Setting Up an ePathology Service at Cleveland Clinic Abu Dhabi

Joint Collaboration With Cleveland Clinic, United States

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• ***Context.***—**The production of whole slide images is the most advanced form of digital pathology, in which a high-resolution digital scanner is used to rapidly scan glass microscope slides and produce a computer-generated whole slide image that can be saved, stored in a network-attached storage device, and accessed through slide management software within the hospital domain and remotely by authorized users. Digital transformation of glass slides has revolutionized the practice of anatomic pathology by facilitating and expediting consultative services, improving clinical workflow, and becoming an indispensable tool in education and research.**

Objective.—**To highlight the institutional need of Cleveland Clinic Abu Dhabi (Abu Dhabi, United Arab Emirates) and the cultural background for obtaining the United Arab Emirates' first comprehensive digital pathology program; to describe a multiphase road map for achieving full implementation of this platform; and to describe the system's clinical applications and its future potential growth.**

Data Sources.—**At Cleveland Clinic Abu Dhabi, we prioritized our efforts to initiate digital consultations (eConsultations) and digital immunohistochemistry services (eIHC) with Cleveland Clinic Laboratories (Cleveland, Ohio). After this, we established an internal archiving system together with a subspecialty-based, organ-specific digital library of pathologic diseases.**

Conclusions.—**We describe the strategic adoption and implementation of digital pathology into the clinical workflow of the pathology and laboratory medicine institute of Cleveland Clinic Abu Dhabi, and we highlight its impact on clinical operations, educational activities, and patient care.**

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Cleveland Clinic Abu Dhabi (CCAD) is an unparalleled extension of the US-based Cleveland Clinic's model of care, specifically designed to address a range of complex and critical care requirements unique to the population of Abu Dhabi, capital of the United Arab Emirates, reducing their need to travel abroad for treatment. The creation of a Center for ePathology within the newly established Pathology and Laboratory Medicine Institute at CCAD was considered at the earliest stages of hospital planning, and has been largely designed to replicate the well-established world-class Center for ePathology at the Cleveland Clinic Foundation (CCF) in Cleveland, Ohio.[1,2] Its foundation marks the first ever comprehensive digital pathology program in the United Arab Emirates.

BENEFITS OF WHOLE SLIDE IMAGE TECHNOLOGY

Whole slide image (WSI) technology is the latest and most advanced form of digital pathology. It uses a high-resolution digital scanner that is able to rapidly scan pathology glass slides and produce computer-generated WSIs, which can be saved in a designated server within the hospital network-attached storage device. Those images can then be accessed through software that performs the function of Web server, database server, image server, and application server. Once uploaded, authorized users are granted remote access to the site, where they can instantly view, browse, and interpret WSIs from anywhere in the world.[3] The digital transformation of glass slides and their transmission to experts worldwide via the Web have revolutionized the practice of anatomic pathology by empowering poorly resourced pathologists to seek expert opinion on difficult cases and receive the results within a few hours of turnaround time. This innovative technologic advance has a positive impact on the health care system at large, and significantly improves patient

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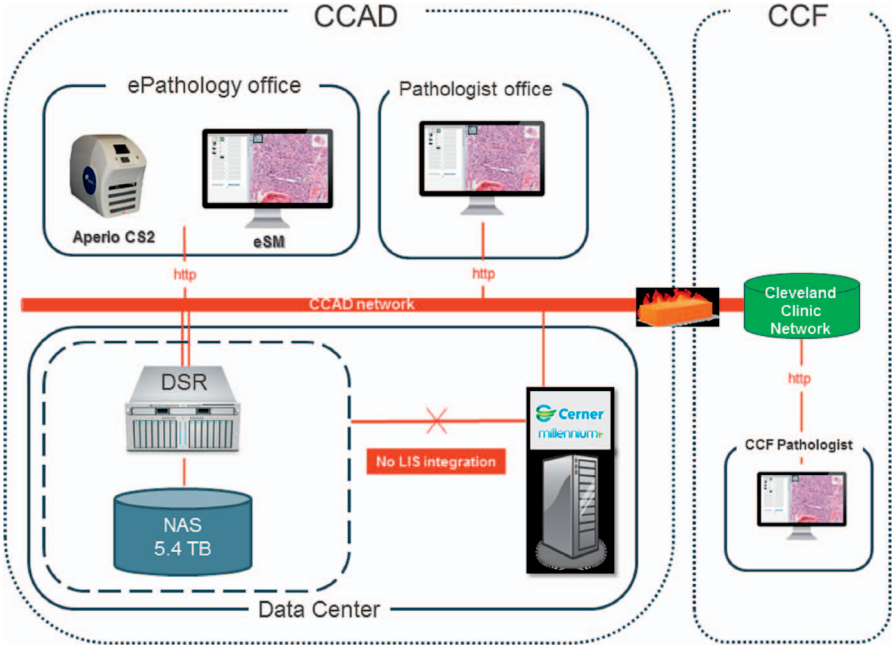

Figure 1. *Architecture display of the information technology (IT) set up of ePathology at Cleveland Clinic Abu Dhabi (CCAD). Abbreviations: CCF, Cleveland Clinic Foundation (Cleveland, Ohio); DSR, digital slide repository; eSM, Aperio managing software eSlide Manager (Leica Microsystems), Cerner Millennium (Cerner Corporation, Kansas City, Missouri), and Aperio CS2 scanner (Leica Microsystems); LIS, laboratory information service; NAS, network-attached storage device.*

care. For example, eliminating the circulation, handling, packaging, and shipping of glass slides increases and preserves the safety and integrity of the patient's precious material by removing the risks of slides being damaged or lost during shipping, and significantly reduces costs related to specimen transportation. Additionally, by reducing the time required to obtain an expert opinion, the patient's hospital stay may be reduced, which translates into not only improved quality of service but also cost savings for the institution.[4] These benefits lead to improved health care outcomes by optimizing patient care, increasing the accuracy of diagnosis, enhancing the medical decision-making process, and leading to better management practice, which ultimately improve physician and patient satisfaction.

TIMELINE FOR THE IMPLEMENTATION OF THE DIGITAL PATHOLOGY PLATFORM

The components of a WSI system, also known as the digital pathology system (DPS), include a scanner with an optical microscope and digital camera for image acquisition, a computer connected to the scanner with software to create and manage image files, a server to store and host images, computer workstations with viewer software that enables image navigation and analysis across a range of magnifications, and secure, stable network connectivity to link the workstation to the scanned slides.

A point-to-point network configuration was established to connect the DPS at CCAD with the DPS at the Robert J. Tomsich Pathology & Laboratory Medicine Institute at Cleveland Clinic Laboratories in Cleveland, Ohio. A point-to-point setting involves 2 sites (on-site and remote site), which are linked only during the consultation process (Figure 1). Five months prior to hospital inauguration, an intrainstitutional and interinstitutional task force representing the Information Technology (IT) department and Network Team at CCAD, Centers of ePathology at Cleveland Clinic Laboratories and CCAD, and Aperio/Leica (Leica Microsystems, Wetzlar, Germany) developed a plan to work toward the establishment of ePathology at CCAD. Thirteen months were required to complete and launch the DPS. The complexity and the diversity of the technical issues encountered were addressed in a timely fashion by a highly experienced team led and guided by the staff of the Cleveland Clinic Laboratories' Center for ePathology. Being a pioneer and one of the world leaders in digital pathology practice and validation, the Center for ePathology at Cleveland Clinic Laboratories was instrumental in smoothly navigating through and accelerating the process of implementation. Below is the phased-in timeline to the implementation of ePathology, summarized in the Table.

Prelaunch System Workflow Verification

As soon as the digital platform infrastructure had been completed, a prelaunch feasibility study between CCAD and CCF was made and was designed to ensure the efficiency and integrity of the entire workflow as a whole by focusing in depth on the technical issues (network, computer, user experience, image viewer, scanning) and professional turnaround time for the efficient and reliable digital pathology consultation service. The study consisted of a mock operation in which 6 anatomic pathology cases of various subspecialties previously verified by CCAD pathologists were scanned at a default setting of ×20 magnification using the Aperio/Leica CS2 scanner (Leica Microsystems, Wetzlar, Germany), collated in eSlide Manager and assigned (electronically transferred) to the CCF ePathology program manager. The final pathology diagnosis was omitted from all cases, leaving the gross description and the clinical information for the purpose of simulating a real consultation environment. The cases were dispatched to the appropriate pathologists and reports finalized within 10 hours to 72 hours. The consulting pathologists successfully accessed the server, and they were satisfied with the section quality and staining. Some of the pathologists experienced slow browsing speed. Although the purpose of this study was mainly technical, ensuring workflow integrity and efficiency, with no intention of testing the diagnostic accuracy of the consulting pathologists, all cases were verified similar to the original diagnosis made by the CCAD pathologists.

Timeline for the Implementation of the Digital Pathology Platform	
November 2014	Data gathering: • Collection of information critical to the implementation and commissioning from CCAD, such as workflow information, location, networking requirement, and IT requirements
December 2014	Scanner installation: • Installation of Aperio Scanner CS2 (Leica Microsystems) with viewing software eSlide manager, and workstation in ePathology suite
January–March 2015	Creation of low-level design document by CCAD IT department, a 40-page detailed document describing: • Network, server, storage, core IT, failover, backup and restore, database, licensing, monitoring, service management, client access, security and privacy, end-user devices, and firewall rules
January 2015	Training and certification: • End-user online training on Aperio Web site (Aperio ePathology, Leica Biosystems, Vista, California) and certification • On-site scanner console hardware training on scanning and software viewing and management
March 2015	• Initiation of interlaboratory CCAD-CCF workflow procedure for establishing eConsultations
April–July 2015	• Account creation of CCF pathologists with usernames and passwords
August 2015	• Connectivity of the scanner with the hospital network established
September 2015	• Transition to production and handover of ePathology to the pathology laboratory
October 2015	• Successful network integration with CCF • 2-day mock operation to test the integrity of the workflow with 6 test cases assigned to CCF, with reports finalized from 10 hours to 3 days
November 2015	• 5-day on-site visit by ePathology manager from CCF to create various scanning parameter settings, pathologists' roles, and an e-library matrix, and to optimize internal ePathology clinical activity, and eConsultations workflow with CCF
November 11, 2015	• Launch of eConsultation services with CCF

Abbreviations: CCAD, Cleveland Clinic Abu Dhabi; CCF, Cleveland Clinic Foundation; eSlide Manager, Aperio/Leica digital pathology management software (Leica Microsystems); IT, information technology.

Technologic Challenges Encountered During Implementations

The most important challenge encountered during the IT setup was implementing the ePathology software on the Virtualized Desktop Environment (VMWare, Palo Alto, California). At the initial phase, the digital pathology solution did not have the ability to be virtualized to have the pathologists work from a virtual desktop. Therefore, a decision was made to use a physical server, which placed limits on future storage expansion and also required a reconfiguration of the desktops used by the pathologists from a virtual desktop to a standard Windows desktop (Microsoft, Redmond, Washington). The standard Windows desktop allowed for the application to be installed locally, with the option of navigating to the virtual desktop through VMware.

Other challenges were related to issues regarding the remote viewing and browsing of the digital consultations (eConsultations) digital slides. Because initially the size of CCAD's contracted bandwidth for transatlantic transmissions was smaller than the contracted bandwidth by CCF, there was some delay in resolving images. To resolve this, the bandwidth on the direct line was increased, along with the creation of an SSH File Transfer Protocol (SFTP) client and process to allow the images to be viewed securely and in a timely manner. Additionally, we have recommended that the CCF pathologists find times of the day that are the most conducive to the best viewing experience. The other challenge was related to the consumption of storage at a faster rate than anticipated. An important factor and initiative that are in progress involve changing the strategy of the storage infrastructure for ePathology from physical storage to virtual storage. This will allow better monitoring of the storage consumption, simultaneously adding the flexibility to increase storage when a threshold is met.

CCAD-CCF INTEGRATED NETWORK FOR DIGITAL CONSULTATIONS AND DIGITAL IMMUNOHISTOCHEMICAL STAIN INTERPRETATION

eConsultations

An Aperio/Leica CS2 digital scanner was purchased, and a point-to-point, network-based, digital pathology platform was configured and deployed, allowing CCAD pathologists access to the large pool of more than 60 expert pathologists at the Robert J. Tomsich Pathology & Laboratory Medicine Institute, Cleveland Clinic Laboratories. This network was intended to facilitate the ability to seek a rapid second opinion digital consultation for difficult cases, particularly in rare subspecialties lacking strong internal expertise, such as neuropathology, transplant pathology, and eye pathology. The ePathology program is directed by a staff pathologist and operated by a full-time medical technologist (1 FTE) and 2 part-time technical assistants (1/2 FTE × 2). There is IT support available on demand provided by an IT manager embedded within the pathology department (0.2 FTE).

A fully digital workflow has been designed to ensure efficient and timely submission of glass slides and their related documents by pathologists to CCAD ePathology technologists who prioritize their scanning over other, less

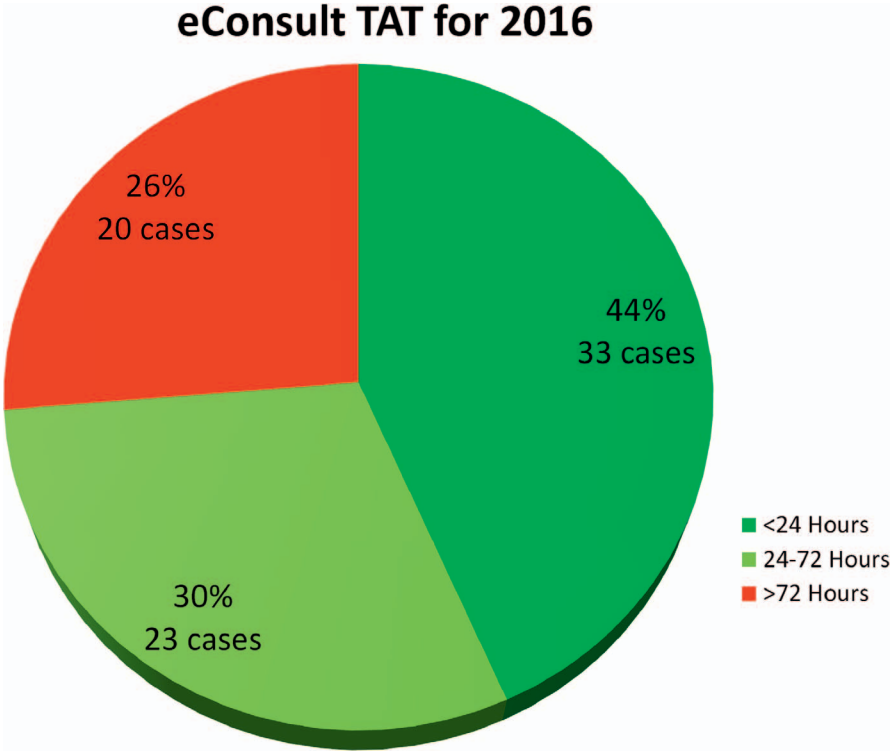

Figure 2. *In 2016, 76 eConsultations were sent to the Cleveland Clinic in Ohio. A total of 33 cases were reported in less than 24 hours, 23 cases between 24 and 72 hours, and only 20 cases exceeded 72 hours. The average turnaround time (TAT) was 2 days and 18 hours.*

time-sensitive scanning activities (archiving, library). They ensure the inclusion of a cover letter detailing the rationale for consultation, a working draft of the report, and any other pertinent information (radiology, laboratory values, others). Two-way alert/notification emails complement the digital workflow, which ensures the immediate awareness of the case arrival to CCF or return to CCAD. The latter alert system is used for calculating turnaround time, which is adjusted to the 8- to 9-hour time zone difference and weekends.

Since launching the service in November 2015, 116 digital consultations have been sent to Cleveland Clinic Laboratories, and results have been completed within 70 hours on average, with the rush cases, such as transplant biopsies, returned within 3 hours. The Center for ePathology at the Cleveland Clinic main campus, in Ohio, follows a key performance indicator of 72 hours of turnaround time for second opinion consultations. In 2016, 74% of cases had a result in less than 72 hours (Figure 2). The delayed reports were attributed to the following reasons: 3 cases required molecular studies; 7 cases required additional special stains and/or immunostains, which were either performed at CCAD or CCF; 1 bone sarcoma required a review by a musculoskeletal radiologist; 6 cases were delayed by long US holidays; glass slides were requested for optimal review in 2 cases; a consensus review was required for 1 case; and a 13-slide case was scanned at ×40 magnification, requiring a longer review process. In 3 thyroid cases, all papillary thyroid carcinomas, the pathologist requested a glass slide review to better assess the nuclear morphology, although the scanning was done at ×40 magnification. This most likely reflects the pathologist's higher level of confidence with light microscopy diagnosis, which has already been reported in the literature.[5]

Digital Immunohistochemistry

In addition to consultative support, the use of digital pathology has helped to reduce cost and facilitate better ordering practices for immunohistochemistry (IHC) and other special stains. Clients seeking special stains without interpretation can send paraffin blocks or unstained slides to a reference lab equipped with digital scanners. Slides are scanned within a few hours of staining, so client pathologists can view the WSI and either proceed with diagnosis or request additional stains. This "eIHC" service allows for less upfront ordering and reduces the need to perform unnecessary stains.

The Center of ePathology at the Cleveland Clinic in Ohio provides this technical-only service not only to CCAD but also to a select number of domestic and international clients. Unstained slides or blocks are sent via express mail. Upon receipt, the stain is performed, and then scanned, and a secure link to the location in which the slide is residing within the Cleveland Clinic server is sent to the requesting pathologist. The latter views and interprets the digital IHC. The stained slide is ultimately returned to the requesting pathologist for review and quality assurance (Figure 3). The laboratory maintains quality assurance records of each IHC interpretation for concordance or discordance. This Web-based review of IHC-stained slides results in faster reporting turnaround time. To date, we have sent 208 eIHC requests, with an average turnaround time of 3.9 days.

Prior to service implementation, all CCAD pathologists participated in a validation project testing their ability to interpret immunostains by glass slides and digitally, equally.[10] Twenty immunostains with variable staining intensity and localizations were scanned and submitted to the pathologists for digital interpretation. The glass slides were then distributed 48 hours later for microscope

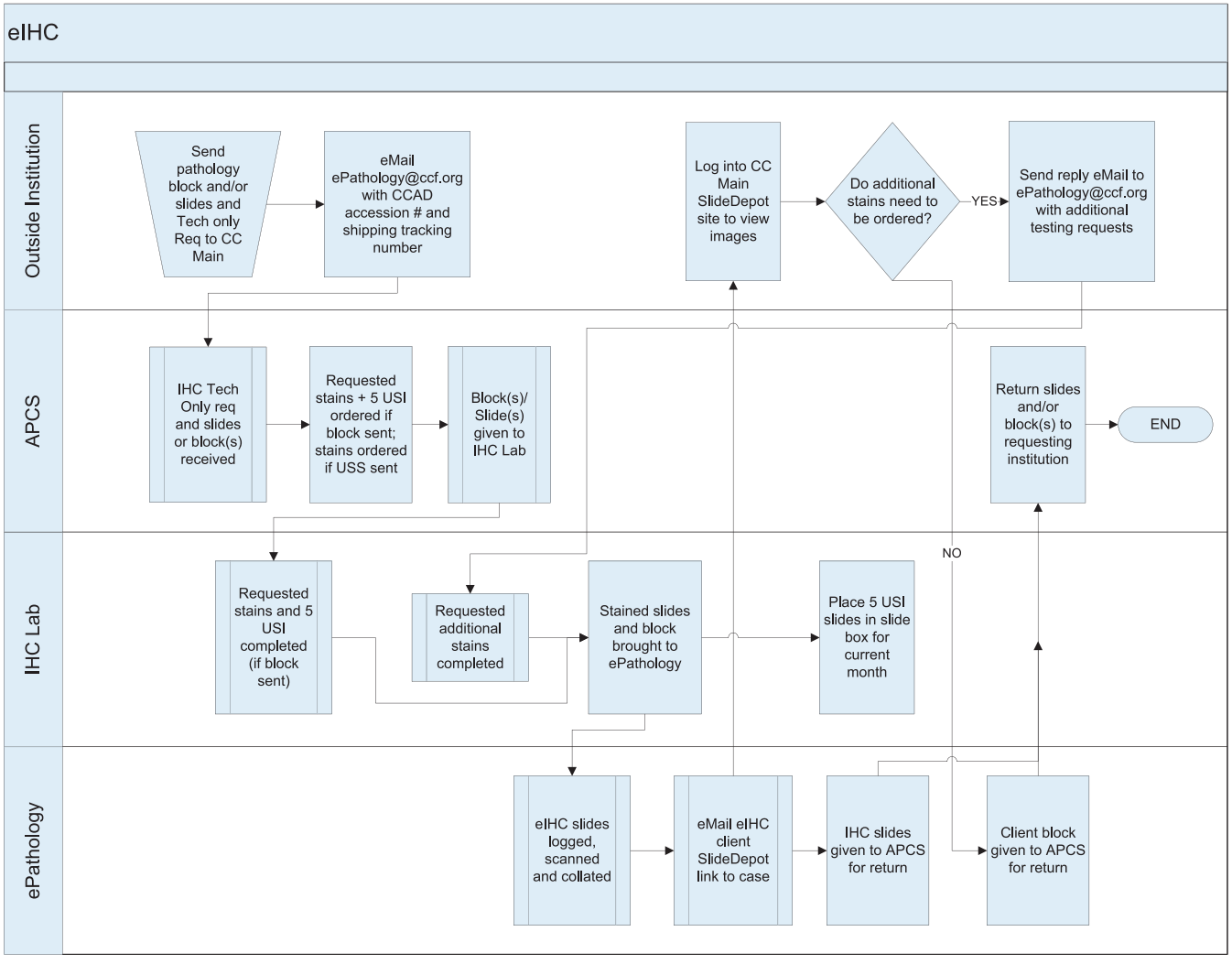

Figure 3. *Flowchart displaying the workflow for handling the electronic/digital immunohistochemistry (eIHC) requests from external clients; eIHC is a service whereby IHC slides are shared via digital pathology. The difference between unstained IHC (USI) and unstained slides (USS) is the section of the laboratory that produces the USS: histology or IHC. Abbreviations: APCS, anatomic pathology consultation services; CC, Cleveland Clinic (United States); CCAD, Cleveland Clinic Abu Dhabi.*

interpretation. The concordance rate between glass and digital interpretation by all pathologists was 100%.

INTERNAL CLINICAL APPLICATIONS

Archiving

In addition to its primary intended use in remote consultations, ePathology is also embedded and integrated into the daily clinical workflow and educational activities of our anatomic pathology laboratory at CCAD. Digital archiving of selected slides and the creation of an educational, subspecialty-based teaching digital library of pathology diseases, are among the most valuable applications.

Prior to the era of digital pathology, and specifically whole slide imaging, reproducing the entirety of the pathologic information present in glass slides was only possible if paraffin blocks were available so recuts could be performed. That meant that cytologic preparations, both gynecologic and nongynecologic, and surgical pathology slides for which paraffin blocks were unavailable could not be reproduced. Full digitization and archiving of all types of glass slides enhances and advances our pathology practice by improving our patient database of pathology records.

In the United Arab Emirates, patients traditionally receive fragmented medical care at multiple institutions and frequently opt for continuity of care abroad, frequently demanding the release of their pathology material for second opinion, which compromises our pathology database.

We have set up a digital pathology archiving workflow in which all pathology material received in consultation from outside hospitals unaccompanied by paraffin blocks is scanned and archived before it is returned, similar to slides requested by patients for second opinion. This ensures conservation, permanent retention and immediate retrieval of patient slides, and consequently improves our patient database.

Internal Quality Control

A good quality WSI starts with a good quality microscopic glass slide. No matter how expensive the scanner, the WSI cannot be superior to the original slide. This is one reason

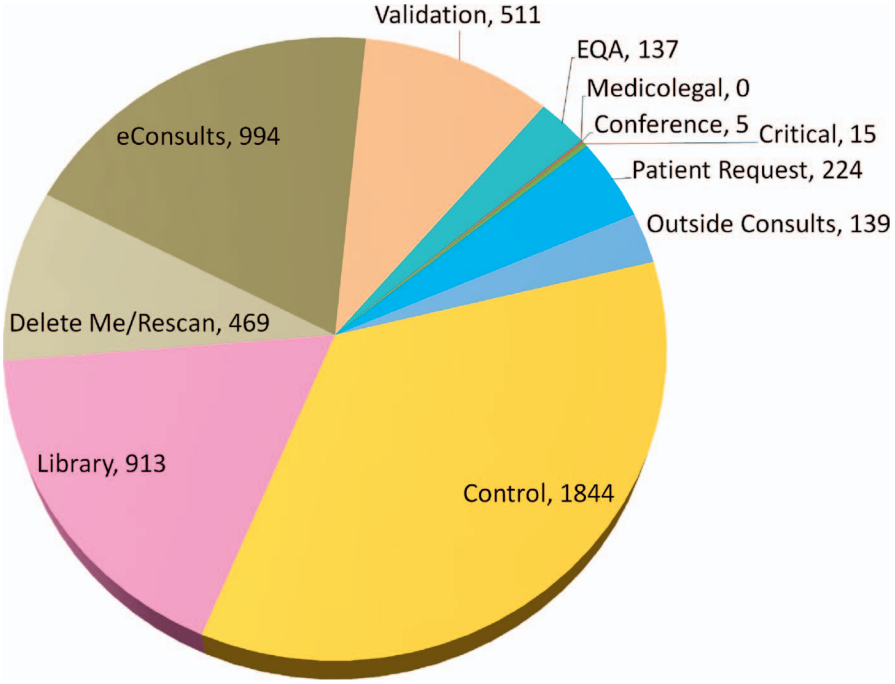

Figure 4. *Pie chart illustrating the total number of slides scanned for various clinical and educational applications. A total of 4621 slides have been scanned to date (511 validation slides refer to the number of slides scanned for possible future validation for primary diagnosis). Abbreviation: EQA, external quality assessment.*

why a background in histotechnology can be helpful for a technician involved with scanning slides.

At CCAD, the entire hematoxylin-eosin staining process has been implemented to mirror the process established at CCF (ie, Ventana Symphony automated hematoxylin-eosin stainer, Ventana Medical Systems, Tucson, Arizona; Leica microtomes, Leica Microsystems, Wetzlar, Germany; and preanalytic processing protocol). In addition, another quality review measure was implemented to safeguard the quality of every glass slide prior to scanning, in which the ePathology technician will reject and return to the lab improperly processed, stained, or mounted slides and will only accept slides of optimal preparation quality. Lastly, the quality of slide staining was assessed by the CCF pathologists during the mock operation (Table).

To improve another key component of our quality control program, we implemented a tissue-preserving, cost-saving procedure of digital scanning and archiving of our daily special stain controls, minimizing the waste of precious control tissue and eliminating the unnecessary circulation and transport of glass slides from the laboratory to the pathologists. Instead of producing a positive tissue control per each pathologist order, only 1 control is performed, scanned, and uploaded to be simultaneously accessed by all pathologists for viewing and interpretation.

We also implemented an entirely digital workflow for the hematoxylin-eosin daily control review. Each pathologist rotates weekly to review the daily scanned hematoxylin-eosin control and records the quality of the stain onto the monthly quality control form, which is subsequently approved and archived each month by the laboratory manager. This digital review not only removes the transport of slides but also allows for a seamless quality control review of prior tests/days, if required.

eLibrary

For educational use, we established a simple workflow by which interesting cases are submitted for scanning and archiving in a subspecialty-based, organ-specific library of pathologic diseases. This digital library enhances the quality of teaching and learning by eliminating many of the inefficiencies associated with maintaining traditional glass slide sets and reducing laboratory costs of preparing extra slides for teaching purposes. To date, we have archived more than 800 subspecialty teaching cases (Figure 4).

DIGITAL PATHOLOGY EXPANSION OF CLINICAL APPLICATIONS

Currently our anatomic pathology laboratory information service is not interfaced with the DPS, and digital archiving is only performed on selected cases. Benefits of the bidirectional exchange integration include the automatic link of scanned images to cases in the anatomic pathology laboratory information service, instant access to a patient's previously scanned specimen for comparison (eg, transplant heart biopsy, prostate biopsies), and automatic metadata transfer from the anatomic pathology laboratory information service to the DPS. This removes the redundant manual data entry of scanned slides and reduces user error. This integration will enable pathologists at our institution to review digital slides on one monitor while simultaneously viewing pertinent case metadata, such as clinical information and gross pathology findings. In addition, data, including WSIs from prior cases, could be instantly accessed and easily reviewed when needed. Transitioning to a digital workflow may save time because it increases efficiency by eliminating manual processes (eg, searching for misplaced glass slides) and improving reporting turnaround time (eg, electronically transferring WSIs of prior cases for review rather than physically searching and delivering glass slides).[6]

Once the interface has been accomplished, we intend to digitally archive, after sign-out, representative slides of all biopsy cases, and pertinent slides from large resections (after diagnostic archiving).[7] A high-throughput scanner will be required for this large scale operation.

The benefits and advantages of postdiagnostic digital archiving are multiple. It will facilitate and expedite

reporting of cases where previous material is required for correlation, because they are instantly accessible. Additionally, the availability of digital slides allows for instant collation of cases for tumor board conference review, and it practically eliminates the time-demanding manual retrieval of such cases. In one report, pathologists saved an average of 1 hour per week in preparing for these meetings, thus cutting their time by 50%. Moreover, whole slide imaging permits real-time flexibility, making it easy to add on cases and show cases side by side. Also, because presenters have access to the entire slide, they are better equipped to address "on-the-spot" questions.[8,9] Furthermore, with a completely digital archive, it becomes possible to store the very heavy and space-consuming physical glass slide archive outside the hospital, or even to discard the slides. Currently, according to the College of American Pathologists, glass slides that are used for primary diagnosis must be retained for 10 years, whereas the retention of WSIs is left to the discretion of the laboratory director. It is not unlikely that in the future WSI may be allowed to become the preferred storage, and glass slide storage deemed optional.

CONCLUSION

We have described the strategic adoption and implementation of digital pathology into the clinical workflow of the pathology and laboratory medicine institute of Cleveland Clinic Abu Dhabi, and highlighted its impact on the clinical operation, educational activities, and patient care.

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