

# Digital pathology and imaging — past, present, and future

By Karen Lynn

The first focus of digital pathology was to automate the microscope. “The ultimate goal was to begin the migration from a physical slide to a digital image and ensure users’ comfort during the transition,” says Jason Christiansen, PhD, senior director of Operations at HistoRx. In its earlier days, image-analysis applications were produced but limited to existing testing paradigms which had less impact than the leap to slide digitization. Fast-forward five years. Today, image quality is virtually identical to viewing a glass slide under the microscope. In fact, pathologists are willing to make diagnoses based on an image versus actual glass.

Viewing slides digitally gives numerous advantages that glass slides do not provide; for example, tumors and areas suspicious for disease can be measured more precisely; images can be manipulated and utilized for consultation and teaching purposes; images can be viewed by more than 100 people simultaneously from anywhere in the world; and automated, quantifying algorithms for estrogen receptors, progesterone receptors, and HER2 have since been developed and FDA-cleared, reports Joon Yim, MD, director of digital pathology at Acupath Laboratories. In addition, digital pathology supports rapid-assessment turnaround time for frozen sections which are critical to surgical protocols, and those slides can be digitally imaged and stored in a central repository.

The next goal of imaging proponents is to have digital pathology fully accepted as a tool in all types of pathology labs, from research to translational to clinical. Rapid exchanges and increased collaboration will allow science and diagnostic decisions to progress faster and improve information flow. As with automation development in other fields, the further integration of all aspects of the entire process will improve workflow. “This means going beyond just providing automatic methods of doing individual tasks that used to be manual; it means the introduction of new methods that were originally unavailable in manual or even in early automation models,” Christiansen says.

From a technology standpoint, scanners will continue to advance and become incrementally better. New algorithms are clearly a candidate for innovation. Methods of collaborating with specialists, peers, and residents will change as well, says Tony Melanson, VP of strategy and marketing for Omnyx. Access to case data and digital images will become more ubiquitous and multimodal. Standards for image formats and data interchanges will be adopted.

Darren Lee, VP of marketing of cellular and tissue analysis for Caliper Life Sciences, foresees analytics — based on integrated solutions consisting of sample preparation steps, staining protocols, and clinically validated image-analysis algorithms — providing prognostic power, as well as diagnostic accuracy and precision, that was previously unachieved. These will arise from better instrumentation, smarter image-analysis algorithms, better reagents, and multiplexing. In addition, fluorescence-based methods will come to the forefront for protein, RNA analysis, and DNA analysis due to improved precision, dynamic range, and novel, independent labeling methodologies (e.g., miRNA, mRNA, FISH in FFPE), optical-imaging technologies, and more advanced image-analysis algorithms, Lee continues.

One change that is not expected is biopsies being replaced by surrogate markers in blood or through imaging because the information that can be retrieved from a biopsy is, by its nature, specific to the disease and is comprehensive. “For the foreseeable future, information from surrogate tests that indicates an issue will likely be followed up by imaging and a biopsy as confirmation,” Lee says.

To advance the field, it is necessary to revisit digital-pathology foundations and examine the field as a whole. “Digital pathology is evolving to become more than just simply imaging; it also includes associated assays and analysis tools,” Christiansen says. For example, typical image analysis today is an automated version of existing scoring methods using a previously optimized assay. The assays and scoring systems were developed prior to the improved quantitative power that is provided by image analysis of digital-pathology results. Thus, new assays and methods are being developed that revisit or replace scoring methods to provide improved results and identify patient groups that were previously not resolved. “This has the potential to improve existing assays and also bring forward the next generation of assays, which may have previously been intractable because of technological limitations,” Christiansen says.

The continuing improvement in many aspects of pathology-lab automation will certainly continue with an eye to increased throughput and improved results. In the future, along with faster and higher throughput imaging, lab scientists can expect to see improved immunohistochemistry automation and, although not as visible on a bench, improved collaboration and image-analysis software. Says Christiansen, “In parallel, we hope that the further integration of all the components in the pathology laboratory will be driven by standards to allow a wider selection of products to users.”

Lee expects to see integrated turnkey sample preparation, labeling, and imaging systems, as well as new visualization software, to help pathologists interpret samples and quickly sort through vastly increased amounts of information made available by new analytics.

Digital pathology’s value is more than just in creating an image. Pathology assays, when imaged digitally, can be inputs, or resources, to analysis methods which provide optimized results. These tests may not exist today because the methods have not existed previously or the resolution of the existing methods has not been sufficient to make the assays useful to the field. “Those working in this field need to look at the entire process as a whole, from the treatment of the sample through imaging to analysis,” Christiansen advises.

Digital pathology, coupled with the combination of improved assays that provide optimized results, allows clinicians as well as researchers to carry science and diagnostics to the next level. “As the scope of digital-pathology automation expands to encompass all laboratory activities, the focus will become less on the actual performance of the technique and more on the valuable results,” Lee concludes. □

Karen Lynn is a medical freelance writer.

## Expanding the lab's reach with digital pathology

By Jared Schwartz, MD, PhD

**A**dvances in digital-pathology systems, including rapid slide creation, data management, and image-visualization techniques are transforming the practice of pathology. A powerful tool in anatomic pathology, advancements in digital pathology continue to enhance efficiency and accuracy, resulting in lower costs, significant workflow efficiencies, and improved patient care.

Digital slides are a complete representation of the entire glass slide, viewable on a computer monitor at any magnification. Web-based pathology picture archiving and communication system, familiarly known as PACS, allow pathologists to work remotely anytime, anywhere, to deliver accurate results faster than traditional methods.

As digital pathology becomes more accessible for the average lab, the ability to work digitally provides opportunities to offer new services and tests, attract new customers, and create new business lines. Implementing an outreach business enabled by digital pathology is an emerging strategy that is helping many labs maintain market share and increase growth and profitability.

*Ketchikan (AK) General Hospital is among the first wave of hospitals in North America to use telepathology in an intraoperative setting.*

### Gaining a competitive edge

Labs are continually challenged to provide fast turnaround time, technology innovation, and good service to deliver the best value, and, in many cases, compete for business. Patients and physicians rely on lab results to make critical healthcare decisions, and test results must be completed and reported quickly and accurately. Labs looking to meet and improve their level of service are increasingly turning to digital pathology.

In large healthcare systems, rural hospitals, and geographically distributed pathology labs, access to specialty pathologists for secondary consults can be very limited, requiring days for the transport of glass slides or to schedule a pathologist visit. With digital pathology, hospitals can leverage remote viewing capabilities by making entire slide digital images of specimens, such as frozen section or blood smears, available over a secure Internet connection for immediate review by an off-site pathologist. Pathologists can work from their homes or a facility hundreds of miles away to provide secondary consults or support the clinical needs of distant hospitals.

For pathology labs wanting to maintain and grow their outreach business, digital pathology provides a competitive advantage by providing access to the right pathologists, facilitating faster turnaround times, improved patient outcomes, lower costs, and increased physician satisfaction.

The flexible adoption of digital-pathology systems allows labs of all types to use the technology in niche applications and later expand the utility of the system to offer outreach services (e.g., slide scanning or secondary consultations) to hospitals in the community, or anywhere in the world.

The value of digital pathology is being realized in many different lab applications. Large reference labs are using digital-pathology systems to scan slides, making them easily accessible via the Internet by their own pathologists for timely interpretation and reporting. Physicians in certain specialties (e.g., oncology) are requesting access to slide images to show their patients specific areas of interest. Toward this end, the adoption of digital pathology, which enables the rapid and efficient management of digital-slide images and supporting case information, is making these uses possible.

### Telepathology

Telepathology offers many new opportunities for pathology. Small rural hospitals without access to pathology expertise benefit by having access to a virtual pathologist, and pathology labs can expand their lab's reach by offering service coverage to a very broad geographic region. Digital pathology makes it possible to solidify and enhance a lab's position in the community by being able to provide the same level of pathology expertise found in any major city, lending credibility and confidence in the diagnosis and treatment process.

More than 30 pathologists at the University of California-Los Angeles (UCLA) are currently using digital pathology to market their sub-specialty expertise and provide real-time pathology consultations to the Second Affiliated Hospital in Zhejiang Province, China, toward helping the country achieve its goal of medical reform. Patients with complex cases or special requests can have their pathological images scanned and reviewed by UCLA for diagnosis; remote teleconferences can be conducted between colleagues around the world to review challenging cases.

A lab group in Bellingham, WA, is providing a new telepathology service to access and view slides in Ketchikan, AK, allowing surgeons in the operating room at Ketchikan General Hospital (KGH) real-time consultation with pathologists in Bellingham. The pathologist can change focus, magnification, and field of view with an online interface to review a frozen tissue slide prepared in Ketchikan.

KGH is among the first wave of hospitals in North America to use telepathology in an intraoperative setting. Digital pathology is especially beneficial to smaller, rural, critical-access hospitals where technical experts may not be readily available. Benefits from using the technology are improving cost, travel, time, efficiency, and slide-management issues to help improve patient care.

### Going digital

As use of digital pathology becomes more widespread, labs of all sizes will see a host of workflow and cost benefits, as well as the ability to expand their reach to provide the best level of service and quality care. □

Jared Schwartz, MD, PhD, brings 30 years of pathology expertise to his role as chief medical officer of Aperio, and most recently served as president of the College of American Pathologists, and director of Pathology and Laboratory Medicine at Presbyterian Healthcare in Charlotte, NC.