



Interoperability between Anatomic Pathology Laboratory Information Systems and Digital Pathology Systems

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Abstract

This white paper offers an overview of the current state of interoperability between Anatomical Pathology Laboratory Information Systems (APLIS's) and Digital Pathology Systems (DPS's). This overview also includes a brief discussion of future work that will impact interoperability.

Both systems rely on data from the other to efficiently deliver full digital imaging functionality to the healthcare provider. Anatomic Pathology (AP) departments and patients will benefit most from imaging workflow when there is a high degree of integration of Digital Pathology information within AP workflow. Implementations of such data sharing already exist via interfaces and standard communication protocols between APLIS's and DPS's, and work continues on these interface standards to improve the degree to which these systems can be used together.

The current state of interoperability provides Pathologists with access to images and image analysis data from within the APLIS or the DPS. This information is then available to the Patient Report.

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Introduction

Digital Pathology is much more than just the capturing of a digital image of a glass slide. It is a term that describes the creation, viewing, management, sharing, analysis and interpretation of these images and includes management and workflow considerations unique to a digital imaging environment.

Some DPS vendors supply all of the functionality described above (end-to-end providers) while others provide individual components intended to be combined with those of other vendors to create a complete DPS (best-in-breed providers).

The process of digitizing glass slides (the fundamental building block of DPS's) has improved dramatically over the last 15 to 20 years. Several vendors now offer scanning products that support digitizing entire glass slides – often called Whole Slide Images (WSI's), digital slides or virtual slides and scan times continue to improve.

DPS's provide pathologists and AP laboratories with new tools including:

- Diagnostic assistance via the quantitative analysis of tissue samples
- Virtual access to samples and subspecialty experts in remote locations
- The creation of digital libraries for reference or education
- Data-mining of digital slide databases seeking similarities and differences in tissue samples of various diseases for research
- Virtual tumor boards or discussion panels where pathologists share and discuss their cases
- Laboratory automation for improved quality control
- Easily accessible image archives for future retrieval
- Side-by-side viewing of slides for comparison
- Precise and accurate measurement tools
- Slide annotations for clarity

These kinds of tools are causing rapid growth in the application of DPS's. Hospitals and laboratories are looking to Digital Pathology to reduce laboratory expenses, better control quality, improve operational efficiency, enhance productivity and improve treatment decisions and patient care.

APLIS's are used by most labs today to manage patient, case, and specimen information. Most pathologists spend a large part of their work day within the APLIS. It manages their cases, workflows and often their final diagnostic reports.

Full and efficient utilization of the tools highlighted above cannot be achieved without their integration into the clinical workflow. Several APLIS vendors and DPS vendors currently support this integration in various forms and to various degrees.

This whitepaper will describe the impact of DPS's on laboratory workflow, potential points of APLIS / DPS data sharing, current approaches to APLIS / DPS data sharing as well as possible future work and the standards involved.

Benefits of Digital Pathology

Before discussing the details of interfacing APLIS's and DPS's, it is appropriate to briefly review the benefits that DPS's bring to pathology. The tools outlined in the Introduction have a tremendous impact on several aspects of pathology workflow and collaboration.

Geographic Dispersal of Pathologists

The inherent dependence on physical tissue places many constraints on the workflow. For example, multi-facility pathology departments must make a trade-off between distributing pathologists to locations near the labs to reduce case turnaround time and centralizing specialist pathologists away from the labs to facilitate collaboration.

Digital pathology provides an opportunity to enable the best of both options by eliminating the constraint of having to transport the glass slides from the lab to the pathologist. Glass slides may be transformed into digital slides by scanners in the histology lab and the images made immediately available to pathologists at multiple remote locations.

Case Transport

The virtual delivery of cases eliminates the waiting time slide folders spend in the lab pending pickup, in transport from the histology lab to the delivery location and in the delivery location until the pathologist checks for their arrival. Virtual cases also eliminate the need for pathologists to repeatedly check a delivery location. These together enable a continuous flow in the delivery of cases from the lab to the pathologist. Delivery of the physical slides is eliminated, resulting in a reduction in shipping and administration costs and the prevention of lost and/or damaged slides.

Case Review

Digital slides enable capabilities not available with physical slides such as side-by-side viewing of multiple slides, quantitative image analysis tools, precise and accurate measurements and slide annotations.

The retrieval of prior studies is instantaneous with digital imaging workflow, resulting in improved patient treatment.

Diagnostic turnaround is improved since digital slides are instantly available without the need for transport.

Access to gross specimen images and/or In Vivo images may also be important in some cases. Several vendors offer interface capabilities with grossing station imaging systems and PACS hardware in order to present these images to pathologists in addition to digital slides.

Additional Studies

When additional studies are ordered by the pathologist for a tissue, the case is traditionally put aside and reviewed again when the results of those studies are available. These studies may either be additional slides with different chemical stains which the pathologist will review or other procedure types (e.g. molecular, flow cytometry, electron microscopy, etc.) with the results reviewed and interpreted by another party. As the studies are received, personnel must currently locate the correct case, check the case for receipt of all ordered studies, and place the case back into the pathologist's review queue when complete.

The digital case work list can automate this management of additional studies by placing the case into a pending status when studies are ordered, automatically matching the studies to the case, and validating the receipt of all studies to return the case to a complete status. This reduces the manual tracking of studies and the time personnel need to spend locating cases, as well as reduces administrative time spent on case management tasks and the risk of unknowingly reviewing an incomplete case.

Diagnosis Entry

Digital slides enable pathologists to associate diagnostic documentation to specific areas of the tissue. This additional information can be utilized to communicate critical information to the ordering clinician to support treatment planning. Snapshot images of regions within the digital slide can also be captured for inclusion in case documentation and reports.

Quality Control

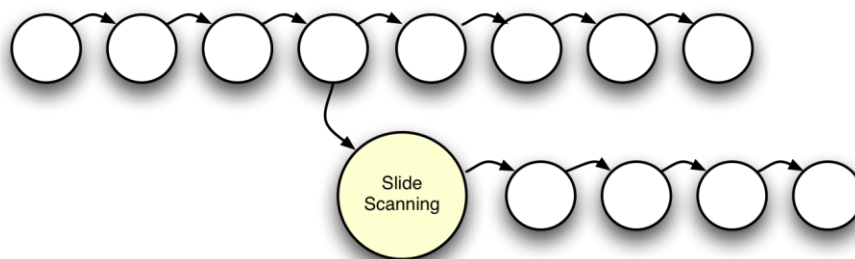
The digitization of slides allows for enhanced opportunities for stain quality control, either offline or prior to reaching the Pathologist when integrated into the laboratory workflow. Automated analyses can ensure that stains remain within acceptable limits.

Benefits of Interoperability

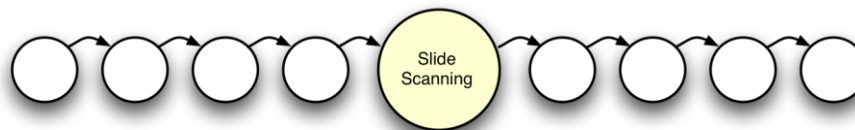
Interoperability between APLIS's and DPS's facilitates the pathologist's utilization of the DPS tools and assists in the achievement of the benefits outlined above by automating data exchange between the systems and providing them within the context of the laboratory workflow. This automation results in a reduction of manual work, case turnaround time and the likelihood of errors occurring.

Digital Pathology within the AP Lab Workflow

Some of the benefits identified so far can be achieved through the creation of digital slides *after* or *in parallel* with the current diagnostic workflow (e.g. QC, education and research). The following diagram illustrates the creation of digital slides outside the diagnostic workflow.



Other improvements however can only be realized when the pathologist is able to utilize scanned images in lieu of or in addition to the physical slide, and therefore requires digital slides to be integrated into the diagnostic workflow¹. The following diagram illustrates an integrated workflow.

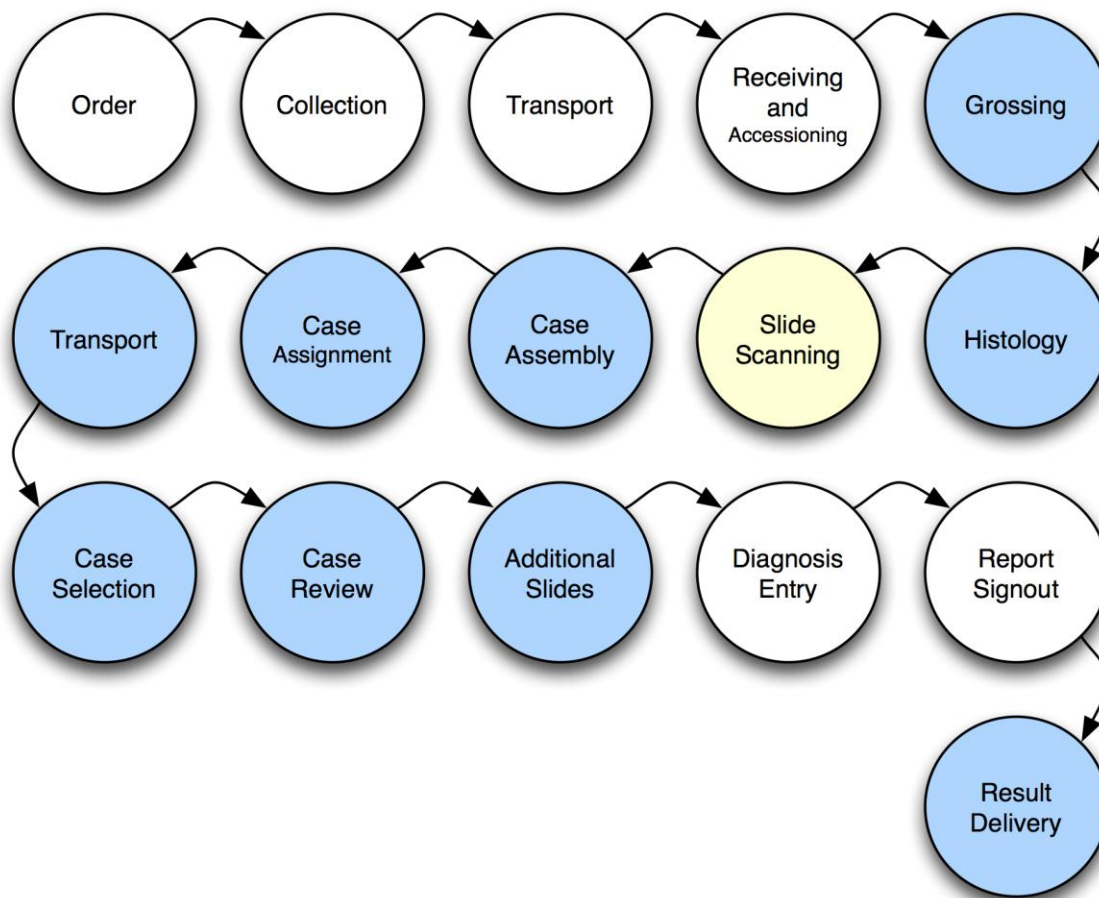


¹ Not yet approved by the FDA for routine surgical cases. For more information refer to the FDA Advisory Committee: Hematology and Pathology Devices Panel at <http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/HematologyandPathologyDevicesPanel/default.htm>.

Integrated Imaging Workflow

As with many technologies there are different degrees of integration possible between APLIS's and DPS's. Each laboratory will have to determine an optimal level of interoperability and integration in order to achieve their specific goals.

The following diagram illustrates a typical laboratory workflow with integrated digital imaging. Slide scanning, the only new step, is a necessary component of this integration and is shown in yellow. Other steps that may benefit from DPS's are highlighted in blue. Each step is discussed in detail in the table on the following page with corresponding considerations for APLIS / DPS interoperability.



Workflow Step	Description	Advantages of DPS Workflow Integration	Interoperability Considerations
Order	The Ordering Clinician identifies the need for an AP procedure and creates an order (electronic or paper requisition).		
Collection	The Ordering Clinician or Surgeon collects appropriate tissues from the patient.		
Transport to Lab	The Order information and tissue specimens are transported to the lab.		
Receiving / Accessioning	The lab receives the tissue samples and order and enters information into the APLIS.		Orders may be sent to the DPS in preparation for scanning glass slides (imaging status shown as “pending”) and may include key tissue information such as source or test performed.
Grossing	Samples of tissue are sectioned and placed into cassettes.	Inclusion of Gross images in the case and/or report possible with the use of a DPS.	Gross images may be associated with the case in the DPS and/or APLIS. Auto-association with the appropriate case is typically achieved using image filenames or folder structures referencing accession information.
Histology	Histology creates stained tissue slides from the cassettes. Slides are ideally bar coded.	Potential for automated QC.	Slides are scanned by the DPS scanner. DPS and/or APLIS are notified. Auto-association of images with the appropriate case is typically achieved using image filenames or attributes referencing accession information.
Case Assembly	Personnel collate slides by case into trays, folders, or boards. Paperwork may be matched with cases.	Auto-association of slides with cases and paperless case assembly can be achieved with integration of APLIS, DPS and slide bar coding.	Case lists may appear in the APLIS and/or DPS.

Workflow Step	Description	Advantages of DPS Workflow Integration	Interoperability Considerations
Case Assignment	Cases are assigned to the appropriate pathologist or specialty.	Remote users have access to digital slides without shipping slides.	For seamless integration of remote users the local APLIS and/or DPS must support accounts for them.
Transport to Pathologist	Couriers separate cases by assignment and transport to the appropriate location.	Physical transport may no longer be necessary with integration of DPS.	
Case Selection	Pathologists identify cases ready for their review and define work order of those cases based on priority and personal preferences.	Physical travel and local proximity no longer necessary with integration of some DPS's.	
Case Review	Pathologists review the slides in conjunction with patient history (available from the APLIS, EMR, radiology studies, or paper documents from the ordering clinician).	Quantitative analysis now available to assist the pathologist in diagnosis.	Pathologists may create Fields of View (FOVs) within the DPS viewer for analysis and/or to be included in the patient report (as pointers or snapshots). Some DPS's include data entry tools which may also require integration with the reporting system. Integration with the EMR and/or PACS may also be implemented at this step.
Additional Studies / Consultations	Pathologists order additional studies and/or request consultations to form and confirm diagnosis. Traditionally this is achieved via entry in the APLIS, paper request forms, fax, e-mail, or telephone communication. If consultations are requested from remote pathologists it also requires shipping slides and/or tissue blocks.	Paper forms, e-mails, faxes, telephone communications and shipping of slides often no longer necessary.	Since remote consultants may not have access to the referring physicians APLIS, several DPS vendors offer data entry fields for consultant observations and opinions. This information, in addition to any FOVs, snapshots or image annotations may then be transmitted to the reporting system (often the APLIS).
Diagnosis Entry	Pathologists document their diagnosis.		Some DPS's include data entry tools which may require integration with the reporting system (often the APLIS).

Workflow Step	Description	Advantages of DPS Workflow Integration	Interoperability Considerations
Report Sign-out	Pathologists review final diagnostic report with consolidated data, providing their expertise in defining medical treatment.		Anonymous case information may be sent from the APLIS to the DPS software to facilitate future use of the images and/or case data for education or research.
Result Delivery	The ordering clinician reviews the final diagnosis together with other patient results and formulates a treatment plan.	Image, markup and analysis data now available in the report. Report may be sent digitally.	Some DPS's and APLIS's offer electronic report delivery.

Examples of Existing Interoperable APLIS/DPS Implementations

As is typical when integrating two software systems, there are multiple ways in which the systems can be linked: from simple to complex or loosely coupled to tightly coupled. The same is true of APLIS / DPS systems. The following are examples of interoperability approaches currently implemented in laboratories that enable the acquisition, management, viewing and quantitative analysis of digital slides within the context of laboratory workflow.

There are two primary interfacing methods for doing so:

- Dual System Metadata Sharing
- APLIS-Integrated Digital Pathology

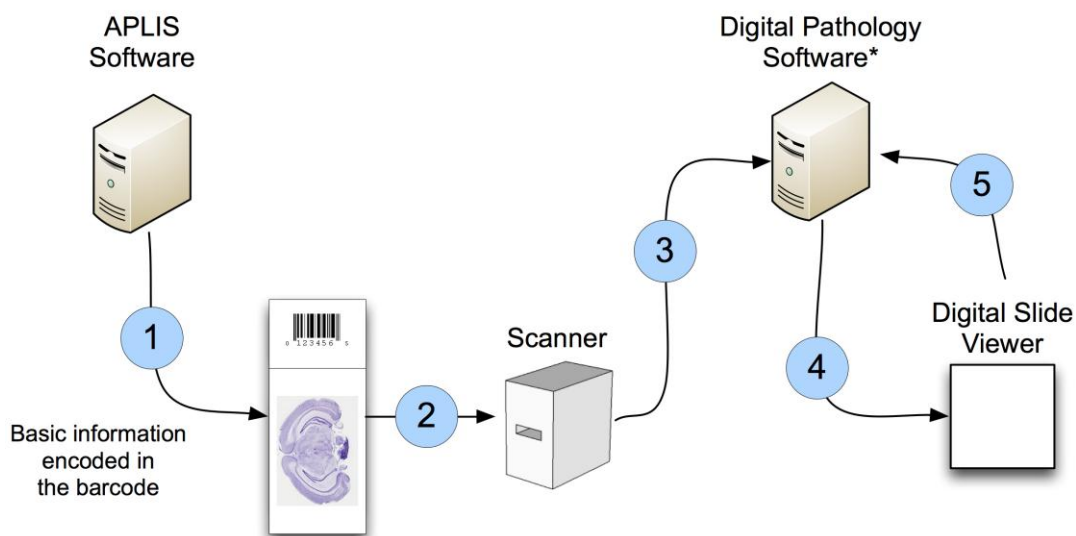
Metadata Exchange

This approach is the simplest form of interoperability. The APLIS and DPS operate independently of each other. The APLIS is the authoritative source of case information and the DPS is the authoritative source of digital slides and associated metadata. The APLIS shares a limited amount of case data with the DPS for the purpose of searching and locating digital slides and presenting relevant clinical information to the DPS user. A pathologist using this interoperability environment would operate two separate software applications – one for the APLIS and one for the DPS.

Metadata from the APLIS may be shared with the DPS in two ways:

- Encoding Metadata in the Slide Barcode
- Sending Metadata between the APLIS and DPS (via a communication protocol such as HL7 or Web Services – either push or pull)

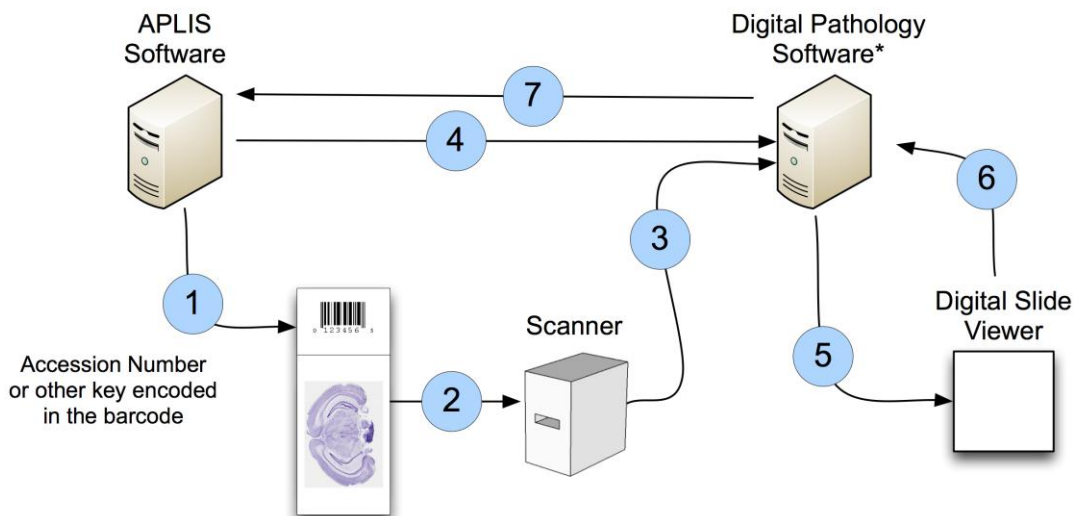
Encoding Metadata in the Slide Barcode



* "Digital Pathology Software" typically includes an image server and application portal (with database). It may also include quantitative analysis tools. As such, it may comprise solutions from one or more vendors which communicate amongst themselves using standard APIs, HL7, Web services, etc.

Step	Description
1	The APLIS software generates a barcode with unique case information sufficient to locate the digital slide within the Digital Pathology Software database. A good example is an accession number.
2	The DPS scanner digitizes the glass slide.
3	The Digital Pathology scanner sends the URL of the digital slide and the decoded barcode text to the Digital Pathology Software.
4	A pathologist can now look up a digital case/slide within the Digital Pathology software using the unique case information from the barcode or APLIS.
5	Annotations and quantitative analyses can be implemented from the Digital Slide Viewer and saved to the Digital Pathology Software as applicable.

Sending Metadata between the APLIS and DPS



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Step	Description
1	The APLIS software generates a barcode with unique case information sufficient to locate the digital slide within the Digital Pathology Software database. A good example is an accession number.
2	The DPS scanner digitizes the glass slide.
3	The Digital Pathology scanner sends the URL of the digital slide and the decoded barcode text to the Digital Pathology Software.
4	The DPS may now query the APLIS using the decoded barcode text to retrieve and associate case and slide metadata (e.g. patient and/or other clinically relevant information).
5	A pathologist can now look up a digital case/slide within the Digital Pathology software using the unique case information from the barcode or APLIS.
6	Annotations and quantitative analyses can be implemented from the Digital Slide Viewer and saved to the Digital Pathology Software as applicable.
7	Information can be sent to the APLIS from the DPS at anytime throughout the process. E.g. case status information, report FOVs, quantitative analysis results, annotations, comments, etc.

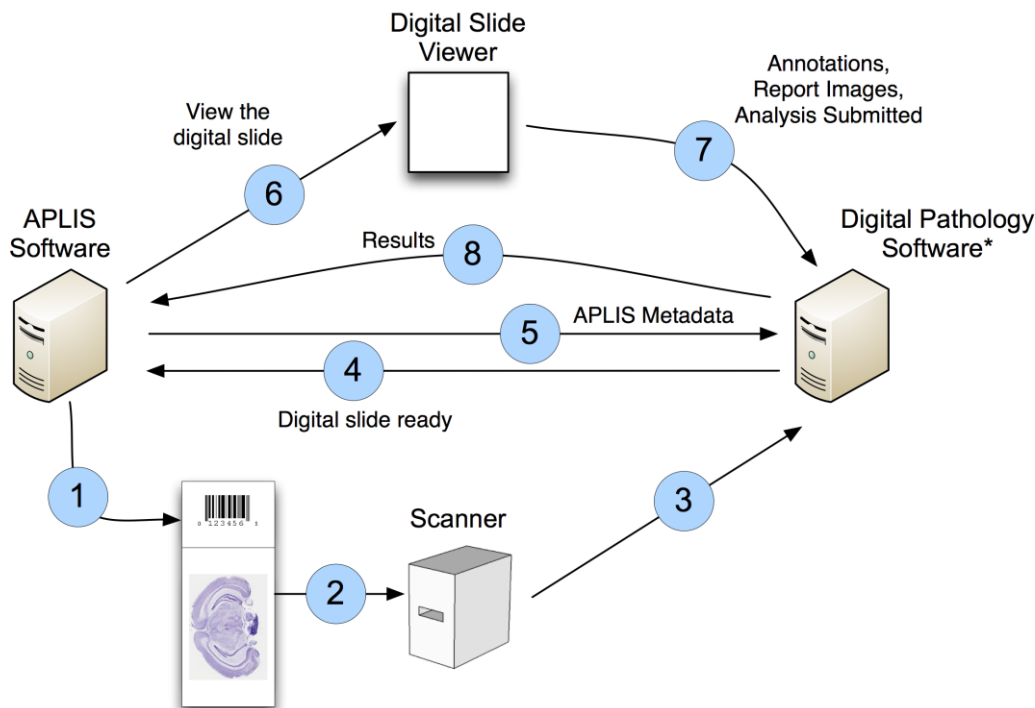
APLIS-Integrated Viewing

This approach results in more tightly integrated systems than the previous process. The APLIS is aware of digital images and provides database and user interface support for them. Digital slide data (including image annotations, quantitative analysis results overlays, etc.) are managed by the DPS software while all other case information is uniquely managed by the APLIS. When a new digital slide is created the DPS sends the following information to the APLIS:

- A digital slide case reference (usually an accession number read from the slide barcode)
- A URL pointing to the digital slide to enable launching of a DPS viewer from within the APLIS
- A thumbnail to represent the digital slide within the APLIS

As in the previous examples, this data is typically transferred using HL7 communications protocols, though other protocols may also be employed depending on the capabilities of the information systems involved.

The pathologist does their work within the APLIS. Once the pathologist is viewing a case they will see an icon, thumbnail or link indicating the presence of one or more digital slides. They can then directly launch the Digital Slide Viewer from within the APLIS.



* "Digital Pathology Software" typically includes an image server and application portal (with database). It may also include quantitative analysis tools. As such, it may comprise solutions from one or more vendors which communicate amongst themselves using standard APIs, HL7, Web services, etc.

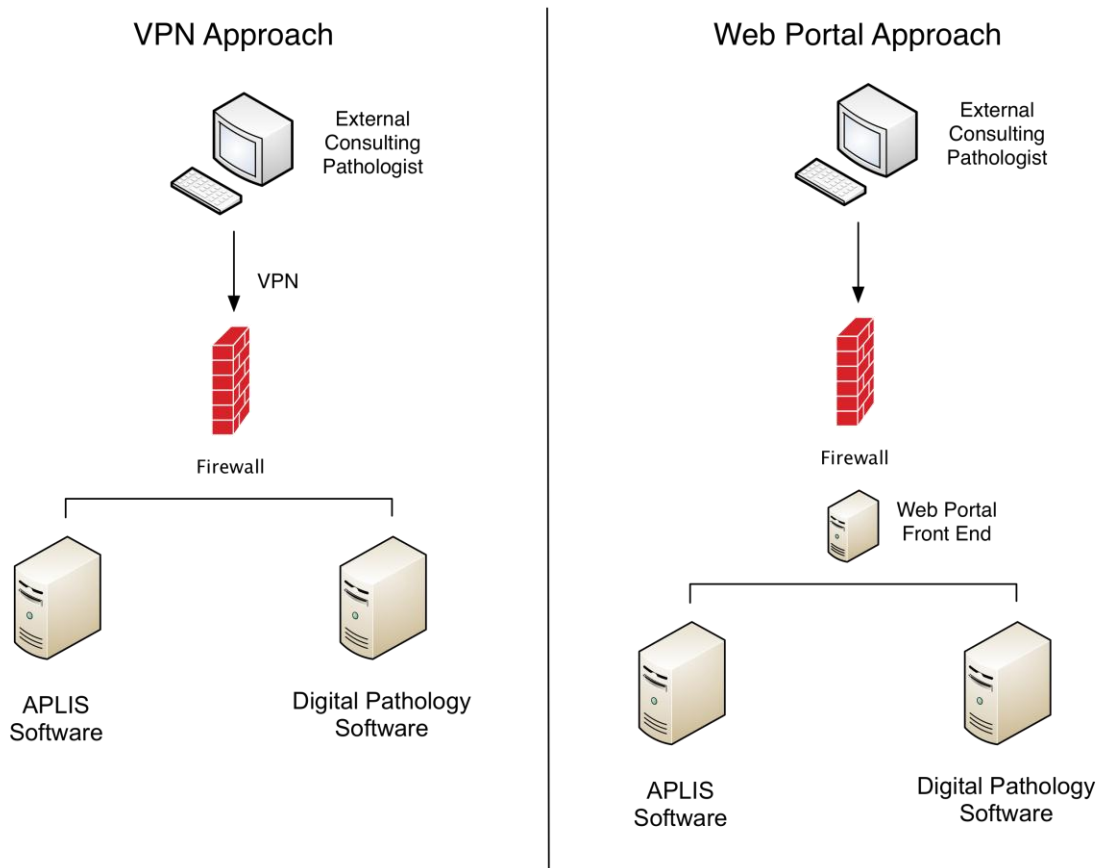
Step	Description
1	The APLIS software generates a barcode with unique case information sufficient to locate the digital slide within the Digital Pathology Software database. A good example is an accession number.
2	The DPS scanner digitizes the glass slide.
3	The Digital Pathology scanner sends the URL of the digital slide and the decoded barcode text to the Digital Pathology Software.
4	The DPS software sends the URL of the digital slide (and an image thumbnail if supported) and the decoded barcode text to the APLIS.
5	Based on the decoded barcode text the APLIS may send metadata to the DPS Software to be shown in the Digital Slide Viewer and/or for later non-diagnostic use (e.g. QC, education and research). Note: A variation of this approach is to switch lines 4 and 5, wherein the APLIS proactively sends an HL7 order message to the DPS software. This pre-populates the DPS software with digital slide and/or clinical information. Once the glass slide is actually scanned the resulting digital slide is automatically associated with the metadata previously sent via the order message.
6	A pathologist can now launch the Digital Slide Viewer directly from within the APLIS case with applicable case information.
7	While using the Digital Slide Viewer the pathologist can create annotations and select FOVs for inclusion in a report and/or to request a quantitative analysis.
8	At any time in the process, the DPS can send status report messages to the APLIS. Finally, any FOVs selected for inclusion in a report and/or quantitative analysis results can then be sent to the APLIS. Should additional image data be created based on these requests they can be managed within the DPS database with their existence and location communicated to the APLIS or other reporting system. Image Analysis results can be forwarded to the APLIS in one of two possible formats: <ul style="list-style-type: none"> • Raw image analysis results. These take the form of key / value pairs and represent the inputs and outputs of the image analysis algorithm. • DPS image analysis report. This report is typically a digested version of the raw image analysis results and is typically the data of interest to the pathologist.

Communications and Collaboration Networks

Discussions of extra-laboratory system interfaces revolve around collaboration and communications (e.g. consultation and remote diagnosis workflow) use cases and address what could be framed as “Laboratory Interoperability” concerns. Cases sent for consultation outside the lab require that:

1. The consulting pathologist be permitted to connect remotely (usually via VPN) to the laboratory’s local area network (LAN); or
2. The existence of a secure (typically SSL-encrypted) Web-based communications and collaboration tool (used via the Internet and/or via a private network).

The following diagram illustrates these two external consultation architectures:



In the VPN approach the APLIS and/or DPS is launched as if the pathologist is on the local network. For each consulting pathologist there is a necessity to create an account to access the LAN as well as an account to access the APLIS and/or DPS. While a simpler approach than the second, it provides no method for synchronizing user or APLIS information distributed across multiple sites and VPN technologies can have a noticeably negative impact on system performance (e.g. viewer performance).

In the Web portal approach the portal software front ends both the APLIS and/or the DPS software. Data is transmitted between systems using one of the interoperability examples highlighted previously. Typically the pathologist will see case data and images via a Web browser. The Web portal approach is easier for IT

departments to deploy and maintain (particularly as external consultation networks grow) and typically offers better system performance from a user perspective. The Web portal may often provide additional functionalities such as electronic ordering and/or reporting.

Some DPS vendors currently offer centralized and/or peer-to-peer Web portal applications intended to enable virtualization, management and user synchronization of pathologists distributed across multiple sites and APLIS's as well as workflow tools for use outside the context of a unique laboratory.

Additional Considerations

Barcodes

As indicated in the interoperability examples outlined previously, bar coding is an important aspect of any real degree of APLIS and DPS integration. While some level of interoperability can be implemented without them, the realization of the full value and integrated clinical workflow is only achievable with the use of barcodes that uniquely identify and track each slide.

Compatibility vs. Interoperability

It is also important to discuss the difference between *compatibility* and *interoperability*, as it can be easy to confuse the two. The former refers to the ability of one system to understand and use information created by another without any communications required between the two (e.g. one DPS vendor's image viewer opens another DPS vendor's image format). The latter refers to the ability of two systems to communicate with each other to achieve a common goal (e.g. one DPS vendor's viewer is capable of requesting analysis from another DPS vendor's analysis system).

These can be important for users of DPS's to understand upfront, since different vendors have different approaches as to which information and tools they do or don't make available to each other (e.g. images, image markup data, quantitative analysis tools, etc.). This is particularly important for multi-site consultation networks which may have multiple DPS's.

Future Directions in Interoperability

Digital Pathology comprises rapidly advancing technologies. Over time we expect improvements to occur in:

- Scanning speeds
- Digital slide viewing tools and clinical decision support
- Backend digital slide storage
- Multi-site communications & collaboration applications

Scanning speeds

To fully integrate Digital Pathology into the mainstream AP workflow, improvements in throughput will be needed. Undoubtedly hardware image acquisition speeds will reach the point where a slide can be digitized in less than 30 seconds. Image storage densities will continue to increase to keep up with number of digital slides that are created and used within the lab.

Digital Slide Viewing Tools and Clinical Decision Support

The digital slide viewing experience will continue to improve. Input techniques that allow the pathologist to quickly and efficiently review digital slides will evolve and image analysis tools that reduce the number of slides that have to be reviewed by a pathologist will improve the throughput of the lab.

Backend Digital Slide Storage

In addition to the trend toward denser file storage other protocols will be adopted creating a standardized environment. For example, Working Group 26, a subcommittee of the DICOM standards body, has ratified a proposal for storing digital slides within a PACS archive. In the next several years PACS software vendors and Digital Pathology software vendors will support this standard. This may increase the interoperability within the AP lab.

Multi-Site Communications and Collaboration Applications

As Digital Pathology enables simpler and more rapid access to sub-specialty opinions, consultation networks will continue to form and grow. The Web-based tools currently providing a platform for these multi-site communications will similarly evolve to offer more applications and integrations with APLIS vendors and other DPS's.

Appendix A – Relevant Industry Standards

HL7 (www.hl7.org)

- Anatomic Pathology Working Group:
<http://www.hl7.org/Special/committees/anatomicpath/index.cfm>
- HL7 Anatomic Pathology Special Interest Group Wiki:
http://wiki.hl7.org/index.php?title=Pathology_SIG
- Most commonly used and supported standard for sharing AP data
- Uses a case, specimen, child-specimen hierarchy
- Supports sending of links and encoded reports (MIME, for example) in addition to structured data elements
- Not designed to send actual images (pointers only) or the 3D information from whole slide images
- Fast transfer speed, easy to implement, widely used, standard is owned by HL7 International and can be purchased
- Moves case information from one system to another

DICOM (<http://medical.nema.org/>)

- Working Group 26 – Supplement 145: Newly ratified standard to define a DICOM standard for whole slide images
- Intended to be the standard for sharing of information about pathology images
- Can offer the transfer of images and more information about the attributes of slides than in HL7
- Adds to the HL7 Specimen model in order to send slide-detail information and images between imaging systems
- Work is being done to improve performance and reduce image size limitations
- Moves an image from one system (image-based modality) to another (image-based modality)

IHE (<http://www.ihe.net/>)

- IHE Anatomic Pathology Wiki: http://wiki.ihe.net/index.php?title=Anatomic_Pathology
- An initiative, not a standard
- Focuses on addressing gaps between the patient information focus of HL7 and the image information focus of DICOM
- Provides “implementation profiles” that show how to use DICOM and HL7 together to achieve user-focused results

HTTP/HTTPS (<http://www.w3.org/Protocols/>)

- Industry standards used for communications with Web-based software