from a single control center, and medical engineering staff can access the device remotely as needed and perform recalibration, for example."

This, he says, has substantially reduced the rate of failures and boosted reliability in the POCT segment in recent years. The quality of blood gas analyses in general has increased steadily and is highly robust. The devices are also becoming increasingly easy to use, which is another way the device is reminiscent of the tricorder. "Even as the insides of these devices become more and more high tech," says Dr. Luppa, "the trend for users is toward low tech."

Frank A. Miltner *has a degree in biology and has been working as a journalist in the healthcare sector for more than 15 years, including as an editor for the newsmagazine* FOCUS*, and editor-in-chief of* NetDoktor.de.

[1] Martin J, Blobner M, Busch R, Moser N, Kochs E, Luppa PB. Clin Chem Lab Med. 2012 Sep 15;0(0):1-8. [Epub ahead of print]

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.

Further Information

www.siemens.com/bloodgas

Efficient Image Analysis for an Entire Region

Offering superior diagnostic services for a widespread area is no small matter. The Associated Radiology Burgenland Central-South (Radiologieverbund Burgenland Mitte-Süd) in Austria has overcome this challenge – through intelligent connection and integration of *syngo*.via in a high-performance combination with *syngo*.plaza.

Text: **Dr. Regina Sailer** Photos: **Manfred Horvath**

Burgenland, on the border with Hungary, Slovakia, and Slovenia, has always been a region with burgeoning business and tourism. In the healthcare sector, the region has seen numerous developments. One impressive example is Oberwart hospital, a vascular center, cancer center, and general hospital, jointly operated by several different medical departments including radiology, in the south of the province. With approximately 400 beds, this facility offers top-quality medicine at an international level.

Services include interventions that just a couple of years ago would have been almost unimaginable in a hospital outside a large city. Procedures such as carotid stent placement, intraarterial cerebral thrombolysis, and endovascular aortic repair were previously carried out at Vienna's General Hospital, which is about 130 kilometers away. The fact that patients can now receive these services without having to travel this far is possible due to several factors. First, there are the many committed physicians at Oberwart, whether they are radiologists, surgeons, or others, and second, there is a new angiography system for planning and performing vascular surgery interventions with accuracy down to the last millimeter. The vascular specialist has the images that are necessary to do this onscreen.

Centralized Image Reading for Four Separate Facilities

Efficient archiving and communication of images has contributed to the healthcare center's success story. The radiology network links Oberwart with three other hospitals in Burgenland – one in Kittsee (130 beds, radiologically taken care of by the Hospital Barmherzige Brüder Eisenstadt), one in Oberpullendorf (208 beds), and one in Güssing (158 beds). They all have been relying on *syngo*®.plaza since early 2012. The picture archiving and communication system (PACS) acts as the technological backbone supporting an efficient communication among the

With the migration to *syngo*.plaza, the radiologists could improve the quality and efficiency of their daily work.

> "We were looking for a new system that could cope with large volumes of image data, and we found it, in *syngo*.plaza and *syngo*.via."
>
> Herbert Langenberger, MD, EBIR,
> Head of Radiology Network Burgenland Central-South, Burgenland, Austria

radiology teams at the four geographically separate facilities. The heart of the Radiology Network Burgenland Central-South, headed by Herbert Langenberger, MD, is located at the largest facility, the hospital in Oberwart. For imaging purposes, each of the four facilities has a computed tomography (CT) system, ultrasound, and fluoroscopy units, as well as mobile and conventional X-ray at its disposal. Magnetic resonance imaging (MRI) and angiography are offered in Oberwart only. Fiber-optic lines connect all of the systems and all medical images can be read in any location, regardless of where the examination is performed.

But the former reading solution, with which the existing devices can be used efficiently and cost-effectively, began to reach its limits. "Over the years, the volume of data at the facilities in the network simply got too large," Langenberger explains. Upgrading the CT units in Oberwart from a four-slice to a 64-slice SOMATOM® Definition Dual Source CT, from a single-slice to 16-slice system in Güssing and Kittsee, and from a four-slice to 16-slice in Oberpullendorf meant a huge increase in data volume. The number of images per scan also multiplied. The SIENET MagicView software that had been running since 2006 was simply no longer able to process the flood of images.

High Image Volume Slows Server to a Crawl

"The data volumes were so high that the server brought the whole system to a crawl," Langenberger recalls. And that came at the expense of speed, especially at night when image reading is done centrally for multiple facilities. "As a result, we started looking for a new system that would be able to cope with these large volumes of image data, and we found it, in *syngo*.plaza and *syngo*.via,"[1, 2] Langenberger explains.

As soon as the new system was selected, the team got to work on migrating the legacy data from the past seven years. At the time of the system shift, in February 2012, the most important diagnostic data from the past one-and-a-half years was already available in the new PACS. "And by the end of this year," Langenberger says, "we will have the entire database on the new server and all of the images will be available directly online."

In addition to a smooth migration, reliability and having a low failure rate for the PACS was "a very essential point" for Langenberger and his team. Everyone was especially relieved in February, when the switchover from the old system to the new one went without a hitch at all of the facilities involved.

"Migrating the system while operations were underway, so that it would work from one day to the next, was something we thought only a very large company could manage, a company that was also already familiar with our circumstances here," Langenberger explains. The service was excellent at every stage of the process, before and during the installation and implementation, and during follow-up care. "We could count on having a service technician available promptly whenever we needed one," Langenberger reports. The remote maintenance also went very smoothly, he says.

Speed: A Crucial Advantage

The team in Oberwart is also happy with the result of the system migration. The key advantage of the new PACS, Langenberger says, is its tremendous speed: "You can really connect multiple hospitals with each other, and you don't even notice that there are multiple CTs and many other systems working at the same time in different locations." Langenberger says that handling the image data has become easier, and loading the data is much more instantaneous. From a clinical perspective, the immediate access of images in every connected facility – regardless of where a patient was examined – leads to faster diagnoses and better coordination with referring physicians. Server-related delays are now a thing of the past. External access is also possible. In emergency cases, such as when patients are experiencing acute bleeding, Langenberger can read the images from home via Internet or via Wi Fi from elsewhere – complying with the most advanced encryption and security codes, of course.[2]

Time Saved During Consultations and Planning

Oberwart was looking for a system that could not only manage large volumes of data efficiently, but could also deliver high-end 3D image processing. And that is exactly what the *syngo*.via 3D routine

Management Summary

Challenge:
- Major increase in data and image volumes due to new, high-performance imaging systems
- Immediate visualization of large image datasets of four decentralized, interconnected radiology departments
- Implementation of a PACS migration at four geographically separate facilities

Solution:
- Decision to work with a partner that is already familiar with local conditions
- Procurement of new server capacity and migration from Siemens SIENET MagicView to *syngo*.plaza
- Realization of efficient 2D reading with *syngo*.plaza and automated pre- and postprocessing with *syngo*.via at the 3D level

Result:
- Time and cost savings through faster consultations, diagnosis, and optimized planning of therapy
- Increased efficiency of entire radiological process through high speed of *syngo*.plaza, even when working over different geographical locations
- Improved quality in visualization and image reading through *syngo*.via, especially in vascular and emergency surgery
- More efficient diagnoses and more goal-oriented treatment methods
- Improved ability to explain matters to patients through *syngo*.via WebViewer, which can be used for non-diagnostic viewing purposes on an iPad
- Efficient, fail-safe 24-hour operation

Loading data in the PACS is still fast, even if several computed tomography scanners within the hospital network are in use.

and advanced reading solution can do. The software has been especially helpful in facilitating the hospital's work with referrers: "With *syngo*.via, I can now show the surgeon a three-dimensional reconstruction where he can see, for example, right where the blood vessels are constricted. That saves us all a lot of time and money when it comes to planning and consultations," Langenberger says, explaining the new system's benefits. The 3D perspective is also often highly important when it comes to diagnostic quality, he says, for example in virtual colonoscopy exams or in visualizing the coronary vessels. "For us as a vascular center, it is extremely important to be able to visualize the vessels in three dimensions, and not only in cross-section," says Langenberger, who, as an interventional radiologist, also performs interventions himself.

Bedside Radiology

Three-dimensional images make it much easier to visualize findings, not only for those of Langenberger's colleagues who plan operations, but also for patients. With this in mind, by the end of 2012 Oberwart will be the first hospital in Austria to use the the *syngo*.via WebViewer[4] application for the iPad[3]. "We will truly do bedside radiology with two mobile information consoles," Langenberger says, evidently happy. "It's really great to be able to explain the diagnosis and treatment to a patient right at the bedside, in a visual format that is easy to understand."

Dr. Regina Sailer *has a degree in communications and writes as a freelance journalist for German-language print and online media. Her topics encompass the fields of medicine, health, new treatments, and research. The author lives and works in Salzburg, Austria.*

[1] *syngo*.via can be used as a stand-alone device or together with a variety of *syngo*.via-based software options, which are medical devices on their own rights.
[2] Prerequisites include: Internet connection to clinical network, DICOM compliance, meeting of minimum hardware requirements, and adherence to local data security regulations.
[3] The iPad® is a trademark of Apple Inc., registered in the U.S. and other countries.
[4] The application is not for diagnostic viewing/reading on mobile devices. Please refer to your sales representative whether the product is available for your country. Diagnostic reading of images with a web browser requires a medical grade monitor.
For iPhone and iPad, country specific laws may apply. Please refer to these laws before using for diagnostic reading/viewing.
For Japan: Applications on iPhone/iPad/iPod are not a medical device in Japan. Use at your own risk. They are not intended to be used for diagnosis.

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.

Further Information

www.siemens.com/syngo.plaza
www.siemens.com/syngo.via

Flat-fee Flexibility

As in many other countries, healthcare managers in the Netherlands face a mounting challenge: to improve the quality of healthcare and meet rising demand while preventing budgets from spiraling out of control. Innovative medical imaging technology is part of the solution. Two Dutch hospitals have teamed up with Siemens to help them in their efforts.

Ziekenhuisgroep Twente (ZGT) comprises two hospitals in Almelo and Hengelo (photo). Siemens not only assumes full responsibility for the quality and uptime of imaging systems, but also ownership.

Over the last decade, the costs of healthcare in the Netherlands have increased at roughly double the rate of Gross Domestic Product (GDP), of which they currently represent around one fifth. The average household now spends 22 percent of its income on a combination of public and private insurance policies. Without substantial cost savings in the healthcare sector, this looks set to rise to 39 percent by 2040 (Source: Dutch Central Bureau of Statistics).

In the face of this challenge, hospitals are busy streamlining their workflow. Investments proposed by the various departments must be carefully assessed to make sure money is used to maximum effect. In many cases, this is made more difficult by the growing demand for (new) healthcare procedures, which shows no signs of slowing down. In radiology, the demand for imaging procedures is growing even faster than the total healthcare budget.

Finding Resources

Nevertheless, the total picture indicates there is a sound business case to be made for investing in better imaging technology. Having access to the latest innovations enables hospitals to increase productivity as well as improve the quality and cost-effectiveness of healthcare through earlier diagnosis and more precise imaging-guided surgery. This is an attractive proposition, especially since Dutch policymakers are keen to encourage competition among hospitals as a way of stimulating innovation, quality improvements, and cost savings.

However, finding the resources to make these investments is not always easy. "Replacing imaging systems takes a big chunk out of the budget," says Peter Wensing, radiologist at Ziekenhuisgroep Twente (ZGT). "That means there's a risk of investments being postponed, sometimes repeatedly, until suddenly you find yourself working with outdated systems – which compromises the quality of care and may even pose safety risks for the patient."

There may, of course, be good reasons to postpone investments. For example, the HagaZiekenhuis, a hospital group with three locations in The Hague, decided not to buy any new systems until a major renovation and extension project had been completed. "Installing new systems and moving them after two years would have been a waste of money," says the Radiology Department's Manager Peter Kraaijeveld. "Unfortunately, the renovation took longer than expected. By the time we were ready to invest in new technology, nearly all systems were in line for replacement or nearing the end of their life-cycle. That meant we were looking at a huge investment."

Functionality-based Contract

Wensing and Kraaijeveld represent two hospitals that have managed to simultaneously boost the quality of their imaging procedures and circumvent financial constraints by entering an innovative partnership with Siemens Healthcare. In the case of the HagaZiekenhuis, Siemens has assumed full responsibility for all imaging technology for a period of 15 years. "The contract is based on functionality. We've agreed on a fixed annual fee, in exchange for which Siemens simply takes care that at any given moment our imaging technology is at least up-to-date and, where necessary, cutting-edge," says Kraaijeveld.

To achieve this, the contract covers maintenance, software upgrades, quality control, and training. Crucially, it also enables systems to be replaced at the end of their life-cycle – or sooner if necessary. Whether that last proviso applies is determined by the speed at which a new technology penetrates the market, explains HagaZiekenhuis' radiologist Herma Holscher. "In strategic areas such as cardiovascular diseases and gynecological and pediatric care, we require cutting-edge technology. Once a particular innovation is available to colleagues in 50 percent of Dutch university hospitals, Siemens will install it here at no extra cost. In other areas, we employ a similar method using the 28 top [non-university] hospitals in the country as a reference."

Already the new systems installed in HagaZiekenhuis have made a significant contribution to improving patient care. In addition to boosting productivity, which results in reduced waiting times for patients, the hospital can now perform prostate biopsies more quickly and precisely thanks to "live" magnetic resonance imaging (MRI). Access to the SOMATOM® Definition Flash computed tomography (CT) system, with its unprecedented low radiation levels, is especially valuable

since one of the HagaZiekenhuis' three locations is a specialized children's hospital.

Better Quality Controls

In the northeastern part of the Netherlands, ZGT, which comprises two hospitals in Almelo and Hengelo, entered a similar though not identical partnership with Siemens. At ZGT, Siemens not only assumes full responsibility for the quality and uptime of imaging systems, but also ownership. This arrangement includes all the Radiology Department's imaging solutions, regardless of make or supplier. This relieves ZGT of the responsibility for technical maintenance as well as the administrative effort of managing hundreds of contracts with dozens of different suppliers.

Although ZGT's Facility Manager Henri Wijers recognizes the cost-saving benefit of this approach, it was not ZGT's primary focus, he stresses. "Our main concern was to introduce better quality controls, especially with a view to patient safety. We felt that a specialized party like Siemens would be able to do that far more effectively. Additionally, we expected this type of contract to give us more flexibility. Technology develops at a spectacular pace, and there is a lot of uncertainty about the way the Dutch healthcare system will develop over the next few years. We wanted to be able to quickly adapt to changing circumstances."

The contract offers such flexibility. For example, ZGT brought forward the replacement of an MRI scanner when demand for MRI procedures grew more rapidly than expected. "At the same time, we wanted to upgrade to a 3 Tesla system, as opposed to the 1.5 Tesla anticipated in the contract, since 3 Tesla was establishing itself as the new standard more quickly than we originally thought."

Finding Service Windows

The flat fee agreement with Siemens enables both hospitals to distribute the cost of such investments evenly. It also represents direct cost savings. Kraaijeveld: "Just looking at purchasing and maintaining systems, we expect to save around five percent per year. And that's without all the time and money we save by not having to start up complicated tender procedures for each new system."

In addition to saving money, the contracts are also designed to improve the continuity of imaging procedures. "We set ambitious goals for the availability of systems, close to 100 percent, and it's up to Siemens to meet them," ZGT's Wensing says. So far, he is more than happy with the way this is handled. "There's always a service engineer onsite. And I'm particularly pleased with the way Siemens organizes planned maintenance. For years, we tried to get suppliers to do their maintenance at times when the systems were not in use. We never succeeded. Now, Siemens takes the initiative to find and exploit these service windows."

Remote monitoring of systems further minimizes downtime, Wensing adds. "On two occasions, such readings indi-

Focusing on Patient Care

"This contract means we are relieved of a substantial amount of work. Hospitals have long tried to do everything themselves. However, instead of trying to manage the ever more complex technology in our hospitals ourselves, I feel it's wiser to focus on those aspects of the care process closest to our core business: looking after people. Of course, the jury is out on whether outsourcing is always the best solution. But in this case, I'm pretty sure it is."

***Meindert Schmidt**,*
CEO, ZGT, The Netherlands

Radiologist Peter Wensing, MD, Meindert Schmidt, CEO, and Henri Wijers, Head of Facility Management, ZGT (from left)

Peter Kraaijeveld, Sector Manager Radiology, and Herma Holscher, MD, Radiologist and Medical Manager at HagaZiekenhuis

cated that the X-ray tube in a CT scanner could give out at any moment, enabling Siemens to install a new one at a convenient time. If a tube breaks while the system is in use, you easily lose half a day worth of scans."
The risk of downtime is further reduced by continuous training of users. Siemens periodically assesses users' knowledge and skills and organizes tailored, web-based trainings to close any knowledge gaps.

Mutual Trust

Both ZGT and HagaZiekenhuis emphasize that this type of partnership requires more than a sound contractual framework. Holscher: "I sometimes compare the contract to a marriage agreement. Of course, you need it. It's there to fall back on if you need to settle questions or disputes or if circumstances change. But it doesn't have to provide for every tiny detail. To make the partnership work, you first need a degree of mutual trust and understanding. That's one of the major reasons we chose Siemens. They understood that this partnership had to be more than the total sum of lots of smaller contracts."
ZGT's Wijers feels that the long-term scope of this type of partnership encourages a more constructive, open way of dealing with each other. "For example, at one point we requested an extension of the support on imaging systems in the trauma rooms to 24/7. Siemens gave us a price but added that they didn't think the investment would be worthwhile as our real problem was of an organizational nature."
Wensing adds: "I certainly don't get the impression Siemens is now resting on its laurels. Quite the opposite, in fact. They seem more involved than ever."
That involvement need not be restricted to ensuring the quality and availability of imaging technology. At HagaZiekenhuis, the partnership encompasses a whole range of activities in which the hospital and Siemens can help each other, including scientific research. Additionally, Siemens will help to analyze the hospital's processes for potential improvements. "We certainly have our own expertise and ideas in that area," says Kraaijeveld.

At HagaZiekenhuis, a hospital group with three locations in The Hague, Siemens has assumed full responsibility for all imaging technology for a period of 15 years.

"But if you restrict yourself to your own vantage point, there's a real risk of developing tunnel vision." He expects Siemens to provide not only international best practices from other hospitals, but also useful insights from completely different environments. "For example, I'm sure they can help us implement LEAN principles in our laboratories, possibly based on the experiences in Siemens production facilities."
At ZGT, where the contract is about to enter its third year, Wijers is happy to build on the level of cooperation achieved so far. "We are considering extending the contract to our nuclear medicine department. We wouldn't do that if the partnership didn't work. Personally, I much prefer this type of cooperation to incidental contracts. The latter take up much energy and relatively high transaction costs. I'd rather invest that energy in a good, meaningful partnership. For me, that's one major, non-quantifiable benefit of this contract."

Management Summary

Challenge:
- Keeping imaging technology up-to-date
- Maintenance and service of imaging technology
- Training of engineers and technicians

Solution:
- Managed equipment service contracts with Siemens

Result:
- Competitive imaging department with up-to-date technology and staff
- Less system downtime
- More flexibility regarding other investments

Further Information

www.siemens.com/healthcare

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.

Under Ruth Brennan's guidance, IT helps Blue Mountain Health System address patient satisfaction and other key strategic initiatives.

Three Community Hospitals Go Digital

The Blue Mountain Health System in the U.S. and the Krankenhaus Düren gGmbH in Germany use Siemens Managed Services IT Outsourcing to support initiatives for improving efficiency and patient satisfaction, and for minimizing human errors. With Blue Mountain starting to implement new applications only recently and Düren operating more than 100 applications, the three community hospitals show how to deal with an increasingly virtualized healthcare industry.

Text: **Lena Schnabl** Photos: **Jonathan Hanson (Lehighton), Siemens (Düren)**

"Our email system often crashed when we received emails with attachements," remembers Ruth Brennan, Vice President, Clinical Services, Blue Mountain Health System, Lehighton, Pennsylvania, USA. The only hospital system in Carbon County comprises two care facilities in northeastern Pennsylvania, including Palmerton Hospital, a 60-bed community hospital, and Gnaden Huetten Memorial Hospital, a 90-bed community hospital in Lehighton. Before Siemens was brought on board, the old telephone system, and the hospital network as well, were issues on a regular basis. When getting a new positron emission tomography scanner, for example, the hospital ran a portion of its data over the vendor's imaging network to keep the data network up and running. A team from Siemens Managed Services spent the last one-and-a-half years rebuilding this infrastructure. Managed Services offers a broad services portfolio that includes a round-the-clock help desk for end-user issues; support for Siemens and non-Siemens applications; and remote monitoring and support for a comprehensive range of information technology. The individual contract depends on the customer. "We were not able to put the money into IT infrastructure nor did we have the expertise in how or where we get the most for our dollars. Siemens brought us that expertise," says Brennan.

Increased Patient Satisfaction

After updating the IT infrastructure, Blue Mountain was able to implement several applications that provided significant support for the organization's patient satisfaction initiatives, such as Patient Assessments. The nurses perform and document their assessments right at the bedside, rather than sitting at the nursing station and documenting on paper. "The patient satisfaction scores increased dramatically the month we rolled out that application," says Brennan. The next jump was after implementing a Discharge Instruction Application. Patients are now getting a printed, comprehensive package of instructions when discharged. "Instructions tended to be handwritten and each doctor addressed something else," Brennan continues, "Now patients or their families know exactly what they have to do and what they must not do after being discharged." In the first full quarter of electronic medical record (EMR) use, patient satisfaction scores for quality of discharge information rose by nearly 10 percentage points.[1]

Next, the pharmacy system was upgraded and Siemens Med Administration Check™ was implemented to support Blue Mountain patient safety initiatives. Through bar-coding and computer technology in the pharmacy and at the patients' bedside, nurses confirm that the right medication is given to the right patient at the right time. "This consistent electronic double check that the right patient is getting the right medication at the right time as ordered by the physician is a huge safety initiative," explains Brennan.

It is not always practical for a community hospital to have all medical professionals on-site. To enable access to these specialists, Blue Mountain installed a program called the George System for burns and infectious diseases. An infectious disease specialist can see the patient through a high-definition webcam while information such as blood pressure and pulse are transmitted to the remote physician while the patient is in the Blue Mountain facility. This enables patients and their families to stay close to home while specialists are working from elsewhere.

According to Richard Rothfleisch, MD, specialist in pulmonary medicine at Blue Mountain, this also brought about a major change to how physicians work at the hospital. When the information does not flow back and forth, there is a high chance of duplication and error. Expensive tests are made twice, patients suffer for it, and expenses go up. Even though healthcare is an information business it is one of the last to go digital. Although the applications support the health system's quality and safety initiatives and help to streamline tasks for staff, the introduction of new technology can often be daunting. Brennan recalls one nurse's initial misgivings about working with the Bedside Mobile Workstations. "But Siemens' team made sure that we had someone right at her elbow the entire day of the launch. By the end of the day, she wasn't afraid of it anymore. Instead, she was feeling comfortable and within a few days, she was ready to mentor somebody else."

> "In one year, Siemens Managed Services had done a tremendous job in moving us forward."
>
> Ruth Brennan, Vice President, Clinical Services, Blue Mountain Health System, USA

The hospital's IT staff was integrated into the Managed Services team, had training, and came back able to solve IT problems that had been unresolved for several years. "They really came out shining," comments Brennan. According to Rothfleisch, this is attributable to a staff that has IT as well as clinical knowledge: One has to know the end-user that is the doctor. If the doctor cannot handle the IT, there will be nothing but sand in the gears, adds Rothfleisch. A help desk is available to provide timely resolution of problems for end users. Lisa E. Johnson, Vice President, Public Relations & Marketing, thinks of the improvements in terms of a "culture change." The staff had to get used to putting in tickets and not directly calling one of the on-site IT workers.

"Before, there was constant complaining that IT was not meeting their needs. Now we have more employees being satisfied quicker," says Brennan.

Financial Turnaround and Reimbursement

Since the cooperation with Siemens Managed Services started, Blue Mountain has not only increased patient and staff satisfaction but also undergone a financial turnaround. Six years ago, the hospital was losing 10 million US-Dollars in one fiscal year. Last year the hospital earned 900,000 US-Dollars. "You can't run a hospital efficiently without the basic IT services in place. When our IT services were failing on us routinely, you just could not practice efficiently. That has all changed. It was dependent on having a stable network, as well as having access to IT specialists. In one year, Siemens Managed Services had done a tremendous job in moving us forward."

The IT evolution of Blue Mountain is directly linked to reimbursement issues. In the USA, healthcare providers can qualify for incentive funds when they can demonstrate a meaningful use of electronic medical records (EMR). As per the American Recovery and Reinvestment Act, these records will be mandatory by 2014. The shift is encouraged through financial incentives provided under the Health Information Technology for Economical and Clinical Health (HITECH) Act. The technology now helps clinicians document more thoughtfully and completely. This new way of documentation supports appropriate charging. According to Johnson, it all comes down to the best care for the patient.

A Leap toward Virtualization

The Krankenhaus Düren gGmbH hospital, community hospital based in Germany, is relying on Siemens to take care of IT services, too. Unlike Blue Mountain which went digital only recently and has been moving forward quickly ever since, Düren outsourced IT services early on and has been working together with Siemens since 2002. Through Managed Services, Siemens is taking care of the remote SAP service (SAP for Healthcare, ERP, the Siemens business intelligence system i.c.m.health, and the hospital information system i.s.h.med) and maintenance to reduce the burden on staff and help increase reliability and data availability. The 491-bed hospital is still keeping some core competencies in-house, especially when the whole institution is affected, such as security, network management, and first-level support. Jürgen Naujoks, graduate engineer, Head of Electronic Data Processing (EDP), was hired in 2004 to purchase and implement medical user systems. Siemens was selected as a suitable vendor because it masters the SAP system as well as user systems. The company is supporting SAP modules and developing its own modules that integrate seamlessly into the SAP system. If needed, the external team can build additional servers or acquire certain hardware. "Only vendors like Siemens are offering the competence and size to make this possible. It is the best vendor we could hope for," says Naujoks. Together with Siemens, Düren hospital implemented a surgery module, a radiology module, the ambulatory billing, and integrated components such as email, web applications, and remote radiology. "Thanks to Siemens, we are well on the way to implementing an electronic medical record. We do not have to think about new information systems but can extend our Siemens components."

At Blue Mountain, Siemens' services help healthcare professionals meet their goals for providing the best care possible.

> "Thanks to Siemens, we are well on the way to implement an electronic medical record."
>
> Jürgen Naujoks, Graduate Engineer,
> Head of Electronic Data Processing,
> Krankenhaus Düren gGmbH, Düren, Germany

An All-Round Package

When implementing the surgery module, a Siemens project manager assisted Naujoks's team. According to the head of IT, the Managed Services team provided support before, during, and after the implementation through training and know-how. When the IT team wanted a modification, Siemens offered developers and consulting on how to realize the new features. IT services are supporting on a second and third level, and controlling the system on a daily basis.

Through an "EarlyWatch Alert," Naujoks and his team are notified via email if the system runs too slowly, or if jobs or computer charging are interrupted or even breaking down. To ensure data security, the Siemens employees log on the IT department of Düren hospital. These logons are registered and watched through the in-house team.
The reliability of the SAP system is supported through synchronized mirroring. To test the new developments, the Siemens Managed Services team helped introduce a method to mirror the production system, anonymized on a regular basis. By simulating a realistic IT environment, new applications can be tested thoroughly.

> "Now we have more employees being satisfied quicker."
>
> Ruth Brennan, Vice President,
> Clinical Services,
> Blue Mountain Health System, USA

Besides the monitoring, the Siemens team is solving IT issues when contacted. "We still have most of the Siemens consultants we started with in 2002. There is not only the competence center, but also the people behind it. When there is a problem, I call them or write an email and get the needed support, sometimes even outside of the working hours. This is important as requests are not scheduled," says Naujoks.
Because the engineer can outsource the SAP knowledge completely, his team can take on other challenging tasks. They are supervising around 100 applications and doing strategic IT development and conception. To keep the end-user in mind, Naujoks consults with physicians about new applications and their implementation. "Physicians are the most demanding customers that I know. It is hard to plan a project when 90 percent of the participants have appointments, such as surgeries, and cannot partake in the whole project and training," says Naujoks. Physicians comment when they feel that data protection is in the way of their work as well. "We try to make data security as transparent as possible, so everybody understands the background."
The radiology and gastroenterology departments in particular drive the digitalization. For example, remote radiology is helping to provide access to data at night or during weekends. Radiologists can access the data through a hospital notebook with a coded hard drive and dedicated log-on right from home.
The gastroenterology department and its chief physician are the most committed, according to Naujoks. There, the medical report is going to be digitalized completely in the near future. The findings would be integrated automatically into the report, including findings from other departments such as ultrasound, for the entire stay of a patient. "These workflows facilitate the work of physicians substantially and raise efficiency. I want to support the departments through the technological developments even better in the future," says Naujoks. Düren hospital strives for a complete digitalization. This is only possible with a cooperation that is flexible enough to adapt to the customers' needs. "What strikes me is Siemens Managed Services sensitivity to our needs and priorities," says Brennan from Blue Mountain. Both hospitals are intending to grow and their IT will grow along with them.

Lena Schnabl, *MA, studied political science and is an editor at* Medical Solutions. *She regularly writes about business and healthcare.*

[1] Press Ganey HCAHPS Summary Report 2011

Further Information

http://healthcare.siemens.com/hospital-it/managed-services

Düren hospital is on its way to digitalization.

Management Summary

Challenge:
- Pressure to digitalize healthcare
- Need to offer reliable and advanced healthcare IT
- Lack of healthcare IT specialists
- Offer specialist medical services in community hospitals

Solution:
- Healthcare IT consulting services
- Implement medical applications
- Enable physician access to eletronic medical records on-site and remotely

Result:
- Reliable healthcare IT support
- Help desk for reliable and timely problem resolution
- Reduced paper-based documentation
- Improved workflow efficiency
- Access to data in the hospital and remotely
- Fewer human errors

Colombia: A Healthcare System in Crisis

By Francisco Jose Yepes Lujan, MD, PhD, Director, Graduate Studies in Health and Social Security Administration, Pontificia Universidad Javeriana, Bogota, Colombia

A 64-year-old woman I know who faithfully paid into the Colombian equivalent of an American Healthcare Maintenance Organization (HMO) for 20 years was rushed to a leading Bogota hospital in August 2012 in excruciating pain from what turned out to be an inflamed gall bladder. After waiting for four hours on an ambulance gurney parked in the emergency room hallway, she was finally examined. The doctor's diagnosis should have led to emergency surgery to prevent a ruptured gall bladder and the risk of fatal peritonitis. But the woman and her family were turned away, sent home. The reason? The hospital refused to authorize the surgery because her HMO had gone broke and for more than a year had not reimbursed this hospital or its doctors for medical services rendered. The woman survived, and her bladder's inflammation later subsided, and she was lucky.

Multiply this woman's experience hundreds of times per day in hospitals and clinics big and small across Colombia and you get an idea of the depths of this nation's medical care crisis. The system is, for all practical purposes, insolvent, and there are many expressions of what that means. In financial terms, the government-run Fosyga, the Spanish acronym for the Solidarity and Guarantee Fund that is responsible for distributing employer contributions to private health plans, owes billions of dollars to the various EPSes, which are the Spanish initials for insurance companies roughly equivalent to HMOs. The EPSes in turn owe $2 billion to the IPSes, the Spanish initials for the generic term for healthcare providers such as hospitals, clinics, laboratories doctors, and dentists that the insurers contract with. As a result, many of the EPSes have been taken over by the government in an effort to try to save them. Cities and townships, which are responsible for administering government-subsidized healthcare to the poor and indigent, have also incurred staggering levels of debt, and many are behind on payments they owe to IPSes.

The most important expression of the crisis is, of course, the decline in standards of healthcare, the congestion in emergency rooms (from which Colombians by law cannot be turned away), and the needless risks and delays that patients face when they become sick or need elective procedures performed. Although the crisis has worsened over time, it has reached a boiling point in recent months due to mounting protests by health professionals and patients and pressure on politicians. The Colombian congress is now considering a new legislative reform, after previous attempts in 2007 with Law 1122 and again in 2011 with Law 1438 failed to right the ship. As before, there is little agreement on how to fix the system, because it is so complicated that almost no one understands it.

What do I think is at the root of the crisis? The central problems are corruption, the failure of the government to adequately fulfill its regulatory function, and the inherent ideological conflicts embedded

Number of Physicians
per 10,000 Resident Population: 1.5 (2010)

Number of Hospital Beds
per 10,000 Resident
Population: 10 (2010)

Number of Nurses and Midwives
per 10,000 Resident Population:

6,2

Total Expenditure on Health
per Capita (2010): US$ 518

$$$$$

Government Expenditure on Health as % of Total Expenditure on Health (2010): 72.7%

Total Expenditure on Health as % of GDP (2010): 7,6

Male Life Expectancy
at Birth (2006):

73

Female Life
Expectancy
at Birth (2006):

80

Population in Thousands (2010): 46,295

Source: WHO Global Health Observatory Data Repository, http://apps.who.int/ghodata/. Last accessed Sept. 10, 2012

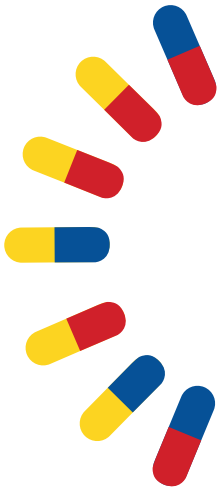
in the system, all of which I will discuss shortly. But first, I will outline the genesis of Colombia's current public healthcare system, which flows from the 1991 Constitution stating that all Colombians have a right to "social security." The so-called "Law" 100 passed by Congress in 1993 refined that right by creating National Obligatory Health Insurance, a system consisting of two regimens. One was called "contributive," for all employers and their formally contracted employees. Together, employer and employee contribute 12.5 percent of each worker's paycheck to the EPSes representing them. The EPSes then contract for services with IPSes – the 30,000 authorized hospitals, labs, clinics, doctors', and dentists' offices in Colombia.

Roughly 44 percent of Colombia's population is covered by 22 EPSes formed to insure "formal," or employed, subscribers in the system, which is a direct descendant of the healthcare insurance system that Bismarck's government designed in late 19th-century Germany.

The other half of the system is the so-called "subsidized" regimen, which provides health insurance for the poor, unemployed, and indigent who cannot contribute. This welfare portion is funded by national and local taxes, royalties from oil and mineral sales, and also a 1.5 percent slice of the 12.5 percent taken from formal workers' paychecks as a "solidarity" gesture. The subsidized system is also supposed to receive any surpluses from Fosyga that are left over from the contributive plan. This half of the public health system covers 51 percent of Colombians and involves 44 EPSes. Taken together, the two regimens were meant over time to give all Colombians, now numbering just over 46 million, access to healthcare, and, so far, 96 percent of the population is at least nominally covered.

The system has worthy social goals, including guaranteeing every Colombian the right to free birth control, including vasectomies and tubal ligations. But there were also some absurd inequalities built into it by which contributive plan members were initially entitled to 40 percent more reimbursements than subsidized affiliates. For example, a poor female participant in a subsidized EPS may have gotten a preliminary diagnosis of cervical cancer, but not the coverage to pay for follow-up procedures to confirm it. That same woman was likely to be denied reimbursement for a mammogram initially, although many of these coverage holes have been filled.

But there are even more critical omissions that have not been corrected. At the top of my list is the government's failure to enforce its regulatory power, evidence of which is very clear in the freedom of the EPSes to commit abuses. Fourteen of the 22 insurers in the contributive system have been sanctioned for collusion, and have been sentenced to pay multimillion-dollar fines. Among the charges against insurers is conspiring to deny coverage and to defraud their affiliated subscribers, and the state as well, by altering information that determines insurance premiums.



> "The central problems are corruption, the failure of the government to adequately fulfill its regulatory function, and the inherent ideological conflicts."
>
> Francisco Jose Yepes Lujan, Director of Graduate Studies in Social Security and Health Administration, Pontificia Universidad Javeriana, Bogota, Colombia

The Office of the General Controller is investigating the EPSes and has found numerous incidences of insurers misappropriating employee contributions, which technically are state funds, and investing them in foreign real estate, in clinics they should not have built, and even in a tourist resort in Villavicencio. So when you talk about this crisis, you have to look at what these insurers have done with the funds that were supposed to go into health services.

The scale of corruption we see is due in part to the fact that regulators have never developed minimum rules and standards for the economics of healthcare delivery,

Facts and Figures

Life expectancy: This figure was 80 years for females and 73 years for men in 2010. That tracks almost exactly with averages in the region, and it has been steadily rising in recent decades with better healthcare penetration, particularly since social security was guaranteed by the 1991 Colombian Constitution. The increases are due partly to the dramatic improvement in infant mortality, as Colombia's under-five mortality rate has dropped from more than 40 per 1,000 births in 1990 to 20 as of 2010. Maternal mortality, however, remains alarmingly high at 92 per 100,000 live births, far above the Latin American average of 63.

Medical care: Colombia has a bifurcated national health insurance system. The "contributive" half covers all employees with formal jobs. They and their employers contribute 12.5 percent of gross paychecks into a national fund that then distributes premiums to the 22 insurers (resembling HMOs) that contract with health service providers. The poor, indigent, and unemployed are covered by the "subsidized" health insurance program funded by national and local taxes, royalties from oil and mining, and a "solidarity" portion of 1.5 percent of the 12.5 percent paid in by "contributive" plan subscribers. Those funds are channeled to cities and townships, which then contract with 44 insurers. When the national health plan was launched in the early 1990s, the aim was to cover all Colombians over time, and currently about 96 percent of the country's 46 million inhabitants participate. Contributive plan participants receive on average about 40 percent more in annual reimbursements than subsidized members, meaning the former are entitled to procedures that the latter are not. Eventually, the gap in reimbursements is supposed to narrow.
Healthcare spending in Colombia is far below the regional average, with US$569 per capita spent in 2009, compared with more than US$3,000 per capita in the rest of Latin America. Total national expenditure on health in 2010 was 7.6 percent of gross national product. Colombia also ranks low as far as medical professionals per capita. There are only 1.5 physicians and 6.2 nurses and midwives per 10,000 inhabitants – considerably fewer than the 20 doctors and 72.5 nurses and midwives averaged in the rest of the region. Colombia ranks close to regional averages in contraceptive prevalence (78 percent), prenatal care (4+ visits: 89 percent), and measles inoculation of one-year-olds (88 percent).

Morbidity and Mortality: The main health risk factor in Colombia is high blood pressure, which afflicts 34.3 percent of the male population over 25, compared with 26.3 percent of men in Latin America generally. Hypertension is diagnosed in 26.5 percent of women, above the 19.7 percent average across the region. But Colombian men are far less vulnerable to diabetes than elsewhere in the hemisphere, with inhabitants having about two-thirds the incidence of raised blood glucose and half the obesity rate seen regionally. Women are also under the regional rate in both diagnoses.

Lifestyle Risk Factors: Recent figures show that 21 percent of Colombian girls younger than age 20 are having babies, up from 13 percent in 1990. In Latin America, Colombia's teenage birthrate is exceeded only by Nicaragua (25 percent), Venezuela and El Salvador (21.6 percent), and Honduras (21.5 percent). By comparison, recent figures for the United States, tallied in 2006, show about seven percent of U.S. teenagers gave birth that year. Colombia also ranks high in landmine victims, with 512 in 2010 (including 54 killed), due to the ongoing armed conflict between leftist rebels, drug gangs, and government forces. The 2010 toll continued a declining trend seen since 2005 and 2006, when about 1,200 were killed and wounded in each year.

Sources: World Health Organization (WHO), Colombian Health Ministry, Guttmacher Institute, Colombian Campaign Against Landmines

which should be their job. Because health services is an imperfect market, regulators need to act as honest brokers of information that some actors in the health market have and that others do not have. The absence of those standards gives the EPSes enormous latitude to commit abuses. A very well-known example is one involving the SaludCoop EPS, which was taken over by the government after it was revealed that its executives were paying themselves enormous salaries while denying services to their affiliates. Another crucial mistake in the system was in not controlling prices that pharmaceutical companies charge for drugs. As a consequence, drug companies are about the only actors, except for corrupt EPSes, that have benefitted from this system. The fact that the drug companies are collecting exorbitant prices for medications is something all critics agree on, and I blame the lack of vigilance by the Colombian state.

The bottom line is that the system gives all the financial incentives to extract money, but absolutely no incentives to promote good health results. There are no standards of health outcomes, and no minimum results for which EPSes and healthcare providers can be held accountable. If an expectant mother dies or someone does not recover from a sickness that we have a cure for, the EPSes, the hospitals, and the municipalities should be responsible for those results. The 2007 law ordered the Health Ministry to come up with those standards within six months, and we are still waiting for them – so we cannot demand them from the actors in the system.

Colombia still has not resolved the inherent clash of interests between those who see healthcare in purely business terms as a commercial asset, and those who feel it is a fundamental human right. One's ideology is bound to affect how one views the crisis and how to fix it, and consensus still seems far away. The government, the World Bank, the Inter-American Development Bank, and a respected think tank in Bogota – Fedesarrollo – think it is a problem of regulation. Others, including many universities, the major medical associations, and big hospitals, think the entire system has to be restructured.

For example, a recent study by Fedesarrollo determined that the current system is salvageable if more resources can be invested. I do not agree. I think it is impossible to determine whether the system as it stands today can be adequately funded while there is so much corruption, when there are so many actors stealing the money. You have to have a system working in an orderly fashion, without the distortions caused by corruption, before you can determine its financial sustainability.

I think the only way out of the mess is to form a new national health system, learning from other experiences like those in the United Kingdom, Brazil, Costa Rica, or Canada. This system would not copy any of those plans, but rather would take elements from each and do away with distinctions between employer-financed and public-financed healthcare insurance systems. Healthcare would be made available to anyone with a Colombian identity card. That approach was the basis of a proposal put forth by a commission on which I participate and which was presented to Colombia's Congress at the end of August 2012. This proposal is based on every citizen's fundamental right to healthcare and the state's duty to respect, protect, and warranty its fulfillment.

The opinions reflected in this article are those of the author and do not necessarily reflect those of Siemens Healthcare.

Francisco Jose Yepes Lujan is Director of Graduate Studies in Social Security and Health Administration at Pontificia Universidad Javeriana in Bogota, Colombia. He earned his medical degree (1964) and his master's degree in public health (1967) at Universidad de Antioquia in Medellin and a master of science degree in health administration (1971) and a doctorate in public health (1979) at Harvard University. Prior to his current academic post, he was a professor at Universidad del Valle Medical School, and a visiting professor at the School of Public Health in the National Institute of Public Health in Cuernavaca (Mexico) and at the Department of Preventive Medicine at the Harvard Medical School. He has held numerous government posts, including Head of Human Resources and Secretary General at the Colombian Ministry of Health and Vice President of the Institute of Social Security, as well as adviser to several health ministers. He also has held several international posts, including consultancies with WHO, PAHO, World Bank, IADB, IDRC, Kellogg Foundation, and several Latin American and African governments. He is the author of numerous articles that have been published in Health Policy and Planning, Cadernos de Saude Publica, and national journals. He has published, with other collaborators, several books on Colombian healthcare reform. The most recent, Luces y sombras de la reforma colombiana de la salud (Highlights and Shadows of Colombian Healthcare Reform) was published in 2010 by Mayol Ediciones and IDRC. He is currently a member of the Commission for the Follow-up of Ruling T-760, which advises Colombia's Constitutional Court, and he has helped prepare a proposal to reform the current healthcare system that is currently being considered by the Colombian Congress.

Further Reading

Siemens offers a variety of customer magazines and information channels. "Further Reading" introduces a selection of articles and topics featured that may be of interest to you. To learn more, follow the link below each article. To subscribe to any of the magazines, see page 87.

Excellence through Lab Consolidation and Automation

Peking Union Medical College Hospital (PUMCH) is an integrated clinical, teaching, and research center. It has 1,800 beds, and an outpatient volume of 10,000 a day. Its Department of Laboratory Medicine, established in 1958, is evolving into an international center of excellence. Siemens is partnering with PUMCH to consolidate and optimize its lab operations and to address current and future strategic business needs. Testing volume is growing at about 15 to 20 percent per year due to the availability of new analytes (e.g., troponin). The demand for preventive care is equally increasing. The department also plans to launch outreach programs to support nearby clinics, as well as reference lab services. By consolidating the labs and deploying two ADVIA® WorkCell™ automation lines, PUMCH will be able to meet the increased demand, enhance quality management, and provide additional services for new business. It also frees staff time for more challenging tasks to continue clinical care and research. Read a case study demonstrating how automation and consolidation is supporting PUMCH by following the link below.

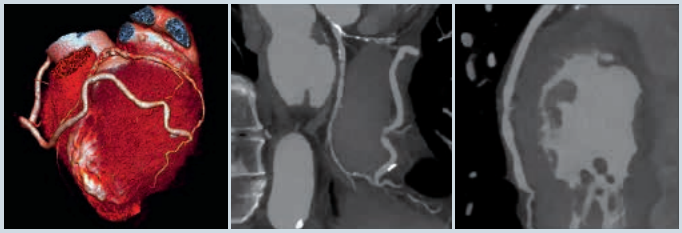
The outcomes achieved by the Siemens customers described herein were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption), there can be no guarantee that others will achieve the same results.

PUMCH continues to explore new testing capabilities.

www.siemens.com/lab-story-peking

Reaching for the Stars: Reducing Dose, Noise, and Blooming

Doctors at the German Heart Center in Munich, Germany, reveal their experience with the Stellar Detector, a new computed tomography (CT) detector technology, in an interview in Siemens' CT magazine SOMATOM Sessions. According to Stefan Martinoff, MD, and Jörg Hausleiter, MD, the new detector offers a better image quality due to reduced noise, less blooming, fewer artifacts, and higher resolution. With images being more accurate, it might be possible, for example, not only to see calcification, but to also evaluate the quality of the plaque and to describe its position more precisely. Besides the image quality, Hausleiter sees an advantage in the dose reduction. Up until now, the doctors could practically only reduce the noise by increasing the dose or they had to accept the noise, if they aimed for the lowest possible exposure. According to Hausleitner, now only 80 instead of 100 kilovolts are required for a CT scan of the heart, or just 100 instead of 120 kilovolts for carotid arteries. Learn more about the Stellar Detector by following the link below.

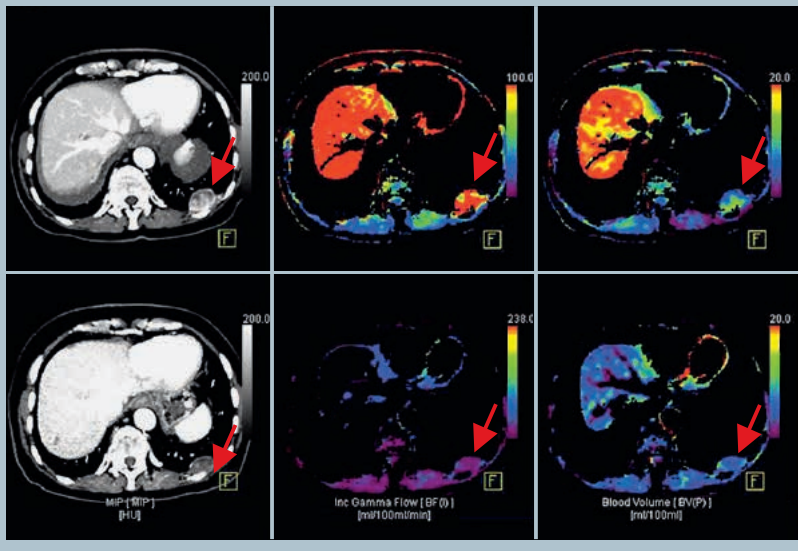


Example of a bypass follow-up study done with the Stellar Detector. *Courtesy of German Heart Center Munich, Munich, Germany*

www.siemens.com/somatom-sessions-stellar

Research on Individualized Oncological Therapies

Siemens Healthcare is contributing to a research project by the Biotech Leading-edge cluster "m4 – personalized medicine and targeted therapy." The project is one of several high-end clusters in Germany, and is funded by the Federal Ministry of Education and Research and by the Bavarian State Ministry for Trade, Transport, and Technology. The main focus of m4 conducted by University Hospital Munich, Großhadern, Germany, is the dedicated development of medical treatments for personalized oncological medicine. One of the projects is researching the non-invasive monitoring of molecular therapies in oncology. Molecular cancer therapies inhibit tumor growth and restrict blood circulation to the tumor as opposed to destroying it cytotoxically. The project is researching the potential of functional imaging procedures with dynamic, contrast-enhanced magnetic resonance imaging (MRI), computed tomography (CT), and contrast-enhanced ultrasound for tumor imaging. Researchers use Siemens medical equipment, such as the MAGNETOM® Verio 3 Tesla MRI scanner, the ultrasound system ACUSON™ S3000 and the SOMATOM® Definition Flash CT scanner. In the initial project phase, the group aims to optimize CT methods and the standardized quantification of tumor perfusion as a noninvasive imaging biomarker of therapy response. Read more about noninvasive radiological and nuclear imaging in primary diagnostics and therapy monitoring by following the link below.



CT perfusion maps of a patient with pleural metastases of a renal cell carcinoma (red arrow; top row: before treatment, bottom row: after treatment).

www.siemens.com/somatom-sessions-cluster-I

Webinar Replay: Bridging Healthcare Providers with HIE

What is a health information exchange (HIE), why should healthcare executives care, and why are provider organizations embracing it? These topics are covered in a webinar featuring experts Denise Abraham, the HIE coordinator for The Washington Hospital, Washington, PA, and Charles R. Vargo, Executive Director of the Washington Physician Hospital Organization Inc. (WPHO). They work closely in The Washington Health Information Network (WHIN), a private HIE that connects The Washington Hospital with physician practices affiliated with the Washington Physician Hospital Organization.

The WHIN uses a private HIE including data based on MobileMD™ technology from Siemens and enterprise access via a physician portal. In the podcast, Abraham and Vargo discuss their experiences with HIE as part of The Washington Hospital's patient care improvement initiatives. The HIE helps physicians, nurses, and key clinical staff secure access to key information such as lab and radiology reports and EKGs. The HIE unites 13 eletronic medical record systems from different vendors via interfaces to provide one data repository that allows enterprise access to more than 375 physicians in central Pennsylvania. More than 90 percent of their physician practices also participate in the physician portal.

The Washington Hospital and its physicians access key data across the care continuum, achieving significant reductions in paper-based communications and the associated staffing costs, expediting billing cycles, and reducing calls to medical records. Physician and staff satisfaction has been very high over the course of the five year project. Click on the link below to access the webinar.

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.

www.siemens.com/hie-webinar

Fastest Turnaround Times

ARUP Laboratories has earned a reputation for some of the fastest turnaround times in the industry. ARUP provides clinical lab service to the University of Utah Hospital and Clinics as well as to hospitals, commercial laboratories, military and government facilities, and public and private clinics. To reach new levels of efficiency and turnaround time goals in its hematology lab, ARUP implemented new rules, based on guidelines from the International Society for Laboratory of Hematology. It also replaced its legacy diagnostic technology with two Siemens ADVIA® 2120i Hematology Systems. The hematology lab's average turnaround time is now 17 minutes, compared to 43 minutes before. ARUP's Immunology Lab represents the other side of ARUP's business model. Like the hematology lab, it also relies on Siemens technology: several years ago, it implemented three ADVIA Centaur® XP Immunoassay Systems for its serologic hepatitis/retrovirus testing, which it selected on the basis of test menu, volume, reliability, cost of ownership, and test accuracy, along with dependability and middleware. Since ARUP switched to the ADVIA Centaur XP system it has, for example, decreased turnaround times for its hepatitis B surface antigen (HBsAg) – the lab's highest volume test – by 36 percent. Average turnaround times on the lab's HBsAg confirmation test have been reduced by 20 percent. Read more by following the link to the right.

ADVIA Centaur XP Immunnoassay System being used at ARUP.

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.

www.siemens.com/ARUP

Optimize Resource Usage with Innovative Automation Solutions

Siemens Healthcare Diagnostics launched Aptio™ Automation, the company's new laboratory automation platform that promises to transform laboratory operations by combining Siemens' industry-leading workflow expertise with peak performance capabilities, adaptability, and intelligent technology. Increasingly, clinical laboratories are turning to automation to help them meet the growing demand for in vitro diagnostic testing in the face of a shrinking labor force. Aptio Automation is an adaptable solution that allows for a phased implementation to accommodate both current and future needs of medium to very high-volume laboratories. The United Kingdom National Health System (NHS) of Tayside, is one of the first laboratories to deploy Aptio Automation. William Bartlett, PhD, Joint Clinical Director of Diagnostics at NHS Tayside, said: "We chose Aptio Automation because it can handle increasing workloads while enabling us to use our staff better. We expect that the implementation of this new platform will allow us to provide a state-of-the-art service that aligns the lab function with Tayside's overall goals for organizational sustainability and improved patient outcomes." To learn more about NHS Tayside's use of Aptio Automation, read the complete case study on our website.

Implementing Aptio Automation

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.

www.siemens.com/aptio

Patient Comfort and Low Dose in Pediatric Cardiology

In the latest issue of Siemens' computed tomography (CT) magazine SOMATOM® Sessions, physicians at the Minnesota Children's Hospital shared their experiences with the SOMATOM Definition Flash Dual Source CT scanner. Low radiation doses, high speed, and high temporal resolution are the main assets of the scanner. The high speed reduces the impact of patient motion and breath hold or sedation of pediatric patients may not be required in all cases. Without the use of sedation, parents can take their children home after the scan, which adds to patient friendliness. In the past, a pediatric CT almost always required intubating the baby and putting the baby to sleep so that an anesthesiologist could hold the baby's breath. According to David Dassenko, MD, Director of the Cardiovascular Care Center at Children's Hospital at Clinics of Minnesota, this paradigm has been dramatically changed with the Dual Source technology of the SOMATOM Definition Flash. The speed of the scanner also helps working more efficiently and saving costs. For the full story, please follow the link below.

Three-day-old baby with an interrupted aortic arch. *Courtesy of Minneapolis Heart Institute and Children's Hospital and Clinics of Minnesota, Minneapolis, USA*

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.

www.siemens.com/
somatom-sessions-flash-children

Saving Dose, Preserving Image Quality

The Inselhospital Bern in Switzerland was the first hospital to introduce the SOMATOM® Definition Edge CT in clinical application. The single source CT scanner uses the recently developed Stellar Detector, which allows for 0.3 millimeter spatial resolution.
While Prof. Christoph Ozdoba, MD, senior neuroradiologist at the Inselspital, describes the images as "cutting-edge," he was positively surprised by the dose reduction as well. Since the installation, Ozdoba and his team have been busy defining the neuro protocols, such as stroke examinations, pre-operative planning of neurosurgical interventions, and controlling of spinal surgery. The low dose aspect makes the scanner promising for the pediatric field as well, and even for cochlea implantations. In these cases, visualizing miniature structures is as equally important as saving dose. For the complete story on the experiences of the Inselspital in Bern, follow the link below.

The SOMATOM Definition Edge at the Inselspital in Bern.

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.

In clinical practice, the use of SAFIRE may reduce CT patient dose depending on the clinical task, patient size, anatomical location, and clinical practice. A consultation with a radiologist and a physicist should be made to determine the appropriate dose to obtain diagnostic image quality for the particular clinical task. The following test method was used to determine a 54 to 60% dose reduction when using the SAFIRE reconstruction software. Noise, CT numbers, homogeneity, low-contrast resolution and high contrast resolution were assessed in a Gammex 438 phantom. Low dose data reconstructed with SAFIRE showed the same image quality compared to full dose data based on this test. Data on file.

www.siemens.com/
somatom-sessions-edgeCT

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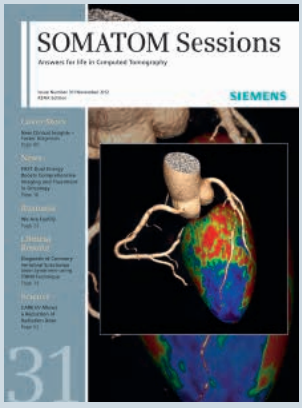

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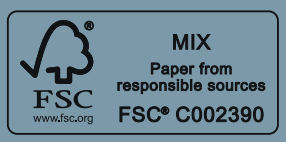

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