Pathology Education Powered by Virtual and Digital Transformation

Now and the Future

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• *Context.*—Myriad forces are changing teaching and learning strategies throughout all stages and types of pathology education. Pathology educators and learners face the challenge of adapting to and adopting new methods and tools. The digital pathology transformation and the associated educational ecosystem are major factors in this setting of change.

***Objective.*—To identify and collect resources, tools, and examples of educational innovations involving digital pathology that are valuable to pathology learners and teachers at each phase of professional development.**

***Data Sources.*—Sources were a literature review and the personal experience of authors and educators.**

***Conclusions.*—High-quality digital pathology tools and resources have permeated all the major niches within anatomic pathology and are increasingly well applied to clinical pathology for learners at all levels. Coupled with other virtual tools, the training landscape in pathology is highly enriched and much more accessible than in the past. Digital pathology is well suited to the demands of peer-to-peer education, such as in the introduction of new testing, grading, or other standardized practices. We found that digital pathology was well adapted to apply our current understanding of optimal teaching strategies and was effective at the undergraduate, graduate, postgraduate, and peer-to-peer levels. We curated and tabulated many existing resources within some segments of pathology. We identified several best practices for each training or educational stage based on current materials and proposed high-priority areas for potential future development.**

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We could just as well be writing this paper with a manually powered typewriter, or with ink drawn from a well by a quill pen, had not a series of revolutionary changes swept the world during the past 200 years.[1] The beginnings of modern pathology, too, date back about that far. The knowledge and skills of pathology's pioneers have been painstakingly transmitted by progressively more ingenious advances that have mirrored the social and technological changes of each successive epoch. Now, standing on the crest of yet another wave of change, driven by artificial intelligence (AI) and machine learning,[2] pathology educators may soon be challenged to convey the best ways to apply these tools to the problems of

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diagnostic pathology to the coming generation of learners and the present corps of practitioners.[3] Hence, this collaborative effort aims to describe the genetic code governing the transmission of pathology knowledge to subsequent generations of medical professionals.[4] We aim to expose not just the code but also the supporting array of catalysts, enhancers, and other cofactors now in place to ensure we have a robust and potent supply of pathologists.

Understanding pathology is fundamental to understanding medicine, and our understanding of pathology is influenced by the tools or means by which our knowledge is derived or demonstrated. Pathology's foundational goal is to advance patient care and disease prevention through the enhanced understanding of pathogenesis, diagnosis, and prediction of therapeutic response. However, the tools that have long been standard for gaining a deeper understanding of diseases, such as the autopsy, the microscope, and laboratory chemistry, have been augmented during the past generation by a dizzying array of new methods and tools. Along with this increase in technology and understanding has come the challenge of teaching pathology, in its ever-deepening comprehension of disease, to both new students entering the field and those currently engaged in practice. For example, the microchip and related digital devices, which have been part of this most recent revolution, have changed not just our understanding of disease but also our capability to teach, in different and perhaps better ways, the increasingly vast knowledge that needs to be understood to treat patients, develop new treatments, and potentially prevent disease. Digital applications in pathology, ranging from digital slide banks to digital texts or virtual reality–driven dissection, are just a few of the promising tools now available to accomplish the educational challenges of modern medical and pathology knowledge and practice.

With the understanding that something new or novel (ie, teaching using digital pathology [DP] tools) is not necessarily better than its traditional counterparts, our purpose in this review of pedagogic tools in the DP era is not just to acclaim the virtues of sensational digital teaching methods for pathology, but to provide a resource and compendium of data and experience that have been demonstrated to be effective, even as a pandemic or other demands have required changes.[5,6] Where possible, best practices are referenced with tangible examples and resource materials. Areas needing further research to demonstrate feasibility and value are also highlighted to motivate further work and creativity.

Social media phenomena have revolutionized how we acquire and share information, and hence will be interwoven into many sections of this work.[7–9] The effective use of social media platforms can enable facile interchange between international experts and novices alike, knowledge acquisition by students and educators to reach vast new audiences. This democratization of teaching and learning is a vital feature of the current pathology educational paradigm, which may help tremendously in coping with the global health care challenges ahead.

The scope of this effort includes resources of digital pathologic images, such as whole digitized slides as well as the surrounding ecosystem (software and related technology) incorporating whole slide imaging (WSI) and similar electronic or virtual resources that will be helpful for students and practitioners at all stages of their professional career. We will identify how digital tools and virtual methods either support or confound the educational process, and highlight what has been gained from 20 years' experience with these tools at the undergraduate level (UME). Going further, we will detail the myriad ways these tools and methods can impact learning in the graduate (residency and fellowship [GME]), postgraduate (continuing medical education [CME]), peer-to-peer, and patient domains and illustrate how the ecosystem associated with these tools can impact both conventional educational settings, such as large pathology professional meetings, and even clinicians' presentation of pathology results to patients. (As used here, peer-to-peer education, as distinct from CME, refers to nonaccredited activities, such as tumor board interactions, the study of commercially provided training materials such as for a newly introduced biomarker, or social media educational interchange between professional peers.)

EDUCATIONAL THEORY, LEARNING EFFICIENCY, AND OPTIMIZATION

Medical education continues to transform. As understanding of how learners learn best accrues, as does that on what circumstances impede learning, it is important to apply that knowledge to the context of pathology education. This new educational paradigm has been recently reviewed by Koch et al.[10] Terms and concepts such as "flipped classroom," "cognitive load," "adaptive learning," and others should be familiar to pathology educators in order to optimally use the newly developing tools in the digital environment.

APPLYING DP IN UNDERGRADUATE MEDICAL, DENTAL, VETERINARY, AND ALLIED HEALTH EDUCATION

Beginning in 1985, this technology has been progressively more widely implemented in undergraduate medical, dental, veterinary, and allied health (nursing, pharmacy, medical technology, etc) education platforms in the United States and internationally.[5,11–26]

As noted above, virtual microscopy laboratories, available on personal devices or in school-based computer labs, have replaced fixed laboratories housing gross specimens, boxes of glass slides, and student microscopes. WSI with links to supplementary resources, such as gross and radiologic images and additional study material, provide enrichment for the teaching and learning experience in the new virtual environment. The ease of deployment of new cases, or of updating existing materials, makes this scenario attractive to course administrators and educators. Additionally, smaller doses of enriched DP material, such as digital slides within a lecture or PowerPoint (Microsoft Inc) slide deck, can be included in courses that may previously not have included lab or microscopy exposure.

Although mastering Kohler illumination and other microscope idiosyncrasies may not be an essential core competency for all practitioners, all medical fields, including allied health fields like dental and veterinary medicine, require a strong understanding of the principles and practices of pathology. Hence, significant exposure to microanatomy and the laboratory methods of pathology underpinning so much of diagnosis, therapy, and management is foundational. DP provides an opportunity to rectify this problem because students using WSI in the virtual setting generally spend more time interacting with the material and performing as well or better on evaluations than historic groups using fixed microscopy laboratories. Additionally, many more students can be reached in this model.

This principle was demonstrated by a recent online pathology course implemented at the University of Washington in Seattle.[15] Cancellation of in-person clerkships because of COVID-19 created a need for online instruction for students as far away as Alaska or North Carolina. The virtual pathology course created to address this need resulted in a large increase in the number of students engaged in pathology education. Learners judged this a success. The lack of in-person contact was more than compensated by the sheer number of students who were engaged.[15] Importantly, although the COVID-19 crisis sparked an immediate need for innovation in online pathology education, the advances that have been made will allow more students to be taught effectively after the pandemic.

It is crucial to remember that effective online learning is more than just lectures delivered via online presentation software. Luckily, virtual learning is especially applicable to pathology because many of our tools (eg, WSI) have been adapted for online use. Obviating the need for microscopes and classroom space, online platforms allow students to explore basic histology and pathology from any location. Using PathPresenter software (https://pathpresenter.net/), University of Washington students previewed curated slide sets and then discussed in small-group settings. WSI was used as part of case-based activities in which students were given a patient presentation and then worked the slides up virtually, ordering lab tests, imaging, and biopsies, and receiving results in real time. These small-group activities encouraged increased participation and helped foster a sense of community.[15]

For those students who are considering a pathology career but cannot complete an in-person elective, traditional clerkship activities can also be accomplished virtually.[16,27] Students can attend sign-out via Zoom (Zoom Video Communications Inc) meetings, during which faculty can share images from microscope cameras, the virtual equivalent of a multiheaded microscope. Furthermore, digital tools create opportunities for even more interaction. For example, Zoom has an annotation function that allows users to draw on the screen. Educators can ask students to circle neoplastic cells or point to mitotic figures. Students can highlight areas they have questions about. These tools make virtual sign-outs arguably better than their in-person counterparts. Similarly, scanning frozen section slides and having students drive the slide, allowing them to direct the examination to develop their own diagnoses, has also been successful.

Although important in any learning model, organization and clear communication are even more essential for online learning. Whether organized locally or globally, a centralized database for accessing class materials, including readings, videos, schedules, and, most importantly, one-click links to real-time sessions, is highly useful. Communication with students should be issued via a single mechanism (eg, email, learning management system, or text) to reduce confusion. Microsoft Teams (Microsoft Inc) or other similar group-work tools have been found to be useful for real-time communication with students while classes are not in session and to address any technical issues while students are trying to access class.

Online education also allows for asynchronous learning, meaning that students can access prerecorded lectures and other materials on their own time. This approach is more flexible for learners and reduces the amount of scheduled time for educators. The Laboratory Medicine course at the University of Washington used this strategy, scheduling time during the week to discuss previously recorded lectures.[28] For pathology education outside of individual institutions, innovative Web sites, such as PathElective (https://www.pathelective.com/), provide free, high-quality, organized, and adaptable pathology elective experiences for any willing medical student. Passive content, such as video lectures, is also an asynchronous option that has been used successfully.[29]

Some newer methods of teaching pathology include incorporation of video games into the curriculum.[13,17,19] For example, in the "Discovering Pathology" serious game, developed by the University of Franche-Comté (Besancon, France), students follow the progress of a pathology specimen within a laboratory and use macroscopic images and digitized slides to come to a diagnosis. Such games challenge students to increase their motivation and offer learners insight into their knowledge gaps. Some programs additionally include 3-dimensional (3D) images of pathology specimens in their virtual slidebox, which also enhances students' learning.[22]

The University of New South Wales in Kensington, Australia, has spearheaded an online repository of biomedical education resources called the BEST network, which stands for Biomedical Education, Skills and Training.[30] The network uses adaptive e-learning techniques consisting of virtual patients, dissecting rooms, clinical laboratories, and diagnostic tools. The site is targeted at students and professionals in medicine and is free to join. "Slice" is the name of its image-based online learning and teaching platform. It contains more than 21 000 digital images for pathology, histology, anatomy, and radiology with more than 200 000 shared annotations. Whole slide images are a prominent feature. Educators can choose from many prerecorded video lectures and presentations. The site includes a course builder, allowing upload of individual content or the use of static and whole slide images from the Slice image repository (Figure 1).

The incorporation of DP into the curriculum has been cited as being user-friendly and advantageous because of the ease of accessibility globally. Furthermore, digital game–based learning in undergraduate pathology courses led to "improvement in academic performance, such as test scores, and increased student satisfaction and engagement."[21] In countries like Australia, DP has helped to improve the quantity, quality, cost, and accessibility of pathology teaching to regional medical schools and rural clinical practices. In dental schools as well, the trend for teaching has moved from light microscopy to virtual microscopy because the latter encourages student-focused learning.[5,11–22,25]

DP IN GME

GME, residency and fellowship, is, in some ways, a natural starting point and stumbling block for digital-empowered pathology education. In a single day, a resident might attend a didactic lecture, present at a tumor board, perform a fine-needle aspiration, interpret cytology and order related molecular testing, review slides from an autopsy, and cut an after-hours frozen section while being

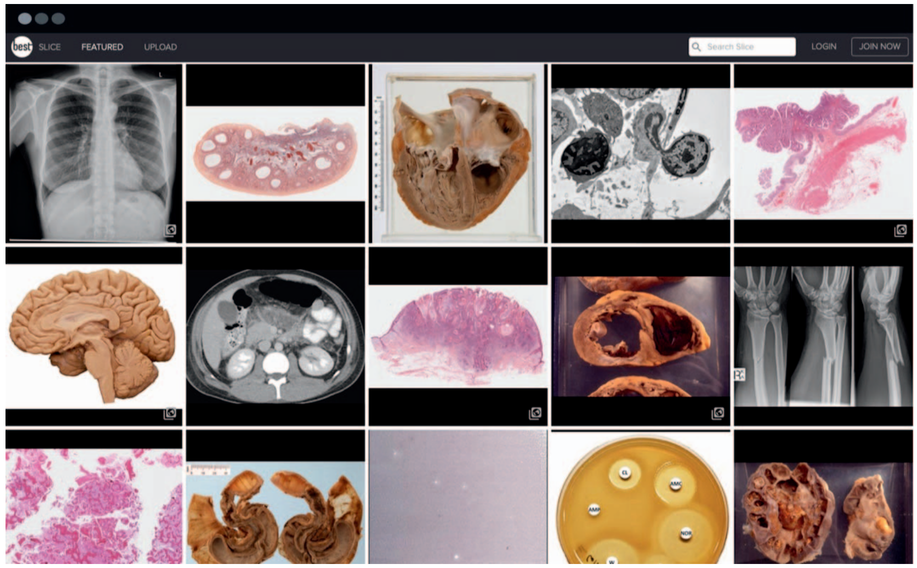

Figure 1. *Sample page from the Biomedical Education, Skills and Training (BEST) network Slice archive.*

on call. Each of these activities presents an opportunity for incorporating DP into their education in a way that enhances the experience.

Anatomic Pathology

Surgical Pathology.—As the main branch of anatomic pathology, surgical pathology practice covers gross and microscopic examination of surgical specimens, including biopsies and resections. Long before DP, most surgical pathology education did not reflect current optimal use cases for technology such as DP. Proficiency with DP or telepathology is understandably not yet mentioned in the Accreditation Council for Graduate Medical Education (ACGME) Milestones or program requirements.[31] Yet, new and accelerated initiatives driven by COVID-19 appear to be moving educators toward greater incorporation of DP (Table 1). In a survey of practicing pathologists, none (n=0 of 34) stated that their experience with DP during the pandemic had caused them to decide against using it in the future.[32] If remote sign-out and conferencing is the new norm, as experienced by students during a pathology elective,[15] they may expect remote residency-level didactics as well. Although many DP resources are available online, lack of updates, inconsistent topic coverage, and stale links pose problems. Endeavors to curate and collate these digital resources have been intermittent, and more recently, an ongoing curated clearinghouse of these materials has been proposed as a part of a *Residency in the Cloud*.[33] The Digital Anatomic Pathology Academy, discussed in the section Confronting Barriers below, also addresses the challenge of quality, curated surgical pathology materials for education by sourcing the digital content from reputable pathologists and institutions.

The utility of DP in surgical pathology education is well established, with many novel and mainstream resources in wide use, as evidenced by the size of Table 1. Core skills, such as feature identification, differential diagnosis, annotation, photography, description, and presentation, are enhanced by the use of DP resources.[3,34,35] The manner of use of these materials also appears to be important in overcoming digital hesitancy in certain learners. Routine incorporation into unknown conferences, teaching sets, and tutorials may enhance and accelerate learning (L.A.H., unpublished data).[35]

Virtual reality may also have a useful role in surgical pathology education, particularly in the area of teaching grossing techniques.[36] Other tools to enhance gross pathology education using digital devices, such as smart glasses, are being investigated but have not yet shown direct educational value.[37,38]

Cytopathology.—Cytopathology is a branch of anatomic pathology that focuses on disease manifestations at the cellular level. Education efforts in cytology have embraced digital tools such as WSI for many years. This includes virtual teaching slide sets, online atlases,[39,40] and proficiency testing (PT). When coupled with the Internet, digital images have proven to be very effective for education. The Cytology Education Learning Lab Web site from the American Society of Cytopathology is filled with digital images to engage learners. Videos showing various aspects of fine-needle aspiration techniques have also been used.[41,42] Videos capturing live sessions of rapid onsite evaluation using video microscopy have also shown promise as an effective teaching tool.

Purely didactic virtual lectures have also been offered by the American Society of Cytopathology in response to the pandemic.[43] Online (virtual) education was useful even prior to the COVID-19 pandemic because end users saved time and money, making high-quality cytology education affordable and within reach of cytologists and trainees around the globe. Since the COVID-19 pandemic, we have seen an even greater transition away from traditional tools (eg, glass teaching slides, textbooks, didactic lectures) and toward more accessible online resources (eg, digital slides, Web sites, webinars, social media) in cytology education and training.[44,45] Today, it has become commonplace in postgraduate training courses for WSI cases to be offered online in advance of conferences, greatly diminishing the complex logistics and costs associated with manually mailing glass slides to participants. Commercial software solutions (eg, PathXL, Koninklijke Philips, Nevada) that support a variety of media, including WSI, are effectively used by some cytotechnology schools in the United States. Eye tracking with digital cytology images has been demonstrated to be effective for tutoring cytotechnologists.[46] Annotated digital slides for cytopathology are included in the high-yield cases section of the Digital Anatomic Pathology Academy as well as through other PathPresenter platforms operated in

Table 1. Digital Pathology and Other Online Resources for Learning Surgical Pathology

Resource	Description	URL[a]
Cases		
American Society of Dermatopathology	Case of the month	https://www.asdp.org/education/case-study-of-the-month/
California Tumor Registry	Case of the month—static images and extensive discussion	http://www.cttr.org/
College of American Pathologists	Case of the month—general pathology, WSI	https://www.cap.org/member-resources/case-of-the-month
Genitourinary Pathology Society	GU pathology, case of the week, static images	https://www.gupathsociety.org/COW-2021-13
International Society of Urologic Pathology	Case of the month—GU pathology, WSI, need ISUP membership	https://isupweb.org/isup/
OSU	Case of the week	https://pathology.osu.edu/COTW/default.aspx
Pulmonary Pathology Society	Pulmonary pathology, static images, case of the month	https://www.pulmonarypath.org/cotm/cotm_current.html
UPMC	Case of the month, static images	https://path.upmc.edu/casemonth/ap-casemonth.html
Atlases		
Leeds	General WSI	https://www.virtualpathology.leeds.ac.uk/
MGH pathology	General pathology, frozen sections WSI	https://learn.mghpathology.org/index.php/WSI:study
Pathpresenter	Platform for sharing slides or images	https://pathpresenter.net/
Rosai Collection	General pathology, Imagescope	https://www.rosaicollection.org/
University of Michigan	General pathology, WSI	https://www.pathology.med.umich.edu/apps/slides/
University of Oklahoma	WSI, quizzes, atlas	https://www.ouhsc.edu/pathologyJTY/OUMC/Default.htm
University of Utah Webpath	Static images covering many areas	https://webpath.med.utah.edu/
Didactic		
Webpathology	Static images	https://www.webpathology.com/
Johns Hopkins Unknowns	Quiz format, static images (email address is requested to access)	http://apps.pathology.jhu.edu/sp/
PathCast	Video didactic lecture series, ongoing, dating to 2016	https://pathologycast.com/index.php?title=pathCast
PathologyOutlines	Opensource textbook with digital slides and video links on many topics	https://www.pathologyoutlines.com/
Other		
DAPA	Requires DPA membership (free to trainees)	https://digitalpathologyassociation.org/digital-anatomic-pathology-academy
Kiko	Platform to share medical data in many formats (requires account; free to obtain)	https://kikoxp.com

Abbreviations: DAPA, Digital Anatomic Pathology Academy; DPA, Digital Pathology Association; GU, genitourinary; ISUP, International Society of Urological Pathology; KiKo, Knowledge in, Knowledge out; MGH, Massachusetts General Hospital; OSU, The Ohio State University; UPMC, University of Pittsburgh Medical Center; WSI, whole slide images.

[a] All URLs accessed December 21, 2021.

collaboration with the International Academy of Cytology and the College of American Pathologists (CAP).

A recent *CAP Today* article nicely summarized progress in virtual cytology education as a result of the pandemic.[45] Table 2 delineates several valuable online resources for cytology education.

Autopsies and Forensics.—Autopsy pathology, including medical autopsy and forensics, represents a unique challenge and opportunity in DP for resident and fellow education, particularly as the number of cases continues to fall at many institutions (Table 3). Studies have shown that residents performing autopsies with supervision over videoconferencing is feasible.[47] At the University of Michigan in Ann Arbor, a new gross pathology video camera was installed for brain cutting, allowing these sessions to be broadcast (Figure 2). This allows for remote education and physical distancing during the COVID-19 pandemic. However, the impact of broadcasting such sessions on resident education is unclear.

Augmented reality technology, such as Google Glass (Alphabet Inc) and Microsoft HoloLens (Microsoft Inc), have been effectively used during autopsies to support remote education, but this currently remains largely experimental and, although promising, more investigation remains to be done.[48] Virtual autopsy and forensic cases are presented by a variety of Web sites, usually with accompanying images and occasionally digital slides.[49] Both of these means offer hope to trainees seeking to develop and retain postmortem evaluation skills as autopsy numbers decline, or for areas where cultural or religious barriers to such examination exist.

CLINICAL PATHOLOGY

Molecular Pathology and DP Education

Molecular pathology is a powerful new subdiscipline of pathology that is key to precision medicine–based approaches in oncology. Thanks to the Human Genome

Table 2. Cytopathology Digital Learning Resources		
Resource	**Description**	**URL[a]**
IAC	60 illustrative cases from Gyn and non-Gyn domains	https://www.cytology-iac.org/educational-resources/case-of-the-month
CELL	Joint endeavor by several organizations on a wide array of topics	http://cytologyedlab.org/?fbclid=IwAR1xMKIB3Mv_Nvk6w73cmL3q-3fBHx2aeeOnGasw7BT4iuCuocD9dYodKAw
Papanicolaou Society of Cytopathology	FNA videos, case of the month, fixed-image atlas	http://www.papsociety.org/education/
DAPA	High-yield cases in cytology (DPA membership required; free to trainees)	https://dpa-dapa.com/
Eurocytology	Virtual slides linked into courses, with assessments	https://www.eurocytology.eu/en/virtual-slides
PathoBasic Cytology	Fixed images of cytology of many organ systems	https://forumep.wordpress.com/
Cytopath1951 (ASC channel)	Video didactics in cytology	https://www.youtube.com/user/cytopath1951

Abbreviations: ASC, American Society of Cytopathology; CELL, Cell Education Learning Lab; DAPA, Digital Anatomic Pathology Academy; DPA, Digital Pathology Association; FNA, fine-needle aspiration; Gyn, gynecology; IAC, International Academy of Cytology.

[a] All URLs accessed January 6, 2022.

Project[50] our knowledge of the molecular basis of disease continues to expand exponentially. Molecular pathology assays have a key role in establishing patient diagnoses (eg, characteristic mutations of *EGFR* in lung cancers and the mutational spectrum in myelodysplasia).

Pathologists have traditionally established diagnoses using histomorphologic assessments of tissue samples. However, the modern pathologist has an armamentarium of supporting techniques (eg, immunohistochemistry and molecular pathology) to diagnose patients, with increasing diagnostic precision. The number of biomarkers at a pathologist's disposal continues to expand each day. This creates a challenge in mastering interpretation of new stains and tests for both trainees and practitioners. In addition to diagnosis, molecular pathology plays a key role in providing information about a patient's prognosis and the therapeutic options available to clinical oncologists.

Interest in understanding molecular-histopathologic correlations drawn from a combination of deep learning/AI techniques and DP images of disease entities continues to increase.[51] For example, in 1 study, colorectal cancer samples were trained using deep learning approaches to infer a genotype using histology.[52] Although it would be naive to hope that all forms of genetic mutations will be identified based solely on histology, such studies indicate that there is an ongoing reassessment of major histopathologic features associated with disease at the genomic level (histogenomic correlations). Studies like these are likely to have a dramatic impact on the adoption and use of DP tools in the near future.

Although there is much excitement around the use of deep learning/AI/DP for both diagnostic and educational purposes, there is also ongoing development of WSI and advanced microscopy techniques for multiplexed molecular biomarker detection.[53] Another key area of interest is in identifying spatial biomarkers in histology slides that are predictive of patients' responses to immuno-oncologic therapies (eg, tumor-infiltrating lymphocytes).[54,55] Thus, DP is enabling quantitative and semiquantitative assessments of histopathology slides in combination with

Table 3. Autopsy and Forensic Resources for Online Virtual and Digital Learning	
Resources	**URL[a]**
Guidelines	
CAP—autopsy reporting protocol	https://documents.cap.org/protocols/ap-autopsy-adult-20-02.pdf
CDC—characteristics of death requiring investigation/autopsy	https://www.cdc.gov/phlp/publications/coroner/investigations.html
CDC—improving cause of death reporting	https://www.cdc.gov/nchs/training/improving_cause_of_death_reporting/
NAME—death certification	https://www.thename.org/death-certification
Royal College of Pathology—autopsy guidelines series	https://www.rcpath.org/profession/guidelines/autopsy-guidelines-series.html
Training courses and other resources	
NIJ—online training courses	https://nij.ojp.gov/nij-hosted-online-training-courses
Virtual autopsy	https://australian.museum/learn/teachers/learning/virtual-autopsy/
	https://www.le.ac.uk/pathology/teach/va/titlpag1.html
Pathology expert	http://www.pathologyexpert.com/links-lectures/
Pathology outlines	https://www.pathologyoutlines.com/autopsy.html.
Case reports	
NAME—cases of the week	https://www.thename.org/educational-activities-committee
Autopsy case reports	https://www.revistas.usp.br/autopsy

Abbreviations: CAP, College of American Pathologists; CDC, Centers for Disease Control and Prevention; NAME, National Association of Medical Examiners; NIJ, National Institute of Justice.

[a] All URLs accessed February 11, 2022.

Figure 2. *Doctors prepare for brain-cutting session with streaming video.*

molecular and genomic biomarkers to drive personalized patient diagnoses and prognoses. Thus, facility with the use of DP becomes a vital pathologist competency in order to provide optimal patient care.

Key developments, such as those mentioned above, in slide-based histopathology and molecular pathology will translate to novel tools for DP education in the near future. DP tools will be useful for general pathology education, virtual interaction and communication, and online and in-person tutoring of pathologists and nonpathologists. These tools and types of interactions are critical because many training and practice settings do not have primary access to vast arrays of molecular testing, but pathologists will play key roles in determining the use and interpretation of data from advanced molecular testing. Importantly, DP tools will be highly useful for molecular tumor boards, a critical nexus to review oncology treatment plans in a highly collaborative and interdisciplinary manner. DP tools, along with the molecular genomic data of a patient, will be key (beyond the anatomic pathology report alone) to communicate complex diagnostic information to clinical colleagues in the near future. Development and research into the optimal means of engaging learners and assessing competency in molecular pathology are areas needing further research.

The fairly recently deployed Training Residents in Genomics, originally conceived in 2010, has begun to fill some of this training gap in molecular pathology, with promising early results.[56–60] Although it was originally developed for team-based learning in person, Training Residents in Genomics now offers a series of online modules that simulate an in-person team-based setting. Comparable materials have been developed for UME and GME as well.[61]

Hematopathology

Hematopathology bridges anatomic and clinical pathology, involving both laboratory testing and morphologic assessment of fluid and tissue specimens. As a result, hematopathology specimens are routinely processed and analyzed by a variety of clinical and nonclinical practitioners. Morphologic assessment of specimens is performed not only by pathologists but also by clinical laboratory personnel and clinical hematologists, all of whom require timely access to materials and appropriate training. DP offers novel solutions to this challenge.

Historically, DP's application in hematopathology has been impeded by the requirement for high magnification, oil immersion objectives, and, in some cases, multiple focal planes.[62] With improvements in scanning technology, these hurdles are becoming less significant, and there is increasing interest in WSI and DP for hematopathology. DP can be used for several hematolymphoid sample types, including peripheral blood smears, bone marrow aspirates and cores, and lymph node and tissue biopsies; each presents opportunities and challenges for educational applications.[63] Of these, DP is currently best established for peripheral blood review.

Identification of peripheral blood elements and leukocyte subsets is essential to the diagnosis of hematologic diseases, and manual analysis of peripheral blood smears is labor-intensive and subjective. Automating this process saves time and money for laboratories and increases consensus.[64] Several companies have developed automated scanners that use computational methods to identify cells via morphology. As early as 2001, the DiffMaster Octavia (CellaVision AB) received US Food and Drug Administration (FDA) approval,[65] followed closely by the CellaVision DM96 (CellaVision AB) automatic hematology analyzer in 2004.[66] Both devices have the capacity to locate and identify peripheral blood elements using image analysis, with end-user verification of results.

Peripheral smear digitization enables multiple users to access materials simultaneously, tag areas of interest for review or education, and share digital slides. As with other WSI, all images can be stored indefinitely. This flexibility facilitates teaching in real time and enables the collection of teaching sets.[67] Additionally, digital platforms can be used as dedicated training tools. CellaVision, for example, offers the CellaVision Classroom Initiative, which is a free program providing tools and resources for laboratory technician educators and students. CellaVision CellAtlas, a cell phone application with mini-lectures and a cell image library, is also available to provide an introduction to cell morphology.[68]

The ongoing challenge of imaging 3D specimens, such as bone marrow aspirate smears and body fluids, has slowed the adoption of DP for bone marrow morphologic assessment. Now, advancements in WSI technology can overcome this challenge by acquiring image data from sequential focal planes, a process called z-stacking.[69] Already, several methods for morphologic assessment of aspirate smears have been developed,[63,70] although none are currently FDA-approved. The rapid development of these technologies will provide expanding opportunities for training in the future.

Urine Sediment Analysis

Despite technologic advances automating the evaluation of urine sediment in clinical laboratories, manual review by trained personnel is still necessary. Examination of urine sediment from a healthy patient is usually unremarkable because it normally is cell-free, contains no crystals, and has very little protein. For patients with urinary tract disease, microscopic examination of urine sediments can provide a noninvasive insight into acute and chronic diseases of the urinary system, including acute kidney injury, acute tubular necrosis, hematuria, and proteinuria.[71]

Automated analyzers and digital analyses of urine sediment in clinical laboratories have become routine in many locations. Studies have shown that the results of automated analyses are similar to those of manual review when comparing identification of erythrocytes, leukocytes, and epithelial cells within the sediment. When evaluating for urinary casts, however, there was no concordance, and manual review provided important additional information.[72]

Before automation and centralization, urine sediment microscopy was performed not only in central laboratories by medical technicians and pathologists but also in clinical settings by nephrologists and other trained clinicians; urine sediment microscopy is also used in veterinary medicine.[73] Despite the need for manual review and the ease by which a specimen can be obtained and examined, provider-performed urine microscopy has diminished, and the skills needed to carefully examine urine sediment are waning. Hence, interobserver reliability of urine sediment analysis shows significant variability.[74] The use of digital microscopy for teaching urine sediment evaluation can help ensure that everyone performing specimen review has the skills needed to provide accurate diagnoses.

Multiple methods for using digital technologies teach and determine competency in urine sediment analysis after training have been attempted, both as private institutional as well as public education resources on the Internet. Training resources vary from single-field digital images, which are the most common, to virtual microscopy teaching sessions using live microscopy.[75] No documented uses of full-slide scanning of urine sediment specimens with annotations or z-stacking have yet appeared.

Single-field digital images have several advantages for teaching urinary sediment evaluation. Digital images are easily captured with a variety of devices, ranging from small handheld phones with microscope adapters to digital cameras integrated or permanently affixed to microscopes that are used for routine evaluation.[76] Captured images are relatively small-sized files, allowing for easy portability, transmission, and use across multiple platforms, from electronic presentation software to Web site integration. Images can also be annotated to enhance value.

Live remote microscopy has several advantages compared with single-field digital capture, including the ability to scan a slide and include multiple planes of focus. Robotic microscopy allows multiple users to drive the slide, but only a single slide on the stage can be viewed. Annotations can be made in real time, and conferencing of multiple users is possible. The ability to use microscopes used for the routine evaluation of urine sediment allows trainees to simulate urine sedimentation examination, per documentation guidance outlined by the Centers for Disease Control and Prevention, which includes multiple magnifications (10× and 40×) and either brightfield or phase-contrast microscopy.[77]

Whole slide digitization of urine sediment specimens in multiple planes would provide ideal real-world training simulation experiences for end users. Trainees could examine an entire slide without annotation to gauge their skills identifying various disease states. Annotation layers can be applied after review to ensure all pertinent findings have been identified. Libraries containing common and rare urine sediment findings for disease entities could be compiled. Issues complicating the use of whole specimen imaging, however, include the current lack of phase contrast or polarization ability.

After training has been completed, multiple opportunities are available for PT, including those offered by the CAP, American Academy of Family Physicians, American Association of Bioanalysts, and the American College of Physicians. Refer to the Competency Assessments and the PT and Competency Assessments sections in this paper for more information.

PEER-TO-PEER AND PATIENT EDUCATION

The days of the stereotypical bashful pathologist trying to share microscopic images with a high-intensity projection microscope or displaying a Kodachrome slide photomicrograph to attempt to communicate pertinent findings to a multidisciplinary tumor board have thankfully mostly faded into remote history. The adoption of WSI for tumor boards has brought the depth and beauty of pathology to the peer-to-peer educational and clinical care sessions in a manner that can compete with the picture archiving and communication system–enabled display of countless radiographic images. High-quality low-magnification images help to bridge the gap between grayscale radiographic gross images and the microscopic anatomy that needs to be understood for precision medical care. Consequently, surgeons' and oncologists' familiarity with microscopic details appears, at least anecdotally, to be increasing far beyond the blue-is-bad level of sophistication.[78]

DP images, whether fixed-field or WSI, have proliferated through social media platforms (Table 4) and become a staple of peer-to-peer education and conversation. The number of pathologists sharing instructional case material via Twitter, Facebook, Instagram, YouTube, and other social media platforms has grown dramatically during the past decade (Table 4). Open links to WSI via PathPresenter, KiKo, and other platforms have greatly facilitated the potential uses and learning value of these teaching and social media venues.[79] Additionally, during the COVID-19 pandemic, virtual meeting platforms became the norm to connect pathologists. Using the share screen function to share digital images from cameras connected to most practicing pathologists' microscopes, peer-to-peer curbside consult in real time became simple and convenient.

Community Pathology and Oncology Practice

Several community-level educational and technological initiatives can serve as models for applying DP to bridge knowledge and access gaps between patients, oncologists, and pathologists.[80] This is important, because as many as 85% of cancer patients in the United States are treated in community settings and yet less than 3% of patients in clinical trials are enrolled at the community level.[81] Additionally, many of these patients do not have access to advanced resources, like AI algorithms and molecular testing data, which often depend on DP technology as an entry point.[82]

Role of DP Education to Advance Community Pathology Practices and Expand Access.—Since the introduction of the technique by Ronald Weinstein in 1986,[83] the field of telepathology has evolved to include the use of static fixed images, WSI, and dynamic telemicroscopy via the Internet for clinical review, quality assurance, and educational purposes.[84] WSIs and telepathology are key enabling technologies for diagnostic and educational purposes, because pathologists' availability is widely uneven throughout the world.[33] The American

Table 4. Social Media Platforms for Digital Pathology Education		
Platform	**Description**	**Distinctive DP Value**
Facebook	Most widely used platform, allows sharing text, fixed photos, short video, links, polls, live streaming	Posts can be directed to public, or specific cohorts of friends. Interest groups (eg, bone pathology) can share cases and opinions
Twitter	Limited text posts but allowing images, links to video/digital slides or other content, Extensive use of #hashtags and potential to target other users and their followers	Wide base of pathology users/contributors. Wide potential reach of tweets
KiKo	Science knowledge sharing platform begun by pathologists. Rich array of content sharing options including digital slides, video	Designed to facilitate WSI sharing and rapid release of scientific knowledge
Instagram	Image-rich format, allows for short videos and text	Can selectively follow #hashtags to enrich content one sees (eg, #GIPath)
LinkedIn	Networking platform with professional emphasis; Posts include text, images, video and links	Lots of DP events are shared here; instructional content is limited
WeChat	Large userbase, especially in China; censored/monitored; images, links, messaging and in-app tools for payment, calling	Access to a large userbase, especially in Asia
YouTube	Video-sharing platform; large userbase, rich array of pathology content; live-streaming capable	Videomicroscopy using screen-sharing or WSI is facile
TikTok	Short videos which could include gross or microscopy, easily shared	Uses conventional #hashtags to allow searching

Abbreviations: DP, digital pathology; KiKo, Knowledge in, Knowledge out; WSI, whole slide imaging.

Society of Clinical Pathology has seeded many WSI-based initiatives to bridge this gap in pathologists' expertise, using case consultation as a training method for pathologists in developing countries.[85] Although pathologists' availability in the United States is nowhere as dire as in developed countries, significant disparities between pathology expertise in rural versus urban settings persist.

Community pathologists play a key role in the delivery of laboratory services to rural populations at large. However, community pathology practice also relies significantly on the consultative, subspecialty expertise of academic pathology experts. For generations, glass slides have been shipped to obtain needed expert consultation, which significantly delays clinical care for patients living in rural areas. With the increasing availability of DP tools and the integration of Web-based viewers, 2-way communication between community or developing country pathologists and academic specialty experts has shortened dramatically the time to diagnosis (D. Milner, oral private communication, February 17, 2021).

DP tools also act as real-time communication tools to educate others and share the latest pathologic advances with pathologists who have limited time and resources. One such application of DP educational tools would be in the standardization of educational content needed to implement consensus guidelines, new grading criteria, or staining interpretation standards into community pathology practices. For example, guidelines developed by a CAP committee or new World Health Organization classification systems could be interactively delivered by committee experts to almost any pathology practice in the world using DP, as is further described in the section below on biomarker standardization.

Role of DP Education in Molecular Tumor Boards in Community Oncology Practices.—Another area in which DP education tools can play an important role at the community practice level is in enabling personalized oncology efforts. Molecular genomic testing is quickly becoming part of the established consensus guidelines for the initial workup of oncology patients with a variety of cancers. Molecular testing can have a significant impact on the initial diagnosis, prognosis, and potentially therapeutic plans for a patient with newly diagnosed cancer. Yet, most experts in molecular pathology work at academic centers, not in community oncology practices. Although local pathologists can send a patient's tumor material for genomic testing, the expertise needed to select and interpret the molecular test results in the broader context of a patient's treatment plan is often lacking at a community level.

Community-level molecular tumor boards help in bridging this gap. In one study, 1725 oncology patient cases were reviewed as a part of a virtual molecular tumor board, leading to enhanced therapy or enrollment into trials based on virtual molecular tumor board recommendations.[86] One of the authors of our current review is involved in a similar community molecular tumor board within the New Mexico Community Oncology Working Group, which is a part of the National Cancer Institute Community Oncology Research Program. Every quarter, molecular pathology case reports are discussed during the New Mexico Community Oncology Working Group tumor board meeting, with interactive participation from pathologists, community oncologists, and oncology nursing teams. Interactive presentations enable education and planning of potential therapeutic modalities for patients living in remote rural areas of New Mexico.

Although the current virtual molecular tumor board efforts use static digital images when feasible, in the future WSI would ideally be incorporated into these efforts, particularly as efforts to derive molecular and other biomarker data from WSI move beyond the investigational stage. Cross-disciplinary tumor boards involving multinational experts are part of the educational outreach of the International Gynecologic Cancer Society using the Extension for Community Healthcare Outcomes platform developed in New Mexico. Digital slides enable US-based pathologists to have meaningful discussions with local pathologists and oncologists about cases from Rwanda, Vietnam, or other developing countries.[87] Potentially, simultaneous participation of academic pathology and oncology teams in conjunction with community pathology and oncology teams could leverage DP educational tools to enable best practices for oncology patient therapeutics for rural oncology patients across the world.

DP Used to Advance Patient Education.—DP also enables pathologists to augment clinician and patient education about biopsy or resection results. Allowing clinicians to directly view pertinent slides either with or without pathologists' commentary and empowering patients to visualize their disease are important educational steps that hinge on DP capabilities.[88] Modern patients regularly consult Internet search engines seeking information about their diagnosis, but obtaining personalized information on their own tumor or condition from the pathologic materials may be more valuable. Data are emerging indicating that patients' primary visualization of their tumors or other pathology findings is beneficial for improving compliance and other predictors of outcomes.[89]

PROFESSIONAL COMPETENCY ASSESSMENTS AND LICENSING

Digital slide materials have been used for certifying examinations for more than 15 years and appear firmly ensconced in this role because of their many logistical advantages for administering examinations. A few studies, both published and not, have demonstrated noninferiority in trainee and student performance using this modality. Primarily speaking in the terminology of ACGME competency, certifying exams using WSI assess the patient care and medical knowledge domains of pathologist competency. However, digital materials offer considerable potential in the assessment of many other areas of competency[34] and, as noted above, mesh well with entrustable professional activities.[90] Building-block skills, such as microscopic feature identification or identifying regions of interest efficiently, can also be assessed readily with digital WSI.[35]

Significantly, the ACGME Milestones do not include any mention of DP exclusive of the more generic category of informatics, but they do make clear that they are not intended to be comprehensive. Researchers at the University of Iowa (in Ames) made an early attempt to use virtual microscopy methods to assess progress toward competency in surgical pathology.[91] The use of this approach faltered, however, as faculty changed. Several institutions have taken another, more public approach in administering periodic assessments of a skill set, such as frozen section evaluation and interpretation skills, by presenting interactive case scenarios built in a Qualtrix (Qualtrix International Inc) platform or with PathPresenter, with immediate individualized feedback for skill assessment. Public sharing of the assessment URL allows access for trainees in a variety of settings.[34]

Digital slide materials have also been used to verify competence as a component of medical credentialing. Beginning in 2008, the Joint Commission mandated the use of Focused Professional Practice Evaluations prior to granting privileges to clinicians in all disciplines.[92] Some pathology departments formalized this by using slide examinations in the particular domain in which a pathologist was expected to practice. Digital slides were shown not to be inferior to glass slides for this purpose and offered the advantage of color and quality consistency over time with repeated use.[93]

As noted above in the Cytopathology section, digital slides can efficiently form the foundation for competency assessments in cytopathology for both cytotechnologists and pathologists. A recent project spearheaded by the Hologic Corporation has offered an ongoing weekly set of quiz cases using digital images and a montage of selected fields, potentially offering a more real-time evaluation of diagnostic accuracy.[94]

Although several efforts have been made to use WSI-driven retrospective and concurrent review as a means of providing quality control during the diagnostic process in surgical pathology,[95,96] the potential for real-time quality control of diagnostic acumen by using intermingled quality control cases within the digital workflow has yet to be adopted by any institution or offered as an enhancement by DP systems. Such systems, however, would allow for the better assessment of critical issues in practice, such as grading standardization, detection limits of rare events, and classification schemes, not to mention intraobserver day-to-day diagnostic variability. Trainee reproducibility of diagnostic acumen could also be affirmed through such means. As we move toward a competency-based rather than time-based qualification scheme, these types of tools are needed.

DP IN CONTINUING EDUCATION FOR PATHOLOGISTS AND NONPATHOLOGISTS

CME aims to help pathologists to keep up to date with current knowledge and advances in their field, retain licensure, and continue practice. Traditionally, pathologists attended conferences, read journals, viewed online lectures, or took courses to obtain the minimum required CME credits each year. The COVID-19 pandemic, however, changed the paradigm of live in-person conferences. DP has provided alternative and often better ways to fulfill this functionality.[97]

The use of WSI, cloud services, and various software programs allows pathologists to earn the necessary CME credits from their homes and offices. Online conferences can be viewed anytime from any device. Faculty upload lectures and attendees can view them beforehand; during the dates of the online conference; and, many times, after the conference, within a generous availability window. Pathologists can attend a discussion based on the lecture during the actual date of the conference and often can view a recording or transcript afterwards. Faculty use WSI or streaming conference-room style presentation in a consolidated online format. Pre and post assessments using WSI allow self-assessment and a potentially better learning experience. Noncredit educational materials using similar hybrid presentation modes, some with links to digital slides, are also becoming more widely used for continuing education for pathologists and other specialists seeking updates pertinent to their practice. These free, noncredit materials have spread widely via social media platforms, such as YouTube and Twitter.

Many conferences have sessions during which, traditionally, a limited number of attendees would pay for sessions with an expert over a multiheaded microscope. DP using WSI or streaming microscopy has allowed this activity to expand to an unlimited number of attendees over the cloud. Some sessions allow preview and postreview of the slides, enhancing the learning experience. In this setting, digital slides are advantageous over streaming microscopy by virtue of consistent high-quality focus and lighting. Digital slides may sacrifice resolution if they have been scanned at a lower magnification. Pixelation or loading delays were previously problems, but they are less common now with higher-speed servers and networks.

Figure 3. *Landmark article from* Archives of Pathology & Laboratory Medicine *linked published images to hosted digital slides via QR codes or hyperlinks, allowing viewers to see the full context of fields chosen for publication. Reprinted from Hwang DH, Szeto DP, Perry AS, Bruce JL, Sholl LM. Pulmonary large cell carcinoma lacking squamous differentiation is clinicopathologically indistinguishable from solid-subtype adenocarcinoma.* Arch Pathol Lab Med. *2014;138(5):626–635, with permission from* Archives of Pathology & Laboratory Medicine. *Copyright 2022. College of American Pathologists.*

The significant positive impact of DP on the delivery of CME programs is evident in the ease of access for pathologists and nonpathologists everywhere, allowing those in the developed and developing world to participate in educational programs via the Internet from almost anywhere, anytime, and on any device. International virtual attendance at major US pathology meetings in 2020 and 2021 is anecdotally reported to have been significantly higher than any previous series of meetings.

Textbooks and Journals

Conventional bound books and atlases have been a tremendous boon to pathology education. These resources can range from multivolume tomes covering a vast expanse of pathology material to single-organ or even single-procedure texts discussing important pathology topics. The transition from mostly black-and-white images to abundant color images was a huge improvement in value for such works. This was followed by the inclusion of a CD-ROM disk containing the high-quality versions of images used in the book, often with additional illustrations that were not included in the print version. Subsequently, books began including a coded link to an online library of the images, thus allowing for a more facile updating of images and potential tracking of purchaser interests and needs. But, surprisingly, although the means to host digital slide libraries have been available for far longer than a decade, major publishers and leading authors have not rushed to embrace this potential enhancement.

Likewise, pathology journals have clung rather tenaciously to fixed images in the publication of pathology-rich articles, with very few exceptions. A pilot article in the *Archives of Pathology & Laboratory Medicine* seems to have been a solitary effort (Figure 3), although some CAP publications subsequently have included digital whole slide materials.[98] *Diagnostic Pathology* has also long offered to host digital slides related to published articles. However, despite reasonably strong evidence of the enhanced value of these kinds of interactive materials[99] and strong advocacy by many,[100] the expanded use of digital slides in journals, even online-only journals, has not ensued.

A noted exception is the appearance of e-book–like PathPresenter Publications, which have showcased the potential value of interactive digital slide–based textbook-quality material to enhance learning. The ready ability to hot-link text to image annotations, include multiple examples of case materials, compare images side by side, and integrate differential diagnostic considerations with slide-based interactive images (Figure 4) vastly exceeds the capabilities of even the most clearly written descriptions in other texts or stand-alone atlases. With 3 publications to date, we anticipate that more publications of this caliber will help accelerate self-paced learning.[101]

PT and Technical Competency Assessments

Laboratories must perform PT on all regulated analytes (moderate- and high-complexity tests) in order to remain accredited by the Centers for Medicare & Medicaid Services or the organizations that have been deemed equivalent as accrediting entities. PT is one of the key elements of a laboratory's quality testing process.

PT samples are typically designed to mimic actual patient samples and are extensively validated under actual testing conditions. This works well for many numerically based laboratory tests, such as chemistry, but it fails for morphology-based evaluations, such as identifying blood cells, body fluids, and urine sediment constituents. All PT products that relied on images first used 35-mm film.

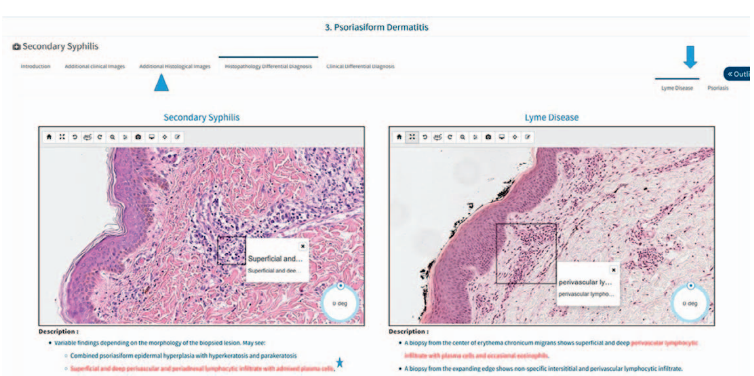

Figure 4. *The learning power of a digital slide–based textbook is demonstrated by the ability to view differential diagnostic considerations side by side, compare multiple differential diagnostic considerations (arrow), view multiple slide examples of a diagnosis (arrowhead), and jump quickly to key features in each via hotlinks to regions of interest (star). (Screenshot taken by Lewis Hassell, from Singh R et al, eds, Dermatopathology for Residents, Publications. PathPresenter.net, accessed May 18, 2021).*

Thousands of slides were duplicated each month and sent to participants. This mass production of film eventually transitioned to color print and online digital images. In each case, cell identification was different, or contrived, compared with a technologist who performed the analysis using a microscope and an actual patient sample.

As DP became more widely available, many PT suppliers turned to WSI to more closely mimic the real-world experience of viewing peripheral blood and other body fluids in a manner that closely resembled the use of a light microscope and stained glass slides. Virtual smears allowed cells to be viewed in context; the entire feather edge of a glass slide or a marrow smear as a whole was available for examination. This fulfilled a central tenet of PT, to make the challenge as close as possible to what actually happens in the laboratory. It also enhanced the educational value of these materials.

Whole slide images were first used for PT by the CAP in 2010 for the bone marrow smear survey.[102] This was the first directed morphologic assessment of marrow-specific hematopoietic neoplastic and nonneoplastic cases. Participating laboratories could assess their competency and knowledge of individual cellular identifications, compare bone marrow differential counting with other participating institutions, and assess the knowledge of particular disease states. The survey provided standardization for morphologic cellular identification across the United States and around the world.

The virtual bone marrow program proved to be quite successful and was quickly adopted for peripheral blood smears. White blood cell differential counts and red blood cell morphology can now be assessed virtually. Today, PT providers offer virtual slides not just for peripheral blood and bone marrow smears but also for body fluids, medical microscopy, parasitology, bacteriology, sperm morphology, surgical pathology, dermatopathology, Papanicolaou smears, and nongynecologic cytology specimens. Virtual whole slide images are also incorporated into in-service, ongoing competency assessment programs aimed at laboratory technologists primarily, which previously relied on static photomicrographs. This is similar to the professional Focused Professional Practice Evaluations assessments described above in the Professional Competency Assessments and Licensing section.

DP is an important resource for continuing hematopathology education as well. Historically, educational or test materials were shared as glass slides or static images. With the broader availability of WSI, conferences and symposia, as well as PT organizations, now increasingly rely on digitized slides to enable the broader distribution of case material. Beginning in 2011, the Society of Hematopathology and the European Association for Haematopathology partnered with Leica Microsystems to use the Digital SlideBox system, enabling participants to access slides for submitted cases on their own digital devices.[103] In 2005, the UK National External Quality Assurance Scheme initiated a trial of virtual slides for the quality assessment of hematomorphology; in 2008, the UK National External Quality Assurance Scheme and the Royal College of Pathologists of Australia conducted a joint quality assurance workshop using virtual slides.[67] In 2018, the CAP publication of a revised hematology atlas based on PT results also included links to digital slide images.[104]

Although cell identification serves a regulatory function, there is significant educational value to PT. PT materials are

BMD-09, 2017 (Marrow, WG, X400)

Identification	Referee %	Participant %
Blast cell (includes lymphoblast)	-	57.9
Monocyte, immature	-	31.4
Erythrocyte precursor, normal	-	2.9
Erythrocyte precursor, abnormal	-	2.1

The arrowed objects are blasts. A blast is a large, round to oval cell, 10–20 µm in diameter. The nuclear-to-cytoplasmic ratio is high, varying from 7:1 to 5:1. The blast often has a round to oval nucleus, but sometimes it is indented or folded, and it has fine, lacy or reticular chromatin. One or more prominent nucleoli may be seen. The cytoplasm is variably basophilic and typically agranular. The morphologic features of a blast cell do not permit determination of the cell lineage (e.g. myeloblast versus lymphoblast). The one exception is the presence of Auer rods, which are diagnostic of myeloid lineage. In the absence of Auer rods, immunophenotyping by flow cytometry, immunohistochemistry on tissue sections, or, less commonly, cytochemical staining (e.g., peroxidase or Sudan black B reactivity) is required to determine the lineage of a given blast cell. Additionally, blasts can be morphologically indistinguishable from lymphoma cells. For identification purposes, one should classify individual cells exhibiting this type of morphology as blast cells when additional confirmatory information is unavailable.

BMD-06, 2016 (Marrow, WG, X400)

Identification	Referee %	Participant %
Blast cell	-	72.5
Malignant lymphoid cell	-	19.7
Lymphocyte	-	2.5
Monocyte, immature	-	2.1

The arrowed cells are blasts. They have large round to oval cells, 10 to 20 µm in diameter, with a high nuclear-to-cytoplasmic ratios and fine, powdery chromatin with variably prominent nucleoli. It is not possible based on morphology alone to further subclassify these blasts by lineage. However, upon immunophenotypic analysis, these blasts were determined to represent blastic plasmacytoid dendritic cells. Although the cells in question have some lymphoid features, the high N/C ratio and open chromatin are consistent with blasts. Some of the blasts have a "hand-mirror" morphology which is not diagnostic of any particular pathology.

Blasts and Blast Equivalents 227

Figure 5. *Sample page from College of American Pathologists* Color Atlas of Hematology *illustrates how QR codes and hyperlinks can directly take the viewer to a digital slide, no matter the platform being used to view the text.* Color Atlas of Hematology: An Illustrated Field Guide Based on Proficiency Testing, *2nd ed., vol. 1.*[104] *With permission from The College of American Pathologists.*

accessible to laboratories to train other personnel and students concurrently and in delayed settings. The need for continuing education became apparent as the PT survey programs gained acceptance and laboratories reported often widely discrepant results. Educational discussions are part of the PT program itself. The summary reports for each PT challenge contain critiques discussing disease pathophysiology and key morphologic features. In the case of the CAP, the writeups are quite detailed and expansive. These educational components formed the basis of the second edition of the CAP *Color Atlas of Hematology*. This 2-volume set included Quick Response (QR) code links to numerous virtual peripheral blood and bone marrow smears so that the individual cells can be viewed along with the entire slide (Figure 5). The CAP *Color Atlas of Hematology* continues to be its most successful publication, emphasizing the added educational value of the linkage to digital slides (CAP Publications Committee, internal communication).

Standardizing Education and Training for Biomarker Testing

Pathology is not static. Device, drug, and other types of innovations engage medical affairs leaders whose roles are pivotal for preparing to launch a new medical product and ensure its safe and effective deployment. Once a drug or medical device passes its development milestones and draws closer to commercialization, medical affairs personnel will lead efforts to provide unbiased clinical and scientific education and product training, address health care professionals' questions, and initiate collaborative activities

Table 5. Comparison of Digital Pathology and Glass Microscopy

Category	Digital Slide Microscopy	Glass Microscopy
Slides and annotations	Standardized images with key findings; annotations preserved over time; annotations can be linked with clinical metadata	Requires ink markings that can only be seen by one user at a time; tissue sections may not present foci of interest, with many slides needed
Working knowledge of microscope	No microscope learning curve/phobia	Depth of field, polarization possible
Staining issues	Image quality is stable	Staining deteriorates over time and slides may accumulate dirt or break
Rare or unusual cases and comparisons	Allows viewing of multiple images simultaneously; rare cases and limited sample types can be stored and shared easily	Requires microscope and glass slides (which require physical space) and learning manual skills, such as focusing; rare or focal findings not easily replicated on heavily recut slide blocks
Access convenience	Files can be accessed on multiple device types and in myriad locations	Maintenance is required for glass slides and microscope
Integrated learning	Digital slides can be incorporated into lectures, included in slide decks, and are readily in focus with optimal lighting	Is more time consuming/clumsy during presentations/ lectures to switch between slides and presentations
Long term cost	Cost-effective over time	Require lab space and other fixed assets

to engage community physicians and key opinion leaders. This step is critical to the success and proper application of the intended medical device or drug.

The main challenge in this roll-out phase is scalability. In essence, the requirement is to deliver effective global education and training in timely manner. This goal is impossible to achieve without digital solutions. For example, a Roche team recently faced this challenge during the launch of programmed death ligand-1 (PD-L1) assays. During their attempt to provide standardized prelaunch education and training, it was impossible to construct a sufficient number of identical glass training sets to accommodate global training for a worldwide set of potential users. In addition, tumor heterogeneity precluded producing matching sets of glass slides, resulting in non-standardized training sets and variable PT outcomes. The well-known glass slide logistical limitations (breakage, loss, slide fading, transportation, etc) and scheduling of global training times are also enormous challenges. In this situation, using digital tools was not only optimal but mandatory.

Roche's recent experience applying a DP model of global training for the Ventana PD-L1 (SP142) Assay as a companion diagnostic was guided by input and endorsement from a Pathologist Training Expert Committee.[105] The group successfully trained more than 1000 pathologists globally for various indications of the assay. The digital training program reported achieving an extraordinarily high passing rate for trainees (99.1%) and overall percent agreement of 98.2%, which attests to the educational effectiveness of the tools and the process.[101] With the anticipated continuing explosive growth of the predictive assay portfolio and personalized health care approaches, we will likely see a parallel expansion of medical affairs' educational role in launch preparations. The need for timely training of the world's pathologists will move digital training tools to the forefront and cement DP's role as a default in these settings.

DRIVERS OF DP ADOPTION FROM EDUCATION STANDPOINT

The 3 pillars of service for most academic pathology institutions include providing clinical care, training new pathologists to enter the workforce, and promoting research by their faculty. Training is traditionally conducted using multiheaded microscopes with glass slides or through PowerPoint-like presentations with static images in conferences. Although this format has performed well for the last 100 years, it is becoming increasingly outdated and has limited scalability, among other limitations. Medical schools, pathology residency training programs, veterinary pathology, and pathology professional organizations have all increasingly moved toward DP education. There are numerous factors propelling this shift toward using DP for education. For example, digital images allow use of the cloud (ie, images can be accessed anywhere) and software programs that can further expand the range of online learning resources and provide readily accessible tools for a larger audience (Table 5).

The most recent driver of using WSI for education has been the COVID-19 pandemic.[6] The pandemic limited traditional meetings using multiheaded microscopes or those within a conference room. Sharing whole slide images over the cloud and using software programs along with screen-sharing services like Zoom have allowed education to continue with few limitations.[106] This has proven to be an advantageous strategy, given the widespread distribution of hospitals, because it allows trainees to log in from anywhere and from any device. The availability of curated digital slide sets allows centers that do not have access to scanners or cases for a particular subspecialty a means to continue their educational activities.

Multiple studies have shown that WSIs, the cloud, and screen-sharing programs have numerous advantages compared with fixed images or didactic materials.[99,107] From a physical resource standpoint, using glass slides for education has significant limitations, as noted in Table 5. The slides can only be shared among a limited number of simultaneous viewers peering at the same field of view on a multiheaded microscope, although streaming techniques expand this greatly. Glass slides tend to deteriorate over time and can break or get lost. In contrast, WSIs can easily be shared with an infinite number of users and can be stored for very long periods without any stain deterioration. Although file corruption, misfiling, or disc failures are possible with WSI, they are less likely risks than those related to glass slides, given modern file mirroring and redundancy protocols. Annotations can easily be made on whole slide images to mark areas of interest (geometric shapes, arrows, texts, etc) and then linked to questions, text, or related areas and made viewable by all users at the same time. Thus, training materials can be more objective and uniform.

Historically, a drawback for using whole slide images was the cost of storage. Each digital slide can consume between hundreds of megabytes and several gigabytes of storage space. At a large scale, this can easily occupy terabytes or petabytes of storage space. However, following Moore's law, the costs of cloud storage have become increasingly more affordable and are projected to continue to keep decreasing in the future, even as storage demands increase.[108]

Case retrieval from the cloud is much easier and faster than retrieving glass slides from fixed distant file rooms or warehouses, potentially offering cost savings. The cost of deploying DP in education, particularly in undergraduate education, has repeatedly proven to be reasonable in light of eliminated costs from fixed laboratory space; microscope purchase and maintenance; and slide preparation, replacement, or maintenance. A student's multipurpose laptop or other mobile device for individual work and a large monitor for group work easily replace costly microscope laboratories. The professional manpower needed to teach using digital slide materials is also often diminished without compromise of student performance. In fact, students' interaction with and understanding of pathologic processes increases using digital slide materials compared with glass slides.[107,109,110]

Another driver helping integrate WSI into education has been the availability of workflows and software programs that mesh easily with conventional AP workflows and simulate current time-tested teaching techniques. For example, traditional teaching allows trainees to preview glass slides, develop a preliminary diagnosis, and then review with faculty; similar digital slide workflows can be easily integrated for most academic institutions. Moreover, software tools allowing for the easy integration of whole slide images with presentation slide tools have been developed and nicely combine conference room–style teaching and instruction at multiheaded microscopes. These conferences can be transmitted live using screen-sharing software, allowing trainees to attend conferences remotely, or recorded for asynchronous learning or review. There is also no limit to the number of people that can be taught through these conferences. Trainees can review the presentations, including the digital slides, after the conference, thus improving retention. The ability to not only preview and review digital slides but to also go back and rereview them at any time or from any place provides significant value beyond conventional glass slide methods.

Digital tools can provide on-demand learning opportunities in variable-sized pieces. Current WSI viewers allow preannotation of areas of interest, annotation during presentations, viewing other whole slide images in side-by-side comparison, simultaneously opened radiology images, hyperlinking slides to references, and slide rotation for good orientation. All these features enhance the pathology teaching and learning experience.

The American Board of Pathology and various other examining boards have now moved to a completely virtual format for slide materials. This makes it mandatory for trainees to become comfortable using WSIs. Software programs now allow integration of WSIs into multiple-choice or short answer questions, which can be used for various prelearning or postlearning purposes. CME programs used for maintaining license requirements are also using WSIs and cloud distribution for virtual attendees.

Social media has been another big driver in applying DP to education.[111] Many residents and pathologists are tuned into social media, and they use WSI and DP to learn and teach pathology on various social media platforms.[7] Questions of the day and cases of the week or month are posted by individuals, institutions, and pathology organizations and further fuel the use of WSIs for education. Again, these allow on-demand learning, whether in microsecond tweets or lengthy lectures streamed live or viewed asynchronously afterward.[79]

Confronting Barriers to Adoption and Implementation

The Digital Pathology Association (DPA) is cognizant of the fact that significant barriers to adoption have stymied the rollout of DP generally and hampered the wider adoption of DP in education. Several fundamental factors contribute to this delayed adoption and implementation.

The Human Element.—Technology must be useful and accessible to be widely implemented. Building a Web site with a library of slides or installing a scanner will not instantly change ingrained pedagogic patterns. The mixed results seen with the adoption of laptops,[112] tablets,[113] and distance learning[114] in the broader field of education should raise caution. The adoption must quench the true urgent needs for the direct user, ideally also benefiting later or downstream stakeholders and needs. In this regard, pathologists have only recently seen the educational platform as facing a crisis.[6] However, human objections related to ease of scanning, user interfaces, and learning curves for new methods are all valid concerns that need to be addressed.

Because of privacy and ownership concerns (see The Institutional Mindset below), most institutions will host some slides internally. However, with those issues adequately addressed, scanning a slide for educational purposes should be as fast and easy as obtaining a physical educational recut. That is, it should be orderable within the usual routine, either electronically or otherwise; the turnaround time should be short enough that the ordering pathologist remembers why it was ordered; it should be free of charge; and it should be orderable by any pathologist or trainee. This short turnaround time allows integration into weekly slide-based teaching conferences, tumor boards, and morbidity and mortality conferences.

Extending the metaphor of educational recuts, departmental digital slide repositories should not resemble a disorganized file room or office, where stacks of slides and slide boxes build up, unlabeled and unused. Facile, preferably automated, linkage to slide and case metadata, including diagnoses and individual slide annotations, are important to avoid this morass and enhance long-term searchability and teaching value.[115]

The Institutional Mindset.—Although some early adopters have freely shared their teaching legacy and added materials freely to the public domain, this practice is not universal. Factors contributing to this reluctance include the hypervigilance in ensuring compliance with privacy standards (such as foolproof de-identification protocols), real threats due to cyberspace attacks (and, hence, increasingly impenetrable firewalls and password protections), and concerns over unethical use of data. Willingness to deploy

Table 6. Summary of Best Practices and Goals for Future Development

Education Level	Key Best Practices	Future Development Needs
Undergraduate	Annotated digital slides for all microscopy work Mentored or small group WSI demonstrations Interactive integrated digital case materials for systems-based curricula and assessments Flipped classrooms, meaningful group work, and game formats lead to enhanced retention and mastery	Virtual reality–based DP materials to link basic disciplines (eg, anatomy and physiology) more tightly with pathology
Graduate (residency) level	Integration of interactive annotated digital slides with didactic slide decks (eg, PathPresenter) for both individual and group study Preview and postview capabilities should be standard options for most learning encounters Standardized digital slide–based assessments to provide essential feedback to individual learners and the training program Digital materials included in clinical pathology disciplines, including those without a high level of pure morphologic emphasis, by means of integrative cases, training sets, simulations, videos, and other digital media Game-based and other interactive learning techniques augmented with digital materials Digital pathology used as an enabling technology for further steps in using virtual reality and artificial intelligence	Enhanced DP assessment materials and methods that are predictive of performance in the real world; DP standardization may enable this Curation and collation of existing materials into widely useable and freely available modules[4] Expanded development of integrated DP materials useful for clinical pathology domains Virtual reality–based DP materials to teach grossing skills and microscopy
Postgraduate training and practice standardization	Incorporation of DP materials, especially digital WSIs, into educational programs Preview and postreview capabilities whenever possible Introduction of new grading, classification, or comparable morphologic nuances and new testing methods (such as companion diagnostics) should be accompanied by DP reference and assessment materials Journal and textbook publishers should endeavor to provide access to WSIs with significant supporting evidence, for morphology-based publications or topics	Enhanced assessment materials and methods that are predictive of performance in the real world, such as real-time QA and QC of pathologist diagnostic performance
Patient education	Provide patient access to digital slide materials to educate patients and help them understand their diagnosis, preferably with the option for one-on-one discussion of the findings	Further research defining optimal means of patient education on pathology-related items

Abbreviations: DP, digital pathology; QA, quality assurance; QC, quality control, WSI, whole slide images.

human resources to create or curate digital material libraries or archives has been low. Commitment of institutional financial resources to the DP infrastructure (eg, scanners, viewers, and especially storage) has also been viewed shortsightedly as offering insufficient financial return on investment.

The Innovator's Conundrum.—Technology startups and behemoths in the DP space have also contributed to the lagging uptake on several fronts. First, the cost of entry has been rather steep, usually only funded by some combination of secondary gains, grant funding, or wider collaboration. When an institution has not adopted it for clinical use, DP adoption for educational use has understandably lagged. Second, the lack of interoperability between platforms both early on and even now was not trivial. Differing file formats, nonobservance of Digital Imaging and Communications in Medicine standards,[116] and other proprietary solutions designed to keep users locked into a particular domain further siloed users, limited collaboration, and contributed to high costs. Thus, torn between pursuing general interests and individual corporate interests, manufacturers have often subverted both.

The Digital Anatomic Pathology Academy Solution.—Many academic centers, especially smaller ones, have not yet implemented DP because of high entry costs, infrastructure requirements, insufficient IT support, and other reasons. This delay may undermine their teaching mission as training candidates choose programs with more enriched DP capabilities.

Digital Anatomic Pathology Academy (DAPA) was recently announced by the DPA, aiming to be part of the solution to this challenge by lowering the barriers to entry into the DP educational world. DAPA can serve as a broad training and educational solution for training programs without their own scanning and archiving capabilities, as well as a resource for those with such abilities. Its mission is to provide easy access to whole slide images of fundamental cases that every resident and fellow should be familiar with before finishing their training program. DAPA simulates conventional teaching and slide-set study, allowing multiple users to view digital slides under mentored tutelage while also allowing independent slide study of high-value cases of curated WSIs annotated by experts. DAPA further leverages the training and learning experience by allowing the creation of enduring video microscopy and mixed media presentations. See, for example, this short video on Chondroblastic Osteosarcoma posted to the social media platform YouTube.[117]

Using software programs created by PathPresenter, DAPA allows for the creation of teaching slide sets of common and uncommon cases and associated relevant information with the whole slide images, such as radiographs, pertinent articles, gross photographs, molecular data, or descriptions and comparison materials. Annotation tools allowed the linkage of microscopic features to fields on the WSIs. The software allows the integration of multiple slides for every diagnosis to showcase the gamut of histologic findings and enables side-by-side WSI comparison for differential diagnosis or histologic-cytologic correlation.

DAPA can be accessed from anywhere in the world using minimal bandwidth and on any device. These kinds of solutions have the potential to transform the delivery of AP education and democratize the availability of educational resources and access to experts throughout the entire world.

Beyond DAPA, other efforts to confront and minimize these barriers are ongoing within the DPA, including joint efforts with other similarly minded societies in Europe (European Society for Digital and Integrative Pathology) and Japan (Japanese Society of Digital Pathology) and in standards organizations like Digital Imaging and Communications in Medicine and other entities.[118] Collaborations with PathologyOutlines, a Web-based interactive textbook, and the National Society for Histotechnology are also ongoing, with similar intent to remove barriers to DP use for educational and clinical intent.

SUMMARY OF BEST CURRENT PRACTICES AND GOALS FOR FUTURE DEVELOPMENT

Our review has identified a number of best practices at each of the various stages of pathology education (Table 6). For undergraduates in particular, annotated digital slides are optimal for all microscopy work and are enhanced by mentored or small group demonstrations. Interactive integrated DP case materials can be used effectively in systems-based curricula and assessments, as such curricula increasingly replace discipline-specific course work. Incorporating flipped classrooms, meaningful group work, and game formats leads to enhanced retention and mastery, all of which lend themselves well to integrating DP.

For graduate-level training, integration of interactive annotated digital slides with didactic slide decks (eg, PathPresenter) is well adapted to all morphologic disciplines for both individual and group study. Preview and postview capabilities should be standard options for most of these kinds of learning encounters. Corresponding digital slide–based assessments can augment didactic sessions and provide essential feedback to individual learners and the training program. Digital materials can be effectively included in clinical pathology disciplines, including those without a high level of pure morphologic emphasis, by means of integrative cases, training sets, simulations, videos, and other digital media. Game-based and other interactive learning techniques augmented with digital materials engender potent engagement and, thus, information retention by trainees. DP is an enabling technology for further steps in using virtual reality and AI that may have future value.

For postgraduate (postresidency) training and practice standardization, incorporation of DP materials, especially digital WSIs, into educational programs is a quality marker, and should be accompanied by preview and postreview capabilities whenever possible. Introduction of new grading, classification, or comparable morphologic practice nuances and new testing methods (such as companion diagnostics) should be accompanied by DP reference and assessment materials. Journal and textbook publishers should endeavor to provide access to whole slide images as significant supporting evidence for morphology-based publications or topics.

For patient-oriented education, pathology departments should endeavor to provide access to digital slide materials to educate patients and help them understand their diagnosis, preferably with the option for one-on-one discussion of the findings.

In each of these phases of education, we see several goals for future development, including the following. (1) Enhanced assessment materials and methods that are predictive of performance in the real world are needed; DP standardization may enable this. (2) Curation and collation of existing materials into widely useable and freely available modules is desirable for training in existing programs and in developing locations.[33] (3) Expanded development of integrated DP materials useful for clinical pathology domains should be encouraged and similarly be made widely available. (4) Virtual reality–based DP materials to link basic disciplines (eg, anatomy and physiology) more tightly with pathology and to teach grossing skills and microscopy may be advantageous.

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