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Beyond economics

Coming soon: Sustainability reporting for hospitals

A company's impact on society, economy and the environment cannot be measured in financial terms alone – and hospitals are no exception. On the contrary: the idea of measuring the quality of healthcare only in economic terms has always been fraught with problems. Hospitals as organizations have always played an important social role, and their environmental impact is increasingly recognized as well.

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Therefore, it may seem only appropriate that many hospitals will soon be legally required to include non-financial data in their yearly reporting. This is required by the EU Corporate Sustainability Reporting Directive (CSRD). The proposal was adopted by the European Commission in April 2021. As soon as the directive comes into effect, it will expand the requirement of non-financial reporting to all EU companies that fulfil at least two of the following three criteria:

- More than 250 employees
- More than 40 million EUR in turnover
- More than 20 million EUR on the balance sheet

This is not the first attempt of the EU to regulate non-financial reporting: the Non-Financial Reporting Directive (NFRD) has been in effect since 2014. However, it is only applicable to large public-interest companies with more than 500 employees: mainly banks, insurance companies and market-listed companies. All in all, according to the NFRD, about 11,700 companies in EU member states are required to issue non-financial reporting – a number that will increase greatly once the CSRD comes into effect. It is estimated that in Germany alone, the number of affected companies will increase sharply from about 500 to 15,000.

From NFRD to CSRD: Prospective contents of required reports

There is another substantial difference between the current NFRD and the future CSRD: Under NFRD, only the fact that companies published their NFRD reports in time was controlled by authorities. The CSRD, in contrast, does not only demand the formal correctness and timeliness of the report – its contents will be audited as well.

But what exactly is corporate sustainability in the eyes of the European Commission? According to the proposal, the new reporting will have to include the following three main sections, abbreviated as ESG:

- Environmental
- Social
- Governance

The environmental section will have to include information on the effects of the hospital's operations on climate change and, vice versa, how they will be affected by climate change. Furthermore, the report will need to contain information on responsible use of water and any effects on seas and oceans; on responsible use of other resources and on recycling (circular or closed loop) economies; on pollution of the environment and on the protection of biodiversity and ecosystems.

In the social sphere, hospitals will have to account for an equal opportunity workplace, regarding for example gender equality, ethnic and cultural diversity, LGTBIQ+ rights and others. Another important point is workplace safety, physically and ergonomically as well as psychologically; and finally, the preservation of human rights and democratic principles. Regarding CSRD-compatible governance, the hospital will have to report on the commitment of board and management to the upholding of sustainability principles; on corporate ethics and anti-corruption guidelines and measures; on political activities including any lobbying the organization might be involved in; and on its relationships to suppliers, partners, and other stakeholders.

Timeline from 2022 to 2024 and beyond

From 2024 on, it will be mandatory for all but the smallest hospitals to include all these information in their annual report. However, details are not yet known. The European Commission is expected to publish guidelines for CSRD, analogous to the existing guidelines for the disclosure of environmental and social information (2017) and for the disclosure of climate-related information (2019). These are available at https://ec.europa.eu/info/business-economy-euro/company-reporting-and-auditing/company-reporting/corporate-sustainability-reporting_en.

CSRD guidelines will most likely encompass general, sector-specific, and organization-specific rules. The first, general set of rules has been announced for October 2022. The sector-specific and organization-specific guidelines will probably follow in 2023.

The European Commission initially intended for the CSRD to become mandatory on January 1, 2024, meaning that the first annual CSRD reports would have to be issued for the year 2023. However, the EU Council requested several changes to these plans, including a grace period of 18 months for member states to implement the new directive. If these changes are accepted, CSRD reporting will not become mandatory until 2025.

How can hospitals prepare for CSRD?

But even if CSRD is put off until 2025, hospitals will have to implement it sooner or later. Now is a good time to take the first steps in preparing for CSRD. While detailed guidelines specifically for the healthcare sector or for hospitals will not be published until some time in 2023, there are other frameworks that can give a first impression of sustainability requirements: existing international guidelines such as those created by the Global Reporting Initiative (GRI), the Sustainability Accounting Standards Board (SASB), the International Integrated Reporting Council (IIRC), and the International Sustainability Standards Board (ISSB), just to name a few. These are supplemented by national guidelines, where applicable, such as the Deutscher Nachhaltigkeitskodex (DNK) sustainability criteria for Germany.

Before detailed CSRD criteria are available, hospitals should not invest massively in CSRD preparations. But some early research into how current quality management, controlling and reporting could be adapted to fulfil CSRD standards will make sure that hospitals are well prepared when the new regulations finally become effective.

Report: Dr Christina Czeschik

DOUBLE MATERIALITY

A central concept behind the CSRD is the principle of double materiality, a core element of the European Sustainability Reporting Standard (ESRS). This is intended to serve as a guideline as to whether a certain sustainability aspect should be included in the sustainability report. Put simply, both the positive and negative impacts of the company's activities on the environment are considered, as well as the opportunities and risks for the company arising from the environment.

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Predicting the future of imaging

What will ultrasound practice look like in the year 2030?

Rapid technical advances in ultrasound and increasingly tight healthcare budgets call for a change in ultrasound practice, experts explained in a session at the European Congress of Radiology in Vienna. Two experts presented possible models for the next two decades.

Ultrasound has become less popular among young radiologists, according to Professor Paul Sidhu, a consultant radiologist in the Department of Radiology at King's College Hospital, UK. 'Trainees are less interested in performing ultrasound than CT or MR,' he said.

In the UK, 90% of the ultrasound is performed by sonographers, nearly all of whom have undergone radiographer training, followed by a two-year apprenticeship in ultrasound, and often also a postgraduate diploma or MSc in ultrasound. This allows for many years of experience prior to independent practice.

By contrast, radiologists have less formal training and tend to use ultrasound only in specialized settings, such as musculoskeletal, paediatrics or contrast-enhanced ultrasound (CEUS). 'Very few of the large teaching centres in the UK would have radiologists performing general ultrasound anymore,' Sidhu said. 'In district hospitals, they're more likely to do general ultrasound once a week, but often only once or twice a week, contrasting with the sonographer's daily practice.'

Unlike most European countries, sonographers in the UK perform both the examination and the reporting, but they're accountable to radiologists, who are still responsible for imaging quality and safety. Ultrasound will thus become less of a radiology tool, Sidhu predicted. 'It's all going to have to change within 20 years,' he told the audience. 'You will get fewer trivial examinations being performed in the radiology-run ultrasound departments. A pleural effusion will be performed at the bedside by the clinician, just prior to the drainage procedure. There will be no need to take a patient to the ultrasound department.'

Finding the right balance

This scenario will be more cost effective for healthcare systems, which are increasingly under financial strain. 'They can't afford a doctor to perform all the ultrasound. The sonographer is less expensive than a radiologist. Healthcare systems have to wonder if it's efficient or necessary to have a physician perform all of the imaging examinations.'

A more sustainable scenario would be to have an ultrasound department run by the radiologists, but used by other practitioners of ultrasound, and staffed by doctors and sonographers. 'The future will be a balance,' Sidhu predicted. 'It takes a lot of training to be able to scan properly. We will see that radiologists delegate more and more ultrasound to well-trained technicians.'

This model will expand slowly and will be initially hospital based, he added. 'The radiologists will always ultimately be in charge because of their imaging background, but it will be a hybrid department where other specialists can use the equipment within the umbrella of the department, which will look at clinical governance, and safety and quality of the imaging,' he said.

This is where the strength of radiology remains in retaining ultrasound, he explained. 'Radiology should not lose it because it's a modality that's so ubiquitous and so useful as a point of care tool that you need it. But trying to convince the younger doctors to understand that is difficult,' he concluded.

The German example

In Germany, some institutions have already established such interdisciplinary ultrasound centres to counter structural problems and high maintenance costs, according to Professor Thomas Fischer, Head of the Interdisciplinary Ultrasound Center of Charité – Universitätsmedizin Berlin, Germany, who also spoke in the session. 'The targeted and time-intensive training of ultrasound specialists, the personnel-intensive staffing of small ultrasound departments, and availability for on-call duty are urgent problems in many departments,' he said. 'Equipment fleets are maintenance- and cost-intensive, and in some cases outdated.'

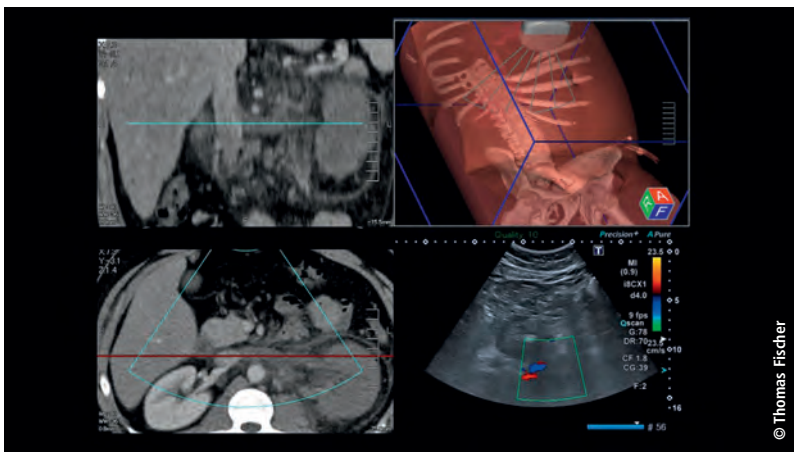
In a recent article, Fischer and colleagues observed how institutions in Berlin, Munich, Regensburg, Rostock, and Trier set up and benefit from an interdisciplinary ultrasound centre. 'They've been able to reduce the number of devices needed in a hospital and more efficient use of available equipment through bedside time optimization,' he said.

Establishing such a centre results in further potential for economic optimization. 'The DEGUM multicentre study PRIMUS showed that hospital stay could be reduced from 8 to 5 days by using ultrasound within the first 24 hours in the emergency department,' he said. 'In some cases, inpatient admission can be avoided, and the number of outpatient treatments can be reduced. The effect on possible therapeutic consequences and targeted diagnostics is high.'

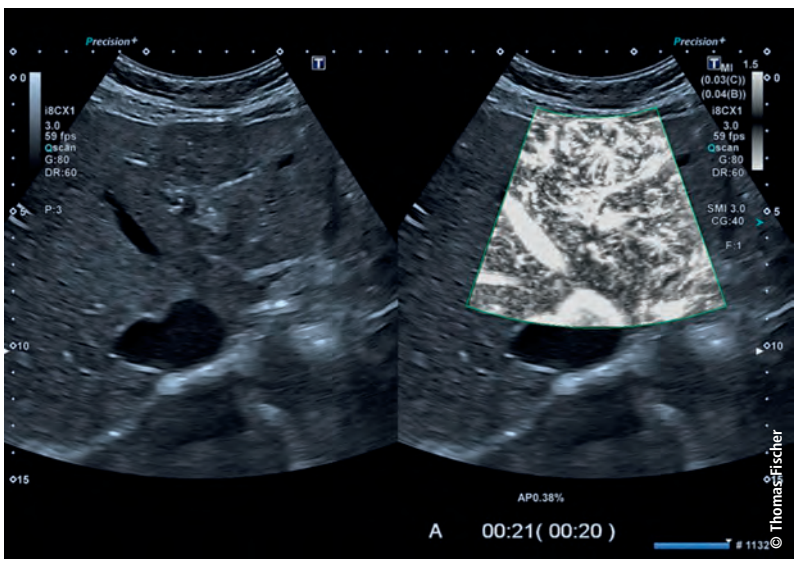
CEUS or image fusion for complex interventions, as well as training of younger colleagues can be centrally organized through the multidisciplinary experience available at such centres, Fischer noted. 'Interdisciplinary centralization also allows standardization and better control of hygiene quality standards. The creation of an interdisciplinary image database based on standardized ultrasound protocols can significantly improve research,' he said.

The challenge will be to coordinate the centralization of the modality with specific organ and disease related processes depending on the local conditions and requirements of the hospital. 'Functional areas have been created in many departments in recent years and are spatially and organizationally oriented on the clinical pathway of the patient – for example, interdisciplinary outpatient breast cancer centres. A high volume of patients and examinations could limit the ability of an ultrasound centre to provide comprehensive sonographic resources,' he concluded.

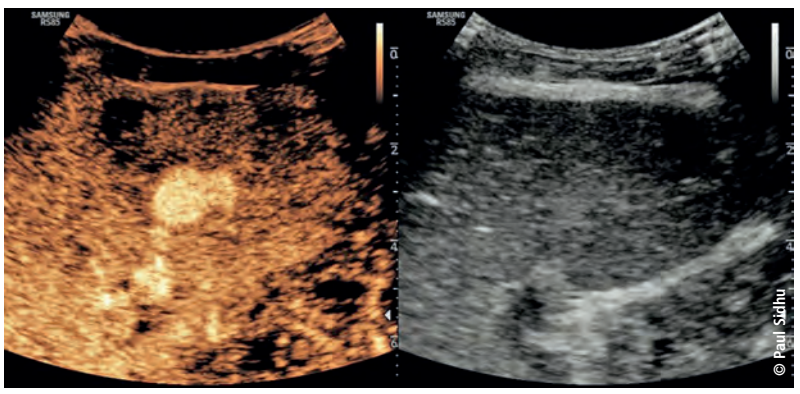
Report: Mélisande Rouger



Nephrology: Example of cooperation with nephrology. CT/US image fusion in renal vein thrombosis. The image planes correspond to an axial section at the level of the left renal vein.



Liver: Cooperation with hemato oncology. A patient comes to the examination of a focal liver lesion. A split-screen mode with B-mode right and special doppler method SMI left after contrast medium administration. The wheel spoke pattern of the FNH is particularly good to recognize.



Aneurysm: Splenic pseudo-aneurysm following trauma with CEUS

Paul Sidhu

Paul Sidhu is professor of imaging sciences at King's College London and a consultant radiologist in the Department of Radiology at King's College Hospital. His research has focused on ultrasound and interventional radiology, and he has published extensively on many aspects of ultrasound, particularly in relation to male health and liver transplantation. Sidhu notably pioneered the introduction of contrast-enhanced ultrasound (CEUS) in the United Kingdom in 1996 and is recognized as an authority in the application of this technique in clinical practice.

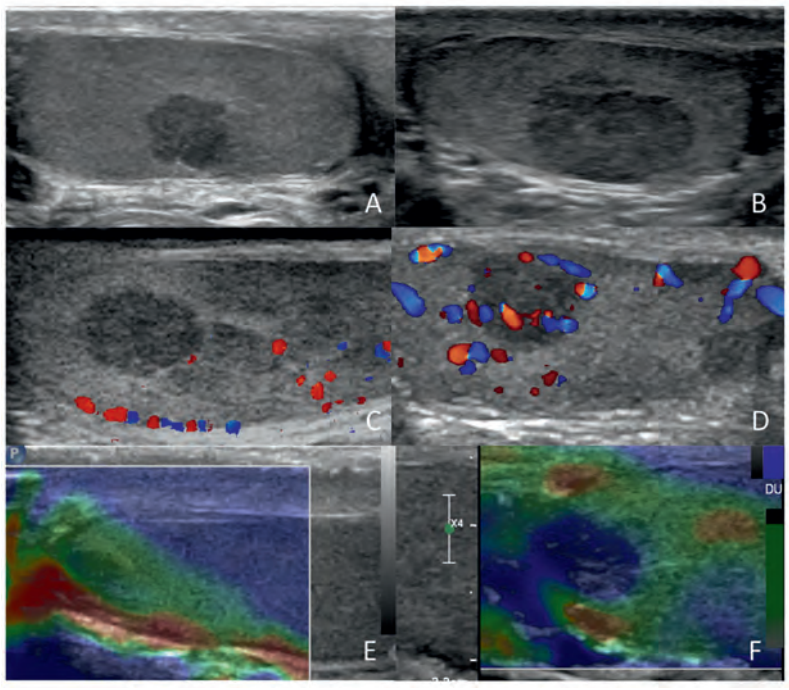
Thomas Fischer

Professor **Thomas Fischer** is Head of the Interdisciplinary Ultrasound Center of Charité – Universitätsmedizin Berlin, Germany, where he founded the Ultrasound Research Laboratory. With a research focus on breast imaging, ultrasound contrast media, US/CT-MRI image fusion, rheumatic diseases, and prostate cancer diagnosis and treatment, Fischer has made important contributions to the development and improvement of new ultrasound techniques like elastography, image fusion, and ultrasound-guided prostate biopsy.

Multiparametric ultrasound

Experts assess usefulness of MPUS in the diagnostic conundrum

Multiparametric ultrasound (MPUS) has proven its value in the abdomen – now, the technique is increasingly moving towards peripheral areas such as breast and testis imaging, experts showed in a dedicated session at ECR 2022.



Suspicious signs for malignancy at MPUS during the follow-up of incidentally detected small testicular lesion. (A-B) The lesion significantly increased in size. (C-D). Lesion vascularity significantly increased. (E-F) The lesion significantly increased in size and in consistency at elastography.

MPUS has been used in breast imaging for many years and the most commonly used features are black-and-white, grayscale and B-mode, Professor Boris Brkljačić, Professor of Radiology and Vice-Dean at University of Zagreb School of Medicine in Croatia, told the audience. 'The majority of our diagnosis and criteria to differentiate benign and malignant lesions are based on B-mode ultrasound,' he said.

Brkljačić routinely uses colour Doppler to assess vascularization of lesions. And in the last 15 years, he has been using elastography to assess lesion elasticity and stiffness. 'Most cancers are stiff, while most benign lesions like adenoma are soft,' he said. 'This difference can be evaluated and quantified with elastography.'

Contrast-enhanced ultrasound (CEUS) in the breast is mostly used for research purposes, but it could help assess treatment response to neoadjuvant therapy in breast cancer that can be treated with chemotherapy and surgery, Brkljačić explained. 'The success of chemotherapy can also be evaluated with contrast-enhanced MRI, which is the standard procedure used for this purpose, but CEUS might have a role to play here, especially since it's far more available than MRI,' he said.

Experience is required

Ultrasound requires a lot of experience and the ability to work with modern equipment that offers software support for special features in B-mode and elastography. 'In B-mode, for example, it's important to use compound and harmonic imaging,' he explained.

Ultrasound can also help guide biopsy or prepare for surgery. 'If you see a lesion on mammography and MRI, it's very easy to perform ultrasound-guided biopsy and deposit clips under ultrasound guidance before neoadjuvant therapy,' he said. 'You can also puncture lymph nodes in the axilla using ultrasound guidance, as it's much easier and faster than under mammography or MRI guidance.' Ultrasound-guided biopsy enables to make a very reliable diagnosis in the preoperative stage, with all the necessary information on oestrogen receptors, progesterone receptors, HER2 status, proliferation, etc. Mammography remains the first modality for breast cancer primary diagnosis and screening. However, the European Society of Breast Imaging (EUSOBI) recommends that women with very dense breasts should be examined with abbreviated MRI protocols. But when MRI is not available, radiologists should not hesitate to rely on ultrasound. 'In dense breasts, accuracy of mammography is lower. An additional test with ultrasound can help detect breast cancer. MRI is better, but we don't have the possibility to screen every woman with MRI, so ultrasound is a good alternative.'

Testis imaging

In the testis, the challenge for MPUS remains to characterize lesions, according to Michele Bertolotto, Associate Professor of Radiology at Trieste University in Italy, who also spoke in the session. 'When you find a small, non-palpable lesion in the testis, although you're able to identify it with very high sensitivity, typically you're not able to characterize it,' he said. 'All lesions, either benign or malignant, look similar on ultrasound.' There is a necessity to improve characterization of such lesions to avoid unnecessary surgery, he argued. '70% of these lesions are benign or non-neoplastic,' he said. 'If you perform orchiectomy each time, there's a lot of over-treatment.'

Urologists still recommend removing the testis when lesions are not characterized well enough, as a risk of cancer remains. 'It's crazy, many patients still undergo surgery for benign lesions,' Bertolotto insisted. But even urologists begin to understand that this is an issue, as the literature increasingly shows the benefits of following up lesions over time, he added. Specificity can often be improved, and CEUS allows to assess with very high specificity whether the lesion is vascularized or not. 'In practice, all the lesions that are avascular on CEUS are benign or non-neoplastic,' he explained. 'If lesions are vascularized, it's more complicated. Still, you can follow up or only remove the nodule, not the whole testis.'

Elastography and Doppler can be useful in that setting. If the lesion remains stable with these parameters, follow up should continue. If vascularization or consistency on elastography increases, it is an indication that the lesion could be malignant.

Ultrasound is a multistep examination, Bertolotto reminded the audience. 'Incidental findings typically occur when a patient undergoes an ultrasound scan for infertility or because he has some pain or discomfort.'

The next step is to carry out a colour Doppler test, to see if the lesion is vascularized or not, what its consistency is on elastography, and then to complete this test with CEUS. 'If you have a soft lesion that becomes harder in time, it's a sign of malignancy. Any change is a sign of potential malignancy,' he said.

If lesions are not palpable and do not show a suspicious behaviour during follow-up, Bertolotto strongly recommends not undergoing surgery. 'Most patients who present with infertility are young. You would reduce their possibilities to conceive if you remove a testis,' he concluded.

Report: Mélisande Rouger

Sponsored · Expansion to AI market

Improving prioritization, quantification and productivity

Bayer recently announced the launch of Calantic Digital Solutions, a new platform delivering access to digital applications, including artificial intelligence (AI) enabled programs for medical imaging.

The offering contains tools which aid radiologists and their teams to improve prioritization, lesion detection, quantification, and productivity. By providing access to AI radiology applications through the Calantic Digital Solutions platform Bayer expands its portfolio beyond contrast media, medical devices, software, and services.

Gerd Krueger, Head of Radiology at Bayer Pharmaceuticals, said: 'With Calantic Digital Solutions, we are entering the fastest growing segment in the radiology market and taking the next step on our way from a product provider to a solution provider, following our mission to provide an ecosystem of third-party and Bayer products to deliver state-of-the-art disease-oriented solutions for radiologists and their teams.'

Providing assistance at critical steps

Calantic Digital Solutions is a suite of digital radiology AI-enabled applications which provide assistance at critical steps within a patient's treatment journey. The vendor-neutral, cloud-hosted platform includes a growing number of applications designed to aid in prioritization, lesion detection and quantification, as well as apps that automate routine tasks and measurements, improve the radiology suites' workflow, and free up time for radiology staff.

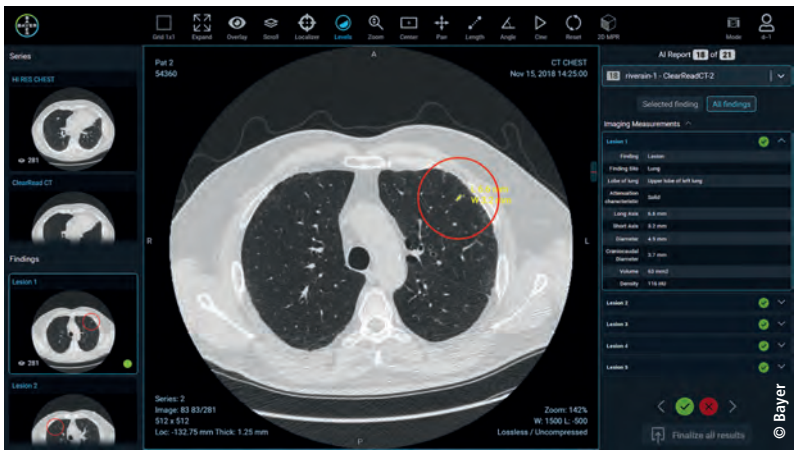
The offering is orchestrated by body region and procedure, initially focusing on thoracic and neurological diseases, such as pulmonary nodule detection. Another area of application is the triage of potential intracerebral hemorrhage (ICH) and large vessel occlusions (LVO), both of which can be associated with stroke.

More disease-specific application packages will be added moving forward, the company announces. Bayer provides services around installation, configuration, and training of the platform and its applications. First launch markets will include the US and several European countries, with more regions to follow.

Increasing demand for AI

The company sees increasing demand for innovation powered by AI: aging populations and changing lifestyles are leading to an increase in chronic conditions such as cardiovascular disease and cancer. Consequently, the need for medical imaging to detect diseases, guide treatment decisions and support therapy planning is growing. AI is the technology to meet these challenges, Bayer concludes, as it comes with the value proposition to accelerate diagnosis and increase the throughput of radiological examinations.

More information:
www.calantic.com



The Calantic Digital Solutions platform

Diversity, transparency, flexibility

Building trustworthy AI systems for cancer imaging

Building artificial intelligence (AI) tools that clinicians and patients can trust, and easily use and understand, are core to the technology being successfully deployed in healthcare settings. AI expert Dr Karim Lekadir focused on the importance of these elements during a presentation at ECR in Vienna, as developers seek to create new AI models to support image-based diagnosis and care.

Lekadir concentrated on different methods for building and validating artificial intelligence workflows, and how federated big data repositories can enhance future AI applications in cancer imaging.

Questioning the performance primacy

He highlighted the creation of trustworthy systems as a key step in AI development. That, he added, has to take into consideration all aspects of the system. 'I will focus on the value of trust in future AI solutions because it is one thing to build an AI solution that is performant, but quite another to build AI solutions that people can trust and will deploy and use,' said Lekadir, who is Director of the University of Barcelona's Artificial Intelligence in Medicine laboratory.

'Until now, people have focused on the performance in relation to accuracy and robustness, but that is not enough. We need to go beyond that and take in other elements, such as fairness. An AI solution may be robust but may discriminate against certain underrepresented groups. It may work well with white patients but not so much with black patients, for example, or with men but not female patients.'

Bringing light into the AI black box

He also pointed out the value of usability and explainability, for both clinicians and patients.

'Because AI models are often complex, users can sometimes be resistant to using them, so we need to make the AI decisions understandable,' he said. Transparency and traceability are also important in light of constantly changing data and users. Models that do not take these factors into account run the risk of quickly losing their robustness, becoming unusable. 'We need to monitor and trace these tools over time, because something that makes AI different from other technologies is that it is highly dynamic and changing over time,' he added.

Inclusive approach to anticipate barriers

The expert argued that adopting a 'highly-inclusive approach when designing, building, validating and deploying the AI solution' is pivotal in its successful introduction into a clinical setting. A crucial oversight of the past, he suggested, was that engagement with clinicians and other stakeholders had been minimal when AI tools were being developed. 'We are realising the importance of having a multi-stakeholder and human-centred approach where we involve developers, clinicians, patients, data experts, ethicists, social scientists, and regulators so we can anticipate some of the implementation barriers,' added Lekadir.

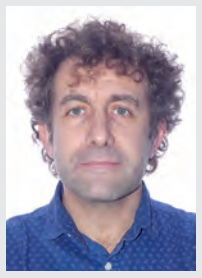
This co-creation enhances technical robustness, applicability, and clinical safety and means problems can be anticipated in advance with appropriate solutions designed and implemented.

Thorough evaluation of AI

He emphasised the role of thorough evaluation, such as ensuring a system covers patients of different ethnic backgrounds. 'If you evaluate without paying attention to ethnic diversity, you may run into problems later when the tool is deployed in practice,' he cautioned. 'It may not work well for certain populations.' External evaluation, in a hospital or centre different to the one where the model was built in, is therefore critical. He also underlined the need for compliance with AI regulations.

For the development of AI, it is important that clinical, technical, ethical and legal aspects are taken into account and that all stakeholders and end users are involved, problems are anticipated and measures are taken to mitigate risks, he concluded.

Report: Mark Nicholls



Karim Lekadir

Dr **Karim Lekadir** is from the Department of Mathematics and Computer Science at the University of Barcelona, and Director of the university's Artificial Intelligence in Medicine laboratory. His research interests focus on big data and AI for biomedical applications.

Medirad project

Increasing the protection from medical radiation

Important findings from a Europe-wide project to improve medical radiation protection for patients and staff were detailed at a session of the ECR in Vienna. The five-year Medirad project sought to enhance the scientific basis and clinical practice of radiation protection in medicine by better understanding and evaluating the health effects of exposure to low-dose ionising radiation resulting from diagnostic and therapeutic procedures.

A multi-disciplinary consortium of various research groups, with 34 partners in 14 countries, looked at areas of dose evaluation and optimisation in medical imaging; the impact of low dose radiation exposure; breast radiotherapy and secondary cardiovascular risks; and the impact of paediatric scanning.

With Medirad having made a number of recommendations for enhancing the effective protection of patients and medical professionals, as well as for identifying further research priorities, the ECR session heard speakers discuss new optimisation methods in chest CT, early cardiovascular changes after radiotherapy, and paediatric CTs and cancer.

Medirad scientific co-ordinator Elisabeth Cardis focussed on CT exposure in childhood to help understand cancer risk estimation for children, retrospective reconstruction of doses, and long-term follow-up. 'The reason we study paediatric exposure to ionising radiation is because there are concerns about potential health impacts of radiation exposure in childhood,' said Cardis. 'Exposure at a young age is associated with a higher relative risk of several forms of cancer.' Highlighting how the number of paediatric CTs has grown dramatically in high income countries in recent decades through improvements in technology and more applications for paediatric patients, she said the project concluded that paediatric CT scanning appears to increase the risk of cancer, particularly in haematological malignancies and brain tumours in a dose dependent fashion. She said the Medirad preliminary findings were that missing doses from conventional x-rays could lead to an underestimation of risk in higher dose categories, though this needs to be confirmed in a full study. However, while final data from the study is still awaited, there appears 'substantial improvements in precision of risk estimates.'

John Stratakis from the University of Crete's Department of Medical Physics, discussed the element of patient-specific radiation dose and cancer risk estimation from chest CT. He also detailed a novel CT dosimetry tool (CTRAD) developed within the framework of the Medirad project.

Stratakis focussed on understanding the limitations of current CT dosimetry methods and tools, the need to appreciate the value of accurate patient dosimetry in CT and the value of patient-specific methodologies for calculating doses and risks in CT. 'CT dosimetry has not escalated in pace with the exponential development of CT technology,' he said. Various alternatives for more accurate CT dosimetry have been proposed over the last two decades, but he suggested they have limitations.

The expert said a high level of accuracy is needed in CT dose measurements because there is evidence of non-cancer effects such as lens opacities, cataracts and cardiovascular disease at relatively low doses; while patients subjected to multiple CT scans and exposed to doses higher than the 100mSv threshold are at significant stochastic risk. He said: 'Inaccurate patient dosimetry can underestimate or overestimate the radiation burden associated with the recurrent CT imaging, leading to wrong priorities and incorrect dose management of these patients. 'We actually need accuracy with dosimetry because accurate dose estimation is the pillar of exposure justification, protocol optimisation, and is invaluable to assess organ radiation doses and radiation use risk of patients. It conclusively governs the management of patients undergoing CT procedures.' He underlined the value of personalized CT dosimetry methods, where a scanner-specific and patient-specific organ-dose estimation is based on a procedure that combines computational techniques and patient CT scans via the CTRAD image-based calculation tool.

A free tool, autoWED, included in CTRAD to automatically calculate Water Equivalent Diameter (WED), enables the correlation of organ dose to patient attenuation characteristics.

CTRAD tool

Stratakis explained that with CTRAD, users can upload a single DICOM image or a DICOM series for dosimetric calculations. CTRAD, he added, can calculate risk and a printable report can provide a summary of the absorbed dose of primarily-irradiated organs as well as the life attributable risks for cancer incidence and mortality. He said the tool has future-proofed characteristics with elements of sustainability, maintainability, reliability, and security; is web-based; and it is easily upgradable with additional data for scanners and anatomical regions.

In conclusion, he said: 'Current CT dosimetry based on simple metrics may have weaknesses, so gold standard combined with Monte Carlo simulations personalized dosimetry can bring a paradigm shift in CT dosimetry, providing accurate organ dose estimates. 'AI has the future potential to accelerate computations and segmentations to eliminate limitations and provide organ dose estimates in real time.'

Report: Mark Nicholls

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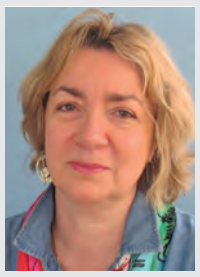
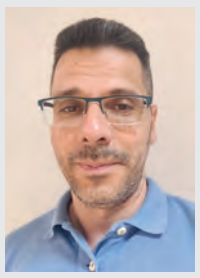


Elisabeth Cardis

Elisabeth Cardis is a research professor in radiation epidemiology at the Institute for Global Health in Barcelona and Medirad scientific coordinator. She is the author of over 100 indexed publications and a member of the board of the MELODI (Multidisciplinary European Low Dose Initiative) platform.



John Stratakis

John Stratakis is a research associate in the University of Crete's Department of Medical Physics and a medical physicist in the University Hospital in Heraklion, Crete.

Overheard at AACC

The complexities of drug testing in urine and hair

Urine screening tests using only immunoassays are the most common procedures used to identify drug abuse. They are inexpensive, automated, and produce rapid results. But they may produce false-positive or false-negative results, which vary based on the drug, drug class, and the assay used. Hair toxicology analysis is another form of drug testing, which unlike urine tests, enable analysis of drug use over a period of time. Hair toxicology tests complement urine tests but can be just as challenging to interpret.

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Mass spectrometry, specifically liquid chromatography with tandem mass spectrometry (LC-MS/MS), is a powerful tool for toxicology analysis. Although more labour intensive, more time consuming, and much more expensive that hair and urine tests, LC-MS/MS is recommended for drug confirmation testing following a positive or inconclusive immunoassay screen. It is highly complex and requires significant expertise but provides definitive results due to its superior sensitivity and specificity.

At the 2022 AACC Annual Scientific Meeting in Chicago, Joe M. El-Khoury, PhD, director of the Clinical Chemistry Laboratory at Yale-New Haven Health, discussed the challenges of interpreting complex urine toxicology cases.

'When in doubt, mass spec it out'

El-Khoury discussed a routine urine test ordered for a patient prescribed opioids and other medications for multiple, chronic, and complex medical problems. Her physician wanted to verify that this patient was not taking additional types of painkillers. The test results were positive for heroine, but other findings were contradictory and confusing. 'Immunoassay screening may not produce accurate results, because antibodies used in the assays for the targeted drug may exhibit cross-reactivity toward other closely related compounds,' said El-Khoury. 'Patients maintained on chronic opioids are often at risk of false positives. The LC-MS/MS test determined that the patient was only taking exactly what she'd been prescribed. When in doubt, mass spec it out.'

He noted that patients taking Suboxone, a drug widely used for treatment of patients with opioid use disorder, are high-risk, and may attempt to stimulate compliance by spiking the pill in urine to pass the screening test. Immunoassays are not specific enough to detect this sample adulteration and patients may get away with it. El-Khoury recommends that quantitative LC-MS/MS testing be the only method used for assessing adherence in patients taking Suboxone. When concentrations of drugs in urine are high, he advised the audience to make sure to rule out pharmaceutical impurities, and to rule out enzyme inhibitors when metabolite patterns are unusual.

Jacqueline Hubbard, PhD, the Laboratory Director of Three Rivers Diagnostics in Pittsburgh, Pennsylvania, gave deeper insights into hair toxicology analysis. Hair grows an average of 1 cm each month. When hair samples are segmented into sections, it is possible to obtain a detailed historic profile of an individual's drug exposure over a specified amount of time. However, the accuracy of the analysis may be impacted by ultraviolet light exposure and diffusion of sweat, which may occur at any time. Cosmetic hair treatments may strip analytes or increase environmental contamination.

Melanin must be considered

A person with higher melanin may show a greater accumulation of drugs compared to a person with low melanin, so this needs to be considered when testing dark hair. Hubbard explained that the Society of Hair Testing (SHT) recommends that hair first be segmented prior to decontamination. The Society recommends use of aqueous washes and an organic solvent to remove oil and external contaminants from the hair. But these processes may still be insufficient. Recent research has suggested that such procedures may lead to the swelling of the hair and may promote incorporation of analytes into the hair itself. Cleansed hair samples need to be cut, ground, and pulverized before they are analysed. 'When drugs are detected in a panel, I recommend metabolite detection to confirm ingestion,' she said. 'The detected presence of drugs in hair may be due to ingestion, incidental exposure from contaminated surfaces, impurities found in the drug, and/or decomposition products of drugs.'

'Hair toxicology interpretation to determine the frequency of use and if a person used specific drugs is not that simple. The amount of drugs detected in hair may not be equivalent to the actual concentration present in hair, and the relationship between the concentration in hair and the amount ingested is not well established,' cautioned Hubbard. 'Drugs in hair are indicative of repeated use and/or exposure, and not of a single use or recent use. Hair as a matrix for toxicology testing has implicit biases, including seeing higher drug concentrations in pigmented versus non-pigmented hair after the same systemic exposure. This test frequently has a longer turnaround time compared to urine tests. But it may be useful to identify if children who have unexplained conditions or may be experiencing developmental delays are living in unhealthy situations,' she said. Hubbard described two cases that demonstrate the utility of hair toxicology testing. A malnourished two-year-old girl showing signs of neglect and developmental delays had a negative urine drug screening test for 11 drugs. However, hair toxicology analysis showed that the child had ingested two drugs, including methamphetamine. A two-year-old boy was admitted to a hospital emergency department with acute encephalopathy and seizures. His urine and lab tests were negative, but when the hair toxicology reports became available 30 days later, they had tested positive for exposure to oxycodone and methamphetamine 'Hair toxicology helped identify an unstable home situation from drug use for both children. For the boy, whose parents were separated, it provided definitive evidence that the mother of the child was a drug abuser, enabling the child to stay with his father. These tests can be invaluable in help keeping vulnerable children safe,' she concluded.


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Report: Cynthia E. Keen

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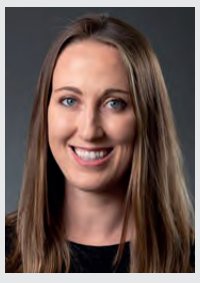
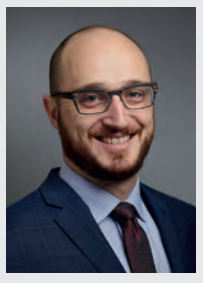


Jacqueline Hubbard

Jacqueline Hubbard, PhD, joined QualiTox Laboratories, now Three Rivers Diagnostics, in 2022 as its Laboratory Director. Her interests include toxicology interpretations, test utilization, and mass spectrometry. She also serves as an MSACL Practical Training scientific committee member and is actively involved in training new users on mass spectrometry. Her research has also focused on developing and validating drugs of abuse assays, driving under the influence of marijuana, and Covid-19 serology research.



Joe El-Khoury

Joe El-Khoury is Director of the Clinical Chemistry Laboratory at Yale New Haven Health in New Haven, Connecticut, and Associate Professor of Laboratory Medicine at Yale University School of Medicine. A fellow of the AACC Academy, his research interests include indicators for monitoring clinical laboratory performance, investigating biomarkers of acute kidney injury and chronic kidney disease, and development of new mass spectrometry-based methods for the measurement of markers in biological fluids.

'Self-destructing' parasite

A solution for drug-resistant malaria?

Over the last 50 years, malaria parasites have developed resistance to seven drugs, but a new way to identify future antimalarials holds promise.

So far, the malaria parasite has defied every method of control, including a vaccine and dozens of drugs – the parasite always makes a comeback.

The currently recommended treatment – an artemisinin combination therapy, a mix of fast and slower-acting drugs designed to treat infection and prevent transmission – fails to cure infections in more than 50% of patients in some Southeast Asian regions. Furthermore, resistance to artemisinins has also now been detected in Africa, where most of the 600,000 annual malaria deaths occur.

Now, an international research team has published a world-first discovery in the journal Science (https://doi.org/10.1126/science.abn0611) showing that a previously overlooked class of chemicals – known as nucleoside sulfamates or "nukes" – can cause malaria parasite enzymes involved in protein synthesis to self-destruct.

Active against all stages of the parasite

Of particular importance, inhibitors of this pathway are expected to be active against all stages of the malaria parasite – effective for both treatment and preventing transmission. Specifically, the nucleoside sulfamates were found to hijack the parasite's own cell machinery, thereby halting processes that are essential for the parasite's survival. 'In short, we discovered a new avenue for targeting pathogens – getting them to be the instrument of their own demise,' says the article's senior author Professor Leann Tilley, from the Department of Biochemistry and Pharmacology at the University of Melbourne. 'The prevention of transmission is very exciting as this will help slow the development of resistance.'

Working with the Medicines for Malaria Venture and Takeda Pharmaceuticals, as well as research labs from across five continents, the team identified a series of compounds that affect the malaria parasite but not human cells. Further work allowed the team to discover that nucleoside sulfamates hijack protein synthesis enzymes to form covalent inhibitor-amino acid conjugates – a bit like super-gluing a key into a lock so that the lock no longer functions. 'Excitingly, we discovered a particular compound, ML901, in the Takeda compound library that targets a single plasmodium enzyme and was non-toxic to mammalian cells,' says Professor Tilley.

Next phase

After solving the protein's three-dimensional structure of the compound, the next phase was to test ML901 in a suite of malaria assays, which are designed to ensure that drug candidates meet the criteria for further development. The team showed that ML901 is active against all stages and strains of the malaria parasite tested. Importantly, ML901 exhibits rapid and prolonged activity that gives potent parasite killing in an animal model of human malaria meeting the criteria for fast and effective treatment of malaria patients. 'The team is now ready to pursue the development of ML901 as a new antimalarial drug candidate,' says Professor Tilley.

Only the beginning

'We believe our work here is just the beginning,' says Dr Larry Dick, an Honorary Fellow in the Department of Biochemistry and Pharmacology, and co-lead author. 'This opens up several important new drug discovery avenues to help address the deadly impact of malaria and other infectious diseases – particularly in developing nations. It could also be used to target other diseases like cancer, neurodegenerative disease, metabolic syndromes including, diabetes and autoimmune disorders.'

According to Professor Tilley, the next step for the team is to tweak the chemical structure to improve the drug-like properties to optimise the absorption and distribution of the compound in the body.

Source: University of Melbourne

Modelling systems for human biology

Organoid technology: new opportunities for drug discovery

Two-dimensional (2D) cultured cell lines and animal models have been the principal research tools for the past decade. 'However, a variety of biological processes unique to humans cannot be fully replicated in animal models or immortalized cell lines,' said Munir Al-Zeer from the Department of Applied Biochemistry at the Technical University of Berlin, Germany.

Since successfully isolating human embryonic stem cells (ESCs) and reprogramming human somatic cells into induced pluripotent stem cells (iPSCs), three-dimensional (3D) cell cultures have become very popular. Classed as one of these new structures, organoids can mimic stem cell niches more closely than 2D cell cultures, particularly gene and protein expression, metabolic function, and host-microbe interactions. 'Organoids are capable of self-renewal, self-organisation, and exhibit organ functionality. Biologists call them organ-like aggregate cell structures,' said Jürgen Knoblich, Scientific Director at the Institute of Molecular Biotechnology (IMBA) at the Austrian Academy of Sciences in Vienna.

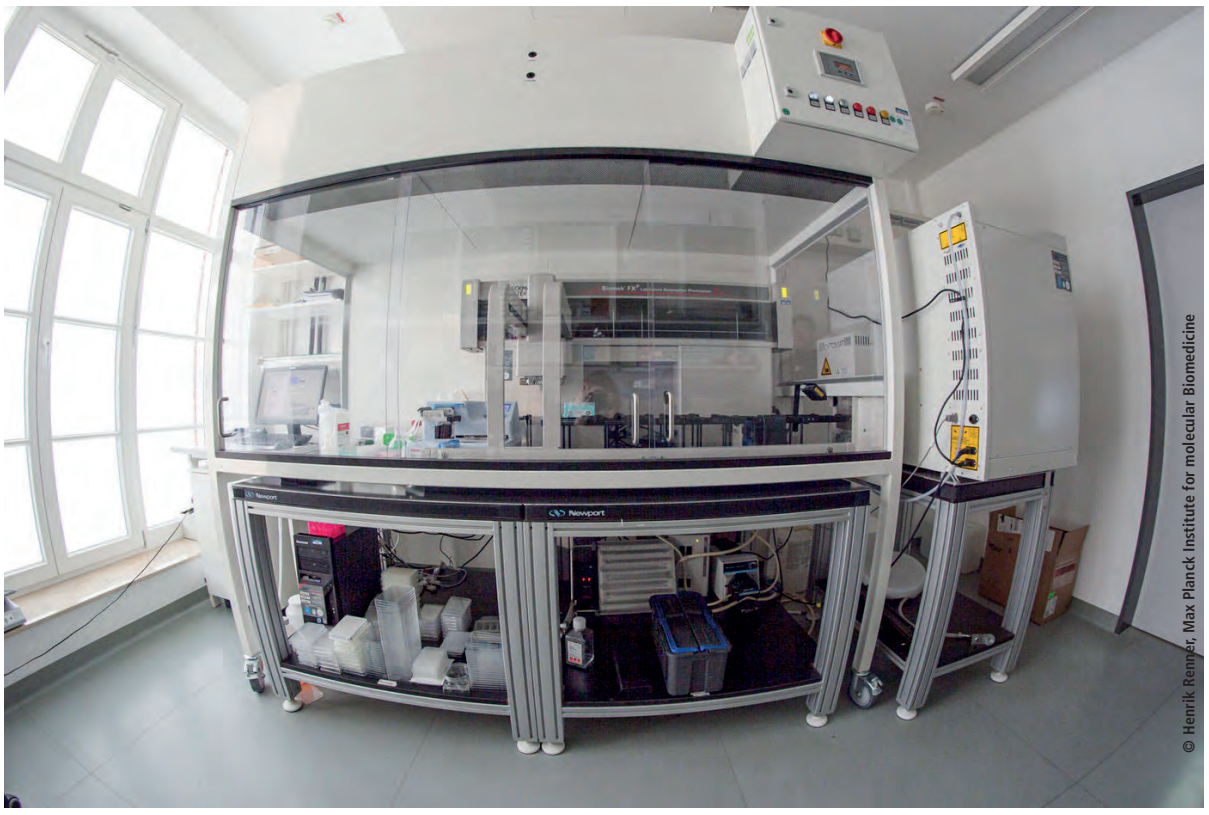
35 human organoids reported for 15 organs

Organoid culture allows specific cell types to be generated that were previously unachievable using 2D cultures. To date, a total of 35 human organoid systems have been reported associated with some fifteen organs from the brain to the bladder, including the retina, the thyroid gland, blood vessels, mammary glands, and the stomach. Consequently, pancreatic, liver, and cardiac organoids have been used for disease modelling, drug efficacy testing and toxicity analysis. Brain organoids are helpful for modelling various neuropsychiatric disorders and neurodegenerative brain conditions. One recent study from the Department of Human Biology at the University of Cape Town Faculty of Health Sciences in South Africa, published in Gene Therapy, has opened up progress in understanding autism spectrum disorders. Lung organoids have been developed from various cell types such as human pluripotent stem cells (PSCs) and alveolar epithelial progenitor cells. These organoids were developed either from PSCs, or adult stem cells (AdSC) and biobanks.

Infections, respiratory diseases, cystic fibrosis, and colorectal cancer

Following the development of human stem cell-based organoids, various human diseases have been modelled using these systems. 'Today, human brain organoids are mainly being used to successfully model human diseases such as microcephaly, a neurological disorder seen during the Zika virus outbreak,' said Jihoon Kim from the Institute of Molecular Biotechnology at the Austrian Academy of Sciences.

Parasitic diseases such as life-threatening cryptosporium diarrhoea and bacterial infections caused by Salmonella typhi and Clostridium difficile have been successfully modelled thanks to organoid systems.



The automated pipetting robots could produce large quantities of organoids

More recently in respiratory disease, lung organoids infected with SARS-CoV-2 were used to demonstrate that the expression of transmembrane serine protease 2 (TMPRSS2) is essential for priming the spike protein of angiotensin-converting enzyme 2 (ACE2) in coronavirus. 'The high-throughput screening of lung organoids has also enabled identification of drugs that inhibit the entry of various coronaviruses into host cells,' observed Yun Kee Jo, from the department of Biomedical Convergence Science & Technology, Kyungpook National University, Daegu, South Korea, in an article published recently in Materials Today Bio.

Resources for precision medicine

Human organoids are becoming important resources for precision medicine They can be useful for selecting an appropriate drug for patients with genetic disorders such as cystic fibrosis, a relatively common specific genetic disorder with approximately 90,000 sufferers worldwide. Organoids can also be used as in vitro cancer models, with high morphological and molecular similarity to their origin, that can be generated from a wide variety of tumours and normal tissue. They can be used as a promising preclinical model for gastrointestinal cancer, and particularly colorectal cancer.

The team from the DKFZ-Hector Cancer Institute at the University Medical Center Mannheim, Germany, collected data relating to around 5.5 million single organoids from 11 different colon cancer patients with more than 500 distinct small molecule perturbations.

Laboratory robots capable of generating up to 20,000 brain organoids a day

A team of scientists at the Max Planck Institute for Molecular Biomedicine in Münster, Germany, has succeeded in using human cells to produce midbrain organoids using a fully automated process. First, a strategy was devised that created mid-brain organoids from small molecule neural precursor cells which can generate all relevant mid-brain cells more quickly and with greater reproducibility than current methods. Henrik Renner's team there then demonstrated that their automated pipetting robots could produce large quantities of organoids. This fully automated high-throughput workflow for 3D-based chemical screening in human midbrain organoids allows scientists to generate, culture and test up to 20,000 brain organoids a day. This technology has been licensed to the American biotech firm StemoniX, which has developed iPSC-based 3D micro-organ tissue constructs, disease models and advanced analytical techniques to ensure that only the safest and most effective compounds progress through the discovery pipelines of their biopharma partners.

'3D organoids are likely to become an indispensable tool for biological research, drug discovery and drug screening within a few years,' said Agnieszka Zuchowska, Chair of Medical Biotechnology at the Warsaw University of Technology Faculty of Chemistry in Poland. New drug development is a long (15 years) and costly process. The average cost of each new drug launched onto the pharmaceutical market is over $1 billion. According to US-based Insight Partners, the market for organoids is projected to reach $3.43 billion globally by 2027. It is expected to grow at a CAGR of 22.1% over the next five years.

Some limitations still to overcome

Although organoids are robust research tools for the study of human development and disease, there are hurdles and limitations associated with using organ-like aggregate cell structures. First, culture techniques are not standardized, hence their heterogeneous nature. Second, the absence of blood vessels impedes the maturation and function of organoids. Lastly, the lack of a native micro-environment precludes studies concerning the interaction of stem cells with their niche or immune cells.

Challenges and limitations

While still in their infancy, organoids face many challenges. They merely imitate a small part of the human body, not the whole thing. Human organoids still lack communication with nearby organs or tissues and are limited to studying the reproduction of organ-specific or tissue-specific microphysiology in comparison to 2D culture and animal models. 'There is a long way to go before implementing the first human multiorganoid model in vitro', Zuchowska concluded.

Report: Bernard Banga

LATEST HEADLINE NEWS

James Hickmann

The FDA announced, that this summer, it is allowed an existing drug to be repurposed based on efficacy data generated using these advanced cell models, or organoids. This represents a true breakthrough in validating the utility of these microphysiological systems and an important advance in finding treatments for rare diseases.

Orlando, Florida-based Hesperos Inc. showed that exposing its model of peripheral motor neuron conduction velocity to serum from chronic inflammatory demyelinating polyneuropathy (CIDP) patients led to increased antibody binding and activation of the complement cascade. A rare autoimmune disease that causes muscle weakness and impairs walking and hand function. CIDP is characterized by immune system hyperactivity sparked by auto antibody production, leading to peripheral nerve demyelination and reduction in nerve conduction velocity.

The data generated provided the rationale for testing Sanofi SA's sutimlimab, a humanized monoclonal antibody used to target C1s in treating CIDP. The product gained US FDA approval under the brand name Enjaymo in February 2022 for the treatment of cold agglutinin disease, in which activation of the complement cascade leads the immune system to destroy healthy red blood cells.

Hesperos aims to replicate that success in other rare diseases for which there are no animal models. 'There are 7,000 rare diseases and only 400 research programs looking at them, as there are no animal models. In some cases, these systems fill a void where animal models don't exist,' said James Hickman, CEO of Hesperos.

Prediction for breast, ovarian, cervical, and endometrial carcinoma

New test detects four women's cancers

What if a test analysing cervical cells from a gynaecological swab could be used to detect four different female cancers at an early stage and also predict cancer risk over a healthy woman's lifetime? Researchers at the European Translational Oncology Prevention and Screening (EUTOPS) Institute in Innsbruck, Austria, are developing tests to do just that for breast, ovarian, cervical, and endometrial cancer detection.

These four cancers account for more than 50% of all cancers in women in Europe. Globally, the World Health Organization's International Agency for Research on Cancer reports that breast cancer was the world's leading cause of cancer incidence in 2020, with an estimated 2.3 million new cases and 685,000 deaths.

It also estimated 604,000 new cases of cervical cancer, 417,000 of endometrial cancer, and 314,000 of ovarian cancer.

Asymptomatic and deadly

Ovarian cancer is especially deadly because it tends to be asymptomatic until reaching an advanced stage, when the cancer has spread within the abdominal cavity or beyond. Over half of ovarian cancer patients die within five years after their initial diagnosis.

Once fully developed and clinically approved, the Women's risk IDentification for Ovarian Cancer Test (WID-OC-Test) has the potential to change these sobering statistics by using DNA methylation analysis from a single cervical smear sample taken during a routine screening.

Prof Dr Martin Widschwendter, principal investigator and director of the EUTOPS Institute, says: 'The identity of a cell is defined by its epigenome, which consists of thousands of tags on the DNA called DNA methylation.'

These tags integrate all factors a cell has been exposed to over a lifetime, leaving a unique "footprint" on the DNA. Examples are hormonal exposures due to childbirth and environmental factors including diet and exercise, the expert explains. 'Changes in the epigenome can increase or reduce the risk of developing cancer. The WID-Test analyses DNA methylation footprints, which can indicate increased cancer risk during a women's lifetime.'

Martin Widschwendter

Prof Dr Martin Widschwendter is Director of the EUTOPS Institute and Professor for Cancer Prevention and Screening at the Leopold-Franzens-University of Innsbruck. He is a Consultant Gynaecological Oncology Surgeon and also holds the position of Professor in Women's Cancer at University College London. In July 2020, he was conferred a Guest Professorship at the Karolinska Institutet in Stockholm. Dr Widschwendter has spent decades researching the role of early detection, risk prediction and prevention of breast and gynaecological cancers.

The researchers explain in detail how they developed and validated each test in articles published in Nature Communications. Samples were assessed from over 3,000 women with and without breast/ovarian cancer from 15 centres in Europe.

They obtained samples from women over the age of 18 years and evaluated the performance of the WID-Test in different age groups, including pre- and post-menopausal women. Their studies are evaluating an individual's risk for more than one cancer by assessing several different epigenetic footprints in a single cervical screening sample.

Results better then estimated

'The results were much better than we hoped for,' said Widschwendter. 'The WID-OC methylation test allowed us to identify 71.4% of women under 50 years of age and 54.5% of women over 50 with ovarian cancers with 75% specificity.

'The fact that the test is not driven by the presence of tumour DNA in the sample suggests that the WID-OC test would have identified women well in advance of their diagnosis.'

Identification of 76.6% of women in the highest risk group

Samples were evaluated with the WID-BC test and with a current method for determining breast cancer risk that combines information on genetic variants. The WID test identified 76.6% of women in the highest risk group, compared with 47.5% using the current method.

Prof Dr Widschwendter tells European Hospital that 'the next research steps will be to demonstrate that the WID-OC and WID-BC tests are able to identify healthy women at risk of developing ovarian or breast cancer in future years. The only way to achieve this is to collect thousands of cervical samples from an entire population, test them, and assign a risk score.

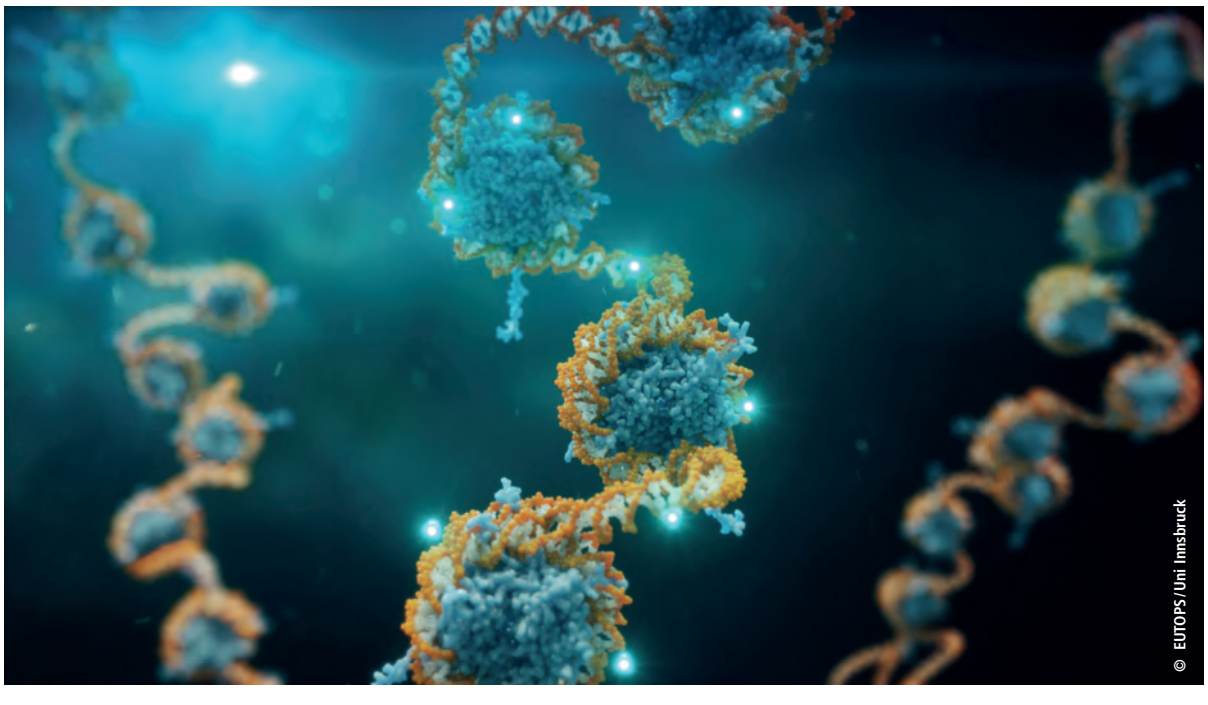
'After waiting for a number of years to identify women in the study cohort who had developed ovarian or breast cancer, we would analyse samples of these women and a control group of samples of healthy women to determine if our test could have predicted which women developed cancer.' Currently, the team is working on the logistics and funding for this large-scale initiative, he reports.

Identifying risk of cancer

'Our goal is to identify women at risk for cancer independently of a BRCA mutation, so that they can take preventative measures potentially decades before they would develop cancer. This could include lifestyle changes as well as regularly scheduled screening tests and preventative medication like tamoxifen for women with breast cancer risk,' Widschwendter adds. 'We also will be conducting research to determine if the WID-Test can be used to monitor cancer risk over time.'

The vision of the EUTOPS Institute is to integrate cutting-edge research in systems biology and oncology to enable real-world implementation of the concepts of P4 medicine (predictive, preventive, personalized, and participatory) and drastically reduce cancer mortality. It was established in 2020 at the Leopold-Franzens-University of Innsbruck.

Report: Cynthia E. Keen



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Visualisation of DNA methylation: Markers on DNA can increase or decrease certain expressions in the cell and leave a corresponding signature on the DNA.

Outbreak prevention and management efforts

Infectious diseases: new challenges for EU monitoring

Avian influenza virus A (H5N1) and A (H7N9), Middle East respiratory syndrome, coronavirus (MERS-CoV and SARS-CoV) and monkeypox virus: outbreaks of infectious diseases are getting more common in Europe. 'Statistically, it is reckoned that nearly 60% of pathogens affecting humans are of animal origin,' said Hadi Kazemi-Arpanahi, from the Department of Health Information Technology at the Abadan University of Medical Sciences in Iran. These emerging diseases threaten global security and challenge traditional surveillance strategies in the EU.


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BIOSECURITY EVENTS IN THE PAST CENTURY

1918: Spanish flu pandemic leading to several million deaths.

1957 and 1968: Asian flu and Hong Kong flu causing about 1 million and 650k deaths respectively

1980: AIDS discovered in human being

2001: Anthrax attack in US

2003: SARS outbreak in China

2009: Swine flu (H1N1) outbreak

2011: Bird flu (H5N1) increased in virulence and transmissibility

2013: MERS outbreak in Middle East, Avian flu (H7N9) in China

2014: Ebola re-emergence in Africa

2020: The Covid-19 pandemic spreads around the world. As of 10 July 2022, just under 586 million confirmed cases and over 6.4 million deaths have been reported globally.

2022: Monkeypox outbreak – geographic areas where monkeypox is not endemic have reported outbreaks of the viral disease. 11,500 cases confirmed across 60 countries.

In 2005, the EU established the European Centre for Disease Control and Prevention (ECDC), to help the 27 member states and two of the three remaining European Economic Area countries (Iceland and Norway) develop surveillance systems for early warning of infectious disease outbreaks. 'This surveillance covers 46 diseases, including severe acute respiratory syndrome, West Nile fever and avian influenza,' said Dr Andrea Ammon, director of the ECDC. The surveillance system is integrated within the national crisis prevention system to support early evaluation and decision-making in response to potential biosecurity threats.

New online portal launched by ECDC

Last year, the ECDC launched EpiPulse. This online European surveillance portal for infectious disease brings together several surveillance systems that were previously independent, such as the highly flexible metadata-driven European Surveillance System (TESSy), the five Epidemic Intelligence Information System (EPIS) platforms and the Threat Tracking Tool (TTT)). This new platform facilitates collection, analysis, and dissemination of indicator- and event-based surveillance data regarding infectious diseases and associated health issues, including global epidemic intelligence, whole-genome sequencing, and health determinants. 'The platform facilitates interdisciplinary collaboration and connects users from different sectors under a One-Health approach,' said Ammon.

The ongoing Covid-19 pandemic, responsible for more than one million deaths in EU countries, 'convinced us of the necessity of ensuring that real capacity is available in the EU to detect possible new variants sufficiently early as well as to monitor them,' the ECDC director said. The struggle is constantly starting over, with the continuous emergence of new mutants/variants such as alpha, beta, gamma, omicron and so on. Traditional surveillance is based on case reports. Syndrome-based surveillance systems actively use data from emergency departments, intensive care units and hospital admissions. Event-based internet surveillance systems are expected to be deployed on a large scale, because effective surveillance will have to use multiple data collected and integrated from several sources. This new approach requires integrating multiple technologies and data resources from various fields including social media, laboratory detection, outpatient or emergency treatment, diagnosis, over-the counter drug sales, insurance claims and even absenteeism. 'The accuracy and timeliness of surveillance can be improved by electronic systems and internet connectivity which could benefit the reach, visualization, and analysis of various data,' said Muyang Yan from the First Medical Center of PLA General Hospital in Beijing. The Covid-19 pandemic significantly accelerated the application of big data in emerging infectious diseases surveillance in order to sooner detect, better predict and better control infectious diseases in the EU and elsewhere. However, Big data is not omnipotent. It also has to deal with the continuous development of "hard" technologies used to diagnosis infectious diseases. Consequently, the rapid development of molecular diagnostics, especially next-generation sequencing techniques, are going to help determine whether an emerging infectious disease occurs naturally or due to genetically modified micro-organisms. Novel biosensors will be able to automatically identify viral, bacterial, and fungal pathogens from patients within a few hours. Novel surveillance systems are improving real-time surveillance capabilities by combining automatic detection techniques with modern networking and communication technologies.

In future, the EU will be fighting on two main fronts: emerging and re-emerging infectious diseases (EIDs), and climate change. 'In recent years, we have seen transmission of traditionally "tropical" diseases in continental Europe: Chikungunya fever in Italy, large outbreaks of West Nile fever in Greece and Romania, and the first local transmission of dengue fever in both France and Croatia,' said Jan Semenza, PhD, ECDC Head of the Health Determinants Programme. Major EID drivers that could threaten control efforts in Europe include:

- environmental change (climate, travel, migration, global trade)
- social and demographic drivers (aging population, social inequality, lifestyles)
- public health (antimicrobial resistance, healthcare capacity, animal health, food safety)

'Climate change is expected to aggravate existing local vulnerabilities by interacting with a complex web of these drivers,' said Semenza. For instance, increasing global trade and travel, in combination with climate change, are predicted to facilitate the arrival, establishment and dispersal of new pathogens, disease vectors and reservoir species. The current acceleration of climate change is creating a "new deal" in the surveillance of infectious diseases in Europe.

Report: Bernard Banga

Covid-19, COPD and cystic fibrosis

Transplant surgery: last hope for patients with advanced lung diseases

Despite treatment, chronic lung diseases such as COPD or cystic fibrosis can become so severe that a lung transplant is necessary. Dr Urte Sommerwerck explains which patients might be considered for transplantation and why follow-up is as important and the surgery itself.

EH: When is a lung transplant necessary?
Dr Urte Sommerwerck: 'For a long time lung transplantation – LTX for short – was considered the last resort when all other treatment options had been used and the patient was at risk of dying from the lung disease within the next two years.

This principle was extended to include a high likelihood of 90-day survival and of five-year survival with mortality due to accompanying diseases.'

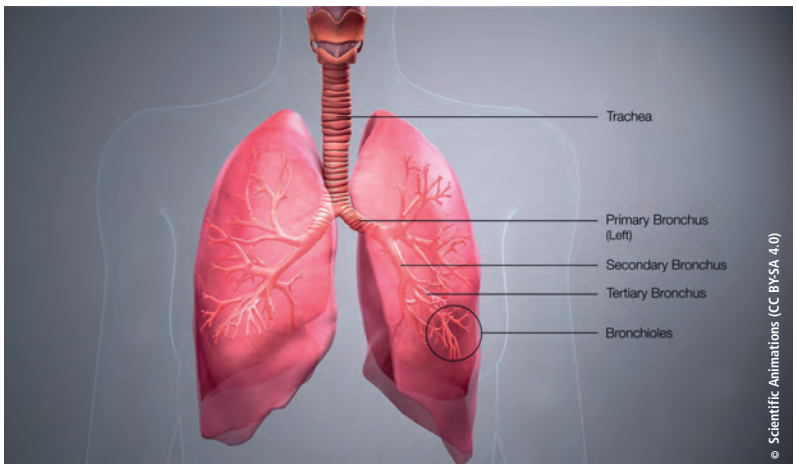
Which requirements does a donor organ have to fulfil?
'The lung has permanent contact to the environment and can be injured, for example due to infections or ventilation. Thus it is an organ that is rarely transplanted. In addition, not every lung of the very few that are donated is suitable for transplantation.

Luckily, modern normothermic ex-vivo lung perfusion (EVLP) allows us to better perfuse the lungs with an optimised electrolyte solution and thus improve the quality of the donor organ. This process has greatly expanded the pool of suitable organs and is the main reason why the number of lung transplants has been stable for the past couple of years despite organ donation scandals and the Corona pandemic. In Germany, an average of 300 lungs were translated per year over the past decade – which is still an extremely low number compared to other countries.'

How is a patient placed on the waiting list?
'In Germany, in order to be placed on the waiting list the patient has to present in one of the 16 lung transplant centres in the country. A 3-person board with the transplant pulmonologist, the surgeon and a further physician decide whether the patient will be placed on that particular centre's waiting list. If a patient is refused, they can approach a different centre.

If the patient is accepted, they are assigned a so-called Lung Allocation Score (LAS) between 0 and 100. This score takes into account the severity of the disease and the outcome prognosis. If the score is between 40 and 60 the transplantation will be performed within the next few months. A lower score means longer waiting times. Is the score above 60, the patients are often severely ill and already in intensive care – which diminishes the survival prognosis. These ethical considerations also apply to extracorporeal membrane oxygenation (ECMO). Patients who have been on a heart-lung-machine for a long time frequently don't have a good prognosis; experience shows that positive transplantation outcomes are rare in these cases. Most patients are severely ill and suffer organ failure; they were not previously trained and screened in the transplantation programme. In addition, it can happen that information on previous diseases is incomplete.'

These patients are too ill?
'Exactly. Exclusion criteria for organ transplant surgery can be on both ends of the scale: the patient status might be too good or already too poor for transplantation.



The ideal patient for transplantation, so to speak, is severely ill but still fulfils the strict criteria, and they have a post-surgery survival prognosis of at least five years. The Covid-19 pandemic has further limited these considerations since all of a sudden many healthy patients suffered from total lung failure and had to be moved to ECMO right away. Currently, it is being discussed whether these patients should also receive a transplant if there is no other regeneration option. But Covid is an infection and at this point we don't know yet whether the transplanted organ will also be affected.'

Who decides which patient will receive a donor organ?
'The allocation of donor organs is exclusively based on medical and ethical considerations. A potential donor organ is registered with the German Foundation for Organ Transplantation, DSO. Eurotransplant, the organisational centre for the allocation of donor organs in eight affiliated European countries, is responsible for the actual allocation. It ensures that each organ is transplanted where it is most urgently needed. Unfortunately, Germany has a very small pool of donor organs. From a patient's point of view it was therefore incomprehensible that in 2020, the German Parliament did not adopt the so-called double refusal solution. That approach considers every citizen a potential organ and tissue donor who did not explicitly refuse to be a donor during their life or whose closest kin do not refuse an organ donation.

This approach is the current legal situation for example in Spain where you have 34 organ donors per 1 million inhabitants. In Germany, there are only 11.2 donors.

In the end, the German Parliament adopted the so-called extended consent solution which means organ and tissue removal is only allowed if the donor during their life or their next of kin consented.'

What is the survival rate after a lung transplant and which complications might occur?
'Obviously, the prognosis depends on the underlying disease. Nevertheless, transplantation follow-up is very important since the lung is an organ in constant communication with the environment: with each inhale, viruses or bacteria can enter the body. Thus, from the very first day the patient body will try to stave off complications. Good chances for recovery require close cooperation between the transplant pulmonologist and the surgeon.

The first few days post transplantation will be shaped by unstable blood pressure, hyperacute rejection reactions and intensive care, including ventilation.

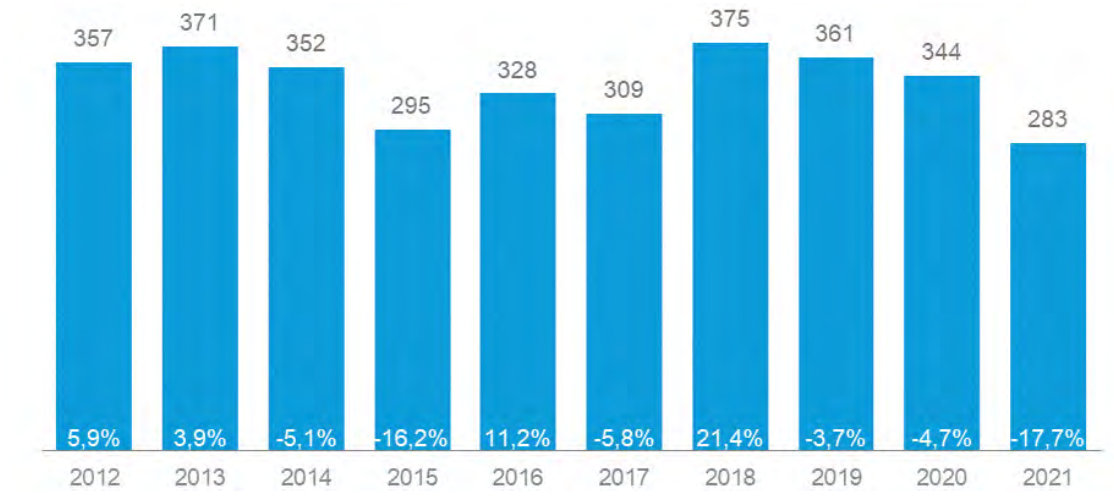
When the patients have survived the first few acute weeks and have been weaned off the ventilator so they can breathe by themselves, the next major challenge follows: in the first year post surgery, the patients are on high doses of immunosuppressive medication in order to avoid rejection of the transplant. That means the body's own immune system is suppressed and the stronger the immunosuppression the higher the probability of an infection. When the patient has survived the first year after the transplantation, immunosuppression will be significantly reduced. Now long-term rather than acute problems need to be managed properly. While the infection risk is sinking, the risk of acute and chronic rejection reactions and side effects of the immunosuppression remain. The immunosuppressive medications are incredibly toxic and can injure any organ. Renal insufficiency or malignant tumours are possible side effects which can appear years after the transplantation.'

What are the specific challenges caused by Covid-19?
'For the patients corona is obviously a particularly difficult challenge since they are high-risk patients. Some of them don't react to the vaccination at all because they don't have the necessary antibodies as the immune reaction is made impossible by the immunosuppressive regimen. Moreover, the patients lose years of their life due to corona. Unlike heart or kidneys, transplanted lungs have a limited life time. Patients gain five or six years with a lung transplant and now, due to the Covid pandemic, they can't leave the house for more than two of those years.'

Report: Sascha Keutel

Urte Sommerwerck

Dr Urte Sommerwerck is Medical Director of the Department of Pulmonology, Allergology, Sleep and Ventilation Medicine at the Augustinerinnen Hospital in Cologne, Germany. The former transplant pulmonologist at University Hospital Essen, is an expert for lung transplantation with the audit committee of the German Medical Association.



Transplanted lungs in Germany. Percentage change compared to the previous year

Keratoplasty

AI for an eye: Performance of corneal

Many consider our eyes to be the windows to the soul. Yet the cornea, the panes of these windows, sometimes need significant repair. Friso Heslinga, PhD, created artificial intelligence models to support surgeons in one of the oldest and most common transplantation procedures.

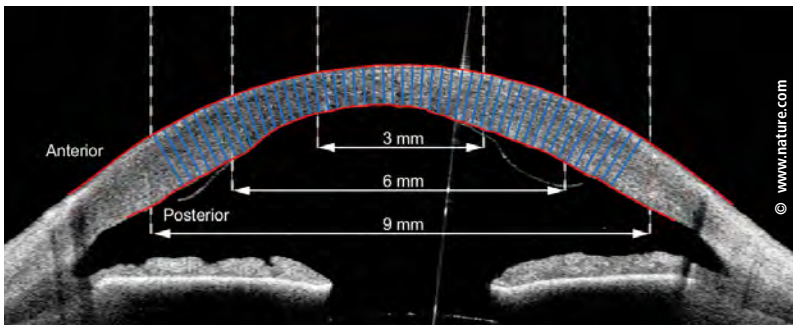
Our eye has several layers. The cornea is the transparent, dome-shaped outer layer that helps focus light, so we can see clearly. The light passes through the cornea and is then focused by the lens onto the retina, where it interacts with photoreceptor cells to generate signals for the brain to process. A damaged or diseased cornea can become less transparent, which can prevent light reaching the retina and cause the transmitted image to be distorted or unclear.
When this happens, the patient might need corneal transplant surgery, in which the surgeon removes all or part of the damaged cornea and replaces it with a healthy layer of tissue. The type of keratoplasty, or corneal graft transplantation, depends on which part is damaged or how much of the cornea needs replacing. 'Over the years, corneal transplantation surgery has improved a lot. Surgeons started by replacing the whole layer. Now, it only comprises the endothelial cells. For the cornea it's only a monolayer, a single layer of cells,' Friso Heslinga, from the Eindhoven University of Technology, said. 'It's an immaculate procedure. They scrape it away from the donor, roll it up, make a small hole in the patient's cornea.
Then they put the roll through that hole and roll it out again and use a small bubble, e.g., air, to push it on the cornea.'

Deep learning research

Heslinga and his collaborators did four projects on the corneal transplantation surgery. First, they developed an AI model to determine intraoperatively whether or not the donor graft is orientated correctly.
'An expert can look at the images and figure it out, but it takes time. And it's not that easy,' the expert said. 'We used intraoperative optical coherence tomography (OCT) imaging to take images intra-operatively. So, the quality is very often suboptimal. It's very hard to see the graft, very often you see only part of it,' he said. With collaborators from the ophthalmology department at University Medical Center (UMC) Utrecht, Heslinga trained an AI segmentation model to automatically assess the orientation of the new layer of tissue. This is important because if it is upside-down, then it cannot be attached to the existing cornea.

Two post-operation projects

Furthermore, they did two post-operative projects: first, to assess the level of attachment of the graft after transplantation surgery. 'We collaborated with corneal specialists from Copenhagen to design a method that finds any spots where the donor tissue is detaching from the underlying tissue.'
For the second post-operation project, Heslinga and his collaborators developed AI models, which were trained using supervised deep learning, to automatically measure corneal thickness at every point in the eye and construct a detailed thickness map. Abnormal corneal thickness is linked to various corneal disorders. 'Corneal thickness is something you could measure by hand; you could draw the lines on the monitor. You still would need a software to do a thickness profile. Again, that takes time doctors rarely have in clinical practice. That is where the AI models come in: to save time,' he said.
For the fourth project, Heslinga developed a model for assessing specular microscopy images. Looking at the individual cells, the technique gives the physician an idea about the state of the cornea. When they zoom in, they can see the number of cells in a square millimetre or differences in cell size. Similar to the corneal thickness maps, these results can then be provided to an ophthalmologist to establish the success of the transplantation procedure and help determine if further treatment is needed.
'For an assessment of these types of images, much depends on the experience of the surgeon. There is quite some information being lost, and that's the part where we think our models will help: by bringing this extra information, we can do measurements and relate these measurements to outcome,' Heslinga is convinced.



Optical Coherence Tomography (OCT) cross-sectional image of the front part of the eye. Visible are the cornea and anterior chamber. Some non-attached parts of the corneal donor tissue are also visible, floating in the anterior chamber (just below the cornea). The red lines indicate the borders of the cornea. The blue lines indicate how the corneal thickness is measured.

Alternative to open surgical procedures gains traction

The future of minimally invasive interventions

In the future, many types of open surgeries will be replaced with minimally invasive interventions, predicts Kevin Cleary, PhD, engineering lead at the Sheikh Zayed Institute for Pediatric Surgical Innovation at Children's National Hospital, Washington, D.C.

Surgeons and interventional radiologists will be able to plan an intervention, perform it, and immediately verify that it achieved desired treatment goals, he told attendees at the International Conference on Computer-Assisted Radiology and Surgery (CARS2022) in Tokyo.

Minimally invasive surgical techniques limit the size of incisions required, lower associated pain and risk of infection, and reduce the time for the wound to heal. Minimally invasive interventions include non-surgical procedures, such as high-intensity focused ultrasound (HIFU), which is used to destroy targeted tissue using heat from sound waves instead of surgical resection.

At Children's National Hospital, HIFU is used to treat osteoid osteomas, painful benign bone tumours. Medical robotics technology was first implemented in 1985, for neurosurgery drilling. Dr Cleary explained that the three classes of medical robots used today are:

- tele-operated, a "master-slave" configuration in which a surgeon sits at a master console and controls a slave robot (e.g., the DaVinci Surgical System);
- cooperative, a robotic system that works synergistically with a surgeon (e.g., Mako SmartRobotics, Stryker) to constrain the cutting plane during knee osteotomy); and
- preprogrammed, a robotic system that executes a pre-programmed plan based on segmentation of medical images (e.g., Cyberknife System, Accuray, for stereotactic radiosurgery).

Image-guided navigation systems also enable minimally invasive interventions. These systems consist of a computer for control and display, a localizer for electromagnetic tracking of instruments, and software for image processing.

Robotics and MRI – a winning combination

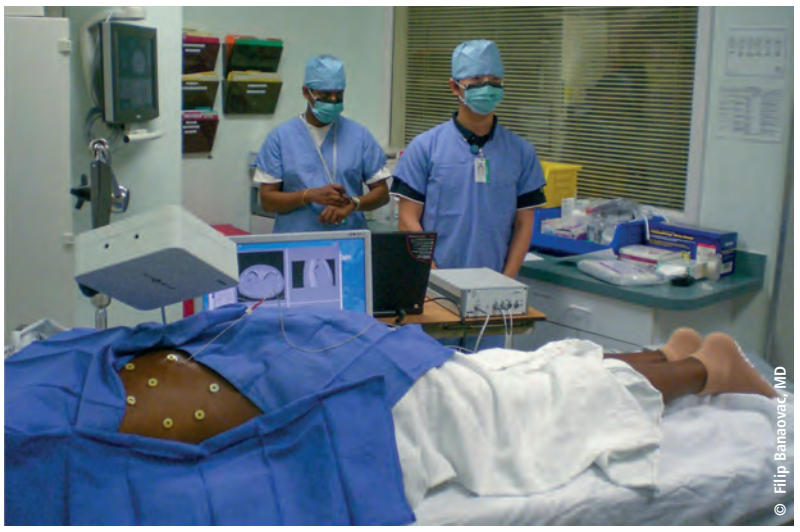
MRI compatible robotics for in-bore interventions are currently under development. These include systems for shoulder arthrography, back pain diagnosis, long bone biopsy, and intracerebral haemorrhage. 'People question why an expensive MRI scanner would be used for minimally invasive interventions, but the images provide exquisite soft tissue discrimination, MRI does not expose a patient to radiation, and other functionality such as monitoring of thermal treatment can be provided,' said Cleary. 'MRI compatible robotics are not hindered by difficult access in a closed-bore MRI, and can enable in-bore interventions that a surgeon logistically would not be able to do. Robots can provide a steady guide for instrumentation, facilitated by real-time MRI guidance.'

'Many challenges need to be overcome,' he added. 'The development of dedicated high quality robotic systems requires the synthesis of mechanical design, electronics, computer science, and control. The strong static and switching magnetic fields and radio frequency pulses used in MRI create a safety hazard and compatibility issues. These exclude the use of conventional robotic technology. It will require clinicians and equipment designers to work together.'

'Medical robotics has the potential to enable new minimally invasive interventions by providing a surgeon the ability to access the anatomy through smaller incisions and in a more dexterous manner than can be done with conventional laparoscopic instruments. Surgical technology is rapidly improving, driven in part by advances in the consumer market, such as high-resolution displays, the rise of artificial intelligence, and new user interfaces,' he said. 'The challenge in integrating consumer-driven advances in an operating room suite includes integration issues that may arise when combining products from different vendors. The regulatory environment requires each individual device to be approved. If devices are to be used as part of an integrated system, the system needs to be evaluated and approved to ensure that it is safe to combine devices. The advantage to the surgeon of such a systems approach would be that a single user interface might be created to operate multiple different devices which would be more user friendly.

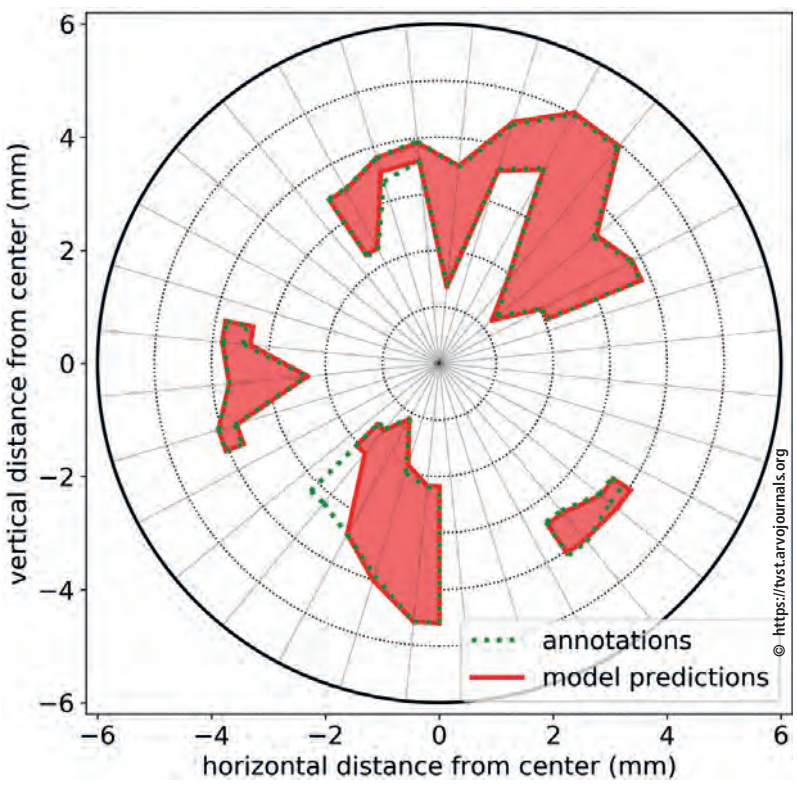
'CARS can help make this happen, because it is focused on bringing engineers, scientists, and clinicians together to develop the next generation of medical technology. This annual conference promotes open exchange and sharing of information. It is continuously evolving to reflect the latest developments in the field,' concluded Cleary.

Report: Cynthia E. Keen



Clinical trial of electromagnetically tracked lung biopsy

transplantation surgery



Results of the deep learning model for measuring the detachment of the donor tissue. The annotations (green dotted line) are made by a cornea specialist and the red is the output of the model.

Currently, the AI models are only used for research. They still need extensive clinical testing and validation before physicians can use them in clinical settings. 'We've shown that the systems work in a specific case using data from the hospital in Denmark. However, showing that the models work for one data set isn't enough. We want to show that it works for different data sets, or patient groups,' Heslinga said.

Collaborations needed

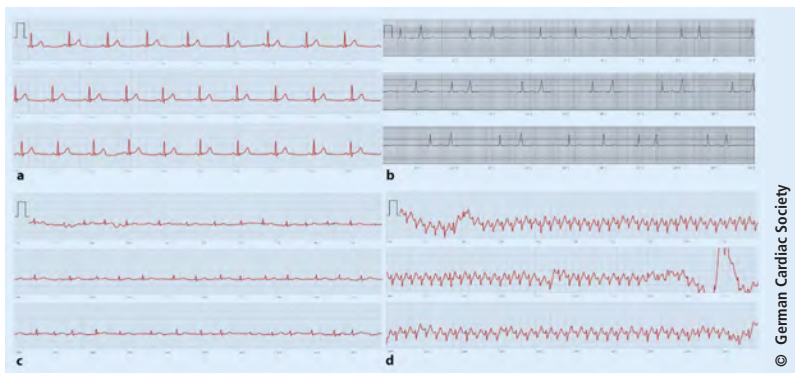
He concluded: 'For good implementation, we need collaborations with the manufacturer of the OCT scanners and validate for all patients using that scanner. That way, we could work on all the images that type of scanner gets from patient groups with different demographics. That would make sure that everything we provide is useful for the patients.'

Report: Sascha Keutel

Algorithms support diagnostics

AI in cardiology: so much is feasible – but is everything useful?

It might sound like science fiction but it is reality in cardiology: with the help of artificial intelligence (AI) physicians can recognize from a patient's headshot whether the person is suffering from coronary artery disease and is therefore at risk of myocardial infarction. But is that knowledge really useful? Professor Dr David Duncker calls for a differentiated and careful assessment of the possibilities and risks associated with AI. He thus recommends the careful selection of the target group in order to recognize at-risk patients early.



ECG curves recorded on Smartwatches: a Sinus rhythm, Apple Watch (Apple, Cupertino, CA, USA). b Sinus rhythm with ventricular extrasystoles, ScanWatch (Withings, Issy-les-Moulineaux, France). c Atrial fibrillation, Apple Watch. d Regular narrow-complex tachycardia, Apple Watch

AI, he says, can help analyse larger data volumes but he cautions that 'An algorithm is always only as good as the person who trained it. Biases and wrong decisions cannot be avoided. This ethical dimension has to be taken into consideration by all means.

'Atrial fibrillation is the most frequent type of arrhythmia,' says Professor Duncker, Head of Rhythmology and Electrophysiology at the Department of Cardiology and Angiology at Hannover Medical School, and adds that "it often causes sequelae such as strokes that can be avoided with early prophylaxis.' He does acknowledge though the potential of AI, particularly when human resources are scarce and patient numbers increase. Algorithms can pre-scan huge data volumes in the background so the physicians have to deal only with suspicious findings. But proper selection of the target group is crucial. 'Today, we can record ECGs with smartwatches and specifically look for arrhythmia,' Professor Duncker explains and adds that 'the users of such smartwatches however, are usually much younger than the group at risk for arrhythmia. Therefore we have to make sure the algorithms are applied to the correct target population.'

Screening recommendations for arrhythmia

Recently, the European Heart Rhythm Association (EHRA) issued new recommendations, co-authored by Professor Duncker, regarding the use of digital devices for arrhythmia screening. Systematic screening is recommended for persons over 75 years and those above 65 years who are at risk. Persons over 75 years without risk factors and those younger than 65 years with risk factors should be screened during their next doctor's appointment. Germany is facing the problem that there are too many people in that age bracket, Professor Duncker points out: 'The physicians simply don't have the resources to review all ECGs. AI would have to preselect a smaller group that needs attention. Specialized apps on the smartphone would be a good alternative to smartwatches for that target group.'

Therapy differences caused by incorrectly trained AI

Professor Duncker, however, underlines that AI does not necessarily make better decisions than human beings: 'Humans make mistakes and are biased. Studies have shown that not every patient receives equal treatment. Factors such as gender, ethnic background or religion play a role. When biases enter AI unchecked, differences in treatment will result which, in the worst case, may harm the patient. This is something we have to be aware of. We have to try to avoid training the algorithms incorrectly.'

Personalised therapies with the help of AI

In a few years, the cardiologist hopes, AI will be able to design personalised therapies, e.g. by calculating the effects of medication and optimally planning surgical interventions. But Professor Duncker warns that 'we should not lower our scientific standards. New pharmaceuticals that are being tested must not be administered to each and every patient. We have to continue scientific studies. These standards also have to apply to AI and randomised studies have to be conducted to assess the effects.'

Report: Sonja Buske

David Duncker

Professor Dr David Duncker is Director of the Hannover Heart Rhythm Centre and Managing Senior Consultant and Head of Rhythmology and Electrophysiology at the Department of Cardiology and Angiology at Hannover Medical School. He is a member of the EHRA board and chair of the EHRA committee for digital communication.

Detecting heart diseases

AI supported vector cardiography to enhance

Cardisiography is a precise screening method for detecting structural, rhythmical, or vascular heart disease. Neuronal networks assess and analyse vector cardiography data. The attending physician receives a report that describes a patient's individual risk. Cardisiography is a decision support tool that guides the targeted follow up for the patient. Meik Baumeister, CEO of Cardisio, gave insight into the development and the operating principle of the method.

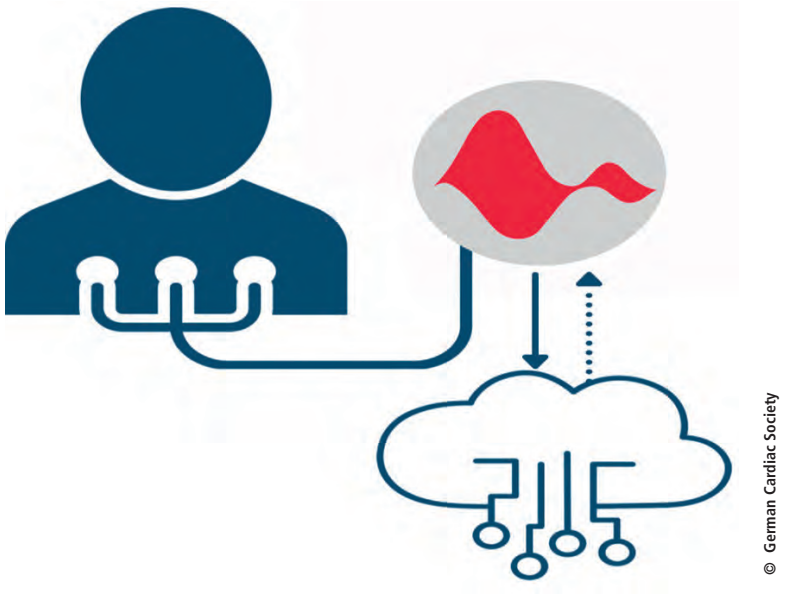
EH: What is the idea behind Cardisiography?
Baumeister: 'In the summer of 2015, we had the idea to breathe new life into vector cardiography and find a way to apply it in clinical practice. The vector cardiography is a 70-year-old idea, with a lot of research on the technique showing great potential. Put simply, the method aims to map the heart and the propagation of the electrical excitation in multiple dimensions. However, interpretation of the multidimensional mapping of the heart is very complex. The mathematical analysis is barely possible with the human brain. Now, in the age of super computers and artificial intelligence (AI), we got a new chance to revive the dormant method using vector cardiography. Cardisiography unites neuronal networks with vector cardiography.'

Many parameters are calculated and analysed

How do vector cardiography and AI work together?
'We measure normal medical parameters, such as the spacing or width of the QRS complexes. The two-dimensional ECG contains information about three angles. The three-dimensional VCG has information about four angles, a volume, and the sheathing surface of the measured loop. All these parameters are calculated and then analysed by the neuronal network. The calculation is followed by statistical evaluation, correlations are ruled out and significant results are identified. We use a big dataset to train the neural network in a supervised learning approach. Each patient is assigned their own set of parameters, which are compared to match the trained results for healthy or sick patients. This way, we can always reconstruct why the algorithm decided the way it did.'

What was crucial for the development?
'Good data. We, as computer scientists, love code, math, and statistics, but without medical know how and good data we are lost. We needed time to get the data and to interpret the data successfully. We also needed – and still need – innovative cardiologists and open-minded medical doctors who declare their interest in the method and the willingness to use it. The cardiologists need to show that they trust the Cardisiography reports.'

How does Cardisiography work?
'Three electrodes are applied to the front of a patient's chest and anoth-



Functional principle of cardisiography: measurement on the patient, data forwarding to the cloud, evaluation of the data by the algorithm in the cloud.

Heart failure with preserved ejection fraction

HFpEF poses increasing burden on health services

Heart specialists are warning of the challenge heart failure with preserved ejection fraction (HFpEF) is posing to health services. With the life expectancy of populations improving, experts believe the rising diagnosis and prevalence of patients with HFpEF will have a significant impact on healthcare services going forward.

Professor Roy Gardner, Chair of the British Society for Heart Failure (BSH) – which has launched the effort to increase awareness of HFpEF – said the condition accounts for an increasing proportion of heart failure-related hospitalisations.

'HFpEF has always been the troublesome aspect of heart failure to manage – difficult to diagnose and even more difficult to treat – but cases are increasingly being recognised,' he added.

Raise awareness, improve diagnosis and care

The BSH has set out a position statement on HFpEF which highlights the challenges HFpEF presents to patients, healthcare services, and population health, and aims to promote discussion regarding measures that can support effective HFpEF diagnosis and care. Drawn up by the BSH Working Group on HFpEF, the statement outlines prevalence, clinical presentation, diagnosis (including recognition of cardiac amyloidosis, which closely resembles HFpEF), treatment, organisation of care, and also looks to the future. In the UK, around one million people are affected by HF, with a further 200,000 newly diagnosed each year and similar prevalence across Europe and globally.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Heart failure with preserved ejection fraction can be diagnosed with echocardiography.

Increasing caseload predicted

With chronic heart failure, the heart is unable to pump blood around the body properly. This usually occurs because the heart has become too weak or stiff. Ejection fraction – the percentage of the blood within the ventricles that is ejected during the cardiac cycle – is one of the most commonly used measurements of heart function. When the pumping action of the heart is obviously reduced, it is referred to as heart failure with reduced ejection fraction (HFrEF); when it is stiff and does not relax properly, it is referred to as HFpEF.

HF specialist and BSH HFpEF working group member Dr Rosita Zakeri acknowledged that the rise in the proportion of patients with HFpEF is partly due to increased recognition and diagnosis of the condition, but also improved treatment and prevention of HFrEF and increasing longevity and rates of comorbidity in the population that might favour HFpEF. She explained: 'There is a strong association between HFpEF, older age and both cardiovascular and non-cardiovascular long-term conditions. Therefore, as life expectancy increases and rates of comorbidities such as hypertension and diabetes increase, we expect to see an increase in the number of people developing HFpEF.'

Appeal for improved quality standards

Among patients with a HF diagnosis, some 40-50% may have HFpEF. The BSH Working Group posit that to reduce existing inequities and achieve quality standards for HF care, including those with HFpEF, significant investment is needed. This includes workforce expansion, training, and greater resource provision to enable widespread access to natriuretic peptide testing and echocardiography in primary care to improve HFpEF detection rates.

Professor Gardner, a Consultant Cardiologist and Heart Failure Specialist at the Golden Jubilee National Hospital in Glasgow, said HF is associated with high symptom burden, frequent and recurrent hospitalisations, and a high mortality rate. 'In many cases the outlook is poorer than those diagnosed with cancer. Despite this, resources to identify and treat heart failure patients in a timely manner are very limited.'

Determine who will benefit from specialist care

The BSH recommendations for a minimum of 3-4 community HF specialist nurses or advanced healthcare practitioners per 100,000 population, Dr Zakeri said. 'We also need ongoing research into new treatments and studies to clarify which patients with HFpEF will benefit from community HF specialist nurse-led care,' she added. Another aim of the BSH position statement is 'to ensure that treating healthcare practitioners are aware of the advances in HFpEF care' and give greater consideration to the causes of HF.

Professor Gardner said: 'Ultimately, we need to ensure that the limited resources we have at the moment are not stretched further. Rather, increased funding for heart failure specialists – cardiologists, HF nurses, and other key allied health professionals – is urgently required.'

Promising leads for better therapy

To achieve a timely and accurate diagnosis, the BSH propose that all patients with suspected HFpEF should be referred to an appropriate heart failure specialist for evaluation. 'With accurate diagnosis and appropriate management, it is possible for people to live well with heart failure,' he added.

Current treatment of HFpEF involves early recognition and treatment of fluid overload (with oral diuretics) to improve symptoms. Dr Zakeri said: 'Looking forward, there is much to be hopeful about with many ongoing clinical trials studying new medications and ways to treat HFpEF. One example, sodium glucose cotransporter-2 inhibitor drugs, have recently emerged as a promising therapy to reduce HF hospitalisations in two recent clinical trials of patients with HFpEF.'

Report: Mark Nicholls

screening precision

er is added on the back. This establishes the "trigonum cardiacum" (heart triangle) and records the third dimension via the back electrode. While many argue that you can also get three-dimensional data with an ECG, that is just a projection. By using the back electrode, we get a native vector which is measured, not calculated. The hardware used to record the Cardisiography has to be adequate to compute all parameters measured. The recording itself is easy and only takes four minutes. After an additional four minutes, the results arrive. The recording does not need to be performed by a doctor; nurses or medical assistants can do it after being trained.'

How should the Cardisiography report be used?

'The general practitioner, who used the Cardisiography, gets the report. He can read it and forward it to a cardiologist, if necessary. He can also hand it to the patient who can take it to other medical professionals. The report gives the specialist a pre-diagnosis, upon which a decision on further diagnostics and possible treatments can be made.'

Analysing the patient's risk

Which information are included in the report?

'Three areas are analysed: the perfusion of the heart, its structural integrity and rhythmology. Three bars (red to green) represent the patient's risk for each of these areas. Information that is more detailed can be added for the expert, to serve as a basis for informed judgement. The additional data helps to identify the pathology of a given result, to exclude physiologically unusual cardiac positions as cause for that result.

'If the algorithm finds a pattern, it is usually not just one parameter that indicates "not healthy". Many patients with an inferior perfusion develop other heart problems. Because of the variable patterns, it is important that their roots are traceable. We use the three main areas to indicate where the algorithm found a pattern. The areas still include various diseases, but it gives the cardiologist a direction to look in.'

Which role do you see for the Cardisiography in the future of patient care?

'Cardiovascular diseases are still the main cause of death. For people over 65, the prevalence is at 40%, with that number rising steeply with age. What this data does not show: people who get diagnosed at 65 started to develop the disease long before. Cardisiography is one part of the puzzle to optimize the prevention of cardiovascular disease. It is a screening tool that is very useful for preventive medical check-ups. If we were to decide, everyone from the age of 30 would be screened. Such an early screening could catch cardiovascular diseases while they are developing and before people go to see their doctor because of their symptoms.'

What is Cardisio's goal?

'We want to send the right patients to the cardiologist. With the method, the primary care physician is empowered to make a more qualified preliminary diagnosis and refer them to a cardiologist when they are at a serious risk.'

Interview: Sara Hoffstedde

Meik Baumeister

Meik Baumeister is co-founder and CEO of Cardisio. He has over 20 years of experience in implementing complex IT projects and leading IT companies. Starting as a consultant for business intelligence and CRM, his career as CEO led him to several medium-sized IT companies throughout Germany. Baumeister has particular expertise in the areas of e-health, cardiology and artificial intelligence.

Women's heart health

The impact of pregnancy and menopause

The critical times in a woman's life of pregnancy and the menopause – and their relation to heart health – was explored in a special session at the European Society of Cardiology congress (ESC). With recognition that heart health treatment and care need to take into account gender-specific factors, the defined field of women's cardiology is becoming an increasingly important area of focus.

'Menopause is an important phase in women's life, affecting changes in cardiovascular disease (CVD) risk factors, the immune system, thrombotic system and several others. The decline in Estrogens start from 30 years onwards and has a huge impact on fertility, CVD risk and many co-morbidities. These appear when women enter their forties, such as thyroid disorders and rheumatic diseases. Women with severe vasomotor symptoms are at higher CVD risk and often develop (early) hypertension. Menopause is therefore an important turning point in life and a good moment to assess an individual's CVD risk,' said Professor Angela Maas.


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Women should pay special attention to their heart health during pregnancy and menopause

Female-specific risk factors

Clinical cardiologist Maas, who is the author of "A Woman's Heart – why female heart health really matters" and Chair in Cardiology for Women at the Radboud University Medical Center in Nijmegen, The Netherlands, said there are a number of key considerations for women during the menopause when it comes to heart health. 'The shift in CVD risk factors is very important and also the consideration of other female-specific risk factors,' she explained. 'Migraine from puberty onwards and high blood pressure in pregnancy are other important female-specific risk factors that are often present in women with early menopause and many vasomotor symptoms.' She also points out that anginal symptoms in women at middle age are importantly caused by coronary spasm and not by stenoses.

Dedicated centres

'The diagnosis is now easy in the cath lab, but still quite rarely done in too few centers,' said Maas. 'Many women walk around without a clear diagnosis and lack of treatment. This needs to change.' With stress increasingly being a crucial risk factor in women, she said that nurses are important co-workers in the outpatient clinic to help women to learn to live with their symptoms. She advocates dedicated centres for women's cardiovascular health to support better diagnosis and prognosis and believes women specific symptoms must be taken seriously, particularly for prevention. Maas emphasised that any comparisons of women's symptoms with those of men is now an outdated approach.

In her presentation on pregnancy and heart health, Maggie Simpson, Lead Clinician with the Scottish Obstetric Cardiology Network, highlighted how CVD is a leading cause of maternal death and morbidity. 'All healthcare professionals who engage with women of reproductive age with CVD have a role in reducing adverse pregnancy outcomes,' she said.

'Women of reproductive age can have pre-existing CVD, risk factors for CVD, and present with new CVD in pregnancy.' She points out that adverse pregnancy outcomes, such as hypertensive disorders of pregnancy and gestational diabetes, are associated with CVD later in life.

Escalation of care

She said awareness of CVD in pregnancy among healthcare professionals is crucial and by recognising their pivotal role in provision of preconception care across a women's reproductive years can lead to better outcomes.

Simpson, who is also Advanced Clinical Nurse Specialist at the NHS Golden Jubilee centre in Glasgow, said recognition of women with CVD can help identify those who may require preconception counselling from experts in CVD in pregnancy, facilitate access to contraception, and refer for follow-up with the Pregnancy Heart Team during pregnancy.

Following recognition of signs and symptoms of CVD presenting in pregnancy/postpartum, healthcare professionals can assess, investigate, make a diagnosis, and escalate care to senior members of the multi-disciplinary team.

Report: Mark Nicholls

Angela Maas

Professor Angela Maas has been a clinical cardiologist since 1988. She has been Chair in Cardiology for Women at the Radboud University Medical Center in Nijmegen, The Netherlands, since 2012, where she focuses on the early identification of women at increased cardiovascular risk and stable and unstable ischemic heart disease in women at middle-age. As one of the most influential female doctors in Dutch healthcare, she was the 2020/21 Women's representative of the Dutch Government to the United Nations.

Maggie Simpson

Maggie Simpson is Lead Clinician with the Scottish Obstetric Cardiology Network and Advanced Clinical Nurse Specialist at the NHS Golden Jubilee University Hospital in Glasgow.

Non-invasive method

Pressure-strain loop to assess myocardial work

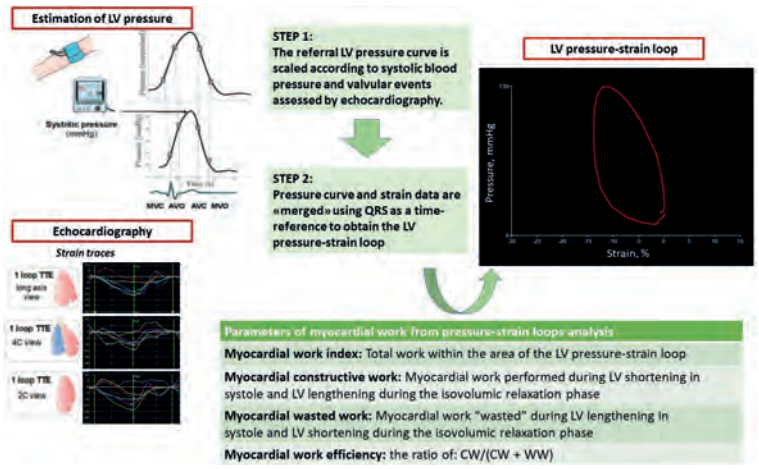

Illustration of LV pressure-strain loop

The value of using left ventricular pressure-strain loops as a non-invasive way to assess myocardial work was outlined in a session on cutting edge echocardiography at ESC 2022 in Barcelona.

Delegates heard how the technique has benefits for cardiologists in terms of diagnosis and prognostic stratification for conditions such as heart failure, ischemic cardiomyopathy, valvular heart disease, or selecting patients for CRT (Cardiac Resynchronization Therapy). The session provided new insights into pressure-strain loops (PSL) analysis for the non-invasive assessment of left ventricular (LV) myocardial work and its potential clinical applications. Dr Elena Galli from Rennes University Hospital in France said the objective is to present the benefits of PSL analysis as a new technique for assessment of left ventricular performance. She said: 'The main aspect of this technique is that it allows an assessment of myocardial work in a way that is reliable and not invasive.'

Not completely precise, but very useful nonetheless

Assessment of myocardial work remains 'a pillar of assessment of myocardial function in terms of mechanics and energy demand,' added Galli. First introduced in the late 1970s when researchers used pressure volume loops to calculate myocardial work, it became the gold standard, but as an invasive measure it is not applicable to patients in everyday clinical practice, whereas PSL offers a non-invasive option.

The non-invasive assessment of myocardial work relies on the measure of blood pressure by an arm cuff sphygmomanometer to estimate LV pressure, and on the measure of LV strain curves by echocardiography. Pressure-strain curves are then obtained (see figure), which allow the estimation of regional and global LV work. LV myocardial work is then assessed. 'It is not a completely precise calculation, but it is a good estimation of myocardial work, and the regional assessment of myocardial work is shown to be directly associated with myocardial oxygen consumption assessed at FDG-PET.'

Since PSL emerged in 2012, it has been validated by various research groups for estimating myocardial work in a reliable fashion in several different pathologies, she added, and most widely shown as beneficial in CRT candidates. 'Studies also show applicability of the method to other clinical conditions; for instance, in patients with hypertension, systolic heart failure, diastolic heart failure, and valvular heart disease, particularly aortic stenosis,' said Galli. 'Also, there are some pioneer studies that have started for the non-invasive assessment of the myocardial work of the right ventricle by the analysis of pressure-strain loops.'

Ready for clinical practice

Other approaches to assess left ventricular function and performance – such as left ventricle ejection fraction and strain – have limitations, she continued, because they simply measure LV fiber shortening and do not take into account the effect of afterload on LV function. As such, PSL seems to provide a more precise and physiological assessment of LV function. 'This is one of the main points of the technique, together with its non-invasive nature,' she said.

Galli believes cardiologists can use PSL to highlight local differences in myocardial work to enable selection of patients receiving CRT and, in the future, it may offer pathophysiological insight into other disease states, such as heart failure and valvular heart disease.

The technique is only slowly entering clinical practice and not being widely applied to patients despite the increasing numbers of studies being conducted in the field. 'We can see that the evidence in research, and interest on parameters derived by PSL analysis, is increasing,' Galli added. 'I think that in the future it could replace some of the parameters that we use now, for instance LV strain, but we need wider evidence to prove it, so we are still at the starting point of the method.'

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