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7-26 ECR SPECIAL reports and more

Progressing towards optical biopsy

PD Dr Thomas Bocklitz studied physics at the Friedrich-Schiller-University in Jena, Germany. He received his diploma in theoretical physics in 2007 and PhD in chemometrics in 2011. Today he heads a junior research group for statistical modelling and image analysis. His research agenda is closely connected with the translation of physical information, measured by Raman-spectroscopy, AFM, TERS, CARS, SHG, TPEF, into bio-medical biological relevant information. This research has led to over 80 reviewed publications and his habilitation. In 2015 he was awarded the Bruce-Kowalski Award for chemometrics and, in 2016, the Beutenberg-Campus Jena e. V. Science Award.

Report: Sascha Keutel

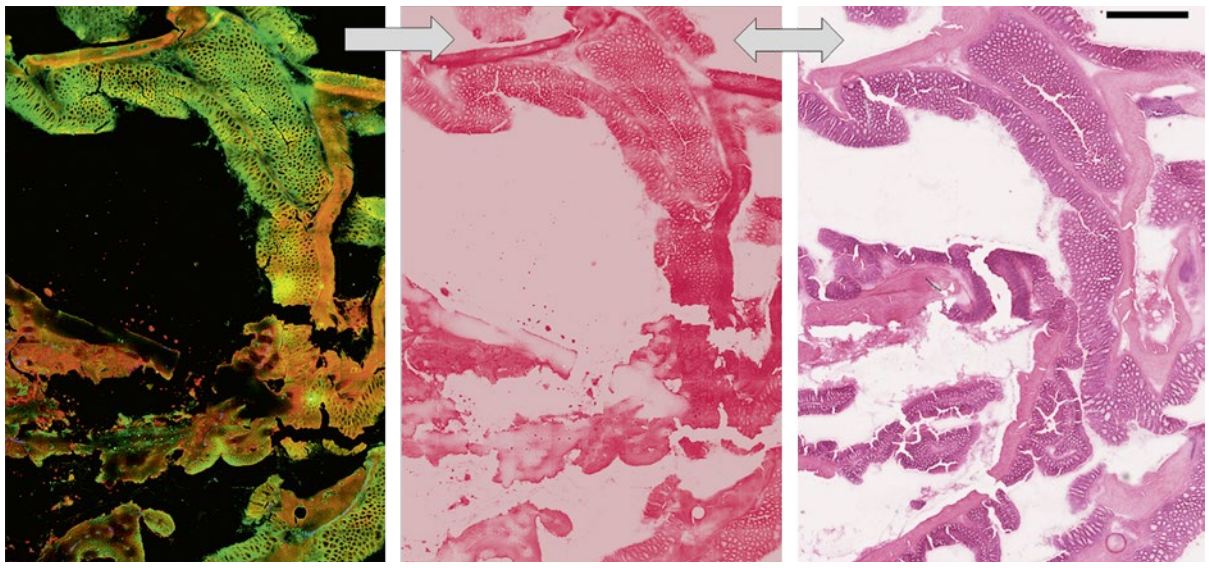
Recognising malignant tissue remains a tricky task. While today, most patients undergo a biopsy, an invasive procedure where tissue is sampled, stained and assessed, researchers are exploring the potential of optical biopsy, the visual assessment of suspect tissue. The interest in optical biopsy 'is indeed enormous,' confirms Dr Thomas Bocklitz, physicist at Friedrich-Schiller University in Jena, Germany. The physicist heads the joint working group 'Statistical modelling and image analysis' at the Leibniz Institute for Photonic Technology and Friedrich-Schiller University Jena, which looks at different aspects of optical biopsy. 'Simply put,' Bocklitz explains, 'in optical biopsy a light beam is directed towards the suspect tissue and the optical response is recorded. (Figure 1)

'In a second step, diagnostic parameters are deducted from this response. In other words, we replace the removal of suspect tissues by direct, in-situ measurement.'

A non-invasive and quick procedure

Optical biopsy offers several advantages compared to conventional biopsy – take, for example, ENT frozen section: in a conventional procedure the patient undergoes surgery under general anaesthetic. The surgeon removes the tumour tissue and takes samples from the tissue margins, which are sent to the pathologist. It can take up to 40 minutes for results to reach the operating theatre (OT) since not every hospital has an in-house lab. If the pathologist detected tumour cells in the margin samples, the surgeon has to remove further tissue, take another sample and send it to the lab again. This cycle is repeated until the sample is tumour cell-free.

'Optical biopsy, however, is performed by a technical assistant at the OT table. The acquired optical images are digitally stained. The results are forwarded to the pathologist – a procedure which saves time and is less strenuous for the patient. Moreover, the optical images contain additional information which can be used beyond sample staining,' explains Bocklitz. (Figure 2)



2) Multi-modal images of the optical tissue response (left) can be converted into digital stains (centre). Digital stains allow histopathology diagnosis. Created non-invasively they can be applied in-vivo. The image on the right shows a conventional haematoxylin and eosin stain (note the 1 mm bar in the top right corner). (Copyright: Leibniz-IPHT)

3) In the MediCARS project, funded by the German Ministry of Research, Professor Popp's working group developed a portable microscope. This can be used to measure multi-modal images in a clinical environment (coherent anti-stokes Raman scattering, second harmonic generation and two-photon excited auto-fluorescence). Using image analysis algorithms, quantitative clinical information can be extracted from these measurement data (Copyright: Leibniz-IPHT / Sven Döring)

1) In optical biopsy, the optical tissue response is measured and diagnostic information is extracted from these responses (Copyright: Leibniz-IPHT / Sven Döring)

researchers are already thinking one step further: they want to implement the measurement directly via fibres and have an endoscopy specialist, or surgeon, assess the results directly. 'The surgeon places the fibres on the tissue and can tell right away whether the tissue contains tumour cells. If yes, he can adjust the tissue mass to be removed. This would mean that really only cancer tissue is removed – healthy tissue will be spared.'

The crucial step in optical biopsies is processing the optical images – the focus of Bocklitz's work. He not only developed the above conversion of optical images into digital stains but also a classification model. This model, a cooperation project with the ENT clinic at University Hospital Jena, offers automated tissue assessment based on images acquired ex-vivo or in-vivo.

Multi-modal imaging enables digital image analysis of tissue samples

The imaging methods Bocklitz and team use combine several optical techniques. 'We simultaneously acquire several types of multi-modal images: coherent anti-stokes Raman scattering, second harmonic generation and two-photon excited auto-fluorescence. These three mechanisms visualise the distribution of lipids and proteins as well as the distribution of the tissue's fluorophores and fibre structures.

'We developed an analysis of these multi-modal images for automated delineation of cancer and healthy tissue as well as algorithms that cull quantitative clinical information from the measuring data,' Bocklitz explains. (Figure 3) His message: 'This is radiomics for pathologists!'

When developing these image analysis algorithms the researchers tried to transfer the standard procedure pathologists use – haematoxylin and eosin staining – to the computer. The pathologist looks at the section and assesses tissue structure and morphology. 'We can teach the computer to recognise patterns," Bocklitz explains. 'We take certain features of the image that quantify morphologies or textures and extract those values.

'Then we apply standard classifiers to differentiate healthy from pathological epithelial tissue. 'These classifiers are used to calculate the significant differences between the two groups and to predict the difference.'

Pattern recognition is the alpha and omega – the acquired skill that allows the computer to tell clear cases from unclear ones and thus reduce the pathologist's workload.

In an initial study, involving ten

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Implementing MDR is complex and expensive and holds little reality

The new Medical Devices Regulation

The heavy burden: By 2020 medical devices manufacturers must document the clinical effectiveness of their devices more extensively. MDR presents a fundamental impact on innovation and price calculation for medical devices

Report: Brigitte Dinkloh

Since the faulty PIP breast implants scandal in France (March 2010), there have been frequent calls for tighter licensing regulations for medical devices within the European Union. The new Medical Devices Regulation (MDR) took effect on 25th May 2017. Following a three-year transition period, from 26th May 2020 this will become mandatory in all EU member states.

The new regulation is creating big problems for regulatory authorities and particularly for small and medium size manufacturers of medical products. Therefore, engineer Christoph R. Manegold, Partner at AC Controls in Germany's Lower Rhine area, and an initiator of the federal network MDR Competence*, is calling for greater common sense in the implementation of this new regulation, and particularly for longer transition periods to master the challenge.

For small and medium size businesses the MDR is especially hard to implement

Safe and also effective

'Small and medium size companies are naturally more nervous than global players, which have had their relevant departments preparing for this for a while. For small and medium size businesses the MDR is difficult for two reasons. Licensing requirements for new products will be significantly increased as documenting the clinical effectiveness of products will become more complex,' the chartered engineer explains.

Previously, the main issue around the licensing of medical devices was patient safety. There were many norms so that patients, users and third parties were not exposed to any harm. The question as to whether a product works as described was clearly given lower priority, depending on the level of risk involved. Where previously it was possible to cover the proof of benefit with simulations or written documentation, clinical studies are now required.

'What we used to refer to as risk management,' Manegold explains, 'initially only relating to the device, then as risk management for the product life cycle (Norm DIN EN ISO 14971), and what mainly related to technical safety, will now have to be extended with studies to cover clinical data collection on product effectivity, and not only when the product first becomes licensed but continuously.' However, small-and medium sized companies, which have an 80% market share in Germany, are not prepared for this.

Studies also required for existing products

The second hurdle manufacturers face is that this will also apply to older devices that have proved their value already. 'This is the biggest problem, and in my view an unjustified imposition,' Manegold laments. 'Clinical data may have to be supplied even for devices which have never been involved in any incidents. And if the manufacturers cannot do this according to MEDDEV 2.7.1 via documentation only, which is what many will try to do, then in a worst case scenario the legislator is forcing them to carry out studies for a device which has been around for several decades.'

Manufacturers don't have the staff for this and no experience, and the authorities do not have the resources to scrutinise and monitor all these studies simultaneously, not even to mention the additional costs involved which have not really been mentioned so far. These will have to be added to the sales price. Manegold estimates that 'the healthcare system will be put under additional financial strain after the end of the transition period; these additional costs will run to around 10-15% for medical devices, dependent on risk category and quantity.' Medical disposables will be less affected than, say, a diagnosis system only used 100 times a year.

Documentation via literature alone is increasingly hard

The situation is aggravated because the fourth revision of the MEDDEV 2.7.1. has been tightened. It stipulates much more intensive work and redefines equivalence criteria. If there is no system on sale that is 100% equivalent for the intended use, settings and diagnostic possibilities then documentation via literature only is not possible. 'You can then only compare apples to apples. In the past, the interpretation of this guideline was a little more practical. For instance, several devices could be compared, but in future manufacturers can only compare their products with devices they already have on the market – because what manufacturer would be happy for the competition to gain access to technical documentation and updates? The legislator has devised something knowing that it is not practicable, which means manufacturers will have to deliver clinical studies to obtain regulatory certification.

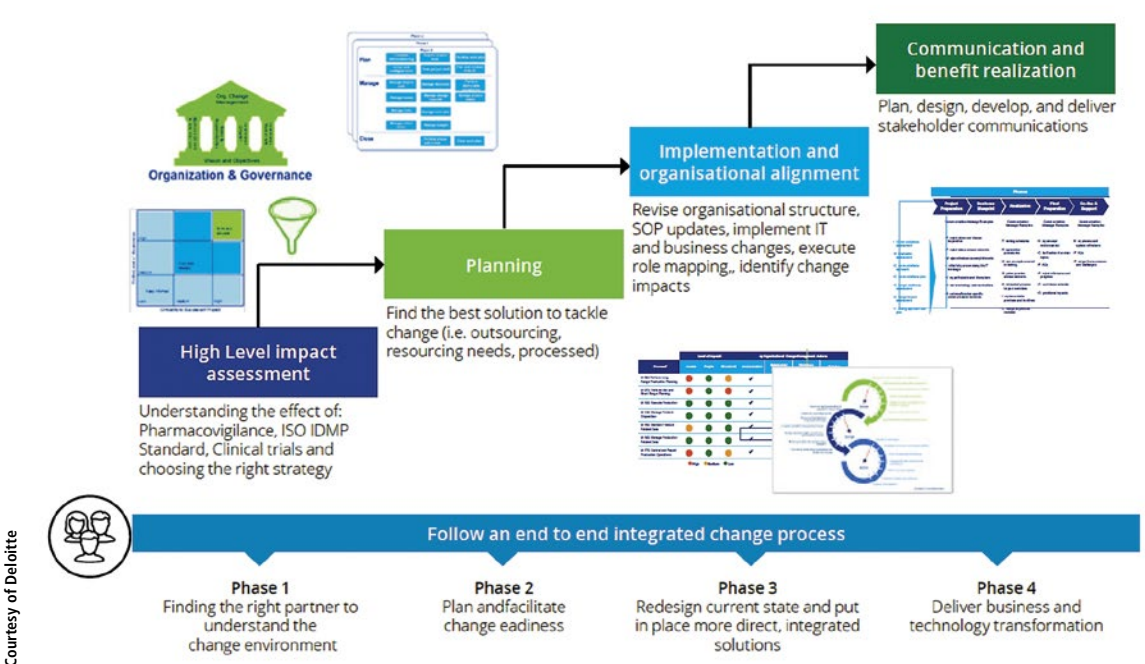
MDR ignores the user safety problem

Manegold criticises the MDR for not picking up real problems. Most incident reports relate to user errors – unlikely to stop even with the new regulation. Take ten ventilators – no two of them will be exactly the same. Unlike the cars that can work in the same way globally, medical devices do not have the same level of assurance. 'The new regulation now proposes licensing procedures similar to those in the pharmaceuticals industry, but this will not lead to more user safety,' Manegold is certain.

The problem with the notified bodies

A further problem is that the MDR 2017 has not only increased requirements for manufacturers but also for the regulatory authorities. The MDR also has applied to the regulatory authorities and notified bodies since 26th November 2017. It contains a re-accreditation of all notified bodies with joint assessments for initial designation, extensions and expansions of the scope, and this is likely to take around 18 months. Therefore, manufacturers will only know in 2019 if the authority previously responsible for them and their products will continue to be so.

In order to develop a regulatory strategy for the implementation of the MDR a coherent sequence of activities can be critical



Courtesy of Deloitte

Documenting the clinical effectiveness of products will become more complex

Source: Jat306 / Shutterstock

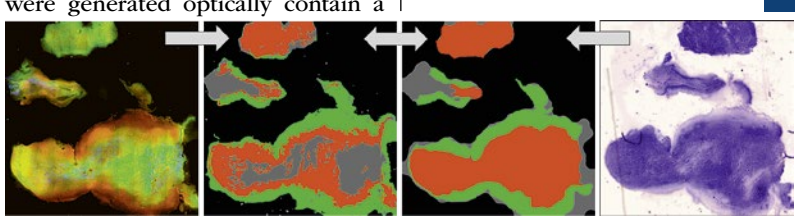
Progressing towards optical biopsy

Continued from page 1

patients, the accuracy rate of the diagnoses was 90 percent. (Figure 4) A multi-centre pre-clinical study is currently being designed to analyse several hundred cases. By increasing the number of patients, Bocklitz hopes to increase accuracy to over 95 percent. Moreover, in this upcoming study the team will perform the measurement in a lab right next to the OT, to be able to integrate optical biopsy into the surgery workflow.

Bocklitz considers the preliminary results of optical biopsy to be very promising. The data that were generated optically contain a lot of information that will improve patient care. 'Initially, there will be a combination of different measuring methods. Each method provides different data, which we will be able to pool.

However, this scenario requires the development of suitable and high-performing algorithms for assessment, because we have created a multidimensional data space that needs to be analysed.' In the long run, Bocklitz predicts, 'optical biopsy will surpass conventional biopsy in terms of accuracy and information value.'



Using image analysis algorithms, multi-modal tissue images (left) can be translated into predictive data (centre, left). In the images above, green areas show healthy epithelial tissue, red areas show cancerous tissue. Histopathological diagnosis (centre right) is based on HE stains (right). When multi-modal imaging is integrated into fibre optic probes, in-vivo tissue diagnostics becomes reality. (Copyright: Leibniz-IPHT)

Biomedical engineer **Christoph R Manegold** also gained an MSc at the European Business School. He began his career as a development engineer and later became technical manager for the Heyer Group in Bad Ems, Germany. In 1995 he founded MT-Consult to develop technologies for life-supporting systems in anaesthetics and ventilation. From 2006-2012 he worked for Pulsion Medical Systems AG in Munich, as development manager and later as CTO, driving company expansion internationally. In 2010 he became the main shareholder of AC Aircontrols and, in 2012 a shareholder in Nano4imaging GmbH.

The number of notified bodies is likely to reduce further, and probably their respective scope will be reduced; already they are hardly taking on any new customers. The regulatory authorities are also desperately looking for qualified staff to implement the new regulations.

Solutions for small and medium size firms

As the 'rescue parachute' for small and medium size medical devices manufacturers (SMU's) demanded by the German Medical Technology Association (BVMed) is unlikely to materialise, the affected manufacturers will need to act and be creative themselves.

Manegold does not foresee the demise of small and medium size manufacturers across Europe but new fusions and increasing mergers & acquisitions activities. To avoid being swallowed by a bigger player, the smaller specialist firms with similar products should cooperate in networks. Manegold: 'The issue is not to fight about each other's intellectual property but e.g. to jointly finance a physician to carry out studies for instance. Just like car sharing they could pool resources, achieving significant cost savings and remaining profitable.

Demands for politicians

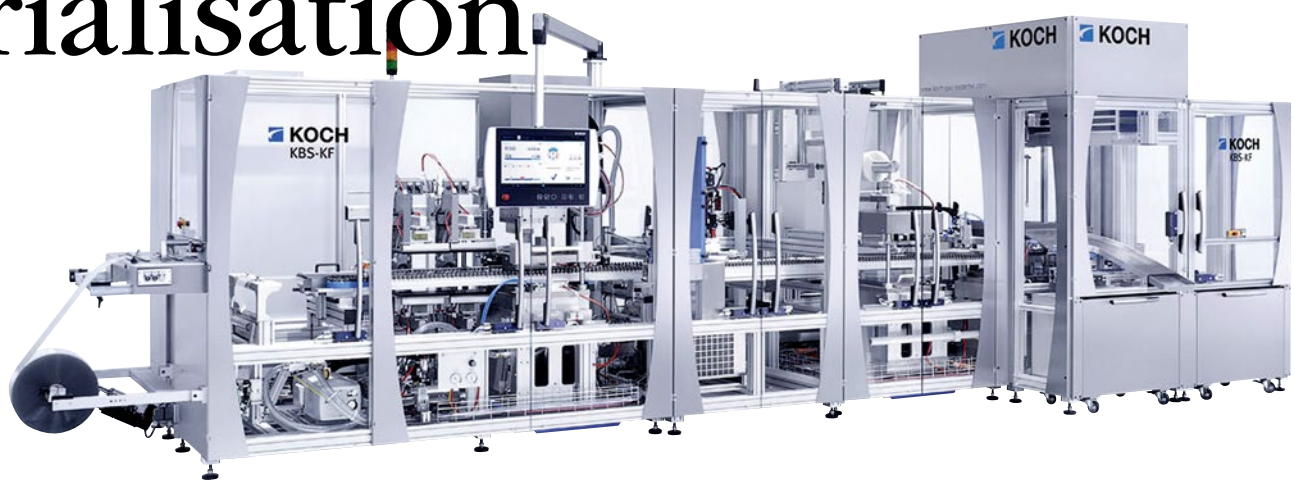
Overall, Manegold and colleagues are disappointed: the MDR is a half-baked text in a half-baked environment, which leaves a lot of room for interpretation. The attempt to harmonise notified bodies was not achieved.

Therefore, their demand is: 'The MDR must be revised using common sense, the transitional periods must be extended and products already on the market need to be evaluated in a different way to how currently stipulated in the MDR. In particular, low risk devices for which no incidents have ever been reported should have their status quo protected in the same way as is handled in the USA, and resources such as the Eudamed Database should also be ready for the new regulation implementation – which is currently unlikely to happen.'

* The non-profit network www.mdr-competence.com, founded to alert manufacturers of impending challenges posed by the MDR 2017, offers eight experts and service providers for licensing, consciously omitting technical development of devices.

At the helm of innovation for Falsified Medicine Directive changes

Track and Trace technology and serialisation



"With the European Union regulation on medical packaging coming into effect February 2019, Track & Trace technology and serialisation have become a key topic in the medical packaging industry. Work processes must now allow for the authentication of products with individual serial numbers printed on each or its packaging, a process called serialisation.

The industry is adapting to the new regulations, by ensuring that, by designing packaging and packaging machines with tracing codes packaging line engineers and machinery can track the life cycle of a product.

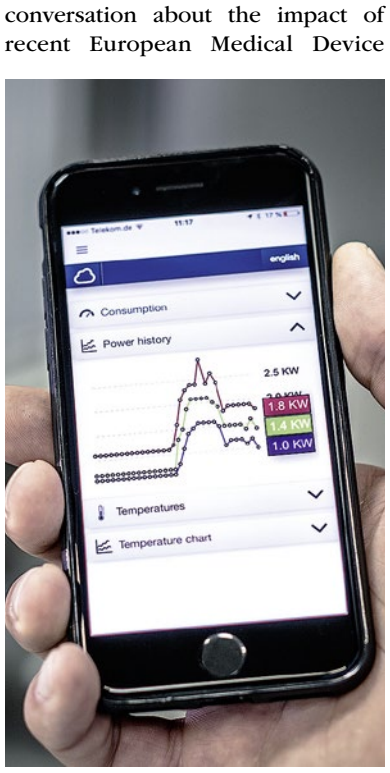
Koch Pac-Systeme, part of Uhlmann, one of the world's leading manufacturers of pharmaceutical packaging machines are ready for these changes. With over 100 electrical, mechanical and software design engineers globally, their wealth of experience helps clients develop blister packaging that is not only bespoke but also ensures they are prepared for regulation changes and that Track & Trace can be seamlessly integrated in the manufacturing line, whether for knee implants or liquid drug formulations.

Workshops and panel discussions on recent regulations

One of the ways Koch Pac stays abreast of changes in the market and supports its customers in navigating manufacturing line changes, is by attending Medtec Europe where, this year, the company will be presenting the Blister machine KBS-KF.

The forming, printing and sealing machine packs individually marked products in modern blister packaging and ensures products are completely traceable, thus providing a one-stop shop solution for Koch Pac customers. It is particularly relevant to the medical technology industry, because packaging can be created in a sterile environment guaranteeing non-contamination of products.

Medtec Europe will also facilitate conversation about the impact of recent European Medical Device Regulations (EMDR) and In Vitro Diagnostic Regulations (IVDR) through panel discussions, keynote speakers, interactive regulatory workshops and breakfast meetings. Jürgen Welker explains that Koch Pac has been attending Medtec Europe for over seven years and looks forward to continuing and building new partnerships within the industry, as well as learning about medical device innovations from across Europe.



Connected app to control the manufacturing line

Koch's Director of Automation and Technology, Jürgen Welker has seen packaging machines evolve during the 28 years he has been with the company: from the individual printing of products to the connection of machines to Internet of Things (IOT) cloud systems and customer enterprise resource planning (ERP) systems.

Packaging machines have come a long way. Nowadays, innovative machines are connected to the Internet of Things, cloud systems and customer enterprise resource planning systems

The company's most recent innovation is the K 4.0 packaging solution that offers digitisation for special-purpose engineering and features state-of-the- art controls.

Koch Pac's connected app allows users to access parameters throughout the packaging process, an innovative solution to ensuring up-to-date control of the manufacturing line from start to finish.

Customers can also use a headset that allows engineers from Koch Pac to direct them through any trouble-shooting in the manufacturing line – showcasing how the firm has adapted to an increasingly digital market by providing integrated, efficient and state-of-the-art support to its customers, wherever they may be.

Updating the production line

With the new regulations about to come into play, the focus for manufacturers is to build three steps into their production line:

- the serialisation of products that can track every item down to its smallest sellable part
- the development of tamper-proof packaging for products
- the back-up of the product serial numbers on a database.

Packaging machines with tracing codes packaging, line engineers and machinery can track the life cycle of a product

These three steps can all be easily achieved with Koch Pac packaging machines; their engineers are trained on how to include these steps into a wide array of manufacturing lines and are able to advise customers on how best to adapt to the Falsified Medicines Directive (FMD).

When the new steps are built-in to the system, Koch Pac can not only virtually assess the impact on the bigger production line, but also train employees on the new machines, ensuring processes are as efficient as possible.

With an estimated two thirds of medical technology companies looking to update their equipment to include labelling, coding or visibility capabilities, Koch Pac is experiencing increasing customer demand for its bespoke engineering solutions and expects to meet and build relationships with many of these new customers during Medtec Europe."

www.medteceurope.com

Source: Koch Pac-Systeme GmbH

Shake-up needs input from students' and lateral thinkers'

High-tech event aims to push progress

Report: Eva Britsch

In the German healthcare system, innovations are difficult – Xpomet boss Ulrich Pieper is certain of this. Not because the system is different, but because the point of view is wrong. 'The system assesses innovations according to how much money they save, and not according to whether they achieve healing,' the industrial engineer explains.

Precisely for this reason, he adds, the three-day Convention for Innovation and High-Tech in Medicine, to be held in Leipzig from 21 March, is a great attraction. The organiser is confident – the next three years have already been solidly counter-financed. The aim of the event is to look beyond the horizon and motivate the system players to dare to take more risks:

'Whoever is willing to take risks will take a new approach, open up and dare to venture into unknown realms, such as through collaboration outside the sector.'

In terms of medical technology, the congress will present some surprising findings, which aim to promote interoperability and better networking of processes, as well as to create greater efficiency for patients.

German emergency medicine needs to become professionalised.

In the run-up to Xpomet, Dr Timo Schöpke, Director of the Emergency Centre of the Barnim Clinic, describes deficits in German emergency medicine. The processes are too complicated; currently there are endless non-necessities, for example in case reports that have to be transcribed up to six times due to a lack of software interoperability. In this, important proficiencies are lost.

Various emergency care representatives will gather at Xpomet to discuss related issues, among them members of the German Society for Interdisciplinary Emergency and Acute Medicine (DGINA) on the opening day. In addition, undoubtedly the focus will be on the emergency care specialist. 'In all other European countries it exists, except for us – we lag behind progress in emergency medicine,' Schöpke asserts.

Industry suppliers see a need for action in this area and offer Xpomet solutions that contribute to increasing efficiency with workflow support. In particular, it is a matter of guaranteeing complete data, which in turn makes 'reliable analyses' possible. On the one hand, this is intended to relieve the physician's workload and, on the other, to provide IT support in his or her judgment. 'Emergency care in Germany must be centralised and professionalised!' the Xpomet organisers demand. In addition to cross-professional information on continuing education and training, and regulations for the allocation of resources in line with demand, require the digitisation of supply processes.

This question is also addressed within the 'OP of the future' showcase, which will show how computer models are used to carry out therapy. At Xpomet, a virtual operating theatre with 'phantom patient', will demonstrate how medical technology based on computer models recognises a surgeon's current surgical stage and calculates the next step in advance.

Patient demands will shape the future

During the event visitors are to be offered 'mixed reality glasses' that have been used in surgical procedures recently, when two novelneurosurgical interventions were performed in Germany for the first time in 2017.

Time and again, a central future medicine topic has been the electronic patient record. The convention aims encourage this by showing what a smooth data flow could be. In an animated video, the networking of companies and their interfaces will be illustrated based on three patient histories. During a related think tank, the question of what the prerequisites are that will make networking interfaces a reality and not simply an imagined Utopia (23 March).

Obsolete equipment, paper stacks, fax machines – Xpomet diagnoses an innovation gap in many medical practices. The medical practice of the future would save doctors and employees time. Visitors will be shown how the initiators envisage an ideal future practice, starting with a simple online appointment.

Why is it not so easy to install innovations in the German healthcare system, when we all handle apps, for example, in many different areas of life?

Pieper sees German politicians as too overstretched to make good decisions. However, he assumes that the healthcare system will change because patients will demand innovations.

Changing communication between doctor and younger generation patients would help them to ask more confidently for innovations and different treatment options.

'At Xpomet we want a bottom-up process,' Pieper explains. In concrete terms, this means that the organisers do not rely on top decision-makers and established names, as in other trade fairs, but rather on students, patients and lateral thinkers who will help shape the future in the healthcare sector.

Following three-years as head physician in the emergency unit at Berlin's Vivantes Klinikum am Urban, in 2015 **Dr Timo Schöpke MD** was appointed for his present role as Director of the Emergency Centre of the Barnim Clinic in Berlin.

Industrial engineer Ulrich Pieper is the Xpomet Convention's Chairman. and the founder and CEO of Business Management GmbH. Since graduating his work has focused healthcare sector for more than twenty years.

In the run-up to Xpomet, deficits in German emergency medicine were outlined

MT-CONNECT exhibition and MedTech Summit

Meeting up with Europe's med-tech and health experts

The international MedTech Summit and MT-CONNECT, an international medical technology exhibition (Nuremberg, 11-12 April 2018) is a key event in Europe. For many years, developments in digitisation and personalised health have been among core elements of the congress, the organiser points out.

Around 1,900 visitors travelled to Nuremberg for the previous MedTech Summit Congress and MT-CONNECT, which provided 96 specialist presentations in the congress and exhibition, which had 189 exhibitors from 11 countries. Medical practitioners and other healtcare and industry experts will benefit from the networking opportunities at this year's event, too, according to Dr Matthias Schier, Managing Director of MedTech Pharma e.V.

Connected Health, Neurostimulation, Personalised Medical Technology, Drug Delivery as well as Implant Technologies are just some of the headliners at the Summit.

Besides technological contents, the congress increasingly focuses on IP Management, Supplier Manufacturer Relations, reimbursement and business models, aiming to build a bridge between development and production on the one hand and application in research and clinics on the other.

The speakers are from renowned companies such as Siemens, Philips, Aesculap, Medtronic und TÜV SÜD Product Service GmbH, and universities and research institutes such as Munich's Technical University in Germany, University Zürich in Switzerland, and several Fraunhofer Institutes, plus clinical application specialists.

The Matchmaking Event will be included again in 2018 to provide an opportunity for participants to network their ideas and needs

The previous MedTech Summit and MT-CONNECT included ninety-six specialist presentations in the congress and exhibition forum

The Partnering event

The parallel 'Partnering' event offers a strong chance to network. In 30-minute cycles, this popular format brings together exhibitors, congress visitors and others.

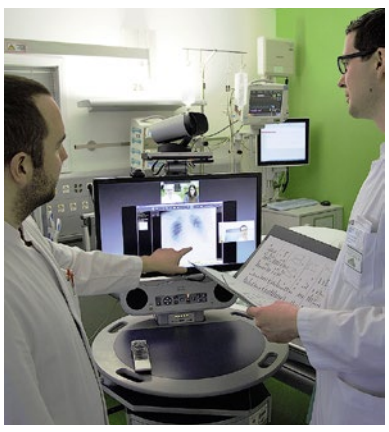
A software program is available to enable participants to arrange appointments quickly.

Details: www.medtech-summit.com

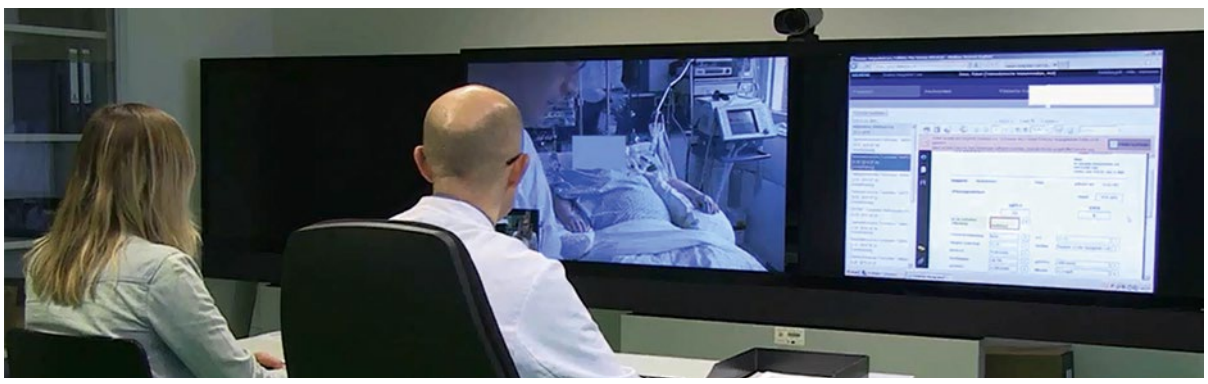
Could telemedicine cure Germany's health system?

Hope for telemedical ward rounds

Doctors discuss treatment options via a videoconference



The telemedical system also transmits X-rays and results



The model project transports digital devices to a patient's bedside or treatment table to conduct the videoconferences

Report: Anja Behringer

The term telemedicine has been around since the 1980s. Ten years later Deutsche Telekom demonstrated the first applications designed to provide medical services to people living remotely such as (based on American ideas) astronauts in space, workers on oilrigs or injured personnel in field hospitals. Since then, the concept of medical care across long distances via telecommunication has not changed. The advantages of fast intervention, diagnostic safety through simultaneous expert opinion obtained via videoconference and ultimately, the associated cost savings still apply – but implementation of the good intentions has been thin on the ground.

A low degree of digitisation

The reason is the lack of digitisation in the healthcare sector, as confirmed by a study commissioned by the Federal Ministry of Economics and Technology last year. The German Federal Association of the Digital Economy believes the most significant reasons why the healthcare sector is lagging behind to be political: rigid legal provisions (around the ban on remote treatment, for instance); rigid structures in statutory health insurance; inertia and the preservation of self-serving interests within the self-governing committees of health insurers and doctors; data protection regulations that are too complex, and a lack of information about the advantages of digital technology provided by the key players in healthcare. At congresses and workshops examples of best practice are conjured up to learn from other sectors that are much more digitised. One example is lean management, as seen in the automotive industry: streamlined process chains lead to shorter waiting times, reduced distances and handing over of error-free results step by step of the process ('zero- error principle'). One attempt at improving processes in hospitals with this principle is the use of digital wristbands. In a model project in Berlin the location of hospital patients is monitored through those wristbands to relieve staff and make processes more efficient.

Model project telemedical networking

The model project TELnet@NRW managed by the University Hospital RWTH Aachen follows a different approach. The objective is the development and evaluation of a comprehensive telemedical network as a new digital care platform. The project is funded with €20 million from a Federal Joint Committee innovation fund and focuses on intensive care medicine. More than 20,000 patients have already participated since the start of the intervention phase in October last year. 'We didn't really count on that many study patients in the first few weeks! We're very pleased,' says Professor Gernot Marx, Director of the Aachen Clinic for Surgical Intensive Care Medicine and Intermediate Care, member of the ZTG-Forum Telemedicine and head of the TELnet@NRW project. 'We are therefore grateful to all participating project partners, hospitals and networks of surgeries to whom we can attribute the success and who deliver vital data for this project.'

An anticipated 40,000 in- and outpatients are being recruited from 21 participating institutions to obtain valid results. The focus will be on patients with infection-related problems and intensive care patients.

A specially created telematics infrastructure facilitates regular tele-intensive, virtual ward rounds by experts from the centres for telemedicine at Aachen and Muenster universities, as well as from partners at the participating hospitals and networks of surgeries.

When the project is completed at the beginning of 2020 it remains to be seen whether the results confirm care optimisation and whether telemedical ward rounds should become part of standard medical care.

Switzerland permits 'remote treatment'

Telemedical treatment in Switzerland has been allowed for the last 14 years. Doctors are available around the clock in designated centres and the experiences have been positive, not even to mention the healthcare cost savings of around 17%. Germany is still way behind.

'The maxim here is still that the first contact between a patient and treatment provider must be personal,' Marx explains. To ensure these specifications are met, a secure video communication link with fast and protected data exchange between the participating organisations is inevitable.

In practice, the Aachen model project transports digital devices, such as computers, monitors and cameras, to a patient's bedside or treatment table so that doctors from different hospitals can discuss the best treatment options via a videoconference.

The devices also facilitate the transmission of a patient's X-rays and results. 'The connection with telemedicine centres at Aachen and Muenster university hospitals is established via highly secured data cables and is therefore well protected,' the expert explains. Professor Thomas Jäschke at the Institute for Health Care Security and Data Privacy (ISDSG) is the external expert for data protection and IT security who advises the project.

Currently there are regular exchanges about infection-related problems between doctors in private and general practitioner (GP) surgeries and specialists in infectious diseases at Aachen and Muenster university hospitals.

Continued on page 6

Professor Gernot Marx MD, Director of the Clinic for Surgical Intensive Care Medicine and Intermediate Care at the RWTH Aachen, Germany, and member of the ZTG-Forum Telemedicine and Head of the TELnet@NRW project, studied medicine (1987-1994) at Hanover Medical School (MHH), Germany, where he also wrote his doctoral thesis in 1995 and habilitation in 2000. In 2004 MHH appointed him as extraordinary professor and, in the same year, he was awarded a C3-professorship for life for Anaesthesiology, Intensive and Emergency Medicine at the Friedrich-Schiller University, Jena, Germany. In 2008 he was awarded a W-3 professorship for life for Anaesthesiology with a focus on Surgical Intensive Care Medicine and Intermediate Care at Aachen University Hospital. His current focus is on the comprehensive introduction of telematics into healthcare, with a view to implementation as standard care.

Soon service robots will find their healthcare niche

Robots: Weak knees and hard facts

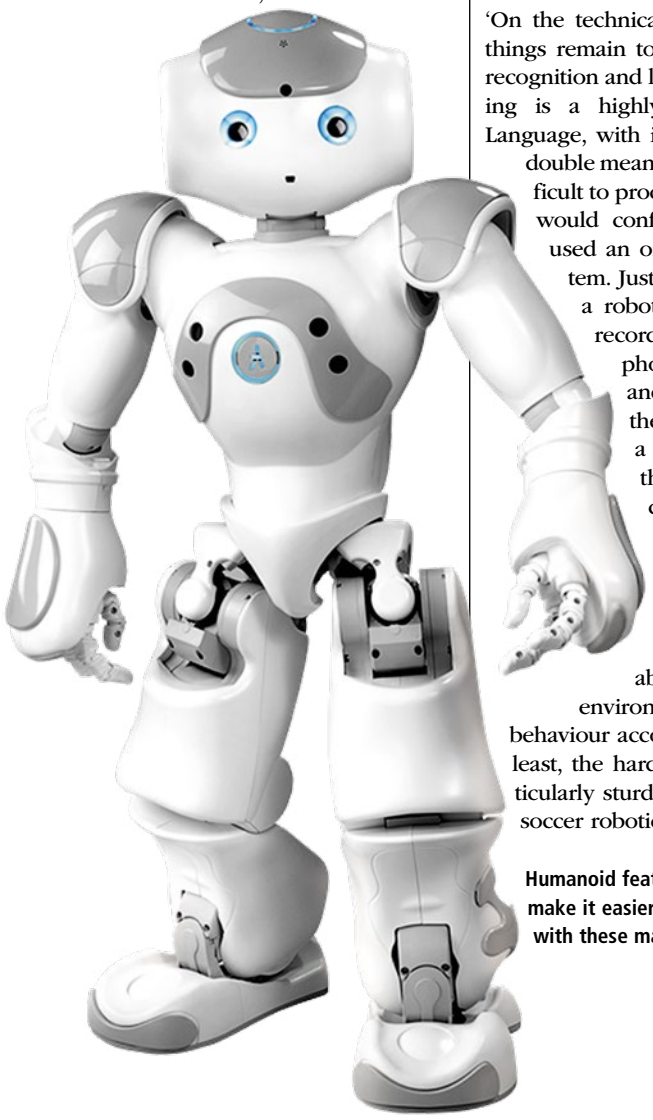
Although robotics is now an established arm of medical technology – with the Da Vinci surgical system a trailblazer – many basic issues need to be resolved before nurse Robot can report for the morning shift in a ward. Surprisingly, among the major problems is the fact that a robot becomes a bit weak at the knees quite easily, explained Mathias Hofmann, researcher at the Robotics Research Institute at Technical University Dortmund, Germany, during an IVAM Microtechnology Network conference. Since centre-forward Robot and nurse Robot are closely related, EH spoke with the developer of soccer robots about current progress

Interview: Lena Petzold

'Service robots in Germany are still quite rare. The robotics industry is new and very few companies offer products suitable for daily use – primarily because a number of basic problems remain to be solved,' explained robotics expert Mathias Hofmann, when asked about their role in healthcare. 'The developers must go back to the drawing board and deal with functions such as language recognition and context awareness. If they don't work properly in a robust and stable system, there will be no marketable products. Service robots, unlike precision systems in the OR, have to perform tasks autonomously – they are much more than a surgeon's extended arm.'

Where can service robots be used?
'They can be used in many areas: obviously, they can monitor and help patients, but they also can bridge waiting times and take over administrative tasks. Theoretically, a robot can perform any task with a low degree of autonomy. In the hospital or the waiting room a robot can entertain patients by playing games with them. Robots can "man" the reception desk – collect data or answer routine questions.

'In the future, robots will also be used to convey information on procedures, or to help children overcome their fear of surgical intervention or certain therapies. Robots might as well monitor the hospital for emergencies and alert the staff. Furthermore, the use of robots is being tested in specific therapies aimed at addiction patients or autistic people. Having said that, one thing remains clear: robots will never be able to replace clinical staff. '



Humanoid features are designed to make it easier for humans to interact with these machines

Then why waste energy on developing service robots?
'The major advantage of service robots is that they relieve staff workload. With their very specific skills, robots are well suited to perform repetitive tasks. In 2014, "Pepper" was introduced, a robot with humanoid features, which, to a certain degree can interpret human emotions and respond appropriately. It is available 24/7 and never under pressure.'

Which technical challenges need to be overcome?
'On the technical side, a number of things remain to be done. Advanced recognition and language understanding is a highly complex process. Language, with its ambivalences and double meanings, is extremely difficult to process – as most people would confirm who have ever used an online translation system. Just like a human being, a robot needs to hear and record language, convert it phonetically into words and respond to it on the cognitive level. 'For a machine to perform those semantic processes and respond to nuances is much more difficult than for a human. Context awareness is another issue: the ability to recognise the environment and adjust the behaviour accordingly. Last but not least, the hardware has to be particularly sturdy – as we can see in soccer robotics every day.'

What problems are you currently trying to tackle?
'We are working on several issues. As a football player, and as a robot, you have to be able to recognise your surroundings; you have to orient yourself; communicate with your team mates, make split-second decisions and move your body accordingly.

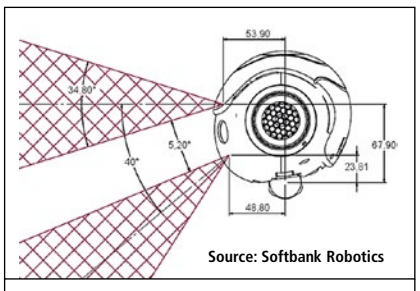
For our research we use NAO, a two-legged humanoid robot that is 58 cm tall and equipped with two cameras, four microphones and speakers as well as several sensors – for example four ultrasound and eight pressure sensors. Just like its human counterpart a robot needs a sense of equilibrium, tactile sense and muscle sense. Under stress the robot's joints run hot and it literally gets weak at the knees. Consequently, NAO needs a system that prevents it from overheating, so to speak.

This is one of the crucial challenges: developing robust systems. In a lab – or on our in-house soccer pitch – the robots tend to function pretty nicely. But, take them out of the lab and things get tricky: the transfer performance is still inadequate. On a smooth surface, NAO can walk without a problem, but what happens when there's carpet on the floor or, even worse, steps?

'Camera settings are another headache: when light incidence changes, the perception of the robot changes. In well-lit rooms this is not so much of a problem, but a service robot also has to function when the light is dimmed or in the dark.'

Beyond technical challenges, are there others?
'Indeed, the legal and ethical obstacles are high. Should robots be allowed at all to act autonomously and take on responsibilities? Take the example above – robots that provide medical information. What about privacy and data security issues when a robot performs administrative tasks?

NAO robots are equipped with cameras, microphones, a gyroscope and acceleration sensors.



Source: Softbank Robotics

NAO camera settings determine images the robot can record and process

What happens in case of an accident? Who is liable – the manufacturer or the operator of the robot? All of these questions are highly complex and none of them has been answered satisfactorily.

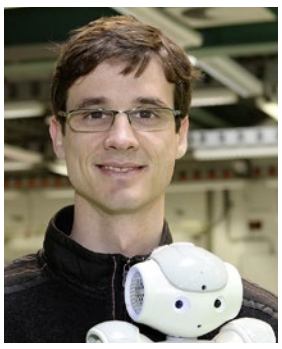
'We are confronted with these issues now with autonomous cars – they are nothing but service robots.

Short, quick movements, as necessary on a football pitch, put strain on robot joints

The use of service robots is moreover a cost issue. It won't suffice to invest in the device; a suitable infrastructure has to be developed at the same time.

'A robot needs to move and orientate itself. Even a human being has difficulties finding his or her way in a hospital where all the hallways look the same. A robot needs unambiguous machine-readable signs, such as beacons or QR codes. This signage has to be developed and implemented.

'A lot remains to be done but I am confident that we will develop suitable solutions. Service robots, I am sure, will soon find their niche in healthcare.'



Mathias Hofmann is a researcher at the Robotics Research Institute at Dortmund Technical University in Germany. Following training as an informatics specialist at Deutsche Telekom AG in Bonn, Germany, in 2005, while also working, he began an informatics BA programme with a focus on business informatics in Darmstadt, Germany. In 2008, he enrolled in an MA programme in informatics with a focus on Intelligent Systems at Dortmund Technical University, while working at the Department of Geo-information Systems at Wupperverband. In 2011, he gained his Master's degree and was offered a position at the Robotics Research Institute. In 2014, he held a six-month research fellowship at the University of Miami in the USA.

Hope for telemedical ward rounds

Continued from page 5

There are daily tele-intensive ward rounds, handovers and case conferences.

'Only around 300 specialists in infectious diseases work in hospitals nationwide,' Marx points out; not enough to provide comprehensive, personal care. TELnet@NRW is to bridge this gap 'because early and joint diagnosis is better and ensures adherence to guidelines'.

Professor Alexander Zarbock, Director of the Clinic for Anaesthesiology, Surgical Intensive Care Medicine and Pain Therapy at Muenster University Hospital is particularly pleased about cooperation between the hospitals: 'By making scientific expertise available to colleagues at any time we support the best possible, close-to-home patient care.'

Next to Aachen and Muenster university hospitals, a further 17 hospitals within the Aachen and Muenster regions are also in the consortium, along with the Techniker Krankenkasse (Technical Health Insurance) and the medical networks Gesundheitsnetz Köln-Süd (GKS), and MuM – Medizin und Mehr.

The consortium is supported by partnerships with the hospital association North Rhine-Westphalia, the Medical Associations North-Rhine and Westphalia-Lippe as well as all statutory medical insurers in North Rhine-Westphalia.

The University of Bielefeld and the Centre provide scientific guidance for Telematics and Telemedicine GmbH (ZTG) in Bochum. The evaluation phases will run to three years.

The data collection method via cluster randomisation and a stepped wedge design allows the project team to compare each hospital with itself and other hospitals over time. Together with continuous data collection this facilitates calculation of the causalities between changes in therapy and diagnosis and the telemedical intervention.

After this evaluation a decision will be taken as to whether telemedical ward rounds can become part of standard medical care.

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SPECIAL ISSUE FOR THE EUROPEAN CONGRESS OF RADIOLOGY

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Hopes for AD prediction

New information on dementia biomarkers is emerging, as increasing results from population studies become available. However, although the list of risk factors lengthens, the value of these predictors, and more generally the cause of disease, remain to be determined, according to Gabriel Krestin, professor and chairman of the Department of Radiology & Nuclear Medicine at Erasmus MC, University Medical Centre Rotterdam.

Report: Mélisande Rouger

Are brain microbleeds predictors of dementia? Ever since radiologists spotted microscopic hemosiderin deposits on MRI, their association with the development of Alzheimer's disease (AD) is increasingly acknowledged.

Gabriel Krestin is the architect of population imaging in the Rotterdam Study, a large epidemiological cohort of 15,000 elderly subjects who have been followed for more than 25 years. He coordinated the installation of a dedicated imaging infrastructure 12 years ago and, since then, more than 14,000 brain MRI and 3,000 CT scans have been carried out to find out what brain features are associated with the development of dementia. For Krestin, there is no doubt that microbleeds and dementia correlate.

Detecting microbleeds

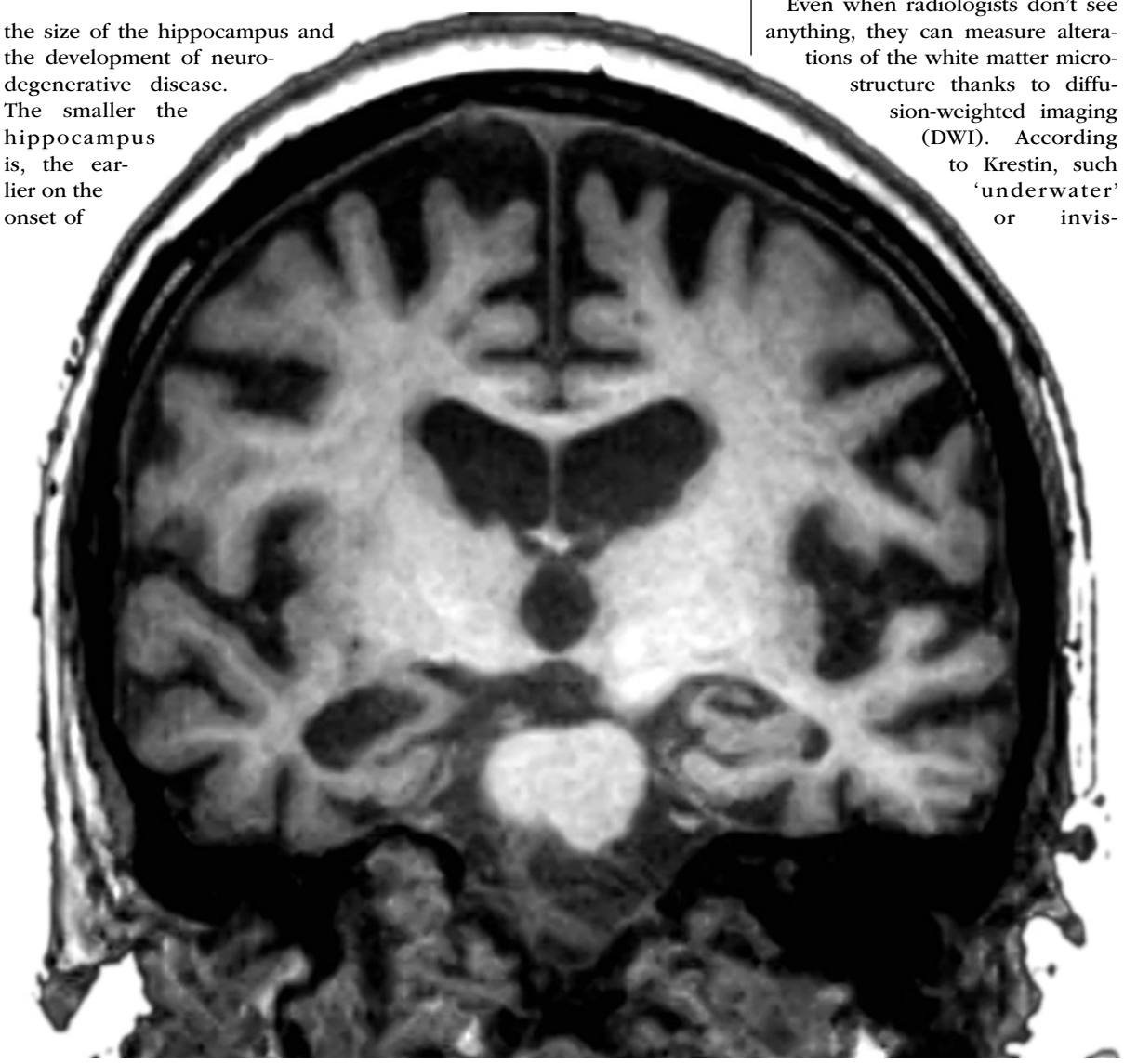
'There is an association between microbleeds, or signal voids, and cerebrovascular disease and the development of dementia. Here we have a potential predictor of an increased risk and development of disease,' he said.

Thanks to MR techniques using susceptibility imaging, researchers involved in the Rotterdam trial have detected a significant portion of microbleeds – enough to be able to prove the link between these lesions and not only AD, but also overall mortality.

'Even one single microbleed increases the risk of mortality; if there are more than five, mortality significantly increases, and so do cardiovascular and other diseases. Microbleeds are a strong predictor of increased mortality,' Krestin confirmed. There is also a strong association between incidence of microbleeds and the use of antithrombotic drugs. But the prognostic value of these haemorrhages has yet to be clearly demonstrated to issue proper recommendations, he explained.

'What is the predictive value of microbleeds? Should we recommend all our patients not taking aspirin? A lot of attention has been given to this information since over the past years. Truth is, we still don't know for sure.'

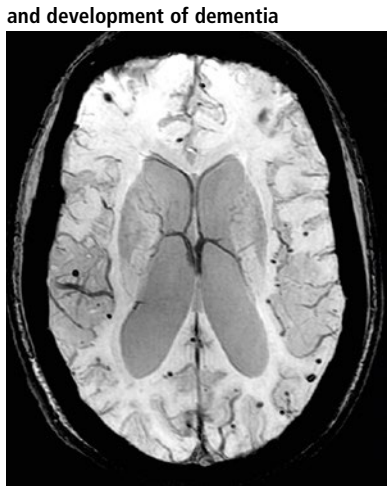
There is a consensus on several risk factors and associated predictive imaging biomarkers of AD, and the best known is hippocampus atrophy. 'There is a relation between the size of the hippocampus and the development of neurodegenerative disease. The smaller the hippocampus is, the earlier on the onset of dementia. The risk of developing dementia increases in individuals with smaller volumes of the hippocampus and amygdala,' Krestin explained.



Coronal T1-weighted MR image of the brain demonstrating hypocampal atrophy (predictive imaging biomarker of Alzheimer's disease)

Volume changes of the hippocampus are even stronger predictors of dementia, and Krestin and his team have shown that accelerated atrophy is even a stronger predictor of AD. 'Even the shape of the hippocampus and the fact that not all its parts are decreasing at the same pace may predict AD development,' he added.

Transversal susceptibility weighted MR image of the brain demonstrating multiple microbleeds (signal voids) associated with cerebrovascular disease and development of dementia



Analysing white matter microstructure

White matter lesions (WML) and silent lacunar brain infarcts are additional acknowledged biomarkers. Early on, the Rotterdam Study showed that the number of lesions was related to cognitive decline. 'The more WML there are, the faster the cognitive decline of the subjects is. Increased periventricular WML load is associated with cognitive decline and the risk of dementia,' he said 'There is also a relationship between silent or small brain infarcts and AD.'

Even when radiologists don't see anything, they can measure alterations of the white matter microstructure thanks to diffusion-weighted imaging (DWI). According to Krestin, such 'underwater' or invisible markers are associated with impaired brain executive functions and may also predict the development of dementia.

His team is now focusing on assessing the microstructure of the white matter to detect invisible lesions in that area. 'The integrity of white matter microstructure is a very strong predictor. Even before lesions are visible, diffusion parameters are measurable and predict the development of disease,' he explained.

Professor Gabriel P Krestin MD PhD is professor and chairman of the Department of Radiology & Nuclear Medicine at Erasmus MC, University Medical Centre Rotterdam, The Netherlands. He is also the Scientific Director of the European Institute of Biomedical Imaging Research (EIBIR).

Using probabilistic tractography, the Dutch researchers have shown that lower tract microstructure integrity was associated with cognitive decline. Krestin believes they could even go a step further and establish relations between the brain's functions and its microstructure and other functions of the body, since there are some associations between kidney function and probably cardiac function and brain microstructure.

The professor and his colleagues are now looking into the disconnectivity hypothesis, i.e. integrating structural MRI and resting state fMRI to build up to the so-called connectome.

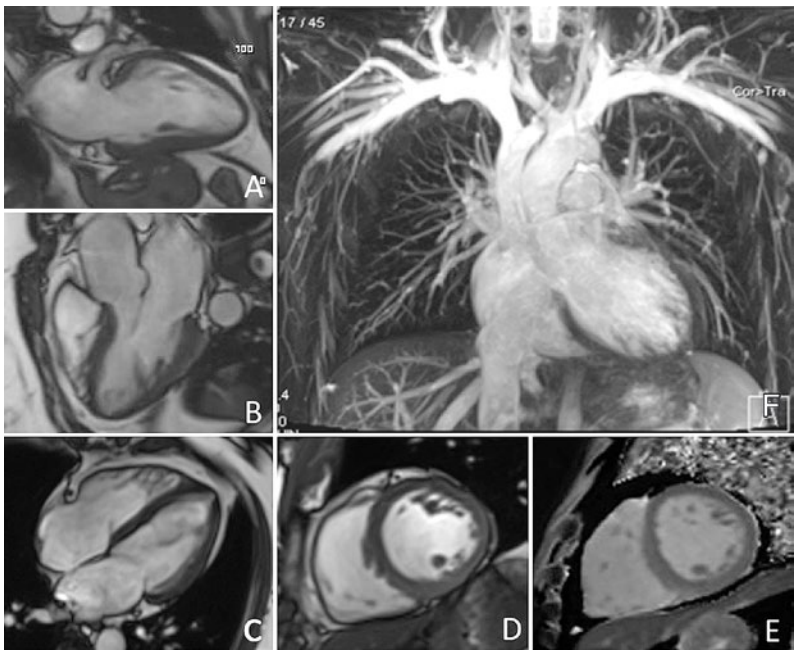
'We want to look at these connections and the function of white matter tracts in order to predict development of cognitive decline at an earlier stage.'

Continued on page 8

Big Data in cohort studies analysis will boost disease prediction

Population imaging

Population imaging is key to determining disease prediction and risk prevention, and Big Data will be key to extracting information and drawing analysis from imaging results, experts highlighted during the annual meeting of the European Society of Magnetic Resonance in Medicine and Biology (ESMRMB) held in Barcelona in October.



Examples of MR images acquired as part of the cardiovascular protocol:
A–C: Long-axis MR images obtained with the cine steady-state free precession sequence
D: Short-axis MR image obtained with cine steady-state free procession sequence
E: MR image obtained with T1 mapping (modified look-locker inversion recovery)
F: Native thoracic MR angiogram

Source: Bamberg F, Kauczor H-U, Weckbach S, et al. Whole-body MR imaging in the German national cohort: Rationale, design, and technical background. Radiology 2015;277:206-220.

Interest in cohort studies has been increasing over the years and population imaging is on the verge of becoming a major medical topic, according to radiologist Professor Fabian Bamberg from Tübingen University.

'Most of our services are based on delivering care to people who are already sick, but a more meaningful approach would be to identify subjects who are at risk for early disease or death at a very early point in time, to modify lifestyle, medication, and just prevent the future development of disease. Ideally, we'd assess genetic determinants right at birth and act accordingly,' Bamberg suggests.

For 15 years the professor has been involved in improving and developing imaging tools. While knowing the determinants – genetic, physiological and environmental information – and outcomes, cancer, dementia, etc., is a key, the issue remains the determination of what occurs in the meantime. 'We don't really know what's in between. I'm convinced that, between determinants and outcome, there is something else to disease, and imaging is a powerful mean to assess and quantify it, and come out with a more individualised risk assessment over time – and this is due to new achievements in MRI.'

MRI can provide new information, but researchers need large data to derive these parameters. Cohort studies can help prove that those imaging biomarkers are really predictive for the occurrence of disease over time.

Famous studies have already stressed the power of population imaging. The Framingham heart study, which observed 3 generations between 1948 and 2017 to predict the occurrence of cardiovascular disease, has helped identify various risk factors, such as high blood pressure, increased cholesterol, diabetes, smoking and family history, by notably using imaging. More recently, the Rotterdam study, which used brain MRI, has revealed that the presence of silent brain infarcts is associated with cognitive decline and increased risk of dementia over time.

The next big thing will be the German National Cohort MRI study, Bamberg said, as it will provide comprehensive characterisation and phenotyping in more than 30,000 participants with 3-T whole-body MRI. 'It's a unique opportunity to substantially impact on imaging-based risk stratification leading to personalised and precision medicine,' he explained.

The study is part of a national, government-funded effort: the GNC study (in German: NAKO), which includes 200,000 participants recruited through 18 centres (and 8 clusters). All participants are invited to take part in physical and medical examinations, collection of biomaterials, personal interviews, and to fill in questionnaires. In 2019, participants will be re-invited for a second examination five years after baseline recruitment.

The participants will undergo complex whole-body imaging sequences – MRA, T-1 mapping of the myocardium, and high-resolution imaging of the neurocranium, torso, hip, and spine – to provide a comprehensive image of the human body and help answer longstanding questions. Results will go along developments in Big Data, radiology, IT and radiomics, to achieve comprehensive characterisation of disease-phenotypes using advanced image-analysis, Bamberg forecasted. 'All this detailed information will help us characterise disease and early disease states much better. For instance, we can cluster patients with lung cancer by applying advanced post-processing methods with similar radiomic expression patterns. Results obtained with this type of imaging analysis are much more relevant and precise for predicting clinical outcome and genetic tumour type,' he pointed out.

Two major challenges to the GNC study remain incidental findings and the internal variability of the MRI studies – although the latter has been addressed by implementing similar MR technology with identical protocols, he explained.

One solution may be related to deep learning, and the field is currently growing exponentially. For instance, convolutional neural network (CNN) has already helped develop and validate a deep learning algorithm to detect diabetic retinopathy in retinal fundus photographs (JAMA, 2017, Gutshan et al.).

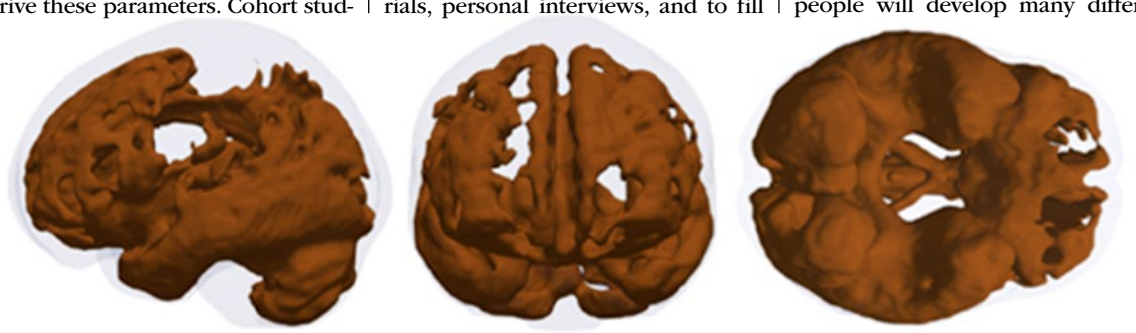
'Prevention of disease is increasingly relevant and there's a high potential of subclinical disease assessment. MRI is an ideal tool for whole-body phenomapping and radiomics is an ideal target for big data approaches,' he concluded.

Paul Matthews, from Imperial College London, presented the UK Biobank prospective longitudinal study, which includes 500,000 women and men aged 40-69 years at the time of the baseline assessment in 2006-2010. The study, which is supported by independent academics, includes extensive baseline questions and measurements, follows up a wide range of disease outcomes by linking to health record systems and direct contact, and will offer adjudication of health outcomes to confirm or refute and to sub classify phenotype.

'Sufficiently large numbers of people will develop many different conditions to assess causes reliably. Having 500,000 volunteers in the study will provide enough power for future cohort designs,' Matthews said. He also highlighted the role of population imaging in defining risk factors, biomarkers of presymptomatic disease and contributory mechanisms for important and common disease.

'Cohort studies create opportunities to investigate gene-environment associations with phenotypic markers and longer-term outcomes. We need to understand disease from the start, decades before they appear. Lifestyle and environment interact with underlying genetic susceptibilities to influence the risks of brain disease. We need to understand how these factors – the exposome* – influence the brain through life,' Matthews explained. 'We can't change your genes, but we can change the environment; people are motivated to do so if we define the risks.' MR

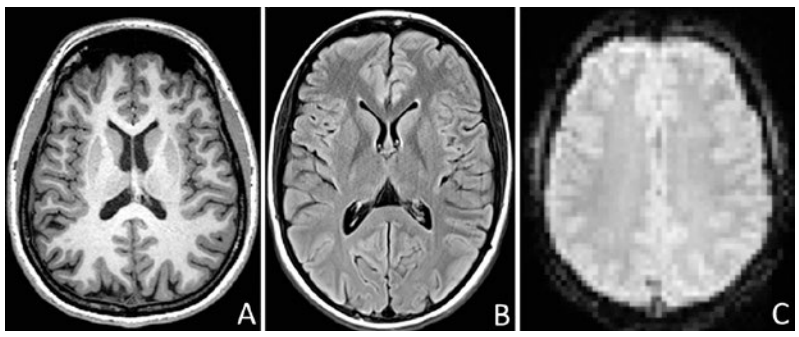
* Exposome: a potential vehicle the better to incorporate environmental components into the study of disease and health.



Brain regions showing age-related atrophy from the initial 5,000 individuals imaged for UK Biobank. To generate this figure, T-1 structural brain MRI images from each of the participants were represented in a common, standard brain space. Age related differences in brain volume across the population were assessed. Those areas showing the greatest change with age are illustrated with a dark brown wash. (Image courtesy of Dr Hideaki Suzuki, Imperial College London).

Paul Matthews OBE, DPhil, FRCP, FMedSci is the Edmond and Lily Safra Professor of Translational Neuroscience and Therapeutics, and Head of the Division of Brain Sciences at Imperial College London, and Associate Director of the UK Dementia Research Institute. He is an NIHR Senior Investigator and lead researcher for the Imperial College Healthcare Trust Biomedical Research Centre Neuroscience Theme. He is also a Fellow by Special Election of St. Edmund Hall, Oxford, UK, and holds other honorary academic appointments in Oxford, Maastricht, McGill and the LKC Medical School of Nanyang Technological University, Singapore.

Professor Fabian Bamberg MPH is currently Associate Chair of Radiology at the Department of Diagnostic and Interventional Radiology at the University of Tübingen, Germany. He received his medical degree from the University of Witten-Herdecke, Germany and gained a Masters in Public Health from Harvard School of Public Health in 2007.
After serving as a faculty member in the Cardiac MR PET CT Program at Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA, he joined the Department of Radiology in Munich, Germany, in 2008, where he completed Residency and Fellowship at the Ludwig-Maximilians University and subsequently directed the MRI program as an attending physician.



MR images obtained as part of the neurologic MR imaging protocol
A: T1-weighted 3-D magnetisation-prepared rapid acquisition gradient-echo sequence
B: Two-dimensional fluid-attenuated inversion recovery sequence
C: 2-D gradient-recalled-echo echo-planar imaging blood oxygen level–dependent sequence (for resting-state functional MR imaging)

Source: Bamberg F, Kauczor H-U, Weckbach S, et al. Whole-body MR imaging in the German national cohort: Rationale, design, and technical background. Radiology 2015;277:206-220.

Hopes for AD prediction remain

Continued from page 7

Meeting the challenges of harmonisation

Genome-wide association studies (GWAS) may contribute to finding associations between genetic alterations and particular imaging biomarkers.

However, there are many challenges ahead. 'You need extremely large populations and to pull the data from different cohort studies possibly including 20-50,000 subjects, to find significant genotypic alterations related to certain imaging phenotypes. You also need a high level of harmonisation in terms of image acquisition, sequencing and data processing,' he added.

The Rotterdam Study collaborates in the CHARGE consortium, including large population cohorts in the Netherlands, Iceland and the USA. A network of researchers in epidemiology genetics and imaging that cooperates to better understand neurodegenerative brain disease. For instance, they found a mutation on chromosome 17, which is associated with WML. They are not sure how to interpret this information yet. 'Is this genetically determined? Is the presence of such mutations associated with earlier dementia onset? We don't know,' Krestin said.

GWAS are only showing associations with and increased risks of developing certain diseases, but not necessarily the cause of disease, he pointed out. 'The utility of these studies is unclear. We find out something about pathophysiology, but not really the cause of this association yet.'

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1. Data on file and from public sources, 2017. **2.** Results from Friedewald, SM, et al. "Breast cancer screening using tomosynthesis in combination with digital mammography." JAMA 311.24 (2014): 2499-2507; a multi-site (13), non-randomized, historical control study of 454,000 screening mammograms investigating the initial impact of the introduction of the Hologic Selenia® Dimensions® on screening outcomes. Individual results may vary. The study found an average 41% increase and that 1.2 (95% CI: 0.8-1.6) additional invasive breast cancers per 1000 screening exams were found in women receiving combined 2D FFDM and 3D™ mammograms acquired with the Hologic 3D™ Mammography System versus women receiving 2D FFDM mammograms only. **3.** In an internal study comparing Hologic's standard compression technology to the SmartCurve™ system (18 x 24cm).

Despite shortages and low recognition

Emergency radiology advances

Emergency radiology is no longer a babbling field; professionalisation will bring more recognition to this young subspecialty, according to Elizabeth Dick, a London-based consultant, who will coordinate part of the new European Diploma in Emergency Radiology (EDER), the European Society of Radiology's new tool. During the International Day of Radiology (IDoR) in November 2017, which focused on emergency radiology, **Mélisande Rouger** interviewed the radiologist, who spoke of her daily practice and why she loves her job.

In London, the Imperial National Health Service (NHS) Trust is a major trauma centre, covering a radius of over 12 miles (20km). 'In the capital this means a lot of people. We also treat abdominal and chest pain, and paediatric emergencies, explained Dr Elizabeth Dick, who estimates her radiology department carries around 20-30 emergency CT scans a day. A consultant for the past 15 years, she has worked in emergency radiology for as long as she can remember. 'I have grown with the specialty, which wasn't established until the late 1990s,' she said.

What's so special about emergency radiology?

'I like the fact that we can make a difference and we are really crucial to the patient pathway. Everybody wants to know what's on CT, so we really influence patient management.

'I enjoy the team approach. We are 15 people in the room, all trying to figure out together how to best treat the patient. Being in emergency radiology myself, I know it's really important in a person's life. No one wants to be there, but if we can make a difference, it's really inspiring.'

Source: Viktor Birkus / Shutterstock

Emergency radiology is a young specialty; as such, this field needs more recognition according to radiology consultant Elizabeth Dick

How do you cope with staff shortage?

'This is not just a local problem; it's a worldwide issue. We prioritise our patients and try to train our juniors very well. We encourage them to ask questions and support them as much as we can. In the end we try to provide a full seven-day service, but we're not able to do that. We provide a full five-day service with emergency cover out of hours, which I find frustrating.

'The hospital is open 24/7 and you will always get good care. But we should have at least daytime consultant lists every day and we're far from that. We have resident juniors with back up from consultants who come into the hospital and are always at the end of a phone.'

Is teleradiology helpful in this context?

'Like every other hospital in the UK, we use teleradiology for all kinds of out-patient imaging. If we can sort those out, that gives us more time for emergency work.

We don't use teleradiology at night, but other hospitals do. It's obviously a very good short-term solution. However, it doesn't really solve the problem of not having enough radiologists.

'I know that a lot of people working in teleradiology work in the NHS, so they are working less directly in their hospital. Additionally, however great Skype or the phone is, it's not quite the same as working together with someone you've known for a while. You lose a lot in translation.'

What other challenges exist for emergency radiologists?

'ER is a young specialty and needs more recognition as such. People often think within their own specialty and that's it. In ER, the skills you need are very broad. Pretty much everyone I know has other interests and that's good because you can bring in different skills. You end up covering the whole body between the staff.'

Is cooperation good with other emergency specialists?

'It's one of the things I really love about emergency medicine in general: teamwork is amazing. Emergency medicine is very young too; we are very much on the same line. Emergency physicians are fantastic to work with; they really want to communicate. That's a real attraction: who wants to work with grumpy colleagues?'

Will Brexit impact on ER?

'Personally I believe Brexit will be a disaster for UK Healthcare. It will have a big impact on our work because about 20% of our healthcare staff comes from Europe. The uncertainty is already driving people home. Instead of thinking of building a future here, people head back. For everyone, their income dropped by 20% when the pound devalued. The impact of the loss of European funding for research and development has already been felt so Brexit is already impacting on healthcare in a variety of ways.'

Are there European trends in emergency radiology?

'More radiology studies are being done. When I started as a radiologist, if people came with an appendicitis they'd go straight to the operating theatre. Now they undergo CT, unless the clinicians are very certain. Imaging definitely increases diagnostic confidence in clinicians before they come to the theatre. Postoperative outcomes are also much better.

'Emergency radiology is not a subspecialty everywhere in Europe. In the UK it is a less established and probably the youngest radiology subspecialty.

'Another big trend is professionalisation within radiology. The ESR has produced diplomas in chest, neuro and now emergency radiology.'

What is the European Diploma in Emergency Radiology?

'This diploma began in January. It consists of 10 webinars and 10 workshops and one exam, so the first candidates will graduate in 2019.

'The idea of having a Europe-wide diploma is great, because it means that wherever you go in the world you'll find someone with the same experience as in your country. This also brings international recognition of their skills to radiologists, and improves their career perspectives abroad.'

Dr Elizabeth Dick is consultant radiologist and lead for emergency radiology at the Imperial College NHS Trust in London, UK. She is president of the British Society of Emergency Radiology and president elect of the European Society of Emergency Radiology (ESER).

Size and mobility is saving time and lives

At the scene: point-of-care ultrasound

Time is of the essence in an emergency, and can be the difference between life and death. Ambulance crews on the front line must decide rapidly whether or not a patient is suffering from a life-threatening condition requiring specialist treatment, and point-of-care ultrasound can provide vital guidance.

SonoSite is at ECR 2018 Hall X5, Stand 503

Geert-Jan Deddens, an emergency care nurse practitioner with the Rotterdam Ambulance Service in the Netherlands, describes the benefits of using hand-carried ultrasound systems to assess suspected abdominal aortic aneurysms, allowing patients to be taken to the most appropriate hospital immediately, avoiding delays due to onward transfer to another medical facility.

'I joined the Rotterdam Ambulance Service in 2006 as an ambulance nurse, going on to train as a nurse practitioner in emergency care five years later. We look after a population in the region of 1.2 million people, covering a large area in and around the city. As a nurse practitioner, I attend emergency call-outs to provide additional support to the ambulance crews when needed, for example, in cases of cardiac arrest.

Geert-Jan Deddens scanning a patient via point-of-care ultrasound

'A couple of years ago, a vascular surgeon at one of Rotterdam's hospitals contacted the ambulance service to discuss the potential benefits of using point-of-care ultrasound to identify and assess patients with an abdominal aortic aneurysm (AAA) in a pre-hospital setting. Without ultrasound, we might suspect the patient has an aneurysm, but we can't be sure. This means that the hospital has to be prepared to carry out emergency surgery, with an operating theatre and emergency room staff on standby to treat this life-threatening condition, when the patient may have a completely different abdominal pathology that is less serious.'

More accurate assessments

'We realised that introducing ultrasound into pre-hospital care would allow us to scan the aorta in the ambulance and make a more accurate assessment of whether or not the patient has an aneurysm, and also to estimate its size. Once we know that, we can quickly transfer the patient to the most appropriate hospital, and provide more exact information to the surgeon much earlier.

'This means that the hospital is better prepared, and does not tie up resources unnecessarily. It also eliminates potentially life-threatening delays caused by avoidable transfers between hospitals, as the patient is taken to the correct medical facility first time.

'At the end of 2015, we began a pilot study – Pre-hospital Assessment Rotterdam Aortic Aneurysm (PARA2) – to evaluate pre-hospital assessment of the abdominal aorta using point-of-care ultrasound (POCUS).

'Fujifilm SonoSite provided two hand-carried ultrasound systems and, together with an emergency physician with extensive POCUS experience, trained three ambulance nurses and two nurse practitioners to scan the abdominal aorta. It quickly became part of our daily routine to scan patients' aortas, gaining as much practice as possible.

'As nurse practitioners, we also received more advanced training in point-of-care ultrasound, including Extended Focused Assessment with Sonography for Trauma (eFAST), to allow additional conditions to be triaged.

950 abdominal scans in the first 16 months

During the pilot study we scanned as many patients as possible, evaluating how easy it was to perform the procedure and the length of time it took to obtain a good view of the aorta. We carried out 950 abdominal scans during the first 16 months, finding 14 patients with an AAA where the aorta measured more than 3 cm.

'Of these, four patients were immediately directed to a vascular surgery team for urgent treatment, potentially saving their lives. At the same time, we were able to identify other life-threatening conditions pre-hospital, for example, differentiating between wet and dry lung problems, looking for blood in the abdomen following an accident, as well as using ultrasound during a cardiac arrest.

'This all helps to ensure the patient is directed to the right facility first time, whether that's a specialist trauma or cardiac centre, ensuring that they receive the most appropriate treatment at the earliest possible opportunity. For patients with an acute AAA, this may well be a life saver.'

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1. Data on file and from public sources, 2017.

New MRI technique visualises seepage that might cause AD

Seeking a leaky blood-brain b

Report: Madeleine van de Wouw

'With our new MRI method, we can finally visualise tiny leaks in the blood-brain barrier. They shed light on the vascular contribution to dementia and may indicate Alzheimer's disease. However, the MRI scan is only a tool to diagnose cerebrovascular damage. We have not yet found a cure for Alzheimer's,' confirms Walter H Backes, medical physicist and professor at Maastricht University Medical Centre.

The blood-brain barrier (BBB) separates blood from the brain tissue and protects the brain by allowing certain substances to pass while keeping others out. Backes, with his interdisciplinary team of Maastricht UMC and Leiden UMC, are hot on the tracks of Alzheimer's disease (AD) as they aim to visualise small vessel leakage in BBB.

Contrast-enhanced MRI

While conventional MRI visualises neither small vessels nor markers or leakage, the dynamic scan traces even extremely low concentrations of the marker fluid everywhere through the bloodstream and brain tissues, no matter how small the vessels are. 'Contrast-enhanced MRI is a combination of vision, technical knowledge and computer power,' says Backes, adding: 'We now can investigate with medical imaging in a non-invasive way and we don't have to rely on post-mortem tissue or spinal tap samples anymore.'

Initial clinical tests yielded exciting insights: 'Since we couldn't test our new scanning method in healthy volunteers with an intact BBB we immediately scanned Alzheimer patients and saw damages in the barrier with fluid leaking from the smallest blood vessels to the brain.'

New insights in the vascular contribution of dementia

Due to the leakage, unwanted substances can enter the brain and damage the tissue. 'At first, blood vessels were not considered a player in the development of AD. While animal experiments had shown leaking blood vessels, these leaks were not thought to be associated with cognitive decline and dementia. What we discovered in the human brain is somewhat of a fluke, an accidental breakthrough. While we can show the leak, we cannot determine yet whether it is AD. This requires further research. Nevertheless, the connection between BBB impairment and AD pathology was strengthened by the fact that the addition of diabetes and other non-cerebral vascular diseases did not change the results.'

The condition of the blood vessel system, Backes concludes, seems to play a very important – and previously underestimated – role in the development of Alzheimer's disease. 'Earlier research focused the deposition of amyloid-beta proteins as a possible cause of AD. This theory appears to be disproven today: When we wipe out the protein stack with medication, the condition of the patient remains unchanged. Finding this leakage is therefore an important contribution to the research on the development of AD. We have shown that in people with Alzheimer's disease not only the brain but also blood vessels are damaged, and that the damage is substantial.'

While there is no cure yet for Alzheimer's, Backes' research might indicate that keeping our vascular system in good condition – with good nutrition and physical as well as mental exercise – could help stave off AD.

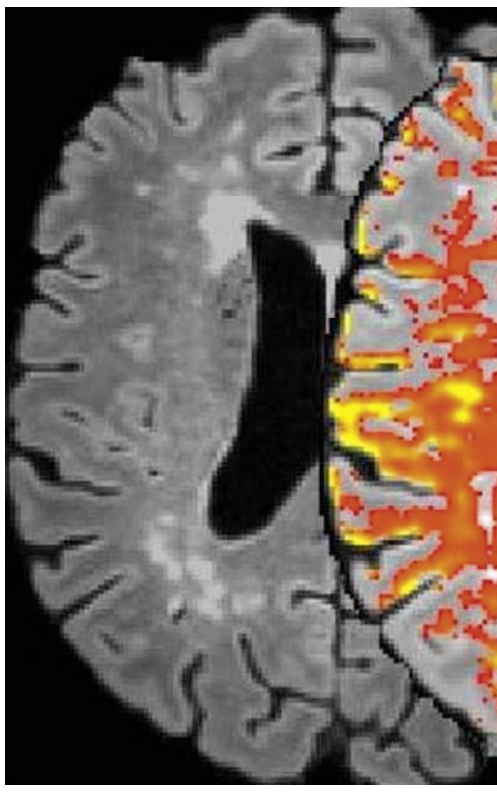
Further research

Unfortunately, the new MRI method is not yet widely available. Therefore, as the physicist explains, 'We are focusing on making the technique easier to apply, so more people can be examined, even those who do not yet show symptoms. With our new knowledge of the leaks, we might be able to send medication to certain places in the brain. However, we don't yet exactly know how vascular medication works in vascular disorders. This will need further investigation.'

Indeed, two follow-up studies are planned, each lasting about four years. Backes: 'In eight years we should have a better understanding of the cause of Alzheimer's. Approximately one hundred people with and without diagnosed AD will participate in each trial.'

Award-winning research

During RSNA 2017, the article Backes and his team published in 'Radiology'* received the Alexander R Margulis Award for the best scientific article of the past year. For Backes the award did not come as a surprise because his research had attracted considerable attention: 'It



Healthcare artificial intelligence

AI – Radiology's next frontier

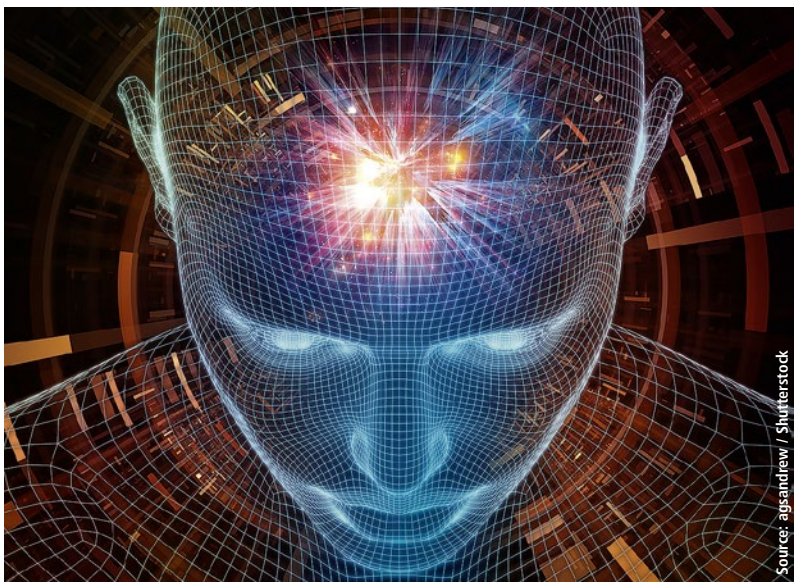
Artificial intelligence (AI) technology and its role and future impact on the radiology profession was the dominant theme at RSNA 2017, whether in scientific presentations or in the technical exhibitions. Keith J Dreyer DO PhD addressed this subject head-on in his presentation 'Healthcare AI – Radiology's Next Frontier.'

Report: Cynthia E. Keen

Dr Keith Dreyer, vice chairman of radiology informatics and chief data science officer at Massachusetts General Hospital in Boston, is an acknowledged expert on information technology (IT) innovations in radiology. His prediction, at a packed lecture hall during the joint RSNA/AAPM scientific session, was that an AI future is very bright for radiology and radiologists. Once AI becomes an established technology in radiology, it will allow radiologists more time to work with both clinicians and their patients. Rather than being diminished, radiologists will assume the leadership role of being aggregators of all data that passes through the diagnostic process. Acknowledging the large number of AI-oriented companies exhibiting for the first time and veteran vendors incorporating the subject of AI into their exhibition booths, Dreyer rhetorically asked where the radiology profession is on the pathway to AI expectations? At the very beginning, he answered.

Potentially diagnostic imaging AI will take decades

Building an AI algorithm can be surprisingly easy, but converting an algorithm into a sophisticated product that works consistently in clinical use is very complex. He disagrees with deep learning pioneer Professor Geoffrey Hinton, a computer scientist at the University of Toronto, whose remarks at the 2016 Machine Learning and Market for Intelligence Conference that medical schools should stop training radiologists now because they will not be displaced by AI technology in five to 10 years made global headlines.


Source: agsandrew / Shutterstock

Digital technology has radically changed the radiology profession: with increasing complex modalities, with electronic health records and the more specialised radiology information systems, with digital imaging and PACS, with cloud storage and global digital image exchange capabilities, and with speech recognition dictation systems and auto-populating structured reporting templates. But these technologies and their adoption have evolved over decades. Diagnostic imaging AI will also potentially take decades because there is a staggeringly large amount of work to do.

The potential for AI has stirred excitement since the 1950's, but deep learning only began to flourish in 2010. The growth in AI applications over the past five years has been fuelled by rapid advances in technology, growth, data, and massive investment from tech titans, by powerful new applications for known AI techniques, the proliferation of open source software, and sharing of advances. Imaging diagnostics is a hot area for investment, and it behoves organisations like the American College of Radiology (ACR) and the RSNA to get very involved.

'What you see on the exhibition floor are very narrow applications of AI, focusing on a very specific radiology application. Is this application needed? Just how good does it need to be? What can it solve better than a radiologist?' Dreyer compared the global diagnostic performance of radiologists to a bell-shaped curve, ranging from random guesses to perfection. What should the standard for an AI algorithm be? He observed that there are many places on the globe where good AI assistance in a very narrow application would be adequate.

Complex work and interaction by multidisciplinary community is needed to have clinical AI take place on a broader scale, and a platform to support all the development of algorithms to deal with thousands of findings and tens of thousands of medical conditions. AI will need to focus on image interpretation, patient care and safety, and radiology practice optimisation for productivity and quality. To show how these AI products reduce costs and improve outcomes will require clinical translation and industrial-grade integration into routine workflow.

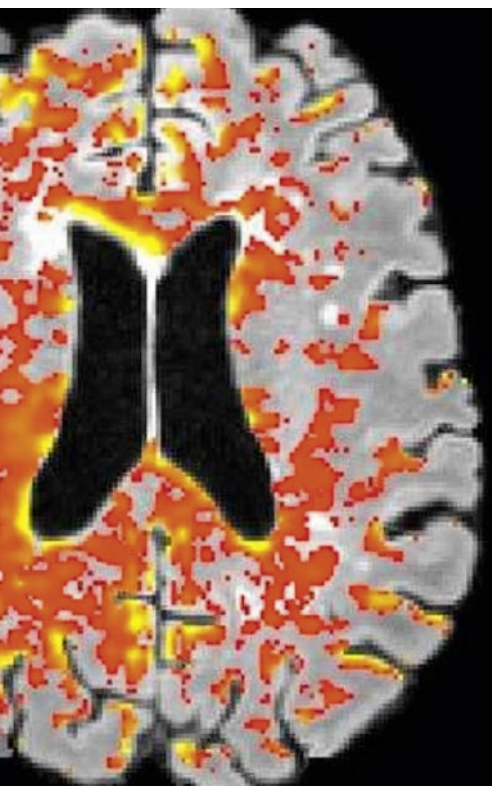
Current obstacles include lack of a healthcare AI ecosystem. No standard methods exist to annotate data for AI model training and testing, nor is there a standard mechanism for clinical integration into existing systems and modalities and future ones. AI healthcare standards need to be developed.

This is a role that the recently established ACR Data Science Institute (www.acrdsi.org) is tackling. Its objective is to advance data science solutions for radiology care that are clinically relevant, safe and effective. The Institute is working with the USA's Congress, federal agencies, the healthcare AI industry, professional societies and the healthcare community. Dreyer discussed in detail the numerous issues that need to be addressed with respect to clinically viable AI applications.

Easing the AI premarket approval process

Radiology has an enormous opportunity to leverage AI to become a centre of intelligently aggregated, quantitative, diagnostic information. This is of great interest to the USA's Food and Drug Administration (FDA), which sees the potential for medical device development tools to ease the process of AI premarket approval and programs such as the National Evaluation System for Health Technology (NEST) to improve post market surveillance through a continuous data feedback loop, as is being implemented by

arrier



provocative investigation that breaks with the current view that blood vessels play no role in the Alzheimer's process.'

So where is AD research heading? 'Since the BBB not only allows nutrients but also medication to pass', Backes explains, 'we might be looking at opening the BBB with sound waves and thus administering medication locally. Many questions remain to be answered: in the event of a leak, the liquid seeps through everything, but how will that work when we open the barrier artificially. Will the opening close again? Will such a procedure improve the quality of life? Can we possibly administer medication indirectly?

In short, the possibility to visualise the leak in the blood-brain barrier opens many doors for all kinds of new research. There is still a lot to be done and even more to be expected.'

Magnetic resonance brain image of an Alzheimer's patient with colour-coded blood-brain barrier leakage

*http://pubs.rsna.org/doi/10.1148/radiol.2016152244

Medical physicist **Walter H Backes** is professor at Maastricht University Medical Centre in the Netherlands, where his research focuses on magnetic resonance imaging of neurological and vascular diseases. In 1999, he established functional imaging of brain diseases for research and clinical examinations. Since then his imaging research expanded to include oncology, vascular and neurologic applications.

Currently, his research examines novel imaging techniques, including (contrast-enhanced) angiography, perfusion and diffusion imaging and functional MRI of brain networks in diabetes, epilepsy, Alzheimer's and small-vessel disease. He initiated and supervises a certified post-academic training program in medical physics and lectures on various radiological imaging topics.

feels very special to get the prize as a physicist. I am not a physician, not a radiologist. It is certainly an incentive to continue. The jury thought it was a

Keith J Dreyer DO PhD is Vice Chairman of Radiology and Director of the Center for Clinical Data Science at Massachusetts General Hospital, USA. He is also Associate Professor of Radiology at the Harvard Medical School. The author of numerous scientific articles and papers is an expert on informatics and focuses his research on various fields including cognitive computing, clinical decision support and digital imaging standards. He has held diverse board and committee positions with healthcare organisations, including the Radiological Society of North America and the American College of Radiology.

the ACR registry process. Financial reimbursement relating to the use of AI tools in diagnostic imaging must be addressed, a separate but related additional layer of complexity.

Once these hurdles are overcome, Dreyer predicts that the combination of radiologists and AI working in tandem will be far better than either working alone. He told the audience to imagine interpreting an exam in PACS that has already gone to the cloud where quantified findings were made, a patient's medical record analysed and compared with data, and structured recommendations and guidelines provided.

Radiologists will be able to work more intelligently, more accurately, and more efficiently. They will be able to do things that they never could do before. Radiology and AI will further expand the impact of diagnostic imaging. It is a goal our entire profession needs to work toward and embrace.

We need to determine the benefits and potential risks

Reason must prevail in debates on GCCAs use

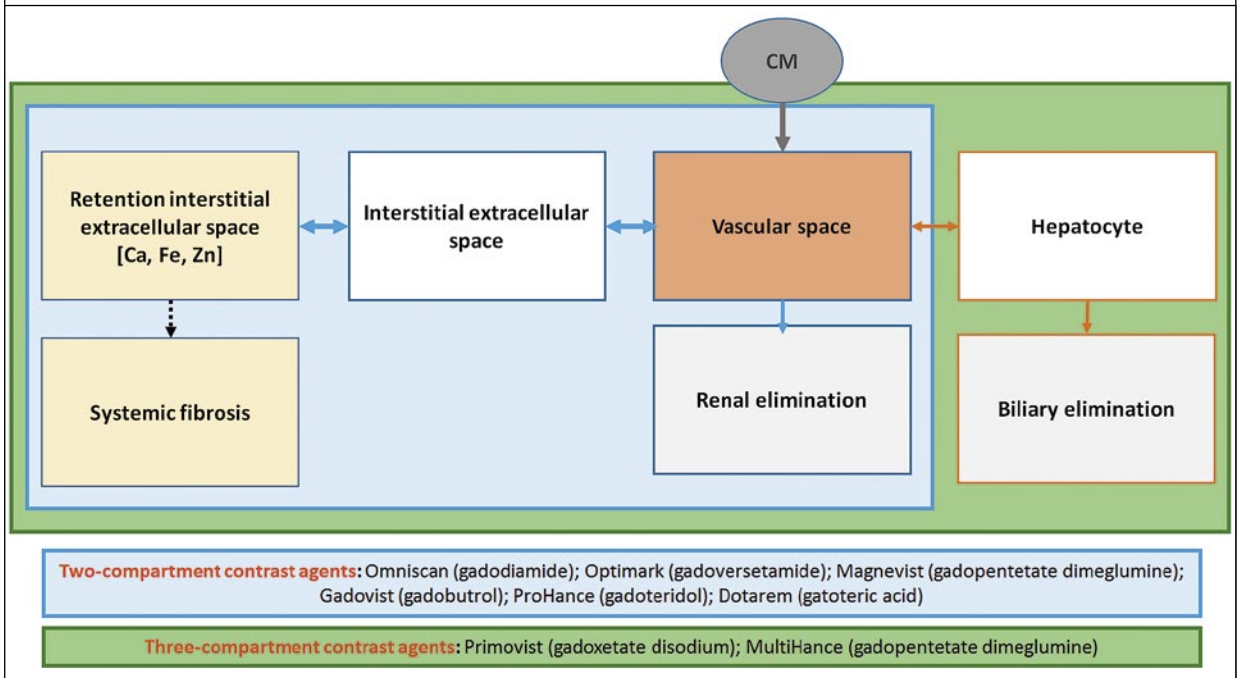
Radiologists must ensure precise scientific data and radiology-based evidence are used to regulate the use of Gadolinium Containing Contrast Agents (GCCAs), a Spanish leading radiologist explained in closed-door leadership meeting earlier this year in Barcelona.

Findings showing GCCAs deposits in different parts of the body have triggered a profusion of publications and decisions that now directly affect radiology practice. The good news is that radiologists can use their abilities to bring science back into the discussion, according to Luis Martí-Bonmatí, Director of the Medical Imaging Department and Biomedical Imaging Research Group at La Fe University Hospital in Valencia, who addressed a panel from the academy and the industry.

'There's been a real tsunami; large quantities of diverse information and opinions that have pushed the authorities to make decisions, which affect our daily practice but are based on neither accurate nor precise data,' he said.

Radiologists now understand the full extent of the deluge. 'We may not have valued these decisions properly at the time. Usually we are not involved in these discussions, so it's not easy to form an initial opinion,' Martí-Bonmatí explained.

In the past three years, concern has grown about gadolinium deposits in the brain of patients undergoing GBCA-enhanced MR examinations. In 2017, the Pharmaco-vigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) recommended suspension of some GCCAs marketing authorisations based on linear chelators, due to the potential risk of gadolinium retention in the human body; the recommendation was further extended by EMA's Committee for Medicinal Products for Human Use. As a result, four linear GCCAs are no longer marketed in the EU lions of patients. GCCAs have been administered more than 300 million times, with a very low frequency of acute adverse events. People tend to overestimate the occurrence of very unlikely events and magnify them in the decisions they make. And generally, people lack abilities to correctly interpret statistical probabilities,' Martí-Bonmatí pointed out.



Administration of gadolinium containing contrast agents

Luis Martí-Bonmatí MD PhD is Director of the Medical Imaging Department and Biomedical Imaging Research Group (GIBI230) at La Fe Polytechnics and University Hospital and Health Research Institute in Valencia, Spain. He is also professor of radiology at Valencia University

(Omniscan, Magnevist, Optimark and MultiHance).

Clear clinical evidence is missing

However, even if long-term safety of GCCAs remains unclear, current scientific evidence for gadolinium retention has several methodological limitations, most experts feel. 'No clear clinical evidence exists indicating that gadolinium retention causes neurotoxicity. We need this evidence to formulate a hypothesis,' Martí-Bonmatí said. 'If we don't use that approach, hypotheses simply do not stand.'

In Spain, the Medicine and Medical Devices Agency is following the EMA recommendation, arguing that clinical benefits do not overcome potential risks. But it still enables the use of Primovist and MultiHance for hepatic studies, an exemption Martí-Bonmatí finds intriguing. 'That's a backroom door! If risks do exist, then they should be relevant in any application and in all contrast media,' he said. 'Even more importantly,' he added, 'we know today that all GCCAs are retained in tracer quantities in different compartments, but without any histological toxicity or clinical sign.'

Debates on potential risks of cutting-edge technology had spurred in the past over the use of radiofrequency and, more recently, magnetic resonance imaging, as an EU directive planned to limit the exposure of workers to magnetic resonance. Eventually, the proposal was withdrawn.

'This draft would have significantly restricted the use of a technique that has showed its benefits in mil-

Precise data to evaluate risks is needed

Radiologists can help evaluate reliability and relevance of risk management investigation using their scientific reasoning. 'What the world needs now are cool, reason-based facts to evaluate risks appropriately. We need to use the scientific method, i.e. to carry out consequent observation using experimentation, measurements, formulation, analysis and hypothesis renovation, to generate evidence,' he said.

However, as they offer their expertise to help advance knowledge, radiologists must demand strong data in return.

'Us radiologists should have a clear idea on how to evaluate data precision, and trust our critical and criteria appraisal for the patients benefit. Each time an institution, academy, committee, person or group approaches us with recommendations on how to act in our clinical practice, we should ask which data and evidence they base their opinion on, to be able to use our reasoning,' he said.

Bias awareness

When faced with the vast amount of studies on the potential risk of GCCAs, radiologists must be aware of bias inherent to scientific investigation. In radiology, bias can originate from samples, tools and data used in measurements and analyses.

But even when trials are carried out properly, results often prove useless, Martí-Bonmatí explained. 'Not only are most investigation results false but also, when they are accurate, they are useless. That's because, deep down, we base our evaluation on statistical probability and we can't or don't know how to, or haven't properly extrapolated small samples' results from the general population. And,' he added, 'we haven't been able to properly manage these small probabilities.'

To this day the only known adverse effect linked with GCCAs use is nephrogenic systemic fibrosis, which had a very low incidence; the risk has almost disappeared since doses are now tailored to each patient. Recent research even suggests it has no effect in patients undergoing dialysis or with chronic renal disease.*

Differentiation is important

Martí-Bonmatí recommends evaluating contrast agents separately, as they have different retention profiles, and conducting prospective controlled trials. Radiologists should also be aware of poorly controlled CA administration numbers and doses, and of the importance of confusion variables, such as age, sex, patient condition and the interval between dose administrations.

'Patients with different diseases and treatments should not be mixed and the effect of pharmacokinetics should be taken into account. We also need histological and/or mass spectroscopy confirmation, as it is absent from most series,' he added.

Last but not least, radiologists use different MR equipment and parameters, and therefore have to watch out for T1 signal variations.

'Retention in bones, skin, liver, or central nervous system is different depending on which CA is being used,' he said. Instead of fighting over which CA is safe to use or not, radiologists should use their energy and skills to determine benefit-risk ratio. Finally, Martí-Bonmatí concluded: 'Political appreciation has ruled in risk management evaluation so far. The time has come to determine which are the benefits and potential risks when using contrast agents.' MR

*https://www.ncbi.nlm.nih.gov/pubmed/28731375

ECR 2018
Wednesday 28, February
16:00-17:30 Room G
Special Focus Session, Level II

SF 4 Gadolinium deposition: is it harmful?

RSNA 2017 highlight – The InnerEye Project

AI drives analysis of medical images

Some time in the distant future artificial intelligence (AI) systems may displace radiologists and many other medical specialists. However, in a far more realistic future AI tools will assist radiologists by performing very complex functions with medical imaging data that are impossible or unfeasible today, according to a presentation at the RSNA/AAPM Symposium during the Radiological Society of North America's 2017 meeting.

Report: Cynthia E. Keen

Research scientist Antonio Criminisi, and colleagues at Microsoft UK's InnerEye project in Cambridge, have been developing machine-learning techniques for the automatic delineation of tumours and healthy anatomy for ten years. Intended applications are extraction of targeted radiomics measurements for quantitative radiology, rapid treatment planning for radiotherapy, and precise surgical planning and navigation. At the RSNA/AAPM Symposium he explained how the team developed algorithms for AI-drive analysis of medical images and their future use.

AI types to simulate human intelligence include robotics, computer vision, and machine learning. Computer vision utilises algorithms for automatic image analysis that understands semantics. Deep learning, just one type of practical machine learning, is part of life – e.g. analysing online buying and consumers' interactions via computer.'

AI research for medical image analysis originated with Microsoft Kinect, developed for game play, Criminisi explained. Kinect uses machine learning that takes input test depth images and, through pixel classification, determines body part segmentation to replicate 3-D human movement. 'Eureka!' The researchers decided that Kinect's technology could help create 3-D images of CT, MRI, and PET scans. Thus InnerEye began a decade of research in automatic semantic segmentation of radiology images.

The goal of automatic 3-D segmentation? To build useful radiomics tools. Criminisi showed how data from two axial slices of the same CT scans overlaid could create 3-D images in seconds. 'Voxel-wide semantic segmentation is difficult to achieve,' he explained. 'The sources of variability factors are huge. These include the same Hounsfield unit (HU) for different anatomies, large deformations, beam-hardening artefacts, different image resolutions, differing degrees of image noise, the presence/absence of contrast medium, and different patient preparations. All these need an algorithm, and the only way to deal with these large sources of variability consistently is through machine learning.'

Algorithms must work with everything, so training data must represent all these variables. For algorithm training, the researchers gathered image data from hundreds of patients in hospitals worldwide, produced by various modalities/models, with different acquisition protocols and image resolutions.

From this, a representation data set was created for segmentation, with each voxel and pixel in an image assigned to an anatomical structure. Supervoxels created from clusters of voxels were taught to associate voxels with anatomical structures. Hundreds of millions of voxels from data of hundreds of patients were used to create a ground truth model.

Decision tree techniques created forests of decision tree layers. A cascade of forest layers, each with unique probabilities, creates a trained deep decision forest model. 'Designing a task-specific algorithm addresses a task at hand, but often doesn't teach us how to address other tasks. When using a decision forest technique, for each new task the model remains the same, as do the training and runtime algorithms. We just enable new families of visual features.

Deep decision forests vs. cellular neural networks

'Once a deep decision forest model for semantic segmentation is developed, it's then applied to previously unseen images to train it, with feedback applied to make improvements continuously. We use the word "deep" because this means we are reusing the output layer to create new layers, each of which improves upon the segmentation image being developed.' At the event, Criminisi then demonstrated the cloud-based radiomics service.

Forests may be better for medical image analysis, so are preferred instead of cellular neural networks (CNN) for the semantic segmentation algorithms. Algorithmically they differ little, but Criminisi advised forests need less training data, may be faster, do not need GPUs, and may deal better with class imbalance.

'Our algorithms have been extensively validated on diagnostic images of both boney structures and soft tissue. In accuracy, there has been no statistical difference between ours and expert radiologists. When compared with comparable regulatory agency-approved algorithms, our algorithms results were as good or better.'

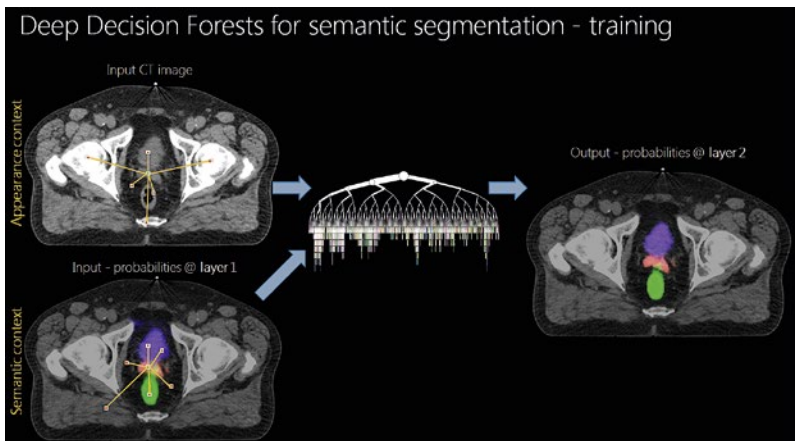
Assistive AI for radiotherapy planning

Currently, the clinical workflow for image-guided radiotherapy is first to acquire a planning scan, perform manual 3-D delineation and calculate the prescribed radiation dose. Manual 3-D delineation and dosimetry takes hours. The InnerEye process takes about five minutes. 'We want to eliminate critical, laborious and tedious tasks for radiologists and dosimetrists,' Criminisi explained.

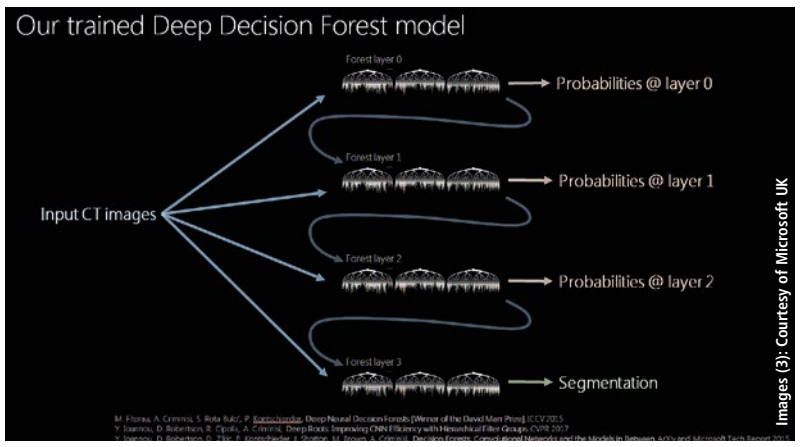
Another application is to monitor disease progression during treatment and perform quantitative radiology automatically. The InnerEye model creates easier visualisation of a tumour from images acquired over time and can create plot lines showing volumes of an active tumour. Criminisi showed a brain tumour that disappeared during treatment – no tumour could be visualised, non-negligible oedema was detected.

'AI can make monitoring cancer treatment effectiveness and disease progression much easier and potentially much more accurate,' he said. 'This is just one aspect of potentially being able to provide more efficient, quantitative image analysis workflow within a clinic. We want to turn this research into a real technology for clinical use,' he concluded, inviting medical software providers into partnership. 'Our expertise is in AI research, not healthcare. InnerEye cloud services are intended to be integrated components in third-party medical imaging software. We invite interested companies to contact us at innereyeinfo@microsoft.com.'

Antonio Criminisi gained his PhD at the University of Oxford in 2000, the same year he joined Microsoft, where today he is a principal researcher at Microsoft Research in Cambridge, UK, working on artificial intelligence, machine learning, computer vision and medical image analysis. He has authored numerous scientific papers and won several awards, including the David Marr Best Paper Prize at the International Conference on Computer Vision 2015 in Chile. He now leads Microsoft's InnerEye project that uses AI to create medical image analysis tools.



The InnerEye researchers prefer to use deep decision forests for their semantic segmentation algorithms instead of cellular neural networks (CNN)



By reusing the output of previous layers as input for the subsequent layer, they are developing a cascade of decision forests that eventually provides more precise results

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The race is on – radiologists must pick up the ball and run!

Liquid biopsy versus radiomics

The development of new procedures to monitor cancer treatments is gathering momentum. One such innovation is liquid biopsy. This new lab technique allows non-invasive identification, characterisation and monitoring of circulating tumour DNA. Thus, liquid biopsy can potentially revolutionise oncological diagnostics – and put a spoke in the wheel of radiology. High time to act, says Professor Dr Jens Ricke, Chair of Radiology at Ludwig Maximilian University (LMU), Munich, and Director of the Clinic and Polyclinic of Radiology at LMU Hospital. He is confident that radiology has several aces up its sleeve – one is radiomics.

Interview: Daniela Zimmermann

Why is liquid biopsy such a success?

'As soon as liquid biopsy has identified circulating tumour DNA, it's also possible to identify gene mutations that might influence the therapy,' the Professor explains. 'This effect can be seen in the personalised therapy of colorectal cancer: an RAS or RAF mutation of the metastasising colorectal tumour impacts systemic therapy. Liquid biopsy can indeed detect this mutation in circulating tumour DNA.'

What does that mean for imaging?

'That's exactly the sore point. Methods such as liquid biopsy are mere lab procedures. They have only recently been introduced and are still under development. This phase, no doubt, will continue for a while. Nevertheless, we radiologists have to get a move on today if we want to actively shape the future of oncological imaging. If liquid biopsy keeps its promise, it may well replace the tight imaging follow-up in oncology. Obviously, that won't mean that radiologists will be out of work. But, we do have to think about our future now and, above all, we need to tap the full potential of radiology. For a long time, we have applied RECIST (Response Evaluation Criteria in Solid Tumours) criteria and accepted their imprecisions. However, we do need unambiguous standards. The current procedure relies on mere volume measurement: tumour growth or regression, however minute, is evaluated. This, however, does not allow a reliable prediction of therapy response. There are better parameters, which have not yet been clinically validated and are thus not accepted as follow-up variables.

'Enter radiomics: future developments in radiomics may well yield suitable criteria to gauge therapy response in oncology. However, as yet there is no proof that the parameters really predict patient survival linked to therapy response. Current data are incomplete and their analysis and successful transformation into criteria will take years. Therefore, we must hurry up.

'The competition is on the ball. This is why we should invest more resources in radiomics. I'm sure we do have the means and the possibilities to create useful alternatives.'

What exactly needs to be done to shape this future?

'Above all, we need validation studies. Firstly, imaging methods need to be established, which might encompass entirely new forms of analyses. The idea underlying radiomics is to cull more information from image data than meet the human eye. This involves complex statistical analyses, what's usually subsumed under the buzzword Big Data: computational drudgery. Every large data set has to be analysed over and over until patterns with predictive value regarding therapy response – or the lack thereof – become visible.

'MRI has already offered promising techniques. But this is just the beginning. The more methods are being developed, the more important is the validation of those methods. Prospective clinical studies that define and show innovative imaging endpoints for therapy response are indispensable.

'Today, FDA and EMA require clinical trials for regulatory approval of a pharmaceutical to be based on the RECIST criteria. However, we also have to think about the validation of potentially new imaging endpoints.'

How quickly can results be produced?

'The validation of such procedures is time-consuming. This is another reason why the projects have to be launched as soon as possible. Validation is always tied to a specific endpoint of the study as such, which might also include long-term survival studies. However, not only studies themselves can take years, the preparation also takes a lot of time.'

Is there political or industry support for these methods?

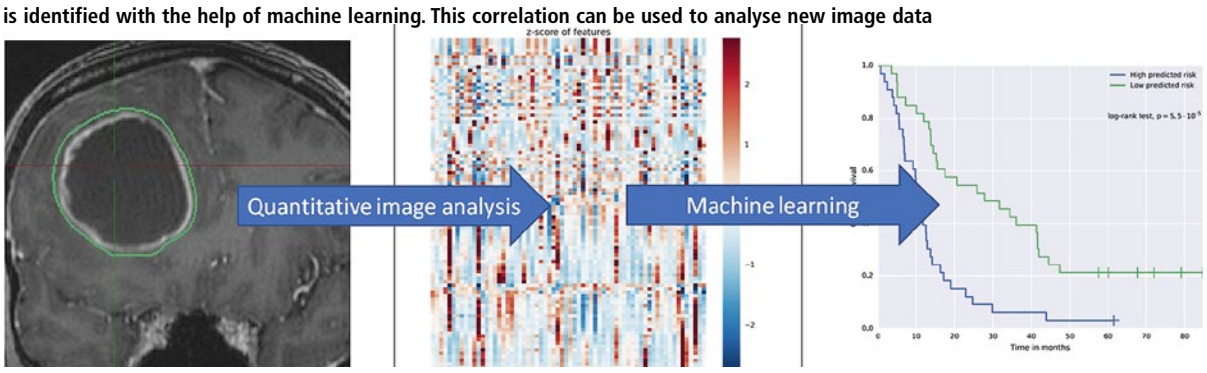
'Such studies are eligible for public funding; but even more interesting is the interest of the pharmaceutical industry. Validation would require clinical trials that include new imaging standards. These studies are rarely publicly funded.

'By the way, within the pharmaceutical industry the awareness that new imaging endpoints need to be defined has markedly increased with the success of immunotherapies. This is because, in the initial phase of immunotherapy, a response in the traditional sense cannot be determined. Quite to the contrary: tumours tend to grow despite an initially positive response. This is caused by tumour infiltrating lymphocytes, which in fact trigger an inflammation. This is an accompanying effect of immunotherapy. These lymphocytes cause pseudoprogression of the tumour, which a conventionally trained radiologist or oncologist might interpret as tumour growth – an undesired outcome – and discontinue the therapy.

However, in many cases, initial tumour growth during immunotherapy turns into tumour regression – the therapy should have continued rather than stopped. To account for these new insights RECIST criteria were expanded: the new so-called iRECIST criteria recommend a different evaluation of immunotherapy response.

'If tumour growth is recorded, further controls are performed in

Radiomics: Radiology images (below, left) undergo feature extraction and quantitative image analysis in order to be converted into a high-dimensional data space (centre). A correlation between this data space and a clinical outcome, such as overall survival (right), is identified with the help of machine learning. This correlation can be used to analyse new image data



Radiology: An era of turbulence and innovation

The birth and rebirth of imaging

The New Horizons Lecture at the RSNA annual meeting is a keynote address that looks to the future, and the inventor of a major innovation in magnetic resonance imaging (MRI) technology, Daniel K Sodickson MD PhD, did just that. His lecture entitled 'A New Light: The Birth and Rebirth of Imaging' looked back at how MRI has evolved and forward at what it will become.

The change will be radical. Today's radiology images may be irrelevant. MR protocols will become obsolete – but radiologists will not be, Sodickson emphasised, because radiologists are in a position to transform the field. 'We invented diagnostic imaging. We figured out how to visualise and understand human inner space. This is both a turbulent age for imaging and a golden age for innovation. We need to embrace the theme of RSNA 2017, and 'Explore, Invent, Transform.' Modern imaging science is information science. Let us be the scientists who create new forms of information. In a world increasingly dominated by information, what more valuable contribution can we make?'

Sodickson explained that the era of continuous, comprehensive imaging data has arrived, and that with this change, the era of the 'carefully framed snapshot' of a high-resolution image will pass. 'Radiology is not just copying our eyes. Instead, it is starting to emulate the way that our brains process multiple, streaming multi-sensory experiences.'

Courtesy of Daniel Sodickson MD and NYU School of Medicine

Daniel Sodickson and the Radiology Research team of NYU School of Medicine, who are involved in the development of new techniques for biomedical imaging

In his lecture Sodickson described the building blocks that created MR technology, from 1973 when the idea was first published to the revolutionary changes and relentless innovation that have ensued. This rapid-fire overview clearly illustrated how radiology progresses, adapts, and advances diagnoses through imaging.

Dramatic improvements of the 1990s

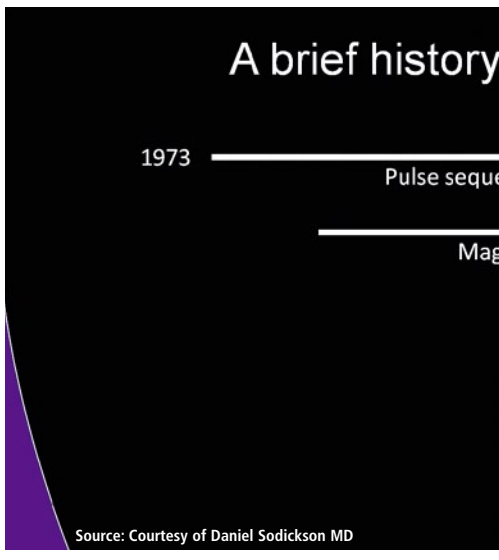
Sodickson spoke of the evolution from the first magnetic field gradients to diffusion imaging. The introduction of functional MRI, implemented in 1990, enabled radiologists to see different types of biophysics, reflecting brain activity. In the 1990's, some dramatic improvements were made to gradients and to radiofrequency coils, enabling advances in speed and image information content. The concept of moving from a sequential imaging device to a parallel acquisition device decreased the time to acquire images. Parallel acquisition made it possible to reduce corruption of images by motion from the abdomen and heart, and also to make the process easier for patients.

In 2007, compressed sensing was introduced. In addition to making the acquisition of images faster, it made feasible the use of multiple dimensions of data, which could be integrated together. Non-traditional data sampling patterns, such as radial patterns, gained new prominence. One particular example Sodickson described used a golden angle radial pattern, which enabled motion robustness during continuous data acquisition.

With the introduction of continuous three-dimensional acquisition, it became possible to perform multidimensional sorting along distinct motion dimensions. This enabled the creation of unique cardiac motion dimensions or respiratory motion dimensions, as an example. More innovations enabled radiologists to determine how the heart contracts and relaxes at any stage, or to look at the morphology of the great vessels or coronary arteries and freeze the images at any stage, thus enabling better heart disease diagnoses.

Creating a dictionary of pre-simulated fingerprints

The addition of 4-D, 5-D, and 6-D image processing algorithms led radiologists away from a mode of carefully tailored and adjusted snapshots toward a much simpler paradigm of rapid and continuous



Source: Courtesy of Daniel Sodickson MD

Professor Jens Ricke qualified in radiology at Charité, Berlin, Germany and, from 2004 to 2006, was professor of interventional radiology at the Department of Radiotherapy there. From 2006 to 2017 he was tenured professor of radiology at Otto von Guericke University Magdeburg, and Director of the Department of Radiology and Nuclear Medicine at Magdeburg University Hospital in Germany. In June 2017, he joined Ludwig Maximilian University, Munich, Germany, where he is Chair of Radiology and Director of the Clinic and Policlinic of Radiology.

short intervals to determine whether this is a bona fide progression or whether the tumour indeed shrinks after a while.

'The oncology community doesn't yet appear to be entirely convinced of the progression/regression dynamics; that's why, in clinical practice, we see immunotherapy medication being discontinued sooner than in the trials. This is obviously to the detriment of the patient, because successful medication is no longer administered.

'At the same time it is to the detriment of the pharmaceutical companies, because their turnover decreases. This is why the pharmaceutical industry, patients, oncologists and radiologist have a common interest in the development of new imaging endpoints. We should pick up the ball and run.'

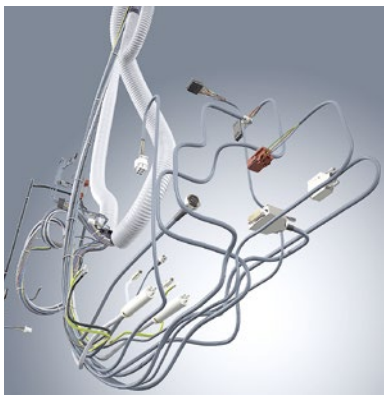
Clever cabling makes devices mobile

The integrated wiring of a medical device imposes great requirements on the cable system's producer as well as the device manufacturer. This calls for a partnership collaboration particularly in development to ensure the system solution exerts a positive effect on mobility, user friendliness and robustness – long-term and reliably.

'Qualified wiring is one of the success factors for large pieces of medical equipment,' Leoni's Healthcare Business Unit confirms. 'Freedom of movement and user friendliness for staff, easy positioning and mobility for multifunctional use in, for example, hybrid operating rooms – the manufacturers' requirements of the system technology are high.

'Installed cables and cable systems must reliably withstand not only sometimes heavy tensile forces or repeated flexing but must also be fitted in such an efficient way that they do not obstruct any other components and allow short maintenance times. The reliability of the permanent transmission of data, signals, power, light and media is meanwhile essential.

'Leoni's Healthcare Business Unit meets the market's challenges concerning innovative system solutions with more than 35 years of experience, know-how and a comprehensive portfolio. We can assist medical equipment manufacturers as early as the development phase of their device and provide input from the "cable's perspective".'



For mobile C-arm X-ray machines, Leoni develops and produces dedicated cable conduits to facilitate permanently smooth mobility of radiators and detector units

Clever cable routing facilitates flexibility

'The key way to develop the wiring of a medical device involves optimally adapting the system technology and related cables to the movement sequences. That sounds easy, but it entails major challenges. Routing can cross rollers, sharp edges, joints or drag chains with the cables and components being pinched, rubbed, worn or dragged out.

'To develop the specific system solution, Leoni's engineers consider the movement sequences and speeds of the device or prototypes on the manufacturer's site. Such early-stage involvement in the development process can yield innovative cable storage modules or spring return systems that reduce the mechanical forces on all components.

Leoni's in-house rigorous testing facility cables are checked for lasting functionality in a mobile application

Leoni is at ECR 2018
Hall X1, Stand 139

'Spare cable length for long travel or high degrees of flex can be cleverly integrated in a device with innovative cable routing. In all cases the jacketing with an additional fabric, or other sleeve, ensures the desired robustness and that the system technology can be more easily disinfected.'

Tobias Höft, Global Business Development Manager of Leoni's Healthcare Business Unit

Less is often more

'In addition to ready-to-connect system technology, Leoni can develop and produce application-optimised cables; such tailor-made cables can give the device manufacturer input on ways to save not only space, but also costs.

'For example, because of the slower speeds involved, standardised drag chains are often a costly solution for medical equipment and do not even provide mobility in all directions. An application-optimised cable can be a more durable alternative.

'In other cases, multifunctional and ready-to-connect hybrid cables can replace complex cable systems and simultaneously increase the mobility and robustness of a device.'

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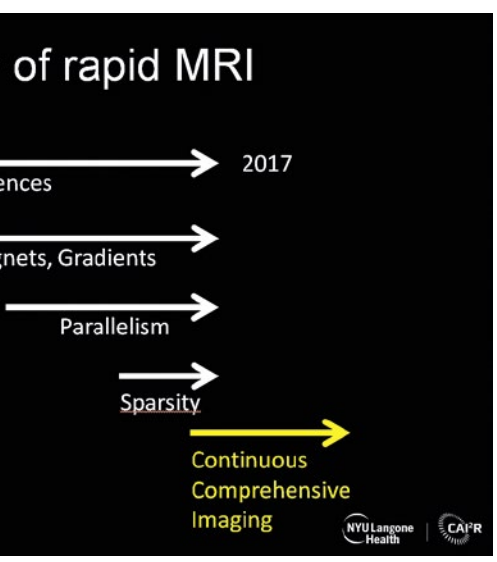
+49 160-90192902

streaming images. A variant of this paradigm, magnetic resonance fingerprinting, was developed in 2013. Rather than standard image reconstruction, MR fingerprinting created a dictionary of pre-simulated fingerprints for different types of tissue and matched acquired singles to these fingerprints to create quantitative maps of tissue properties.

MR fingerprinting offers the promise of scanner- and operator-independent scanning. If this promise is delivered, the feasibility of conducting clinical trials in radiology with tens of patients could easily expand to thousands, thus making clinical trials more accurate.

Findings of such huge clinical trials could advance precision radiology.



Assessing a continuously acquired multidimensional data stream

Enter artificial intelligence (AI). 'The artificial intelligence I see benefiting radiology is not merely image interpretation but rather data interpretation,' Sodickson said. 'AI neural networks can learn the various tricks of parallel imaging, compressed sensing, and other transforms we don't know yet.

'These could create images that are better than ones any existing image processing algorithms can produce and by doing so, they can help radiologists to make better diagnoses."

This is happening now, he said; but is happening with single slices and static images. What if you could have an AI neural network to assess a continuously acquired multidimensional data stream? AI would be the perfect way to economically produce actionable information, with biological fingerprints of disease as the output.

However, if AI could determine all this, would images even be needed? And how would MR scanners change? Could MR scanners be stripped down to the bare minimum of simply acquiring continuous data with the push of a button? And what would be the role of radiologists?

Sodickson has suggested that, in the new era radiologists are facing, they would be information traffic controllers. They need to control and interpret the information content and context, and make it relevant for the treatment of patients.

Courtesy of Daniel Sodickson MD and NYU School of Medicine

Daniel K Sodickson MD PhD is vice chair for research in the Department of Radiology, director of the Bernard and Irene Schwartz Center for Biomedical Imaging, and Professor of Radiology, Physiology and Neuroscience at the NYU School of Medicine in New York City, USA. He also chairs the National Institutes of Health (NIH) study section on biomedical imaging technology. He is credited with founding the field of parallel imaging, which allows distributed detector arrays to gather MR images at previously inaccessible speeds. As a result of his discovery, most MR scanners have parallel imaging hardware and software, and parallel imaging acceleration is used routinely in clinical MRI examinations and research imaging studies worldwide.

'We too are a force for change, a juggernaut of extended vision and expanded mind. If we embrace emerging paradigms of technology and information, and put them to good use, we will continue to see what was once invisible. If we stay true to our rich history of invention,' he concluded, 'we are bound to see things in a new light.' CK

New cancer treatments present radiologists with new imaging questions

Understand the treatment to understand an image

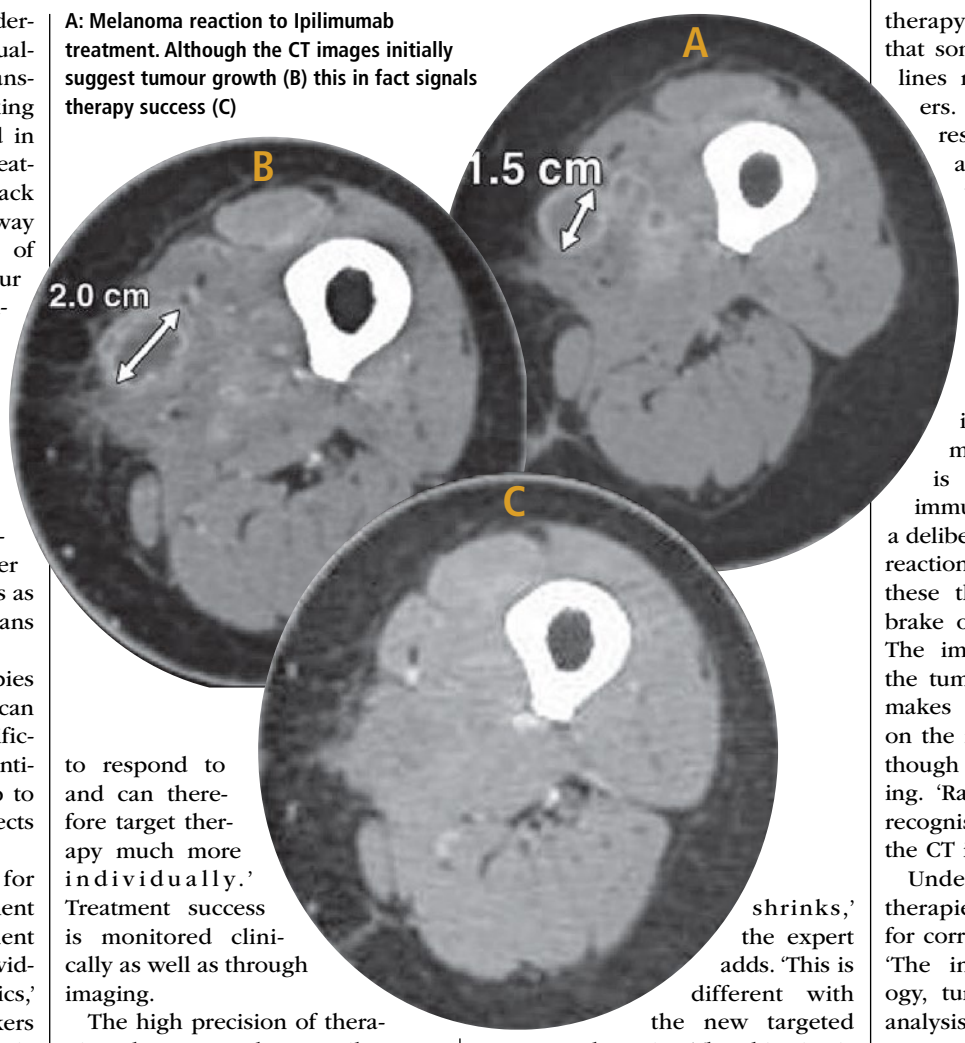
Conventional chemotherapy in oncology is increasingly yielding to new procedures such as targeted therapy and immunotherapy. The result is changes for radiologists because new procedures require familiarisation with certain imaging to ensure that the treatment process is interpreted correctly. During a recent CT symposium Professor Hans-Christoph Becker, radiologist at Stanford University Medical Centre in California, USA, discussed aspects of such changes. Wolfgang Behrends reports

'To begin with it's important to understand how the new therapies actually work,' radiologist Professor Hans-Christoph Becker advised, speaking at the CT-Symposium 2018 held in Garmisch, Germany. Targeted treatment and immunotherapy attack tumours in a very different way from chemotherapy. 'The point of chemotherapy is to destroy tumour cells. Targeted, i.e. specific cancer therapy works, for example, with specific messenger substances that activate signal paths, and explicitly interfere with the metabolism of tumour cells.' The advantage of the new treatments lies in their higher precision. 'Chemotherapy is comparatively non-selective,' Becker explains. 'It damages tumour cells as well as healthy tissue, which means it causes collateral damage.'

By comparison, targeted therapies attack the tumour cells, which can be identified with high specificity with the help of surface antigens, for instance. This can help to reduce the severity of side effects for patients.

Therefore, the objective for researchers is to make the treatment as precise as possible. 'Each patient has tumours with a certain, individual combination of characteristics,' Becker points out. These markers are determined histologically via biopsies. 'We can now differentiate with much more precision which treatments tumours are most likely to respond to and can therefore target therapy much more individually.' Treatment success is monitored clinically as well as through imaging.

A: Melanoma reaction to Ipilimumab treatment. Although the CT images initially suggest tumour growth (B) this in fact signals therapy success (C)



The high precision of therapies, however, also entails some new difficulties: 'With chemotherapy, treatment success is usually confirmed by the fact that a tumour shrinks,' the expert adds. 'This is different with the new targeted therapies. The objective is not necessarily only the destruction of the tumour tissue but also a significant impact on its metabolism.' This reduces the blood supply to the tumour. 'It leads to effects which look different from those of conventional chemotherapy.' Tumours are usually heterogeneous, i.e. they consist of different cell lines. Targeted therapy has become so specific that sometimes only some of these lines respond to it, but not others. 'This leads to a peculiar response where some tumours and metastases may shrink, whilst others even grow at the same time.'

With other procedures, such as immunotherapy, the tumour initially clearly looks bigger in the CT image – however, this does not mean that the tumour is not responding to treatment. 'To the contrary, this is a classic phenomenon of immunotherapy and the result of a deliberately induced inflammatory reaction,' Becker explains. 'Some of these therapies release the handbrake of the body's immune cells. The immune system then attacks the tumour with leucocytes, which makes the tumour appear larger on the image. What it really means though is that the treatment is working. 'Radiologists must be able to recognise these effects to evaluate the CT images correctly.'

Understanding how different therapies work is also essential for correct interpretation of images. 'The interaction between pathology, tumour treatment and image analysis is increasingly complex,' says Becker. 'Linking these areas in a meaningful way will be among the big challenges in the future.'

From 2001-2014 **Professor Hans-Christoph Becker** was a senior consultant at the Institute for Clinical Radiology at Ludwig-Maximilian-University (LMU), in Munich, Germany. In 2009 he was appointed Professor of Radiology, focusing on non-invasive cancer imaging. About three years ago he received a generous budget to set up a cancer research laboratory at Stanford University, California, USA, similar to the one he established at LMU in Munich.

AI analysis presents great potential

Automated evaluation of such imaging phenomena is also conceivable. Artificial intelligence (AI) could detect the specific reactions of tumours in the data sets and therefore measure treatment success. Stanford University Medical Center is already working on the development of such algorithms. 'The procedure is still in its infancy, but it's very exciting. It is likely that AI-supported evaluation will soon have a major impact in radiology.'

The 'new' cancer therapies referred to here are actually not that new: 'Hormone therapy was already in clinical use 20 years ago,' Becker points out. 'However, subsequently, more and more therapies have been discovered and the number of licensed targeted therapies also continues to increase.

'Many different drugs are currently being trialled, and studies into combining these with conventional treatment, as well as dose-ranging studies will continue to run.' Fundamentally, the new therapies can be used anywhere that conventional chemotherapy is used.

ECR 2018
Friday 2, March
08:30-10:00 Room C
New Horizons Session, Level III

NH 9 Immunotherapy: a revolution in cancer care?

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» CT: looks bigger, but it's better [A-386]
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» The MR armoury in follow-up [A-387]
D.-M. Koh; Sutton/UK
» Systemic and immunologic effects of image-guided interventions in oncology [A-388]
S.N. Goldberg; Jerusalem/IL
» Panel discussion: How should radiology improve imaging to support this revolutionary care?

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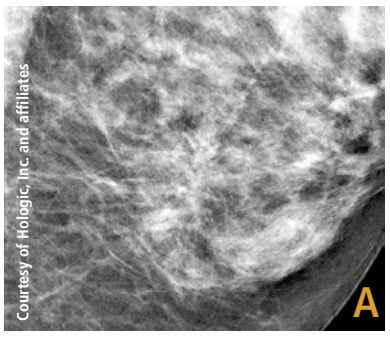
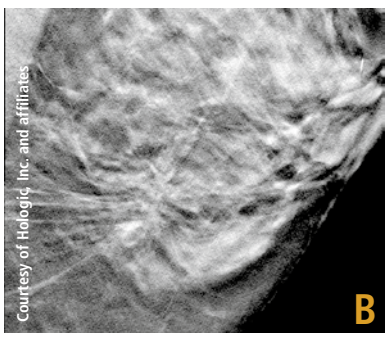
The clinical implications of breast tomosynthesis

Catching more invasive cancers earlier

What beats digital mammography to detect breast cancer in asymptomatic women? Digital breast tomosynthesis (DBT) – was a big discussion at RSNA 2017. Sarah M Friedewald MD, medical director of the Lynn Sage Comprehensive Breast Center of Northwestern Memorial Hospital in Chicago and its division chief of breast and women's imaging, discussed the clinical implications of DBT for routine mammography screening.

When digital mammography (DM) equipment was introduced in the USA its adoption by accredited women's imaging centres and hospital radiology departments was cautiously slow. By comparison, the adoption of digital breast tomosynthesis technology skyrocketed, fuelled by studies that prove its superiority in breast cancer detection.

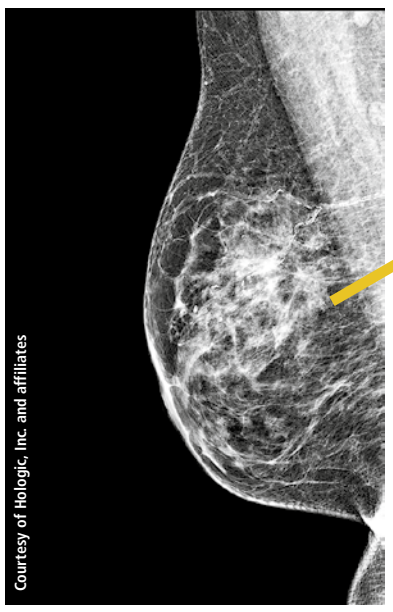




Digital screening mammography shows no definite lesion at the area of interest, left 8-9:00 position. Breast tomosynthesis demonstrates architectural distortion and shows the area for targeting for image-guided biopsy or localization. Histopathology revealed Radial scar and Ductal Carcinoma in Situ. This lesion, seen on breast tomosynthesis imaging (B), was occult (not visualized) on routine digital screening mammography (A)

In June 2005, five years after the first full-field DM system received 510(k) clearance from the USA's Food and Drug Administration (FDA), out of the 13,621 mammography systems in use at 8,911 facilities, only 6.4% systems were digital. In June 2016, five years after clearance of the first DBT technology systems, 20.8% of 16,155 systems in use were DBT capable. Just 18 months later, this has increased to 29%, with 43% of all accredited facilities having at least one DBT-capable system.

This surge is based in part on radiologists' familiarity with and recognition of the fact that full-field DM systems do increase early stage cancer detection rates. Numerous studies conducted in Europe and North America show that DBT offers even greater benefits. The USA's National Comprehensive Cancer Network (NCCN) 2016 guidelines recommend that DBT be considered for breast cancer screening exams



Occult cancer obscured on conventional mammogram is easily seen with tomosynthesis

in average-risk patients over the age of 40, thus increasing payment coverage for many women through private health insurance.

Advantages of digital breast tomosynthesis

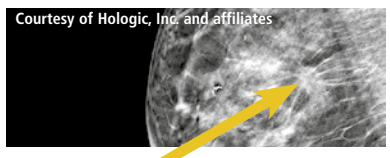
DBT improves on mammographic performance by minimising the impact of overlapping breast structures, making it easier to see invasive cancers. It improves lesion conspicuity and by removing tissue superimposition, improves evaluation of margins and localisation. Recall rates for additional testing are lower. And, for some patients, when suspicious findings of screening mammograms merit additional testing, breast ultrasound exams may be performed in lieu of diagnostic mammograms, thus avoiding additional exposure to ionising radiation.

While many think DBT is only useful to identify cancers, this is not the case. Friedewald explained that findings from a study of over 450,000 women showed that, while DBT did identify more cancers than DM, recall rates also reduced significantly. This 2014 study evaluated mammography findings and recall rates of 281,187 screening exams at 13 institutions for 12 months before they implemented DBT, with mammography plus DBT from the date of implementation through December 2012, for 173,663 screening exams. The 13 participating facilities were geographically diverse, both academic and non-academic, and with breast specialists and non-specialist radiologists interpreting the exams.

'The results from this diversity of screening centres were very exciting – they confirmed that DBT increased cancer detection and reduced recall rates, the two main criticisms of screening mammography. After tomosynthesis implementation, the invasive cancer detection rate increased from 2.9 to 4.1 per 1,000 women screened, a relative increase of 41%,' she said. Recall rates reduced by 15% overall,

Lowering the recall rate

'Of particular interest was that, when recalls were divided into categories of dense-breasted and non-dense women, there was statistically



significant improvement in recall rate reduction for both categories. And, when we divided patients into the four density breast categories, we discovered that more cancers were being identified with DBT use in women with fatty breasts. The fat surrounding the cancers enabled us to see them better with DBT,' said Friedewald. 'For this group, the use of mammography plus DBT identified 38.2% more cancers.'

Further analysis based on stratifying the patient cohort in 10 year age groups, adjusted for breast density, showed performance outcome in identifying cancers with the use of digital mammography plus DBT screening, for women aged 40-49, was almost equivalent to digital mammography alone of women in their 50s. While there were gains from DBT use in all age categories, the relative increase in detecting invasive cancers was 69% for women in their 40s.

Friedewald also referenced a study conducted at the University of Pennsylvania in Philadelphia evaluating recall rates over three years breast screening examinations using DBT. This demonstrated that, over time, the benefit of imaging patients with DBT shifts from cancer detection to recall rate reduction. In the study, there were only 59 recalls per 1,000 examinations in the third year compared to 130 recalls per 1,000 exams in the first year of imaging.

Complicated transition from DM to DBT

In addition to cost, the disadvantages of adopting DBT technology is that radiologist need a learning curve, which may also result in increased recall rates during the time it takes for them to become proficient with the technology. 'The transition from DM to DBT is complicated because there are many more images to interpret. The time it takes to read a screening examination is two to three times as long as digital mammography. However, with the reduction in recall after screening with DBT, the volume of diagnostic imaging should decrease concomitantly, and radiologist interpretation time can then be shifted to screening,' Friedewald explained.

She advised that the way her breast centre made the adjustment and incorporated DBT into the breast imaging practice was with the initial purchase of a single system. This was used to image patients in the diagnostic setting. Because a longer amount of time was allocated for patients having diagnostic imaging, this extended time enabled the physicians to become accustomed to the new images and reading times. It also allowed the breast radiographers time to become familiar with the technology. Today, DBT is used for all routine and diagnostic breast screening examinations.

'There are many ways to deploy this exciting technology,' she said.

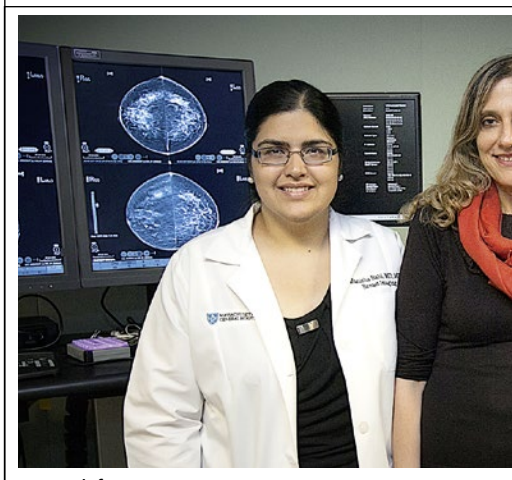
Sarah M Friedewald MD is medical director of the Lynn Sage Comprehensive Breast Center of Northwestern Memorial Hospital in Chicago, USA and its division chief of breast and women's imaging. She is also an Assistant Professor of Radiology at Chicago's Feinberg School of Medicine. In 1998 she gained her doctorate at the Columbia College of Physicians and Surgeons in New York City, followed by her internship in the surgical department at Union Memorial Hospital, in Baltimore, USA. After her residency in radiology at Johns Hopkins Hospital, she started her Women's Imaging fellowship at the University of Pennsylvania Hospitals.

'The women's imaging centre at Baylor College of Medicine in Houston, TX, began by using DBT for routine screening to maximise the technology's benefits in increasing detection of early cancer and reducing recalls. After 24 months, a hybrid model was adopted based on room availability and specific scenarios that needed DBT, such as asymmetries and architectural distortion.'

Friedewald did not present statistics relating to digital breast tomosynthesis adoption in Europe, but expressed hope that imaging centres in all countries that have converted to digital mammography will add DBT to their cancer-fighting arsenal of imaging examinations: 'It's a very exciting technology that is helping to save lives.' CK

Artificial I
to detect

Scientists are using Artificial Intelligence to detection. The researchers at Massachusetts Science and Artificial Intelligence Laborator (MGH), and Harvard Medical School, are us whether breast lesions identified from a bio



From left:
Manisha Bahl MD is a breast imaging radiologist and director of the Breast Imaging Fellowship Program at Massachusetts General Hospital/Harvard Medical School in Boston, USA. After graduating from the Harvard School of Public Health with an MPH in Health Policy and Management, she completed a radiology residency and breast imaging fellowship at Duke University Medical Centre and joined the faculty at Massachusetts General Hospital/Harvard Medical School in July 2016.

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Out of 335 high-risk lesions the system correctly diagnosed 97% as malignant

Intelligence helps breast cancer

o support more effective breast cancer Institute of Technology (MIT) Computer ry (CSAIL), Massachusetts General Hospital ing the machine learning system to predict opsy will turn out to be cancerous.

(Photograph: Jason D

a member of the Computer Science and Artificial Intelligence Laboratory at the Massachusetts Institute of Technology. USA. Her research focuses on natural language processing and applications of deep learning to chemistry and oncology.

Constance Lehman MD is a Professor at Harvard Medical School in Boston, USA, and chief of the Breast Imaging Division at MGH's Department of Radiology. After graduating from Duke University and receiving medical and doctoral degrees at Yale University, she became Professor and vice chair of Radiology and division chief of Breast Imaging at the Seattle Cancer Care Alliance before her recent move to Massachusetts General Hospital.

The hope now is that this research could help reduce the number of unnecessary breast cancer surgeries because it could pinpoint which lesions are cancerous more accurately and more efficiently.

In the study, the system was trained on information about such lesions and looked for patterns among a range of data points, including demographics, family history, biopsies and pathology reports. When tested on 335 high-risk lesions, it correctly diagnosed 97% as malignant. The researchers suggest that such levels of accuracy could lead to a reduction in the number of unnecessary surgeries by more than 30%.

While mammograms can detect cancers, there is also a risk of false positive results that can lead to unnecessary biopsies and surgeries – often from 'high-risk' lesions that appear suspicious on mammograms and have abnormal cells when tested by needle biopsy. The researchers say patients have the lesion surgically removed but often it is benign and the operations were unnecessary.

To address this, the team developed the machine learning system to predict if a high-risk lesion identified on needle biopsy after a mammogram will upgrade to cancer at surgery.

'Because diagnostic tools are so inexact, there is an understandable tendency for doctors to over-screen for breast cancer,' Dr Regina Barzilay, MIT's Delta Electronics Professor of Electrical Engineering and Computer Science, pointed out.

'When there's this much uncertainty in data, machine learning is exactly the tool that we need to improve detection and prevent over-treatment. A model like this will work anytime you have lots of different factors that correlate with a specific outcome. It hopefully will enable us to start to go beyond a one-size-fits-all approach to medical diagnosis.'

Using a method known as a 'random-forest classifier', the model resulted in fewer unnecessary surgeries compared to the strategy of always doing surgery, while also being able to diagnose more cancerous lesions than the strategy of only doing surgery on traditional 'high-risk lesions'.

Dr Constance Lehman, Professor at Harvard Medical School and chief of the Breast Imaging Division at MGH's Department of Radiology added: 'To our knowledge, this is the first study to apply machine learning to the task of distinguishing high-risk lesions that need surgery from those that don't. We believe this could support women to make more informed decisions about their treatment, and that we could provide more targeted approaches to healthcare in general.'

It is hoped that MGH radiologists will begin incorporating the model into their clinical practice over the next year. 'In the past, we might have recommended that all high-risk lesions be surgically excised,' Lehman said. 'But now, if the model determines that the lesion has a very low chance of being cancerous in a specific patient, we can have a more informed discussion with our patient about her options. It may be reasonable for some patients to have their lesions followed with imaging rather than surgically excised.'

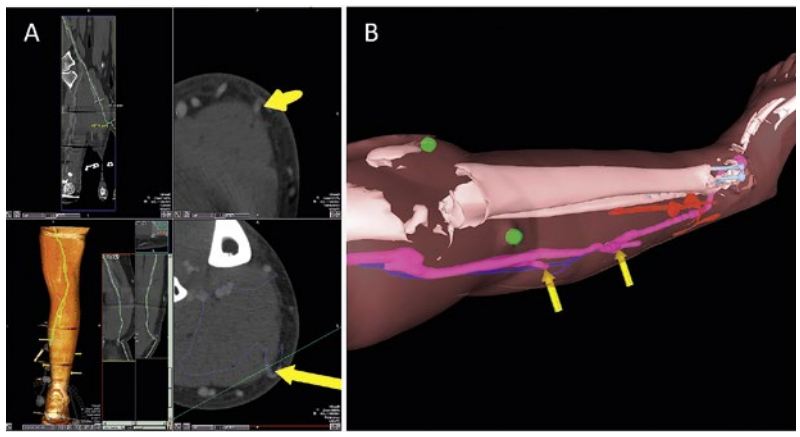
The team – which also included Manisha Bahl, director of the Massachusetts General Hospital Breast Imaging Fellowship Program – says that they are working to further evolve the model and in future hope to incorporate the actual images from the mammograms and images of the pathology slides, as well as more extensive patient information from medical records. MN

A valuable tool for reconstruction

Augmented reality lets surgeons 'see' inside limbs

Report: Mark Nicholls

Researchers at Imperial College London (ICL) have shown how the Microsoft HoloLens headset can be used during reconstructive lower limb surgery. Surgeons at London's St Mary's Hospital are using the device, a self-contained computer headset that immerses the wearer in 'mixed reality', enabling them to interact with holograms visible through the visor. In effect, the limb's interior is visible during the procedure.



a) Yellow arrows in CTA image indicate perforating arteries arrows; b) example of HoloLens rendering of segmental polygonal models

a) AIR overlay of models as viewed from remote HoloLens; b) co-ordination of perforator location with audible Doppler ultrasonography c) Case with overlay of bounding box with arrows highlighting position of d) Sural metal and e) posterior tibial perforators

Identifying critical blood vessels under the skin

Testing the technology, the ICL team used the system to overlay images of CT scans – including the position of bones and key blood vessels – on to each patient's leg so the surgeon could better locate and reconnect key blood vessels during reconstructive surgery. 'We are one of the first groups in the world to use the HoloLens successfully in the operating theatre,' Dr Philip Pratt, a Research Fellow in the Department of Surgery and Cancer, confirmed.

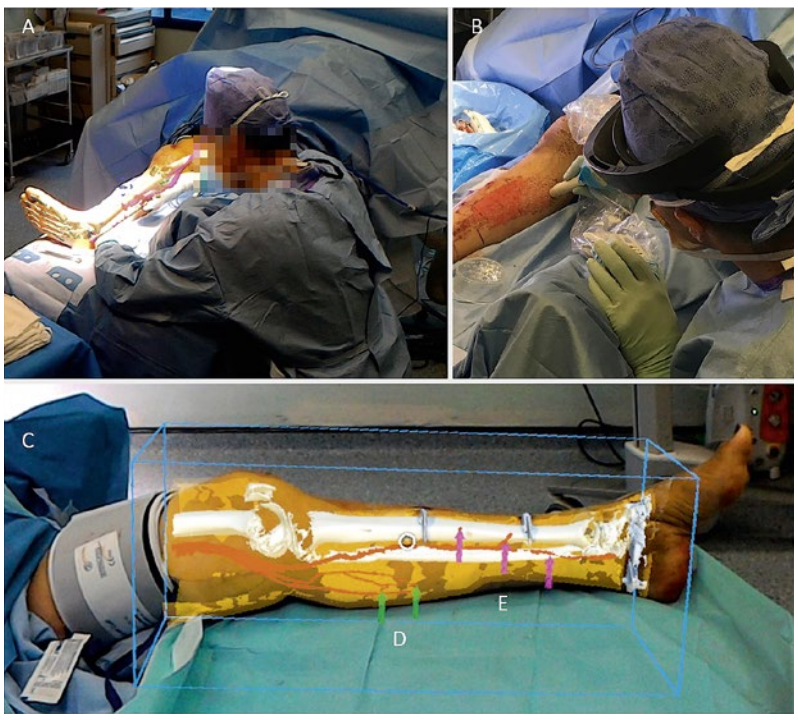
'Through this initial series of patient cases we have shown that the technology is practical, and that it can provide a benefit to the surgical team. With the HoloLens, you look at the leg and essentially see inside of it. You see the bones, the course of the blood vessels, and can identify exactly where the targets are located.'

When a patient sustains serious injury, with tissue damage or open wounds, they may require reconstructive surgery using fasciocutaneous flaps of tissue taken from elsewhere on the body, including the skin and blood vessels, to be used to cover the wound and enable it to close and heal properly. Successfully connecting the blood vessels of the new tissue to those at the wound is a vital step in the process. Presently, handheld scanners using ultrasound are used to identify blood vessels under the skin. 'Augmented reality offers a new way to find these blood vessels under the skin accurately and quickly by overlaying scan images onto the patient during the operation,' Pratt explained.

Virtual 3-D arrows guide the surgeon

During initial trials of the technology, five patients requiring reconstructive leg surgery underwent CT scans to map the structure of the limb, including the position of bones and blood vessels.

Images from the scans were then segmented into bone, muscle, fatty tissue and blood vessels by Dr Dimitri Amiras, a consultant radiologist at Imperial College Healthcare NHS Trust (ICHNT), and loaded into intermediary software to create 3-D models of the leg. These models were then fed into specially designed software that renders the images for the HoloLens headset, which in turn overlays the model onto what the surgeon can see in the operating theatre.



The HoloLens is used to identify where the blood vessels are in 3-D space and uses virtual 3-D arrows to guide the surgeon. Clinical staff can then manipulate the augmented reality images to make fine adjustments to correctly line up the model with surgical landmarks on the patient's limbs.

Jon Simmons, plastic and reconstructive surgeon at Imperial College Healthcare NHS Trust, carried out the trial procedures. Already, the hospital's surgical teams believe that the HoloLens approach is more reliable and less time-consuming than the ultrasound method of locating the blood vessels.

Dr Philip Pratt is a Research Fellow in the Faculty of Medicine, Department of Surgery & Cancer at Imperial College London, UK. Initially working in the banking sector, he began to explore research opportunities at the Institute of Biomedical Engineering, Imperial College, which ultimately led to a career change. He was appointed Research Fellow at the Hamlyn Centre for Robotic Surgery, Imperial College. From within the Department of Surgery and Cancer, he now undertakes very active research in image-guided surgery, and has successfully translated new technology and software into clinical practice in the operating theatre.

Improving the system for future use

While the first cases have been carried out on legs, which have clearly visible surgical 'landmarks', using this technique for surgery on the abdomen may be more complicated. However, as the technique is refined it could be used in other areas of reconstructive surgery requiring tissue flaps, such as breast reconstruction following mastectomy.

'In future we hope to automate the process further,' Pratt added. 'We can use software to improve the alignment and will attach markers to the patient when they have the scan, with the same markers present during the operation to use as additional points of reference.'

With further trials planned in a larger set of patients, he acknowledged that further improvements are needed, but said that from the number of cases so far the technique could be a valuable tool during reconstructive surgery.

MobileDaRt Evolution MX8 Digital Mobile

Superior functionality a

'With Your Stories – lifetime healthcare support': this future-driven approach combines the best of two worlds, using Shimadzu's insights and expertise in medical imaging systems and laboratory instrumentation to benefit patients through ever improving prevention, diagnosis, treatment and follow-up.

In 2018, the year of the 50th anniversary of the opening of Shimadzu's European headquarters, the company has released the new MobileDaRt Evolution MX8 version digital mobile X-ray system. This features its first telescoping support column to increase convenient drivability and improve forward visibility; a large completely flat monitor screen; a lockable FPD housing compartment; an extensive selection of options and improved operability.

Digital mobile X-ray systems become increasingly essential for qualified radiography in hospital rounds, or to examine emergency patients, in neonatal intensive care units or other highly urgent medical applications. Shimadzu MobileDaRt series digital mobile X-ray systems are already used in over 60 countries around the world, with more than 3,500 units sold to date.

Shimadzu is at ECR 2018 Expo Hall X2, Stand 218

In September 2017, Shimadzu received the 'Global General Radiography Product Line Strategy Leadership Award 2017'. The award is presented to a company that introduced products and services demonstrating the highest leadership in international markets for diagnostic X-ray imaging systems in the previous year and for employing the best strategies for success. A part of the company's portfolio contributing to this award has been covered by its DR solutions.

Multifaceted support

The newly redesigned MobileDaRt Evolution MX8 version has been developed to provide users with multifaceted support based on Shimadzu's extensive technology and track record cultivated thus far.

The most important features: Collapsible column enhances forward visibility and drivability. The new design features an X-ray tube support column that can be extended or retracted and a more compact system width. The previous model was 1930 mm tall during travel; the new design is only 1270 mm tall and 560 mm wide, becoming 20 mm narrower. This shorter profile due to the collapsible column dramatically improves forward visibility during travel and the more compact size makes it easier to use the system in narrow spaces such as bedside.

Various functionalities and options help to improve hospital round efficiency. The MX8 features a new completely flat 19-inch monitor, which improves operability. The maximum X-ray focal point height is also increased by 15 mm, making it easier to examine patients on higher beds.

Security features are also considered, such as the addition of a new locking function for the FPD housing compartment. New optional features, such as a wireless hand switch for X-ray exposure operations

We need strategies to maintain quality healthcare in Spain

Our education plan is completely obsolete

When it comes to radiographers, Spain has one of the shortest curricula in the world. But advanced imaging and the continuously rising demand for imaging studies require properly trained imaging graduates, and universities have a role to play in the debate, according to Salvador Pedraza Gutiérrez, Associate Professor of Radiology and Director of the School of Diagnostic Imaging Technicians in Girona.

Spain has a two-year education plan for radiographers – half the time considered necessary worldwide.

'While the Spanish model was correct 40 years ago, advances in CT and MR technology have made it completely obsolete. It's just not enough and the curriculum needs to be updated. We need to have properly trained graduates in medical imaging,' explained Salvador Pedraza.

'All other countries have a three or four-year education scheme. The European Federation of Radiographers Societies is pushing a bachelor's level. The situation in Spain doesn't make any sense.'

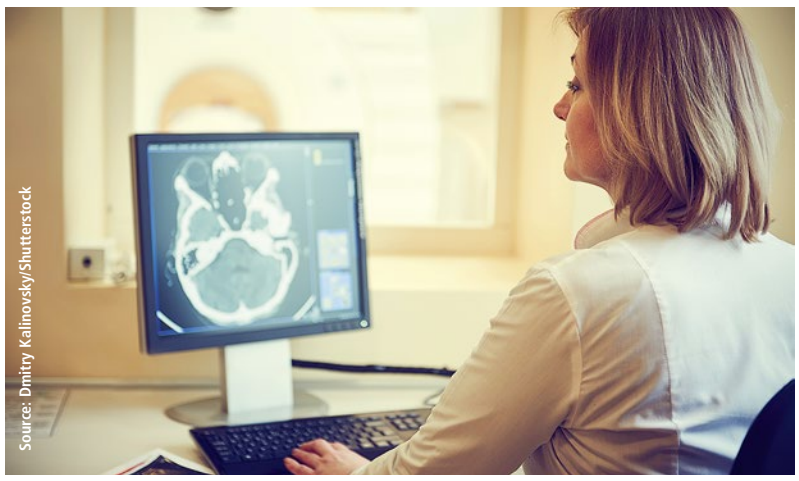
Radiographer is a new profession

'For the past 20 years, those who had a good relationship with their radiology colleagues improved their knowledge and skills in their daily practice. But these were exceptions and this was never meant to last.

'Some radiographers went abroad, for instance to Coimbra, Portugal, for further education. The problem is that when they want to validate their degree in Spain, it's not possible. The Education Ministry cannot recognise their diploma because Spain has no such university degree.

'Besides, graduates in medical imaging are not listed as healthcare professionals. So those who invested extra time and efforts cannot obtain recognition, and we cannot profit from this education in return.

'The Spanish Health Ministry has to understand it's important to include a new profession in their list and Spanish universities must obtain approbation, so these graduates can work in a public hospital. If we do both, we could have medical imaging graduates with a university level within four to five years.



Source: Dmitry Kalinovsky/Shutterstock

Imaging complexity and the increased need for advanced studies makes it compulsory to have adequately trained medical imaging graduates, Professor Gutiérrez emphasises

'Right now we are educating technicians who cannot work abroad. This goes against work flexibility and circulation in the EU.'

Could other medics do the job?

'We need technicians who can perform CT and MR scans with a good knowledge of technical issues, and who can improve parameters, avoid artefacts and perform advanced imaging. We also increasingly rely on post-processing imaging.

'Radiographers already carry out standard ultrasound examinations on their own. This has been happening every day for the past 30 years in medical practice.

'Imaging complexity and the increased need for advanced studies makes it compulsory to have adequately trained medical imaging graduates.

'In the UK, radiographers write reports. It's a specific scenario; I'm not sure that solution can be applied to other countries. I feel more comfortable with sonographers doing the examination and radiologists then writing the report. The UK also has a cruel lack of radiologists.'

Is there a similar shortage here?

'Yes. Most hospitals outside big cities have hiring problems. Young radiologists want to work in hospitals with advanced techniques and the possibility to do everything. We need to keep equity in our healthcare system. Whether you live in the city or countryside, you are entitled to receive proper healthcare.

'There are 5,000 radiologists in Spain, but many of us will retire in the next ten years. Physician workforce is expected to drop by 20%. So today's problem will be worse tomorrow. We need strategies to keep healthcare quality and one of them is to have properly trained medical imaging graduates.

'The administration tends to not react fast enough to changes. In this case it's easy. Spain must realise that other European countries have agreed to train medical imaging graduates in three or four years, so they should just copy this model.'

'The University of Barcelona has just launched a medical imaging degree, and the radiogiology society is supporting this initiative, along with the national societies of nuclear medicine and cardiology.

'This initiative could be the first step in convincing the Health Ministry to include medical imaging specialist in the list of healthcare professions. 'The EU has expressed its support for this proposal. Having an official statement from Brussels on radiographers' education would also help.' MR

Salvador Pedraza Gutiérrez is Director of the Diagnostic Imaging Institute (IDI) in the Radiology and Nuclear Medicine Department at Dr Josep Trueta Hospital and Santa Caterina Hospital in Girona, Spain. He has been Associate Professor of Radiology at the University of Girona (UDG) since 2006 and he directs the School of Diagnostic Imaging Technicians in Girona.

X-Ray System

nd drivability

and a height-adjustable grip bar, help to improve efficiency on hospital rounds. Selectable FPD series enables flexible system configuration. FPD models are available to meet a wide variety of clinical needs, such as physical size, sensitivity and data transmission. FPDs of various sizes can be added. A liquid resistance and the combination with a lightweight FPD makes daily handling much easier. High-sensitivity compact FPD for paediatric care. The compact FPD fits inside the cassette tray of an incubator, which enables imaging neonates or infants. A high-sensitivity FPD helps reduce radiation exposure, providing powerful support for paediatric care.

Tools to support radiation management: The system is in conformity with today's needs for radiation management. The estimated Dose Area Product (DAP) is displayed prior to exposure, and the calculated DAP value is stored for post-exposure management. A DAP chamber can also be mounted if required.

Designed for sterile equipment covers: For daily use, extra storage spaces are provided to store wipes, pens, markers, etc. Grooves have been added for holding the FPD vertically while putting a sterile cover on it.

Details: Shimadzu Europa, www.shimadzu-medical.eu

The new MobileDaRt Evolution MX8 digital radiography solution provides superior drivability and functionality. It is used for hospital rounds and to examine patients in emergency rooms, neonatal intensive care units or other highly urgent medical applications.

EU v. USA – a comparison

Used imaging equipment

by Phillip F Jacobus

I've watched the used imaging equipment market for the last 40 years and it seems like every year, at ECR, I have a conversation with friends comparing the USA and EU markets. Clearly, the market is more developed in North America than it is in Western Europe. Why?

Let's look at the numbers

I think it's fair to say that DOTmed.com, a company that I started in my apartment almost 20 years ago, is one of the most important medical equipment/parts/service websites on the internet. People made fun of me because our website was free, but it proved to be a good strategy. Today, out of over 274,521 registered users there are 25,975 used equipment dealers. 18,442 are in the USA and 2,640 are in the EU, with another 881 in non-EU, European countries. There are 17,350 service companies in the US, with only 2,806 in the EU.

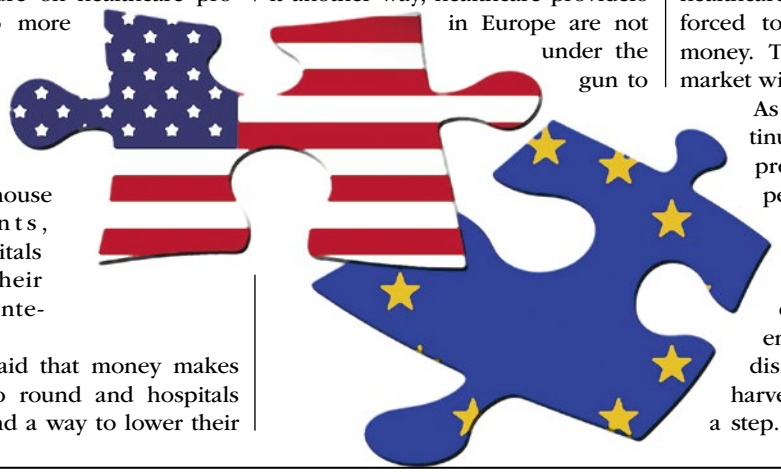
As far as postings of parts or equipment for sale, there are 119,220 total equipment listings with 103,994 in North America and 10,085 in Europe. There are 677,545 total part listings with 369,551 in North America and 83,159 in the EU. So, if your instinct tells you that the market for used imaging equipment is bigger in the US than in the EU, then you're probably right.

DOTmed.com is at ECR Expo Hall X2, Stand 203

Why?

There's that old conundrum... Which came first, the chicken or the egg? In the US we have a healthy pre-owned equipment industry because we have a healthy independent service industry, and we have a healthy independent service industry because we have a healthy independent spare parts industry. All of this is motivated by financial pressure. In the US there's pressure on healthcare providers to do more with less for more patients. This has carried over to in-house departments, where hospitals provide their own maintenance.

It's been said that money makes the world go round and hospitals not only found a way to lower their operating costs by servicing the equipment themselves, but now in the US there are alternative parts vendors that help these hospitals. In fact, some of these alternative parts vendors are shipping equipment to Europe and will continue to do so until the independent parts industry in the EU grows big enough to meet demands.



In my opinion, it's all a question of priorities. Europe enjoys a better rail infrastructure than North America because the governments in Europe have made it a priority. Healthcare is also a priority in Europe, even at the cost of higher taxes in some cases. In the US, healthcare is a political football whereas in Europe it seems to be an inalienable right. Or, to put it another way, healthcare providers in Europe are not under the gun to find ways to save and economise to the same extent as they are in the United States. There is an abundance of trained service labour available in the USA. Coupled with an entrepreneurial spirit, this labour has formed ISOs to offer lower cost quality alternative service to the OEM prices. Then add a robust spare parts market and you have strong alternative service options.

Will this change?

There are more people alive today in the world than there were 100 years ago and we have succeeded in making people live longer. It seems to me that it's only a matter of time before this larger population places financial pressure on European healthcare providers and they are forced to look for ways to save money. The pre-owned equipment market will be that answer, I predict.

As the rest of the world continues to grow, the need for pre-owned equipment and perhaps more importantly, pre-owned parts, will grow as well. The market in Europe will have to develop some independent engineering groups to dismantle equipment and harvest parts without missing a step. Some of these engineering groups will be asked to provide maintenance. First, they'll be asked to provide maintenance in a pinch, and then in the future, they'll probably be called upon for regular maintenance.

It's my prediction that, just like in the USA, the EU market will have a place for OEM service, in-house service and independent service. It's only a matter of time.

In the meantime, just a few companies are going to be big winners, as they dominate that space.

The President and Founder of DOTmed.com, Inc., **Philip F Jacobus** publishes HealthCare Business News magazine and HealthCare Business News online. He is also President of Owen Kane Holdings, Inc. and its subsidiaries. Jacobus was a used equipment dealer (1977-1996) and pioneered the exporting these goods to China, visiting that country 70 times. He has also sold equipment in over 30 countries. A business partner/investor in more than 90 imaging centres, he was instrumental in installing the first proton therapy system in Russia.

New monitor generation produces natural, precise colours

The i3 series improves diagnosis

JVC reports a complete redesign of its display line-up, bringing the i3 series to market. 'At first glance, the new housing design stands out; the displays bezels are much narrower than in the previous generation,' JVC points out. 'Also new are function buttons on the screen with virtual descriptions. These customisable buttons give users direct access to various functions.'

Beyond the visual, the devices have been further developed; they also offer some technological innovations. The new 3-D lookup table, for example, enables the best possible colour reproduction, the firm reports. 'By also calibrating primary colours, colours have never been so natural and precise,' says Marcel Herrmann, Marketing Manager Totoku at JVCKenwood. 'This also ensures that the image impression is the same on every monitor in the entire facility. In combination with the new colour front sensor, we can guarantee this for the entire life of a display.' As the first display systems on the market, the calibration is executed autonomously and independently from the PC, the company adds. 'The procedure is very simple: The user defines the calibration time and date, for example at night. This scheduled calibration will start automatically even if the workstation is not operating.'

JVC is at ECR 2018 Expo Hall X5, Stand 528

The sensor system of the new i3 monitors consists of a front sensor and an ambient light sensor. 'The front sensor measures continuously luminance and colour of the display and corrects those in real time. This ensures a very stable brightness and high colour stability,' Herrmann explains.

In addition, the i3 series devices include a human sensor. This detects whether someone is sitting in front of the screen, which helps to save energy when the monitor is not in use. For example, JVC adds, it can be ensured that a doctor is not disturbed by the quality control when he is busy doing his reporting.

The i3 series devices include a human sensor that detects whether someone is sitting in front of the screen, which helps save energy when the monitor is not in use

Patients' complaints must be taken seriously

Benign gynaecology specialist centres are needed

Report: Madeleine van de Wouw

The recently opened Uterine Repair Center (URC) in VUmc (Amsterdam) serves women suffering non-cancerous gynaecological disorders, such as myomas, adenomyosis (endometriosis of the uterus), niches (caesarean scar defects) or congenital uterine abnormalities. Gynaecologist Professor Judith Huirne leads the clinic – but has greater aspirations.

As a professor of benign gynecology, in her inaugural lecture in December 2017 she argued for the expansion of the number of benign centers for gynecology. In these specialist centers doctors can make better diagnoses using the latest diagnostic techniques, and perform treatments that are scientifically validated. 'Research shows that one in three women has severe menstrual problems,' Huirne points out. 'Approximately 70% will postpone making a doctor's appointment. When she finally does, she's often told her complaints are "normal" – part of being a woman. But, severe menstrual complaints should be investigated. That's also why these specialist centers are needed.'

Taboo on menstruation

Many women dislike talking about their periods: 'Through history, and in certain religions, there is a menstruation taboo. It's seen as impure and therefore, for example, you can have no sexual intercourse. The taboo is stronger than we realise. Additionally, Dutch women don't want to whine, so leave things as they are. Or they find a solution: one of my patients had such severe bleeding that she set an alarm twice a night to change her sanitary towels, or have to change the bed. This should not be acceptable. We need to increase women's awareness, so they can recognise what's normal and what isn't.'

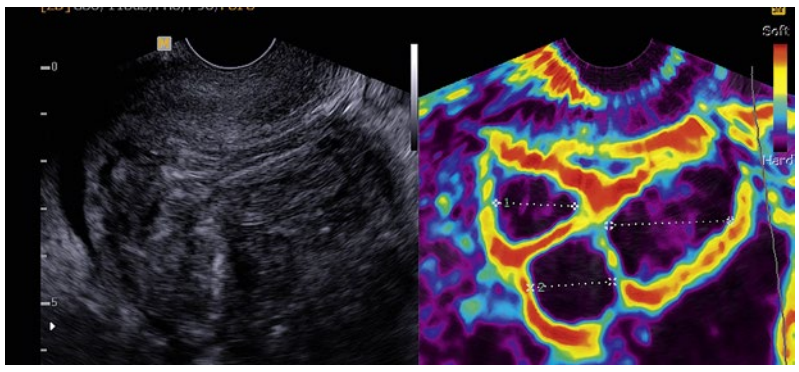
Take women seriously

According to Huirne, GPs and gynecologists also need to change their attitude with women who consult them with menstrual complaints. Often hormones are prescribed, but these suppress the symptoms and are not the solution. Also placing an IUD, or removing the uterus, are often a remedy, which does not work when a woman wants a child.

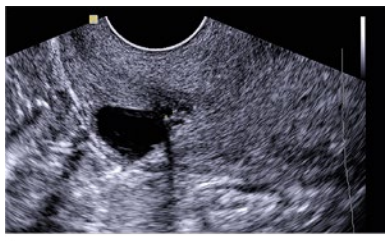
A lack of knowledge

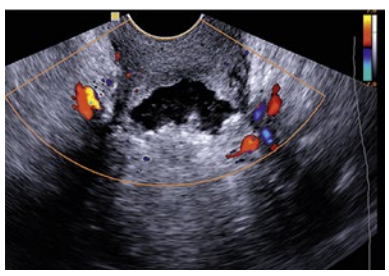
The main issue, Huirne believes, is lack of research into menstruation problems. 'Myomas are often the cause. When you ignore them, they continue to grow, and minimally invasive treatment will no longer be possible. Myomas also can lead to fertility problems. In our clinic we see many women in their late 30s, early 40s, who want a baby and have tried to become pregnant for years. Often they were also in an unsuccessful IVF trajectory. Had they come before or after their first IVF, the problem could have been solved sooner.'

The first diagnoses can be done quite well in hospitals, Huirne says. 'But you need expertise and specialisation to make every diagnosis and to discuss and perform all possible treatments and alternatives. Not every treatment is suitable for every patient. All those specialties are present in benign clinics.'

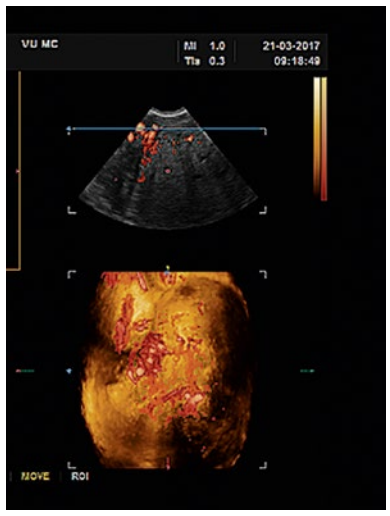


Myomen presenting during sonoelastography and a normal grey echo (1)





Uterus defect presenting during echoscopy (2)



The growth of myomen is predictable on the basis of the vasculair index measured with a 3-D power doppler (3)

Adenomyosis

Alongside myomas, adenomyosis often causes menstrual problems. This form of endometriosis is located in the uterine wall between muscle tissue. Yet, this condition is not always recognised. 'This also needs specialist clinics. There are new echo techniques that help to detect this condition. Also, better treatments should be developed and investigated – presently a new treatment is being investigated in the Uterine Repair Center.'

Caesarean section effects

The Uterine Repair Center is the most specialised center in the Netherlands to treat patients with 'niche complaints'. About 60% of women have a uterus defect after a caesarean. 25% of them even have large defects. The findings are that women with niches are three times more likely to develop abnormal bleeding after menstruation and an increased risk of fertility problems.

'This also needs research, because niches can sometimes reduce the chance of a next pregnancy,' Huirne points out. 'Not every niche needs treatment. In our URC we determine whether womb repair is necessary, and examine the added value for women who want children.'

Another task for benign centers is providing second opinions. If a treatment is non-beneficial, or the patient wonders whether the treatment is correct, the general practitioner can seek a second opinion. We often arrive at the same answer, and it resassures the patient if we propose the same treatment and refer her back to her own gynaecologist.'

Specialisation through centralisation

How many centers are needed depends on how often a condition occurs. For Huirne one center is enough to treat caesarean section niches. For all other conditions five centers would be sufficient.

'The Netherlands is a small country, so maybe you have to travel for an hour or so to find all the expertise you need in one place. In the center we can do research and treat niche resections and congenital abnormalities, like placing straps around the cervix via endoscopic surgery. That's not a common procedure so it's not desirable to do it in every hospital in the country. To become an expert, you need practice. You can't be a specialist by doing things now and then. Through centralisation you can specialise, increase possibilities and can do much better research.'

Research is necessary

Huirne gained her doctorate on hormone regulation after IVF, but switched to benign gynecology. 'I was surprised to learn there has been incredibly little research in this area. Only by chance we discovered how many women have problems with menstruation after a caesarean. How can that procedure be performed so often and we don't observe what happens afterward? We know that over half the women between 40 and 50 years have myomas, but we have no clue as to why that is.

'As for cervical straps, mostly they are placed during pregnancy when there is already dilatation. That's not always effective. We think for women with higher risk it is more effective if a band is applied before the next pregnancy. But that procedure is not suitable for everyone, because it involves endoscopic surgery, and the baby can only be born via a caesarean section. Our job is to find out whether it's indeed effective and who is eligible.'

The VUmc currently runs several research lines in collaboration with gynecologists, radiologists and laboratory technicians. 'We now supervise many PhD students who research myomas, adenomyosis and niches, etcetera. 'Money is needed for all these studies, which is problematic. We want to do more research into the underlying cause of various problems, to develop more focused and effective treatments. Ultimately, this would bring down healthcare costs.'

Awareness

Huirne believes that, to function properly and take research and care to a higher level, more transparency is needed between doctors. 'Tell your colleagues what you do, about any complications, or what you have encountered. Collaboration is important. Fortunately, in the Netherlands, we already often do so.

'To make these clinics a success we need doctors to participate and refer patients to benign clinics. Colleagues in the clinics have to make standard agreements about researches and treatments. Everything must be discussed to give reliable information to the patients.'

Huirne stipulates that it doesn't matter whether a doctor is male or female. 'Doctors don't need to have disorders themselves to know what they are talking about. The most important thing is that complaints are taken seriously and that per patient the best treatment is considered.'

The Uterine Repair Center has already been established, and will start a collaboration with AMC shortly. 'I'm convinced that, if we continue to cooperate we can achieve so much when we offer good quality of healthcare and provide the right information in any way. There will be more centers. That is logical, since specialised clinics exist for all kinds of disorders, such as oncology.

'Finally, we want to tell women to see a doctor! Both women and doctors must realise that severe or painful menstruations are not normal. Awareness. That's where it all starts with.'

Following a minor invasive surgery period at Ulleval University Hospital, Oslo, in 2007 gynaecologist **Professor Judith Huirne MD** joined VUmc Amsterdam, where she became professor of benign gynaecology in 2017. She now heads the gynaecology unit, specialising in minimally invasive treatments of uterine abnormalities including myomas (fibroids), adenomyosis (endometriosis of the uterus), niches (caesarean scars defects), congenital uterine abnormalities and cervical insufficiency.
She has been involved in development of various new diagnostic techniques and treatments for uterine abnormalities, and founded the European expert group on uterine abnormalities. In 2017 the uterine recovery centre was founded.

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LC-MS/MS enters the medical laboratory

Changing analytic parameters

Interview: Walter Depner

Over the last four years, Dr Thomas Stimpfl and his team have integrated mass spectrometry into routine analysis.

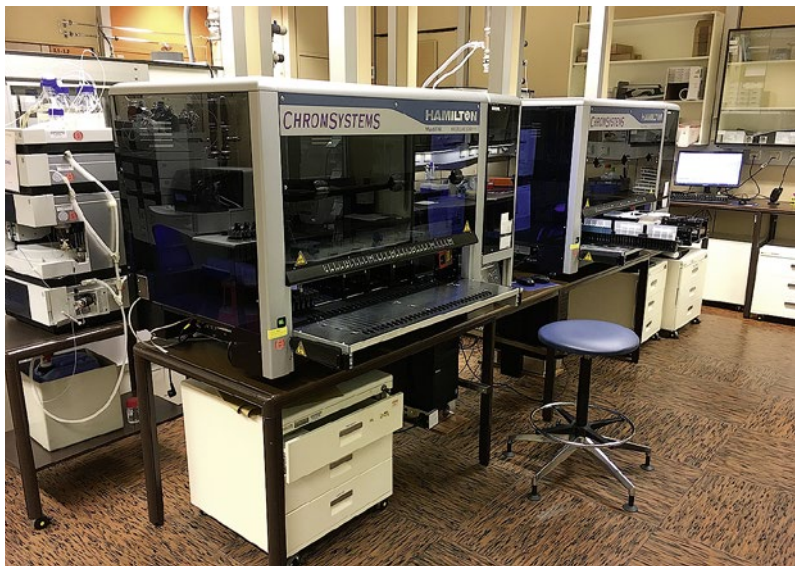
The analytical technique liquid chromatography–mass spectrometry (LC-MS) combines the physical separation capabilities of liquid chromatography (or HPLC) with the mass analytical capabilities of mass spectrometry (MS).

LC- and MS procedures were not originally developed for clinical/medical diagnosis; their introduction in the diagnostic laboratory has been problematic and taken longer than some had hoped. LC-MS, however, has already enjoyed notable success in Vienna and it is evident that this technology will be much more widely used in medical laboratories in the future.

Our EH Correspondent spoke with Assistant Professor Thomas Stimpfl, head of Therapeutic Drug Monitoring and Toxicology at the Vienna General Hospital, about the implementation of the new LC/MS procedures.

Why was a largely non-medical analysis procedure introduced into the laboratory, and how long did that take?

'Mass spectrometry, a standard procedure in forensics, was previously used for only a few specific analytes in laboratory medicine here. These analyses were complex, difficult to reproduce and prone to errors. Furthermore, only a few, select specialists in the field of biomedical analysis could carry them out. Making further developments in this field required much persuasion at all levels to prove the qualitative as well as economic superiority of mass spectrometry and its suitability for routine use. This is an on-going process and leads to a continuous expansion of parameters, which we determine via liquid chromatography–mass spectrometry '



A fully automated robotic system for the determination of immunosuppressants in Stimpfl's laboratory

LC-MS procedures need more technical application than conventional medical analysis. Was the staff affected?

'In the beginning it was difficult for LC-MS to find widespread acceptance for the expansion of the parameter list. We had to use a lot of persuasion and some intensive training to familiarise staff with the more complex technology.
Simplifications in handling and data evaluation, but also further developments of LC-MS systems towards classic medical analysers will make them easier to use in the future. Meanwhile, we now have 15 specialists in biomedical analysis in Vienna who can analyse the 85 LC-MS parameters independently (and also on weekends). '

In your lab, which TDM parameters have changed to LC-MS/MS, and with what success? And which are also planned?

'Immunosuppressants are now determined fully automatically via LC-MS, and this also includes aliquoting blood from the original sample tubes sent in. This step is essential for the repeatability of the overall process, since it has been observed that manual aliquoting of whole blood leads to significant variability. Moreover, after manual sample preparation, the same LC-MS systems are also used to determine psychopharmaceuticals, HIV-therapeutics, antiepileptics, antimycotics and cardiac agents. These analyses will soon be extended to antibiotics and endocrinological parameters.

'Its success lies in the enormous quality gain due to each sample now being given an isotope labelled, internal standard, and the current quality management, which is based on analytical batches, becoming focused on individual patients.'

Which classic laboratory procedures – e.g. immunoassays (ELISA, RIA), photometry – have MS procedures replaced, or are some earlier procedures still used in parallel?

'Immunoassays have been replaced, with the different analytic strategies to be viewed as complementary. In the future, qualitative and also economic factors will determine the use of the different technologies. Decisive for the success of LC-MS will be the automation of sample preparation, reliability and ease of handling of the analysers, complete LIMS integration and fast support from product specialists and service technicians.

'The development of a robust and easy to use LC-MS analyser will be key to extensive expansion of this new technology, also enabling its use around the clock. As mass spectrometry can be used in very wide-ranging ways, this technology specifically lends itself to the establishment of new parameters and the closure of potential analytical gaps in the parameter spectrum.'

What about the economic aspects of LC-MS?

'The widespread establishment of LC-MS is still a challenge due to high costs involved (devices, laboratory adaptation), as well as the higher level of staff expertise required. In the long run, however, running costs will be lower, with higher flexibility and quality. The use of commercially available reagent kits offers a wide range of parameters. In our case this has led to a centralisation of services, where the University Hospital is now offering this service to hospitals throughout the city of Vienna.

'This also facilitates new financing concepts – such as including necessary analytical devices in the reagent kits and paying a price per reported result, which lowers the threshold for the establishment of LC-MS considerably.'

Which systems do you use to achieve what capacities?

'We use in-vitro diagnostic reagent kits from Chromsystems. The sample aliquoting and preparation for an annual total of 35,000 immunosuppressant determinations is carried out with a Hamilton device (as a batch) combined with Sciex mass spectrometers.

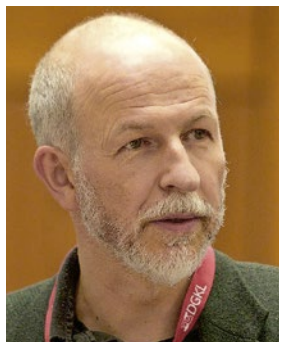
'The sample preparation for a further 15,000 LC-MS determinations a year is done manually because we don't yet have the appropriate random-access automation. We are beginning to see some promising developments among some of the device manufacturers in this field.'

New device/system/method integration into existing infrastructures is important in the modern laboratory; what happened in yours?

'The minimum requirement in order to introduce LC-MS was defined as equivalence with the existing systems. Therefore, from the start, we aimed for the full automation of all processes and full integration into the LIMS; for instance there is no longer any manual data transmission. At the same time, we have been able to increase reliability and quality of results considerably.'

Would you say the reliable and harmonic integration of MS into an existing diagnostic laboratory is a complete success?

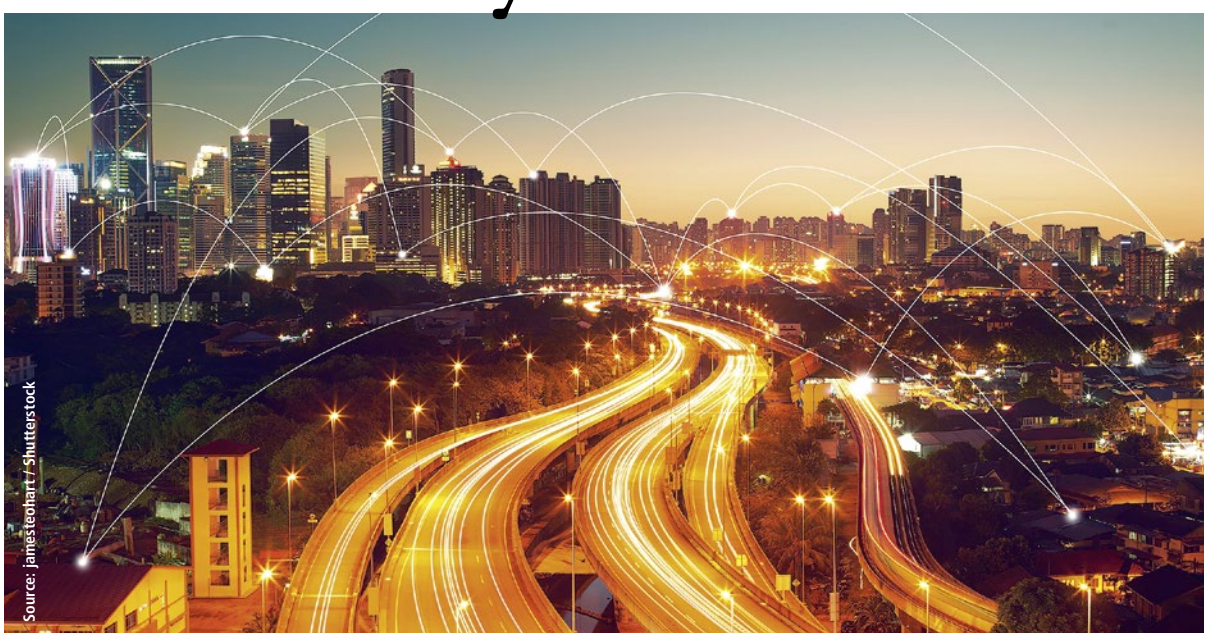
'We can say that mass spectrometry has been successfully established as a routine procedure in our laboratory. However, I believe this is only the beginning of an exciting development – we will see an increasing presence of clinical mass spectrometry in medical laboratories in the future.'



Assistant-Professor Thomas Stimpfl PhD studied pharmacy and earned his doctorate in forensic chemistry at the University of Vienna in Austria. He worked as a forensic toxicologist both in Vienna and at the University Hospital Hamburg-Eppendorf in Germany before he moved to the Division of Medical-Chemical Laboratory Diagnostics at the Vienna General Hospital – Europe's largest university hospital. He also heads a GLP-certified LC-MS laboratory at the Medical University of Vienna.

Network consolidation continues across the globe

The changing face of laboratory medicine



Source: jamesteohart / Shutterstock

In Quebec, a provincial reorganisation process of laboratory services is taking place to save millions of dollars a year, requiring the transportation of about 70% of all test samples to centralised hubs

Report: Mark Nicholls

Laboratory networks are consolidating across the globe as they seek to deliver a more efficient and cost effective service. The latest developments on several continents were outlined at the FiLM 2018 – Frontiers in Laboratory Medicine congress held in Birmingham, UK in January.

With consolidation viewed as a way to deliver economies of scale, it was a recurring theme at the congress with topics covering the pros and cons of consolidating pathology services, and exploring whether one size fits all when it comes to models of laboratory consolidation.

The Dark Report editor-in-chief, Robert Michel, drew on examples of Sonic Healthcare Ltd from Sydney, Australia, as a leader in consolidation and LabCorp and Quest Diagnostics in the USA as major global players, although he pointed to other examples in Japan, with one major laboratory processing 100,000 patient specimens every night.

In a round up that focused less on Europe and Asia, and more on North America, Australia and New Zealand, he offered an insight into what was happening in terms of laboratory consolidation within the sector in these regions.

Approaches differ internationally

From a situation in 2000, when New Zealand had multiple private lab providers, the country now has 'sole source' tenders to reduce competition, concentrate testing and lower the cost of pathology whilst, in Australia, hospital clusters have set up regional pathology networks.

'Canada has been consolidating both hospital and laboratory services since the late 1990s,' he pointed out, 'though that concentration is generally happening within the boundaries of each province.

'There is currently tension between private pathology companies and the public health care sys-

Mass spectrometry is advancing laboratory practice

95% of samples analysed within 14 days

Mass spectrometry is moving laboratory medicine to increasingly automated discrete analysis methods, resulting in ever faster and more reliable results. It is also leveraging economies of scale as an increasingly cost-effective tool, says Craig Webster, Consultant Clinical Scientist and Clinical Lead, Department of Biochemistry and Immunology at Heartlands Hospital in Birmingham.

Speaking about 'Advances in Mass Spectrometry – future diagnostic uses' during FiLM 2018 – Frontiers in Laboratory Medicine congress this January, Webster outlined how mass spectrometry is being automated for common analytes and how this may change laboratory medicine practice.

Advances in mass spectrometry and lab automation began growth in the mid-1990s and although some issues still include lack of sensitivity, cost, the highly specialist nature of the technique, ion suppression, sample variation, and some concern over standardisation of assays, he confirmed that mass spectrometry had emerged as the gold standard method for analytes. However, he added: 'Because you have a fixed cost in the equipment you get better investment leverage from the technology if you put a massive workload through; you then get the benefits from the investment.'

From 20 samples a week to 65,000 per year – and more

Webster, a consultant clinical biochemist for more than a decade, outlined the evolving use of mass spectrometry in Heartlands through the example and testing for Vitamin D deficiency, which started in his area 2006, and how that has moved forward in the last decade or so.

With the initial technology his team examined 20 samples weekly, rising to 3,200 samples a year and then 4,500 in 2008, upgrading the Sciex API mass spectrometry system with a Tecan automated workflow solution and cutting the chromatography time from 10 minutes to two-and-a-half minutes.

'Further workflow steps were automated with pipetting and removing of hexane, and online extraction meant we could take more costs out of the system,' he said. 'We had high quality extraction, achieved really clean samples, had good equipment, better uptime and less cleaning.'

By 2010 they handled 35,000 samples a year and 65,000 by 2013, introducing barcode recognition and an interface into the Laboratory Information Management System (LIMS) as the workload increase.Webster said his lab is at a stage where a medical laboratory technician could operate the system with minimal running costs, few sample rejections, and very few repeats.

Cost per sample is now £3.10 with 95% done within 14 days. The team is moving towards multiplexing assays with mass spectrometry and simultaneously measuring multiple analytes in one run, but he also warned of disadvantages

'The advantages are that the sample only has to be prepared once; there's faster turnaround time, combined calibration and controls and it offers extra clinical information,' Webster said.

'However, there are difficulties in method optimisation and troubleshooting and the extra clinical information can often lead to over-investigation of patients.'

One more general issue is that the technological advances have exposed a lack of skills from informatics training. 'It's not just about putting a computer on the system; it's about how that fits in with workflow and the people who work within that,' Webster continued, adding: 'More informatics training is important because without the IT we do not get full automation.' With more trackable systems and electronic transfer of results, Webster said the system is now moving increasingly towards discrete analysers and an automated chemical analyser with the instrument performing tests on samples kept in discrete cuvettes in contrast to a continuous flow analyser. Mass spectrometry, he concluded, is now fully integrated into the LIMS and workflow at Heartlands, and needs less skilled staff, with an expansion into more analytes. MN

Dr Craig Webster, Consultant Clinical Scientist at Birmingham Heartlands Hospital, is the clinical lead for Biochemistry and Blood Sciences, responsible for R&D in the department of Biochemistry and Immunology. He has developed a number of projects utilising LC/MSMS. His technical background is wide-ranging, with major interests in HPLC, mass spectrometry, capillary electrophoresis and information technology.

Source: Juergen Faelchle / Shutterstock

As the workload increased, the laboratory introduced bar code recognition and an interface into the Laboratory Information Management System (LIMS) in 2013

tem and, after almost 30 years, most provinces do not have much left to "squeeze out" of pathology testing via consolidation.'

In the USA there are private independent lab companies and speciality testing companies, but hospitals are forming ever-larger integrated health systems with the hospital inpatient labs being the first clinical service to be consolidated.

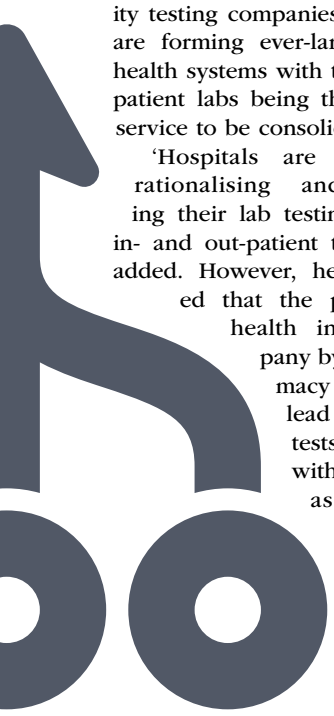
'Hospitals are consolidating, rationalising and standardising their lab testing services for in- and out-patient testing,' Michel added. However, he also predicted that the purchase of a health insurance company by a major pharmacy brand would lead to pathology tests being offered within pharmacies as consumers sought greater convenience.

Options to adopt consolidation

Earlier, Ralph Dadoun, Senior Advisor with the Optilab Project in Montreal, detailed the latest progress on the Optilab project, which is part of a provincial re-organisation of laboratory services intended to save tens of millions of dollars a year and requiring the transportation of about 70% of all test samples to centralised hubs over large geographical distances in Quebec.

Meanwhile, Chris Fourie, Director of laboratory performance consultancy LTS Health, in the UK, discussed the model for consolidated pathology services in England. Fourie has worked alongside NHS Improvement to develop operational metrics to centrally assess pathology data across England with the data being used by Trusts to benchmark their laboratories.

Delegates heard there were five main options for adopting consolidation in England: better networking and stronger collaboration between trusts; consultants interaction being critical to achieve success; a more modern IT infrastructure to act as a catalyst to improvement; convenience becoming a key value added factor; and innovative funding models.



All around the world, laboratory networks are looking for consolidation

Source: Micromaniac / Shutterstock

Robert L Michel is Editor-in-Chief of The Dark Report, a business intelligence service for pathologists and laboratory executives. A respected commentator, consultant, author, editor, speaker and entrepreneur, he is a leading expert on the management of clinical laboratories and anatomic pathology group practices. He received his BA in Economics from the University of California, Los Angeles, USA, and currently lives/works in Austin, Texas, USA.

AMR: the world's biggest health threat

'End animal growth drugs'

A major summit meeting in London, Great Britain, has seen politicians, doctors, scientists, farmers and other experts come together in a bid to tackle the growing global antimicrobial resistance (AMR) crisis. Among these experts was Dame Sally Davies, England's Chief Medical Officer, who described AMR as a 'problem without a face' because most patients are not told they have a resistant infection.

She also called for an end to drugs being used for growth promotion within the farming sector within five years.

The forum, held in Westminster, aimed to put the issue of AMR on the political agenda and raise awareness to the problem in developing countries

Call for support

The event was organised by the Bureau of Investigative Journalism with MP Kevin Hollinrake, who has campaigned on the issue of AMR. 'AMR,' he emphasised, 'is an increasingly serious threat to global public health and it requires action from around the world.

Without effective antibiotics the success of major surgery is compromised, medicines become ineffective, infections persist and spread and the cost of healthcare increases. 'So, it's hugely important that we continue to build on the UK's global leadership on this very important issue and continue the momentum which has built up in the UK to tackle it.'

He also called for support for an Innovation Fund, which is helping more small-scale researchers with finances to increase the chances of finding a solution to the AMR crisis.

AMR has been called the biggest global health threat the world faces.

The forum, held in Westminster, aimed to put the issue on the political agenda and raise awareness to the problem in developing countries and saw several leading authorities on the subject take part in a discussion before opening the floor to questions from the audience.

Increasing transparency

Lord Jim O'Neill, a former finance minister and economist who chaired the government's review into AMR and his report published in 2016, said that there had been a lack of action in three areas: pharmaceutical companies developing new antibiotics, new diagnostic tests, and using vaccines in livestock to mitigate use of antibiotics.

He felt that new diagnostic tests were crucial in the ongoing fight against AMR and that by 2020 all governments should make it mandatory that doctors only prescribe antibiotics if a patient's infection has been diagnosed by a state-of-the-art test.

He called for more transparency from drug companies around antibiotic effluent released as part of drug manufacturing and said that all antibiotics important in human medicine should be banned in agriculture.

Dr Thomas Van Boeckel, a scientist at the Swiss university, ETH Zurich, who has mapped the use of antibiotics in animals, said the reduction of antimicrobial use in animals in the UK was 'remarkable' but that this was in stark contrast to the situation across the globe

'The real tragedy of AMR is that millions of people do not have access to antibiotics because they cannot afford it,' he said. 'When these people will finally be able to afford antibiotics they will not work. Not because they misused it, but because we did. And because we used a lot of it to raise chicken and pigs.'

Kevin Hollinrake is a Conservative Party Member of Parliament for Thirsk and Malton constituency in Yorkshire, England. A former businessman, he has held this political seat since May 2015 and has worked to raise awareness of the global threat of Antimicrobial Resistance.

Other speakers included Dr James Tibenderana, global technical director at the Malaria Consortium, which runs health programmes around the world, and Dr Clare Chandler, a medical anthropologist who runs the AMR Centre at London School of Medicine and Tropical Hygiene.

She also talked about how antibiotic use is related to the wider political and economic context as they speed up recovery so that people can get back to work more quickly, and increase productivity. MN

Going for high-performance hospital hygiene

H_2O_2 disinfects air, surfaces and

Room decontamination using hydrogen peroxide (H_2O_2) has proved to be a powerful solution for complete surface and final disinfection as well as outbreak management in modern hospital hygiene.

Most final disinfections in hospitals are carried out using the scrub and wipe method, the specialist disinfection company Diop GmbH and Co. KG explains. 'However,' the firm adds, 'this essential disinfecting measure entails dangerous risks, such as unnecessary gaps in surface disinfection (up to 70%), incorrect chemical dosages, human errors due to time pressure and lack of validation possibilities. Who seriously wants to take a contamination risk of at least 30%? 'Inadequate final decontaminations can lead to losses in disinfection quality (contaminated surfaces + equipment), high personnel costs (e.g. by repetition of disinfection processes) as well as to an increasing number of infections, such as Methicillin-resistant Staphylococcus aureus (MRSA), Clostridium difficile-associated diarrhea (CDAD) etc. This places heavy financial burdens for economically weak hospitals.'

Validation and difficult, expensive cleaning and disinfection

'Mechanical and automated disinfection methods can be reliably validated, such as the hydrogen peroxide-based room disinfection,' Diop confirms. 'In recent years, the so-called cold nebulisation, aerosolised hydrogen peroxide (aHP), or aerosol disinfection has emerged from these H_2O_2 procedures as being the most practical, user-friendly and most cost-effective disinfection method for final disinfections and outbreak situations in over 20 application areas. These include leading pharmaceutical manufacturers, federal institutes in the field of animal health, research centres, hospitals and food production.

'Especially in highly contaminated patient rooms, toilets, laundry services and other hospital environments, the residual risks and gaps of the disinfecting work carried out by humans can be mechanically secured by way of validation. These serve as microbiological proof of the disinfection performance,' Diop assures.

Recommendations

For the simple, safe and fast implementation of a conclusive validation, closed germ carriers (e.g. DioFog-Controller or DioSpore-Controller) are recommended. These special bio-indicators virtually exclude the risk of recontamination by humans and the environment because they have no handling problems, transport complications or storage risks.

Depending on requirements, bio-indicators for either bacterial activity (incubated with the reference germ Enterococcus faecium or Staphylococcus aureus) or sporicidal disinfection (inoculated with Geobacillus stearothermophilus) can be used.

'The validation itself is quite simple and accompanied by chemical

The H_2O_2 nebulization method can eliminate hygiene risks like gasps in surface disinfection and recontamination by humans

Two pillars of preventive medicine

Vaccination and infection control

Synchronised efforts between preventive medicine and immunology enable powerful vaccination strategies in a Spanish seniors hub. Efficient prevention also comes with proper infection control and regulating antibiotics use in primary care, local expert in preventive medicine explained in an exclusive interview with EH.

Working in a small structure has its perks, one of which is that departments can join strengths easily on many occasions, according to Antonio Valdivia, head of the Preventive Medicine Department at Denia Hospital in the Valencian Community. 'Having everything under one roof enables us to do everything,' he said. When it comes to cooperation, Denia's preventive medicine and immunology departments have quite a successful track record, which culminated with the launch of a campaign on pneumococcus vaccination last year. 'When preventive medicine is combined with immunology, vaccination strategies can be implemented. We are more determined to vaccinate sick or immunosuppressed patients. Pneumococcus infection causes one out of three pneumonias, recent studies have shown, so it's important to fight bacteria which have such a huge disease burden,' Valdivia pointed out.

The Denia Hospital is a small Spanish institution – its size allows close collaboration, especially between the preventive medicine and immunology departments

Recruiting patients from primary care

His department first asked to access databases of patients under immunosuppressive treatment, which makes them particularly vulnerable to pneumococcal infections. The Spanish doctors then crosschecked if these patients had received appropriate pneumococcus vaccination – and if not, initiated the process.

'We have been identifying patients and checking their antecedents for about a year and a half. We've been recruiting patients directly from primary care to vaccinate them against pneumococcus,' Valdivia said. The strategy has brought results: out of a 160,000-population in the Denia area, 2,000 individuals have been vaccinated just by cross-checking risks. Annual tests measuring pneumococcus infection in the region revealed a 15% decrease in the number of cases since the campaign started. Such initiatives can prove effective in areas with high densities of seniors, as they are more prone to develop bacterial infections with life-threatening and expensive outcomes. With its idyllic weather, the Valencian community is a hub for retired Europeans; it also has low birth rates, as a consequence of the financial crisis. This combination is an extra squeeze on already drained resources, Valdivia explained.

'We have a lot of elderly foreigners and overall population, and they consume a lot of healthcare resources. Birth rate is low and we don't have enough young people to take care of our senior patients. Our budget is low because of significant cuts started in 2007, so we have to find creative and efficient solutions to care for our patients,' he pointed out.

A major pitfall in Spain is that healthcare professionals tend to refrain from vaccinating vulnerable, immuno-depressed populations, based on out-dated knowledge, according to Valdivia.

'Twenty years ago, a significant portion of our vaccines used the very viruses or bacteria we vaccinated against. But now most vaccines use a completely different formula. Unfortunately the majority of people, including healthcare professionals, are not aware of that,' he said.

Information systems, and particularly the electronic patient record, have enabled to improve hygiene and infection control, two main axes of preventive medicine. 'The electronic patient record is a powerful tool and increasingly enables us to include all patient data – lab results, vital signs, and so on,' he said. 'It's a great resource to carry out clinical trials and improve infection surveillance in the same region.'

The Denia Hospital team uses patient listings, in which it updates infection status across the community, highlights any potential antibiotic resistance and triggers appropriate chain of actions – change of treatment plan, identification of infection sources (catheter, etc.) and raising the alarm if necessary.

Managing antibiotics use

Recently, Valdivia has noticed a significant increase in multiresistant bacterial infections, especially those acquired inside the hospital. 'Nosocomial infections have multiplied by three in my department over the past two years. We have also seen many cases of multiresistant bacterial infections in patients who came from retirement homes,' he observed.

Training professionals appropriately, directly in a hospital and retirement homes, is key to manage infections properly, Valdivia believes.

Another clear trend he identifies is multiresistant bacteria infection in patients who have received high spectrum antibiotics in the three months prior to the infection, a common scenario in urinary tract infection treatment. 'We are now coordinating our efforts with the infection committee, pharmacies and hospital management systems to try and regulate antibiotics use.'

Their main objective is to reduce the administration of fluoroquinolonas, a commonly prescribed antibiotic, to only absolutely necessary cases, as they found out it was responsible for more than 30% of resistance cases.

Another antibiotic Valdivia does not recommend to treat urinary tract infections is Amoxicillin, unless lab tests strongly indicate so.

Fosfomicinas, an antibiotic developed in Spain, could be an ideal alternative, according to Valdivia, who plans to push the idea directly at general practitioners. 'We are getting serious about antibiotics control in primary care. About 80% of our patients with multiresistant bacterial infections have been treated with fluoroquinolonas or Amoxicillin – and in many cases, this was totally unjustified,' he concluded. MR

Antonio Valdivia, head of preventive medicine at Denia Hospital in Spain, specialised in immunology at Hospital Clinico San Carlo in Madrid, Spain, and in preventive medicine and public health at Madrid Community's teaching unit focused on those fields.

He holds a master's degree in patient safety and quality assistance and a postgraduate degree in investigation methodology.

l rooms

indicators which proof the visible completeness of the disinfection process by automatic discoloration,' Diop points out.

What disinfection results can be achieved?

'Extremely difficult disinfecting processes, e.g. Acinetobacter baumannii, multi-resistant pathogens in general, norovirus outbreak or Clostridium difficile spores cannot be managed manually. In order to get these germs, viruses and spores inactivated and under control (microbiologically and financially), the H_2O_2 nebulisation technology demonstrates its impressive performance at manageable costs and investments.

'H_2O_2 can cover the complete microbiological spectrum of activity (bacteria, fungi, yeasts, viruses and spores). For this purpose, approximately 4 ml per m³ of a disinfectant (for example, Diosol) tested according to EN standards are applied via an aerosol generator (e.g. DiosolGenerator) covering also hard-to-reach areas, such as shafts, ducts and air-conditioning systems.

'Neither expensive training nor a time-intensive additional training is mandatory for the application of the H_2O_2 nebulisation method,' Diop concludes. 'Serious providers offer users in hospital hygiene a 2-3-hour expert training.'

Advanced technology results in more difficult and complex interventions

Anaesthesia is a story of great success

Report: Michael Krassnitzer

Technical innovations and the implementation of quality standards in anaesthesia have immensely increased patient safety. 'Over the past 60 years, patient safety during anaesthesia has improved more than in any other medical discipline,' according to Professor Achim von Goedecke MD MSc, Director of the Institute of Anaesthesiology and Critical Care at Landeskrankenhaus Steyr in Upper Austria.

Good news, since anaesthesiology plays a crucial role in reducing perioperative mortality and increasing patient safety. Today, industrial nations report perioperative complications in three to 16 percent of surgical interventions; 0.4 to 2.0 percent of these cases result in permanent damage or death, as explained by von Goedecke at the annual meeting of the Austrian Society of Anaesthesiology, Reanimation and Critical Care (ÖGARI) in Vienna.

Major improvement

'While each incident is one too many, the statistics reflect a remarkable success story: The number of anaesthesia-associated deaths dropped from 100/100,000 cases in the 1940s to the current level of 0.4/100,000,' he says (see box), and adds that 'a major improvement has been reported since the late 1980s, when further safety standards and improved training were implemented.'

In 2010, the European Board of Anaesthesiology (EBA) and the European Society of Anaesthesiology (ESA) jointly published the Helsinki Declaration on Patient Safety.

At the same time a special Task Force was founded to ensure implementation of the actions identified in the declaration. In 2013, a European platform was established that collects and publishes safety warnings and recommendations by the European incident reporting systems.

Important as they might be, standards ensuring safety and quality in anaesthesiology as well as recommendations to manage critical clinical situations are only one success factor. The dramatic reduction of mortality and concomitant progress in patient safety are, to a large extent, due to medical technology innovation:

- Pulse oximetry. Continuous and non-invasive measurement of blood oxygen saturation is a parameter of respiratory function and the heart-lung system because it shows the peripheral pulse waves.
- Expiratory CO2 monitoring (capnometer and capnography) is a gas exchange parameter that provides data on the pulmonary and circulatory function as well as on the correct placement of the ventilation tube.
- Neuromuscular monitoring. Intraoperative relaxation monitoring of muscle function is important with regard to ventilation tube placement and in certain interventions, such as abdominal laparoscopy.
- Invasive haemodynamic monitoring allows, among others, intra-arterial pressure measurement, which in turn offers data on important cardio-vascular parameters.

Source: B&K - Nicholas Bettschart

Professor von Goedecke outlined major improvements in anaesthesia practice at the annual ÖGARI meeting

Anaesthesia-associated mortality per 100,000 surgery patients	
1940s	100
1960s	80
1970s	10-30
2016	0.4

'In the past decades, these innovations have helped to save many lives and they are contributing significantly to patient safety,' Goedecke underlines.

Source: gespag

Professor Achim von Goedecke MD MSc studied medicine at RWTH in Aachen, Germany. As a medical officer in the air force (1985-95), he became junior physician for anaesthesiology and critical care at the German Armed Forces Hospital in Berlin. He joined the Anaesthesia and Critical Care department at Philipp University Hospital, Marburg, Germany, in 1996, and completed his specialist training. In 2001 he became senior physician at the Anaesthesia and General Critical Care Clinic in Innsbruck University Hospital, Austria. Public health studies and his habilitation thesis were undertaken between 2004-2006. He has directed the Institute of Anaesthesiology and Critical Care at Landeskrankenhaus Steyr in Upper Austria since 2008, and is a board member of the Austrian Society of Anaesthesiology, Reanimation and Critical Care (ÖGARI).

A slight perioperative mortality increase

'Nevertheless, recent figures show a slight increase again in anaesthesia-specific and perioperative mortality in general. 'This is not related to any deterioration of the safety standards but simply to the fact that more older and multi-morbid patients undergo anaesthesia and surgery,' the expert points out. In Germany, the number of surgical patients over 75 years rose from 2.3 million in 2006 to 3.9 million in 2016, which translates into an increase from 18 to 23 percent of all patients. 'In addition, advances in medical technology have led to more difficult and complex interventions. Today surgery, as such, is associated with many more risks,' he explains. Among patients without relevant systemic diseases anaesthesia-associated mortality is stable at 0.0004 percent, whilst in patients with severe multi-morbidity the number increases by factor 100. The conclusion, von Goedecke says, is simple: 'We have to put even more effort into patient safety.'

Easing ARDS and AECOPD

Innovative 'artificial lungs', which help the patients to breathe, offer less traumatic treatment for severe diseases such as acute respiratory distress syndrome (ARDS) or chronic obstructive pulmonary disease (COPD/AECOPD).

Respiratory failure is one of the most frequent causes of ICU admission. It may occur inter alia in patients with ARDS, a dangerous condition when the respiratory system can no longer provide the important exchange of carbon dioxide and oxygen.

Mechanical ventilation

Conventional therapy for ARDS patients, and also for patients with exacerbation of chronic obstructive pulmonary disease (AECOPD), relied on invasive mechanical ventilation.

However, mechanical ventilation has several major drawbacks: sedation has to be induced and the air being pressed into the lungs with positive pressure can damage the pulmonary alveoli or the diaphragm. Moreover, even maximum ventilation frequently does not provide adequate gas exchange.

The extracorporeal 'artificial lung'

An advanced and easy-to-use alternative to such a trauma-associated invasive procedure is an extracorporeal 'artificial lung'. It usually comprises a pump-driven pulmonary support system that removes carbon dioxide from the blood and adds oxygen.

A key component of such a device is the so-called membrane ventilator which 'breathes' outside the body for the patient and carries out some of the gas exchange work of the native lung and at the same time relieves the respiratory muscles.

A plasma-tight diffusion membrane is, for example, connected femorally to the body via a vascular access. It is supported by a blood pump that can be adjusted precisely, and instruments to control blood flow. The membrane ventilator can be used on the patient for up to 29 days.

Many advantages

The 'artificial lung' offers a broad range of support tasks – from efficient removal of carbon dioxide to full oxygen supply.

The approach offers many benefits to patient and healthcare staff alike. Reduced stress on the patient's respiratory system gives the lungs time to heal and the treatment is significantly less traumatic and more effective than conventional invasive procedures.

The lung assist system does not require sedation, which means the patient is actively involved in the therapy and can eat and communicate. The entire hardware fits on a trolley, providing patient mobility during therapy.

Easy to use

Physicians and nurses can quickly height-adjust the membrane ventilator as needed in any particular situation, e.g. when the patient wants to lie down, sit up or be moved around. Subsequent therapies can follow sooner which translates into reduced length of stay and thus reduced costs.

Source: Xenios AG, Heilbronn, Germany.

The membrane ventilator 'breathes' for the patient, outside the body