EUROPEAN HOSPITAL

Technology-based therapy approach

Self-administered brain stimulation as a novel tool for depression treatment

Including **EH@ECR**

The stark reality of depression is evident in the latest World Health Organization (WHO) statistics, indicating that around 280 million people worldwide suffered from depression in 2019. National estimates showed a doubling or tripling of depression prevalence in many European countries. Unfortunately, traditional treatments for depression, primarily medication, have shown limited efficacy. According to the Economist Group, in Europe "Only 40% to 60% of patients achieve remission after initial antidepressant treatment, regardless of the chosen drug. Psychotherapy also faces challenges such as limited success, restricted access and long waiting times. These factors contribute to a substantial number of patients classified as partial or non-responders, leading to a lower quality of life, increased comorbidity, and social and occupational disability. With the WHO predicting major depressive disorder to become the leading cause of disability globally by 2030, the outlook is grim.

Given the limited success of traditional therapies, recent years have witnessed the emergence of technology-based interventions for depression. One such intervention is transcranial electromagnetic stimulation (TMS), a noninvasive use of magnetic fields to stimulate the brain, approved by the Food and Drug Administration (FDA) in 2008. However, it is considered costly and trials have concluded that TMS is associated with a small risk of seizures.

Another promising noninvasive brain stimulation technique is transcranial direct current stimulation (tDCS). tDCS, with its potential cost-effectiveness, easy application, and safe profile, applies a weak direct current through scalp electrodes to modify neuronal excitability. Clinical trials have shown tDCS to have a similar impact as antidepressants, with fewer and less severe side effects.

To enhance tDCS's therapeutic efficacy, it has been integrated with psychological interventions and is mainly used by licensed physicians in clinical settings.

Bringing tDCS home with Flow

Daniel Månsson, a clinical psychologist with a BSc in Computer Science, recognized the need to make depression treatment more accessible: "I can treat five to eight people per day, but this is not enough given the large number of people affected by it". Teaming up with neuroscientist Erik Rehn, they founded the neurotech company Flow Neuroscience and developed Flow. Unlike other medical-grade tDCS devices, Flow is designed for home use, empowering individuals to self-manage their treatment. The solution aims to provide effective treatment without the drawbacks of side effects, long waiting times, high costs, or social stigma associated with traditional approaches. While Flow does not aim to replace traditional treatments, it seeks to expand therapeutic options and provide a complementary approach to existing treatments. "I think it's extremely important that people have access to a large toolbox. We are here to provide something that augments current treatment options or acts as an alternative", Månsson said.

How Flow works

Flow combines a medical-grade tDCS headset with an app-based behavioral therapy program, offering a holistic approach to depression treatment. The Flow headset, with two electrodes placed on the frontal part of the head, delivers a noninvasive treatment by sending a weak current into the left side of the brain, which activates neurons on the left, influencing feelings, thoughts, and inner mental processes. The overall effect is comparable to antidepressants but without the associated side effects. Månsson explained: "What is unique about Flow is that it is a medical-grade, one size fits all tDCS treatment for depression that can be used at home. "

Flow's track record

Flow's effectiveness and safety are supported by real-world data and clinical evidence from a large randomized placebo-controlled trial.

The Flow 2023 study conducted among 174 participants in the UK and the US showed that 56% of them experienced a complete removal of depression symptoms (remission) within 10 weeks, whilst an additional 6% were measured to have an improvement in symptoms of at least 50%. No major side effects were reported from the treatment group. Overall, a greater than threefold increase in the odds ratio of substantial improvement with active treatment compared to placebo/sham stimulation were measured. Flow's effectiveness surpasses the average effect size witnessed in trials for the 21 best-selling antidepressants in the UK and the US.

Scaling up efforts

Flow has received CE approval in the EU, Great Britain, and Brazil, with FDA approval expected by mid-2024. Currently, Flow has approximately 17,000 users and its largest market is the UK. Worldwide over 150 clinics deploy Flow, most of them based in the UK, some are in Switzerland, Germany, and Brazil. However, Flow is available over the counter in all EU countries and some Asian countries have also shown interest in the product.

User endorsements and future outlook

Flow has garnered broad endorsement from users, although the company acknowledges that individual outcomes may vary. More research into the longer-term effects of tDCS treatment are needed.

The company is looking into expanding the duration of the treatment regime as well as its geographical reach. Additionally, it explores cooperating with psychiatrists, general practitioners, clinical psychologists, and other healthcare professionals. Flow's broader application to conditions like bipolar disorder, post-traumatic stress disorder (PTSD) and pain management shows promise, indicating the potential of stimulating neurons in addressing various brain-related disorders. ∎

Report: Cornelia Wels-Maug

Woman wearing brain stimulation device on her head to treat depression © YouTube/Flow Neuroscience

CONTENTS

E-skin patches

# How "intelligent" skin could highlight cardiac conditions

Two companies are combining their unique expertise to develop intelligent e-skin patches to "self-sense" cardiac events in patients. The flexible patch platform will deliver a comprehensive understanding of both electrical and mechanical heart activities and has the potential to enable cardiologists to better monitor their patients.

The initiative, which sees STMicroelectronics and DuPont Liveo Healthcare working to develop the wearable platform, was outlined during a presentation by Oriana Di Marco from STMicroelectronics and DuPont's Jennifer Gemo at Medica in Dusseldorf in November.

Speaking to European Hospital after the conference, Di Marco, who heads EMEA Strategic Business Development for Health &Well-being at STMicroelectronics, said: 'The companies' respective contributions to this development is our long-term vision for an intelligent electronic skin patch that can self-sense a cardiac event and act immediately at the point of need.' For the e-skin project, STMicroelectronics provide a smart, flexible electronic board with innovative sensing, low power management, processing, and in-sensor and microcontroller AI capability embedded in a single module. This technology pairs with the DuPont Liveo silicone technology with electrically conductive properties.

Durable, but gentle

Gemo, who is Global Strategic Marketing Leader with DuPont Liveo Healthcare, explained how medical professionals can use Liveo Soft Skin Conductive Tape as a skin electrode for biosignal monitoring. She emphasised that good skin conformability, no drying over time, and repositionability with gentle adhesion and atraumatic removal are vital. 'The conductive tape can be used in single electrodes for short-term monitoring, as well as in medical wearable patches for long-term monitoring
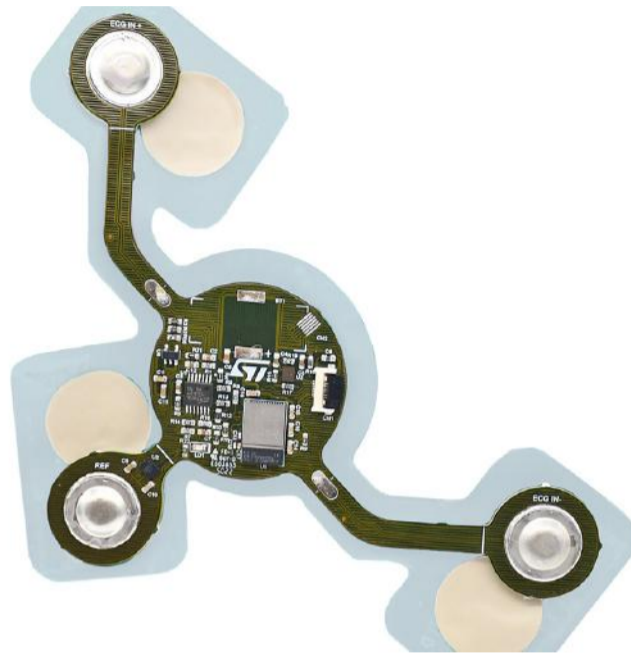
Smart Biosensing Patch concept © Liveo

lasting seven or more days,' she continued.

DuPont – which carried out the full design, processing, and assembling of the patch prototype solution – also provides a toolbox for wearable medical devices that includes biomedical grade elastomer for hardware encapsulation and soft skin adhesive for skin gentleness,

Oriana
Di Marco

Oriana Di Marco is Head of EMEA Health & Well-being Vertical, Strategic Business Development at STMicroelectronics. With a master's degree in Biological Science and an Executive MBA, Di Marco has a distinctive scientific background combined with advanced semiconductor knowledge from 20 years at ST. She is a recognized expert in molecular diagnostics, drug delivery for diabetes, microfluidics technologies and medical devices.

repositionability, and long wear time of the patch onto the body.

Synchronized and contextualized measurements

Di Marco outlined how the flexible patch platform prototype supports heart monitoring. As electrocardiography (ECG) and seismocardiography (SCG) signals are detected in the same sensor, they are

Jennifer Gemo

Jennifer Gemo is Global Strategic Marketing Leader for DuPont Liveo Healthcare at DuPont Industrial Solutions. She is responsible for developing and driving the global growth strategy for DuPont Liveo and supports the development and commercialization of several growth innovation platforms for Liveo. Prior to her current role, she was the global segment leader for Medical Devices.

fully synchronized as they occur. 'Moreover, by using the artificial intelligence capabilities embedded in the sensor and in the microcontroller, it's possible to contextualize the measurement within the wearer's daily activities as well as supporting the derivation of other vital signs like non-invasive blood pressure, in addition to respiration rate and heart beats,' said Di Marco.

Clinicians benefit from a better understanding of the heart rhythm and main vital signs during a patient's visit and once they have left the doctor's practice. 'The patch's intelligence lets it detect changes in normal patterns and alert the patient, who can share the data with the physician,' she added.

Catering to cardiologists' requirements

Patient benefits are related to the characteristics of the wearability of the patch. The patch can be worn longer without irritating the skin and it is flexible, lightweight, and can be repositioned easily. In terms of how this is advancing the field and patient care, Gemo said: 'The cardiac market is one of the most advanced in technological adoption, with cardiologists demanding longer wearability, better data, and superior design. They are clamouring for small, flexible, and waterproof patches that deliver improved comfort, longer wear, and higher signal quality over time.'

Such requirements are driving the trend for continuous and remote cardiac monitoring outside of the hospital and in patient's homes, where patient comfort leads to improved compliance. The two companies have provided a toolbox of technologies to address these needs and delivered a prototype that improves signal quality and patient comfort over time.

Next step

The patch is also suited to applications beyond cardiac monitoring. It can be positioned in various

places of the body and use different algorithms to detect other biological functionalities.

For DuPont Liveo, the next step is to build prototype patches for further testing and to provide reference designs and components to build similar patches to monitor other functions. While acknowledging that vital-sign monitoring is a high-growth market, Gemo said its key needs are improved signal quality and patient comfort.

STMicroelectronics and DuPont have portfolios suited for wearables and electronic skin patch applications. DuPont Liveo Healthcare enables next-generation wearables through its toolbox of technologies, including medical-grade elastomers, adhesives, resins, and thermoplastics; while ST is developing a new class of motion sensors with an embedded vertical analog front end that opens new categories of human-centric applications. ■

Report: Mark Nicholls

Soft Skin Conductive Tape © Liveo

Timely project

Improved care after heart attack on AI-powered telemedicine platform

Coronary artery disease (CAD) causes more than 1.8 million heart attacks each year in Europe, 300,000 in Germany alone. In most cases, rehabilitation helps the patients to return to their everyday life. But what happens once the patients have left the rehab clinic? PD Dr. Boris Schmitz launched the Timely project to find out. The project aims to develop a patient-centered platform that provides early cardiac risk prediction and supports prevention and intervention in post-rehab care for CAD patients using eHealth and artificial intelligence.

In a rehabilitation clinic, CAD patients learn how to change their life styles in order to be able to continue living with the disease for as long as possible and without reinfarction. A healthy diet, exercise, and stress reduction are the most important issues, but once back in their home many patients don't follow through with the behavioral changes they learnt in rehab. 'The first six months after rehab are crucial,' says biologist and sports scientist Schmitz since 'only during this period behavioral changes will become a habit.'

A senior scientist at the Center for Clinical Rehabilitation at the Königsfeld Clinic, Schmitz wanted to find out how CAD develops after treatment has been completed in order to be able to influence the patients' state of health post rehab. But post-rehab care does basically not exist: the guidelines require only a single follow-up visit at a cardiologist's after six months. Too little and far too late, says Schmitz. With his randomized, controlled clinical study, he wants to show that cardiovascular risk decreases with the help of the Timely platform. For this purpose, 360 adult patients were recruited who had undergone myocardial revascularization after being diagnosed with CAD as well as follow-up care as part of cardiac rehabilitation. The project is conducted in three study centers in Germany, Spain and the Netherlands and 13 partners from industry, the outpatient sector and the clinical environment are participating in the development of the platform.

### Equipped with wearables and app
In order to design the platform with the patient front and center, Schmitz onboarded the potential participants right at the beginning of their rehab in the form of a 'living lab'. 'We interviewed the patients', explains Schmitz, 'asked them about their wishes and needs, tried out several approaches and tested the user-friendliness of the app, among other things. It was important to us that all participants felt comfortable with the app – no matter how old they are and regardless of their previous technical knowledge.' After a thorough

medical examination, the participants are equipped with various wearables for six months. In addition to a portable, wireless 3-lead ECG, they received a blood pressure monitoring device to measure resistance in the vessel and the speed of blood flow. Moreover, an activity tracker provides information about stress levels, exercise and activity calories. The 'heart' of the study is the Timely app. It provides the patients with information on all aspects of rehab such as diet, stress management, weight loss or exercise and each participant can set their personal goals. Personal messages, push notifications and a chatbot regularly

offer positive reinforcements to keep motivation up. Artificial intelligence processes large amounts of data and detects arrhythmias at an early stage. 'A change in sleep rhythm or an increased stress level can indicate arrhythmias,' says
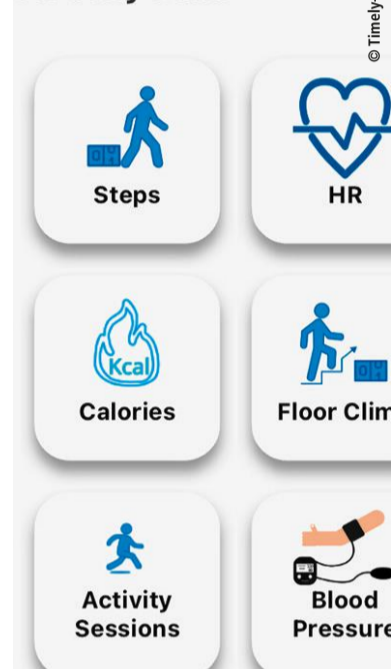
Schmitz and adds that in such cases the team 'responds directly and contacts the patients who need immediate support.'

Digital dashboard
Via a digital dashboard, physicians, therapists and case managers access all data and the individual risk profile of each patient, which is

automatically evaluated and interpreted. In the event of abnormalities – for example, when someone has not been exercising for a long time – the person is called on the phone to adjust the therapy if necessary or to arrange other kinds of help. The data is transmitted automatically via the mobile network and via secure systems in Germany, Schmitz emphasizes.

After six and twelve months, the study participants return to the rehab facility for further extensive examinations. The last patient is expected to undergo this final exam by mid-2024. The primary endpoint of the EU-funded study is a biomarker score, which reflects the risk of mortality over the next ten years, and a test to assess physical performance. In addition, changes in diet and exercise behavior are analyzed. Schmitz wants patients to continue using the app for the rest of their lives, whenever they need it. 'Intensive use over six months is enough to internalize the content. However, there are always setbacks in life, perhaps career changes or other illnesses that make it necessary to return to work. My vision is that the app can be prescribed as a digital health application, a so-called diga, and be used not only for aftercare, but also for prevention.' ∎

Report: Sonja Buske

Boris Schmitz

PD Dr Boris Schmitz is senior scientist at the Königsfeld Clinic, Center for Medical Rehabilitation. A biologist by profession, he also holds a doctorate in sports science. He spent most of his professional career in Münster as a research assistant, project and laboratory manager as well as a private docent. Schmitz is a member of the European Society of Cardiology (ESC) and works as a reviewer for various journals.

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Settings

Help & Support

Timely — Fitrockr

Net ECG — Vivosmart

Tel-O-Graph eConnect — Other Issues

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Activity Data

Steps — HR

Calories — Floor Clim

Activity Sessions — Blood Pressure

EUROPEAN HOSPITAL @ ECR 2024

Interview with ESR President Carlo Catalano

ECR 2024: Focus on technologies and research – surprises guaranteed

Our author Mélisande Rouger spoke with ESR President Professor Carlo Catalano from Rome, Italy about the meeting's content and its intriguing theme.

What does 'Next Generation Radiology: Embracing the future and redefining the field of radiology' entail?
'The demand for imaging studies is increasing worldwide. To face this rising demand, we need to use all the technology that is available now. It may come from AI and more widely digital medicine. AI does not just comprise of tools that aid diagnosis, but also to help improve workflow – for example, by expediting time consuming administrative tasks. Improving exam quality may sometimes be impaired because of the number of studies we have to deal with. In many places, it is really challenging to provide quality service.

But technology is improving, with very high-quality radiology equipment coming out every day. Soon, we will use technology with a different approach, and just focus on not just anatomical information but also functional information. Radiology will be part of a much wider system, and possibly integrate with other diagnostic tools, for instance laboratory tests, to provide the best possible solutions for the patient. The radiologist's profession is also changing and becoming increasingly clinical. Radiologists must have a subspecialty to be able to deal with the patient directly and take part in decision making. We also have a leading role in clinical activity, research and education.

An increasing number of young physicians now understand what radiology is and means in terms of diagnosis and intervention. The next generation of radiologists will have a different profession, with technology that has improved and a different approach as to how we perform our exams.'

What are the current trends in AI, radiomics and, more generally, technology?
'Technology has led changes in radiology and needs improvements that are not related to hardware, but to the way we use our tools. Significant improvements are being made in speed and precision with AI, which means also greater comfort for the patient, and a better possibility to analyse imaging and data. Technology can also help reduce dose to the patient. Dose remains a problem, especially when

you consider how many exams are performed worldwide. There are staff shortages everywhere. With AI, we can also speed up processes, and better use our staff resources to get closer to patients.

AI can help us make earlier diagnosis and gain confidence when doing so. AI can really become a companion for radiologists, providing real support and helping them increase the quality of their services. We need to use new tools that can help us to continue doing

so many exams. At ECR, we can educate radiologists and show them what can be done, and how technology could be used. Technologies such as quantum computing, 3D printing, and molecular imaging are very promising beyond AI.

More into the future, we will move forward the Digital Twin concept, i.e. using all the different tools together with AI to get the best data provided by different resources. To guide therapeutic response, the

digital twin will be applied the way it has already been applied in the aerospace industry, by learning on a simulator. We hope all the information we have can be used by each of us, to create a twin or avatar, to try and understand exactly diseases in the patient.'
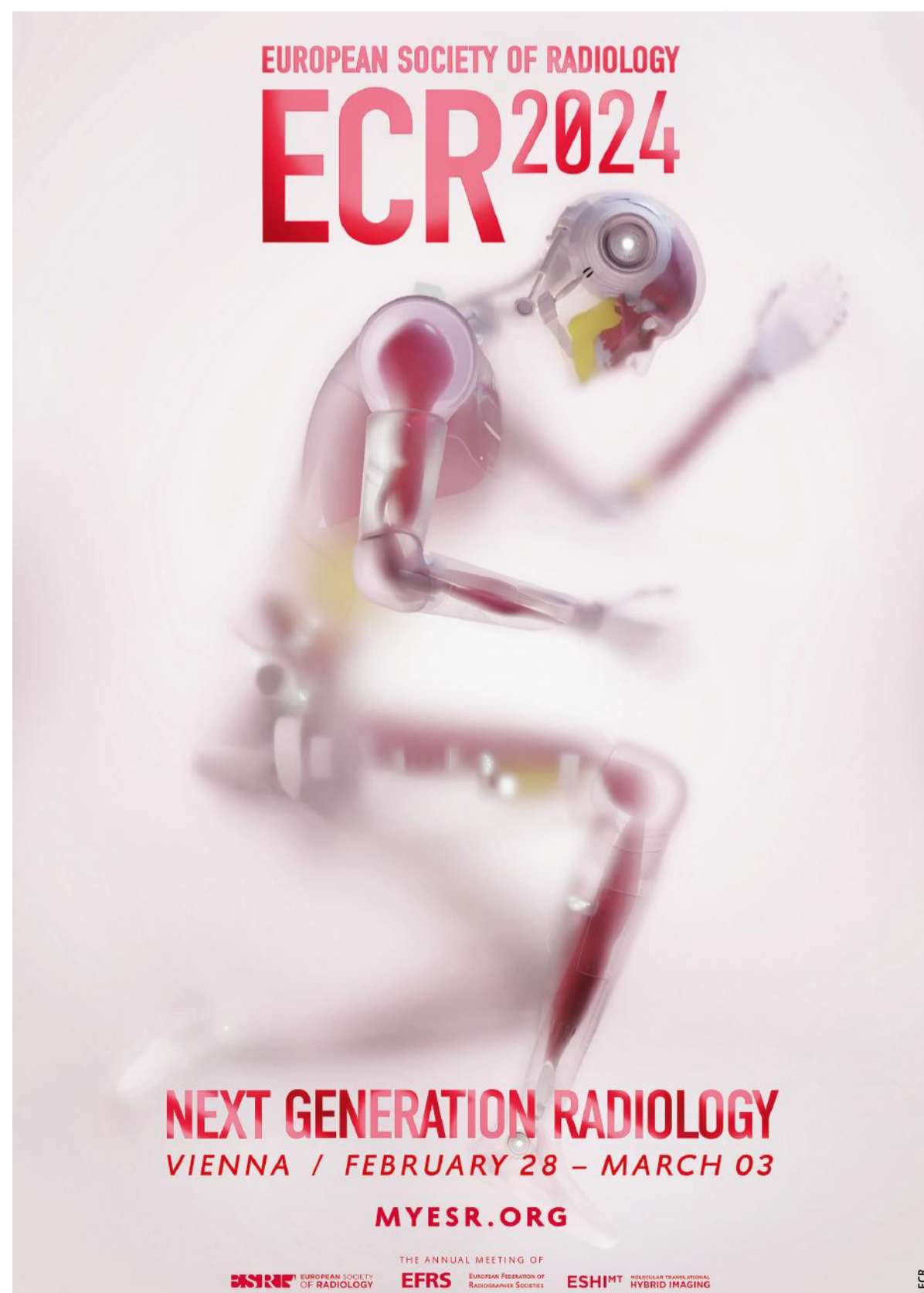
What will be new at ECR this year?
'The Plenary Lectures will be done in a different, more informal format, which will be like Ted Talks. The topics will surprise everyone. For example, the pro-

gram will explain how AI changes radiology from a clinician and company's point of view.

The focus will be on how research activity is changing medicine and how medicine is now delivered everywhere. I always recommend young radiologists to go to the Cube, the ECR's popular interventional radiology area. It shows a different part of radiology. We talk a lot about technology and AI, but all these tools can be used for not just diagnostic purposes but also intervention.

Minimally invasive therapies have advanced and grown a lot in oncology, in vascular diseases etc. The Cube somehow differentiates ECR from other congresses, generalist congresses where interventional radiology is sometimes left behind.

Finally the opening ceremony will be slightly different this year. Talks will be much shorter and we will use new technology to talk about technology. Brace yourselves for surprises!' ◾

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ECR 2024
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Carlo Catalano

Prof Carlo Catalano is a full professor of radiology and chairs the Department of Radiological, Oncological and Pathological Sciences at the Sapienza University of Rome, Policlinico Umberto I. He obtained his medical degree at the Sapienza University of Rome in 1990 and completed his training in radiology at the University of L'Aquila in 1994.

Imaging in characterisation and classification of tumour types

Taking a closer look at breast cancer

Breast cancer has no "one size fits all" therapy approach: subtypes differ significantly in malignancy, progression, and treatment response. Therefore, the more is known about the type of carcinoma in a patient, the better the outcome. At the annual scientific EUSOBI meeting in Valencia, Dr Ramona Woitek pointed out the potential of novel imaging techniques and computational image analysis for classification and characterization of breast cancer as well as treatment response prediction.

Molecular imaging can provide valuable insights into cancer characteristics, Dr Woitek, a Professor of Radiology at the Research Center for Medical Image Analysis and AI (MIAAI) at Danube Private University in Krems, Austria, outlined. It can help differentiate cancers via hallmarks such as increased self-proliferation, deregulated cellular metabolism and tumour vasculature. In a best-case scenario, imaging can help identify – potentially actionable – mutations, and select those patients who will benefit the most from undergoing tumour tissue sequencing.

Beyond standard-of-care imaging such as conventional mammography, ultrasound and MRI, functional imaging can provide more specific information, the expert explained: ^{18}F-FDG PET is mainly used in metastatic breast cancer, but can also help understand a tumour's microenvironment and biology, while ^{18}F-FLT PET and ^{18}F-FMISO PET show cell proliferation and hypoxia in tumours, respectively. Another tool that can help make better treatment decisions is ^{89}Zr-Trastuzumab, a tracer that identifies tumour heterogeneity between metastatic lesions. Waiting in the wings are advanced MRI techniques using hyperpolarised carbon-13 (^{13}C) and sodium (^{23}Na), which show promise in treatment response prediction and early response detection by distinguishing between actual progression and pseudoprogression.

Additional insights from semantic descriptors and heatmaps
Semantic descriptors in MRI images serve as an effective way to distinguish between breast cancer subtypes, Woitek pointed out. 'It has been shown in several studies that some of these descriptors are more frequently found in certain subtypes.' These distinctions can provide valuable and actionable information, especially in settings where assessment of the KI-67 marker is not available. 'For example, irregular borders and persistent enhancement are most frequently found in Luminal A cancer types, while Luminal B is characterised by more heterogeneous enhancement. HR-/HER2+ breast cancers typically feature smooth borders, washout, and are more frequently associated with multifocality.' These insights can be
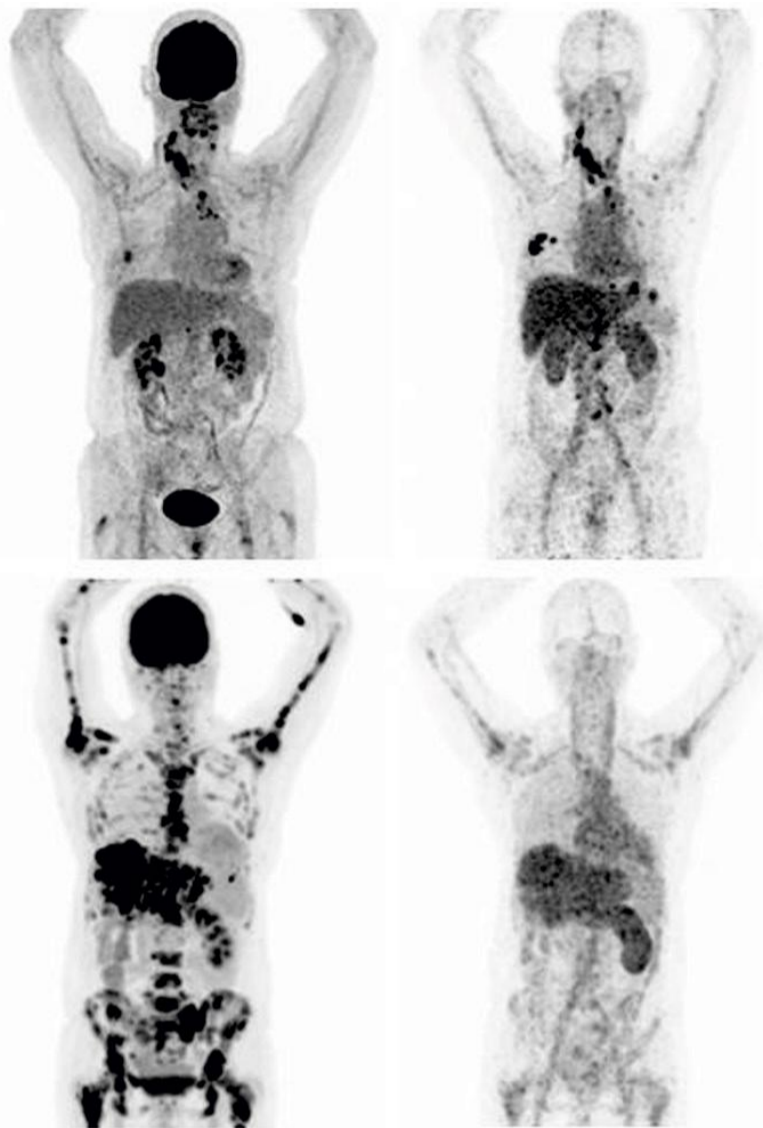
Molecular imaging can help identify heterogeneity in HER2 expression in metastatic breast cancer: ^{18}F-FDG (left) and ^{89}Zr-trastuzumab PET scans (right) of two patients © Bensch et al., EJNMMI 2018 (CC BY 4.0)

further exploited via radiomics, where quantitative features such as shape, volume or texture of a tumour can be extracted. Using dynamic contrast-enhanced MR imaging (DCE-MRI), this provides high-accuracy information especially for distinguishing luminal B-type cancer from other forms, often outperforming semantic or clinical features, Woitek reported. Using convolutional neural networks (CNN), high-quality information can also be extracted from multimodal ultrasound imaging (B-mode, colour Doppler and shearwave elastography). 'These networks use deep learning to find the relevant features to classify the tumours by themselves, and they are getting better and better at this. Usually, the more types of data from different sources and the more modalities are put together, the higher the chances of developing really good predictors.'

As with most AI algorithms, this approach is somewhat of a black box. However, this can be overcome using special heatmaps. These class activation maps show how much any pixel of a given diagnostic image contributes to the algorithms classification or prediction, leading to interpretable results. For example, if the algorithm derives its findings mostly from pixels which are far away from the actual tumour site, it is likely that the interpretation is not trustworthy. On the other hand, if the heatmap stays focused on the cancer, the result has high predictive value.

A more profound understanding of cancer types
'Usually, oncologists' decisions on whether or not to give targeted anti-HER2 treatment are based on single biopsies from single metastatic sites or even from the primary tumour,' Woitek pointed out. 'But scans and tracers like this really allow us to get an idea about the heterogeneity of cancer, the receptor status and the expression of HER2 in different sites of the body, and that can actually have a huge effect on treatment decisions.'

Computational image analysis, combined with novel imaging techniques, holds great potential to help characterize cancers, the expert summarized. 'Especially with novel treatments, our focus on functional techniques will grow. It is our task to identify the key questions we want to answer in the prediction, classification and characterization of cancer, and how this can have the biggest impact on our patients and improve their outcomes.' ∎

Report: Wolfgang Behrends

Ramona Woitek

Dr Ramona Woitek is Professor of Radiology at the Research Center for Medical Image Analysis and AI (MIAAI) at Danube Private University in Krems, Austria. Her work focuses on the analysis of medical imaging data for the development of quantitative biomarkers, and the use of AI to predict the presence of disease, its progression or treatment response.

The next generation of CT contrast media injectors

The Accutron CT-D Vision is the next generation of Medtron AG's leading CT contrast media injector. Focusing on the user's needs, the latest stage of development of the Accutron CT-D improves the usability of the CT injector and optimizes its integration into the radiological environment.

Radiographers and radiologists are working mostly on screens throughout the day, monitoring examinations and analysing images. With high resolution touch screens, of 10" on the injection unit and 12" on the remote control, Accutron CT-D Vision improves the comfort of use and helps to reduce eye fatigue. The new graphical user interface provides a comprehensive overview of each examin-ation. The wireless injector Accutron CT-D Vision benefits from the recently launched Intelligent Battery Management System to optimize the duration of the battery charge and further increase the working availability. With the new medical grade casters the injector can be moved with less effort and quieter on imaging room floors.

Enriched user experience

The upgraded graphical user interface of Accutron CT-D Vision focuses on providing a comprehensive view of each parameter. It visually highlights the key parameters. Choosing and selecting from lists and a saved profiles library now simplify exam management. This leads to an easier, clearer and more precise programming in less time. Trackability of contrast administration does not only mean recording the contrast dose. It also involves the way the dose was administered. By recording the puncture site location and the size of IV catheter as well as the contrast media type directly as part of the injection data, Accutron CT-D Vision provides comprehensive trackability and documentation of contrast administration.

Improved readability in the console room

Inside the exam room, the choice of the light mode display on the injector screen enhances the readability of key parameters. In the low light of the console room, the operator can choose the dark mode display to reduce visual disturbances and allow the focus on the imaging procedure. Ac-cutron CT-D Vision is equipped with several substantial new features that optimize its integration into the radiology environment.

Injection data Sharing

Providing a RIS/PACS interface based on the DICOM standard, the new IDS software option offers direct access to the modality worklist from the RIS for the operator to associate each contrast injection results with the related patient images and data and save it in the PACS. Currently exporting these injection data as a secondary capture or as an ePDF, IDS is a flexible solution able to offer customized access to shared injection data.

Accutron CT-D Vision © Medtron AG

Point-of-care ultrasound (POCUS)

Returning e-FAST 'to its roots'

Stagnation, under-use, unfulfilled potential: At the EUSEM congress in Barcelona, leading emergency physician Dr Joseph Osterwalder describes how e-FAST (Extended Focused Assessment with Sonography for Trauma) – a key point-of-care ultrasound technique for trauma – has changed over the last two decades, and not necessarily for the better.
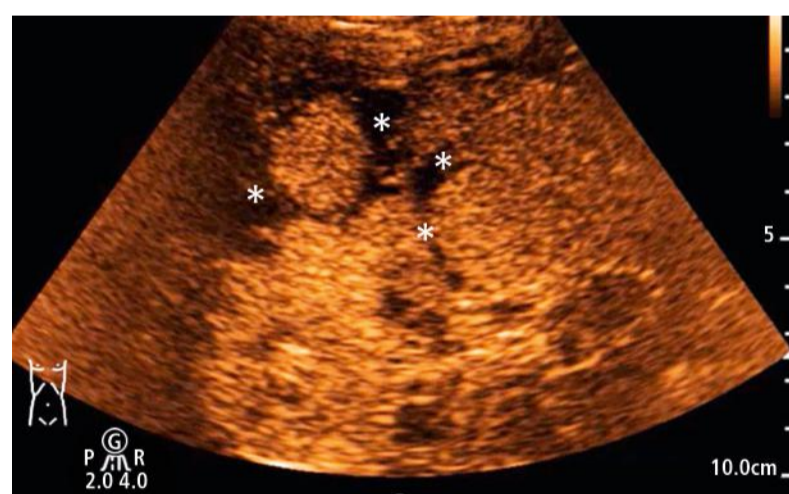
Despite ultrasound having made great progress in terms of technology, price and indications, e-FAST – a standardized protocol-based POCUS that looks for bleeding in the chest and abdomen and pneumothorax – has seen a marked, the expert added. Originally intended for the primary survey in the ATLS (advanced trauma life support) system, it is now being used for wider applications and lesser conditions.

At the European Emergency Medicines Congress in Barcelona (EUSEM 2023) in September, Osterwalder outlined how he believes that e-FAST should 'return to its roots' to re-define its place in imaging. 'The traditional use was intended for unstable or non-stabilizable patients to detect large haemorrhages in the peritoneal, pleural and pericardial cavities as well as a large pneumothorax within a maximum of 1 to 2 minutes using ultrasound,' said Osterwalder, who, until 2017, was Head of the Emergency Department at Kantonsspital St Gallen in Switzerland.

Use cases in the shock room

In stable patients, he said it should be used to detect small bleedings in the peritoneal cavity by means of four additional sonographic views; include the examination for retroperitoneal bleeding/hematoma; injuries to the spleen, liver and kidney; and free intraperitoneal air in the patient with repeat examination as necessary in the shock room. It was also intended to apply the long-established ultrasound indications during the emergency 'ABCDE' protocols in e-FAST patients: to look for airway obstruction, false intubation, pulmonary contusion, intracranial hypertension, retro-orbital haematoma, fractures and assist in monitoring and volume management.

Osterwalder continued: 'Because musculoskeletal injuries are the most common injuries in moderate and severe trauma patients, MSK ultrasound should also be used as part of the secondary survey, especially as its diagnostic accuracy is often equal to MRI.' Since the 1990s e-FAST has been extended to

stable patients and those with mild to moderate trauma. However, he believes this led to exaggerated expectations with users not fully aware of the limitations of the technique, and even resulted in studies questioning the usefulness of e-FAST. He points to clear benefits for clinicians from e-FAST:

more certainty for decision-making on further procedures such as an indication for CT, operating theatre, interventional radiology, and hospital admission for monitoring. 'It also enables faster processes,' he added. 'There are no waiting times for CT examinations. It saves resources for teams that care for and monitor the patient, makes the attending physician more independent and also increases the degree of satisfaction.'

Patient benefit

Benefits for patients include reduced risks from CT examinations such as radiation exposure, allergic reactions and renal insufficiency from the contrast medium. The technique also avoids the need for emergency intubation in children and restless patients before a CT scan can be performed. 'There is no evidence to date that this reduces mortality and morbidity, nor that CT leads to better results,' explained Osterwalder, who remains convinced that redefining e-FAST has opportunities to advance the field.

'It can improve the diagnosis and treatment of moderate and minor injuries in places with limited resources, especially CT scanners, and lead to faster assessment and care of patients in highly-specialized institutions.' He also feels there is an opportunity for industry to work more closely with clinicians.

Wide range of applications

Osterwalder, who has significant experience operating as a field medic, further pointed out the potential of e-FAST in disaster, expedition, and military medicine. The technique is already being used in all emergency situations, not only in EDs but also pre-hospital, in the offices of general practitioners, hospital wards, ICUs, ships, expeditions, and theatres of war, he said. Application ranges from trauma, unclear shock, women of childbearing age to abdominal pain during and after resuscitation.

However, he said: 'e-FAST has not developed any further for over 20 years, even though ultrasound has made huge progress in this time regarding technical innovations such as Microflow, better and high-resolution probes, CEUS; falling prices,

hand-held devices and countless new, scientifically well-founded indications.'

He hopes that the profile of e-FAST can be raised and re-defined to ensure it is used for optimal medical and clinical benefit. ■

Report: Mark Nicholls

Example for highly location for fluid: Subdiaphragmal * © Osterwalder

Joseph Osterwalder

Dr Joseph Osterwalder was Head of the Emergency Department at Kantonsspital St Gallen in Switzerland (1988-2017) and Associate Professor for Emergency Medicine at the University of Geneva. A former delegate of the International Committee of the Red Cross, he is a Fellow of the Swiss Society of Rescue and Emergency Medicine, the European Society of Emergency Medicine, the Swiss and German Society of Ultrasound in Medicine and is a pioneer of emergency medicine and emergency ultrasound in Switzerland.

Additional findings from the MIPA study

Benefits of preoperative breast MRI

Ordering preoperative breast MRI exams of diagnosed breast cancer patients used to be controversial: Did they aid surgical planning better than the combination of mammography and breast ultrasound? Or did their findings cause overtreatment, specifically mastectomy, when breast-conservation surgery would have sufficed? New research has now settled the issue.

The real-world analysis of nearly 6,000 patients having surgery as the primary treatment for biopsy-proven breast cancer in 27 centres in Europe, Australia, the United Kingdom, and the United States showed that breast MRIs did not cause overtreatment. And as study data continues to be analysed, it confirms that when breast MRI is ordered, primarily by radiologists and/or breast surgeons, it positively impacts the quality of staging and choice of surgical treatment.

Although data from the MIPA (Multicenter International Prospective Analysis) observational study revealed that 9% more mastectomies were performed than initially planned by surgeons for patients who had a bilateral contrast-enhanced breast MRI, this subgroup of women were at higher risk than those who just had conventional breast imaging. In fact, for a handful of women, breast MRI confirmed the feasibility of breast conservation surgery instead of planned mastectomy.

Screening lead to increased mastectomy rate
Initiated by the European Network for the Assessment of Imaging in Medicine, and funded with an un-

conditional research grant from Bayer AG, the study recruited 7,245 patients ages 18 to 80. Of these, the data of outcomes for 5,896 were able to be analysed. Based on the recommendations of their physicians and the protocols of their treatment centres, 53.1% had a breast MRI supplementing conventional imaging. In addition to a larger number of women in the breast MRI cohort being younger and pre-menopausal, 17% more had dense breasts, 15% more had tumours larger than 20 cm, and 9% more had a higher rate of invasive lobular histology than the conventional imaging group.

Mastectomy had already been planned for 547 (22.4%) prior to the breast MRI. Post MRI screening, this number increased to 791 women (32.4%), and ultimately 773 were performed based on surgical recommendation.

An additional 50 women self-opted to have a mastectomy. By comparison, only 398 (14.4%) of women had planned mastectomies based on conventional imaging findings. This ultimately increased to 432 women, with 19 of this group electing to have a mastectomy instead of recommended breast conservation surgery.

'MRI did not alter the surgical planning based on conventional imaging in 84.5% of cases,' wrote principal investigator Prof. Francesco Sardanelli, MD, of the Università degli Studi di Milano, Italy, and co-researchers in European Radiology.

The surgical planning value of breast MRI is also reflected in reop-

eration statistics. The MRI group had a significantly lower reoperation rate, at 8.5%, compared to 11.7% in the non-MRI group. By itself, this finding has major implications for the welfare of the patients and medical cost savings as well.

Identifying cancers that otherwise may be missed
In a subsequent analysis published in European Radiology, Sardanelli and colleagues compared mastectomy rates and reoperation rates among three groups:

- women for whom breast cancer had already been identified and breast MRI had been ordered for ipsilateral staging, contralateral screening, and surgical intent (79.7%),

- women for whom a diagnostic exam had been ordered, primarily as follow-up to equivocal conventional imaging find-

ings (16.6%),

- and women for whom breast MRI was ordered for breast cancer screening (3.7%).

The screening MRI subgroup proved to be women at the highest risk: younger, with complex cases, larger lesions, the highest rates of small and single-focus cancers, and the highest percentage of familial or personal genetically proven increased risk. The researchers were not surprised that this highest risk subgroup had the highest rate of mastectomies, at 39.5%. By comparison, the rate of mastectomies for the diagnostic group was 24.1%.

Reoperation rates for close or positive margins among the three groups were not significantly different, ranging from 8.2% to 10.5%. However, the difference between the MRI and conventional imaging only groups was. 'These findings

reinforce the fact that breast MRI identifies cancers that may not be seen -- or clearly seen – on mammography and breast ultrasound,' they commented.

Impact on DCIS in a patient matched analysis
The most recent MIPA data-related study, also published in European Radiology, evaluates the influence of preoperative breast MRI on mastectomy and reoperation rates in patients with pure unilateral ductal carcinoma in situ (DCIS). Six hundred eighteen patients selected from a group of 1005 with biopsy-confirmed DCIS were equally matched 1:1 to eliminate bias. Three hundred nine had breast MRIs and 309 did not.

The findings again confirmed breast MRI has a positive impact on surgical outcomes. Although the overall mastectomy rate was 23.3% in the group of patients who had breast MRI exams prior to surgery compared to 17.8% in the conventional imaging group, the reoperation rate of the MRI group was dramatically lower. At 23.3%, the reoperation rate of the conventional imaging group was more than double the 10% of the MRI group. 'The increase in the overall mastectomy rate engendered by preoperative MRI is less than half the corresponding reduction in reoperation rates,' the authors advise. ◼

Report: Cynthia E Keen

Using low-frequency electromagnetic fields

Detecting breast cancer in two minutes

The innovative technology aims to be more accurate as well as cheaper to provide than today's most common diagnostic tools such as X-ray mammography, ultrasound and magnetic resonance imaging (MRI).

Test runs have been completed in two minutes and used less energy than a smartphone. It would also be safer than X-rays, which expose patients to high-level radiation that can damage DNA and cause cancer. 'We are coming very close to providing a method for breast cancer detection at an early stage that is inexpensive and harmless for women,' said Dr Omar Ramahi, lead researcher and a professor in Waterloo's Department of Electrical and Computer Engineering. 'We're

trying to make a serious contribution to women's health and create an alternative that is clinically and commercially viable.'

Ramahi began exploring new ways to detect early-stage breast cancer in 2001 and, for the past five years, has been studying the potential of low-frequency electromagnetic waves. Ramahi and his research team made what he described as "a big discovery," namely that very low electro-magnetic frequencies "travel in straight lines."

The diagnostic device they created somewhat mimics X-ray mammography but without its drawbacks. In place of X-rays, low-frequency electromagnetic energy is emitted from an antenna, like the

one found in a smartphone. Once the energy penetrates a patient's breasts, it is picked up by a meta-surface, or circuit board, consisting of end-to-end pixels, each pixel acting as a receiver. The AI then interprets the pictures coming from the circuit board, removing the need for a human technician to review the results. The technology can locate the size and location of a tumour, even in breasts with dense tissue, something current diagnostic systems can miss.

Ramahi has tested his system on breast phantoms. Next steps are to develop a system that can be tested on human subjects. ◼

Source: University of Waterloo

Nanotechnology and ultrasound

Innovative solution: Reducing over-treatment of rectal cancer

An innovative solution based on nanotechnology and ultrasound that could prevent over-treatment of patients with rectal cancer. The magnetomotive ultrasound system uses nanotechnology for reliable diagnosis of any spread of rectal cancer to nearby lymph nodes.
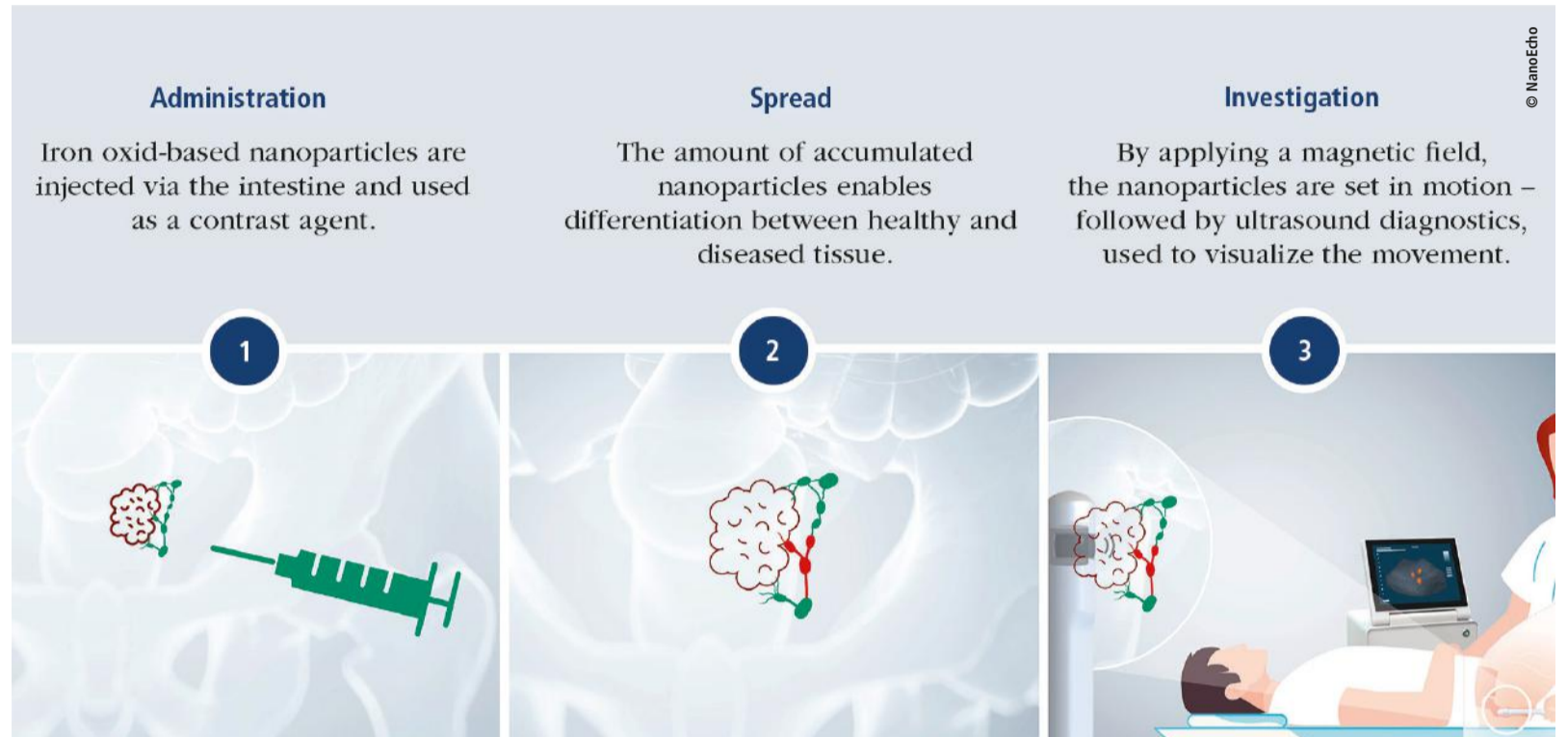
The system is designed to address indications of unnecessary surgery, caused by the current lack of a definitive method to identify this spread. With high resolution imagery harnessed to offer a better assessment of rectal cancer in patients, iron oxide-based nanoparticles injected locally around the tumour are utilized as a contrast agent to enable a probe to differentiate between healthy and unhealthy tissue in the rectum.

At the Medica trade fair in Dusseldorf, Kristina Hallström outlined the benefits benefits of the system developed by NanoEcho, a Swedish company founded by a research group at the Department of Biomedical Engineering at Lund University. In her presentation, the NanoEcho marketing director highlighted how the company has developed the diagnostic rectal cancer technology.

600,000 people are diagnosed with rectal cancer

The focus is specifically on rectal cancer, which makes up a third of the colorectal cancer group – the second most common type of cancer after breast cancer for women and prostate cancer for men. Hallström said: 'Every year, 600,000 people are diagnosed with rectal cancer globally, with that expected to increase due to ageing populations and western lifestyle. Early detection and reliable diagnostics are crucial. In rectal cancer, it is important to identify whether there is a spread of cancer cells to the nearby lymph nodes, especially in the early stages.'

However, she pointed to research suggesting that many patients suffering rectal cancer are overtreated. 'To ensure all cancer cells are removed, most patients diagnosed with early rectal cancer undergo a

Administration

Iron oxid-based nanoparticles are injected via the intestine and used as a contrast agent.

1

Spread

The amount of accumulated nanoparticles enables differentiation between healthy and diseased tissue.

2

Investigation

By applying a magnetic field, the nanoparticles are set in motion – followed by ultrasound diagnostics, used to visualize the movement.

3

© NanoEcho

major surgical procedure resulting in permanent stomia,' continued Hallström. 'But research has shown that this was unnecessary in nine cases out of 10, because in those cases there was no cancer spread to nearby lymph nodes and a

healthy and diseased tissue. The injected iron oxide-based nanoparticles it uses are super-lymphatic, are the right size to go into the lymph system, and are spread differently depending on whether the tissue is healthy or unhealthy.

risk of incontinence, as well as freeing up healthcare resources. 'NanoEcho addresses a growing unmet medical need to provide correct diagnosis of rectal cancer spread to nearby lymph nodes,' added Hallström. 'This ensures rec-

uled for 2024 and an aim to place the product on the market in 2026.

Report: Mark Nicholls

NanoEcho by the bed. © Nano Echo

minor intervention would have sufficed.' NanoEcho's solution aims to reduce this unnecessary overtreatment by differentiating between

When a probe with an integrated rotating magnet is inserted into the rectum, applying a magnetic field, the nanoparticles start to move.

Hallström said: 'Ultrasound is used to visualise the movement of the nanoparticles on the screen in real time. The amount of accumulated nanoparticles enables differentiation between healthy and diseased tissue.'

Individually adapted, effective, and less risky treatment

Better diagnostics, she continued, mean the patient can receive an individually adapted, effective, and less risky treatment. 'It is especially important for patients with stage 1 or 2 rectal cancer, and this is a group that will increase due to ongoing implementation of screening.' The aim is to avoid patients undergoing major surgery and the

tal cancer patients receive a correct diagnosis and an optimal individualized treatment, which would free-up resources, reduce costs for society and increase quality of life for the patients.'

The system developed by Nano Echo and its partners includes advanced software, an ultrasound device with an integrated magnet, with the nanoparticle developed by an external company.

While the focus is on rectal cancer diagnostics, the company believes the technology has other potential applications such as the detection of prostate cancer, the identification of plaques in blood vessels or as a tool for stem cell therapies.

The system is now under the verification and validation process with further clinical assessment sched-
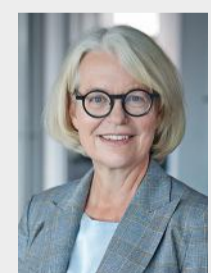
Kristina Hallström

Kristina Hallström leads the marketing and communication efforts along with quality and regulatory affairs at NanoEcho. An experienced professional at the intersection between healthcare and business with a Master of Business Administration from Lund University and a background as a physiotherapist, she combined a focus on both clinical aspects and business development. Her career spans large international MedTech companies, as well as start-up companies with innovative products.

Diagnostic imaging collaboration

Canon Medical and Olympus team up for endoscopic ultrasound

Two major players in diagnostic imaging combine their expertise in the field of endoscopic ultrasound (EUS): At a press conference in Tokyo, Japan, Canon Medical Systems Corporation and Olympus Corporation announced their collaboration agreement, which includes introduction of a new, jointly developed system that takes advantage of both companies' experience in endoscopy and sonography.

As part of the collaboration, Canon Medical will develop and manufacture diagnostic ultrasound systems for EUS procedures, while Olympus will perform the sales and marketing efforts. With the traditional handshake, Frank Drewalowski, Head of the Endoscopic Solutions Division at Olympus, and Toshio Takiguri, President and CEO of Canon Medical, affirmed the agreement. Both expressed their enthusiasm for the collaboration, highlighting the two companies' rich history of technological innovation in the respective fields of endoscopy and diagnostic ultrasound. In this new constellation, both manufacturers aim to expand their business in diagnostic imaging markets, including Europe.

Image quality to rival CT and MR imaging

In a first demonstration of the cooperation, the companies unveiled a combined setup of Canon's Aplio i800 diagnostic ultrasound system

Frank Drewalowski, Executive Officer and Endoscopic Solutions Division Head, Olympus Corporation (left) and Toshio Takiguchi, President and CEO, Canon Medical Systems Corporation (right) at the global press conference in Tokyo. © Olympus

for EUS and Olympus' Ultrasound Endoscope. Equipped with Canon's proprietary imaging enhancement features such as differential tissue harmonic imaging (D-THI), superb micro-vascular imaging (SMI), shear-wave elastography (SWE) and attenuation imaging (ATI), the system can be used as a tool for a wide range of imaging applications.

Taking full advantage of the technology, the combined EUS setup is designed to provide image resolution and quality compared to CT

and MRI, Takiguri said. With the new device, the companies hope to enhance diagnostic efficiency, for example in the detection of smaller lesions in pancreatic cancer and bring benefits in other pancreatobiliary diseases, which affect more than 60 million patients worldwide, added Drewalowski.

Endoscopic ultrasound – which combines a sonography probe to the tip of an endoscope to assess diseases of the gastrointestinal tract and nearby organs, such as the liver, pancreas and gallbladder

– has a range of diagnostic applications, said Hironobu Kawano, Endoscopic Solutions Division Head at Olympus. However, the modality is often considered tricky, requiring a high level of expertise in sonography. The enhanced imaging features in the new EUS system allow for more consistent image quality and improve access for difficult-to-reach areas of the body, he pointed out.

Going into more detail on the technology, Akihiro Sano, General Manager of the Ultrasound Systems

Division at Canon Medical Systems, showcased the strengths of the embedded features: D-THI provides clearer images at greater depths, while SMI shows more and thinner vessels compared with conventional Doppler ultrasound, enabling a better visualisation of blood flow. Further, ATI is used to quantify and color-code changes in the tissue composition (e.g., fat content of the liver).

Coming to European markets this summer

'We have a long history in diagnostic ultrasound systems and have developed unique technologies that contribute to the early detection of diseases in cooperation with doctors around the world,' Takiguri said. 'We are very pleased to collaborate with Olympus, a leading endoscope manufacturer, in the EUS field, which we have not been able to cover adequately until now, to deliver superior solutions to more patients.'

Drewalowski added: 'In the field of EUS, diagnostic ultrasound systems are very important, and we are pleased to have a cooperative relationship with Canon Medical, which has advanced ultrasound imaging technology.'

Introduction of the EUS system to European and Japanese markets is planned for June 2024, Takiguchi said, while the timeline for US markets is still pending. (WB) ■

Study examines diagnostic quality

Special probes for obese patients

A new study at the University of Leipzig Medical Center with support from the Helmholtz Institute for Metabolic, Obesity and Vascular Research (HI-MAG) shows how obesity in patients leads to decreased image quality of ultrasound scans of the liver and kidneys.

Ultrasound of the abdominal organs is a central diagnostic tool and is recommended as the first-line approach for many medical conditions. However, the accuracy of this method is usually limited in obese individuals because the imaging quality of anatomical structures is impaired. To date, the degree of obesity at which ultrasound diagnostics are no longer suffi-

ciently precise has not been sufficiently researched.

In the clinical study, researchers found that the quality of ultrasound scans of the liver and kidneys was significantly lower in obese patients. 'The results showed that as the body mass index of the patients increased, the image quality of the ultrasound decreased. It also became clear that modern probes with matrix technology improve the quality of ultrasound imaging,' says Professor Thomas Karlas, head of the study. The matrix probes have an improved transmitting and receiving performance and therefore achieve greater penetration depth into the tissue. This allows for better diag-

nostic accuracy in high-risk patients. The performance of matrix probes in obese individuals has not yet been scientifically validated.

The current data show that these relatively expensive special probes for ultrasound equipment can provide significant added value. The 40 participants in the study underwent a highly standardised ultrasound examination of the abdomen with three different probes. The liver and right kidney were examined in people with varying degrees of obesity, and the quality of the ultrasound imaging was scored.

Source: Leipzig University

Study

First test for the early detection of head and neck cancer being developed

Most head and neck tumours are discovered in late due in part to the fact that there is no established method for early detection. To close this gap, a team at oncgnostics, a biotechnology company based in Jena, Germany, is participating in a study which aims to develop an early detection test.

In Germany alone, every year 17,000 people are diagnosed with head and neck cancer, i.e. malignant tumours of the oral cavity, throat, larynx, nasal cavity, paranasal sinuses and outer neck, especially the thyroid gland. Often, tumours develop from so-called leukoplakia, conspicuous white patches in the mouth and throat. Since they do not cause any symptoms, however, very few patients consult a doctor, explains Dr. Alfred Hansel, biologist and CEO of oncgnostics, and adds that 'most patients see a doctor only when they have severe difficulties swallowing. By then the tumor is often advanced and requires chemo-

© Eberhard Schorr, oncgnostics

therapy or surgery – depending on the location and type of tumor. At that point, cure rates are low. Therefore, we would like to develop a test that detects tumours early.'

Study in five centers
To achieve this goal, the biotechnology company has launched a

broad study in five centres. In a first step, a liquid biopsy is performed in patients diagnosed with a head and neck cancer prior to treatment in order to detect DNA methylation markers in saliva. If this is successful, further saliva or swab samples are taken during follow-up to monitor the markers and

assess relapses. 'Going forward, we might be able to search for precisely these biomarkers in patients with an increased cancer risk, for example patients with leukoplakia,' Hansel is confident. First test kits could become commercially available after the conclusion of the study in mid-2026.

According to Hansel, screening the entire population is neither realistic nor necessary. Instead, he supports the idea of a standardized screening programme for groups at risk, i.e. smokers over 50 years of age and patients with an HPV infection. Similar to a Covid-19 test, Hansel says, the people in these groups could take the saliva samples themselves and send them to a laboratory. 'To the best of our knowledge,' he adds, 'this process would be unique worldwide.' ∎

Report: Sonja Buske

© Sonja Buske

Alfred Hansel

Dr Alfred Hansel is CEO of oncgnostics GmbH. After his doctorate in in molecular microbiology, he gained many years of experience in the field of project management through work at domestic and foreign university institutions and was in the industry in the areas of product development product development, sales and marketing.
The spin-off of oncgnostics GmbH is based on his scientific work in the functional area of gynaecological molecular biology" as well as a project group led by him.

Large-scale international study

Head and neck cancer in older patients: Increasing the chance of survival

Should patients over the age of 70 with head and neck cancer receive aggressive combined radiotherapy and chemotherapy? This is a controversial issue among patients, their families and health professionals. A large-scale international study involving Leipzig University Hospital proves the effectiveness of this combined treatment in older patients.

As a result of demographic change, the proportion of older oncology patients is rising sharply. Compared to younger patients, cancer treatment is highly individualised due to more frequent and sometimes severe comorbidities, increasing age-related infirmities and reduced physical fitness.

Considering the side effects of treatment
It is also important to consider the side effects of treatment, which can affect quality of life. The standard treatment for head and neck cancer is either surgical removal of the tumour followed by radiotherapy, or organ-preserving radiotherapy in combination with chemotherapy. The use of concomitant chemotherapy is particularly controversial because of the physical strain and side effects in older patients. So far, there is only a limited amount of trial data on the best treatment.

Combining chemotherapy and radiotherapy is associated with a better chance of survival
An international study involving twelve university hospitals in Europe and the US has investigated the extent to which older head and neck cancer patients benefit from a combination of radiotherapy and chemotherapy on the one hand, or an alternative drug therapy with an antibody against a growth factor receptor (EGFR) on the other. This clinical study shows that adding chemotherapy to radiotherapy is associated with a better chance of survival compared to radiotherapy alone. This benefit was particularly pronounced in patients between 65 and 79 years of age and in those with good general health and few comorbidities. 'In particular, fit older patients with minor comorbidities should not be denied this effective therapy simply because of their advanced age," explains study leader Professor Nils Nicolay: "In contrast, radiotherapy combined with taking the growth factor antibody showed no survival benefit compared to radiotherapy alone.'

To find out, the researchers analysed data from 1,044 older patients with head and neck squamous cell carcinoma of the oral cavity, pharynx or larynx who were treated with radiotherapy and, in some cases, in combination with a

drug between 2005 and 2019. Led by Leipzig University Hospital, a prospective international registry for older patients diagnosed with head and neck cancer is currently being set up. More than 20 centres from Europe, the US and Australia have already expressed an interest in participating.

Recording parameters in addition to oncological data
In addition to oncological data, the registry will record other parameters, including a comprehensive geriatric assessment, data on health-related quality of life, and the frequency of 'decision regret', i.e. the regret of the patient in choosing a particular therapy. "In collaboration with other international research groups, additional modelling of the biological parameters will be carried out to better predict which older patients would benefit from combined radiotherapy and chemotherapy," explains Dr Alexander Rühle, lead author and co-leader of the study. "Tools will also be developed to facilitate joint therapy decisions based on individual patient data," adds Professor Nicolay.

Professor Nils Nicolay and Dr Alexander Rühle started the study at the University of Freiburg Medical Center and completed it when they moved to Leipzig. Nicolay has been
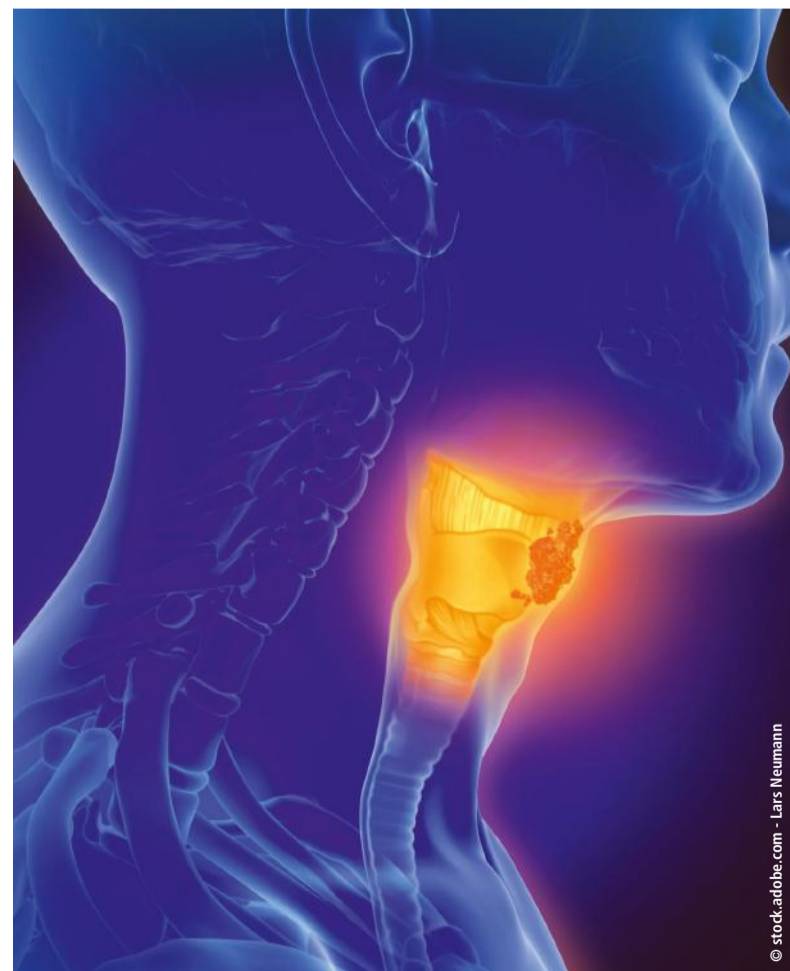
© stock.adobe.com - Lars Neumann

Professor of Radiotherapy and Radiooncology at Leipzig University's Faculty of Medicine since September 2022. The appointment also entails directing the Depart-

ment of Radiooncology at Leipzig University Hospital. ∎

Source: Leipzig University

Improving quality and efficiency

Preparing for artificial intelligence in clinical laboratories

Some year in this decade, AI tools will become ubiquitous within clinical laboratories. AI has the potential to increase the accuracy of laboratory testing and improve the quality and efficiency of operations and service of testing labs.

Clinical laboratorians must prepare to help lead this initiative, for their knowledge will be the key to successful implementation. They need to learn how AI algorithms are developed and validated, how to justify and analyze impact from the perspective of clinical laboratory medicine, and how to implement them to best benefit the patient and the hospital. Several scientific sessions at the 2023 Association for Diagnostics and Laboratory Medicine (formerly the AACC) Annual Scientific Meeting focused on this topic.

AI is in its naissance in medical lab development, and this was very apparent in the technical exhibition of the ADLM/AACC meeting. David McClintock, MD, Chair of the Division of Computational Pathology and AI in the Department of Laboratory Medicine and Pathology of Mayo Clinic, pointed out that only 30 out of the 941 exhibitors at the meeting included the terms "artificial intelligence" (AI) and/or "machine learning" (ML) in their product/company descriptions on the AACC exhibitor website.

Ten companies included 'analytics' in their description, but only four were separate analytics-based companies selling clinical lab AI/ML software. 'This is an emerging space, just as radiology PACS was 30 years ago,' McClintock said. 'Now is the time to learn about it or perhaps even start to developing models that can benefit your lab.'

Uses of AI/ML in the lab
There are numerous ways that both simple and complex AI tools can aid a clinical laboratory. These include:

- Automated spectroscopic data analysis and disease detection; multivariate analysis of disease conditions; test interpretation;

- Digital image analysis for microbiology, haematopathology, immunology, and forensics;

- Data entry automation for specific tasks and processes;

- Creating standardised reports for lab test results and automated entry into Laboratory Information System (LIS);

- Minimising laboratory testing for inappropriate test orders, predicting test results from other available data on patient chart, and reducing redundancy and duplication of lab tests, based on prior type and date of tests already performed;
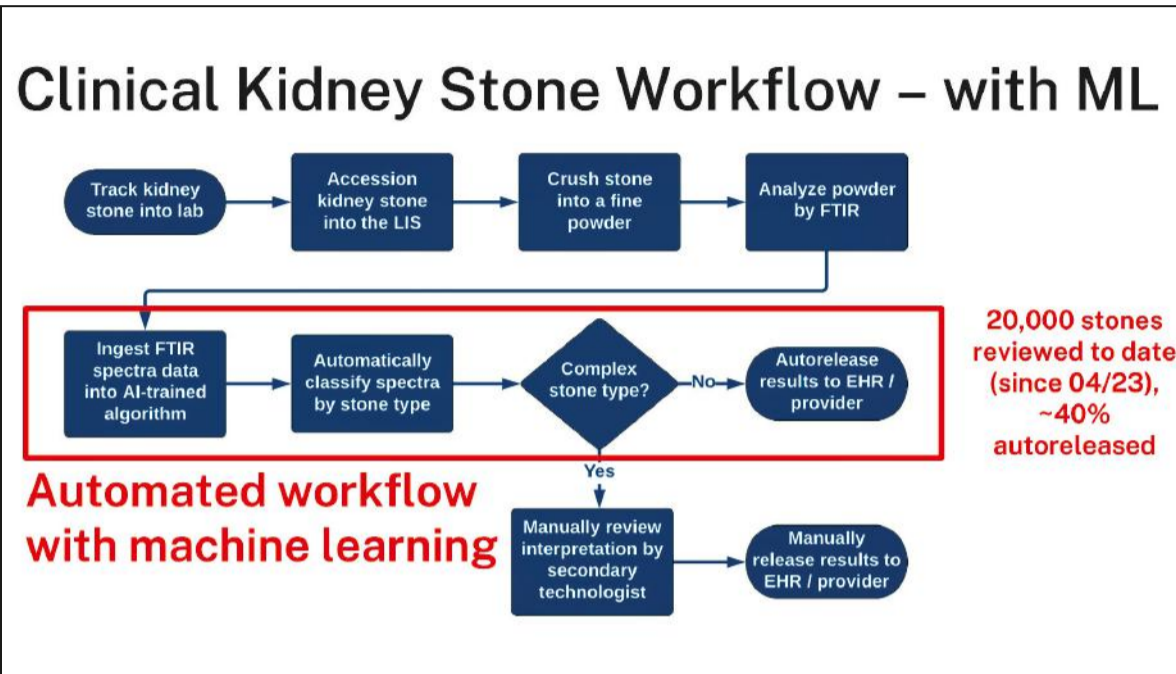
- Data analytics for laboratory operations planning, such as predicting volume workflow, employee staffing requirements, etc.;

- Identifying and alerting for abnormal test results;

- Auto-verification of test results for quality control.

Automating spectral analysis for kidney stones and fecal analysis
Mayo Clinic spent six years developing an AI model to automate the spectral analysis of stones passed by patients. It is based on the classification of 708 unique kidney stone types. In the first 90 days of implementation, commencing April 2023, 20,000 stones have been reviewed, 40% of which were newly able to be bulk auto-released to patients' medical records (EHR).

Before the model was implemented, the conventional workflow began with cleaning and drying the stone, after which it was ground into a fine powder and manually analyzed with FTIR spectroscopy. A technician manually entered the results into a LIS, followed by a second technician reviewing the interpretation. Only then are results uploaded to a patient's electronic medical record (EHR).

AI tool to automate multiple processes
After evaluating how AI could improve workflow, reduce costs, and increase efficiency, the Kidney Stone lab at Mayo Clinic Rochester, in conjunction with an AI team from Mayo Clinic Florida, created an AI tool to automate multiple processes following FTIR spectra analysis.

The AI model was trained on 70,000 kidney stone spectra and validated with 16,491 kidney stone spectra. Quality assurance required 81,517 kidney stone spectra. 'This is a lot of data, which took a lot of

work, and a lot of computing time,' commented McClintock. 'But now the process is automated and is achieving our expectations. If a stone is not complex, the AI system classifies it and then the information is automatically entered into the LIS and subsequently released to the patient's EHR. When it identifies a stone as complex, the results produced are manually flagged for review by a technician. The lab is now saving a lot of time, which equates to tangible cost savings and opportunities for laboratory staff work reduction/redirection.'

Other applications of AI in the clinical labs also exist, such as commercially developed AI tools in clinical microbiology to detect fecal ova and parasites (O&P). For most labs, up to 95% of O&P cases can be negative, and thus the process of reading slides can be monotonous. The investigational AI-assisted screening tool (Techcyte, Orem, UT) uses a convolutional neural network to identify and count parasite cysts and trophozoites, yeast, and red and white blood cells and groups them by class.

Techcyte claims the tool is five times more sensitive than manual examination, with a sensitivity of 98.9%. It produces findings within 30 seconds instead of the average five minutes, automatically uploading negative findings to a LIS. Positive samples are flagged for technologist review and assessment. At Mayo Clinic, this test has just been implemented, with initial impressions positive by laboratory staff who can now remotely review slides, improving employee experience.

What clinical lab managers need to think about
'Don't get enamoured with AI for your lab,' McClintock cautioned. 'Always remember a clinical lab's primary objective: to deliver the right information to the right per-

son at the right place and right time in the right way. No system today can integrate all potential outputs of AI tools,' he emphasized. 'LIS, EHR, and middleware solutions take considerable effort to integrate with any AI tool without encumbering the pathologist, laboratorian, or clinician. For starters, you need to think about data governance, data pipelines, regulatory guidelines, ethical review, custom programming and coding, computational computing power, either locally or in the cloud, cybersecurity, and risk management.

'Don't forget the cost and availability of AI maintenance, support and quality control, which all require new IT support skills. There are also AI specific tools, such as algorithm drift. And then, in the end, will the AI tool save you enough money or at some point be reimbursable so that it can pay for itself?'

Understanding the barriers and challenges
Experts recommend that lab managers need to focus on generating clinical evidence for AI benefits and understand the barriers and challenges to implementation when they select a tool. New training on AI is essential. In general, experts recommend implementing the new tool while still keeping the existing system functioning, to give practitioners time to learn and get comfortable with AI while maintaining the status quo as back-up.

McClintock also described a new framework for clinical AI life cycle implementation, from idea generation to final validation, go-live, and system maintenance. By adopting a similar AI lifecycle, he encouraged attendees to embrace the potential of AI in their labs.

Co-presenter Christopher Lee Williams, MD, Assistant Professor of Pathology at the University of Oklahoma Health Sciences Center,

concurs. 'Will AI be replacing staff in labs?' he asked rhetorically. 'Probably not. The practice of laboratory medicine has been constantly evolving, often due to increasing automation. I think that AI will be another tool in our tool bag, to aid in efficiency and quality control. With a steady increase in an aging population in the United States, we are going to need all the help we can get.' ∎

Report: Cynthia E Keen

Mayo Clinic clinical kidney stone workflow with machine learning. © Dr. David McClintock, Mayo Clinic

Christopher Lee Williams

Christopher Lee Williams, MD, is the Director of Informatics in the Department of Pathology at the University of Oklahoma Health Sciences Center in Oklahoma City, where he also serves as an Assistant Professor Dr Williams' current research interests include how to operationalise AI tools for analysis and reporting in the laboratory setting, and in optimizing UI/UX design for laboratory workflows.

David McClintock

David McClintock, MD, is the Chair of the Division of Computational Pathology and Artificial Intelligence within the Department of Laboratory Medicine and Pathology at Mayo Clinic in Rochester. His primary clinical interests include clinical informatics, laboratory workflow optimisation, digital pathology implementation, analytics, and clinical ML/AI model deployment. His research interests include understanding the role and effects of digital pathology within the clinical laboratories and the use of AI and ML for improved diagnostics, more efficient workflows, and better patient outcomes.

Pros and cons of diagnostic techniques

Liquid biopsy vs. tissue biopsy: Getting the best of both worlds

Tissue biopsy and liquid biopsy can increasingly be used as complementary or alternative approaches, with advantages and limitations to each. While speakers at the recent 35th European Congress of Pathology in Dublin were quick to highlight that liquid biopsy was not about to replace tissue biopsy, the focus looked at the benefits and challenges of each through the lens of four expert speakers.

For his presentation, Professor Paul Hofman focused on the advantages and limitations of liquid biopsy versus tissue biopsy in thoracic oncology. In looking at how both biopsy techniques can be complementary, the Professor of Pathology and Head of the Laboratory of Clinical and Experimental Pathology at the Pasteur Hospital and Director of the IHU RespirERA, Nice, examined the landscape in thoracic oncology therapeutic decision making. Hofman further explored emerging biomarkers and molecular testing in thoracic oncology, provided insights on when and how to use tissue biopsy and liquid biopsy, and outlined recent developments of cf-DNA testing.

With more and more targeted genome alterations in thoracic cancer, looking for disease is a growing challenge, Hofman said. He emphasised the need to use NGS (next-generation sequencing) to address this. 'We also need to consider what is not targeted; there is at least 40% of patients in Western countries without any genomic alteration with an associated drug, which is much too high.' He under-

lined the importance of following ESMO (European Society for Medical Oncology) recommendations and guidelines but also noted that with some differences in US guidelines, there was a pressing need for global harmonization.

Emerging biomarkers call for complimentary approach
The benefits of using both liquid and tissue biopsy become evident in the context of emerging biomarkers, Hofman pointed out. Some of these markers are not detectable on liquid biopsy and may only be detected on tissue biopsy. 'This is particularly true for an increased number of proteins, including some targets of antibody drug conjugates, which can be detectable and quantified only on tissue biopsy.'

With future and current biomarkers for non-small cell lung cancers (NSCLC), he advocated seeing tissue and liquid biopsies as complementary. 'For our patients, we need to be sure about the right sample, so this is why now we need to think about the integration of liquid biopsy. Because sometimes it is a complementary approach but not an alternative approach if tissue biopsy is not available.' While he pointed out that in the US, liquid biopsy was a first line approach, he suggested Europe was not yet at that stage.

Mix and match to suit clinical needs
When dealing with lung cancer and the use of small tissue specimens, he felt blood specimens should be integrated into the process. 'By tissue biopsy, we can see some mechanisms of resistance
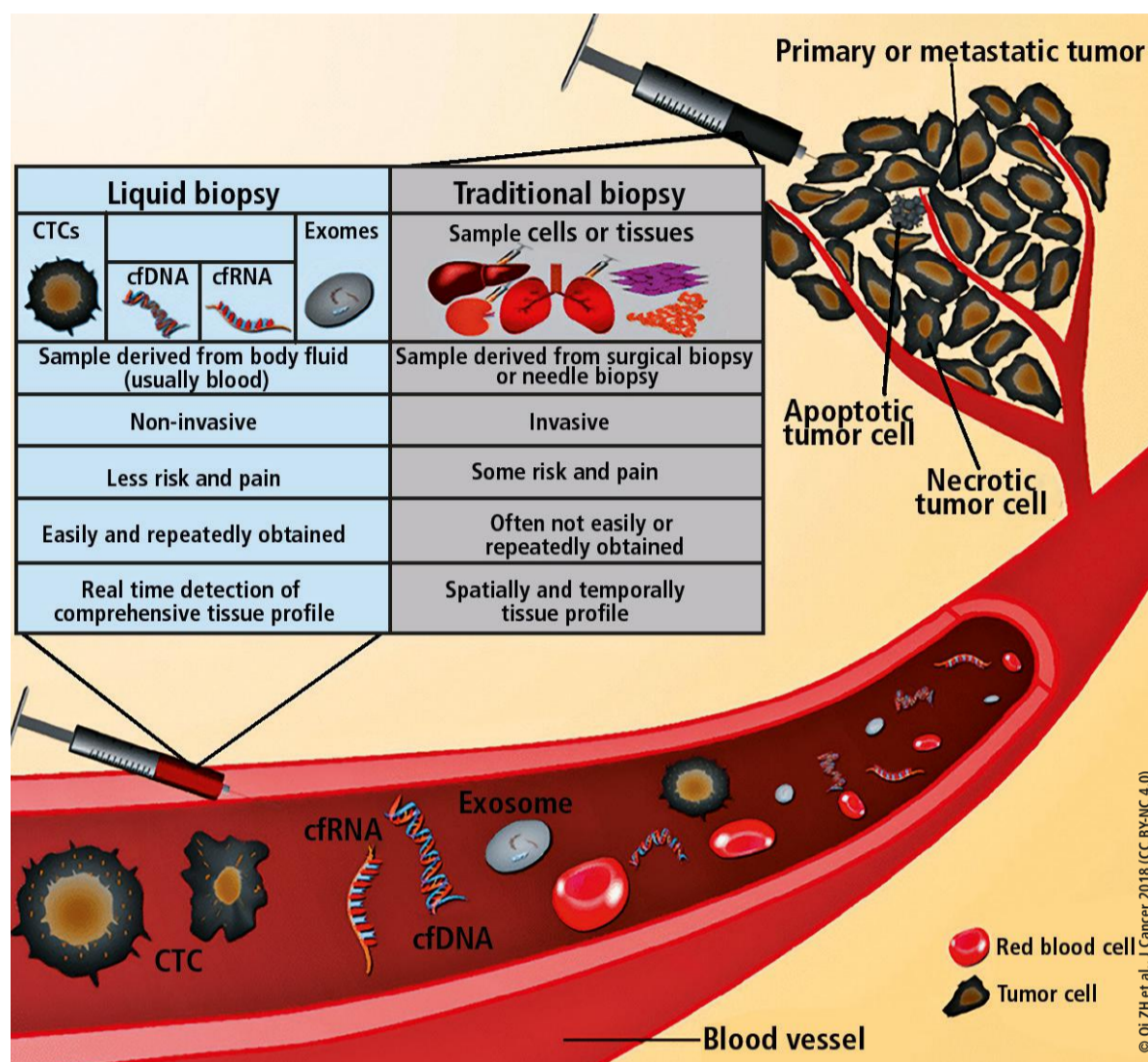
that we cannot see in liquid biopsy. For example, we know that expressions of some proteins are only on the tissue. 'In tissue biopsy, gene amplification and detection of large gene deletion is probably higher than in liquid biopsy, but there are advantages of doing liquid biopsy, such as we do not need hospitalisation.'

He further pointed to technical, logistical, and biological issues and limitations that come with both approaches. Liquid biopsy is non-invasive, repeatable, can be done as an outpatient, and is cost effective but with no histological evaluation and cancer diagnosis. Turnaround time for tissue biopsy is always longer, creates the need for hospitalisation and is invasive, but offers histological evaluation, standardisation of workflow and sensitivity for fusions/amplification. 'The best strategy is to match tissue and liquid biopsy at the same time,' said Hofman.

Use cases and challenges in lung cancer
For advanced lung cancer, doing tissue and liquid biopsy provides an opportunity to increase detection of actual genomic alterations and create global molecular portraits of the tumours. This can increase the number of target possibilities, though he pointed out concordance was around 70%. 'If we have negative results on tissue, then we have to look at the liquid biopsy results and vice versa,' he added. Additional challenges for integration of liquid biopsy in tho-

racic oncology include screening and the detection of minimal residual disease and when post-surgery to take the blood sample, but there is still a gap in introducing that into daily practice, the expert reported.

Tissue exhaustion becomes a growing challenge
To avoid tissue exhaustion, he said NGS should be performed in-house as sending samples outside the lab will not be sustainable in the near future.

Against a backdrop of current and emerging biomarkers, Hofman concluded: 'We need to work hand in hand for tissue biopsy and liquid

biopsy because we have more and more biomarkers to look for with less and less tissue, so we need to avoid tissue exhaustion. If there is tissue exhaustion, we can switch rapidly to liquid biopsy.' However, he warned that as the next generation of pathology emerges, there is a need to be aware of false negative results in liquid biopsy. ■

Report: Mark Nicholls

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