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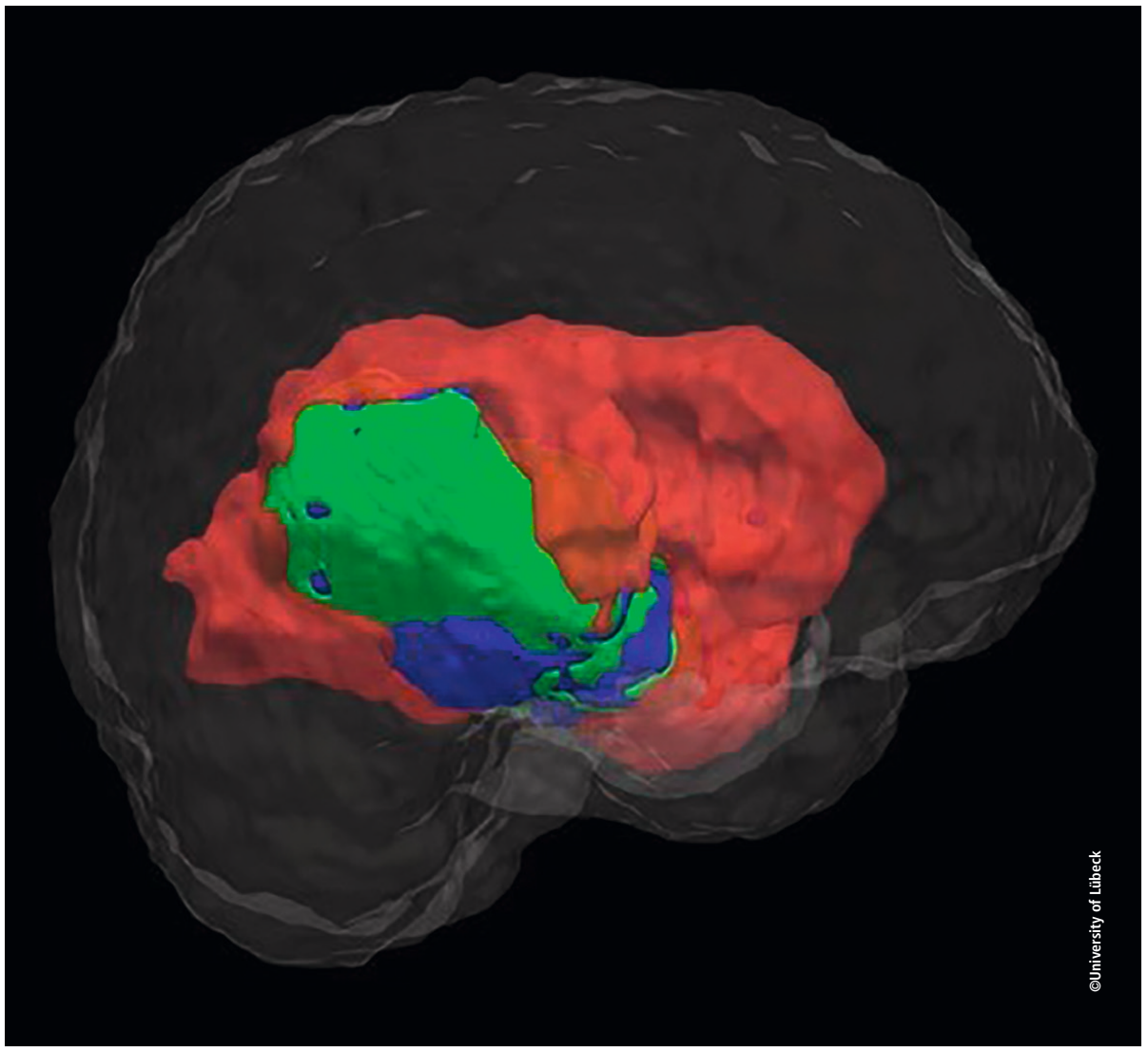
AI imaging

More accuracy in the segmentation of brain tumours

Diagnosing cancer and managing a patient's respective treatment path requires a precise segmentation of the affected anatomical structures. Defining the different semantic objects in an image such as disease patterns, lesions, biomarkers, organs, tissues etc. is at the core of this. Such a segmentation enables radiologists to distinguish the three subcategories of a tumour – the active core, the necrotic disintegrated area and oedemas – among others. A range of medical decisions are based on this classification: e.g., radiologists determine the volume of a tumour, monitor its development, design the concept of a personalised radiation therapy and subsequently administer it. In the realm of surgery, image segmentation is used for planning and navigating operations.



Grün: Peritumorales Edem; Gelb: Gadolinium-verstärkter Tumor

Heinz Handels

Prof Dr Heinz Handels
Director of the Institute of Medical Informatics, University of Lübeck

To best support patients, clinicians need this segmentation to be as accurate as possible. However, segmenting medical images is a key challenge of medical image processing. The Research Department Artificial Intelligence in Medical Image and Signal Processing (AIMedI) at the Lübeck site of the German Research Center for Artificial Intelligence (Deutsches Forschungszentrum für Künstliche Intelligenz or DFKI) has been working on the development of a high-precision three-dimensional viewer software for medical image data. Using AI and deep learning methods, the software analyses medical image data, bio signals along with other patient data and automatically interprets them. In this way, it can delineate pathologically altered image areas and detect diseases.

Prof Dr Heinz Handels, Director of the Institute of Medical Informatics, University of Lübeck, and Head of AIMedI explains: "Our aim is to support clinicians with the classification of cancer tissue of malignant brain tumours such as glioblastoma. This also helps with the volumetric measurement of a brain tumour for which we need to be able to define which pixels form an object."

Annotated medical data in short supply

Methods to measure the volume of tumours already exist, but their accuracy is still wanting. To this end, the research group around Handels, AIMedI, developed a procedure that allows to automatically segment and recognise objects such as tumours at an exact pixel-level in the brain. It uses deep learning methods tailored to image processing, which deliver a higher accuracy of the segmentation. These deep learning methods autonomously learn from training data. To facilitate this, the algorithm requires original images that must be manually marked by an expert to create a so-called annotated image.

This approach has already been successfully used in many areas of public life, such as for the analysis of traffic, where non-specialists perform the annotation of the images. Nevertheless, this is different in the field of medicine where an expert is required to do the annotation. As it takes several hours to annotate a 3D dataset, only few exist: "I reckon that in my research community there is globally only a limited number of such annotated datasets, which are all part of a global initiative. The data is held on central servers so that the images can be accessed from everywhere. This allows to compare generated images to those annotated by experts", says Handels. However, deep learning algorithms deliver more reliable results, the more data is available.

Using U-Nets for optimised results

To overcome the constraints of limited manually annotated training data, scientists in the AIMedI group have trained a U-Net, a convolutional neural network developed for image segmentation. The U-Net architecture is suited to work with fewer (annotated) training images whilst achieving a more precise segmentation. Furthermore, the researchers investigate the safety and possible explanations of the generated results.

The evaluation of the methods and systems developed is still ongoing and done in close cooperation with medical cooperation partners based on practical applications.

The future: Generating annotated synthetic image data

At the heart of this endeavour is the aspiration to generate annotated synthetic brain tumor images to free up experts' time, which they anyhow only unwillingly bestow on annotating 3D datasets. Handels explains: "We aim to generate new data, so-called synthetic image data, where the labeled data is automatically generated, using generated adversarial networks (GANs) or diffusion models." However, this type of network poses its own challenges like its substantial storage requirements.

Furthermore, synthetic data would circumnavigate data protection requirements as mandated per the General Data Protection Regulation. "In our research, we investigate to use only synthetic data for the training of neural networks. This will be of enormous value for research purposes as this data will be freely available", concludes Handels. This is a relatively new research field, and more work is needed. ■

Article: Cornelia Wels-Maug

CONTENTS

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PACS administrators as quality control monitors of algorithms

The “watchdogs” of AI radiology tools

Artificial intelligence (AI) products are starting to demonstrate that they can improve efficiency and quality in medical imaging. Radiology software vendors are rapidly developing AI tools, and government regulatory agencies are starting to clear them for clinical use.

Radiology AI products are a whole new world. So is running them safely and efficiently in production. However, radiology AI quality control “watchdog” tools for monitoring and assessment have not been deployed as rapidly. New skills and resources are needed to use radiology AI tools safely and cost effectively, Raym Geis, MD, told attendees of the Samuel J. Dwyer III Memorial Lecture, the most prestigious event of the 2024 Society for Imaging Informatics in Medicine (SIIM) Annual Meeting.

Avoiding the “Challenger Shuttle moment”

He warned that as radiology AI tools proliferate and begin to automatically communicate with each other, making independent decisions based upon their interactions, they will quickly evolve into highly complex models. These will require sophisticated, quantitative monitoring to prevent human injury, or as Geis calls this, “the Challenger Shuttle moment”. If an incident in which AI tools were to cause harm to many people, clinical medical imaging AI would come to an abrupt halt, pending lengthy investigation.

Geis’ lecture, entitled “Reliability Engineering for Intelligent Medical Imaging Systems”, suggested that radiology Picture Archiving and Communication Systems’ (PACS) administrators are best qualified to perform this role, but will need to learn challenging and sophisticated new skills. He believes SIIM should take the lead in this new initiative, as it is the professional medical society that pioneered radiology PACS development and implementation.

Geis, a radiologist and a radiology informatics specialist, Adjunct Associate Professor of Radiology at National Jewish Health in Denver, Colorado, and Clinical Assistant Professor of Radiology at the University of Colorado School of Medicine, foresees a remarkable new future for SIIM: Leading the experts to make medical imaging AI into reliable, safe, efficient, and cost-effective clinical systems.

‘PACS administrators already do many things that AI will need: installation, monitoring, management, repair and rollback. Radiology lags behind other industries in systems reliability engineering (SRE), but this works for us. We can adopt a lot of what other people in different industries have developed and are using,’ Geis said.

‘SIIM should take the lead to educate current members on the practice and methods of SRE as it applies to our specialized field, to promote and to define the research we need to understand, and to define best practices to operate these AI systems in medical imaging,’ emphasized Geis. ‘SIIM members’ strength is not to build these AI models, but to know how to manage these systems reliably so that there will be no medical catastrophe.’

The inevitable downward drift of AI tools

The challenges are manyfold. ‘The initial one is that there is no way to predict which best AI tool will work over the long haul,’ he noted. ‘AI-modelled behaviour is determined by data. If the training data changes, the model changes. Accuracy will change. A PACS administrator currently doesn’t know which data features are the most critical,’ he explained.

‘What we do know is that any AI tool works better on the data it was trained on than the data it utilizes in a real-world clinical application. Unless the model is trained solely on your data, and even if you never change a tiny thing about how to generate the data, your results will be worse,’ said Geis. ‘The AI tool may work well on some of your exams, but not all. But you won’t know until you try it and then evaluate it.’

‘Even if initially perfect, your AI tool’s results will get worse over time. Usually this is because the input data changes. Your department changes techniques and protocols. The patient population changes. The diseases change. A new scanner has been purchased that produces slightly different data. Who knows what else? You need to be observant through monitoring. All of these changes are ultimately going to happen and your results are going to drift downward. AI tools fail silently, slowly, and subtly.’

Higher stakes

Geis noted that if an AI model used by Google fails, advertisers may lose money. But nobody dies. But in radiology, rigorous monitoring is essential. In his lecture, Geis described the steps to evaluate, adopt, monitor, retrain, and decommission an AI model. He emphasized the importance of understanding and being able to access the data a vendor used to train the model, and the importance of logging versions of both the vendor software model and data set(s) tested. He explained the concept of “banded assessment monitoring”, where specific groups of features are assessed for QC and performance accuracy. Some questions for evaluation include: What is the accuracy level stated by the vendor and how does it compare? Is AI accuracy consistent among imaging locations, different models/vendors of an imaging modality? What is the impact of different radiotherapists performing the exam, or radiologists interpreting it? How does an AI tool interpret atypical exams?

Setting the standards

Geis exhorted SIIM as an organisation to develop model card templates for medical imaging. In other industries, model cards contain model number, use case, architecture, information about training data and how it is evaluated, ethical considerations when the AI tool should not be used, and contact information to enable direct contact with the creators. He urged SIIM to set the standard for vendor AI software tool model cards, and to be the preeminent decider of information needed for monitoring to make AI tools safe and reliable.

‘Monitoring is expensive. It is essential. PACS administrators need to grasp the emerging opportunity to become well paid Reliable Systems Engineers. Compared to other professional organizations, SIIM is positioned develop a Certified Intelligent Imaging Informatics Professional credential.’ He concluded, ‘This is a really exciting time. SIIM needs to grasp the opportunity and rejuvenate, to again become the leader and pioneering medical society of AI in radiology.’ ■

Report: Cynthia E. Keen

Raym Geis

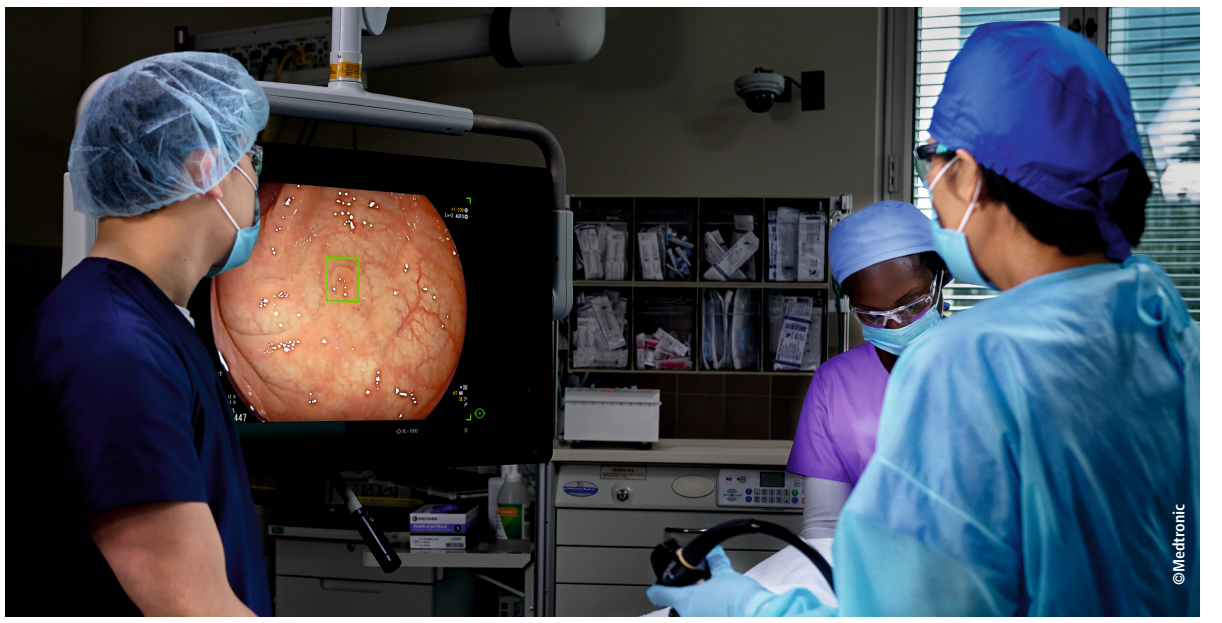
Raym Geis, M.D., a radiologist and imaging informaticist, is Adjunct Associate Professor at National Jewish Health in Denver, CO, and a Clinical Assistant Professor at the University of Colorado School of Medicine in Aurora. His interests include systems engineering for medical imaging AI, as well as radiology data, standards, and ethics of new data science approaches for medical imaging. Geis is a past chair of the Society for Imaging Information in Medicine and former Vice Chair of the American College of Radiology Informatics Committee.

GI Genius enters NAIAD large-scale clinical trial

–Advertorial–

AI making earlier detection of colorectal cancer possible

Early detection is crucial for effective treatment of colorectal cancer, but the initial stages are easily missed during endoscopy screenings. With GI Genius, Medtronic presents an AI-powered tool to help detect precancerous lesions in real-time. In an upcoming large-scale trial, the intelligent endoscopy module will demonstrate its benefit in the clinical context.



The intelligent endoscopy module detects and marks precancerous lesions in real-time

Colorectal cancer is among the most common in developed countries and is responsible for more than 150,000 deaths per year in Europe alone.[1] On the other hand, 90% of patients can recover when the cancer is detected at an early stage.[2] While small benign polyps can start to grow in the colon, they can become adenomas and from that, progress into cancer.

This process can take years, often without symptoms, so early detection is essential. To prevent undetected progression, many countries have established endoscopy screening programmes. However, since the initial polyps may be very small, and the procedure covers a considerable distance of the colon, abnormalities can be easily missed, even by experienced endoscopists. This is further exacerbated by an increasing workload in the specialty.

A second set of eyes – but not a replacement for human skill

To mitigate this problem, GI Genius system acts like a "second set of eyes" to support gastroenterologists during colorectal cancer screening. The system reviews the colonoscopy images, in real time[3] and throughout the procedure, highlights suspected regions that the clinician may use to confirm whether the area contains a lesion. This overlay marker may be accompanied by an additional AI assessment of the area, categorizing it as either adenoma, non-adenoma or no prediction. The final decision remains with the expert endoscopist, but the technology is designed to increase the level of confidence[4] in the optical diagnosis, and, unlike the operator, whose vigilance may deteriorate after several hours of looking at similar images, the AI remains laser-focused on its task, supporting the detection of colorectal polyps of various shapes, size, location and histology.[5,6]

The increased diagnostic confidence can also bring financial benefits. Current practice is to remove almost every suspicious finding from the colon and send it to histopathology for further analysis, which can be time-consuming and a significant cost burden. The international guidelines suggest that a highly accurate optical diagnosis should permit the implementation of cost saving strategies such as resect-and-discard and a diagnose and-leave. AI-assisted polyp characterization with high accuracy could expand the uptake of optical diagnosis, increasing the cost–effectiveness of colonoscopy.[7]

Large-scale clinical study puts AI to the test

GI Genius is the most studied AI system in endoscopy which so far proved its credentials in a series of studies: Research found an increase of adenoma detection rate of 14.4% and approx. 50% reduction in adenoma miss rate when the system was used.[8,9] Especially the detection of smaller lesions (≤ 5 mm) improved significantly when the AI assisted the endoscopists.[8] The system also contributes to maintaining a consistency of care by increasing diagnostic confidence of less experienced examiners, another study found.[10]

Two new major pieces of research are underway to further evaluate GI Genius

COLO-DETECT is a randomised control trial that evaluated whether colonoscopy assisted with the GI Genius improves the detection of abnormalities such as polyps and cancer compared to standard colonoscopy. 2,000 participants, across 11 sites in the UK, have been randomised to receive either GI Genius assisted colonoscopy or standard colonoscopy. The study has found that GI Genius significantly increased the adenoma detection rate and increased sessile serrate polyp detection, overall, it recommends GI Genius to be in used in all colonoscopies.[11]

In addition, a large-scale study which was made possible by the NHS award, is designed to assess the system's diagnostic performance and its impact on endoscopists in a "real-world" clinical setting has kicked off in the UK. The National study of Artificial Intelligence in Adenoma Detection for colonoscopy (NAIAD) is led by King's College London. The trial will be carried out over two years and eventually involve the deployment of 60 AI systems across 20 hospitals in the UK National Health System (NHS) in England. The study is the result of set-up funding from NHS England, which ran a competition to identify and fast-track AI technology into clinical services.[12] "Our NAIAD study is set to explore the use of AI in a 'real world' setting, and how it might influence endoscopists in their day-to-day practice," says Dr Bu Hayee, Consultant Gastroenterologist and Principal Investigator of the study at King's College Hospital.

The use of AI in endoscopies is set to expand as GI genius has the possibility to host multiple real-time applications which will support development and access to these tools. AI in endoscopy has a bright future and has the potential to continue to improve patient outcomes. ■

GI Genius™ intelligent endoscopy system

Indications for use

The GI Genius™ module is a computer-assisted reading tool designed to aid endoscopists in detecting colonic mucosal lesions (such as polyps and adenomas) in real time during standard white-light endoscopy examinations of patients undergoing screening and surveillance endoscopic mucosal evaluations. GI Genius™ computer-assisted detection device is limited for use with standard white-light endoscopy imaging only. This device is not indented to replace clinical decision-making.

Risks

If the device is used outside of Instructions For Use, it could potentially lead to inappropriate diagnostic information being displayed to the user (e.g. to analyze images from an unintended patient population, on images acquired with incompatible imaging hardware or incompatible image acquisition parameters).
Incorrect detection or characterization of lesion(s) may lead to false positive or false negative which may result in incorrect patients' management with possible adverse effects: Unnecessary treatment, unnecessary additional medical imaging and/or unnecessary additional diagnostic workup such as biopsy, complications, including incorrect diagnosis and delay in disease management.
Device failure could lead to the absence of results, delay of results or incorrect results, which could likewise lead to inaccurate patient assessment. In the event of unrecoverable failure, please switch off and revert to Non AI enhanced colonoscopy.

Important: Always refer to the Instructions For Use (IFU) packaged with the product for complete instructions, indications, contraindications, warnings and precautions.

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[1] *Colorectal Cancer burden in EU-27. ECIS Accessed 15th March 2024. Available at: https://ecis.jrc.ec.europa.eu/pdf/Colorectal_cancer_factsheet-Mar_2021.pdf*

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[3] *IFU v2.0.0 GI Genius FINAL*

[4] *Hassan C, Balsamo G, Lorenzetti R, Zullo A, Antonelli G: Artificial Intelligence Allows Leaving-In-Situ Colorectal Polyps; Clinical Gastroenterology and Hepatology 2022; https://doi.org/10.1016/j.cgh.2022.04.045*

[5] *Wu J et al.: Comparison of efficacy of colonoscopy between the morning and afternoon: A systematic review and meta-analysis; Digestive and Liver Disease 2018; https://doi.org/10.1016/j.dld.2018.03.035*

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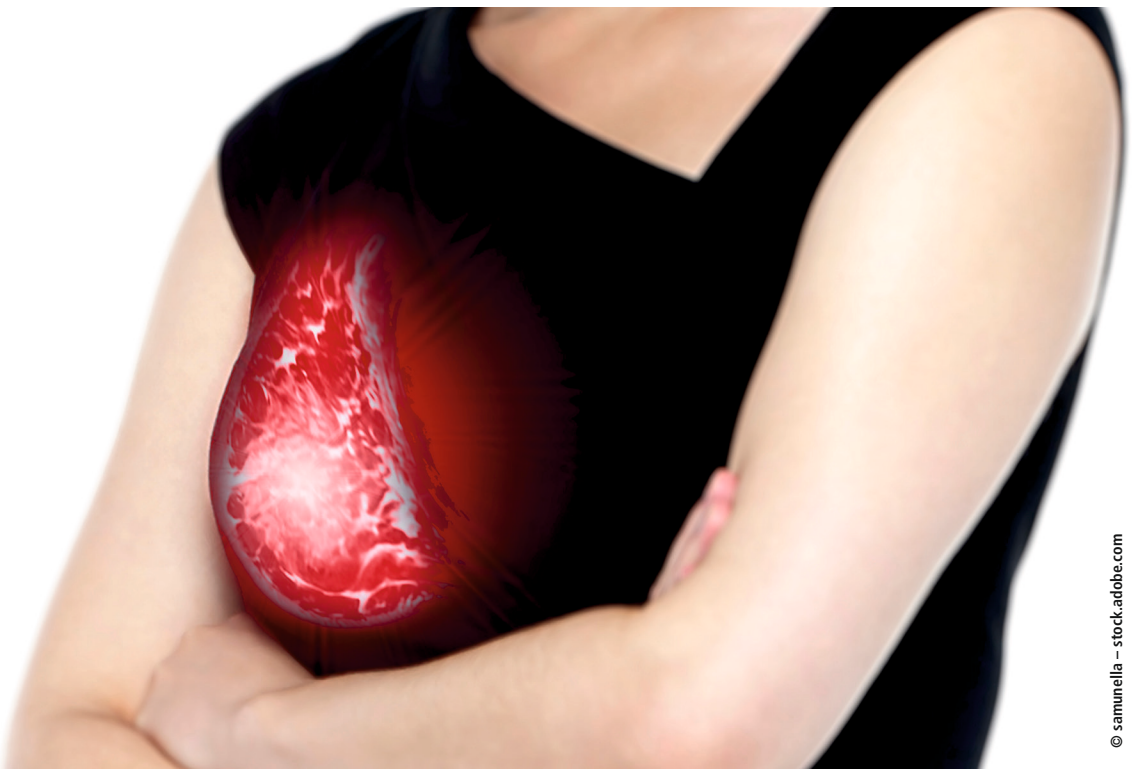
[11] *Seager A et al.: Polyp detection with colonoscopy assisted by the GI Genius artificial intelligence endoscopy module compared with standard colonoscopy in routine colonoscopy practice (COLO-DETECT): a multicentre, open-label, parallel-arm, pragmatic randomised controlled trial; Lancet Gastroenterology & Hepatology 2024; https://doi.org/10.1016/s2468–1253(24)00161–4*

[12] *King's trials AI to aid early detection of bowel cancer; Kings College Hospitals NHS Trust website/news; https://www.kch.nhs.uk/news/kings-trials-ai-to-aid-early-detection-of-bowel-cancer/ Last accessed February 2024*

AI, modern mammography, and more

EUSOBI 2024: Breast imaging breakthroughs

Minimally invasive surgical interventions, innovative imaging and the use of AI: At the EUSOBI congress in Lisbon, experts presented and discussed the latest advances in breast imaging. We spoke with Tanja Brycker, Vice President, Strategic Development, Breast & Skeletal Health and Gynecological Surgical Solutions at Hologic, ahead of the event about new trends in women's health, the company's investment in innovation and education, and what the future of mammography looks like with the rise in AI.



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EH: What are the most significant trends in women's health that you've observed recently, particularly in diagnostic imaging, and how will these be highlighted at the congress?

Tanja Brycker: 'Minimally invasive surgical interventions for breast cancer, artificial intelligence (AI) and contrast-enhanced mammography (CEM) and biopsy (CEBx) are amongst the most significant current trends in women's health. The increasing focus on minimally invasive surgical interventions for breast cancer is driven by the potential to improve patient outcomes and well-being, while also benefiting healthcare facilities through reduced demand on resources and a potential reduction in costs.

'Diagnostic imaging is also no different from other healthcare fields, with AI continuing to be a hot topic, despite having been in use for over a decade. While it is used to manage and clarify diagnostic images, the impact of AI also extends to driving workload efficiencies and the potential to support more personalized medicine.

'Research has already shown that the next generation of deep-learning technology, such as Hologic's Genius AI Detection solution, can help significantly enhance performance, surpassing traditional machine learning Computer-Aided Detection (CAD) algorithms in specificity and overall effectiveness.[1]

'Finally, to mention the growing focus on CEM and CEBx. The synergy between CEM and CEBx has the potential to accelerate cancer diagnosis and workflow efficiencies. CEM pairs 2D and tomosynthesis images, all under one compression, providing anatomical and functional imaging in one exam.[2] The contrast agent accumulates where lesions are forming and growing, enabling radiologists to identify it on the Hologic Selenia Dimensions and 3Dimensions systems. When a breast lesion is identified, CEBx enables radiologists to target and acquire tissue samples with the same contrast agent.

'These three trends are reflective of the growing awareness of how technology can help address radiologist workload, drive workflow efficiencies and improve patient comfort and satisfaction. By delivering technologies that support diagnostic accuracy, we can improve the experience of everyone involved in the breast diagnostic imaging process.'

What did Hologic showcase at the EUSOBI congress?

'Hologic highlighted a series of innovations designed to help radiologists improve workflow efficiency and diagnostic accuracy – from AI solutions designed specifically for breast cancer diagnosis, to expanded breast biopsy solutions. Attendees could visit Hologic's booth at the Lisbon Conference Centre to explore:

- Contrast-enhanced Mammography Solutions that enable clinicians to identify and target lesions that are not visible in 2D or 3D mammography images.
- Hologic's integrated Breast Health AI Software Suite that improves early detection and diagnosis of breast cancer, helps to accelerate workflow, and enables personalized patient care with automated breast density assessment.
- The Brevera Breast Biopsy System, the world's first vacuum-assisted breast biopsy solution that integrates tissue acquisition, real-time imaging and verification, and post-biopsy handling. With the newly launched 7-gauge needle, the system now empowers radiology professionals with enhanced clinical versatility to sample larger volume tissue specimens.

'Additionally, we provided a complete medical education program featuring wide-ranging reading and interventional workshops that provide participants with hands-on experiences. After last year's successful CEM education workshops, Dr. Jacopo Nori, chief of breast imaging at Careggi University Hospital, returned to lead another series on CEM with his team. He was also joined by Dr Julia Camps-Herrero, Head of the Radiology Department at University Hospital de la Ribera in Alzira, Valencia, Spain, to discuss new research about using CEM in managing patients with a personal history of breast cancer.

'We also welcomed Dr. Sarah Friedewald, associate professor of Radiology and chief of breast imaging at Northwestern Memorial Hospital, for an interactive hands-on reading workshop with our 3DQuorum imaging technology. Additionally, Dr. Adnan Duhovic, radiologist at Goldenes Kreuz Private Hospital in Vienna, Austria, shared his experience and learnings for digital breast tomosynthesis (DBT) and the best use of the technology in a nationwide screening programme.'

Why does Hologic specifically invest in education within the diagnostic imaging sector?

'At Hologic, we have a longstanding commitment to investment in clinical education. It is essential for radiologists to understand how to correctly use a system for optimized performance and accuracy. CEM is a great example of this, and of the significant investment we have made in an education strategy that supports adoption of, and confidence in, the technology. Chief of Breast Imaging at Careggi University Hospital, Dr. Jacopo Nori, has been a great advocate for CEM education, helping EUSOBI attendees learn about CEM image interpretation, its use in pre-surgical planning, and other medical education workshops. We're proud to work with Dr. Nori on these sessions to build on last year's activity at our EUSOBI symposium.

'Additionally, we continue to sponsor the EUSOBI Breast Imaging Grant for ten Young EUSOBI Club members to attend the congress as part of our dedication to invest in the future of diagnostic imaging. We believe that future radiologists should have the opportunity to network with their peers and build relationships with industry leaders, while having access to the latest educational opportunities.'

Can you share any partnerships or collaborations your company has engaged in to foster innovation and education in the field, and were any of these highlighted at the event?

'Through our collaboration with BARCO, we are excited to announce the arrival of a new monitor for PACS and breast imaging this year. The Coronis Uniti monitor is the biggest and most equipped display system yet available for general radiology and breast imaging. The full-size, 12-million-pixel screen presents images with crystal-clear precision on a large, flexible, bezel-free image area, providing an uninterrupted view of large images, numerous smaller studies, or various combinations and overlays in any layout. EUSOBI congress attendees were able to see it on BARCO's booth.'

How is AI transforming the field of mammography, and what specific advancements has Hologic made in this area? Was this also showcased at the EUSOBI congress?

'AI is revolutionizing mammography by enhancing early detection and diagnostic accuracy, assisting radiologists with identifying subtle abnormalities with greater confidence. As we look at AI today and into the future, it can help empower clinicians to deliver more personalized patient care.

'As a global leader in breast health, we see AI playing a major future role in breast imaging. Because of this, we continue to make significant investments in research and innovation related to AI. Our suite of AI solutions is reflective of this, and can help radiologists with optimizing their work, including triaging patients, reading images, and planning for surgery. At our booth at EUSOBI, we did showcase this suite of integrated breast health AI solutions for attendees to explore.

'Most notably, we introduced attendees to our new Genius AI Detection solution – which can help radiologists categorize and prioritize cases by complexity, to optimize workflow and expedite patient care. This new deep-learning AI software is designed to help radiologists detect subtle potential cancers in breast tomosynthesis images. With higher specificity than Hologic's previous AI solution, the deep-learning software can help detect hard to identify lesions for further examination by the radiologist. Research shows a difference of +9% in observed reader sensitivity for cancer cases using Genius AI Detection technology.[3]

'Also at our booth was our 3DQuorum imaging technology, which assists radiologists by reducing the number of DBT images they need to review by creating high-resolution, overlapping 6mm „SmartSlices" to expedite reading time. When a radiologist reads SmartSlices instead of 1mm slices, the number of DBT images to review is reduced by two-thirds3–5, leading to an average interpretation time savings of one hour per day.[4]

'AI will continue to revolutionize mammography for years to come and will help improve the radiologist experience. Our suite of integrated AI solutions can help facilitate the workflow efficiency and diagnostic accuracy that they are looking for.' ■

Interview: Wolfgang Behrends

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[1] Performance of a traditional machine learning computer-assisted detection (CADe) algorithm versus a deep learning artificial intelligence (AI) algorithm on digital breast tomosynthesis (DBT) studies. Authors: Manisha Bahl (MGH), Constance Lehman (MGH). Accepted as electronic poster.

[2] Burhenne LJW., Wood SA., D'Orsi CJ., et al. Potential Contribution of Computer-aided Detection to the Sensitivity of Screening Mammography, Radiology 2000; 215:554–562

[3] Based on analyses that do not control type I error and therefore cannot be generalized to specific comparisons outside this particular study. In this study: The average observed AUC was 0.825 (95% CI: 0.783, 0.867) with CAD and 0.794 (95% CI: 0.748, 0.840) without CAD. The difference in observed AUC was +0.031 (95% CI: 0.012, 0.051). The average observed reader sensitivity for cancer cases was 75.9% with CAD and 66.8% without CAD. The difference in observed sensitivity was +9.0% (99% CI: 6.0%, 12.1%). The average observed recall rate for non-cancer cases was 25.8% with CAD and 23.4% without CAD. The observed difference in negative recall rate was +2.4% (99% CI: 0.7%, 4.2%). The average observed case read-time was 52.0s with CAD and 46.3s without CAD. The observed difference in read-time was 5.7s (95% CI: 4.9s to 6.4s).

[4] Data on File: Clinical Study Report CSR-00116 Rev. 004

Molecular meets digital

Single-cell multiplex imaging: a powerful tool for digital pathology

Multiplex imaging can play a critical role in unravelling the tumour microenvironment. The potential and benefits of the emerging approach – a way to extract information from human tissue samples by visualising many more biomarkers than traditional microscopy – was highlighted in presentations during the 36th European Congress of Pathology in Florence, Italy. Speakers also discussed novel technologies to transform clinical care and deep learning for pathology biomarkers for precision oncology.

In his presentation, Dr Teijo Pellinen indicated that understanding the diverse cell states and molecular composition within the tumour microenvironment is crucial for improving risk stratification and predicting therapy responses. The Senior University Researcher at the Institute for Molecular Medicine Finland (FIMM) at the University of Helsinki, Finland, said multiplex tissue imaging is 'a great tool' for discovering 'clinically meaningful associations' and can answer different scientific questions.

Explaining the digital image processing and analysis steps in multiplex tissue profiling, he discussed different spatial tissue imaging approaches, from IHC-based systems, immunofluorescence, mass spectrometry and tyramide signal amplification systems. 'Some are more simple and high-throughput, meaning that they can cover large numbers of samples, while others are more suited to deep biological profiling and can cover up to 100 protein targets but are typically limited to fewer sample numbers with expensive infrastructure costs,' said Pellinen. 'Basically, the choice of multiplexing system depends on the biological and scientific questions.'

A more advanced way of doing image analysis

Pellinen highlighted how his FIMM group has developed an in-house approach that combines tryamide signal amplification and cyclic immunofluorescence in an affordable high-throughput system using basic histo-laboratory commercially available fluorescence scanners. With cyclic staining and digitisation, machine learning (ML) is used to annotate the artefacts, followed by cell segmentation and classification, though human input is still required, and multiple challenges remain to improve the automation.

He said multiplexing offers more accurate phenotyping and the ability to measure distances between cells. 'It is a more advanced way of doing image analysis. The difference in tissue research is that you can map those phenotypic clusters and cells on top of the tissue as we have coordinates for every single segmented and classified cell and that gives a lot of data as well.'

The FIMM team has recently launched a pan-cancer multiplex tumour microenvironment project aiming to profile over 40,000 tissue samples. By analysing samples, survival data and pathological data, they are using five different antibody panels to cover 33 different tumour microenvironment markers to discover both 'unique and common cellular profiles in these cancers.' they state.

The importance of spatial context

He gave an example of identified multimarker-defined fibroblast subsets in non-small cell lung cancer with different associations of patient survival, mutations and immune features, highlighting CAF (cancer-associated fibroblast) subsets with some showing better prognosis and survivability than others. 'The study highlighted that there are different types of fibroblast subsets and also suggests that different CAF subsets can have tumour permitting and tumour inhibiting functions in cancer,' said Pellinen.

The team also examined the prostate cancer tumour microenvironment, focusing on the behaviour and density of CD3 immune cells in benign and tumour areas and discovered highly interesting spatial interactions between CD3+ immune cells and epithelial cells with prognostic significance. 'This example,' he said, 'highlights the importance of spatial context in cancer and really tells us that large scale immunofluorescence profiling of cancer can reveal spatial patterns with highly interesting clinical associations that would be missed with technologies not preserving the tissue integrity.'

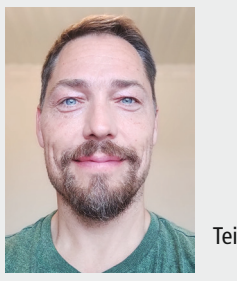
Transformative potential of liquid biopsy

In her presentation, molecular pathologist Dr Heather Dawson from the Institute of Tissue Medicine and Pathology at the University of Bern, Switzerland, said that while novel technologies have the potential to transform, transition from basic research to clinical practice can take a long time.

Focusing on the example of liquid biopsy to illustrate a technology with transformative potential for healthcare, Dawson said the technique can be used to measure markers such as circulating tumour cells, exosomes and circulating tumour DNA (ctDNA).

Illustrating the point through the patient journey, she highlighted how liquid biopsy can be used for early diagnosis of cancer, minimal residual disease (MRD) after an intervention, therapy monitoring, and detection of mutations and resistance mechanisms in advanced disease. She said: 'The introduction of liquid biopsy, especially for the application of early cancer diagnosis and MRD, opens the door for molecular testing in patients with localised disease.' ■

Report: Mark Nicholls



Teijo Pellinen

Dr Teijo Pellinen is a Senior University Researcher at the Institute for Molecular Medicine Finland (FIMM) at the University of Helsinki, where he leads team focusing on and developing advanced imaging technologies, especially on cancer specimens.

Heather Dawson

Dr Heather Dawson is Medical Director of Molecular Pathology at the Institute of Tissue Medicine and Pathology at the University of Bern in Switzerland. Her research focus is the investigation and use of prognostic biomarkers in the diagnosis of colorectal carcinoma.

Keynote on integrated diagnostics

Predicting – and shaping – the future of modern pathology

Complex diseases could require complex biomarkers for accurate diagnosis in the years ahead, according to a leading pathologist. In a keynote address to the 36th European Congress of Pathology in Florence, Italy, Professor Manuel Salto-Tellez highlighted this as one of the major future challenges for the discipline. However, he also believes pathologists will sit at the core of modern medicine.

As he opened his address, the Professor of Integrative Pathology at the Institute for Cancer Research in London (ICR) and Professor of Molecular Pathology at Queen's University Belfast (QUB) reflected on the last two decades looking in pathology and how at the turn of the millennium, he suspected few would have been able to predict the advances, and the speed at which they have been made, in the intervening years.

In his presentation, Salto-Tellez also referred to the challenge in 1999 from Dr Harold Vamus, Nobel Prize winner, pioneer of oncology and Director of the US National Institute of Health, for the scientific community to change the basis of tumour classification 'from morphological to molecular characteristics.' Despite the pessimism it created then about the future of the discipline, Vamus said: 'Could we have predicted that 25 years later, there were more samples than ever coming into pathology departments with an increase of 5% per year and that many of the predictive markers we used in personalised medicine are actually driven by good old immunohistochemistry?'

Disease vs biomarker complexity: levelling the playing field

'So, how do we start predicting the future?' asked Salto-Tellez. While there are new drugs, clinical trials and technologies, he focused on new biomarkers as pivotal in translating discovery into applicability and prediction of treatment response.

Focusing on immuno-oncology (IO) and advances in pathology, particularly with the advent of artificial intelligence (AI), he discussed the complex biology of the tumour microenvironment, the complex biomarkers and what pathologists can offer today in IO diagnostics with PD-L1, microsatellite instability, tumour mutational burden, and – in the boundary between clinical trials and diagnostics – the analysis of T-cell response and tumour infiltrating lymphocytes (TILS). 'We are dealing with complex disease with very simple biomarkers,' he said. 'But it could be that complex disease need complex biomarkers. To me, this is going to be that challenge that we are going to see over the next few years.'

Advancing that can mean extracting the complexity that exists in images; harnessing new technologies; or better use of information available in hospitals and 'begin to integrate that in new algorithms that are hopefully going to better help our patients.'

The future is digital

He pointed to studies in digital pathology and AI that 'tell us that a pathology service that is digitised is better. But this is only the beginning because we know that the in-silico image is going to allow us to extract significant information for the future.'

Such tools, however, need to be intuitive to use, meaningful for the pathologist and scientist, quantitative, and correlate with clinical outcomes. The AI architecture, with numerous tools now available to pathologists, can be used to identify histological features better, predict molecular biomarkers and quantitate single and multiple biomarkers.

New methods against PD-L1 'madness'

Prof Salto-Tellez also reflected on the current complex pathology pathway in the realms of molecular diagnostics. 'It is fragmented and as pathologists, we probably need to start thinking about how we rationalise this.' He expanded on this by referring to the 'madness' with PD-L1, where pathologists are dealing with multiple scoring systems associated with individual drugs, antibodies and auto-stainers which have to be scored and defined differently, depending on the cancer type.

His QUB team is working to create prototypes to match the H&E and PD-L1 staining to mark the area of tumour and then render a potential result. When translated into an AI in a system together with other potential prognosticators, he said that can begin to tell the prognosis of individual patients. 'Through the tools we have today, we are beginning to generate new complexity,' he said.

Medical information talks – if we let it

Further ICR work, he said, has examined tens of clinical trials and is using tools to identify every potential member of the tumour microenvironment. 'An important component of what we do in the future is associated with clinical trials, but until now clinical trials have been the lost opportunity to develop biomarkers meaningfully,' he suggested. 'The trend we see is that we probably apply AI too late in the process. It may make sense to bring this forward and start generating AI tests up front.'

A critical step in delivering integrative diagnostics into hospital settings and generate new algorithms to help patients involves accessing information in real life in the hospitals, the expert pointed out. 'The reason we are not able to extract information for patients immediately and start applying these tools is because that information is in siloes – lab information management systems (LIMS), electronic health records (EHR), other records, images, are not talking to each other. That is the main bottleneck.'

'Custodians of multiplex diagnostic opinion'

A survey of clinicians suggested genomics, histopathology, digital pathology tools, AI results, radiology and radiomics, EHR and LIMS should be integrated. However, three main questions must be answered to overcome this challenge, Salto-Tellez said:

- are we ready in our hospital to manage that information in that way?
- do we have computation technology to create that integration?
- how can accreditation be brought to a test that is an amalgamation of different systems?

'This is important because to me, the main custodian of that multiplex diagnostic opinion should be the pathologist,' said Salto-Tellez. 'We should be the ones leading this opinion. My prediction is that we are looking at a fourth revolution: how to integrate our resources and how we bring that information into our patients is going to dictate the future.' ■

Report: Mark Nicholls

Manuel Salto-Tellez

Professor Manuel Salto-Tellez is Professor of Integrative Pathology at the Institute for Cancer Research in London (ICR), and the lead of the Royal Marsden Hospital/ICR Integrated Pathology Unit. He is also the Chair of Molecular Pathology at Queen's University Belfast (QUB), a clinical consultant pathologist and the Lead of QUB's Precision Medicine Centre of Excellence, and author or co-author of more than 320 internationally peer-reviewed articles in translational science, molecular pathology and diagnostics.

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Generative AI

Large language models: enabler or eroder of cardiovascular care?


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Large language models (LLMs) have potential in healthcare settings to help support both patients and clinicians. Cardiologist Dr Robert van der Boon believes they could have several applications, including patient communication and education, clinical decision support and administrative tasks. Delegates to ESC 2024 in London heard roles explored for LLMs in areas of clinical decision-making, patient care, research, and scientific writing. But experts in the session also raised concerns over trustworthiness, bias, privacy and security.

Van der Boon, from the Cardiovascular Institute at the Erasmus Medical Center in Rotterdam, gave a specific presentation on how to improve patient care with LLMs. He said: 'As healthcare has become very data and text heavy, LLMs have the potential with natural language processing capability to improve efficiency but also provide better outcomes for our patients.'

Robert van der Boon

Dr Robert van der Boon is a cardiologist at the Cardiovascular Institute at the Erasmus Medical Center in Rotterdam, the Netherlands. His research interests are in heart failure, telemonitoring and digital health.

For patients, one of the most appealing options is interaction with LLM-powered chatbots, but there is risk that these models may start to "hallucinate" – provide incorrect or incomplete information – and thus have a detrimental effect. 'One way we tackle this problem is to implement human oversight instead of letting LLMs answer patients directly,' van der Boon said.

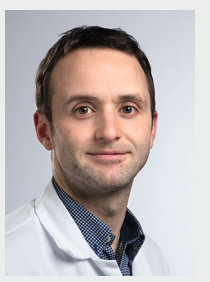
A recent study showed that LLM-powered chatbots can improve physician efficiency and interphysician agreement. He also pointed to research that suggested LLMs may even be more empathetic than clinicians, though the results of the studies should be interpreted with caution.

A future goal would be to develop LLM-based chatbots enabling patients to talk to their doctor in the form of an Avatar 24/7. 'But we are not there yet,' the expert added.

Reducing administration

The technology also shows promise in regards of diagnostics skills, van der Boon said: 'LLMs do fairly well on exams – but we know from medical school that answering questions is not the same as being a doctor.' Instead, he explained, a key area of benefit lies in reducing administrative tasks for doctors, particularly in an outpatient clinic where one hour of clinic creates up to two hours of administration, leading to stress and burnout in physicians.

However, barriers to implementation such as accuracy of models, trustworthiness, bias, security and privacy remain. The expert said: 'We need to prove the safety and effectiveness of these models in pragmatic, prospective randomised controlled trials before widespread implementation. LLMs have the potential to revolutionise patient care and will likely expand in the near future, but challenges remain and integration into clinical practice requires careful consideration.'



Stéphane Fournier

Dr Stéphane Fournier is an Attending Physician at the Interventional Cardiology Unit, in the Department of Cardiology at CHUV in Lausanne, Switzerland. His research is primarily focused on coronary physiology but also includes the implementation of large language models (LLMs) in clinical practice.

Potential for education

During the session, Dr Stephane Fournier, Head of the Cath Lab at University Hospital Centre Vaudois (UHCV) in Lausanne, Switzerland, discussed the impact of the technology on cardiovascular education. He elaborated on how LLMs offer better and equitable access to information, enable 'shy' students to ask questions without feeling uncomfortable in front of peers, are time efficient, deliver updated information and language assistance, and facilitate exam preparation and can even create clinical skill scenarios.

However, he said a risk was that students would lose the ability to communicate, and posed the question: 'Can someone who knows everything but can no longer communicate still be a good doctor? We have to keep in mind that the communication with our patients and colleagues is extremely important.' While there is no data about the impact of LLMs on cardiovascular education, he believes there is a huge opportunity for them to improve education.

Impact on scientific publishing

Tomasz Guzik, Editor-in-Chief of the journal Cardiovascular Research, looked at the challenges and opportunities of LLMs in scientific publishing. Noting that scientific research should be impactful, he explained that 'in order to be impactful, research needs to be visible. LLM and AI can help authors to achieve this.'

While highlighting a view that AI could foster integrity and help researchers 'navigate the digital age', he pointed to an alternative view that overuse of LLMs 'will lead to the destruction of current scientific process.'

Prof Tomasz Guzik is a Regius Chair of Physiology and Cardiovascular Pathobiology of the University of Glasgow and a Professor of Medicine at Jagiellonian University, Poland. His research focuses on vascular biology, hypertension, and cardiovascular immunology.

Evidence suggests some researchers are using LLMs to prepare scientific literature and he felt this can improve grammar, consistency and formatting, streamline literature searches and reference management, and may also increase objectivity and reduce bias. Guzik, who is Chair of Cardiovascular Medicine at the University of Edinburgh, added that it also facilitates continuous learning, data analysis and interpretation. But there are risks too, he pointed out. These include loss of originality and authenticity in content, misinterpretation of data visualisations, and overuse may remove need for collaboration. It may, he continued, also lead to the introduction and perpetuation of biases, and an over-reliance on AI may lead to an erosion of critical thinking. ■

Article: Mark Nicholls

Emergency departments voice concerns

Understaffed and overcrowded: survey highlights ED safety fears

A survey of emergency medicine practitioners across Europe has highlighted major concerns over safety and overcrowding in Emergency Departments (ED). Understaffing, too few doctors and the risk of burnout were also among the issues highlighted in the Europe-wide survey by the European Society of Emergency Medicine (EUSEM). While AI technology may help alleviate some of these issues, its implementation is connected to new challenges.

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Provisional findings of the survey, which is still in progress, were presented at the EUSEM 2023 congress in Barcelona by Dr Said Hachimi-Idrissi in a session which also focused on how technology can impact safety and quality within the ED. During his presentation, he admitted that the scenario was complex with no clear solutions. 'The objective of the survey is to get an insight on Quality and Safety programme initiatives across Europe and more specifically in emergency departments and/or in Pre-Hospital EM settings,' added Dr Hachimi-Idrissi, who is Clinical Chief of the Emergency Department (ED) at UZ Ghent in Belgium.

More than a matter of mere discomfort

A key finding of the survey so far is that about 90% of professionals feel that at times the number of patients in their ED exceeds the capacity of the department to provide safe care and that overcrowding is a regular and serious problem. Dr Hachimi-Idrissi added: 'Overcrowding is not just an issue of discomfort or loss of dignity, but carries a substantial risk of harm and increased mortality. Understaffing was another major contributory factor.'

He said there are far too few doctors for the volume and complexity of many of the patients. This increases the risk of harm to the patient, and of morbidity and mortality, when the length of stay at the ED is too long. In addition, this imbalance is imposing stress, which may result in burnout, practitioners leaving the profession, impacting relationships and use of illicit substances. The expert hopes the survey findings help lead to changes in emergency care practice, increase awareness of the risk, and mitigate and tackle that risk to deliver improvements. Administrators, nurses, physicians, and patients all have a role to play in achieving that, he added, naming development of clinical interventions to reduce adverse events, better monitoring, the use of KPI (key performance indicators) and benchmarking as viable option to move towards this goal.

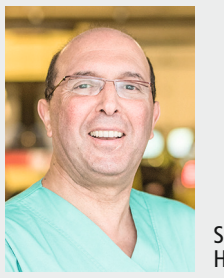
AI: a new hope for the ED?

Technology could also have a role to play in making more efficient use of time in the ED and impact positively on quality and safety, such as use of Artificial Intelligence (AI) tools.

'AI and machine learning would help to monitor patients and integrate data, vital signs and symptoms to define the population at risk, though more research in this area is needed,' Dr Hachimi-Idrissi said. However, he remains concerned that the current environment in EDs across Europe is a health hazard for patients and healthcare providers.

The session also included presentations looking at how hi-tech can catch impact positively on quality and safety in the ED; the use of big database and AI on continuous quality and safety improvement in emergency medicine; and how to integrate patient satisfaction in big databases to improve performances in the ED.

*In a separate EUSEM session, findings were presented from a study that indicate the AI chatbot ChatGPT performed as well as trained doctors in suggesting likely diagnoses for patients being assessed in the ED[1].



Said Hachimi-Idrissi

Dr Said Hachimi-Idrissi is Clinical Chief of the Emergency Department at UZ Ghent in Belgium and Professor of Critical Care Medicine at the University of Ghent as well as Professor at the Free University Brussels. A Past President of the Belgian Society of Emergency and Disaster Medicine, he is Director of the Global Network on Emergency Medicine, a council member of the paediatric section of the EuSEM and has published extensively in peer-reviewed international publications.

While researchers at Jeroen Bosch Hospital, s-Hertogenbosch, The Netherlands acknowledge that more work is needed, their findings suggest the technology could support doctors working in emergency medicine, potentially leading to shorter waiting times for patients. ■

Report: Mark Nicholls

Real-time drug identification

AI camera detects incorrect medication transfers

With high proficiency, a deep-learning model identified contents of vials and syringes, confirming whether medication transfers were correct. A team of researchers says it has developed the first wearable camera system that, with the help of AI, detects potential errors in medication delivery. In a new test, the video system recognized and identified, with high proficiency, which medications were being drawn in busy clinical settings. The AI achieved 99.6% sensitivity and 98.8% specificity at detecting vial-swap errors.

The system could become a critical safeguard, especially in operating rooms, intensive-care units and emergency-medicine settings, said co-lead author Dr. Kelly Michaelsen, an assistant professor of anesthesiology and pain medicine at the University of Washington School of Medicine. "The thought of being able to help patients in real time or to prevent a medication error before it happens is very powerful," she said. "One can hope for a 100% performance but even humans cannot achieve that. In a survey of more than 100 anesthesia providers, the majority desired the system to be more than 95% accurate, which is a goal we achieved."

Drug administration errors are the most frequently reported critical incidents in anesthesia, and the most common cause of serious medical errors in intensive care. In the bigger picture, an estimated 5% to 10% of all drugs given are associated with errors. Adverse events associated with injectable medications are estimated to affect 1.2 million patients annually at a cost of $5.1 billion.

Syringe and vial-swap errors most often occur during intravenous injections in which a clinician must transfer the medication from vial to syringe to the patient. About 20% of mistakes are substitution errors in which the wrong vial is selected or a syringe is mislabeled. Another 20% of errors occur when the drug is labeled correctly but administered in error. Safety measures, such as a barcode system that quickly reads and confirms a vial's contents, are in place to guard against such accidents. But practitioners might sometimes forget this check during high-stress situations because it is an extra step in their workflow.

The researchers' aim was to build a deep-learning model that, paired with a GoPro camera, is sophisticated enough to recognize the contents of cylindrical vials and syringes, and to appropriately render a warning before the medication enters the patient. Training the model took months. The investigators collected 4K video of 418 drug draws by 13 anesthesiology providers in operating rooms where setups and lighting varied. The video captured clinicians managing vials and syringes of select medications. These video snippets were later logged and the contents of the syringes and vials denoted to train the model to recognize the contents and containers.

The video system does not directly read the wording on each vial, but scans for other visual cues: vial and syringe size and shape, vial cap color, label print size. "It was particularly challenging, because the person in the OR is holding a syringe and a vial, and you don't see either of those objects completely. Some letters (on the syringe and vial) are covered by the hands. And the hands are moving fast. They are doing the job. They aren't posing for the camera," said Shyam Gollakota, a coauthor of the paper and professor at the UW's Paul G. Allen School of Computer Science & Engineering.

Further, the computational model had to be trained to focus on medications in the foreground of the frame and to ignore vials and syringes in the background. "AI is doing all that: detecting the specific syringe that the healthcare provider is picking up, and not detecting a syringe that is lying on the table," Gollakota said.

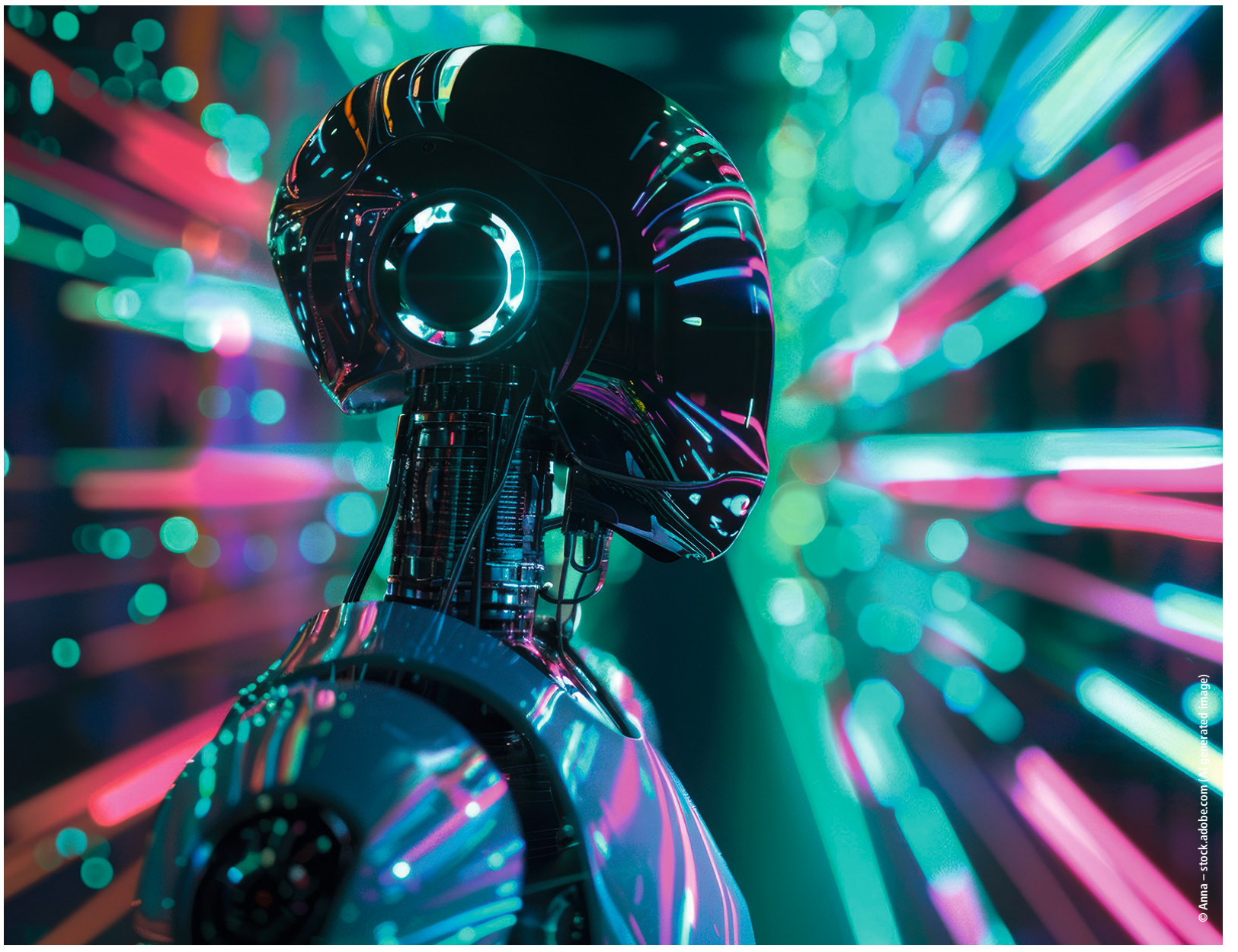
This work shows that AI and deep learning have potential to improve safety and efficiency across a number of healthcare practices. Researchers are just beginning to probe the potential, Michaelsen said.

The study also included researchers from Carnegie Mellon University and Makerere University in Uganda. The Toyota Research Institute built and tested the system. The Washington Research Foundation, Foundation for Anesthesia Education and Research, and a National Institutes of Health grant (K08GM153069) funded the work. The authors' declared their potential conflicts of interest in their paper, which will be made available on request. ■

Source: University of Washington School of Medicine

Artificial intelligence meets internal medicine

Medical AI: Enter ‘dea ex machina’



In the world of theatre, the ‘deus ex machina’, the god from the machine, is a dramaturgical trick to resolve seemingly unsolvable conflicts. Can artificial intelligence (AI) also be such a universal problem solver for internal medicine? At the Annual Congress of the German Society of Internal Medicine (DGIM) in Wiesbaden, Dr Isabella Wiest explored the potential – and limitations – of AI helpers.

The research associate at the Else Kröner Fresenius Centre (EKFZ) for Digital Health at TU Dresden and resident physician at Mannheim University Hospital explained that the aspect of generative AI in particular shows enormous potential.

Every person generates a large quantity of health-related data on their way through doctors‘ surgeries and clinics, but also in their private lives, and this data could be analysed by an AI for clinically relevant patterns, the expert pointed out. Examples include medical reports, radiology images, histopathology scans as well as genome and sensor data.

However, the availability of this wealth of data is only half the battle, Wiest pointed out: around 80% of data is stored in unstructured form, and the free text of findings often contains relevant additional information that goes beyond the structured data. In order to use this information quantitatively, much manual rework has been necessary up to now. Traditionally, tasks such as transferring the data from doctors‘ letters into a table have fallen to the doctoral students.

Locally-run language models help protect sensitive data

This tedious and unrewarding work could be delegated to a generative AI, explained the expert, referring to what is currently probably the best-known application: The large language model (LLM) ChatGPT from OpenAI. This program has been trained on large text corpora and is able to generate new content on this basis. This also includes extracting information from unstructured texts. One recent study has demonstrated useful results in retrieving TNM stages (tumour/node/metastasis) from pathological reports – even if these had not been digitised.

However, the OpenAI solution cannot be used in these cases, as the sensitive patient data should never be transferred to the US company‘s servers, Wiest pointed out. A viable alternative would be locally-run language models such as Llama-2, which can be installed on a computer on site. ‘This means that the data stays where it is generated and does not leave the hospital or practice.’ Despite having far less computing power, the local AI model delivered good results in tests with gastroenterological endoscopy findings, the expert reported.

AI-generated summaries free up more time for patient care

Initial studies suggest that the LLMs also perform well when summarising the content of clinical texts. Although these summaries are by no means flawless, Wiest recognised that the AI-generated texts contain fewer misinterpretations and inaccuracies than those of human experts. The expert argued that the use of these tools could ‘make work easier and increase efficiency, leaving more time for the patient and less time for documentation’.

However, for LLMs to provide medically accurate information without producing the infamous “hallucinations”, the input has to be right, Wiest pointed out: for example, current guidelines would have to be entered into a database in the form of machine-readable vectors so that the corresponding prompt results in well-founded answers. This approach, known as ‘Retrieval Augmented Generation’ (RAG), has already produced some good results in initial trials, according to the expert. ‘This is a promising technology that doctors can use to have up-to-date treatment recommendations available when they are needed.’

One algorithm for all – or all for one?

The increasing digitalisation of health data opens up numerous other potential applications for AI, Wiest explained: From predicting microsatellite instability (MSI) to detect genetic changes in histopathology, through organ segmentation to support surgical treatment planning, to assessing radiological images. However, she emphasised that irrespective of the specialist area, it is fundamentally important to have a solid data basis and to validate the trained models thoroughly. ‘We need to scrutinise generative AI very critically and develop good metrics.’ She concluded that the transparency of the models and explainability of the results must always be ensured.

As an alternative to the current models, which are tailored to narrowly defined tasks, more recent research is moving in the direction of a “generalist” AI. This is designed to integrate any data modalities from the clinic and practice into an application and thus enable a holistic view of medical issues – such a model might at least come close to the concept of the deus ex machina.

‘Whether such a model will exist at all remains to be seen,’ said the expert, pointing out the high level of complexity required. Instead of having a single “jack-of-all-trades” AI, she suggested that individual, specialised models might also be orchestrated with the help of a parent AI – a so-called LLM agent. Depending on the clinical task, this supervising algorithm would “consult” the appropriate AI in order to generate a diagnostic or treatment recommendation based on its expertise.

The final hurdle that Wiest addressed was the integration of the models into existing healthcare infrastructures. ‘Interoperability of digital systems is urgently needed for this.’ This means there are still a few challenges to overcome before AI can make the leap from digital assistant to a fully-fledged clinical dea ex machina. ■

Report: Wolfgang Behrends

Transformative technology

Debating the case for AI in pathology

Artificial Intelligence (AI) remains a divisive topic within the discipline of pathology with a range of opinions over its current value and applicability in clinical settings. While most experts agree that the technology will not replace pathologists, it might still spell bad news for those who do not embrace AI in their daily practice. On the other hand, reservations persist about whether pathologists are ready to achieve this adoption this in the first place.

The topic was discussed during a lengthy session at the 36th European Congress of Pathology in Florence, Italy, where speakers argued the pros and cons of AI within pathology in a lively debate. Delegates were also asked to add their views during real-time surveys on pertinent questions regarding AI.

Will Europe be left behind?

Yet it was a powerful opening from a leading AI expert that set the tone for the session. Dr Ricardo Baptiste Leite, CEO of HealthAI – a Geneva-based global agency for responsible AI in health – said the global AI healthcare market was worth $11bn in 2022, with China taking a lead with 61% of patents in 2015–22, compared to 21% from America and a mere 2% from the UK and the EU. The market worth is estimated to reach nearly half a trillion US Dollars in 2032.

'We are on the verge of tremendous geopolitical tensions in which Europe really needs to reposition itself if it wants to be an active player,' he said. Leite indicated that AI may be accelerating healthcare inequalities and that it was important to bring the human factor into the conversation and ensure that the 'use of technology can lead to better health outcomes' for patients.

Navigating the "wild west of AI"

The expert pointed out key AI trends, including healthcare analytics, medical diagnostics, telehealth, robotics, management and clinical trials. On the other hand, significant challenges remain, such as cybersecurity risks, regulatory and ethical issues. There is also global fragmentation with different requirements, approval processes and timelines across different countries.

While AI shows clear potential to save lives, Leite underlined the need to get regulation right. 'Lack of effective governance of AI in health increases risks for citizens, and we are living in an age that I would define as the "wild west of AI". In many contexts, people are using this technology with no oversight, and companies are putting this technology in countries where there is no data protection.' As a former Parliamentarian, he therefore advocates 'light legislation, effective regulation' for AI and expressed his belief that politicians relinquish power on the topic more to regulatory bodies.

Prediction: AI will change pathology – and pathologists

As the session moved on, the panel debated whether pathologists are even ready for AI in practice.

Arguing in favour, Prof. Dr Falko Fend from the Institute of Pathology at Tübingen University Hospital in Germany, discussed what pathologists want from AI, such as increased diagnostic accuracy and extraction of "invisible" biologic and prognostic features, and looked at the AI tools that are needed in pathology. But he warned: 'To use it in a technical way, we need an integrated digital pathology system; we need expertly curated cohorts, clinically and diagnostically valid questions, intensive collaboration with computer scientists, stringent evaluations in practice settings, and data.'

Bottlenecks to AI are the availability of digital pathology, computing power and storage, and a need for regulation. While there are doubts over jobs and skills erosion, the expert said there is a need to foster a 'pragmatic attitude' to AI. 'Pathologists need to be involved right from the beginning, testing algorithms rigorously in clinical diagnostic setting,' he continued. 'In the end, AI should not replace expertise in pathology, but pathologists should use AI tools to make a better diagnosis and not see AI as a replacement for expertise. Perhaps AI will make us better pathologists, but different ones to before.'

Exploratory phase

Providing the con counterpart to Prof Fend's pro-arguments, Dr Catherine Guettier from the Department of Pathology, Hôpital Bicêtre, Paris, suggested pathologists are not ready for AI in practice. She declared that AI in pathology is still in the exploratory phase, with only very few early adopters. To back up this claim, the expert pointed out that, as of April 2023, there were fewer than ten AI-enabled medical devices in pathology approved by the FDA – compared to nearly 400 in radiology.

'The integration of AI in pathology has been limited by a range of obstacles: the slow diffusion of digital pathology, which is the basis of AI, uncertainties about the quality of AI algorithms and the regulatory constraints,' she said. Elements missing for large-scale adoption of AI in real life settings include seamless integration of algorithms in the pathologist workflow, a sustainable economical model and lack of an in-depth reflection on the strategy for using AI within the discipline.

However, in a survey during the session, more than half of delegates found themselves supporting the "pro" side, agreeing, or even strongly agreeing, that pathologists are ready for using AI in practice.

How much do we need to understand?

A second debate focused on interpretability and explainability in AI and whether it is necessary. Vincenzo L'Imperio, Assistant Professor of Pathology at the University of Milano-Bicocca, Monza, Italy, argued that it is. 'Interpretability and explainability in AI can be of help when applying these algorithms for diagnostic purposes,' he said. However, Diana Montezuma Felizardo from the clinical laboratory group IMP Diagnostics in Portugal, argued against the question. She said: 'AI has made significant advances in various fields, including pathology. As AI models become more complex, the topics of interpretability and explainability have risen as key concerns. The real issue often lies in the delicate balance between making AI understandable while maintaining its sophisticated capabilities. ■

Report: Mark Nicholls

Falko Fend

Professor Dr Falko Fend is Medical Director at the Institute of Pathology and Neuropathology and Head of the Department of General and Molecular Pathology and Pathological Anatomy at Tübingen University Hospital in Germany.

Catherine Guettier

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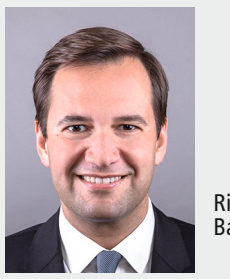

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Hyperbaric oxygen therapy to reduce toxic effects

HBOT shows promise after breast cancer radiotherapy

Hyperbaric oxygen therapy (HBOT) treatments could offer relief to breast cancer patients who experience late toxicities following radiotherapy treatment. To date, the handful of completed clinical trials only produced inconclusive or contradictory results. Therefore, results from the latest trial, named HONEY (Effect of Hyperbaric Oxygen Therapy on Breast Cancer Patients with Late Radiation Toxicity), were anxiously awaited. However, the researchers' insights, published in JAMA Oncology, also do not provide much definitive evidence of HBOT's benefit.[1,2]

HBOT provides 100% oxygen for inhalation inside a pressurized treatment chamber. The therapy is used to treat a large variety of medical conditions, including toxicities caused by cancer treatments, by increasing the amount of oxygen that the blood can carry throughout the body and by delivering oxygen-rich plasma to hypoxic tissue. This can help strengthen immune responsiveness and encourage new collagen deposition and endothelial cell formation.[3]

The HONEY trial

A multi-institutional team in the Netherlands conducted the hospital-based randomised clinical trial to assess the effectiveness of HBOT to reduce or eliminate moderate or severe breast, chest wall, and/or shoulder pain in combination with edema, fibrosis, or movement restriction 12 months or longer following breast irradiation. Three hundred eighty-eight (19.1%) patients out of 2,029 survey responders (who had been participants in a previous breast cancer clinical trial) reported they were experiencing these late toxic effects. A total of 189 were eligible to participate in the HONEY trial.

The researchers invited 125 women to receive 30 to 40 HBOT sessions 120 minutes in duration over a period of six to eight consecutive weeks. Eighty-five women declined the treatment, with 70 saying that the time commitment required to participate was too great. An additional 61 were selected as the control group.

Ultimately, only 31 women completed the HBOT treatment, which consisted of breathing 100% oxygen through an oxygen mask during four intervals of 20 minutes at an atmospheric pressure of 2.5 ATA (or bar). Principal investigator Prof. Helena M Verkooijen, MD, PhD and colleagues evaluated these patients at baseline and at three- and six-months post-treatment. They report that in follow up, moderate to severe pain was not statistically different between the HBOT group (50%) and the control group (62%). However, the HBOT treatment participants experienced a significant reduction in fibrosis.

In an accompanying editorial, Dr Ezra Hahn of the Princess Margaret Cancer Centre in Toronto, Prof. Dr Aron Popovtzer of the Hadassah University Medical Center in Jerusalem, and Prof. Dr Benjamin W. Corn of the Hebrew University Faculty of Medicine in Jerusalem, write: 'We now have modest evidence to justify the use of HBOT in treating the chronic morbidities associated with breast irradiation. […] In terms of the next steps, adequately powered randomized, sham-controlled, double-blind trials will be necessary to truly determine the benefit of HBOT.' [2]

Breast cancer-related HBOT clinical trials in progress

Two clinical trials are currently underway in Asia to evaluate how HBOT may reduce toxicities caused by radiotherapy to treat breast cancer. South Korean researchers at the Cha Ilsan Medical Center, a woman's hospital in Goyang-si near Seoul, are conducting a clinical trial to determine the efficacy and safety of HBOT to prevent radiation dermatitis. Patients receiving adjuvant radiotherapy following breast conservation surgery for localized invasive breast cancer are either randomized to receive HBOT three times a week after completing five fractional radiotherapy treatments (for 60 Gy total) or to receive standard education in dermal care. Principal investigator Assistant Professor Jee Young Lee advises that the study, which started November 2023, is measuring the incidence and severity of radiation dermatitis in each group, as well as evaluate any self-described quality of life improvements. [4]

A large randomized clinical trial of nearly 400 breast cancer patients receiving treatment at Guangdong Provincial People's Hospital in Guangzhou, China, is evaluating if HBOT treatments can prevent radiation pneumonitis caused by chemotherapy and radiotherapy. Radiotherapy can cause radiation lung injury, leading to pulmonary fibrosis. [5]

'Hyperbaric oxygen can improve the tissue after radiation by promoting the function of vascular endothelial cells and fibroblasts, and reducing the secretion of inflammatory factors, thereby inhibiting the process of fibrosis and fiber atrophy after radiotherapy, and promoting tissue repair. Therefore, it has the potential value of treating chronic radiation injury,' explains principal investigator Prof. Kun Wang, MD, PhD.

Half of the patients are receiving standard-of-care treatment. The other half are receiving 30–40 hyperbaric oxygen therapy treatments immediately after the end of radiotherapy. Researchers will evaluate the incidence of radiation pneumonitis 12 months following completion of treatment for both patient cohorts, and the type and severity of symptoms among both groups of patients who develop radiation pneumonitis. ■

Article: Cynthia E. Keen

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Brain cancer immunotherapy

Turning immune cells against glioblastomas

Glioblastoma is the most common and most aggressive primary brain tumour, with an average survival after diagnosis of less than two years, and against which current treatments remain ineffective.

In recent years, immunotherapies have given patients renewed hope, albeit with relatively modest success. A team from the University of Geneva (UNIGE) and the Geneva University Hospitals (HUG) has succeeded in identifying a specific marker on the surface of tumour cells, and in generating immune cells carrying an antibody to destroy them. Furthermore, these cells, called CAR-T cells, appear to be capable of targeting diseased cells in the tumour that do not carry this antigen, while sparing healthy cells. These results, published in the journal Cancer Immunology Research, are a first step towards the development of clinical trials with human patients.

Glioblastomas carry biological characteristics that make them particularly difficult to treat. Able to induce a microenvironment that limits the attack of the immune system, they escape standard treatments and recur rapidly.

Denis Migliorini, assistant professor in the Department of Medicine at the UNIGE Faculty of Medicine, holder of the ISREC Foundation Chair in Brain Tumour Immunology, member of the Translational Research Centre in Onco-Haematology (CRTOH) and attending physician in charge of the HUG Neuro-oncology Unit, is an expert in CAR-T cells (for chimeric antigen receptors T-cells). This immunotherapy consists in collecting immune T cells from patients, modifying them genetically in the lab to make them express antibodies capable of detecting elements specific to tumour cells, before reinjecting them so that they can specifically target the tumour.

"For several years we have been trying to identify the protein markers expressed by glioblastoma cells," explains Denis Migliorini. "One of these markers, PTPRZ1, proved particularly important: we were able to generate CAR-T cells carrying antibodies targeting PTPRZ1. This is a first step towards CAR-T cells effective against malignant gliomas."

Most CAR-T cells are generated using viral vectors, a technique that has proved its worth in certain diseases but is not very suitable in the brain. "Indeed, they persist for a very long time in the context blood cancers. The brain is a fragile organ, and this persistence can generate a risk of toxicity," explains Darel Martinez Bedoya, a post-doctoral fellow in Denis Migliorini's laboratory and first author of this research. The scientists therefore introduced in the T-cells the messenger RNA encoding for the desired antibody. The cellular machinery is then responsible for producing the right protein to build the receptor that will take place on the T-cell surface and recognise the tumour target. "This technique has a number of advantages: CAR-Ts offer a flexible platform, allowing multiple adaptations according to the specificities and evolution of the tumour," explains Darel Martinez Bedoya.

To check that CAR-Ts only attack tumour cells, the Geneva team first tested them in vitro on healthy and tumour cells. "To our surprise, not only did CAR-Ts not attack healthy cells, but they were also capable, by bystander effect, of identifying and fighting tumour cells not expressing the PTPRZ1 marker," Denis Migliorini is delighted to report. "In this context, CAR-Ts are probably capable of secreting pro-inflammatory molecules that are responsible for eliminating tumour cells even in the absence of the original marker when co-cultured with target positive tumour cells."

The second stage involved testing the treatment in vivo in mouse models of human glioblastoma. Tumour growth was controlled, prolonging the lives of the mice remarkably well without signs of toxicity. "By administering CAR-Ts intratumourally in the CNS, we can use fewer cells and greatly reduce the risk of peripheral toxicity. With this data and other unpublished yet, all lights are green to now envisage a first clinical trial in humans," the scientists conclude. ■

Source: University of Geneva

Experts explore the future of CSP, CRT, ICD

Implantable cardiac devices: which techniques are ready for prime time?

Opposing views on new implantable cardiac devices were aired in a Great Debate session at the European Society of Cardiology's annual 2024 congress in London. Experts discussed emerging techniques and technologies and debated whether they are actually ready for clinical application. At the core of the session was the issue of whether conduction system pacing (CSP) should replace cardiac resynchronisation.

Speakers firstly discussed the pros and cons of whether CSP – a cardiac pacing technique that uses the heart's natural conduction system to help the ventricles activate in a physiological way via leads in the organ's conduction system – should replace cardiac resynchronisation, a treatment for heart failure (HF) that involves implanting a device to help the heart's ventricles pump in a coordinated way.

A second element to the Great Debate focused on whether patients with an ICD (implantable cardioverter-defibrillator) but no indication for bradycardia pacing should receive an extravascular ICD (EV-ICD), where the lead is placed below the breastbone and is outside of the heart.

CSP: A proximal solution for a proximal problem

Arguing the case for CSP to replace cardiac resynchronisation therapy (CRT), Dr Jacqueline Joza from McGill University Health Centre in Montreal in Canada, felt the debate should actually focus on whether CSP should replace biventricular (BV) pacing as both methods resynchronise the heart. Her key points were to suggest that the HIS-Purkinje system was meant to conduct rapidly and synchronously (so it should be used); that the block in LBBB (left bundle branch block) occurs most often at a location within the HIS (the cardiac muscle cells that transmit electrical impulses), so it is a case of delivering a proximal solution for a proximal problem; and that BV-CRT is an inefficient and dyssynchronous method of delivering CRT.

Joza conceded: 'The only time BV-CRT may be a better fit is when there is no HIS-Purkinje disruption at all.' But she added that CSP performs well in patients with RBBB (right bundle branch block) and HF indication for pacing.

Just a 'new kid on the block' in need of evidence

Putting the case against CSP replacing CRT was Cardiologist-Electrophysiologist Professor Kevin Vernooy from Maastricht University Medical Centre in the Netherlands. He argued that there are many trials that show BV pacing is much better than just an ICD in these patients[1] with much evidence to suggest that BV in patients with LBBB and HF is an 'awesome therapy.'[2,3,4]

While acknowledging CSP in HF is a 'new kid on the block', he expressed surprise that clinicians seem to be moving towards it 'without evidence' when he believes there is such a good existing pacing therapy. 'We have so much evidence that biventricular pacing is doing a good job,' added Vernooy. 'Even though CSP is theoretically an alternative for BV pacing, the implantation requires new skills and knowledge with limited success rates in patients with heart failure with the current tools. Therefore, we still need BV as a bail-out strategy, so I think we should not go too quickly.'

He concluded that while CPS is a 'promising' pacing strategy, clinical routine is shifting towards it 'without evidence'; that training, education and EP understanding is 'essential'; and that CSP does not seem to be the 'optimal strategy' in many patients.

Transvenous leads: only for those that need them

In a second debate in the session, Professor Lucas Boersma from St Antonius Hospital in Nieuwegein, the Netherlands, argued the case for patients with an ICD but no indication for bradycardia pacing, receiving an extravascular ICD (EV-ICD).

While acknowledging that ICDs save lives and the Transvenous ICD (TV-ICD) has become the 'workhorse' over the last 3–4 decades in everyday clinical care for Sudden Cardiac Death (SCD), he said TV-ICD therapy comes with a price of morbidity and mortality and that leads can become infected or break down.[5] 'We used to take that for granted because there was no alternative,' he said. 'But if we place the lead outside the vasculature, that may avoid unnecessary complications.'

S-ICD (subcutaneous) was an important first step but he pointed to further advantages of EV-ICD: smaller devices, lower defibrillator energy, greater longevity, pacing with a single device, anti-tachycardia pacing, asystole pacing support and post-shock-pacing. Boersma concluded by pointing out that EV-ICD and S-ICD have high conversion rates and similar efficacy for transforming ventricular arrhythmias back to sinus rhythms and they avoid harmful vascular complications. 'For patients that do not need pacing, these devices with no transvenous lead in the heart are the way to the future; we should not give transvenous leads to patients that don't need them.'

TV-ICD: 'still a lot to offer'

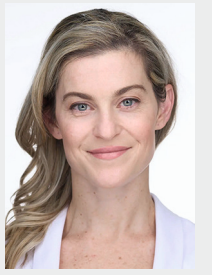
Offering the opposing view was Professor Jeanne Poole from the University of Washington in Seattle. Her institution is a high user of S-ICD, which has been FDA approved for 14 years, so she suggested it is already 'prime time' in appropriate patient groups, whereas EV-ICD has only been recently approved in the United States and has not been adequately tested in real world prospective registries or randomised controlled trials. 'So, categorically, it is not ready for prime time,' she said.

The expert discussed the risk of lead fracture, though acknowledged future transvenous leads are likely to be more robust and smaller, and that infection rates are now significantly lower. Pointing to additional considerations in favour of TV-ICD systems, she said they still have the lowest inappropriate shock rates and set a 'high bar' with tens of thousands of patients enrolled in clinical studies. There is also excellent sensing with endocardial leads, expanded diagnostics, long battery life, well-established surgical techniques, no need for general anaesthesia, painless ATP for patients, and offer flexibility in programming.

In summary, Prof. Poole said that all patients with an ICD indication but no indication for bradycardia pacing should categorically not receive an EV-ICD. 'Transvenous ICD systems still have a lot to offer, they are the only option for many ICD indicated patients and they will be around for many years,' she concluded.■

Lucas Boersma

Professor Lucas Boersma is an Electrophysiologist at St Antonius Hospital in the Netherlands and was Head of the Cardiology Department from 2008–2016. He is the past chairman of the Committee for Science & Innovation of the Netherlands Society of Cardiology and endowed Professor of Cardiology at the University of Amsterdam since 2017.



Jacqueline Joza

Dr Jacqueline Joza is an associate professor of medicine and cardiac electrophysiologist at the McGill University Health Centre, Canada. Her research focuses on CSP, atrial fibrillation and syncope.

Jeanne Poole

Professor Jeanne Poole is an electrophysiologist and the Section Head of Electrophysiology at the University of Washington in Seattle, US, and is Editor-in-Chief for the Heart Rhythm O2 Journal.

Kevin Vernooy

Professor Kevin Vernooy is the medical director of the heart and vascular center and chairs the Department of Cardiology at the Maastricht University Medical Center in the Netherlands. His research focuses on the invasive treatment of cardiac arrhythmias in patients with heart failure.

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