Understanding the value of digital pathology

By John Wellbank

To better understand the history, roadblocks, benefits, and future of digital pathology, it's helpful to look at an earlier digital transformation in radiology. Picture archiving and communication system, or PACS, is a familiar term to all healthcare institutions that harbor radiology services. It came into vogue in the 80s, went mainstream in the 90s and allowed the storage, transmission, viewing and interpretation of digital data acquired with radiology digital imaging equipment, ranging from simple digitized chest radiographs to more sophisticated CT and MR exams.

By doing so, PACS and this digital revolution facilitated a number of advantages over analogue film X-Ray devices. A common communication protocol called DICOM (Digital Imaging and Communications in Medicine) was developed by the National Electrical Manufacturers of America and the American Society of Radiology. It allowed different device manufacturers and healthcare institutions to communicate their digital image data with each other.

Storage of this digital information is cheaper, quicker and easier to access, and space requirements were vastly reduced. That meant resources could be more effectively diverted from the darkroom, film room, reading room, and the archives toward more efficacious capital investments. Provision of an interpretive digital data set increased speed of data transmission, viewing and interpolation, improved the quality of diagnosis thus benefiting the patient, the caregivers, institutions, research, and industry, or in short, the overall patient care continuum.

Implementation of PACS is an IT-intensive process, but well understood, with most of the hurdles overcome, and it has a clear ROI. Subsequently, through the course of time, several other areas of medical imaging, such as nuclear medicine and cardiology, have been added to the DICOM communication standard.

Bringing digital advantages to pathology

Digital pathology (DP) is the common term applied to the digitization of conventionally produced fixed formalin paraffin-embedded block slides by utilizing a machine called a digital slide scanner in lieu of, or as a complement to, the microscope. The digitized image can then be viewed, manipulated, analyzed through the hospital intranet, or anywhere in the world that has internet.

The scanners come in an assortment of varieties produced by many different manufacturers, some large and familiar and some boutique. There are differing technologies, which creates various price points dependent on requirements based on volume, speed, image quality, type and size of tissue specimen, clinical, and research demands. The digital slide scanner, much like its radiology counterparts, such as the CT, MR or digital chest stand, requires varying degrees of peripheral equipment, such as digital storage media and devices (digital disk, tape, chip) , a user interface (monitor, touchpad, keyboard), software (management, user and interoperability, quantitative) .

DP for clinical use is primarily used for bright-field imaging (a white light source, typically LED based) for H&E slides, composing the clinical majority, and special slides, such as IHC; and there are also scanners that address FISH (fluorescence in situ hybridization) and other more research based purposes.

The digitization of pathology is producing many (and promises many more) of the same benefits we saw when PACS transformed radiology 30 years ago. Some benefits, rationale for adoption and use cases include:

- Tumor board meetings are clearly beneficial, since representatives from different specialties and subspecialties (including patients) can virtually convene, show and discuss multiple disciplinary findings in order to identify best treatment courses.
- Software is available that allows straightforward tissue identification, type and structure classification as well as nuclear, membrane cell and density quantification for IHC.
- Frozen sections from surgery can be immediately viewed by digitally scanning the slide in or near surgery without having a Pathologist on hand in the surgery department, thus saving time and money.
- Teaching software is available that provides customized education that can be quickly adjusted and enhanced for new content, learning and testing.
- Analogue data such as slides are impossible to mine, as computers require ones and zeros in order to perform calculations. Massive databases can be developed from gathering institutional, local, national, and genome correlated populations, allowing specialized discoveries in personalized medicine thorough mining and machine learning. This, along with digital input from other medical disciplines, should benefit outcome-based medicine through more accurate drug development and treatment.
- Consolidation of laboratory services is enabled as digital images can be moved and reviewed anywhere there is internet.

- Remote diagnosis and second opinion can be set up as ancillary services.
- Quality control on slide processing can be automated.
- Workflow can be streamlined and automated in regard to subspecialty slide distribution, interpretation difficulty, workload and availability
- In the near future, algorithms performed on slides scanned and in system workflow will have the ability to redirect the slide for additional needed stains based on preliminary findings through artificial intelligence, improving turnaround times.

Limitations and overcoming hurdles

DP digitally copies but does not replace the glass slide. The equipment, cost, and space for instruments required to produce the glass slide are not eliminated, thus antagonizing the ROI when compared to radiology. The lack of a satisfactory pathology DICOM standard complicates the interoperability of an institution's DP equipment, and the integration into other software such as HIS and LIS. Efforts from DICOM, the DPA (Digital Pathology Association) and other organizations should soon prove successful in eliminating this barrier.

Another barrier to adoption was the FDA's former requirement that DP be approved as a Class III or PMA product, thus adding to the expense and difficulty of development and production costs. This clearance standard was more or less appealed to the FDA by a consortium of major manufacturers representing the DPA, and with some guidance the first of the manufacturers was able to achieve *de novo* clearance (which requires less manufacturer burden) for WSI (whole slide imaging) for clinical diagnosis in August of 2017. There now appears to be a short list of other manufacturers who are pursuing Class II clearance, which is the current requirement for WSI from the FDA, based on predicate devices.

To summarize the three aforementioned hurdles, the U.S. is most impacted by the FDA and this hurdle has been more or less eliminated (the Class III requirement), with routine clinical trials remaining the only impediment for other interested manufacturers to achieve Class II clearance. Another, the lack of a DICOM standard, will be overcome through perseverance, as it has in the other major imaging disciplines. And in the meantime, with careful planning and diligence, most digital communication issues can be avoided.

In conclusion, the current market conditions exhibit that DP is readily available in different forms of sophistication and utility to the clinical, research and the pharma industry. Adoption has been steadily progressing in all three areas around the developed world, the laggard being the clinical market in the U.S. (over the past several years Europe has adopted at a much faster rate), which finally appears to be adopting at an increasing rate. Soon there will be more than one choice of FDA cleared product and manufacturer, allowing a more complete variety of choices and a more custom fit for solutions. The FDA may soon loosen up in terms of what is required of a "cleared" DP product making even more choices available.

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The last, and perhaps the biggest obstacle, the ROI, deserves its own paragraph as it remains to be fully proven and will not manifest in the straightforward way that it did in radiology. What appear to be accepted among the vast majority of users are the following findings:

- The workflow of the department, the specimen and the pathologist can be better tracked and directed, and the elimination of paper tracking, routing and monitoring is more efficient.
- There are no longer books of slides traveling the department, as the slides can be immediately stored/archived (still an FDA requirement for 10 years after production) after they are digitally imaged. Lost and broken slides due to transport around and between offices and institutions can be eliminated.
- Pathologists are becoming more adapted to DP (and it to them through various user interfaces and software improvements) and there is less and less resistance by pathologists insisting that they can manually read a slide via microscope faster than they can on a monitor. One study, of which there are few, claims an improvement in pathologist efficiency be 10-20 percent.
- Second opinions by experts are readily available all across the world, since the digital slide can be transmitted in seconds rather than the days of delay caused by shipping a slide. This is also relevant for pulling archived glass slides, which might be stored hours away, if required to be reviewed again.

More benefits will be forthcoming as more companies, especially those in the artificial intelligence space, enter the marketplace, and the ROI will become more and more tangible. Digitization appears to be inevitable in all sophisticated areas of our lives, so if you have a practical use case now, you will probably have more in the future. Consider starting the ball rolling, as implementation takes time and planning.

About the author: John Wellbank is a full time consultant for Thermo Fisher Scientific, AP division, working with them in the digital pathology (DP) space. Prior to this he led Global Sales, Service and Marketing for Philips Digital Pathology, the first company to achieve FDA clearance for DP Primary Diagnosis. John currently serves as a board member and president of the Digital Pathology Association Foundation, a foundation set up by the Digital Pathology Association, where he previously served 2 years as president and chaired several committees.

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