Spring 2025
#100

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100th Issue

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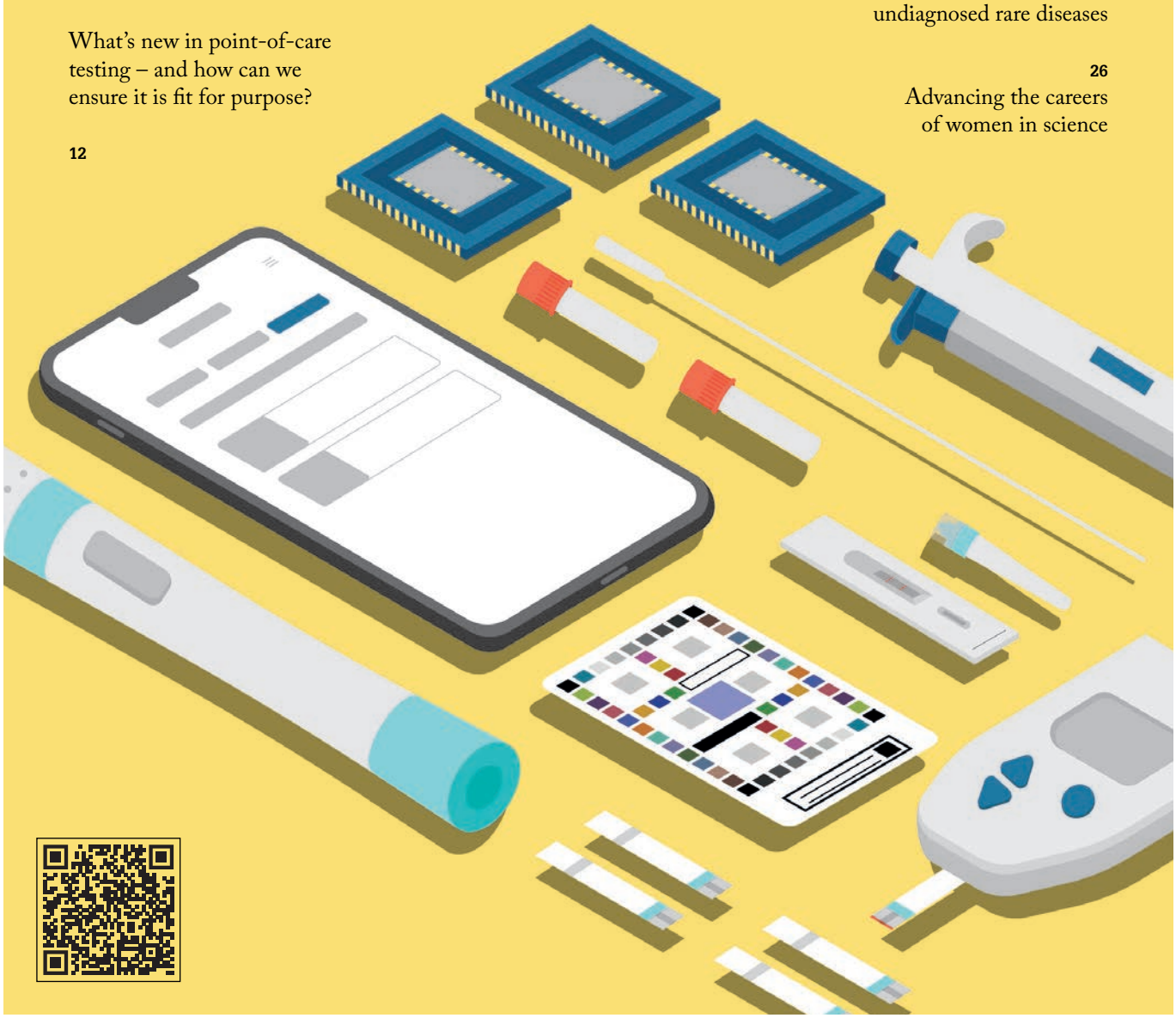

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Patients love point of care testing, but what about labs?

Frank always honored his scheduled appointments at the diabetes clinic, but often missed follow-up appointments to discuss test results due to work commitments. When his clinic introduced on-site A1C testing, Frank received his test results and counseling on diabetes management in his routine appointment. The result showed Frank's A1C levels had been increasing over the last two years, and his diabetes nurse discussed affordable lifestyle changes he could make to improve his glycemic control. At his next appointment, the care team were pleased to see that Frank's A1C level had decreased.

Sofia was desperately worried about chlamydia infection. Rather than wait a week for a GP appointment, she presented at the emergency room. The clinicians there ran a test on their benchtop PCR analyzer. Whilst, unfortunately, it confirmed Sofia's suspicions, the fast result allowed her to start treatment that same day.

Nadiya was insistent that her child needed antibiotics for a sore throat. Her doctor took a swab and ordered a point of care test for Group A Streptococcal pharyngitis while Nadiya waited. The negative result spared the child from an inappropriate antibiotics prescription, and Nadiya was advised on how to manage the symptoms.

Point of care testing (POCT) is undoubtedly beneficial from a patient perspective. And it relieves pressure on labs. But how do laboratory medicine professionals feel about non-specialists carrying out sensitive tests? What are the error rates? Are clinicians able to maintain their competencies in POCT amongst all their other tasks?

As well as sharing some of the latest developments in POCT technologies, our feature article takes an in-depth look at the pros and cons of POCT. After hearing our experts' take, why not share your views with The Pathologist? What are your hopes and fears for POCT? Join the debate: *edit@thepathologist.com*

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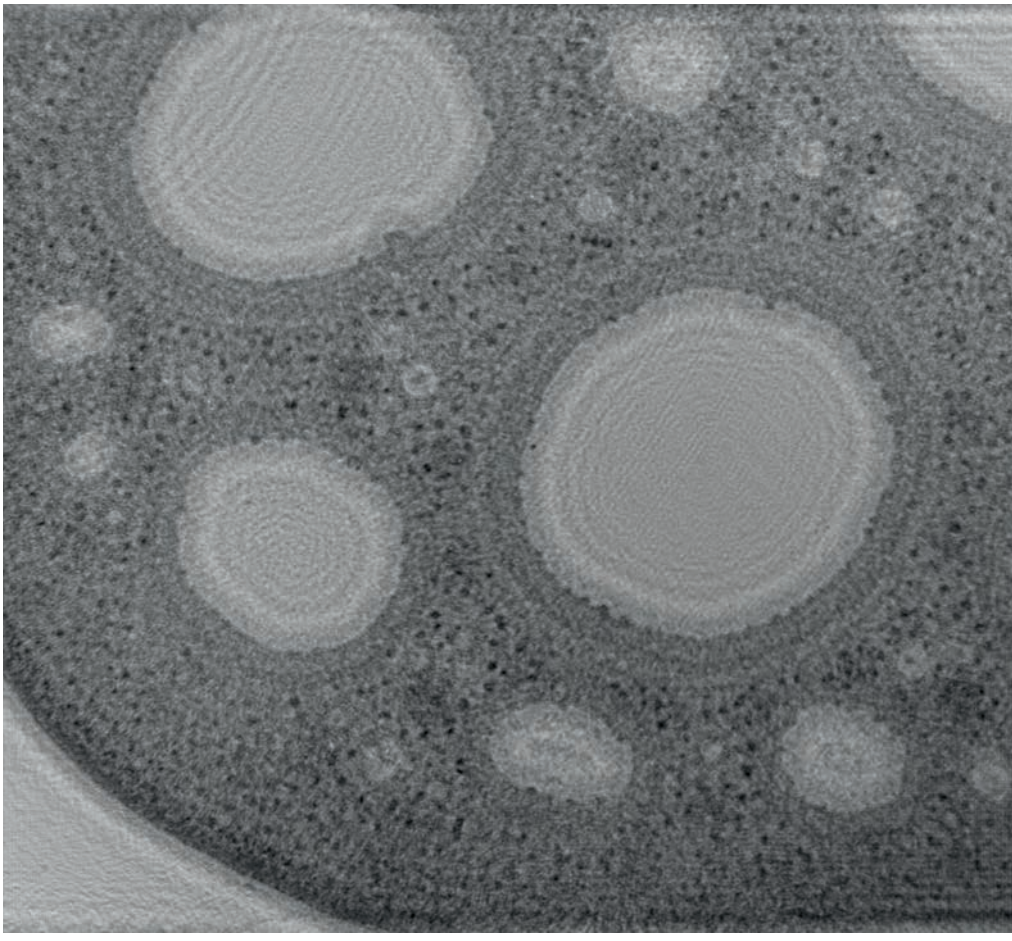
Multidimensional Precision

How smartphone-based microscopy opens up imaging at the point of care



Credit: Yuki Nagahama

A new smartphone-based digital holographic microscope (DHM) allows users to make precise 3D measurements with a broad range of applications (1). Here, lead researcher Yuki Nagahama shares more about this exciting development.

How does your smartphone-based DHM device differ from traditional systems?
In this DHM system, laser light illuminates the object, creating interference fringes by combining light that passes through the object with light that does not. These fringes, called holograms, are recorded. A computational system then simulates light propagation on the hologram, allowing the object to be focused and observed later.

Unlike traditional microscopes, DHMs capture both the amplitude and phase information of light. This enables the observation of transparent objects, such as microorganisms and cells, without the need for staining.

How could this device enhance point-of-care (POC) testing, particularly in remote or resource-limited settings?
We estimate this device will cost only tens of dollars in materials. With smartphones becoming more widespread, offering a microscope at this low price makes it far more affordable than typical options. This affordability could allow for the development of POC testing environments in a variety of locations.

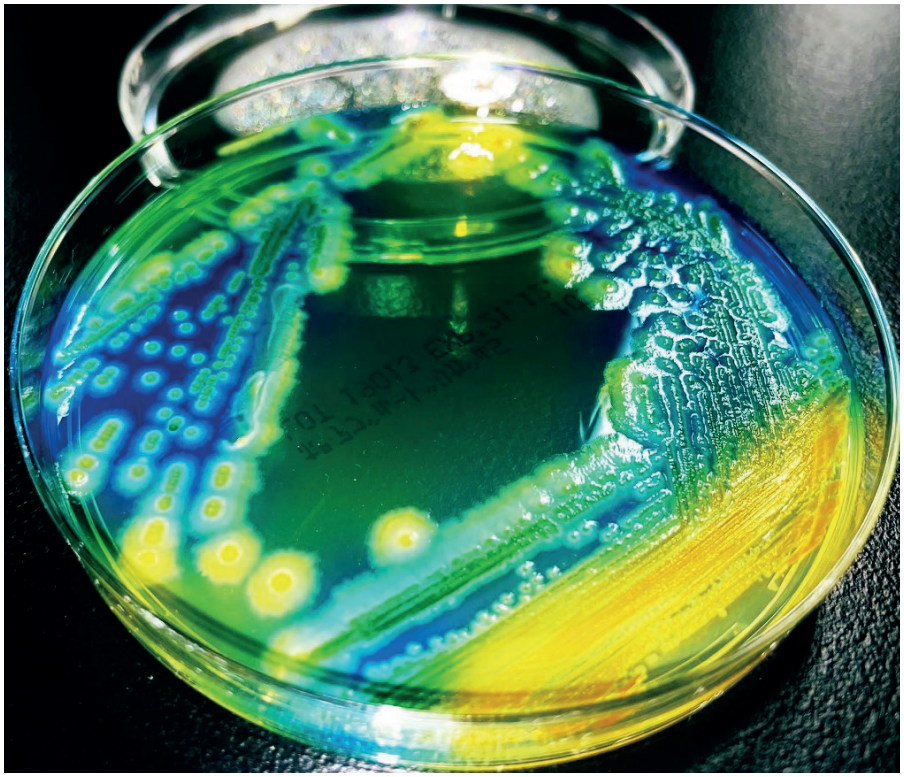
What diagnostic advantages does this system offer for clinical pathology?
The phase information can be used to estimate the object's thickness, aiding in the identification of microscopic features.

Unlike typical microscopes, this DHM system doesn't use physical lenses, like eyepieces or objectives, to magnify images. Instead, it uses a touchscreen zoom function powered by optical simulation. This allows users to zoom in without changing lenses, enhancing convenience and usability.

How could the device be improved to broaden its applications in bio-imaging or enhance its value in clinical diagnostics?
We are exploring ways to enhance image quality with deep learning. DHMs often produce unwanted effects, like conjugated images, that overlap with the observed image. Our research focuses on using deep learning to remove these unwanted elements through image conversion.

More broadly, how do you anticipate POC technologies will evolve over the next decade?
With the growing demand for telemedicine, patients may increasingly perform tests at home or in remote areas and share results with medical professionals for diagnosis. Linking these devices with wearables and smart devices will also allow patients to monitor and manage their health. To enable this, a secure system for managing POC data and a robust communication infrastructure are essential. Additionally, providing support to help patients use POC devices effectively will be crucial.

References available online.



Colorful Coli

Our image of the month comes from Wataru Hayashi, who says "this image showcases colorful escherichia coli colonies on Drigalski lactose agar."

Credit: Wataru Hayashi, research scientist at the National Institute of Infectious Diseases, Japan

QUOTE *of the month*

"We need to ensure that tests are performed by well-trained individuals to achieve high-quality results. If other people perform the tests, there should be a system – preferably overseen by someone with pathology and point-of-care experience – to monitor and track quality; it's important to look for unusual patterns, track data, and manage the system in real time to maintain high standards of care."

Linoj Samuel, clinical microbiologist at Henry Ford Health, USA

Read the full interview at https://bit.ly/3Q3YA76

Solving Disease Mysteries

Genomic reanalysis boosts rare disease diagnoses across Europe

Credit: Adobe Stock

In an effort to address undiagnosed rare diseases, the Solve-Rare Diseases (Solve-RD) Consortium identified molecular diagnoses for 13 percent of previously unsolved cases through comprehensive genomic reanalysis.

This pan-European initiative, detailed in *Nature Medicine* (1), systematically reanalyzed genomic data from 6,004 families affected by rare diseases, providing diagnostic clarity for 506 families (8 percent) through systematic reanalysis and an additional 4 percent via expert ad hoc reviews.

Examples of Solve-RD success include the discovery of a missense variant and deletion in B4GALT1 that resolved a neurological disorder, and a mitochondrial mutation (MT-TL1) that explained varying symptoms in a mother and son. Pathogenic variants found in PIK3CA and MN1 also ended long diagnostic searches in intellectual disability cases.

Solve-RD's scalable framework demonstrates the potential of reanalysis to address undiagnosed rare diseases globally. Future research plans to expand to additional rare diseases and adopt advanced sequencing technologies.

Reference

1. *S Laurie et al., Nat Med, Online ahead of print (2025)*

Invest in the Future

Setting up a department fund could open the route to departmental innovation, including digital pathology and AI

By Bob Tessier, co-founder and panelist for the Panel of National Pathology Leaders

Credit: Panel of National Pathology Leaders

When it comes to laboratory upgrades, departmental needs and ambitions can often be thwarted by a lack of funds. Hospitals are reluctant to support the introduction of new technologies, such as digital pathology and AI, because there is no reimbursement for these services. In other cases, budget limitations do not allow the department staff to explore best practices or bring in outside consultants to improve efficiency. So, what is the route forward to improved workflows and expanded services?

Well, when external funding is not forthcoming, it might be prudent to look for an internal solution. I would advise establishing a department fund.

A department fund is a special purpose account within a nonprofit hospital, which has been established to allow tax-deductible contributions that are earmarked for the benefit of the pathology and laboratory department.

In nonprofit hospital departments, department funds offer a mechanism for pathologists – who have an exclusive contract – and patients, who have benefited from their services, to contribute to the department. The funds can then be used to sponsor innovation and make upgrades that are not within the normal operating or capital budget.

The first step in setting up a department fund is for the hospital to establish a separate account for this purpose. The contributors – usually pathologist partners in the private practice group – determine how much each will contribute to the fund and, together with the hospital's C-suite, they decide how the monies will be used. In many cases, the hospital is willing to match physician contributions or provide a portion of performance-based incentive payments, which both parties agree to reinvest in the department. Other funding sources include outside donors, strategic partnerships, and foundations.

It is important to remember that, in a nonprofit hospital setting, financial contributions can be classified as charitable contributions, which are tax exempt. Contributions might also be in the form of expertise – including serving on hospital committees/boards and charitable organizations.

Patients may also donate to the fund, on the basis of positive outcomes from diagnoses/treatments they received. In one instance, a patient who had significant laboratory work made a donation which was used to update blood bank automation. In another case, a friend of the Department Chair left money in their will which funded equipment purchases in Chemistry and Microbiology.

So, what are the potential benefits of dividend reinvestment in the pathology department? Let's consider the advantages of investing in digital pathology and AI. The department might be able to offer external subspecialty expertise, generating an additional income stream for the hospital. Metrics suggesting improved turnaround times and diagnostic accuracy could lead to "world class" community hospitals integrating with regional centers of excellence. That, in turn, might lead to big cost savings on courier services, as samples are transferred digitally.

Finally, it's worth considering the benefits to department members. Recently graduated pathologists prefer to work in a setting with cutting-edge technology and greater efficiency, and they will be drawn to hospital settings that have these. This is essential for successful recruitment and retention. Additionally, the pathologists' work-life balance can be greatly improved with digital pathology and AI. In Toronto, one pathologist who did not live near the hospital saved two hours of commuting time a day because they were able to work from home. In another example, a pathologist did not need a six-month medical leave to care for a family member.

Beyond technology upgrades, department funds might enable access to a host of other expenditures: department promotion and public relations initiatives, website development, outreach projects, non-funded clinical research, staff training, hosting a distinguished lecture series, or strategic planning.

Pathology Meets Industry

Why translational pathology should be included in pathology residencies

By Tengfei Wang, pathology resident PGY3, Department of Pathology, Baylor Scott and White Health, Temple, Texas, USA

Credit: Baylor Scott and White Health

The landscape of pathology is evolving rapidly with the advancements in AI, digital pathology, and precision medicine. These shifts are shaping the practice of pathology, demanding a new generation of pathologists who are knowledgeable and adaptable across diverse applications beyond traditional laboratory roles. Should we not be building those demands into pathology training?

Integrating translational pathology – an industry-based experience that bridges the gap between research and clinical application – into pathology residency training offers a unique opportunity to enhance educational outcomes and expand career options. Emphasizing and supporting this approach within residency programs can prepare future pathologists to contribute more effectively to the evolving field.

Translational pathology focuses on taking scientific discoveries from bench to bedside. Industry settings, particularly within biotechnology and pharmaceutical companies, are often at the forefront of these advancements, developing and refining novel diagnostic tools and therapeutics. Collaborating with these industry partners brings pathology residents multiple benefits.

Firstly, industry rotations provide residents with hands-on experience in advanced technologies, offering insights into their practical applications and how they can enhance diagnostic accuracy and efficiency. For instance, pathology residents gain exposure to cutting-edge tools and methodologies – from advanced companion assays to AI applications or digital algorithms – which they may not encounter in a traditional training setting.

In an industry setting, residents learn not only how to use innovative tools but also how these tools progress from concept to market. This involves exposure to regulatory and commercial aspects of pathology, such as the development, approval, and post-launch evaluation processes for new diagnostics and therapeutics. Familiarity with regulatory frameworks gives residents insight into the critical steps required to bring a new diagnostic test or treatment to clinical practice. Learning about quality assurance, regulatory compliance, and safety protocols also broadens their understanding of healthcare innovation.

Industry-based training also helps cultivate a mindset of innovation and adaptability – traits that are essential in a field that is advancing as rapidly as pathology. Working in such dynamic industry settings encourages residents to develop a creative, solution-oriented approach to problem-solving. This innovative spirit can inspire residents to approach clinical diagnostics with a fresh perspective, ultimately improving patient outcomes.

Some may argue that industry involvement poses risks, such as prioritizing commercial interests over education or patient care. However, these concerns can be effectively managed with clear ethical guidelines and structured programs that prioritize learning objectives. Residency programs and accrediting bodies should work together to establish transparent partnerships with industry that align with the highest educational and ethical standards. By offering structured rotations or electives in translational pathology, residency programs can ensure that residents gain valuable industry experience without compromising their primary clinical training.

From a practical standpoint, implementing structured industry rotations in residency programs can broaden career prospects for pathology residents, giving them exposure to a variety of professional opportunities beyond traditional roles. Pathologists who have experience in translational pathology are well equipped for positions in biotechnology, pharmaceutical companies, and regulatory bodies. Such roles provide a unique chance to impact patient care on a large scale by contributing to the development and implementation of new diagnostic tools and therapies. This expanded career path offers flexibility for those who may wish to pursue non-traditional roles while also providing essential expertise in a growing area of healthcare.

Furthermore, incorporating translational pathology into residency training helps prepare a pathologist who is equipped to lead in a future where the scope of pathology continues to expand. As more pathologists engage with AI, digital pathology, and other advanced diagnostic technologies, they will play an essential role in shaping the future of healthcare. With the right training, residents can become leaders in both clinical practice and innovation, pushing the boundaries of what is possible in pathology.

In conclusion, incorporating translational pathology into residency training prepares future pathologists to be leaders in both innovation and clinical practice. Collaborating with industry partners should not be viewed as a divergence from traditional pathology education, but rather as an enrichment to the training experience. By embracing translational pathology, residency programs can cultivate a workforce that is knowledgeable, adaptable, and ready to make a meaningful impact in a healthcare system where pathology's role is rapidly expanding.

As we explore new paths for pathology education, it is time for residency programs and educators to recognize the invaluable role of translational pathology in preparing residents for a forward-thinking, innovative, and impactful career.

Igniting Innovation

How curiosity in pathology leads to better patient care

By E. Blair Holladay

If you were to ask the average person how they see the laboratory interacting with patients, they'd probably tell you that they don't see it at all. As pathologists and laboratory medicine professionals, however, we know that our role in healthcare is first and foremost patient-centric, and that the laboratory is where science meets patient care.

Continued innovation by the laboratory strengthens the connection between these two essential elements. Innovation, however, doesn't often happen by accident. Rather, it requires active participation and, most importantly, derives from staying curious.

Change in the medical laboratory is happening at a rapid clip, with no prospect of slowing down. The adoption of cutting-edge tools like molecular diagnostics, AI, or next-generation sequencing has transformed the landscape of laboratory medicine. These innovations enable faster, more precise results that can guide timely and effective treatment decisions. These tools not only enable us to provide high-quality care like never before, but they also free up valuable time that can otherwise be used to envision and put into motion what the next level of individualistic, personalized care can look like for patients.

But only if we stay curious.

Curiosity ignites innovation.

In the medical laboratory, curiosity can take on many forms. It can mean questioning the status quo or exploring solutions from different angles – even if they may seem unconventional. Staying curious means committing yourself to a learning mindset and being open to change. It empowers pathologists and laboratory professionals to adapt to changes more easily, ensuring that our work remains relevant and impactful. Staying curious can also mean fostering collaboration across disciplines to address complex healthcare challenges: How can you leverage your own knowledge with the knowledge of other fields to maximize results?

In a rapidly changing field such as patient care, staying curious is vital to ensuring we are giving our best to and for our patients. Today's patients are more engaged and informed about their health than ever before. Helping empower patients to take an active role in managing their health can't happen without our leadership to help drive that change. It can't happen without pathology and laboratory leaders being inquisitive about patients' needs or without the knowledge that a patient's understanding of their diagnosis is the foundation for effective treatment plans.

Innovation in the medical laboratory is not a luxury; it is a necessity for advancing patient care in an increasingly complex healthcare landscape. By staying curious and embracing a culture of continuous learning and experimentation, laboratory professionals can drive meaningful innovation and progress that benefits patients worldwide. From improving diagnostic accuracy to enhancing accessibility and empowering patients, the impact of innovation is far-reaching. In the end, it is the relentless curiosity of pathology and laboratory professionals that ensures the laboratory remains the cornerstone of modern medicine.

"Innovation in the medical laboratory is not a luxury; it is a necessity for advancing patient care."

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State of the Digital Nation

Three experts – Catherine Guettier, Sheeba Irshad, and Anthony M. Magliocco – reflect on Owkin's international survey on the opportunities and challenges for digital pathology and AI solutions

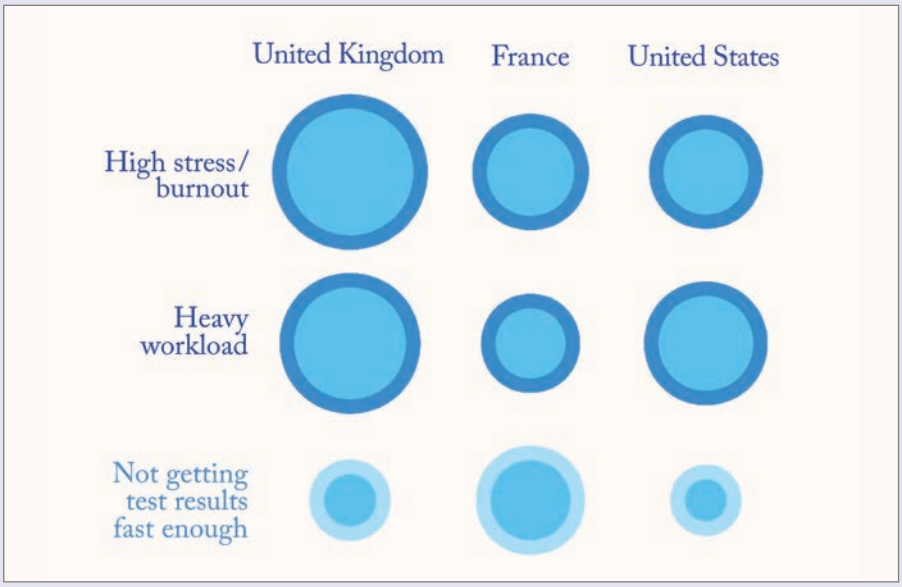
Despite the potential for digital pathology and AI tools to relieve the burden on pathologists – particularly in the complex field of precision oncology – uptake of these technologies has been slower than anticipated (1).

To better understand barriers to adoption, AI biotech company Owkin commissioned the State of the Nation survey in July 2024 (2). A total of 120 pathologists and 192 oncologists – in France, the UK, and the USA – took part, sharing their opinions on workloads, budgets, AI support solutions, and the future of the lab.

To explore the meaning behind the data, Owkin invited representatives from the three regions to comment on the survey results in a webinar hosted by The Pathologist (3).

Here, we report on their observations.

Different regions show concern for different burdens



Results from Owkin's State of the Nation Survey

The Panelists

Catherine Guettier – Emeritus Professor of Pathology, Paris-Saclay University, France

Sheeba Irshad – Clinical Reader in Medical Oncology, Kings' College London, United Kingdom

Anthony M. Magliocco – Founder & CEO of Protean BioDiagnostics, Protean BioDiagnostics, USA

Burdens detrimental to patient care

When asked about the burdens they were currently experiencing at work, survey respondents in the UK reported the highest levels of burnout and heavy workload.

Sheeba Irshad attributes this to a disconnect between expectations and reality, saying, "Diagnostics and treatments are both becoming more sophisticated, but, in the UK, infrastructures are not yet in place to deal with this increased sophistication. Whilst technology is moving forward, our workflows just aren't geared up for it yet – and that creates stress for healthcare professionals."

In the US, the increasing complexity – but also volume – of work is undoubtedly contributing to burnout, comments Anthony Magliocco; "We have more complex forms to complete, synoptic reporting, more challenges with new therapeutics, and so on."

Added to this, he says, "Trying to interface with the variety of electronic form document systems – particularly EMRs – can really take a lot of effort from medical staff."

In Owkin's survey, only 49 percent of respondents in France ranked their mental health as "good," compared with more than 60 percent in the US and UK. This could suggest that, in France, the problem of burnout is worse or it impacts mental health more significantly.

Catherine Guettier attributes this situation to declining efficiencies in the French healthcare system, leading to increased delays in diagnosis and treatment. "French oncologists and pathologists are watching the gradual decline of the health care system and the deterioration of working conditions – particularly in hospitals, with no hope of rapid improvement," she says.

Opportunities for digital pathology and AI to relieve these burdens

Owkin's survey found that US and French pathologists are more optimistic about the impacts of digitizing pathology than UK pathologists. This pattern held for cutting waiting times for tests and treatment, democratizing access to tests, and relieving pressure on pathologists.

Sheeba Irshad thinks that optimism in the UK might be curbed due to the slow pace of technology upgrades in the

National Health Service. Nevertheless, her institution has had positive experience with using AI to identify HER2 status in breast cancer. "The model identified 95 to 97 percent of all HER2-low and HER2-positive tumors in the validation cohorts," she says. "But what was really exciting was that it outperformed the average agreement between senior pathologists."

Anthony Magliocco spoke on the theme of using AI as a digital assistant to relieve workload pressures, saying, "Humans can get tired and miss details on slides. A diagnostic AI assistant can act like a pathology fellow that works with you day and night – and never tires. And if we exploit digital pathology to share cases with other experts and seek second opinions, errors will be a lot less likely."

Though French survey respondents are currently using AI less than their UK and US counterparts, their enthusiasm for the potential of AI in the lab was on a par. Catherine Guettier shared that her department has recently implemented an AI tool for grading prostate biopsies and has already seen measurable time savings per slide as well as improved diagnostic accuracy.

Catherine Guettier also reported the successful integration of Owkin's research tool for predicting breast cancer recurrence with her lab's image management system, adding, "In my opinion, this type of seamless integration is the best way to work with AI in real life and to boost adoption of AI by pathologists."

Breaking down the barriers to entry

When asked about the main barriers to digitization of pathology, the survey respondents cited lack of operational resources, prohibitive costs, lack of funding, and risks around ethical issues and the accuracy of the solution.

Reflecting on the survey's findings, Sheeba Irshad believes that the major barrier in the UK is the lack of adequate infrastructure. Once that is overcome, she says, "Training the healthcare professionals who will be deploying these tools is vital. Only with effective education of the workforce and patients will the tools fulfil their potential."

The financial challenges are the primary bottleneck to digital implementation in France, says Catherine Guettier. Being able to demonstrate a return on investment will be key: "French pathologists must obtain reimbursement for the use of AI from the French Social Security, and this will be achieved only by the demonstration of a true improvement in the quality of care."

Encouragingly, Catherine Guettier explains that data on AI performance in pathology is already being collected in prospective multicenter trials. What's more, she continues, in France, "Some pathologists working in academic departments have begun to request the possibility of using in-house algorithms derived from their own translational research."

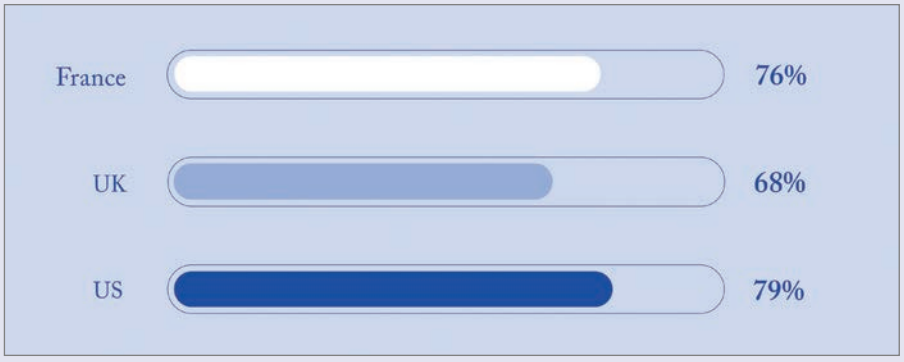
Meanwhile, in the US, the lack of reimbursement for digital pathology and AI from the health insurers is still a major barrier to implementation. Despite this, Anthony Magliocco remains optimistic that the tide is turning. "Some companies are now receiving payments from CMS for digital services," he says. "And once there's a pathway to reimbursement, that changes everything. In the US, once there's money to be made from technology investments, you'll find the adoption will happen incredibly quickly."

An appetite for research into AI capabilities is also driving interest in the US, explains Anthony Magliocco. "At Protean, we are very keen to evaluate and implement new algorithms in both the research and the clinical side," he says. "I'm very optimistic about the future of these technologies."

A virtuous circle

Our panelists' experiences suggest a future where AI can catalyze digital pathology adoption via specific use cases that help alleviate the burdens placed on pathologists and oncologists by modern medicine, helping patients in the process. A collective thought appears to be that the barriers to entry could be overcome through the willingness of pathologists and healthcare systems, alongside the close collaboration of AI tool developers with end users. And it seems clear that a continued drive to prove – to both regulatory authorities and payer systems – the invaluable nature of digital pathology and AI solutions through the generation of clinical evidence will also lead to wider adoption.

Are you optimistic that AI can cut waiting times for testing, oncologist review, and treatment?



Results from Owkin's State of the Nation Survey

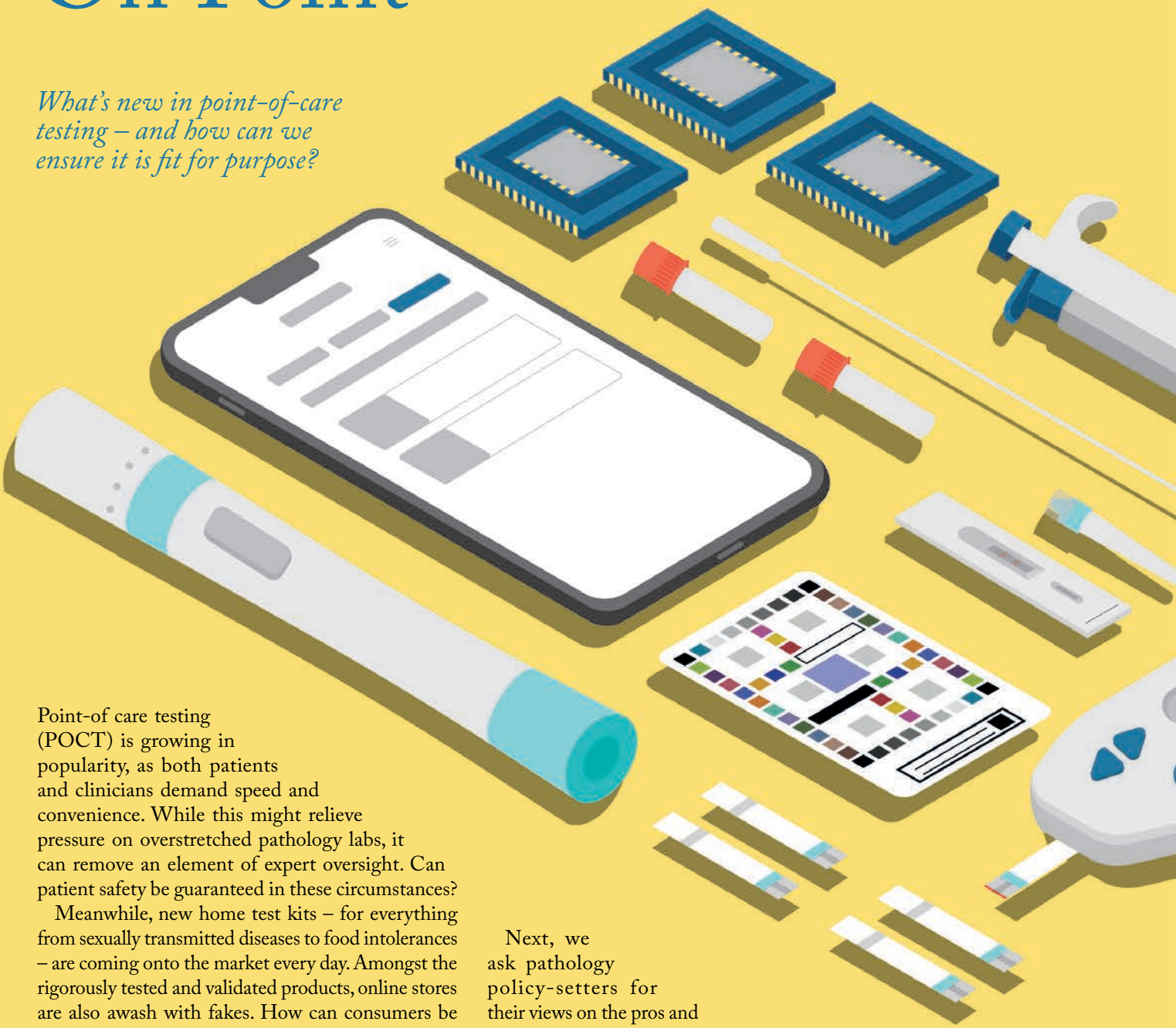
References

1. *A Khanduja and C Tang, "Beyond Digital," The Pathologist (2021). Available at: bit.ly/4gX0S3o*
2. *Owkin, "State of the Nation: Opportunities and Challenges for Digital Pathology and AI Solutions," (2024). Available at: https://www.owkin.com/connect/state-of-the-nation*
3. *Webinar: "State of the Nation: Interrogating the Benefits and Obstacles to Digitization and AI Adoption," The Pathologist (2024). Available at: https://bit.ly/4axW5Dr*

OWKIN

On Point

What's new in point-of-care testing – and how can we ensure it is fit for purpose?



Point-of care testing (POCT) is growing in popularity, as both patients and clinicians demand speed and convenience. While this might relieve pressure on overstretched pathology labs, it can remove an element of expert oversight. Can patient safety be guaranteed in these circumstances?

Meanwhile, new home test kits – for everything from sexually transmitted diseases to food intolerances – are coming onto the market every day. Amongst the rigorously tested and validated products, online stores are also awash with fakes. How can consumers be sure they are accessing reliable and useful products?

Our feature first examines some exciting new developments in the landscape of POCT. From a biosensor for kidney disease that could replace ELISA testing to a colorimetric test that can be analyzed on a smartphone – these innovations will blow your diagnostic mind.

Next, we ask pathology policy-setters for their views on the pros and cons of this testing paradigm. Are standards for POCT keeping up with the upsurge in developments – and are they being adhered to? Are labs being consulted in the development of new POCT schemes? How do pathologists feel about at-home testing? Read on to find out…

GIVE IT A (COLD)SHOT

Developing improved diagnostic methods for Kaposi's sarcoma

Researchers have developed a simplified DNA extraction method to streamline the diagnostic process for Kaposi's sarcoma (KS) (1). We spoke with corresponding author David Erickson to learn more.

Why focus on the KS diagnostic workflow?

The study was inspired by the need for faster, more accessible diagnostic methods for KS – particularly in regions with limited access to centralized laboratories. Previous work showed that extracting DNA from skin biopsies was the bottleneck in point-of-care (POC) diagnostics using loop-mediated isothermal amplification (LAMP). This research aimed to develop a simpler, equipment-free DNA extraction method to streamline the process, ultimately enabling quicker and more effective KS diagnosis in low-resource settings.

What is ColdSHOT?

ColdSHOT is a simplified, ambient-temperature DNA extraction method using sodium hydroxide (NaOH) to lyse cells without the need for heating or mechanical homogenization.

Traditional methods like spin column extractions involve more steps, such as tissue digestion, multiple buffer washes, and centrifugation, which require equipment and are time-intensive. In contrast, ColdSHOT uses a basic NaOH solution followed by neutralization, allowing for DNA extraction from small tissue samples without significant equipment.

How does ColdSHOT, without significant equipment, manage to achieve comparable DNA yields to spin column extractions?

ColdSHOT achieves comparable DNA yields by leveraging the high alkalinity of NaOH, which effectively breaks down cellular and nuclear membranes to release DNA. While it lacks the purification steps of spin columns, the NaOH lysis in ColdSHOT provides enough disruption to extract DNA from submillimeter tissue samples. Although it does not fully homogenize the tissue, it extracts sufficient DNA for the LAMP-based detection of targets like the KSHV, making it suitable for use at the POC.

What challenges did you encounter during your research – and how did you overcome them?

One challenge was achieving consistent DNA yields without using heat, which is traditionally employed to accelerate alkaline DNA extraction. This was addressed by optimizing the NaOH concentration and incubation time to balance yield with the simplicity of the method.

Another challenge was ensuring that the extracted DNA was compatible with LAMP assays despite the presence of non-target tissue components, which required careful testing of assay conditions and verification of DNA integrity.

What limitations do you anticipate with the ColdSHOT method in clinical use?

ColdSHOT's efficiency might be affected by temperature variations, as DNA extraction at ambient temperatures might differ in hotter or cooler climates. Additionally, the method may not fully digest larger tissue samples, potentially limiting its use to small biopsies. Sample stability in different storage conditions also poses a challenge, requiring further validation to ensure DNA integrity if samples cannot be processed immediately or stored properly.

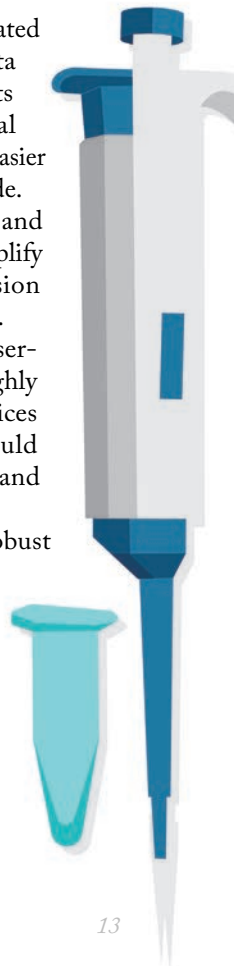
How do you see POC diagnostics evolving in the next 5–10 years?

POC diagnostics are likely to become more integrated with digital health tools, enabling real-time data sharing and analysis. In oncology, advancements in molecular diagnostics, including isothermal amplification techniques like LAMP, could make it easier to monitor cancer biomarkers directly at the bedside.

Additionally, improvements in microfluidics and portable sequencing technology could further simplify complex diagnostic processes, bringing precision oncology closer to patients even in remote settings.

POC technologies will likely become more user-friendly and automated, reducing the need for highly trained personnel. Integration with mobile devices for data analysis and cloud-based storage could enable rapid feedback loops between patients and healthcare providers.

To maximize their potential, investment in robust supply chains, reliable power sources, and training programs for local healthcare workers will be crucial. Collaboration between researchers, industry, and public health organizations will also play a key role in scaling up these technologies to meet diverse clinical needs.



Reference

1. *JC Manning et al., Sci Rep, 14 (2024). PMID: 38877073.*

DIAL D FOR DIAGNOSIS

Introducing a smartphone-enabled, paper-based assay for point-of-care diagnostics

A new smartphone-enabled, paper-based colorimetric assay solution combines affordability and portability with the precision of modern diagnostics, enabling real-time results in resource-limited settings (1). We connected with Nidhi Menon, head of R&D at HueDx, to dig into the details.

Credit: HueDx, Inc.

Why focus on paper-based assays?

Current methods for clinical chemistry diagnostics are time-consuming, labor-intensive, require exorbitant equipment, and are inaccessible in many regions. Paper-based assays represent an affordable, accessible, and sustainable solution to this problem. These assays are not only cost-effective but also easy to produce and distribute, making them particularly valuable in resource-limited settings.

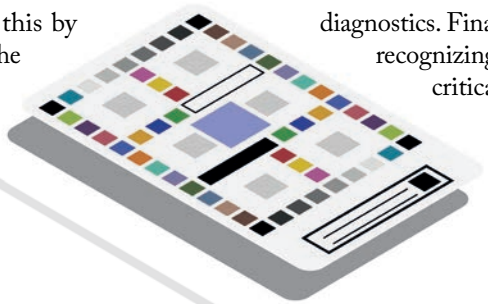
Additionally, the widespread adoption of smartphones has transformed them into powerful tools for diagnostics. With advanced imaging capabilities, processing power, and connectivity, smartphones offer a versatile and cost-effective alternative to traditional reader systems. Together, they pave the way for innovative solutions that improve healthcare access and outcomes, especially in underserved communities.

How does your system improve upon other colorimetric point-of-care (POC) methods?

Our system combines colorimetric chemistry with paper-based microfluidic technology and a smartphone app powered by AI and machine learning. At its core is a customizable HueCard, which holds the paper-based assay. The card includes a color sticker to standardize the colorimetric results, ensuring accuracy even with different lighting conditions. This helps improve the precision of analyte concentration measurements, meeting regulatory standards for POC and at-home testing.

Traditional colorimetric POC diagnostics typically provide qualitative or semi-quantitative results, which can limit clinical decisions. Our system advances this by providing truly quantitative results without the need for expensive or complex equipment.

Additionally, the system can be used with existing qualitative tests, allowing them to be adapted for quantitative analysis. This makes diagnostic testing more useful for both patients and healthcare providers, offering clearer and more reliable results in various settings, such as clinics or at home.



Can you share any details behind the development of the assay?

Developing this assay was both exciting and challenging because we were creating a new technology. One of the main challenges was ensuring the color results could be interpreted accurately in any lighting, which can vary significantly. To solve this, we created custom color correction software that adapts to different lighting conditions, making the color changes clear and consistent in any environment.

Another challenge was turning the test into a precise, quantitative tool. This required integrating advanced AI, computer vision, and signal processing to detect subtle color changes and provide accurate measurements. We also needed to make the assay compatible with mobile devices, overcoming limitations in mobile operating systems and hardware. To do this, we developed a custom app that simplifies the image capture process, ensuring reliable results on any device.

Finally, we built a cloud-based system using AWS to securely store images and process results quickly. This infrastructure ensures high-quality data storage and fast analysis, providing users with reliable workflows without compromising result quality.

How do you see POC technologies evolving over the next decade?

I anticipate POC testing will expand to include a broader range of biomarkers and clinical analytes for quantitative testing. Recent advancements in nanotechnology, microfluidics, and the integration of AI and machine learning have enabled technologies to enhance sensitivity and accuracy of detection and quantitation. Integration with digital health systems will allow for continuous monitoring, enabling patients to advocate for their health and healthcare providers to make faster, informed decisions for improved patient outcomes.

Support in the form of investments in new technologies, public awareness and education, regulatory support, and collaborative networks will be essential for the widespread adoption of POC diagnostics. Financial models and reimbursement policies recognizing the potential of POC diagnostics will be critical in making tests accessible to patients.

Reference

1. *N Menon et al., PLoS One (2024). PMID: 39365798.*

BYE, BYE ELISA?

A new biomarker sensor for low- cost, high-speed kidney disease detection

Over 850 million people worldwide are affected by kidney disease – more than double those living with diabetes. Though various diagnostic methods are used in clinical settings, they can be invasive, expensive, and uncomfortable.

Researchers at Chung-Ang University, South Korea, tackled the issue head on, developing an innovative diagnostic method based on a peptide receptor that specifically binds to symmetric dimethylarginine (SDMA) – a key biomarker of kidney disease (1). By attaching this receptor to a functionalized electrode, the team achieved precise detection of trace SDMA levels using electrochemical techniques.

We connected with Jong Pil Park, lead researcher on this study, to find out more.

How do you envision clinical laboratories benefiting from this technology?

The well-established ELISA technique, which uses antibodies, is costly, time-consuming, and prone to denaturation under certain conditions. In contrast, the peptide receptor identified in this study offers advantages like low molecular weight and easy chemical modification. With further testing on real samples like urine or blood, this sensing system shows potential for clinical diagnostic applications.

What breakthroughs enabled sufficient sensitivity for trace-level detection?

Gold electrodes are commonly used in these sensor applications due to their high electrical conductivity, but they're unable to detect specific molecules in their regular state. To improve sensitivity, we enhanced conductivity and other properties by using a novel nanocomposite made of nickel, chromium, and layered double hydroxides. Developing this nanocomposite required significant time and effort to ensure quality and consistency through repeated analyses.

Could your sensor technology be expanded to other biomarkers?

This study aimed to develop a new system to replace current kidney disease diagnostics. Though further research is needed to validate its use as an in vitro diagnostic tool, advancing the core technology could enable broader applications in medicine, including cancer diagnostics. However, as the research is still in its early stages, extensive additional studies are necessary to make it practical for clinical use.

"The well-established ELISA technique [...] is costly, time-consuming, and prone to denaturation under certain conditions."

Reference

1. *JH Shin et al., Biosens Bioelectron, 267 (2025). PMID: 39461099.*

THE TROUBLE(S) WITH POINT OF CARE TESTING

Bernie Croal – President of the Royal College of Pathologists in the UK – says much needs to be done to guarantee the safety of testing outside the laboratory

The COVID-19 pandemic saw a huge expansion in the availability of lateral flow testing. This opened patients' eyes to the possibility of carrying out their own diagnostic tests at a time and location suitable to them. The resulting appetite for self testing has seen a growing market for test kits and wearable sensors that empower the patient and relieve pressure on the health care services.

But are these initiatives sustainably funded? And with laboratories removed from the testing equation, who is overseeing quality assurance for these tests?

The Pathologist team met with Bernie Croal, President of the Royal College of Pathologists (RCPath), to discuss the point of care testing (POCT) situation in the UK.

Could you give some examples of POCT routinely used in the National Health Service (NHS)?

Within secondary care, we see POCT used in places like intensive care and emergency medicine, for tests such as blood gas analysis, where very rapid results are required. We also see POCT used for things like blood glucose measurement, mainly for convenience.

Similarly, in primary care, POCT provides convenient on-site testing for blood electrolytes, blood glucose, C-reactive protein, and other markers. There are also specific tests for things like D-dimer and natriuretic peptide. However, there is huge variation in the types of testing offered by general practice surgeries.

Community and home testing increased in the wake of the COVID-19 pandemic, thanks to the prevalence of lateral flow tests. And thanks to sensor technology, many patients are now wearing sensors to monitor blood glucose and guide insulin use. These have been very successful.

What are the current gaps in POCT in the NHS, in your opinion?

We're seeing increased pressure on the NHS in every area. So the option to use POCT to enable fast-track decision making is certainly seen as being of potential value. Unfortunately, there does not appear to be joined up funding for these initiatives. That can lead to a lot of backdoor entries for POCT, where it's not really set up or evaluated properly, and the quality assurance processes are missed out.

That situation leads to the second problem – that of quality in POCT. It's important that the central laboratories have oversight of POCT: across training, implementation, and maintenance of the services, as well as the reporting of results. These are areas that are frequently neglected and rarely standardized.

Whilst quality standards and accreditation, via the UK Accreditation Service (UKAS), are available, it appears that very little POCT in the UK is accredited. This is likely because a lot of POCT isn't even known to the central labs, never mind under their control.

We need to fix these gaps in order to avoid significant errors being made both in procurement and in patient safety.

How did the development of the National Strategic Guidance for at Point of Need Testing evolve?

That was the result of discussions between RCPath, the Institute of Biomedical Science, and the Association for Laboratory Medicine along with other bodies within NHS England. We recognized that, coming out of the pandemic, POCT had expanded significantly and would need to continue to do so in the future because of the planned expansion of community health care. It seemed timely to update the existing guidance.

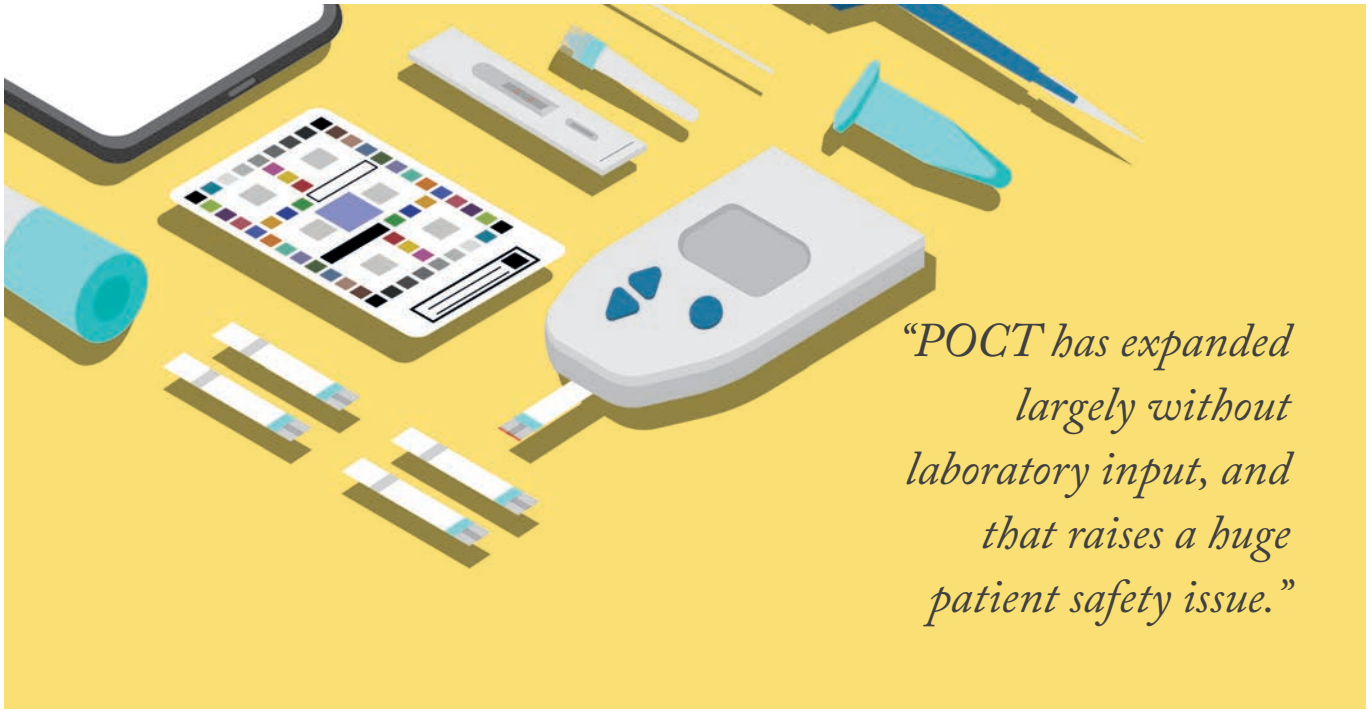
Aimed at those who have responsibility for choosing, implementing, monitoring, and maintaining POCT, the guidance suggests the minimum standards to ensure appropriate testing that is safe for patients and staff.

How do you think the guidance will influence POCT standards and patient safety?

My view – based on anecdotal evidence – is that POCT has expanded largely without laboratory input, and that raises a huge patient safety issue.

The new guidance advocates that any new POCT services that are developed are fully funded, including the laboratory element. There needs to be support in place for the development, procurement, implementation, training, and quality monitoring. Additionally, the IT aspects must be in place to ensure that the test result is securely recorded and added to the patient's medical record.

It's a huge challenge, but we need to ensure that that is the standard we have in place going forwards, otherwise we will see inappropriate POCT being introduced and significant patient safety compromise as a result.



"POCT has expanded largely without laboratory input, and that raises a huge patient safety issue."

How can the RCPath influence the UK Government's NHS spending plans?

In recent years, we have set up an all-party parliamentary group that involves pathologists, scientists, and members of parliament. We have used that as a platform to highlight the importance of pathology testing. And, indeed, in the last year, we have looked at the development of community diagnostic centers and the important role that POCT and pathology testing in general may have in that area. And that's something we'll be looking to continue with the new parliament.

What is the RCPath's position on direct-to-consumer testing?

A lot of lateral flow type tests are now available to buy online for anything from cancer to liver disease. Many are fakes, with fake CE marks, that simply don't work. Alarmingly, they are now being used heavily by the public – probably in response to the fact that they can't easily access health care.

Our second concern is around appropriateness. We are seeing a lot of these tests being used in inappropriate circumstances, with no guidance provided on their interpretation or next steps. And, of course, there's no connection to the NHS, either, so it is an expanding area of concern.

Whilst a lot of the walk-in clinics and testing labs are of a very high quality, I would question the appropriateness of carrying out high volumes of tests with no good purpose. It raises anxiety, it raises problems, and it's usually done purely on a commercial basis.

Then there are the genetic testing services that advise you about your ancestry but also give risk scores for various diseases. That is likely to cause huge anxiety for consumers, which is why they've been banned or severely limited in many countries around the world. So it's important that we raise some concern around them.

What do you think is the way forward for POCT?

Technology has moved forward tremendously fast in recent years – to the point that we now are able to do some fantastic things diagnostically. We have access to mini analyzers, health monitoring devices, and lateral flow tests, and that has changed the health care delivery landscape. But in order to ensure that we do things that are appropriate and safe for patients, we absolutely need to ensure that those quality aspects and laboratory oversight is in place for everything that we do at the point of care. And that is where the huge gaps are.

Within the UK healthcare system, because of the relative lack of funding of laboratory services to fund that expansion, there is a danger that we will see extended use of POCT without that oversight and that will not be good for patient care.

So our message is quite clear. We need to ensure that laboratories are given the training, the oversight, and the funding to allow POCT to expand appropriately as it should do.

HEALTH CHECKS WHILE THE KETTLE BOILS

What is the Association for Diagnostics & Laboratory Medicine's position on the at-home testing market?

From gonorrhea to gluten intolerance and from colorectal cancer to iron deficiency, patients are opting to check their health in the comfort of their own home rather than at the clinic. Is this a good thing?

Here, we present the answer to this question and more from Anthony Killeen, President of the Association for Diagnostics & Laboratory Medicine (ADLM, formerly AACC), Professor and vice-chair for clinical affairs, department of laboratory medicine and pathology, University of Minnesota, Minneapolis.

What are the drivers for the increased demand for at-home tests for medical conditions?

In the last few years, one of the biggest drivers of this increased demand has been the COVID-19 pandemic. At-home testing was integral to managing the pandemic, and it led people to become much more comfortable performing self-collection of samples and using kits to test themselves and others for COVID.

The public and healthcare providers came to really trust results from at-home COVID tests, using them to make critical decisions about travel, personal/social interactions, and other behaviors. This, in turn, has increased trust in at-home testing across the board.

What are the advantages of at-home testing to patients?

A major goal of the ADLM – and the laboratory medicine community at large – is to improve patient access to testing, something that at-home testing is definitely helping us to accomplish.

Another positive is that at-home testing empowers people to take a more active role in their own medical care and may help reduce the burden on the healthcare system when used appropriately.

What about the disadvantages?

As with all new healthcare paradigms, we must be aware of and mitigate the downsides of at-home testing in addition to embracing its benefits. One of these is that at-home tests may not be as reliable as testing that is performed in clinical laboratories.

It is also important to help patients understand that results of at-home tests cannot be used in isolation to provide a diagnosis. The test result counts of course, but clinical context must be carefully considered when acting on that result. The ADLM advises patients who are using at-home tests to consult with their healthcare providers and use evidence-based guidance when interpreting the test results.

We must also consider that the unnecessary use of single-use at-home tests is wasteful on resources. We experienced this at several points throughout the pandemic as the demand for at-home tests surged – sometimes without clear necessity or supporting proof of the value of testing – resulting in inadequate supply.

Finally, the potential of increasing health anxiety in patients is another issue that at-home testing raises. For instance, if an individual were to get a false-positive result on an at-home test saying that they have an infection or condition that they don't actually have, that could certainly cause undue stress.

To reiterate what I've said above, this is yet another reason why it's so important that people consult with their healthcare providers when interpreting home test results and deciding what action to take in response to them.

How do pathology labs benefit from patients performing their own testing?

One of the biggest operational challenges that clinical labs in the US are facing is that they have been chronically short-staffed for many years. Since the pandemic, we have also been dealing with ongoing shortages of some essential supplies.

Increasing the use of at-home tests could help with both of these issues by alleviating the burden on clinical labs – and, in fact, this is exactly what we saw happen during the height of the pandemic. At-home tests played an integral role in helping clinical labs keep up with the demand for COVID testing in the midst of staffing and supply chain shortages.

Are pathology labs generally supportive of at-home testing?

The laboratory medicine community as a whole is very supportive of expanding patient access to testing through the advancement of home tests. At the same time, we do believe that it's important to balance innovation in this area with the need to ensure that home tests are accurate and used appropriately. We want patients who use these tests to access the care they need, and also to ensure that we are not overutilizing testing and healthcare resources.

ADLM, therefore, continues to recommend that patients and consumers consult with their healthcare providers and evidence-based guidelines for when to test and how to interpret home test results. This advice also applies to determining the best course of medical care based on these results.

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A Panoramic View of Disease

How transformational technologies are advancing precision medicine in oncology

This article has been commissioned and funded by AstraZeneca.

Translational science plays a pivotal role in developing precision medicines. This rapidly developing field is expanding our knowledge of tumor biology and the mechanisms of action of therapeutic agents, pioneering state-of-the-art biomarkers, and informing the design of innovative clinical trials that have the potential to transform outcomes for patients.

Developments in artificial intelligence (AI) and computer vision are enabling a transformation in how biomarkers are discovered, developed, and, ultimately, delivered clinically. Computational pathology is becoming invaluable not only to replicate the tasks that pathologists do or to infer the presence of specific molecular alterations that can be identified by genomics, but also to understand mechanisms of action of targeted therapies and to identify patients who are most likely to benefit from specific treatments. In fact, computational pathology allows for a more holistic characterization of the tumor with precision, accuracy, and reproducibility, bringing together features to both target biology and tumor biology.

Recognizing the criticality of deeper biological understanding in precision medicine for oncology, AstraZeneca is committed to developing advanced computational pathology tools. We connected with Jorge Reis-Filho, Vice President of Cancer Biomarker Development in Oncology R&D, to learn how AstraZeneca is bridging the gap between early-stage drug development, biomarker identification, and clinical practice.

What priorities are driving AstraZeneca's approach to precision medicine in oncology?

Patients can have vastly different responses to treatment – despite sharing the same cancer diagnosis. These differences in response can be due in part to variations in their genetic make-up, epigenomic landscape, target expression, and more.

Our approach to precision medicine is based on understanding these unique variations between patients and developing treatments that could ultimately benefit patients at the right time during their treatment journey.

How is AstraZeneca using computational pathology to identify novel digital biomarkers for patient selection?

The vast majority of the therapeutic agents in our early oncology pipeline at AstraZeneca apply a precision medicine approach. This involves leveraging advancements in computer vision and AI to derive target and tumor biology insights. With this approach, we achieve levels of precision, reproducibility and accuracy that far surpass those attained by the human eye – while also increasing our understanding of tumor biology. These new biomarkers are transforming patient selection and enabling the delivery of more personalized treatments.

Our most advanced computational pathology biomarker solution is Quantitative Continuous Scoring (QCS) – a fully supervised AI-based platform that assesses the expression of targets in specific subcellular compartments of cancer cells. By applying QCS to digital whole-slide images of samples analyzed by immunohistochemistry (IHC), we can assess the number and distribution of biomarker-positive tumor cells. The technique allows us to calculate the staining intensity of biomarkers both on the surface of and inside every tumor cell.

QCS can enable enhanced decision making by pathologists – in a more precise, objective, reproducible manner than with traditional methods. It can also detect and quantify the presence of target expression heterogeneity in cancer cells within tumors. Based on the assessment of seven classes of human interpretable features, QCS helps develop new biomarkers that identify patients who are most likely to respond to certain treatments.

"QCS can enable enhanced decision making by pathologists – in a more precise, objective, reproducible manner than with traditional methods."

These QCS-based biomarkers also have the potential to identify new patient populations – such as patients who express low levels of a biomarker that may not be detected using traditional pathologist scoring.

How is multiomics being used to interrogate tumor biology at the molecular level?

At AstraZeneca, we are accelerating innovation to inform the development of next-generation diagnostics that have the potential to improve patient outcomes. We are developing multimodal biomarkers through AI-powered deep multiomic analyses – integrating molecular, genetic, transcriptomics, and single cell genomics data, with data derived from computational pathology and radiomics.

Unlike traditional biomarkers, which typically assess only a single variable, multimodal biomarkers provide a panoramic view of the disease, enabling an integrated approach to diagnosis and treatment. Our approach for the delivery of these multimodal biomarkers, however, is to reduce them to the most parsimonious set of biomarkers required for treatment decisions. This allows us to better define treatment strategies that are tailored to a patient's unique tumor profile, while keeping the assays clinically deployable.

How is AstraZeneca using circulating tumor DNA (ctDNA) technologies to enhance precision medicine approaches in cancer treatment?

There is no one-size-fits-all solution to cancer diagnosis and treatment. And that's why we have assembled a systematic framework for the technical benchmarking and deployment of ctDNA technologies. These technologies will allow clinicians to detect and intercept cancer earlier, track tumor dynamics, and monitor treatment responses. They also offer unique opportunities to identify patients whose tumors may be responsive or resistant to specific treatments in much greater molecular detail.

By detecting cancers earlier and being able to characterize their genomic and epigenomic features, we may be able to enable physicians to intervene sooner. In this way, they can offer personalized treatments that may be effective and durable, helping to transform the treatment journey of our patients.

How do you envision AstraZeneca's pursuit of transformational technologies shaping the future of cancer care?

Given the incredible development pace of new AI-driven technologies, it is clear that we are at an inflection point in oncology and pathology. AI applied to pathology is undoubtedly making an impact, but generative AI and foundation models will result in greater generalizability and accuracy of the biomarker solutions developed. Eventually, this will change the way we integrate data to understand patient trajectories even further – allowing for more personalized treatment based on predictions with a much greater level of accuracy.

A key challenge in our industry is navigating the multitude of therapeutic agents available to patients and how they can be combined or sequenced to maximize benefits. Traditionally, the pharmaceutical industry has focused on a one-biomarker-per-drug approach. At AstraZeneca, we are now using transformational technologies to develop the next generation of biomarkers for all classes of therapeutic agents in our pipeline. This advanced approach allows us to explore how to optimize combination therapies to attack cancer effectively from multiple angles.

We are pursuing exciting new, transformative technologies, including:

1. Foundation models – with the goal of developing a multi-cancer, cross-indication QCS, potentially allowing us to deliver QCS solutions across our portfolio for assets that target cell surface markers.
2. Multiplex biomarker solutions – potentially enabling us to quantify the expression of multiple targets and mechanisms of resistance on the same tissue section in a precise, reproducible, and quantitative manner.

How do you see these innovations transforming patient outcomes over the next few years?

AstraZeneca is leading the digital and computational pathology revolution – and we firmly believe that in addition to providing more precise, accurate and reproducible biomarkers, it will drive the democratization of access to biomarkers. This is the next step in transforming how precision oncology is practiced and enabling the delivery of our potentially life-saving drugs to patients at the right time in their treatment journey.

You can learn more about AstraZeneca's approach to computational pathology at https://www.astrazeneca.com/what-science-can-do/topics/data-science-ai/computational-pathology-potential-transform-cancer-diagnostics.html.

AstraZeneca

MOLECULAR PATHOLOGY

Rare Disease Detectives

How collaborative consortia are solving medical mysteries

By Nina Gonzaludo and Sukhvinder Nicklen

By definition, rare diseases are individually rare, but they are collectively common across the global population. There are more than 7,000 types of rare disease in existence, meaning the burden on families and healthcare systems is significant. Around 300 million people worldwide have a rare disease, waiting an average of 4–5 years for a diagnosis.

Aside from great personal cost, research has found the complex diagnostic process for rare diseases has a huge economic impact. In the UK, NHS England has spent more than £3.4 billion over the past ten years on rare disease patient care. Meanwhile, under the private system in the US, the annual cost of rare disease patients is estimated to be $2.2 trillion per year. Despite this great expense, around 60 percent of people still don't receive a diagnosis.

Finding the underlying causes of rare diseases presents a significant challenge as the vast majority of conditions are suspected to have complex genetic origins. One of the major contributing factors to breakthroughs in rare disease research is the growing number of international consortia and research partnerships. These efforts bring together the best minds and cutting-edge technologies in genomics today. Investment in such collaborative efforts is critical to unlocking the secrets of rare diseases' genetic origins, enabling faster and more accurate diagnoses, and improving patient outcomes.

The diagnostic odyssey

Many families start the often years-long diagnostic odyssey with some form of genetic testing. Gene panels, microarrays, and exome sequencing are amongst the chosen methods for investigating the genetic cause of rare disease. However, these technologies do not resolve all cases.

Gene panel tests look for variants in more than one gene, and can be useful if symptoms are well characterized and specific causative abnormalities are suspected. Microarrays can potentially detect more variants, as well as chromosomal abnormalities, but are biased to only detect known genomic variants. Exome sequencing, which in many countries is the first-line test for suspected genetic disease, is a form of sequencing that captures genetic changes primarily in exonic coding regions. However, many of the variants associated with rare diseases are novel, much longer, or occur in non-coding regions, so often go undetected. These standard testing methodologies may require prior knowledge of which genetic variants to investigate, meaning they are only effective when specific known genes or variants are the suspected cause of disease. If the disease-causing variant is novel, complex, or in a poorly covered region, legacy testing technologies may fall short.

When exome sequencing doesn't reveal the cause, the next logical step may be short-read whole genome sequencing (srWGS) to examine the rest of a patient's genome. This method begins with library preparation that breaks the genome into small fragments, sequences each, then maps variants against the accepted reference genome. This comparison – known as variant calling – helps to identify potential disease-calling variants within a patient's entire genome. While most of the genome is characterized by srWGS, the technique is more expensive than exome sequencing and only provides a modest increase in solving rare disease (approximately 10 percent). Additionally, certain types of variation like repetitive sequences, which are known to be clinically important to rare diseases, are still challenging to map back to the reference genome using srWGS – imagine a puzzle where all the pieces look the same.

In short, current testing techniques and interpretational challenges leave families navigating a maze of appointments and enduring uncertainty. In contrast, long-read sequencing, which can capture long stretches of DNA at a time, is revolutionizing

the diagnosis of rare disease. This technology can capture genomic variation that other types of genetic testing miss.

Rather than studying rare diseases in silos, a growing number of universities, technology companies, and patient groups are pooling their resources to accelerate research and find answers for families. There is real hope that long-read sequencing will improve diagnostic rates which will ultimately lead to better patient outcomes.

The undiagnosed hackathon

A powerful example of a research consortium in action is the 2024 Undiagnosed Hackathon; initiated by The Wilhelm Foundation and held at Radboud University Medical Center (Radboudumc) in Nijmegen, the Netherlands. More than 120 experts from 28 countries, including doctors, geneticists, bioinformaticians, and AI specialists, collaborated in a 48-hour sprint to aim to diagnose some of 42 families with previously undiagnosed diseases. The results were extraordinary: ten conditions were diagnosed in just two days – a significant breakthrough for families who had been waiting years for answers.

Key to these discoveries was access to advanced genomic technologies at the event, including a type of highly accurate long-read technology called HiFi sequencing. By sequencing the genome in much longer stretches, HiFi enables researchers to accurately call all variant types, including those which are more complex and often misassembled by traditional tests. Lisenka Vissers of Radboudumc explained at the event, "Unless you use long-reads, there is no test that captures nearly all medically relevant variants. Only with this technique have we gained the way to look at the human genome."

In a retrospective clinical study by the Radboudmc team, HiFi sequencing was found to identify 93 percent of pathogenic variants, and led to 8 out of the 10 solves from the event. Events like the hackathon are critical to proving the value of such advanced technologies and encouraging investment from hospitals and research institutions in rare disease research. Events are also key for educating and engaging the rare disease community, from patient groups to scientists. For many participants, such as lab specialists and bioinformaticians, who typically do not have contact with patients, meeting the families added a deeply emotional dimension to their work. Seeing their research in action provided extra motivation, driving the team to relentlessly pursue diagnoses within the 48-hour window.

The journey ahead – a group road trip?

The Hackathon did an amazing job at showcasing the power of cutting-edge technologies and enabling researchers to see the real-life applications of their work. But, at its heart, the event was about building the rare disease community and bringing hope and answers to families left in the dark for years. Radboudmc's Alexander Hoischen commented on the event, "The beauty of the undiagnosed hackathon is that it will continue and is still growing. We have to bring the latest innovations including long-read sequencing to the patients."

"By pooling expertise, data, technology, and patient understanding, consortia can accelerate research, improve diagnostic accuracy, and find solutions more efficiently."

Rare disease research is not a solitary endeavor – it's a shared journey between patients, their families, and all who are committed to solving their condition. No single institution has all the resources or knowledge needed to investigate the complex genetic and biological factors behind rare diseases. By pooling expertise, data, technology, and patient understanding, consortia can accelerate research, improve diagnostic accuracy, and find solutions more efficiently. As the Hackathon proved, advancing rare disease research on a global scale relies on greater collaboration and investment in the field.

Nina Gonzaludo is Global Lead of rare disease and clinical/translational research at PacBio; Sukhvinder Nicklen is EMEA lead for rare disease at PacBio.

INFECTIOUS DISEASE

Better, Faster, Cheaper

Robin Patel talks infectious disease diagnostics – from fighting antimicrobial resistance to molecular genomic approaches in lab

The 2024 AMP annual meeting and expo was filled with exciting talks and innovative research. Early into the event, Robin Patel, Professor of Individualized Medicine at Mayo Clinic, presented "Infectious disease diagnostics – from gram stain to next-generation sequencing." Now, she joins us to share more about her experience with infectious disease research and combating persistent bottlenecks with modern diagnostic tests.

Can you tell us about your work to increase understanding of infectious diseases?

There's often a misconception that medicine has all the answers about infectious diseases, but that's far from true. Many infectious diseases exist that we haven't identified yet. For example, mosquito- and tick-borne diseases that have been discovered in recent years, including by our group, are not new – they've been around, but we didn't recognize, name, or diagnose them. Today, there are patients we could help if we knew more about infectious diseases – in other words, there is more to discover.

I also highlighted examples of diseases that were previously not considered infectious but are now known to be caused by infections. A well-known example is *Helicobacter pylori*, which causes peptic ulcer disease, initially thought to be linked to lifestyle factors like stress or smoking. We now know it's an infectious disease, and therefore treatment has drastically changed as a result.

Another fascinating example is hyperammonemia syndrome in lung transplant patients. A small percentage of lung transplant recipients develop high blood ammonia levels in the immediate post-transplant period, which can cause brain damage (encephalopathy) and even death. Previously, this was thought to be a metabolic disorder, and treatment focused on managing the biochemical abnormality – often unsuccessfully.

Our team and others discovered that the cause is *Ureaplasma* (*Ureaplasma urealyticum* or *Ureaplasma parvum*). These bacteria produce high ammonia levels through the enzyme urease. Once we identified this, patients were treated with antibiotics targeting *Ureaplasma* species, enabling a cure. This was a breakthrough, as we hadn't historically considered this syndrome to be infectious.

These cases highlight how much we still must learn about infectious diseases and the potential to discover and treat conditions we don't yet fully understand.

How can modern diagnostic tests help curb the emergence of anti-microbial resistance (AMR)?

This overuse of antibiotics – especially broad-spectrum agents – contributes to resistance. With better diagnostics, we can identify exactly who needs antibiotics and which ones are appropriate, reducing overall use and favoring narrower-spectrum options that are less likely to drive resistance. We can do better for both current and future patients by using antibiotics more wisely.

Why is digitization so important for the lab of the future?

In traditional microbiology laboratories, much of the work was manual – people recorded observations with pens and paper. This approach made it difficult to standardize, analyze, and fully use the data. To improve, all data – written notes, test results, and visual observations like stains and plates – needs to be digitized.

When data are digitized, they can be analyzed and even reanalyzed with new and improved tools as they become available. For example, if a new analytic method is developed, we can quickly apply it to existing digital data without redoing tests. This enables rapid adoption of faster, better, and less expensive diagnostics over time.

Digitizing also helps integrate lab data with patient information, giving a clearer picture of what's happening in the lab and with the patient. Because we live in a digital world, continuing to expand digitization will enhance patient care. We've made progress, but the more we digitize, the better the outcomes we can achieve.

To what extent do you think POCT and at-home testing will shape the future of infectious disease diagnostics?

POCT and at-home testing will play a major role in the future of infectious disease diagnostics. The COVID-19 pandemic showed that people can successfully collect their own specimens and run their own tests, when given the right resources. Many infectious diseases could be diagnosed this way – in other convenient locations close to the people that need them. This shift will greatly benefit humanity; we are already moving in this direction and will continue to do so.

Full article available online.

DIGITAL PATHOLOGY

Institut Curie – A Digital Case Study

Building a digital pathology lab of the future

By Rob Monroe

In this follow-up to our three-part series showcasing how pathology laboratories in New Zealand, Germany, and Portugal have successfully tackled the transition to digital, Rob Monroe, Chief Medical Officer at Leice Biosystems, highlights the efforts to build a successful digital pathology laboratory at Institut Curie in France.

Institut Curie was founded in 1909 and today treats more cancer patients than any other center in France, as well as more breast cancer patients than any center in Europe. Now, more than a century after it was founded, the medical center and its affiliated institutions are also leading France in digital transformation.

Institut Curie boasts two hospitals and a research arm. Yves Allory, Head of Pathology at the Institute's hospital in Saint-Cloud, notes that digital tools will help Institut Curie embrace cutting-edge research for years to come. "I see many, many advantages for us. I think it's our future."

Initially, though, Allory had his doubts about the clinical adoption of digital pathology. "I was afraid that people would stay in their own offices without spending time talking together," he says. However, the opposite happened – the digital approach enhanced teamwork, allowing Institut Curie's locations to share cases and reach diagnoses faster, ultimately benefiting patients.

Instrument selection

Institut Curie's pathology labs began their digital transformation with a high-quality scanner. Instead of sharing physical glass slides, the labs now scan and distribute virtual slides digitally, streamlining storage and distribution but adding a step for technicians. "Simplicity for the technicians is important," says Lab Manager Magalie Toutain. Image quality was crucial, and the scanner needed to fit seamlessly into workflows. The lab selected the Leica Biosystems Aperio GT 450 scanner, which Allory says is "very easy to use for the technician and produces high-quality images for the pathologist."

Workflow design and optimization

Next, the Institut Curie partnered with vendors to map out its entire workflow, covering pre-analytic processes, scanning, image quality control, virtual slide distribution, and instrument maintenance. "It's important that you put a lot of energy into optimizing all these steps," observes Allory.

Much like traditional pathology, however, a successful digital transformation still depends on strong pre-analytics. The new scanner required meticulously prepared glass slides, with consistent histologic sectioning. "The sections must be correct, without folds, without holes," emphasizes Toutain, who notes that the lab examined and refined every step of their process, including analog practices, to ensure digital success.

The digital transformation team ensured all key stakeholders were involved. "It is very important to have the lab technician, the histotechnologist, the lab manager, the pathologist, and the IT department," says Allory. They also collaborated closely with vendors to plan the project thoroughly.

"Much like traditional pathology, however, a successful digital transformation still depends on strong pre-analytics."

Starting small was essential. Toutain highlights the importance of trusted vendor partnerships and implementing one tool successfully before scaling up. Initially, introducing the Leica Biosystems Aperio GT 450 scanner felt daunting. However, collaboration among internal teams and external partners made the transformation a success, and served to simplify the ongoing maintenance, service, and support.

The lab then added a Leica Biosystems HistoCore SPECTRA Workstation for H&E staining. Toutain describes the staining workflow as straightforward and easily adaptable to the pathologists' expectations. "Maintenance is very important in the workflow, but everything runs optimally," she notes.

With a streamlined digital workflow, the lab's hospitals and research arm can collaborate more efficiently and review cases quickly. The transition to digital also brings additional benefits. Remote work is now an option for some staff, helping them to balance their work and personal lives. Further, Allory points out that remote flexibility can attract qualified staff and address the broader shortage of pathologists.

To the future

As Institut Curie looks to the future, it's clear that digitization is key. Storing slides digitally reduces the need for physical storage and transportation, helping to minimize waste and lower the lab's carbon footprint, according to Allory. Moreover, as Toutain highlights, digitization lays the groundwork for adopting AI technologies in both clinical and research settings. AI enables labs to leverage their data for innovative solutions while delivering more accurate and timely diagnoses.

Building on its history of innovation – beginning with the introduction of radium for cancer therapy – Institut Curie's digital transformation could now help to shape the future of pathology in France.

Rob Monroe is Chief Medical Officer at Leica Biosystems

"Workplaces should allow people with families to be just as successful as those without."

Laboratory Mentor Extraordinaire

Sitting Down With… Ann M Gronowski, Co-Division Chief of Laboratory and Genomic Medicine at Washington University School of Medicine

What initially drew you to laboratory medicine?
My dad was science-oriented and taught us a lot, so I felt a pull to work in science. I always wanted to be a veterinarian, but somehow I changed course. Now, I have a PhD with training in endocrinology and reproductive physiology, and I later transitioned into laboratory medicine. I've got no regrets – it's been a great career. However, I still feel a pull toward animal science, so maybe I'll return to it when I retire!

What have been your career highlights?
Firstly, my research in women's health and maternal-fetal medicine. My main focus has been on hCG, the marker of pregnancy, and I'm proud of how our work has changed how and who we test.

Another was mentoring young laboratorians – particularly women. When I began training in this department, there were no female faculty members. We eventually welcomed our first woman faculty member and, over time, our faculty has grown. It's been incredibly rewarding to support the next generation.

Additionally, for the past two and a half years, I have been the division chief within the Department of Pathology, overseeing the Division of Laboratory and Genomic Medicine as well as serving as the CLIA medical director for all our pathology services. As a female PhD, I am proud of this role, which has also allowed me to continue mentoring the talented individuals we've recruited to our department.

How do you stay motivated and continue to push boundaries in a field that is both demanding and rapidly changing?
My initial response is that it's easy because I love my job and I love that there's no steady state. That said, like everyone, there are definitely days where I wake up and think, "Oh no." My personal mantra is that I'm allowed a pity party for one day – but no more. After that, I need to come back, figure out what's wrong, and address why I felt the need for that pity party in the first place. I think it's important to allow yourself to feel down or frustrated, but you also have to challenge yourself to move beyond it. Life is about acknowledging your feelings – validating them – but then tackling the issues and not letting them bring you down.

As an advocate for bringing more women into the field of laboratory and genomic medicine, what changes do you think are still needed?
Pay equity is still an issue. Although our school has worked to close the gap between men and women, the problem persists. Creating a better work environment for people with families is another important factor. This is true for both men and women, but women still bear a disproportionate share of family care, including childcare and eldercare.

Workplaces should allow people with families to be just as successful as those without. That means not scheduling meetings at inconvenient times, like early mornings or late evenings. Though this is difficult in medicine, where surgeries often start early, more flexibility is needed.

Finally, certain tasks, such as managing a division newsletter or mentoring (which is important but often undervalued) should be distributed equally among men and women. These contributions are essential but don't always translate into big line items on a CV. Addressing these issues can help narrow the gap at the top.

What role does mentorship play in advancing the careers of women in science?
Having role models who mentor is crucial, as it shows that work-life balance is possible and helps overcome stereotypes and preconceived notions about women in the workplace. For example, there's a lot of data showing that women often don't negotiate and, when we do, there's a perception that we don't negotiate well. In reality, studies show that women actually negotiate better than men in many cases because they focus on long-term outcomes and equitable solutions.

Mentoring women on these insights can empower them to realize they're not bad at negotiating, but may simply avoid it – particularly when negotiating for themselves. Interestingly, women tend to negotiate better when advocating for others.

In my career, after becoming a full professor, I wanted to give back to the women in my department. When I started, there were no women faculty, and I was determined to ensure that didn't happen again. I created a professional development group for women, initially for faculty, but later it expanded to trainees.

As a division chief, I now look after all our faculty, but I've thought about focusing again on supporting women when I retire. Ideally, by the time I retire, such efforts won't be necessary because parity will have been achieved. At that point, we can focus on whatever gaps remain.

What lessons have you've learned throughout your career that are essential for those entering the field today?
My advice is to be inquisitive. I'm a strong advocate for critical thinking. Looking back, I realize that many of us, especially when we're junior, are afraid to ask questions because we fear we'll sound foolish. We all experience a bit of imposter syndrome, but you're likely smarter than you think.

Don't be afraid to ask questions, challenge the norm, and explore why things are done a certain way – or whether they can be done better. Sometimes we stick to certain habits just because that's how it's always been done. And though that can sometimes be necessary, there are other times when change is needed. Don't shy away from it.

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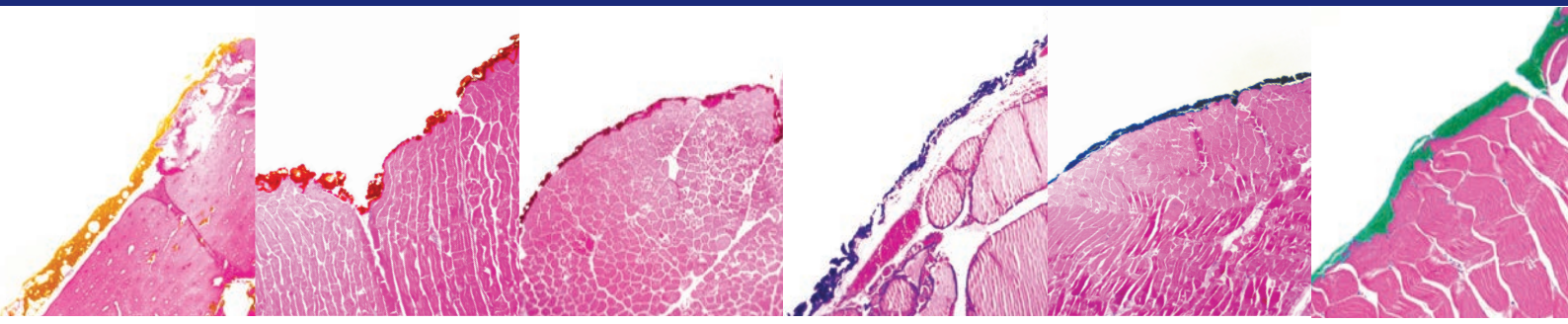

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