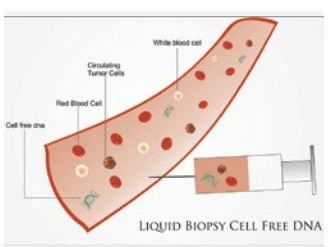
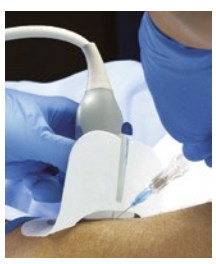
VOL 27 ISSUE 5/18 • Oct/Nov 2018

EUROPEAN HOSPITAL

THE EUROPEAN FORUM FOR THOSE IN THE BUSINESS OF MAKING HEALTHCARE WORK

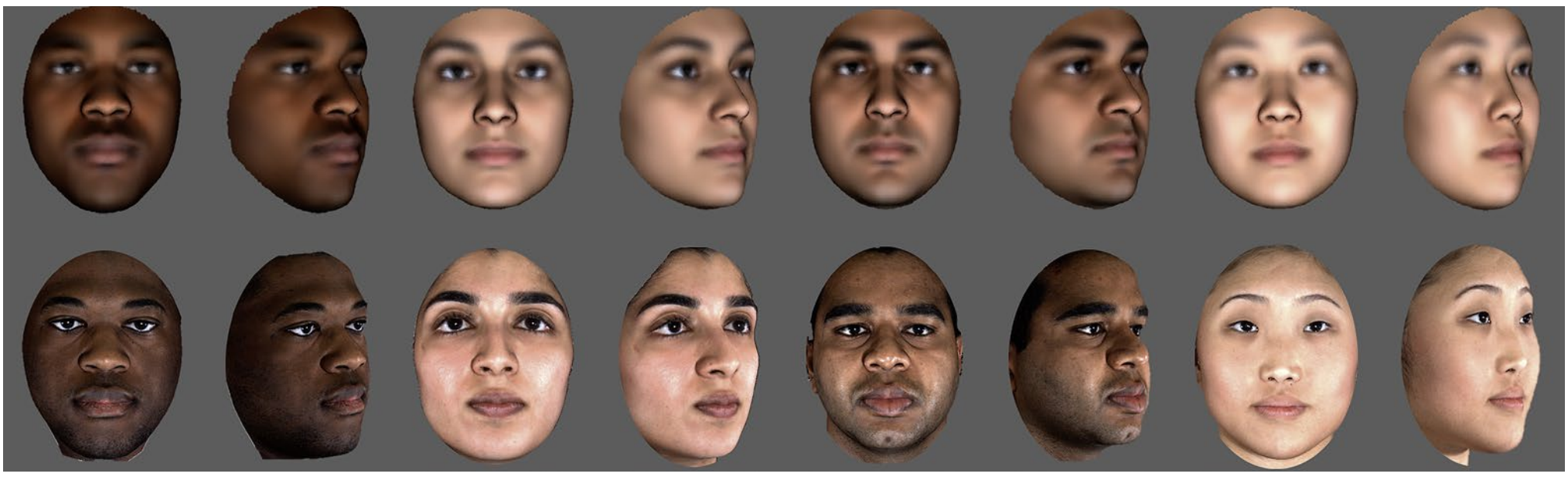




DRESS FOR SUCCESS
Introducing the World's First Barrier and Securement Dressing
ULTRADRAPE™
UGPIV Barrier and Securement

The revolution escalates

New procedures in medical image analysis based on artificial intelligence offer numerous opportunities but still have their limitations, Michael Krassnitzer reports.



Face reconstruction from solely contextual properties (a set of gene variants responsible for facial development, supplemented with age, BMI and gender). Top: reconstructed face. Bottom: real face, unknown at the time of the reconstruction. The model was built using a database of 3-D pictures, DNA, age, BMI, and gender of an admixed population. (Courtesy of Professor M. Shriver, Pennsylvania State University, and Dr Peter Claes, KU Leuven. Reprinted from Paul Suetens, Fundamentals of Medical Imaging 3rd edition, Cambridge University Press, 2017.)

'Is image computing an opportunity or a threat?' asked Dr Paul Suetens, professor of Medical Imaging and Image Processing at University Hospital Leuven. During the recent European Radiology Congress 2018 held in Vienna he also provided his own answer: 'It's an opportunity if the radiologist takes advantage of this supporting technology. It's a threat if it is discarded by the radiologist – "I am too busy now" are words I often hear; then it's other specialists who are gratefully adopting this technology.

'Image Computing, including image analysis, artificial intelligence, artificial neural networks und deep learning, is starting a revolution,' Suetens is convinced. Artificial Intelligence (AI) is not new – research in this field was carried out as far back as the 1950s – but, whilst in the early days AI learnt from image descriptions, it now learns directly from the images, such as photometric image characteristics.

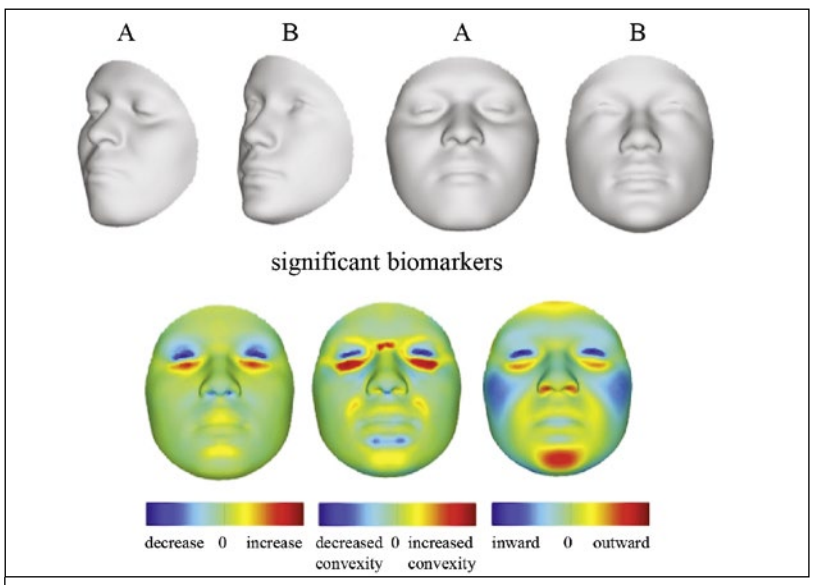
Suetens was involved in a project that used MRI images with BOLD contrast – with the image signal depending on the oxygen content in red blood cells – for a detailed investigation into which areas of the brain are active during hearing and processing of language. Other types of image computing are based on geometric image characteristics, such as segmentation of thoracic images.

Detecting mutations via facial analysis

Image computing also includes the exciting field of image genetics, in which Suetens is also involved. As a member of an international research team, he linked a database containing 3-D facial images with genetic information. One of the results was that biomarkers, which point towards genetic mutations, were found in the image data. Certain characteristics of human faces suggest a mutation of the SLC35D1 gene, which is associated with chondrodysplasia with snail-like pelvis, a very rare, lethal form of skeletal dysplasia.

A further use of this link between facial images and genetic information is the reconstruction of faces from human DNA, making it possible for instance to reconstruct the features of well-known persons of whom, long after they have died, only artistic

Continued on page 5



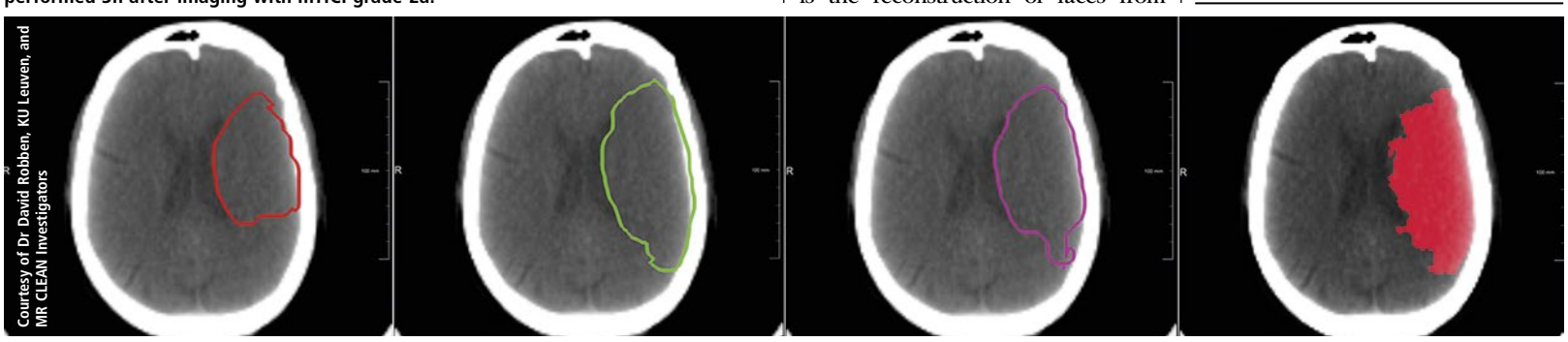
Result of a study of a selected set of SNP genotypes in a normal population. Faces A and B show the effect of two extreme SNP variants in gene SLC35D1. Mutations in this gene cause Schneckenbecken dysplasia. The colour images show the differences between faces A and B of some local features (from left to right: strain, curvature change and distance). Significant local differences, such as at the orbits, may define characteristic biomarkers for this particular genetic disorder. (Courtesy of Dr Peter Claes, KU Leuven. Reprinted from Paul Suetens, Fundamentals of Medical Imaging 3rd edition, Cambridge University Press, 2017.)

Example of deep learning to predict thrombectomy outcome in acute stroke based on CT perfusion images. A Convolutional Neural Network was trained on the following data:

- **180 CT perfusion images in the acute phase.**
- **Y/N followed by an intra-arterial thrombectomy. About 50% of the training set received an endovascular treatment.**
- **The time between imaging and the end of the thrombectomy.**
- **Occlusion present Y/N.**
- **A follow-up CT scan after 5 days with a delineation of the final lesion.**

Left three images: the prognosis showing 3 cases: (left) a complete reperfusion except for the core; (middle) no treatment, hence, the final lesion consists of core and penumbra; (right) predicted lesion after thrombectomy 3h after imaging with a presumed mTICI grade 2a.

Right image: the follow-up scan after 5 days with the final lesion. Thrombectomy was performed 3h after imaging with mTICI grade 2a.



www.healthcare-in-europe.com

CONTENTS

Will transplant medicine have a future in Germany?

Numbers of organs and qualified surgeons drop

Report: Anja Behringer

'Do we want transplant medicine? And if yes, what are we prepared to change in public policy, society and medicine?' This question characterises the current situation within this medical discipline. Since the 2011 transplant scandal, there has been a steady decline in organ donations according to the German Foundation for Organ Donation (DSO).

Although there were some 1,200 transplant donors annually from 2006 – 2011, the number of organs donated had already declined to just 800 in 2017. The reasons are numerous. Certainly, significant damage was done to the image and confidence in German transplant medicine. However, health policy and social structure improvements are also necessary: Despite measures taken to create transparency and quality assurance in the transplantation field – such as mandatory interdisciplinary case consultation in the transplant conference prior to a transplant and a newly introduced central registration at the German Medical Association – there were just as few organs transplanted in 2017 as had been in 2002, according to the German Foundation for Organ Donation (DSO). Some 10,000 patients await a donated organ. Media attention has been drawn to the discussion about the so-called opt-out solution proposed for a new organ donation bill, by German federal health minister Jens Spahn. However, the concept is nothing new. The opt-out option has already been used in many European countries for a long time:

In line with societal consensus, the opt-out solution means that if one rejects a potential organ donation, one must actively reject it when alive. Nonetheless, in most countries this does not happen without the consent of the patient's family. This 'double opt-out solution' also applies in Spain, for example. That country has led Europe for years, in having 47 donors annually per million inhabitants. By contrast, Germany is closer to the bottom of the list with nine donors per million inhabitants.

According to Professor Jörg C. Kalff, president of the German Society for General and Visceral Surgery (DGAV) and director of the clinic for general internal, vascular and thoracic surgery at University Hospital Bonn, the current debate is more than welcome. However, an introduction of the opt-out solution – double or simple – no matter how sensible, in isolation will probably not automatically yield higher donor numbers. A study in the German Ärzteblatt says there are also problems in Germany both with registering potential organ donors and with accomplishing the donation itself.

Economic pressure is high, especially on small hospitals, if they are also to identify all potential donors and register them with the DSO. To do this, however, they need to employ specially trained transplant officers and the sensitivity and readiness of medical personnel to contribute to an organ donation has to be correspondingly high. If the identified potential organ donor is actually to be used, (i.e. with consent given and no medical objections to an organ donation) then, following a process strictly regulated by law (here, cerebral death diagnosis), the extracting hospitals must maintain operative and intensive care capacities at high cost.

As Kalff explains: 'Assistance for organ donation and transplantation ought not to become a loss-making business for the extracting hospitals, otherwise higher registration rates will not be achievable in periods where economising is necessary.

Biomedical designers must increase safety

Cut device-related pressure ulcers

Whilst acknowledging that state-of-the-art bioengineering approaches are being applied in preventing Medical Device Related Pressure Ulcers (MDRPUs), Professor Amit Gefen, from the Department of Biomedical Engineering at Tel Aviv University, believes there are gaps in knowledge and technology in this area and therefore more must be done to improve patient care and avoid additional healthcare costs.

During a 'Wound Care from Innovations to Clinical Trials' (WCICT 2018) conference held in Edinburgh last June his 'Gaps in technology in prevention of MDRPUs' presentation analysed approaches to mitigate the problem and discussed emerging technological solutions.

'MDRPUs are injuries associated with the use of devices and equipment applied for diagnostic or therapeutic purposes, where the injury has the same configuration as the applied device,' explained Gefen, who is also the WCICT president. 'In intensive care units, MDRPUs caused by endotracheal and nasogastric tubes are common, both in adult and paediatric settings.'

MDRPUs, which, by definition, are hospital-acquired pressure ulcers (HAPUs) and considered in many countries to be an adverse event, may also be associated with the use of electrodes and wiring, pulse oximeters, catheters, compression stockings, and even bedpans.

'Studying the root causes of MDRPUs and effective means to mitigate their risk will lead to improved quality of life for patients and considerable cost savings which can otherwise be invested in further prevention and treatment of the primary comorbidity,' Gefen pointed out. 'Development of experimental and computational biomechanical models is essential for creating laboratory standards to test the safety of medical devices which come in contact with the surface of the body.'

His team in Tel Aviv has developed experimental systems equipped with thin flexible force sensors, as well as models of adult and paediatric patient heads to simulate tissue loads during interactions with devices, such as tubing, electrodes and wiring, masks and head supports. 'These physical and computational three-dimensional anatomical model systems facilitate rigorous empirical and simulation-based investigations of commonly encountered conditions and scenarios at which MDPRUs may occur.'

'Based on our findings,' he continued, 'we feel that the design of many edical devices and equipment used in ICUs should be revisited, since currently, there appears to be no attention to the safety of use with regard to the device-associated pressure ulcer risk.'

Gefen suggests that much can be done concerning the engineering design of device structures, selection of materials and integration of mechanisms that minimise the risk. Tubes, wires, electrodes and other equipment can be made safer, he said, and selection of more adequate, softer materials and devices, such as development of soft electrodes made of conducting textiles and similar ideas, can reduce the occurrence of MDRPUs.

Several examples were discussed during his presentation, based on data from the team's recent experiments and computer simulations of scenarios where there is high risk for MDRPUs.

Exploring new technologies

Advanced materials (particularly smart materials and structures), sensors and tele-monitoring systems, physiological signal analysis and data management, all have a role to play.

HAPUs are commonly considered an adverse event. MDRPUs, which are always HAPUs, compromise patient safety, lead to increased costs for potential additional hospitalisation days, interventions and treatments to manage the MDRPU condition, and also in association with the risk of litigation costs.

'From all perspectives,' he continued, 'the best strategy is prevention and dedicated technologies, including investments in new technologies, are required for that,' Gefen concludes.

'MDRPUs are a major portion of HAPUs and hence, mitigating MDRPUs will save vast financial

© shuttersock/Tyler Olson

BIOTRONIK
excellence for life
From Vision to Impact.
That's Excellence for Life.
From University Spin-Off to High-Tech Solutions.
biotronik.com

Prof Dr Jörg C. Kalff heads the Department of general, visceral, thorax and vascular surgery at the University Hospital Bonn, Germany, and is president of the German Society for General and Visceral Surgery (Deutsche Gesellschaft für Allgemein- und Viszeralchirurgie (DGAV)). The course of his medical career has also led Prof Kalff to the United States several times, where he worked in Washington, DC, and Pittsburgh, PA

Where increasing economic pressure creates disincentives and clinics do not (or no longer) participate in organ transplants for economic reasons, these systemic problems need to be remedied. Nonetheless, adjusted remuneration for the extracting hospitals can only be one measure.'

Policymakers have also recognised this, hence strengthening of transplant officers and adjusted remuneration for extracting hospitals is part of the bill now submitted by the German Federal Health Ministry (BGM).

Lacking organs plus surgeons

There remains a systemic problem, probably still underestimated: the lack of new potential surgeons.

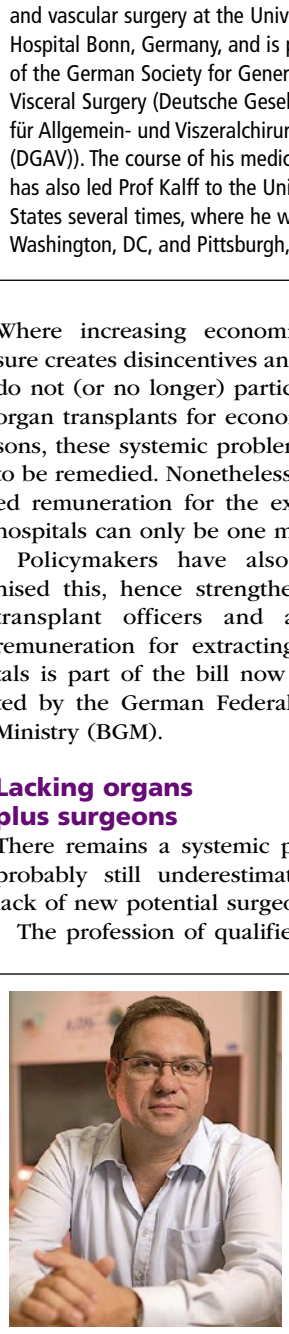
The profession of qualified transplant surgeon has become unattractive. The German Society for Surgery already warned of this two years ago. At the Visceral Medicine Congress in September 2018, the impact of the lack of new potential for this high-tech medicine was debated even more deeply.

Transplantation medicine is work characterised by the greatest degree of sub-specialisation – both in surgical method (including for organ extraction) and patient care prior to and after the transplant. 'Whereas, a few years ago, ten extraction operations were necessary, today some 25 assisted organ extraction operations are needed before one can work for the DSO as an independent extraction surgeon,' Kalff notes. The declining number of organ donors and transplants makes it ever more difficult for young surgeons to obtain the necessary operative experience for solid expertise.

A few years ago, transplantation surgery was considered a difficult and prestigious 'supreme discipline' among internal medicine surgeons. Today, it has become increasingly unpopular due to the constant availability of operating surgeons, operations that are difficult to plan, reliance on large centres, possibly also negative publicity and possible legal pitfalls. For example, the number of independent extraction surgeons working for the DSO declined nearly 18 percent between 2013 and 2017 (DSO press office).

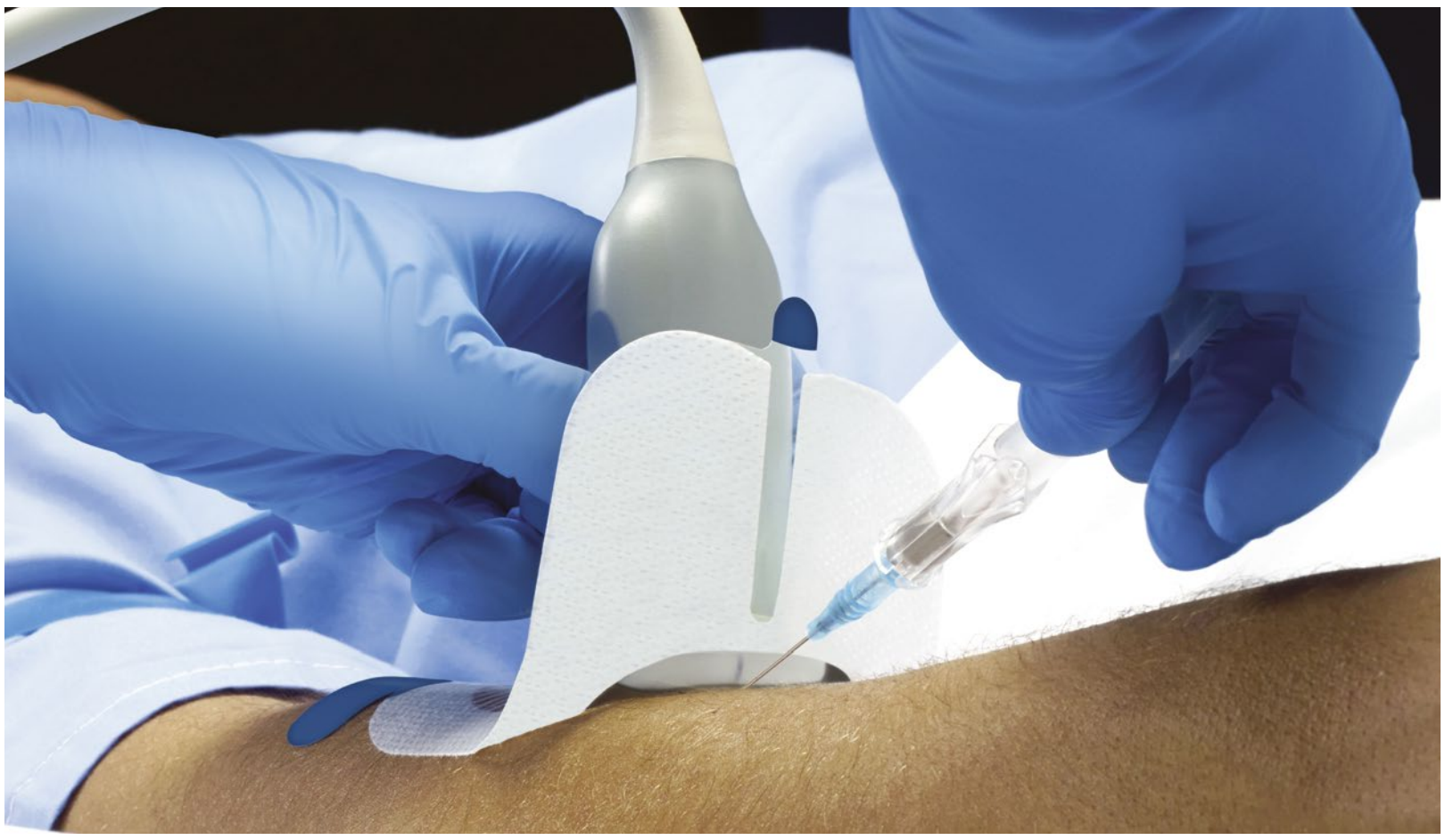
Germany still has no specialised education for a transplant physician or transplant surgeon, something quite normal in other countries, which is why it is important, more than ever, to train medical students as well as nurses and medical personnel in organ transplantation and to strengthen the acceptance of transplant medicine in society, Kalff emphasised.

The DGAV has already formed a commission to promote the education of young transplantation surgeons. Good news for the patients urgently waiting for an organ: the DSO reports a slight increase in donor numbers and transplants for the first half of 2018 compared to the previous year.



Amit Gefen is Professor of Biomedical Engineering and the Herbert J. Berman Chair in Vascular Bioengineering in the Department of Biomedical Engineering, Faculty of Engineering, at Tel Aviv University in Israel. He is also President of the Wound Care from Innovations to Clinical Trials (WCICT 2018) conference, which was held in Edinburgh.

and physical resources to medical facilities, which could potentially be invested elsewhere, for the benefit of patients, care givers and society.'



DRESS FOR SUCCESS

Introducing the World's First Barrier and Securement Dressing

Minimize cost and eliminate secondary cleaning procedures with UltraDrape™ from Parker Laboratories. UltraDrape is cost-efficient compared to the alternative use of sterile gels and covers, while its inventive design allows a no-touch, aseptic procedure.

UltraDrape… the first-of-its-kind, sterile barrier and securement dressing uniquely designed for UGPIV.

ULTRADRAPE™

UGPIV Barrier and Securement

To learn more about UltraDrape visit parkerlabs.com/ultradrape

60 PARKER The Sound Choice For 60 Years

Patent www.parkerlabs.com/ultradrape.asp ISO 13485:2016

Parker Laboratories, Inc. **The sound choice in patient care.™** 973.276.9500 parkerlabs.com

©2018 Parker Laboratories, Inc. UltraDrape and The sound choice in patient care are trademarks of Parker Laboratories, Inc. AD 34-15-3 REV 2

Chronic peripheral inflammation and schizophrenia

France boosts mental illness research

European Hospital correspondent Jane McDougall spoke with Dr Guillaume Fond, lead author of an exciting new paper* that explores the association between chronic peripheral inflammation and poor response to treatment in schizophrenia patients.

As European health services are pressured to provide the best possible care for best possible value, some medical fields are now very much the poor relation; this is particularly true for mental health.

Mental illnesses represent a great health burden and cause huge financial and societal pressure in terms of direct and indirect costs from repeated hospitalisation and treatment failures, while funding for research directed to improve diagnosis and treatment into these disorders is lacking.

To help rectify this problem and tackle the heterogeneity of available care and lack of organisation in the field, in 2007 the FACE network (FondaMental Academic Centres of Expertise) was set-up, with funding from the French Ministry of Health. Encompassing 39 different expert clinical centres throughout France, the network has created an original and innovative model to treat patients with mental disorders. By integrating clinical research into the patient's routine care, they have created a huge cohort of motivated individuals living with mental illnesses within society, but with closely monitored and carefully coordinated medical support.

This allows observed findings to directly guide treatment changes in a way that circumvents the normal downtime required for adjustments to guidelines to be made and paradigm thinking to shift before new medical ideas and concepts are adopted.

Concentrating on four disease areas: schizophrenia, bipolar disorder, treatment-resistant depression and high-level autism, in a multidisciplinary environment, the network provides newly referred patients with a two-day assessment, leading to a complete treatment plan tailored to their and the families' needs. A comprehensive report, plus details of prescribed medication, psychotherapy and suggested lifestyle changes are sent to the patient's own psychiatrist or general practitioner (GP) while additional annual follow-up with the expert centre's psychiatrists is proposed.

This latest scientific publication from the network comes from drawing on their cohort of schizophrenic patients and comparing them with the sub-population of patients within it (~10%), who develop ultra-resistance to psychotic medication (ultra-resistance to treatment in schizophrenia [URTS]). These patients are defined in the paper as demonstrating symptoms with a score greater or equal to 70 on the Positive and Negative Syndrome scale for Schizophrenia (PANSS) despite being treatment compliant.

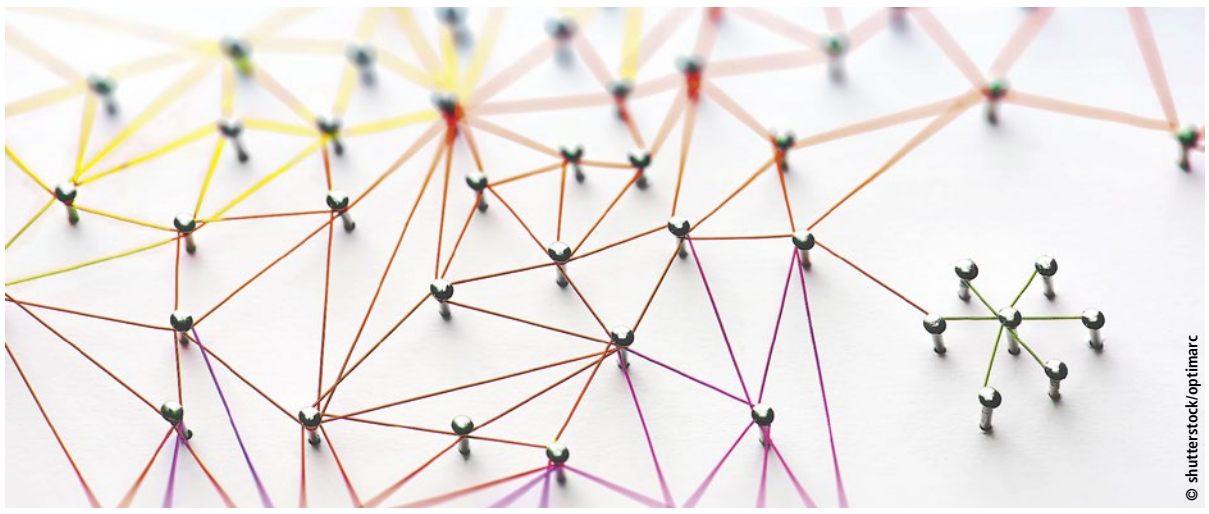
Blood tests revealed that these patients had elevated levels of highly sensitive C-reactive protein (hsCRP), which was independently associated with chronic peripheral inflammation (OR = 2.6 [1.2–5.7], p = 0.01). Confirming results from other studies in which increases in inflammatory biomarkers have been associated with poorer outcomes and treatment response in schizophrenia. Inflammatory blood markers have also been suggested to be predictive for treatment response to antipsychotics and high levels of CRP have been associated with cognitive impairment in both schizophrenia and Alzheimer's disease.

The mechanism whereby inflammation causes treatment resistance is as yet unknown. It may be speculated that chronic low-grade inflammation at the level of organs. such as the liver and pancreas, might alter drug absorption and/or metabolism, diffusion through membranes (blood/brain barrier) might also be compromised and possibly there is a more direct effect, on the brain receptors themselves, which has been postulated for Alzheimer's disease. Therefore, should schizophrenics be prescribed complementary anti-inflammatory treatment?

Presently, Fond suggests patients should be actively encouraged to reduce inflammation by lifestyle changes, such as taking more exercise, having a healthy diet with plenty of vegetables and increasing their intake of vitamin D and omega 3. In this way the patient's general physical health and wellbeing will improve, which can only be positive for their mental health.

Photo ©Tijana Feterman

Dr Guillaume Fond is associate professor, psychiatrist and coordinator of the national Schizophrenia Expert Centre Network and local head of the Resistant Depression and Schizophrenia Expert Centre, Marseille, France. He is affiliated with the AP-HM medical information department, researcher at the Group EA 3279: CEReSS – Health Service Research and Quality of Life Centre and Lecturer at the University Aix-Marseille-La Timone. Fond has coordinated the national Schizophrenia Expert Centre Network since November 2012.



© shutterstock/optimarc

* Fond G et al. Chronic low-grade peripheral inflammation is associated with ultra-resistant schizophrenia. Results from the FACE-SZ cohort. Eur Arch Psychiatry Clin Neurosci. 2018 May 28. doi: 10.1007/s00406-018-0908-0. [Epub ahead of print] PMID: 29808267 FACE-SZ details: www.fondation-fondamental.org/

The more powerful management is the least creative it becomes

Dutch homecare goes global

Home care in the Netherlands worsened. 'The organisations grew bigger, involving more and expensive management,' observed nurse Jos de Blok. 'Registration procedures became unnecessarily complicated. I enjoyed my job when I started in 1986, but that feeling changed. I knew there should be an easier way, without managers and at a lower cost. So, in 2006, I began the Buurtzorg concept.'

This is similar to the way district nurses in the Netherlands formerly worked: autonomously and using their own initiative. Buurtzorg has self-managing teams of ten to twelve people, who give one to one care for about fifty patients each. When multiple care or other expertise is needed, several team members can handle it. Patients know their carers and care is tailored to their current needs. 'This makes it measurable: care becomes cheaper, less care is needed, and patient self-reliance can be increased,' de Blok explained.

The teams hire their own colleagues and organise the work, planning, training, assessment, etc. Everything revolves around questions: What's happening? How are you solving it? What's the result? There are no policy plans to meet, and therefore no complaints from employees; everyone focuses on their expertise and professionalism. 'We started with four employees; now there are 14,000. I'm still impressed by all those who quit their jobs in the early days to work with us. Families also made Buurtzorg known around the country. It's all viable now.'

Care at home is like invisible holding hands.

https://stock.adobe.com/slonme

The organisation is frequently acclaimed as the Netherlands' most attractive employer. 'We have just one office in Almelo to support the teams,' de Blok explained. 'All the support, including our software packages, were created by employees. Sixty other Netherlands organisations now use Buurtzorg's supporting software. Problems? No. But we face a shortage of new qualified staff.'

The concept's first year was financed by De Blok's consultancy firm, although his wish to introduce it to other organisations did not initially materialise. 'My ideas about less management and autonomous teams were too frightening. Some were willing to adjust, but all wanted to keep their management. I'm convinced that top down rules don't work, so I started Buurtzorg as an autonomous company. The best ideas come from work in the field, not from management. People must have the opportunity to come up with their own solutions.'

Example: In 2010 an employee initiated the 'walker race', after an 87-year old said there are no races for people using a walker. 'She raised 10,000 euros to get the race started. It became the Rolympiade, an annual walker race covering 400 or 800 metres. Last year six over 90-year-olds – oldest 104 years – participated.' This improves mobility, and reduces loneliness, he noted. There are around 100 more Buurtzorg projects.

Beyond the Netherlands

De Blok now sells Buurtzorg abroad. 'The concept runs in Japan, China, Australia, Germany, England, France, Switzerland and Austria. Recently, I explained at a conference how to implement the system in a test environment and adapt it to local conditions. The universal components, such as teams, self-organising process, back office and IT support, work everywhere.'

Financing can be done through government or insurer reimbursements and, for example, in partly through private contributions, as in China and India.

In the Netherlands healthcare is covered by Social Security Systems and health insurers. In the early years, De Blok faced finance problems: the system was too unfamiliar. 'Now there are good agreements with insurers. We signed three-year contracts based on results and not, as with other care-giving organisations, on fees, costs and volumes.'

Nurse and entrepreneur

Although De Blok sees himself primarily as an entrepreneur, he maintains patient contact. 'It inspires me, he explained. 'For example, I received a letter, after her death, from a 31-year-old breast cancer patient. She thanked us for the great last months of her life.

'She had four new (caregiving) girlfriends who even took her on a stretcher to places she wanted to visit, one last time.'

The future

'It's crazy that management is the least creative when it has the most power,' he observed. 'Buurtzorg has 14,00 creative brains which invent and develop beautiful innovations with an enormous impact on self-

The revolution escalates

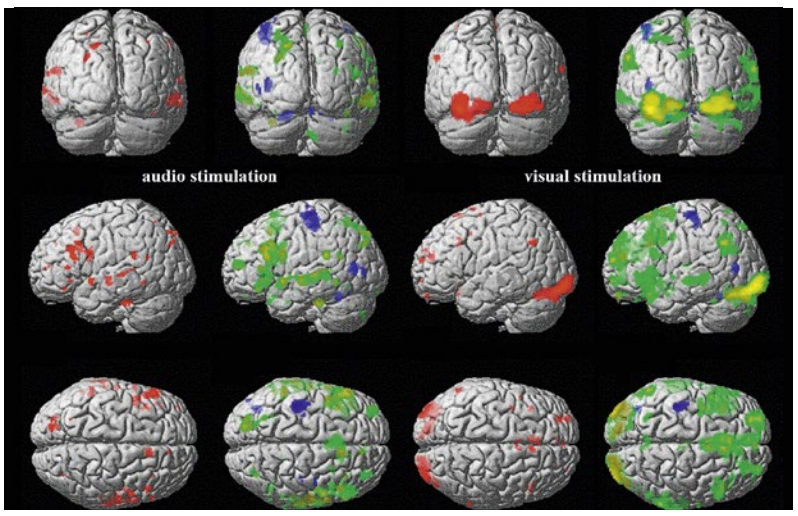
Continued from page 1

representations have been available. Respective reconstructions based on saliva samples from living test subjects achieve astonishing resemblances.

These applications are based on deep learning, which entails an artificial system learning from examples, then itself recognising inherent patterns and regularities. The basis of this is so-called artificial neural networks that are modelled on the workings of the human brain. 'Deep learning is a new paradigm with a strong impact on medical image analysis. It is sufficiently accurate and fast to compete with the human expert for specific narrowly defined tasks,' says Suetens.

However, deep learning still has its limitations. 'Deep learning is still in its infancy,' admits Suetens. If only a limited amount of data is available, or where the issue is around complex forms and deformations, neural networks do not function very well. 'A neural network is nothing other than a large number of individual data processors which are linked with one another – comparable to neurons in the human brain,' explains Suetens.

However, the human brain has around 86 billion nerve cells, whilst an artificial neural network only has 20 million nodes. 'When we increase the number of nodes the results become worse – and we don't yet know why this is,' Suetens admits.



Activation areas in fMRI language study. Column 1 and 3: hearing and seeing words (red) during respectively auditory and visual stimulation. Column 2 and 4: subsequent semantic decision (green) and right-hand response (blue). The yellow colour is a mixture of red (perception) and green (interpretation). (Figure courtesy of Professor S Sunaert, Department of Radiology, UZ Leuven. Reprinted from Paul Suetens, Fundamentals of Medical Imaging 3rd edition, Cambridge University Press, 2017.)

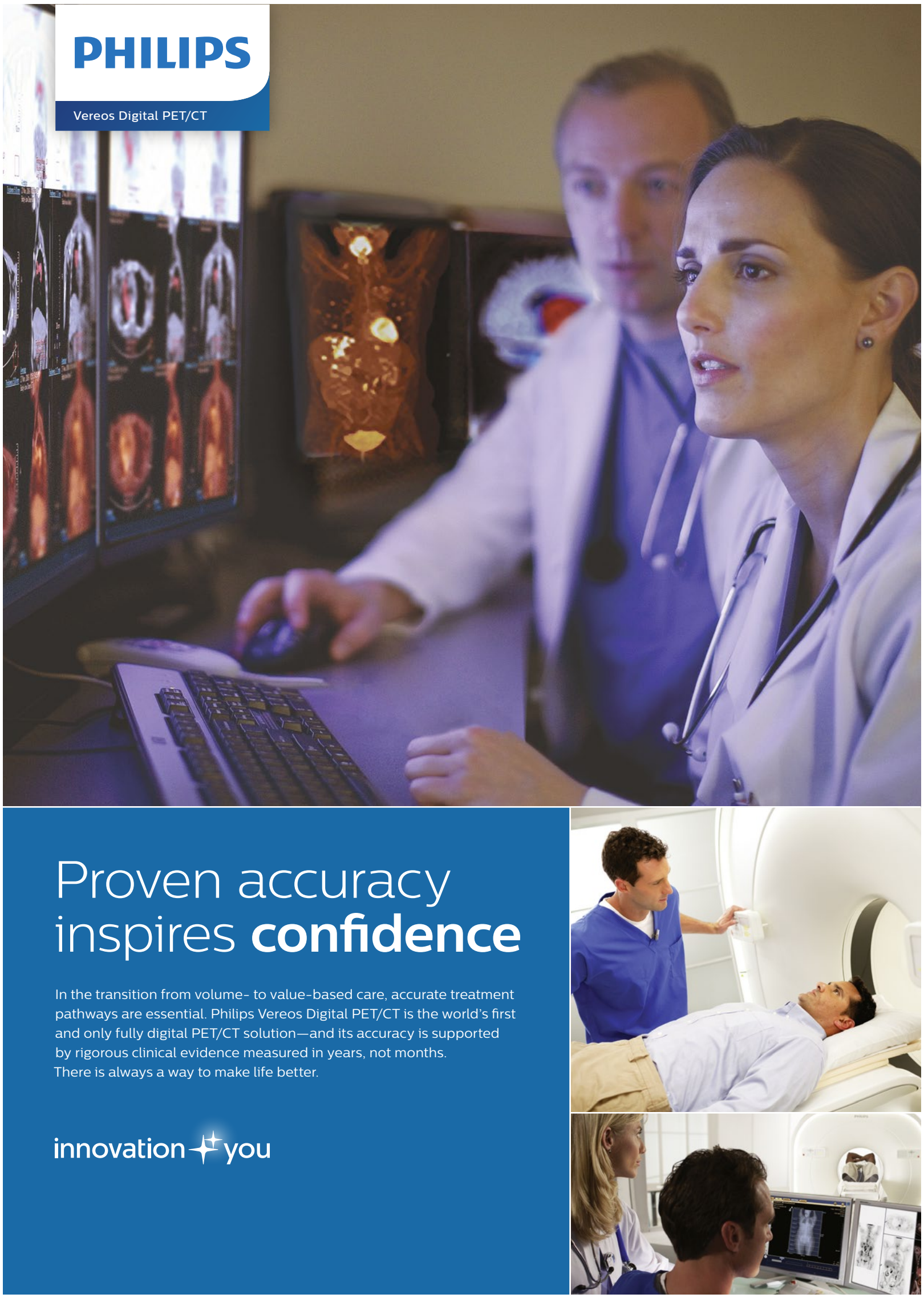
Professor Paul Suetens heads the Division Image and Speech Processing in the Department of Electrical Engineering at Katholieke Universiteit (KU) Leuven, Belgium. He is also chairman of the Medical Imaging Research Centre at University Hospital Leuven. His research focuses on medical imaging and medical image computing, which methodologically lies in the domains of computational science and machine learning. He has authored more than 500 peer-reviewed papers in international journals and conference proceedings and is author of the book 'Fundamentals of Medical Imaging' (3 editions, 2002, 2009, 2017).

Jos de Blok was awarded the prestigious Albert Medal from The Royal Society of Arts (RSA). 'I received a letter from London about the nomination. I thought it was a joke, until they called me and explained they wanted to recognise the innovation and global impact of the concept. So, in 2014, I received this award, placing me on the same list as physicist Stephen Hawking. I feel really honoured.'

reliance and well-being.

'I predict that, in five to 10 years many organisations worldwide will have reversed their approach, defeated by their own weapons: saving. And those savings will not be at the expense of healthcare providers and healthcare receivers.'

Buurtzorg is essentially a modern form of old Dutch community nursing. Now it is the largest provider of care. In addition, there is Buurtdiensten for community service, household and family assistance, like family care in the past.



Discharged ICU patients need careful rehabilitation

Aftercare after intensive care

Care models that go beyond rehabilitation services and are aimed at a smooth transition from intensive to aftercare are not established in Germany. A working group around Professor Dr Christian Apfelbacher at the Institute for Epidemiology and Preventive Medicine, Regensburg University, is currently developing a concept for intensive out-patient aftercare. 'The project is to help improve the care of patients after prolonged treatment in the intensive care unit (ICU) and to close the gap in the transition from intensive care to aftercare,' the professor explained during an interview with Sascha Keutel.

Prolonged treatment in intensive care frequently leads to chronic physical and psychological impairments, also described as Post Intensive Care Syndrome (PICS). This description relates to new or worsening physical (pulmonary, neuromuscular, physical-functional), cognitive (such as memory- or concentration problems) and psychological (anxiety disorders, post-traumatic stress disorder and depression) problems in patients, which occur due to illness requiring treatment in intensive care and persist after hospital treatment,' Professor Christian Apfelbacher explains.

'On-going, comprehensive diagnostic investigation, as well as adequate multidisciplinary care with coordination of services, are imperative for patients who have received intensive care. Patients find coordinated, needs-based medical care after being discharged helpful. It can also help to reduce the large share of patients who have to be readmitted after being discharged: Care models would be desirable that go beyond the services provided by rehabilitation clinics and are customised to patients' needs during the post-ICU phase.'

A continuum of care

Patients who are discharged after a lengthy stay in intensive care are rarely completely recovered and most are still dependent on help. Therefore, the study project is not only aimed at patients but explicitly also their relatives, as 'they are also affected by the continuous morbidity. PTSD, depression, anxiety and adjustment disorders can be potential implications. In recent publications these psycho-pathological reactions among relatives have also been described as PICS-Family (PICS-F),' Apfelbacher adds.

However, persistent psychological - and physical morbidity after discharge, or transfer, has so far not been sufficiently addressed; this is where the study comes in. The working group wants to specify patients and relatives needs, with the help of primary and secondary data and to develop a concept for intensive out-patient aftercare on this basis. 'Intensive out-patient aftercare would improve the processes - coordination of therapeutic services, referrals based on specific medical needs, contact with GPs, involvement of relatives – and close the gap in care,' Apfelbacher said, who also explained that the project is carried out alongside Professor Dr Thomas Bein from the Anaesthesiology Clinic at Regensburg University Hospital.

A participative approach

The study includes adult patients who have spent more than five days in intensive care, have had organ replacements and have a predicted life expectancy of more than six months. The first step is to investigate the uptake of care as well as existing care requirements of patients and their relatives after discharge from the ICU, with the help of guided interviews. Recruitment of around 25 patients, plus their relatives, is done via stratified quota sampling with regards to age, gender and severity of illness among the participants and consortium partners. In parallel, an analysis of

In 2003, **Professor Christian Apfelbacher PhD** gained a master's degree in philosophy at the Munich School of Philosophy, followed by a Master of Science in Public Health at the London School of Hygiene and Tropical Medicine (DLSHTM) in 2006. Two years later he became a Doctor of Humanistic Sciences at the Medical Faculty of Heidelberg University. Then came a PhD in Philosophy at Brighton & Sussex Medical School in 2013. In the same year he qualified to teach medical sociology. In spring 2014, Apfelbacher became Professor for Medical Sociology at the Institute for Epidemiology and Preventive Medicine at Regensburg University.

The interdisciplinary challenge

Evaluating ICU care for cancer patients

Progressive treatments offer new chances for cancer patients, but also could result in as yet unknown complications. The number of cancer patients transferred to the ICU for cancer-specific and internal medicine related reasons is on the increase. Caring for them on the ICU is a complex challenge, with interdisciplinary cooperation playing an essential part.

Certain criteria need to be met for the admission of a cancer patient to the ICU, according to Dr Peter Schellongowski, specialist in internal medicine and intensive care and senior consultant in the ICU at Vienna's Medical University. The Austrian ICU specialises in the care of critically ill cancer patients suffering from, for instance, acute respiratory failure and infection related problems such as sepsis or toxic reaction.

Admission criteria

'We need to consider several factors when deciding whether critically ill cancer patients should be cared for in the ICU. Apart from the patient's general condition, we must evaluate the probability of surviving acute organ failure(s) along with the expected long-term survival and therapy options after intensive care treatment. The latter can be very strenuous and even traumatising and affect the remaining quality of life, which is why the admission criteria are important,' Schellongowski explains. 'Patients in the early stage of a still treatable disease, whose life expectancy is likely to be more than a year, patients who should receive curative treatment, and patients in remission from their primary disease are usually admitted. They are given a full code management, receiving the entire range of intensive care treatments available. However, if treatment options have been exhausted or intensive care is unlikely to improve a patient's life expectancy or condition we would refrain from treatment.'

For patients receiving palliative care who may have a good chance of longer-term survival due to treatment progression, such as patients with low-grade non-Hodgkin Lymphoma, for instance, or patients in partial remission from diseases like multiple myeloma or solid tumours, admission to the ICU can also make sense.

'The group of patients who may benefit from intensive care continuously expands due to the broad range of cancer treatments available. Oncology is continuously evolving, making a close cooperation between intensive care medics and oncologists so important: It guarantees the best treatment for the patient,' Schellongowski explains.

Close examination

Despite structured criteria and guidelines, the decision-making process on treatment and admission objectives is often very complex. 'A minimum "one-year survival" objective obviously does not mean that a patient with an 11-months survival prognosis will immediately fall outside the scope. Each case is intensively examined.

'If the situation is not clear-cut,' he adds, 'we often start a multi-day ICU trial to examine whether the patient responds positively to the treatment. Then we decide if it makes sense to continue with intensive care.'

In some cases, limited intensive care treatment is considered, excluding certain procedures such as intubation. 'A study has confirmed that this approach also helps many and that survivors suffer from post intensive care syndrome (leading to anxiety, depression or post-traumatic stress syndrome) no more frequently than patients without therapy limitations.'

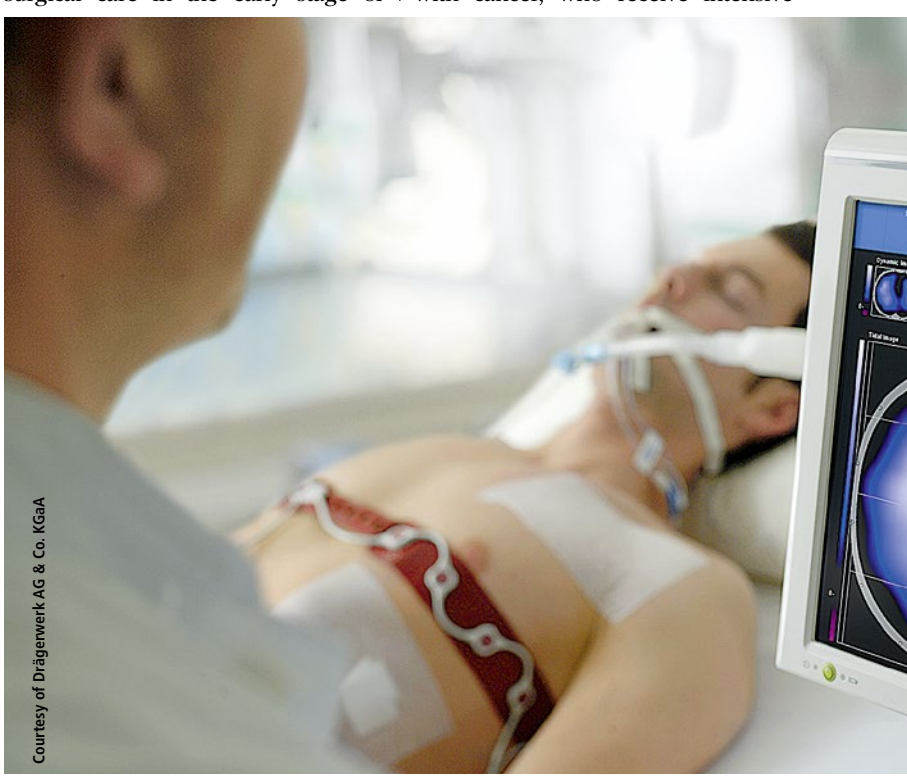
Frequent ICU admissions

Patients in the early stages of a cancerous disease are in particular need of intensive care. Five to six percent of cancer patients with solid tumours are admitted to the ICU for primary surgical care in the early stage of the disease. Further, up to 18% of patients with aggressive, haematological cancers require intensive medical care during the early disease stage, either because of early complications or because of aggressive initial treatment that has caused secondary complications, both ultimately leading to organ dysfunction.

Specific treatment

The most common cause for ICU admission is acute respiratory failure, followed by complications from sepsis. Haematological diseases in particular often lead to pulmonary complications, caused by infections or complications arising from leukaemia itself. 'This complicates treatment, because chemotherapy can aggravate an infection. At the same time, chemotherapy cannot be suspended for too long.

'Close cooperation between haematologists and oncologists is therefore of extraordinary importance and very desirable,' Schellongowski emphasises. 'It's scientifically well documented that intensive care patients with cancer, who receive intensive



Courtesy of Drägerwerk AG & Co. KGaA

ACEM

MEDICAL LIGHTING SYSTEM

ACEMSO15F

FOCUSABLE LED LAMP FOR EXAMINATION AND MINOR SURGERY

ACEM SPA | Medical Company Division
ARGELATO, BO - ITALY
PH +39 051 721844 | FAX +39 051 721855
info@acem.it | WWW.ACEM.IT

MEDICA
12-15 NOV 2018
DÜSSELDORF
HALL 10 | STAND B60

routine data from health insurer AOK Bavaria will be carried out to capture the objective care requirements.

All those involved in the care process will be asked about their knowledge of the care requirements, their views as to the possibilities and challenges of interdisciplinary cooperation and their expectations regarding the practicability of intensive out-patient aftercare in focus group discussions.

The group setting and resulting dynamics of interaction are to evaluate subjects and statements that go beyond the contents provided in the guidelines. Five focus group discussions are anticipated, with up to eight participants each. To ensure each group is heterogeneous, participants will have mixed educational backgrounds and professions.

'An elementary building block of care'

Based on these results, the study group will develop a concept for participative, intensive out-patient aftercare. In the second step, this will be tested in a model project. 100 patients will be split into two groups of equal sized, with one group receiving intensive out-patient aftercare and the other conventional care. Data from both patient groups is to be compared for certain parameters to measure success, with further discussions conducted. The research questions relate to the feasibility of intensive out-patient aftercare, acceptance amongst patients and effects of intensive outpatient aftercare on physical and psychological quality of life.

The participative approach of the concept means that the subject of transferability to the treatment situation in everyday life is an inherent feature. 'We see the focus of the intensive out-patient aftercare in examination, diagnostic investigation and coordination of therapeutic services, with cooperation between surgeries and therapists being an elementary building block of care,' Apfelbacher concludes.

© Werner Krüper

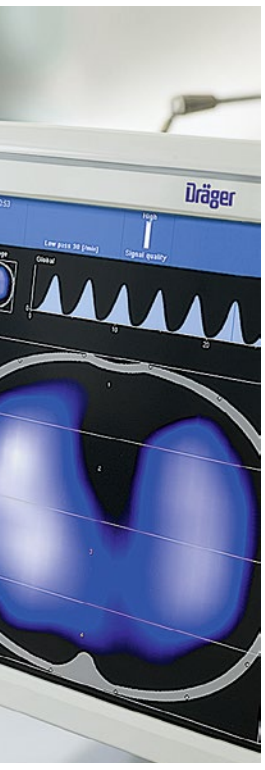
Prolonged intensive care can lead to chronic impairments

Source: MedUni Wien F. Matern

Associate Professor Peter Schellongowski MD PD, internal medicine and intensive care specialist and senior consultant in the ICU at Vienna's Medical University, heads the working group on haemato-oncological intensive care medicine at the Austrian Society for Internal Medicine and General Intensive Care and Emergency Medicine (ÖGIAIN) and is deputy spokesman for the working group for intensive care medicine at the German Society of Haematology and Oncology (DGHO).

interdisciplinary care, have a better outcome."

A German-Austrian consensus recommendation on this topic is due to be passed and published shortly.



Patients in the early disease stage, those who should receive curative treatment and patients in remission from their primary disease, are usually admitted to the ICU and given so-called full code management

Advertorial

MEDICA 2018: Greater efficiency through medical technology – Made in Taiwan.

Taiwan is a country founded on technology and the relentless drive for innovation. It benefits from the ambitions of its individual researchers, their institutes and companies and from the engagement and support from the Taiwan External Trade Development Council – TAITRA. At this year's MEDICA, TAITRA presents an elite group of 15 companies - the recipients of TAITRA's Taiwan Excellence awards – displaying technology to improve efficiency, process and, ultimately, outcomes to the world's doctors, caregivers, and patients.

The ability for doctors to reach rapid, accurate conclusions is key to diagnosis and continued evaluation. Leltek Inc. offers this through a best-in-class cordless ultrasound subsystem. Of particular interest is their system's bring-your-own-device compatibility, its ultra-light design at only 330 grams, and the exceptional battery life of three hours – overcoming the issues associated with previous cordless ultrasound solutions. Another company featured through Taiwan Excellence, AmCad, leverages existing ultrasound diagnostic equipment to achieve the most cost-effective sleep apnea (OSA) diagnosis. As the understanding of the denigrating effects this condition plays in the general population becomes established, AmCad's UO system delivers standardized ultrasound-head positioning and output data analysis to achieve an accurate diagnosis within 10 minutes on a fully awake patient, thereby eliminating the need for expensive overnight evaluation.

The world's population is aging and becoming more connected. This fact is of utmost importance to Taiwan; its commercial sectors are focused on issues associated with a citizenry maturing in-stop with the West. Rehabotics Medical Technology Corporation has just brought an exceptional aid to the market, MirrorHand, which enables robot-assisted rehabilitation of the hands after a stroke. Weighing only 750 grams, it is by far the lightest robotic rehabilitation device for the hand. The mirrored motion from healthy to compromised hand and the programable passive motion rehabilitation functions support neuromuscular regeneration.

Some unique technologies are just as beneficial at either end of life. The Opro9 Smart Diaper from Civicloud is an example of just that. By offering a diaper with networked moisture monitoring, this technology is an excellent low-cost, multifunctional device. Whether in a NICs unit where renal function monitoring is a key aspect to positive outcomes, to an assisted living center where the care must remain efficient but responsive and flexible, this simple system can alert staff to needs of each patient and ensure an exceptional quality of care while offering valuable data-points into the EHR.

These Taiwan Excellence recipients and others organized by TAITRA will be presented during the MEDICA in Dusseldorf, Germany, from November 12th through the 15th in hall 17 Stand A61. All are interested in realizing opportunities for technological cooperation and business development with the global medical community. Stop in for a conversation. Hosts are on-hand and individual tours are available to meet your goals.

Visit our press conference:
Tuesday, November 13, 2018
10:30 am - 12:00 am, Hall 8b, Room 814A
www.taiwanexcellence2018.de/pc/

www.taitra.org.tw

Multidisciplinary care is key to cardiac disease management

Research with 7-Tesla MRI

New 7-T MR methods could potentially shed light on cardiomyopathies' principles, according to a leading French radiologist who also stresses the importance of teamwork between radiologists, cardiologists, surgeons and anaesthesiologists.

Report: Mélisande Rouger

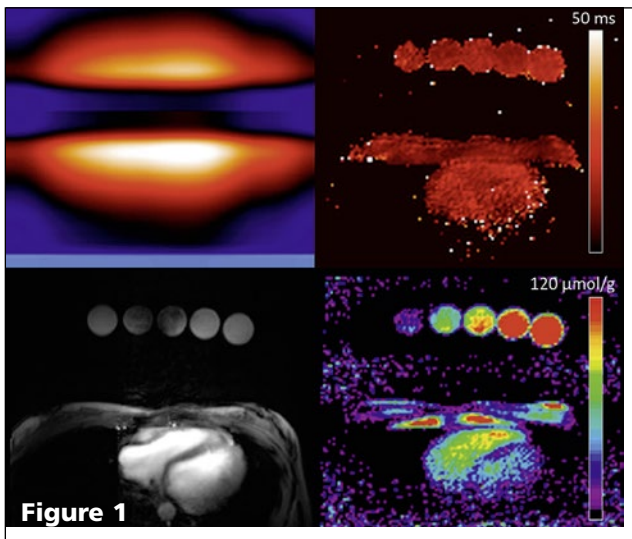


Figure 1

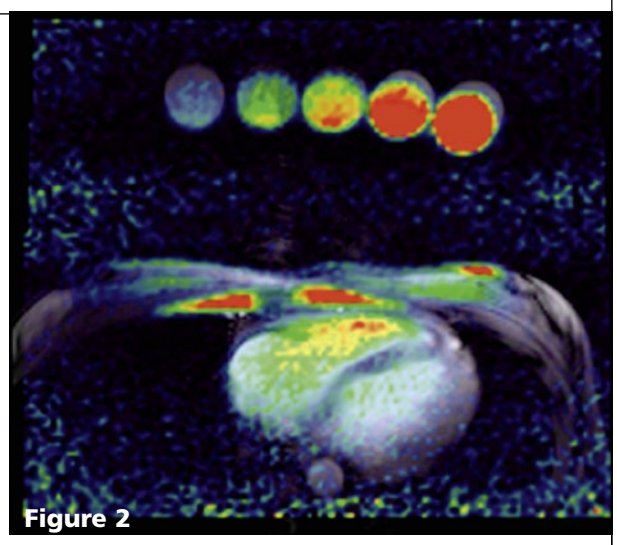


Figure 2

Sodium mapping of the heart using 7 Tesla MRI

Higher signal-to-noise ratio (SNR) using 7 Tesla MRI allows to map sodium in the human heart. The isolation of the long relaxation sodium component (using a long echo time) and the compensation of concomitant signal modulation (T2star and B1+/B1- from transmit-receive coil) allows for a single slice to be mapped within 5min at a resolution of 2x2x10 mm3. Reference sodium concentration vials attached to the coil serve as calibration of the sodium MRI signal.

Figure 1: Top-left is B1+/B1- map, Top-right is T2star map, Bottom-left is anatomical MRI image of the heart using conventional 1H-MRI, and bottom-left is the map of long-relaxation sodium concentration after corrections of the sodium MRI signal using the maps at the top.

Figure 2: Overlay of long-relaxation sodium map onto the anatomical MRI.

Morphologic and dynamic information of the myocardium is achieved with millimetric resolution (0.9x0.9 mm2). Strong intensity variations characteristic of 7-Tesla MRI can be observed from anterior to posterior myocardial segments.

New tools provided by industrial partners and used by cardiovascular surgeons and radiologists are improving treatment of thoracic aorta pathologies. An increasingly used technique is fusion imaging, in which pre-treatment MR and CT scans of the patient are being fused with angiography images to guide stent-graft navigation through the vascular structures of the patient during the intervention, according to Alexis Jacquier, cardiovascular radiologist at Timone University Hospital in Marseille.

'Fusion imaging enables to lower radiation dose and to reduce the amount of contrast media that are traditionally required in this type of surgery. It avoids having to inject iodine to know where we're at,' he explained.

The hospital also hosts the Timone Aortic Centre (CAT in French), a leading regional multidisciplinary centre that covers full aortic pathology management, from diagnosis to patient care and follow-up, with a strong connection with the university. The CAT includes vascular and cardiac surgeons, radiologists, cardiologists, vascular physicians and anaesthesiologists.

The objective is to provide a multidisciplinary approach to provide the best medical care; for instance all thoracic stent-graft procedures are performed by a multidisciplinary team comprised of vascular surgeons, radiologists and anaesthesiologists at CAT.

Imaging has become key in thoracic aorta treatment with the boom of minimally invasive procedures. Besides thoracic disease, Timone Hospital is one of the main centres in France offering endovascular interventional radiology skills to treat patients with carotid and renal disease, which Jacquier and colleague Vincent Vidal perform daily, along with the full suite of cardiovascular interventional radiology procedures – endoprostheses and stent placement, small vessels and tumour embolisation, etc. Furthermore, the hospital is located close to the medical and biology MR centre (CRMBM), one of the few labs in Europe that work with 7-T MRI for diagnostic imaging research.

This proximity enables Jacquier and team to test 7-T methods using sodium instead of proton imaging, a possibility that opens brand new perspectives in heart imaging. 'Sodium electrolytic disorganisation in the myocardium can have an electrical and mechanical impact on heart function. 7-T will enable the development of new applications in the field. It is still a complex task, but we are working hard on different papers on sodium quantification in the myocardium and potential clinical applications' he explained.

Cooperation with cardiologists is essential in myocardial disease management, according to Jacquier, who again stressed the importance of the multidisciplinary approach during patient treatment. 'Patients are now being care for within the heart team, a model increasingly followed by healthcare facilities in France and beyond,' he explained, adding, 'whether it's for TAVI procedures, diagnosis or follow-up. Medicine is becoming hyper specialised and mixing profiles and specialties enables us to significantly improve patient care.'

Another significant development in France was the reform of the radiology residents' training scheme, which was introduced in 2017. Radiology residents must now undergo a three-step training, including successively: base training (one year), dedicated to emergency radiology; in-depth training (three years), to ensure that every subspecialty in radiology has been covered in their education; and consolidation training (one or two years), providing certification for one or two subspecialties.

The French Council of the Teachers of Radiology (CERF) has been piloting the change for radiology. The French Society of Cardiovascular Radiology now provides e-learning material to ensure homogeneous teaching and training program across the country. In September, the series became freely available for French residents on the CERF website, and also available for all radiologists on the website of the French Society of Radiology.

This change is a substantial improvement in the training scheme, because it reflects daily routine better, Jacquier added. 'Cardiac imaging studies are being prescribed every day by all sorts of physicians: GPs, endocrinologists, surgeons, and even oncologists, for instance in pre- and post-chemotherapy evaluation.'

As for cardiology, the French Society of Cardiology and the French Society of Radiology established a working protocol in 2005; according to this, the cardiologist prescribes the CT and MR scans and radiologist performs the technical assessment and writes the report – and then sends it to the cardiologist. Jacquier: 'This division of tasks promotes the best possible medical care, but everything really depends on the physician's skills. A lot of things may need to be updated as we gradually introduce artificial intelligence.'

Radiologists must also homogenise the way they write the imaging report. Introducing the structured report to exploit data at national level will prove essential for their future. Another priority is to improve communication not only with patients but also other medical specialties, he said.

Jacquier will participate in the International Day of Radiology (8 November 2018), an initiative to highlight the radiologist's role in cardiac care.

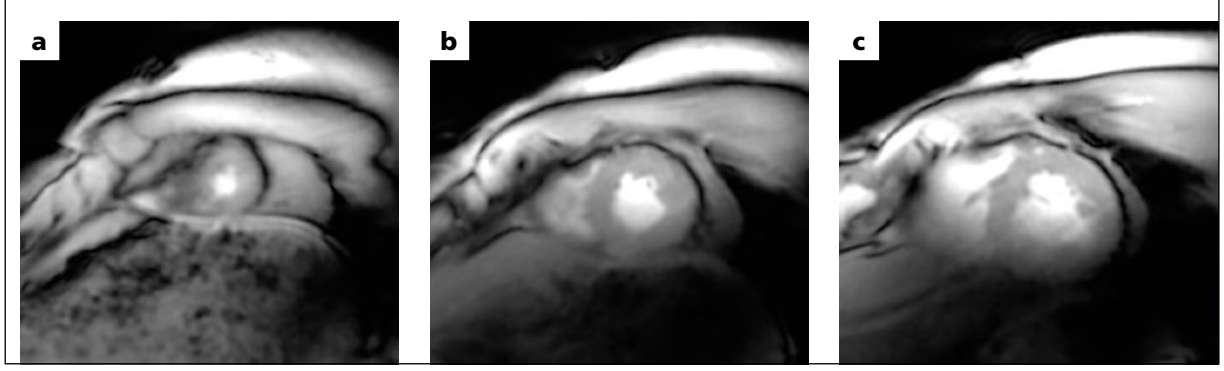
'Radiology is not a medico-technical specialty, although French administration still classifies us as such. We're a medical discipline. The old-fashioned image of the radiologist reading scans alone in a basement and not having contact with anyone else in a hospital is outdated. The radiologist,' he emphasised, 'is now at the centre of patient care and healthcare.'

Cardiovascular radiologist **Professor Alexis Jacquier**, at Timone University Hospital, Marseille, France, trained in Marseille and Lyon and gained his PhD in San Francisco, USA, supervised by Maythem Saeed and Charles Higgins. In 2006 he integrated the cardiovascular group in the CEMEREM research lab (http://crmbm.univ-amu.fr). He is author and co-author of more than 90 peer-reviewed publications and has presented numerous lectures, tutorials and refresher courses internationally. He also chaired the European Society of Cardiac Radiology membership committee and is current vice president of the French Society of Cardio-Vascular Radiology (Société Française d'Imagerie CardioVasculaire, SFICV).

High-resolution Simultaneous Multi-Slice (SMS) dynamic MRI of the heart at 7 Tesla

Increased signal-to-noise ratio from the 7 Tesla MRI is harnessed for refined imaging of heart. Simultaneous Multi-Slice (SMS) cardiac dynamic MRI (cine) permits the acquisition of three thin-slices (4 mm) within a 10 s breath-hold. Robustness to patients motion and limited breath-hold capacity is guaranteed through a dedicated self-calibrated SMS technique tailored for cardiac imaging. Morphologic and dynamic information of the myocardium is achieved with millimetric resolution (0.9x0.9 mm2). Strong intensity variations characteristic of 7 Tesla MRI can be observed from anterior to posterior myocardial segments.

Figure 3: SMS cine acquired within 10s showing diastole (relaxed phase of the cardiac cycle) of the apex (a) mid-ventricular (b) and base (c) slices.



Accutron® CT-D

New with **Pre-Inject**

Testing of the patient's access prior to the injection!

Easy activation with a single keystroke!

Automatic profile adjustment!

Update now!

Contrast medium injectors and consumables for CT, MRI and angiography

Hauptstrasse 255 · 66128 Saarbruecken
For more info: www.medtron.com

MEDTRON® AG

Nanomedicine is deemed valuable in cardiovascular care

Manipulating atoms and molecules

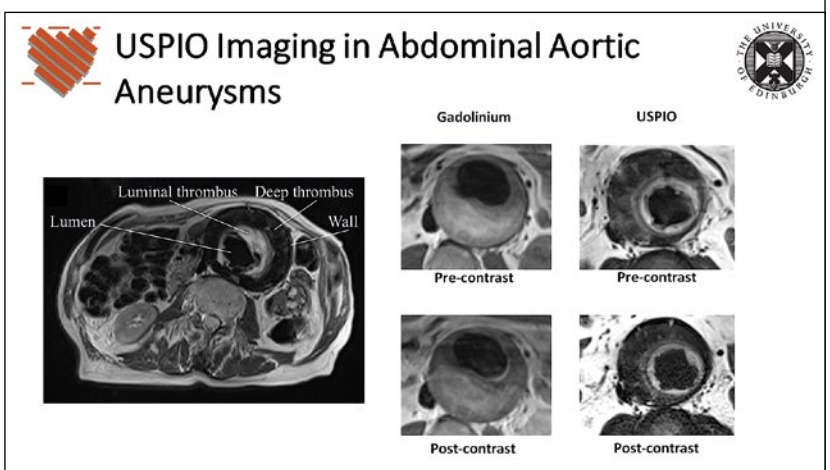
Report: Mark Nicholls

Nanomedicine is set to play an increasingly important role in the future diagnosis and treatment of cardiovascular disease.

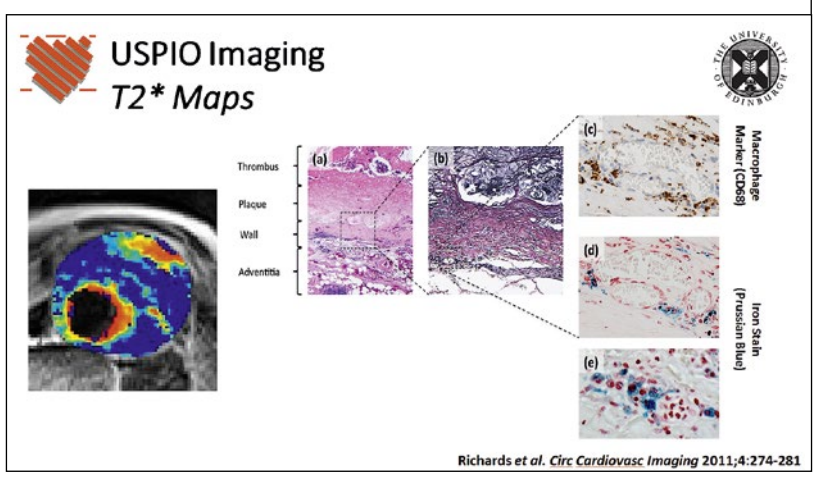
Understanding the importance of nanomedicine was enhanced by four experts who spoke at the British Cardiovascular Society conference held in June. The technology – dealing with dimensions and tolerances of less than 100 nanometres and especially the manipulation of individual atoms and molecules – is a critical component in increasingly more precise detailed approaches to cardiac care.

The speakers tackled areas such as nanomaterials for cardiovascular repair and regeneration, magnetic nanoparticles for atherosclerosis and the development of novel MRI tools to assess atheromatous plaque inflammation and stress analysis.

Professor Dave Newby spoke of 'magnetic nanoparticles in clinical cardiovascular disease' highlighting how magnetic resonance imaging agents have an application to cardiovascular disease, predominantly with macrophages.



USPIO imaging in the Abdominal Aortic Aneurysm



Richards *et al. Circ Cardiovasc Imaging* 2011;4:274-281

Tracking active inflammation

'Macrophages are important in lots of cardiovascular diseases – plaque rupture, heart attacks and aneurysms, for example – and resolution of injury and inflammation within that,' said Newby, who is Professor of Cardiology at the University of Edinburgh in Scotland.

Nanomedicine and advanced imaging to study biology are currently particularly topical.

'It's not just body structure,' he said. 'It's also about what the tissue in the body is actually doing. Nanoparticles can tell us about where there is active inflammation and where macrophages are active.

'That can be useful because it helps us understand disease biology – where injury is happening, how diseases are occurring and how the body heals.'

Experts are using MRI, PET and other technologies to exploit the role of nanomedicine in this field as they assess arterial blockages and the disease dimension. 'What we need to know is whether the biology is dormant, is it just going to lie there and stay unchanged for the next 10 years and never cause a problem, or is there a heart attack around the corner and what can we do to stop it happening?'

Newby outlined his work to identify ongoing inflammation using ultra-small superparamagnetic iron oxides (USPIOs) to identify hot areas within the aneurysm that are growing.

His study showed that, if the aneurysm lights up with the MR agent, it will grow bigger and t surgery is necessary, or the likelihood of the aneurysm bursting increased.

Understanding cardiac injury

Newby also described how the heart heals after myocardial infarction and how, via iron nanoparticles, imaging can show how much inflammation there is in the heart and how this activity relates to the resolution and scarring of the heart attack.

'We do not know yet whether modifying cellular inflammation will make things better or worse, because it could go either way,' Newby pointed out. 'If a heart does not heal well, it can burst and rupture but if it overdoes it and heals too much then you get remodelling and heart failure.'

Work with nanomedicine in this area, he said 'are the first steps towards trying to understand how the heart is responding to injury from a heart attack.'

The speakers also included Dr Iwona Cicha, from the University Hospital Erlangen, Germany, who focused on magnetic nanoparticles for atherosclerosis - in vitro and in vivo preclinical studies. Also, Professor Patrick Hsieh, research fellow and affiliate attending surgeon at the Institute of Biomedical Sciences, Academia Sinica, Taiwan spoke of nanomaterials for cardiovascular repair and regeneration.

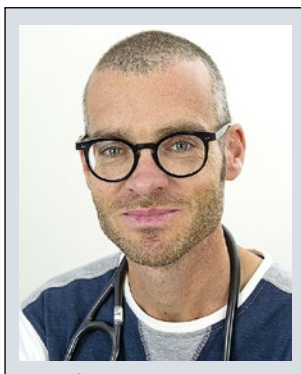
The development of novel MRI tools assessing atheromatous plaque inflammation and stress analysis was the focus of Professor Jonathan Gillard, Professor of Neuroradiology at the University of Cambridge, United Kingdom.

David Newby is the British Heart Foundation Professor of Cardiology at the University of Edinburgh, and Director of the Edinburgh Clinical Research Facility, plus a Consultant Interventional Cardiologist at the Edinburgh's Royal Infirmary. His principal research interests are in advanced imaging with particular relevance to acute coronary syndromes, valvular heart disease and heart failure.

What kind of workflow can maximise clinical benefit?

Looking again at IN-TIME

The IN-TIME study remains the only major trial to show a clear mortality benefit for remote monitoring in heart failure (HF) patients. A recent analysis by Hussar et al. suggests workflow processes such as daily, multiparametric data transmitted using Biotronik Home Monitoring, may be key to this benefit. Dr Wilfried Mullens, Head of the Heart Failure and Cardiac Rehabilitation Section at Ziekenhuis Oost-Limburg, in Genk, Belgium looks at the implications for telemonitoring in the future.



Dr Wilfried Mullens heads the Heart Failure and Cardiac Rehabilitation Section at Ziekenhuis Oost-Limburg, in Genk, Belgium

According to the recent Hussar et al. analysis, workflow processes might make a clear difference in remote monitoring's clinical benefit. How should we now look at the IN-TIME?

Wilfried Mullens: 'IN-TIME is a great study, but you have to incorporate it into a disease management strategy. Telemonitoring is a great tool if you know how to use it within a daily work schedule. If the study showed something, it was that when you react to telemonitoring signals in an appropriate and individualised manner, it can be beneficial.

'There's a lot of technical signals coming out of devices that don't lead to a lot of clinical benefit. You need someone to filter those before they reach the physician or healthcare professional. You have to get to know your patient as well because some alarms will be important for some patients but not for others.'

How is an efficient remote monitoring workflow managed in your practice?

'We've installed mandatory phone calls for certain alerts. In these phone calls, the nurses ask patients specific questions. Our EP nurses, who are absolutely fantastic, will sometimes say everything is fine. My heart failure nurse might call later for the same alert and be able to tell whether something's wrong.

'If you keep a direct link to that patient, you can then reinforce better adherence to medical therapy, for example. Telemonitoring can be a challenge in a lot of hospitals because it can take a lot of time to process technical alerts. We would look to manufacturers to make that more efficient.

'At hospitals, we need to improve the way we look at data, by training two types of nurses—those who handle device problems and those who specialise in heart failure.'

For telemonitoring, what should the next step be?

'I think telemonitoring is here to stay and it's going to expand. I think patients want some kind of self-empowerment and we're almost there. For example, if I had paroxysmal atrial fibrillation only once every three months and I have an implantable device, why do I have to take anti-coagulants all the time?

'If I see an alert on my phone saying I have to take an action to avoid a thrombolytic event, that would be a step forward.

'The second thing is to train nurses to see what's important in telemonitoring and to act on that information as independently of the physician as possible.

EUROPEAN HOSPITAL
European Hospital Verlags GmbH
Theodor-Althoff-Str. 45,
45133 Essen, Germany
Phone: +49 (0)201 87 126 850
Fax: +49 (0)201 87 126 864
E-mail: info@european-hospital.com
www.healthcare-in-europe.com

Editor-in-Chief: Brenda Marsh
Art Director: Olaf Skrober
Editorial team: Wolfgang Behrends, Sascha Keutel, Brigitte Dinkloh, Marcel Rasch
Senior Writer: John Brosky
Executive Director: Daniela Zimmermann
Founded by Heinz-Jürgen Witzke
ISSN 0942-9085

Correspondents
Austria: Michael Kraßnitzer, Christian Pruszinsky.**China:** Nat Whitney **France:** Jane MacDougall. **Germany:** Anja Behringer, Eva Britsch, Annette Bus, Walter Depner, Emelie Hofstetter, Cornelia Wels-Maug. **Great Britain:** Brenda Marsh, Mark Nicholls. **Malta:** Moira Mizzi. **Spain:** Mélisande Rouger, Eduardo de la Sota. **The Netherlands:** Madeleine van de Wouw. **USA:** Cynthia E. Keen, i.t. Communications, Lisa Chamoff.

Subscriptions
Liane Kaiser, Theodor-Althoff-Str. 45, 45133 Essen, Germany

Subscription rate
6 issues: 42 Euro, Single copy: 7 Euro.
Send order and cheque to:
European Hospital Subscription Dept

Printed by: WVD, Möhrfelden, Germany

Publication frequency: bi-monthly

Representatives
China & Hongkong: Gavin Hua, Sun China Media Co, Ltd.
Phone: +86-0755-81 324 036
E-Mail: gavin_hua@163.com

Germany, Austria, Switzerland:
Ralf Mateblowski
Phone: +49 6735 912 993,
E-Mail: rm@european-hospital.com

France, Italy, Spain: Eric Jund
Phone: +33 493 58 77 43,
E-Mail: ej@european-hospital.com

GB, Scandinavia, BeNeLux:
Simon Kramer
Phone/Fax: +31 180 6200 20
E-Mail: sk@european-hospital.com

Israel: Hannah Wizer, International Media Dep. of El-Ron Adv. & PR Co., Ltd.,
Phone: +972-3-6 955 367
E-Mail: hw@european-hospital.com

South Korea: CH Park, MCI
Phone: +82 2 730 1234,
E-Mail: mci@unitel.co.kr

Taiwan: Charles Yang,
Phone: +886 4 232 236 33,
E-Mail: medianet@ms13.hinet.net

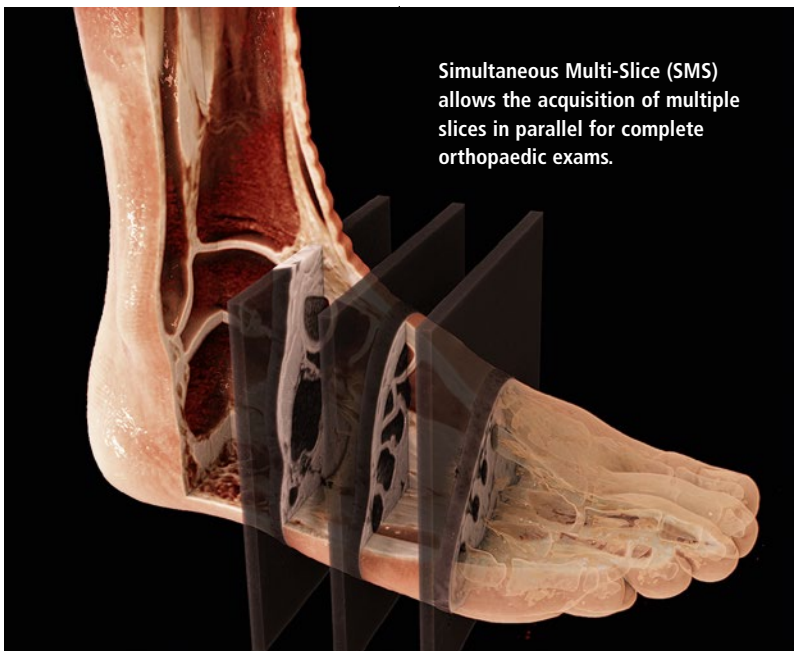
USA & Canada:
Hanna Politis, Media International
Phone: +1 301 869 66 10,
E-Mail: hanna@media-intl.com

All company, brand and product names in this publication are the property of their respective holders. Users must obtain permission from those holders before copying or using the owner's trademarks, product and company names or logos.

Coping with individual patient's characteristics

Refined imaging despite movements

The new 1.5 Tesla MRI from Siemens Healthineers, Magnetom Sola, is packed with helpful algorithms and other functions. AI-supported systems monitor patients and scan parameters and ensure consistent image quality. Whilst visitors at this year's ECR-Expo admired the new device, Prof. Ulrike Attenberger has already tested it in practice. The Vice Chair at the Institute of Clinical Radiology and Nuclear Medicine, University Medical Centre Mannheim, talks about the effect of the new functions in clinical routine.



Simultaneous Multi-Slice (SMS) allows the acquisition of multiple slices in parallel for complete orthopaedic exams.

Report: Wolfgang Behrends

BioMatrix is the technology used by Siemens Healthineers to partially control MRI scanning with the help of artificial intelligence (AI). The focus is on three new functions: heartbeat, head movements and breathing – the biggest interference factors to date – which are calculated out of the image in real-time. 'This is a central issue for the precision medicine which we are aiming for,' Attenberger explained. 'We need standardised, robust and comparable diagnostics for this purpose, but this has not yet been possible because the examination result is strongly influenced by which doctor or MRI assistant carries out the respective scan.'

With long-term investigations in particular, this reduces the comparability of data enormously, even for the same patient in the MRI scanner. Different patients' individual characteristics also cause additional inconsistencies: 'Obesity impacts on image quality and so, does arrhythmia, for example. Some patients cannot hold their breath, which used to cause us huge problems.' The new technology also helps the examiners here. 'We enter patient data into the system, i.e. height and weight, how long they can hold their breath, and then the algorithm calculates the settings that will achieve the best image quality,' Attenberger said. 'This has worked very well during the first practice runs.'

The manufacturer already implemented the new functions in the 3-Tesla System Magnetom Vida. 'However, the introduction in the 1.5-T range makes the technology available to a much larger range of users, especially in clinical practice,' added Dr Christoph Zindel, Senior Vice President and General Manager of MRI at Siemens Healthineers.

Even MRI novices adapt quickly to the system

'During the test phase,' Attenberger pointed out, 'we made a point of selecting our most junior MRI assistants who are being coached by skilled assistants but don't yet have much MRI experience. After three days of training on the simulator they then used the device in practice, and it turned out the handling is so intuitive that there were no problems during the introduction.'

The first test phase began with only one of the three sensors, i.e. the respiratory sensor, and even just this one component convinced Attenberger and her team. 'The system works perfectly in practice. Movement is always a big problem for us: patients in our centre are becoming increasingly older and sicker, which leads to high fault rates through motion artefacts with conventional MRI scanners. The BioMatrix technology now counters this problem very effectively. The new system makes the image quality far better.'

It also has a significant impact on the examination time: 'We aim to reduce the time spent in the examination room by around 50%, from an average 50 minutes to 25 minutes. Having used the new device for the first few weeks now, we can foresee this should be achievable.'

The new simultaneous multi-slice technology also contributes towards this because it facilitates simultaneous images of several slices. This function really excels during musculoskeletal examinations.

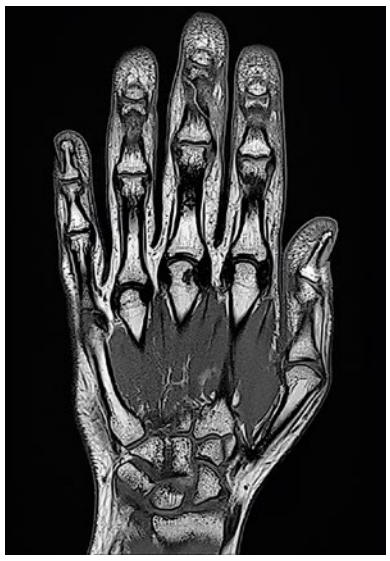
In cardiac and abdominal imaging, patients benefit from compressed sensing. The technology enables the examination of cardiac function with free breathing through mathematical reduction of the acquired data. 'You simply start scanning and continuously acquire images over a three-minute period, without the need for the usual breath-holding commands,' Zindel observed. 'Afterwards, the intelligent algorithm automatically selects the best images from this data jungle.'

Professor Ulrike Attenberger is Vice Chair and Medical Director at the Institute of Clinical Radiology and Nuclear Medicine, University Medical Centre Mannheim. After gaining her medical degree in Munich, a doctorate focused on 'The importance of MRI in the diagnosis of pulmonary hypertension' followed in 2006. Her current research is on MRI for tumour diagnosis and capturing therapy response. The professor received an RSNA Fellow Award for her work on optimisation and dose reduction for contrast-enhanced MR angiography.

Wish list during development

It is no coincidence that the Mannheim-based radiologist is currently carrying out the test run with the Magnetom Sola. Her institute collaborated with Siemens Healthineers during the conception of the new device and provided input for the developers. 'We contributed our ideas and requirements from a clinical routine perspective,' Attenberger said. 'This type of cooperation with Siemens Healthineers has a long tradition.'

Is she pleased with the result? Yes. 'All our suggestions have been implemented.' Along with the new functions these also include connection to the Teamplay software, which delivers an analysis of the clinical processes and optimises MRI capacity.



Simultaneous Multi-Slice TSE enables full hand coverage with thinner slices and all relevant contrasts

FUJIFILM
Value from Innovation

SonoSite

YEARS

SONOSITE ULTRASOUND HAS LED THE MARKET FOR THE PAST 20 YEARS

Fujifilm SonoSite celebrated its 100,000th system installed worldwide and remains focused on the same mission that started the company:

Helping clinicians bring ultrasound to any patient, anywhere, anytime.

"Why do more clinicians prefer SonoSite ultrasound systems than any other brand?"

Contact us online and a SonoSite ultrasound expert will be in touch for a consultation, in-person or virtual demo of any of our ultrasound systems.

www.sonosite.com/uk/sales/contact

SONOSITE and the SONOSITE logo are trademarks and registered trademarks of FUJIFILM SonoSite, Inc. in various jurisdictions.
FUJIFILM is a trademark and registered trademark of FUJIFILM Corporation in various jurisdictions. All other trademarks are the property of their respective owners.
Copyright © 2018 FUJIFILM SonoSite, Inc. All rights reserved. Subject to change.

MKT03222_UK 07/18

More than just MRI accessories

allMRI

www.allmri.com

AI shapes the future of radiology

System allocates cases to the right radiologist

Report: Daniela Zimmermann

Synergy is key to ensuring Artificial Intelligence (AI) can play a critical role in helping radiologists raise their game.

Integrating AI with innovative platforms to optimise workflow and make diagnosis more efficient, whilst also creating more accurate reports, offers enormous potential benefits to patients, clinicians and hospitals, according to industry specialist Tomer Zonens, Worldwide Product Manager at Carestream. Thus it is among the latest systems the company is developing to speed up reporting and eliminate the most mundane tasks radiologists undertake.

Speaking at the recent Roeko German Congress of Radiology, Zonens discussed AI radiology solutions and the challenges to overcome in order to achieve the advances radiologists and patients need and demand.

Carestream, which delivers medical and dental imaging and IT solutions, has worked with Zebra Analytics, a third-party software company that provides tools to enhance the quality and speed of diagnosis and reporting for radiology imaging exams. The resulting algorithm-enabled Radiology Assistant can boost diagnostic confidence while simultaneously improving productivity and containing costs. AI can quickly calculate and provide incidental findings, critical findings and quantitative assessments, which can help streamline radiologists' reading workflow and allow earlier treatment. Zonens pointed out a range of ways in which Carestream's AI applications can support the radiologist, stating that 'Synergy is the key.' While the automotive industry has been a driver within the AI space, followed by the gaming sector, he explained the technology also has huge potential within healthcare, and particularly in radiology.

Carestream is collaborating with a number of centres to harness AI and deep learning to identify and analyse mainstream images. These include customers, university health systems and private practices.

The company's AI systems can already automatically populate reports and even offer triage. 'For example,' said Zonens, 'If the AI algorithm detects a brain bleed, Carestream's new Workflow Orchestrator system automatically escalates the exam. The radiologist may be seeing an out- or in-patient for a non-urgent exam, but once the brain bleed is spotted, that patient will jump to the top of the list and, thanks to a particular icon on the system, the radiologist will already know something has been identified.'

Carestream is constantly working to add more algorithms to the system. It will, for example, soon be possible to search all a patient's data who is being screened in hospital, perhaps for an un-related event, so as to tell the clinician and patient if there are any signs that need follow-up. With interactive reports, hyperlinks to findings can be included, leading to more comprehensive reports and increased patient confidence.

'The viewer can see the report, and as it is interactive they can make comparisons more easily, which is much better than just getting a piece of paper,' Zonens pointed out.

Findings can be added and filters created, with access made possible across multiple facilities and for multiple subspecialists at multiple locations.

Going to the best specialist

Above all, Zonens affirmed, the new technology avoids wasted time for radiologists. This is largely because Carestream's Workflow Orchestrator directs the study to the best radiologist for each case, based on subspecialty, location and affiliation.

'We want studies to find the radiologist rather than the radiologist having to look for a study,' Zonens continued. 'We therefore have a system for matching exams to radiologists, based on intelligent rules, and we are working on applying AI to this process. We can imagine a system where an AI algorithm actually guides or directs the flow of studies in the optimum way towards the radiologist.'

Carestream's AI Orchestrator tool also has the ability to automatically spread hospital workloads more effectively. 'If, in the hospital, there is some division of the workload, the system will use this as feedback and optimise the load in future until the best result is achieved.'

AI can already use the information in scans and text to 'extract more value' from reports, by taking the clinical data and plainly making sense of it. Yet, Zonens sees far more potential for AI within radiology in the years ahead. 'Maybe in the future the machine will scan the patient and the reports will come directly out of the system,' he said. 'They will not even need images; all the information will be in the machine, and AI will do everything. But I think this is very far in the future. Until we get to that point we need to consider if we truly want to maximise the value from AI.

'We will only achieve this by integrating AI within an enterprise platform while also working to create better reports and optimise workflow, making radiologists more productive and improving results by allowing them to focus on their main task: treating the patient.'

With 14 years' experience in developing, launching and marketing medical technology solutions, **Tomer Zonens** is Worldwide Product Manager at Carestream and responsible for three product lines in the Healthcare Information Solutions division. Formerly an algorithm engineer, he developed automated sleep medicine analysis systems following studies in Biomedical Engineering at Technion, Israel Institute of Technology.

AI Orchestrator details: carestream.com

Real Python code developing screen. Programing workflow abstract algorithm concept. Lines of Python code visible under magnifying lens.

TRISON

Ultrasonic baths for robotic instruments, rinsable MIS and standard instruments

Made in Germany

The new standard in the pre-cleaning of robotic instruments

- Modular compilation of the system according to the types of instruments
- Time optimized and coordinated cleaning processes depending on the types of instruments
- Cleaning – gentle and in shortest time
- Robotic and rinsable MIS instruments: safety by rinsing of single channel and single examination

More information about our ultrasonic baths and the cleaning of medical instruments you will find on the website bandelin.com/branchen/medicine or by phone +49-30-768 80-212.

You meet us here:
Hall 12 A30 MEDICA®

BANDELIN
Ultraschall seit 1955

Canon – a bright future in healthcare.

Healthcare IT

Offering leading-edge diagnostic support systems and network solutions utilizing ICT.

In-vitro Diagnostic Systems

Supporting examination workflows with high resolution and rapid analysis of blood and other specimens taken from patients.

Introducing Canon Medical Systems

As of January 4, 2018, Toshiba Medical Systems Corporation has changed its name to “Canon Medical Systems Corporation”.

Technology that’s made for life.
Canon—having welcomed Toshiba Medical Systems Corporation,
a company renowned in the field of medical imaging,
into the Canon Group—celebrates today on January 4th, 2018,
the birth of Canon Medical Systems Corporation.
Made for Partnerships. Made for Patients. Made for You.
Based on our “Made for Life,” philosophy, we aim to support the wellbeing,
safety and security of humankind globally.

Canon Medical Systems will contribute to even further developments in healthcare
through three pillars of advanced technology: Diagnostic Imaging Systems,
Healthcare IT and In-vitro Diagnostic Systems.

Diagnostic Imaging Systems

Meeting clinical needs with
high resolution imaging
from CT, MRI, X-ray and
Ultrasound systems.

Images are for reference purposes only.

Canon

©2018 Canon Inc. **global.canon**

Comparison is still pending

On-going malignant astrocytoma vaccine tests

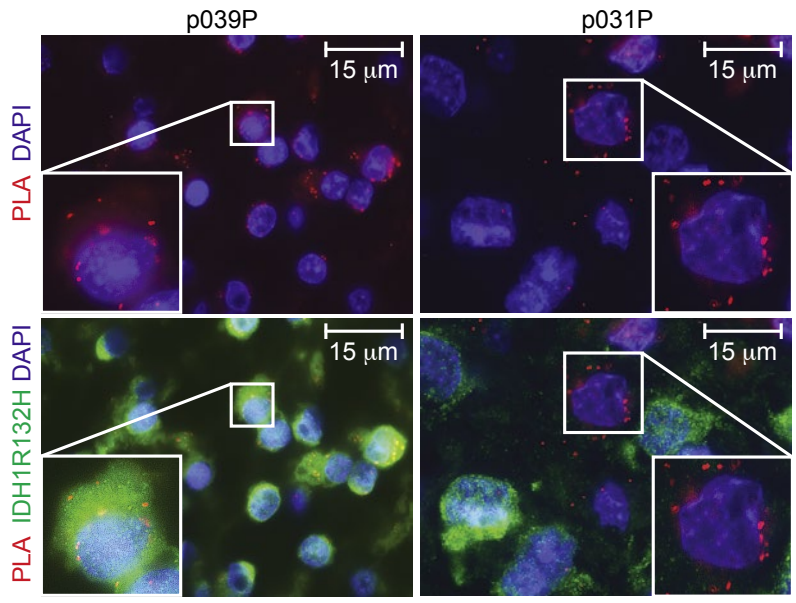
A new vaccination for malignant astrocytoma brings such patients hope. However, research is still in its infancy. Eva Britsch of European Hospital spoke with Professor Michael Platten, Medical Director of the Neurological Clinic at Medical University Mannheim, about the present state of research and the serious opportunities this presents. During the interview, he also revealed how cooperation with the pharmaceutical industry is developing and why the current results are only conditionally resilient.

From July 2015 to July 2017 Professor Michael Platten and colleagues treated 33 patients with newly diagnosed malignant astrocytoma with a novel vaccine.

What is the current state of affairs?
MP: 'We have completed the study and are in the follow-up phase. The patient data are currently evaluated. However, over the next few months we will collect and evaluate further data on the patients' progress. At the same time, we are currently conducting intensive research on the patients' blood samples to gain a better understanding of the immune reactions.'

EB: Can definitive statements be made about the vaccination reducing the risk for astrocytoma and oligodendroglioma* patients to recur?
'No. In addition to vaccination all patients received effective radiation and chemotherapy, which also prevents recurrent tumour growth, even if only for au limited period. Whether this recurrence risk is further reduced by vaccination can only be answered in a comparative study. We can start such a study once we have fully evaluated the current study.'

How does the new vaccination work and how can it be seen in combination with previously known treatment options?



Brain tumour cells producing the mutated protein molecule IDH1R132H (green) carry this on their cell surface (seen in red). Thus, tumour-specific changes are visible to the immune system

'The vaccination is intended to sensitise the immune system of patients concerned to a protein molecule that is characteristically altered in the tumours of the patients, namely by the exchange of a single building block. We call this change IDH1R132H.

With the vaccination we can sensitize the immune system so specifically that only the altered protein molecule in the tumour cells, IDH1R132H, but not the healthy form, IDH1wt, which can be found in all healthy body cells, is recognized. We hope that this specific sensitization of the immune system through vaccination will lead to the targeted treatment of tumours, as we have observed in animal experiments. We also assume that radiation therapy of the tumour, a proven therapy for these tumours, helps the sensitized immune system to fight the tumour.

You and colleagues are currently evaluating the immune reactions of patients to the vaccine – how do you evaluate the reactions?
Very positive. The vast majority of patients develop specific antibodies against IDH1R132H as a result of vaccination, but also T-cells, two important components of the immune system. We are currently evaluating which factors influence the strength of the immune reactions and, of course, whether these have an influence on the further course, i.e. freedom from recurrence. We are also interested in finding out why individual patients have not experienced an adequate or delayed immune reaction.'

Does the vaccination have (previously known) risks?
'The only relevant risks we have observed are vaccination reactions at the injection site with redness and itching. This reaction is to be expected and is mainly the result of the necessary vaccination booster.'

Could a similar vaccine be developed for other cancers?
'In rare cases IDH1R132H can also occur in other types of tumours, for example in bile duct carcinomas. In principle, all tumour types in which IDH1R132H is present are suitable for vaccination.

'On a super-ordinate level, mutated protein molecules are found in practically all tumours, but they are usually patient-specific. If we succeed in defining these specifically modified protein molecules for each individual patient and in developing a tailor-made vaccination therapy, then such a vaccination could in principle be used for all types of tumours. However, this would then be a real individualised cancer immunotherapy that could not simply be taken out of the medicine cabinet.'

Michael Platten MD is Medical Director of the Manheim Medical University Neurological Clinic and professor of clinical neurology, neuroimmunology and neuro-oncology at Heidelberg University. In recent years he has also led brain tumour immunology at the German Cancer Research Centre (DKFZ) in Heidelberg, Germany.

Could your research lead to new treatments for multiple sclerosis, which you are also researching?
'We always try to learn from other diseases. For the current vaccination we use many findings and models, including multiple sclerosis, because an unwanted excessive immune reaction occurs in the brain there. If we understand the mechanisms that lead to this excessive immune response, then we can better control the immune responses in brain tumours.

'Conversely, many of the breakthrough technologies we use to analyse immune responses in brain tumour patients can also contribute to a better understanding of multiple sclerosis.'

How does the pharmaceutical industry respond to your research?
'Let's say: with cautious interest. But, we have now begun a cooperation with the industry that combines our vaccination approach with an approved cancer immunotherapy drug. Through this intelligent combination, we hope to make our vaccination therapy even more effective. This clinical trial will start in the next few weeks.'

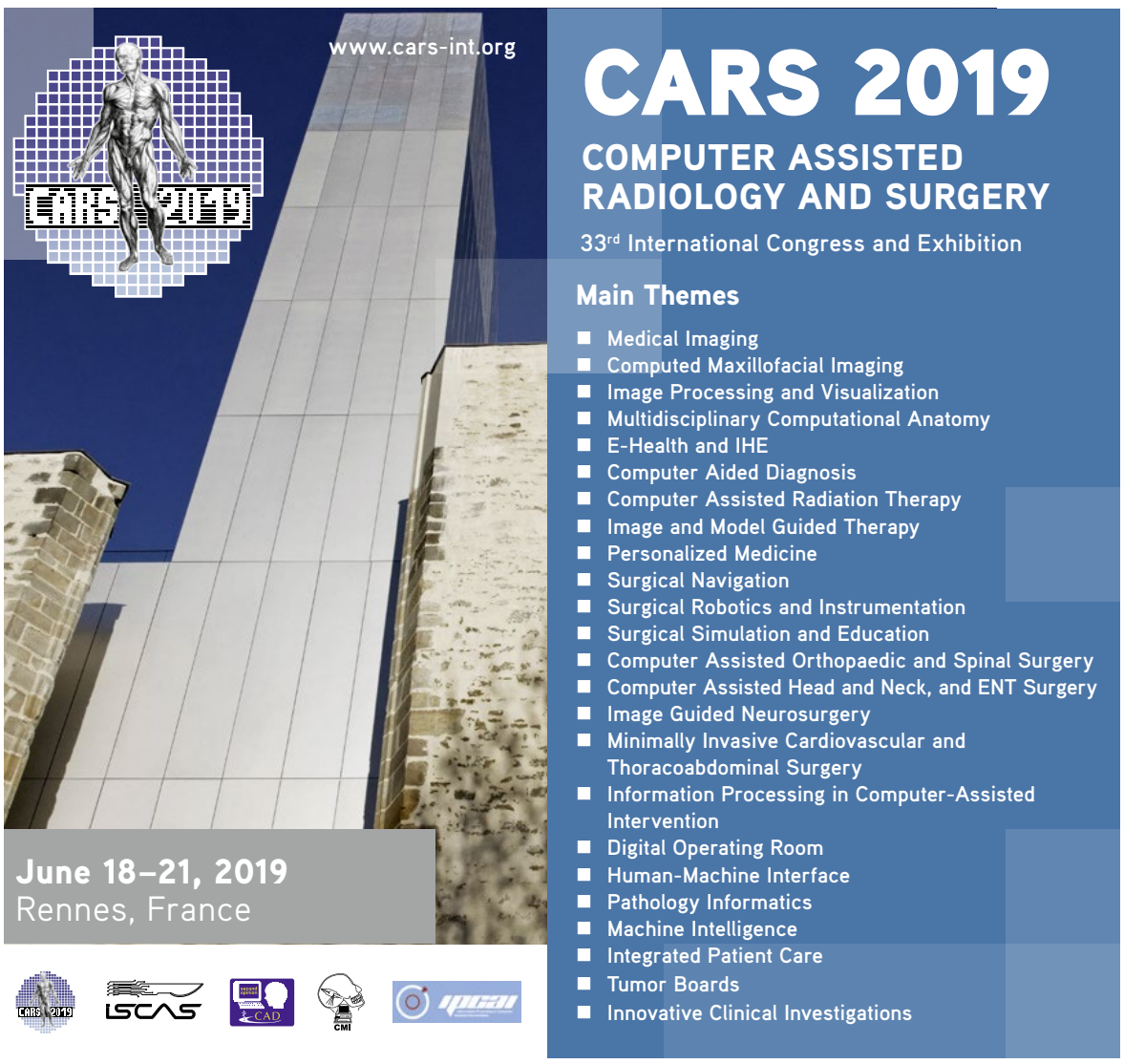
What hampers your work?
'Financing is certainly a major obstacle; so far we have financed all studies from public subsidies. The German Cancer Research Centre, the National Centre for Tumour Disease, German Cancer Aid and the Federal Ministry of Education and Research have given us considerable support, for which we are very grateful. Without this support, implementation would not have been possible.

'We are also very grateful for the good cooperation with the Paul Ehrlich Institute, which actively supports us in these innovative therapeutic approaches.'

Could patients hope to receive vaccination beyond their research status?
'It's probably too early for now. We are currently focusing all our efforts on the follow-up study. Until we can say for sure whether the vaccination therapy will actually work and, if so, in which patients and under what conditions, research in the form of clinical studies will be a priority.

'However, we are very pleased that the patients affected and their relatives are supporting us by participating in the studies.'

* A rare, slow-growing tumour that begins in oligodendrocytes – the cells covering and protecting nerve cells in brain and spinal cord.



CARS 2019 President
Pierre Jannin, PhD (F)

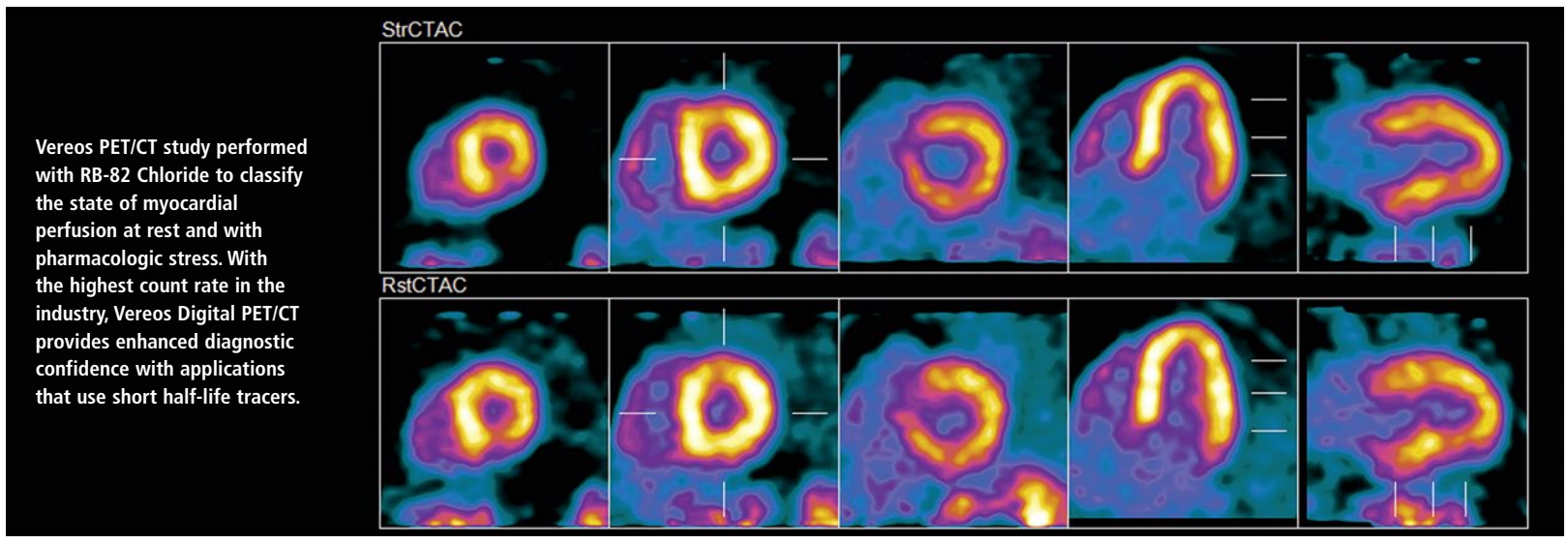
Congress Organizing Committee
Christos Angelopoulos, DDS (USA)
Elizabeth Beckmann, BSc (UK)
Leonard Berliner, MD (USA)
Ulrich Bick, MD (D)
Davide Caramella, MD (I)
Kevin Cleary, PhD (USA)
Mario A. Cypko, PhD (NL)
Takeyoshi Dohi, PhD (J)
Kunio Doi, PhD (USA)
Volkmar Falk, MD, PhD (D)
Allan G. Farman, PhD, DSc (USA)
Hubertus Feussner, MD (D)
Guy Frija, MD (F)
Miguel Ángel González Ballester, PhD (E)
Makoto Hashizume, MD, PhD (J)
Yoshihiko Hayakawa, PhD (J)
Javier Herrero Jover, PhD (E)
David Hilderbrand (USA)
Kiyonari Inamura, PhD (J)
Pierre Jannin, PhD (F)
Leo Joskowicz, PhD (IL)
Tina Kapur, PhD (USA)
Heinz U. Lemke, PhD (D) (Chair)
Kensaku Mori, PhD (J)
Hironobu Nakamura, MD, PhD (J)
Nassir Navab, PhD (D)
Terry M. Peters, PhD (CDN)
Osman M. Ratib, MD, PhD (CH)
Hans G. Ringertz, MD, PhD (S)
Yoshinobu Sato, PhD (J)
Ramin Shahidi, PhD (USA)
Akinobu Shimizu, PhD (J)
Hiroyuki Yoshida, PhD (USA)

Surmounting conventional photomultiplier limits

Digital Photon Counting (DPC)

Interview: Daniela Zimmermann

Built as the first commercially available scanner to deliver truly digital PET, the Vereos PET/CT, from Philips, offers revolutionary Digital Photon Counting technology. The science behind this scanner evolution is 'quite complicated', agrees Piotr Maniawski, Director of Clinical Science Nuclear Medicine at Philips Healthcare, yet the improved performance is significant, particularly when compared with an analogue system.



Vereos PET/CT study performed with RB-82 Chloride to classify the state of myocardial perfusion at rest and with pharmacologic stress. With the highest count rate in the industry, Vereos Digital PET/CT provides enhanced diagnostic confidence with applications that use short half-life tracers.

That performance includes a reduction in scan time, lower dose, improved diagnostic accuracy and better detection of small lesions as well as applicability across oncology, cardiology and neurology, for example in dementia assessment.

Maniawski outlined how proprietary Digital Photon Counting (DPC) technology sits at the core of the new Philips PET system, and was developed to overcome the limitations of conventional photomultiplier technology.

With PET, scintillating crystals are used to collect high-energy photons and convert them to visible light, which is then picked up by a light sensor, and the output constructs the resulting image. With DPC technology, light is counted as individual single photons.

'This is very technical talk,' Maniawski concedes, 'but what it means is that we have far more precise information about the characteristics of that light signal. We have a better way of determining when the signal was detected and also more precise localisation of that signal.

The primary benefit of the improved resolution is the detectability of smaller lesions and that eventually translates into more acute diagnostic accuracy.'

Additional to DPC, other advances making digital PET possible are 1:1 coupling between the scintillator and the light-sensing element and faster Time-of-Flight (TOF) technology.

Philips' DPC technology was developed to overcome the limitations of conventional photomultiplier technology and the 1:1 coupling and enhanced TOF allow the Vereos system to offer approximately double the volumetric resolution, sensitivity gain, and accuracy of a comparable analogue system.

Maniawski emphasised how better images benefit patient management with the ability to see disease that has traditionally been difficult to image or the recurrence of disease. 'This can change patient management if, for example, there are extra lymph nodes that were not seen before. Significant patient decisions are made on the accuracy of the detectability of the disease.'

PET tracers are enhancing personalised medicine in, for example, the area of immunotherapy and marking antibodies with PET imaging isotopes. 'These antibodies will go only to places where they are sent; that's a very targeted, personalised precise therapy. However, before therapy, we can image to make sure the patient receiving this immunotherapy is going to respond,' he said, adding that the latest clinical evidence for cancers that utilise glucose for growth is that PET and PET/CT is the most accurate staging modality.

With immuno-PET developed to help guide immunotherapy, researchers investigate if a therapy works in tumour response. 'Here again digital PET has potential, because it's much more quantitative, more reliable in absolute uptake. We can do studies and track if a patient is responding in the way we anticipate,' Maniawski explained.

A number of academic sites are currently using Vereos PET/CT for high-end research and have developed their own radio tracers to work with Philips, using those tracers for investigational and clinical applications.

Other areas where Vereos is applicable, in addition to oncology, are cardiology and neurology, such in diagnosis of different types of dementia, where various tracers are used, such as amyloid tracers of amyloid plaque, and tau (an antibody that expresses in dementia).

'What you want in a PET scan for dementia is high resolution,' Maniawski pointed out, 'because we are looking at very small changes and we want to detect these changes before clinical symptoms of cognitive dementia show up.'

Another key area of evaluation from Vereos is in coronary artery disease (CAD) with heart scans conducted at peak exercise and at rest to assess the supply of blood in the myocardium.

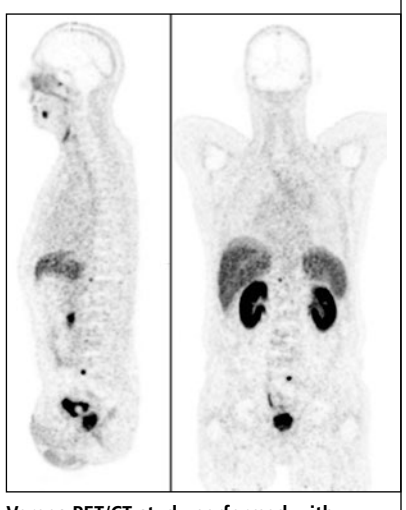
An issue with conventional PET myocardial perfusion imaging is that, in patients with multi-vessel disease, it cannot fully distinguish where the coronary arteries are diseased. 'However, if we are able to characterise the absolute flow in millilitres per minute per gram of tissue, we can then see in absolute terms if the flow is normal or not – even in patients with multi-vessel disease – with new PET/CT scanners,' Maniawski said.

This is where the 1:1 coupling offers a critical benefit, because it allows more accurate quantification of the flow.

Artificial Intelligence (AI) – or adaptive intelligence as Philips prefers to call it – also undergoes significant developments with PET, notably for example with adaptive protocols that are specific to patients.

'Patient image quality suffers with larger patients,' Maniawski observed, 'but the system can adapt the protocol either through automisation or reconstruction.'

Piotr Maniawski is a clinical physicist and Director of clinical science for nuclear medicine and advanced molecular imaging at Philips Healthcare. He worked in a multitude of positions, including as radiation safety officer in Zabrze, Poland, as research associate at Yale University and as software engineer in Cleveland. The focus of his work is in nuclear imaging, especially PET/CT, for which he develops clinical protocols and quality control tools.



Vereos PET/CT study performed with F18-PSMA on patient with prostate ca for staging. Increased activity in prostate identified and multiple areas of increased uptake in the pelvis are consistent with lymph nodes. Also identified is a very small lesion anterior to the spine in the upper abdomen

This research is as vital as understanding the human genome

Exploring the human microbiome

During the International Forum for Laboratory Medicine, being held at MEDICA 2018, one seminar (on 12 November} will focus on infectious diseases. Professor André Gessner, from the Medical Microbiology and Hygiene Department at Regensburg University, will lecture on 'The human microbiome, an explosive 'climate' topic,' he explained to EH reporter Walter Depner.

WD: Generally you know the kind of audience you face during gatherings of specialists in your field. However, there's no certainty about who will be among the MEDICA delegates attending your lecture. Could this make your job difficult or perhaps more exciting?
AG: I have given many lectures to heterogeneous audiences and find the challenge of explaining complex relationships in the most comprehensible way to be very exciting and positive.

Often, I have received very stimulating questions – especially from colleagues in other fields.

About three years ago, at the University of Regensburg, you lectured on The Intestinal Microbiom as the Centre of Health and Illness, and included in the invitations physicians, chemists, nutritionists, microbiologists, dieticians, technical consultants and health journalists – a very heterogeneous audience. Could that experience help with the Düsseldorf seminar?
Yes, certainly. The conference is a good example for what the participants see as a successful interdisciplinary forum.

Modern medicine and healthcare demands an interdisciplinary approach. Do such events, as in Regensburg and now Dusseldorf, help to reach this goal?
The challenge is to transmit the latest scientific knowledge, with a critical appraisal, in such a way that it is well understood and to 'condense' without over-simplification, which distorts the information. For me it is important to stay realistic and above all not to raise hopes among physicians and their patients too early that cannot (yet) be fulfilled.

There is considerable focus on the role of microbial intestinal flora as a basic component for staying healthy. You have described modern, high-throughput sequencing technology as a source of dramatic knowledge growth. Why?
Without high throughput sequencing technology, together with appropriately qualified bioinformatics, microbiome analysis would be impossible. It was this technology that first made this enormous knowledge growth possible – currently more than 65,000 publications in just over ten years.

MEDICA'S LABMED FORUM

- **Monday, 12 Nov 2018 10.45 – 11.15 a.m.**

The human microbiome – diagnostic and therapeutic aspects
Speaker: Prof. André Gessner, Director of the Institute for Medical Microbiology and Hygiene at Regensburg University

Are their approaches going in the right direction?
The technological potential in analysis is developing rapidly. Here we need improved standardisation of analyses, quality controls and hope to gain ever increasing 'read lengths', that is to say DNA sections that can be sequenced in one piece, lower sequencing error rates and naturally lower costs for examinations.

Especially important here is also a significantly better comprehension of the functional relationships between microbiome and various diseases, so that rational new therapies can be developed in the future.

Along with interdisciplinary scope, the internationality question plays an important role. What is the state of cooperation, exchange in research, teaching and practice?
Microbiome research is particularly characterised by numerous already well-established international cooperation efforts, among academic institutions such as universities, and increasingly among very many firms.

The exchange is extremely intensive, not only through scientific publications but also via Internet fora and more than a dozen international congresses annually on microbiome topics.

Having studied medicine and molecular biology at the University of Hamburg, **Professor André Gessner** received his medical doctorate in infection immunology and a PhD in molecular virology. Following five years' basic research at the Heinrich-Pette Institute, Hamburg, he established his research group at the University of Erlangen, where he qualified as a specialist in medical microbiology and infectious disease epidemiology. His scientific work focuses on molecular infection immunology, infectious diseases and the role of the microbiome for diseases. He is an expert and reviewer for several international journals and scientific societies and, between 2008 and 2010 he received four calls regarding chairs for medical microbiology. Since 2010 he has been a professor and director of the Institute for Medical Microbiology and Hygiene at Regensburg University, where 150 employees focus on all aspects of infectious diseases. In 2015, Gessner became the Dean of research at the Regensburg medical faculty.

Infection control in orthopaedics and trauma surgery

Local antibiotics improve results

Hip and knee joint surgeries are among the most common procedures in orthopaedics and trauma surgery and complications can occur. Rare, but serious, among these is periprosthetic infection (PJI), which causes high costs in healthcare and stress for patients. PJI is caused by microorganisms that form a biofilm on the surface of the implant and, in this sessile state, they are difficult to diagnose and treat. Successful management of a PJI is therefore based on prevention and prophylaxis so that infections cannot develop in the first place.

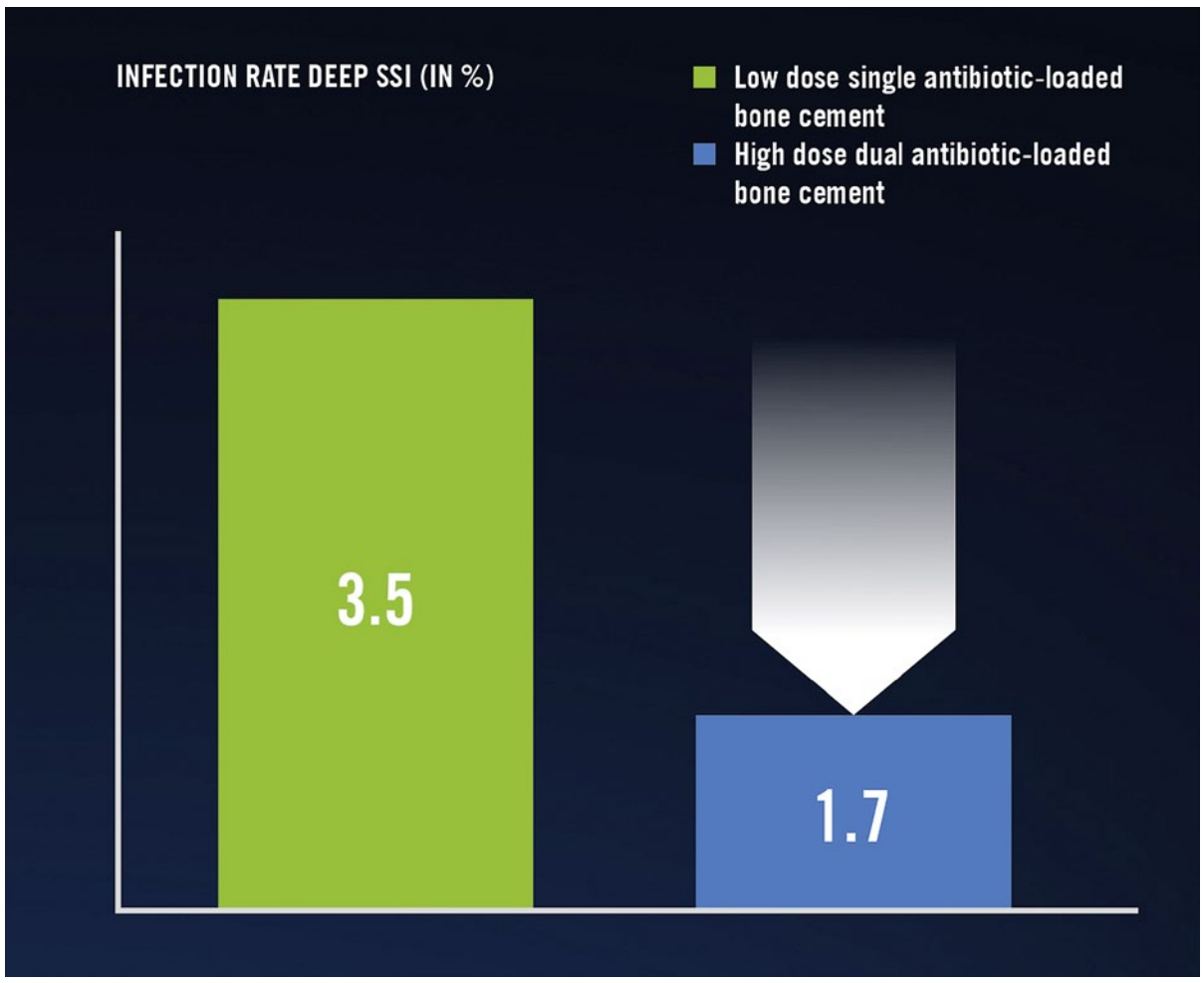
Antibiotic prophylaxis using antibiotic-loaded bone cement

Polymethylmethacrylate (PMMA) bone cement, which is primarily used to fix prosthetic implants, can support effective infection management in primary arthroplasty, revision and the treatment of periprosthetic infections. The local release of the antibiotic from the bone cement supplements standard systemic antibiotic prophylaxis. The advantage lies in the considerably higher local concentration of the antibiotics with a low systemic load.

Choosing the right treatment algorithm is a critical factor for successful prevention and reduction of PJI. Combinations of antibiotics – systemic and local – are advantageous for effective infection management for revisions, in trauma cases after femoral neck fracture and occasionally in primary arthroplasty. When choosing the antibiotic, the current resistance situation and prevalence of microorganisms responsible for PJI should be considered. The COPAL bone cements Copal G+C and Copal G+V, for instance, contain combinations of antibiotics (gentamicin and clindamycin and gentamicin and vancomycin respectively) that tackle most of the microorganisms responsible for PJI. Synergistic effects of the combinations of antibiotics enable a high local antibiotic concentration in situ.

In revision, the range of treatments includes one-stage replacement with good soft tissue conditions and known susceptible pathogens, as well as two-stage replacement with precarious soft tissue conditions and unknown resistant pathogens. In both cases the effectiveness of the treatment can be increased by using bone cement with combinations of antibiotics. The combination of antibiotics used should be determined after completing diagnostics and an antibiogram.

69% reduction in the rate of deep infections following femoral neck fracture when using high-dose antibiotic-loaded bone cement. Source: Sprowson et al.



For revisions due to verified resistant microorganisms (MRSA/MRSE), the use of Copal ® G+V is recommended. This contains the antibiotic gentamicin combined with vancomycin which, as a reserve antibiotic, is an option for use with known bacterial resistance to MRSA/MRSE, for example.

For septic loosening or chronic infections, a spacer made of antibiotic-loaded bone cement is often inserted as a temporary joint replacement to eliminate infection. Articulating spacers with an implant-like design, e.g. from Copal knee moulds, should be given preference here to preserve the joint function and to prevent the formation of contractures and scar tissue.

Risk of deep infections can be considerably reduced

In primary arthroplasty patients, who are particularly at a high risk of infection, are recommended for combinations of antibiotics for antibiotic prophylaxis, and thus the use of Copal G+C bone cement. The risk factors that can increase the likelihood of infections include diabetes, osteoporosis, limited mobility, excess weight and dementia.

When treating femoral neck fractures with a cemented hemiarthroplasty using Copal G+C, it can be verifiably demonstrated that the risk of deep infections (surgical site infections, SSI) can be considerably reduced by using dual antibiotic-loaded bone cement.

Pioneering the clinical use of mass spectrometry

Mass spec needs experienced operators

Report: Mark Nicholls

As mass spectrometry proves to be a more consistent and accurate tool in biochemical measures, with acknowledged advantages over immunoassays, its role in diagnostics has escalated.

Headed by Professor Ruth Andrew, the pioneering Mass Spectrometry Core Facility at the University of Edinburgh, aims to offer researchers access to expert scientists and specialist resources to support clinical research.

With high-cost state-of-the-art equipment hosted through a Core lab, the costs of installation, maintenance and on-going support can be shared. The facility is staffed by mass spectrometry specialist scientists who can advise researchers on the correct way to address their scientific questions at all stages of the project.

They also assess the potential of innovations that could benefit clinical research and find ways to resource and incorporate new technologies.

Mass spectrometry is already playing a greater role in diagnostics. 'Over the last decade,' Andrew pointed out, 'MS has become more extensively utilised in clinical biochemistry, primarily because it is recognised that other biochemical measures – such as immunoassay – have inherent errors and can be variable between manufacturers. This causes offsets between data generated by different hospitals.

'MS overcomes the non-specificity of antibodies used in immunoassays, generating more accurate results that can be standardised nationally. MS instruments have improved in their sensitivity and robustness, making them more attractive and approachable to clinical labs. Investment in warranty contracts will enable a lab to operate with less downtime, but are costly.'

In the UK, analysis of testosterone and Vitamin D are now routinely conducted by MS, while the US Endocrine Society has recommended that MS should become used across hospital labs for steroids assays. There are various quality control schemes in the USA, EU and UK to align data between labs with samples being sent to multiple centres and compared.

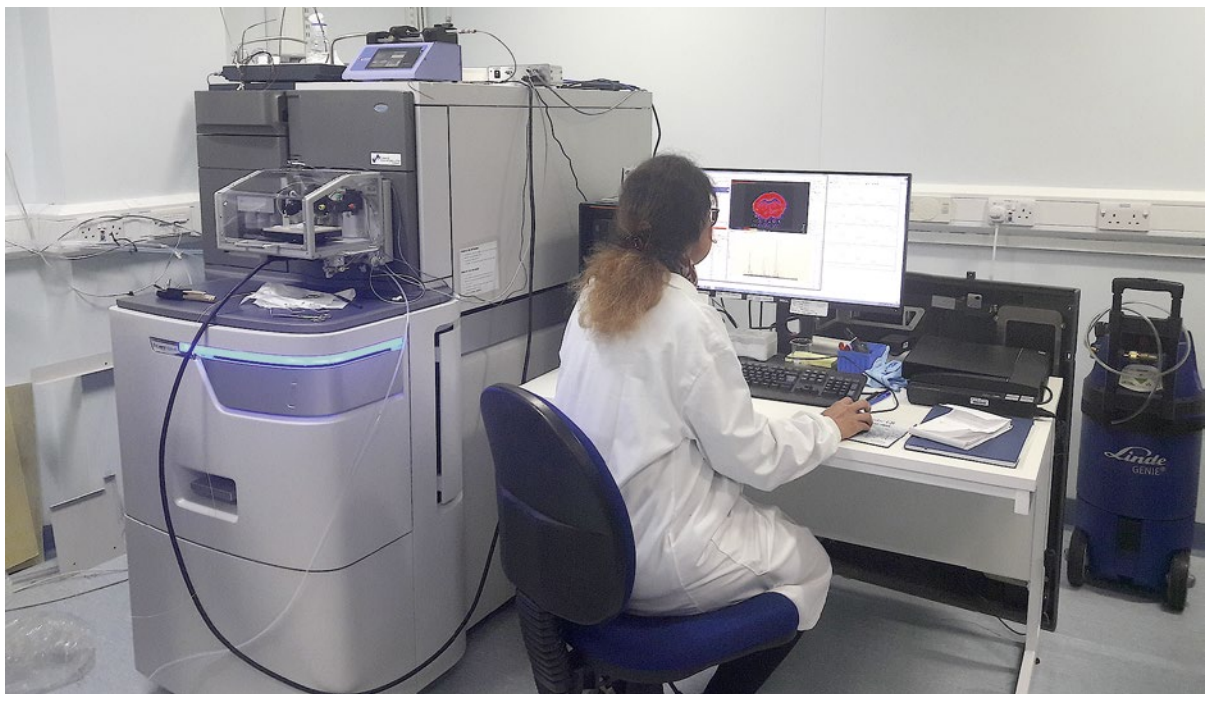
However, MS is still generally only available in regional hospitals and sites of specialist expertise, such as for use in paediatric labs to diagnose inborn errors. 'MS is complementary to other techniques but, due to the expertise required, it cannot be easily managed by non-specialist scientists and normally does not have as high a throughput as other analytical approaches,' Andrew added. 'However, this may be offset by the fact that multiple components can be measured in one run.

Making MS more user friendly

'With time, sample preparation has become more automated and throughput is increasing. Some of the instrument companies have invested in kits and software to make the system more user-friendly, such that less experienced operators can use the system. However, the systems still need to be embedded in labs with expert staff to ensure efficient running, method development and to troubleshoot problems.'

While MS is more precise, albeit more complicated, there are clear advantages, particularly with specificity, which allows greater reproducibility and reliability of data.

'For hormone analysis, for example, this means there is less likelihood that other components in the blood can artificially raise the results,' Andrew explained.



'In the research field, metabolomic profiling of the fingerprint of a large number of biochemical species by MS may be used to predict disease risk or drug responses, but this approach is in its infancy and the data hard to handle in a standardised manner, so some way from clinic. However, this could pave the way for personalised medicine.'

There is a promising future for MS in diagnostics, she confirmed, but also warned not to expect the same pace in advances in quantitative tandem MS/MS over the next decade as in the previous 10 years.

'Accurate mass systems offer improved specificity but are not yet as sensitive or as accepted for quantitation (e.g. narrower linear range). However, these instruments may in time take a bigger role in the clinical lab but are not common place.'

The new technique of REIMS (Rapid Evaporative Ionisation Mass Spectrometry) to sample from surfaces is highly exciting for real-time surgical diagnostics and also for pathology.

'REIMS may also gain a role in rapid microbiological testing,' she said. 'These approaches are speeding up diagnostics and I expect to see these applications extended with improvements in MS imaging. However, again, these are highly-specialised and expensive and, to my knowledge, only one manufacturer is building instruments that are specifically designed to meet the quality requirements for clinical diagnostics.'

Professor Ruth Andrew is Personal Chair of Pharmaceutical Endocrinology Centre for Cardiovascular Science, University of Edinburgh, and Director at the Mass Spectrometry Core Facility, where her main role is to facilitate, lead and conduct biomedical research in the MS Core in all stages of clinical research projects, including preclinical development. Within the MS Core she assesses the potential of new innovations and brings new ideas forward that may then be consolidated in clinical research.

Analysing physical/chemical properties of particles

Flow cytometry rises to new challenges

Report: Mark Nicholls

Flow cytometry has proved an invaluable diagnostic tool for leukaemia and lymphoma for almost three decades. Now, however, this is evolving in applications to seek out residual disease in cases and in fusion with molecular testing to advance its diagnostic potential.

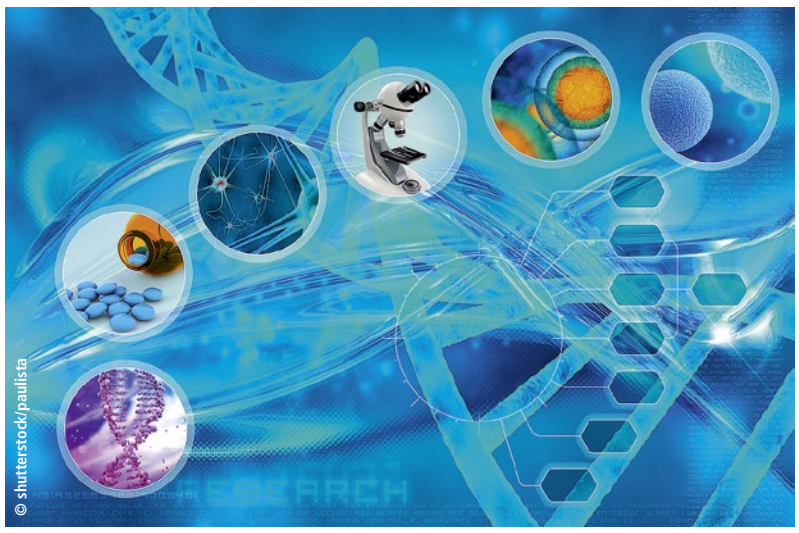
However, although recognised as fast, flexible and accurate, flow cytometry suffers from a lack of standardisation, according to Professor Brent L. Wood from the University of Washington (UW) School of Medicine in Seattle.

Wood addressed those issues when describing the impact of flow cytometry on the clinical laboratory at the joint European Federation of Clinical Chemistry and Laboratory Medicine/European Union of Medical Specialists (EFLM/UEMS) conference, which was held this October in Turkey.

Flow cytometry is a technology that analyses the physical and chemical characteristics of particles in a fluid as it passes through a laser. Wood, who directs UW Medicine's Haematopathology and SCCA Pathology, could reflect on his experiences with flow cytometry for over 20 years.

He has been involved in developing flow cytometry in various contexts, such as identifying residual leukaemia after therapy and demonstrating its clinical utility and significance in assessing patient outcome.

Flow cytometry has been a technique for diagnosis since the 1970s, particularly of neoplasms, and came to the fore in clinical laboratories in the 1980s with the spread of HIV before evolving as a methodology in the 1990s for diagnostics of leukaemia and lymphoma and diseases that were easier to create cell suspensions from such as peripheral blood and bone marrow.



© shutterstock/paulista

Recently this advanced to focus on next generation sequencing and examining the concordance and relative merits of those two techniques.

As a technology, flow cytometry is flexible, facilitating the design of a variety of different assays to create panels of re-agents that are suitable for diagnosing leukaemia and lymphoma.

'The application to monitoring for residual disease involves looking for much smaller populations of cells of similar type and distinguishing them from their normal counterparts,' Wood said.

'That's one of the thing's that this technology is particularly adept at doing – distinguishing normal from abnormal.'

However, he emphasised that looking for relatively small populations of cells is a more technically-demanding process, requiring more attention to detail in terms of technique, consistency and artefacts, and interpretation. An area of concern, said Wood, is that while the technology is widespread, it is 'very poorly standardised'. This can see different laboratories having their own panel of reagents that they have validated themselves and their own ways of processing samples and collecting and interpreting data.

'Interpreting data is the subjective component of this type of analysis, which requires someone with experience and training,' he pointed out. 'In that sense it is different to many other tests we do in clinical laboratories, where instruments provide a numerical data or results that are reviewed and released.'

Steps are being taken to address standardisation; for example, the Euroflow group is working to create standardised panels of reagents in Europe and has made some progress. The issue, he said, is more problematic in the USA, with little incentive for labs to adopt such panels, although an exception has been in minimal residual disease testing, where the FDA has required standardised testing for certain clinical trials. 'Some manufactures are beginning to make reagent combinations that are premixed in a stabilised format, so that makes it easier for people to bring that data and to standardise them,' Wood said. 'That may have been a step forward,'

Where flow cytometry shows a clear advantage is its speed. 'When a sample arrives in the laboratory,' Wood explained, "it can be processed rapidly and results are generated in a few hours; that's difficult to match with antibody-based techniques that require a more lengthy process.

'It is also inherently multi-parametric with its ability to look at large numbers of individual single cells very rapidly in a multi-parametric fashion, and so provides a high degree of sensitivity and specificity for the identification of abnormal hematic cell populations.'

As for the future, Wood believes flow cytometry technology is capable of providing more information about the inherent biology of leukaemia and lymphomas. 'We can begin to understand the end-line biology and which has the markers or antigens associated with a particular response to a therapy or outcomes,' he explained. 'There is a potential role to assess the biomarkers as they are identified in a relatively efficient or cost-effective manner, but it requires some discovery of what those markers are to drive the application.'

Another area of potential is in residual disease monitoring, where the assessment of both prognosis or eventual outcome and response to therapy is becoming an application increasingly carried out by a variety of laboratories.'

Pathologist **Professor Brent L Wood** is director of UW Medicine's Haematopathology and SCCA (Seattle Cancer Care Alliance) Pathology laboratories and UW professor of Laboratory Medicine and Pathology. A past president of the International Clinical Cytometry Society, his laboratory serves as one of two national reference laboratories in Canada for flow cytometric identification of minimal residual disease in childhood.

Of further interest is to extend the technology to solid tumours, although this has been more challenging because preparing samples for them is difficult and there is a limited amount of data known about the expression patterns of proteins and antigens in solid tumours.

'One of the real opportunities lies in the fusion of flow cytometric technology with molecular testing,' he said, 'increasing capability to do single cell molecular-based techniques that can incorporate some of the flow cytometric features to a system identifying cell populations, but also then extensively characterising them at a molecular level and providing much more insight into the biologic nature of subpopulations of cells in any given tumour and potentially their relative response to therapy.

'I think hybridisation of flow cytometry with molecular testing is an important area going forward,' Wood concludes.

An asset to improve cancer management

Liquid biopsy has enormous potential

Report: Mark Nicholls

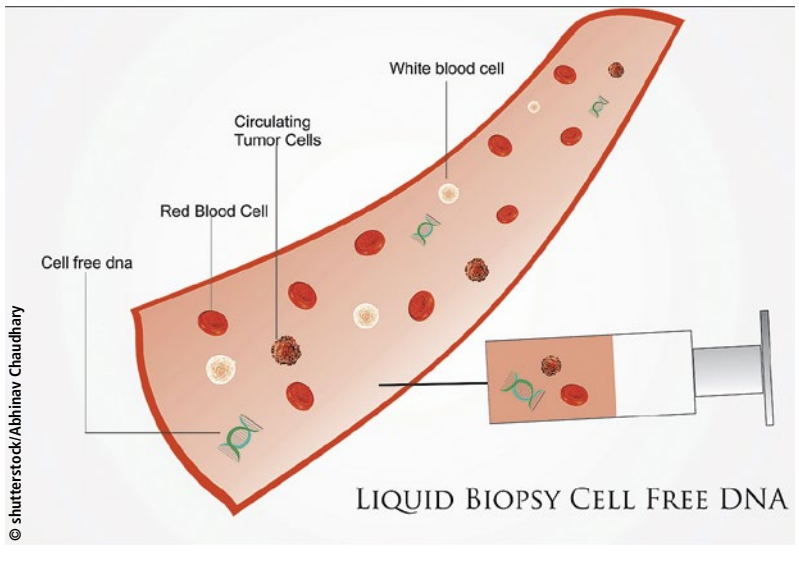
It is non-invasive, delivers a chance of early diagnosis, prognostic information and sequential monitoring, and, believes Professor Francesco Salvatore, the enormous potential of liquid biopsies has still to be reached. However, the positive results obtained so far have 'opened the door to a promising new multifaceted group of tumour markers, at present collectively designated "liquid biopsy",' he explained.

While liquid biopsy is a relatively new term, Salvatore suggested the real essence of its meaning is much older in laboratory medicine: haemochromocytometric analysis to search for altered blood cells was one of the first tests used in medical diagnostics and thus can be considered the first real liquid biopsy.

With the test later extended to molecular aspects of nucleic acids (DNA and RNA) in terms of their quali-quantitative analyses, the diagnostic performance of oncohaematological tests became more sensitive. Today, femtomole amounts of specific nucleic acid sequences are routinely used in leukaemia and lymphoma patients.

In 1997, Salvatore's group was among the first to produce evidence of the presence of RNA sequences in the blood of patients with solid tumours. Soon after, the molecular analysis of nucleic acids was integrated into pathology practice.

The concept of liquid biopsy is evolving, he said, with clinical trials under way with various technologies – such as next generation sequencing of nucleic acids and other high productivity 'omics, analyses – to try to reach high diagnostic sensitivity in body fluids. With cellular and molecular markers that can be visualised, analysed and investigated, there is great potential for cancer treatment. 'Since cancer is a genetically driven disorder the sequencing of tumour derived DNA and RNA is very promising, not only in terms of understanding the pathogenesis of cancer, but also in the early identification and monitoring of tumour derived material thereby acting as biomarkers of the affected tissue or organ.'



© shutterstock/Abhinav Chaudhary

One of the benefits of liquid biopsy, he added, is the ability to identify tumour-associated cells and molecules within body fluids, primarily blood, at the earliest opportunity – leading to better prognosis.

'Obviously, this procedure must be accompanied by highly sensitive methodology that can capture even minute amounts of material. Consequently, nucleic acid sequences, which may be amplified also in the case of a tumour, are crucial for an early diagnosis,' Salvatore pointed out.

Because it is minimally-invasive – unlike needle biopsy – the liquid biopsy approach can be repeated and used to monitor tumour progression and therapy.

Other advantages of liquid biopsy include: prognostic information; easy sequential monitoring; planning treatment monitoring; identification of molecular modifications before and during tumour development; RNAseq studies; detection of infectious agents; and post trauma monitoring, plus the technological advantage of increased sensitivity and specificity of nucleic acid NGS and other products of omic sciences.

Among the tumour components that are shed into the circulation, Salvatore explained, the three that are most likely to be clinically useful and have the greatest potential are: circulating tumour cells, circulating tumour DNA, and tumourderived exosomes.

'Evidence is increasingly appearing regarding the possibility of using these cells and cell components as markers of early diagnosis, recurrence and metastatic spreading, which will also serve to characterise tumour material at molecular level with a view to customised treatment,' he said, predicting that this could see clinical advances over the next decade, in the fight against cancer diseases, particularly in the standardisation of samples from patients affected by tumours; their conservation; transport to specialised analytical centres and storage in certified biobanks; continuous improvements in technological approaches and methods in terms of increased analytical sensitivity and the detection of minute variations; as well as advances in sophisticated bioinformatic tools and methodologies that can help cancer scientists to identify novel gene pathogenic variations.

However, markers have, so far, been approved for only a few examples of specific tumour types and therapy.

Convinced there is a bright future for new tumour markers – at present collectively designated 'liquid biopsy' – he said that, in time,

The general data protection regulation involves all

Ensuring your safe GDPR compliance

The General Data Protection Regulation (GDPR) requires changes in the healthcare sector. It is Greiner Bio-One's aim to optimally fulfil these requirements with the help of its GeT system solutions, the company reports.

The data protection basic regulation came into force on the 25th May 2018. This regulates the protection of ordinary people with regard to processing personal data. One of the few measures expressly mentioned in the GDPR that supports those responsible in complying with the regulation is pseudonymisation. This means the processing of personal data in such a way that it can be allocated to people without the need for additional information.

In the case of the software and hardware solutions from Greiner eHealth Technologies (GeT), the health and personal data (e.g. name, date of birth or hospital stay-related data, such as ward name, diagnosis, etc.) are pseudonymised using a barcode on the patient's wristband and on the blood collection tubes. This means that no data is visible to third parties and integrity and confidentiality are maintained at all times.

Personal data are pseudonymised before the first treatment step. Patients are equipped with pre-coded patient wristbands and numbered tickets upon registration. During blood collection, the patient's wristband is scanned to obtain the corresponding laboratory order. The filled Vacuette barcode tube is scanned again after blood collection and electronically linked to the patient's laboratory order. This ensures optimum protection of the patient's personal and health data from third parties, even during transport of the sample to the laboratory.

Greiner Bio-One is committed to ensuring that customers can optimally meet the requirements arising from the GDPR with the help of GeTs software and hardware solution.

We reduce personal data to a minimum and find a suitable deletion routine together with our customers, to ensure data protection compliance. This guarantees the patient adequate protection against unauthorised processing as well as the knowledge of his data by third parties. It is inevitable that the GDPR itself will lead to significant changes in the healthcare system. The goal of making the blood collection process more transparent and secure is achieved by using the GeT system.

© Greiner Bio-One GmbH

Pseudonymisation by using Vacuette Barcode Tubes combined with GeT.

Francesco Salvatore is Emeritus Professor of Human Biochemistry at the University of Naples, Italy, and until recently was President and Scientific Director of CEINGE, a biotechnology research consortium with over 200 researchers and core facilities for post-genomic research applied to biomedicine. He founded the centre and is an active PI at the institution. Over 400 publications bear his name, including more than 200 original papers, mostly published in international peer-reviewed journals. His many prestigious awards include the Gold Medal from the Ministry of University and Scientific Research and the Gold Medal from National Academy of Sciences.

liquid biopsy tests should gradually acquire the 'canonical characteristics' of laboratory medicine, of standardisation, reproducibility, correct mutational analysis, high sensitivity and specificity, and be validated in internal and external quality controls.

SHIMADZU
Excellence in Science

50th ANNIVERSARY Shimadzu Europa

Unique solution to overcome the bottleneck in sample preparation

Whole in one

CLAM-2000* – the world's first fully automated sample preparation module for LC-MS

The CLAM-2000 is the world's first system able to perform all steps fully automated from pre-treatment of the sample to LC-MS analysis. The CLAM-2000 provides a "whole in one solution" in the areas of clinical, pharmaceutical and pathological research, biological and immunological analysis, or medical laboratories.

Dramatically improved workflow
with better safety and higher reproducibility for clinical research

Large choice to adapt to sensitivity needs
through compatibility with the LCMS-8040, -8045, -8050 and -8060 systems

Uniform pretreatment times between samples
improving analysis accuracy

Integrated and easy to use
online sample pretreatment and LC-MS controlled by a GUI on a touch panel

www.shimadzu.eu/clam-2000

*For Research Use Only. Not for use in diagnostic procedures. Not available in the USA, Canada and China.

Raising the chances of survival for cancer patients

Hungary is steadily digitising pathology

Hungary has one of the worst outcomes when it comes to cancer. Early detection and accurate diagnosis could significantly reduce the costs of oncological treatment. Pathology plays a crucial role in diagnoses, but is crippled by severe shortage and fragmentation. Digital pathology could help overcome those difficulties – and two projects underway seem particularly fit to help, László Fónyad, a pathologist from Semmelweis University, Budapest, explained during ECP 2018 held last September in Bilbao, Spain.

Photo: Attila Kovács - Semmelweis University

In 2004 **László Fónyad MD PhD** graduated from the Faculty of Medicine at Semmelweis University (SU), in Budapest. Following his pathology residency, he became a faculty member at the first Department of Pathology and Experimental Cancer Research, in SU. There, in 2015, Fónyad received his PhD in digital pathology, an interest that began when a student. He was the first to introduce digital slides into graduate education in Hungary, and has headed numerous pilot projects to adopt digital slides in routine surgical pathology. As a part of his PhD program he received a grant from the Hungarian-American Enterprise Scholarship Fund's (HAESF) and was a visiting research fellow at the Pathology Imaging and Communication Technology (PICT) Centre, Massachusetts General Hospital, in Boston, USA, where he worked with Yukako Yagi, and John Gilbertson.

The distortion of resources for pathology impacts on efficiency and simultaneously worsens the quality of and access to healthcare, according to pathologist László Fónyad. 'We have 76 hospital pathology departments in Hungary and around 200 pathologists, who deal with approximately 550,000 cases per year.

'In terms of pathology service diversity, the situation is frightening,' he said. 'Some labs only have a thousand cases while others have 30,000. There are numerous small labs with no fulltime pathologist available, or only one –usually a retired pathologist who is still working. It's unjustifiable and everybody knows that the result is long turn around times of findings, which can take two to four weeks, a lack of consultations that would be needed in complicated cases, and lack of rapid diagnostic aid during surgeries,' he said.

Individual digital initiatives

Digital pathology solutions could potentially improve the situation, Fónyad explained, and there have been a number of initiatives in that sense in Hungary since 1994, with the implementation of an early telepathology network connecting various hospitals and pathology labs, using still images and sharing live images of robotised microscopes.

From the mid 2000s, digitisation has spread to other fields of pathology, such as graduate and postgraduate histopathology teaching, research and routine diagnostics, thanks to the cooperation between Semmelweis University and a Hungarian spin-off company in digital pathology. 'For many years, efforts to introduce telepathology on a local, regional and national level have been driven by enthusiastic volunteer pathologists and have not been financed by the Hungarian government,' Fónyad pointed out.

Recent developments

In 2015 the European Union and the Hungarian government co-financed the Social Renewal Operational Programme and issued a nationwide comprehensive report on pathology services in Hungary, which highlighted the importance of enhanced laboratory automatisation, workflow management and digitisation as tools to improve quality.

In 2016 the Human Resources Development Operational Program, also co-financed by the EU and Hungary, launched an initiative to develop pathology services throughout the country, with a budget of approximately €11 M.

The objective is to provide labs with both traditional and high-end equipment – tissue processors, microtomes, strainers, etc. – and equipment of safe lab sample tracking, such as cassette and slide printers, and barcode readers.

Another goal is to develop a nationwide dedicated pathology information system (nwPIS), which will connect all the pathology labs and be interfaced with each lab's own hospital information system (HIS).

'The nationwide pathology information system will enable real time data collection of all aspects of pathology workflow and resource management. Synoptic reporting and solutions for automated or semi-automated medical coding and billing are also planned,' Fónyad said.

The system will be integrated into the Electronic Health Care Service System, a recently installed cloud computing service connecting various HISs throughout the country. Pathologists will be supplied with computers suitable for digital pathology with ultra-high resolution large-format displays.

A nationwide telepathology consultation network

Hungary is also working on a nationwide telepathology consultation network, to digitise, store and share slides for intraoperative fresh frozen specimens, second opinion and primary diagnosis.

The project is primarily being conducted by Semmelweiss University, which recently received a €6.72 million grant from the public health program of the Norwegian Financial Mechanism, an organisation that regularly injects money into EU states initiatives.

The project also includes the design of a qualification program for histotechnicians, expanding their competence to handle surgical samples that are intended for intraoperative pathology telediagnostics, a quality assurance system for the digital network and a detailed project plan for the implementation of the network when resources become available.

Discussions about funding the implementation have begun with the Ministry for Innovation and Technology. Ideally, the teleconsultation system should be fully equipped by 2019, but workshops should be held for users and the medico-legal aspect should be clarified before the network launches, Fónyad pointed out. 'If necessary, the pathology community should address the issue and counsel the governing bodies on matters of patient privacy, security of patient data and informed consent, licensure, malpractice and liability or reimbursement,' he added.

The current decentralised model of pathology departments is a challenge to good service, and digitisation could also help overcome this difficulty, he explained. 'We have a physically fragmented service. We're thinking of a reasonable centralisation of the pre-analytical processes into several labs, and to distribute the task. or several tasks. of the analytical phase. This is where digital pathology comes in.

'If you want to centralise, you end up with enormous amounts of data and physical samples to process. You need to have a dedicated information system and software to track your samples and trace back any errors. The planned nationwide telepathology consultation network enables distribution of diagnostic tasks between pathologists all around the country.'

The consultation network could improve the human resources capacity of pathology services, but will not solve the low-cost effectiveness rooted in fragmentation, Fónyad warned.

'It has to be clear that implementing digital pathology could help to overcome some of our difficulties but not all, while it is a prerequisite for lab centralisation.'

'Digital pathology is just a tool, not an end,' he concluded.

MR

We listened.
We learned.
Now we lead.

"Analytical performance of POC instruments for HbA1c can be seen to be continually improving. However, there are still some instruments that do not perform to the desired level when different quality targets are applied.

Quo-Lab met all criteria."

Lenters-Westra E, English E. Evaluation of Four HbA1c Point-of-Care Devices Using International Quality Targets: Are They Fit for the Purpose? Journal of Diabetes Science and Technology. 2018; 12: 762-770.

Find out more at
ekfdiagnostics.com

EKF Diagnostics for life

'It will be worthy and cost effective'

Belgium sets up a DX pathology platform

As in many other countries, Belgium faces a significant shortage of health professionals – particularly pathologists to guarantee the diagnostic quality necessary for adequate therapeutic choice. A digital pathology platform can be a true ally; the Brussels Erasmus Hospital opted for that solution. Project manager Dr Ali Ramadhan shared his experience – the good, the bad and the ugly – at ECP 2018 last month in Spain.

Belgium has a dense population –370 inhabitants/km2– and life expectancy is around 81.4 year. Chronic disease numbers, such as diabetes, are rising – in 2018 there were 540,000 diabetics, according to countrymeter.info.

Healthcare expense represents 10.2% of GDP and the main issue is staff shortage, which will increase. 'By 2035, it is estimated that we will have 40% less workforce. With one pathologist per 56,515 citizens, pathologists are a particularly rare species,' Ramadhan pointed out.

In that context, switching to digital pathology is a relief, he added. 'We are all aware of the ongoing complexity and burst of demands for the pathological diagnosis. We have become aware of what technology could bring to pathology in terms of benefits, and thought that digitisation could solve most of our issues. The truth is, it is. It's the cure to most of our problems.'

Therefore, Professor Isabelle Salmon, head of the pathology department at Erasmus Hospital, decided to integrate digital technology into the existing surgical pathology services for specific uses. 'The floor wasn't ready for full digitisation. So, Professor Salmon thought it more beneficial to use digital and the conventional services together and gradually and partially adopt the new technology,' Ramadhan explained.

SecundOS

Four years ago, Erasmus Hospital pathologists stepped in that direction, launching into the creation of a digital pathology platform called SecundOS (second opinion simplified) with the financial support from the 'Fond Yvonne Boël', a non–profit organisation, to purchase diagnostic solutions and scanners, and to secure the operational budget for the project infrastructures.

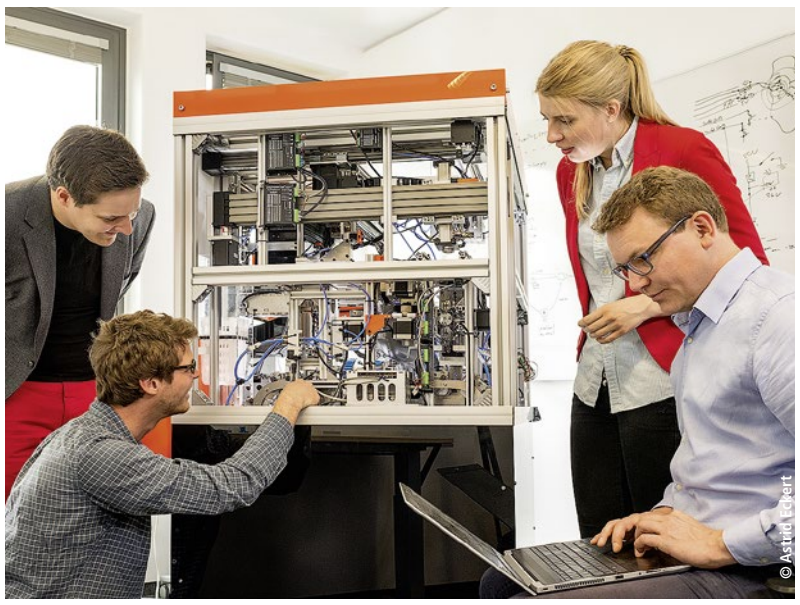
Continued on page 22

Professor Isabelle Salmon heads the pathology department at Erasmus Hospital, and directs Curepath (Centre Universitaire inter Régional d'Expertise en Anatomie Pathologique Hospitalière). She is also co-director of DIAPath, a transdisciplinary and interfaculty research unit at Faculties of Medicine and Brussels School of Engineering, alongside Professor Christine Decaestecker.

Ali Ramadhan MD graduated from Mosul University School of Medicine, in Iraq in 2004 and did his residency at Jordan University of Science and Technology, King Abdullah University Hospital between 2007-2011. He is board certified (Jordanian and Arabic) in anatomic pathology and joined Nineveh Medical College as a lecturer in pathology. Beside teaching and mentoring pathology residents, since 2012 he has worked as a pathology consultant in Mosul. He became a postdoctoral fellow at Université Libre de Bruxelles ULB, in Belgium. Ramadhan is also project manager of the digital pathology platform (SecundOS) at the pathology department in Erasmus Hospital.

Aims to liberate labs from manual processes

Striding towards automation



Inveox founders Dominik Sievert (left) and Maria Driesel (right) discussing details of the automation device with two of their engineers.

Often referred to as the 'Achilles' heel' of histopathology, the sample entry has posed considerable challenges in pre-analytics for several decades. European Hospital visited the Munich-based lab automation start-up Inveox GmbH. Is digitisation and automation really a game-changer in histopathology?

A decades-old problem

Time-intense, highly manual processes in labs are expensive, error-prone and the most common reason for irregularities in cancer diagnoses. In Germany alone, every year hundreds of patients are misdiagnosed or treated incorrectly due to false-positive/negative laboratory findings, that cause fatal medicinal, psychological and personal consequences for patients and families.

Of course, that is the worst-case scenario. However, the traditional process of sample entry in histopathology labs is almost always described as very lengthy and inefficient. The exposure of lab staff to the carcinogenic substance formalin, in which the tissue samples are transported, is often associated with occupational health hazards.

The solution: innovation and automation

Inveox has developed an automation system consisting of three components –a data and communication platform, proprietary biopsy containers and an innovative automation device for the sample entry. 'It defines a new standard in patient safety while providing a long-sought boost in lab efficiency and profitability' co-founder and CEO Maria Driesel claims.

An innovative biopsy vessel with integrated filter facilitates automated processing of tissue samples.

Web-based data and communication platform

The diagnostically relevant data (e.g. imaging, precise macroscopy, tracking) which could not be recorded and leveraged in the traditional process, are now collected in an IT database and made available to pathologists in their existing laboratory information system. Using the inveox web-based, encrypted data and communication platform, physicians and pathologists are automatically informed about the status of a sample in real time - from the extraction of the tissue sample to diagnosis.

Intelligent sample container

Whilst nowadays biopsies must be manually repacked into different vessels and re-labelled several times in the process, Inveox has combined these vessels into a single sample container with an integrated filter. This way, the sample always remains in a single container, eliminating potential mix-ups, loss or contamination. Furthermore, the sample container is provided with a unique and permanent ID, additionally increasing processual safety and allowing for data transfer, track & trace and process control.

An automation device for sample entry

The lab automation device is designed to enable several dozens of sample containers to be inserted at a time and, be processed automatically, seamlessly and simultaneously: The sample data is collected, formalin removed, and the tissue photographed 360° for documentation and additional diagnostical information.

The subsequent innovative technology computer vision opens up a multitude of new possibilities in Visual ID, Machine Learning/AI, which are yet to be explored and leveraged in processual, analytical and diagnostic terms.

The sample is then discharged from the machine, still sitting in the same coded part of the original sample container, the biopsy cassette, and can be seamlessly transferred to the next step in the lab's workflow. 'Inveox is also working and actively researching artificial intelligence. We are determined to create the greatest possible impact and improve lives.' co-founder Dominik Sievert emphasises.

Pathology 4.0 – The laboratory of the future

Every good therapy begins with a precise, reliable and comprehensive diagnosis. Therefore, the future of healthcare begins in the laboratory. 'Our goal is a fully automated, connected laboratory including sample tracking as well as collection and leveraging of process data. Process mining and an algorithm to understand what happens to a sample on its long journey from tissue collection to diagnosis are sources for further insights.' Maria Driesel points out. Combined with diagnostic data, e.g. from pathologists and radiologist, as well as patient profiles, this could form the basis for a reliable, holistic diagnosis – cross-location and in real time.

The revolution escalates

Continued from page 21

The project was carried out in a multistep setup, and divided into three phases: creating the platform (call and set up phases), testing the feasibility of the platform and digital service in general (test phase), and starting the production and the actual use (production phase).

This approach enabled re-evaluation of results after each step and to assess different kinds of obstacles that were faced, and already been thoroughly described in the literature.

By mid-2015, the SecundOS team began an eight-month test phase to study project workability, to identify functional problems, issue recommendations, establish expertise flows and make improvements for optimal use.

'Our team had many difficulties during that phase, as did all those who have tried to set up digital pathology in the lab,' Ramadhan recalled. 'We first bought a scanner and put it in DIAPath, where we used to do the scans, and delivered the slides through shuttle bus and received the images though our web-based sharing system. We noticed a lot of disadvantages: turnaround time went really high, and we had considerable risk for slides loss and breaking. So, we stopped, and bought another scanner to put in our hospital.'

The SecundOS team also noticed there was no perfect link between the platform and the hospital's laboratory information system (LIMS). 'Instead of making benefit of time, we had to do all the additional administrative work. This was a burden to the technologist and pathologists, and was not practical,' he confirmed. 'Eventually we succeeded in performing matches between the platform and LIMS. Both systems linked perfectly and it became a matter of mouse-clicks. All the information was uploaded and sent remotely.'

Team SecundOS. Ramadhan: 'You still need an excellent team with the motivation and spirit working with you to make use of the tool.'

After they analysed the statistics of the test phase, the Belgian pathologists launched the production phase and noticed encouraging data concerning the numbers of cases sent for second opinion for around 600 cases, compared to the 100 cases that were sent during the test phase. 'We also observed increased and more diversified uses of the platform, as we added multiple features. Besides second opinion (24%) and primary diagnosis (2%), new applications, such as using the images for teaching purposes, MDT meetings and research, have been successfully added.'

A topic that still triggers discussion and controversy is the wide use of the platform for academic purposes at the expense of clinical uses such as primary diagnosis, second opinion and frozen section consultations, he noted.

A motivated team

The adoption of the SecundOS by all the pathologists inside the department proved particularly challenging. 'You can have the perfect workflow, perfect DX platform, but you still need to have an excellent team with the motivation and spirit working with you to make use of the tool,' Ramadhan said.

Not having a properly specialised technician to work in this environment as it develops complicated things. 'Image quality was not satisfying at first, we had to work on that,' said Ramadhan, who also recommended having an IT specialist on a daily basis for the platform to run smoothly.

Further issues are compatibility with the rest of the IT systems inside the hospital, to rely on strict criteria upon selecting second opinion experts and to comply with the Belgian and European Union legislation in this framework. The platform must be used across all departments in the hospital to have real value. 'This must be a multidisciplinary tool: we need to make a stand in our network, make it multidisciplinary, and all specialists are welcome,' he said.

Ramadhan and team must now to link the platform to their biobank. 'We need a digital library, an archiving system, which is going to be a very important source of information for researchers, patients, stakeholders… We've done fifty percent of the job and we still have to do the remaining half.'

Integration of artificial intelligence tools to obtain diagnosis and access the biobank is also a significant goal, and cooperation with the DIAPath team, who are already using the technology in their daily work, will be central.

Connected to pathology image server

Other objectives are including more users on the platform and having LIMS connected to the pathology image server, to use all the data in teleconsultation, primary diagnosis, second opinion analysis, interdisciplinary meetings, education and archive.

'Having a platform is a long journey, you have to work in a team and overcome different kinds of problems. It's a must, but not an option to have a digital platform in a hospital,' he concluded. 'It takes a lot of time to integrate this platform into our daily work, but it will be worthy and cost effective.'

WORLD FORUM FOR MEDICINE

MEDICA

Leading International Trade Fair

DÜSSELDORF, GERMANY
12–15 NOVEMBER 2018

www.medica.de

Member of MEDICAAlliance

- The medical world on its way into the digital future
- Worldwide overview: Only at MEDICA 2018

BE PART OF THE NO.1!

Messe Düsseldorf GmbH
P.O. Box 10 10 06 _ 40001 Düsseldorf _ Germany
Tel. +49 211 4560-01 _ Fax +49 211 4560-668
www.messe-duesseldorf.de

Basis for Business

Messe Düsseldorf

Canon
CANON MEDICAL

Women's health solutions

Made possible.

Made For life

Working together to understand your needs and challenges drives valuable outcomes that positively impact you and your patients' future.

Canon Medical's vision and commitment to improving life for all, lies at the heart of everything we do. By partnering to focus on what matters, together we can deliver intelligent, high quality solutions.
With Canon Medical, true innovation is **made possible.**

http://eu.medical.canon
