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EUROPEAN HOSPITAL

THE EUROPEAN FORUM FOR THOSE IN THE BUSINESS OF MAKING HEALTHCARE WORK

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Pioneering women in medical imaging informatics: Katherine P. Andriole

From the cradle of digitization to the dawn of AI in radiology

The Society for Imaging Informatics in Medicine (SIIM) has done more than any other professional society to promote the digital conversion of medical imaging from X-ray film and 35 mm slides. The pioneering research of its members over the past 40+ years transformed timely access to radiology exams and created a sea change for radiology department operations and how data from imaging could be analysed. Although a mostly male dominated field, women did and are increasingly making important contributions in the technology. SIIM is producing a "Women in Informatics" webinar series, launching it with a profile of Katherine P. Andriole, Ph.D., a leading expert and one of the first women to enter the field.

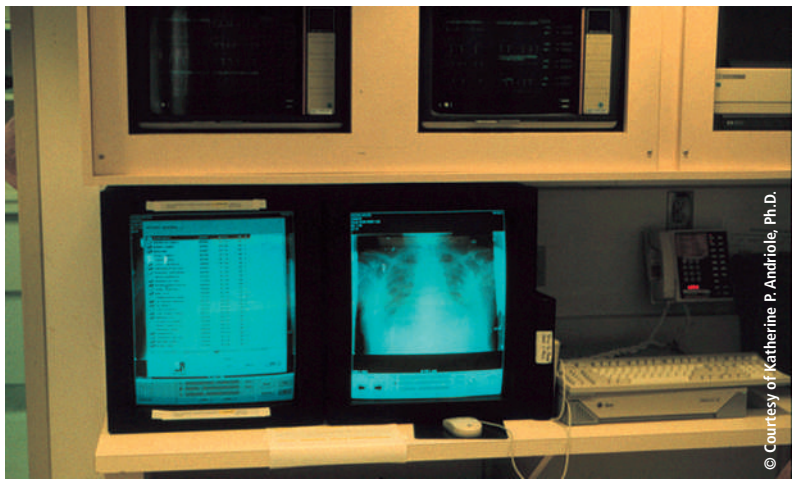
Andriole is lauded by numerous medical societies and organizations for her many technical accomplishments, and for her leadership role to promote medical imaging informatics. She was instrumental in helping design, build, and implement one of the first precommercial hospital Picture Archiving and Communication Systems (PACS). She is now focusing on the use of artificial intelligence (AI) systems in medical informatics. Andriole has authored or co-authored more than 160 peer-review journal articles.

European Hospital talked with Andriole about the evolution of medical imaging informatics, experiences she has had, and her advice to those – both women and men – who want to enter the field.

The impact of timing: starting a career at the dawn of a revolutionary era in radiology

Andriole points out that the ubiquity of digital medical imaging didn't happen overnight. It is the result of the collective efforts of an international group of radiologists, engineers, computer scientists, medical device and software product developers, medical information technology specialists, and medical physicists to develop methods to extract, organize, share, and utilise data and images from digital modalities.

Medical imaging informatics has evolved over decades, eventually becoming a subspecialty of radiology. It has crucial role in exchanging and utilizing medical images within complex information systems. By combining information science, computer science, and healthcare, informatics optimize the acquisition storage, retrieval, and utilization of healthcare information, enhancing accessibility and quality.



© Courtesy of Katherine P. Andriole, Ph.D.

ICU and ER PACS viewing workstations

None of this existed when Andriole entered college. Her parents, both healthcare professionals, and especially her mother, were influential in stimulating interest in math and physics as applied to biology and medicine, and in showing what a powerful, determined woman could achieve. Andriole earned a Ph.D. in electrical engineering and medicine at Yale University, with an emphasis on classical machine learning and image processing.

'My initial work with imaging devices was to manually measure carotid arteries seen on CT scans,' she said. 'At the time, no efficient means existed to acquire digital data directly from CT images. This was a different era. MRI was relatively new, PET was a novel toy, radiology reporting was dictated to a tape recorder and manually transcribed to paper records, and exam scheduling was done by phone.'

A chance encounter at a medical conference with H.K. Bernie Huang, D.Sc., a leading PACS pioneer, led to a fellowship in radiology to work on research in digital imaging and PACS development, first at University of California, Los Angeles (UCLA), and subsequently at the University of California, San Francisco (UCSF).

EH: You have experienced some seismic changes in radiology. What had the greatest impact? How did you adjust to change?

Andriole: 'In my opinion, the establishment of the DICOM standards and systems integration of RIS/PACS/HIS were foundational elements. With these, capabilities and functionality soared. Continuous improvements in computing power and network capabilities, plus dramatic reduction in the cost of digital storage also had a huge impact.

'The DICOM standards enabled us to extract accurate data in an orderly manner from any vendor's proprietary imaging scanner or PACS, enabling interoperability. An image interchangeability DICOM demonstration among technical exhibition vendors at the 1995 RSNA annual meeting was a monumental event.

'Image storage has evolved from a walk-in refrigerator sized magneto optical disk storage system holding a maximum of 1 terabyte of data to laptop computers with that capacity and accessibility to cloud storage. The improvements in network data transfer, combined with dramatic cost reduction of transmitting data, were game changing. The technologies became affordable and adoptable.'

'I was a member of a multi-specialty team at UCLA and UCSF whose goal was creating a sea change using technology innovations to improve radiology. I had brilliant, supportive mentors. The late Theo C. Pilkington, Ph.D., a pioneer of biomedical engineering, taught me how to approach projects with many unknowns. He ingrained the mandate that if you are going to do anything, you need to understand the fundamentals of a science or technology and its impact.

'Huang insisted that his PACS team embed itself prominently in the clinical environment to understand what tools are needed, how they will impact workflow, and what benefit they will have. What makes a tool useable and compelling, improving upon an older method of doing something or introducing something totally novel but potentially beneficial? What characteristics of a tool or a process cause a user to like or to hate it?'

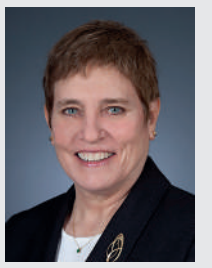
You are a RSNA 2022 Gold Medal recipient for rendering 'remarkable service to the science of radiology'. What do you think your greatest contributions are to medical imaging in your career as a medical informaticist?

'What I have achieved has been as a member of a team. Informatics is teamwork. It requires team science, clinical domain experience, IT experience, and implementation science. The teams I have worked with demonstrated how to develop innovative beneficial technology constructively working with all the players, including vendors, convivially and having fun.

'I am proud of the work we did to be among the first to acquire data from computed radiography (CR) scanners and to show that CR-generated data could be used even though spatial resolutions were challenged. CR scanners were designed at the time to transmit data only to X-ray film printers. We had to do reverse engineering using ACR/NEMA standards and then DICOM standards.

'I also am proud of developing simple, easy-to-use interfaces for PACS viewing-only workstations for ICU, neonatal ICU ward, and Emergency Department physicians. And with David E. Avrin, M.D., Ph.D.,of UCSF for developing software for automated image prefetching of relevant prior exams to a PACS diagnostic workstation cache for comparison with a new exam being interpreted. These both were revolutionary at the time.'

Is medical imaging informatics a good career choice for women? What is your advice for entering this specialty?



Katherine P. Andriole

Katherine P. Andriole, PhD, is the Director of Academic Research and Education of the Mass General Brigham AI Office, formerly the MGH & BWH Center for Clinical Data Science (CCDS). She is currently an Associate Professor of Radiology at Harvard Medical School, Brigham and Women's Hospital.

'Most definitely. There will be a growing need for medical imaging informaticists, especially as AI tools become commonplace aids to radiologists. Someone has to validate their need and monitor their use and performance. People who are inquisitive and who like to solve problems enter this field with many different backgrounds.

'I encourage anyone interested in the field to attend society meetings such as SIIM25, in person. I can't emphasize this enough. It's where you meet the pioneers and leaders, make connections, and can ask questions. Proactively network with end users and with vendors. I also recommend the National Imaging Informatics Course, an accelerated introduction to this specialty. It's a five day long deep dive into the field. Tuition scholarships are available from its SIIM and RSNA sponsors.' ■

Article: Cynthia E. Keen

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EUROPEAN HOSPITAL @ ECR 2025

Congress preview

ECR 2025: Welcome to Planet Radiology!

Science, sustainability, and society – these are the three cornerstones of this year's European Congress of Radiology (ECR) in Vienna, Austria. Following the motto "Planet Radiology", the congress focuses on the environmental impact of diagnostic imaging while exploring ways to advance equitable global healthcare access. Congress President Prof. Andrea Rockall provides a preview on the upcoming event, discussing highlight sessions and new formats – and how radiologists can contribute to fixing our planet.

As radiologists from around the world have come to expect from ECR, this year's scientific programme is again packed with insightful sessions from high-profile speakers. During its five-day runtime (Feb 26-Mar 2), the congress will explore cutting-edge advances in radiology, provide an overview of the latest and most exciting findings from clinical trials, and demonstrate how innovative interdisciplinary approaches bring new benefits for patient care. Visitors will also be sure to get their fair share of eye candy during the opening ceremony on the first day of the congress, auspiciously titled "Wonder".

In view of the extensive and distinguished programme, Prof. Rockall is confident that the congress will be a truly one-of-a-kind experience for all congress attendees: 'With the theme "Planet Radiology", ECR 2025 will take the concept of planetary health and explore its key parts, including global sustainability, healthcare equity and scientific innovation.'

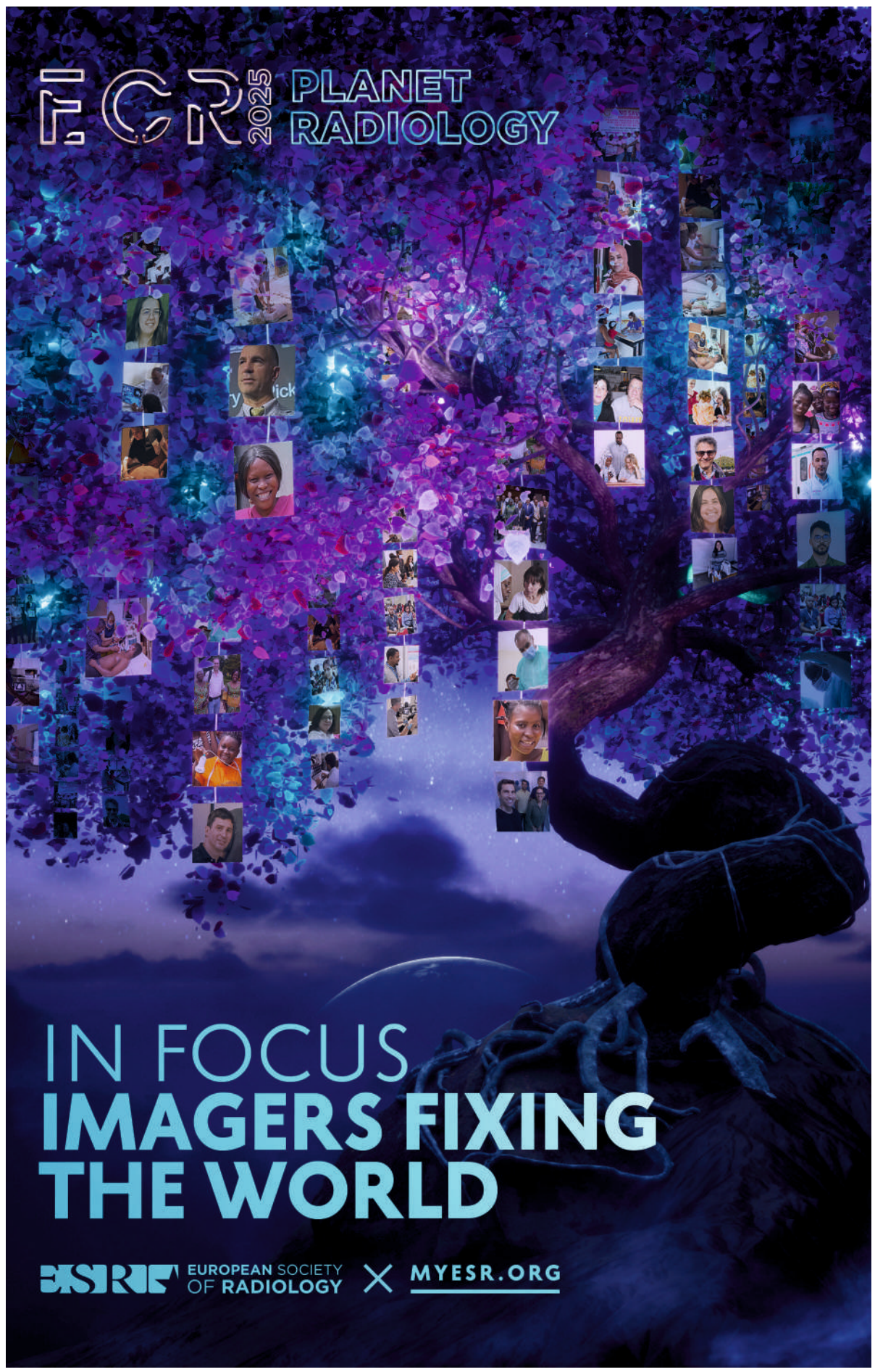
Striving to make the event more environmentally-friendly than ever, the organisers have introduced new ways to weave sustainability into the DNA of ECR. Prof. Rockall emphasizes: 'As climate impacts grow, radiologists are positioned to be leaders in adopting greener practices and sustainable healthcare models. As such, you can expect educational sessions dedicated to this critical issue. These are supported by a number of green initiatives we have implemented at ECR 2025, including the offer of discounted rail travel to reduce attendees' carbon footprints.'

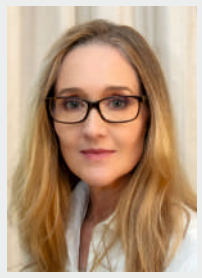
ECR 2025 brings back popular favourites like the image interpretation quiz, open forums and the AI Theatre (Room D2 on level –2), while introducing fresh elements such as the all-new "Ask Me Anything" sessions. In these sessions, participants can directly engage with leading experts in their respective fields, who will share in-depth knowledge through a short lecture followed by an open discussion.

How to fix the world (as a radiologist)

Another notable addition to ECR is a format called "Imagers Fixing the World" (Room O2 and the In Focus Lounge on Level 1), which will showcase the impact of radiologists worldwide: 'From providing teleservices in conflict zones and bringing ultrasound to the remotest regions to harnessing the power of AI and driving radiology's green transition, Imagers Fixing the World will celebrate the people and projects that are advancing global health equity and planetary sustainability for the future,' the organisers say.

Following congress tradition, ECR 2025 features several partner countries: During the "ESR Meets" sessions, attendees will learn how radiology is practiced in Morocco, Brazil, the UK and the Baltic countries. Working on the finishing touches for this year's event, Prof. Rockall says: 'I want to express my sincere appreciation to everyone who has worked and continues to work so tirelessly in making ECR 2025 a reality. The dedication and passion of so many, often behind the scenes, has shaped this congress into something truly special. I greatly look forward to welcoming you to Vienna, where we will explore "Planet Radiology" together.' ■





Andrea Rockall

Professor Andrea Rockall is the Clinical Chair of Radiology at Imperial College London and President of the European Society of Radiology. She is also the Congress President for this year's European Congress of Radiology (ECR). Her work focuses on genitourinary cancer research and machine learning in radiology, earning her the BIR/Mayneord Memorial Award for her contributions to the field.

Imaging modality comparison presented at RSNA 2024

Photon-counting CT advances identification of pancreatic cystic lesions

Pancreatic cystic lesions – indicating an increased risk of pancreatic cancer – are an occasional incidental finding in routine computed tomography (CT) abdominal imaging. New research suggests that the superior image quality of photon-counting CT (PCCT) can help detect more of these lesions. At the RSNA annual meeting, an expert outlined the benefits and limitations of the imaging technique for early detection.

Patients with pancreatic cysts may be at increased risk for pancreatic cancer. Therefore, an MRI scan with intravenous contrast for follow-up of incidental cystic lesions is usually performed, and guidelines recommend follow-up CT imaging on an ongoing basis.

The lesions are only identified as incidental findings in fewer than 3% of routine abdominal CT scans performed, compared to up to 44.7% in MRI examinations. Recent research at multiple academic centres explores the effect of improved CT image quality on detection rates for pancreatic cystic lesions. [1]

Researchers at the University of Freiburg evaluated the image quality and diagnostic accuracy of PCCT compared to conventional energy-integrating detector CT (EID-CT), with MRI serving as the reference standard. They reported at a RSNA 2024 scientific session that PCCT does improve detection and delineation, particularly for smaller cystic lesions. Additional benefits included significantly lower radiation exposure while producing higher image quality and generating higher diagnostic confidence by readers. [2]

Improved differentiation

Principal investigator Stephan Rau, MD, and colleagues' database included 106 consecutive patients with a median age of 62.7 years, who had a portal venous abdominal PCCT, an EID-CT, and a multi-parametric abdominal MRI performed within a six-month period. A total of 46 simple cystic lesions were confirmed on MRI: 14 greater than 10 mm, and 27 between 5 mm to 9.99 mm in size. The researchers assessed diagnostic accuracy, and qualitative and quantitative image accuracy.

Dr Rau reported image quality, lesion conspicuity, and diagnostic confidence were rated superior for PCCT vs. EID-CT on 5-point Likert scales by three independent radiologists in a blinded reading. Sensitivity for the detection of cystic lesions was significantly higher for PCCT for all lesion categories: 76.8% vs 59.4% overall, 86.4% vs 71.6% for lesions 5 mm to 9.99 mm in size, 90.5% vs. 83.3% for lesions equal or greater than 10 mm.

Photon-counting CT also provided better material decomposition, resulting in higher cystic parenchyma contrast.

'From my point of view, this is the most interesting finding of the study,' Dr Rau commented. 'It shows that PCCT provides better evaluation of cysts components, in this case, water-like fluids. Thereby, a new possibility for future studies on differentiation of cystic lesions based on their attenuation/material decomposition could be feasible and should be evaluated.'

Complimenting MRI, not replacing it

'The University of Freiburg has already integrated PCCT technology for clinical applications, including abdominal imaging,' Dr Rau told European Hospital. 'The results of the study underline its value in improving diagnostic workflows for detecting pancreatic cystic lesions, especially in routine scenarios or where MRI access is restricted. Adoption for broader use in the specific context of pancreatic cystic lesions detection will likely depend on further advancements, including multispectral imaging capabilities for lesion characterisation.'

Asked about the potential of PCCT as an appropriate substitute for MRI, Dr Rau advised, 'MRI remains the reference standard, particularly due to its superior contrast resolution and ability to characterise cystic lesions in greater detail, such as distinguishing malignant from benign features. MRI's unmatched soft tissue contrast, especially on T2-weighted sequences and diffusion weighted imaging, is critical for comprehensive pancreatic cystic lesion evaluation.'

He added, 'MRI remains indispensable for follow-up imaging or cases with non-conclusive CT findings. And it does not use ionizing radiation.' Dr Rau believes that PCCT, with its higher image quality and lower radiation dose, demonstrates great promise as a complimentary tool to MRI. 'It may even be a substitute on scenarios where MRI availability is limited, or patients are contraindicated for MRI,' he said.

Diagnostic boon, but a burden on workload

But while PCCT's higher sensitivity for detecting small pancreatic lesions is a significant advantage, this technology has brought a new challenge: what should radiologists do about these increasingly common incidental findings?

Dr Rau explains that current guidelines, based on conventional CT technology, recommend follow-up imaging for all pancreatic cystic lesions. 'This approach may impose a substantial burden on healthcare systems without clear evidence of benefit. Balancing early detection with the cost and practicality of follow up care is an important consideration for future research and policy discussions.' ■

Author: Cynthia E. Keen

Stephan Rau

Stephan Rau, MD, is a radiologist specializing in computed tomography at the Clinic for Diagnostic and Interventional Radiology at the University of Freiburg, Germany. He has conducted extensive research in the diagnostic capabilities of photon-counting detector CT technology. His clinical research includes PCCT imaging of cystic renal lesions, the spine, head and neck scans in patients with dental hardware, multiple myeloma, and of patients with metal artefacts.

References:

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Digital solutions for healthcare

Telemedicine as a lifesaver?

Using VR glasses, external doctors can participate in the discussion of a shared patient case via the digital platform „Mona." © Sonja Buske

The future of healthcare requires rethinking and innovative approaches. Given demographic changes, increasing care needs, and a growing shortage of skilled workers, the integration of digital solutions is essential, as Dr. Gerald Gaß, Chairman of the German Hospital Federation, and Prof. Gernot Marx, Chairman of the German Society for Telemedicine, emphasized during the special exhibition „Hospital of the Future" at MEDICA in Düsseldorf. Both associations are therefore calling for a stronger use of telemedicine in hospitals in a joint position paper.

'Telemedicine offers promising opportunities to enhance the quality of patient care and create equal living conditions—especially in rural areas, which are often affected by care shortages,' said Marx. He cited stroke care as an example, which can be ensured in remote areas thanks to telemedicine connections. 'Experts from specialized centers are digitally involved in the treatment. This reduces transfers to major care centers and enables local care, even for complex diagnoses,' explained Marx. He thus advocates moving away from the notion that good care can only be provided on-site. Another key aspect is the future use of data in patient care. Electronic patient records, combined with AI-supported analysis, could help refine diagnoses and target telemedicine interventions more accurately. This would not only improve care but also allow for a more effective use of scarce resources. However, according to Gaß, political and structural changes are needed to realize these advances. He appealed to those responsible to create innovation spaces and overcome outdated structures. 'Telemedicine services must be adequately funded, and existing legal hurdles must be dismantled.'

Dr. Gerald Gaß (left), Chairman of the German Hospital Federation, and Prof. Gernot Marx, Chairman of the German Society for Telemedicine, advocate for the increased use of telemedicine. © Sonja Buske

Flexible handling of financing mechanisms

Currently, certain telemedicine services cannot be billed like their analog counterparts. Gaß stated, 'This hinders the integration of digital solutions.' A flexible handling of existing financing mechanisms, such as case-based payments, could provide relief without injecting additional funds into the system. Moreover, a shift in mindset is required that shifts the focus from technical details to medical quality. 'Telemedicine should not only be perceived as a technical addition but as an integral part of modern medical care. This change in awareness must also be reflected in political and regulatory decisions to promote the acceptance and use of digital medicine,' Marx added. The goal is a connected healthcare system that breaks down barriers, increases efficiency, and ensures quality. Marx and Gaß emphasized that it's not about investing more money, as many often believe. 'It's more about making these new forms of treatment permissible and billable within existing volumes.' Stroke care served as an example again: If a regional stroke unit consults telemedicine expertise from a neurological center, the treatment cannot be billed. To act economically, the patient would have to be transported to a clinic and treated there, although the treatment could have been provided telemedically. 'It must become possible for us to bring telemedicine expertise to the patient and receive part of the case payment for this service,' Marx clarified. He is not aiming to design an additional billing system but rather to handle the existing funds more flexibly.

How the medicine of the future can already be implemented today was demonstrated by the company Clinomic with its digital platform for intensive care medicine 'Mona.' The integrated solution acquires, analyzes, and visualizes patient and operational data. Experts can be digitally consulted to review a case together with colleagues. Mona thus enables interdisciplinary telemedicine consultations with internal and external specialists for optimal intensive care. 'This is a breakthrough in the care of critically ill people,' Marx finds, and concludes by emphasizing: 'If we do not fully utilize the possibilities of digital medicine, we will not be able to overcome the challenges we face in patient care.' ■

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Research presented at Spanish cardiology congress

New data on heart attack puts pressure on governments to promote social justice

Environmental factors such as low temperatures and carbon monoxide levels in the air have long been underestimated as risk factors for triggering a heart attack. At the Spanish Cardiology Congress (SEC24) in October in Bilbao, an expert presented new research results, which offer insights on the disease causes and put pressure on policy makers to reduce pollution and promote equal access to energy.

The data, which was acquired in a retrospective study, sheds light on population risk factors that are often disregarded, according to main author Prof. Alberto García-Lledó, Head of the cardiology service at the Príncipe de Asturias hospital in Madrid. 'In infarction, we usually think of individual factors such as cholesterol or work that affect an individual, but there are also environmental factors that affect society,' he said. 'These variables are those that periodically increase the risk of infarction when certain diseases come along, such as the flu in autumn.'

Shattering a myth

García-Lledó's team has observed heart events in the Madrid region to identify the environmental factors that can influence the risk of suffering from a heart attack. The researchers found that fewer heart attacks occur in August than in November, thereby contradicting a longtime belief related to heat waves. 'Temperature has an influence, but heat waves are not associated with infarction,' he said. 'In Madrid, the colder it gets, the higher the risk. With heat waves, we were able to demonstrate that there was no increase in the risk of suffering from a heart attack.'

With low temperatures, vasoconstriction occurs to avoid cooling the inside of the body. Adrenaline is secreted, and the skin is left with less blood to keep it warm inside the body. The process creates increased tension in the body that is similar to the mechanism of stress. 'The cold causes stress and this reaction increases tension of the arteries as they tend to close,' he explained. The phenomenon, called snow attacks, is a well-referenced risk factor of myocardiopathies.

Another classic trigger for cardiovascular events is the association with respiratory infections, but there used to be a problem of statistical analysis differentiating between cold and flu, he explained. 'In our continental climates, flu and cold go together,' he said. 'Determining the relative contribution of one and the other – whether it is the flu or the cold that influences the risk – was an important issue to demonstrate.'

García-Lledó and his team have shown that both influenza and cold are independent risk factors in triggering myocardial infarction. In addition, they have observed that pollution factors, some of which tend to cluster with cold temperatures, also present a risk for heart attack. 'Cold, flu and carbon monoxide act as independent associates in the risk of suffering a heart attack. All three have a pathophysiological explanation,' he said.

Vaccination and fairer health policies

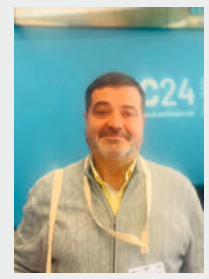
An efficient strategy to decrease those risk factors is to get vaccinated against the flu, a vaccination that also protects against other cardiovascular events such as stroke. 'We have evidence that of all respiratory infections, the influenza virus is the one that is most correlated with cardiovascular accidents,' he said. 'The flu vaccine has been around for many years, and we have a lot of experience and published work on its efficacy. In the general population, the vaccine reduces the risk of myocardial infarction and the risk of stroke.' Vaccination in Spain is among the best in Western Europe, third only to the UK and Portugal's that is close to or exceeding 60%, the target set by the WHO.

The importance of social justice

The new vaccine against the Respiratory Syncytial Virus (RSV) could also prove efficient on population risk. 'All respiratory viruses and pneumococcus have an influence,' said García-Lledó. 'Any infection increases the risk of heart attack and stroke because it produces inflammation of atherosclerosis plaques.'

The most relevant part of the study, however, is how it could help implement health policies that reduce both pollution and energy poverty, García-Lledó believes. 'We will have to support the reduction of pollution and the promotion of social justice, so that the less wealthy have access to heating,' he said. 'We are working to incentivize social assistance, because the risk of heart attack is higher in populations with higher unemployment rates and lower income. These issues have to do with social policy, and are also relevant for the clinician, in order to promote vaccination against influenza.' ■

Author: Mélisande Rouger



Alberto García-Lledó

Alberto García-Lledó is Head of the cardiology service at the Príncipe de Asturias hospital in Madrid, Spain. He is also an associate professor of cardiology at Alcalá de Henares University near Madrid. His special interests are general cardiology and epidemiology.

Digital pathology discussion panel

The AI tools pathologists want and need

Linder, Moore, Bodén and Sadimin at the DPAI © Mark Nicholls

The evolving role of AI tools in digital pathology was explored at an open discussion during the annual Digital Pathology and AI Congress in London with a high-level panel of practitioners looking at current and future technology options. The panel of pathologists, scientists and academics assessed the tools they currently use, and those they would like to see available in the future as AI plays an increasing role in pathology.

The experts also looked at how the adoption of AI into clinical practice is reimbursed and whether digital pathology is delivering on its promise.

Taking part in the discussion was Professor Evita Sadimin, Chief of the Division of Pathology Informatics and Data Science at the City of Hope National Medical Center in California; Dr Anna Bodén, Chief of AI governance at the Region Ostergotland and clinical pathologist at the Department of Clinical Pathology and Department of Biomedical and Clinical Sciences at Linköping University in Sweden; Consultant Pathologist Luiza Moore, Senior Director of Clinical Diagnostics with AstraZeneca; and Professor Nina Linder, Guest Professor of Medical Diagnostic Artificial Intelligence at the Department of Women's and Children's Health, Uppsala University, Sweden.

Challenging beginnings

The panellists highlighted what they consider the most current promising use of AI.

This included delivering diagnostics to patients in remote locations, supporting the introduction of new biomarkers and improved medical screening. However, all acknowledged the implementation of AI into practice and workflows has had challenges.

Looking back to when her department began to introduce digital pathology, Bodén believes having more structured data from the outset would have made implementation easier. Linden added that establishing good ground rules was an ongoing problem as she believes end points are still not good enough to train algorithms.

While 'fantastic tools' are becoming available, Moore stated: 'We are very conscious of how this is going to fit into individual real-world labs and with interoperability and we are looking at ways to deploy AI that minimises disruption.' Sadimin, who offered a US perspective, said: 'For us, the number one challenge of introducing AI algorithms into clinical practice is regulatory, which is very tricky to navigate, as well as having the constant requirement to produce return on investment.'

New approaches to reimbursement needed

In terms of improving diagnostic accuracy, Moore said greater acceptance of novel biomarkers for computational pathology will be essential but rather than simply being a multi-industry response, a 'societal response' is also required with wider public and governmental acceptance of AI.

All panellists agreed that demonstrating return on investment (RoI) is a major hurdle, and with relatively few laboratories that are digitised, reimbursement remains fragmented. Bodén favoured a longer-term perspective towards reimbursement and hopes to see health systems become more data driven to provide a better understanding. Sadimin said the main circumstances where it has been easier to show a RoI with AI in pathology is whenever pathologist shortages arise, or they are required to work in remote locations. As for showing benefits to an organisation, she said: 'That is more challenging and very much depends on who you ask and people's levels of experience and comfort with AI.'

The issue of bias and ethics in AI use in pathology was raised, with concerns over reliable ground truth but also dogged by a lack of institutions using the approach.

Sadimin added: 'We need to get as many institutes as possible using it and across sites with different demographics.'

Slow take-up seen as a major hurdle

The future of AI tools in pathology hinges on a few key factors, the panellists concluded: A major concern remained the limited take-up of the technology. 'With only 4–5% of hospitals in the US currently digital, without digital slides, we are not going to have AI,' Linder pointed out the importance of wider adoption globally.

Bodén suggested a need for more AI use on assisting with reporting as well as improved search functionality to reduce the need for outside data sources. Moore said: 'There are so many biomarkers in the pipeline, that digital pathology biomarker assessment is coming and there is going to be more than one biomarker on one slide, so multiplex too. The sooner we can embrace that the better. Tumour volume is going down because of early detection programmes, so with less tumour, we will need more biomarkers.' ■

Author: Mark Nicholls

Anna Bodén

Anna Bodén is Chief of AI governance at the Region Ostergotland and clinical pathologist at the Department of Clinical Pathology and Department of Biomedical and Clinical Sciences at Linköping University in Sweden. She is co-lead of the European project Bigpicture on AI-driven digital pathology, has spearheaded digital pathology in her department and aims to integrate AI into clinical practice.

Nina Linder

Nina Linder is a Guest Professor of Medical Diagnostic Artificial Intelligence at the Department of Women's and Children's Health, Uppsala University, Sweden, and a researcher at the Institute for Molecular Medicine (FIMM) at the University of Helsinki in Finland. Her research focus is on the development of novel AI-based solutions for cancer and infectious disease diagnostics.

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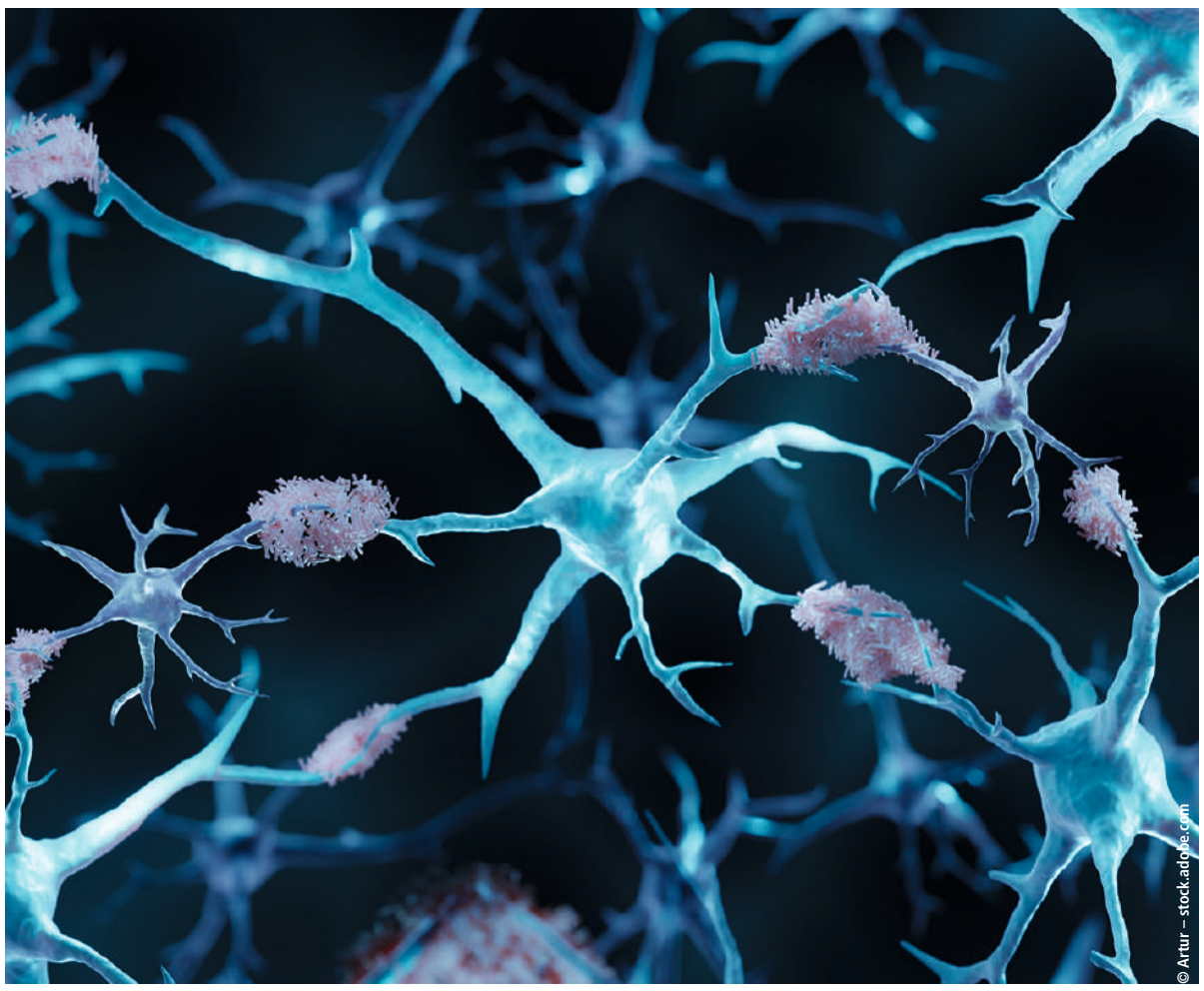
Promising, but in need of further validation

Implementation challenges of blood biomarkers for Alzheimer's disease



Blood-based biomarker (BBB) tests may represent the best weapon to combat the soaring rates of Alzheimer's disease (AD) throughout the world. Existing clinically validated tests are currently deployed to facilitate diagnosis, to monitor disease and effectiveness of treatments, to quantify progression, and to determine if a patient is appropriate for treatment or participation in a clinical trial.

Historically, diagnosis of AD has been based on clinical observations and apparent symptoms, and, for those with access and the funds to pay, lumbar spinal puncture for a cerebrospinal fluid (CSF) test or for a PET imaging scan.

With the proliferation of BBB tests in clinical development, and with increasing levels of accuracy attained, they are expected to become a global tool to fight this most common of dementias. However, there are many challenges to be overcome yet, both with the tests themselves and with their clinical implementation.

Test equipment challenges

The most accurate tests today use mass spectroscopy, which outperform immune-based methods of measuring plasma in accuracy and reliability. Korean researchers from Hanyang University College of Medicine in Seoul conducted an in-depth review of current methodologies used in published research to measure Amyloid-beta (Aβ) plasma. They discovered 'considerable variance in the diagnostic efficacy of plasma Aβ, contingent upon the measurement techniques employed. Ionization-mass spectroscopy exhibited superior performance, while single molecule array (SIMOA) technology did not yield comparable results,' wrote lead author Hyuk Sung Kwon, MD, PhD.[1]

Mass spectrometry-based assays require specific expertise and infrastructure, are time consuming, and yield lower throughput with immunoassays. The equipment is expensive and not available in many hospital and clinic laboratories.[2]

However, immune-based methods are currently used for CSF analysis. In addition to immunoassays producing less accurate results of BBB tests they are also subject to batch-to-batch variation, antibody reproducibility, and potential cross-reactivity. They offer automated processing, lower cost, and can deliver rapid turnaround time for point-of-care testing capability. And equipment is in the lab. These factors make a strong case for the development of BBB tests specifically designed for immunoassays.

Standardisation challenges

Another challenge relates to collecting viable samples for processing in remote or low-economy geographic areas with inadequate laboratory infrastructure. Expansion of testing capability of more robust samples, such as dried blood spot, could help resolve such issues.

When multiple tests are available from multiple vendors, the cost of blood biomarker analysis is expected to drop. While this is expected to make BBB testing more accessible throughout the world, standardisation for blood biomarker measurements is imperative. Reproducible, accurate, and consistent results are essential. The Global Biomarker Standardization Consortium of the Alzheimer's Association has been overseeing this critical issue as well as the development of certified reference material.

Both tasks are enormous in scope and scale, but essential for widespread global adoption.

Prof. Michel Schöll, Ph.D., of the University of Gothenburg and the Wallenberg Centre for Molecular and Translational Medicine, and colleagues, write: 'Standardisation challenges will vary greatly depending on the blood biomarker and analytic approaches used for its measurement.' They add, 'True standardisation will require the derival and validation of cutoffs that are translatable between methodological approaches for respective blood biomarkers.'

Standardisation reference values are made more complex by the fact that the requirements for the diagnostic performance of a biomarker are determined by the BBB test's context of use. As an example, a test to "rule in" AD needs a higher specificity cut point to minimise false positives, whereas a "rule out" test needs a high sensitivity cut point, to minimize false negatives.[3]

Challenges of population ethnic diversity, medical comorbidities, and confounding factors

Most BBB tests have been tested and validated in clinical trials with patient cohorts of non-Hispanic Caucasian people, who have few health-related comorbidities, and who live in developed economies in countries north of the Equator. Research is starting to reveal that co-morbidities, such as chronic kidney disease, hypertension, history of cancer and/or cardiac arrest, diabetes, and some prescription drugs, can each impact biomarker concentrations in the blood.

Alzheimer's BBB research of the diverse ethnic, genetic, cultural and demographic factors, and socioeconomic different populations of Africa, South Asia, Central America and South America has just begun, and is sparse compared to research in Europe, North America, China, Korea and Japan. Yet, approximately 60% of people living with dementia are estimated to be from low-income and middle-income countries in these under-researched areas.[4]

This is a massive and complex challenge. 'The unavailability of reliable reference intervals for highly diverse populations could lead to the misinterpretation of laboratory test results and contribute to misdiagnosis and inappropriate clinical intervention in a diverse real-world setting with greater heterogeneity among individuals,' writes Schöll and his multi-national team of co-authors.

Harald Hampel, MD, PhD, Chief Medical Officer and Senior Vice President, Neurology from Japan-based pharmaceutical company Eisai, and co-authors are more blunt: 'While the performance of BBBs in highly selective populations provides initial information, a broader understanding of how these biomarkers behave within the global community at large is needed to provide clinical guidance. It is imperative to conduct rigorous validation studies in more representative, real-world populations to determine which measures perform most consistently and to establish cutoffs and reference intervals that perform reliably across all patient groups.'

BBB tests in current clinical use are making diagnoses and AD monitoring more precise, and are facilitating AD research through better selection of patient cohorts for clinical trials. Still, it is going to take years before BBB testing can reach the lofty but much needed goal of stemming the epidemic of AD. ■

Author: Cynthia E. Keen

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Detection of neurodegenerative condition

Developing blood biomarkers to diagnose Alzheimer's

There is no known cure for Alzheimer's disease (AD), although prescription drug-based treatments that can slow AD progression in some patients are starting to enter clinical use. Biomarkers, quantifiable characteristics of biological processes or pathological conditions, are making it possible to help identify and measure the presence and extent of AD and its degenerative progression.

A blood plasma biomarker test received international media attention in July 2024 when results of a large clinical trial showed it to be 91% accurate in diagnosing AD in patients who had been clinically evaluated and diagnosed, compared to 73% by dementia specialists and 61% by primary care physicians. The study involved 17 primary and secondary care centres in Sweden treating 1,213 patients over 65 years old experiencing symptoms ranging from subjective cognitive decline to dementia. Half had pathologically confirmed AD.[1]

The significance of this research becomes clear in light of experts predicting that in 2025, 10 million people will develop AD. Leading organisation Alzheimer's Disease International (ADI) further estimates that the disease will escalate from 55 million cases worldwide to 78 million by 2030 and more than 139 million cases by 2050.[2]

Benefits for diagnostics and research

When blood biomarker tests for AD do become clinically available, unlike the current testing methods of expensive positron electron tomography (PET) imaging scans and invasive lumbar spine puncture for a cerebrospinal fluid test, they will offer many advantages. These are expected to be widespread availability, low cost, easy acquisition from patients, and accurate laboratory analysis. But they are not going to be a commonplace screening tool soon.

Many clinical research challenges await. Sebastian Palmqvist, MD, PhD, Associate Professor in the Clinical Memory Research Unit at Lund University and principal investigator of the Swedish study, advised during a JAMA Medical News podcast that the test is not a standalone diagnostic AD test, but rather something that should accompany the standard clinical evaluation. However, he emphasized that ‚you need biomarker tools to accurately identify AD, because the clinical symptoms aren't specific for that disease and can be caused by many other ideologies.[3]

The development of blood biomarker tests will greatly aid drug-related clinical trials. In a review on this topic, lead author Tharick A. Pascoal, MD, PhD, an Associate Professor of Psychiatry and Neurology at the University of Pittsburgh, along with an international team of co-authors, state that ‚the importance of biomarkers in drug development is growing exponentially' and that they ‚are expected to serve a wide range of contexts of use in clinical trials focusing on AD and other dementias.' [4]

‚The lack of biomarkers for population selection [of early clinical trials targeting Amyloid-beta] has raised the possibility that their negative results could be because other brain pathologies, unaffected by the drugs being studied, were causing symptoms in many participants,' they write. ‚Furthermore, the lack of biomarkers to track therapeutic response has raised questions about whether drugs reach their targets and produce the expected biological effects. The lessons learned from these clinical trials have highlighted that it is imperative to use biomarkers for more informative drug development in the field of AD.'

Categories and complexities

Blood biomarkers for AD do not have a single category, but three. The first class includes biomarkers associated with the presence of beta-Amyloid plaques and p-tau tangles, both of which are classic pathological hallmarks. The second class is associated with neuronal loss, neurodegeneration, or synaptic degeneration. The third class includes processes related to neuroinflammation related to glial cells.

The US Food and Drug Administration and National Institutes of Health created a Biomarker Working Group in 2016, which defined and established nine types of biomarkers. These are categorized in diagnostic, predictive, prognostic, susceptibility, response, monitoring, and safety categories.[5] Diagnostic biomarkers are most publicly associated with blood laboratory tests being used in clinical trials and in development.

Better diagnostics lead to increased need for care

Assuming that blood biomarker tests become clinically approved and low in cost, what then? Commenting about the accuracy of the blood plasma test used in the Swedish clinical trial in a JAMA editorial, dementia specialist physicians from Australia and the United States point out the need for a significant increase in nurse practitioners, nurses, and care navigators.[6]

Lead author Stephen Salloway, MD, of the Departments of Psychiatry and Neurology of Warren Alpert Medical School of Brown University in Providence, Rhode Island, and co-authors write, ‚Advances in the diagnosis and treatment of Alzheimer disease will require important changes to care models. It will not be possible to provide high-quality dementia care in a new molecular era within the already overburdened practice settings without providing additional resources and staffing.'

This by itself is a huge challenge, and is not being achieved to effectively deal with the needs of today's AD patients and their caregivers, even though an estimated $1.3 trillion is being spent, according to ADI. ■

Author: Cynthia E. Keen

Sebastian Palmqvist, MD, PhD is Associate Professor in the Clinical Memory Research Unit at Lund University. He also is a Consultant Neurologist at Skåne University Hospital in Malmö, Sweden. Palmqvist is principal investigator of ADetect, a 24 month long AD detection study launched in January 2024, and a research participant in Lund University ongoing EDAP (early prognostics of Alzheimer's disease) project.

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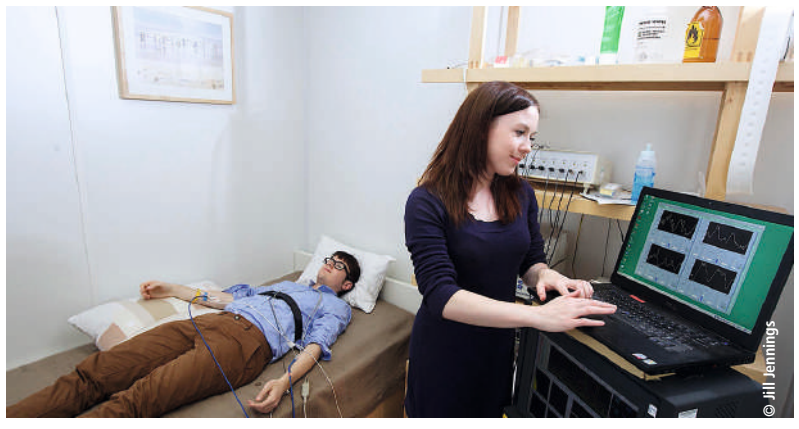
New approach to detecting Alzheimer's



Researchers combined non-invasive measurements of brain blood flow and electrical activity with novel analysis methods

Research led by Lancaster University has revealed clear evidence that changes in the orchestration of brain oxygenation dynamics and neuronal function in Alzheimer's disease contribute to the neurodegeneration.

The study "Neurovascular phase coherence is altered in Alzheimer's Disease" is published in Brain Communications. The lead author is Aneta Stefanovska with Juliane Bjerkan, Gemma Lancaster, Peter McClintock and Trevor Crawford from Lancaster University and Bernard Megli and Jan Kobal from the University of Ljubljana Medical Centre in Slovenia. Professor Stefanovska said: "Alzheimer's can be hypothesised as being a result of the brain not being appropriately nourished via the blood vessels (vascular system)."

Dr Bernard Megli, clinical coordinator of the study, said: "The vascular system and the brain work together to ensure that the brain receives sufficient energy. In fact, the brain needs as much as 20% of the body's overall energy consumption despite contributing only about 2% of the body's weight."

The "neurovascular unit" (NVU) consists of vasculature connected via brain cells called astrocytes to neurons and ensures that this cooperation is successful. To assess the function of the NVU, researchers combined non-invasive measurements of brain blood flow and electrical activity with novel analysis methods developed by Lancaster's Nonlinear and Biomedical Physics group. They measured the brain's electrical activity and oxygenation using electrical and optical probes on the scalp while an electrocardiogram (ECG) measured heart rate, and a belt wrapped around the participant's chest measured breathing. Simultaneously measuring blood oxygenation, brain electrical activity, respiration and electric activity of the heart let the researchers capture physiological rhythms and their imperfect timings. Efficient functioning of the brain depends on how well all these rhythms are orchestrated. To assess the efficiency of the NVU, both the strength and the coordination of these rhythms were assessed by computing their "power" and "phase coherence" using mathematical algorithms.

Researchers found that the median respiration rate was approximately 13 breaths per minute for the control group, and approximately 17 breaths per minute for the Alzheimer's group. Professor Stefanovska said: "Quite unexpectedly, we also detected that the respiratory frequency at rest is significantly higher in subjects with Alzheimer's disease. This is an interesting discovery – in my opinion a revolutionary one – that may open a whole new world in the study of the Alzheimer's disease. It most likely reflects an inflammation, maybe in the brain, that once detected can probably be treated and severe states of Alzheimer's might be prevented in the future."

Dr Megli said: "With disappointing results from protein-focused drug trials, the vasculature and neurovascular unit are promising targets for future treatments of Alzheimer's disease." Professor Stefanovska said: "We show clear results of our approach and how Alzheimer's can be detected simply, noninvasively, and inexpensively. The method has a great potential, and we are discussing possibilities to create a spin-out or start-up company to proceed with it. Of course, more research is needed." ■

Source: Lancaster University

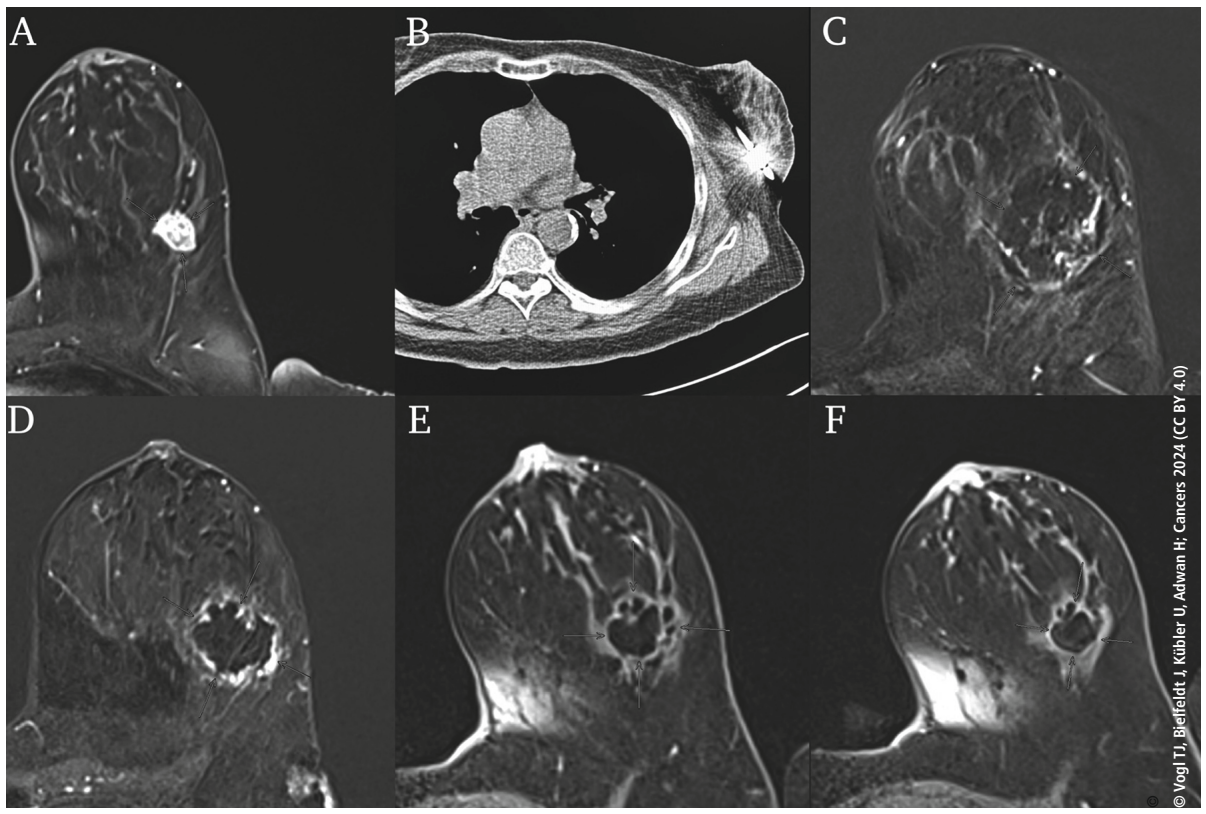
Freezing cancer cells

Cryoablation: A treatment option for low-risk early-stage breast cancer patients

Cryoablation, the destruction of malignant cancer cells by freezing them, is increasingly becoming an alternative to having conventional lumpectomy for patients diagnosed with early-stage, localised, low-risk breast cancer. Findings from numerous recent clinical trials show that cancer recurrence rates are very low and are comparable to breast conservation surgery (BCS).

Unlike in BCS, however, no breast tissue is removed, and scarring is minimal. The procedure is performed in outpatient hospital radiology departments, with local anaesthesia and ultrasound or MRI guidance, taking less than an hour. Patients experience little discomfort and can resume normal activities within a day or two.

Mild-to-moderate adverse effects for patients having the procedure include bruising, localised edema, freeze-related skin burns, rash, bleeding from needle insertion, local hematoma, tenderness, pruritis and rash. They resolve rapidly without complications or long-term residual effects.



59-year-old female patient with cancer in the left breast. The Cryoablation was performed with two 9 min freeze cycles with a 9-min passive thaw cycle in between. (A) Pre-Ablation contrast-enhanced T1-weighted MR images. Tumour localized in left lower lateral quadrant. (B) The cryoprobe is inserted in the lesion during the CT-guided ablation procedure. (C) First post-ablation images, 24 h after ablation. The ablation zone can be seen in the contrast-enhanced T1-weighted MR images. (D) Ablation zone in the 3-month post follow-up MR-images. (E) Ablation zone in the 6-month post follow-up MR-images. (F) Ablation zone in the 9-month post follow-up MR-images. The patient showed a complete remission and had a survival time of 16 months starting at the date of ablation until last contact.

‘Cryoablation is most effective when treating small lesions without extensive intraductal component,’ say Lauren M. Kopicky, MD, a breast surgeon at Cleveland Clinic and Debra A. Pratt, MD, Medical Director of breast services of the Moll Cancer Center of Fairview Hospital in Ohio.[1] They caution that breast cryoablation is appropriate only for select patients, and is currently authorized by the US Food and Drug Administration (FDA) only in clinical trials. According to cryoablation technology developer IceCure Medical, the technique is approved for use in Europe for breast cancer and fibroadenomas (benign breast tumours) for over two decades and is considered a well-tolerated outpatient procedure.

Promising trial results

Much awaited five-year outcomes of the ICE3 Trial, initially presented at the 2024 American Society of Breast Surgeons (ASBrS) Annual Meeting, may spur FDA approval.[2] This is the first and largest-to-date prospective, multi-centre clinical trial of breast cryoablation for breast cancer. One hundred ninety-four women, ages 55 to 94, received cryoablation treatment at 19 hospitals, with imaging follow-up only and no subsequent tumour excision for 194 patients. None had lymph node involvement. Almost 80% of participants received adjuvant treatment, predominantly (63.9%) endocrine treatment.[3] Seven patients (3.7%) experienced cancer recurrence. Two patients (1%) developed distant metastasis and died.

Principal investigator Richard E. Fine, MD, of the West Cancer Center and Research Institute in Germantown, Tennessee, reported that at 54 months, the overall ipsilateral breast tumour recurrence (IBTR) rate was 3.7%, 3.2% for patients who subsequently received endocrine surgery. This gives a five-year IBTR survival rate of 4.3% and 3.7%, respectively. Five years following treatment, 100% of patients and physicians were very satisfied with cosmetic results: a normal-looking breast with a small scar from the cryoablation needle.

CT-guided cryoablation for curative intent and metastatic local tumour control

In Germany, cryoablation is being used to treat patients with localised recurrence, auxiliary node involvement, and metastasis. Researchers at University Hospital Frankfurt report their treatment of 56 tumours in 45 patients using liquid-nitrogen based CT-guided cryoablation in Cancers.[4]

The study cohort consisted of breast cancer patients who did not want to undergo surgery or who had unresectable tumours who underwent cryoablation between May 2019 to May 2023. They ranged in age from 31 to 86 years. Thirteen with newly diagnosed breast cancer and 11 with breast cancer recurrence were treated with curative intent. Twenty-one with metastases were treated for local tumour control. All patients completed the treatment, and none experienced any complications.

Patients had a planning CT-scan prior to cryoablation to locate an appropriate incision point and plan the trajectory of the cyroprobe shaft. Breast MRI scans were performed 24-hours post-treatment. If any residual contrast-enhanced tumour tissue was seen at ablation margins, another cryoablation procedure was performed to ensure complete ablation of the tumour.

Principal investigator Prof. Thomas J. Vogl, MD, PhD, Director of the Clinic of Radiology and Nuclear Medicine, and colleagues advise that they selected CT-guidance instead of ultrasound guidance for the ablation procedure to enable an exact visualisation of the cryroprobe, the malignant tumour, and the ice ball in all dimensions and to ensure a sufficient safety distance to adjacent structures.

They say that the advantages of using a liquid-nitrogen system are that it is cost-effective, time-efficient for both patient and clinicians, and has a notably better cosmetic outcome. It does not require specific security measures, because liquid nitrogen is not stored in a pressurised container. The disadvantage is that the procedure takes considerably longer than either microwave or radiofrequency ablation procedures. ■

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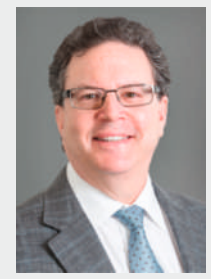

Richard E. Fine

Richard E. Fine, MD, is a breast surgeon at the Margaret West Comprehensive Breast Center in Germantown, Tennessee. He has the distinction of being one of the first surgeons in the United States to perform image-guided breast biopsies and has extensive experience in new breast biopsy methods. Dr Fine is a past president and Chairman of the Board of the American Society of Breast Surgeons.

Prof. Thomas J. Vogl, MD, PhD, an interventional radiologist, is Director of the Clinic of Radiology and Nuclear Medicine at University Hospital Frankfurt, Germany, specializes in interventional oncology and vascular procedures. He also is Professor for X-ray Diagnostics of the Goethe University Frankfurt am Main. Dr Vogl’s research has resulted in worldwide optimisation of imaging procedures and surgical methods. He was involved extensively in the evaluation of contrast agents and developed an angiography robot with the ability to deliver high-resolution diagnostic images from inside the body to detect previously undiscovered tumours.

ProSense Cryoablation System. © IceCure.

Hyperbaric oxygen therapy to reduce toxic effects

HBOT shows promise after breast cancer

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. ■

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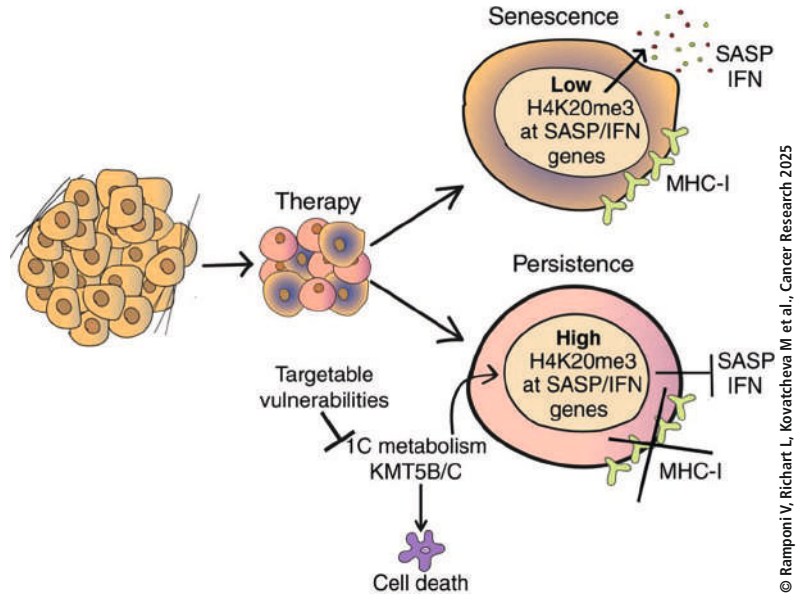
New approach to crack persister tumour cells

Cancer therapies do not always succeed in eliminating tumour cells. Some of these cells enter a state of senescence—a latent, non-dividing state that is generally irreversible.

Others, however, enter a state known as ‚persister,' where dormancy is temporary and reversible. This state allows the cells to begin growing again after the treatment has ended, leading to cancer recurrence.

A team led by Dr. Manuel Serrano at the Institute for Research in Biomedicine (IRB) Barcelona has discovered a key strategy through which these persister cells evade the immune response and resist cancer treatments. Specifically, the study reveals that persister cells block the genes responsible for inflammation through an epigenetic mechanism that acts as a ‚molecular lock,' preventing these genes from becoming activated and alerting the immune system. This lock stops the immune system from detecting and eliminating these cells, allowing them to resist treatment.



Graphical abstract of the new research

This contrasts with senescent cells, which are highly inflammatory and use different mechanisms to evade the immune response.

"This epigenetic silencing is a weakness of persister cells and could be leveraged to design new therapeutic approaches," says Dr. Serrano, head of the study and currently working at Altos Labs (Cambridge, UK).

The study, first-authored by Dr. Valentina Ramponi, has been published in the journal Cancer Research.

In addition to identifying this mechanism, the study shows that inhibiting the epigenetic mechanism could unlock inflammatory genes and compromise the viability of persister cells, thus paving the way for the development of new therapies. "The goal is to be able to develop drugs that selectively target persister cells and strengthen the effect of conventional treatments," concludes Dr. Ramponi, now a postdoctoral researcher at the AIRC Institute of Molecular Oncology.

This discovery marks a step forward in the fight against resistance to cancer treatment. By targeting persister cells, the likelihood of relapse could be reduced, thus improving patient prognosis.

This study has been done in collaboration with the Rovira i Virgili University, the Queen Mary University of London, the CIBER de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), the AIRC Institute of Molecular Oncology, and Altos Labs' Cambridge Institute of Science. The study was funded by the European Research Council (ERC), the Spanish Association Against Cancer, the European Molecular Biology Organization (EMBO), and the Barcelona Institute of Science and Technology (BIST). ■

Source: Institute for Research in Biomedicine Barcelona

San Antonio Breast Cancer Symposium (SABCS)

Young women and breast cancer: research in focus

At the San Antonio Breast Cancer Symposium (SABCS) in December, three experts presented new approaches and study results for the treatment of breast cancer in young women.

In her lecture, Camila dos Santos explained that the development of the mammary glands is strongly controlled by hormones that promote cell growth and cell division. 'During pregnancy, there are significant structural and functional changes in the breast, such as the expansion of cells and the production of new proteins to prepare for milk production,' said the Associate Professor at Cold Spring Harbor Laboratory, New York.

'These hormonal influences not only change the growth pattern of epithelial cells but also affect the collagen structure of the breast and its alignment, as shown by microscopic techniques such as collagen staining.' She emphasized that pregnancies leave epigenetic changes that permanently affect the gene expression of breast cells. 'Early pregnancies can reduce the risk of breast cancer by 30–40%, depending on the subtype and genetic mutations. This protective effect often lasts into postmenopausal age,' explained dos Santos. Using mouse models, it was shown that pregnancies promote cell aging, which inhibits tumour development. It was also discovered that pregnancy affects the immune system by infiltrating certain types of T cells that can alter the tissue environment of the breast and inhibit tumour growth.

Urinary tract infections promote tumour growth

The systemic effects of urinary tract infections (UTIs) on the breast are still relatively unknown. They lead to a systemic inflammatory reaction and increased collagen deposition in the breast. In mouse models, it was found that UTIs cause hyperplasia of the mammary gland ducts and changes in cell behaviour. These changes can accelerate tumour growth in genetically susceptible models. 'Pregnancy and systemic factors such as infections can influence breast development and breast cancer risk in multiple ways. These findings could lead to the development of preventive therapies that modulate the immune system or influence epigenetic changes to reduce breast cancer risks,' summarized the expert.

Suppression of ovarian function

In her presentation, Prudence Francis looked at various approaches to suppressing ovarian function in premenopausal women with early breast cancer. The medical oncologist breast cancer clinician-researcher at Peter MacCallum Cancer, Melbourne, Australia, pointed out that ovarian function can be reversibly suppressed by GnRH agonists, which is particularly suitable for young women to avoid permanent menopause. 'Alternatively, surgical menopause is an option for women close to the natural menopausal age,' said the expert.

Monitoring estradiol levels is also important to ensuring effective suppression of ovarian function. 'In clinical practice, this is often not done routinely unless specific symptoms indicate that suppression is inadequate. However, studies show that younger women, women without chemotherapy, and those with higher BMI are at increased risk of not achieving persistent suppression,' Francis explained. Ovarian suppression is particularly indicated in premenopausal women with a high risk of recurrence, for example in very young women or those who are to be treated with an aromatase inhibitor. For premenopausal women with estrogen receptor-negative breast cancer, ovarian suppression is increasingly being discussed as a means of reducing the risk of premature menopause. 'Although there is no oncological benefit in this group, the quality of life and health of women could be improved by avoiding premature menopause,' the expert made clear.

Aftercare and treatment: a multidisciplinary approach

Dr Jenni Sheng addressed the various aspects of follow-up care and treatment for young women with breast cancer in her presentation. The Assistant Professor in the Department of Oncology at the Johns Hopkins University School of Medicine, Baltimore, emphasized that a multidisciplinary approach is necessary to optimize survival and quality of life, as this patient group is often underrepresented in studies. 'There is a particular focus on fertility and family planning, including the importance of early fertility preservation discussions. Studies show that pregnancy after breast cancer does not worsen disease-free survival or overall survival,' said Sheng. Another key point of her presentation was psychosocial health: 'Younger patients often suffer from higher levels of psychological stress. The fear of relapse is widespread, but can be reduced through cognitive interventions,' the expert made clear, emphasizing the importance of couples therapy to improve coping strategies. Problems such as insomnia could be successfully treated with a combination of cognitive behavioural therapy and light therapy.

Finally, Sheng discussed support programmes for young adults. These should cover a broad spectrum, from psychosocial support and fertility counselling to the treatment of menopausal symptoms. 'However, the implementation of such programmes is hampered by limited financial and human resources,' she criticized. ■

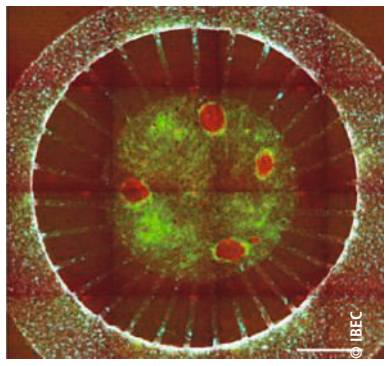
Report: Sonja Buske

Replicating tumours to assess cancer immunotherapy efficacy

The Micro Immune Response On chip (MIRO) allows tumours and their environment to be replicated in order to understand their response to immunotherapy-based treatments.

The device, which has already been successfully tested on breast cancer samples, could be key to developing new treatments and determining the most appropriate therapy for each patient in a personalized way. The work, published in Nature Communications, is the result of a collaboration between the Institute for Bioengineering of Catalonia and the Research Institute of the Hospital del Mar.

The MIRO device makes it possible to fill a gap in the creation of treatments against cancer cells. Many developments offer promising results in the laboratory, in vitro and in mouse models, but they do not work as well when transferred to humans. "MIRO enables to recreate not only the tumour, but its environment and the interaction they have with the cells of the immune system. This relationship is vital for the success of immunotherapy-based treatments which, despite their curative potential, currently only work in between 20 and 40% of patients" explains Dr Anna Labernadie, who designed the microfluidic system during at IBEC and now leads the Cell Behavior and Tissue Bioengineering laboratory at the Príncipe Felipe Research Center (CIPF) in Valencia.



Representative image of MIRO co-culture on day 10

The researchers who have developed this technology have already tested it with breast cancer samples known as HER2-positive. This type of cancer cell has very high levels of the HER2 protein, which promotes rapid tumour growth, but at the same time, can be treated with therapies that specifically target this protein.

The tests carried out have made it possible to verify the importance of the environment surrounding breast tumours in protecting them from the most common treatment in this type of cancer, the monoclonal antibody trastuzumab. "Thanks to MIRO, we have been able to track the immune cells, see how they lose speed, movement, as they approach the tumour, which makes the treatment not work. They encounter a barrier formed by the tumour environment and become blocked", explains Dr Alexandre Calon, head of the Translational Research Laboratory in Tumour Microenvironment at the Hospital del Mar Research Institute.

The MIRO device, which has already been tested with other types of solid tumours, such as lung or colon tumours, is manufactured using microfluidic techniques. These techniques allow fluids and cells to be manipulated on a very small scale. MIRO includes cell cultures of different types, separated into compartments in order to direct and observe their evolution. This model, the first of its kind created with these techniques, makes it possible to recreate and study in detail the interaction between cancer cells, their connective tissue and immune responses. "This model allows us to directly test the treatments that would be used with patients," explains Dr Xavier Trepat, ICREA research professor at IBEC, where he leads the Integrative Cell and Tissue Dynamics group, and member of the University of Barcelona (UB).

The device's ability to analyse the functioning of different treatments, the emergence of possible resistance and even identify new biomarkers individually for each patient, represents a great advance in the design and personalisation of immunotherapy treatments in oncology. In this sense, Dr Joan Albanell, head of the Medical Oncology Service at Hospital del Mar and director of the Cancer Research Program at his research institute, pointed out that "MIRO is an innovative preclinical model that can help improve the success rate and efficacy of new strategies with immunotherapy once we transfer them to clinical trials".

As for future work, IBEC, ICREA and Hospital del Mar Research Institute have already filed a joint patent application for MIRO's technology. "Our goal is to transfer this technology to the pharmaceutical industry and hospitals to be able to apply it to patients," explains Dr Anna Labernadie.

The study described is part of Alice Perucca's PhD thesis at IBEC. Her work focuses on investigating the role of the immunocompetent ecosystem in cancer progression.

The work also included the collaboration of the Institute for Research in Biomedicine (IRB Barcelona), the University of Barcelona (UB), the Bioengineering, Biomaterials and Nanomedicine Networking Biomedical Research Centre (CIBER-BBN), Pompeu Fabra University and the Oncology Networking Biomedical Research Centre (CIBERONC-ISCIII); and has received partial funding from the "la Caixa" Foundation. ■

Source: Institute for Bioengineering of Catalonia

From chatbot to medical assistant

Generative AI: prompt solutions for healthcare?

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Anyone who has exchanged a few lines of dialogue with a large language model (LLM), will probably agree that generative AI is an impressive new breed of technology. Beyond their use as chatbots, LLMs show great potential in addressing some of the most urgent challenges in healthcare. At the Medica tradefair in Düsseldorf, several expert sessions were dedicated to the topic of generative AI, its potential medical applications and current caveats.

The above fact that almost everyone has tried their hands at interaction with a chatbot is testament to what some experts believe to be a key benefit of the technology: 'LLMs are a game changer in that they make generative AI approachable for more people, not just data scientists,' explained Dr Bertram Weiss during a discussion at the Medica Health IT Forum. 'This is because you can talk to them using normal language instead of code,' the Pharma Lead from Berlin-based AI developer Merantix Momentum added.

It is this high level of accessibility that could help hospitals offload a number of basic, but time-consuming tasks, such as appointment scheduling, or patient case documentation. For example, generative AI has shown promising results in transcribing doctor's notes into structured formats, said co-panellist Dario Antweiler from the Fraunhofer Institute for Intelligent Analysis and Information Systems IAIS. Even though results still need to be checked by a human, 'this takes away hours of daily work from medical professionals,' the expert pointed out.

Everyone hallucinates sometimes

Pointing out the need for human validation of the AI-generated content brought about one of the technology's major issues: results that look plausible at first glance but may turn out to be inaccurate or even completely made up by the algorithm – a phenomenon that has gained notoriety as AI "hallucinations".

Since these fabricated findings cannot always reliably be excluded, safeguards should be established, suggested Antweiler. For example, different AI models could be running independently on the same task to reveal inconsistencies. Also, human operators should always be aware of the possibility of such errors. 'However, we should not forget that humans also "hallucinate" – we make mistakes, and we tend to be less critical about them than we are about AI hallucinations,' the expert cautioned. 'Therefore, we should establish fair comparisons, to not vilify this powerful technology.'

Baked-in bias

Prof Dr Reinhard Heckel pointed to insufficient data as a major cause for underperforming AI models. Rare conditions are by nature underrepresented in most datasets, and variations in image quality may increase existing misinterpretations, the expert from the Technical University of Munich's School of Computation, Information and Technology said, adding that inclusion of diverse data could mitigate some of these issues. However, some technologies have biases deeply embedded into their functionality, he explained. For example, some imaging modalities are optimized for lighter skin tones, which inherently leads to superior results in these patients. 'This is a social issue,' Antweiler said, pointing out the need to establish groups that should be especially protected from this kind of bias.

Of further note were the IT requirements of generative AI, especially regarding computing power. More general models are often considerably more demanding, barring their use for solutions that need to be locally based to ensure data security. In these cases, smaller, more specific AI models should be implemented, the experts agreed.

Need for "AI literacy" among medical professionals

Despite the current shortcomings of generative AI models, many experts consider their clinical adaptation to be almost inevitable. Heckel noted that US-based companies are especially adept at translating AI models to marketable products, while European developers tend to have more high-end models, but are more cautious in their implementation. In medical settings, an AI may process highly sensitive data, which calls for a thorough analysis of benefits and potential risks, Weiss pointed out. 'We should not blindly push for implementation when the side-effects are unclear,' he concluded.

The aforementioned US companies were of course also at the tradefair, to present their generative AI solutions. Notably, Hadas Bitram, Partner General Manager, Health AI at Microsoft Health & Life Sciences, addressed the issue of responsible use of medical AI at the Medica Innovation Forum. She highlighted safeguards in the company's own products against AI hallucinations and omissions. For example, the LLM gives reference to the sources a given information is based on, to enable validation and provide clinical context. 'Still, there should always be an accountable medical professional in the loop,' Bitram said.

The expert also highlighted "AI literacy" as a crucial skill for future clinicians: 'The work of medical professionals will become increasingly sophisticated,' she predicted. Assessing and using the right AI tools, interpreting their results and making the right calls based on their input will therefore be essential. AI may not replace doctors, she concluded, but doctors who use AI will replace those who don't. ■

Author: Wolfgang Behrends

AI keeps an eye on health AI

Using a pioneering artificial intelligence platform, Flinders University researchers have assessed whether a cardiac AI tool trialled in South Australian hospitals actually has the potential to assist doctors and nurses to rapidly diagnose heart issues in emergency departments.

"AI is becoming more common in healthcare, but it doesn't always fit in smoothly with the vital work of our doctors and nurses," says Flinders University's Dr Maria Alejandra Pinero de Plaza. "We need to confirm these systems are trustworthy and work consistently for everyone, ensuring they are able to support medical teams rather than slowing them down."

Developed by Dr Pinero de Plaza and her team, PROLIFERATE_AI is a human-centred evaluation tool that uses artificial intelligence alongside researcher analysis to assess how well AI tools work in hospitals. "In order to understand if the AI systems are viable, we look at how easy they are to use, how well doctors and nurses adopt them, and how they impact patient care," says Dr Pinero de Plaza, a research fellow in Flinders' Caring Futures Institute. "It's not just about making AI accurate; it's about making sure it's easy to understand, adaptable, and genuinely helpful for doctors and patients when it matters most."

Published in the International Journal of Medical Informatics, the study used PROLIFERATE_AI to assess the RAPIDx AI tool; designed to help emergency doctors quickly and accurately diagnose cardiac conditions by rapidly analysing clinical and biochemical data.

With chest pain one of the most common reasons for ED visits, the South Australian health system has been part of an NHMRC-funded trial being run across 12 hospitals in metropolitan and rural South Australia, which is currently analysing its 12-month patient outcomes. Before and during the trial, the PROLIFERATE researchers evaluated the tool, with medical and nursing staff at the participating hospitals being provided the opportunity to share their insights on interacting with the RAPIDx AI tool.

The results showed that while experienced clinicians, such as ED consultants and registrars, demonstrated high comprehension and engagement with the RAPIDx AI tool, less experienced users, including residents and interns, faced usability challenges. Registered nurses also reported strong emotional engagement with the tool, recognising its potential to enhance patient safety by reducing diagnostic uncertainty. "What sets PROLIFERATE_AI apart is its ability to provide actionable insights," says Dr Pinero de Plaza. "Rather than focusing solely on technical performance, we evaluate AI tools based on real-world usability and clinician trust, ensuring that these technologies are not just innovative but also practical and accessible."

While the research demonstrated consultants and registrars benefited most from using RAPIDx AI, the study also highlighted the need for targeted training and workflow-aligned interfaces to improve adoption rates among new users.

"Our goal is to create AI solutions that empower doctors and nurses, not replace them," says Dr Pinero de Plaza. "Technology alone cannot solve the complexities of emergency care. We need AI systems that work seamlessly with clinicians, support decision-making under pressure, and integrate smoothly into existing workflows. We are committed to enhancing our AI tools to ensure they are instinctively user-friendly and to develop customised training programs that meet the diverse needs of healthcare professionals and others." ■

Source: Flinders University