VOL 30 ISSUE 1/21 • March/April 2021

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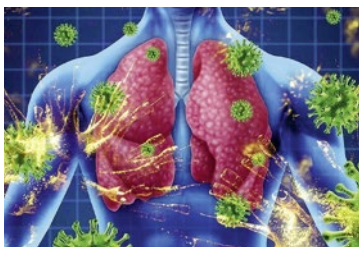


The Chaimeleon project

A new EU-wide repository for health-related imaging data could boost development and marketing of AI tools for better cancer management. The open-source database will collect and harmonise images acquired from 40,000 patients, spanning different countries, modalities and equipment. This approach could eliminate one of the major bottlenecks in the clinical adoption of AI today: Data bias.

Report: Mélisande Rouger

The project, named 'Chaimeleon', has been injected with €9 million from the European Commission to create a homogeneous dataset, by 2024, to predict tumour behaviour with the help of AI. Eighteen partner institutions and external providers will select and analyse images that have been acquired at different European sites in patients who have and will be diagnosed with breast, colorectal, lung and prostate cancer between 2015 and 2024.

The researchers will design a multimodal analytical data engine to facilitate the interpretation and extraction of the relevant information stored in the database. Leading developers will validate applicability and performance for AI experimentation, and the selected tools will undergo early validation in observational clinical studies.

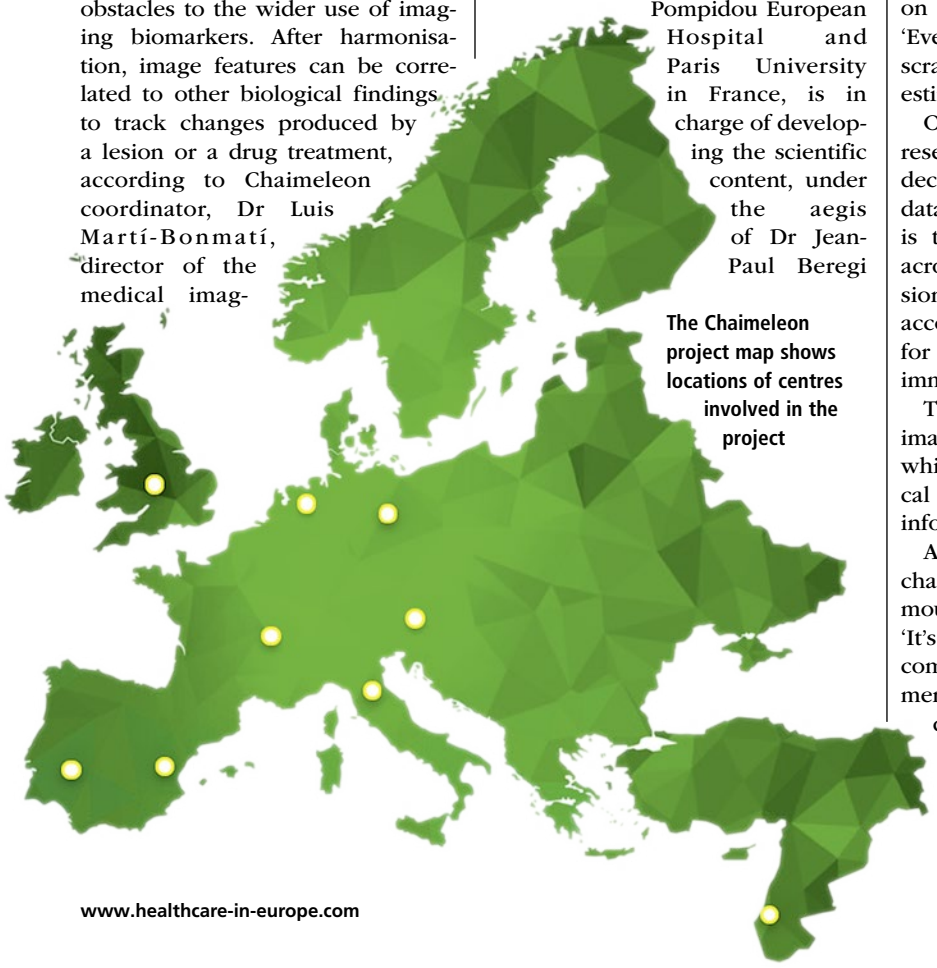
Harmonising images of 40,000 patients

A key step of the project is to harmonise images. This enables the algorithms to obtain relevant data from them which will help clinical practice. The developers are confident that this will help overcome data heterogeneity, one of the main obstacles to the wider use of imaging biomarkers. After harmonisation, image features can be correlated to other biological findings to track changes produced by a lesion or a drug treatment, according to Chaimeleon coordinator, Dr Luis Martí-Bonmatí, director of the medical imaging department at La Fe Hospital in Valencia, Spain. 'We want to be able to predict tumour behaviour using images regardless of the equipment, protocol or version used for their acquisition,' he said. 'Reducing variation between imaging studies is critical for AI to have a real impact.'

Images obtained from different hospitals or even different departments within the same hospital will always produce heterogeneous results. Variations in imaging equipment and constantly evolving technologies make it near-impossible to reliably generate comparable images in clinical practice, even when following the same imaging protocols. However, working with heterogeneous images may compromise data impartiality in the quantification phase. 'When images come from different centres and scanners, you run the risk of working with biased data,' Marti-Bonmatí said. Because of its wide scope, the data repository should be applicable to other forms of cancer across the EU.

Selecting relevant use cases

Chaimeleon will tackle regulatory, technical and ethical issues, and then include pertinent clinical use cases. Dr Laure Fournier, professor of radiology at the Georges Pompidou European Hospital and Paris University in France, is in charge of developing the scientific content, under the aegis of Dr Jean-Paul Beregi and the French radiology teachers association (CERF). 'From image acquisition to imaging biomarkers reporting, the project is focused on inciting AI research,' she said. 'Everything has to be built from scratch; that's one of the most interesting aspects of the project.'



The Chaimeleon project map shows locations of centres involved in the project

Dr Ángel Alberich-Bayarri is CEO and co-founder of Quibim, a medtech company based in Valencia, Spain. With a PhD in biomedical engineering, he served as scientific-technical director of the biomedical imaging research group (GIBI230) and as a board member of the European Society of Medical Imaging Informatics (EUSOMII) and the European Imaging Biomarkers Alliance (EIBALL). He has more than ten years' experience in the development of quantitative image analysis solutions and their integration in clinical practice. He has co-authored more than 60 research papers and has participated in numerous international research projects in medical imaging.

Once the database is structured, researchers will have to feed it and decide what kind of images and data they want to put in. Their aim is to find a model that is viable across the EU. Criteria for inclusion in the dataset will be defined according to the clinical question - for example, to predict response to immunotherapy in lung cancer.

This determines which kind of images should be sorted out and which type of biological and clinical data can help provide relevant information.

Although harmonisation is a huge challenge, diversity of data is paramount to avoid being too specific. 'It's very important that the images come from different sites, equipment and acquisition methods, with different slice thicknesses, etc.,' Fournier explained. To achieve this, a proper balance between quantity and feasibility must be found - which inevitably leads to trade-offs: 'The more relevant data you collect, the fewer patients you have.' The selected imaging data must also add value to existing clinical practice, for example PSA in prostate cancer, she pointed out.

Dr Laure Fournier is professor of radiology at the Georges Pompidou European Hospital and the Université de Paris, France. Her time is divided between clinical work on urogenital cancers and imaging research in the INSERM U970 imaging research lab. She works on functional imaging, radiomics and big data, to extract quantitative parameters from images reflecting tumour physiology and biology, more specifically to define response to therapy. She organises the curriculum on AI for French radiology residents and is a member of the scientific committee of the DRIM France AI national image database and the medical imaging chair in the PRAIRIE interdisciplinary AI institute.

Pioneering new combinations to explain AI

The Chaimeleon repository will also be an opportunity to test combinations of advanced computational techniques, in order to make AI more understandable. Researchers will evaluate the combination of self-supervised learning and Generative Adversarial Networks (GANs) to enhance reproducibility of radiomics features and parameters extracted from cross-vendor and cross-institution CT-MR-PET/MR imaging data.

The effort will be led by the Imperial College of Science Technology Medicine in London, UK, with GE Healthcare and Quibim, a medtech company that extracts imaging biomarkers from radiology images. 'Our goal is to demonstrate that this combination is possible to reduce the bias in quantification, by building models that are more explainable,' explained Angel Alberich-Bayarri, CEO and co-founder at Quibim. 'Think of an iPad – you never give the instruction manual to a kid, they learn by interacting with the tool. In self-supervised learning, you interact with the data to find patterns within.'

Thus the researchers want to explore the use of self-supervised learning as a paradigm shift in AI, where models are autonomously developed without the need of annotated data. In self-supervised schemes, part of the data contained in the images is withheld during the training process. This way, the algorithm learns to predict hidden parts from the knowledge acquired from complete images.

The project will also build on tools that have been validated for image harmonisation of multi-vendor or multicentric data and interpretability of AI.

Quibim will notably use its experience in building the cloud-based platform of another EU project called PRIMAGE, which gathers thousands of paediatric oncology cases by integrating hospitals' repositories from all across Europe.

Dr Luis Martí-Bonmatí is professor and chairman of radiology and director of the medical imaging department at La Fe University and Polytechnic Hospital, Valencia. He is a full member of the Spanish Royal National Academy of Medicine representing radiology and was founder and director of the research group on biomedical imaging (GIBI230) within La Fe Health Research Institute. He has presided over the European Society of Magnetic Resonance in Medicine and Biology (ESMRMB), Spanish Society of Radiology (SERAM), Spanish Society of Abdominal Radiology (SEDIA) and European Society of Gastrointestinal and Abdominal Radiology (ESGAR).

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CONTENTS

What EU/UK deals may mean

Post-Brexit and future cancer research

Mark Nicholls reports on an online experts debate focused on how Brexit could affect research

Despite Brexit uncertainties, four leading UK cancer research experts expressed optimism for continued pan-European collaboration and innovation during the online panel debate 'Brexit deal: What it really means for cancer research and innovation' hosted by the National Cancer Research Institute (NCRI). The experts, Dr Sheuli Porkess, Professor Richard Sullivan, Emlyn Samuel, and Jim Elliott, were chaired by Professor Pam Kearns, Chair of Clinical Paediatric Oncology at the University of Birmingham.

Steep challenges

Having reviewed the current UK research and innovation landscape, the panellists discussed the outlook from the perspective of key UK organisations. Also considered was the potential impact of the coronavirus pandemic on cancer research, science, innovation, funding and treatment in the future, and also the long-term economic effect of Covid-19 internationally.

Porkess noted that Brexit and the pandemic had brought disruption to global R&D and healthcare systems, but had motivated the Association of the Britisch Pharmaceutical Industry (ABPI) to be even more focused on being internationally competitive with commercial clinical trials.

Concerns include continued participation in EU programmes, data adequacy, clinical trial supplies, moving products for research and additional hurdles for equipment and consumables imports, regulation of trials, and immigration factors. 'It's tough at the moment with the effects of Covid-19 and we also know some practicalities of Brexit have not been worked through,' Porkess said. 'But, we have a recovery resilience and growth programme in place that gives us opportunities we've not had before to get through those changes, to ensure recovery from the pandemic and drive that growth in research that we all want to see.'

The Cancer Research UK (CRUK) has worked with the UK government, and across Europe, on the implications of Brexit since the 2016 referendum to ensure, whatever the outcome, that 'cancer patients and research is protected as far as possible', Samuel pointed out.

Continuity across borders

Key topics were the regulatory environment for clinical trials, immigration and movement, as almost a third of CRUK trials involve patients from EU member states.

'We've also been working to ensure that patients can continue to access new and innovative medicines as well as the supply of existing medicine across borders, and also working on monitoring broader research environment with the Horizon Europe Association – one of the real positives to come out of the deal,' Samuel added. 'There was a huge relief that there was a deal; it provides a platform for further development and negotiation of the UK relationship with the EU.'

Sullivan said his team had examined the effect of Brexit on cancer research with regards to the socio-economic impact; the mechanistic aspects of collaboration and partnership, such as policy changes around the ability for people to move freely across borders; and the political attitude to collaborations. While the UK had previously enjoyed an enormous amount of EU funding, he feared it now risked no longer being centre stage in major initiatives.

Elliott commented that it still remained difficult to see clearly what the issues may be because of the pandemic, but added: 'The characteristic of the cancer patient movement is a "can-do" attitude, so I'm reasonably confident that the UK research community will find ways to carry on and collaborate across Europe, as we do in the rest of the world.'

Research in a laboratory

Copyright: CRUK

Emlyn Samuel leads the policy department at Cancer Research UK and a team of policy, public affairs and campaigning experts who work to drive policy change up to international levels.

Jim Elliott is a member of the National Cancer Research Institute (NCRI) Consumer Forum and is part of the NCRI Consumer Involvement Advisory Group.

A new relationship

Pre-Brexit free movement, 'a significant enabler of collaboration', has gone, causing Elliott concern over paediatric oncology and rarer cancers, and the possibility that UK patients may not be eligible to take part in trials being run in the EU. He warned of continuing uncertainty as a new relationship is developed with the EU on immigration and regulatory status '…and how we will continue to partner with the EU on clinical trials and research going forward'.

Discussion flowed on. Question: Might the UK, being outside the European Medicines Agency (EMA), offer speedier approval of drugs and therapies from the Medical and Healthcare products Regulatory Agency (MHRA), making it an attractive test bed for innovation?

Sullivan said the new Horizon Europe programme remains important, with the Erasmus programme no longer accessible to the UK and replaced by a 'global talent visa', with concerns that movement between the UK and Europe for research would become more complex and costly.

How will Brexit affect funding that enables cross border research? While Covid has impacted on charitable income, the panel felt UK participation in the Horizon Europe research and innovation framework programme was important. 'The UK has some of the best early phase clinical trial activity, not just in Europe but probably in the world,' Sullivan said, pointing out the UK's 'amazing infrastructure for clinical research' to run complex trials. Data protection and exchange of personal data with GDPR regulations is still an issue, but confidence remains over an agreement on data adequacy for data flow. CRUK funds 30% of research fellows, and 43% of post-doctoral researchers from the European Economic Area (EEA) who will hopefully be able to 'work around Brexit'. On the upside, the Brexit deal provides 90-day visa-free visits.

In conclusion, Kearns questioned the panel's optimism about post-Brexit cancer research. Porkess is optimistic about UK-EU research collaborations, and Sullivan believes research relationships built up over years will remain strong. Elliott added that patient anxiety could be eased with good communication and engagement, while Samuel feels positive about conversations over 'moves to bolster' the UK's life sciences and clinical trial environment.

Professor Pam Kearns is Chair of Clinical Paediatric Oncology at the University of Birmingham, an Honorary Consultant Paediatric Oncologist at Birmingham Women and Children's Hospital, and Director of the University of Birmingham's Institute of Cancer and Genomic Sciences and Director of the Cancer Research UK Clinical Trials Unit (CRCTU).

Pharmaceutical physician **Dr Sheuli Porkess** is Interim Medical Director at the British Pharmaceutical Industry Association. She began her career in the NHS and has held numerous medical leadership roles in companies at a national, regional and international level.

Richard Sullivan is Professor of Cancer and Global Health at King's College London, Director of the Institute of Cancer Policy, and co-Director of the Conflict and Health Research Group.

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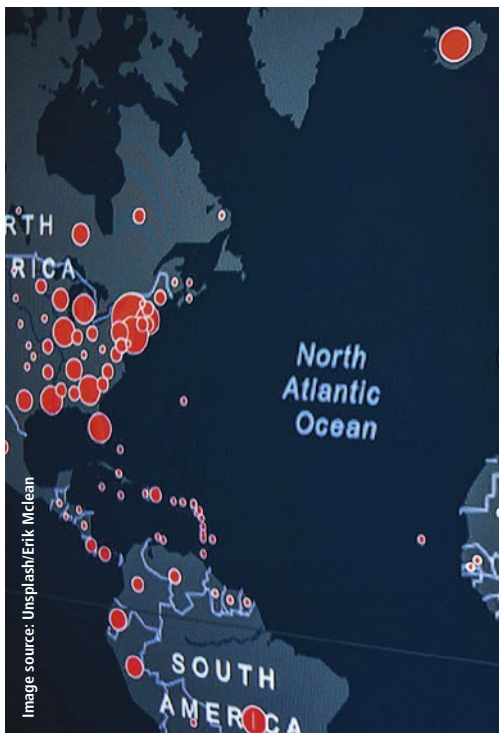


Image source: Unsplash/Erik Mclean

Due to compromised immune systems, cancer patients are at higher risk of contracting infections. How does cancer impact on patients who also contract Covid-19? To collect this data, four cancer registries, one in the EU, one in the UK, two in the USA, have been established.

Report: Cynthia E. Keen

The first large, multi-institution study of the impact of Covid-19 was conducted in Wuhan, China, and presented at the virtual American Association for Cancer Research (AACR) Annual Meeting 2020 in April.

The study included 105 cancer patients and 536 age-matched patients without cancer, and showed that Covid-19 patients with cancer had higher risk in intensive care unit (ICU) admissions and mortality. However, at the same conference, researchers from Gustave Roussy Cancer Campus in Villejuif, France, reported that 137 cancer patients diagnosed with the coronavirus in March did not have more lethal or aggressive disease than patients without cancer in the global population. Such conflicting reports supported the urgent need to acquire long-term global data.

The UK Coronavirus Cancer Monitoring Project

The UK Coronavirus Cancer Monitoring Project (UKCCMP) (www.ukcoronaviruscancermonitoring.com), established in mid-March 2020, was the first Covid-19 clinical registry to enable near real-time reports to frontline physicians about the effects of Covid-19 on cancer patients. Its objective is to monitor the impact of Covid-19 and enable oncologists to gain crucial insights and inform clinical- and infrastructure-based decision making. A live clinical data dissemination system provides a daily update to an interactive website; weekly reports are sent to individual UK cancer centres and clinicians. In its first five weeks

The importance of Covid-19 registries for cancer patients

ng robust fic tools

The Covid-19 map.

of operation, the UKCCMP accrued the largest prospective database of symptomatic and asymptomatic Covid-19 cancer patients globally. Approximately 80% of UK adult and 100% of paediatric cancer treatment centres are currently participating. As of mid-August, the cases of 2,314 adult and 61 paediatric cancer patients were enrolled in the database.

'Our objective is to identify and learn from every case of Covid-19 in cancer patients in the UK,' said Leonard Y W Lee MD PhD., an honorary research fellow of the Institute of Cancer and Genomic Studies of University Hospitals Birmingham and an executive lead of the project.

'The number of cancer patients with Covid-19 in the UK is relatively small. But approximately 2.5 million individuals live with or have a history of cancer in the UK, with an estimated 1,000 new diagnoses each day. A substantial number of new cases require, are undergoing, or are recovering from surgery and complex treatments. One of the things we want to determine is if specific cancer treatments may differentially contribute to the risk of developing Covid-19.'

In results of a Covid-19 mortality study* of 800 cancer patients who contracted Covid-19 between 18 March and 25 April revealed that patients receiving or who had received chemotherapy and/or radiotherapy within the past 30 days were not at greater risk of dying when compared with other cancer patients. (*Conducted by the UKCCMP project team and published in *The Lancet* 20/6/2020). However, age and comorbidities were significantly associated with Covid-19 related death of 28% of these patients, the researchers reported.

'We also determined that cancer patients were at increased risk from Covid-19,' Lee told *European Hospital*. 'Globally, a mortality rate of 20-35% is being reported. It's important for patients to undergo regular rapid Covid-19 testing, especially prior to each cycle of chemotherapy. Oncologists need to take decisive and active steps, such as screening regularly for Covid-19, to prevent infection while administering effective anti-cancer treatments for patients who have a rapidly progressive tumour.'

The Covid-19 and Cancer Consortium (CCC19)

The Covid-19 and Cancer Consortium (CCC19) (www.ccc19.org), also established in mid-March, is collecting data to study the characteristics and course of illness among patients age 18 and older diagnosed with Covid-19 and a current or past diagnosis of invasive solid or haematologic malignancy.

Currently, 120 institutions are participating, of which 11 are located outside the USA. The 11-member steering committee includes Professor Solange Peters MD PhD, head of the Medical Oncology Service of the University Hospital Lausanne, and the current president of the European Society for Medical Oncology (ESMO).

CCC19 is actively analysing and reporting findings from its registry, including a cohort study on the clinical impact of Covid-19, published open access in The Lancet (28 May 2020), and a study on the utilization of Covid-19 treatments and clinical outcomes among cancer patients, published open access (22 July) in *Cancer Discovery*.

The clinical impact study included 928 invasive cancer patients from Canada, USA and Spain who received treatment for Covid-19 between 17 March and 16 April 2020. The study's primary endpoint was all-cause mortality within 30 days of Covid-19 diagnosis. This is an ongoing clinical trial (NCT04354701) with an accrual goal of 10,000 patients.

Patients ranged in age from 18 to 90 years, with a median age of 66. The cohort had 20 different types of cancer in all stages, with 32% stable or responding to treatment, and 45% in remission or presumed cured. Three percent had surgical treatment within 30 days of contracting Covid-19, and 39% had received anticancer treatment in this time frame.

The majority had two or more comorbidities; 51% had no smoking history. Thirteen percent died from Covid-19 within 30 days of contracting it. This highly detailed, early report suggested that cancer patients appear to be at increased risk of mortality and severe illness.

The treatment utilisation study included 2,186 adults, with a median age of 67, of whom 47% had mild, 40% moderate, and 12% severe baseline Covid-19 severity. Patient demographic and cancer characteristics, Covid-19 treatments received, and outcomes are discussed in detail. Sixteen percent died from Covid-19 within 30 days of contracting it, again reinforcing the vulnerability of cancer patients to the novel coronavirus.

ASCO Covid-19 and Cancer Registry

The American Society of Clinical Oncology (ASCO) launched the ASCO Survey on Covid-19 in Oncology Registry (www.asco.org/asco-coronavirus-information/coronavirus-registry) in early April, inviting oncology practices across the USA to share information about patients. ASCO established this registry to collect both baseline and longitudinal data on how the virus impacts on cancer care and cancer patient outcomes during the Covid-19 pandemic and into 2021. Data being collected includes characteristics of cancer patients most impacted by Covid-19, estimates of disease severity, treatment modifications or delays, implementation of telemedicine in the cancer treatment setting and clinical outcomes related to both Covid-19 and cancer.

Richard L Schilsky MD, ASCO executive vice president and chief medical officer, explained that whilst the ASCO Registry and CCC19 Registry have very similar objectives, the ASCO Registry collects more information on cancer treatment and outcomes, whereas CCC19 collects more data on Covid-19 treatments.

Data is also updated on different schedules, with ASCO requesting that practices update their patients' Covid-19 status on a weekly basis and cancer status on a monthly basis. CCC19 is requesting 30- and 90-day outcomes.

'As of mid-August, 45 oncology practices and cancer treatment centres have submitted data about 300 patients with 33 different types of cancer,' Schilsky said. 'ASCO is interested in collaborating with other Covid-19 and cancer registries to extend our findings and maximise our learning from data collection on the impact of Covid-19 on people with cancer.'

ESMO-CoCARE Registry

Launched on 29 April, this registry provides Covid-19 data to cancer centres and organisations internationally (but not North America). With the most diverse geographic enrolment in the world, it is led by a steering committee of nine oncology experts from France, Germany, Portugal, Switzerland, the UK and the USA. As of mid-August, participation of cancer treatment centres was 111 – Europe, 23 – Middle East; 8 –Africa; 48 – Asia, and five – Oceania. To increase global data collection ESMO Co-Care also partnered with the CCC19 Consortium, which covers North America,

The Registry's demographic data includes age, sex, place of residence, ethnicity, and nationality. Clinical history data includes prevalence of major comorbidities and the parameters defining a patient's malignancy, including histology, stage, organ dysfunction, and molecular features.

Antineoplastic therapies administered within two months from Covid-19 infection, including chemotherapy, immune check point inhibitors and targeted therapies, surgery, and radiotherapy are being recorded.

Richard L Schilsky MD is executive vice-president and chief medical officer of the American Society of Clinical Oncology (ASCO).

Leonard Y W Lee MD PhD is an honorary research fellow of the Institute of Cancer and Genomic Studies of University Hospitals Birmingham and executive lead of the UK Coronavirus Cancer Monitoring Project.

Wako ß-glucan test

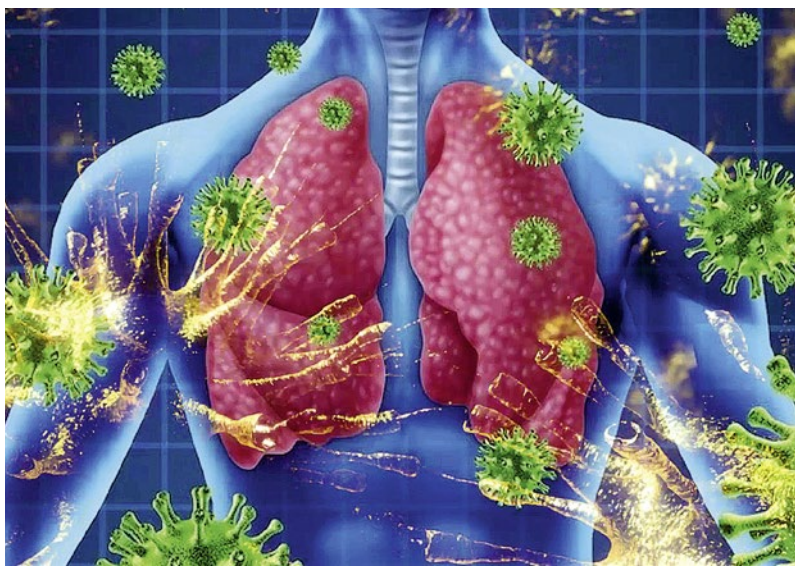
Better detection and diagnosis of fungal infections

Beta-glucan tests are proving to be pivotal in the better detection and diagnosis of fungal infections. As a robust complimentary test for traditional testing techniques and biomarkers, it is helping clinicians deliver rapid results and offering greater reassurance in more accurately identifying such infections. ß-glucan testing, which is an in vitro diagnostic test, is regularly used at University Hospitals Leuven in Belgium. 'Although it is not a specific test for a particular fungal disease, the value is its use in conjunction with other conventional tests, such as microscopy and culture, and biomarker detections,' explained Professor Katrien Lagrou, head of the Molecular Diagnostics department at the university.

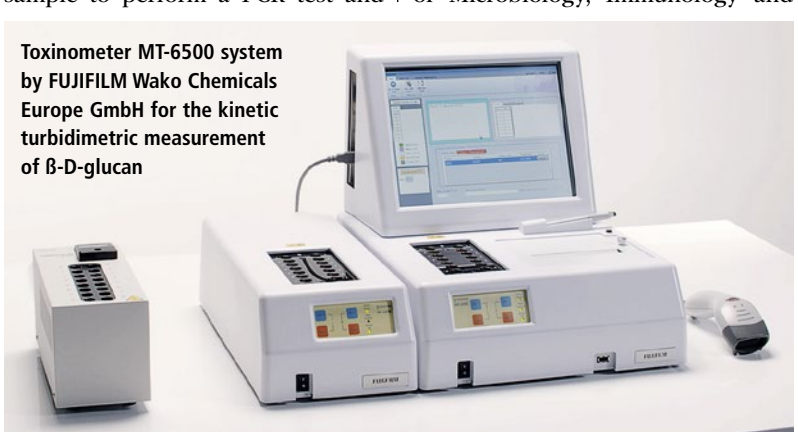
Report: Mark Nicholls

Invasive fungal diseases are a major worldwide health problem and affect immunocompromised patients, such as those undergoing intensive-care treatment, and people with chronic disorders – particularly lung diseases. Most infections are caused by Aspergillus, Candida and Pneumocystis jirovecii, with early recognition and diagnosis crucial to improve patient outcomes. Guidelines from the European Confederation of Medical Mycology for Candida – which will be updated imminently – and Aspergillosis, recommend the use of a ß-glucan test for their detection.

In addition, PCR (polymerase chain reaction) is the first line test in non-HIV Pneumocystis jirovecii Pneumonia but it has drawbacks that the ß-glucan test can help overcome. 'It's not always possible to have a bronchoalveolar fluid sample to perform a PCR test and we also know the PCR test is supersensitive and may detect colonisation and not infection, said Lagrou, who also heads the Department of Microbiology, Immunology and Transplantation and also heads the National Reference Centre for Mycosis at University Hospitals of Leuven.



Patients with an impaired immune system are at risk of invasive fungal infections



Toxinometer MT-6500 system by FUJIFILM Wako Chemicals Europe GmbH for the kinetic turbidimetric measurement of ß-D-glucan

'If it's not possible to conduct bronchoalveolar lavage, the ß-glucan test may be used to evaluate the likeness of Pneumocystis infection. In addition, this test may also be of value in the discrimination between infection and colonisation.' What it offers as a complimentary test, she added, is an extra level of reassurance – either to support a diagnosis or exclude the diagnosis.

In vitro diagnostic test

'The diagnosis of fungal infection is complicated and you need to put together different tests and they all have their own value and they do provide complimentary information, and the ß-glucan test is one of those tests.'

The Wako ß-glucan test – evaluated at the Leuven centre – is an in vitro diagnostic test for the quantitative determination of (1→3)-ß-D-glucan in serum or plasma and a marker of invasive fungal infections. The assay is performed on the Toxinometer MT-6500 device developed by FUJIFILM Wako Pure Chemical Corporation.

The test may also have a role with Covid-19, where invasive aspergillosis is a complication in Covid patients and also a known complication with influenza patients. But, Lagrou added, 'The diagnosis with Covid patients is not easy and it's good to combine different tests. These patients might also have an invasive Candida infection, especially among those in the ICU. As yet, we are in the learning phase about the incidence, disease characteristics, and still evaluating these tests. It is too early to say what the exact value of the ß-glucan test is in this instance.' However, there are aspects of the Wako ß-glucan test that make it an appealing option for clinicians.

The single sample test: a real advantage

'One of the things that appeal is the fact that you can run it as a single sample test,' Lagrou said. 'That's a real advantage because we are in a setting of several life-threatening infections where it is important to get the information as soon as possible and to be able to put together the results of different tests we are conducting. It's also a robust test and the reproducibility is very high.'

Other advantages, she pointed out, are that the test adds additional information, is not difficult to implement or execute, and staff can be trained to use it relatively easily, and it also delivers rapid results with clear benefits for prompt patient care. Lagrou believes there will be future areas where the Wako ß-glucan test can be of value and this will evolve as the sensitivity can be improved by lowering the cut-off value, with high sensitivity of particular importance when diagnosing invasive fungal infections.

Professor Katrien Lagrou is Head of the Department of Microbiology, Immunology and Transplantation at the University of Leuven and also heads the National Reference Centre for Mycosis. She is also Professor at the Faculty of Medicine of the Catholic University of Leuven. Her major interest is the diagnosis of fungal and viral infections in severely immunocompromised patients, with a focus on invasive pulmonary aspergillosis. Lagrou also presides over the Belgian Society of Human and Animal Mycology and is former General Secretary of the European Confederation of Medical Mycology.

Stabilisation from the start

Precise glucose testing

Diabetes mellitus is one of the most common metabolic disorders in the world, and plasma glucose levels are essential for its evaluation, as well as gestational diabetes. The breakdown of glucose (glycolysis) in venous blood samples is of great significance in pre-analytics, particularly in relation to the diagnosis of diabetes mellitus and gestational diabetes.

Effective glycolysis inhibition: determining in vivo blood sugar content precisely with the Vacuette FC Mix Tube

Greiner Bio-One produces the Vacuette FC Mix Tube. This special additive mixture not only reduces the pH value and blocks the pH-dependent enzymes which would be active in the initial stage of the glycolysis cascade. The tube can also stabilise the sample immediately after collection for up to 48 hours.

The time from collection until separation of plasma and cells, temperature as well as cell count strongly affect glucose levels, possibly leading to false low results. Unfortunately, fluoride alone cannot stabilise the real in-vivo glucose level completely.

Vacuette FC Mix Tubes are citrated and therefore can help to prevent the initial loss of glucose within the first few hours from collection until fluoride shows its effect. Buffered Na2EDTA, citric acid, sodium citrate and sodium fluoride are used to decrease the pH and block the pH dependent enzymes, which would be active in the initial stage of the glycolysis cascade.

The shatter-proof tube is made of polyethylene terephthalate (PET). PET is important for the stability of the vacuum, Greiner Bio-One points out, adding that the safety cap is particularly easy to open and facilitates hygienic working. The transparent plastic label provides an optimum view of the tube contents.

Powder additive

'The powder additive in the Vacuette FC Mix Tube has no dilution effect. There is no need to take a conversion factor into consideration. Inverting ten times ensures that the tube additive is completely dissolved and well mixed with the sample.

'Should the tubes be stored longer than 24 hours at room temperature, samples should be centrifuged after blood collection. Centrifuged aliquots from FC Mix Tubes can be stored for up to 48 hours at room temperature. Tubes should be centrifuged within 20 minutes after blood collection. Cooling of the samples is also suitable for 48 hours glucose stabilisation.'

Details: www.gbo.com

Optimising clinical laboratory management in a pandemic

Covid-19: Overcoming unprecedented challenges

During a pandemic, the demands for laboratory testing challenge routines in an efficiently run clinical laboratory. Gold standard procedures may need modification, or to be discarded, and the more nimble, resilient and receptive a lab is to change, the better off it could be.

Source: Shutterstock/bleakstar

During a pandemic, laboratories need to cope with unprecedented challenges and must therefore change their workflows

Report: Cynthia E. Keen

Senior managers at ARUP Laboratories in Salt Lake City, Utah, a large clinical reference laboratory that offers over 3,000 diagnostic tests and test combinations to client laboratories throughout the USA, describe how they coped with 'unprecedented challenges in a world turned upside down' during the first six months of the Covid-19 pandemic, in their article in the January 2021 issue of the American Journal of Clinical Pathology.

Communication and collaboration

Communication and collaboration are the primary means of creating and maintaining a flexible, resilient organisational structure, explain chief operating officer Jonathan R Genzen MD PhD, and Brian R Jackson MD, medical director of support services, IT and business. Before the pandemic struck, ARUP management prided itself on enforcing essential-only meetings and e-mail messaging policy to maintaining good communications without sacrificing workforce efficiency. In-person department and medical directors' meetings were held monthly.

However, from March 2020 in-person meetings were cancelled, to be replaced with virtual meetings held once weekly to convey news and information and more rapidly deal with and implement necessary operational and policy changes.

The underpinning of all initiatives was decision-making collaboration across teams, departments, and divisions. 'Laboratory operations, R&D, supply chain, finance, human resources, business development, IT, safety, and facilities all have an essential role in this coordinated response. Each is affected by how the laboratory should respond to the crisis, and conflicting departmental priorities can hinder the ability to successfully implement initiatives in a timely manner,' the authors wrote. 'Collaboration facilitated effective conflict resolution.'

Also in March, ARUP's chief executive officer, Sherrie L Perkins MD PhD, began to send daily e-mails to the 4,000+ member workforce. Content included news updates about the lab, safety announcements, positive highlights of individual department achievements, and employee wellness tips.

To promote inclusiveness to all employees, ARUP conducted video 'town halls' as another means to respond to workforce questions and concerns. 'It's important to be informative and transparent during such stressful times,' the authors pointed out. 'This facilitated sensitive discussions about work reduction that included hourly and salary reductions across all departments and jobs, voluntary leaves of absence, and the lab's financial health due to significant reductions in routine tests.'

FAQ for staff

The lab also developed a frequently asked question (FAQ) list to address clinical questions from staff and physicians. This was updated and expanded as needed. The answers provided were aligned to guidance provided by the World Health Organisation, the United States Centers for Disease Control and Prevention, and existing internal policies and procedures regarding safe handling of respiratory specimens. Additionally, a Covid-19 Communications Group, comprised of marketing and communications staff, immediately developed a new website page of links to published resources, podcasts, material, and a free public laboratory test selection support tool.

Supporting staff in turbulent times

Prior to the onset of the pandemic in late February 2020, this nonprofit enterprise of the University of Utah's Department of Pathology processed over 60,000 clinical tests a day. Routing testing volume dropped with the pandemic. ARUP pivoted to divert some lab and financial resources and staff to support SARS-CoV-2 molecular testing by its Molecular Infectious Disease and Molecular Genetics laboratories to maximise capacity for Covid-19 diagnostic test orders and serology, including cytokine testing.

Keeping the employee base intact and safe

Because clinical laboratory staff represents a highly trained scarce resource that cannot be easily or quickly replaced, ARUP's guiding principle is to keep its employee base intact and safe during the pandemic. This has included a mix of offering work flexibility options, including remote working, where feasible; temporary leaves of absence; implementing temporary work and salary reductions fairly to both workers and managers; maintaining health benefits for all, and stringently implementing and enforcing safety measures.

The increase in remote work options necessitated bolstering information technology services to support increased network use.

Fiscal budget changes

The authors note that, because laboratory cash flows tend to be relatively stable and predictable, creating an operating budget for the following year tends to be a simple process of minor modification.

The impact of a pandemic changes this. They recommend that because expenditures need to be evaluated based on cash availability, lab managers should adopt a dynamic budget mindset. ARUP implemented a rolling forecast model and has suspended non-emergency spending. Its objective is to preserve cash and available resources wherever possible and to justify expenditures based on immediate and Covid-19 related clinical needs.

'The clinical laboratory environment is very regulated and therefore adverse to quick change, but the crisis has required big decisions to happen fast,' Genzen pointed out. 'We've learned to be nimbler and more efficient, but cautiously, so as not to compromise quality.'

Jonathan R Genzen MD PhD is chief operating officer at ARUP Laboratories in Salt Lake City, Utah.

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ISSN 0942-9085

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Subscription rate

4 issues: 32 Euro, Single copy: 8 Euro.

Send order and cheque to:

European Hospital Subscription Dept

Printed by: WVD, Möhrfelden, Germany

Publication frequency: quarterly

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EUROPEAN HOSPITAL @ ECR 2021
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SPECIAL ISSUE FOR THE EUROPEAN CONGRESS OF RADIOLOGY
ONLINE EVENT
VIENNA • AUSTRIA • MAR 03-07 2021

Awareness is key for breast screening services

Daniela Zimmermann speaks to Samir Parikh, Hologic's Global Vice-President (Research & Development and Clinical Affairs), about the company's approach to raising post-Covid awareness of breast screening.

The impact of Covid-19 has been devastating; countless lives lost, millions of infections worldwide, health systems overwhelmed and economies rapidly shrinking. In addition, routine operations have been cancelled, patients have avoided Emergency Departments for fear of catching coronavirus or hampering health workers, and others have failed to seek help when they should have consulted a physician.

Health experts fear this is storing up a negative health legacy for years ahead as patients present with worse symptoms than if they had sought timely help.

Screening, such as for breast or cervical cancer, is an area particularly affected, with numerous appointments delayed.

It is against this backdrop that Hologic is working to pave the way for a return to a degree of normality for when the coronavirus pandemic passes.

Raising awareness

Central to that is a role in raising awareness among women about the importance of breast cancer screening, alongside helping health systems reduce backlogs and restore screening to pre-Covid-19 levels. Within that are also steps to help clinician workflow and offset any increased workload.

Samir Parikh has outlined how the company is raising awareness of breast screening with consumer education campaigns, and developing innovations to support clinicians and health systems deliver effective screening programs post-Covid.

At present, global health systems have a realigned focus to cope with Covid-19, which is having a significant effect on preventive screening and will impact future outcomes.

He pointed to evidence in the UK that postponement of clinical cancer diagnostics and treatment may lead to 18,000 more deaths over the next year, while a French study found 38% of people avoided screening over Covid-19 concerns, and 28% did not want to further burden healthcare workers. Studies elsewhere in the world reflect a similar picture.

"Breast cancer screening, cervical and other procedures being postponed has created an additional burden on health systems as they move out of Covid" said Mr Parikh, who has been with Hologic for 24 years and from the start of the company's digital journey.

Addressing the backlog

With early detection a critical part of the breast cancer journey, awareness and access to screening are important messages for women as services pick up, but he acknowledged patients need to feel "comfortable" about coming back to screening services. Healthcare facilities are taking precautions, but that is adding to workload and means procedures will take longer.

"The biggest challenge," he continued, "is how do we address the backlog and get back to that routine of annual screening for everybody, not just breast cancer? We believe this is where Artificial Intelligence will play a significant role."

Mr Parikh highlighted how Hologic's Genius AI™ technology can improve workflow efficiency by enabling radiologists to read images more efficiently and help reduce backlogs. "AI is core of where we are going," he said. "We believe AI will continue to help how we improve, not only in cancer detection or operational efficiency, but also affecting clinical outcome across the whole pathway."

Digital breast tomosynthesis (DBT) remains a proven technology within the mammography sphere, but having images sliced into 1mm segments in some systems can lead to fatigue with a 5cm area of breast resulting in 50 slices to scroll through.

Hologic's Genius AI solution sees the company's 3DQuorum™ Imaging Technology, Powered by Genius AI™, create 6mm SmartSlices where each high-resolution SmartSlice overlaps the previous one by 3mm, ensuring there is no loss of 3D image data and continuity in scrolling.

HIghlighted regions of interest

"This not only overlaps, but with the AI underneath we are making sure regions of interest that are important to a radiologist – lesion, classification, masses – are highlighted and that helps reduce the workflow time," he said. With 3DQuorum, resolution and detection are better, he pointed out. It is an integrated solution that reduces the number of 3D images to review by two-thirds, improves workflow efficiency and can literally take an hour of work off an eight-hour shift.

Educating consumers

As a global leader within breast health, he underlined Hologic's commitment to patients and customers during the pandemic. This has seen Hologic reach out directly to patients with educational resources to raise and maintain awareness of the importance of breast cancer screening.

In the United States, Hologic launched a "Back-to-Screening" consumer education initiative which focused on reminding women of the importance of mammograms and not missing examinations, and how facilities were working to be Covid-safe. In Europe, a similar breast cancer awareness campaign addressed women directly, but targeted via social media. The European campaign will continue in 2021.

Another element supports customers on tomosynthesis breast cancer screening and products such as ultrasound technologies, hand-held and surgical devices, with a medical education team established to deliver an educational and technology support structure. He said: "For us, the biggest learning point from Covid-19 was that it reinforced our commitment to providing insight-driven innovative solutions throughout the patient pathway. It is at the heart of what we do; it is about how we connect the dots from risk to screening, to diagnosis, biopsy, surgery, pathology, and to treatment and how we integrate our solutions for improving workflow and driving critical patient outcomes in a lifesaving way."

AI-led technology, he added, can improve efficiencies, reduce cost and burden, and "the impact of the backlog along the entire pathway."

Samir Parikh is the Global Vice President of Research & Development. In this role, he is responsible for leading and driving innovative advanced solutions across the continuum of care to drive sustainable growth of the Breast and Skeletal Health division. Samir joined Hologic in 1997 and held positions of increasing responsibility over the years.

Commitment for women's health

While Hologic has extended its portfolio with the acquisition of SuperSonic, he explained, that it will continue to see its portfolio evolve over the medical spectrum, with AI playing a crucial role but emphasized Hologic's commitment to, and core focus on, women's health.

Having structured the company's innovation – internally, organically and through acquisitions – underlines a sharp focus on the global pathway.

"But this is just the starting point. Our goal is to impact a billion women in the coming years and we will not be able to do this unless our mission and purpose is very focused," he concluded. "Hologic remains a leader in breast health and our commitment to that through innovation and technology remains our primary focus."

Hologic's 3DQuorum technology

Introducing ATEM Mini

The compact television studio that lets you create training videos and live streams!

Blackmagic Design is a leader in video for the medical industry, and now you can create your own streaming videos with ATEM Mini. Simply connect up to 4 HDMI cameras, computers or even technical equipment. Then push the buttons on the panel to switch video sources just like a professional broadcaster! You can even add titles, picture in picture overlays and mix audio! Then live stream to Zoom, Skype or YouTube!

Create Training and Educational Videos

ATEM Mini's includes everything you need. All the buttons are positioned on the front panel so it's very easy to learn. There are 4 HDMI video inputs for connecting cameras and computers, plus a USB output that looks like a webcam so you can connect to Zoom or Skype. ATEM Software Control for Mac and PC is also included, which allows access to more advanced "broadcast" features!

Use Professional Video Effects

ATEM Mini is really a professional broadcast switcher used by television stations. This means it has professional effects such as a DVE for picture in picture effects commonly used for commentating over a computer slide show. There are titles for presenter names, wipe effects for transitioning between sources and a green screen keyer for replacing backgrounds with graphics!

Live Stream Training and Conferences

The ATEM Mini Pro model has a built in hardware streaming engine for live streaming via its ethernet connection. This means you can live stream to YouTube, Facebook and Twitch in much better quality and with perfectly smooth motion. You can even connect a hard disk or flash storage to the USB connection and record your stream for upload later!

Monitor all Video Inputs!

With so many cameras, computers and effects, things can get busy fast! The ATEM Mini Pro model features a "multiview" that lets you see all cameras, titles and program, plus streaming and recording status all on a single TV or monitor. There are even tally indicators to show when a camera is on air! Only ATEM Mini is a true professional television studio in a small compact design!

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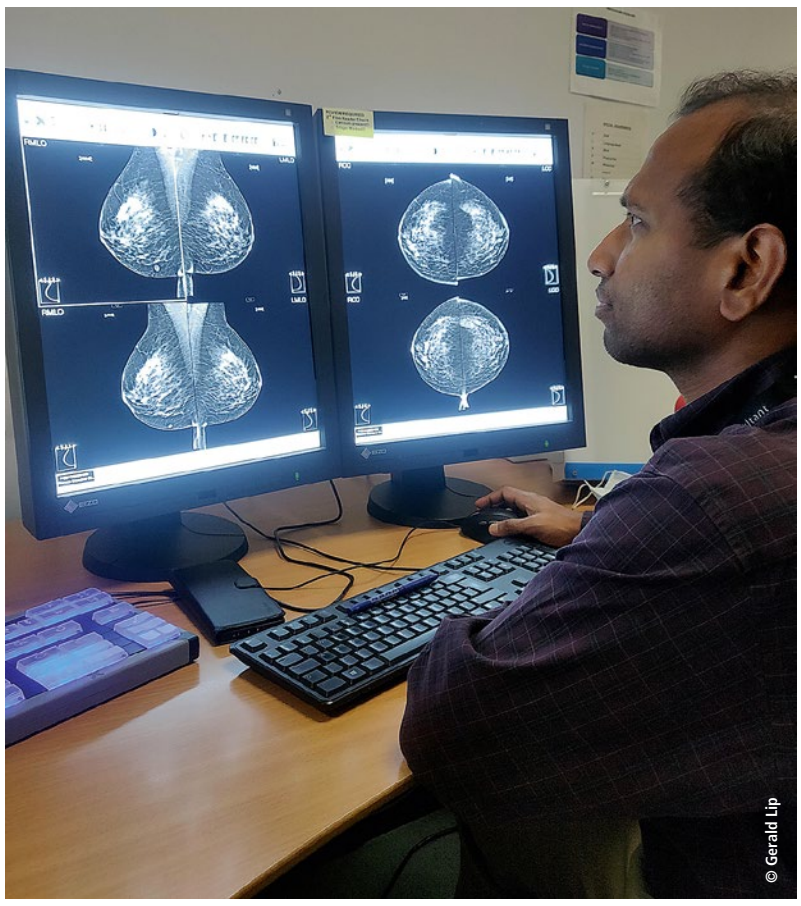
The iCAIRD project – evaluation and the route to adoption

AI to aid Scottish breast screening

Implementation of artificial intelligence into Scotland's national breast screening service is moving closer following an initial success with a trial project, Mark Nicholls reports



Mammography images being viewed as part of the iCAIRD project to implement AI into the Scottish breast screening service.

While Scotland's breast screening trial has delivered highs and lows, significant hurdles have been overcome in terms of approvals, governance and patient acceptance. The ongoing process of bringing AI into the mammography programme was outlined at the virtual Artificial Intelligence in Practice event organised by the British Institute of Radiology, in association with the Royal College of Radiologists.

In his presentation 'Experiences with mammography AI evaluation, analysis and route to clinical practice in the iCAIRD (the Industrial Centre for Artificial Intelligence Research in Digital Diagnostics) project', Dr Gerald Lip, Clinical Director of the North East of Scotland Breast Screening Service, outlined how AI is being lined up as an independent reader of mammograms in Scotland.

Lip, who is also the Chief Investigator of the Mammography AI project as part of iCAIRD, explained that the process began in November 2018 with an Innovate UK grant, with contracts signed and data processing and information agreements set up as the partnership involving Kheiron Medical and Canon, the University of Aberdeen, National Screening Services in Scotland and NHS Grampian took shape. 'Most of 2019-20 was spent on physical infrastructure, getting permissions, meetings, satisfying information governance and building a virtual workspace for anonymising 80,000 mammograms from over four years in the North East of Scotland,' Lip explained.

With the Scottish breast screening system already paperless, the data was readily available in a highly-structured data extract and transferred into the 'safe haven' for the project.

Work progressed well in 2020 despite Covid, from Phase 1 of establishing feasibility and prototype, and into Phase 2 of development and clinical evaluation, clinical efficacy and safety data, with the project expecting to submit its first scientific papers.

Entering Phase 3

With the Scottish breast screening sy

The project is now set to enter the Phase 3 stage of real-world testing, subject to research grants looking at the feasibility for implementation across multiple sites, regulatory approval, working through the health economics and subsequently into Phase 4 with initial health system adoption.

'Phase 3 is the hard divide,' Lip pointed out. 'In a clean retrospective analysis in Phase 2 you can get good results but moving into clinical practice is a different story, especially in screening, because we are looking at evaluating this as an independent first or second reader.'

He also explained that the data used in the evaluation stage was not curated or enriched and covered four years with over 80,000 women, 240,000 images, and 700 cancers. As the project team knew what was there, they were keen to see what conclusions AI came to.

80-90% of women accept AI

Patient engagement has been important and positive with patient group surveys on women's attitudes to AI in screening mammography. 'In our population, 80-90% of women were very happy to have AI read their mammograms, particularly if a radiologist was involved,' Lip reported. 'Women who had an understanding of AI were more accepting of AI and if they could get results back faster, but safely, they were very happy with that process.'

Engagement with stakeholders such as the Scottish government and national screening services and research, advisory and governance bodies was a critical, yet time-consuming, step. 'I've probably spoken to or corresponded with 40-50 different committees in the last two years, trying to put away misconceptions about AI. You find there are people in a different place to you and not all these groups were in perfect agreement,' Lip reflected. 'Covid was also an issue; there was a lot of prioritisation of Covid-based projects and suspension of non-Covid projects.

'We had ups and downs, but there were some highs: after six months of getting permission to move the anonymised data from 80,000 women into our safe haven, it was done over a weekend without affecting the network. Similarly, when we ran our first results trial for the AI project, it was 240,000 images in two days.'

The Scottish government has been supportive, as has NHSX, which has responsibility for setting national policy and developing best practice for NHS technology, digital and data. The project is now checking validation and clinical evaluation of the AI algorithm to ensure there is no bias as they look to moving into real-world practice.

Lip explained that, in breast screening, the usual cancer detection for a single reader is 6-8 cancers in 1,000 mammograms, whilst two radiologists combined may find 10-12 cancers. 'The idea of AI, when it's replacing a reader, is not to be the same as the average reader but to be as good as an experienced reader,' he added.

To move this forward into the Scottish breast screening system, the iCAIRD project team is designing a training module with AI integrated into it, that will read opinions and compare with expert readers. This is planned to be rolled out across six centres covering 20,000 mammograms a month to deliver 'granular level of understanding' of the data in the platform.

The data training module, he explained, will act as a form of health technology assessment, rather than a formal randomised controlled trial, which will help the decision-makers and regulatory authorities to determine whether this can be adopted into the breast screening programme.

Questions remain about IT, data protection agreements, the use of the cloud and how screening readers get feedback on performance, but Lip is optimistic that, over coming months, the AI project will move closer towards implementation in the Scottish breast screening programme.

Gerald Lip MD MSc is Clinical Director of the North East of Scotland Breast Screening Service, the Chief Investigator of the AI mammography project and an honorary senior clinical lecturer at the University of Aberdeen. He is a graduate of Trinity College Dublin where, along with his medical degree, he gained an MSc in Health Informatics.

Managi breast l

Report: Cynthia E. Keen

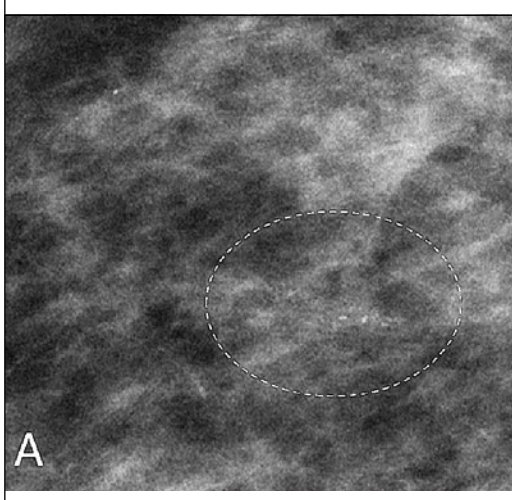
The management of biopsied breast lesions that are diagnosed as abnormal but are not definitively malignant is challenging and controversial. Treatment ranges from diligent follow-up, with imaging and subsequent biopsy, to surgical excision.

Researchers at the Medical University of Vienna (Medizinische Universität Wien), Austria, have developed and validated a software algorithm designed to stratify the risk of a breast lesion of uncertain malignant potential, known as a B3 lesion. This could help define the best treatment or follow-up and prevent unnecessary surgeries. Because B3 lesions have an increased risk of malignancy and an increased risk of subsequent development of invasive breast cancer, the practice in many countries is surgical excision.

Thus, many women with ultimately benign lesions have unnecessary surgeries. Additionally, with a steadily increasing number of B3 lesions being diagnosed by biopsy, due to improvements in mammography imaging and the worldwide increase in breast cancer screening programmes, more precise methods of predicting malignancy are needed.

Currently, the risk of missing a malignant component in a B3 lesion ranges from 2-58%. Writing in the February 2021 issue of the European Journal of Radiology, the researchers attribute this wide range to characteristics of the type of biopsy performed (core needle or vacuum-assisted); the lesion type; and diverseness of imaging features, which include microcalcifications, masses, and architectural distortions.

The researchers advise that B3 lesions are identified in 3-11% of stereotactic-guided vacuum-assisted stereotactic biopsies (VABB) performed for suspicious microcalcifications. Their aim was to create a machine learning risk stratification method for VABB diagnosed B3 lesions using a combination of imaging, pathological, and clini-



Two cases that underwent stereotactic vacuum-assisted calcification. Case A (perimenopausal woman) revealed histopathological examination, no history of breast car to the risk stratification algorithm. Follow-up instead o was proven. The postmenopausal woman in case B was cancer on in the right breast. The microcalcification clu revealing atypical ductal hyperplasia. This intermediate meeting and surgery suggested, revealing an invasive

AI tool might reduce surgery

ng cancer-questionable lesions

Pascal Baltzer MD is an associate professor specialising in breast imaging at Medizinische University Wien, where he has worked for the past nine years. Currently he is also Secretary-General of the European Society of Breast Imaging (EUSOBI) and executive board member of the breast imaging working group of the Deutsche Röntgengesellschaft. In July 2020, he was appointed editor-in-chief of the European Journal of Radiology.

cal features. The data set used to develop the algorithm included 99 patients with B3 lesions diagnosed and surgically excised at AKH Wien.

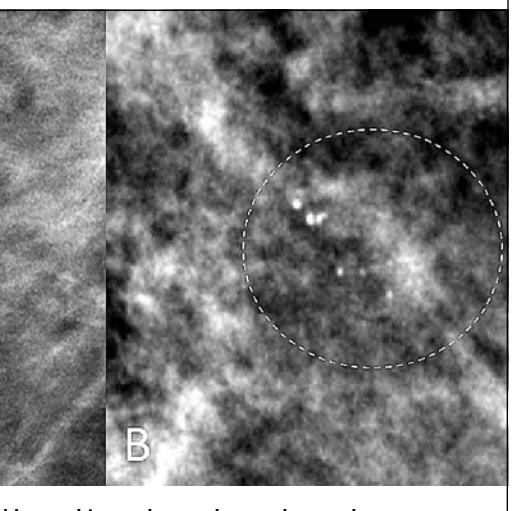
The study included a training cohort of 76 patients diagnosed between 2013-2015 and a testing cohort of 23 patients diagnosed in 2016. There were 10 malignant and 66 benign B3 lesions in the training cohort, and six malignant and 17 benign lesions in the testing cohort. The malignant lesions included one invasive ductal carcinoma and 15 ductal carcinomas in situ. Benign lesions in both cohorts included adenosis, fibrocystic changes, and fibrosis, and papillomas in the testing cohort only.

The algorithm utilised clinical information of each patient regarding age at diagnosis, personal history of breast cancer, presence of a concomitant breast cancer, histology of the biopsy and surgical specimens, and diagnostic imaging, which included a BI-RADS classification. Radiologists assessed lesion size, morphology, microcalcification distribution, presence of associated soft-tissue mass, and architectural distortions. Principal investigator Professor Pascal A T Baltzer MD, and colleagues at the Department of Biomedical Imaging and Image-guided Therapy, reported that the algorithm identified malignancies in more women who had highly suspicious microcalcifications and a concomitant cancer. Their findings suggest that surgery should generally be recommended for microcalcifications with a highly suspicious morphology, and follow-up only with patients who have less suspicious microcalcifications, with round punctate, amorphous, and/or coarse heterogeneous morphology.

If the risk stratification algorithm had been used with these 99 patients, surgery could potentially have been avoided in 25 cases.

Baltzer told *European Hospital* that the team now plans a larger, multi-centric retrospective validation study. They are currently looking for partners, and would like interested hospital researchers to contact Baltzer (pascal.baltzer@meduniwien.ac.at).

'Our exploratory analysis gives us only a clue about the number of avoidable surgeries,' he pointed out. 'This number needs to be substantiated by confirmatory studies. Also, such research could establish whether the missed cancers are indeed biologically minor, or whether we could miss "killer" cancers by the suggested therapeutic de-escalation. We are pursuing this and possibly a prospective multi-centric randomised clinical study.'



d breast biopsy due to clustered amorphous l flat epithelial hyperplasia, no atypia upon ncer. The case would be classified as low risk according f surgery was initiated and stability over five years s recently diagnosed with invasive lobular breast ster shown was found and biopsied in the left breast, e risk lesion was discussed in the multidisciplinary ductal cancer G2.

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Viewing through a 'window' empowers management

How to shape a blueprint for progress

Hospital data from a wide range of disciplines, departments and specialties strongly influences crucial decision-making and planning. Agfa HealthCare's Business Intelligence solution, for example, uses data to measure, understand and predict developments, and aims to present this information in an accessible and transparent way so that administrators need not even ask for in-house generated reports. Agfa's Business Intelligence product manager Tommy Vansteenkiste, and Willy Rosé, representing Agfa's Imaging IT solutions marketing division, discussed the firm's solution with Mark Nicholls.

There is a solution that amalgamates all hospital data – e.g. involving personnel, equipment, patients' waiting times, room occupancy, age groups and regions from which they have been referred, workflows and bottlenecks, and the use of an imaging device (e.g. if one CT scanner is used more than another, indicating further equipment investment). The solution reveals multiple aspects of the organisation, helping to streamline operations and processes, accreditation, capacity and investment planning. It also monitors trends and helps with billing accuracy and quality improvement.

Vital assessments during the pandemic

This ability has proved particularly important during the coronavirus pandemic, during which assessment of workflow, capacity, and performance has been and is crucial.

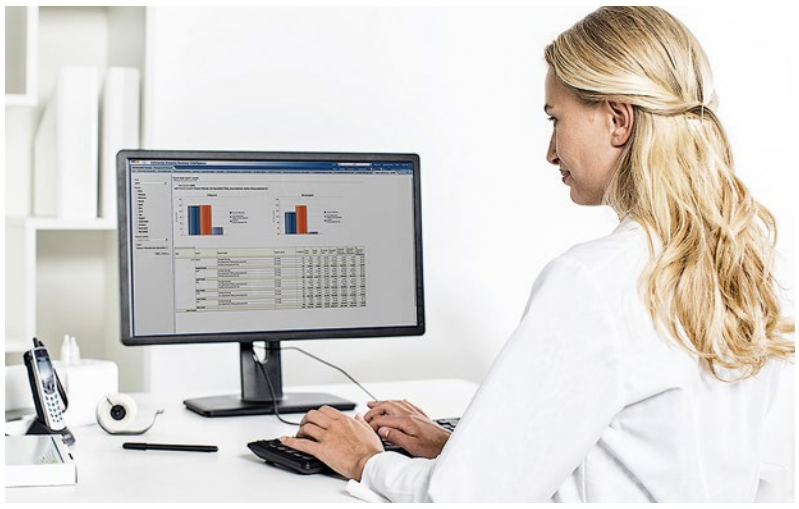
As Business Intelligence product manager Tommy Vansteenkiste observed, 'The solution brings data to the fingertips of the end user.' A department head can identify where there is room for improvement, view market information, assess a shift in the use of certain equipment, or where investment is needed. Clinical staff can also assess workflow, performance and future workloads. 'It helps with resourcing and planning, patient waiting times to see if there are peaks that can be flattened to provide a better patient experience, and how fast a report is delivered to the ordering physician,' he added. 'It's about ensuring the operation runs smoothly, and also keeps a quality of service.'

Benefits can be measured in many ways, such as time efficiency and tracking how long it takes to provide a service, whilst also offering a checkpoint on a system's quality. Here, identifying peaks and supporting changes in the scheduling and planning of examinations, for example, can improve treatment delivery. More recently, the solution has tracked the growth of coronavirus and associated changing service demands and delivery. 'What we are seeing is where there are dips in certain procedures and those coming back in again. That can give input on resourcing and what is coming up and what a hospital might need to plan and change,' Vansteenkiste pointed out.

Diving into something strange

A key facet is how Business Intelligence allows users to explore the data in detail. 'The end user can explore data and add certain attributes or "slice and dice" the data in a different way,' he explained. 'Often, you do not know what you are looking for until you see it. The whole point of Business Intelligence is that you see something strange and dive into it and look what the issue is. We are not only giving the data more to the end user, but we are enabling them to explore the data.'

Agfa HealthCare's Business Intelligence solution



After a 15-year engineering career at Agfa Gevaert, **Willy Rosé** transitioned to the role of Head of Marketing IT Europe at Agfa HealthCare. Leading a team of 10 highly skilled professionals, he connects the dots between regional sales organizations, R&D, finance and solution management.

Willy Rosé, from Agfa's Imaging IT solutions marketing arm, confirmed that the tool's value lies in identifying areas that need improvement and where problems lie. 'You can use it to mine the data, see where a problem is; fix or improve, and measure again.' He further outlined the solution's capability to focus on human performance. 'If you can measure how many duplicate examinations you do, you can investigate if it's because of equipment, people, or the process and, by doing that, you can increase operational efficiency and avoid unnecessary examinations. That is where Business Intelligence comes together with clinical intelligence.'

Tommy Vansteenkiste joined Agfa HealthCare in 2004 as part of the IT R&D department and has been active in different roles in both R&D and Global Services. Currently he is Product Manager for Enterprise Imaging's Business intelligence solution bringing actionable insights to Medical Imaging providers.

Identifying staff who need support

If the analysis system reveals that some personnel take longer to perform a task, this may suggest a need for support, or question whether the workload is being effectively distributed across devices – for example, not overloading CT scanners. The Agfa Business Intelligence solution is also a powerful tool in terms of monitoring performance; producing reports for accreditation and documenting improvement, and measuring patient and referrer satisfaction.

In a nutshell: The solution aims to transforms data into actionable insights leading to more informed decision-making and improved operational efficiency. With easy access to all operational data and reports, it can help to detect productivity gaps, maximise modality utilisation, and optimise resource utilisation and performance. As Rosé summed up: 'The Business Intelligence system is a window on a hospital's data, workflows, and performance.'

Integrated radiogenomics improves clinical outcomes

Images and patient data com

Harnessing radiomics power and adopting an integrated way to combine imaging and patient data could improve cancer outcomes. Now, clinicians can explore a non-invasive method to identify the heterogeneity of a tumour and more accurately target regions for biopsy.

During a presentation at ECR 2021 in March, Professor Evis Sala will underline the importance of integrating data to build a clear, non-invasive diagnosis and potentially cut down on the need for biopsies, as imaging and radiomics builds up a clear view of a lesion.

Her current research focuses on integrated diagnostics through the clinical development and validation of functional imaging biomarkers to rapidly evaluate treatment response using physiologic and metabolic tumour habitat imaging. Sala's presentation, 'Linking radiomics features to other omics data in clinical practice', will review potential applications of emerging radiogenomics, and discuss how to analyse big data. The Cambridge team combines multi-layered data – radiomics, clinical, and blood data (CA 125 in the case of ovarian cancer) – with e-genomics, including circulating tumour DNA, and patients' history, to develop algorithms to predict treatment response.

Robust data to create a robust biomarker

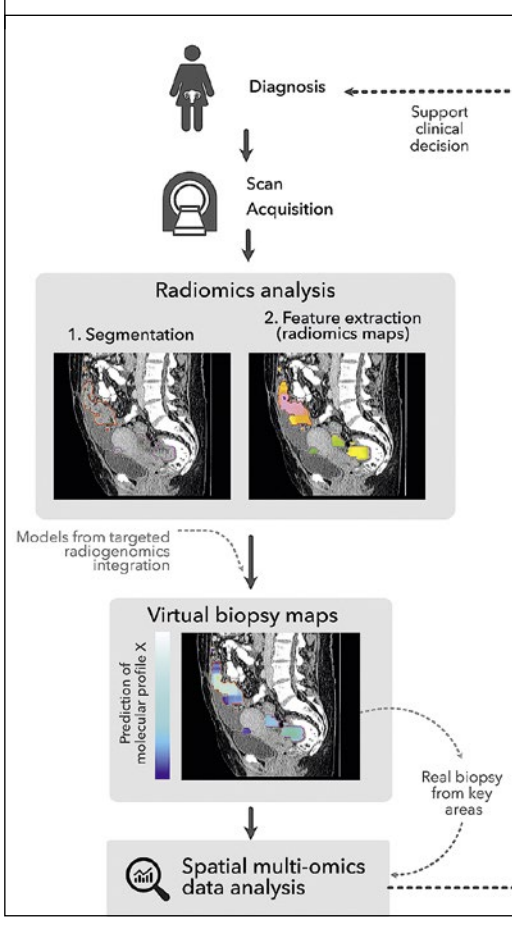
Underlining the need to have robust data to create a robust biomarker, Sala's examples will concentrate on CT scan and ovarian cancer. She also emphasises the importance of keeping the research grounded in everyday practice, to ensure the developed biomarkers actually will be useful in the clinic.

A challenge lies in making the transition from qualitative research and data to quantitative findings and turning that image data into numbers. 'That's not going to be pretty to the eye,' she acknowledged. 'As radiologists we are visual, but we have to extract things we don't see with our bare eye because that's where the quantitative information is.'

Sala, whose work integrates quantitative imaging methods for evaluation of spatial and temporal tumour heterogeneity with genomics, proteomics and metabolomics, points out that the additional features to acquire the quantitative information rely on heterogeneity, which is imperceptible to the human eye.

'It might not be exciting to radiologists, but it is so crucial to feed that information into the algorithms that can actually predict response and outcome.'

To extract the quantitative features from an image, the first major step is to segment the lesion. Whilst laborious in metastatic disease, this has led to the development of automatic segmentation. Once the lesion is segmented and the radiomics data extracted, it is fed into the treatment prediction algorithm with other clinical and molecular data. Her team is working on the use of this tool to create a 'virtual biopsy' to reduce the number of biopsies needed, by more precisely targeting the optimum site



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Clinical audits in radiology to promote high quality medical care

The QuADRANT project

Report: Mark Nicholls

Clinical audit within radiology departments can help promote high quality medical care and improve patient experience, as well as provide educational and teaching opportunities.

Aiming to see consistent delivery across Europe, clinical audit is currently under the initiative 'Diagnostic and Interventional Radiology, Radiotherapy, and Nuclear medicine including Therapies'.

The latest project is being conducted on behalf of the European Commission (EC) by a consortium led by the European Society of Radiology (ESR), including the European Society of Radiotherapy and Oncology (ESTRO) and the European Association of Nuclear Medicine (EANM).

QuADRANT progress will be updated during an ECR 2021 session led by Professor David Howlett. This aims to help radiologists understand the principles of clinical audit, as well as deliver an update on the ESR Esperanto audit project. Howlett, who chairs the ESR Audit Standards subcommittee and leads the QuADRANT project, explained that the EC launched this in January 2020, to improve quality and safety in radiology, radiotherapy and nuclear medicine through clinical audit ('a systematic process whereby medical radiological practice is examined against agreed standards with modification of practice if needed').

'The EC want us to look at clinical audit across Europe,' he explained, 'to find how and where it's being done well; what are good practices, and what the barriers are to clinical audit, but with a particular emphasis on clinical audit as mandated within the EU Basic Safety Standard Directive (BSSD)' (2013/59/Euratom).

The project looks at clinical audit implementation and procedures against a backdrop of seeing it embedded in clinical practice in support of the BSSD, which is now mandatory within the EU. The ESR has also developed the EuroSafe Imaging initiative to support and strengthen medical radiation protection across Europe. The session will explain five key work packages of the 30-month project. Howlett will examine the importance of clinical audit; review the role of audit within the BSSD; examine ESR audit-related initiatives; review the project, examining timelines and outputs of work packages; and consider challenges and potential benefits for QuADRANT.

Consultant radiologist **Professor David Howlett** is with East Sussex Healthcare NHS Trust and is also Honorary Clinical Professor of Radiology at Brighton and Sussex Medical School, UK. He specialises in head, neck and symptomatic breast imaging. He is also chair of the European Society of Radiology Audit and Standards subcommittee and project lead for QuADRANT.

The five work packages included an initial conference webinar meeting in December – to give background and current practices in member states.

Dr Adrian Brady, Head of Department and Consultant Radiologist at Mercy University Hospital, in Cork, Ireland, and ESR Second Vice-President, will update outcomes and recommendations from that session, while EC project officer Georgi Simeonov will discuss the project from the EC perspective.

The next step will see the project survey clinical audit practice, process and infrastructure in all EU member states, plus the UK, Norway, Iceland and Switzerland. A further conference is planned for December 2021, with the fifth and final phase producing a summary conclusion and recommendations for the EC. Howlett said clinical audit is becoming increasingly recognised within the clinical governance process.

'It's part of quality improvement and an important tool in looking at practices and processes, and benchmarking against what is considered good practice,' Howlett explained. 'It has shown to be a very effective tool in improving outcomes for patients and staff, but can also look at areas such as costs and enable departments to assess whether they are hitting targets and how things can be improved.'

The ESR has been active in audit-related initiatives, notably via the Esperanto document, launched at ECR 2019, which gives a background to clinical audit and discusses BSSD requirements, and also contains audit templates to allow departments to undertake their own audits. A new version of Esperanto is scheduled for 2022, with an upgrade in line with the project's output findings.

'QuADRANT will establish a roadmap of clinical audit activity across the EU, providing the EC, and thereby Europe, with a way forward for clinical audit that will help implementation and develop infrastructure, improving practice and process.'

Source: Shutterstock/LEDOMSTOCK

bined

for biopsy. 'With imaging, this can track the entire tumour border, not just one lesion, and point out the region for biopsy.'

Sala believes the concept is close to deployment in the setting of a clinical trial and validation. 'It's about understanding the biology of what we are seeing, how we can use this cross-scale investigation and interrogation to then limit the number of biopsies, or biopsy the most useful part of the tumour.'

A key learning point from this ECR session will be that maximum benefit is achieved from integrating the data. 'Integrating them will give a more powerful, robust way of predicting an outcome,' Sala added.

She also emphasised the importance of radiologists enhancing their contribution by gaining knowledge of oncology; teamwork; having a multi-disciplinary approach with algorithm developers working closely with clinicians to develop the AI; and bringing patients into the research phase for the perspective they offer. (MN)

Overview of workflow leading to the creation of virtual biopsy maps from key areas which can be used, along with real time biopsies from key areas, to inform clinical decisions. Source: P Martin-Gonzalez et al (2020). Integrative radiogenomics for virtual biopsy and treatment monitoring in ovarian cancer (https://doi.org/10.1186/s13244-020-00895-2). Insights into Imaging. Republished under a Creative Commons Licence.

Professor Evis Sala is a consultant radiologist at Addenbrooke's Hospital, Cambridge, UK, and, since late 2017, has been Professor of Oncological Imaging at the University of Cambridge, having previously served as Chief of Body Imaging Service at Memorial Sloan Kettering Cancer Center. Sala leads the Radiogenomics and Quantitative Imaging Group in the Department of Radiology and co-leads the Cancer Research UK (CRUK) Cambridge Centre Integrative Cancer Medicine Theme and Advanced Cancer Imaging Programme.

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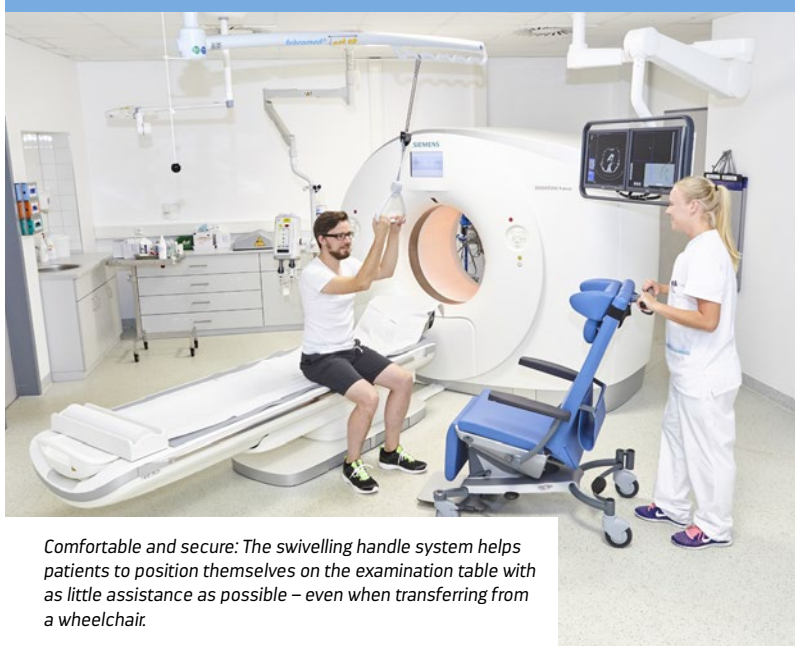

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The "get up" handle system can not only be mounted on the ceiling, but also on the wall. Photos: Febromed

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Portable ultrasound demonstrates versatility in all specialties

Covid-19 – Testing time for people and devices

Due to the coronavirus, hospitals and medical staff developed new work practices involving, in acute settings, social distancing, rigid use of personal protective equipment (PPE), handwashing, and disinfection of equipment every day.

Additionally, portable, highly-mobile and versatile equipment came to the fore in point-of-care (POC) – particularly when wards and operating theatres are spread across several floors and access to specialist devices is at a premium.

This proved the case in operating theatres, wards and intensive care units (ICUs) at the Utrecht University Medical Clinic (UMC) in the Netherlands, where portable ultrasound has supported swift and effective diagnosis of Covid-19 patients and supported treatment pathways.

Anaesthesiologist Dr Karina de Roos-Baron, who works across the ICUs and operating theatres at UMC, said that during the second wave of the pandemic cases, and deaths remain high, with extra ICU beds opened up to cope with increasing numbers of Covid-19 patients. Here, ultrasound is playing a vital role.

With wards and operating theatres spread across two floors at UMC, and not every unit having an ultrasound machine, the five highly portable and versatile Mindray TE7 machines are proving to be real workhorses.

Elective surgery has been cut by half as operating theatre staff are redeployed to care for Covid-19 patients, meaning the portable TE7 is playing an increasingly important role. 'This is a very mobile unit,' de Roos-Baron confirmed. 'It's available at point-of-care, does not need a constant energy supply and is easy to disinfect. In the operating theatre, we use it for venous and arterial canulation and, in ICU, for vascular access.'

Anaesthesiologist **Karina M M de Roos-Baron** heads the regional anaesthesia working group at University Medical Centre Utrecht (UMC), the Netherlands. After completing medical school in Amsterdam, she gained experience in anaesthesiology and intensive care as a resident and fellow at the UMC and other Dutch hospitals. Keen to educate new staff, Roos-Baron is an instructor for the Acute Trauma Life Support (ATLS) training programme as well as for the Dutch Association of Regional Anaesthesia (DARA).

The hospital's five Mindray TE7 systems are also being used by colleagues in, for example, neurosurgery, vascular surgery and urology. Also, with a programme starting for POCUS (point-of-care ultrasound), that role is set to expand further.

The TE7 offers superior image quality, simple touchscreen operation and intelligent tools to help speed up ultrasound examinations in demanding POC environments such as critical care, emergency and anaesthetics.

It features a 15-inch high-resolution anti-glare touchscreen display which is easy to use and is responsive, even with gloves and gel. It can also connect seamlessly to the hospital's electronic patient record (EPR) system.

With a wide range of pre-sets to cover all POC exams, the device has full calculation packages included as standard. Three transducers can be connected at once with easy on-screen selection; there are 23 probes available ranging from 1 to 20MHz for high-definition imaging, and the machine boots up in less than 25 seconds, or three seconds from standby.

At UMC, the TE7 is used in the recovery ward and to perform echo on patients' lungs, heart and abdomen. Also, should a patient need an emergency operation, it can be used to check whether the stomach is empty, or not. 'We use a mobile machine because we do not have enough ultrasound devices to go around the 23 theatres we have, which are also on separate floors of our hospital,' de Roos-Baron explained.

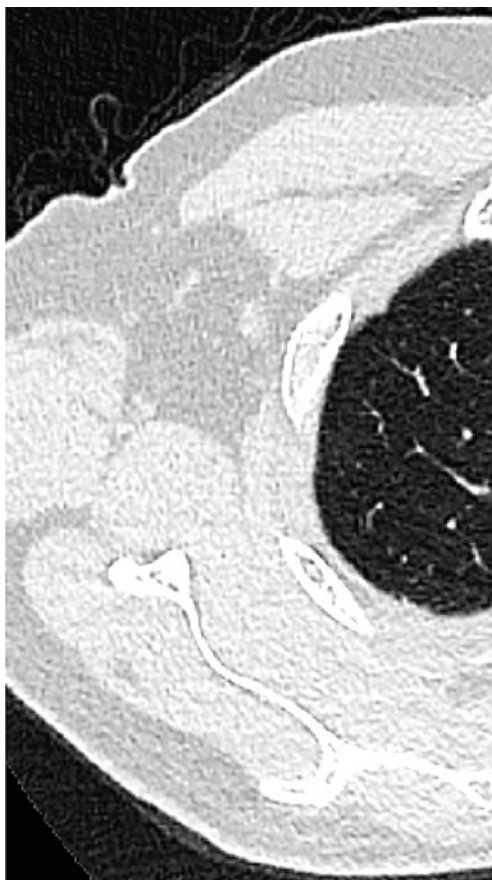
Careful logging of equipment keeps track of where on site the five Mindray machines are at any time.

Another advantage is that the device can last for 1-2 hours on battery, and then be plugged in or re-started promptly when needed.

This is a robust machine – particularly important in the Covid environment where constant disinfection is necessary – and it is easy and straightforward for ICU and theatre staff to cover the machines, the flat screen, and the probe with plastic protection. 'What's changed during Covid is that there is a lot more disinfection of machines,' de Roos-Baron pointed out. This is in addition to the constant use by staff of PPE and the time taken to put that on. While the theatres are working at reduced capacity, the ICU is very busy with Covid patients and, at UMC, additional ICU space has been created, with older wards reopened, re-purposed and re-equipped for coronavirus patients. Covid patients are also being treated on general wards, but can be moved to ICU if their condition deteriorates.

In a nutshell, the benefits of the Mindray TE7 have become increasingly apparent to UMC staff during the coronavirus pandemic due to their mobility, performance, flexibility and reliability. 'In the beginning, I was sceptical, but we are pleased to have them,' the UMC anaesthesiologist concluded. 'As the person in charge of them, I think this is a very good machine.'

Dr Karina de Roos-Baron at work



Pan-European lung cancer

Report: Mark Nicholls

Pan-European lung cancer screening is challenged due to the range of approaches in different countries. As attitudes towards smoking and smoking cessation programmes vary, experts are attempting to establish more unified lung cancer screening.

The introduction of consistent pan-European lung cancer screening will be outlined at a special session during the online ECR 2021, with presentations highlighting the current position in several countries.

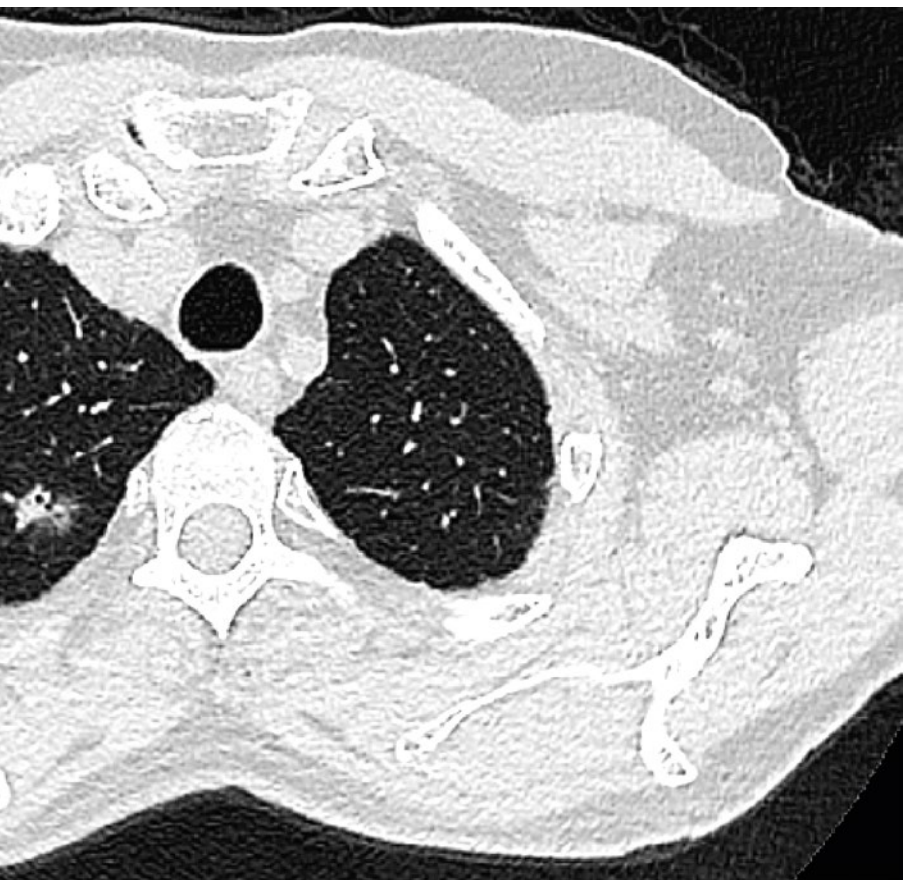
The session, entitled 'Lung cancer screening implementation in Europe: where are we now?' will be chaired by Dr Annemiek Snoeckx, from the Department of Radiology at Antwerp University Hospital and the University of Antwerp in Belgium.

With lung cancer causing 1.76m deaths a year worldwide (5,726 deaths a day), she will look initially at the pivotal aspects of a lung cancer screening service, focusing on the 10 key points of eligibility criteria (who should be screened), plus shared decision-making; image acquisition; imaging review; good communication; smoking cessation; a multi-disciplinary approach; quality assurance; cost effectiveness; research and Artificial Intelligence.

'From there,' Snoeckx said, 'the session will focus on the struggles different countries encounter in the implementation of lung cancer screening. I think the biggest problem now in Europe is that there are not yet any European recommendations.'

Welcoming the recent move to include lung cancer screening in Europe's Beating Cancer Plan, she gave a prediction. 'I think one of the conclusions from the session might be that different countries have different problems because they have different healthcare systems, but that there also are challenges that

Updates: France, Germany, the UK, Croatia, Hungary, Poland, Russia



Chest CT: lung cancer in the right upper lobe

ropean lung screening

are common and need to be tackled from a European level.'

Snoeckx, a co-founder of Flemish Lung Cancer Screening Task Force, explained that, in Belgium, lung cancer screening is organised on a regional level. She advocates a MDT (multi-disciplinary team) approach, including radiologists, medical physicists, tobacco cessation specialists, pharmacologists, surgeons, radiotherapists, and epidemiologists and underlines the importance of the smoking cessation aspect to screening.

Prepare to implement lung cancer screening

Without clear European recommendations, she noted there is reluctance in Belgium – and other countries – to press ahead with implementation of formal and unified lung cancer screening programmes, though her advice is for nations to start preparing to be ready to implement lung cancer screening.

It is crucial, she underlined, for the EU to make recommendations on lung cancer screening and that pressure from member states could push that along. As another speaker in the session, Dr Marie-Pierre Revel, Head of the Radiology Department at Cochin hospital, University of Paris, will outline the position on lung cancer screening within France and ongoing plans to develop this. Her presentation will provide an overview of lung cancer screening studies in France, will discuss pilot programmes, as well as explain how French radiologists are being prepared for large-scale screening.

Revel also has a role overseeing the European Society of Thoracic Imaging (ESTI) Lung Cancer Screening Certification Project (supported by ESR) to introduce the European certification in nodule assessment and lung cancer screening as a qualification to standardise training and expertise quality across Europe.

Speaking to European Hospital ahead of the presentation, she explained that in 2016, France rejected lung cancer screening, mainly because of the high level of false positives from USA trials, and that European trials at the time did not confirm mortality reduction. However, that position has now changed following further studies in Europe. 'What we know now is that lung cancer screening works and European trials have confirmed that there is a reduction in lung cancer related mortality,' she said. 'So, we believe that now, the major reasons why lung cancer screening was not considered in France are not valid anymore.'

Funding has been granted for a national pilot study in France focusing on women aged 50-74 (the same catchment as for breast cancer). 'We consider that women invited for breast cancer screening, if they are eligible in terms of smoking history, could also benefit from lung cancer screening, and we also need more data on women.' Another area of the work is in validating readings to enable reliance on a single radiologist rather than double reading, said Revel, who also has a key role in a verification programme at European level, based on e-learning to train radiologists in screening.

Marie-Pierre Revel is professor and head of the Radiology department, Cochin hospital, University of Paris, and oversees the European Society of Thoracic Imaging (ESTI) Lung Cancer Screening Certification Project to introduce the European certification in nodule assessment and lung cancer screening.

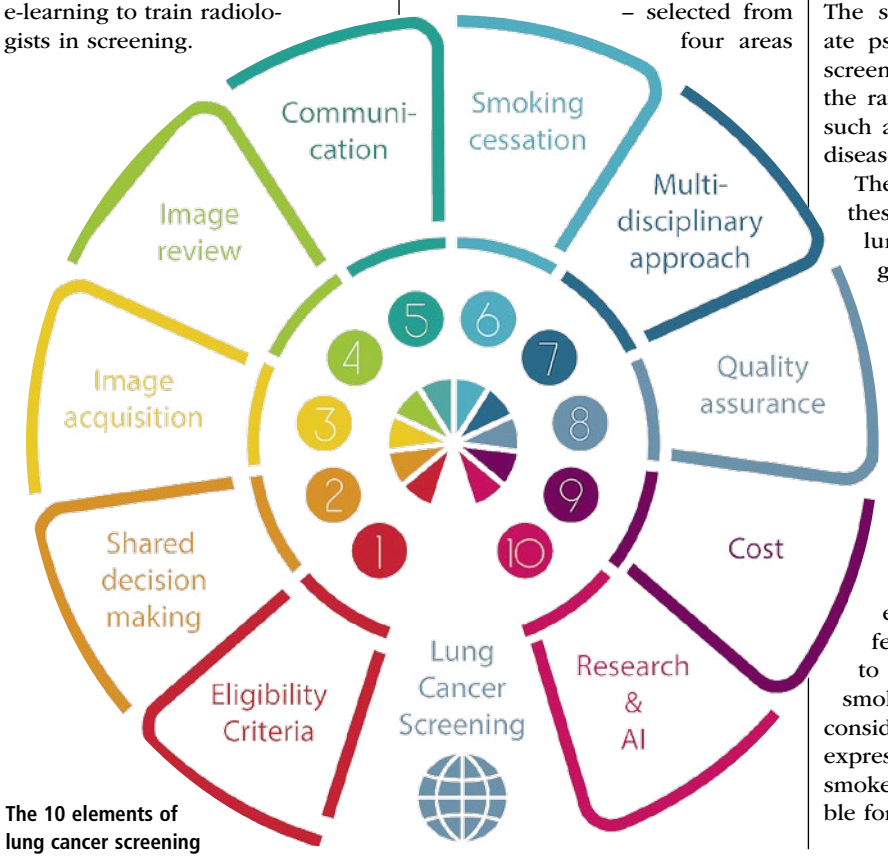
The French pilot study

2,400 females are participating in the French pilot study – selected from four areas of France with different socio-economic profiles. Radiologists will be trained to use artificial intelligence in the process, with the work also evaluating AI as a unique reader. The study will additionally evaluate psychological consequences of screening among participants and the rate of detected co-morbidities, such as COPD and coronary artery disease.

The hope, she explained, is that these trials will help shape future lung cancer screening programmes in France.

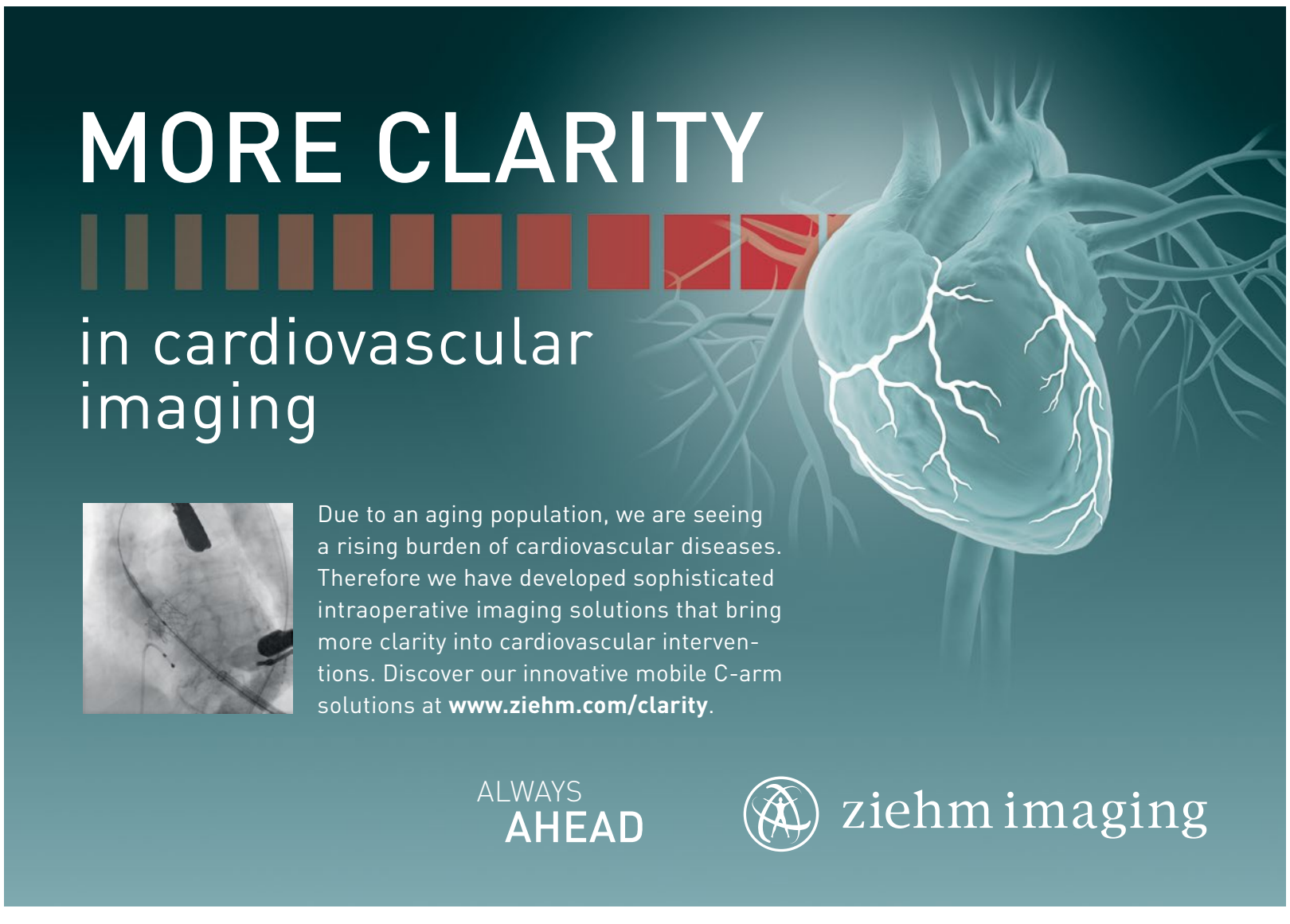
However, Revel stressed that only eradicating smoking will resolve the health threat, pointing particularly to rising cases of women of much younger age now presenting with Stage 4 lung cancer.

'The smoking situation in France – and Spain – is really worrying. We have an epidemic of lung cancer in the female population. We need to change the way we consider smoking; for years it has been considered a way of life, as the expression of liberty, but being a smoker is a disease and is responsible for so many deaths.'



The 10 elements of lung cancer screening

Dr Annemiek Snoeckx is a chest radiologist at the University Hospital of Antwerp and the University of Antwerp and is a co-founder of the Flemish Lung Cancer Screening Task Force. Her interest and research focuses on AI and biomarkers in lung cancer imaging, pulmonary nodules and screening.



Agfa's SmartXR

AI gives the digital radiography workflow a boost

In the move to evidence-based medicine, healthcare budgets put more pressure on efficiency, while quality of care has to meet ever increasing standards. Agfa has chosen to direct its development of artificial intelligence (AI) solutions towards helping radiology departments meet these challenges.

Agfa's SmartXR AI upgrades for its digital radiography portfolio focus on supporting operational efficiency and clinical consistency, as Gert Merckx, Product Manager Radiology Solutions for Agfa, explains.

An 'intelligent' approach to doing more with less

"Eliminating waste, supporting quality care, and enabling an efficient workflow are certainly not new challenges! With our legacy in imaging going back 120 years, we have worked hand-in-hand with our customers to enable continuous improvements. But AI technology allows us to completely rethink the equation," begins Product Manager Merckx.

He continues, "One of the most pressing challenges for managers of imaging departments is a shortage of skilled technicians combined with more limited training on radiography. This raises problems that impact departmental quality and efficiency, including avoidable errors, high exam variability, and more."

Agfa is addressing these issues with SmartXR, which adds targeted AI-based features to its DR solutions. SmartXR acts as an 'intelligent assistant' to the technician, enabling a smoother and more efficient daily imaging workflow and more consistent images.

SmartXR Assistant X-Ray Intelligence at work

Defining what hospitals want from AI

"The original ideas for possible features came from my time as an image processing researcher, working with X-ray equipment in the lab. I found that I made a lot of mistakes and realized AI technology could potentially help me to avoid some of them," Gert Merckx explains.

To select which features to include in SmartXR, Agfa went directly to radiology managers and users. "We started by conducting customer workshops and data mining our workstation usage patterns to evaluate radiographers' pains and needs. We found the greatest interest was in AI tools for optimising dose, improving positioning, and avoiding the nuisances that drive inconsistent imaging."

Based on these findings, Agfa developed SmartXR, which currently includes four sets of AI features that are available for use with Agfa's DR 600 and mobile DR 100s[1].

SmartXR at a glance

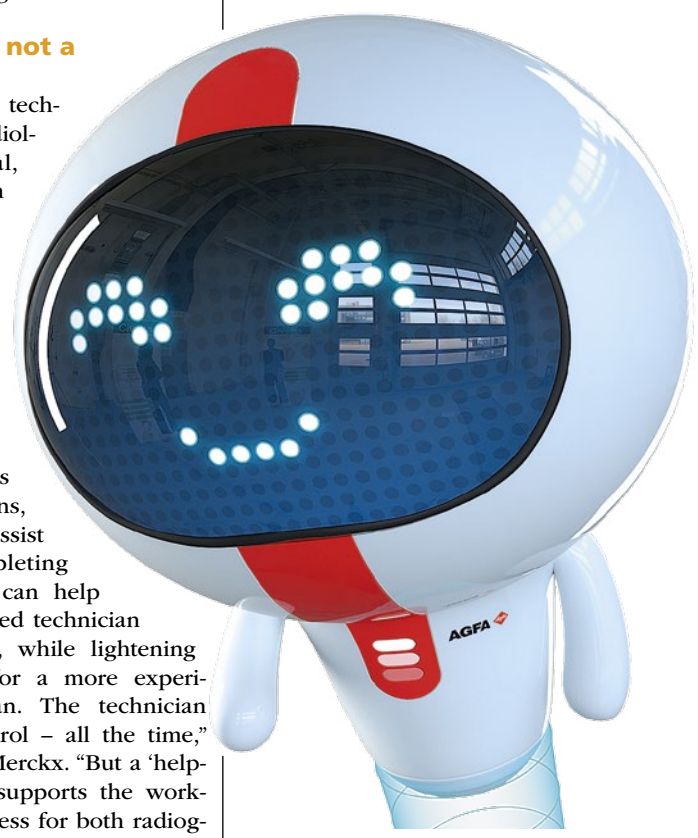
- SmartPositioning augments a live camera stream of the patient by projecting the image area and the AEC X-ray feedback sensor positions onto the patient's body. This helps the technician speed up positioning, while making it more accurate and consistent to reduce retakes.
- SmartRotate uses deep learning to auto-rotate images to their standard orientation based on the image content. Fewer post-processing actions are needed, while image presentation on both workstation and PACS is more consistent.
- SmartAlign uses advanced sensing to give live feedback on the accuracy of the tube-to-panel alignment during bedside or out-of-bucky exams. Alignment is faster and more accurate, with fewer retakes due to grid cutoff and more consistent projections.
- SmartDose uses 3D machine vision to determine the thickness of the patient, and then tailors the exposure parameters. This helps the technician to speed up the configuration of exposure settings, reduce retakes, improve image consistency, and ensure the ideal dose for the patient.

Two SmartXR packs are available: the Convenience Pack includes SmartRotate and SmartAlign; and the Performance Pack includes the full set of intelligent features.

An assistant, not a replacement

The role of the technologist in radiology is critical, not only from a technical standpoint but also from the perspective of their interactions with patients. "SmartXR is not intended to replace the tasks of the technicians, but rather to assist them in completing those tasks. It can help a less experienced technician to avoid errors, while lightening the workload for a more experienced technician. The technician remains in control – all the time," describes Gert Merckx. "But a 'helping hand' that supports the workflow reduces stress for both radiographer and patient." At ECR 2021, Agfa will introduce SmartXR to the European radiology field. Gert Merckx explains, "With SmartXR, we have given our imaging solutions eyes and a brain, we've made them aware of their environment and we have taught them their first skills. We are only bound by the limits of our imagination now."

[1] SmartXR SmartDose and SmartPositioning on DR100s is a work in progress. Contact your local sales representative for more information on the availability on the SmartXR tools in your region.



Liv, the friendly face of Agfa's SmartXR Imaging workflow assistant

NEW: The CL-S1200 colour 30.9-inch monitor

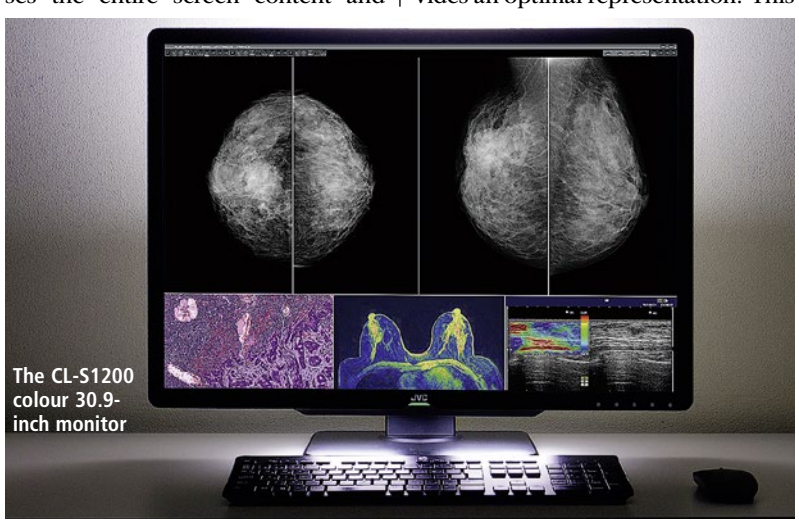
Analysing several scans on one screen

Displaying medical images of different modalities, such as CT, CR/DR, MR, ultrasound or mammography and pathology, on one screen? That's a radiologist's dream – indeed, many place several medical displays side by side to see several scans at the same time. With its new 30.9-inch CL-S1200 colour monitor ,JVCKenwood has eliminated this awkward practice.

With 12 megapixels (4,200 horizontal and 2,800 vertical), the device can display a variety of medical images side by side. The windows arrangement can be freely selected, and the large screen, without a centre bar, creates a comfortable environment for radiological diagnostics. With a maximum brightness of 1200 cd/m² and contrast ratio of 1500:1, the monitor is also suitable for mammography.

Latest technology integration

The display contains the latest technology. The patented Dynamic Gamma function, for example, analyses the entire screen content and selects the correct gamma curve for each individual pixel in real time. This applies to all images, whether ultrasound, endoscope, pathology or nuclear medicine, and always provides an optimal representation. 'This succeeds even with moving images without any problems, although millions of operations per second are necessary here,' explains Marcel Herrmann, Marketing Manager of Medical Imaging at JVCKenwood.



The CL-S1200 colour 30.9-inch monitor

The innovative Turbo Luminance function can increase the brightness and contrast of the screen for a maximum of 30 seconds to magnify recognisable gray scales, the manufacturer reports. 'This allows radiologists to reliably assess even low-contrast lesions on mammograms. The effect is further enhanced by the Visual Point mode.

'Luminance and colour temperature are automatically adjusted in real time on the CL-S1200. The built-in colour front sensor on the screen constantly measures colour temperature and adjusts changes over a long period of time,' Herrmann explains. This is gentle on the examiner's eyes – as is the built-in illumination on the back of the monitor and the indirect illumination of the keyboard and mouse, the company confirms.

Control via PACS

Another new feature of the CL-S1200 is the ability to control the display directly from the picture archiving control system (PACS). JVC has developed and integrated a special interface to do this. 'It allows the user to start the Visual Point Mode, for example, from within his familiar working environment and within the workflow. This darkens the areas outside the region of interest and enhances the contrast within,' Herrmann points out. In addition, the presets, i.e. the defined default settings of the display for certain images, can also be switched from the PACS. 'In doing so, the PACS transfers the respective DICOM tag to the MS-S1200, which then selects the appropriate pre-set,' he explains. If a mammogram is to be found, the monitor would work with a brightness of 500cd/m², and with a CT scan with only 250cd/m².

Sanitation

Additionally, the smooth, flat design of the CL-S1200 ensures that both the monitor and the wide-angle swivel can be disinfected and thus maintain hygiene.

Details: http://healthcare.jvc.com

Radiomics, pathomics and deep learning

Computational imaging furthers precision medicine

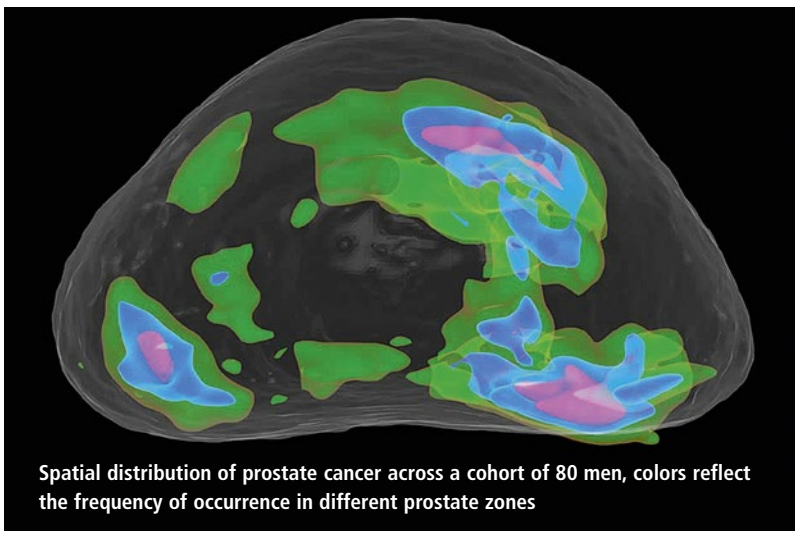
The advent of digital pathology provides the means to develop computerised image analysis to diagnose disease and predict outcomes for cancer patients from histopathology tissue sections.

Report: Mark Nicholls

Such advances can help predict the risk of recurrence, disease aggressiveness and long-term survival, according to leading expert Professor Anant Madabhushi, of Case Western Reserve University, Ohio, USA. Speaking to online delegates at the 7th Digital Pathology and AI Congress, Madabhushi outlined how tools are being developed to advance this area of diagnosis, prognostics and prediction.

His team has developed a suite of image processing, computer vision and machine learning tools specifically designed to predict disease progression and response to therapy via the extraction and analysis of image-based histological biomarkers derived from digitised tissue biopsy specimens. These have already been applied in the context of several different disease domains including breast, lung, oropharyngeal, prostate, ovarian cancer, and endomyocardial biopsies.

He suggested the tools would serve as an attractive and cost-effective alternative to molecular based assays, which attempt to perform the same predictions. His presentation, 'Computational Pathology as a Companion Diagnostic: Implications for Precision Medicine', looked at the implications of such tools for precision medicine against a backdrop of cancer diagnosis and mortality in the USA. With 600,000 deaths annually and 40% of the population receiving a cancer diagnosis, he noted: 'There is some discrepancy between those two statistics.



Spatial distribution of prostate cancer across a cohort of 80 men, colors reflect the frequency of occurrence in different prostate zones

'Some of the reasons why diagnostic incidence is high and mortality for the disease not in the same ball park is because we have become more aggressive about cancer detection, screening and imaging.'

Overdiagnosis harms patients

Madabhushi warned that overdiagnosis is harming patients – not only physically due to the treatments and side effects of therapy, but also financially with a high proportion of cancer patients having to invest their life savings in their treatment.

While finding disease earlier leads to a more favourable outcome, he suggested computerised image analysis could play an increasingly important role in the cancer diagnosis and therapy evaluation. Immunotherapy is a game-changer for cancers such as melanoma and lung cancer, he said, but they are expensive and have a limited success rate of 20-25%, and no clarity on which patients will benefit or respond to these therapies.

This, he pointed out, underlines the need for better diagnostic, prognostic and predictive tools that will identify the presence of disease, as well as predict disease outcome and progression and the response to treatment. 'AI, deep learning and machine learning can really aid the pathologist, but there is a real unmet clinical need for these tools which can benefit the clinician, the one who is interfacing with the patient and having to make treatment and management decisions.

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'This will support precision medicine by using prognostic and predictive tools for tailoring therapy for a given patient based on a specific risk profile.'

His group is working to understand the full value to be gained from the data gleaned from tissue biopsies and the unprecedented opportunity to use computational machine learning tools on the digitised slides. 'This will not only identify presence or absence of disease,' he said, 'but also mine data for digital interrogation of data from the perspective of mining digital biomarkers, to identify features that can tell us about the risk of progression of disease, aggressiveness of disease, and how likely patients are going to respond to chemotherapy or immunotherapy.'

Studies prove benefit

To illustrate this potential, Madabhushi highlighted a series of studies from his group where AI and machine learning had been shown to suggest which patients would benefit most from which treatment. These included one focusing on disorder of collagen fibre associated with risk of recurrence in Oestrogen Receptor Positive (ER+) breast cancers in ECOG-ACRIN E2197 & TCGA. 'This goes to show the value of these diagnostic tools to aid the clinician in figuring what the outcome is and how to treat these patients,' he confirmed. 'This is also true in early-stage disease.'

In other examples, Madabhushi outlined how a combination of computer extracted features of nuclear morphology, tubular formation and mitotic count predict disease-free survival in ER+ breast cancer, and also how computer extracted images of nuclear shape, orientation disorder and texture from whole slide imaging are associated with disease-free survival in ductal carcinoma in situ. He further detailed possibility of using similar approaches predicting post-surgical recurrence in prostate cancer, lung cancer, ovarian cancer, endometrial and cervical cancer.

'Computational analysis with routine imaging could help address questions in precision medicine, specifically prognosis and predicting response to therapy,' Madabhushi concluded. 'The relatively low-cost aspect of computational diagnostic tools could also have global benefits, especially in low- and middle-income countries.' And, he predicted, 'the importance of establishing the connection to the molecular underpinning of the features, moving away from an abstract representation, is going to be a really important driver for clinical adoption and clinical utility.'

Anant Madabhushi is the Donnell Institute Professor of Biomedical Engineering, Case School of Engineering, Case Western Reserve University, Cleveland, Ohio, and also Director of the Centre for Computational Imaging and Personalised Diagnostics. In the School of Medicine he is Professor in the Departments of Pathology, Radiation Oncology, Radiology, Urology and General Medical Sciences. His research interests include quantitative image analysis, radiomics, pathomics (a central source for computational pathology), cancer imaging, and digital pathology.

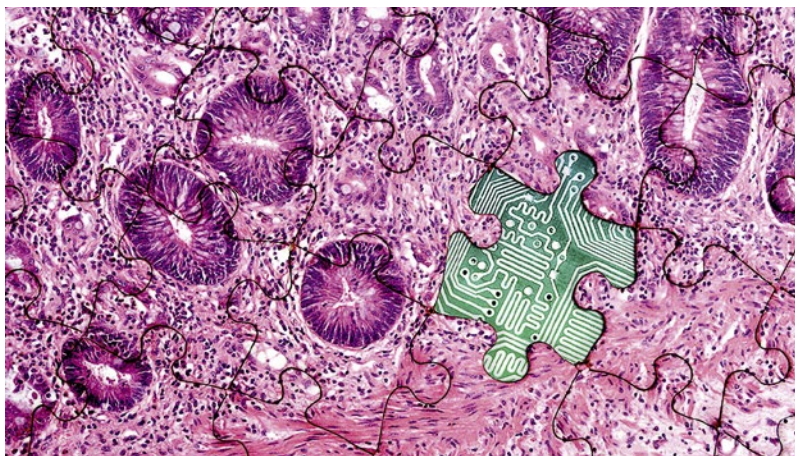
Digitisation dawns in developing world

The future of digital pathology is assured

Pathologist Dr Talat Zehra reports from Pakistan

Given the rapid transition towards digitisation, digital pathology is now unquestionably the future. However, some pathologists, particularly in underdeveloped countries, are still reluctant to accept its place in their labs. Among their many reasons, some feel that histopathology is a very complex and subjective field and artificial intelligence (AI) software cannot cope with all the issues. Conversely, pathologists are also scared that AI might replace them completely.

Last but not least, a large number of pathologists, particularly senior ones, or those who have not worked in the developed world, are not familiar with new modalities, so they are reluctant to adopt them.



Pathologists in many countries are eager to go fully digital – however, in some cases, crucial pieces are still missing (Image courtesy of Dr Alex Wright, University of Leeds)

As for Pakistan, the bottleneck here is either the absence of pathology slide scanners, digital microscopes or manual whole slide image (WSI) software; if available ,they are mainly used for educational or research purposes only. The use of AI is almost negligible, indeed very few pathologists know about this novel entity.

Initially, I did some pilot projects to validate the results of AI software on previously diagnosed cases. For this I am highly thankful to *Aiforia Technologies Oy*, which gave me its demonstration version and training on AI software. Using this, I carried out some pilot projects on chorionic villi and malarial parasite detection and gained a good concordance of around 84%. We accomplished this project without a scanner or digital microscope.

Despite slow adoption in many institutions and countries, the digital slide image is slowly replacing the glass slide. Aided by AI-based image analysis software, we can improve the much weaker and fragile healthcare delivery in developing countries. These carry most of the world's endemic disease workload but,

Continued on page 16

Dr Talat Zehra MBBS FCPS is assistant professor at Jinnah Sindh Medical University (JSMU) and consultant Histopathologist at JSMU Diagnostic Lab, Karachi, Pakistan. She gained her Bachelor of Medicine, Bachelor of Surgery degree in 2007 from Dow Medical College, University of Karachi, Pakistan, and her fellowship in Histopathology at the College of Physicians and Surgeons of Pakistan. Zehra's field of interest is digital pathology and the use of artificial intelligence in tissue imaging. Zehra has written a few articles internationally to highlight the issues in delaying adoption of digital pathology techniques in the developing world. Currently, she is also a member of the education committee of the Digital Pathology Association (DPA).

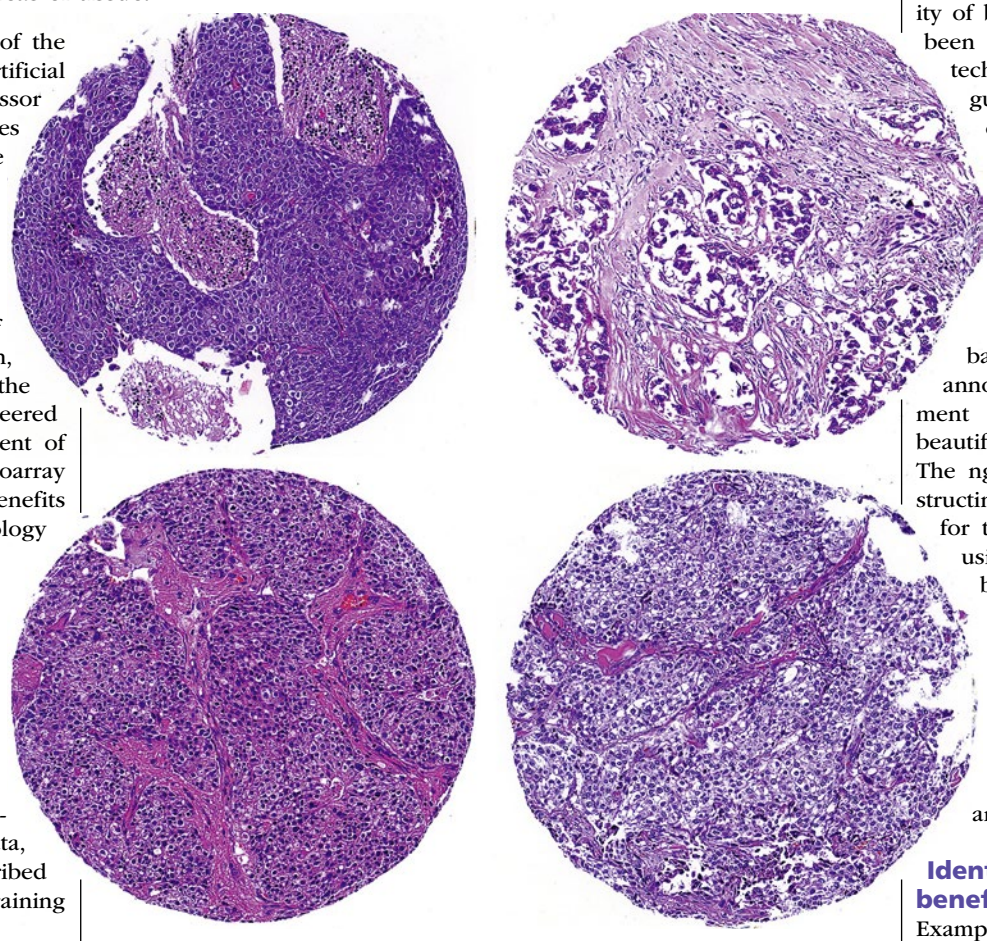
Multiplexing, DNA/RNA sequencing and AI applications

An exciting new era for tissue microarrays

A new generation of tissue microarrays are delivering more efficient, time-effective solutions to answer complex clinical and scientific questions, digital pathology allows specific and targeted analysis of small areas of tissue.

During an online presentation of the 7th Digital Pathology and Artificial Intelligence congress, Professor Inti Zlobec outlined advances 'From artificial intelligence to multiplexing: exciting avenues for next-generation Tissue Microarrays'.

As Head of the Translational Research Unit (TRU) at the Institute of Pathology, University of Bern, Switzerland, Zlobec explored the potential of an approach pioneered through her unit's development of next-generation Tissue Microarray (ngTMA), and looked at the benefits of coupling with digital pathology in translational research.



TMA of breast cancers with brain metastasis

A virtual goldmine

The TRU has assembled a massive repository of pathologist-annotated images through the ngTMA Facility, including whole slide and tissue microarray spots, linked to corresponding clinical and histopathological data, to create what the team described as 'a virtual goldmine for training machine learning algorithms'.

'Exciting new avenues for investigation using tissue microarrays include multiplexing, DNA/RNA sequencing and artificial intelligence applications,' she said. Underpinning their research at the Institute is the Tissue Bank Bern (TBB), a platform on which their collections of different tissues are used and stored for different studies and analysis. This includes a frozen collection of 12-13,000 different tissue samples stored at -80°C. Outlining the evolution of TMAs from the late 1990s, Zlobec pointed to the benefits of having tissue cylinders in one block, making it easier to identify an area of focus. 'It's an incredible tool because they are easier to evaluate and it's a research tool lasting years, depending on the quality of the associated clinicopathological data. They create the same experimental conditions but with less resources and less material.' Her group has focused on a subgroup of cells in colorectal cancer (CRC), called tumour buds, which are heavily related to CRC prognosis.

'Tumour budding appears in many, or most, solid cancers and is a route to dissemination and metastasis,' she added. 'We wanted to capture these tumour buds and study them in terms of heterogeneity of biomarkers. This would have been impossible using old TMA techniques because there is no guide to punch out very specific areas. However, the way to do that would be to use a digital slide.'

That enables researchers to mark certain areas of interest and placing annotations on an image.

'It is a digital pathology-based solution and works with annotation of a scan and alignment with a block and creates beautiful TMAs,' she pointed out. The ngTMA process is about constructing a TMA that is very specific for the research project and, by using digital pathology as the basis, more questions can be answered.

They can be used for precision medicine, tumour heterogeneity, rare diseases/scenarios, to target histological areas, perform animal studies, and establish antibodies and new methods.

Identify patients who will benefit most

Examples include PD-L1 in colorectal cancer, to identify patients who will benefit most from immunotherapy and the use of ngTMAs to answer the question about PTEN deletion, a known major cause of PTEN protein loss, correlating with aggressive characteristics and worst outcome. In addition, ngTMA has been used to compare the protein expressions for breast, brain and pancreatic cancers. Future trends in ngTMA include multiplexing, DNA/RNA sequencing and AI. Multiplexing can be expensive; scanning – and analysis – can be time consuming, but can lead to increased precision due to smaller areas/cores on which to concentrate.

'Scanning time can be avoided if you have a smaller number of slides,' Zlobec explained. 'One of the examples of multiplexing that we have helped to contribute to is CODEX, the application in co-detection by indexing.'

With colon cancer, the researchers plan to look at two different special types of immune cell infiltrates and investigate cellular neighbourhoods to orchestrate antitumoral immunity in CRC, processes that would not be possible using regular TMA processes. The ngTMA process also facilitates quality control, traceability and can support image analysis.

With AI, the biobank offers a massive repository of images for machine learning and is a huge resource for training algorithms, though the challenge remains over management and efficient retrieval of the data.

'TMAs are a highly valuable biobank collective,' Zlobec confirmed. 'While useful for conventional reasons, such as screening of biomarkers, they have an application in the new areas of multiplexing, genomic analysis and computational pathology.' (MN)

Inti Zlobec is professor and head of the Translational Research Unit and the Bern Tissue Bank at the Institute of Pathology, University of Bern, Switzerland. She leads the digital pathology project for routine diagnostics as well as the colorectal research group which develops computational approaches to address clinical questions.

The future of digital pathology is assured

Continued from page 15

unfortunately, being less equipped with diagnostic techniques, the results are delayed diagnoses which, in turn, are associated with increased morbidity and mortality rates. The digitisation of pathology resources opens the door for the use of the massive potential of AI in pathology, which can speed up more accurate and reliable diagnosis. Additionally, integration will help to ease large data storage and predict the future outcome of disease, as well as personalise care plans for each patient, and forecast oncology trends particular to specific geographies. In this way, pathologists could suggest proactive approaches to prevent disease progression.

Thus, AI-enabled digital pathology use will transform the horizon of pathologists' traditional clinical practice, which has been unchanged for many decades. The rise of the pandemic that penetrated the globe without discrimination, further enhanced the need for telepathology, which I and other pathologists belonging to my organisation use to send digital images to senior colleagues in hospitals in Karachi to avoid unnecessary travel and exposure. However, the bottleneck in most of our setup has been the lack of pathology slide scanners or digital microscopes through which WSI can be sent easily. So, the idea of 'working from home' through devices emerged, which resulted in new norms in the thought process of pathologists, even in Pakistan, and will leave its impact even after the pandemic completely resolves.

Additionally, an important and serious issue in digital pathology adoption is that a large number of technical, ethical and legal questions still need to be answered, particularly in developing countries with a weak monitoring system. A very important issue, which may not be a very big deal for developed countries, is the high cost of scanners and AI-based software – among the reasons for delayed adoption of low resource setups and countries.

That accounts for the delayed adoption of this novel technique in our area of the world. We sent the cases for second opinion in the form of digital images that we took through microscope cameras, which cannot produce a detailed image; so a second opinion is not always easy. Many times, senior pathologists ask us to come to their location because digital images are not enough to give a reliable consultation, particularly in difficult cases. So, due to the lack of scanners and digital microscopes, we have used digital images largely for research and educational purpose, not for routine clinical diagnosis.

The role of world leading organisations of slide scanners and of AI software could be of great importance. They could participate with pathologists and technical staff in developing countries, which are potential sources of big data, in terms of training, as well as to offer scanners, digital microscopes and software at a relatively affordable price, i.e. to put them within the budgets of low resource organisations.

Finally, I will conclude on the note that digital pathology and AI is in the forefront of modern pathology and its emerging use within healthcare is now being realised. The novel technology is at our doorstep and it is better to welcome and accept it, otherwise a large proportion of the world population will suffer.