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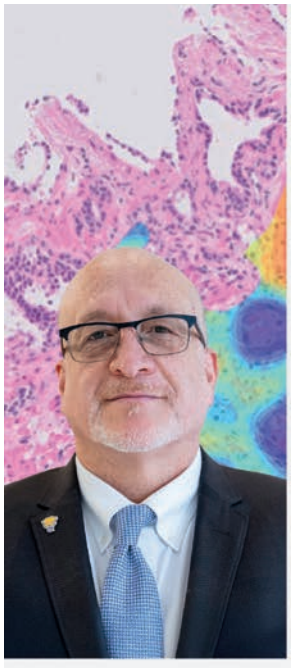

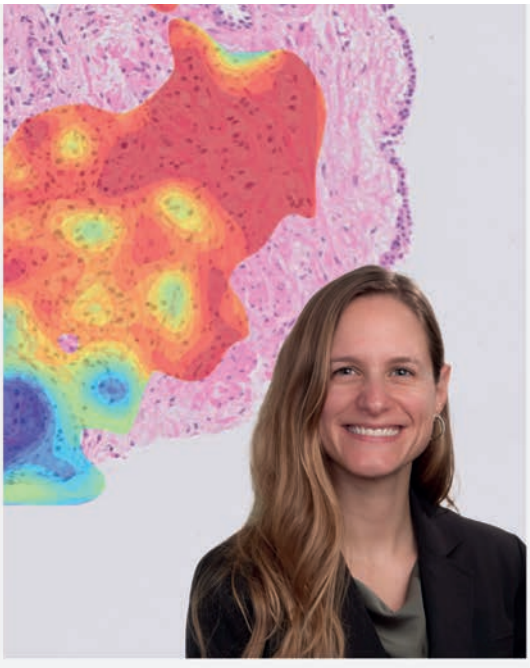

AI in the lab

Introducing computational pathology is "simply the right thing to do," say experts

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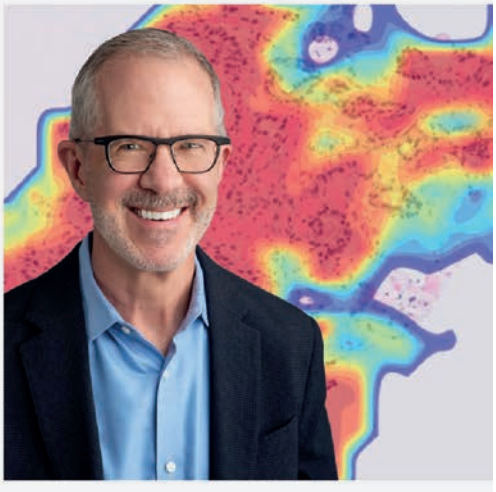

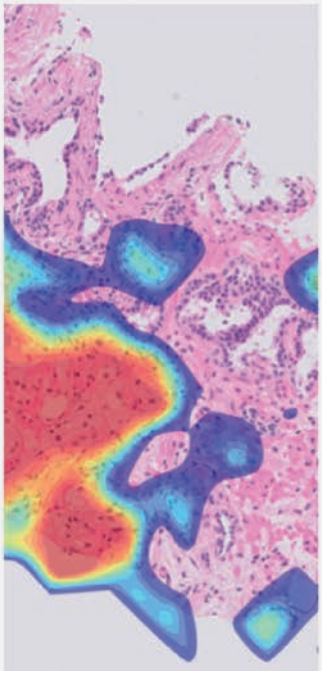

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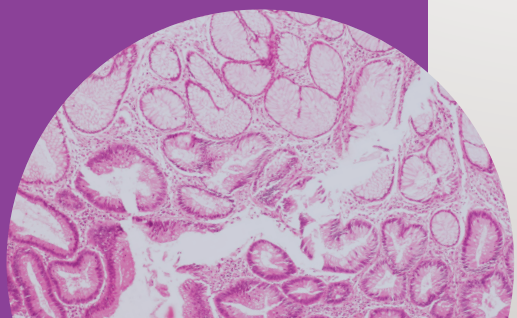

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AI: We Owe it to the Patients

Among the many benefits of AI technologies, the most important is better patient outcomes

Artificial intelligence (AI) is redefining the landscape of pathology through cutting-edge advancements in image analysis, data interpretation, and report generation. These technologies are enabling unprecedented accuracy and efficiency in diagnostics – allowing more patients to receive their test results more quickly, while minimizing diagnostic disparities.

But improved turnaround times are just the tip of the iceberg in terms of AI-augmented pathology. To truly deliver personalized medicine, we must integrate AI tools that go beyond diagnostics, enhancing every stage of a patient's journey toward recovery.

Prognostics are now being advanced by machine learning. AI models can be trained to predict the progress of diseases, helping the clinician to have a more informed discussion about outcomes. And in research, by efficiently matching patients to clinical trials for companion diagnostics, AI opens doors to early and more specific treatments and therapies. During trials, AI tools can also monitor patient responses, providing real-time insights to researchers and clinicians.

As these models continue to evolve and improve, it is our responsibility as clinicians to ensure they are inclusive and equitable, enabling every patient to access personalized treatment and achieve better outcomes.

The basis of all these models is data generated in the pathology department and, by embracing these innovations thoughtfully and rigorously, pathology can truly emerge as a cornerstone of cognitive excellence in medicine.

Rajendra Singh,
Co-Founder, PathPresenter, and Director of Dermatopathology and Digital Pathology, Summit Health

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AI Outperforms Pathologists in Celiac Disease Diagnosis

Could machine learning eliminate the subjectivity and variability of current diagnostic practices?

Research published in the *New England Journal of Medicine AI* presents a machine learning model that can correctly identify whether a patient has celiac disease or not from a duodenal biopsy image – in 97 percent of cases (1).

Here, Florian Jaeckle, Visiting Research Associate at the University of Cambridge's Department of Pathology, explains the research and its implications.

What inspired this research?
Our group, led by Elizabeth Soilleux, first started working on celiac disease after she and her children were diagnosed with the condition more than seven years ago.

The disease is diagnosed via duodenal biopsies, which are often deprioritized due to the duodenum's low malignancy rate (2). Alongside that is the problem of low diagnostic consistency; in a study we conducted, inter-pathologist agreement when diagnosing celiac disease was only around 80 percent (3).

Professor Soilleux's personal experience, combined with these pressing clinical needs, inspired us to develop AI tools for celiac disease diagnosis.

How was the machine learning model trained and evaluated?
The AI model was trained using more than 3,300 scanned biopsy slides sourced from four hospitals, scanned on five different devices. We used the original clinical diagnoses made by reporting pathologists as the ground truth during training.

For evaluation, the model was tested on over 600 cases from an entirely separate, previously unseen hospital to assess its real-world generalizability.

What were the key findings of the study?
In an inter-observer study using biopsy slides from a previously unseen hospital, we compared the AI's diagnostic performance with that of four experienced pathologists. We found that any given pathologist was just as likely to agree with the AI as they were with another human pathologist. This suggests that the AI achieves a level of diagnostic accuracy on par with experienced professionals.

We further found that the model performed consistently across adult patient subgroups, regardless of age or sex.

What impact could these findings have on celiac disease diagnostics?
With an overall accuracy of 97 percent, alongside specificity and sensitivity both exceeding 95 percent, our AI tool demonstrated pathologist-level performance. These metrics, combined with our inter-observer findings, indicate that the tool could significantly reduce diagnostic variability and improve reporting consistency and turnaround times across pathology services.

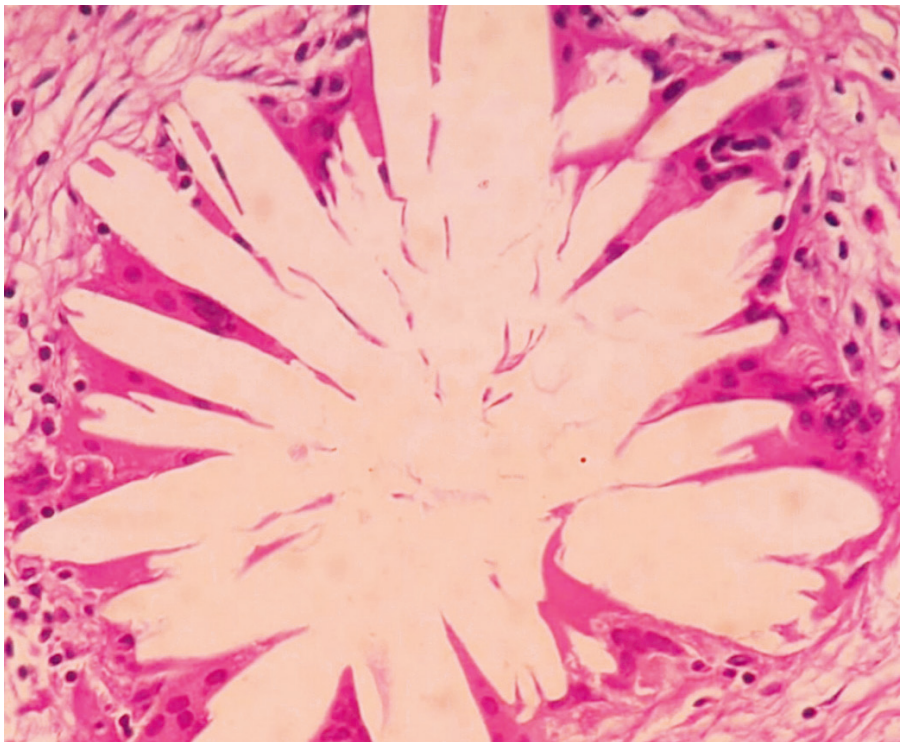
How do you envision this tool being used in clinical workflows?
Initially, we see this tool functioning as a decision-support aid, helping pathologists improve diagnostic accuracy and consistency when assessing for celiac disease.

In the longer term, our team is actively developing additional AI tools designed to pre-screen and filter out a proportion of normal duodenal biopsies. By integrating these with our current model, we aim to create a more comprehensive pipeline that prioritizes abnormal and ambiguous cases for pathologist review.

This integrated approach has the potential to significantly reduce reporting backlogs – especially in resource-limited or high-throughput settings – while maintaining diagnostic safety and accuracy.

References

1. *F Jaeckle et al., "Machine learning achieves pathologist-level celiac disease diagnosis," N Engl J Med, 2, 4 (2025).*
2. *V Shenoy et al., "Determination of the relative frequencies of expected diagnoses in duodenal biopsies: an essential step in developing an artificial intelligence approach to diagnostic classification" (2025). Available at https://doi.org/10.20944/preprints202503.2274.v1.*
3. *J Denholm et al., "CD, or not CD, that is the question: a digital interobserver agreement study in coeliac disease," BMJ Open Gastroenterol, 11, 1 (2024). PMID: 38302475.*



Symphony of Cholesterol

Fantastic florals captured in our image of the month

Our image of the month comes from Syed Salahuddin Ahmed, who says, "Cholesterol crystals in tissue sections are always attractive. This particular H&E stained image shows deposition of cholesterol in the tissue section giving a floral look."

Credit: Syed Salahuddin Ahmed, Senior Consultant in the Department of Pathology at Delta Hospital, Dhaka, Bangladesh

QUOTE *of the month*

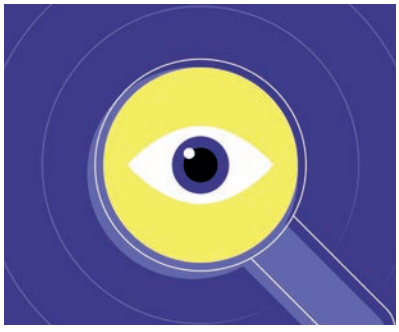
"Forensic pathologists are a forgotten asset in the world of public health; being the final doctor for many patients and by way of our procedures being the most thorough in physical disease assessment, we have the potential to change the public's perception of disease. We pull back the curtain for both others in the medical field and the general public."

Darin Wolfe, Forensic Pathologist, Indiana, USA (@the_dead_letter on TikTok and Instagram, @drdarinwolfe on Substack, and Knife After Death on YouTube)

Read the roundtable article online: https://bit.ly/42FD9R6

Improved Outlook for Eye Cancer Diagnostics

Digital biobank aims to improve early detection of rare ocular cancers



Researchers at the University of Liverpool have launched an initiative to advance our understanding of cancers of the eye. The Eye Cancer Artificial Intelligence Digital (EYE-CAN-AID) Bioresource, combines a digital eye cancer biobank with AI-driven analysis. It is hoped the resource will help to develop better diagnostic tools to inform personalized treatments.

"EYE-CAN-AID collates all the ocular images of eye cancer patients into one trusted research environment, linked together with clinical treatments and outcomes, genetics and histology of the tumors," says Sarah Coupland, Director of the Liverpool Ocular Oncology Research Group. "This will allow for their detailed analyses with respect to tumor size and location with the eye, and how this influences therapy choice, treatment dose, treatment success, and side effects. It will also enable predictions of which patient group is most likely to respond to certain treatments."

United in Outcomes: Molecular and Pathology Data

Why these diagnostic data are equally valuable to precision medicine

By Nathan Buchbinder, Chief Strategy Officer at Proscia

If the pursuit of precision medicine were a race, molecular data might seem like the sprinter who burst out of the starting gate. Molecular data have fueled groundbreaking advancements, powering new therapies and diagnostics that have accelerated our fight against some of humanity's most challenging diseases. Consider what happened during the COVID-19 pandemic: over 5 million viral genomes were sequenced globally to track variants, a clear demonstration of the tremendous potential of molecular insights (1).

Yet, despite serving as the foundation of diagnosis for over 150 years, pathology data is now shifting into high gear. It's not just keeping pace – it's rapidly moving into a leadership position in this new era of care.

On your mark: Understanding molecular and pathology data

Before we zoom to pathology's growing impact, let's review how we got here. Molecular data – including DNA and genomics – offer a unique window into what makes each of us biologically distinct, making them a natural catalyst for breakthroughs in personalized medicine. Molecular data are also highly quantifiable, reinforcing their value in research and diagnostics.

Though molecular data provide crucial insights into the individual, they yield only an indirect understanding of the disease he or she may face. These data reveal a portion of the blueprint that contributes to the condition but lack direct phenotypic representation of the condition itself.

Pathology, on the other hand, offers a clear picture at the tissue, cellular, and subcellular levels. For decades, though, its promise has been limited by traditional microscopy, depending largely on qualitative assessment and the human eye's interpretive ability. As a result, extracting deeper insights about disease has been somewhat elusive.

Until now.

Get set: Whole slide images are laying the foundation for pathology's precision medicine era

Quality and efficiency gains might be the commonly cited advantages of digital pathology, but another significant benefit deserves recognition; each whole slide image captures billions of pixels providing one of the most direct – and detailed – profiles of diseases like cancer. These images introduce a new data modality that's roughly ten times richer than a typical radiology image.

Moreover, whole slide images make it possible to apply AI to pathology data – a breakthrough that represents the biggest development in the field since the introduction of the light microscope 150 years ago. AI taps into the wealth of data within these images – unlocking insights invisible to the human eye and quantifying characteristics that could reshape our understanding of disease.

Go! Unleashing the power of pathology data

Among their many use cases today, AI algorithms count mitoses in breast cancer biopsies, determine the prevalence of biomarkers, and provide objective data for tumor grading. These tools bring to pathology the same objectivity that gave molecular data its early edge.

Compared to their molecular counterparts, pathology-based tests are often cheaper and faster to run so that more patients can start the best treatment sooner. They also typically preserve more of the original tissue since DNA, RNA, and proteins do not need to be extracted – making it easier to conduct further testing down the line. So, does this mean that pathology data is poised to pull ahead of molecular data?

Not so fast.

A team effort, not a race

Though we are clearly entering a new era of pathology, it isn't one that will be defined by a competition among data types. Instead, we are at the start of realizing the impact of an increasingly collaborative, multi-modal approach.

Precision medicine, at its core, hinges on both the individual and the disease. Molecular and pathology data form a dynamic duo that work in concert – likely even with other modalities – to provide understanding unlike anything before. They are not racing against each other but rather accelerating towards a shared finish line: better health outcomes for all.

Reference

1. *G Berno et al., "SARS-CoV-2 variants identification: overview of molecular existing methods," Pathogens, 11, 9 (2022). PMID: 36145490.*

AI's Imminent Revolution in Medicine

Algorithm-assisted tools will become standard and could reduce siloes in clinical practice

By Derya Unutmaz, Professor, Jackson Laboratory, Farmington, Connecticut, USA

The laboratory medicine community is aware that healthcare stands on the cusp of a profound AI-driven transformation. Pathology faces daunting workloads. Examining tissue samples for cancer or other abnormalities under the microscope can be exceptionally time-consuming, and human attention inevitably varies. AI systems have recently demonstrated remarkable speed and accuracy in detecting malignant cells, allowing pathologists to cut review times dramatically.

In one study, using an AI-assisted workflow sliced the time spent per slide by more than half, while also boosting cancer detection rates. Over time, this should reduce missed cases, lower costs, and expand access to high-quality pathology services across more regions.

Pathology and laboratory medicine are not alone when it comes to the inevitable shift towards AI-powered solutions. Particularly in other specialties that are dependent on image interpretation, we are already seeing AI match or even exceed human performance in key diagnostic tasks. The AI revolution is both real and urgent, promising faster, more accurate, and more accessible patient care.

Take radiology, for example, which takes the lionshare of over 700 AI algorithms that have already been cleared by the FDA to support clinicians. The need is clear: radiologists – like pathologists – interpret countless images and must grapple daily with fatigue, growing caseloads, and the risk of missed findings. Studies suggest that AI can quickly pinpoint subtle abnormalities that even the most seasoned radiologists might overlook after hours of image review. In one large study of mammograms, an AI-assisted approach flagged 20 percent more cancers than radiologists working without computer aid, while simultaneously reducing overall workload. Such results highlight the promise of an AI that can elevate quality, reduce errors, and ensure more consistent outcomes.

Dermatology is another specialty profoundly impacted by AI's image-recognition prowess. Deep learning algorithms can already identify melanoma and other skin cancers from photographs of suspicious lesions with a level of accuracy that surpasses many dermatologists. Shifting resources from unnecessary biopsies to earlier essential biopsies could have a tremendous impact on patient outcomes; early detection is often the key to successful cancer treatment.

Ophthalmology is witnessing similar breakthroughs. AI systems such as IDx-DR, approved by the FDA, can independently diagnose diabetic retinopathy from retinal images without a specialist's interpretation. This innovation allows primary care clinics to catch eye disease early, offering a lifeline for many diabetic patients who might otherwise skip yearly eye exams.

Beyond these visually oriented fields, primary care and internal medicine may experience their own seismic shift. Large language models (LLMs) like ChatGPT excel at analyzing patient histories, symptoms, and lab data to suggest possible diagnoses or triage levels. In recent trials, LLMs often matched or surpassed general physicians in diagnostic accuracy, correctly ranking the eventual diagnosis among their top suggestions in most cases. These systems could act as triage "assistants," helping frontline doctors capture subtle red flags or identify which patients might need urgent care.

Meanwhile, consumer-facing apps are evolving into robust symptom checkers that guide patients on whether to seek immediate attention or try home remedies first. Tools that let individuals photograph moles or ear infections for instant analysis, or wearables that detect arrhythmias in real time, help identify serious issues early or spare unnecessary office visits.

Future scenarios might feature a suite of smart home devices, including scales, blood pressure cuffs, and even camera-enabled kits-that continuously relay health data to AI systems. When a significant deviation is detected, a prompt alert could direct the patient to contact a healthcare provider for intervention, shifting the focus from reactive treatment to proactive prevention.

The true revolution, then, will be in bringing these disparate systems together to achieve a truly holistic health care approach. Only when our digitized systems are truly interoperable will AI be able to interrogate a patient's entire health profile. The apps and algorithms must be built around a connected system to deliver on AI's potential to expand access to expert level care.

Imagine a future with pathology and laboratory medicine at the center of that network, with AI acting as the glue that binds these previously siloed specialties.

Advancing Prostate Cancer Diagnostics

Why biomarker-based urinalysis should replace the PSA test

By Dave Taylor, CEO of Valley Diagnostics

Awareness of the incidence and challenges around prostate cancer has been rising in recent years, with a number of high-profile public figures – including cyclist Chris Hoy and restaurant critic Giles Coren – bravely making their diagnoses public. The resultant visibility has added to the rise in voices calling for easier, earlier, and more accurate testing, and a properly implemented screening programme.

The statistics back this up, with a worldwide annual death rate from prostate cancer of over 375,000 men (1). In the UK, over 12,000 men die every year from the disease – equivalent to 33 men every day (2). In the USA it is around 100 men every day (3).

Prostate cancer tests are usually offered only when symptoms are present. As the majority of early-stage cases are non-symptomatic, testing often happens too late, when the cancer is at stage 3 or 4.

What we have

Men aged over 50 are encouraged by healthcare providers to take the industry standard prostate-specific antigen (PSA) test for indicating prostate problems, including prostate cancer.

PSA is a protein produced by normal, as well as malignant, cells of the prostate gland. Both prostate cancer and several benign conditions – particularly benign prostatic hyperplasia (BPH), and prostatitis – can cause PSA levels in the blood to rise. The established PSA test is therefore regarded as only an indicator of potential prostate-related problems.

If the test shows an abnormally raised level of PSA, then the patient is generally referred for additional testing, including: an internal examination, a magnetic resonance imaging scan, a biopsy, and additional genetic tests. All of these add significant extra costs.

What we need

The current testing process is expensive, time-consuming, invasive, and unlikely to detect prostate cancer at an early stage.

What's more, the overall accuracy of the PSA test has been shown to be extremely low. False-positive test results are common – at around 6 to 7 percent – and only about 25 percent of patients who eventually have a biopsy due to an elevated PSA level are found to have prostate cancer (4). In fact, in the USA, the PSA test is not recommended for routine prostate cancer screening in the general population.

There is an urgent need for better prostate cancer testing methods.

Several tests are in development, primarily using blood. The problem is that they all involve molecular tests that require special expertise and are logistically complex, time-consuming, and expensive. The turnaround time from taking a sample to the return of the results can be five working days or more.

However, an alternative testing method is now being developed that could overcome these challenges…

Bring in the biomarkers

Several biomarkers have been identified in the urine of men with prostate cancer – leading to development of a multi-biomarker variant of the lateral flow test (LFT) that can be performed at the point of care and gives results within minutes.

This test will have the ability to diagnose early-stage prostate cancer as well as distinguishing prostate cancer from BPH. Another advantage is that it will require only a naturally expressed urine sample, avoiding the need for an invasive blood extraction.

The greater accessibility of the LFT means it is more likely to be used by younger men, detecting the cancer at a much earlier stage when effective interventions can be made.

Biomarker LFTs provide 95 percent accuracy, are low-cost, and easy-to-use in comparison with the current standard of testing. With the potential to save thousands of lives every year across the UK and the world, LFTs must be the way forward for decentralized testing and personalized care for men.

References

1. *International Agency for Research on Cancer, "Global Cancer Observatory" (2022). Available at: https://gco.iarc.fr/today/home*
2. *Prostate Cancer UK, "About Prostate Cancer" (2025). Available at: https://prostatecanceruk.org/prostate-information-and-support/risk-and-symptoms/about-prostate-cancer*
3. *Centers for Disease Control and Prevention, "Prostate Cancer Stat Bite" (2024). Available at: https://www.cdc.gov/united-states-cancer-statistics/publications/prostate-cancer-stat-bite.html*
4. *RL Grubb 3rd et al., "Prostate cancer screening in the prostate, lung, colorectal and ovarian cancer screening trial: Update on findings from the initial four rounds of screening in a randomized trial," BJU International, 102, 11 (2008). PMID: 19035857.*

Embracing AI to Advance Patient Care

Why the laboratory must take the lead in AI implementation

By E. Blair Holladay, CEO, American Society for Clinical Pathology

Artificial intelligence (AI) has transformed health care over the past decade and will undoubtedly continue to do so. As pathologists and medical laboratory scientists, the use of AI is not a novel concept in the laboratory – we have been using AI in different forms for decades. But, as diagnostic testing underpins nearly every aspect of patient care, embracing the integration of AI into pathology and laboratory medicine presents an unparalleled opportunity to enhance our role, as well as patient outcomes.

The laboratory must take the lead in AI implementation and application. When we do, we drive innovation that prioritizes patient-centric care and further strengthens the critical role of laboratory medicine in healthcare. AI has the potential to improve numerous processes that can directly impact the health and experience of our patients, including test result interpretation, quality control, workflow automation, and disease detection.

With AI, we have the potential to improve diagnostic precision, reduce turnaround times, and better enable personalized treatment approaches. By embracing and leading the incorporation of AI in the laboratory, we put the focus squarely on delivering the high-quality care that all patients deserve. We can better guide clinicians in the therapies that are best suited to a patient, or flag at-risk patients before their symptoms even develop.

There is so much untapped potential for AI in the medical laboratory, and the time is now to unlock it. We, as the diagnostic experts, possess the knowledge needed for best practices in integrating AI. As leaders in healthcare, we can attest that AI-driven innovation aligns with laboratory best practices and patient care. We can ensure that further incorporation of AI in the medical laboratory is done so with patient safety, data privacy, and ethical decision making at the forefront. We can oversee the validation of AI systems, ensuring they are unbiased and used in ways that, importantly, prioritize patient wellbeing.

The laboratory is the bridge between cutting-edge AI technologies and their practical application in patient care. Our expertise is crucial in translating AI-generated insights into meaningful clinical recommendations that improve patient outcomes. Successfully adopting AI to play a larger role in the medical laboratory means we must educate ourselves on the knowledge and skills needed to do so. We should continue to advocate for AI education in the laboratory to ensure that future pathologists and laboratory professionals are prepared to work with AI-driven tools.

As AI continues to revolutionize the medical laboratory with new ways to enhance diagnostic accuracy, improve efficiency, and promote patient-centric care, we are the needed leaders to ensure its proper integration into patient care. AI is by no means a replacement for laboratory expertise, but a powerful tool that, when guided by skilled professionals, has the potential to redefine patient care for the better.

"By embracing and leading the incorporation of AI in the laboratory, we put the focus squarely on delivering the high-quality care that all patients deserve."

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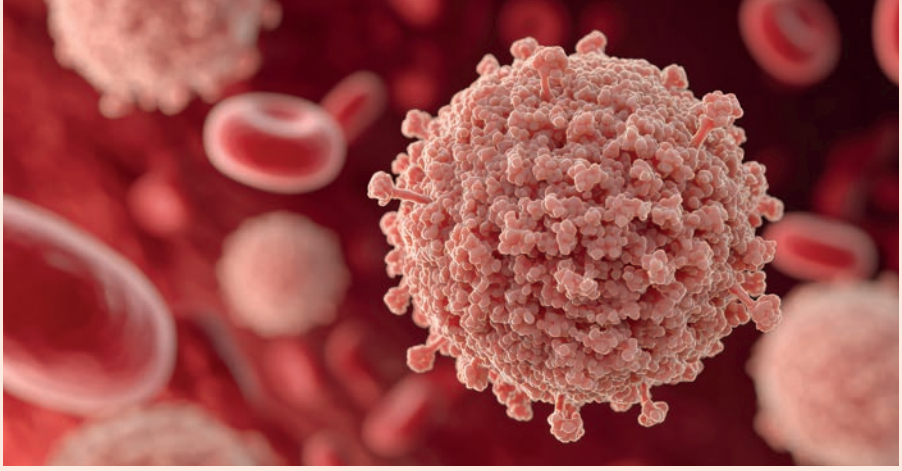


Democratizing Liquid Biopsy-Based Precision Oncology Biomarkers in the United States

Four national thought leaders discuss the latest advancements and practical applications of liquid biopsy in cancer diagnostics and treatment

In April 2025, Thermo Fisher Scientific™ hosted a webinar designed to explore the latest headlines in liquid biopsy news and provide a comprehensive update for the precision oncology community.

From actionable plans to improve access to testing, to recent changes in reimbursement and coding in the United States, and the need for decentralized liquid biopsy testing – we bring you the essential highlights.

Liquid Biopsies for Precision Oncology

Simon Heeke, Head of the Liquid Biopsy Translational Working Group at MD Anderson Cancer Center™ in Houston, Texas, began by guiding us through the current landscape for liquid biopsies in precision oncology.

Heeke detailed how circulating nucleic acids act as biomarkers in blood biopsies, before going on to explain how pathologists use RNA-based fusion detection to identify multiple fusions for cancer classification.

Of course, liquid biopsies go beyond blood. Heeke illustrated how cerebrospinal fluid (CSF) liquid biopsy can be used to identify oncogenic drivers in lung and breast cancer. Another example, he said, is fine needle aspiration (FNA) supernatant, which allows rapid molecular profiling and demonstrates good correlation to cytology analysis.

On a heat map of the US, Heeke showed how access to oncology care differs across the various states – with a scarcity of care apparent throughout Middle America. To expand access, he argued, more liquid biopsy centers are urgently required. While tissue samples require specialist expertise and equipment to collect and process, liquid biopsies are easily collected in the community, with minimal training.

Liquid biopsies, Heeke continued, can offer clinicians a "minimally invasive approach to obtaining real-time insights into tumor biology," allowing for rapid patient turnaround times, helping to better guide treatment and therapy decisions, and potentially expanding access to care due to the ease with which they can be sampled.

Creating Equitable and Widespread Implementation of Liquid Biopsy for Cancer Care

Lauren Leiman, Executive Director of the Blood Profiling Atlas in Cancer (BLOODPAC) Consortium, reported on how the organization is helping to break down implementation barriers for liquid biopsy testing.

BLOODPAC brings together global collaborators from academia, government, diagnostics developers, pharmaceuticals, private payers, and not-for-profit organizations. For years, its working groups have been generating evidence in support of introducing liquid biopsy into routine clinical practice.

"Liquid biopsies for solid tumors go beyond blood."

The Accessibility Working Group has been looking into the barriers to adoption of liquid biopsy testing. According to their findings, levels of skepticism are still high. A lack of awareness or education, uncertainty over the performance of liquid biopsy tests, and concerns about the costs all stand in the way of implementation.

With its paper, "Recommendations for the Equitable and Widespread Implementation of Liquid Biopsy for Cancer Care," the Accessibility Working Group now hopes to effect change (1). The article lays out specific, practical actions to help ensure equitable access to all patients.

In summary, Leiman emphasized three important messages:

- Significant barriers still exist to the adoption of liquid biopsy tests across the US healthcare system – particularly for underserved communities.
- Liquid biopsy tests have the potential to influence access to treatments and improve outcomes for cancer patients.
- A roadmap for action in helping ensure these innovations benefit all communities is clearly laid out in BLOODPAC's accessibility paper.

Reimbursement for Liquid Biopsy in the US

Charles Mathews, Partner at ClearView Healthcare Partners™, reported on the recently updated reimbursement model for comprehensive genomic profiling (CGP) via ctDNA testing.

From the payers' perspective, tissue-based CGP is still widely used for cancer diagnostics. But what happens when tissue biopsy is not feasible or there is insufficient tissue to test?

There is good news: In 2025, a series of new Current Procedural Terminology (CPT) codes were created to describe liquid biopsy tests for solid tumor testing. Codes for genomic sequence analysis, cell-free nucleic acid (e.g., plasma), and interrogation for sequence variants – DNA analysis or combined DNA and RNA analysis, CNV, and rearrangements – are now available. Additional codes include microsatellite instability and tumor mutational burden testing, reported Mathews.

However, with so many limitations on reimbursement for liquid biopsy, is there any incentive for manufacturers to develop and commercialize them? Mathews cited some emerging trends that might improve the situation.

First, the body of evidence supporting the clinical utility of ctDNA approaches continues to grow. With that, test regulation and quality control work, carefully balanced with the need for laboratory developed tests, is helping to improve confidence in test performance. Furthermore, the increasing number and significance of technological innovations that rely on liquid biopsy testing cannot be ignored. Minimal residual disease assessment and HER2 serum extracellular domain testing are two examples seeing rapid growth in uptake.

The tide seems to be turning for liquid biopsy adoption, said Mathews. With more applications now emerging, more reimbursements will – necessarily – open up.

Precision Medicine and Liquid Biopsy: The Patient Perspective

In the final presentation, Nikki Martin, Senior Director of LUNGevity Foundation™ Precision Medicine Initiatives, advocated for a more engaged approach to patient care in precision medicine and liquid biopsy. Providing clear explanations, using patient-friendly language, and involving patients in the testing process, is the key to their empowerment, she argued.

It is also crucial to understand the factors that prevent individuals from having biomarker testing, said Martin. LUNGevity's work has revealed a wide variety of potential barriers – including English as a second language, socioeconomic disadvantage, and a lower level of education.

Using data taken from LUNGevity patient focus groups, Martin also examined what patients themselves reported about their experiences with liquid biopsy. Interestingly, while the groups did appreciate the less invasive nature and potential for real-time disease monitoring, many still have concerns over the accuracy and limitations of liquid biopsy tests. There was some documented confusion as to what liquid biopsy actually entails and how it differs from other tests, such as minimal residual disease assessment.

Words are important, Martin continued, emphasizing that unclear terminology and technical jargon does nothing but present communication barriers for patients. Patients' understanding of their cancer can lead to them pursuing better, more efficient treatment options.

To this end, LUNGevity has developed – with patient input – a cancer decision tree to empower patients to better navigate communicating about biomarker results with their healthcare providers. You can find it here: *https://bit.ly/4jTasWh*.

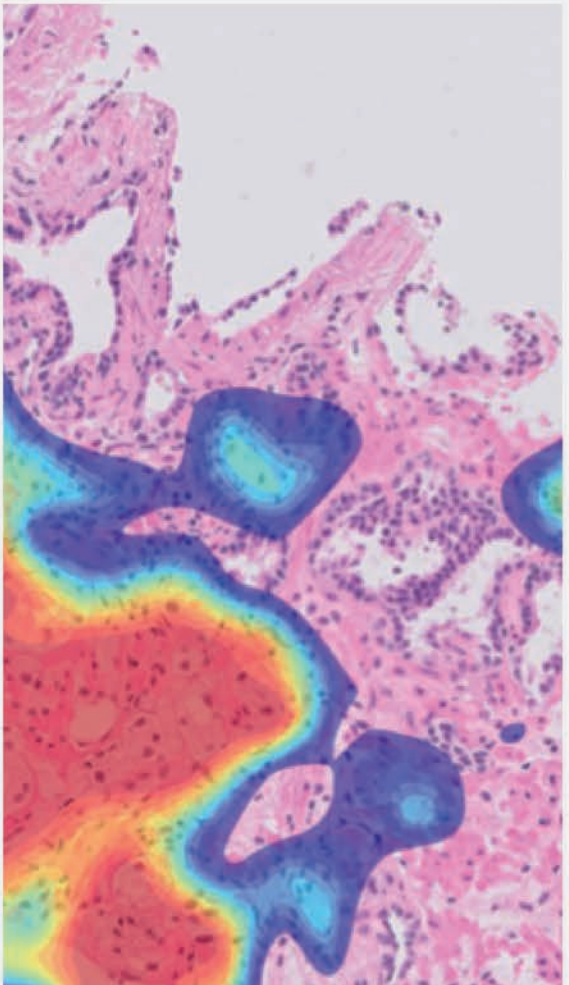
The Future Standard of Care for Cancer Diagnostics

As this exploration into the transformative potential of liquid biopsy-based precision oncology concluded, it is clear liquid biopsy holds the key to revolutionizing cancer diagnostics and treatment. The insights shared by thought leaders underscore the urgency and promise of democratizing access to these potentially life-saving technologies. Now is the time for laboratories across the United States to embrace liquid biopsy, breaking down barriers and expanding access to help ensure that all patients, regardless of their location or socioeconomic status, can benefit from precision oncology. Liquid biopsy may one day be a standard of care that transforms lives and brings us closer to a future where cancer is a manageable condition for all.

"There is good news: In 2025, a series of new CPT codes were created to describe liquid biopsy tests."

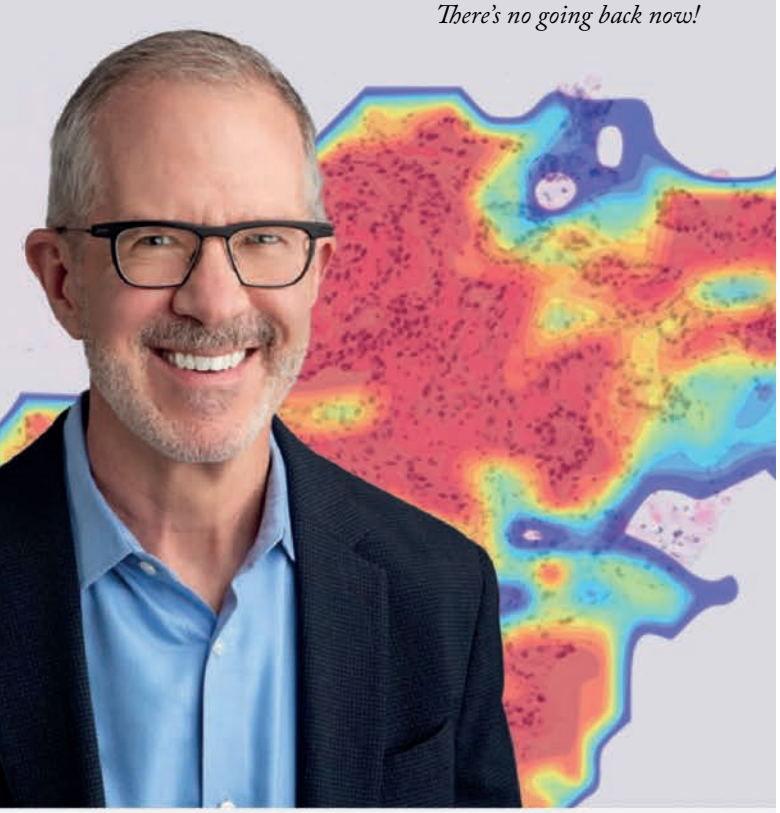
References

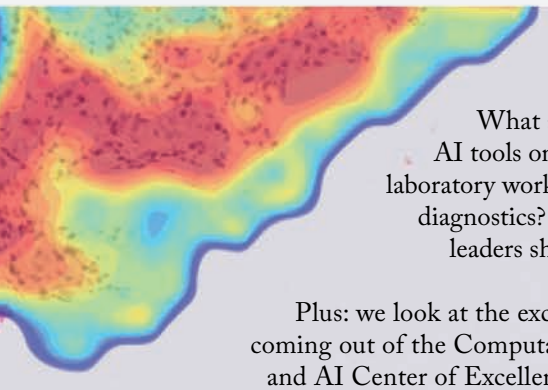
1. *P G Febbo et al., "Recommendations for the Equitable and Widespread Implementation of Liquid Biopsy for Cancer Care," JCO Precision Oncology, 8 (2024). PMID. 38166232.*



AI *in the* Lab

Meet four pathologists for whom AI-augmented workflows are enhancing efficiencies and outcomes on a daily basis. There's no going back now!





What are the impacts of AI tools on clinical research, laboratory workflows, and cancer diagnostics? Three technology leaders share their insights.

Plus: we look at the exciting innovations coming out of the Computational Pathology and AI Center of Excellence in Pittsburgh.

AI-powered digital pathology images supplied by Ibex Medical Analytics

Next Gen Clinical Research

Amanda Hemmerich, Director of Pathology at IQVIA Laboratories, shares her experience of working for a clinical research organization and how digital pathology and AI have transformed the efficiency and reach of clinical trials.

How did you get started in computational pathology?

John Cochran, Chief Medical Officer and Chief Pathologist at IQVIA Laboratories, recognized that my skills would translate well to oversight of the digital pathology initiative. And I was up for the challenge!

First, I learned all about the various scanning technologies, file formats, image management systems, and data storage options for the research space. Next, I looked into image analysis, exploring the answers to key questions: How does machine learning happen? What does deep learning and artificial intelligence do? What's a foundational model? How many different image analysis vendors are there?

I needed to navigate how our IT system would deal with digital pathology, what the audit trail would look like, and how to train our personnel to work with it. It has also given me the chance to collaborate internationally with our labs across the world, in Scotland, the US, Singapore, and Beijing.

Setting up the digital pathology system has been a huge (and exciting) learning curve. It has also been a lot of fun.

How is clinical research harnessing image analysis software?

AI introduces a useful tool for pattern recognition, but it has taken a long time to get it right. Imagine training an algorithm to recognize a dog. It would learn from a set of 100 dog images. But what if you challenged it with an image of a cat. The program sees two ears, four legs, a nose and a tail and recognizes it as a dog. Now, with newer foundational models, the training starts with images of normal, healthy tissue. So, when it's shown cancerous tissue, the model can recognize it as abnormal tissue.

Currently, we're at the stage where we can start using these tools for image analysis. Indeed, trained algorithms can give highly accurate percentages of stained tumor cells on IHC slides or calculate ratios like cytoplasm to membranous staining.

We're also seeing the emergence of companion diagnostic algorithms, which are allowing us to analyze tissue sample images from patients on specific drugs and calculate cell ratios to see if the patient is actually benefiting from the treatment. It is simply not feasible for a pathologist to come up with that sort of scoring system just from looking at a glass slide, which makes these tech-enabled solutions vital supplements to our expert eyes.

"It's critical that pathologists are involved in clinical trials because they can advise on any discrepancies between the assays in the trial environment and how they are likely to be performed in the real world."

Hopefully, in the future, we will have image analysis algorithms that predict the most likely alteration in a specific type of tumor, so we know where to focus our testing. Not only are these sorts of targeted approaches highly efficient, but they are also helping to deliver more personalized patient care, which is ultimately the goal.

How is digital pathology and AI enhancing clinical trial efficiency and access?

Even if hospitals have to send slides to a centralized lab for scanning, the resulting digital whole-slide images allow trials to be location agnostic, which really helps with efficiency and workflows. For example, we could have our pathologist in Mumbai, India, look at a case so that when the patient in the UK wakes up, their results are ready and waiting for them, confirming whether they can start the clinical trial that day. In that way, pathology becomes much more of a 24/7 operation.

There are other practical benefits when you have pathologist specialists spread across various locations around the world. For example, if our hematopathologist in the UK was unavailable but we needed someone else to look at the cases, we would have had to package the glass slides up and ship them to California, adding weeks to the timeline. With digitized slides, the diagnostic workflow is no longer hampered by delays or complications due to shipping.

Something as simple as annotation tools on image management systems also make a huge difference to collaborative working. Pathologists in different locations, who are looking at the same digital slide, can now share notes and second opinions on a case as if they are in the same room.

Another aspect is quality control. We have AI tools that can assess the quality of staining on slides, so we can adjust accordingly to achieve more consistency. There are also algorithms that can assess the diagnostic accuracy of the pathologists themselves and spot any trends that emerge, which helps us plan training.

Meet Amanda Hemmerich

I am board certified in anatomic and clinical pathology. After completing residency training at Duke University, I moved to the University of North Carolina to do a specialized surgical pathology fellowship. I also gained specialized experience in gastrointestinal and liver pathology there.

A few years into my pathology career, I felt that I was more suited for and interested in working in the life sciences industry, whether consulting or in another business role. I took a position with Foundation Medicine – a purely molecular company offering next-generation sequencing (NGS) testing of tumors. There was also a huge explosion in PD-L1 testing for checkpoint inhibitors while I was there, and I was involved in developing different immunohistochemistry (IHC) assays.

With that molecular experience under my belt, I transitioned to IQVIA Laboratories and joined its molecular hub in Research Triangle Park, North Carolina. While at this innovation lab, I assisted with research in exploratory biomarker development that largely looked at the expression of proteins of interest via IHC assays.

It's crucial that pathologists are involved in clinical trials because they can advise on any discrepancies between the assays in the trial environment and how they are likely to be performed in the real world. For instance, if a particular scoring system is used in the study, it's important to make sure it's reproducible in a regular lab in an everyday clinical setting.

What innovations or trends do you predict will emerge in the computational pathology space?

I expect that the regulators may start to insist on standardized file formats. Hopefully, it will be the DICOM standard, which has been proven to aid interoperability in radiology.

I also predict more capitalization of IHC image analysis to develop companion diagnostics in oncology and beyond in the next two or three years.

AI-integrated Companion Diagnostics

They are coming to a lab near you soon, predicts Douglas Clark, Chief Pathologist for Companion Diagnostics at Agilent

Why do we need AI-powered companion diagnostics?

In oncology, one driver is the need to evolve diagnostics to meet the type of drugs we're working with. For example, there is a dense pipeline of antibody–drug conjugates coming through, for which the mechanism of action is very complex.

If we look at HER2-positive breast cancer, the first companion diagnostics were simply looking for overexpression of HER2. But antibody–drug conjugates might have efficacy in low expressors, so we will have to examine the entire dynamic range of expression. And that adds complexity to the diagnostic tests.

Immuno-oncology drugs have an even more complex mechanism of action because the body's immune cells are involved. Here, we need to develop the next generation of PD-L1 assays to match the complex biology of the treatments.

The second driver for introducing AI is information content. There is so much information contained in a single digital whole-slide image – and digital pathology and AI can really help us unlock it.

What's in it for the various stakeholders?

For our patients, our primary goal in all this is better prediction of response or nonresponse to treatments.

From the pharmaceutical industry perspective, it's about gaining approval for drugs, which means running the most robust clinical trials. They want better tests.

In the clinic, we want the right drug for the right patient at the right time, which requires the most powerful diagnostic tests we can make.

Tools for better quantification of biomarker expression are the very foundation of precision medicine. Right now, biomarker testing is in a semiquantitative – and admittedly somewhat subjective – state. As I said before, quantitative tools that measure the whole dynamic range of expression offer an incredible opportunity for all stakeholders.

So that's where AI-assisted companion diagnostics come in. There are two main classes. One is an assistive algorithm that examines digital images in the same way a pathologist does and assembles the observations into an output. The opportunities there would be faster and more accurate classification.

Meet Douglas Clark

I started my career at Johns Hopkins doing research and teaching alongside diagnostic pathology. From there I moved to the University of New Mexico to become Chair of the pathology department, where my interests in digital pathology and AI really took off.

I moved to a Chief Medical Officer role at Tricore – a large reference lab. I set up the infrastructure for digital pathology at Tricore, which served two different groups – the University of New Mexico's group and a private group of pathologists. That taught me that there is no one ideal model for digital pathology.

Later, working at a pathology AI company, I was involved in one of the first clinical trials for software as a medical device in pathology – specifically, detection of prostate cancer in needle core biopsies.

All that varied experience led me to join Agilent two years ago. One of my main tasks is to find AI solutions to navigate the various disease scoring systems we use in pathology to help make treatment decisions. Because AI is great at quantification tasks, it can make these companion diagnostics work better for patients, as well as providing valuable tools for pathologists.

Credit: Agilent

But, for me, the Holy Grail is what's called an augmentative algorithm that can extract a feature from an image that a pathologist cannot see easily – or cannot see at all. It can bring more of the information content to the companion diagnostic.

Should we approach this technology with caution?

I predict that AI tools will integrate into our jobs quite naturally. But, with that, we pathologists need to look very carefully at how we use them. It has to be "pathologist plus algorithm." When a pathologist looks at a digital slide image and an algorithmic output, ultimately they have to make the diagnostic decision. I'd like to reassure your readers that we are very far from AI taking our jobs.

But we should also consider the opportunities AI affords to enhance our direct diagnosis. There is a really intriguing opportunity for us to learn from the algorithms. If the algorithm does spot a small cancer or some feature that we have missed, it provides the pathologist with an opportunity to learn in a best case scenario.

What needs to change for these tools to be more widely adopted?

The big change is that diagnostics companies like Agilent are actively working on developing AI-integrated companion diagnostics. Once they are approved for clinical use, every lab will need to be digitally enabled to access the best diagnostics and treatments for their patients. That will be a real catalyst for change.

Precision and Progress

Sam Terese, President and Chief Executive Officer at Alverno Laboratories, discusses AI's impact on laboratory medicine

What motivated the decision to digitize your labs?

Beyond logistics, you have to think about the impact on patients and providers. When a patient is waiting for a diagnosis – especially for something like cancer – even if they're told it's routine, they're still anxious. If we can take even a day out of that waiting time, it's a significant benefit.

Digitization also improves efficiency, making it easier for pathologists to work in different environments, within regulatory guidelines. During the pandemic, for example, we had to ensure that pathologists could access images whether they were in the hospital, at home, or elsewhere. Digital pathology became not just a matter of efficiency but also a safety issue.

It's true that determining the return on investment for digital pathology can be challenging, but I see it as a foundation, not an endpoint. It opens the door to AI and advanced analytics. If you think short term, it may seem hard to justify, but in the long term, it's essential.

How did you approach the digitization project?

The FDA approved the first scanner for primary reads around 2017. At the time, it was the only option available at scale. We knew we couldn't move forward until we had FDA-approved technology. So, the moment we got the email announcing the approval, we decided to move ahead because it directly solved our turnaround time and logistics challenges.

We formed a team of pathologists and administrators to evaluate the market. We brought in four different scanners and tested them by scanning sample slides, which we sent to pathologists across our system for review. From there, we narrowed it down and sent pathologists abroad to see the technology in action. That step was key to getting their buy-in because they became invested in the process.

The next hurdle was integrating it into the workflow. Scanning slides adds an extra step compared to simply packaging them for transport, so we had to figure out how to ensure everything was still ready by 8 am the next morning. This meant investing in 10 to 12 scanners to maintain efficiency and turnaround time. Today, our entire system is fully digital and has been for several years.

What were the barriers to implementation – and how did you overcome them?

Each organization had its own security protocols, infrastructure, and bandwidth considerations, so we spent a lot of time understanding these factors before even bringing in the scanners. We had to determine where servers would be located, how data would be transferred, and how to ensure images were routed to the correct sites securely. Labeling, barcoding, and access controls were key components of this process.

Cost is always a factor, of course. For us, as a multi-site system, it was easier to justify because the logistical efficiencies were clear. But for a single hospital where the histology lab is just across the hall from the pathologist, the return on investment is harder to quantify.

How did the lab teams take to the new way of working?

Here, I can share a story that is very telling. One of our sites was subject to a cyber-attack, which meant that we had to sever all connections and stop sending digital images through to them. The team there had to revert back to glass slides and microscopes – but the pathologists refused to work in that way. They said, "Don't send me glass; send me to a different site where I can read my digital cases on their network!"

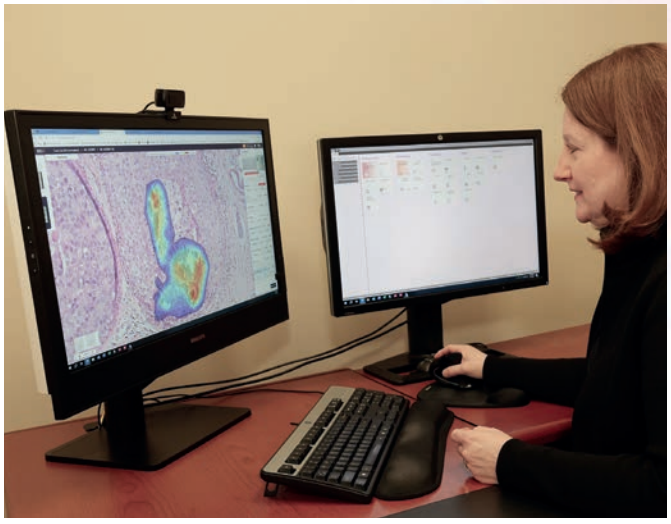
Credit: Alverno Laboratories

Meet Sam Terese

I've been in the laboratory field for a little over 45 years. Believe it or not, I started out as a phlebotomist! Over time, I moved through various management roles in different settings.

My entire career has been dedicated to diagnostic laboratory medicine, except for about a decade in pure research. Since then, I've worked in hospital laboratories in different leadership roles, and today, I serve as the CEO and President of Alverno Laboratories. We operate a large, integrated laboratory network, servicing over 30 hospitals, 34 patient service centers, multiple free-standing emergency departments, and numerous physician practices.

AI-powered digital pathology. Credit: Alverno Laboratories



"We still have much to learn about cancer, but if AI helps us detect it earlier and manage it more effectively, then every lab should be using it."

Slide scanners in the lab. Credit: Alverno Laboratories

The digital workflow very quickly became the new normal – with a lot less hassle.

Why did you decide to introduce AI tools to the lab?

For us, it was simply the right thing to do. Just like we strive to improve lab tests over time, we should take advantage of every technology that enhances outcomes and quality of care. AI is just another step in that continuous improvement – much like how apps have made our personal lives easier, AI can do the same in pathology.

Introducing AI to pathologists is different from digitization because there's often a fear that AI will replace them. But that was never the intent. AI is a tool to support them, improving diagnostic accuracy and reducing even the smallest margin of human error. Pathologists themselves acknowledge that, as humans, errors are always possible.

AI is not meant to replace pathologists but to support them by reducing errors and mitigating risk. It has been well accepted among our pathologists because they see its value. After all, AI is trained by pathologists, not independent of them.

What difference have these tools made to both the lab and patients?

Measuring impact is challenging, but we can confidently say that we are providing a higher level of accuracy to patients and physicians. This isn't just about having cutting-edge technology – it's about improving patient outcomes.

Studies show that some cancer cases – perhaps 5 percent – are missed or underdiagnosed. Even if we only improve that rate by 1 percent, that's still meaningful. If 2 out of 100 patients experience a delayed or missed diagnosis, that delay can have significant consequences, especially in cancer. Early detection is key, and AI helps achieve that.

We still have much to learn about cancer, but if AI helps us detect it earlier and manage it more effectively, then every lab should be using it.

Democratizing AI, Globally

A computational pathology and AI center is a must in every pathology department, says Hooman Rashidi

The Computational Pathology and AI Center of Excellence (CPACE) is an AI center in the University of Pittsburgh, School of Medicine.

We connected with Hooman Rashidi, Executive Director of CPACE, to learn about the work of the center and how its innovations are impacting the practice of pathology.

How would you summarize the work of CPACE?

Liron Pantanowitz, Chair of Pathology at UPMC, puts it nicely – we're built to be problem solvers. If people are looking for basic science research in AI, they should not come to us. We are all about translational research. We want the models we design and build to directly impact patient care and improve workflow efficiencies.

Credit: UPMC

Meet Hooman Rashidi

Before medical school, I was a graduate student with a focus on bioinformatics at the University of California (UC) San Diego – but I decided to switch tracks and pursue a career in medicine instead. The plan was to enhance medicine through my bioinformatics and machine learning skills. The reality was that I spent many years trying to persuade my institution to introduce bioinformatics and machine learning into clinical practice, but nobody was interested.

Then, about 10 years ago, things changed. The CEO and Vice Chancellor of UC Davis invited me to become the AI Director for the whole health system. We built AI models for both laboratory and clinical applications, including sepsis and acute kidney injury.

From there, I moved to Cleveland Clinic to set up an AI center there. Alongside that, we deployed the first no-code AI course, with the aim of democratizing AI literacy for the whole medical landscape.

Finally, I was recruited by UPMC and the University of Pittsburgh to create the new CPACE initiative.

Could you elaborate on your machine learning solution for automating the whole-slide image analysis building process?

It's an automated machine learning framework for building, validating and deploying whole-slide image analysis for specific disciplines.

Traditionally, building a model to, say, detect prostate or colon cancer, or predict PD-L1 status, can take anywhere from several months to over a year. That's because whole-slide images are massive files, and the process of creating triage models is extremely resource-intensive.

Our goal was to streamline this entire pipeline – from model creation to clinical deployment – using a fully automated framework. We designed it to work across different pathology disciplines, with the ability to rapidly generate highly specialized models.

Because the process is now automated and runs on our high-performance computing infrastructure, what used to take months we can now complete in just a couple of days. Instead of producing four or five models a year, we're capable of building hundreds.

What were the main considerations for CPACE in designing open-source chatbots for laboratory medicine?

If you've ever used a chatbot like ChatGPT, you'll know that your data is shared with a third-party cloud provider – whether it's OpenAI, Google, or Microsoft via Azure. That's fine for many use cases, but in healthcare or any setting involving sensitive data – like patient information or proprietary content – you have to be cautious. Anything you input could potentially be used to train future models. So, if privacy matters, that's a major concern.

The second issue is cost. If you're building a custom chatbot and hosting it through a commercial platform, every user interaction incurs an API or usage fee. That can become financially unsustainable, especially if you're scaling to hundreds of thousands of users.

This is why open-source models are so exciting. Platforms released by companies like Meta are now incredibly capable – on par with some closed-source models. The open-source approach allows you to deploy the model on your own infrastructure, completely privately, with no API fees – just the cost of running your own servers.

We've already built frameworks around this approach, offering fully private, cost-effective alternatives to commercial generative AI tools, including one called Pitt-GPT+ and a newer one called Nebulon GPT.

How are PITT GPT+ and Nebulon GPT used in clinical or operational settings?

With Pitt-GPT+, users can upload their own documents – say, 1,000 laboratory reports – and interact with them directly through the chatbot. It has a much lower tendency to stray into unrelated topics or pull in external information. If you ask something outside the scope of your documents, it will simply respond, "I don't know." That's what makes it so powerful – it stays in its lane and focuses solely on your uploaded materials.

Nebulon GPT is designed for more general-purpose queries. If you want to ask questions like you would with ChatGPT – based on global knowledge, not your own files – but still want to do so in a private environment, that's where Nebulon GPT comes in. The whole idea is to allow users to run queries securely and confidentially without sharing data with external platforms.

What impact is that having on laboratory workflows?

The reason people really like this tool is because it addresses several long-standing challenges in pathology reporting.

The first is time. Bone marrow reports, for instance, are lengthy – and they take a long time to write. Fatigue also becomes a real concern, and when people are tired, the risk of errors increases – which can have serious implications for patient safety.

Second, there's a lack of standardization. Reports vary significantly between institutions and even between pathologists. While we try to keep formats consistent, in reality, the content is often scattered and inconsistent.

Third – and this is a big one – traditional dictation methods like Dragon software or transcriptionists don't offer in-document quality control. Our model runs automatic quality checks throughout the report to catch inconsistencies, and helps ensure structured data are captured more accurately, which benefits downstream analysis and clinical decision making.

What does the future hold for CPACE?

We plan to move ahead, full force, with democratizing AI globally. We want what we do here to be translated to other centers of excellence. We're firm believers that a computational pathology and AI center is a must in every pathology department.

MOLECULAR PATHOLOGY

Insights from the Microbiome

In conversation with the makers of an at-home microbiome testing service

It's not every day that you have the opportunity to meet a true pioneer of medical technology. But Mark Driscoll – having developed one of the very first next-generation DNA sequencers (NGS) – certainly falls into that category.

After leading the way on research into the human genome for many years, he switched his attention to using NGS technologies to investigate the human microbiome – and Intus Bio was born.

It was after Driscoll had published a paper on using microbiome NGS to improve infection control in a neonatal intensive care unit that he teamed up with biotechnology business leader Paul Denslow. Denslow recognized the life-changing potential of the technology and had the vision to develop it for primary health care use. Joining forces with long-read sequencer developers PacBio, they launched GutID – a microbiome home testing service that delivers actionable insights for patients.

The Pathologist chatted with Denslow and Driscoll to learn more about the GutID technology and its implications for health care.

What is GutID and how does the service work from the patient perspective?

Mark Driscoll: GutID offers an end-to-end microbiome testing service, from sample collection, through genomic analysis, to a comprehensive gut health report.

Patients receive a test kit for collecting a small stool sample, which is then mailed to our testing lab. The sampling method ensures the stability of the samples – they can be stored at room temperature for many months without the bacterial content changing.

Paul Denslow: We extract the bacterial DNA, analyze and interpret it, map it, and send the patient a detailed report of their gut health. It gives scores for indicators like microbial diversity, richness, and evenness, which can be indicators for both gut and overall health conditions. Patients can either use the reports by themselves or work with a health practitioner who can suggest actions to improve the patient's gut health, which can have a massive impact on overall health.

Who are your customers?

PD: The patients who use the service essentially fall into three categories. First there are the "bio hackers" who are really trying to take control of their own data and their own health outcomes. They already believe in the importance of the gut microbiome to overall health, and want to access the best possible data on that. James Kinross, one of the UK's top colorectal cancer surgeons and a leading microbiome researcher, is on record saying that our test is the only one he trusts, because it's complete, accurate, and detailed.

Another group of customers have unexplained gut function issues. Usually they have seen a doctor, been referred to a gastrointestinal specialist, had multiple tests, all have come back negative, and they are still living in pain and discomfort. They want to know why, and what can be done about it.

The third group generally come to us via doctor referrals, when the doctor or the patient thinks that a broader health condition might be linked to gut health, and wants to either rule it in or out.

What are the technologies powering the GutID platform, and how do they work together to achieve strain-level resolution?

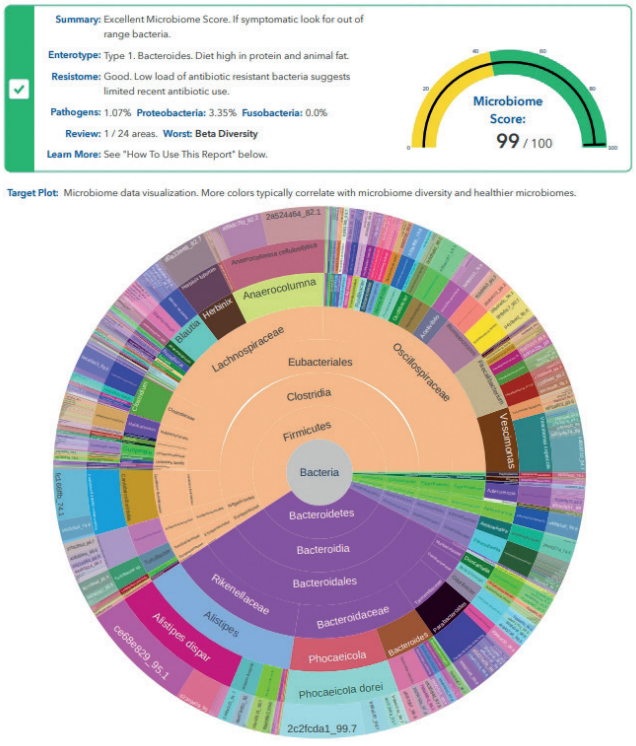
MD: The first challenge is cracking open the bacteria in the sample to release the DNA. We're dealing with millions of different types of bacteria: some fall apart easily, and others require beating with a hammer, so to speak. But when going in heavy to crack the tough bacteria, you don't want to destroy the DNA in the weaker ones. We had to invent a whole new system for doing that. So the first technology we use is our patented high-throughput cell lysis method.

Next comes the DNA sequencing. We use PacBio long-read sequencers because they give us exactly the right information for identifying the bacteria at strain level. We worked with PacBio to increase the capacity of the sample hoppers to maximize efficiency in our workflow.

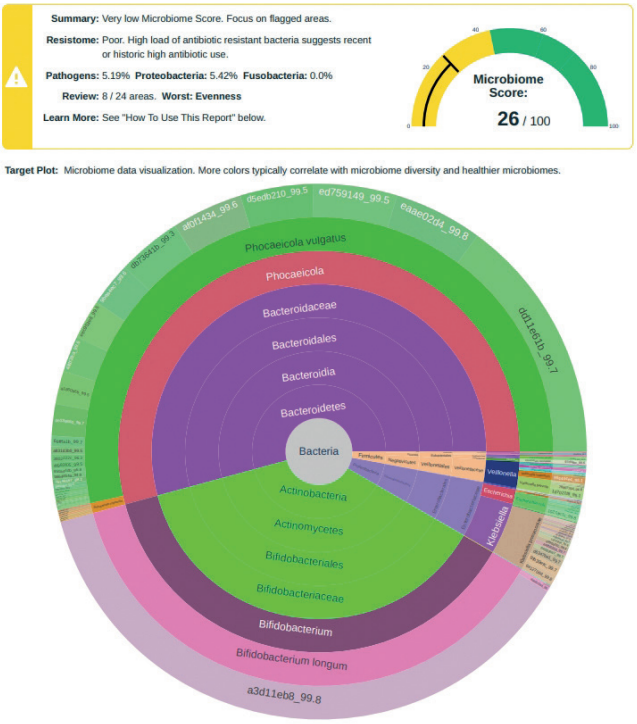
The sequencing results are massively data heavy, so we use machine learning to analyze it. Our machine learning tool was developed in house, and performs analysis, assembly, and mapping of the results. It is also trained to recognize cancer biomarkers.

PD: The combination of the highly accurate long reads from the PacBio DNA sequencer and our unique assay allow us to see the entire colony of gut bacteria. We separate each individual strain of bacteria

Credit: Intus Bio



Example of a healthy microbiome



Example of an unhealthy microbiome

and represent them in the outer ring of our target plot data visualization. From there, we work inwards, mapping species and genus, all the way to phylum and domain.

This strain or outer ring led approach is what allows us to generate data for the entire microbiome – something other approaches can't do in a practical way. Our machine learning tools then use the data to generate GutID reports, which highlight issues, make recommendations, and contain accurate microbiome health metrics, like evenness and diversity – a true first for the industry.

How do you respond to the criticism that microbiome tests fall short on scientific accuracy?

PD: There are a lot of myths out there that the microbiome is always changing, and is therefore not a reliable source of information. But our research shows that the microbiome is incredibly stable. We have tested samples from the same individuals over time and our assay returns virtually the same result month after month.

These results also speak to the incredible stability of our assay. We have seen repeatability testing with other assays that show very different results from the same sample. If we run two tests from one sample on our system, the results are essentially identical.

Ours is a very data-driven company. Scientists should be celebrating the insights our assays generate because they are backed up by solid data. Our technology is transforming an area of health care that was previously very ambiguous and gray into one that can be quantified and monitored.

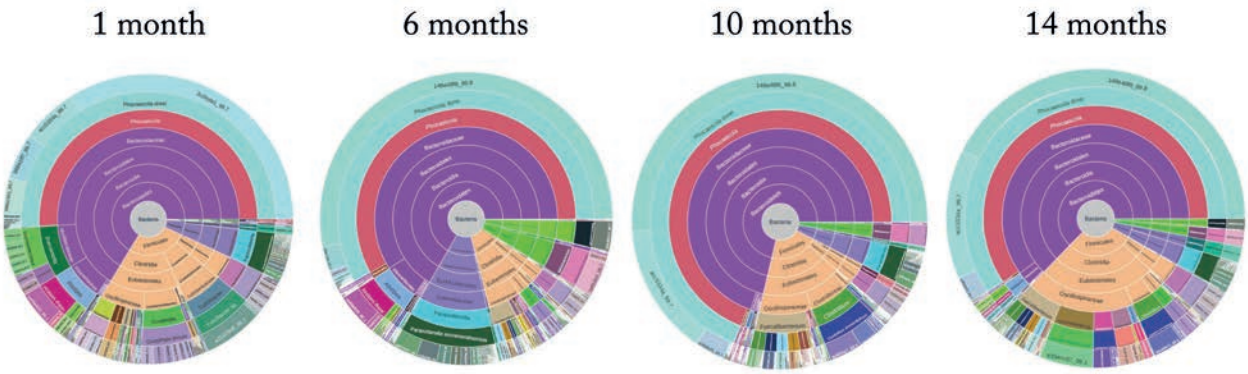
Could you elaborate on how the GutID test results are translated into clinical or lifestyle interventions for the patient?

MD: I can give you an example where I was the test subject! As inventor of the test, I wanted to take the test and prove that my microbiome is excellent. However, the test results showed straight away that it's not so great.

In the interest of science I retested my microbiome every month for 14 months, without making any lifestyle changes, and – sure enough – the results kept coming back the same. This demonstrates what Paul was saying: if you just live your life, the microbiome is incredibly stable.

For years I had experienced gut pain after eating. And I'd never really addressed it – it was just part of my life. When I showed my microbiome map to Intus Bio's nutritionist, Elena Panzeri, she started asking me about my diet and lifestyle. I explained that I'm healthy; I run, I lift, I eat well. She said, "But you're not eating any vegetables." I said, "I am!" Well, it turns out that peanuts are not vegetables.

She recommended taking a very specific supplement to make up for the deficits in my diet. I thought, "Given the stability of my microbiome for the past 14 months, this is never going to work." But, sure enough, when I ran the GutID test just a few weeks



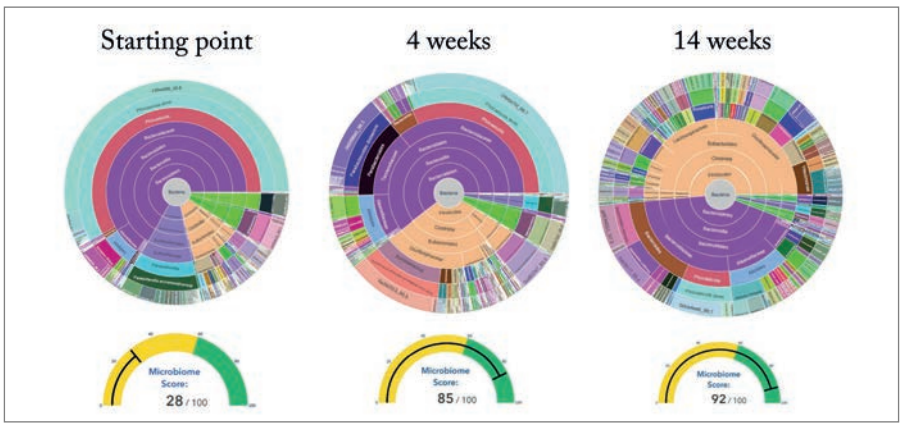
Driscoll's stable microbiome. Credit: Intus Bio

later, the change in my microbiome was very noticeable. What's more – I felt better. The post-meal cramping that I had experienced for years totally went away. I was able to walk the dog and help with the dishes after meals, instead of lying on the couch clutching my stomach.

The GutID test reports do make some general recommendations for patients. But my experience demonstrates the value of talking to a qualified professional who knows your story in order to hear a personalized recommendation.

PD: We believe in presenting microbiome data in an actionable manner. Clinicians don't want to spend hours wading through data – they want to see the headlines at a glance, on the first page of the report. Is there a problem and does it need further investigation? Our reports show target plots and microbiome scores on page one, which indicate from the offset whether an intervention might be required. Subsequent pages give more detailed information on the biodiversity, beneficial bacteria, disease-related bacteria, species related to digestive health, and so on, which can inform the nature of those interventions.

The other way microbiome testing helps is in proving whether the interventions are working or not. A patient's doctor or dietitian might recommend they take a probiotic. But there are so many different ones on the market – how does the patient know which one to pick, and whether it's making a difference? Mark's example of "before and after testing" shows that our test provides the answers to those sorts of questions.



Driscoll's improving microbiome. Credit: Intus Bio

How do you see strain-level microbiome analysis impacting broader areas of healthcare?

PD: The first group of clients we had for GutID in the UK were all being treated for mental health conditions. They wanted to understand the impact of gut health on those conditions. A lot of patients in the mental health space have gut function issues. We can show them the link between those issues and their microbiome, and present something that can be measured and improved – gamified, in a way. That can be very powerful.

We are now doing some research with The Delamere Clinic in the UK with patients with alcohol use disorder that is showing some very strong signals.

MD: We're also working with some leading cancer centers in the States, looking at microbiome testing for diagnosis of early-stage pancreatic cancer. Because the pancreas dumps into the fecal space, we can detect the bacterial biomarkers in the poop, and then we can give an early warning for disease. And it's a non-invasive test.

If approved, we could build it into our microbiome analysis software so that all of our customers are screened for pancreatic cancer as standard.

PD: We have this incredibly powerful platform, and it's very sample hungry. If we can access any kind of samples of specific patient cohorts – be it spit, stool, swabs, even tissue – we can run them on our analyzer. And the results will very clearly show whether or not there's a microbiome correlation with the condition in question.

So the thing that is holding our research back is not the technology, it's the samples to train and build the data to run these applications. In that respect, here is a call to action for readers of The Pathologist: if you are looking to develop an understanding of the link between the human microbiome and a specific condition, and you have samples from a cohort, please get in touch.

INFECTIOUS DISEASE

Preventing the Next Pandemic

Why we must urgently boost biosurveillance for zoonotic pathogens

By Neil Ward, Vice President and General Manager, PacBio

According to global health experts, we are living in an "era of pandemics" (1). COVID-19 was at least the fifth global health pandemic since the Great Influenza Pandemic of 1918 (2). Zoonotic pathogens – disease-causing microorganisms that can spread from animals to humans – pose the greatest threat to global society. Hundreds of thousands, maybe millions, of viruses exist in mammals and birds, many of which could infect people (3).

Recent years have seen high levels of avian flu, which is mutating and jumping from birds to other animals with an ever-increasing pandemic threat, according to the European Centre for Disease Prevention and Control. Meanwhile, the Coalition for Epidemic Preparedness Innovations has identified seven priority pathogens – including COVID-19, Ebola, and Lassa Fever – all of which are zoonotic.

While the extraordinary global response to the COVID-19 pandemic enabled containment and control of the disease through vaccines and therapeutics, this is not a sustainable approach. Future pandemics may well be more virulent, borne from pathogens significantly more complex to tackle. So, how should the world respond?

To navigate this era of pandemics, a seismic shift in mindset and policy is needed – from a reactive to preventative approach that mitigates their spread.

Genomic sequencing lifts the lid on dangerous pathogens

The good news is that we have the means and the methods available to reduce the impact of zoonotic pandemics. Through modern biosurveillance techniques, we can actively monitor, detect, and analyze zoonotic pathogens and pre-emptively gauge their threat to humans.

In particular, genomic sequencing has become an invaluable tool to analyze genomic data from a variety of sources to identify potential pathogens and variants. Sources can include animal species known to harbor zoonotic pathogens – such as bats, rodents, primates, and livestock – and individuals who work in close contact with animals, such as farmers, veterinarians, and market workers. Samples from these sources can be sequenced to identify mutations and detect new strains. Another useful source of information is wastewater, which can be analyzed to track resistance rates among microbes in local populations.

The ultimate goal – as characterized by the World Health Organization's International Pathogen Surveillance Network – is a world where every country has equitable access to genomic sequencing and analytics as part of its public health surveillance system.

However, while governments are starting to expand their biosurveillance of zoonotic pathogens, many are still relying on one type of genomic sequencing technology – called short-read sequencing – to do so. While short-read sequencing has many uses, it analyses a pathogen's genome in small fragments rather than one long, continual "read", which can lead to parts of the genome being missed or contribute to high error rates. This, in turn, can lead to incorrect interpretation of the transmission mechanisms of pathogens, as well as how they evolve to become drug resistant.

This matters because if we are tackling a pathogen that is more complex than COVID – which was comparatively simple to amplify and sequence – then an early, accurate picture is absolutely essential.

The time to act is now

To keep the threat of a potentially devastating pandemic at bay, governments urgently need to employ the latest advances in sequencing technology. Modern long-read sequencing technologies enable the sequencing of much longer DNA fragments, simplifying the interpretation of the sequence data and enabling sequencing of variants that current short-read sequencing technology struggles with. Therefore, long-reads enable a much clearer picture and deeper analysis of pathogens and their potential threat.

The latest generation of accurate long-read sequencers are becoming rapidly more accessible. As advances in the technology bring down cost, it is becoming more feasible to establish large-scale disease surveillance networks for many more nations, enabling a preventative approach to pandemics worldwide.

Addressing the threat – together

The threat of zoonotic pathogens is increasing. Urbanization is increasing the risk of rapid transmission; meanwhile, climate change is altering the habits of mosquitoes and ticks creating greater opportunity for diseases like malaria, dengue, and Lyme disease to spread.

Now is the time to act. By introducing the latest generation of sequencing technology as part of a national biosurveillance plan, governments can help to identify dangerous zoonotic pathogens before they spread. Alongside technology, international collaboration and data sharing will enable the world to shift towards a preventive approach, avoid global public health crises, and help to make the era of pandemics a thing of the past.

References

1. *UN Environment Progamme, "Escaping the 'Era of Pandemics" (2020). Available at: https://bit.ly/3Ej1CSA.*
2. *A Casadevall, "Pandemics past, present, and future: progress and persistent risks," J Clin Invest, 134, 7 (2024). PMID: 38557492.*
3. *J Paoli, "Viruses 101: what's multiplying in you?" (2013). Available at: https://bit.ly/4lSCT8J.*

DIGITAL PATHOLOGY

The Beginner's Guide to Spatial Image Data Science

All you need to know about the AI-driven image analysis unlocking the complexity of disease

Spatial biology is offering fresh insights into cancers, neurodegenerative diseases, and autoimmune disorders, and helping researchers identify new biomarkers to improve diagnosis and treatment. But what is spatial image data science – and how does it fit into the picture?

Here, Gourab Chatterjee, Director, Product Strategy and Management, and Lorenz Rognoni, Senior Director, Image Data Science, at Vizgen, guide us through the fundamentals.

What is spatial image data science – and why is it becoming increasingly important in modern pathology?

Spatial image data science uses advanced imaging combined with computational analytics to map and quantify the locations, interactions, and heterogeneity of cells and molecules in tissue.

Its rise in importance is driven by the increasing need to understand complex tissue architecture in diseases. It can provide context that traditional single-marker or bulk measurements can't offer, ultimately leading to more informed decisions and strategies in therapeutic development.

What unique insights does spatial biology provide over traditional histopathology and genomic approaches in understanding tissue microenvironments?

Spatial biology presents a high-resolution view of tissue architecture and cell-to-cell relationships. Unlike traditional histopathology approaches that predominantly provide morphological details or genomics approaches that mostly examine molecular averages, spatial biology provides quantitative data on cell types, their locations, and interactions.

This spatial image data is particularly valuable in understanding complex diseases like cancer, where the tumor microenvironment plays a critical role in disease progression and treatment response.

What are the biggest challenges in analyzing spatial image data – and how can pathologists leverage data analytics tools to make the most of this information?

One of the main challenges is managing the volume and complexity of generated data, including storage and processing issues. Additionally, collaborative data access is already difficult. Combining methods to align multiplexed images, standardizing analysis across platforms, and integrating multi-modal datasets are also challenging.

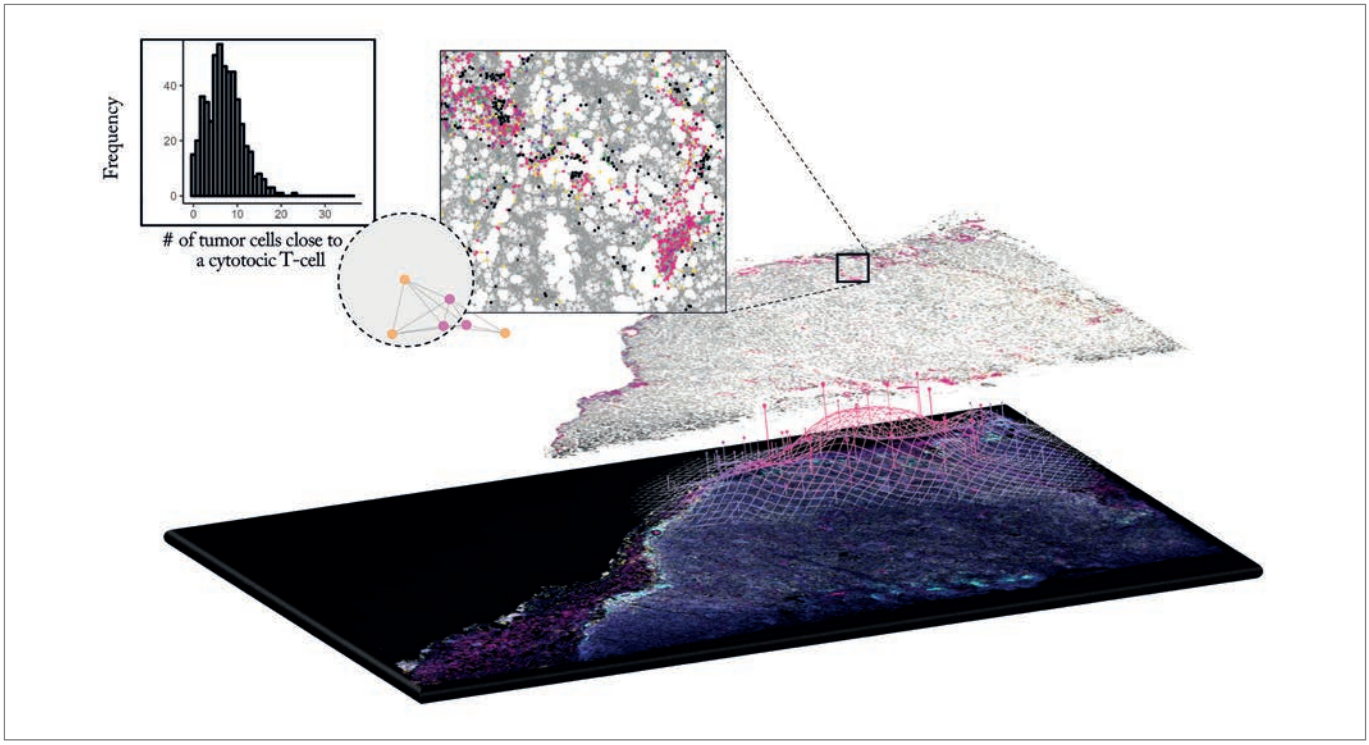
Leveraging advanced data analytics and machine learning tools can help pathologists automate and standardize image processing, quantify features objectively, and integrate spatial insights with molecular and clinical data – ultimately leading to more accurate, reproducible assessments.

How does the integration of multiplexed imaging with spatial analytics improve the accuracy of biomarker discovery and disease characterization?

Multiplexed imaging allows for the simultaneous visualization of numerous biomarkers in a single tissue section. Coupled with spatial analytics, pathologists can identify different cell types and decipher their complex interactions with the microenvironment.

"AI-powered image analysis has revolutionized pathology by removing rigid thresholds and adapting to tissue and signal variability, allowing for the detection of complex patterns that are challenging to assess manually."

This integrated approach refines biomarker discovery precision and enhances disease characterization. It can uncover subtle shifts in cellular interactions that may indicate early therapeutic resistance or disease progression, such as increased tumor infiltration of cytotoxic T-cells.



Spatial imaging of the tumor microenvironment. Credit: Vizgen

What considerations should pathologists keep in mind when interpreting data from spatial imaging platforms?

Pathologists must account for variability in tissue sample preparation, imaging artifacts, and analytics pipelines. The sparse 2D sampling of histology sections should also be acknowledged. It is crucial to validate findings across different modalities and consider each technology's limitations.

Integrating spatial data with other diagnostic modalities offers a more comprehensive view of the disease, but requires careful correlation and validation to ensure accuracy and relevance.

How is deep learning enhancing spatial image analysis?

Deep learning has greatly improved the analysis of complex spatial patterns in tissue images. It detects subtle cellular differences, recognizes morphological patterns in high-dimensional data, and discovers new features that may be overlooked manually.

In multiplexed immunofluorescence, deep learning-based cell classification allows for threshold-independent positivity classification, which enhances the precision of tissue-based diagnostics by minimizing human error, increasing throughput, improving analysis accuracy, and reducing variability.

Can you provide examples of how AI-powered image analysis has changed the way pathologists assess disease progression or therapeutic response?

AI-powered image analysis has revolutionized pathology by removing rigid thresholds and adapting to tissue and signal variability, allowing for the detection of complex patterns that are challenging to assess manually.

For instance, AI can analyze continuous biomarker data. One model – quantitative continuous scoring (QCS) – was used to assess the normalized membrane ratio for TROP2. This offered nuanced insights into disease progression and therapeutic response in patients with non-small cell lung cancer.

This technology enhances expert analysis by highlighting critical areas in tissue samples and expands access to advanced diagnostics, ultimately improving patient care.

How do you see deep learning shaping the future of digital pathology and personalized medicine?

Deep learning is set to become a cornerstone in the evolution of digital pathology and personalized medicine. As these algorithms advance, they will enhance diagnostic accuracy and integrate multi-modal data – combining imaging, genomic sequences, and clinical information into comprehensive computational models.

In the future, we will see a shift towards fully personalized treatment plans that allow pathologists and clinicians to use data-driven insights to tailor therapies to each patient's unique disease landscape.


"I had been told by several of my respected mentors that I would be wasting my career in microbiology. Fortunately, I had come to my own conclusions and had other supportive mentors to guide me on my way."

Infectious Enthusiasm

Sitting Down With… Bobbi S. Pritt, Professor of Laboratory Medicine and Pathology, and Chair, Division of Clinical Microbiology, Mayo Clinic, USA

How did you find your way into clinical microbiology?
I was a late comer to clinical microbiology, selecting it only towards the end of my third year of pathology residency. Based on my interest in the gross and microscopic morphology of various pathologic states, I had originally planned on becoming an anatomic pathologist. However, I realized that I was better suited to the clinical pathology workflow, where I could have a wide variety of responsibilities and activities.

Having different things to do every day – and even every hour of the day – appealed to me. I was worried that I would become restless if I sat at a microscope all day long. I also found infections fascinating!

Finally, I realized that I was more interested in the pathology of infectious diseases than malignancies, and was very excited about the opportunity to combine my anatomic and clinical pathology training to diagnose infections from both traditional microbiology and histopathology specimens.

Could you please share your career highlights?
One was being hired – right out of fellowship – to direct the Clinical Parasitology Laboratory at Mayo Clinic, leading the team that discovered two new tick-borne pathogens in the United States. I also had the opportunity to serve as Vice Chair of Education for the department, Division Chair of Clinical Microbiology Division (my current role), and Interim Chair of the Department of Laboratory Medicine and Pathology.

In this last role, I was responsible for over 170 physicians and PhD scientist laboratory directors, and over 3000 staff. Though I wasn't interested in the permanent position, I was honored to lead our department during a dynamic and exciting 16-month period.

Perhaps my biggest career highlight to date, however, is being elected to the Board of Governors for the College of American Pathologists.

What key leadership lessons did you learn as interim departmental chair?
There were so many! There are plenty of books on how to be a good leader, so I won't repeat the wisdom held within. Instead, I'll focus on three practical points I learned during the 16 months I was in this role.

First, it's important to take control of your calendar – as much as possible at least – to ensure that there is time for the important things you want to accomplish. Otherwise, it's easy to end up in 10 hours of back-to-back meetings that are focused on other people's priorities.

Second, remember that all eyes are on you as the leader, and that people who were colleagues – or even previous mentors – will now look to you for approval. It took me a while to get used to this change in how people saw me.

Finally, it's important to reflect on your performance regularly so that you can improve. Take some time to talk through challenging issues with a trusted advisor if you can. Good leadership is a skill that can be learned through effort, reflection, and practice.

What achievement brings you the most pride?
My accomplishments in education and mentorship give me the most pride. I had the honor of being inducted into the pathology educator hall of fame by being selected as Educator of the Year in clinical pathology six times in my first nine years at Mayo Clinic. I also received the highest-level award for educational excellence offered by Mayo Clinic.

Though I am proud of my achievements in clinical care, research, and leadership, I feel that my legacy will be the students, residents, and fellows that I have had the privilege of teaching.

What do you like most about your job?
I love the ability to contribute in so many different ways, from the teaching and mentorship I just mentioned, to creating innovative new tests and signing out cases in ID pathology, a subspecialty of anatomic pathology.

I am lucky enough to work with diverse teams of health care professionals, providing individualized consultation for patients and physicians around the world. Although I probably say "yes" to too many things, I am constantly stimulated by my work and the people I get to work with.

What advice would you give to pathology residents in choosing their subspecialty?
Remember that what you are doing as a resident will not be the same as an attending. I really enjoyed grossing as a resident but realized that I was unlikely to spend much time doing this as an attending.

Second, pick the area of pathology that truly excites you the most – even if it is not what your mentors had in mind for you. I had been told by several of my respected mentors that I would be wasting my career in microbiology. Fortunately, I had come to my own conclusions and had other supportive mentors to guide me on my way.

Finally, don't worry if few residents specialize in the area you are drawn to. As long as there are job opportunities, it doesn't matter if you are the only one in your group to specialize in that field. Being a rarity might even make you more highly sought after!

Few pathologists move into microbiology, for example, but pathologist-trained microbiologists can do things that other microbiologists can't easily do, such as sign out surgical pathology cases and cover other areas of the clinical laboratory. This may make you a more attractive job applicant.

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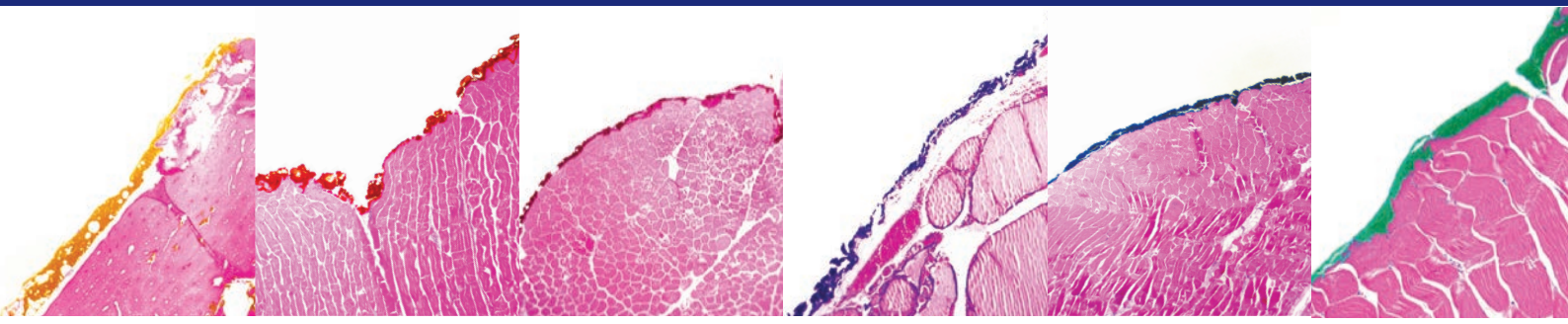

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