Pathologists Are Reinventing Their Role Through ePathology
Rapid changes in how pathologists must do their job today require tools that can help them quickly adapt, continue to work efficiently, and provide accurate answers to the critical questions related to patient care.

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Introduction

With the healthcare system being redefined by the adoption of the electronic medical record (EMR), emergence of accountable care organizations (ACOs), advances in technology for histologic sample collection, the rapid growth of molecular technology as the heart of personalized medicine, significant decreases in reimbursement, and increased patient demands for quality of care, the pathologist now finds themselves in the position of reinventing their role as a healthcare provider in order to adapt and survive in this new healthcare environment.

The landscape of patient care is taking many new routes. An aging population and the large influx of patients into the healthcare system in the near future are being met by a growing primary care physician shortage that is only expected to get worse, according to the American Academy of Family Physicians.1 Already, this type of care is seeing a shift to being administered by the growing field of nurse practitioners and physician assistants, who are capable of writing prescriptions and utilizing clinical and pathology laboratory services. There is also rapid growth and adoption of telemedicine as a driving force for the future care of many patients. States are quickly passing laws that are expanding the use of this new electronic technology to cover a multitude of patients, including the underserved.2 Lastly, more new physicians coming out of medical school are following the path to becoming specialists; and many are going on to subspecialize within many of the medical specialties such as gastroenterology, pediatrics, etc.

These new groups of basic care providers and specialty/subspecialty physicians face the inevitable task of providing the high-quality care that Americans have come to expect, and at the same time, meeting efficiency goals that are being driven to reduce the cost of healthcare in this country. Specialized physicians are also requiring access to new molecular technologies and access to “specialized pathologists,” either directly or through their own local pathologist, to help get the diagnostic answers they need for treatment-planning decisions.

Thus, as this new trend matures, treating physicians are going to require more guidance from the pathologist and the laboratory. “Pathologists, PhDs, nurse practitioners, and physician assistants all have an opportunity to play a significant role as consulting advisors in a most cost-effective way by helping to solve the problem of cutting down on inappropriate testing,” says Jared Schwartz, MD, PhD, past president of the College of American Pathologists (CAP) and currently chief medical officer, Leica Biosystems, Vista, Calif. “It doesn’t mean not allowing tests to be ordered. Where the pathologist and the laboratory team can assist is in making sure the right tests are ordered to answer the physician’s specific questions related to the treatment of a patient. Thus, the pathologist can become a more active member of the patient’s team and provide the role of an interpretive director and clinical advisor.”

With these new healthcare demands and the increased growth of “electronic medicine,” digital pathology is opening new doors for the pathology laboratory in the aim for better patient care. As part of reinventing the pathology laboratory’s role, pathologists must look for, and adopt, a variety of new tools that can help them successfully meet the demands for quick analysis, increased precision, immediate access, and expanded service. Today’s electronic technology is an accelerator, and digital pathology is quickly becoming a “prized tool” in the pathologist’s tool kit to help him or her in this transition. Digital pathology is allowing pathology laboratories in the clinical healthcare and life science arenas to engage, evaluate, and excel in a whole new dimension of transparency, consistency, and collaboration.

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Digital Pathology Yesterday and Today

History of Digital Pathology

Digital pathology has actually been around for several decades. It essentially started as photo microscopy the first time pathologists attached cameras to their microscopes and took static pictures that could be used for publications or to produce Kodachrome slides used for educational purposes. With the ability to utilize monitors and telecommunication services, telepathology was introduced in 1986, which then opened the door to practice pathology long distance using digital images.

Today, digital pathology has expanded to include whole slide images, whereby the glass slides can be converted into digital slides that can be viewed, managed, and analyzed; thus, increasing the tools pathologists need for providing today’s expanded diagnostic answers and services. Digital companies have been working diligently to develop and refine a variety of hardware and software solutions to fit in and improve the workflow of the anatomic pathology laboratory. Scanning throughput time has improved significantly and is beginning to solve the broad concerns many held around producing images quickly. Software and connectivity improvements are helping digital slides to be presented and managed in ways that mimic, and even improve upon, the current standard processes pathologists use with glass slides.

ePathology

The art of pathology is inherently a collaborative practice. Before rendering a diagnosis on a tissue sample, the pathologist relies on clinical input from the treating physician along with access to any additional test results (clinical or anatomic) that can supply information to be used in understanding the diagnostic questions that need to be answered from the specimen he or she is reading. Traditionally, pathologists may only get a small amount of clinical information from the treating physician. As technology now expands, the pathologist is gaining the ability to access information from other systems (ie, radiology, etc). The need to have all of the relevant information in a format that is easy to view while the tissue specimen is being read is being solved with ePathology and laboratory information system (LIS) connectivity.

ePathology provides an environment for managing and interpreting pathology information that is enabled by the digitization of a glass slide that presents with excellent color and fine structure resolution. ePathology’s goal is to allow the pathology lab to more easily and efficiently support patient care and assist in determining the patient’s proper treatment regimen.

Benefits and Advantages

An example of how far this technology has expanded its capabilities is Leica Biosystems’ Aperio ePathology Solutions™, which provides pathologists the ability to capture, manage, and move electronic images (eSlides) to help accelerate services such as remote access and sharing with their colleagues and/or collaborators anywhere in the world. Aperio ePathology is supported by an IT network backbone that allows managing and sharing eSlides by either a customer-managed database (within their own IT network), or by use of a remote secure cloud.

Once a digital scanner produces an eSlide, software-management programs provide a multitude of image-management options for the streamlining of accessioning, sorting, searching, and archiving. eSlide images can be presented and managed in eSlide folders that resemble the cardboard folders currently used in the lab (see Fig. 1). One can quickly pan and zoom the images just like moving a glass slide under the microscope and moving lens objectives. eSlides can be integrated into the laboratory LIS, and instantaneous recall of an eSlide replaces having to wait while a glass slide is pulled from a storage area, thus helping to improve workflow and turnaround time.

Aperio’s ePathology Solution is able to support remote, simultaneous, real-time viewing and convenient distribution of eSlides for intra-operative consultations and collaboration with other institutions and pathologists, thus saving transportation time and costs. The system also provides easy-to-use eIHC precision quantification tools, empowering the pathologist with advanced analytic capabilities that help standardize quantification of biomarkers to
improve accuracy and to work in tandem with today’s growing molecular programs, especially for targeted therapies.

The open and nonproprietary system also allows customers the opportunity to use their own solutions, which can be especially beneficial in the life sciences arena. Finally, digital images can be archived—eliminating the need to constantly pull glass slides from remote-site storage locations.

ePathology is not meant to replace the microscope entirely. “Pathologists are no longer asking if digital pathology is going to become a standard part of the operations of the laboratory,” Schwartz says. “They are now asking how is this going to be done, and how fast can they implement it within their own laboratory.”

**How ePathology is Reinventing Pathology’s Impact on Patient Care**

As discussed, advances in ePathology and the emergence of super electronic connectivity are being rapidly accepted for a multitude of purposes to improve workflow and help meet the challenges that clinical and research pathologists face associated with the growing and diverse biomolecular and genomic technology fields that are now driving personalized patient care.

Although whole-slide imaging for primary diagnosis is not FDA-approved on any of the digital pathology instruments in the United States, its promise of adoption has been boosted by such approvals in Canada and Europe. **Recent guidelines released by CAP** now provide laboratories with a rigorous guidance they can utilize to perform a CLIA validation of whole-slide imaging for diagnostic clinical use within their own laboratory.

Digital pathology is becoming a key player in the new healthcare paradigm, as witnessed by other companies such as GE and Philips (who led the digital revolution of radiology), now entering the pathology space with their own digital and software solutions. Thus, the drive to revolutionize and bring the art of pathology into the electronic age is taking on a whole new persona.

**The Shrinking Biopsy**

One of the biggest problems faced by pathologists today is the size of biopsy samples. Schwartz, along with Eric Glassy, MD, chairman, Digital Pathology Working Group, CAP, and medical director, Pathology Inc, Torrance, Calif, agree that the biggest problem pathologists face is that biopsies are getting smaller, leaving less tissue to work with as more biomarkers are introduced. They also note that tissue is becoming very valuable, and the pathologist must use every tool available to efficiently get every piece of information for a diagnosis.

As knowledge has grown that the biology of tumors is most often heterogeneous, pathologists are now faced with having to work with an increased number of stains along with molecular and genomic applications for many cases. These predictive and prognostic ancillary procedures are putting the pathologist in the role of writing an “Rx” for the diagnosis. This leads to a multitude of new procedures the pathologist must perform in addition to the normal H&E reading. Where in the past, pathologists were only required to review one or two ancillary IHC and special stained slides, now they often have to look at, compare, and quantify intensities of several stains across multiple slides. This involves the labor-intensive method of having to switch from slide to slide, remembering what was just seen on the previous slide, performing manual quantification for each stain, and then manually compiling the data for the report. ePathology now allows imaging of all stained slides, automatic quantification of the IHC stains, and then presentation of all of the tissue images (including H&E) side by side on one screen, for faster evaluation. The results are improved workflow and accuracy (see Fig. 2).

ePathology also assists the pathologist in accurately identifying specific areas of the tissue for application of new genomic technologies. With small tumor sections often nestled within a biopsy sample and the need to acquire adequate DNA sampling, viewing images at high resolutions and marking these small areas of tumor can help guide micro-dissection and ensure enough tumor sample is being retrieved for analysis. “Without the Aperio system, we would be stuck in the time-consuming practice of taking multiple low- and high-magnification images to share,” says Sean Downing, PhD, Foundation Medicine, Cambridge, Mass. “The latter practice is just not practical for our level of cases and doesn’t give you the ability to zoom as the images are static.”

**Collaboration**

Another key role that ePathology can play in helping pathologists become an active part of...
the patient's team and improve patient care is in the collaboration with internal and external colleagues. As molecular and genomic technologies rapidly secure their place in medicine, the demand for multi-physician collaboration of difficult cases is rising. Being able to quickly and easily share and view all of the multiple case images at one time with colleagues reduces time and costs, and helps provide a timely answer for the anxious patient.

Intraoperative consultations and radiology/pathology conferences are two examples of how digital images with connectivity solutions can further improve decision-making, reduce costs, and improve patient care.

**Intraoperative Consultations**

Intraoperative ePathology is showing promise as a way to address the costly procedure of the pathology department having to transport a pathologist from one hospital to another in order to cover frozen section procedures in both rural and urban settings. Rural settings often consist of hospitals that are 50-plus miles apart and are divided by natural barriers such as two-lane roads, mountains, water passages, etc. Pathologists who service multiple hospitals for frozen section service must drive these routes on a regular basis, which is costly, especially if only for a couple of procedures.

ePathology allows the pathologist to remain at his or her central laboratory and perform the specimen grossing via real-time viewing of grossing with the technician at the surgical site (see Fig. 3). Then, the intraoperative consult can be performed on the pathologist’s computer with digital images developed and electronically posted from the remote laboratory.

An example of how ePathology intraoperative consultations can reduce travel time and costs is illustrated by Northwest Pathology PS, Bellingham, Wash, which utilizes this electronic technology to provide services to PeaceHealth Ketchikan Medical Center, Ketchikan, Alaska. Miles of waterways separate the rural setting of the hospital from Northwest Pathology, resulting in long and expensive ferry rides for a pathologist to perform frozen sections. “This type of ‘intraoperative’ consultation using telepathology is just as accurate and timely as if the pathologist was right in the Ketchikan lab,” noted Berle Stratton, MD, FACP, in an interview with the Juneau Empire newspaper in 2010. “Now we can have immediate analysis of a frozen tissue sample for any type of surgery, even emergencies, conducted during normal business hours without the delay and expense of arranging for an on-site visit.”

Intraoperative ePathology and additional IT connectivity within the KU system, they were able to set up ePathology multidisciplinary conferences program that was developed at the University of Kansas Medical Center (KU), Kansas City, by Ossama Tawfik, MD, PhD, professor and director, Anatomic and Surgical Pathology, and Mark Redick, MD, PhD, assistant professor of radiology, Section of Breast Imaging.

**Radiology/Pathology Conferences**

Another example of how ePathology collaborations can provide better patient care and enable cost savings can be illustrated in a pathology/radiology audio-video conference program that was developed at the University of Kansas Medical Center (KU), Kansas City, by Ossama Tawfik, MD, PhD, professor and director, Anatomic and Surgical Pathology, and Mark Redick, MD, PhD, assistant professor of radiology, Section of Breast Imaging.

Literature studies have shown a radiologic-pathologic discordance of breast biopsies to be in the range of 1% to 6%, with 2% of benign cases being discordant. By developing a web-based, multidisciplinary audio and video conference in which pathology and radiologic images could be analyzed together, Tawfik and Redick set their goal to address the issue of any discordant results between mammography and radiology findings for all patients with benign diagnosis undergoing image-guided biopsies in the KU system. As radiologic imaging advances have emerged, radiologists are finding a significant decrease in the size of suspicious lesions to biopsy, which leads to those areas making up only a small part of the total tissue sample submitted to pathology. As part of their goal, Tawfik and Redick also wanted to ensure that adequate sampling had taken place, error reduction was recognized, a proper diagnosis had been reached, and that proper surgical/treatment plans had been realized.

The KU pathology department is located 1.5 miles from the cancer center. Finding time to travel between the two institutions to discuss cases was difficult for both physicians. Thus, with the ability to digitize slides and use ePathology and additional IT connectivity within the KU system, they were able to set up ePathology multidisciplinary conferences
where they could view the mammograms and the digital tissue images side by side and hold a discussion (see Fig. 4). Cases can include patients with mammograms +/- calcifications, masses, abnormal sonograms, etc.

Due to the continued demand by radiologists to further evaluate calcifications in tissue blocks that didn’t match imaging findings, a special radiology tray was invented for tissue sections that allows the radiologist to put the biopsy core in the tray, x-ray it, and mark the areas of interest. The lab was then able to embed the tissue in the same orientation as it was by the radiologist, thus providing a tissue “carbon copy” of the x-ray pictures.8

Results have been quite impressive for this KU program. In its first year (2009), with 534 total cases reviewed, discordant cases with a major impact to patients equaled 4.4%. As the conferences continued, a steady decline was seen in major impact discordance (2010: 2.9%, 2011: 1.6%, 2012 Q1: 1.3%).9

The results of this program have provided significant benefits to breast cancer patients at KU. “Once we started the pilot study, we never went back,” Tawfik says. “Our surgeons, oncologists, radiologists, pathologists, and even hospital administrators are demanding it now.” The pathology department is working to expand this type of collaboration with other services, starting with KU’s orthopedic oncologic surgeons who practice at a satellite hospital.

The KU conferencing program also drew the attention of the US Department of Health and Human Services. The department invited Tawfik and representatives from the University of California, Los Angeles (UCLA), (where video collaboration conferences are also performed), to Washington, DC, to discuss their programs and their benefits to patient care. As a result, the department published a report recognizing this type of electronic collaboration as a major step forward in improving workflow that could provide optimal communication of patient data and improved patient care.7

Research

Finally, just as the clinical healthcare sector is looking for new tools and solutions, so is the field of life sciences, which is responsible for the development of the new market of targeted therapies and companion biomarkers being used in the clinical space. Biopharma companies are faced with slowing pipelines, the need for reducing times for decisions to go forward or not with drug development, identifying predictive markers for stratification of populations, and providing safety/efficacy data. Research institutes are trying to leverage their expertise and provide new revenue streams through licensing of their discoveries. Contract research organizations (CROs) are looking for ways to differentiate themselves in a growing, competitive environment, while trying to retain costs. Similar to the clinical healthcare environment, life science players are faced with decreases in budgets, increases in workload, increasing needs for team communication (globally), and increases in accuracy and consistency so that the products they develop can clinically improve patient care.

Many of the same tools and solutions that ePathology is able to provide to the clinical side of medicine are being used in these research efforts. Specific research-related applications also provide a full menu of solutions that can help these institutions meet their new challenges and goals in a more cost-effective manner.

ePathology Benefits to Research

ePathology provides the ability for life science institutions to view eSlides from anywhere in the world, streamline collaborations with other institutions, perform external peer reviews, quickly summarize study results with integrated project tools, develop audit trails, and archive locally or in the cloud. All of this can be accomplished while meeting Good Laboratory Practice (GLP) compliance. ePathology also provides unique workflow solutions helping technicians, pathologists, CSOs, and IT departments in providing high throughput for large studies, while reducing time and costs.

ePathology provides an opportunity for the monitoring of imaging across integrated sections throughout development of a drug. Key image modalities can be brought together with the histopathology results. Thus, “A drug candidate can be treated like a patient,” says Steve Van Adestine, global digital imaging specialist – Early Development, Covance Laboratories Inc, Princeton, NJ.

Precision tools also exist for brightfield or fluorescence microscopy, allowing quantitative analytic capabilities for identifying predictive biomarkers using IHC or tissue microarray (TMA). As the new field of multiplexing (applying large numbers of biomarkers to one piece of tissue) expands, it is opening a whole new world for evaluating protein signatures in a tumor that can aid in determining how aggressive the tumor may behave and what courses of therapies may produce the best results. Digital imaging and ePathology analysis are playing an important role in this valuable technology.

Just as ePathology provides substantial improvements in clinical healthcare, these tools also provide key benefits critical to study results. “The virtual microscopy-based methodology increases accuracy and reproducibility. Moreover, it provides a permanent record of retrievable data with full transparency in clinical trials,” as noted by Barisoni, et al, in a recent study on using quantitative methods by virtual microscopy in patients with Fabry Disease.10
The Future of ePathology

The applications of ePathology are limitless, just as we have seen with the expansion of other electronic technologies. The future of ePathology will be driven not only by the need for its presence in the everyday life of the pathology laboratory, but also by the visions of pathologists to expand its capabilities as it becomes a standard in laboratory operations. Already, applications can make it possible to retrieve data and view eSlides on other electronic devices such as smart phones and tablets. With secure connectivity solutions, a pathology report with digital images can allow the physician to click the image and open the entire digital slide to review or share with a patient. “ePathology will continue to become more useful to the pathologist,” Glassy says. “There will continue to be gradual adoption over many niches. Adoption will also be driven by unique software and workflow improvements that will continue to increase the ability for tasks to be done digitally that can’t be done with glass slides, even on H&E slides.” ePathology will also provide more standardized criteria for areas with high variables such as cytology and cervical intraepithelial neoplasia (CIN) cervical cases. “Consistently applying criteria across pathologists’ computers will also improve quality control (QC), accuracy, allow more consistent sharing, improve income sources, and ultimately improve patient care,” Glassy says.

In summary, as the pathologist now steps into his or her new role as interpretive director and clinical adviser, ePathology provides a flexible and powerful tool that can help pathologists meet the challenges and reinvent the role of the pathology laboratory to one of a dynamic leader in today’s new healthcare environment.

REFERENCES

Applications make it possible to view eSlides on multiple electronic devices.
Leica Biosystems and Aperio ePathology: Stronger Together

With its acquisition of Aperio, Leica Biosystems now offers a full range of products for each step in the pathology process, from sample preparation and staining to imaging and reporting. Combined with the Leica Biosystems capability, the Aperio ePathology solution suite now enables users to manage images from the complete range of ePathology capture platforms for H&E, IHC, FISH and immunofluorescence samples through a single interface, ensuring secure and rapid access to eSlides for remote, real-time viewing and distribution. Now, pathologists can have the right tools on a seamless pathology image management platform.

PATHOLOGISTS HAVE THE RIGHT TOOLS WITH LEICA – APERIO PARTNERSHIP

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HOW ePATHOLOGY IS BEING USED TODAY

More than 30 pathologists at a major California university are currently using ePathology to market their sub-specialty expertise and provide real-time pathology eSlide sharing. Patients with complex cases can have their pathological images scanned and reviewed for expert opinions.

A lab group in Washington provides ePathology services to access and view slides in Alaska, allowing surgeons in the operating room interoperative consultations with pathologists in Washington.

A well-known US Clinic employs a multi-site implementation to “connect” their pathologists, eliminating slide shipping, reducing recuts, and ensuring that patients have ONE experience and access to the pathology expertise of the entire organization.

Let us show you how our integrated system can convert your glass slides to electronic format and allow you to compare different information, conduct quantitative image analysis, and use the right tools to gather information from the patient’s sample so that you can more easily share findings.

For more information please visit: www.LeicaBiosystems.com/ePathology

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