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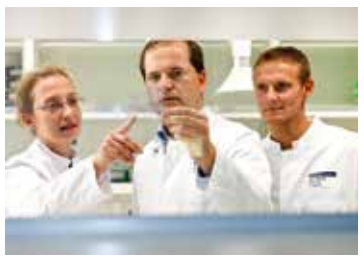

Pain is the point of departure for medical interaction

Research on the sensation is notably difficult to better understand how pain occurs and how it can be treated

Report: Anja Behringer

Pain is the point of departure of any medical interaction. When a body sends out pain signals to say that something is wrong, the person in pain will react – either by self-medication or by consulting a physician. In the latter case, the person becomes a patient and the physician turns into a detective who tries to detect the source of pain.

That's where misunderstandings in terms of communication and knowledge begin. Where does the patient feel the pain and how does he or she express the pain? Is the physician sufficiently trained and experienced to understand the patient? Which factors, such as gender, age or cultural background, play a role in the communication process? Can a subjective phenomenon such as pain be objectively described?

Little knowledge about pain

Those are some of the questions all actors in the 'pain play' have long tried to answer. The fact is that European medical training does not sufficiently address the issue of pain (see EH 5 2013, p. 2). Physicians are not the only ones needing 'pain training', patients also need to understand their situation on the biological, psychological and social level. Thus the physician needs to be a good trainer. At this year's German Pain Congress), co-organised by the Deutsche Schmerzgesellschaft e.V., the German section of the International Association for the Study of Pain (IASP) in Hamburg, several sessions focused on this complex issue. The panellists agreed that little is known about pain, since it is difficult to research such a subjective condition. In everyday healthcare work, however, the way to start is for patient and physician to meet on a level playing field, ideally equipped with a tool that can record the characteristics of the pain as objectively as possible. While physicians regularly collect information on basic pain characteristics, such as intensity, duration, minimum, maximum and quality, anything beyond this fundamental information, e.g. instruction, scales, etc., still varies significantly.

Moreover, the interpretation of the pain-related information differs from physician to physician. 'The patient feels pain in places where the surgeon would not expect pain to occur and even small interventions can cause severe pain,' explains Professor Esther Pogatzki-Zahn, from the Department of Anaesthesiology, Post-surgical Intensive Medicine and Pain Therapy at the University Hospital Münster. 'While there are several predictors for pain intensity currently being researched, it may well be that these predictors change with patient age.'


Artist: Matthew Wardell

> *"The patient, physician and insurer need to continue to focus on three basic ethical principles: do well, don't do any harm and respect the autonomous individual."*

Morphine: still the gold standard

The idea of the 'pain-free hospital' took hold in Münster ten years ago aiming to dispense adequate medication. Painkillers, above all opiates, are usually under-dosed for fear of dependency and for financial reasons. Professor Michael Überall, President of Deutsche Schmerzliga e.V. (DSL – German Pain League), presented his experience of treating chronic non-cancer pain with strong opioid analgesics. There is considerable discussion as to whether the pharmacological differences between the opioids that are subject to German regulation are clinically relevant and should thus be the basis of an individualised pharmacotherapy or not.

Relevant differences

A large Swedish register study evaluating 50,223 patients with chronic non-cancer pain concluded that patients with non-cancer pain who initiated treatment with CR (controlled-release) morphine had a 19% higher risk of opioid rotation than patients initiated with CR oxycodone (Journal of Pain Research 2013; 6: 379-386). These results correspond to the pharmacological differences between the two opioid agonists oxycodone and morphine as well as to the clinical experience of many pain therapists.

The differences between the currently available opioid analgesics are even more significant when the range of analysed active ingredients is expanded to include available combination products.

Prof. Überall explains that, apart from cancer patients, those who benefit from opioids are, above all, patients with chronic pain, e.g. patients with inflammatory-degenerative joint disease, back pain and neuropathic pain. However, opioid dispensation can be problematic. 'Patients with chronic pain are already on medication. During hospital admission they receive different drugs with other side effects, or the active ingredients don't work well together. The patient has little say in his or her medication.'

Important financial considerations

As anywhere, these also have a role, the professor points out. 'Apart from the fact that a pain-free patient can be discharged sooner, consider this figure: in Germany alone we could save €19 billion just by optimising medication. Two thirds of this amount can be saved because patients comply much better when, from the very beginning, they receive the right medication at the right dose.'

Dr Überall emphasises that, in healthcare, the patient, physician and insurer need to continue to focus on three basic ethical principles: do well, don't do any harm and respect the autonomous individual.

In 1990 **Professor Michael Überall** graduated in medicine at Friedrich Alexander University Erlangen-Nürnberg, Germany, where, in 1996, he became Head of Epilepsy Outpatient Services at the Clinic and Policlinic for Children and Adolescents and later senior resident at the Neuropaediatrics Department.
In 1988 the university hospital's new social-paediatric centre introduced outpatient services for paediatric headache patients and Dr Überall focused on difficult-to-treat epilepsy patients, hydrocephalus patients with cerebral shunts and spina bifida patients.
Following his habilitation in paediatrics, Dr Überall was appointed Medical Director of the Institute for Neurosciences, Pain Management and Paediatrics (IFNAP) in Nuremberg in 2003. In the same year he became Vice President of the German Society of Pain Therapy (DGS).
The professor has headed the Institute for Quality Assurance in Pain Therapy & Palliative Medicine since 2004 (IQUISP).
In 2011 he received a special award from the DGS.
He has also been President of the Deutsche Schmerzliga (DSL) since 2012

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The Hospital Surve

Very few European healthcare institutions use it, nor is data collection unified and organised as in the USA

Report: Bettina Döbereiner

A Swiss and German researcher asked whether, where and how the Hospital Survey on Patient Safety Culture (HSOPS) is used in Europe and how relevant this survey – developed in the USA ten years ago and where it is widely accepted today – is in the European context. Last October, one of the two researchers, Dr Antje Hammer, sociologist at the University of Cologne, presented the initial results of her study at the 12th Congress on Care Research, held in Berlin.

It all began with *To Err is Human*, a report by the Institute of Medicine (IOM) published in the USA in 2000. This showed an inordinately high number of medical errors in the country's hospitals. To increase patient safety, the report concluded, a culture of safety needed to be established within hospitals. The Agency of Health Research and Quality (AHRQ) acted by commissioning the development of an instrument to measure hospital safety culture, the *Hospital Survey on Patient Safety Culture* (HSOPS).

This questionnaire is free and can be downloaded from the AHRQ website. With 42 questions (in English and Spanish) addressed to hospital staff it covers twelve relevant areas for safety culture. Versions for nursing homes, medical offices and pharmacies have been added. Participating hospitals can – but do not have to – enter their survey results in the AHRQ database once a year, to face national comparison. Moreover, AHRQ performs an annual analysis of the data; in 2012 1.128 US hospitals were evaluated – a substantial percentage of the 5,700 hospitals nationwide.

Since its inception in 2004, healthcare institutions worldwide increasingly use HSOPS and today, next to the Safety Attitudes Questionnaire (SAQ), this is considered the most widely applied safety culture measurement tool in healthcare. Dr Antje Hammer and her colleague Professor Tanja Manser, psychologist and Associate Professor SNSF at the University of Fribourg, Switzerland, looked at HSOPS application and found that the original survey was translated, adapted and used 44 times in 20 European countries.

Even if the researchers do not claim that their users list is exhaustive, their results do provide important insights: Spain tops the list with seven users, followed by Ireland, Italy and the Netherlands. In most cases, as in the USA, the survey measured the hospital safety culture – very few nursing homes and medical offices used it. While in the US most surveys are conducted on the initiative of the individual hospital, this is not so in Europe, where only a few institutions, e.g. in Spain and Italy, proactively worked with HSOPS. The majority of the hospitals conducted the survey in the framework of a research project.

In a second step, Dr Hammer and Prof. Manser examined whether HSOPS is suitable for European healthcare systems by comparing 14 of the studies that had evaluated the questionnaire. 'We arrived at the conclusion that the questionnaire can be used very well in Europe although it needs to be adapted to each national environment,' said Dr Hammer. Only very few aspects of the HSOPS are less suitable. 'The questions concerning staffing and organisational learning don't work that well in Europe,' Dr Hammer explained, adding that she and her colleague have not yet looked into the reasons why this might be the case but they venture an educated guess: the different framework conditions in European hospitals. With regard to staffing, for example, the survey includes questions on agency staff but, in some European

Pathogens lie dormant or grow slowly within biofilms

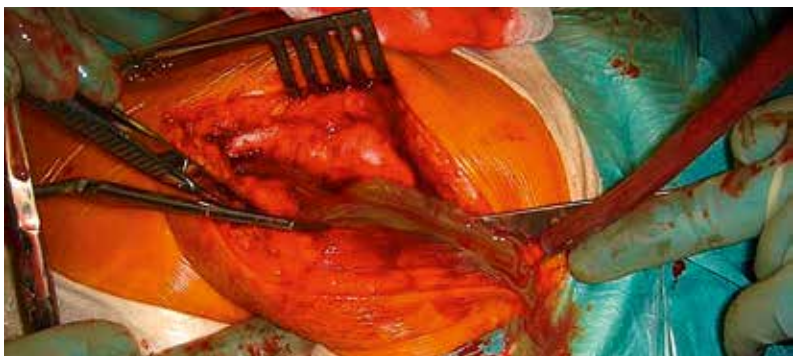
Transplants under sile

The number of patients treated with implants – from cardiac pacemakers, heart valves and vascular implants to artificial hips and knees – is rising worldwide. On average, implants remain functional for 10 to 15 years but, depending on the kind of implant, a significant number of patients may develop implant-associated infections. On this subject, EH interviewed infectious diseases expert Professor Andrej Trampuz, from the Centre for Musculoskeletal Surgery in Charité University Medical Centre in Berlin, who specialises in implant-associated infections and biofilms.

'The body is well equipped to fend off pathogens entering via skin, mucosa, airways etc. However, Prof Trampuz adds, 'implants are foreign objects inserted deep into the body and are designed to stay there. While it takes a million pathogens or more to start an infection via the usual entry paths, only 100 bacteria are sufficient to initiate an infection if they are present on an implant. In joint implants, infections are common in 1-2% of patients after primary implants and in 5% of revisions. Given the low number of bacteria sufficient for an infection, it is almost impossible to lower considerably the incidence of infections by additional hygiene measures.'

What are the symptoms of implant-associated infections?

'In most cases there is no full-blown infection with fever and elevated inflammation markers in the blood. Implant-associated infections usually are low-grade and the bacteria are often associated with biofilms, in which they are dormant, or display very slow growth for quite some time. Symptoms vary considerably: implanted joints or teeth loosen, breast implants deform and become painful, and patients with infections associated with vascular implants often develop sepsis and detect blood in their stools.'



An infection around a hip implant after incision; S. aureus was detected in the pus

How are implant-associated infections diagnosed and treated?

'In the first years after implantation, every painful prosthetic joint must be punctured to obtain joint fluid for culture and leukocyte counting. However, bacteria are enclosed in a biofilm and often show only poor growth. Therefore, cultures are not sensitive enough and may lead to false-negative results, especially in patients previously treated with antibiotics.

'In the treatment of prosthetic joint infections there's a tendency to retain the infected implants if symptom duration is short, i.e. less than three weeks, the implant is stable and the soft tissue coverage is sufficient. Otherwise, the implant is removed and replaced after a short or long interval, typically with an antibiotic-loaded bone cement spacer. In this case, the diagnosis of infection is challenging as well.

'Therefore, sonication of the removed implant was developed by Bandelin electronic (BactoSonic) to remove attached biofilms, which can then be detected in the sonication fluid. This fluid can be used to either culture the pathogens or to perform a PCR analysis.'

What needs to improve?

'We need diagnostic methods with high sensitivity and the ability to identify the pathogens involved, even if only present in small numbers, dead, dormant, or only slow growing. These methods should be able to deal with biofilms and also tell us about the antibiotic resistances the pathogens are carrying so that we can chose the right drug, avoiding empirical treatments and the use of broad-spectrum antibiotics. At present, patients with implant-associated infections are treated sub-optimally, so the infection often persists or recurs. Consequently they need mutiple revisions, leading to worsening performance of the implant. In the case of joint implants this can lead to side effects such as stiffening, Girdlestone arthroplasty or even amputation.'

Are new technologies being developed?

ey on Patient Safety Culture

countries, such as Switzerland, the use of agency nurses is currently rather rare.

The researchers thus conclude that, in Europe, HSOPS is useful and suitable to gain a first impression on the safety culture in a hospital. Thus they strongly recommend that HSOPS application as well as studies on the survey be coordinated and the parties involved be linked in a network. The concrete adaptation of HSOPS needs a balanced view of the healthcare framework and suitable translation – linguistic and content – into the national context. 'In addition we recommend including other important aspects, such as the staff's perception and attitudes on mistakes by colleagues or advanced training and improved knowledge regarding safety issues,' Dr Hammer says, adding: 'currently such questions are not in HSOPS but in our opinion they are crucial aspects of hospital safety culture.'

Nevertheless, one basic question remains to be answered: To date, 13 years after the demand of the IOM and 10 years after the introduction of HSOPS, there is no systematic analysis if there is indeed a relationship between a hospital's safety culture and patient safety.

A meta-analysis performed by Patricia Groves (pub: 2012; *Western Journal of Nursing Research*) did not indicate a significant correlation albeit the meta-analysis was based on a very small data pool. No matter, though, whether the safety culture in a hospital directly affects patient safety outcomes, HSOPS no doubt raises awareness among hospital staff. In its 2012 report AHQR describes a change over time for 650 hospitals that submitted data more than once.

* The research results of Dr Antje Hammer and Prof. Tanja Manser will be published in Patient Safety Culture: Theory, Methods and Application, edited by Dr Patrick Waterson, Ashgate.

Dr Antje Hammer is a state-registered nurse and sociologist. Since 2008 she has been a research associate at the Institute for Medical Sociology, Health Services Research and Rehabilitation Science (IMVR) at the University of Cologne. For her dissertation, she analysed data of the German version of the HSOPS, specially adapted for medical directors.
In her latest project, she collaborated in the EU-funded research project *Deepening our Understanding of Quality Improvement in Europe* (DUQuE), focusing on European hospitals.
She was national coordinator (Germany) and supported the IMVR as partner in the DUQuE project. Her main research focuses on organisational culture, safety culture, patient safety and healthcare quality.

nt attack

'One technology currently under development is the i60 implant and tissue infections cartridge for the Unyvero System of Curetis AG. This cartridge, which is not yet fully validated clinically, covers 91 pathogens and 23 resistance markers.
Unyvero is already on the market with a cartridge to detect pneumonia-causing pathogens and their antibiotic resistances and obtains a result in less than four hours in a fully automatic manner. If Curetis and its partner Heraeus Medical can establish the clinical validation for i60 and demonstrate a high sensitivity, this will be a breakthrough for the diagnosis and treatment of implant-associated infections.

Andrej Trampuz MD is a Professor at Charité University Medical Centre in Berlin, where he heads the interdisciplinary Department for Infections at the Centre for Musculoskeletal Surgery. He is a co-initiator of the European Implant Cohort Study (EICS) and has been the principal investigator for many clinical trials related to infectious diseases, in particular surgical implant-related infections. Prof. Trampuz has also co-authored over 80 publications in peer-reviewed journals and books dealing with implant-associated and biofilm infections, and rapid microbiological diagnostics etc.

Male and female doctors

The need to include women at all levels is a reality, says Moira Mizzi

Whether it was a constitution of sorts writ on cavernous rock at the dawn of mankind no one knows. What is clear is that since the inception of the first rudimentary societies the male always expected to rule and the female to follow and obey. Despite the fact that the woman has proven time and again that she can perform as well as her male counterpart in most sectors, this ideology still holds today, albeit more subtly, even in one of the most developed of continents like Europe.

In the medical field this scenario still holds strong. Although the number of female doctors in European hospitals and in medical schools – UK (70%), Germany (61%) – has risen steadily since the 1990s, men still dominate the profession with their presence and ideology thus making it logistically difficult for female counterparts to thrive, especially if they also have a family to tend. In Germany the number of female doctors has risen from 42% to 55% since 2000; of these only 25% achieve professorship and 11% are found in leadership positions ('glass ceiling' phenomenon). In most EU countries female doctors are often found working on a part-time basis in specialisations that allow them to cope with all their responsibilities.

Luckily, in the last four decades there has been a gradual shift of focus to gender issues bringing social power relations and hierarchies more to the forefront even in the medical profession. The World Health Organisation is in fact highlighting the deleterious health effects gender inequality has on both sexes. In the EU gender equality has become part of a Strategy for equality between men and women (2010-2015) which is targeting equal economic independence; equal pay for equal work and work of equal value; equality in decision-making; dignity, integrity and ending gender-based violence, and gender equality in external action policy.

The EC recently launched (April 2012) a Working Document on an Action Plan for the EU Health Workforce in which the key challenges, e.g. the increase in labour demand (aging population) compounded with a decrease and unequal distribution in health professional workforce are highlighted and measures to promote a sustainable workforce are addressed.

Belgium recently launched a multi-annual plan addressing the workload (increase worker pool), wages and incentives for further academic growth; Finland addressed certain tasks that can easily be shared between physicians and nurses (redistribution of tasks) supporting this initiative with state grants, legislation and national strategies, while Ireland set up an Expert Group on Future Skills Needs (EGFSN) to assess balanced supply and demand in many sectors of healthcare under different scenarios.

This helped to set an integrated approach in the level and type of service offered while regularly addressing workforce planning. Spain proposed a more radical healthcare upheaval by evaluating new models of services, namely ambulatory surgery and home care, defining different competencies of different healthcare specialities and change in citizens' health behaviours (self-care, informal care providers) thus reducing the workload from central hospital systems.

Medics with children

Despite these measures, reconciling work, family and private life is still a challenge for many European women; in fact, there are 12.1% fewer women with children than without on the labour market compared to 8.7% for men. In Germany, the Federal Ministry of Health is working on arrangements that encourage a balance between family and medical work, which can include parental leave, company leave because of a sick child, the right to reduced working hours for a period of time, and support for, or the offer of childcare facilities even in medical school.

In the UK, all NHS staff, including general practitioners, has access to childcare; recently other forms of support – after-school clubs, holiday play schemes, child-minding networks and childcare vouchers – are being considered. Plymouth hospitals also offer options for paternity leave, flexitime, term time working and annualised hours where necessary. In Norway, three months parental leave is offered to both parents to ensure the woman is not forced to leave her job.

All these measures support the family, especially the woman, giving more flexibility for other aspects of her life. However, there are other perspectives, namely a work environment free of sexual/sexist harassment and one in which she is appreciated for her academic prowess, relations acumen, motherhood and so on. Supporting a woman to fit into a male world will do nothing to enhance her individuality and health and that of those around her, including male colleagues.

Malta's Director of Health Promotion and Disease Prevention, Dr Charmaine Gauci asserts: 'If I look back through my career, I can positively say that the fact that I'm female did not affect my progress at all. I firmly believe that it is not gender that affects being chosen for a particular job but how much you really work hard for it and for what you believe in. I feel that females do have some skills that males do not have, and vice versa but, if one maintains balance and respect, gender will not make a difference. What you sow you reap.'

Dr Gauci admits that it was particularly hard for her to juggle between work, family, studies and personal time. 'Usually, time for oneself is the first to suffer but I'm very adamant about "my time", which I enjoy either in outdoor activities or watching a movie with the family; that is the healthy part of it all.'

Family support is essential

She also speaks of vital family support when her son was very young. 'I wonder if my career would have progressed as it did if they weren't there to take care of him. I strongly believe it would have been harder for me to succeed had I been forced to spend four years out of the workforce.'

Dr Natasha Azzopardi Muscat, Chief Medical Officer at the Ministry for Health for Elderly and Community Care, also talks of positive gender experience in her career: 'I've not encountered discrimination; if anything I've encountered some real encouragement and support from older male mentors along the years.' She also refers to a gender revolution over the past decade. 'In 2001, I was the only female director in a group of 13 within government departments and one of two within the ministry. Since 2008, half the headship positions have been taken by women.' Her biggest challenge is also balancing work with the needs of three children with different schedules and commitments. 'For me, everything is triple,' she moans, 'school concerts, sports days, parents days, not to mention holiday time, which is a nightmare – especially since the pace has become hectic with electronic devices requiring one's availability 24/7.'

Electronic devices are not society's only heralds of change, particularly in recent decades. The inclusion of women at all work levels is a reality we all experience in our daily lives. As we are collectively accustomed to having technology readily available, I believe we also need to become acclimatised to all the realities that go with it, including family and quality of life. As Oscar Wilde insists, 'To deny one's own experiences is to put a lie into the lips of one's own life.' That, of course, is entirely up to us.

Alfried Krupp Hospital in Essen, introduced 50 different part-time models including:

- Qualified part-time employment (15–93% of full-time employment)
- Job sharing, particularly for managerial functions
- Coordination of duty rosters of couples across different departments
- Establishment of time accounts (plus and minus hours)
- Flexible working hours (flexitime), with family-oriented core times.

The U**niversity Hospital Charité,** Berlin, established a "fathers representative", who advises men on questions concerning family–work balance.

In Hanover, the Medical University provides financial incentives for departments that attract female doctors back to work from parental leave within one year.

Sources: Bundesministerium für Familie, Senioren, Frauen und Jugend, 2009 (34); Müller B, 2005 (35).

Dr Natasha Azzopardi Muscat is the country's Chief Medical Officer and a lecturer in Health Services Management at the University of Malta, from which she graduated in medicine and surgery in 1995. After gaining her Masters degree in Public Health in 1997, she was awarded a Chevening Scholarship and went to the London School of Hygiene and Tropical Medicine London, there gaining a Masters with Distinction in Health Services Management. She became a Member of the Faculty of Public Health (UK) in 2003 and three years later an elected Fellow of the faculty of Public Health. In 2001, aged 27, she accepted her first Headship position in the Public Service of Malta, and worked on European and International Health Policy, particularly focusing on healthcare preparations for Malta's EU accession. From 2007-2011, Dr Muscat served as Director General (Strategy and Sustainability), and was then appointed Chief Medical Officer. She is a founding member of the Malta Association of Public Health Medicine and its President between 2006 and 2007. She is actively involved in the European Public Health Association and Section President for Public Health Policy and Practice.

Dr Charmaine Gauci is a consultant in Public Health Medicine and currently occupies position of Director of the Health Promotion and Disease Prevention Directorate within the Ministry for Health, Elderly and Community Care. She graduated as a medical doctor in 1991. Over the years she has developed skills in the wide aspect of the public health specialty. She pursed her studies with masters in public health medicine. She has also specialized in fitness and nutrition. She attained her PhD Degree in communicable disease epidemiology in 2006. She is a fellow of the Faculty of Public Health in UK. As a senior lecturer at the University of Malta she lectures on public health, with a special focus in Epidemiology and Communicable Diseases and is currently co-coordinator for the Public Health MA course. Also active in research, she supervises a number of undergraduate, masters and PhD students. Currently, Dr Gauci is President of the Malta Association of Public Health Medicine, and also acts as a focal point for a number of bodies within the EC, including ECDC, WHO and Health Security. Her life's motto is: 'If there's no wind, row. If you want it, make it happen.'

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Need we say it? Males and females are different

Gender medicine

Report: Anja Behringer

The insight that psychological, social and environmental conditions affect a person's health is insufficiently considered in medical training and in the every-day diagnosis and treatment of patients. Apart from gender-specific diseases, there is little medical research on 'women's health' and 'men's health'.

Gender medicine as a research area was founded in the mid-1980s by the US-American cardiologist Marianne Legato who also coined the term. 'Gender' refers to the social construct, meaning the social and cultural roles of women and men and their tasks in every-day life, while 'sex' refers to the biological sex constituted by the biological differences between the genders. English is the only language that makes this distinction.

Gender medicine starts from the vantage point that diseases can manifest differently in men and women and thus diagnosis, therapy and medication have to be gender-specific. These differences might stem from biological (anatomy, hormones, chromosomes) as well as the psychosocial differences (lifestyles, culture, environment) in men and women.

'Gender-specific research continues to confirm the impact of psychosocial and psychological variables of diseases. The variables influence the course of the disease as well as recovery and are thus important factors of the clinical outcomes and well-being of patients,' says Professor Vera Regitz-Zagrosek MD, who directs the Institute for Gender Research in Medicine (GiM) at Charité, Berlin. The Institute also hosts the pilot project Gender Medicine, which monitors and classifies research on gender medicine issues and makes it publicly available.

National and discipline-specific differences

One way or another, many countries incorporate gender medicine. For example, in Sweden healthcare policy actively promotes gender equity. In Austria, gender medicine is a mandatory topic in medical training and also looks at patients and their gender-specific reaction to physicians and staff. According to one study, patients have the highest confidence in older male physicians and the least in younger female physicians.

Today, gender medicine is quite well established in cardio-vascular, pulmonary and autoimmune diseases as well as in rheumatology and endocrinology. Significant gender-differences are also known in neurological and gastroenterological diseases. The issue of medication, however, is severely under-researched. Many trials are still conducted exclusively with male subjects although it has been known for quite some time that many drugs act differently in men and women. Moreover, men and women communicate very differently. Men tend to be reluctant to express pain, whereas women, frequently more in tune with their body, describe pain in a more detailed way. Thus, in the USA and the United Kingdom gender-specific interview methods and communication training have been incorporated in the medical curricula.

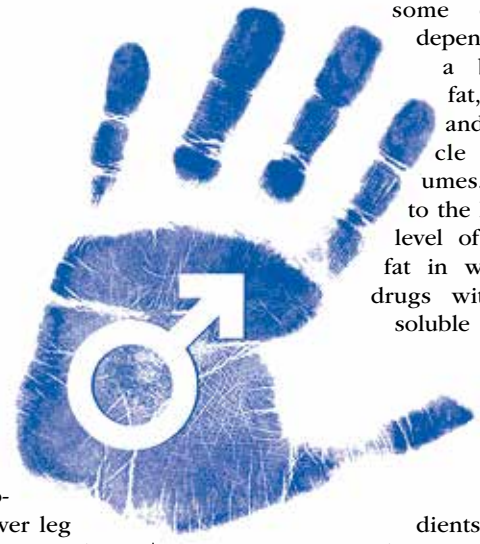
Consequences for diagnosis and therapy

Gender medical research has shown that the classification of diseases as 'typically male' or 'typically female' can have a fatal effect: these stereotyped diseases are not recognised in the other gender, also because they tend to show different symptoms in men and women. Gender and age differences can be present in bone density, vessel thickness and metabolism. Moreover, there are differences in the size of internal organs, cardiac activity, body water/fat ratio and last but not least in physiognomy, size and weight. Women, for example, tend to have a smaller patella than men and due to the female pelvis anatomy have a higher risk of wear in the knees. Yet, it was 2007 before these differences began to be considered in knee implant construction.

Significant gender differences are confirmed in rheumatic and cardiovascular diseases. Today we know that myocardial infarction and stroke are by no means typically male diseases. Nevertheless heart attacks in women remain frequently undetected, or are detected too late simply because physicians still do not expect them in women. Moreover the symptoms of a myocardial infarction tend to be different in men and women: in women the event is associated with rather unspecific symptoms, such as pain in the upper abdomen and the back, lower leg oedema, fatigue or sleeping disorders. The typical male symptoms such as chest pain radiating to the shoulder and down the arm are also present in women, but are rarely immediately associated with a myocardial infarction due to the wider range of symptoms.

These are not the only differences. More women than men suffer migraine or irritable bowel syndrome. Pain perception is different between men and women. On the other hand, more men than many physicians tend to acknowledge suffer from the allegedly typically female disease osteoporosis – and die from it. In patients with diabetes, blood sugar levels in women are more difficult to adjust than in men.

The fact that men and women respond differently to certain medications is only partially due to the differences in body size and weight. Gender-specific metabolisms and hormonal makeup also play a significant role.



Moreover, the processing of active ingredients to some extent depends on a body's fat, water and muscle volumes. Due to the higher level of body fat in women, drugs with fat soluble ingredients tend to have stronger effects in women, while other active ingredients take longer to be flushed out by the liver and are filtered to a lesser degree in the kidney.

Neglecting these physiological processes can lead to dangerous adverse reactions and overdosage – and toxicity can occur. Consequently, in years to come the young discipline of gender medicine will most likely put a special focus on gender differences in response to drugs, especially regarding medication for heart diseases, seizures and coagulation modifiers.

Economic benefits of gender-specific perspectives

In geriatrics, gender factors are also frequently neglected because the costs are allegedly prohibitive. However, providing old patients with gender-specific treatments is above all a question of organisation, not funds.

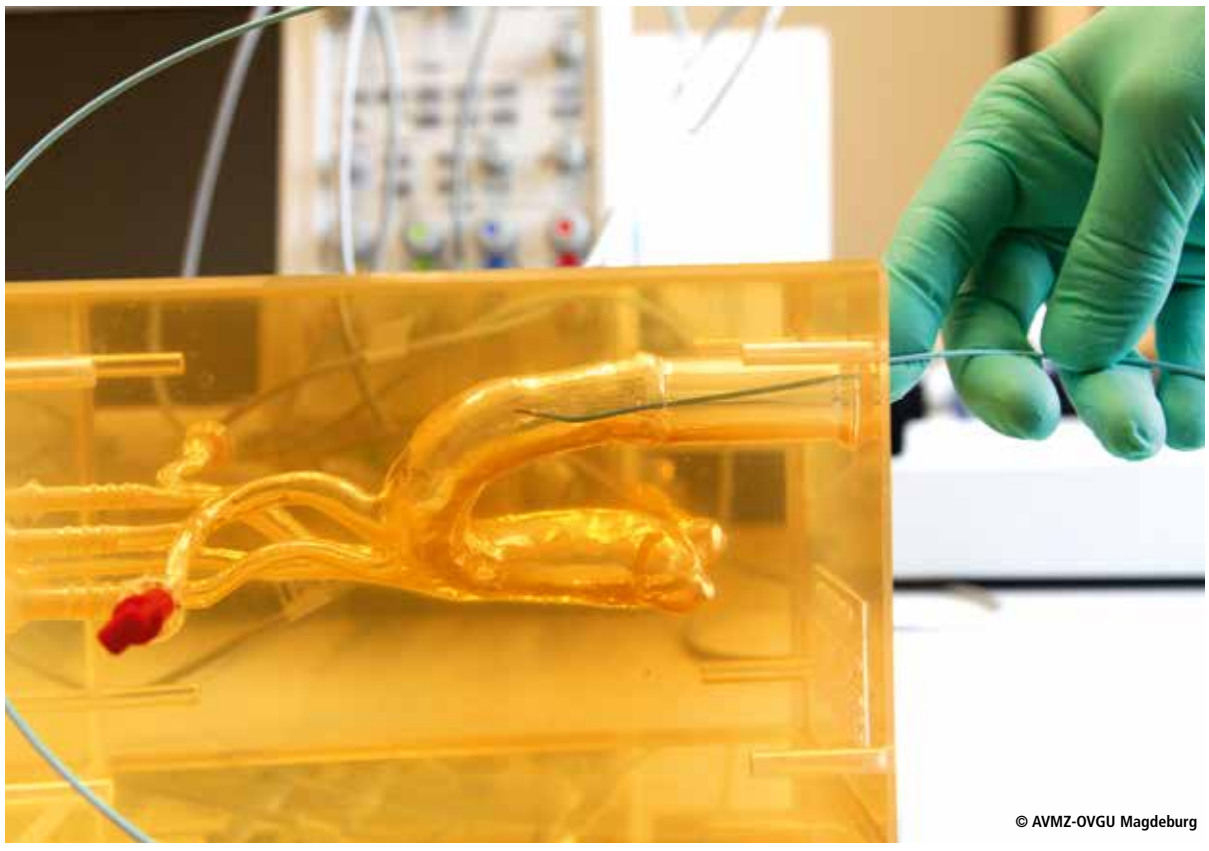
One argument: Gender-specific medication is too expensive, in effect meaning that personalised and patient-centred medicine is too expensive. Conversely, the advocates of gender medicine maintain that gender-specific medication saves money and has better outcomes, in the long run. Additionally, they deplore EU funds being channelled to biogenetic research rather than to behavioural, environmental or prevention research.

Professor Vera Regitz-Zagrosek MD is co-founder and Director (since 2007) of the Institute for Gender Research in Medicine (GiM) and a Member of the Board (from 2012) of the Centre for Cardiovascular Research (CCR), both at Charité Medical University in Berlin. Following her habilitation in internal medicine at the Free University Berlin the professor joined the Berlin-based German Heart Centre as a senior physician. She has also served as Vice Director of the Centre for Cardiovascular Research (CCR) at Charité (2003 to 2008). In 2002 the professor designed the graduate course *Gender-specific mechanisms in myocardial hypertrophy.* She also initiated the foundation of the International Society for Gender in Medicine (IGM) and the German Society, of Gender Medicine. For the European Society of Cardiology (ESC), Prof. Regitz-Zagrosek heads the *cardiovascular diseases in pregnancy* task force and coordinates the Berlin site of the German Centre for Cardiovascular Research.

Electrical engineers, doctors and biologists are developing an instrument for early diagnosis of arteriosclerosis

Characterising plaques with millimetre-waves

The Plaque-CharM project funded by the German Federal Ministry of Education and Research is to develop novel sensor technology that can characterise arterial tissue in the smallest space – the tip of a catheter. This could help to diagnose arteriosclerosis at an early stage, leading to improved prevention of heart attacks and strokes. Dr Chafik Meliani, the project co-ordinator at the Leibniz-Institute IHP (Innovations for High Performance Microelectronics), discussed the venture with EH correspondent Bettina Döbereiner



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The image shows a catheter phantom. It describes a typical case where a catheter equipped with a millimetre-wave sensor system could be used. The scale becomes particularly clear: the phantom is oriented on the original size. The sensor to be developed needs to fit into the small catheter-top to detect fatty- and calcareous plaques in the arteries.
The partners of the Plaque-CharM project, based at the Leibniz Institute IHP (Innovations for High Performance Microelectronics), are: Primed Halberstadt Medizintechnik GmbH, the Chair for Healthcare Telematics and Medical Engineering and the Institute of Micro and Sensor Systems at the Otto-von-Guericke University Magdeburg, the Chair for Electronic Circuit Technology at Ruhr-University, Bochum, and the Clinic for Cardiothoracic and Vascular Surgery at University Hospital, Giessen and Marburg GmbH.

The interdisciplinary research project began when Professor Sebastian Vogt MD, Head of the Research Laboratory at the Cardiothoracic and Vascular Surgery Clinic in Philipps University of Marburg approached Professor Wolfgang Mehr, Director of the Leibniz Institute IHP. Prof. Vogt's request: the development of a novel diagnostic instrument to help characterise arterial tissue to detect dangerous plaques and distinguish these from asymptomatic plaques. At IHP Prof. Vogt was knocking on an open door.

The project, involving five partners, rolled out in September 2012 to begin a three-year schedule financed with €2.3 million by Germany's Federal Ministry of Education and Research.

The term Plaque-CharM is derived from the characterisation of plaques via millimetre-waves. 'What we would like to prove is that in the frequency range of millimetre-waves we can determine characteristics of the arteries that we cannot necessarily see with other procedures,' Dr Meliani explains. This especially includes the distinction between fatty and calcareous arterial plaques and healthy arterial walls. 'The frequency range of the millimetre-waves has not yet been fully researched for medical applications, we really are at the very beginning.'

The IHP-MICMOS technology developed and planned for the sensor at the IHP is indeed innovative, with add-ons also developed at the Institute, which facilitate on-chip antenna for the integration of biosensors, for example. The research project is currently in its first phase. The objective is to prove the principle experimentally, to systematically characterise tissue in the Gigahertz range and to build a first demonstrator. Already the first success has been observed with initial test structures – a sufficient phase difference was determined during transmission measurements for different types of tissue in the 30 Gigahertz range. 'This is proof for us that we can indeed see a difference in tissue structure with the application of microwaves,' Dr Meliani confirms.

In phase two, the objective will be to miniaturise the sensor to such an extent that it fits into the top of a catheter, with a diameter of around 1 millimetre to 500 micrometres and a length of a few millimetres. There will also be issues of biocompatibility, such as the question of temperature, because the sensor must not warm up in the bloodstream. However, a resolution for this issue is already being examined. Even if at first glance the warming up of a sensor may appear inconsequential from an electrical engineer's perspective, it isn't from a medic's point of view.

That is exactly what Dr Meliani finds so fascinating about this project: 'Traditionally, electrical engineers are not that familiar with doctors and vice versa. We each have our own ideas that we contribute to the project, making everything extremely dynamic. This is something new for everyone involved – and it is extremely exciting.'

Chafik Meliani MSc PhD gained his electrical engineering degrees in 1999 and 2003, from the University of Denis Diderot, in Paris and from 2000 to 2003 he was working for Alcatel in Paris, on the design of high bitrate circuits for optical communication systems. In 2003, he joined the Ferdinand-Braun-Institut für Höchstfrequenztechnik (FBH) in Berlin, where he was involved in IC design for communication and radar systems and, from 2008 to 2011, led the institute's power amplifier group. Dr Meliani joined the Leibniz Institut für Innovative Mikroelektronik (IHP) in 2012, heading the research group mm-wave Wireless.

From MIS to optimally invasive cardiac surgery

'The smallest incision is not always the best'

Report: Bettina Döbereiner

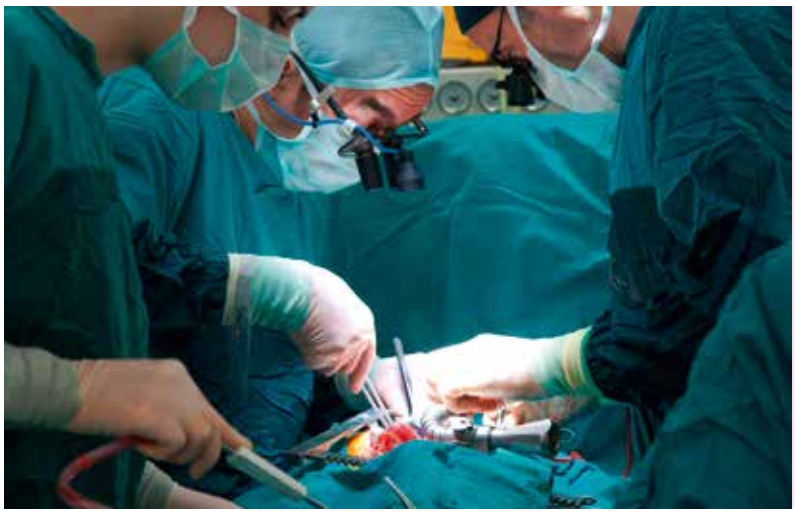
Since minimally invasive surgery (MIS) entered cardiac surgery in the mid-1990s it became unthinkable not to use this medical specialty. However, MIS procedures do not always result in the best outcome for patients. Thus, at the German Heart Institute in Berlin (DHZB - Deutsches Herzzentrum Berlin) the preferred term is 'optimally invasive' surgery – a description attributed to Professor Roland Hetzer, the Institute's Medical Director. In an August medical technology gathering, the concept was explained in a lecture by his colleague Professor Onnen Grauhan, Consultant at the DHZB Department of Cardiothoracic and Vascular Surgery.

In early days of MIS the prevailing belief was that the smaller the incision, the better for the patient – and talk was of keyhole or buttonhole procedures. However, the term, at least in cardiac surgery, generally has a broader meaning. Prof. Grauhan: 'Minimally invasive heart surgery nowadays is primarily aimed at minimising what is harmful and traumatic for the patient.' Naturally, this continues to include the choice of incision and, if possible, minimisation, but not always exclusively – the reason why the preferred term at the DHZB is optimally invasive surgery. This more aptly expresses what really matters: finding the optimum level of invasiveness for each patient – and that doesn't always have to be the procedure with the smallest incision.

Explaining the concept, Prof. Grauhan spoke of mitral valve surgery. Here, a 10-15cm long incision for an anterolateral thoracotomy, i.e. incision on the side of the chest between the ribs, is optimally invasive and has clear advantages compared to a typical, 3-5cm minimally invasive incision. He cites four reasons why: First, cannulation for the heart-lung machine (HLM) can be done via the primary incision on the aorta and vena cava (left atrial approach) and does not require an additional incision in the groin; next, visibility is considerably better with the longer incision because the view offered by the cameras used with the smaller incision is not comparable to the direct view.

Third, myocardial protection, i.e. measures to protect the heart muscle during surgery, is easier when the incision is larger, as the quality of myocardial protection is easier to monitor.

His final argument for optimally invasive surgery is that a larger incision improves cardiac de-airing: 'In our estimation and experience, de-airing is much easier with a larger incision. As banal as it may sound, you just take one hand and shake the heart a little, which makes the air rise up and out of the hear.' Surgery is generally carried out with CO2 – if too much air reaches the brain via the blood this can cause significant damage.



However, it's not only the ability to free the heart from any remaining air, but also the chance to have one's hands in situ, which the professor feels is a clear advantage for a cardiac surgeon. In this example, the concept of optimally invasive surgery strikes a balance between traditional, median sternotomy and a classic, minimally invasive procedure.

However, one should mention that any intervention on the side of the chest, rather than via the sternum, would always be more painful in terms of wound healing. Mitral valve surgery at DHZB is always discussed with patients beforehand, along with any aesthetic considerations because, particularly in the case of MIS, the procedure involves several, smaller incisions for clamps, lighting and HLM cannulae, resulting in several scars. Although these tend to heal somewhat quicker than a longer incision, a patient might be concerned by this multitude of scars later. Another example is bypass surgery. Patients often have several

Onnen Grauhan gained his medical degree and doctorate (thesis: 'Man in microgravity") at the Institute of Physiology, Free University Berlin. He was a resident at the department of Cardiothoracic Surgery at DHZB and the department of General Surgery at the Charité, University Medicine Berlin, and in 1994 became a consultant in DHZB's cardiothoracic department. In 1999, at the Charité Medical Faculty, his PhD thesis covered 'Humoral rejection after Heart transplantation'. In the same year he became a University Lecturer at Charité. Since 2003 he has repeatedly stayed in Bosnia Herzegovina to support the development of a cardiac surgery unit at the University of Sarajevo.

stenoses in different parts of their coronary arteries, or on the posterior wall, so that minimally invasive direct coronary artery bypass surgery (MIDCAP) is not possible. In these cases, if possible the off-pump-coronary-artery-bypass (OPCAB) procedure, i.e. open-heart bypass surgery, is performed. 'We also feel that OPCAB can be considered as optimally invasive here because it avoids the HLM and prevents limitations in renal and respiratory function and averts cerebrovascular events,' Prof. Grauhan explains. However, in recent times, doubts have been raised about the OPCAB procedure due to unfavourable long-term results.

Coronary stents, an alternative hotly debated over the last two decades, he points out, are used at DHZB in agreement between cardiologists and cardiac surgeons according to the *National Medical Guidelines on Chronic Coronary Heart Disease* (2006). The recently published final results of the international, multicentre Syntax Study (Synergy between PCI with taxus and cardiac surgery) confirmed that, in around two thirds of patients with complex three-vessel disease or stenosis of the left main stem, bypass surgery is definitely superior to stent implantation. Therefore, he urged all cardiologists present to be more closely guided by the jointly developed medical guidelines in future. Too many stents, he says, continue to be implanted in cases where, taking into account current study results, bypass surgery would be better.

Prof. Grauhan is convinced that the trend will clearly continue towards minimalisation of incisions and interventional cardiac surgery, especially as patients are increasingly older so classic heart surgery is not an option. He does not want optimally invasive surgery to be perceived as a regressive concept but rather as a cardiac surgery strategy adapted to the overall outcome for the patient. The DHZB performs numerous interventional operations in the hybrid operating theatre (opened 2008), such as transcatheter aortic valve implantation (TAVI) and hybrid operations where surgery via incisions and catheter-based interventions are performed simultaneously on the same patient.

Manufacturing World Osaka 2013

Manufacturing World Osaka 2013 consisted of three exhibitions covering Mechanical Components & Materials Technology, Design Engineering & Manufacturing Solutions and Medical Device Development & Manufacturing.

Given the acknowledged design quality of Japanese goods, it's not surprising that October's event drew in its largest-ever number of overseas exhibitors – 91 came from nine countries – China, Germany, Hong Kong, Korea, Mongolia, Taiwan, Thailand, Turkey and the USA. Among these, Korea, Taiwan and Thailand presented their products in national pavilions.

The actual number of exhibitors was 863 and visitors numbered 39,972 (this figure includes people visiting the highly-functional Material World Osaka 2013, but excludes seminar participants, members of the press and exhibitors).

Inevitably, the increasing globalisation and Japan's economic recovery lead to important international exchanges between exhibitors and visitors, the organiser Reed Exhibitions Japan Ltd reports, adding that this trend is expected to continue next year.

Running over three days, Manufacturing World Japan and Manufacturing World Osaka will take place on 25-27 June 2014 in Tokyo and Osaka, and be on a larger scale than ever, the company adds. 'Following the huge success of the previous show, many applications have already been rushing in to Show Management. If you are interested in exhibiting, please contact Show Management immediately,' the firm advises.

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The complex science behind microbubbles

PART II: Ultrasound activation – from diagnosis to drug delivery

In European Hospital issue 5/2013, *François Tranquart, General Manager of Bracco Suisse S.A. (picture),* explained how microbubble technology is used for ultrasound diagnostics. Continuing his discussion with Daniela Zimmermann and Ralf Mateblowski he examines the potential of drug-guiding microbubbles.

'Bubbles,' François Tranquart explains, 'could improve local drug delivery because they make it easier for the tissue to take up the drug. You send the microbubble and the drug together to the site where you apply ultrasound waves – high acoustic pressure – to make the bubbles burst. These explosions create tiny lesions within a vessel wall which could facilitate the passage of the drug from the vessel to the tissue and maybe even to the cells.'

At the Ultrasound Medical Department of Bracco Imaging in Germany, Dr Christian Greis points out the nanotechnology potential of microbubbles: the microbubble cavity allows the incorporation of active substances, making microbubbles a vehicle for drug delivery. 'Microbubble-encapsulated drugs can be injected intravenously and released locally, either by short ultrasound-mediated microbubble destruction or by retarded release after local binding of target-specific microbubbles,' he explains. 'Using such drug delivery systems, a high local drug concentration and effect can be achieved with a markedly reduced systemic effect.'

Is this nanotechnology a promising approach ?

'Indeed the concept of encapsulating drugs is amazing,' François Tranquart agrees. 'However, today very few drugs are available as nanoparticles because the new drug needs to be developed first and then you can think about a nanoparticle. This is a long and costly process. We are talking about approximately 15 years. 'Moreover, prior to clinical use, regulatory authorities have to review the process and at this point we do not know if and for how many indications we would get clearance. Therefore, my preference today would be to disconnect bubbles and drugs and have one bubble and one drug—and to inject them simultaneously.'

When microbubbles carry or accompany drugs to a disease site in the body, the microbubble technology moves from the purely diagnostic to therapy. Apart from the technological challenges such a development presents, there is the fact that it will bring two other players on the stage: the regulator and the pharmaceutical company. As far as the regulator is concerned, 'typically authorities care about safety, not efficacy,' François Tranquart points out. 'Their primary role is to ensure that your invention is safe for patients. Secondly the regulator will ask whether you are changing the clinical outcome for the patient that is, whether you improve life expectancy.'

As far as the second new player – the pharmaceutical company – is concerned, he is convinced that drug-delivering microbubbles 'cannot be achieved without close collaboration between a bubble and a pharma company. We have to demonstrate in a clinical environment that we can improve local delivery and, more complex, that we are improving the clinical outcome.

'To translate a concept from the research level to clinical use requires a huge amount of work. Not to mention investments. The current research on targeted agents requires a lot of resources. The next step will be targeted indications. No doubt, this is an exciting issue and we'll see how the pharmaceutical industry will get involved in this.'

Lower dose adds value to improved delivery

'With improved local delivery we might be able to decrease the injected dose, thus we could also decrease the number of adverse events – a real benefit for patients, and obviously for pharma companies. In general, all the involved parties need to cooperate, including pharma companies and authorities. If we want to improve treatment efficacy and local delivery a global effort is necessary. Bracco cannot solve all problems by itself. Microbubbles are one solution among many, albeit a very significant one.'

Microbubbles and ultrasound: a match made in heaven

Microbubbles and the hardware they are being used with need to work hand in glove. Therefore, the ultrasound manufacturers approach Bracco to test their technologies. 'We work with all ultrasound companies and they come here to test equipment because we know how to use the bubbles, François Tranquart explains. 'Since we are the only remaining company with a large research lab it's a win-win situation.'

Microbubbles are a complex research object where a host of factors has to be taken into consideration: gas, shell, equipment, properties, organs, etc. Bracco's General Manager takes on the challenge eagerly. Even more: he is proud that ultrasound and microbubbles lead the way. While iodine compounds for CT and gadoline complexes for MR are established technologies, he says, ultrasound 'is really innovative. We are still changing and creating something new.'

Research is one step in the value chain, but how can the physicians on the ground be motivated to adopt new technologies? François Tranquart is well aware that simply telling the physicians 'Buy SonoVue!' won't suffice and as a marketing strategy it does not do justice to the enormous potential of ultrasound and microbubbles. 'Obviously, we need to convince the users that they can get more relevant information when using bubbles. We need to help them to be more confident with sonovue in different indications, how to apply it, quantify and analyse the results. More importantly, though, the focus is not on the microbubbles per se but on the integrated unit of the modality – ultrasound – and microbubbles. It is a powerful global solution.'

Ultrasound vs. MRI – a passionately debated issue

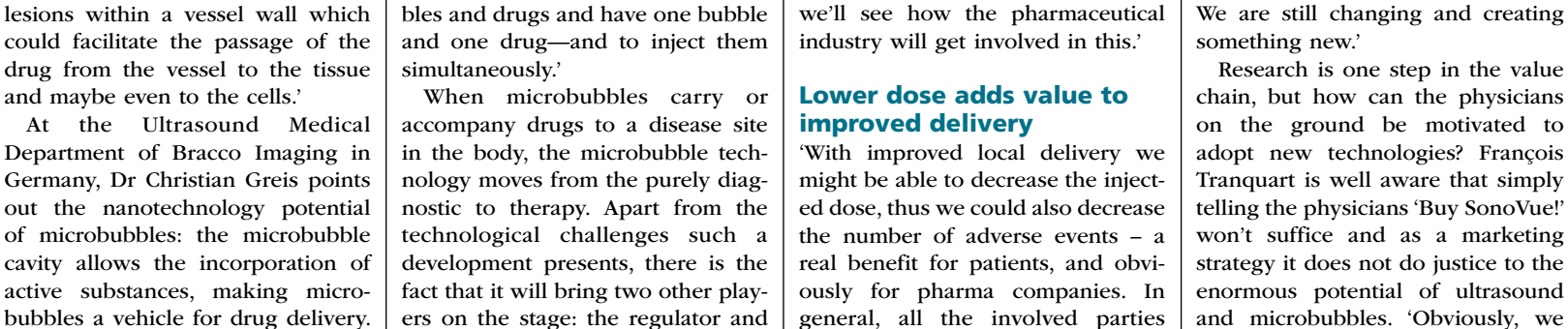
'Controlled trials have shown that there is no difference in quality between contrast-enhanced ultrasound and MRI,' François Tranquart points out, but adds: 'we do know that for some indications, contrast-enhanced ultrasound is probably better than other modalities, for example to detect liver metastasis. However, we must acknowledge the significantly lower costs of ultrasound. It makes no sense to insist on very expensive methods that could be replaced by more cost-effective technologies – such as contrast-enhanced ultrasound.

Contrast-enhanced ultrasound is not only cheaper than MRI, it is also quick, efficient and patient-friendly, he says. 'You can find a nodule in five to ten minutes and get results with contrast-enhanced ultrasound. Thus it is really important, in terms of costs and patient anxiety.

'When you discover a lesion you can inject the microbubbles in the same session get unambiguous results in no time. Imagine you discover a liver lesion in a breast cancer patient. For a CT or an MRI scan she has to wait two or three weeks, whilst with contrast-enhanced ultrasound you can tell her within five minutes: "Don't worry; it's benign" – or, you could also start the treatment three weeks earlier.

'In my opinion it's a pity that contrast-enhanced is underused, because it might be able to solve some of the imaging issues prevalent in many countries. Certainly a new MRI unit and new CT scanner often can be helpful – but not for a knee examination. We should use the right technologies for the right indications. No doubt: MRI cannot be replaced for brain imaging and CT is best for lungs. But for certain indications, contrast-enhanced ultrasound is the method of choice.'

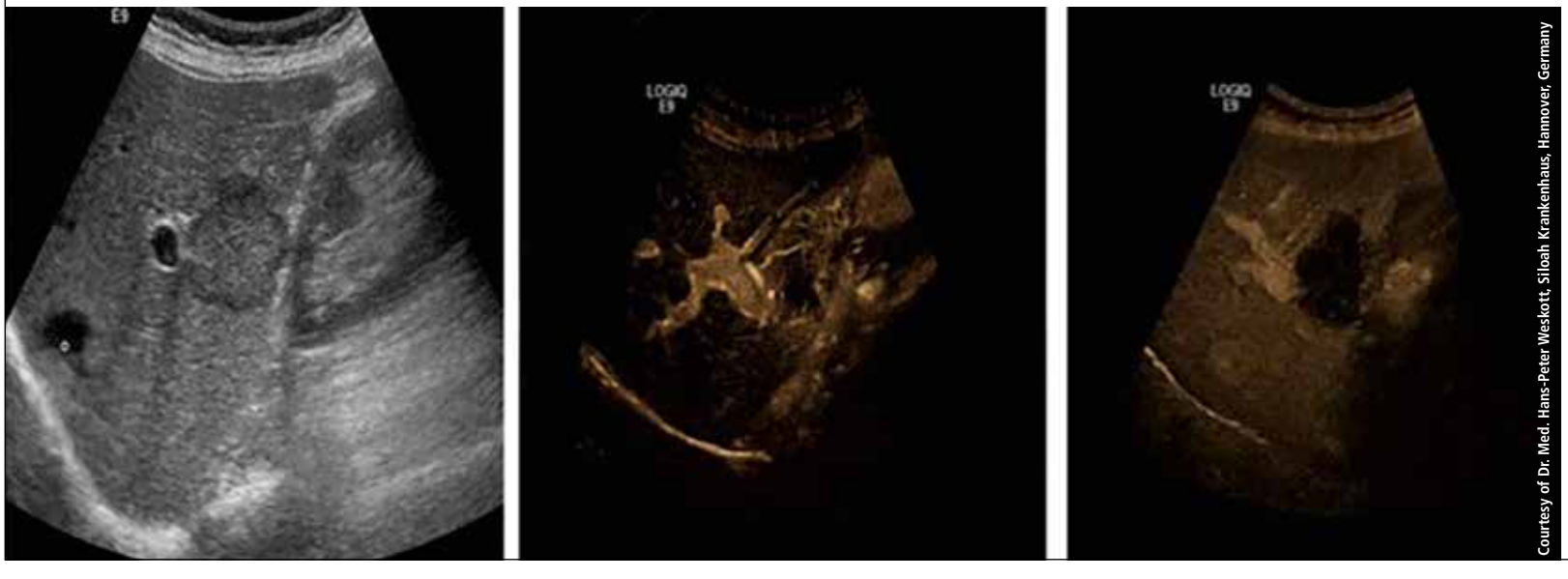
In vitro gene delivery with lipofection (left) and sonoporation (right) demonstrating a clear superiority of ultrasound mediated transfection



Left: Lipid-mediated plasmid internalisation. MAT B III cells were incubated with LF 2000/(DNA/YOYO-1) lipoplexes and observed with a fluorescent microscope at 5 min and 1h.

Right: Ultrasound-mediated plasmid internalisation. MAT B III cells were sonoporated with YOYO-1 labelled DNA and observed with a fluorescent microscope at 5 min and 1h.

Liver metastasis for this 63-year-old patient with normal liver tests and a known history of an ovarian cancer



Left: A liver lesion is found at baseline ultrasound.

Middle: After SonoVue injection, the lesion enhances during the arterial phase with a rim enhancement. The enhancement shows a central ischemic area.

Right: The lesion starts a rapid wash-out in portal phase typical of a liver metastasis.

A revolutionary tool on the horizon for radiologists and clinicians

Intelligent virtual assistants

Report: Cynthia E. Keen

Starting in the mid-1990's, PACS technology revolutionised radiology departments. Now, some 20 years later, intelligent virtual assistant (IVA) technology is expected to do the same. RSNA 2013 attendees at a business analytics scientific session received a tantalising glimpse of a product in development that marries artificial intelligence, natural language processing and speech recognition, all seamlessly interfaced to healthcare IT software.

Consumer versions of intelligent voice command technology developed by Nuance Communications (Burlington, MA) are currently used in smartphones and mobile tablets, for controlling televisions, and in some automobiles to initiate commands. In late 2014, or early 2015, Nuance plans to commercially introduce Florence, a virtual assistant for physicians named after Florence Nightingale, the world's most influential nurse. One of its specialised applications will be for radiologists.

'Virtual assistants will provide an intelligent layer between radiologists and the RIS or PACS they use,' said Jonathan Dreyer, director of mobile solutions marketing for Nuance's health care division. He explained that with the ability to actively listen, have the artificial intelligence to understand the contextual meaning of a request, and rapidly search multiple sources of data and information, virtual assistants would be able to streamline the process of information gathering that radiologists now must perform "manually" without automation using non-intuitive point-and-click software.

Florence is programmed with a conversational user interface to make interactions seem natural and human-like for its clinical users. In addition to "understanding" a verbal request for information, or command, to perform an action, Florence will be programmed to prompt for all necessary information, ask for clarification if needed, and identify/alert radiologists to obvious discrepancies.

IVA software will be designed to be interfaced with electronic health records, computerised physician order entry/clinical decision support software for ordering diagnostic imaging exams, laboratory information systems, and e-prescribing systems. IVAs will be able to access RIS/PACS as well as critical results reporting systems. At some point in their technology development, they may be able to search patient databases for critical information, such as previous cases with similar symptoms, outcomes data for patients with similar symptoms, relevant articles in peer-review journals, and electronic libraries of diagnostic images that may help a radiologist make a difficult diagnosis. IVAs are being designed to search for information within a patient's medical record, navigate complex healthcare applications, identify missing data that is relevant to the verbal request made to it, and streamline end-to-end clinical documentation.

Jonathan Dreyer gave several examples of how the first commercial clinical virtual assistants for radiologists could be used to increase their productivity and performance.

These included:

- Accessing prior reports and specific report content
- providing real-time insight on clinical guidelines
- reviewing a narrative report and determining if there are inconsistencies or information missing
- verbally navigating a PACS work list (i.e. show me all unread chest CT cases)
- streamlining transmission of critical, or unexpected, results to the ordering physician.

He also reported key findings of a survey of United States physicians that was commissioned by Nuance early in 2013. The top three roles that the respondents identified that they would like virtual assistants to do would be to provide accurate, real-time information to support patient care, alert them to missing information in patient records, and authenticate their identity by voice. The top five ways that doctors felt virtual assistants would change healthcare delivery would be by improving access to data and navigation within a patient's electronic medical record, help navigate diagnosis and prescription options, improve communication among multiple healthcare providers, and improve follow-up communications with a patient, especially with respect to a patient discharge from a hospital.

Jonathan Dreyer, director of mobile solutions marketing, Nuance health care division

In summary, 80% of the survey respondents felt that IVAs would drastically change healthcare by 2018 – and that's less than five years away.

LED colour displays for diagnostic use

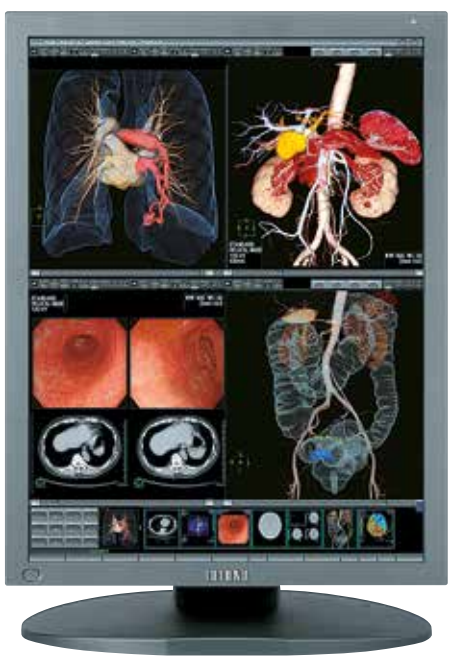
The Japanese Display vendor Totoku has extended its i2 line-up with a two and three megapixel display. 'The CCL258i2 and CCL358i2 are high brightness colour displays with a very high contrast ratio,' the firm explains. 'That's why both can be used for primary diagnosis or critical applications like thorax exams.'

These are the first colour models with the new LED backlight, providing ecological, financial and qualitative benefits, Totoku points out. 'Compared to CCFL monitors, LED displays save up to 20% electricity and have a longer life span by about 30%. This has a positive effect on the budget of the user. Furthermore, the CO2 emission decreases due to reduced energy production.' Specifically, the displays use 15% less power than their predecessor, with almost double the lifetime and disposal is much more environmentally friendly, since LEDs don't contain critical elements such as mercury, Marcel Herrmann, Marketing Manager at Totoku Medical displays, sums up.

In addition to ecological benefits, due to the newly developed power supply of the i2 series, standby power consumption has been reduced by 80%. 'Together with the backlight dimming function hard cash is saved,' Totoku points out.

All new i2 models offer the new display port interface. 'This enables the user to connect not only DVI signals or video cards, but also the latest Display Port cards from various vendors, for example Matrox, ATI and NVIDIA. Another benefit from Display Port is the improved greyscale reproduction,' the company continues. 'Display Port offers, for the first time, true 10-bit greyscales on a colour display and true 11-bit for the greyscale products.

Details: www.totoku.eu



November's successful first-year international gathering

The German Stem Cell Network

More than 400 international scientists headed for the Max Delbrück Centre in Buch, near Berlin for updates on stem cell biology findings and discuss how to develop synergies between basic research, regenerative medicine and pharmacology, as well as strategies to cope better with researchers' needs. The three-day event was the first annual conference of the German Stem Cell Network founded at the beginning of 2013.

Bettina Döbereiner reports

In his opening remarks, Professor Oliver Brüstle, the then Acting President of the German Stem Cell Network (GSCN), outlined the importance of the foundation of this, as he called it, second-generation stem cell network. 'The networks that were initiated ten years ago primarily had the mission to bring scientists together for the first time and thus create a stem cell community,' he explained. Now, however, to justify the establishment of GSCN, the manifold requirements of this grown community must be channelled and managed, he added. The Network is funded by the Federal Ministry of Education and Research (BMBF) with around €300,000 for the initial yearlong phase.

The annual conference programme was pretty much structured by the contents, covered by the particular working parties of the GSCN. These fairly autonomous and self-reliant groups deal with purely scientific topics as well as strategic network interests. Among their main topics was pluripotency and stem cell reprogramming.

Due to restrictions on human embryonic stem cell (hES) research – only the import but not the establishment of hES is allowed in Germany - many laboratories there pin their hope on the iPSCs research and the transdifferentiation technique. However, Prof. Frank Emmrich, member of the executive board of the GSCN, curbed expectations. 'Nowadays nobody can say whether human embryonic stem cells are really dispensable.' Hopefully in the next ten years, contrasting studies of human embryonic cells and iPSCs or transdifferentiated cells will reveal this

Other important topics were somatic stem cells and their development, stem cells in diseases such as cancer stem cells, stem cells in regenerative therapies and stem cells in disease modelling and drug development.

Prof. Brüstle gave a comparison of the strategic groups' topics with those from already existing stem cell networks. 'Our strategic groups are in charge of preparing better funding strategies, career development for our researchers, bundling information about clinical trials and regulatory affairs, outreach activities for teachers and scholars, patient information and stem cell technology development.'

The latter strategic group had the most registrations for stem cell technologies. Following the group's first workshop at the annual conference, Prof. Frank Emmrich, one of two speakers from this group, said: 'The need to obtain knowledge of new methods and of learning from the others seems to be enormous.' Many participants in the predominantly young audience, he said, had pleaded to create an interactive internet platform in which to exchange competencies in stem cell technologies.

Other main technology needs were also discussed in this group – initially the development of a quick (within minutes) and reliable quality assurance tool for in vitro bred cell cultures to be injected into a patient by a medical practitioner for therapeutic purposes; then the need to learn more about the so-called stem cell niche - where stem cells are located in the body - and their micro-environment to enable a future reproduction of the niches and, consequently, of stem cells themselves in a bioreactor; and finally, the request for more cell culture media or nutrient solutions to raise stem cells. 'The development of such cell culture media generally takes years, because so many unknown variables must be checked, but we hope we can find ways to accelerate the process using bio-informatics instruments,' Prof. Emmrich explained.

To hit all those goals the GSCN promotes close cooperation with the stem cell related industry, Prof. Brüstle pointed out. Consequently, the network also includes industry – currently five enterprises. However, the network is backed primarily by more than 250 personal memberships and six institutional memberships.

Apart from industry, the GSCN pursues a close exchange with other national and international stem cell research networks. All-in-all, this was notably accentuated by the four keynote lectures, given by distinguished stem cell researchers from abroad, including Prof. Michele De Luca from Italy, who presented his successful treatment of traumatic destruction of the conjunctival epithelium with cultured human limbal stem cells. Presently the GSCN is pursuing a second funding phase by the BMBF. Then, beyond 2017, the network will be run from membership fees. ■

Frank Emmrich MD is a clinical immunologist, specialist in cell biology, a professor at the Faculty of Medicine at the University of Leipzig, head of the Fraunhofer Institute for Cell Therapy and Immunology and also director of the Translational Centre for Regenerative Medicine (the latter two are Leipzig-based). Along with management tasks, he researches tolerance induction; with his team he recently developed a method intended to avoid the Graft-versus-host disease in patients with allogeneic blood stem cell transplantation. With animal studies completed in 2013, as soon as financial support is assured, the technique will enter a clinical study.

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From left: Daniel Besser MD, GSCN coordinator and treasurer of the executive board, MDC/Berlin; Oliver Brüstle MD (1st GSCN acting president); Tobias Cantz MD, member of the extended board, Medzinische Hochschule Hanover, and Andreas Trumpp MD, from DKFZ Heidelberg, who is now the Network's new President

Neuropathologist and specialist in stem cell research, **Oliver Brüstle MD**, directs the Institute of Reconstructive Neurobiology at the University of Bonn, and is scientific director of Life & Brain, a university-affiliated enterprise. The professor's research is dedicated to the use of pluripotent stem cells for neurogenerative diseases. He was an initiator and the Founding President of the German Stem Cell Network (GSCN) and is now succeeded Prof. Andreas Trumpp MD for the coming year. Prof. Brüstle is also speaker for the Federal State of North Rhine Westphalia Stem Cell Network, founded a decade ago.

GLOSSARY

Induced pluripotent stem cells (iPSCs) – These are former adult cells, for example cells of the blood, liver, brain or pancreas that were re-programmed into their prior pluripotent condition aiming to turn them back into a wide variety of cells. In 2012, Prof. John B Gurdon, leader of the group Re-programming of Gene Expression by Nuclear Transfer at the Wellcome Trust/ Cancer Research UK Gurdon Institute, part of Cambridge University, and Prof. Shinya Yamanaka, director of the Centre for iPS Cell Research and Application at Kyoto University, received the Nobel Prize in Physiology or Medicine for the discovery that mature cells can be reprogrammed to become pluripotent.

Transdifferentiation – The word describes the branch of research in which scientists try to bypass cell re-programming by directly programming one cell-type into another, as presented recently at the World Conference on Regenerative Medicine, in October in Leipzig), for example, for haematopoietic cells: somatic cells (fibroblasts) have been directly converted into primitive and mature haematopoietic cells by Dr Mick Bhatia from the McMaster Stem Cell and Cancer Research Institute (SCC-RI), in Canada.

Literature: Foundational concepts of cell fate conversion to the hematopoietic lineage. Salci KR, McIntyre BA, Bhatia M.: Curr. Opin. Genet. Dev. 2013 Oct; 23 (5): 585-90.

Earlier detection of Down's syndrome

UK researchers develop a new non-invasive test for routine screening

Report: Mark Nicholls

Down's syndrome (also referred to as trisomy 21) is a genetic disorder caused by the presence of all or part of an extra copy of chromosome 21 in a person's DNA.

Current screening for Down's syndrome and other trisomy conditions includes a combined test done between the 11th and 13th weeks of pregnancy. This involves an ultrasound screen and hormonal analysis of the pregnant woman's blood.

Methods such as chorionic villus sampling (CVS), which involves taking cell samples from the placenta, and amniocentesis (sampling amniotic fluid), are also used to detect abnormalities but both are invasive and carry a risk of miscarriage.

Led by Kypros Nicolaides, Professor of Foetal Medicine, researchers from King's College London and King's College Hospital have developed a new test that they report can be given earlier in pregnancy and is more accurate than current checks. Their findings have been published in two papers in the journal Ultrasound in Obstetrics & Gynaecology.

Several studies have shown that non-invasive prenatal diagnosis for trisomy syndromes using foetal cell free (cf) DNA from a pregnant woman's blood is highly sensitive and specific, making it a potentially reliable alternative that can be done earlier than the current screening for the condition. With colleagues, the King's researchers have now demonstrated the feasibility of routine screening for trisomies 21, 18, and 13 by cfDNA testing.

Testing done in 1,005 pregnancies at 10 weeks had a lower false positive rate and higher sensitivity for foetal trisomy than the combined test done at 12 weeks. Both cfDNA and combined testing detected all trisomies, but the estimated false-positive rates were 0.1% and 3.4%, respectively. Professor Nicolaides: 'This study has shown that the main advantage of cfDNA testing, compared with the combined test, is the substantial reduction in false positive rate. 'Another major advantage of cfDNA testing is the reporting of results as very high or very low risk, which makes it easier for parents to decide in favour of, or against, invasive testing.' A second Ultrasound in Obstetrics & Gynaecology study by the group, which included pregnancies undergoing screening at three UK hospitals between March 2006 and May 2012, found that effective first-trimester screening for Down's syndrome could be achieved by cfDNA testing contingent on the results of the combined test done at 11 to 13 weeks. The strategy detected 98% of cases, and invasive testing was needed for confirmation in less than 0.5% of cases.

The research team concluded that screening for trisomy 21 by cfDNA testing contingent on the results of an expanded combined test would retain the advantages of the current method of screening, but with a simultaneous major increase in detection rate and decrease in the rate of invasive testing.

Kypros Nicolaides is Professor of Foetal Medicine at King's College London. His research interests are on foetal medicine with special reference to haematology, and on pre-term diagnosis of chromosome abnormalities. At King's College Hospital, Prof. Nicolaides also heads the Harris Birthright Research Centre for Foetal Medicine, a leading clinical unit and research centre for the assessment and treatment of unborn babies, caring for more than 10,000 patients annually.

Point-of-care-testing in emergency

Advice: test, test and test again

Report: Cynthia E Keen

Over the past decade the use of point-of-care testing (POCT) in European and North American hospitals has steadily increased, stimulated by the objectives of accelerating diagnostic treatment, increasing efficiency and improving patient outcomes. Its use, however, remains controversial. Last month the American Association for Clinical Chemistry (AACC) conducted a three-day online conference on the role of POCT in patient care.

For many hospitalised patients, POCT begins in an emergency department (ED). In one conference session, a pathologist and a supervisor of POC services for two different multi-facility healthcare enterprises discussed how their organisations used POCT and what needed to be done when implementing a POCT programme in an emergency department.

Dr Valerie Ng PhD, Chair of pathology for Alameda Health System, is also director of clinical medicine at Highland General Hospital, one of the seven healthcare facilities in the California county east of San Francisco Bay. She believes that the adversarial attitude about POCT that existed between laboratory and hospital departments has changed dramatically in the last five years. 'There's a role for POCT in emergency departments.'

Most hospital emergency departments are seriously overcrowded. If a POC test is performed appropriately and accurately according to protocol, if trained members of staff are available, if turnaround time for results is faster, and if the POCT achieves a goal that can be financially justified, Dr Ng is in favour. POCT can help make an ED function more efficiently and help improve patient outcomes.

It also can seriously harm or kill a patient, such as when the blood type of a patient needing a transfusion is mixed up with another patient. 'It just doesn't succeed without thorough analysis and preparation. Much work needs to be done to determine if a specific POCT procedure is appropriate. Some will be. Others won't – and don't assume that having an electronic medical record system will make things easier. It actually complicate the process because transactions with every element must be tested and validated,' Dr Ng cautioned.

The two key points to consider are how quickly a result is needed. Will POCT decrease a patient's length of stay? How will it affect patient management? Sonya Evans, POC coordinator of Greenville Health Systems, with six hospitals located across some 280 kilometres in northwest Georgia, agrees. Her organisation established a multidisciplinary POC Committee to assure standardisation, clinical utility of any POC test, cost effectiveness, and clinical staff/regulatory compliance. Written policies and procedures are mandatory and enforced by both organisations, as well as standardised training. Staff members who don't complete training updates are electronically 'locked out' of access to electronic POC testing forms.

The use of a POC D-dimmer test to exclude pulmonary embolism was an example given. ED physicians at Dr Ng's hospital opt for a three-to-six hour rule out rather than a 90-minute one. For this reason, that test is performed by the central lab. Using POCT to identify elevated lactate that indicates sepsis is different.

Speed in treatment is of the essence, not only for patient survival but also, in the USA, to meet federal metrics that determine financial performance incentive payments or penalties.

The ease of performing a POCT must also be evaluated, as well as the precision required to achieve accurate results. Only lab professionals should administer some tests, Ms Evans advises. Equipment or test kits may not function as well in an ED as a lab.

The cost of a test must be evaluated against reimbursement and its value to patient and hospital. A POC creatinine test is more expensive, but has rapid turnaround. For this reason, the additional cost can be justified for a patient who needs a MRI exam. Efficient workflow without scheduling delays in a MRI suite is very important and worth the higher POCT cost.

Other advice: test, test and test again. Review all procedures with the staff members who will be performing the POCT to determine obstacles or hidden pitfalls before the implementation date. Monitor often and consistently. Be prepared to make adjustments immediately – and test them – when points of failure are identified. Use written procedures. Develop checklist forms. Establish metrics for ongoing measurement. Train, train and retrain. Involve the IT staff if electronic records are involved. Make sure that data transfer from point-to-point-to-point are comprehensive and accurate and that everyone who needs to see the data has electronic access to it.

Finally, keep hospital administration informed. Otherwise, budgets may be affected.

From petri dishes to DNA chips

50 years old and still growing

In 1963 Greiner Bio-One came into being with the opening of the Greiner Labortechnik production centre for laboratory products in Nürtingen, Germany. In Austria, in 1974 the firm began to produce petri dishes surfaced for cell cultivation. Two years later, a sales office opened in the Netherlands and a partnership was formed in Spain.

Although the idea of collecting blood via a vacuum originated in the 1940's, it was Greiner Labortechnik in the 1980s that applied the technology to produce the first evacuated blood collection system with a safety plastic cap that could sustain the vacuum for 18 months. The Vacuette range for specimen collection systems had arrived.

In 1988, in Frickenhausen, the company built one of the most modern injection moulding plants, covering 15,000 m². The firm's growth continued in the '80s and '90s with the opening of sales branches in Belgium and France (1988), the UK (1989), Japan (1990) and the USA (1995) along with new production centres in Austria (1992) and Hungary (1996).

During 1997 and '98, the company took the leap from research in high throughput screening into the further development of micro plates. The still-used 96-well plate, plus the 384-well plate and much denser 1536-well plate were developed.

The new millennium saw Greiner Labortechnik investing in a new modern production facility in Monroe, N. Carolina, USA. Then, in 2001, the firm was re-named Greiner Bio-One International AG. In the following years new safety products to protect against needlestick injuries were successfully launched; Vacuette Premium Tubes combined with a unique safety twist cap could now protect medics from potential infection risk.

Specialising in plastic laboratory products, Greiner Bio-One International AG, a member of the Austria-based Greiner Group, today consists has four divisions – Preanalytics, BioScience, Diagnostics and OEM – which generate a €364 million turnover

Over the past decade Greiner Bio-One has also developed new molecular biological analysis methods, which include the DNA-chip that precisely identifies bacteria or viruses in biological and pharmaceutical research. The company also launched the DNA arrays PapilloCheck for cervical cancer, CarnoCheck for food analysis and CytoInspect, a mycoplasma test kit.

The latest innovation is the Vacuette® Tube-Touch safety holder, a passive activation safety product. The safety mechanism automatically activates when the first blood collection tube is inserted in the holder.

'With more than 1,700 employees and seven production locations (Austria, Germany, Hungary, USA, Brazil and Thailand), as well as 24 sites in addition to our international distribution partners, Greiner Bio-One is represented in more than 100 countries worldwide,' the company reports, in the year that it celebrates half a century of manufacturing. 'The unique combination of tradition and innovation should be a firm basis for a successful future together with our worldwide customers.'

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Baaske Medical

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Showcased at this year's Medica, DTR Medical's Rotating Cervical Biopsy Punch is a timely development in light of the increasing need for cervical cancer screenings and human papilloma virus (HPV) testing.
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The rotating jaw provides first time sharpness and a precise cut with a cleaner wound that heals quickly. Alternatives commonly lack a precise cutting jaw, creating poor biopsies with continued wound trauma which leads to longer patient recovery time.
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* NEW for VeriDoc 2C: A second ValiPrint label printer can be optionally connected to the new VeriDoc 2C. This means that 2 printers with 2 different labels (e.g. STEAM and VH202) can be operated with one system. The VeriDoc 2C systems also have a USB port, via which the process data for electronic documentation and tracking purposes or for statistical analysis can be transferred to a USB stick or external hard drive.

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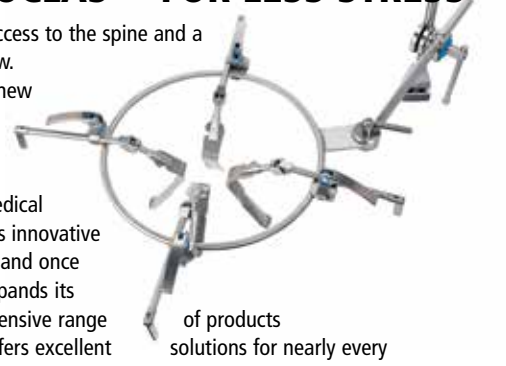

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As a result of the development in medical imaging over the past 20 years, digital medical imaging has replaced the conventional film imaging in the majority of all hospitals. The greatest challenge with regard to design is the parallel use of film-based diagnostics and softcopy reading in one room. The reading room environment plays a significant role in diagnostic accuracy. The new test procedure for acceptance testing will therefore include the measurement of the ambient light and also the control of pixel defects on the screen. The measurement device to be used for the ambient light measurements needs to be a luxmeter which is calibrated and can be recalibrated.
The spotmeter to be used for the display measurements must comply with class B of DIN 5032-7. As the luminance characteristics will be tested and calculated, the use of a software package for assistance in all test stages is recommended in the draft version of DIN 6868-157. Changes are also underway internally. The new IEC 62365-1 is published as a draft version. IEC publications have been issued in the form of recommendations for international use and are accepted accordingly by IEC National Committees. The IEC 625613-1 international standard has been prepared by subcommittee°62B. It includes diagnostic imaging equipment and electrical equipment in medical practice. In order to keep ambient conditions on a constant level, it is always recommended to use an ambient light control system.

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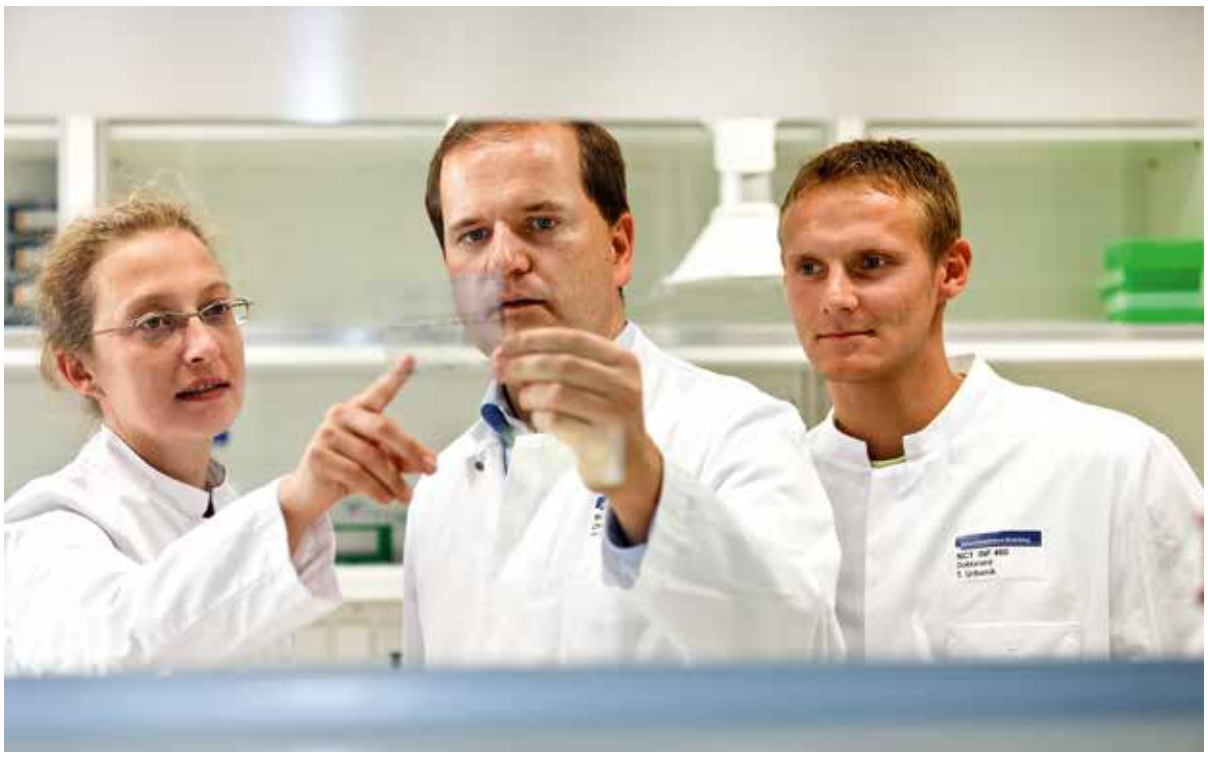
New cancer research targets

More treatments – but many more patients due to early detection

Report: Michael Reiter

'We aim to develop an understanding of which novel research activities could bring benefits for patients,' explained Professor Christof von Kalle, Director of the Department of Translational Oncology, NCT (German National Centre for Tumour Diseases) and the German Cancer Research Centre (DKFZ), speaking on translational activities during the New Cancer Targets gathering in Heidelberg this September. 'We structured our conference according to radiotherapy, targeted drugs mostly derived from genetics, the identification of novel targets which may not yet be targetable, as well as immunotherapy and prevention.'

This year the NCT will report about 11,000 new cancer cases and perform more than 35,000 therapies. DKFZ aims to organise patient-related research and treatment under one roof; in addition to implementing best established clinical processes involving interdisciplinary tumour conferences, the group does its best to make available the most recent study protocols and trials for patients. Roughly, ten percent of patients are enrolled in clinical trials and the aim is for this figure to rise. The conference focused on putting activities in Heidelberg in the context of international research.



Christof von Kalle, Director of translational oncology at NCT and DKFZ

Geneticist and Nobel Prize winner Mario Capecchi from the University of Utah

Translating into clinical routine at a faster pace

'We are witnessing an acceleration of discoveries translating into clinical diagnostic or therapeutic procedures', the professor noted. 'This holds particularly true for discoveries transferring from one tumour entity to another.' An example of this transfer is how BRAF gene mutations originally studied in skin cancer are suddenly found in rare forms of leukaemia, with trials following quickly to verify whether skin cancer drugs have an effect on those leukaemia conditions.

'In this meeting we are trying to 'shake the tree' to understand what the key developments will be in the field.' A lot of the presented work was about navigating the landscape of genetic discoveries and identifying what could be put to clinical use; this included, for example, new interpretations of epigenetic modifications in cancers.

Druging the cancer genome

Using old tricks in new applications was another approach offered: tissue hypoxia and the role of the tumour stroma for the radiation process are returning to the agenda. A research area showing continued growth is druging the cancer genome, with interventional studies that aim to inhibit tumour-specific mutations. Intelligent combination therapies are also experiencing widespread interest. Innovative anti-cancer targets are focusing on more recent developments in brain tumours, in particular glioblastomas, with a focus on molecular issues.

Prof. von Kalle pointed out that there are many clinical immunotherapy trials: 'Various groups are working on new agents, antibodies, and vaccines as well as T-cell preparations to harness tumour immunity.'

Prevention is a field that is still in its introductory phase in Germany. 'However, in a sense it is probably the most important one. Known risk factors, such as smoking, excessive alcohol use, and obesity can be addressed. We need to identify the risk groups and engage in preventive measures.' Cohort studies are conducted to observe the population and demonstrate which individuals in those groups develop cancer. 'Studies already indicate that risk factors for cardiovascular diseases also play a role in the development of cancer or in the rate of tumour growth – as is the case with elevated insulin levels.

'After some time of stagnation, today a lot is happening in oncology, with the rate of discoveries going up drastically over the last three to five years. We expect this to continue for probably another decade. Even if the out-patient scenario may become more important, the rate of discoveries and early diagnosis will still lead to ever larger numbers of patients requiring conventional procedures.'

Utilising cancer fingerprints

Sarcomas primarily afflict children, adolescents and young adults. These extremely aggressive cancers are not as common as carcinomas, which may be the reason why they have not received as much attention, explained Nobel Prize winner Dr Mario Capecchi, Distinguished Professor of Human Genetics and Biology and co-chairman of the Department of Human Genetics at the University of Utah in Salt Lake City. 'What our team is performing on mice appears to be very similar to what happens in a human body. Many genes are, for example, turned on and off when a cancer emerges, and each cancer has a different fingerprint. We use that fingerprint in a mouse to find whether a certain cancer faithfully recapitulates the same cancer in humans.' Each cancer is different and goes through critical events; each type of cancer therefore requires a different approach to therapy, he concluded. 'Progression of the cancer in the mouse can be studied in much greater detail than can be done in humans – where we are typically confronted with the final stages of the cancer – we can find out in mice how the cancers develop and progress, and can use the same mouse model as a platform to develop new therapies.'

Prof. Capecchi's team is currently studying and modelling four sarcomas. 'They differ very much at the molecular level,' he said. 'Understanding those characteristics will help us design the highly different therapies required.' The metastasis stage is the most critical phase.

Sarcomas are simpler than carcinomas, but both types of cancer have rules in common as to what cancer cells do. 'Therefore, what we are learning from modelling sarcomas will also be applicable, in later stages, to carcinomas,' Prof. Capecchi emphasised.

Tumour heterogeneity

A challenge for oncologists

Report: Michael Krassnitzer

'The disease "cancer" is increasingly classified into sub-groups. Today, we are already dealing with a number of orphan diseases,' says Professor Richard Greil MD, head of LIMCR at University Hospital Salzburg, This is due to tumour heterogeneity, a major topic at the annual meeting of the German, Austrian and Swiss Societies for Haematology and Medical Oncology held in Austria this October, chaired by Professor Greil as Congress President.

Generally speaking, tumour heterogeneity means that tumours differ depending on site, surrounding tissue and genetic predisposition of the patient. Thus, breast cancer is different from lung cancer and a brain tumour is different from a bone tumour. Cancer cell genes can have a high mutation rate but only a few of these mutations are so-called driver mutations, which are relevant for the development and evolution of cancer. While in lung cancer 180 of such mutations were found, in breast tumours only 30 driver mutations have been identified to date. 'This explains why tumours evolve at different speeds and why they show different degrees of severity,' Prof. Greil explains.

A patient's age can be another important factor: the older the patient the higher the tumours' genetic diversity from patient to patient. In brain tumours, for example, children show a much lower number of mutations in the cell genome than adults. 'Therefore,' he points out, 'cancer is easier to treat in children than in adults.'

Tumour heterogeneity is even more complex: Genetic variation exists within individual tumours, so-called intra-tumour heterogeneity. 'If you perform a biopsy at different tumour regions you can get significant differences in the gene expression profile,' he underlines. The same holds true for a primary tumour and its metastases, he adds. 'The specific environment of a tumour creates a specific selection pressure and influences the further evolution of a tumour.' Moreover, cancer cell genotypes change over time. 'In a targeted therapy we focus on a certain mutation but it may well happen that after two months the genetic profile of the tumour cells has changed and other driver mutations are dominating the development.

'A single biopsy is not representative of a tumour and its metastases,' he explains, referring to current research. 'We need entirely new study designs and new diagnostic tools to get a picture of the genetic variation of a tumour. This is where we are entering a new era of molecular medicine. We have to gather sufficient information to get a complete picture of the genetic variation and how this variation is controlled.' The Austrian oncologist has a clear idea where the development of new diagnostic tools could start: Every day three percent of the entire mass of a tumour's DNA is released into the patient's blood flow. New screening methods might help to cull relevant information from this process.

Senior consultant and university professor **Dr Richard Greil** has directed the Third Medical Department for Oncology, Haematology, Haemostaseology, Rheumatology and Infectiology and Head of the Laboratory for Immunological and Molecular Cancer Research (LIMCR), University Hospital Salzburg. Austria since 2004. Before this, the Austrian oncologist headed the molecular-cytological lab and haematology out-patient services at the Department of Haematology and Oncology, at Innsbruck Medical University, where he had trained in medicine. A member of many international medical associations, e.g. s the American Association of Cancer Research and American Society of Haematology, he conducts reviews for many international medical journals, such as Lancet Oncology. In Austria, he founded and is current chair of the Oncology Board that advises the Minister of Health on oncology issues and he was commissioned to design a national oncology strategy.