

Integrating the Health-care Enterprise Pathology and Laboratory Medicine Guideline for Digital Pathology Interoperability

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Abstract

Integrating the health-care enterprise (IHE) is an international initiative to promote the use of standards to achieve interoperability among health information technology systems. The Pathology and Laboratory Medicine domain within IHE has brought together subject matter experts, electronic health record vendors, and digital imaging vendors, to initiate development of a series of digital pathology interoperability guidelines, called “integration profiles” within IHE. This effort begins with documentation of common use cases, followed by identification of available data and technology standards best utilized to achieve those use cases. An integration profile that describes the information flow and technology interactions is then published for trial use. Real world testing occurs in “connectathon” events, in which multiple vendors attempt to connect their products following the interoperability guidance parameters set forth in the profile. This paper describes the overarching set of integration profiles, one of which has been published, to support key digital pathology use cases.

Keywords: Digital pathology, integrating the health-care enterprise, interoperability

INTRODUCTION

Integrating the health-care enterprise (IHE) is an international initiative to promote the use of standards to achieve interoperability among health information technology (HIT) systems and effective use of electronic health records (EHRs). IHE provides a forum for care providers, HIT experts, vendors, and other stakeholders in several clinical and operational domains to reach consensus on standards-based solutions to critical interoperability issues. The primary output of IHE is system implementation guides, called IHE Integration Profiles. IHE publishes each profile through a well-defined process of public review and trial implementation and gathers profiles that have reached final text status into an IHE Technical Frameworks (TFs). For more information regarding IHE in general, see www.ihe.net. For more

technical information, see the IHE TFs General Introduction (http://www.ihe.net/Technical_Frameworks/#GenIntro). For on-going development work, see wiki.ihe.net. This paper delineates use cases and associated integration profiles that support interoperability among various components that comprise a holistic digital pathology workflow solution. The integration profiles are presented at a high level in this document. Each profile will be fully specified and published

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as a supplement to the IHE Pathology and Laboratory Medicine (PaLM) TF.^[1] The intended audience of this IHE PaLM paper is:

- Technical staff of vendors participating or considering participation in the IHE initiative in the scope of the PaLM domain
- Pathology and laboratory subject matter experts.

IHE International welcomes comments on this document and the IHE initiative. They can be submitted by sending an e-mail to the co-chairs and secretary of the PaLM domain committees at palm@ihe.net. If possible, please describe your organization's vision and anticipated role within the workflow outlined under this initiative.

BACKGROUND

This paper lays out the vision and use cases for digital pathology and calls for a collection of future integration profiles to replace the former Anatomic Pathology Workflow (APW) profile.^[2] One of the primary objectives is to document holistic use cases that comprehensively represent the future workflow in pathology laboratories, considering the latest advancements in digital imaging. These use cases are not intended to be exhaustive; they currently primarily span two phases of anatomic pathology, but also imply possible coverage of some clinical pathology workflows (e.g., hematology blood smear imaging). The two phases targeted are:

- a. The gross/macroscopic examination, which generally involves manual methods and leverages a digital camera to capture digital images one at a time
- b. The histologic/microscopic examination incorporating whole slide imaging (WSI) technology, which may be manual or fully automated, and leverages slide scanners to capture images one at a time or in volume through use of one or many slide racks.

Both phases generally require a hardware device to be paired with image management software that assists with acquisition of a digital image from an imaging modality (e.g., slide scanner), review of this image, quality adjustments, embedded manual or automated annotations, and transmission of the image into some types of archive for long-term storage.

This paper breaks down the former APW profile,^[2] which modeled the entire digital pathology workflow, into a set of smaller, easier to implement building blocks that each focus on one key aspect of the digital pathology workflow. These workflow components include ordering and reporting pathology studies, digital image scheduling, acquisition, display, storage, management, annotation, analytic processing, and second opinion requests and responses. The expectation is to collect feedback from a wide spectrum of stakeholders of digital pathology (vendors, pathologists, and health-care institutions) to confirm and/or refine a set of profiles to encompass one or more workflow components before starting to build them as new supplements to the PaLM TF,^[1] leveraging existing integration profiles,^[3-5] and work completed by

other organizations such as HL7^[6] and DICOM^[7,8] whenever possible.

THE FUTURE OF ANATOMIC PATHOLOGY: DIGITAL EVOLUTION OR REVOLUTION?

Recent advancements in whole slide digital imaging technologies serve to significantly alter traditional workflows within pathology laboratories.^[7,8] Digital imaging in pathology typically spans two primary aspects of the conventional workflow, namely, the gross/macroscopic examination and the histologic/microscopic examination. In Europe and Canada, digital technologies have been leveraged in the past few years to compensate for shortage of expert pathologists. Implementations have evolved and advanced rapidly, and data support the benefits of digital pathology over routine microscopy,^[9,10] especially the downstream analytical benefits of a digital format.^[11] In the United States, Food and Drug Administration (FDA) approval of the first WSI system for primary diagnosis^[12,13] has reignited focus on use cases and value propositions for various vended solutions that in aggregate would support digital pathology. However, currently, there is minimal formal literature that speaks to optimal interactions among vended solutions. Our goal is to fill this gap through the precise documentation of how best to accommodate the most prevalent needs or "use cases" within the clinical domain.

While the EHR focuses on the integrated care of a single patient, the anatomic pathology laboratory information system (AP-LIS) focuses on the production, storage, and conveyance of the diagnostic interpretation of stained tissue. AP-LIS is transitioning to become modules of larger EHR systems, and during this transitional period, the implementation of these systems is quite variable across the market. WSI will drive additional evolution and/or reinvention of the AP-LIS. There is more to digital pathology than supporting WSI and associated instrumentation, but this innovation will be a catalyst for change and an enabler of significant evolution of workflow and advancement of the field. During this period of change, the guidelines provided in the IHE Profiles can be important resources for coordinating product development and ensuring the incorporation of best practices into new system designs.

INTEGRATING THE HEALTHCARE ENTERPRISE PROFILES SUPPORT THE DISCIPLINE OF DIAGNOSTIC PATHOLOGY

Anatomic pathology is one of the two major branches of diagnostic pathology, the other being clinical pathology. Both branches are concerned with the diagnosis of disease, the definition and prediction of disease course, and the delineation of disease causes. The primary goal of anatomic pathology disciplines is the generation and communication of pathologic diagnoses based on examination of the morphology of excised organs, tissue, isolated cells, or cell-free material from a human subject. Hence, anatomic pathology is specimen driven

and morphology centered. For the purposes of constraining the scope of this discussion, our focus will be on traditional surgical pathology workflows with the recognition that related variants (e.g., cytopathology, autopsy, and hematology) will need to be examined in more detail in subsequent efforts to identify their fit into this framework and their distinct features that remain to be addressed.

IHE profiles define a framework of electronic messages through which systems participating in specified workflows may request and send data. These systems are free to implement internal processes that request, create, and manage data in innovative ways, but the communications between these systems and the workflows that they support are standardized. The systems may act under the control of various types of users, or they may be autonomous. In IHE profiles, participating systems or roles are referred to as actors and the way in which actors interact are referred to as transactions. Actors and transactions are enumerated and “registered” in IHE to standardize implementations across vendors in a manner that promotes interoperability and reuse. For vendors that implement an IHE profile, their products can therefore be thought of as “actors” performing specific roles through discrete “transactions” that facilitate interaction between systems and devices involved in specified workflows. This abstraction layer frees vendors to innovate and implement novel functionality that best suites the development roadmap for their products while still supporting interoperability. For example, consider an Electronic Medical Record (EMR) vendor that wants to support an interoperable electronic ordering profile to work with multiple LIS platforms. A typical use case will include a surgeon that wants to send specimens

to a pathologist to render diagnoses. The surgeon will typically use an EMR to place a laboratory order, playing the role of an “order placer actor.” A pathologist in the lab will receive and process the specimen and its associated order, using an LIS to return a result, playing the role of the “order filler actor.” The pathologist may use diagnostic instruments, referred to as “analyzer actors,” to automate parts of the diagnostic process. In this scenario, the original laboratory order is transformed into more atomic “work order steps” that an analyzer follows as part of the diagnostic process. This discussion is organized from “outside in” with respect to a laboratory employing digital pathology, i.e., we begin by considering the high-level external interactions required for digital pathology [Figure 1] and subsequently move to internal workflows.

ORDERING A TISSUE EXAMINATION

Clinicians order tissue examinations using the Order Placer Actor, which is generally implemented as an order entry system that may be a module in the EMR or EHR. The order is posted to the pathologist who handles it using the order filler actor, typically implemented by the AP-LIS [Figure 1].

Two transactions are needed between the order placer actor and order filler actor to support order placement and fulfillment, as depicted in greater detail in Figure 2:

- Placer order management is a process, in which the order transmits from the clinician (order placer actor) to the pathologist (order filler actor) and keeps the order placer and filler systems synchronized on any further update of the order
- Report management is the process which transmits reports, results, and references to digital assets from the pathologist (order filler actor) to the clinician (order placer actor).

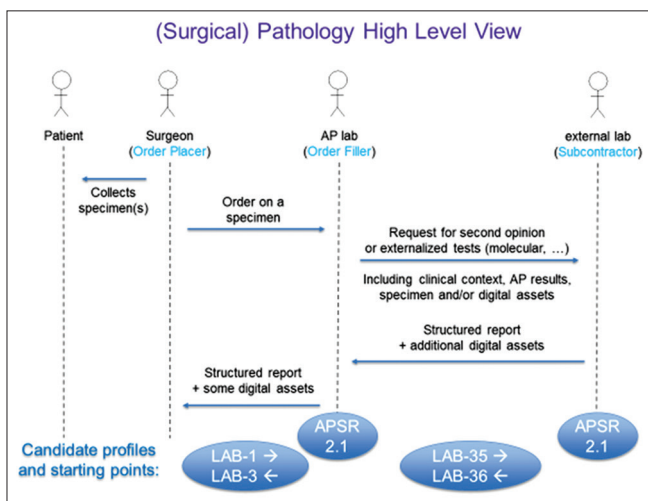


Figure 1: External interactions of the laboratory involved in digital pathology workflow. Four actors and their communications are shown, symbolized by stick figures. The user/entity roles are shown under the symbols, with the generic actor type in parentheses under the roles. Communications are shown as horizontal arrows, and the vertical dotted lines depict a timeline during which the sequence of communications takes place. Existing profiles pertinent to these generic actor types that may contribute to this discussion are shown in ovals at the bottom

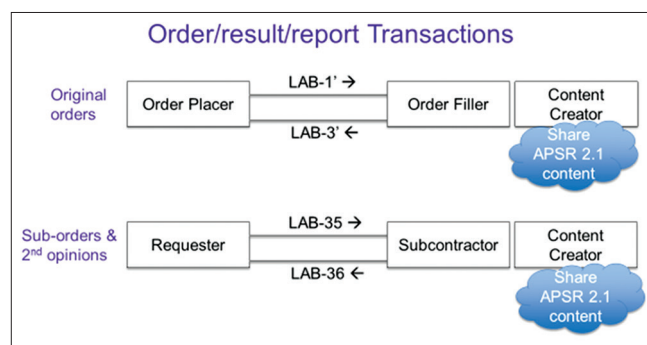


Figure 2: Actors and transactions supporting external interactions. The transaction numbers refer to defined transactions in existing integrating the health-care enterprise Profiles. Transactions LAB-1 and LAB-3 were designed for clinical pathology orders/results, whereas transactions PAT-1 and PAT-3 were designed for anatomic pathology orders/results. This paper recognizes the need to build a set of two new transactions merging the prior two sets. This new set is temporarily tagged LAB-1' and LAB-3'. Each anatomic pathology laboratory information system is also expected to produce and send or share an anatomic pathology structured report conformant to the Anatomic Pathology Structured Reports 2.1 profile (<https://pubswiki.ihe.net/index.php/APSR>)^[3]

In a situation where some of the examination or testing is subcontracted to an external lab or where an external pathologist is solicited for a second opinion, two additional transactions replicate the same kind of workflow between the primary lab and the subcontractor [Figure 2].

Most EHR systems create a single order for submitting one or more tissue specimen(s) to a AP-LIS. Typical specimen-specific order questions may include:

- Requested procedure (e.g., histology, cytology, frozen section, etc.)
- Source (e.g., skin)
- Collection procedure (e.g., shave biopsy)
- Target site (e.g., right cheek).

Other data elements include:

- Placer order number or placer order group number
- Patient name and medical record numbers
- Collector ID, date/time stamp
- Barcoding of documents and containers:
 - 1D for most liquid specimen containers used in clinical lab automation
 - 2D for small containers.

INITIAL FOCUS ON SURGICAL PATHOLOGY CLINICAL CARE WORKFLOWS

The production of a glass slide in surgical pathology is depicted in Figure 3 (omitting the specimen collection step). There are separate, existing IHE integration profiles^[4,5] that speak to ordering, collecting, labeling, and tracking specimens into a pathology laboratory. These are touched upon in the text of this paper insofar as these activities are critical to support the acquisition of a digital image and subsequent events in the digital pathology workflow. Most of the steps that occur after receiving a specimen in a laboratory reflect manual manipulation and human observation of the specimen with

documentation in an AP-LIS. This functionality is important but generally will not directly impact the components of the digital workflow. It is important to recognize that production of a glass slide remains a prerequisite for digital imaging in most surgical pathology laboratories. Certain facets of the production of a glass slide will likely need to be modified in most laboratories to support digital image acquisition. Requirements and assumptions include:

- All glass slides contain barcodes that encode a unique identification for that physical asset. As an example, the slide identifier can be built algorithmically following this construct: prefix (alpha) + two digit year (numeral) + delimiter (e.g., a hyphen) + a case number (representing the sequential creation of pathology examinations for the year) + delimited (usually a space character) + a number representing the block + the number representing a slide level (representing the sequential depth of cut into a block). Example: SP19-000321 A1-1
- Digital asset identification will present new challenges in supporting chain of custody, auditing, and digital annotations more granular than current physical ones. Examples include potential many-to-many mappings between digital and physical assets as physical assets are modified and as multiple digital scans of the same physical asset are acquired or modified through digital processing, and definition/annotation of digital regions of interest (ROIs) within scans. These challenging issues remain to be addressed in future
- The focus of this initial discussion is on the most common clinical care-related tissue specimen workflows. The following use cases are important but are not covered here:
 - Multidisciplinary tumor boards represent an important clinical care activity, which will be examined in a future multidomain cooperation within IHE
 - Interlaboratory cooperation such as digital consultations, subcontracted further testing, and

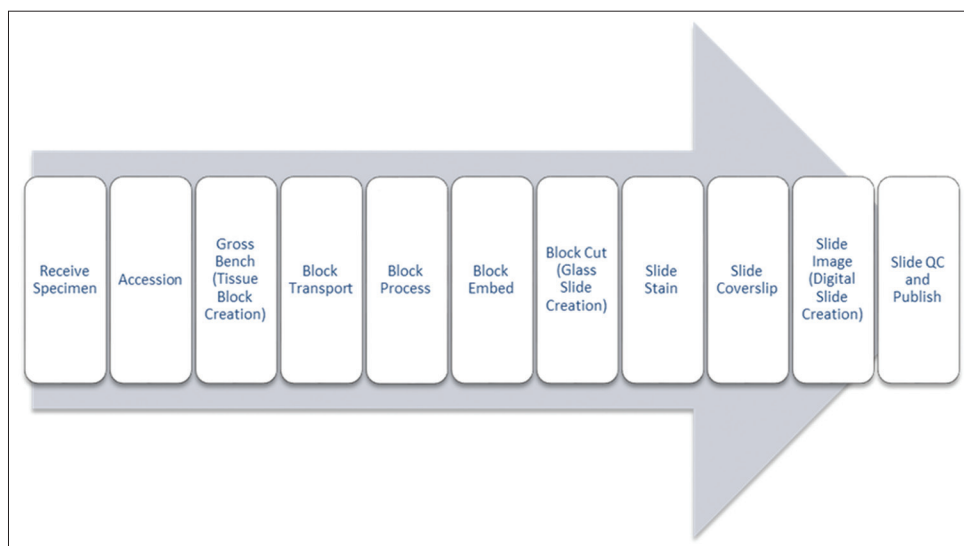


Figure 3: Steps performed on specimens from arrival in lab to creation of slide images

second opinions represent an important aspect of clinical care diagnostics have already been addressed in the recent past by the PaLM domain with the Inter-Laboratory Workflow Profile^[5]

- Research workflows vary by protocol and are not explicitly investigated here. Neither are public health and environmental testing
- Tissue microarrays represent a special use case, in which tissue from multiple sources is incorporated onto a single glass slide. This use case is currently left out of the scope of this paper as specimens from multiple patients are typically not intermingled in clinical scenarios.
- Every digital asset will have a single parent (and the root node in the data model is the specimen; in alignment with the HL7 specimen domain analysis model [SDAM]^[6]). On-slide tissue controls remain a challenge to be addressed in future
- *In vivo* microscopy is not explicitly considered given its immaturity in clinical tissue-based diagnostics today
- Fine-needle aspiration ultrasound images and specimen radiographs are key clinical workflow elements but are out of scope of this discussion. Radiology profiles exist today to support ultrasound and radiographic instrumentation and may be referenced for use in a pathology laboratory.

digital images and associated data during one or more steps in the overall workflow [Figure 4]. In the diagram, the “order placer” is usually an EHR, the “order filler” is usually an AP-LIS, an “acquisition manager” is typical image management software, an “acquisition modality” is typically a WSI scanner, an image manager/archive may be a picture archival and communication system (PACS) or a vendor neutral archive (VNA), an “evidence creator” may be a digital analysis algorithm, and an “image display” may be a whole slide image viewer. An implementer of this profile needs not follow these typical designations, however. For example, the image acquisition profile (Digital Pathology Image Acquisition [DPIA]) requires that an “acquisition modality” create a DICOM compliant object. This does not explicitly require that this must be accomplished within the physical hardware of a scanner. A vendor may combine a WSI scanner together with a workstation and image acquisition software as representing their implementation of an “acquisition modality.”

As depicted in Figure 4, the scope for proposed new profiles (of which only DPIA has currently been published^[14]) includes:

1. The ordering process to initiate the tissue collection and subsequent pathology exam and to report the results back. This first part of the workflow needs two transactions that will be derived from the combination of the original transactions LAB-1 and LAB-3 designed for clinical pathology and PAT-1 and PAT-3 from the former anatomic pathology TF. This will be detailed in the digital pathology ordering and reporting integration profile that will be designed to support ordering and

DIGITAL PATHOLOGY AND ASSOCIATED INTEGRATING THE HEALTH-CARE ENTERPRISE INTEGRATION PROFILES

Digital Pathology augments the traditional APW by creating

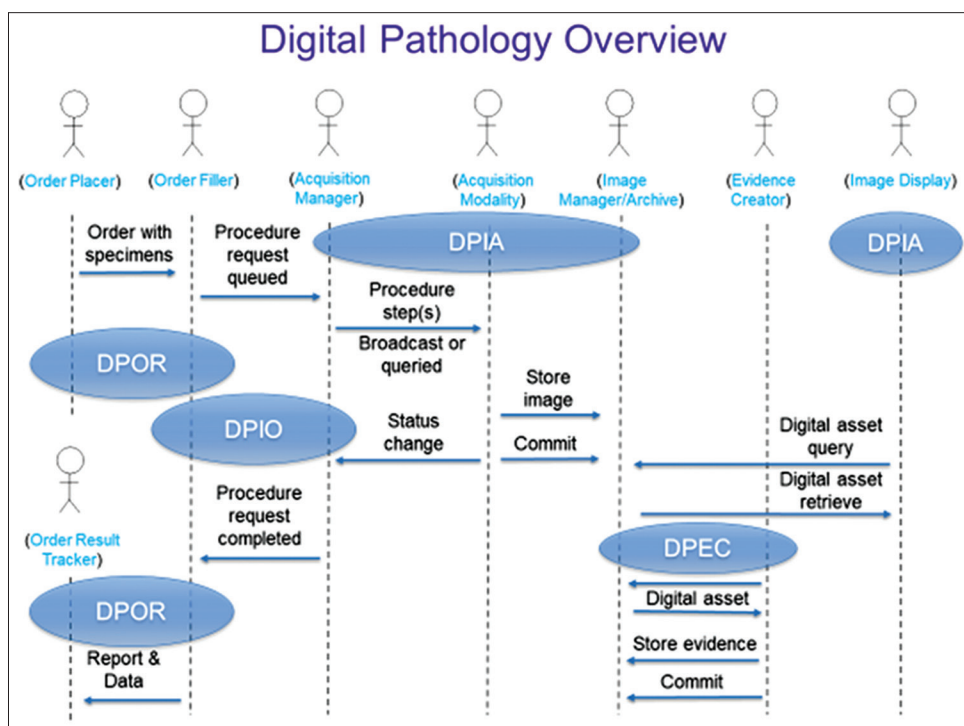


Figure 4: Actors and transactions involved in the digital pathology workflow. The digital pathology image acquisition profile has been published. Digital pathology ordering and reporting, digital pathology image ordering, and digital pathology evidence creation profiles represent future development

reporting for both clinical and anatomic pathologies. This new set of transactions is temporarily tagged LAB-1' and LAB-3' [as depicted in Figure 2]

2. Following the pathology examination, any subsequent acquisition of digital assets and digital processing steps would be detailed in the Digital Pathology Image Ordering integration profile slated for the future development
3. The acquisition of a digital image covers the minimal set of actors and transactions also necessary for preservation of the image, namely, storage in DICOM format with notification of availability to the relevant actor. This is documented in the recently published DPIA profile.^[14]
 - a. Digital asset identification represents an important component of image acquisition.
4. The display of stored digital images. This is documented in the DPIA profile
5. The storage and retrieval of digital images as needed for display, processing, and new evidence creation. This is documented in the DPIA profile
6. The manipulation of digital images by humans and machine algorithms, potentially resulting in the creation of new evidence or alteration of existing digital assets. This will be documented in the Digital Pathology Evidence Creation workflow.

The pathology laboratory may study both physical specimens and digital specimens. The production of observations (margin measurements, recognition of morphologic abnormality, histologic type, etc.) on digital specimens combines actors and transactions of existing IHE profiles with actors of future digital pathology-specific profiles. Figure 5 depicts how existing IHE profiles may be leveraged to support interoperability of analytic data within a digital pathology workflow leveraging the existing Laboratory Testing Workflow and Laboratory Analytical Workflow profiles.

ORDER FULFILLMENT

The AP-LIS needs to manage the “manufacturing process” of

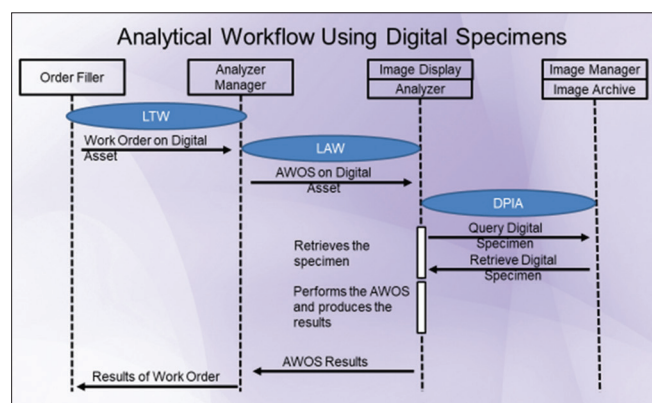


Figure 5: Actors and transactions involved in analytic data exchange for digital pathology with analytic work order steps performed on digital assets returning a quantitative result (such as measurement of a digital feature) or a digital specimen (such as a new image with a certain feature highlighted)

the digital image(s) and the final pathology diagnostic report, usually including structured and unstructured data. The AP-LIS may break down the clinical order into a set of work orders similar to what is done in the clinical laboratory space. Work orders are in turn broken down into granular “work order steps” for instrumentation to follow for a given type of specimen and lab test to be performed. Middleware is uncommon in AP laboratories today, but it may be reasonable to assume that it will play a larger role as instrumentation and automation advances within AP laboratories. Specimen processing “events” tracked by an AP-LIS are largely captured manually or using barcodes today, but technologic advances should allow for greater automation and granularity in future. It is important to recognize that many tasks fulfilled by the AP-LIS today involve physical processing of the tissue (e.g., creating an unstained slide or then applying a stain to it), but in future, these may include processing of digital images (e.g., applying a mitotic count algorithm to a designated region of interest [ROI] on a whole slide image). It is also possible that vended systems outside the AP-LIS take on some of these roles (i.e., specialized “evidence creator” actors taking on greater roles rather than relying solely on “order filler” actor functionality).

Work order steps are typically performed by instrumentation actors (slide scanners, analyzers, etc.) on physical specimens or digital assets. Work order steps that acquire digital assets are defined as Imaging Work Order Steps. Work order steps that produce analytical observations on physical or digital specimens are called Analytical Work Order Steps. Work order steps representing a single operation to be performed on a specimen by an automated device (e.g., transferring a glass slide specimen container from a cover-slipper to a whole slide scanner) are termed specimen work order steps (SWOS, reference LDA in PaLM TF10.0^[1]). Work order steps may be performed on both physical specimens and digital assets for patient diagnosis and quality control (QC) purposes.

DIGITAL IMAGE ACQUISITION

Image acquisition workflow may be categorized into a few different paradigms with actors and transaction depicted in Figure 6:

- A. An order/step driven workflow; this may also be described as a scheduled or queued workflow. An acquisition modality instrument will typically query an acquisition manager for instructions on how best to acquire a digital image after recognizing the presence of a physical asset. This is felt to likely represent the most common implementation in the near term. This will require a bidirectional interface between the acquisition manager and the acquisition modality, and it reflects a relatively standard workflow in radiology today (querying of an imaging modality work list). Situations in which a physical asset unexpectedly appears within an imaging modality may also be readily accommodated within this acquisition paradigm
- B. A unidirectional interface representing a broadcast

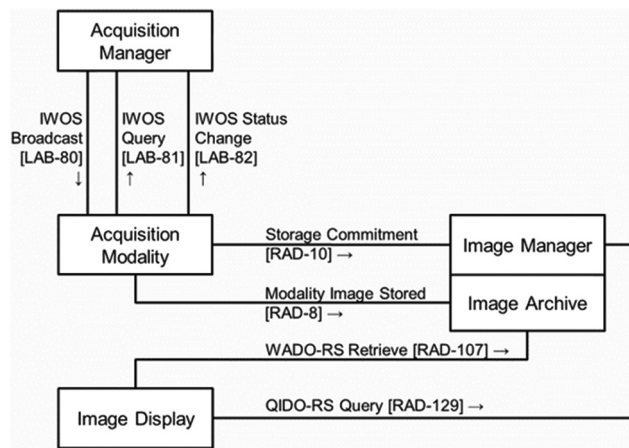


Figure 6: Digital pathology image acquisition profile: Transactions to acquire, store, and display images. IWOS stands for “Image Work Order Steps”

message from an acquisition manager to one or more acquisition modalities represents a simpler paradigm for managing image acquisition. In this scenario, physical asset identifiers along with acquisition “protocols” will typically be broadcast to all acquisition modalities that are capable of acquiring a digital image from the physical asset. When the physical asset is recognized within any of the acquisition modalities, digital image acquisition can begin according to the previously broadcast parameters

- C. Variant/reconciliation workflows represent a category of exception handling to manage situations that fall outside the scope of paradigms “A” or “B” above. Typically, these situations will require some level of manual intervention by a technologist. The technologist will have to guide the acquisition modality in situations where the instrumentation is not able to ascertain how to acquire an image due to a workflow or instrumentation fault of some kind (e.g., unreadable label).

It should be noted that an AP-LIS may not use a traditional PACS in the sense of an image workflow and communication tool, but rather leverage the AP-LIS for workflow, image management software for digital asset organization, file format specific image viewer(s) for display, and use an image archive for local, networked, database, or cloud storage. Vended software may choose to incorporate the roles of multiple actors, for example, a “Pathology PACS” might choose to serve as an image acquisition manager, image viewer, and image archive.

REPORTING THE RESULTS OF A TISSUE EXAMINATION

The results fulfilling the order of tissue examination are messaged from the order filler (e.g., the AP-LIS) to the actor tracking results for orders, called order result tracker. This actor is an application used by the clinicians. Most often, it is a role performed by the EMR/EHR, but it may also be a standalone application dedicating to result tracking and serving.

The “result” is represented by the preliminary or final pathology report, which may include digital assets too. Management of digital assets and physical assets are part of the workflow and transactions.

USE CASES FOR DIGITAL PATHOLOGY WORKFLOWS

The following use cases represent high priority, high prevalence needs within the clinical domain as determined by a group of subject matter experts spanning the pathology and lab domain, clinical informatics, and technology vendor space. The list is nonexhaustive and the descriptions are described only insofar as key interoperability requirements and themes are clear to the implementers of the integration profiles.

Use case #1: Managing digital assets for primary diagnosis

These workflows include the use of whole slide images for primary diagnosis. The first workflow described is a general workflow for glass slide production in a surgical pathology laboratory, followed by modification for a digital pathology sign out rather than direct transport of slides to the pathologist for viewing under a microscope. These workflows assume that all specimen containers, tissue blocks, and glass slides are barcoded with a unique identification schema, in which every specimen is related to a parent specimen from which it was derived. Primary workflow steps and considerations to create digital copies of all glass slides for primary diagnosis begin with traditional glass slide production:

- Specimens are collected and transported to the receiving area of the pathology laboratory
- Specimen gross examination is performed with possible digital imaging and annotation, generally to include specification of what tissue has been placed into what cassettes for later correlation with microscopic review. Data describing the examination are either transcribed or directly entered as free text or structured templates into the AP-LIS
- Tissue blocks are transported in formalin to a specimen processing area in the laboratory
- Blocks are removed from the tissue processors and embedded in paraffin
- Slides are generated through block cutting, usually involving a barcode scan of the tissue block with associated slide label generation. An important (and today, entirely manual) QC check involves correlation of the tissue profile in the cut face of the paraffin block with that observed on the glass slide. Vended systems for digital capture that are capable of cataloging of the face of the tissue block for later comparison to the microscopic image remains a gap in the market today
- The glass slide may be manually stained or placed in an automated stainer, which might be optionally interfaced with the order filler (e.g., AP-LIS) to draw forth information on precisely what type of stain should be performed on the unstained tissue present on the glass slide

- The stained slide is cover-slipped using mounting medium and a thin glass coverslip or possibly optically neutral plastic tape
- The stained slide is dried sufficiently to be placed into a digital scanner for image acquisition.

Once glass slides have been generated, these are placed into a WSI scanner (“acquisition modality”) for image acquisition. The scanner reads the label on the glass slide and interprets the barcode, which typically reflects the case accession number, block, and slide level to uniquely identify the glass slide. This schema is not always followed. Some information systems leverage only a simple numeric identifier, but this still uniquely identifies the glass slide within the organization. The barcode may be preceded and followed by a delimiter so that interpreting software recognizes the presence of a scanning event. Many scanners can be programmed to automatically insert these delimiters at the time of a scanning event, so the delimiters may not be necessary to store as part of interface messages or within the information model.

- For example, \SP18-000555 B3-L2\, would indicate the 555th case accessioned in the year 2018, the second container designated “B,” the third block of tissue submitted during gross examination of that container, and the second deepest level of the block cut by the histotechnologist for placement on a glass slide. The delimiter is the backslash character “\,” which allows the information system to recognize a barcode scan event
- Please note that other elements of the slide label represented as human readable text are generally not encoded in the barcode. Some data elements such as patient identifiers are included in the interoperability profile transactions, while others such as the pathology laboratory or hospital name will be included in the DICOM metadata that is packaged with the image data.
- The “acquisition modality” (scanner) may communicate with an “acquisition manager” (image management software or AP-LIS) to adjust parameters specifically for the glass slide being scanned.
 - A unidirectional interface may push parameters into a buffer in the scanner in expectation of physical loading of the glass slide OR
 - Upon completion of scanning and storage of image, the image storage system may indicate to the acquisition manager the availability of a digital resource for viewing and linkage to an AP-LIS case
 - A bidirectional interface may request and receive parameters from the acquisition manager as glass slides are recognized as having been loaded into the scanner
 - Upon completion of scanning and storage of image, the scanner will indicate to the acquisition manager the availability of a digital resource for viewing.
- The acquisition manager must be able to track and identify when digital assets are available for viewing by a technologist for QC review. Similarly, a mechanism must exist for a pathologist to recognize when all physical assets have a QC-verified digital counterpart ready for interpretation
- The scanner may flag images requiring manual intervention
- Digital images are ultimately deposited onto a local hard drive, a network file share, VNA, or PACS
- The acquisition modality will need to be configured to identify new digital assets in a way that allows other actors to recognize the parent specimen from which this new digital asset was derived.

Those glass slides that are unable to be scanned must be sent to the pathologist for review. Envisioning a future in which many (hundreds or thousands of) glass slides are routinely in the process of being scanned by several different scanning devices, glass slides need to be electronically tracked to enable timely retrieval by laboratory staff. The IHE Specimen Event Tracking profile may be leveraged to provide this functionality.

Today, the AP-LIS presents a work list to the pathologist and perhaps in conjunction with additional software (e.g., PACS or image management system [IMS]) clearly indicates the presence or absence of digital assets and/or pending status. If a glass slide could not be scanned, it should be clearly called out to the pathologist so that he/she may ensure that all diagnostic materials are reviewed prior to verification of the diagnoses for a case.

Digital slides should be rapidly accessed and reviewed for interpretation by the pathologist taking into account the following considerations:

- It should be clear what slides have been viewed completely, partially viewed, or not viewed at all
 - Different pathologists may have different interpretations of what “viewed completely” entails and as such should be configurable by the end user organization (e.g., review of all tissue at a certain magnification must occur).
- Pathologists should be able to annotate images to flag features or ROI (these should be customizable by the pathologist)
 - Pathologists should be able to quickly go back to an annotation by searching for metadata.
- Pathologists should be able to flag certain digital assets for review by a consultant
- The system should maintain an audit trail of all viewing and annotation activities
- The system should uniquely “stamp” all digital assets at the time of case verification by the pathologist to preserve them in their current state for future review
 - If a digital asset is rescanned, deleted, further annotated, it should be clear if this occurred before or after case verification and/or if a pathologist has viewed, been informed of, and/or approved of the activity.

Storage considerations should be harmonized with the laboratories policies for retention of diagnostic material in accordance with local, regional, and national regulations. Harmonization with policies for send out testing also deserves consideration. Rather than the maintaining digital versions of all glass slides, a process for culling may be considered, in which only key slides are retained (e.g., for a cancer case, only representative tumor, closest margins, lymph nodes, etc.). A pathologist may manually annotate which slides should be retained in perpetuity or a configuration option may be set to indicate that any slides with annotations should be preserved. All other digital versions of slides should be able to go through an archiving or deletion process to reduce the storage footprint for a case. Different types of slides may undergo different processes (e.g., cytopathology z-stacked slides may lose all but one plane or may undergo postprocessing to have the most in-focus tile maintained while others are deleted).

For every step in the life cycle of a pathology specimen, digital artifacts (metadata) may be created. Most are small and primarily for management and tracking (identifiers and timestamps), but digital images made of case material can be large and complex. The images fall into two main categories, images used in the formation of the clinical diagnosis of the case and those obtained as either “proof of work” or for QC purposes. A full audit trail should be retained for all modifications to the digital image to provide a full digital “chain of custody” and confidence in what information was available to the pathologist at the time of review. Examples of clinical diagnosis images include:

- Photographs of the specimen being removed in the operating room
- Pictures of gross dissection of specimen upon arrival in the laboratory
- Microscopic images from slide review.

Examples of “proof of work” images include:

- Picture of specimen/container upon arrival in the laboratory
- Picture of tissue section to be embedded
- Image of immunohistochemical QC slide (positive and negative controls).

Use case #2: Image slides for historical review/secondary review/consultation

There are numerous contexts for consultation requests which have subtle but important differences from each other. Understanding these contexts and the pertinent variations for workflow is necessary to optimize systems design to fulfill user needs for secondary reviews.

1. Historical review of digital images of prior pathology for a patient reflects a critical, high yield use case. Being able to confirm that a tumor in a current biopsy is morphologically identical to that seen in a prior biopsy can reduce the turnaround time to render a diagnosis. The usual lengthy wait time to retrieve physical glass slides from storage can be eliminated

2. Pathologist requested consults, requested in advance of, or in support of establishing the primary diagnosis, or possibly to confirm an already published primary diagnosis. Only a subset of the total set of data associated with a case may be submitted for consultation. The requesting pathologist determines the relevant subset in these circumstances, but the consultant generally has the option to request additional material.
 - a. Intra-institutional: The pathologist is requesting an opinion (through digital review) to another pathologist at their institution, either at the same site or another site in their network
 - b. Inter-institutional: The pathologist is requesting consultation from an outside hospital, usually due to the challenge of the case or the need for an external subspecialist
 - c. Concomitant review by multiple pathologists to arrive at a consensus diagnosis is an important variant for intra-institutional consultations but may become more prevalent for inter-institutional consultation as digital pathology platforms remove barriers for collaborative review
 - d. A related scenario involves subcontracting of special analyses (e.g., immunohistochemistry [IHC], fluorescence *in situ* hybridization [FISH], or other molecular studies) to a molecular laboratory, which usually results in the creation of new evidence, either in the form of data (e.g., flow cytometric analysis) or a new physical specimen (immunohistochemically stained tissue on a glass slide) or both (KI-67 stained slide with computer aided quantified results indicating proliferation rate).
3. Patient requested additional opinion, postprimary diagnosis
4. Physician requested additional opinion, postprimary diagnosis
5. Legal review, postprimary diagnosis. A full audit trail associated with digital images and confirmation of what digital assets were available at the time of original sign out would be important requirements to fulfill. Any additional annotations or alterations to digital images undergoing legal review that may obfuscate these requirements should either be prohibited or clearly designated by the information system
6. Consultation for intraoperative interpretations of frozen section or rapid FNA slides. Time is of the essence for this variant of a digital consultation. Most health-care organizations require rapid diagnosis (15–20 min) from the time tissue is sent to a pathology laboratory from the operating room.

Use case #3: Immunohistochemistry positive control slides

Creating digital copies of IHC-positive control slides to preclude the need for creating multiple positive control slides for distribution to pathologists can represent a significant cost savings.

The value proposition for this use case is in savings in application of expensive IHC antibody to multiple glass slides. Standard workflow calls for distribution of positive control stained tissue on glass slides to pathologists interpreting patient tissue reactivity to a particular antibody. If a single glass slide can be created for a single antibody being run in a particular batch and have that slide digitized and made available to all pathologists electronically, the quantity of expensive antibody reagents utilized can be reduced.

- Request for IHC stain processed as usual
- Only one distinct IHC-positive control is run per batch, in which a particular antibody is requested as part of an order on a patient sample
- IHC0positive control slides are imaged and saved to network folder
- Positive controls are not distributed as physical glass slides, resulting in cost savings
- Glass IHC slides are reviewed by a pathologist, but the same positive control is reviewed digitally by all pathologists for a given IHC (e.g., only a single cytokeratin positive control slide is created during a batch run even if requested across many different patient samples).

Please note that this imputes the need to have one slide associated with multiple cases. However, typical workflow today does not require a formal linkage between the positive control and specific patient case records within LISs. Having metadata that reflects the date of testing (or more specifically, the batch identification number) for both the IHC testing on patient slides and the creation of positive antibody controls will be sufficient. If a positive control fails completely, IHC laboratory QC should hold patient material and repeat testing. In most circumstances, there is subtle variation in antibody staining, for which review of positive control staining is imperative. Once this has been performed, persistence of this digital asset needs not be maintained based on current laboratory practices. Most laboratories will dispose of positive control slides when submitted for filing. Some pathology departments may favor maintaining positive control images for a period of time. *Information systems that manage digitized positive control slides should be able to organize slides not just by case accession number but also by a lab-specific batch number and/or by date of testing and have those images explicitly dissociated with an AP-LIS patient case record but readily retrievable at the time of initial case review for primary diagnosis applications.*

Use case #4: Sharing and cooperating on gross examination images

Definition: Gross examination is the first step of sample preparation. It involves macroscopic examination during which the sample is examined visually to identify that subset of tissue that are clinically relevant for microscopic examination.

Workflow: The process of grossing is performed in a meticulous and systematic fashion including all of the following main steps:

- Verify specimen labeling and patient identification

- Review clinical information
- Examine and palpate all external surfaces of the specimen
- Understand the resection margins
- Inking resection margins
- Dissecting and sectioning the specimen
- Examining the dissected specimen for clinically relevant findings
- Preparing samples for microscopic review in designated “cassettes”
- Capturing and annotating images at various points in the above workflow may be helpful in conveying complex findings and correlating gross and microscopic tissue relationships
- Sharing and collaborating/consulting on gross examination images brings value and may be critical for evaluation of complex specimens where anatomic details must be well understood before pathologists can make educated judgments about the extent of the patient’s condition and need for further resection
- Preanalytic variables such as cold ischemia time, specimen fixation, and transportation conditions are essential for minimizing downstream analytic errors and improving specimen quality. A combination of SET and the HL7 SDAM may be leveraged to help qualify the sequence of events and issues that the digital image currently under review may have been affected by
- Correlation between a gross examination feature and a microscopic feature may be critical for accurate diagnostic interpretation (e.g., “the tissue sections marked with a triangle were noted to have a clip in them”). An end user should be able to move between related gross and microscopic images (e.g. “show me the positive margin identified on the gross specimen”)
- Grossing “benches” with image and voice recording devices make it possible to record a number of specimen details in both pictorial and textual forms. The macroscopic image and the related clinical and gross examination findings provide critical context for subsequent microscopic review and diagnosis.

Pathologist diagnostic interpretation is optimized when microscopic images are coupled with macroscopic ones. In the era of the digitalization of pathology, it should be now possible to access microscopic and macroscopic images in an intuitive and seamless manner.

Use case #5: Incorporation of legacy digital images

Legacy digital images may exist today in laboratories in a number of different file formats and include both still images (gross and microscopic) as well as whole slide images (microscopic only). File formats for whole slide images today include those originally produced by Aperio (.svs,.tif), Hamamatsu (.vms,.vmu,.ndpi), Leica (.scn), MIRAX (.mrxs), Philips (.tiff), Sakura (.svslide), Trestle (.tif), Ventana (.bif,.tif), and generic tiled TIFF (.tif). The DICOM standard for whole slide images reflects a hierarchy of tiles that allow for efficient transfer of data relative to both the source information and

the destination display/device capability and requirements. DICOM facilitates the association of patient, case, specimen, and image metadata as part of a data “wrapper” around the actual image data.

With the implementation of an AP-LIS, EHR, IMS, or archival system (PACS or VNA), the bulk transfer of existing digital assets (DICOM and non-DICOM) will likely be required to facilitate at least rudimentary association between a patient, anatomic pathology tissue collection event, and various digital assets that might be available associated with that particular patient encounter. It is possible that the format of image data and associated metadata are in different formats during different time periods during which legacy information systems were utilized to acquire and manage the digital assets that exist in an organization as “legacy digital data.” The value of these data will increase if future vended solutions recognize the need for association of this existing data with pathology “cases,” “specimens,” and/or patient “encounters.”

Due to ever-increasing prevalence of digital assets, consistent growth of information technology systems, and occasional turnover of AP-LIS platforms, the need to maintain and incorporate “legacy” digital assets in laboratory pathology workflows will continue to be a necessary aspect of future digital pathology workflows. Legacy migration will consistently come from multiple perspectives including migration to a new primary AP-LIS/digital cockpit, migration to a new image management system (WSI integrated solution, PACS, or VNA), addition of a new postanalytic system, and increasing scope of asset collection (biobanking, etc.). The legacy asset incorporation/conversion use case shares boundaries with several other use cases, especially including consultation workflows, notably including incoming asset identifier management, transfer of asset ownership, replication of existing case structure and patient data, and varying quality of source data that cannot be guaranteed. However, it maintains several unique features including the (relatively) massive scale of content covered compared to other workflows, potential value versus complexity in handling internal audit and tracking data on historical cases, and the likelihood that nearly all organizations engaged in digital pathology practices will need to account for this situation regardless of their business scope and participation in other use cases.

Central challenges to legacy asset incorporation are:

1. Identifier management (patient, case/report, specimen, block/slide/container, provider, user/technologist, physical labeling, etc.)
2. Replication of case structure, prior process and result data, and associated relevant patient information
3. Accurate bulk assignment of legacy digital images to the correct patient, encounter, case, and associated more granular physical assets (specimens, blocks, slides, etc.)
4. Resultant data integrity challenges such as duplicate images or inaccurately assigned images.

Use case #6: Image analysis, machine learning, and in silico workflows

Data analytics and machine learning promise to provide significant value to those that embrace digital pathology workflows. Recent publications have demonstrated the capability of machine learning algorithms to fulfill complex diagnostic tasks such as identification of lymph node metastases on digitized H and E images of lymph nodes.^[15] Some studies purport that these machine algorithms already have the potential to exceed the capabilities of human pathologists. For example, a LIS may allow ordering of analytic “tasks” on digital assets, similar to the paradigm, in which IHC might be ordered as tasks to be performed on physical tissue today in AP-LIS platforms. In addition, AP-LIS systems should be able to recognize when certain digital assets routinely require analytic tasks to be performed in a particular sequence as part of a digital “protocol.” For example as part of the routine processing of whole slide images acquired of sentinel lymph nodes of breast, the deep learning algorithm for metastasis identification might be run automatically immediately after whole slide scanning has been completed.

It should be permissible for these algorithm “tasks” to irreversibly modify digital assets through a layered annotation process as well as return metadata to store in to the AP-LIS as a relevant diagnostic data point (e.g., Ki67 proliferation index for a ROI), or finally create a dataset (“evidence creation”) for further process by downstream “tasks” that are part of a larger analytic process or protocol.

Use case #7: Quality control/quality assurance and error correction workflows

QC and quality assurance (QA) represent important processes in the creation of glass slides for clinical diagnoses today and must be extended to ensure the production of high-quality digital assets for digital pathology. Quality evaluation (QE) events represent periodic data collection mechanisms to facilitate tracking quality metrics over time. QE events should include preanalytic factors and can be broken down further into prescan and postscan evaluations. Standard operating processes and policies should detail all routine QEs, QC, and workflow steps. It should be noted that the ability for all participants involved in a QC exercise to evaluate exactly the same histological section has obvious advantages over sequential sections sent out on multiple glass slides to multiple participants.

Preanalytic, prescan evaluations include:

- Quality of tissue placement/alignment in block
- Correct processing steps in processor given size and fat content of tissue
- Quality of embedding orientation and placement into paraffin
- Quality of sections cut and placed onto a glass slide
- Quality of barcoded label placed onto glass slide.

Preanalytic, postscan evaluations include:

- ROI appropriate for tissue placement on glass slide
- Accuracy of barcode interpretation

- Appropriate white balance, magnification, focus, and image file generation
- Appropriate assignment of imaging order to digital image asset created
- Appropriate filing of digital asset to the image archive.

Postanalytic evaluations include:

- In initial validation or verification within a laboratory prior to clinical implementation, most validation studies/processes end with an adjudication panel of pathologists reviewing glass slides through microscope and WSIs to evaluate discrepancies/discordances between interpretations and determine root causes. A similar process can be extended to include imaging and histology/lab personnel to provide ongoing QC
- On slide color, white balance, contrast, and spatial resolution calibration does not exist today but may represent a consideration for future automated digital QC
- Departments may wish to do periodic conferences to evaluate quality issues and improve QC processes. This may be especially important for a feedback loop to laboratory and scanning personnel and iron out complex problems.
 - Many systems may allow for tagging images for QA review at a later time; this should correlate to QE/QC data
 - There may need to be QA processes for certain cohorts of tissue types, stains, subspecialties, or diagnosis types
 - Aggregation of specific cases for inspection for regulatory purposes may be pursued proactively or retrospectively. For example, digital images that lead to safety events might be flagged for later audit or QE
 - Adverse event reporting in some scenarios, groups may want or need to report adverse events of systems to vendors, FDA, or other relevant outside groups
 - Randomized reinterpretation of digital cases through microscope (similar to cytotechnologist QC or regular surgical pathology QA processes)
 - Periodic re-verification/validation of image analytic results (i.e., occasional ordering of FISH evaluation to assert her2 image analysis functions remain predictive)
 - Randomized or periodic testing or auditing of equipment precision
 - Real-time manual QA reporting would ideally be incorporated at any point where there is human interaction with the digital image
 - Although not currently assigned to any specific actor in a profile, proper support of a digital pathology workflow (most likely the “order filler” but possibly the “acquisition manager”) should have the capability to warn the user if digital images have not been viewed (e.g., if a physical asset has not yet been scanned or a scanned digital image has been overlooked) prior to report verification

- Any automated algorithms implemented as part of a digital pathology workflow should have QA metrics incorporated to reflect the possibility of performance failure over time. For example, preanalytic variables such as a delay in tissue fixation could result in staining artifacts and algorithm failure.

QC and assurance for image management, file management, and network management might be automated in more sophisticated image managements systems.

- Log file aggregation and analysis for systemic errors
- Random audit of tracer cases to verify image availability
- Monitoring of network load, network speeds, and other measures of network performance
- System backups and auditing of file integrity (both for main archives and backups)
- Network security or vulnerability audits.

Use case #8: Digital pathology in support of clinical conferences

Categories of conferences include consensus conferences to reach a primary diagnosis (usually of a first diagnosis of a malignancy for a patient), internal QA conferences (usually to ensure performance levels of equipment and personnel), and multidisciplinary subspecialty boards (usually to discuss complex patient cases). The use of digital pathology in the review of cases for discussion at multidisciplinary meetings represents a vast improvement in efficiency and safety. In a nondigital environment, significant time is spent collecting and collating glass slides for review. These conference cases usually share some common characteristics:

- It is commonplace for slides to be imaged specifically for the purposes of such conferences. If digital images already exist, specific images may be flagged as most relevant for conference review. Specific ROI disclosing key pathologic findings may systematically be identified (e.g., positive margins, lymph node involvement, lymphovascular invasion, etc.)
- Most of these conferences focus on key images for specific patient tissue collection events and may need to dynamically obscure protected health information such as patient name, medical record number, or accession numbers, for displaying to a large audience of medical professionals
- Many digital pathology thin client systems allow for the organization of multiple cases, even for disparate patients, into sets or be indexed together in other forms, which can help assist in the process of organizing rapid, efficient, accurate switching between cases for multiple patients in these settings
- While conferences are not generally tied to billing, from the perspective of cost accounting (saving multiple physicians time), they are extremely valuable. Documenting time spent on best practice of diagnostic reviews for patients is valuable for capture and later reporting.

Use case #9: Image registration functions

Image registration involves the creation of a cross-image coordinate system of multiple images for the same object(s) or “scene” to allow for useful image comparisons across different digitized images of different glass slides for the same tissue block. A classic use for this functionality stems from the need of a pathologist to overlay glass slides to recognize which cells are co-labeling for specific IHC antibodies. An imaging system that can identify landmarks for digitized tissue sections for correction of orientation facilitates recognizing the same cell cohorts in different tissue sections. Images may be displayed side by side or layered on the top of each other with variable levels of transparency.

Use case #10: Digital pathology in support of intraoperative procedures

Intraoperative consultations occur frequently to help guide surgical procedures and/or assess the diagnostic adequacy of tissue removed during surgical or a biopsy procedures. Typical staffing models to cover this type of clinical service generally involve a single pathologist supporting the needs of multiple operating rooms for a period of time (e.g., 24 h). This coverage model pragmatically allows for the efficient use of limited pathologist resources. Situations often arise where this isolated individual may need to call upon the subspecialty expertise of others. Rapid imaging of frozen tissue sections provides a mechanism for remote viewing by the pathologist on call as well as consultation from the primary pathologist to a subspecialty pathologist. Requirements for digital histology imaging in this context require rapid image acquisition. There is no mandated turnaround time in the USA for intraoperative procedures, but most laboratories target <20 min as a quality metric for turnaround time from fresh specimen receipt in the laboratory to communication of a result following microscopic review.^[16] The overall process may require linkage to other data elements including the gross image for orientation, clinical history, and procedural context (i.e., why the patient is undergoing a procedure, why tissue is being sent for evaluation, specific questions to be answered to guide the procedure, etc.).

It should be noted that while demographic information must always be present in association with tissue submitted for intraoperative consultation, many laboratories may choose not to immediately create/accession a new case into the AP-LIS due to time constraints. An image management system should be able to accommodate situations, in which case creation and permanent glass slide identification in the AP-LIS are deferred to the point in time, in which the surgical procedure has been completed and all specimens are ready to proceed with gross examination. In this situation, digital assets labeled with patient demographic identifiers only need to be supplementally identified to create linkage to the appropriate AP-LIS case.

The whole slide image produced during intraoperative consultation may be at varying “levels” of depth as the tissue is cut through to obtain a full-thickness cross section and will almost always be accompanied with a deeper “permanent

section” that represents the tissue remnant following standard histologic processing. Correlation between the frozen and permanent sections is a documentation requirement in most laboratories and usually occurs as the attending pathologist signing out the case reviews the final set of microscopic images. This activity represents an opportunity for future automation.

DATA MODEL AND ASSOCIATED ELEMENTS

The data model for the interoperability profiles will leverage the HL7 SDAM, which has been aligned with what started as DICOM supplement 122 “*Specimen Module and Revised Pathology SOP Classes*” and is now part of DICOM Part 3: Information Object Definitions that includes a specimen module (C.7.6.22).^[6-8] Some of the data elements below represent data that may be relevant in a digital pathology environment but are not required for implementation. If implemented, these may be considered for addition to the HL7 SDAM to enhance interoperability.

Data elements for gross specimen imaging

- Before case accessioning should include medical record number, patient name, and date/time stamp
- Following case accessioning the container identification number should be integral to the metadata or be derivable from the file name
- Annotations that generally include ROI coordinates and textual information such as a part of the specimen sampled into a specific tissue block.
- Examples include block designations, clip designation, biopsy site, calcifications, mass or lesion, closest margins, hemorrhage, necrosis, and vascular invasion.

Data elements for whole slide microscopic images

- Label
- Identifiers
 - Patient level, case level, block level, slide level, and scan level identifiers may be associated with today’s whole slide images.
 - Barcode, 1D versus 2D.
- Control tissue (positive and negative controls)
- Diagnostic tissue
- Multiple fragments
- Coded fragments (e.g., 2 lymph nodes and 1 bisected and inked).

Metadata for digital pathology workflow support

- Slide scanning order(s)
- Magnification, Z-stacking, digital filters
- Slide received in machine
- Slide scanning started
- Slide scanning completed
- Slide scanning errors/warnings
- Slide manually retouched
- Operator ID, date/time stamps begin/end, and audit trail of functions applied
- Slide received/available in AP-LIS/PACS

- Slide viewing started
- Start time, end time
- Audit trail of X-Y-Z at Mag M
- Audit trail of digital filters applied at time point
- Tissue annotations, for example, ROI, tumor outline, nodal metastases, and margins.
 - Margin (designate), distance to margin, benign neoplasia, dysplasia, *in situ* malignancy, invasive malignancy, infectious finding, inflammatory finding (acute, chronic, specified, and unspecified), cell classification, structure classification, uncertain finding (ROI not otherwise classified), tumor size (with axis designations), tissue floater, mitotic figure, mitotic hot spot ROI, capsule invasion, and lymph node metastasis (size, extranodal)
 - Mark up coordinates relative to slide origin or ROI origin.
- Slide annotations, for example, stain type (H&E, IHC, special stain, etc.), thickness, and level of depth into block
- Stain issues (too pink), cutting issues (too thick, fragmented), and visibility issues (frozen section artifact and air dry artifact)
- Slide viewing completed
- Slide viewing inquiry
- Viewer ID (years in practice and area of specialty)
- Start time, end time
- Slide ID to include stain (H&E vs. IHC, etc.)
- Case type (breast, GI, lung, and b9 vs. neoplastic dz, etc.)
- Percent of tissue not viewed
- Percent of tissue not viewed twice
- Percent of tissue not viewed at higher than $\times 10$ mag
- Size of tissue on slide (area of polygon).

CONCLUSION

The benefits of digital pathology have been established, use cases supporting many of those described in this paper have been voiced by others, and a recognition that digital pathology will play a larger role in anatomic pathology seems clear.^[17,18] Many organizations are beginning to reap the benefits of numerous vended products in the market. What remains a significant gap is the consensus among technology solution providers in the digital pathology space on how best to work together to facilitate interoperability. This gap precludes customers from picking and choosing among best of breed products to pair a particular image management system or pathology PACS with an AP-LIS and have them work “out of the box” in a “plug and play” manner. Typical solutions today involve building proprietary interfaces that serve only to connect specific vended products to achieve a fixed set of goals for a single customer. Editorials have been published with a plea for greater interoperability among vended solutions to preclude the necessity for proprietary customization efforts by individual vendors.^[19] IHE attempts to create a consensus among all stakeholders, including multiple vendors, on how best to establish interoperability for the most common use

cases leveraging existing standards and best practices. With the recent publishing of the first digital pathology integration profile focused on image acquisition (DPIA),^[14] a solid foundation has been established upon which to build a robust digital pathology interoperable ecosystem for addressing the primary clinical use cases described in this paper. Future work and effort with greater engagement by the vendor community and customer stakeholders are required to fulfill the promise of this early interoperability effort.

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