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ECR SPECIAL ISSUE: 7-22

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Forensics identify victims and terrorists

'I am sorry, the electricity will be cut off because we're going to simulate an attack, or emergency exercise, this morning,' explained Dr Wim Develter, when he suddenly delayed his interview with Mélisande Rouger of European Hospital. They were about to discuss computed tomography, and its role not only in advanced healthcare and other more unexpected areas, such as the arts and forensics, but in recent years as a forensic tool in police investigations into terrorism. During ECR 2017, this leading forensic pathologist, from Leuven University Hospitals, will describe the procedures and practices within his work.

Seasoned forensic pathologist Dr Wim Develter has worked on disaster victim identification (DVI) in four major catastrophes, including the terror attacks in Brussels airport in Zaventem, in March 2016.

At the department of Forensic Medicine Department at Leuven University Hospitals, in the Netherlands, he trains forensic pathologists. In its DI and crime scene investigation work, the department organises simulations in which an invasive attack or disaster takes place and the personnel must act accordingly.

In his latest exercise, Develter put mannequins with prostheses in a plane to train staff towards the identification model as well as to test whether Leuven's facilities were big enough and if everyone was sufficiently trained. 'We also tested the psychological support for the families. Shortly after that exercise,



Memorial for the victims of three bomb attacks at Brussels airport and a metro station. Left: Forensic scientists were trained with damaged mannequins and, below, mock cases to identify victims

the Brussels bombings occurred, so we were well prepared,' he added.

The examination of disaster victims and their remains often begins with CT exams, first to rule out dan-

ger in the bodies – hidden explosives or biohazard – and then to organise the identification process (complete bodies, body fragments or body parts). CT also helps by

showing the pathologists whether the victims were wearing jewellery or metallic devices, such as prostheses, at the time of the disaster, information that can help to iden-



Wim Develter MD is a trained clinical pathologist and an expert in corporal damage. As such, he specialises in forensic medicine in the Department of Forensic Medicine at Leuven University Hospitals. He is also Secretary for the Royal Belgian Society of Legal Medicine.

tify them. Once this information is gained, the forensic team can track down where he or she received surgery or where objects were bought.

Develter could not speak of the contents of the on-going investigation regarding the Brussels attacks at the time of our interview, but he said the identification process of a terrorist or victim is similar. 'After an attack you have a lot of extra information that can be useful for your investigation. I am one of the leading forensic pathologists in this enquiry, so I cannot say anything about the contents of the investigation because of the instruction's secrecy,' he said. However, during

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Chemiluminescence Immunoassay Focused Supplier

120 countries exported 7000 units installed globally

Tumor Markers Ferritin AFP CEA Total PSA f-PSA CA 125 CA 15-3 CA 19-9 PAP CA 50 CYFRA 21-1 CA 242 CA 72-4 NSE S-100 SCCA	Thyroid TPA-Snibe Pepsinogen I Pepsinogen II Gastrin-17 H.pylori IgG β ₂ -MG HCG/β-HCG Calcitonin Tg(Thyroglobulin) Proinsulin *proGRP *AFP-L3	Fertility TSH(3rd Generation) FSH LH HCG/β-HCG PRL Estradiol free Estriol Progesterone Testosterone free Testosterone DHEA-S 17-OH Progesterone *AMH *SHBG *Androstenedione	Anemia Vitamin B ₁₂ Ferritin Folate	Immunoglobulin IgM IgA IgE IgG	Hepatic Fibrosis HA PIIIP N-P C IV Laminin Cholyglycine	Glyco Metabolism C-Peptide Insulin ICA IAA(Anti Insulin) Proinsulin GAD 65 IA-2	Bone Metabolism Intact PTH Calcitonin Osteocalcin 25-OH Vitamin D	Inflammation Monitoring hs-CRP PCT(Procalcitonin)	Cardiac CK-MB Troponin I Myoglobin NT-proBNP Aldosterone Angiotensin I Angiotensin II D-Dimer LP-PLA2 hs-cTnI hs-CRP *Direct Renin *H-FABP	Infectious Disease HBsAg Anti-HBs HBeAg Anti-HBe Anti-HBc Anti-HCV Syphilis Chagas HTLV I/II Anti-HAV HAV IgM HIV p24 Ag HIV Ab/Ag combi	Autoimmune TGA(Anti-Tg) TRAb TMA Anti-TPO ICA IAA(Anti Insulin) GAD 65 IA-2 *Anti-CCP *Anti-dsDNA *Anti-Sm *Anti-Ribosomal-P *ANA *ENA *Anti-Scl-70 *Anti-CENP-B	Kidney Function β ₂ -MG Albumin	TORCH Toxo IgG Toxo IgM Rubella IgG Rubella IgM CMV IgG CMV IgM HSV-1/2 IgG HSV-2 IgG HSV-1/2 IgM	EBV EBV EA IgG EBV EA IgA EBV VCA IgG EBV VCA IgM EBV NA IgG EBV NA IgA	Others GH(hGH) IGF-I Cortisol ACTH	Prenatal Screening cAFP free β-HCG PAPP-A HCG/β-HCG free Estriol	Snibe * Available soon
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Forensics identify victims ...

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the ECR, he will share his experience in disaster victim identification in other mass disasters.

As a trained pathologist, Develter started working in forensics in the wake of the Tsunami in Thailand in 2004 and, a decade later, worked on the MH17 Ukraine plane crash. In both events, high-end CT imaging proved very helpful in victim identification but its use depended very much on the circumstances of the event.

Whilst the plane crash victims could be related to a passenger list, things were far more difficult after the Tsunami. 'It was an open disaster, people were in their swimsuits; they were not wearing any clothes, or had cell phones or keys, there was nothing to identify them.'

'DNA was very important then and we were very lucky that China offered free DNA investigations for all victims.'

The aftermath of the tsunami, which caused 227,000 people from all over the world to lose their lives, became the catalyst to improve international Disaster Victim Identification (DVI) protocols.

'We realised that we needed to have an international protocol because we were all working in more or less the same way, but some countries, such as Germany and the UK, had much more experience than others. So the results could be different and that's something that cannot be; if you are performing one (international) investigation everything needs to be on the same level and by the same criteria,' Develter explained.

Whereas in Europe the team often relies on mobile CT services, which can be available within one or one and a half days in the entire continent, protocols can change according to the situation and the forensic team must adapt to local circumstances. 'Everything is digitised now,' he pointed out. 'Back then, twelve years ago in Thailand, everything was written on paper.' In addition, Develter and colleagues dealing with the tsunami victims had to choose between ventilation and lighting to be able to operate their devices, including the X-ray machines.

Things were expedited after Thailand; forensic pathologists established a protocol, which they extend annually. The International Criminal Police Organisation (Interpol) in Lyon, France, is responsible for establishing and revising the protocol every four years. Every year Develter and his DVI pathologist colleagues participate in an Interpol meeting to discuss the approach to global disasters, and exchange experiences and discuss protocols.

His field has also benefited tremendously from popular TV series such as CSI. 'Forensics became popular a few years ago thanks to these series. If you are not well known it's hard to find funding or grants for scientific projects. Though still tough, that (program) has certainly helped our discipline. It's an upward spiral.'

The field is multidisciplinary, among other specialities involving toxicology, microbiology, biochemistry, radiology and pathology and police investigative skills. 'You need all these disciplines to answer just one question: What happened? That's why the other fields are also interested: we're all working to solve a mystery.'

Spanish expert separates fables from facts

Seasonal over-indulgence

In the early months of a New Year many of us are tightening our belts after Christmas gastronomic indulgences. However, the belt may not be as long as it used to be and the gym treadmill may be the only answer, Mélisande Rouger reports



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In Spain, the Christmas holiday period culminates in the arrival of the Three Kings on 6th January, giving everyone one more week to relish festive delicacies, including the delicious calorie bomb Roscón de Reyes (Three Kings Bread, made with sugar, flour, yeast, eggs, milk, orange extract and salt)

In fact, according to the Vithas Xanit Internacional Hospital in Benalmádena, Andalusia, as much as 80% of the Spanish population put on an extra 1 to 5 kilos each year after Christmas.

Typical of Spain? Yes and no
'In Southern Europe every holiday is an excuse to stop taking personal care and break up our healthier routine. Whether it's Christmas or

Easter, people tend to relax and forget about healthy habits,' said Dr Rafael Estrada, dietician at the hospital.

Because many foreigners choose to live in attractive, sunny southern Spain, Estrada tends various nationalities and he acknowledges that cultural differences have an impact on food habits and eating schedules, even though many people in the Western world put on a little weight after Christmas. The traditional Spanish way of life – eating and going to sleep late – may seem at odds with a healthy lifestyle. 'We are crippled by our work timetables, which affect another lifestyle. Your wife, husband or friends work until 8 p.m., so you want to wait for them to have dinner or go out for a drink,'

Estrada pointed out. Many Spaniards live in line with the rest of Europe, he nuanced, mentioning all the different patient profiles he treats at his practice. 'I attend patients with hypertension and diabetes,' he said, 'as well as very thin patients, children, sportsmen and parents who want to develop better food habits once their child is born.'

Food disorders are often a manifestation of deeper emotional issues and, in that case, a dietary treatment comes hand in hand with psychological therapy.

Christmas, for example, is an emotionally packed period and some patients might find it difficult to resist temptations or not compensate with food around that time.

One thing most patients have in common is their addiction to sugar, which is partly fed by the food industry. 'Sugar is the hardest thing to give up. You have to read all the labels carefully when you go grocery shopping, and beware of those who read 'low calorie input' or '0 fat' because they are typically full of sugar. Being selective is time-consuming, but there's truly a need to raise public awareness on this issue.'

Patients are increasingly aware that they must take care of themselves and Estrada has been treating an increasing number of patients ever since he began work at the hospital six years ago.

To recover from celebratory excess, the dietician recommends



Rafael Estrada heads the Dietetics and Nutrition Department at the Obesity Surgery Unit, Vithas Xanit Internacional in Benalmádena Hospital in Malaga, Spain. In addition he is head of Dietetics and Nutrition of the Medical Centre 2002 in Malaga and a dietician at the Vithas Xanit Limonar Centre in the Alicante province of Spain.

reintroducing good sleeping and eating schedules, minimising the intake of sugar while increasing the amount of fruits and vegetables, and practicing physical activity.

Eat fives time a day

The best thing to do to keep in shape is to eat five times a day, and reduce portions as the day goes by. 'Some people decide to skip breakfast or dinner, but this is a terrible mistake because you need to distribute the energy needed by the body without feeling hungry. A trick is to progressively reduce the amount of energy throughout the day. For instance, start with a strong breakfast, and then have a fruit or yoghurt snack, followed by a varied and healthy selection of aliments (meat/vegetables) for lunch. Later, you can have a snack followed by a light dinner because, as the day goes by, you need less energy input,' he explained. The key to success is to be constant and keep up with a routine diet that adequately fits one's needs, he added. 'It's useless to adopt a new daily routine for just a few weeks; it's also useless to reduce the amount of food we consume for a while, because this could endanger our health and badly reflect on our organism.'

Increase in medical school places will cost £100 million from 2018-2020

The UK will train more doctors

Report: Mark Nicholls

The British government has pledged to increase the number of places available at United Kingdom medical schools by 25 per cent by 2018 in a bid to boost the number of home-grown doctors within the National Health Service (NHS).

Presently, a quarter of the 150,000 NHS doctors were trained outside the UK but the move is designed to see the country become 'self-sufficient' in training doctors with medical school places rising from 6,000 to 7,500 a year.

The announcement, made by Health Secretary Jeremy Hunt at the annual Conservative Party conference, came in the aftermath of Britain's decision to leave the European Union, sparking fears that it will become harder to recruit doctors from overseas in future.

It was also made against a backdrop of a long-running dispute between the British government and junior doctors over working conditions, which has seen young doctors taking strike action.

With an estimated nine per cent of UK doctors also due to retire within



Mark Porter, Chair of the British Medical Association

five years, Mr Hunt said: 'We need to prepare the NHS for the future, which means doing something we have never done properly before - training enough doctors. Currently a quarter of our doctors come from overseas. They do a fantastic job and we have been clear that we want EU nationals who are already here to stay post-Brexit.'

'But is it right to import doctors from poorer countries that need them while turning away bright home graduates desperate to study medicine?'

However, as medical degrees take five years to complete, it will be



Patients' Association CEO Katherine Murphy

2024 before the impact of these extra places is felt.

The rise in training places will cost £100m from 2018 to 2020 but, in the long-term, the government hopes to recoup money by charging foreign students more than it does now.

In addition, medical students will be expected to work for the NHS for at least four years - or face penalties that could include them having to repay the cost of their training, which currently stands at £220,000 to the taxpayer over the five-year medical degree course.

However, the British Medical Association - which represents NHS

doctors - said the plan would not prevent the NHS from needing to recruit overseas staff and urged the government to tackle the causes of the workforce crisis, such as extra workload, demoralised staff and lack of funding.

BMA council chair Mark Porter said: 'This announcement falls far short of what is needed. The Government's poor workforce planning has meant that the health service is facing huge and predictable staff shortages.'

'We desperately need more doctors, particularly with the Government plans for further seven-day services, but it will take a decade for extra places at medical school to produce more doctors.'

This initiative will not stop the NHS from needing to recruit overseas staff. International doctors bring great skill and expertise to the NHS. Without them, our health service would not be able to cope.'

The Patients Association in the UK welcomed the plans to drive up the number of British doctors working in the NHS. 'One of the central quandaries in how the NHS can overcome the challenges it faces in 2016 and

Down to earth devices

On sale now: a novel monitoring patch tried and tested in the International Space Station. John Brosky reports

Space missions are famous for driving innovation, from Mylar blankets to microchips. So when French scientists learned one of their compatriots would be aboard the Soyuz MS-03 spacecraft to reach the International Space Station (ISS), they gathered cutting edge technologies for him to carry into orbit.

On 17 November 2016 the European Space Agency (ESA) astronaut Thomas Pesquet was launched into space with NASA astronaut Peggy Whitson and Russian cosmonaut commander Oleg Novitsky for the six-month Proxima Mission.

Inside Pesquet's space gear were equipment and materials for two assignments, the Matiss project designed by the French National Centre for Space Studies (CNES), and the ESA's EveryWear program.

The EveryWear tablet computer serves as the data platform for two devices from BodyCap, a start-up based in Caen, France, which collaborated on a zero-gravity study of wearable technology with the CNES laboratory focusing on microgravity science and the Swiss Institute for Space Medicine and Physiology.

Monitoring sensors

A sensor in the e-TACT patch worn by astronaut Pesquet combines activity tracking, skin temperature monitoring and body position detection; data is sent wirelessly in real time or stored on the device for subsequent analysis. The patch can be worn on any body area for some time, monitoring chronic diseases, sleep disorders and overweight people, for example.

'As there is no gravity in the ISS, the astronaut needs to be attached to the bed to avoid drifting around the capsule, which makes it difficult to sleep. What becomes important



is an ability to quantify movement during his sleep, as this is a very good indicator of sleep quality, a measure of whether he is truly sleeping or is restless,' explained Sébastien Moussay MD, a co-founder of BodyCap.

The other device from BodyCap is the Blood Pulse Wave sensor finger-worn device to detect changes in the blood pulse of the carotid artery when the astronaut presses his finger against his neck. This tonometer is being used as part of a study of modifications to astronaut Pesquet's cardiovascular system during long-term exposure to microgravity.

Without the resistance of gravity,

Finger worn Blood Pulse Wave sensor is a tonometer that checks on modifications to the cardiovascular system

Moussay said, the heart does not need to force blood flow to the brain and it progressively weakens, requiring a period of therapy for recovery once Pesquet returns to earth in May 2017.

The pulse wave sensor is a work-in-progress, Moussay pointed out, but e-TACT is a CE-approved product with down-to-earth medical applications in programs for the obese and diabetic patients where physical activity is a vital measure, as well as for sleep labs. An

example is patient compliance to prescribed physical therapy routines in the period following bariatric surgery.

Connected watches and other activity trackers popular with consumers do not make the grade with clinicians, he said.

'What's very important for doctors and medical staff is a measurement of metabolic change linked to activities such as walking and swimming. They are less interested in measuring hand movements of someone playing a video game, which is the data provided by connected watches,' Moussay explained.

The Matiss project is a test of

smart surfaces to resist bacterial colonisation inside the spacecraft with an eye on the future.

'If we are going to send people to Mars, we don't want them to get sick on the way, nor do we want them scrubbing and cleaning all the time,' said Guillaume Nonglaton, the project manager for the Matiss experiment at the Grenoble-based Leti research institute.

Housekeeping in the space station takes up an inordinate amount of the astronauts' time, which could be better spent performing their scientific mission.

Keen housekeeping is a vital task

Astronaut Pesquet installed four plaques in spots regularly frequented by fellow astronauts, such as the kitchen area. Each plaque holds 20 different samples of hydrophobic materials that will be exposed to the air in order to come in contact with water droplets circulating within it, each possibly carrying bacteria.

The sample surfaces were each designed to repel the droplets so that they remain in the air and can be filtered, rather than being absorbed on a surface where they may take root.

Advanced materials developed for the experiment include a fluorinated thin layer, an organic silica and a biocompatible polymer, all chosen for their hydrophobicity, and ability to be manufactured on an industrial scale.

The materials also have practical benefits back on Earth for germ-free medical device surfaces and even elevator buttons.

Nonglaton: 'One never knows where the next good idea for practical applications will come from; perhaps this time it will come down from space.'

Doctors

beyond is the need for more trained health and social care practitioners, including doctors,' said the association's Chief executive Katherine Murphy. It's reassuring to hear the Secretary of State recognises that, at present, the demand is not being met and take action to solve this.

'The Patients Association has always heralded the hard work and dedication of all staff that work in the NHS, wherever they trained, or whatever their nationality. But we also recognise the importance of giving opportunities to British students wanting to pursue a career in health, and the unique value this adds to our world-famous, great, British institution that is the NHS.'

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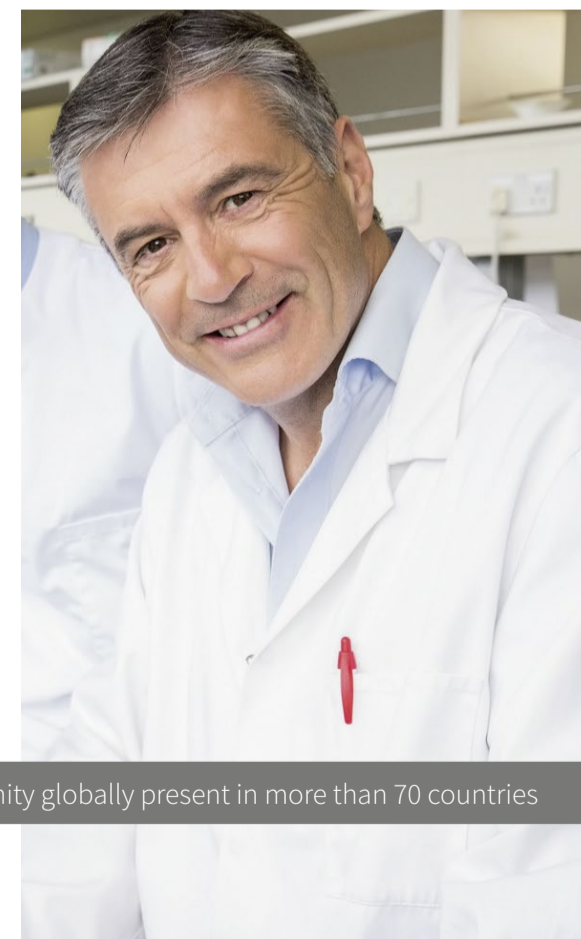
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Dutch healthcare givers and receivers want a higher care level

Divisions need revisions

Report: Madeleine van de Vow

Dutch healthcare is internationally viewed as high level. However, the cost of care continues to rise, despite all the cuts. Additionally, both health consumers and healthcare professionals in the Netherlands experience a lack of focus on patients and cooperation in healthcare. The cause: divisions that exist in the Dutch healthcare system. It is time for a 'Next Level in Healthcare'.

The divisions are the barriers between and within health institutions, healthcare providers, health insurers and the government. To gain insight into these divisions, research agency SIRM, under the initiative of the Association of Innovative Medicines, Pharmaceutical Committee of AmCham and Enterprise organisation VNO-NCW, performed an investigation. The results were presented in December to all parties and politicians involved.

Not really new

'Divisions are not new,' says Jan Peter Heida, partner and consultant of research firm SIRM, which noted three types of divisions/partitions:

- **Financial divisions**, created by the spending of healthcare providers and health insurers, which are determined within different legal frameworks. Healthcare for most patient groups is paid via one or more of these budgets. Siphoning money from, for example, hospital to primary care proves to be difficult.
- **Regulation**. Divisions are organised by type of care and type of insurance. This compartmentalised legislation leads to undesirable effects. For instance, exempt from VAT makes it less attractive for hospitals to hire



The report shows that by tearing down the divisions the quality and accessibility of healthcare in the Netherlands remains high and affordable

specific services (cleaning, accounting).

- **Practical divisions**, which are mainly maintained by the power of habits and cultural barriers between categories of healthcare providers, for instance between general hospitals and university medical centres and between specialties.

Islands in care

'Especially thinking in islands is a problem,' says Merit Boersma, head of communications of the Association of Innovative Medicines. 'The compensation now depends on the practitioner, while funding should actually follow the patient and his treatment.'

The collaboration between, and even within, hospitals should improve because it's a finding that doctors from different medical disciplines are having trouble communicating with each other.

Specialists will have to align their treatments so that patients do not always have to tell the same story and double treatments, examinations etc. can be avoided. It is even more difficult when different par-

ties, such as a general practitioner and a medical specialist have to coordinate the best care for this patient. For instance, it can be much more pleasant for the patient and cheaper for the healthcare system to receive chemotherapy at home and have a consultation via e-health, than having to go to hospital each time. But because the hospital cannot bill this to the healthcare provider, this is not happening, or at least too few.'

Also in prescribing medication there is a lot to win.

Boersma: 'Health insurers reimburse expensive drugs or treatments only if they are prescribed by a university hospital, but not when prescribed by a regional hospital or doctor,' Boersma explains.

'A good example: the drugs for schizophrenia,' Heida adds. 'In mental healthcare pills are prescribed. When patients forget to take them they may end up institutionalised. There is also the "depot medication", wherein the drug is delivered subcutaneously, so that forgetting is impossible and ending up in a hospital will not be necessary. However, only the pills are reimbursed. They

seem initially cheaper, but depot medication is eventually definitely more cost effective.'

'Lunatics in care'

Within healthcare there are already great examples of breaking down barriers: such as the birth centres, the ParinksonNet and chance@home. All these local initiatives aim to link the care islands to one another and to focus on the patient. National rollout of these initiatives proves difficult because they are not reimbursed. 'These "lunatics in care", we call entrepreneurs simply must have the opportunity to care future-oriented' said Hans de Boer, chairman VNO-NCW in presenting the report.

What needs to be done?

There are many causes and reasons why the barriers and islands are held in position,' Heida points out. 'Breaking the practical barriers, which often have to do with the culture of care, is a crucial first step towards being effectively patient-oriented. A shift in care and re-organisation of this "living on an island" culture is needed – from current supply-driven care to targeted group care. We will also need financial incentives to change, as well as space for entrepreneurship.'

Boersma adds: 'The way our healthcare is set up is typically Dutch: GPs act as gatekeepers for referrals and treatments in hospitals. And the healthcare insurance companies monitor the quality and purchase of healthcare.' He also agrees that pharmaceutical companies play a role in Next Level healthcare.

'In total, the central government spends about €70 billion a year on healthcare. Of this, €5 billion goes on medicines from which five percent is destined for the more expensive drugs. We are constantly look for better ways to deliver the best medication to the patient, while keeping healthcare sustainable affordable.'

'For example, we are working on a money-back system for the hospital in case the patient does not have a benefit of the prescribed medicine. And we work with hospitals and others to gather data so that we can know when a drug for a patient is effective.'



Merit Boersma is head of communications for the Association of Innovative Medicines

The future

According to the report, there is no need to overhaul the current system immediately. Within the existing system a lot already can and needs to be achieved. Not least because the study shows that patients suffer more from the lack of cooperation over healthcare thinking.

By tearing down the divisions and not dwelling on islands, the quality and accessibility of healthcare in the Netherlands remains high and, above all affordable, with the potential to achieve a saving of over €1.5 billion over the next four years. Here lies a task for the government; collaborations, and shifts of budgets should be enabled from politics within the current system, possibly with an adjustment of legislations.

Therefore the report and recommendations are also extended to the next government with the call to trigger the removal of barriers, so that Next Level Healthcare can be for real.

About the SIRM research:

- The overview of advances in care and possible solutions (tilting agenda) set by SIRM based on fifteen interviews and own project experiences. The three species found all three divisions are on five levels.
- Intermediate results of this study were discussed with a number of healthcare administrators, officials of Health and the Ministry of Finance and a group of health economists.
- Results from more than 60 local initiatives and studies translated for the Netherlands SIRM lead to the conclusion about potential savings.

UK faces severe financial restraints

Healthcare needs a radical rethink

Report: Mark Nicholls

Leading clinicians, scientists, academics and crossbench peers have urged a radical rethink of the approach to health in the United Kingdom.

Against a backdrop of Brexit and the 'troubled' state of the NHS, the powerful group has taken the bold step of setting out a manifesto for a 'health creating society' across Britain with a fundamental shift of provision of care from hospitals to the community at its heart.

Writing in *The Lancet*, they presented their vision of how the UK can promote and improve health and at the same time strengthen the country's economy.

Lord Nigel Crisp, crossbench peer and former NHS Chief Executive said: 'The NHS faces severe financial constraints, and leaving the EU is likely to exacerbate many problems,

including staffing.

'With a new government comes the opportunity for a clear, bold new strategy. We need a new approach to health that recognises on the one hand the enormous contribution health and biomedical sciences make to the economy and, on the other, that every part of society has a role to play in improving health.'

In the report, entitled 'Manifesto for a healthy and health-creating society', the authors propose action in four closely linked aims:

- 1: The UK should strengthen its role as a global centre for health and the biomedical and life sciences; that should be at the centre of the UK's industrial strategy and vision for the future as an outward facing country and help to shape the future health, prosperity, and security of the UK and the world.



Professor Robert Lechler is Vice-Principal (Health) and Executive Director of King's Health Partners Academic Health Sciences Centre and President of the Academy of Medical Sciences. Formerly Dean of King's College School of Medicine, his research interests revolve around transplantation tolerance.

- 2: The transformation of the health and care system from a hospital-centred and illness-based system

to a person-centred and health-based system needs to be accelerated and funded. This will require a massive increase in services in homes and communities and new ways to empower front-line staff, enabled by technology, to manage the complex needs of patients across different services and organisations.

- 3: The UK needs to develop and implement a plan for building a health-creating society, supported by all sectors of the economy and the wider population, in a way that addresses health inequalities. Current plans for health promotion and disease prevention are too small scale and fragmented and need to be replaced by a larger scale, society-wide effort.
- 4: Health, care, and scientific institutions should help develop and restore a healthy society in the

UK, but a health-creating society can only be built in a society that itself is healthy.

However, the authors warn the success of the aims will crucially depend on having an effective and sustainable health system which can provide a platform for the development of science, expertise and products.

David Stuckler, Professor of Political Economy and Sociology at Oxford University, said: 'For too long, the NHS has been fire fighting. The system is struggling to maintain old services whilst creating new ones – and as a result is facing double running costs and failing to invest in the future. We need to fund modern services and take some of the strain off the NHS by creating a society where everyone has a role in promoting health.'



Jan Peter Heida is partner and consultant of research firm SIRM

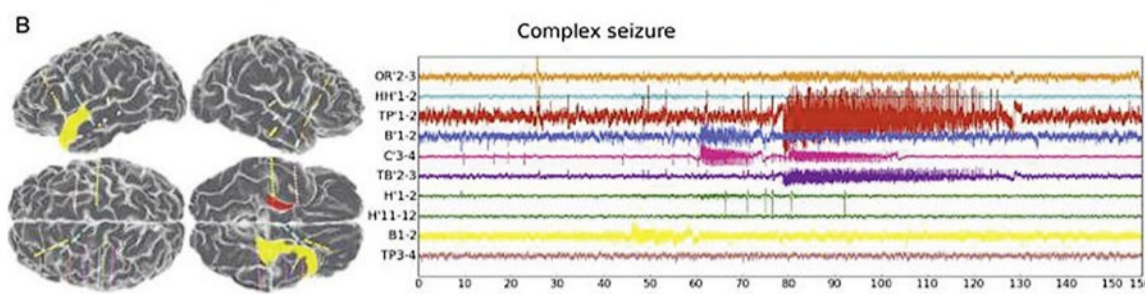
Cutting into a virtual brain areas to assess curative results

Computer model simulates epileptic events

- In December, reporting was offered to Hans de Boer of VNO-NCW.
- Kantar TNS did an additional study (care monitor), in addition to the SIRM study.
- 1,430 people (18+), representative of the community, were invited to participate in this study. 943 Dutch finally filled in the questionnaire.
- 351 healthcare professionals (148 doctors, 58 pharmacists and 145 medical specialists) completed the questionnaire
- For this study the CAWI (Computer Assisted Web Interviewing) method was used.
- The average questionnaire completion time was 12 minutes.
- The questionnaire for both groups was largely similar. A single question was asked only to healthcare professionals.
- The fieldwork ran from 21 February 2016.

Some results

- Compared to the past, 70% of healthcare consumers believe that care has become less patient-centred. Among caregivers that percentage was 44%.
- 45% of consumers see care co-operation worse than before (56% think it better) against 20% of caregivers (80% consider it better now).
- Both healthcare professionals and healthcare consumers identify the fact that the problem is that healthcare professionals are thinking about too many islands.
- More than three quarters of care consumers find it very important, or essential, that something is done to improve collaboration between healthcare providers and healthcare professionals.



Approximately one percent of the world population are epileptic; in France alone, an estimated 600,000 people regularly experience seizures. During an epileptic event cortical neurons suddenly discharge, forcing their rhythm onto other nerve cells. This unusual and always temporary activity differs from person to person: it may manifest itself in a wide range of symptoms, from slight jerking of some muscle groups to serious convulsions and impediments of speech, memory, movement and behaviour. Brigitte Dinkloh reports

In the past, research instruments that could gather knowledge on epilepsy were limited because, in about 50 percent of those affected, neither MRI nor electroencephalography (EEG) show any visible brain anomalies. However, now researchers at the Centre National de la Recherche Scientifique (CNRS), the national institute of health and medical research (Inserm), Aix-Marseille University and the General Hospital Marseille (AP-HM), have succeeded in creating a virtual brain that not only allows modelling the originating sites and trajectory of abnormal brain activity but which can also optimise the planning of surgical interventions.

In 70 percent of epileptic patients the seizures can be managed by medication. 'When medication is not sufficient, however, surgery has to be considered,' says Dr Fabrice Bartolomei, Medical Director of the

Simulation of a patient's epileptic seizures: Seizures started in the right hippocampus (channel B1-2) before spreading to the contralateral hippocampus (channel B 1izu and further spreading in the left temporal lobe (d'après Jirsa et al, 2016)

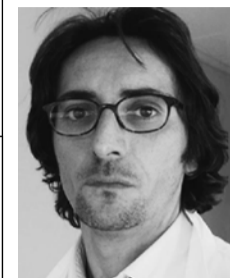
Department of Neurophysiology at Hôpital de la Timone in Marseille, France. 'In a first step the epileptogenic area is identified and, in a second step, it is removed or neutralised.'

An MRI head scan is performed to localise the abnormal brain activity. MRI offers both an anatomy snapshot and – helped by the 3-D modelling technique tractography – the reconstruction of the course of larger neural tracts. A second source of information is EEG. 'Brain activity is recorded by electrodes which, under general anaesthetic, were implanted into the brain by the neurosurgeon,' Bartolomei explains. 'The electrodes are placed in areas the surgeon considers important to understand the origin of an epileptic event and its propagation in the brain.'

Innovative and less invasive techniques are currently being tested, such as magneto-encephalography (MEG), which discovers and maps changes in the magnetic fields on the surface of the skull. An entirely new approach is the 'virtual brain', which '...allows us to personalise a mathematical model for each individual patient,' explains Dr Viktor Jirsa, Director of Neuroscience Systems at CNRS, 'and provides a visualisation that enables individual simulations.'

By visualising brain activity and detecting the origins of an epileptic event and its spread in the brain, the virtual brain technology offers a more precise diagnosis. Surgeons can mark the surgery regions of interest and plan and even test the most effective and least invasive surgical cuts. Thus different scenarios and their effects on the brain can be simulated. Bartolomei explains: 'In a first step the MRI and EEG data are transferred to the model. In a second step, electrical impulses are applied to nodes in the model, particularly in the areas that are most likely epileptogenic. Thus epileptic events can be triggered and visualised in the virtual brain and the source, as well as spread of abnormal activity, can be reconstructed.'

In each patient the interaction of nodes in the brain is different. The virtual model allows prediction of the effects of a given surgical intervention at a given node. The surgeon can remove certain areas of the virtual brain and see whether the epileptic events continue to develop, or whether cutting the connections, so to speak, has stopped the event. This technology increases plan-ability and efficacy of epilepsy



Neurologist Fabrice Bartolomei, specialist in epilepsy, is a professor at the Aix-Marseille University (<http://edu.univ-amu.fr/en> or <http://edu.univ-amu.fr/en>) in France, leading the neurophysiology service clinic. He is also medical director of the Centre Saint-Paul at the Henri Gastaut Hospital (<http://www.hopital-gastaut.com>), one of Europe's oldest hospitals to manage epilepsy, after a few pioneers established epileptology following WWII. Today the hospital treats 3,000 adults and children annually. Bartolomei has published numerous epilepsy studies, particularly on the concept of Epileptogenic Networks and on the relationship between stress, emotions and epilepsy. He has largely contributed to the promotion of EEG/SEEG analysis in focal epilepsies and is the co-inventor of the Epileptogenicity Index, a method to assess epileptogenicity of brain regions.

surgery. The model, however, cannot predict any surgical side effects.

In Marseille, the virtual brain is almost already used to plan interventions. An evaluation of the patients who underwent surgery remains to be done. There is a long way to go for researchers: they need to assess whether the virtual brain indeed provides an accurate picture of the epileptic event.

Bartolomei estimates another 18 to 24 months before the model can be used in a clinical setting. Since, in epilepsy, electrical biomarkers are very specific, transfer of the model to other neurodegenerative diseases will not be easy



Professor David Stuckler is Research Director and Professor of Political Economy and Sociology at the University of Oxford. His research integrates political economy and public health and he currently focuses on macro-social and economic determinants of health, political economy of global health and development, and comparative social welfare.

Dr Richard Horton, Editor-in-chief of The Lancet, said: It's time to write a new contract between the UK's NHS and society. The relationship between Government and the medical profession is broken. It's there-

fore urgent to set out a new, positive vision for health and the health service - a modern NHS that delivers the best care for patients wherever they live, supports world-class scientific research, is supported by all sectors of society working to create a healthier nation.'

Professor Sir Robert Lechler, President of the Academy of Medical Sciences, said the significant health challenges facing society as a result of an ageing and growing population, rising obesity levels and environmental and economic change cannot be ignored.

'Finding ways to keep the population healthy matters - a healthy society is also a wealthy and happy one.'

Other authors included Professor Dame Sue Bailey, Chair of the Academy of Medical Royal Colleges; Professor Maureen Baker, Chair of the Royal College of General Practitioners; Martin McKee, Professor of European Public Health, London School of Hygiene and Tropical Medicine; Heather Henry, co-Chair of the New NHS Alliance,



Lord Nigel Crisp is an independent crossbench member of the House of Lords, where he co-chairs the All Party Parliamentary Group on Global Health. He works and writes extensively on global health. A former chief executive of the National Health Service (NHS) and Permanent Secretary of the United Kingdom's Department of Health, he is a Senior Fellow at the Institute for Healthcare Improvement and an Honorary Professor at the London School of Hygiene and Tropical Medicine.

a grassroots organisation of 10,000 individuals and organisations working to improve community health; and Professor Cathy Warwick, Chief Executive of the Royal College of Midwives.

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Smart phone technologies

Fujifilm reinvents high-end endoscopes

Two technologies from consumer electronics are at the core of a next-generation endoscope that throws a new light on exams in gastroenterology, John Brosky reports

Light emitting diodes (LEDs) and complementary metal oxide semiconductor (CMOS) cameras can be found on a billion smart phones internationally. Fujifilm Medical Systems is the first to introduce them on a flexible endoscope, the Eluxeo 700 Series.

LED is a new light in the closed, dark world where gastroenterologists work. The industry-standard for all other endoscopes is a xenon light source.

The firm's innovation in applying everyday LEDs is to use four independently controlled light sources, each responding to a specific wavelength across the spectrum from blue-violet at 400 nanometres up to red at 650 nanometres.

The ability to alter combinations of spectral wavelengths at the source splits radically from a decade that has seen the widespread use of light filtering to enhance contrast levels and aid clinicians in distinguishing neoplastic lesions from healthy mucosal tissue.

'This is a next generation endo-

scope, the first with specific spectral settings to target mucosal layers, and also the first to use CMOS technology,' explained Jacques Bergman MD, a specialist in gastroenterology and endoscopic intervention at the Academic Medical Centre in Amsterdam, the Netherlands.

'LED excitation is new, instead of xenon light in a fibre running down the endoscope, and four light sources presents enormous potential for investigating ways of highlighting disease.'

Endless possibilities

Bergman believes there is no end to the possibilities for this system. 'These are very promising tools for the assessment of GI diseases,' added Emmanuel Coron MD, from the University Hospital Nantes, France, 'and we should validate the clinical impact of this technical achievement.'

In February 2016, a paper published in *Clinical Endoscopy* directly compared filtering a single xenon light source against combinations of

the technologies used by Fujifilm; it demonstrated that filtering light limited the ability to distinguish lesions distant from the immediate view of the endoscope camera, but that by adding a greater intensity of white light, while boosting hues in the red region of the spectrum, microstructures as well as microvasculature were highlighted.

The short wavelength of blue light LED illumination corresponds with the light absorption of haemoglobin at 410 nanometres, which is why microvasculature shows up more brilliantly.

The variable LED combinations can also increase contrast in the 650-nanometre wavelength, which improves detection of inflammation or the delineation of tumour margins.

The Eluxeo offers push-button switching between three pre-set modes for white light, blue light illumination (BLI) and linked colour imaging (LCI), each holding advantages for detecting, characterising and delineating the margins of dis-



Four independently controlled light sources each respond to a specific wavelength across the blue-violet to red spectrum

eased tissue.

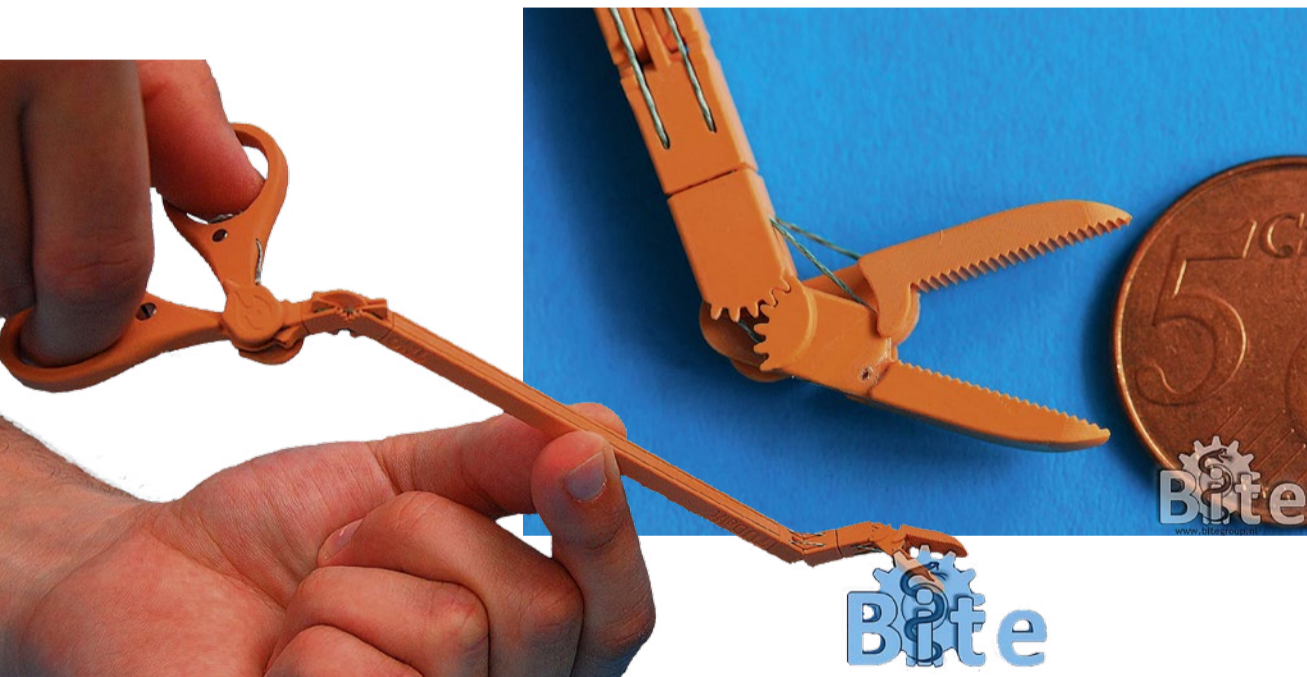
'The BLI created by four LEDs provides a high contrast in white light and I believe the contrast enrichment with BLI is the future,' said Helmut Neuman MD, University of Mainz, Germany. 'But also, by using this CLI imaging mode, white becomes even more white, while red gets more red, and this becomes a very interesting technology for the early detection of lesions and delineation before performing an endo-

scopic therapy.'

With a useful life estimated at almost 10,000 hours, LEDs should also prove to be more cost-effective than xenon lamps that need to be changed after 500 hours, according to Ronald Grieger, head of the endoscopy marketing group for Fujifilm Europe.

The 3-D printing revolution

Re-named 'additive manufacturing' and making products increasingly functional and creative.



Report John Brosky

Inexpensive and readily available, 3-D printers accelerate innovation in the design of medical devices from university laboratories to the factory floor.

At the Delft Technical University they call themselves the Bio-Inspired Technology Group, or BITE. And their claim to fame is in having created DragonFlex, the world's first steerable surgical instrument made entirely by 3-D printing.

While the prototype is more likely to earn doctoral degrees for the inventors than to win a CE certification for use by surgeons, it demonstrates the emerging robustness for 3-D printing technology.

'It's cheap, it's accessible, and 3-D printing helps students to rapidly try out their product ideas,' said Robert Webster, a visiting speaker at TU Delft from Vanderbilt University School of Engineering.

'As the prices come down dramatically and performance goes up, it's reasonable to think that in a few years, the idea of a hospital having a 3-D printer in the basement to create on demand patient-specific implants or customised instruments for surgery, is absolutely feasible,' he said. 'The hospital could take any scan, print it and create a 3-D model.'

According to Amir Zadpoor, Director of the Additive Manufacturing Lab at TU-Delft,

when rapid prototyping using 3-D printers first became feasible, academic projects made up 80 percent of the activity.

Device designers in industry quickly caught up, calling it 'additive manufacturing' instead of 3-D printing. While this year more than \$3 billion will be spent as companies find new applications to convert traditional manufacturing processes, this investment is expected to reach \$20 billion annually in just a few more years.

Zadpoor notes that medical devices today account for 40 percent of that spending '... because there is such a great added value to these products that justify the increased cost associated with the technology'.

Making money? 3-D printing prices will drop dramatically; then hospitals will have 3-D printers to customise implants or surgical instruments

The pioneer in additive manufacturing applied to orthopaedic devices is Warsaw, Ind.-based Zimmer-Biomet Inc., which began developing products 15 years ago.

Using what is called a build plate, industrial 3-D printing involves building up micro layers of titanium powder that are burned with a laser to solidify the powder into a metal with nano-precision to match the design model.

By the end of 2015 manufacturers had installed around 300 machines for 3-D printing of implantable prostheses.

Whereas in 2010 there were just four 3-D-printed implantable devices approved by the United States Food & Drug Administration, by 2014 twenty-five products had been FDA approved.

According to Kevin Lobo, CEO at orthopaedics leader Stryker Corporation, additive manufacturing is 'having an impact on our knee business as well as spine, and we have a huge line up of other divisions with ideas and prototypes to get into 3-D printer titanium product'.

In 2016 Stryker began construction of its second 3-D printing facility in Cork, Ireland.

Orthopaedics market specialist Ali Madani, from Avicenne Medical in Paris, said that titanium spinal cages made by additive manufacturing processes constitute the most dynamic orthopaedic segment and that these products are steadily

eroding the market share for polymer-based PEEK cages.

In Europe, Madani pointed out that Italy is home to the most advanced companies in additive manufacturing where challengers like Lima Corporate, based in San Daniele del Friuli, and Milan-based Adler Ortho have invested massively in the technology and each year sell thousands of 3-D printed hip cups, shoulder implants, knee tibial plates, or mini-hip stems.

Robin Stamp, the associate manager for Advanced Technology at Stryker Orthopaedics explained that for over 20 years, Stryker has milled and machined metal implants using complicated, multi-step manufacturing processes based on coating materials with rigid requirements that limit design options.

'What 3-D printing does is give design freedom, an ability to try exotic designs, build channels into the surface, create roughness, give a product any feature needed for essentially the same cost as building a standard model,' he said. 'Where we are really seeing a difference is in the speed of design iterations.'

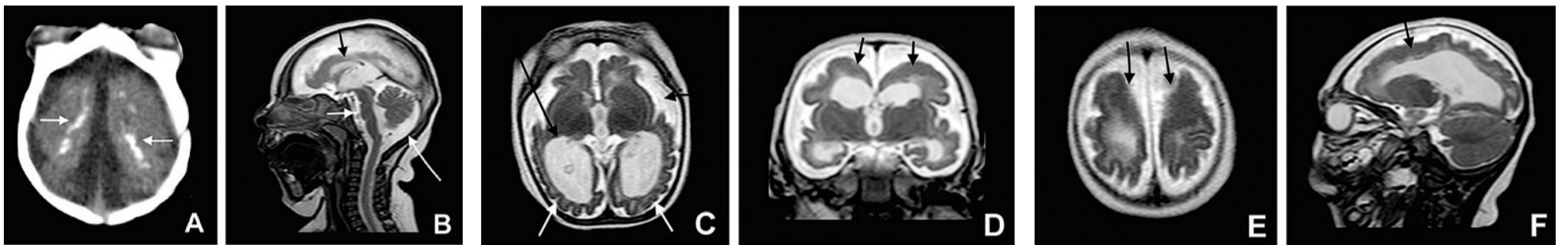
Instead of a product development cycle of 18 to 24 months with a high cost for making changes, he said that today, using additive manufacturing, his group can produce a design and within one week, give the part to a panel of surgeons and rapidly iterate, based on the panel's suggestions to further develop the design.

'This is phenomenally powerful,' he said. 'We are capable of doing so many more iterations, putting much more functionality and creativity into products.'

ECR 2017

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Zika birth defects decrease, but...

ECR 2017 Guest Lecturer Maria de Fatima Vasco Aragao, a radiologist from Pernambuco state, Brazil, has been tracking the Zika virus ever since it broke out in her country in 2015. She will highlight how CT and MRI can help reach diagnosis, especially in the absence of microcephaly. In an exclusive interview with European Hospital correspondent Mélisande Rouger, the radiologist warned there might be more to come regarding the spectrum of Zika syndrome, with possible outcomes such as epilepsy and cognitive impairment.

'We do not follow patients routinely in order to prevent sedation of infants and ionising radiation. Control studies are only indicated after identification of clinical signs of a complication, for instance hydrocephalus and seizures. 'Microcephaly and brain malformations can be diagnosed with ultrasound during pregnancy.' 'When a baby is born with microcephaly in an epidemic area, the paediatrician and neuropaediatrician usually suspect congenital Zika syndrome, whether or not the mother recalls a rash during pregnancy. But we are beginning to see cases in which neuropaediatricians don't suspect congenital Zika syndrome, because the babies don't have microcephaly, but have normal-size heads.' They undergo MRI examination due to unspecific neurological signs, e.g. delayed neuropsychomotor development and motor deficits. Here, radiologists must be alert, as the indication is not Zika virus or microcephaly, and microcalcifications may be subtle, so could be missed. 'Not only the presence of calcification, but also its location at the cortical subcortical white matter junction needs to be identified,

as it is highly suggestive of congenital Zika syndrome.

'Another suggestive finding is malformation of cortical development predominant in the frontal lobes. In addition, these children are around one year and, therefore, specific IgM test for Zika virus can be negative, even if the child has the disease. Therefore, the radiologist's responsibility is even more important in case of congenital Zika syndrome without microcephaly, to suggest the diagnosis to the paediatrician and neuropaediatrician. In these cases, radiology is the only tool we have to make the diagnosis. So radiologists must be alert.'

'Imaging is important, especially in less severe cases, for early detection of congenital Zika syndrome, allowing rehabilitation to start quickly, to help improve their development. If microcephaly is absent and clinical signs appear when infants are several months old, the most important way to diagnose the syndrome is through imaging studies, so radiologists need to detect microcalcifications at the cortical subcortical white matter junction, which can be difficult on MRI, and malformations of cortical development, predominant in the frontal lobes.



Radiologist Maria de Fátima Viana Vasco Aragão is president of Pernambuco Radiology Society, professor of radiology at the Maurício de Nassau University and Scientific Director of the Multimagem Diagnostic Centre in Recife.

development, predominant in the frontal lobes.

'Imaging is also important in identifying complications of the disease, such as hydrocephalus, in which the indication for surgery for ventricular derivation is important, to prevent neurological deterioration.'

How many cases are there?

'Since its peak in October/November 2015, new cases of congenital Zika

Microcephaly, cortical malformation, and brain calcification; Axial CT image (A) shows many small dystrophic calcifications in the junction between cortical and subcortical white matter (white arrows) and noticeable reduction of the brain parenchyma thickness. Sagittal T2 weighted image (B) shows hypogenesis of the corpus callosum (black arrow), enlarged cisterna magna (long white arrow), and pons hypoplasia (white arrow). Axial T2 weighted image (C) shows simplified gyral pattern (white arrows), ventriculomegaly (long black arrow) widely open Sylvius fissure as well as enlargement of subarachnoid space (black arrow). Coronal T2 weighted image (D) shows pachygyria in frontal lobes (black arrows). Note the bilateral cortical thickness in the pachygyric frontal lobe (black arrows), shown on axial and sagittal T2 weighted images (E and F).

syndrome decreased throughout 2016. Two possible explanations: the population is gradually becoming immune to the virus in north-east Brazil and prevention has become more intense, with people knowing how to protect against the Aedes aegypti, the mosquito responsible for Zika infections.. 'The WHO revealed that, as of 14 December 2016, 75 countries and territories, especially in Latin America, reported evidence of mosquito-borne Zika virus transmission. Up to then 29 countries, particularly in Latin America, had reported microcephaly and other central nervous system malformations; four were without endemic transmission. After Brazil, Colombia (67) and the USA (37) had most cases.'

Observational studies to understand the spectrum of this syndrome ongoing. 'The fact that some children do not present with microcephaly but image alterations raises questions of great importance for public health. Perhaps we've seen the tip of the iceberg with the most severe brain damage cases associated with microcephaly.' Researchers want to know the real size of what is submerged, where minor changes without microcephaly could cause future problems, e.g. epilepsy and cognitive impairment..

'Other groups are trying to evaluate prospectively the risk of developing

microcephaly and other abnormalities after Zika infection during pregnancy. Besides congenital microcephaly, neurologic complications have been found in adults.' According to the WHO, up to 14 December there was an increase in Guillain-Barre cases and/or laboratory confirmation of Zika virus infection among Guillain-Barre cases in 20 countries. Myelitis and encephalitis have also been identified. 'As radiologists, we try to help the scientific community to understand the pathophysiological process of the disease.'

Is there hope of a treatment?

'There is neither specific treatment nor a vaccine. Although vaccination can be developed, a treatment for the lesions caused by the virus is extremely unlikely. This does not mean there is nothing to do. Once the disease is recognised, rehabilitation must begin immediately, especially in less severe cases, to provide the chance of better neuro-psychomotor development for the children and support for their families.

'Treatment and support must also be directed towards other disease manifestations, - seizure, ophthalmologic and auditory deficits, arthrogryposis and possible complications, e.g. hydrocephaly.'

Demands for high quality education

ECR focuses on youth

'Youth' is the central theme of this year's ECR. More than 25,000 delegates from over 100 countries are expected for the 29th conference at the Vienna's Austria Centre to take part in the annual meeting that promotes science and innovation..

The Youth focus is reflected throughout the 2017 program, to which end the planners considered the demands of a young generation of radiologists for high-quality education, delivered in an efficient and customer-friendly way. The more interactive session will attract junior radiologists.

Professor Paul M Parizel is the first person to occupy the new role of a combined ESR and ECR presidency. The participants expect a varied program. There will be three state-of-the-art symposia, 10 professional challenges sessions, 19 special focus sessions, more

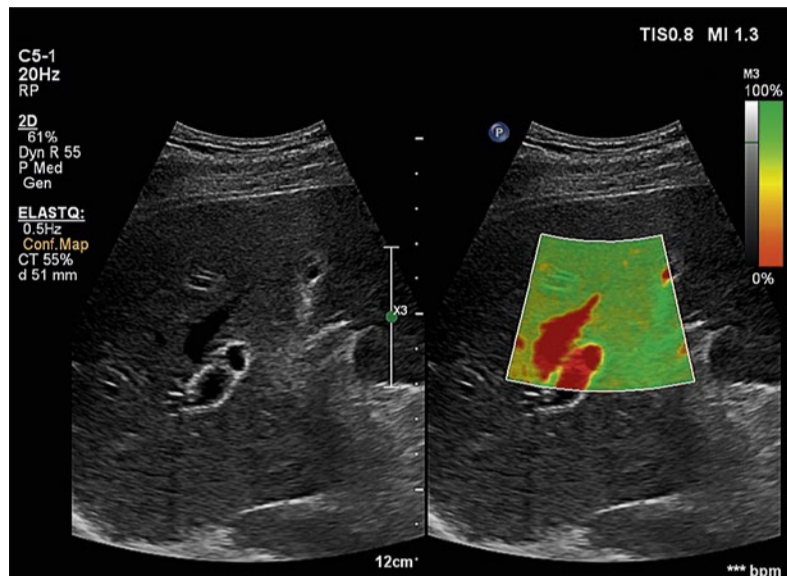


Neurologist Professor Paul M Parizel, who leads Antwerp University Hospital's radiology department, has been appointed the first ESR/ECR President

than 70 refresher courses and four multidisciplinary sessions, which feature radiologists, oncologists, gynaecologists and surgeons involved in the interdisciplinary treatment of patients. The good relationship between the ESR and the European Federation of Radiographer Societies (EFRS) also has a strong impact on the program. 'The quality of our performance depends on the strength of the entire team,' Parizel observed. 'I am so happy that the ECR collaborates closely with radiographers, and the scientific program for 2017 will reflect this growing symbiotic relationship.'

New ElastQ Imaging, real-time shear completes Philips solution for liver a

NEW: Evolution 3.0 EPIQ ultrasound upgrade offers high-res PureWave crystal transducer technology, shear wave elastography, contrast enhanced ultrasound, and image fusion. Could you ask for more?



Philips has released the EPIQ Evolution 3.0, an upgrade to its range of high-end ultrasound scanners – and a device that combines a number of innovative technologies to improve image quality and processing. Professor Dirk-André Clevert, head of the Interdisciplinary Ultrasound Centre at Munich University Hospital, explains what sets this new system apart from any competition.

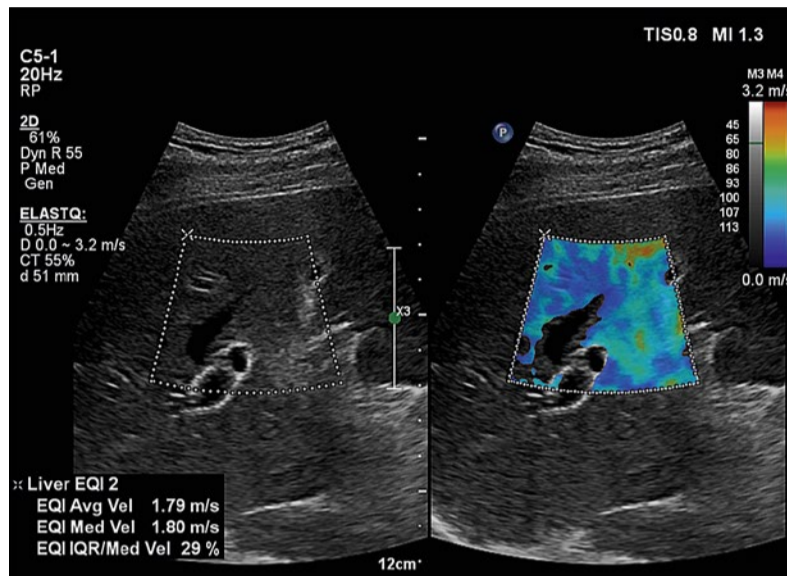
Asked why the specific focus in development of the EPIQ-platform was liver imaging, he pointed out that the liver is the largest and central metabolic organ, with many pathological processes manifesting within it. 'This applies primarily to tumour metastatisation but also to parenchymal changes other than liver cancer, such as fibrosis or cirrhosis. The liver is therefore an

The confidence map captures areas with high (green) and low (red) measurement accuracy. Shear waves cannot propagate through liquids, so the veins captured are coded red

organ of great interest to all medical disciplines for oncological, inflammatory, vascular and parenchymal questions.'

What does Evolution 3.0 mean in this context?

'The special feature is the combination of different advanced elements in one system: *high resolution PureWave crystal technology, shear wave elastography technology (ElastQ Imaging), contrast enhanced ultrasound (CEUS) and image fusion.* This covers all four mainstays of liver imaging.



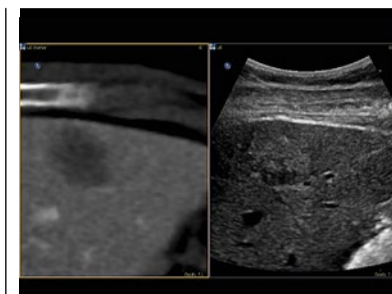
'The first is image quality, i.e. the B-mode image, which diagnosis hinges on, and for which we require high resolution transducers that can detect even the smallest, deep-lying lesions. Newly developed data processing algorithms additionally ensure fast image reconstruction.

'The second mainstay is contrast enhanced ultrasound, because only the use of contrast media enables us to fully utilise the diagnostic relevance of ultrasound images. The system offers high frequency transducers, providing optimal resolution with sufficient depth of penetration, which can additionally be combined with contrast-enhanced ultrasound.'

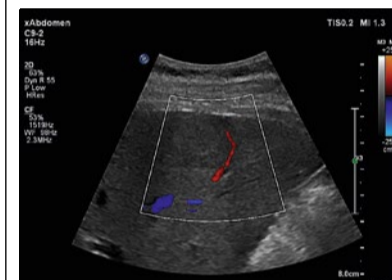
'Elastography is the third mainstay. ElastQ Imaging is a colour coded, quantitative measuring system to evaluate tissue elasticity in real-time. Rigidity measurements indicate

potentially pathological changes not yet visible on the B-mode image, and whether the tissue is becoming softer or harder after treatment. Image fusion is the fourth mainstay. This procedure can sonographically detect pathological changes seen on CT or MRI scans and can substantiate a firm diagnosis.'

Shear wave elastography shows clearly increased liver stiffness, with the medium velocity of the shear wave propagation around 1.79 m/s, indicating cirrhosis. The colour gaps in the measurement box correspond with a hepatic vein and a branch of the portal vein



The CT scan has detected a suspected liver lesion. Good CT-Ultrasound fusion imaging with definition of suspected, hyperechoic liver lesion



Increased vascularisation of this liver lesion cannot be defined in the colour coded duplex ultrasound scan



In the contrast-enhanced ultrasound examination the liver lesion shows a distinct wash-out after around 50 seconds, indicating a liver metastasis

Moving centre stage in liver interventions

3-D simulation includes haemodynamics

New 3-D simulation models that include haemodynamics enable better treatment of hepatic tumours via radio-embolisation, according to eminent Spanish radiologist José Ignacio Bilbao Jaureguizar

Report: Mélanie Rouger

In radio-embolisation, an endovascular technique currently used almost exclusively in liver cancer therapy, particles are liberated in the arterial flow of a vessel feeding hepatic tumours, to deploy the particles within the arterial tumoural network.

Interventional radiologists use a microcatheter through which they inject particles loaded with yttrium-90, which emit radiation in a diameter between 2.5 and 11 mm for about 64 hours.

Crucially, the particles must be placed within the tumour, so that the total radiation goes only there. However, doing so remains a challenging exercise, mainly due to the blood stream.

Depending on the arterial flow, areas of the tumour may receive more or less particles, according to José Ignacio Bilbao Jaureguizar, professor of radiology, head of interventional radiology and consultant radiologist at University Clinic of Navarre in Pamplona, Spain.

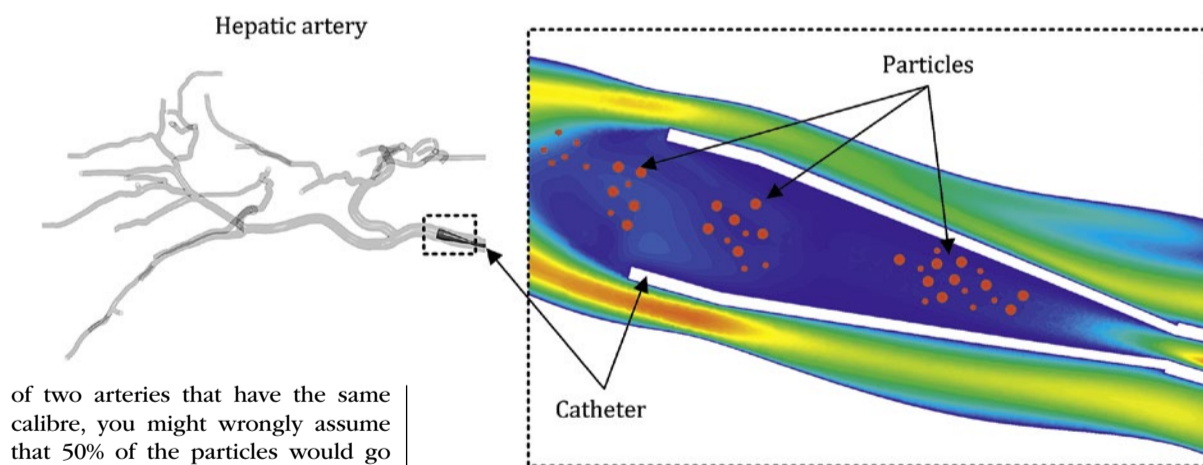
'This is one of the problems we

have,' he explained. 'We use angiography and selective catheterisation techniques to homogeneously distribute the particles, but it all depends on blood flow in the end. So some areas will be treated appropriately, and others won't – or not as much.'

Because they needed to understand vascular flows better, Bilbao's department decided to team up with the University of Navarre (UN) School of Engineering in neighbouring San Sebastian, to help develop a computational simulation model based on the anatomy, to study all possible scenarios of particles distribution. (See: Numerical investigation of liver radio-embolisation via computational ... <https://www.ncbi.nlm.nih.gov/pubmed/27751569>).

The simulation model takes into account all the available information, such as what kind of catheter will be used and its shape, or its distance from the next arterial bifurcation.

'There are many parameters to factor in and countless scenarios in which particle distribution is not as homogenous as it should be,' Bilbao explained. 'For example, if you place a catheter close to the bifurcation



of two arteries that have the same calibre, you might wrongly assume that 50% of the particles would go left and 50% right. But blood stream is a complex physiological process, and a catheter, even if only a 1mm calibre, may interfere with it,' he said. 'You may also obtain different results if you place the tip of the catheter close or further to the bifurcation, in a central or lateral position in the vessel, or if you liberate particles at high or low speed.'

The UN researchers came up with a large amount of possibilities and findings using and analysing real-sized 3-D models, according to Bilbao, who compared particles distribution to cars in highway traffic. 'We are learning a tremendous set of things. Simulation models enable us to test new catheters and see if

they work, or not, understand how our equipment works, and issue appropriate user recommendations, among others. It opens up a lot of possibilities.'

Radiology began to take an interest in haemodynamics study a few years ago, when a team in the USA showed the value of studying blood flow in prosthesis placing to correct aneurysms in the aorta (Basciano CA. Computational particle-haemodynamics analysis applied to an abdominal aortic aneurysm with thrombus and microsphere-targeting of liver tumours. PhD Thesis, North Carolina State University, Raleigh, NC, 2010.)

Anterior view of the patient-specific hepatic artery modelled by Jorge Aramburu Montenegro in his thesis for computational simulations and a detail of the particle-haemodynamics in the vicinities of the injection

Studying smaller mobile vessels in the liver is just as interesting an option for radiologists, but they must learn to focus on functional imaging, Bilbao believes. 'We can't work with morphological criteria alone any more; we need function. Radiology is a wonderful morphological technique and we're particularly fond of studying microanatomy in depth. However we must get

wave elastography, assessment

'The platform offers a large range of transducers, with three different transducers available for abdominal scanning alone. This choice of transducers makes it possible to utilise the technology developed for the liver for other applications and organs as well. For patients with acute stroke, CT and ultrasound data can be fused to check for any severe brain damage, and for patients with prostate cancer it facilitates precise positioning of lesions detected on the MRI scan to help carry out biopsies.

'This means that the technology promotes the interdisciplinary utilisation of image data that would otherwise go to waste. Instead, doctors can feed radiological image data into their systems and use it for progress monitoring. Viewing a CT or MRI scan next to an ultrasound scan makes it possible to track whether a lesion has become smaller, larger or has remained the same over longer periods of time.'

Which trump cards does the new shear wave elastography offer?

'This technology is primarily used on the curved array transducer. The large measurement window makes it possible not only to view and measure partial liver segments but also larger areas of the parenchyma.

'Along with colour coding, which indicates whether tissue is hard or soft, a mean numerical value can also be determined. This can be used to monitor treatment and see whether the values are changing. The system edits the data and converts it directly into a structured patient report, which simply needs to be printed.'

'Another special feature is the ability to acquire more data within the field of view during post-processing, in addition to the data sets already stored. This means that specific smaller, partial segments of interest, within a larger field of view, can be evaluated and documented later on.'

'The system also makes a so-called confidence map available during the examination, which indicates the quality of the signal by colour: green means high, yellow means moderate and red means low. It's therefore always possible to get the best out of the images.'



Professor Dirk-André Clevert MD heads the Interdisciplinary Ultrasound Centre at Munich University Hospital (founded in 2004), where all ultrasound activities in the hospital converge. He

is also head of the Radiology Section of the German Society for Ultrasound in Medicine. As course director and president, Clevert organises numerous national and international ultrasound courses and congresses. On the 80th anniversary of the founding of the Medical Faculty at Tbilisi State Medical University, the professor, as head of the Interdisciplinary Ultrasound Centre, received an honorary doctorate.

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gadobenate dimeglumine

Now also indicated for MR imaging of the whole body and MR Angiography in adults and children over the age of 2 years



José Ignacio Bilbao Jaureguizar is professor of radiology, head of interventional radiology and consultant radiologist at University Clinic of Navarre (UCN) in Pamplona, Spain. He is also former chairman of UCN radiology department. He gained a medical degree at Navarre University's medical faculty. Training followed in interventional radiology at MD Anderson Cancer Centre, Houston, USA and he received his PhD, cum laude, at Navarre University. His research interests are percutaneous treatment of tumours including chemotherapy and embolisation, especially in liver tumours.

involved in function and find out more about fluid dynamics.'

In the future, 3-D simulation models should be tailored to every patient. This would prove of tremendous help in brain cancer surgery for instance, Bilbao added. 'We still have a lot of work ahead. Developing a simulation model takes thousands of hours on a super computer. It's not only about money, but also techniques. It could take years, but things go so fast now, so who knows?'

MULTIHANCE - SUMMARY OF PRODUCT CHARACTERISTICS For prescribing information please refer to the approved SPC in your country. **MultiHance, 0.5 M solution for injection - Composition** 1 ml of solution for injection contains: gadobenic acid 334 mg (0.5 M) as the dimeglumine salt. [Gadobenate dimeglumine 529 mg = gadobenic acid 334 mg + meglumine 195 mg]. **Excipients** Water for injections. **Therapeutic indications and dosage** This medicinal product is for diagnostic use only. MultiHance is a paramagnetic contrast agent for use in diagnostic magnetic resonance imaging (MRI) indicated for: - MRI of the brain and spine in adults and children above the age of 2 years, where it improves the detection of lesions and provides diagnostic information additional to that obtained with unenhanced MRI. - **MR imaging of the whole body in adults and children** (above the age of 2 years) including **head and neck region, thoracic space** (including the **heart and female breast**), **abdomen (pancreas and liver), abdomen (gastrointestinal tract), retroperitoneal space (kidney, adrenal glands), pelvis (prostate, bladder and uterus) and musculoskeletal system** where it facilitates identification of abnormal structures or lesions and helps in differentiating normal from pathological tissues. - **Magnetic Resonance Angiography (MRA) for the assessment of stenoses, occlusions and collaterals in adults and children** (above the age of 2 years). - **Specific applications in the heart include measurement of myocardial perfusion under pharmacological stress conditions and viability diagnostics ("delayed enhancement")**. **Contra-indications** MultiHance is contra-indicated in: - patients with hypersensitivity to the active substance or to any of the excipients. - patients with a history of allergic or adverse reactions to other gadolinium chelates. **Special warnings and special precaution for use** The use of diagnostic contrast media, such as MultiHance, should be restricted to hospitals or clinics staffed for intensive care emergencies and where cardiopulmonary resuscitation equipment is readily available. Patients should be kept under close supervision for 15 minutes following the injection as the majority of severe reactions occur at this time. The patient should remain in the hospital environment for one hour after the time of injection. The accepted general safety procedures for Magnetic Resonance Imaging, in particular the exclusion of ferromagnetic objects, for example cardiac pace-makers or aneurysm clips, are also applicable when MultiHance is used. Caution is advised in patients with cardiovascular disease. In patients suffering from epilepsy or brain lesions the likelihood of convulsions during the examination may be increased. Precautions are necessary when examining these patients (e.g. monitoring of the patient) and the equipment and medicinal products needed for the rapid treatment of possible convulsions should be available. Insignificant quantities of benzyl alcohol (< 0.2%) may be released by gadobenate dimeglumine during storage. Nonetheless, MultiHance should not be used in patients with a history of sensitivity to benzyl alcohol. As with other gadolinium-chelates, a contrast-enhanced MRI should not be performed within 7 hours of a MultiHance-enhanced MRI examination to allow for clearance of MultiHance from the body. Impaired renal function **Prior to administration of MultiHance, it is recommended that all patients are screened for renal dysfunction by obtaining laboratory tests**. There have been reports of nephrogenic systemic fibrosis (NSF) associated with use of some gadolinium containing contrast agents in patients with acute or chronic severe renal impairment (GFR < 3.0 ml/min/1.73 m²). Patients undergoing liver transplantation are at particular risk since the incidence of acute renal failure is high in this group. As there is a possibility that NSF may occur with MultiHance, it should therefore be avoided in patients with severe renal impairment and in patients in the perioperative liver transplantation period unless the diagnostic information is essential and not available with non-contrast enhanced MRI. Haemodialysis shortly after MultiHance administration may be useful at removing MultiHance from the body. There is no evidence to support the initiation of haemodialysis for prevention or treatment of NSF in patients not already undergoing haemodialysis. **Elderly** As the renal clearance of gadobenate dimeglumine may be impaired in the elderly, it is particularly important to ensure that NSF may occur with MultiHance, it should therefore be avoided in patients with severe renal impairment and in patients in the perioperative liver transplantation period unless the diagnostic information is essential and not available with non-contrast enhanced MRI. **Undesirable effects** The following adverse events were seen during the clinical development of MultiHance. Common (≥ 1/100, < 1/10): **Nervous system disorders**; Headache. **Gastrointestinal disorders**; Nausea. **General disorders and administration site conditions**; Injection site reaction, including, injection site pain, inflammation, burning, warmth, coldness, discomfort, erythema, paraesthesia and pruritus. Uncommon (≥ 1/1,000, < 1/100): **Nervous system disorders**; Paraesthesia, Hypoaesthesia, Dizziness, Taste perversion. **Cardiac disorders**; First-degree atrioventricular block, tachycardia. **Vascular disorders**; Hypertension, hypotension, flushing. **Gastrointestinal disorders**; Diarrhoea, vomiting, abdominal pain. **Skin & subcutaneous tissue disorders**; Urticaria, rash including erythematous rash, macular, maculo-papular and papular rash, pruritus, sweating increased. **Renal and urinary disorders**; Proteinuria. **General disorders and administration site conditions**; Chest pain, pyrexia, feeling hot. **Investigations**; Electrocardiogram abnormalities, Blood bilirubin increased, Blood iron increased, Increases in serum transaminases, gamma-glutamyl-transferase, lactic dehydrogenase and creatinine. Rare (1/10,000, < 1/1,000): **Immune system disorders**; Anaphylactic/anaphylactoid reaction, Hypersensitivity reaction, Anaphylactic shock. **Nervous system disorders**; Convulsion, Syncope, Tremor, Parosmia, Loss of consciousness. **Eye disorders**; Visual disturbance, Conjunctivitis. **Cardiac disorders**; Myocardial ischaemia, Bradycardia, Cardiac arrest, Cyanosis. **Respiratory, thoracic and mediastinal disorders**; Dyspnoea, Laryngospasm, Wheezing, Rhinitis, Cough, Respiratory failure, Laryngeal oedema, Hypoxia, Bronchospasm, Pulmonary oedema. **Gastrointestinal disorders**; Faecal incontinence, Salivary hypersecretion, Dry mouth Oedema mouth. **Skin & subcutaneous tissue disorders**; Face oedema, Angioedema. **Musculoskeletal, connective tissue and bone disorders**; Myalgia. **General disorders and administration site conditions**; Asthenia, Malaise, Chills, Injection site swelling. **Investigations**; Blood albumin decreased, Alkaline phosphatase increased. **Additional safety information** Laboratory findings were mostly seen in patients with evidence of pre-existing impairment of hepatic function or pre-existing metabolic disease. The majority of these events were non-serious, transient and spontaneously resolved without residual effects. There was no evidence of any correlation with age, gender or dose administered. In patients with history of convulsion, brain tumours or metastasis, or other cerebral disorders, convulsions have been reported after MultiHance administration. Injection site reactions due to extravasation of the contrast medium leading to local pain or burning sensations, swelling and blistering and, in rare cases when localised swelling is severe, necrosis have been reported. Localised thrombophlebitis has also been rarely reported. Isolated cases of nephrogenic systemic fibrosis (NSF) have been reported with MultiHance in patients coadministered other gadolinium-containing contrast agents. Paediatric population Common (≥ 1/100, < 1/10): **Gastrointestinal disorders**; Vomiting Uncommon (≥ 1/1,000, < 1/100): **Nervous system disorders**; Dizziness. **Eye disorders**; Eye pain, Eyelid oedema. **Vascular disorders**; Flushing. **Gastrointestinal disorders**; Abdominal pain. **Skin & subcutaneous tissue disorders**; Rash, sweating increased. **General disorders and administration site conditions**; Chest pain, injection site pain, pyrexia The adverse reactions reported among paediatric patients treated with MultiHance during clinical trials and tabulated above were non-serious. The adverse reactions identified during post-marketing surveillance indicate that MultiHance safety profile is similar in children and adults. **Please note** The peel-off tracking label on the vials should be stuck onto the patient records to enable accurate recording of the gadolinium contrast agent used. The dose used should also be recorded. Consult the locally approved package insert. The Marketing Authorisation Holder, the Marketing Authorisation number and the date of approval may be different in different countries. **Date of revision of this text** September 2016.

Your Insight,
Our Solutions



BRACCO
LIFE FROM INSIDE

Seeking a quick route into healthcare management

Big firms forge a new partnership

An alliance between Siemens Healthineers and IBM Watson Health aims to support service providers in the healthcare system, such as hospitals, health networks and other providers. A top-class technical solution consisting of three main components is to help ensure better treatment for many, at lower costs per head. 'I believe we can make an important contribution towards evidence based medicine,' says Arthur Kaindl, General Manager for Digital Health Services at Siemens Healthineers

Report: Julia Geulen

Enterprise Performance Management is one key component and can be compared with a storage archive. Looking at a group of hospital patients, the management system is used to analyse classic performance indicators, such as average duration of patients' stay, or the adherence to standard guidelines during treatment. The data required is networked between the different in-house IT systems, consolidated and evaluated. It forms the basis for reimbursement of the services provided on the part of the health insurers and other operators and it can also be utilised to optimise processes and reduce costs.

Looking at the individual

A further component, i.e. the Watson Care Manager, comes into play when the issue is not the analysis of a defined group but the individual care of patients. Example diabetes management: This platform consolidates and processes all avail-

able patient data. This includes data from the hospital information system along with image and laboratory data. Based on this data, the system can then help doctors and nurses to choose the best treatment. The high added value of this solution, and – unique on the market to date – the combination of all image, laboratory and pathology data, complemented by information from the patient file, is analysed in real-time.

'The treatment path is available immediately after the image has been generated,' Kaindl points out. This is a big advantage during the diagnosis and treatment process, especially when there is an acute problem, such as a potential stroke. In view of the increasing number of chronically ill patients the extension of this solution to out-patient care is a declared objective. The plan is to network in the individual, vital data generated at home so that it can be integrated and analysed – to achieve better out-patient management.

One vital requirement is adherence to the necessary data protection regulations. Siemens has a clear

competitive advantage in this field because the company holds two certifications for a cloud-based networking solution: ULD for Germany and EuroPriSe, which corresponds with the new European data protection regulation.

Technical challenges

Several hurdles must be overcome during implementation of the solution: Quantitative analytics has not yet been sufficiently implemented in radiology, for instance. However, the prerequisite for clean data analysis is the supply of discrete data based on a structured, quantitative evaluation. Although there appears to be a change in awareness, Kaindl says, because it is recognised that the referring practitioners often do not have time to read pieces of prose, and because inconsistencies are also dangerous.

A further requirement for effective implementation is the clean networking of different IT systems, with one to two dozen of these systems usually found per hospital. Networking can easily and quickly

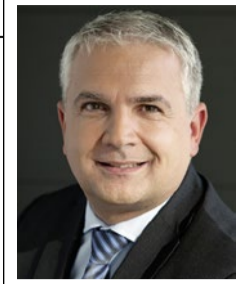
be achieved with standard interfaces. However, without these interfaces the process is more time consuming and sometimes also requires assistance from other IT companies.

Nothing works without curation

When data from the respective IT systems has been aggregated it must be curated. Kaindl: 'This is a complex as well as unavoidable step to ensure we actually receive comparable data. Curated data is a must.' This process is carried out manually during development of the hospital database and takes a certain amount of time. It must be ensured that all information is input correctly into the data structure envisaged. This can often take several months.

The actual analysis of the data can only be carried out afterwards. 'Otherwise there would be a danger of "rubbish in, rubbish out"', which must be avoided at all costs.' Initially, standard analytics is carried out with the help of known algorithms.

After licencing, the data is later



Arthur Kaindl MSc PhD is General Manager of Digital Health Services at Siemens Healthineers. He first worked for Siemens after gaining his Engineering Diploma at Friedrich-Alexander University, Erlangen-Nuremberg (1988-95). In 2001 he received a PhD in Electrical Engineering from Leibniz University, Hanover. Following this, he held various magnetic resonance management roles and then, in 2005, was awarded an MSc in Ceramics Engineering at Alfred University, New York.

specifically evaluated with the help of a new deep learning engine.

Jumping on the train

Siemens Healthineers are looking for a quick route into healthcare management. IBM Watson Health is delivering important components. The newly established partnership is based on a distinct win-win situation. 'The respective strengths and domains ideally complement each other – ultimately also to the advantage of our customers,' Kaindl is convinced.

There is optimism regarding competition in this field. Although Google, for example, is trying to position itself with respective projects and the resulting predictive analytics, there appears to be a lot of distrust amongst consumers – particularly regarding healthcare data.

European and USA radiology societies unite to validate reporting templates

Devising structured reports

Report John Brosky

Structured reporting in radiology is easier to say than do. Initially radiologists must agree on the structure of the report itself. Then they need to agree on what to report. Those two very different challenges help to explain why migration into the Digital Age of radiology reports is moving at Ice Age speed.

The expectation, according to Emanuele Neri MD, Chair of the eHealth and Informatics Subcommittee for the European Society of Radiology (ESR), is that templates for structured reports should be reviewed by diverse specialty professional societies aiming to validate a format for each specialised practice area.

In 2013, the ESR announced a collaborative initiative with the Radiological Society of North America (RSNA) to accelerate the process of developing complementary templates, and to open up that process for a wider participation by European national societies of radiology as well as specialist and subspecialty societies.

In 2015, the ESR and RSNA signed a Memorandum of Understanding that includes the creation of a common working group called the Template Library Advisory Panel (TLAP) to serve as a bridge between the two societies to create and review proposed structured reporting templates.

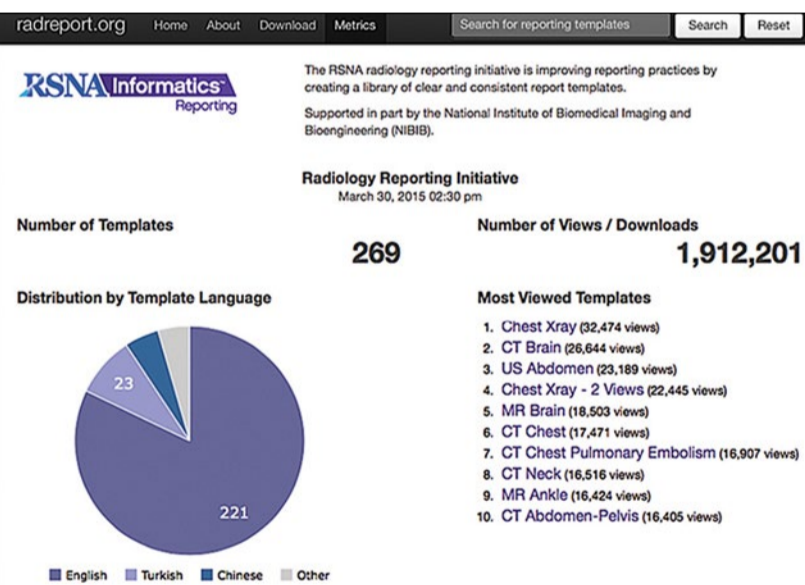
The TLAP wish that many ESR subspecialty societies will step forward to collaborate, working through the open, online template library established by RSNA to select and then validate clinical content and technical formatting for their respective practice areas.

Through the agreement, ESR members have full access on the RSNA website, and not only the ability to download and review materials, but also to upload templates as a credential member.

'We find ourselves at an intermediate stage where the separate elements, such a reporting templates for different specialised practices, are increasingly available but have not yet come together,' said Neri, who is also a member of the RSNA Informatics Committee. 'There are many subspecialty societies federated by ESR, whether abdominal, neural or cardiac,' he pointed out. 'And it becomes extremely important that each society with its expertise reviews and validates those templates created for a specific area of expertise, that they agree with it.'

Validation of templates by European professional societies and the subsequent publication of the template will mark a milestone, he said allowing the initiative to expand and advance toward adoption of templates.

Neri outlined three strategies for the implementation that will unfold



in parallel to this.

First will be the promotion of templates by ESR through its diverse activities, and targeted promotion by the specialty societies to its members.

Many of these societies are committed to structured reporting, he said, citing as examples the European Society of Gastrointestinal and Abdominal Radiology, the European Society of Oncological Imaging and the European Society of Medical Imaging Informatics.

Concurrently, there will be a progressive integration by manufacturers of validated templates into imaging equipment. 'Today when

a hospital buys a CT scanner, the manufacturer has already pre-loaded imaging protocols, which facilitates the work for a clinician with validated, predefined parameters for an examination programmed into the console. PACS vendors can do the same with reporting templates, which will encourage and motivate radiologists to use appropriate reporting formats,' Neri believes.

A third push toward wider implementation will come through multidisciplinary interactions, such as a radiologist participating on tumour review boards. 'In these settings, the use of structured reporting is growing because, with the reports, the

radiologist improves communication with other clinicians asking for specific information for tumour measurement or staging of the disease. In this oncology context a structured report provides specific information to respond to specific clinical questions. And it is very effective.'

Yet, there remain multiple challenges to widespread adoption, some of which are uniquely European. 'The difference from the United States is that different countries in Europe not only have different healthcare payment systems,' Neri pointed out, 'there is also a language issue, which is one of the major challenges we face for implementation.'

Here the advantage of structured reporting is that it standardises reporting formats so that even where the language changes, the same information is presented in the same order.

As a pan-European group, he said, ESR can help diverse societies establish structure, provide guidelines, and give direction.

'Still, reports must be translated,' he added. 'Here's where we find the challenge.'

Beyond language there is the challenge of ontology, the terminology used to describe an imaging finding.

'The risk is having a report with the correct structure, but with a wide variation in the terms. For this

Mobile X-ray around the globe

Since launching meX+ DR solutions in 2009 the imaging and X-ray solutions producer medical ECONET has installed the range internationally. Physicians in diverse areas and fields of expertise, medical crews on ships and oil-rigs, paramedics in military ambulances, as well as disaster relief forces in conflict areas, report satisfaction regarding the lightweight and flexible meX+ X-ray devices in their daily work, the manufacturer reports. 'A highly beneficial factor is the user-friendly handling of the self-explanatory meX+ Image acquisition software, which contains a full integrated positioning guide and proposals for adequate dose values.'

With a specific focus on mobility and flexibility, medical ECONET explains it 'supplies radiography solutions that are equipped with a worldwide unique hybrid-powered technology. This smart technology allows operation of the meX+ portable X-ray generators by the integrated battery, or by an external power supply, while charging the battery. These durable lithium-ion batteries can produce over 500 exposures, with only one full charge, and generate clean diagnostic images by high frequency technology.'

In addition, the firm's range of wired and wireless digital radiography detectors come in three imaging sizes (10x12, 14x17, 17x17 inch) and can be provided as customised solu-

tions for mobile, stationary and retrofit applications. 'And,' the company adds, 'due to the equipped wireless file transfer and the Automatic Exposure Detection (AED), the user can work in a most comfortable way without any disturbing cables.'

Details: www.medical-econet.com

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EPIQ Evolution 3.0: The ultimate ultrasound solution for liver assessment

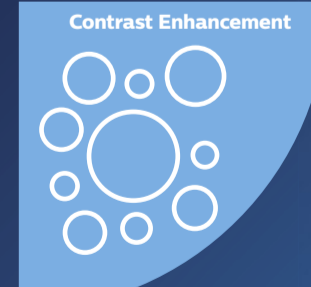
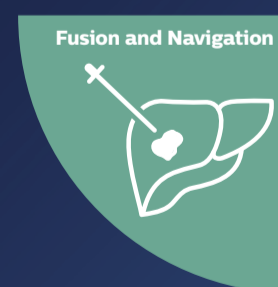
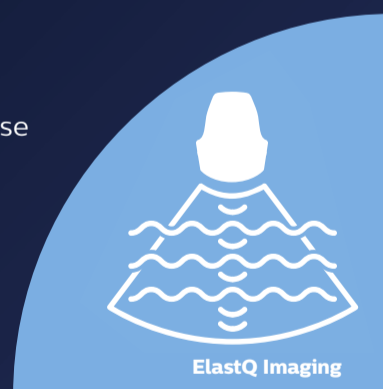
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Professor Emanuele Neri chairs the eHealth and Informatics Committee of the European Society of Radiology (ESR), and the ESR EuroSafe CT Dose Repository, he is also a delegate for Imaging Biobanks of ESR Research Committee and member of the RSNA Radiology Informatics Committee. At the University of Pisa, Neri is Associate Professor of Radiology, devoting most of his research focus on Gastrointestinal and Oncologic imaging and Imaging Informatics, with special interests in Structured Reporting, Imaging Biomarkers and Biobanks.

reason in parallel with development of standardised reports is an effort to arrive at standard terminology, a lexicon,' Neri said. 'RadLex, developed at RSNA, will probably be the example to follow.'

Finally, reports are not just a matter of text but also convey a wealth of quantitative information, such as measurements of volume, length, density, or contrast uptake. Some of this data may be captured and reported automatically where software vendors can reliably transfer the measures into the report.

'But,' he added, 'this will not always be the case.'

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Age-appropriate disease? Doesn't exist

What can we learn from population studies? According to Gabriel Krestin MD PhD there are things that we can un-learn, as well as learn, from population imaging studies.

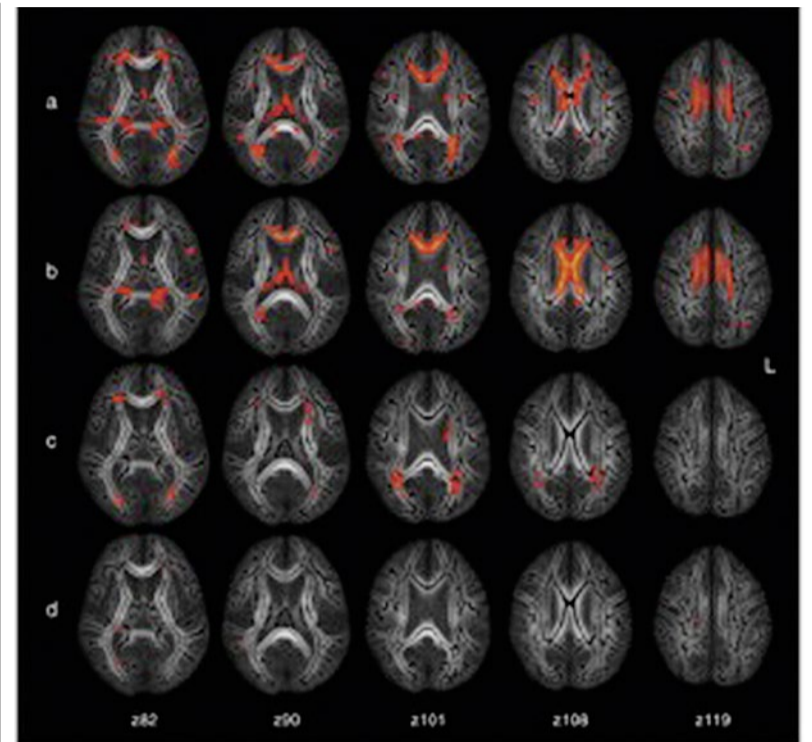
Interview Daniela Zimmermann

The Chair of the department of radiology & nuclear medicine at Erasmus University Medical Centre, Krestin also leads the European Population Imaging Infrastructure (EPI2), an initiative of the Dutch Federation of University Medical Centres and Erasmus University.

Population imaging is the large-scale application and analysis of medical images to find imaging biomarkers that enable the prediction and early diagnosis of diseases. The EPI2 coordinates data acquisition at diverse locations and times and is a flagship node of the EuroBioImaging initiative, one of the large distributed life-sciences infrastructures on the European Strategy Forum for Research Infrastructures Roadmap. Pan-European participants include radiologists and research organisations from Austria, Finland, France Germany, Norway, Sweden, and the United Kingdom.

At the Garmisch MR 2017 Symposium, held in January, Krestin focused on brain imaging in the Rotterdam Scan Study to challenge the widely held concept that there is an age-appropriate approach in medicine. 'There is no such thing,' he stated during our EH interview, defying this largely accepted idea in what he acknowledges is a provocative talk.

'In the past the term "age-appropriate" has been used to relate a lot of alterations to the process of aging. The changes that we attributed to age are, in fact, caused by symptomatic and sometimes pre-clinical or asymptomatic disease. Aging is not a so-called normal process. There is no such thing as a normal aging of the brain. It is not normal that you lose or deteriorate in your brain



Effects of age, global white matter atrophy and white matter lesions on fractional anisotropy values of normal-appearing white matter. Images are shown in the Montreal Neurological Institute (MNI) stereotactic space, with MNI coordinates for axial levels (z) depicted for each column. The white matter skeleton (black) is projected onto the axial MR images. Yellow-to-red colors represent normal-appearing white matter regions with reduced fractional anisotropy (FA) in relation to (a) increasing age, adjusted for sex only, (b) global white matter atrophy, adjusted for age, sex and white matter lesions, (c) white matter lesions, adjusted for age, sex and white matter atrophy and (d) increasing age, adjusted for sex, white matter atrophy and white matter lesions. With increasing age, multiple regions show significant decreases in FA (a). However, after adjustment for white matter atrophy and white matter lesions, only few regions remain (d). Global white matter atrophy (b) relates to decreases in FA in the hippocampal region (z82), fornix (z90), corpus callosum (z90 to z108) and along the cingulate bundle (z119). In contrast, white matter lesion burden (c) is associated with reduced periventricular FA (z82 to z108).

M.W. Vernooij, M. de Groot, A. van der Lugt, M.A. Ikram, G.P. Krestin, A. Hofman, W.J. Niessen, M.M.B. Breteler: White matter atrophy and lesion formation explain the loss of structural integrity of white matter in aging. *NeuroImage*, Volume 43, Issue 3, 2008, 470-477. <http://dx.doi.org/10.1016/j.neuroimage.2008.07.052>

function with age, that the brain becomes senile.

'What we see is the influence of many external factors, many risk factors, many related diseases, or perhaps of genetic predispositions. But it's not necessarily the number of years you have lived that lead to

these changes.

'In population studies, when we started we were looking for very simple things, such as the different volumes of the brain across subjects of different ages. We were taught in medical school that, after adolescence, the number of neurons in

New system helps physicians to choose suitable devices

Simpler MR-conditional cardiac device selection

The ProMRI Configurator made by Biotronik is an online tool that enables physicians to select from a series of MRI requirements for a patient and subsequently generates a recommendation of all suitable MR-conditional cardiac device and lead combinations available in a particular country, thus helping physicians to choose the most suitable MR-conditional cardiac systems for each patient.

Many of the firm's implantable cardiac devices are not only MR-conditional but also take advantage of the company's award-winning MRI AutoDetect functionality, Biotronik reports. 'This feature allows a device's built-in sensor to detect an MR environment automatically (within a programmable window of up to 14 days) and to switch the device to and from MRI mode



for the duration of an MRI scan. This means that patients implanted with a cardiac device can receive optimal therapy for the maximum amount of time without requiring multiple

visits to their physician for manual configuration for MRI scans.'

Its portfolio of MR-conditional devices and systems is extensive, so possible combinations for physicians

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dy produces provocative insights



Professor of Radiology **Gabriel P Krestin** chairs the radiology and nuclear medicine department at Erasmus MC, University Medical Centre in Rotterdam, the Netherlands. A graduate of the University of Cologne, Germany, his residency in radiology was completed in 1988. He was later appointed radiologist and head of the MRI Centre in Zürich University Hospital, Switzerland, where he became associate professor of radiology and head of the clinical radiology service, before moving to his present position.

predictors of certain outcomes, of dementia, but also of stroke.

'Still, all of this is only the tip of the iceberg. There's a lot more that we cannot see with our eyes that are under the water line, let's say. Today we can measure with sensitive tools such as diffusion weighted MRI, the microstructural integrity or damage of the white matter. With these measures, what we find in longitudinal population studies is that even in the non-affected white matter, which appears to be completely normal on conventional MRI images, a change

in these diffusion metrics appears long before the white matter lesion becomes visible – years later. On the other hand the microstructure of the white matter is linked to cognition, and damage is associated with impairment of cognition.

'We have also done functional connectivity studies and we can see these white matter damages that we attributed to aging are quite extensive. Yet they have nothing to do with age. When we correct for all the risk factors, and a lot of other factors that can play a role, we see

that there's not much remaining. Instead of a change with age these aging people are increasingly affected by other diseases or impairments related to cardiovascular risk factors, diabetes, decrease of brain perfusion or impaired microvasculature.

'Again, my message is that what we relate to age is not, in fact, due to the so-called normal aging process but is part of a process that has to do with some disease pathophysiology.

'The reason that assessment of such imaging alterations becomes important is that these measures are

biomarkers that can predict certain outcomes. People who have damage to the microstructure of the white matter, or show a high level of atrophy, or white matter lesions, will have a higher risk to develop dementia or stroke.

'Over the past fifty, years we have increased life expectancy due to the fact that today we have a much better understanding of these risk factors and thus a better prevention, by decreasing the number of predisposing or external factors.'

the human brain is decreasing with age. Yet, when we were looking at volumes of brain structures, measuring grey and white matter, what we saw was that, with increasing age, the grey matter is not changing in volume. It's the white matter that changes in volume. If we look deeper we find that it is not the grey matter that atrophies so much as the white matter.'

'Another process that we relate to age is the formation of white matter lesions. With some sequences in MRI we can identify those small, high-signal intensities, even if we don't know exactly the histopathology and pathophysiology of these lesions.

'We assume that these white matter lesions are related to degeneration, and at the same time, we know that the number and the load of white matter lesions increase with age.

'From population imaging studies we learned that white matter lesions are associated with a certain number of risk factors. For instance cardiovascular risk factors, like smoking, hypertension, or diabetes, lead to an increased white matter lesion load. And, finally, we also learned that these white matter lesions are also

to select can be overwhelming. The ProMRI Configurator relieves concerns by channelling MR-conditional systems and devices into a single online platform with an easy-to-use interface. In a step-by-step process doctors are directed to possible cardiac implantation combinations for their patients' MRI needs.

The ProMRI Configurator marks the second offering of the ProMRI Check online platform that the manufacturer offers physicians. 'The first tool, the ProMRI SystemCheck, was launched in 2014 and helps physicians to determine whether an implanted Biotronik system is MR-conditional.'

This is a 'retrospective tool', the firm points out. 'The ProMRI Configurator enables physicians to be proactive in their approach – to determine beforehand the best system or device to implant based on the physical needs of the patient.'

As Manuel Ortega, the company's Senior Vice President, confirmed: 'We are determined to maximise patient accessibility to MRI scans as far as possible.'

Details: www.promricheck.com

www.healthcare-in-europe.com

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'Very few people have a carbon hyper-polariser'

From the extremely new, but not generally available, to the somewhat new... very available and highly useful... Walter Kucharczyk outlines potentials and practicalities in advanced brain tumour imaging

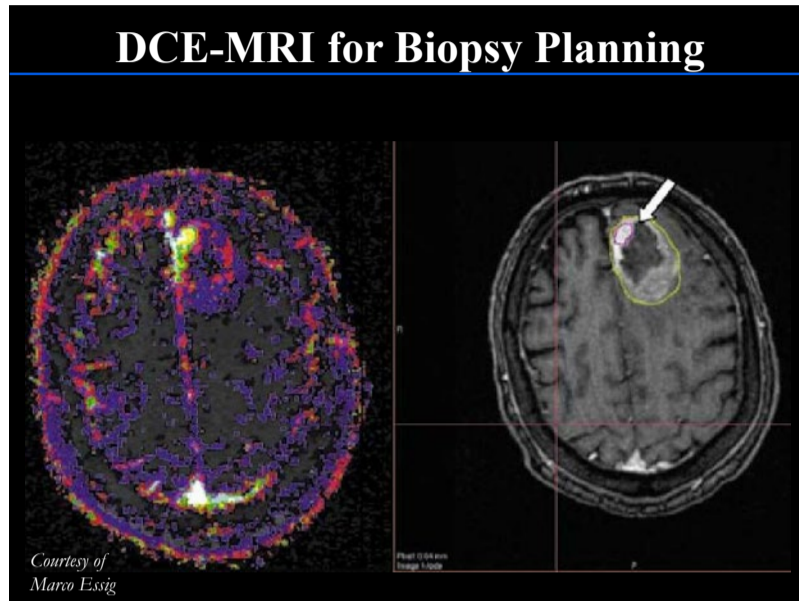
Report: John Brosky

When the organisers of Garmisch MR 2017 (22 January) wanted to hear about the newest developments in neuro radiology, they turned to Walter Kucharczyk MD FRCPC, one of the event's most experienced presenters, having delivered lectures at this MRI Symposium since 1991.

His experience also includes having served as the President of the International Society of Magnetic Resonance in Medicine (ISMRM), the largest research and education group in the world devoted to developing and teaching magnetic resonance to doctors and scientists, and as previous Professor and Chair of the Department of Medical Imaging at the University of Toronto for sixteen years. He is a renowned veteran lecturer with a decades-long record of international lectures.

The faculty's proposed title for the talk was terse, yet ambitious: 'Brain tumours: what is new?'

Among those attending his presentation, Kucharczyk had predicted that, while many would be interested in and aware of the very newest developments in neuroradiology, most practitioners would not have had access to such equipment and methods, so they would look for advanced, "somewhat-new" techniques that might not be the newest, but are available, are of proven value, and have stood the test of time. 'For this reason, I divided the lecture into two, between readily available, useful



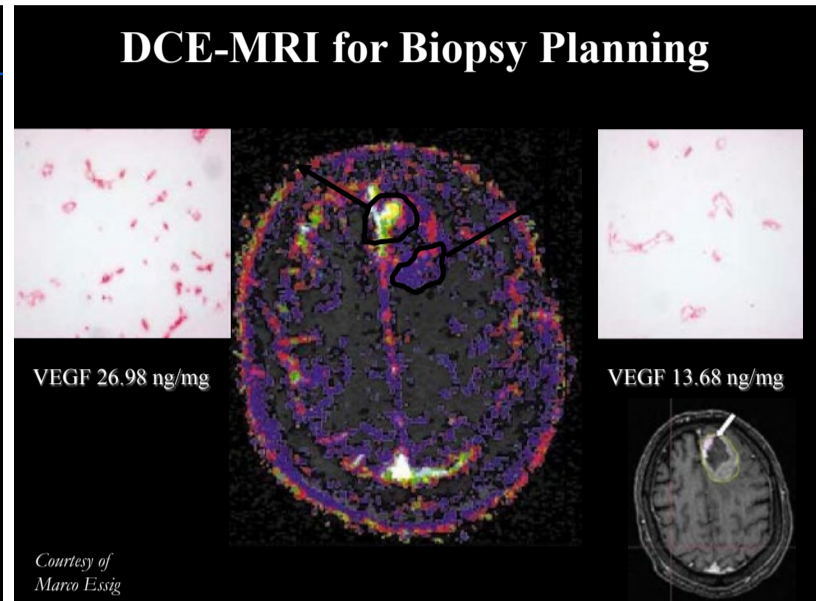
methods, that may not be extremely new, and what is truly new, but not readily available, is also complicated to analyse, and thus not particularly useful to most radiologists today,' he explained. 'I hope both parts of the lecture were of interest to the audience - letting them know what all of them can do today and giving them a taste of what might be useful in the near future.'

After setting a context in reviewing the not-so-new, but well-proven techniques, Kucharczyk advanced into more recent developments in techniques that are sufficiently available for everyone to use, and which are useful for a variety of applications, including diffusion weighted imaging, tractography, perfusion MRI, and MR spectroscopy.

The very newest techniques are mostly performed in a research environment to investigate and help solve yet unsolved problems. But, they are not widely practiced because not every medical imaging centre has the hardware, software, cyclotron,

combined MRI-PET scanner, carbon hyper-polariser, or specialised personnel to perform these techniques. 'I don't think we are there yet with many of the very newest things,' he pointed out.

The usefulness of the most readily available radiotracer, 18-FDG, to image brain tumours is limited, he said, because radiotracers based on



glucose provide poor image contrast between the tumour and normal brain. Brain tumours and healthy brain tissue both avidly take up the glucose. 'As a result you need to go to other novel formulations of radiotracers, which are very expensive and have very short half lives,' Kucharczyk explained. 'These necessitate having a cyclotron.'

Similarly, hyper-polarised carbon species carry similar logistic and cost issues of requiring a very expensive carbon hyper-polariser, he added, 'but they do enable the radiologist to study carbon-based metabolites, such as pyruvate, through its biochemical pathways and potentially assess the effectiveness of therapeutic drugs. But very few people in the

New digital mobile X-ray systems for higher operator satisfaction

MobileDaRt Evolution MX7 series

Digital mobile X-ray systems equipped with a Flat Panel Detector (FPD) are used to examine patients during hospital rounds and for urgent cases in A&E and neonatal intensive care units (NICUs). Leading medical equipment manufacturer Shimadzu (www.shimadzu-medical.eu) reports that its new MobileDaRt Evolution MX7 digital mobile X-ray systems provide ultra-modern and extensive mobile digital radiographic (DR) system functionality. 'The MX7 series expands the level of support for medical personnel involved in mobile imaging work. The system includes new

software functions, an extremely operator-friendly design, and a built-in large 17-inch LCD monitor that increases resolution and also provides better visibility and touch-panel operability.'

Storage and more

Other new features include storage space for smaller items as well as grooves in the console top side-walls, to maintain stability while placing a cover over the FPD unit, for example. 'The MX7 still features the popular smooth and quiet drive system, the "all-free" button to freely position the unit with a single button, and the ability to display images in about two seconds after exposure,' Shimadzu

adds. 'These help operators to work quickly in typical healthcare environments.'

Trusted performance

The firm reports that, in a customer satisfaction survey by USA-based Research Firm KLAS, Shimadzu MobileDaRt Evolution was acknowledged as the 2016 "Category Leader" in Digital X-ray Mobile. 'Thus, MobileDaRt Evolution can offer proven first-rate healthcare support.'

To date, Shimadzu has sold over 3,000 digital mobile X-ray systems worldwide. 'With the steady growth of digitalisation in clinical environments, MobileDaRt is a globally well-known product appreciated by numerous customers in professional healthcare organizations,' the manufacturer reports. 'The 3,000+ units have been installed in more than 60 countries.'

The MX7 features, an integrated power management function Smart seCURE, which gives users a selection of choices to create the best system for their clinical needs. Based on superior communication between the main unit and DR system, this management function utilises the battery more effectively by minimising unnecessary power consumption. 'In addition to a start-up time of about one minute for the DR system, the system also includes other new features designed to meet the needs of healthcare providers, such as a

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lay – and not yet

world have a carbon hyper-polariser because it costs something north of a million dollars, and then it has to be placed beside the scanner because the tracers have very short half-life.'

Following the lecture a discussion of developments fell into the category of automated image analysis, big data and machine learning, he said. 'There is work being done on very interesting concepts based on automated image analysis and machine learning. When we humans look at an image, we see patterns that are based on the spatial location of dots, their Grayscale or colour, and shapes. But digital images can yield additional information already embedded in them, based spatial frequencies and similar features, that can only be extracted by various mathematical operations and transforms, and not appreciated by the human eye,' he explained.

'When we analyse this scatter image we can't say whether it's a picture of a human brain or a giraffe. But, with appropriate software, a computer can recognise patterns that we cannot, potentially finding unique patterns that may ultimately prove diagnostic of certain diseases. By analysing sufficiently large sets of such image data, perhaps soon automated analysis will enable us to distinguish between various types of brain tumours, grade them, and possibly even inform us of their genetic makeup.'

Looking ahead, Kucharczyk said he hopes that radiologists, like

machines, can learn from the detailed correlative analysis of clinical information, images, and pathology studies to deliver findings that increasingly correlate with the ultimate pathology report. 'As radiologists, we are quite accurate in macroscopic diagnosis. We can see many things about a brain tumour that a pathologist does not: the extent of a tumour, its size, and whether there is more than one tumour. And we can provide a fair estimate of the grade and histopathology of the tumour.'

'Today, the pathologist has the

final say in brain tumour diagnosis and, by definition, has the definitive opinion on grade, mitotic rate, histopathology and genetic profile, with terms such as: 1p19q co-deletion to determine the chromosomal type, IDH 1 and 2 mutation [isocitrate dehydrogenase], and the MGMT promoter methylation status,' he said. 'These are all important in determining diagnosis, prognosis, and probability of treatment response.'

Then, he speculated: 'Wouldn't it be cool if we could actually determine the same findings from the

images as the pathologist does from the microscopy?'

Continuing: 'Ultimately our objective should be to be able to do everything the pathologist does, but to do it in vivo, by extracting that information from images. Our objectives should be to determine all features of the diagnosis and prognosis without having to operate on the patient, without having to extract tissue. Are we there yet? No way. Will we ever get there? Probably not completely, but we are moving in that direction,' Kucharczyk concluded. ■



Walter Kucharczyk, MD, FRCP is the Director for Research at the Joint Department of Medical Imaging of the University of Toronto and a hands-on Neuroradiologist there, as well as a Professor of Medical Imaging and Neurosurgery.

on



The team of the Neonatal Care Unit, Portsmouth Hospital NHS Trust with the mobile digital X-ray systems

larger image display monitor and convenient storage space,' Shimadzu adds.

Scatter Correction software

'The Scatter Correction software enables more efficient work, due to the elimination of grid misalignments,' the firm points out. 'Whereas a grid physically reduces scatter and increases image contrast, the software mimics this process virtually. It generates a scatter model, which is subsequently subtracted from the image. The result is an image with reduced scatter and increased contrast.'

Finally, Shimadzu adds that the state-of-the-art control software incorporates new functions and optimises the pre- and post-processing workflow. 'The anatomical programs (APRs) can be selected easily via a body mask to perform the recommended radiographic examinations.' Further information: Shimadzu Europa, www.shimadzu-medical.eu ■

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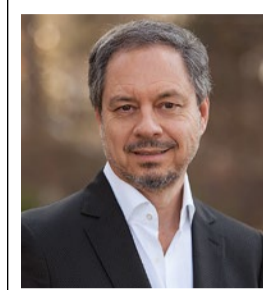


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ECR 2017– Eminent radiologist stresses adverse work issues

Radiologists suffer burnout and gender inequality

In an exclusive interview with EH Correspondent Mélisande Rouger, **Mauricio Castillo** president of the American Roentgen Ray Society (ARRS), spoke about the impact of dissatisfaction and gender discrimination in radiology, the focus of his Wilhelm Konrad Roentgen Honorary Lecture at ECR 2017



Mauricio Castillo MD is the James H Scatcliff distinguished professor of radiology as well as chief and program director of neuroradiology at the University of North Carolina in Chapel Hill, N. Carolina. He is also the current president of the American Roentgen Ray Society. Dr Castillo completed his radiology and neuroradiology training at the University of Miami School of Medicine, Jackson Memorial Medical Centre, and Emory University School of Medicine, Affiliated Hospitals in Atlanta. His research interests include paediatric neuro-imaging, application of new imaging techniques and medical literature editing. Within the latter, he has authored more than 640 articles and 25 books including the famous *Neuroradiology Companion* (now in fifth edition), a reference work covering the fundamentals of neuroradiology for residents, fellows and practitioners.

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Burnout, dissatisfaction and gender inequality are recognised phenomena among physicians, and recent studies reveal they increasingly affect radiologists. 'We're hurting in these aspects,' confirmed Dr Mauricio Castillo, the JH Scatcliff Distinguished Professor and head of neuroradiology at University of North Carolina, in Chapel Hill, USA.

Radiologists are among the best-paid physicians in the USA. In 2011 they earned more than any other specialty and ranked sixth in 2015. 'We earn more than in 2011, but our salaries have not increased at the rate of other specialties. But we still do very well,' Castillo agreed.

However, only around 50% of radiologists felt fairly compensated and satisfied with their career choices, according to a study conducted among almost 20,000 physi-

orities is to take care of our own, by making sure that people have appropriate psychological help and achieve a life-work balance.'

To take care of its staff, UNC has launched a three-year program, in which it will inject US\$300,000.

This is an essential step, Castillo argued, as radiologists usually don't receive help in their daily work and find themselves increasingly squeezed by finances.

'We do a lot more studies than ever before, which has made our salaries go up, but also lead to burnout. Radiology used to have fixed schedules similar to anaesthesia. Now you can never leave,' he said. 'Studies always have to be read, turnaround time has decreased and we are expected to have everything ready within minutes. We are teaching that to residents. Getting that



cians by Medscape in 2016. (<http://www.medscape.com/features/slide-show/compensation/2016/public/overview?page=1>)

Evidence collected over the past few years has also increasingly shown that radiologists are depressed. And worse, they suffer burnout.

A 2015 study led by the Mayo Clinic showed that burnout affected over 39,000 physicians in the USA especially family doctors, urologists, physical medicine and rehabilitation specialists... as well as radiologists.

'Ten years ago, the proportion of radiologists seeking counselling was negligible. Today this figure has increased by 400% and more radiologists are quitting their jobs for positions inside the industry,' Castillo pointed out.

The neuroradiologist became alarmed after a study conducted at his university revealed how disheartened radiology residents felt. In a questionnaire sent to 504 residents about the issue of feeling extremely tired or burnout, those who said they were the most exhausted were the surgeons and radiologists.

'I was surprised. But burnout has been on everybody's mind, including the American College of Radiology, which has taken a significant interest in this issue to ensure it is being properly tackled in medical schools,' he said. 'At UNC, one of our top pri-

turnaround time in less than one hour is compromising what is being learned, but it's how we work nowadays. We're held accountable for how many studies were read within the 60 minutes threshold. It's the same during the weekend, and this, of course, increases burnout.'

The profession's inherent lack of contact with people also adds up to burnout and creates a sense of frustration.

Castillo believes these factors have led to a significant decrease in interest from medical students in radiology, an alarming fact as experts predict the profession will need 20% more radiologists by 2025 when the last baby boomers retire. Radiology has become even more unpopular among women medical students.

'Radiology has one of the lowest percentages of women in medicine and that's amazing when you think that 50-60% of all medical

students who are now graduating are women,' Castillo observed. In 2013-14, radiology was not even in the top ten of entering in the pipeline women applicants, students and residents, according to the Association of American Medical Colleges (AAMC). The unattractive, poor life/work balance experienced in radiology is possibly one of the main reasons why women disregard radiology as a career choice, he suggested; but gender inequality in salary and career advancement may not be far behind.

Studies in this field show that women in medicine make an average 25-35% less than men for an equal position, and the number of women becoming full professors in medicine is small compared to the number of men. 38% of a medical faculty are women, and only 21% are full professors and 16% are deans, according to the AAMC.

The USA has done the most research on this topic, but the problem is also very much present in Europe and probably the rest of the world, and it should receive more attention from everyone, Castillo believes. 'In Western Europe and Scandinavian countries the question of gender inequality seems a little less obvious than in the USA. However, when you speak to women in Europe they feel that there's inequality of gender in respect to free time, advancement within the career and between salaries, so this has become an issue there, too.'

* ECR 2017. 1-5 March. Vienna, Austria
* ARRS Annual Meeting. 30 April – 5 May. New Orleans, USA.

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Closing gaps in the hygiene chain of medical devices

Trusted cable systems

Ever more imaging devices are characterised by very extensive movement sequences while simultaneously being compact. Both device manufacturers and suppliers must consider mounting dynamic requirements when developing their products and ensure their long-term system integrity.

Furthermore, antimicrobial products are of interest not only for minimally invasive or invasive applications because of the increasingly discussed risk of nosocomial infections, but can also close unwanted gaps in the hygiene chain of medical devices. Systems supplier Leoni reports that it supports customers '...as early as the development phase of their medical devices with cable routing, specification, design and manufacture of complex cable systems and ready-to-install subsystems. These solutions for imaging processes decrease installation time while supporting the device properties in providing maximum patient safety, excellent image quality and long-lasting dynamic operation.'

Incorporated components conform to either national or international standards, the firm adds, with proven reliability in numerous tests. Leoni adds that the firm itself executes verification and documentation in standard and increasingly complex customised testing procedures as an add-on service for its customers.

Comprehensive testing proves reliability

In addition to transferring a growing bandwidth, cables and cable systems for imaging devices nowadays must cope with an increasing range of movement. 'Devices are becoming more mobile; horizontally, vertically and orbitally,' Leoni points out. 'Cable breakage and consequently required service calls are as unwanted as ever.'

'The best preparation for durable wiring is optimum routing, as well as the corresponding specification of individual components and the whole system. Involving a solution provider like Leoni in the development phase of an X-ray machine can minimise the interference on the wiring at an early stage.' As a systems provider, the firm reports that it scrutinises the long-term manoeuvrability of its solutions in extensive tests. 'Alongside using standard set-ups in compliance with national and international standards (such as UL), Leoni will, on customer request, simulate non-standard movement sequences with prototypes or device models designed in-house. A Leoni add-on service – basic or complex test set-ups can be established in 2-D or 3-D, and individual components can be rapidly produced by means of 3-D printing. Leoni is thereby able to document and verify the system integrity of its solutions when subjected to customised movement sequences in long-term tests.' Leoni's

antimicrobial cables and systems can help to enhance the hygiene of imaging procedures and patient safety. The integration of only a small quantity of a metal oxide to the sheath material significantly reduces contamination to >99.99% on the surface. Similar to the skin's protective shield of acids, germs, bacteria, viruses and fungi are killed at a pH level of <4. 'During normal handling (involving contact with sweat and proteins), the antimicrobial

effect is retained well, throughout a range of times and concentrations,' Leoni continues. 'This is an important difference compared to conventional methods using silver or copper.'

**At ECR 2017
Leoni's Business Unit
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To give plastic surfaces an antimicrobial effect, Leoni adds a metal oxide to the polymer during the extrusion or moulding process, which then lowers the pH level on the surface as a result of escaping acid ions.

A basic principle for wiring is to route hardwearing cables close to the motion sequence. Thorough system solutions for dynamically durable wiring of imaging devices can involve drag chain structures, abrasion-proof bulkhead receptacles, cable reservoir modules or spring return systems

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Whole breast ultrasound reveals minute cancers in minutes

Built for comfort; created for speed



Mark Stribling is President and CEO of iVu Imaging Corporation. Stribling introduced an innovative approach with Sofia and set up his own start-up company in Texas. Partnering with Hitachi Ltd. In Tokyo, Japan, Stribling could take Sofia to the next level.

The new Sofia 3-D breast ultrasound system solves all the economic and logistic challenges associated with whole-breast ultrasound by using a full-field radial scanning method, the firm reports. The resulting throughput, efficiency, and patient comfort make Sofia an ideal solution for women with dense breasts

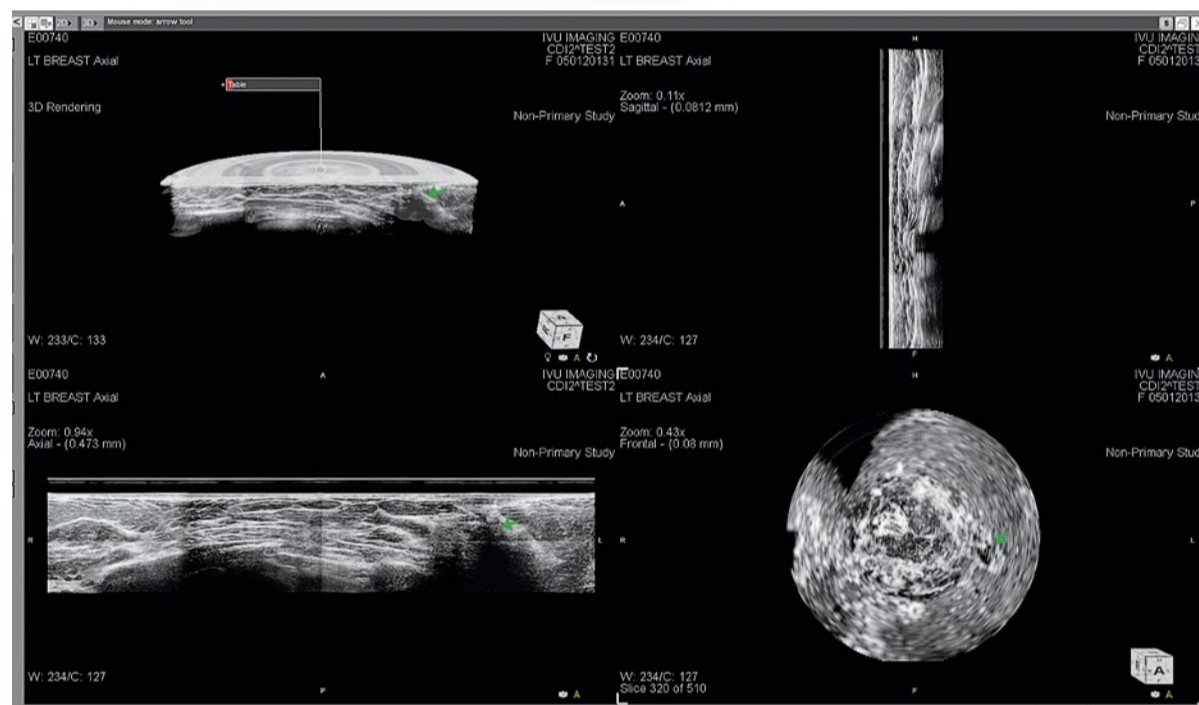
Combining Hitachi's high-end ARIETTA ultrasound with iVu Imaging has resulted in the Sofia 3-D whole breast ultrasound system. 'By consistently finding cancers of five millimetres to one centimetre early enough, we are likely to find they are localised to the breast and pre-metastatic,' explained Mark Stribling, CEO of iVu Imaging Corporation. 'That's the goal, to find these occult cancers by surveying the (dense) breast quickly.'

It is understood that women with dense breast tissue face a four to six times greater risk of developing breast cancer. 'This is a high risk population, and all the literature tells us that conventional mammography is going to miss these tumours for four women in every thousand examined,' he added.

Speed up the process

Yet supplemental ultrasound exams performed manually to detect hidden cancers are time-consuming, and a good outcome for a woman depends heavily on the experience of the operator handling the probe. To solve these clinical challenges, Stribling introduced an innovative approach with Sofia, an examination table that automates the examination and speeds up the process developed in Texas through his start-up company, iVu Imaging Corporation.

Partnering with Hitachi Ltd, in Tokyo, Japan, Stribling could take Sofia to the next level. In September 2016 he introduced 3-D radial acquisition of whole breast images using a long linear transducer (92mm width), which was then linked to the Hitachi's 'Noblus' ultrasound system.



Following the latest development steps, Sofia now also can be operated in conjunction with Hitachi's premium performance Arietta platforms. 'The Arietta platform is the game-changing breakthrough for 3-D whole-breast ultrasound,' Stribling pointed out. 'Hitachi ultrasound now enables the Sofia system to scan eight times faster than our first configuration, while at the same time tripling the resolution.'

A full bilateral exam requires just 10 minutes from the moment a patient enters the exam room until she leaves. As a result, clinics equipped with Sofia can schedule more patients for supplemental imaging per day requiring no additional consumables and no time-

consuming pre-scan preparation. Sofia does not require a room dedicated to whole-breast ultrasound. Instead, the adjustable height table and the Arietta platform create a new multi-use examination room for a wide variety of diagnostic ultrasound exams or interventions.

Confirm findings

Sofia also offers women the most comfortable of any breast exam experience, the firm points out. They lie on a padded table and, unlike suffering the breast compression involved in other devices, the breast is positioned in a recessed cone in the table and then, in a single automated radial sweep of only 30-seconds, a full image is acquired. 'We can present a single breast volume to the radiologist, clearly showing breast structures in their natively-acquired radial plane along with the reconstructed coronal, sagittal, and oblique views if desired,' Stribling said. 'The result is an average interpretation time of about one minute per breast.'

The 900 images Sofia captures are reconstructed into a 3-D volume that looks more like an MRI image than a conventional ultrasound image, yet with the anatomical detail that ultrasound can provide. 'This view gives clinicians the ability to review the exam like a breast tomosynthesis or MRI image that they are familiar with. In fact, all our customers who use MRI for supplemental dense

breast exams also use Sofia for a second look to confirm findings, because of the number of false positives in MRI images,' he added.

The automated acquisition also assures consistent and reproducible results, thereby eliminating the user-dependency of manual breast exams using traditional ultrasound. Because the Sofia is powered by the Hitachi Arietta platform premium ultrasound system, it comes equipped with a host of powerful imaging capabilities. Arietta family's Symphonic Technology optimises data fidelity along the entire signal handling chain, from transducer to display monitor, the company pointed out. The system also dynamically focuses at the pixel level, improving resolution and image uniformity.

'Anything Arietta is capable of doing, the examining clinician can do with Sofia,' explained Stribling, who added that Hitachi engineers are already working with iVu Imaging to bring an innovative capability to Sofia with automated eFlow Doppler scanning and mapping in 3-D.

'Hitachi's eFlow can depict very specific intra-nodular vascularity so that we will not only see abnormal anatomical structures but with the push of a button can provide functional information showing any abnormal vascularity, such as angiogenesis,' Stribling said. 'This new functionality is not very far away.'

Way for ultrasound

Report: Mark Nicholls

It is collaboration could push vascular imaging to a new level. Researchers from the University of Manchester and IVS Ltd (Independent Vascular Services) – an independent UK company providing clinical services and running vascular ultrasound departments for the NHS – is pairing Mindray's Resona 7 with Piur Imaging's tomographic ultrasound device to develop 3-D tomographic ultrasound (tUS) to enhance vascular diagnosis.

The collaboration is underpinned by a €2.6m European Horizon 2020 grant, in a research initiative that Charles McCollum, Professor of Surgery and head of the Academic Surgery Unit in the Institute of Cardiovascular Sciences at the University of Manchester, believes will significantly enhance the imaging of carotid disease as the cause of stroke and advance monitoring and treatment of aortic aneurysms, as well as many other conditions.

Duplex ultrasound imaging, such as that achieved by Resona 7, is already regarded by the team as the first line of investigation for arterial and venous disease throughout the body, apart from the heart and chest arteries.

Safe, pain-free and delivering high quality imaging, it avoids the disadvantages of MR, which can over-estimate the severity of stenosis, or CT with the risk of ionising radiation and nephrotoxic X-ray contrast, Professor McCollum explained.

'For the investigation of carotid disease, varicose veins, deep vein thrombosis, peripheral arterial disease and arterial and venous malformations in the limbs, it can't be bettered,' he added. 'For aortic aneurysm, ultrasound is the way you make the diagnosis. But what we are showing now with 3-D tomographic ultrasound with the Piur Imaging solution, is that it is the best way to measure the aneurysm; for surveillance and to detect endoleaks, or problems after Endovascular Aneurysm Repair.'

'In my view the future is 3-D tomographic ultrasound. It will not be necessary for all applications of colour Doppler, but for quality imaging that a surgeon can interpret, 3-D tomographic ultrasound will be the way forward.'

McCollum added that the 3-D tomographic approach will produce images that a surgeon can look at from every angle, as well as inside the artery, and images he/she can

WHAT IS V-FLOW?

Mindray's new ultrasound system, Resona7, delivers a technology that dynamically visualises blood flow.

Called V-Flow, it displays the fluidity with dynamic arrows indicating the flow process, rather than a series of static images, with both the magnitude and direction of the flow measurable at any location in the vessel, avoiding the inconvenience of angiography.

The platform uses an extremely high frequency yet remains flexible due to the availability of arbitrary beamforming methods. Consequently, multiple image lines are obtained after a single transmission. Continuous Doppler transmission can

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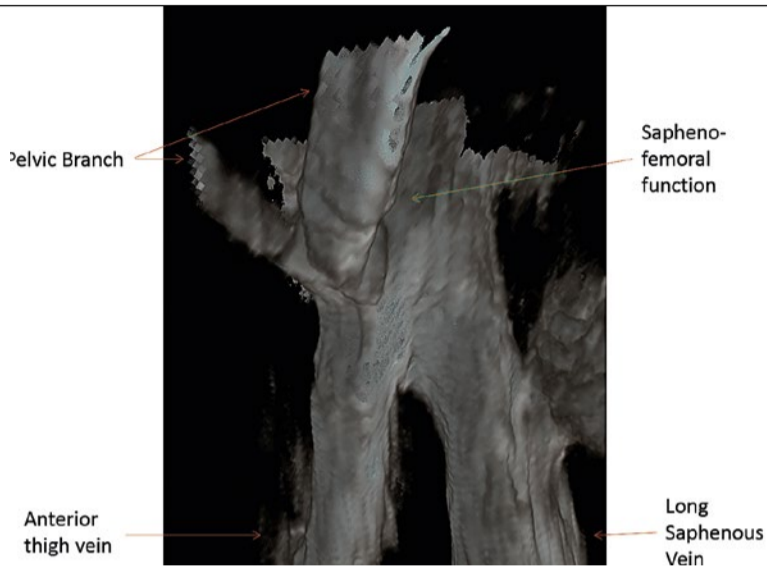
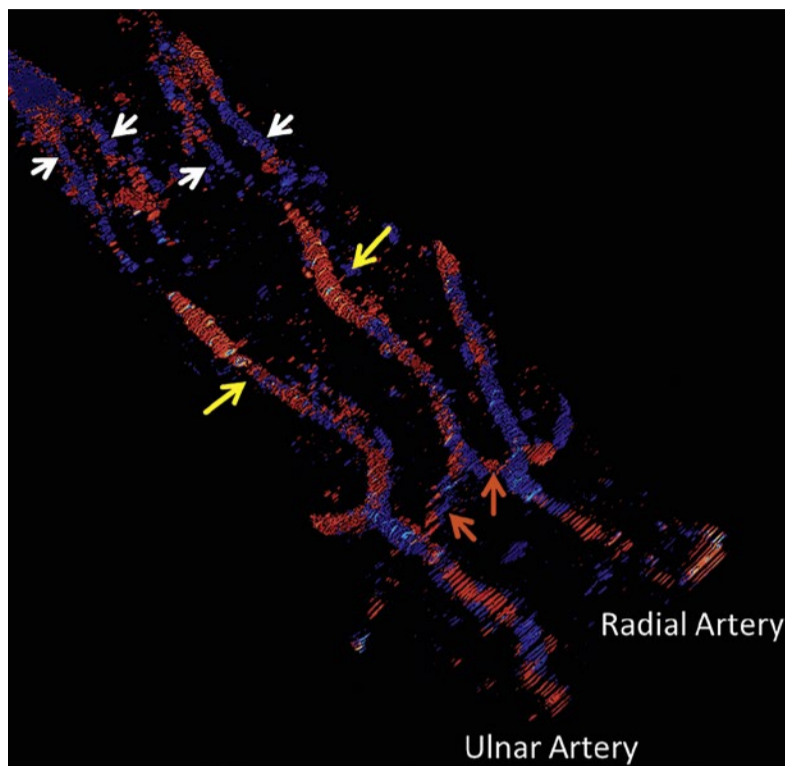
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Delivering a new dimension to vascular imaging

Forward: 3-D tomographic and



Charles McCollum is Professor of Surgery at the University of Manchester and an honorary consultant surgeon at University Hospital of South Manchester, with a tertiary referral practice in carotid artery disease, cerebral perfusion, complex aneurysms and venous disease. Leading a research team of lecturers, fellows, scientists and technicians, his collaborations are with various disciplines including epidemiology, neuro-imaging, dementia services, stroke medicine, cardiology, mathematics, engineering and industry. He has published over 450 papers including 350 on original research.



have confidence in when making surgical decisions.

The greatest impact, he believes, will be in stroke intervention due to evidence suggesting that emboli (elements of thrombus or atherosclerotic material discharged from the plaque and blocking arteries in the brain) are more important in the causation of stroke than stenosis. 'We've found that the volume of plaque is a very important association with stroke symptoms,' he said. 'If the risk of stroke is over 5% then, to detect people with carotid plaques, population screening becomes worthwhile. We can use the Resona 7 tomographic ultrasound solution to measure the

volume of the plaque.'

This is now a major focus for McCollum and team; he also believes that the same combination could increase accuracy in aneurysm screening.

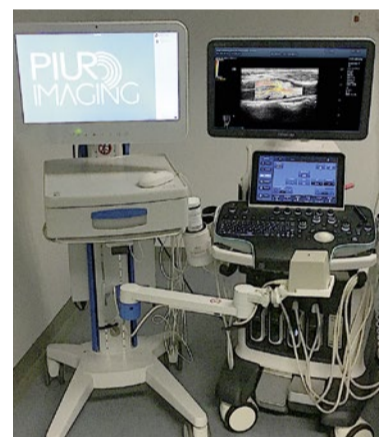
Resona 7 incorporates a novel ultrasound-based technology called V-Flow which can visualise blood flow and, rather than a series of static images, the fluidity will be displayed with dynamic arrows indicating the flow process. McCollum said it is particularly suited to this latest research, especially with high quality images and Mindray's flexibility in responding to clinicians' needs in developing the equipment and associated techniques.

In addition, with IVS performing more than 80,000 vascular ultrasound investigations a year, there is demand for robust and reliable equipment to achieve such high volume.

'It needs to have excellent image quality and a very good user interface; that's why we chose Mindray Resona 7,' explained Steven Rogers, an academic clinician with IVS. Piur Imaging provides the tomographic ultrasound device that couples to the Resona 7 to produce the tomographic ultrasound images.'

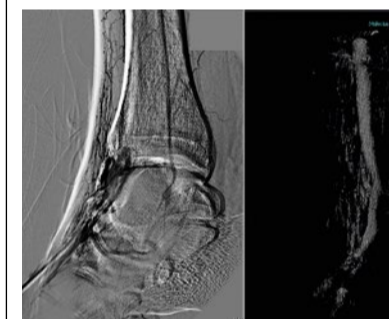
There are four key research areas the team aims to advance tomographic ultrasound use in the vascular surgical market in addition to aortic aneurysms: carotid plaque volume for plaque vulnerability in the prevention of stroke; arteriovenous fistula for haemodialysis access; vein mapping for cardiac and vascular bypass; tomographic ultrasound angiography to produce angiogram-like images for planning peripheral arterial disease surgery.

'For certain aspects at present, previous ultrasound was not good enough to make a surgical decision, which means surgeons have to rely on traditional forms of angiography, whether CT, MR or catheter angiogra-



phy,' Rogers said. 'Finding an imaging modality that allows us to make surgical decisions, that does not involve radiation and nephrotoxic contrast media, is of the utmost importance to the European market and would save the European economic area a significant amount of money each year.'

'That's what we are trying to achieve with the Resona 7 tomographic ultrasound solution. Effectively, it will use both devices to replace angiography as the next step in vascular surgical planning.' Being able to view the vascular system in the 3-D, he pointed out, opens up new ways of measuring, monitoring and assessing a range of diseases.



Steven Rogers is an academic clinician, providing clinical services for IVS and conducting 3-D ultrasound research using Piur Imaging equipment and Mindray's Resona 7. As a senior clinical vascular scientist and research associate, his research interests include 3-D ultrasound within vascular surgery focus on carotid disease, aortic aneurysms, peripheral arterial disease and venous disease. At the Vascular Societies' Annual Scientific Meeting 2016, Rogers was awarded the Ann Donald Scientist of the Year Award and a prize for Best Proffered Paper for his presentation on Tomographic 3-D Ultrasound on peripheral arterial disease.

be achieved, avoiding a transient state, enabling continuous filtering for removing clutter. To derive the direction of flow velocity, multi-directional transmissions and receptions are employed. A true velocity with accurate direction calculated via angle-compounding technology, shows an example where compounding and regression analysis of two angles is applied giving more angles. This is supported by innovative display technology with colour arrows. Clinical results have already shown that this new method gives much more detail with different types of flow in the carotid artery, compared to conventional ultrasound colour flow mapping (CFM).

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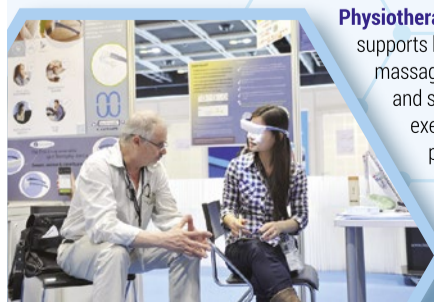
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Training in radiography and medical technology is mainly academic

ECR significantly expands radiographers program

Report: Sylvia Schulz

The job title radiographer has a firm place in many European and non-European countries. The academic training reflects the complex range of responsibilities the role entails. Michaela Rosenblattl M.Ed, who heads the radiology degree course program at the University of Applied Sciences in Wiener Neustadt, Vienna, reports on the Austrian situation. As president of the Austrian Society of Radiological Technologists (rtAustria), a founder member of the European Federation of Radiographer Societies (EFRS), also presents a European perspective.

Since 1960, Austrian training for this profession used to require students to have passed their Matura (equivalent to A-levels), Rosenblattl explains. In those days, training

centres were mostly affiliated to hospitals. The Bologna Process, a pan-European harmonisation of degree courses and degrees and trans-national academic reform, aiming to achieve international mobility for students, accelerated further developments. In 2004 the title 'radiographer' was officially introduced (in Austria) and, in 2005, training was integrated into the universities for applied sciences. The degree course is now available at seven of these universities across Austria.

Radiology department assistants can perform less challenging radiological tasks, requiring fewer qualifications. They work closely with radiographers and are only allowed to carry out certain procedures, such as bone density measurements and mammograms. Radiographers are on a level with doctors. 'Doctors can avail themselves of our competen-

cies. Since 2004 they have been entitled to administer contrast media and, since 2012 they have also been able to administer radiopharmaceuticals. 'Dosage calculation has always been part of our duties. The application is obviously always carried out in agreement with doctors, with the degree of risk governing the intensity of this cooperation. It is important that doctors are available in case of any incidents,' explains Rosenblattl.

Accordingly, radiographers in Austria have extensive competen-



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Training for radiographers is academically based in almost all European countries, Rosenblattl points out. Only Germany and Spain lag behind, with the latter now making amends. 'I don't understand why things should be so difficult in Germany of all countries,' she observes. In many non-European countries, including Australia, training is also organised on an academic level. 'This is even the case in Nigeria, with an entire institute being managed by a radiographer.'

The academic training is demanding because the course includes physics, technology and IT. But even those without A-levels can enrol, as long as they pass the additional examinations required. 'The permeability of our education system is quite high and we put this principle into practice,' Rosenblattl explains. Training also continues to be important once graduates have completed the course and work in the profession, because radiology is a very innovative field, both from a medical and a technological perspective. 'Our organisation also offers its own programs to promote further training.' More importantly, an exchange across national borders is

What's best for a radiographer: the clinic or industry?

You can't compare an apple with an orange

Usually radiographers work in a clinical environment, are specialised in CT, MR or ultrasound and take care of patients and their treatment. Not so Patrick Doherty, Siemens Healthcare Regional Business Manager, Dublin undergraduate who worked in a University Hospital for five years before switching to work within the healthcare industry. Conclusion? 'It's a daily challenge,' he confirms. In the ECR's Rising Star Session he describes 'Working in the industry'. Earlier, he outlined his experiences for European Hospital.

Report: Marcel Rasch

Asked why there no standardised education for radiographers in

Europe, Siemens Healthcare Regional Business Manager Patrick Doherty pointed out that, for a start, countries

use a different term for radiographers – e.g. radiological technicians. 'In European countries the educational

approach for radiographers and radiological technicians differ very considerably,' he added. 'There appears to be no established standard yet and indeed it seems to be difficult to agree on an educational standard.'

'I did my undergraduate degree in Dublin – on a four-year undergraduate degree program – the only one in Ireland for diagnostic radiography. 'In the United Kingdom there is a three-year undergraduate program, but this can vary based on content. And in other countries, such as the USA, where they call radiological technicians MTAs, one undergoes an educational diploma in a particular area of a radiologi-

cal department, for example general X-ray scanning, and this is what they do after examination, all day, every day – general X-ray scanning. Whereas the undergraduate degree that I took was a broad-based degree, covering all the imaging modalities and topics, so that we were essentially able to go into the departments fully qualified.'

What opportunities are there when working in the industry?

'When I started to work in the industry, I went into direct sales, for a local Irish medical distributor, selling an array of products. That was real learning by doing and a quick immersion into the world of sales and being nimble and entrepreneurial. It broadened my perspective because it was a hard challenge for this small distributor to compete in an environment where all the big companies, like GE, Siemens, Philips and the national big players as well, are placed. For me it was a big learning curve, having gone from the clinical environment and essentially being a customer to now seeing the industrial view.'

'Back to your question: typically radiographers who work for companies such as Siemens are specialised in a certain area. When the company sells an MRI Scanner, for example, the radiologist or radiographer explains how to use it and how to interact with the system. That would be the first step of I would say 75 percent of radiographers going into industry. The advantage is that you start with a lot of the tasks you would have done in your clinical work routine. From there you can develop into different areas.'

What are the benefits of working in the industry?

'It's a different approach. Working in a hospital is a busy, hectic job with all the subjects you have to address from patient to paper work. Working in the industry is a different challenge. There are pros and cons in each role.'

'In the industry I miss, on one hand, the clinical interaction with patients but, on the other hand, it opened my eyes to the complexity of what the companies and the industry

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Patient management and care alongside technical ability

The role of a radiography assistant



Michaela Rosenblattl M.Ed heads the radiology degree course program at the University of Applied Sciences in Wiener Neustadt, Vienna, and is president of the Austrian Society of Radiological Technologists (rtaustralia).

welcome. As mentioned, Rtaustria is a founder member of the European Federation of Radiographer Societies (EFRS). The EFRS represents more than 100,000 radiographers in member organisations across Europe and supports the ECR, which hosts the Educational Wing Annual Meeting with an integrated program for students of radiography. 'The ECR is important for exchange amongst our members,' Rosenblattl points out. 'We are pleased that the program for radiographers has been significantly expanded this year.'



Patrick Doherty is Regional Business Manager Western Europe and Africa at the Advanced Therapies department at Siemens Healthineers in Forchheim, Germany. He gained his radiography undergraduate and master's degrees at University of Dublin School of Medicine, Ireland

is trying to do for our patients to make clinical decisions faster, easier and more comprehensive. Having been on the clinical side I can appreciate quicker what already has been achieved by the industry. You cannot compare the clinical to the industrial environment. This is like comparing an apple with an orange.

'My personal message about the advantages and disadvantages of working in the industry is a very realistic one. There exists a perception in the clinical environment that people in industry have a good life, because they may receive benefits like a company car, bonuses, and the company supports you very well. Yes, that's right. However, the industry is, in fact, a tough environment; it's challenging. For example you might not have to work a night on call but the working days are typically longer than those in the clinical world

'The step to change from a clinical environment to industry should not be undertaken just because you want a company car. It sounds great to travel the world, go to conferences and events, and those are elements of the job that you can have. But, I would encourage the thinking that these are the primary benefits of working in the industry.

'There is a high application rate of clinical based people who want to go into industry, with the majority staying in their original position for only about three years, before they either return to the clinical environment or move within the company. That's what I have seen personally.'

'Breathe in. Hold your breath. Then we press the button' – the times when this brief summation could be made about a radiography department assistant's (RDA) work are long gone. As an imaging support worker, the radiology assistant helps qualified radiographers with procedures such as biopsies, and also performs clerical tasks, such as handling appointments.

With rapid technological and innovative advances in radiology, plus transformation of the field, this assisting role has developed increasing importance and is now an essential part of the smooth operation of radiology, nuclear medicine, radiotherapy and medical physics. Responsibilities in radiology are manifold, needing a multi-talented approach.

An RDA's tasks fall into three main areas: logistics, management and examination. They manage patients from admission to discharge, acting as a constant contact for reassurance



and information during radiology department visits, as well as transporting patients between wards and departments.

Radiology assistants also help to maintain image processing systems

and accessory equipment and report on faulty equipment.

They assist the radiographer in logistics, such as the management of materials needed for the radiological process. Some have a huge degree of responsibility being, for example, authorised to order materials costing as much as a luxury car.

An RDA also needs concentration and precision to help perform the rising numbers of complex examinations and interventional procedures. Incorrect or incorrectly processed images lead to wrong diagnoses, or more work if the formatting must be redone – losing time and costing more. In other words, the quality of a radiography assistant's work can underpin fast, precise diagnosis.

Last but not least, good teamwork is a vital prerequisite for any successful radiography assistant, by relating well with radiology department colleagues, physicians, nurses, auxiliaries, porters and all others involved in patients' welfare.



Claus Becker qualified as a radiography assistant at the Training College for Radiography Assistants in Grosshadern, Munich in 1997 and launched his career in the Radiology Department at Regensburg University Hospital. In 2011-12 he completed further training in Esslingen, qualifying him to teach prospective radiography assistants. In 2006 Becker was appointed senior radiography assistant at Regensburg. He has also chaired the Board at the Association for the Medical Technical Professions (VMTB), since May 2015.

Reviewer workshop

Interested in publishing your work or reviewing for a journal? Attending ECR in Vienna this March? Join the Radiography Editorial Team for an interactive and informative author or reviewer workshop. Saturday 4th of March, 16:30 - 17:30

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Julie Nightingale; Salford/UK

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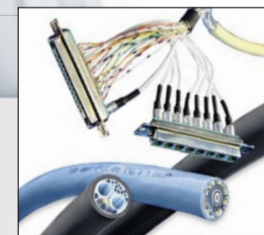
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Radiographer calls for increased cooperation with radiologists

By Mélanie Rouger

The increased demand for imaging studies and workforce shortages have put strain on radiology services while technological advances enabled other medical disciplines to perform their own imaging examinations. To hold their ground, radiologists and radiographers must work together and develop common strategies, an expert will argue during a dedicated professional challenges session organized by the European Federation of Radiographers Societies (EFRS) and the European Society of Radiology (ESR) at ECR 2017.

"Workforce shortages, workload increase, workplace changes, new technologies and budget challenges put quality of medical imaging and radiology at risk," Dr. Graciano Paulo, professor of Medical Imaging & Radiotherapy at Coimbra Health School in Portugal, said.

Assessing opportunities and challenges facing radiography and radiology has become mandatory because medical imaging is being taken over by other specialists, Paulo, co-founder of the EFRS, explained.

"While the number medical imag-

ing procedures has risen sharply over the past fifteen years, there is evidence of a shortage in the number of radiologists and radiographers. This can only mean that the imaging procedures are being fragmented and slowly being taken by others. Cardiologists, orthopedists and many other specialists now perform their own interventional procedures and imaging investigations. Technology is becoming more available, smaller and easier to use, so the boundaries of the profession are disappearing," he said.

Many experts agree that radiologists need to have more contact with patients and within the clinical team to secure their position.

One solution would be to delegate part of their workload to radiographers, Paulo suggested.

"Training an advanced-practice radiographer to work in close cooperation with a radiologist would enhance patient care and increase the visibility of the radiologist. The radiologist would have more time to do clinical work and interact with patients and his peers instead of sitting behind his/her screen filling reports," he said.

In some countries like the UK,

where the number exams is increasing every year, radiographers already fill in the imaging report for plain x-ray examinations and in close cooperation with the radiologist.

The radiographer has a special position in the imaging chain, and this role could benefit both the patient and the radiologist, according to Paulo.

"The radiographers are gatekeepers to radiological equipment and act as real pivots between referrers, patients and radiologists. Allowing and improving skill mix and joint guidance between the two professions can give the radiologist more time to do clinical work and meet the patient," he said.

Radiology, an increasingly deserted specialty, would become more attractive in return; similarly, more young people would decide to become radiographers if training included disease knowledge, Paulo believes.

"If we manage to bring the two professions together towards a new paradigm in the way we provide service to the patient, this will increase professional satisfaction of both radiologists and radiographers and make both professions more

attractive," he said. Radiographers education and training programs level across Europe should be harmonized, and include a minimum European Qualification framework (EQF) level 6 of Knowledge, Skills and Competences (KSC) and a 240 ECTS program. Some countries are currently lagging behind.

"In Spain, the radiographer profession has one of the lowest qualifications in the world. It's not a university degree and training lasts only two years. Almost everywhere else, radiographers must train four years (240 ECTS). Many Spanish radiographers are actually training in Portugal to have their skills recognized internationally. So we are currently working on convincing the Spanish government of the necessity of training radiographers more appropriately," he said.

Besides, imaging services need to use a common coding system across Europe to make sure they are comparing the same type of data, regardless of the country or institution. Departments should also adopt workflow performance metrics, clinical indication oriented protocols, audit and accreditation systems, Paulo recommended.



Graciano Paulo is a full time professor of medical imaging & radiotherapy and vice president of IPC-Escola Superior de Tecnologia da Saúde in Coimbra, Portugal. He is a co-founder and past president of the European Federation of Radiographers Societies (EFRS). Dr. Paulo has a bachelor's degree in radiography, a master's degree in health economics, and a PhD in health sciences. His main area of research is radiation protection.

"With these pillars, we would be able to increase the visibility and recognition of radiology in health-care systems. But we can only do this together in Europe," he said.

In the end, the future of medical imaging will depend on both professions' capability of working as a team, based on roles and responsibilities, bearing in mind that the patient should be always in the center of the process, with a holistic approach, he added.

"We should be proactive in finding a solution because when we want to be reactive, at that point, it will be too late."

Pivotal role in patient care for radiographers

By Mark Nicholls

Delivering consistent levels of education and training throughout Europe remains an important challenge as radiographers play an increasingly pivotal role in patient care and patient safety.

As the European Congress of Radiology in Vienna prepares to hold a record number of sessions

for radiographers, including many focused on the evolving roles of radiographers, Dr Jonathan McNulty, vice president of the European Federation of Radiographer Societies (EFRS), believes that delivering Europe-wide levels of education, qualification and training for radiographers is critical in raising standards of care, diagnostics, therapeutics and patient safety. He

acknowledged that, whilst radiographers in Europe are generally well educated, and often trained to masters or doctoral level, access to bachelor degree level training in some countries is still limited.

"In Europe, the quality of imaging services is generally good, however, there are some discrepancies so an important body of work at European level is to try to work with radiographers, national societies and education institutions to enhance the education and training of radiographers," McNulty added.

ECR 2017 has a strong education and scientific program for radiographers, including a number of sessions delivered with partner organisations and, this year, ECR is recognised as the official congress of the EFRS for medical imaging.

There are sessions looking at professional challenges, patient safety and refresher courses across all specialist areas of radiography.

McNulty, from the School of Medicine at University College Dublin, also stressed the importance of using the skills of radiographers to their full potential. "There remain issues in countries around Europe where the knowledge and skills of radiographers are somewhat under-utilised at a time when there are huge opportunities for radiographers to play a more significant role in medical imaging and radiology."

However, while radiographers have been viewed as technicians in some nations, in others their role has advanced significantly with their increasing knowledge, experience and responsibility with some working as advanced practitioners or the equivalent of consultant radiographers.

"It's not just about giving more opportunities to radiographers," he

continued, "but there's a very good evidence base showing that when radiographers are used more effectively - when challenged and allowed to take more advanced roles - there can be improved patients outcomes as well, so there is a big benefit to the patient from better utilising the workforce across Europe."

The European Society of Radiology and EFRS have a Memorandum of Understanding as a blueprint for greater collaboration at a time that radiographers are playing these ever greater roles in radiology services.

"Radiographers are a key piece in the jigsaw, which makes for a modern state-of-the-art diagnostic or therapeutic service being provided by radiology departments," he said.

"It is essential that radiographers are the experts in terms of the technology that is at the heart of a modern radiology department and radiographers have the key role to play in optimising the use of that technology.

"An equally essential role - that people can often overlook - is that radiographers work closely with their patients. They interact with them on a daily basis and have an important role to play in patient care and patient safety in a modern imaging department.

"If it is an imaging modality using ionising radiation, they make sure the radiation dose to the patient is minimised. From being seen as a technician, they need to be seen as the expert in that area who can really get the most out of the technology and play that important role in patient care, patient management and in a safe way as well."

What is also important, he added, is that radiographers - whether diagnostic or therapeutic radiographers - must work to raise the identity and profile of their profession among the public and other members of the health service."



Dr Jonathan McNulty is an Assistant Professor and Head of Subject, Radiography, in the School of Medicine, University College Dublin, Ireland where he oversees the BSc Radiography programme along with over 20 postgraduate programmes and as a University Fellow in Teaching and Academic Development, he has led University-wide educational research projects. Since 2014 he has sat on the Board of the European Federation of Radiographer Societies (EFRS) and is currently Vice-President of the EFRS. Having delivered more than 100 conference presentations and contributed to over 50 journal articles, he has held significant national and international research grants. His research interests include medical and healthcare education, optimisation and benefit-risk communication, neuroimaging and image perception.

McNulty said a team approach and closer collaboration with other health professionals remained important in terms of achieving patient safety and the best clinical outcomes. McNulty is presenting a session, looking at the challenges in education and training and implementing the theory of patient safety into clinical practice.

He said a challenge lay in achieving agreement on the scope of patient safety within radiology.

"A message I'd like to get across at ECR is to make people reflect more on what we are doing in our educational programmes, in clinical practice, and to identify patient safety-related deficits which may exist and what steps we might be able to take to try and address some of those areas."

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Lab medicine in Norway, Serbia and France

Laboratory medicine delivery, regulation and accreditation vary between countries, e.g. Norway, Serbia and France recently aired at FiLM 2017. Leading figures explained the shape, scope and funding of healthcare and lab services and roles played by different professionals and challenges they face, Mark Nicholls reports.

Norway – Professor Sverre Sandberg spoke about this sparsely populated country of five million people, with healthcare systems arranged to meet those needs.

Laboratory medicine is funded and shaped with services to meet the demands of 80 hospitals, four medical universities, 4,000-5,000 general practitioners (GPs), four health regions, care homes and nursing homes, military installations and oil platforms.

Sandberg, who directs NOKLUS (see profile) and is a University of Bergen professor, said the government funds the healthcare systems and laboratory medicine but Norwegians increasingly have health insurance.

In terms of lab services, most hospitals have laboratories, and also take samples from GPs and nursing homes.

Public laboratories receive a basic reimbursement from hospitals and some have an internal reimbursement system paid by clinical departments.

The government reimburses services for GPs; negotiations continue for reimbursement for tests in hospitals. The government reimburses one major private lab, depending on whether it's a simple or complicated analysis.

GP surgeries perform a basic repertoire of tests (Hb glucose, urine strips, HCG), with specific reimbursement negotiated annually; lab

med participates in the negotiations.

Sandberg said all data is closely monitored, with evidence collected on numbers of samples, though variation exists between health regions. Key to this, and monitoring costs, is an open dialogue with clinicians, he said. 'We want to maintain that close contact, regular discussions over the number and type of tests, so we can provide evidence about laboratory testing.'

With demands to cut the budget, he said services must become more effective and, 'The best way to cut down requesting by clinicians is by talking to them regularly'.

Norway's laboratory medicine



As a counsellor for public health at the Fédération Hospitalière de France (FHF), **Bernard Gouget** monitors national public hospital programmes involving, for example, health and safety. He was assistant professor at University Hospital, Paris-Descartes, a member of the steering committee overseeing medical laboratories reform and is a medical biology expert for the EU.



Snezana Jovicic heads the Clinical Laboratory for Cardiac, Vascular and Endovascular Surgery, Cardiology and Pacemakers, at the Centre for Medical Biochemistry, Clinical Centre of Serbia. She teaches at the Medical Biochemistry Department, in the Pharmacy Faculty, University of Belgrade and is an Executive Board Member for Serbia's Society of Medical Biochemists.

involves microbiology, immunology, genetics, pathology and medical biochemistry with 300-400 lab specialists, 4000-5000 medical technologists, IT staff and a small number of biochemists and scientists. 'Twenty years ago, medical doctors led hospital laboratories; now all but one has a medical technologist as director.'

While they have logistics and technical skills, the biggest challenge is professional knowledge to lead the sector effectively in the future, he added.

POC testing is a key element of Norway's laboratory medicine, with NOKLUS established for delivery and monitoring by advising what should be analysed and where, ensuring correct results, supporting, advising on problems, equipment, education and e-learning courses.

NOKLUS has 2,990 participants in GP offices and nursing homes, is expanding to homecare, and covers 21 military installations and 50 oil

platforms, visiting 50-60% of them annually. With 22 Norwegian locations and main centre in Bergen, it is important to Norway's lab services, given the country's demographics. Healthcare takes 9.6% of the gross national budget.

Serbia has a seven million population, 161 community health centres, 41 general hospitals and 35 specialist hospitals, 37,500 hospital beds, 10% of GDP spent on healthcare – funded via citizens' contributions to mandatory health insurance, alongside state financing for those not in the mandatory system, such as the unemployed, refugees, and welfare recipients.

Dr Snezana Jovicic, Head of the Clinical Laboratory for Cardiac, Vascular and Endovascular Surgery, Cardiology clinics and Pacemakers, in the Serbian Centre for Medical Biochemistry, explained that laboratory medicine covers biochemistry, laboratory haematology, microbiology, immunology, immunohaematology, toxicology, cytogenetics and molecular genetics, tissue typing and histopathology.

Clear guidelines and strong education cover the sector, e.g. through the Medical Biochemistry Unit at the Pharmacy Faculty, University of Belgrade.

Serbia has many medical biochemistry labs, including 261 state laboratories and 193 private laboratories, with 295 medical biochemists, 227 medical biochemistry specialists and 276 clinical biochemistry specialists. 'Medical biochemistry laboratories are organised according to the healthcare level – primary, secondary and tertiary – and according to the guidelines for Providing Healthcare,' Jovicic said.

The Serbian Society also aims to unite its specialists to promote and develop all branches of medical bio-



Sverre Sandberg directs the Norwegian quality improvement of primary care laboratories (NOKLUS) and the Norwegian Porphyria Centre (NAPOS) and is a University of Bergen professor. He has chaired the Committee on Evidence-Based Laboratory Medicine; published 240+ peer reviewed papers and is President of the European Federation of Clinical Chemistry and Laboratory Medicine.

chemistry in healthcare provision. 'It aims to achieve uniform work standards in clinical biochemistry laboratories and provide continuous education for all medical biochemists at all academic levels. Professional interests are ensured through the Chamber of Biochemists of Serbia,' Jovicic said.

Laboratories and services activities are clearly defined, with all stages of work subject to standardisation by the implementation of a Total Quality Management System (TQM) – plus external quality control – and an accreditation body.

As with other countries, pressure to save money continues, with service users cutting budgets yet wanting the same levels of service and numbers of tests, she said.

France – Over recent years, medical biology has been reformed, aiming to enhance 'medicalisation' of the profession; harmonising public/private practice, and to ensure medical biology tests quality by implementing mandatory accreditation.

The country has 10,442 medical biologists (2,975 medical doctors and 7,467 pharmacists) medical

Continued on page 24

This is the era when tests must have proven consequences

Facing up to many new challenges

Medical laboratories must be pro-active if they are to meet the new challenges being presented to the sector globally, according to Dr William Morice from the renowned Mayo Clinic in America.

Report: Mark Nicholls

With clinical laboratory medicine providers facing a number of challenges across various health systems and countries, Morice offered a USA perspective from his role as Professor and Chair of the Department of Laboratory Medicine and Pathology at the Mayo Clinic and President of Mayo Medical Laboratories.

In his presentation – *Leadership challenges for laboratory medicine* – delivered during the Frontiers in Laboratory Medicine conference FiLM 2017, held in Birmingham, UK, he suggested laboratories need to reach out to partners, offering their knowledge to a wider sphere, and also seek to exert influence if they are to take a leadership, rather than a 'back-office', role.

He was speaking as clinical laboratory medicine service providers face 'interesting and challenging' times ahead, against a backdrop of ris-

ing demand, falling reimbursement, technological innovation, enhanced quality and governance, and the need to recruit and retain a skilled workforce.

He looked at how the changing USA's healthcare environment was impacting on the Mayo Clinic and Mayo Medical Laboratories.

Laboratories have seen rapid growth, but there have been utilisation issues, a drive to decrease spending and then a need to look at the consolidation of lab activity in the United States.

Further uncertainties loom with the FDA proposing a 'risk-based' classification system for laboratory-developed tests and the as yet unknown changes that might arrive under the very new Presidency of Donald Trump.

Morice told delegates that, within the laboratory medicine sector globally, there was often not enough money available to pay for health-

care – even in countries such as China – at a time that the profession faces market disruption.

Earlier, the FiLM 2017 delegates had heard from senior figures in the UK's pathology, biomedical sciences and clinical biochemistry sectors about changing demands on services within the National Health Service (NHS) against a continuing backdrop of needing to reduce costs and make financial saving through service reconfiguration.

Mayo Clinic's Department of Laboratory Medicine is part of an integrated practice with 10 divisions and 63 labs, providing the full gamut of care for patients, with some 24 million tests performed last year by Mayo's labs.

One of the biggest challenges, he said, lay in the sector looking to exert its influence and leadership at a time that some were viewing it as a 'back-office' function. 'When I took the job, we were not seen as an integral part of our practice care activities, although laboratory testing,' he said, 'provides a significant proportion of Mayo Clinic's top line

and bottom line revenue.'

Morice acknowledged that Mayo Clinic has been seen as 'unique and singular' in the past, in terms of US healthcare provision. 'But the way we responded, and to survive,' he explained, 'is that we have built bridges and collaborations; we have started to work with the diagnostic and insurance companies – we strive to become part of the solution process.'

The big change, he pointed out, is in shifting away from the fee-for-service environment towards value-based healthcare and that labs were now in the era where tests must have proven consequences – if they are to be paid for – with consumer choice of laboratories driven by cost transparency.

However, he added: 'We also know that, at times, the cost of not doing the test is more than the cost of doing the test in terms of the overall care cost for patients.'

Morice emphasised how lab managers can use data to shape patient care and drive down costs. 'If we make the right test, we will deflect away from other tests and save money – by using lab data correctly to drive patient care,' he added.

Mayo labs are engaging with partners – particularly in IT and other areas of healthcare areas – applying knowledge into the systems of partner organisations, and bringing money back into the already finan-



Dr William Morice is chair of the Department of Laboratory Medicine and Pathology at the Mayo Clinic, Rochester, USA, and President of Mayo Medical Laboratories. A graduate of Mayo Medical School (1987-1994), he was previously Chair of the Division of Haematopathology at Mayo. His research interests include Lymphoproliferative disorders of cytotoxic T-cells and natural killer (NK) cells and the laboratory evaluation and diagnosis of plasma cell proliferative disorders and B-cell disorders with plasmacytic differentiation.

cially-strong department, which uses its returns to support the research and education mission of Mayo Clinic, a non-profit entity.

'We have moved to a period of frequent change, particularly with next generation sequencing, and we have to be much more proactive about understanding what is happening in our environment and then participating in it from a leadership perspective,' Morice concluded. 'We have to get people engaged so we feel we are driving some of the change, rather than just responding to it.'

Circulating biomarkers – the great white hope of liquid biopsy

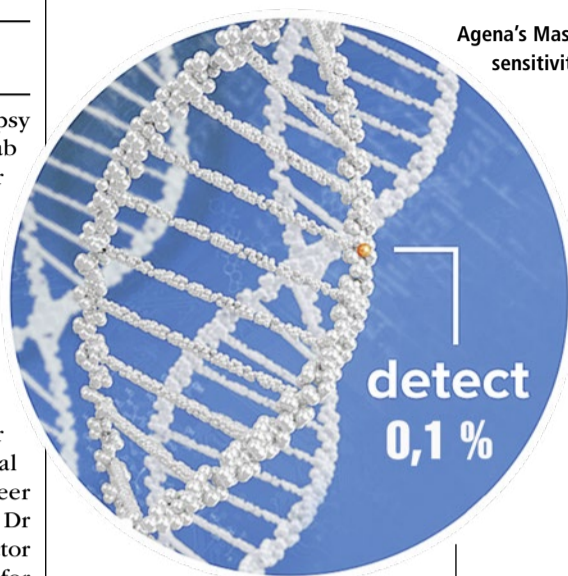
Walter Depner and
Daniela Zimmermann

About six years ago, liquid biopsy appeared on the diagnostic lab stage. Last December, a seminar offered by Agena Bioscience in Frankfurt, Germany, was set to explore the enormous potential of this new technique for oncology. European Hospital talked about the promise of liquid biopsy – and about its risks – with Professor Dr Klaus Pantel, Director of the Institute of Tumour Biology at University Hospital Hamburg-Eppendorf, a pioneer in liquid biopsy, and Professor Dr Jörg Kriegsmann, Medical Director at the Medical Service Center for Histology, Cytology and Molecular Diagnostics, Trier, Germany.

Liquid biopsy is a blood sample used to detect, characterize and monitor cancer non-invasively. A growing tumour always sheds dead cells containing DNA and releases them into body fluids. Once in the bloodstream, this circulating so-called cell-free DNA (cfDNA) can be isolated and amplified with PCR (polymerase chain reaction) and analysed with new molecular methods such as Next Generation Sequencing (NGS) or Agena's Mass ARRAY technology which is based on Matrix-assisted laser desorption/ionisation Time-of-flight (MALDI-TOF). While the fact that tumour cell fragments float in the blood has been known since the 1990s, modern genome analysis methods are required to exploit the potential of liquid biopsy and make this diagnostic procedure available for oncology.

In current cancer diagnostics tissue biopsy is the gold standard, albeit it has a major drawback: invasive sampling is risky for the patient. Moreover, certain regions, such as the brain or the lungs, are difficult to access with a biopsy needle and the interventions cannot easily and immediately be repeated. Liquid biopsy samples of circulating tumour cells (CTC) or circulating cell-free tumour DNA (cfDNA) in the blood are easy to obtain, and after thorough validation, can complement the invasive tissues biopsy.

Professor Pantel explains the hopes and objectives associated with liquid biopsy: "In oncology, our major aim is to detect a tumour as early as possible since early



Agena's MassARRAY has a sensitivity of 0.1%.

detection immensely increases the chances to cure the cancer. What we envision in fact is screening every person from a certain age for all major tumour types in order to be able to react quickly. Furthermore we are interested in issues such as cancer progression and the development of metastases."

For Professor Pantel's oncology team, as for research teams in many other clinical disciplines, therapy monitoring plays a crucial role. Cancer therapies are stressful for the patient and incredibly expensive; patients as well as the healthcare system would benefit from discontinuing unsuccessful treatments. Research on therapeutic response includes the precise identification of the target groups for certain therapies and aims to obtain insights into resistance mechanisms – where and in which patients do they develop?

In view of these objectives R&D today is looking for liquid biopsy tests with a broad range of applications. First-generation tests are commercially available and are being used successfully. But Professor Pantel warns of exaggerated optimism. He is sure it will take a while before the "ideal" blood test is found: "We have to aim for particularly high specificity because the older we get the more mutations our cells develop. Most of them are entirely harmless and won't lead to cancer, even when they are found on tumour cells. False-positives are especially vicious as they mean we see indications of cancer cells where there is no reason for concern. At the same time certain tumour types cannot yet be identified with the minute traces we find."

Professor Kriegsmann focused his presentation on cell-free tumour DNA (cfDNA). The concentration of cfDNA in cell fragments is increased in the presence of certain diseases, including certain types of some cancer. Thus, cfDNA is used as a diagnostic biomarker.

Tumour composition is heterogeneous. This is why a standard tissue biopsy cannot detect aggressive tumour clones. Liquid biopsy finds DNA molecules of the entire tumour. It might thus be a valuable complement of tissues biopsy. cfDNA also provides important information in prenatal diagnostics, in transplant medicine and with regard to autoimmune diseases.

Today, says Professor Kriegsmann, NGS has become part of the stand-

ard workup in mutation analyses. The Mass ARRAY technology, however is a sensitive and cost-effective alternative to NGS in complex analyses of clinically relevant mutations. With its high sensitivity, robustness and quick availability of final this method is very well suited for clinical practice. In addition, it is easy to perform and requires little "hands-on time" compared to NGS.

At the seminar, Professor Kriegsmann presented impressive images to illustrate the progress that has been achieved in the field. But he also addressed the problems and limitations of liquid biopsy, for example when "false readings" can happen. Promising studies demonstrated the ability of liquid biopsy to quickly and reliably detect resistance mutation in lung cancer. Liquid



Benchtop MassARRAY mass spectrometry system identify somatic mutations using single base extension with mass distinction of extended primers.

biopsy further provides sensitive and fast analysis of KRAS and BRAF mutations which in turn allows the

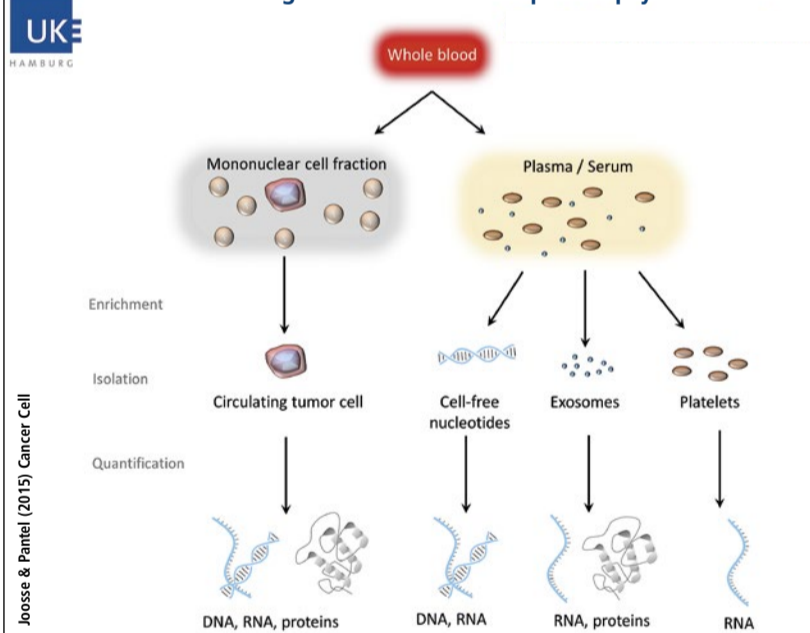


Prof Klaus Pantel is Chairman of the Institute of Tumour Biology at the University Medical Center Hamburg-Eppendorf. The institute is part of the Centre of Experimental Medicine and the University Cancer Center Hamburg (UCCH). The pioneering work of Prof Pantel in the field of cancer micrometastasis, circulating tumor cells and circulating nucleic acids (ctDNA, microRNAs) is reflected by more than 400 publications in excellent high ranking biomedical and scientific journals. Moreover, Prof Pantel coordinates the European TRANSCAN group "CTC-SCAN", the European IMI consortium CANCER-ID (www.cancer-id.eu) on blood-based "Liquid Biopsies" and serves on the Editorial Boards of international cancer journals (e.g., Clin. Cancer Res., Breast Cancer Res., Cancer Res.).

design of individualised therapies for patients with colorectal cancer.

"The availability of a new and highly sensitive DNA analysis method enables oncology researchers to chart entirely new analytic territory. Liquid biopsy, particularly when used to detect cfDNA, shows immense potential to complement the diagnosis of primary tumours. Today there is no standardized comprehensive quality management that covers all steps from sampling to sample processing and reading the results – which is an essential component of all analytic methods used for diagnostic purposes. Due to the easy availability of blood and the automation potential of the analytic process, liquid biopsy however can be a valuable complement to standardized histopathology methods. It seems to be a very attractive method, particularly in view of the fact that no tissue samples need to be obtained," Professor Kriegsmann concluded.

Circulating tumor markers as liquid biopsy



Lab medicine in Norway, Serbia and France

Continued from page 23

biology represents 2.5% of medical specialists and covers all sub-specialties in lab medicine.

Total spend on medical biology in France, supported by the national healthcare system is €4.3bn euro in the private sector and 2.4bn public.

Dr Bernard Gouget, counsellor for public health at the National Federation of France, believes mandatory accreditation has directly impacted on the consolidation of private labs with the modernisation of healthcare, setting up the territorial hospital groups for public hospitals, revitalising cooperation in medical biology. France has 953 medical labs operating in a pressured healthcare system heading for reform, but with patient satisfaction high. Different funding arrangements based on the type of provider, with a mix of public and private

health with regional differences.

'Challenges include maintaining funding through the national welfare system, despite spending growth restraints,' he said. 'There are social and regional inequalities in health, adapting to epidemiological changes with chronic disease levels and an ageing population as well as technological evolution.'

Another issue: while digital development supports healthcare, hospitals have too many different systems making regional communication difficult. French biology reform gave a central place for biological diagnosis improving diagnosis pathways and clinical outcomes by a better service closer to clinicians and more efficient, with new tools, technologies and evidence based medicine.

Gouget believes practice accreditation will succeed, achieving its

explicit and specific purposes to benefit all groups – including patients. 'I want to be very positive about the sustainability of lab medicine. As specialists we have many strengths and a central role in prevention, diagnosis and therapy monitoring, quality and efficiency.'

'Due to globalisation and rapid development in scientific communication, European and International collaboration is the way forward to harmonise scientific training, standardisation of tests and to improve quality and impact of research findings.'

Whilst the outlined practices operate within different healthcare systems – they face similar challenges: to be more efficient and cost-effective as they embrace technological advances to meet patient expectations.



Professor Jörg Kriegsmann MD, Dr. phil. a specialist in Pathology, is co-founder and head of the Medical Supply Centre for Histology, Cytology and Molecular Diagnostics in Trier, and co-founder and partner of the cross-regional professional association for histology, cytology and molecular diagnostics in Trier, Düren and Düsseldorf.

Small molecules of genetic material can help choose therapy

Ascertaining the value of microRNA

Michael Krassnitzer reports on a new approach in molecular diagnostics introduced during the IASLC World Conference in Vienna

'Molecular diagnostics is the basis of increasingly individualised, and therefore more effective treatment for lung cancer,' explained Professor Robert Pirker MD, President of the 17th World Conference in December organised by the International Association for the Study of Lung Cancer IASLC.

One of the objectives of molecular diagnostics is to detect certain mutations in tumour DNA, which can be used to predict whether particular types of treatment will be successful.

A study presented at the conference demonstrated that the analysis of DNA is not the only procedure that molecular diagnostics needs to rely on. In the case of pleural mesothelioma, a rare but dangerous type of cancer, microRNA can be used to help select the best treatment strategies. MicroRNAs are small molecules of genetic material that serve as important regulation mechanisms for gene activity, specifically for switching genes off. Swiss and Australian researchers have succeeded in the development of a score based on six microRNAs that could be used as a decision aid in the treatment of mesothelioma.

Pleural mesothelioma develops in the layers of tissue that wrap the lungs. Among patients, there is one group with a markedly longer survival rate than others. Dr Michaela B Kirschner, at the Department of Thoracic Surgery, University Hospital Zurich and colleagues at the Asbestos Diseases Research Institute, in Sydney, have introduced the miR-Score, a prognosis marker for mesothelioma that can be used to identify these patients.

The researchers examined and analysed the miR-Score of pleural mesothelioma patients prior to, and after chemotherapy, using tissue samples obtained either for the purpose of diagnosis or during tumour surgery – i.e. radical removal of the pleura, lung, pericardium and parts of the diaphragm. Radical tumour surgery can increase the rate of survival, with induction chemotherapy aimed at reducing the tumour bur-

den prior to surgery.

The miR-Score was determined under these conditions through examination of the microRNA from 34 tissue samples obtained during diagnostic examinations (i.e. prior to chemotherapy) and 34 tissue samples obtained during surgery – i.e. after induction chemotherapy.

Chemotherapy is aimed at causing maximum damage to, or death of, the tumour tissue. The question was therefore whether microRNAs from the tissue samples removed and examined for diagnosis also remain significant for the prognosis of the expected disease progression after chemotherapy (and after surgery).

The analysis showed that, although chemotherapy changed some of the micro-RNAs in the miR-Score, two of

them (miR-30e and miR-221) were basically resistant. 'If they can be detected in the diagnostic tissue sample, this can very likely be used to help assess a patient's prognosis,' Kirschner reports. The next objective is to determine how the administration of different cancer drugs (cisplatin, pemetrexed, gemcitabine) affects micro-RNAs because different chemotherapeutic agents have different effects on the malignant cells.

Between 15 and 20 cases (dependent on country statistics) of mesothelioma per million are diagnosed in Europe annually. Compared to non-small cell lung cancer, for example, this type of cancer is rare but, due to its aggressiveness, is one of the lung cancers with the worst prognosis. It has been clearly documented that exposure to asbestos fibre is the cause of most cases of pleural mesothelioma. ■

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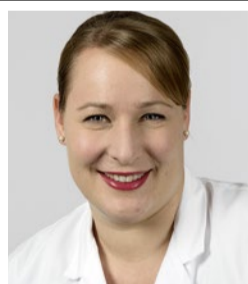


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Michaela Barbara Kirschner is a postdoctoral Research Fellow at the Division of Thoracic Surgery, University Hospital Zurich, Switzerland. As a molecular biologist she has a strong background in microRNA and mesothelioma research. Dr Kirschner trained at the University of Heidelberg, Germany, and the German Cancer Research Centre. As part of her biomarker-focused research, she has developed robust methods to detect microRNAs in the circulation; her research also led to the discovery of novel potential blood-based microRNA biomarkers. In the last six years she has published 19 papers, seven of these as first author, presented regularly at national and international conferences, and has received a number of travel grants.

Identifying fundamental mechanisms in cancer progression

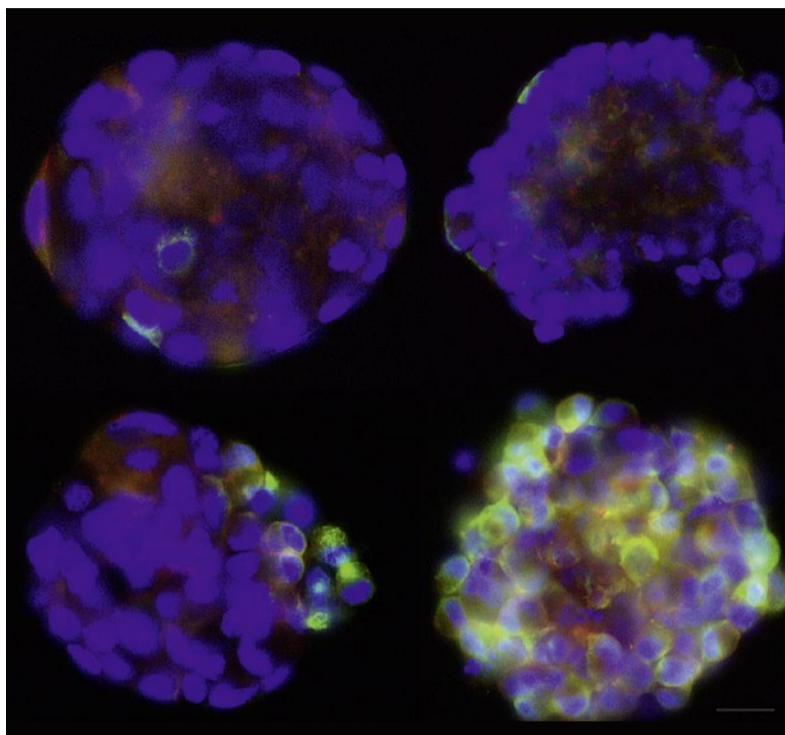
Proteomic mass spectrometry

Scientists at a UK university are using the power of mass spectrometry to research critical processes in human prostate cancer, Mark Nicholls reports

Dr David Boocock is leading a group at the John van Geest Cancer Research Centre at Nottingham Trent University, with a key research focus on the discovery of new markers that can predict prostate cancer metastasis. The research will feed into the immunotherapy stream of

the centre.

'We have been working on creating and characterising a model that can help us predict prostate cancer metastasis,' he explained. 'To do this we have cloned prostate cancer cell lines to generate new cell lines that have varying degrees of EMT



Examples of four clone prostate cancer cell line spheres with differing levels of EMT. The green stain shows cells with high levels of vimentin, a mesenchymal marker, and red/orange shows E-cadherin, an epithelial marker, all cells show blue (DAPI) nuclear stain

(epithelial to mesenchymal transition), which is thought to be a critical process in cancer invasion and migration that relates to metastasis.

'We generated a cell line that undergoes a "spontaneous" transition from epithelial to mesenchymal phenotype, which we believe may better represent the biological process in cancer than current methodologies that use exogenous factors to induce EMT in vitro.'

This work was recently published in Nature Publishing Group's Scientific Reports (<http://www.nature.com/articles/srep40633>).

For his research Dr Boocock, Senior Research Fellow and Group Leader in Clinical Proteomics and Biological Mass Spectrometry in the John van Geest Cancer Research Centre, primarily uses proteomic mass spectrometry (Next-Gen Proteomics) to look for differentially expressed proteins between different samples. 'At the most basic, it's comparing cancer and non-cancer samples to identify cancer related proteins,' he explained, 'but, we also have looked at response to therapy and prediction of disease status.'

'To do this, we use quantitative mass spectrometry to measure the differential expression of the peptides/fragments of proteins following high performance liquid chromatography (HPLC) of the complex samples.'

Boocock reports significant findings result from the model developed in the present work, which provide a valuable resource for the investigation of EMT in human prostate cancer.

'Unlike artificially-induced models of EMT,' he added, the EMT derived cells in this study express endogenous levels of EMT-associated proteins. As such, these clones can be utilised to derive an authentic EMT-signature, which could be extended to clinical applications. These cells have been studied in vivo, using a mouse xenograft model, which showed that the clone with high spontaneous EMT gives rise to a much larger, faster growing tumour.'

For the studies, the instrumentation from Sciex, used by Boocock, includes the TripleTOF 6600 and 5600+ mass spectrometers, along

with the Eksigent 400 series nanoLC HPLC system.

He said the TripleTOF system allows him to identify 3-3,500 proteins in a complex cell lysate with an hour's gradient and then use the information to create a 'spectral' or 'ion' library for that specific sample type.

From there, using a different technique called SWATH, or Data Independent Acquisition (DIA), his team can gain quantitative information on every protein in the sample (up to 4,500 in an hour's LC gradient). This enables us very quickly to run a batch of samples with two or more classifications - cancer; non-cancer, or aggressive vs. non-aggressive, for example - and get a relative quantitative readout for each protein.

'Sciex provides an excellent cloud based software platform (OneOmics), which has revolution-



Dr David Boocock is a Senior Research Fellow and Group Leader in Clinical Proteomics and Biological Mass Spectrometry in the John van Geest Cancer Research Centre at Nottingham Trent University. With his colleagues, his research focuses on three main areas of cancer - prostate, breast and leukaemia - in both biomarker discovery and cancer immunotherapy. It incorporates state-of-the-art technologies for discovering the genetic basis of the disease and developing new methods of diagnosis and treatment. His research on biomarker discovery utilises biological mass spectrometry to identify protein biomarkers as predictors of disease status and response to therapy, particularly in prostate and breast cancer.

ised the laboratory throughput and allows us to upload our raw data and process it far faster than would be possible locally, with a great user interface.'

At present, while the studies are at an early stage, a next step is the continuation of the work with novel prostate cancer cell clones. With the full transcriptomic and proteomic (SWATH) characterisation of the cell lines under way and several key molecular drivers of EMT and metastasis already identified from the data, the group is working toward further publications in the near future.

'These clones provide a significant resource and considerable scope for future studies that are focused on interrogating the fundamental mechanisms involved in cancer progression. They will also be of significant value for studies based on biomarker discovery and the identification of drug-able or immunotherapeutic targets that can be exploited to develop new approaches for prostate cancer treatment and management.'



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Travel transports viral trouble

Virologists are today's universal necessities

Globalisation has been a defining term in this 21st century: with almost anybody able to visit any place at any time, diseases, viruses and bacteria can be travel companions. Thus virology is gaining increased attention. Walter Depner interviewed Professor Barbara Gärtner, President of the German Association of Virology, about the issues and challenges arising from this development.

Virology, as an independent discipline, is not necessarily in the public eye, but is increasingly important – is this the case and where would you position your discipline today?

Prof. Gärtner: 'I think it's an accurate observation that virology is gaining importance, primarily due to so-called epidemics. Whilst, a few years ago, HIV dominated the headlines, today people are more interested in influenza or tropical viruses such as Zika or Ebola, which in turn are covered more widely and frequently in the non-medical media. Think of the situation in the run-up to the Olympic Games in Rio de Janeiro 2016 when the Zika virus was a big issue in the media.'

Germany has two professional associations – the DVV, of which you are President, and the Society of Virology, GfV, with the latter representing virologists not only in Germany itself but also in all German-speaking countries. What are the tasks of the DVV compared with GfV and where do they cooperate?

'DVV supports public health services with a focus on influenza. Thus we organise an international influenza congress every three years. Other important issues are viral disinfection, infections during pregnancy,

virus safety and noroviruses as well as vaccination and antiviral therapy.

'Since we primarily represent the public health services sector, private individuals cannot become members of DVV. Our members are, inter alia, the German Federal Ministry of Health and almost all State Ministries of Health. DVV aims to support the public health services sector in fighting viral diseases. Thus, the organisation clearly focuses on applied research.

By contrast GfV is a medical professional society, an association of individual researchers and scientists in the area of virus infections.

Obviously these two organisations share many interests and tasks. All virologists working for DVV are members of GfV and there are a number of joint working groups – this leads to very tight cooperation.'

Would you describe the increasing importance of virology over the past 10-20 years and where is the discipline heading?

'Firstly, the increasing importance of virology is clearly linked to the fact that we know more and more viruses, understand their links to certain diseases better and that epidemiology looks at certain viral infections



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in new ways: all of a sudden we recognise viruses where we did not see them before.

'A case in point: Zika virus diseases, or the spread of the Chikungunya virus, which, over the past few years has been conquering many new areas. However, at the same time as the viruses were spreading, our diagnostic capabilities were expanding immensely and viral therapy has seen groundbreaking progress. Take, for example, modern hepatitis C therapies with antiviral medication – they have all but revolutionised conventional therapies that were fraught with side effects.

'With the on-going globalisation virus infections will continue to spread. Treating the triggers and diagnostics will become more important – for all intents and purposes that will no doubt hold true for the entire discipline of virology.'

New insights, as well as external influences, are already forcing virologists to become specialised. Going forward, does a virologist have to be even more of a specialist and what does that mean for interdisciplinary work?

'As far as basic research is concerned, specialisation is doubtless the name of the game. However, when it comes to clinical virology a broader approach is still possible. Having said that, I should add that new developments in antiviral substances are highly demanding. While in bacteriology, the microbiology specialist physician routinely provides treatment recommendations, in virology the clinical specialists who frequently treat viral infections such as HIV, hepatitis C or CMV in immunosuppressed patients, decide on the therapy.

'Virology should aim to move beyond diagnostics and be more directly involved with the patients.'



Professor Barbara Gärtner, President of the German Association of Virology (DVV) is Interim Director of the Institute of Microbiology and Hygiene at University Hospital in Saarland, Germany. The professor is also in charge of microbiology at the Saarland public health consulting service.

Close cooperation with other disciplines, such as microbiology, hygiene and other clinical fields seems to be vital.'

With people being ever more mobile, viruses and diseases also travel. What does that mean for national medical societies?

'The pathogens will spread as human mobility increases and vector-borne diseases will definitely spread, too. Another issue to deal with in the future is close contact between humans and animals. Many diseases that turn into epidemics are originally zoonoses, meaning they developed in animals, for example, influenza and Ebola. Large-scale – industrial – livestock farming increasingly happens in so-called developing countries. We import those products, which exacerbates the problem.

'Thus international cooperation to fight epidemics is imperative. Nevertheless national professional societies will remain important because many aspects have to be implemented nationally. And, in the end, international organisations are made up of national member countries.'

Disheartening patients organisation study results

Hepatitis control must be accelerated

Report: Sylvia Schulz

Last year the WHO launched a global strategy on viral hepatitis aiming to eliminate hepatitis B (HBV) and C (HCV) as public health threats by 2030. Among the goals: a 90% drop in the number of chronically infected people and a 65% mortality rate reduction, as untreated chronic viral hepatitis can cause irreversible liver damage leading to cirrhosis or cancer.

The global health organisation, clearly demonstrating that hepatitis is not only a problem among third world countries but is also a current European issue, set up an action plan last September. Europe records around 57,000 newly diagnosed acute and chronic cases of hepatitis B and C annually. On top of that, an estimated 10 million Europeans are believed to have chronic hepatitis B and C infections without knowing it or being treated.

As the monitoring and evaluation framework of the WHO hepatitis strategy is not expected to become operational until 2018, the European Liver Patients Organisation (ELPA) surges ahead, compiling facts about state of the art care concerning this

disease. It commissioned a broadly based, the Hep-CORE study, to shed light on the policy response to hepatitis B and C engaging with ELPA member organisations.

Based at the University of Barcelona and Copenhagen, the research team carried out the survey, with data collected from local specialists in each country. The researchers asked one patient group in each of ELPA's 27 member-countries to complete a 39-item survey about various aspects relating to HBV and HCV: overall national response, public awareness and engagement, disease monitoring and data collection, prevention, testing and diagnosis, clinical assessment, and treatment. The plan is to repeat the patient-led monitoring tool on a regular basis, to compare results between countries and follow individual country progress over time.

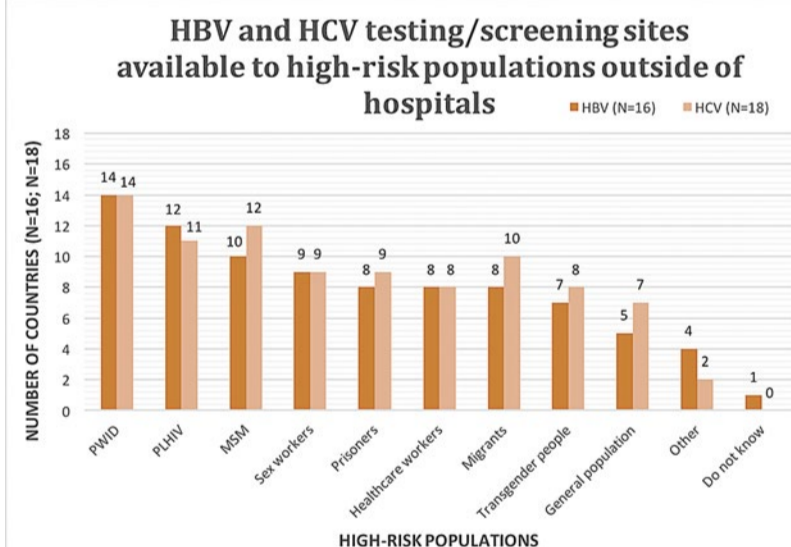
In brief, the study reveals serious gaps in policies concerning hepatitis control. 52 per cent of the 27 European countries surveyed lack national strategies to address viral hepatitis B or C despite the WHO's Assembly resolution calling on all countries to have one. Only

three of those countries have access to the new, highly effective medicines (direct-acting antivirals) for hepatitis C without restrictions. The director of studies, Professor Jeffrey V Lazarus, from the University of Barcelona, said: 'These Hep-CORE results serve as an unprecedented analysis of regional and national gaps, clearly showing where there are deficient policies and, by default, what action needs to be taken.'

No national register

For example, despite an urgent need for broad monitoring and disease surveillance, this study found that 17 countries (63%) have no national hepatitis B virus (HBV) register and 15 countries (56%) have no national hepatitis C virus (HCV) register. Basic access to testing and screening facilities is vital for patients, especially those from high-risk groups, such as people who inject drugs, or prisoners.

Despite this, patient groups from 10 countries (37%) reported that there are no HCV testing or screening sites outside of hospitals for the general population in their countries. Even more alarming, patient groups from 12 of the countries



(44%) reported that there are no such sites outside of hospitals that provide testing or screening services for high-risk populations.

Another section of the survey asked a set of questions oriented towards understanding hepatitis prevention in each country. This section focused on the availability of harm reduction – services that target the reduction of negative health consequences associated with drug use, such as the spread of viral hepatitis.

It was reported that clean needle and syringe programmes are available in at least one area of a patient group's country in 22 cases (81%), that opioid substitution therapy is available in at least one area of a patient group's country in 24 cases

(89%), and that drug consumption rooms are available in only five cases (19%). The study shows that significant gaps in harm reduction regarding reported coverage and availability remain.

Lazarus concludes: 'The 2016 Hep-CORE Report findings are a resource that can aid the efforts of all those working to eliminate HBV and HCV as public health threats in Europe, and beyond, in line with WHO's global strategy. We now have a starting point from which we can systematically scale up hepatitis prevention, treatment, and care – and monitor the much-needed progress. Viral hepatitis must be combated on a large scale and this requires individual country and concerted pan-European action.'

Cancer diagnosis is likely to take a dramatic shift from scanning

Liquid biopsies challenge imaging

Novel blood or urine tests can now detect a tumour and but might in future be able to say what type of cancer is developing in which organ, John Brosky reports

During the meeting of United European Gastroenterology, Sarah Bohndiek PhD was tasked with arguing against the rapidly emerging class of liquid biopsies that are challenging traditional imaging diagnostics techniques. But, she just couldn't bring herself to do it. 'Liquid biopsies are incredibly relevant,' said Bohndiek, a Group Leader at the University of Cambridge, England, who, as a physicist, was expected to promote the merits of scanners over chemistry kits.

'The evidence for these tests is building. The technologies are increasingly sensitive and there is evidence that, through epigenetics, we may even be able to work out the specific organ of origin,' she said.

The term liquid biopsies covers an ever-widening number of diagnostic test kits, some using blood samples, others urine samples. Thanks to the convergence of powerful computer processing with the discoveries of genomic, proteomic and metabolomic biomarkers, these simple tests have the potential to identify a specific cancer and even stage the severity of tumour development.

There is a veritable gold rush underway as companies complete clinical phase testing of novel assays, including Johnson & Johnson's Janssen Diagnostics and Genomic Health in the United States, MDxHealth based in Herstal, Belgium and Berlin-based Epigenomics.

In the pathology of colorectal can-

cer alone, a successful liquid biopsy test could capture a market opportunity estimated at US\$2 billion.

Bohndiek believes that, as these tests are likely to become more widely adopted for first-line screening than traditional diagnostics such as X-ray mammography, while using whole body imaging or endoscopy to detect tumors will become a second line of testing.

Shifting image for imagers

'There will be a bit of a shift in how we see ourselves as imagers, perhaps the imaging community will see the advances of these liquid biopsies as an affront in coming years,' she said. 'Traditionally, we have been the go-to technology for early diagnostics in screening programmes, but I think it is likely that a liquid biopsy of some sort will become the go to technology.'

The benefit to healthcare systems will be cost savings as patients migrate from specialised centres back to the primary care setting where these tests can be administered.

For example, colorectal cancer screening using the gold standard of colonoscopy creates long queues of patients, especially in public payer systems, such as the United Kingdom's National Health Service, she pointed out. 'There are very long waiting lists at specialised centres, which is not very good if our goal is to detect cancer early.'

This is where the two diagnostics are complimentary and not competitive, she said, allowing a rapid movement for the patient through the pathway.

Once disease is detected the role of imaging is to specifically map the tumors, determine those with a



With a doctorate in radiation physics and postdoctoral work in molecular imaging, Sarah E Bohndiek has led Cancer Research at the Cambridge Institute in the United Kingdom since 2014, working through the VISION Laboratory, also known as the 'Bohndiek Lab'. In her own words, she describes her group as 'a small, highly interactive and international research team, whose passion is using new technological innovations to improve our understanding of metabolic processes in disease. We hope to use these innovations to improve cancer patient survival, by finding routes to overcome drug resistance and eventually enabling earlier cancer detection.'

high risk of progression, then guide interventions and monitor the effectiveness of treatment.

About a third of the work in the Cambridge lab that Bohndiek directs is dedicated to developing endoscopic technology.

Improving image processing

Analysing images pixel by pixel

Sometimes innovations face a long journey before becoming a final product. This particularly applies to medical displays – due to very high quality demands and strong regulations that are mandatory in this segment.

In the past, the Japanese display vendor Totoku implemented a couple of innovations into its products, among them Dynamic Gamma. In many cases, safe diagnosis needs simultaneous onscreen display of Grayscale and colour images. This is a real challenge because Grayscale and colour images require different gamma curves. Grayscale images require DICOM and colour images are best displayed with a Gamma of 2.2. This is where Dynamic Gamma shows its advantage.

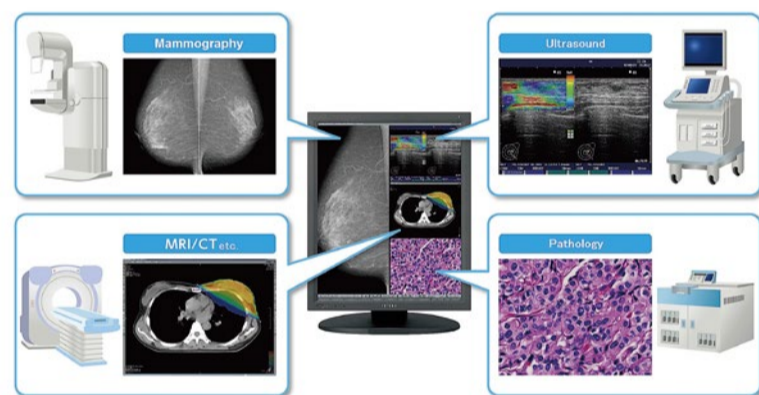
'Dynamic Gamma,' explains Marcel Herrmann, Totoku's Marketing Manager, 'analyses the screen content pixel by pixel and applies different gamma curves to each pixel, even when working with moving images in real time. Using the latest hardware technology we can handle this without delay, even though it requires millions of operations per second.'

Brighter is not always better

'From the beginning customers wanted highly bright colour displays. However, such brightness is not always helpful, for example in case of text processing or reporting,' Herrmann pointed out. 'The auto-

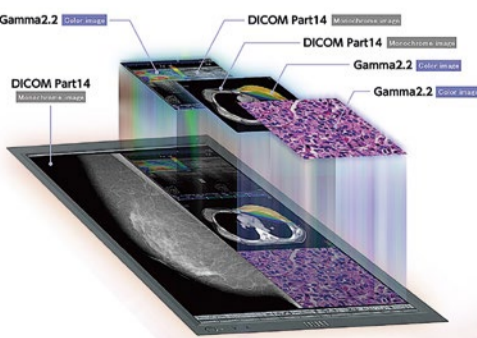
matic text mode detects those bright areas and reduces their brightness. Any other area remains untouched, which enables continuous precise diagnosis. This works like Dynamic Gamma without any configuration from user side.'

These functions are added to all current i2 units from Totoku.



Ideally, Grayscale and colour images are displayed together on a monitor

For an optimal display of differently coloured images, each individual pixel is read out separately



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