

Virtual Imaging Peer Review (VIPER) – A Case Study

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Introduction

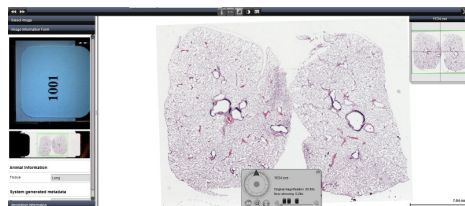
Histopathology peer review is a vital part of preclinical toxicology studies and has typically been conducted by on-site pathologist evaluation using glass slides viewed under a light microscope. With emerging digital pathology technologies, successful remote peer review may now be achievable. For many years pathologists have utilized photographic and digital images, both high magnification and whole slide tissue sections, for ad-hoc peer reviews and alternate opinions. And in some instances, in-house peer reviews have been conducted using digital media but pathologist's experiences have not reported. This case study presents pathologists' experiences in conducting a peer review process utilizing digitized tissue sections and remote access of the images.

VIPER Process

1. A previously peer-reviewed and closed study was used to study remote peer reviews processes. The study was anonymized and pathologists were blinded with regards to candidate drug data.
2. Whole tissue sets from all animals in control and high dose groups and target tissues from other dose groups were scanned and housed on a dedicated server.
3. Individual animal data and a link to the images were provided to three veterinary pathologists, with extensive peer review experience of nonhuman primate tissues, who accessed and evaluated slide images from remote locations (other than the physical server location).
4. Pathologists recorded lesion identification and concordance based on study derived and standardized nomenclature.
5. Pathologists completed a questionnaire to assess their experiences and to gather feedback for refinement of the remote peer review process.

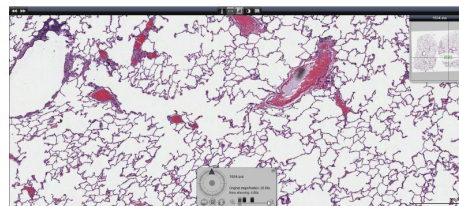
VIPER Goals

1. To test the process of remote pathology peer review when pathologists use digital images of tissue slides in lieu of microscope slides
2. To query the study peer review pathologists' experience with remote peer review
3. To gather data in order to make the process more time efficient and productive for future remote peer reviews. This information will enable hardware and software vendors, and fellow veterinary pathologists to understand the pros and cons of remote peer review.
4. To determine if the peer review pathologist could identify previously diagnosed lesions and assess the primary pathologist's evaluation.
5. To determine if current state of digital scanning, storing and retrieval of slides from preclinical tissue allowed for adequate peer review.



A low magnification view of lung tissue using SlidePath viewing software. Slide label information and animal and tissue information is present on the left side of the image and a whole slide representation is available for visual scanning of the entire tissue (equivalent to 1-2 x magnification).

A high magnification view of lung tissue using SlidePath viewing software. Pathologists used slide movement and magnification tools located at bottom center and upper right corner of image. Note measurement tool on the lower right corner (automatically adjusts with changes in magnification)



Materials and Methods

Preclinical study:

A completed and closed nonhuman primate study was provided by MedImmune. The study was previously peer reviewed during the course of its completion. The study was chosen based on histopathological findings in target organs in all dose groups and anonymized to remove references to candidate compound and original study and peer review pathologists.

Individual animal data and target tissue selection:

IAD from all study animals was provided by MedImmune and complied for the review pathologists by EPL, INC using proprietary peer review software. Animal data and data on target tissues were provided to the review pathologists. EPL provided a dictionary of study lesion nomenclature and nomenclature specific to digital review (e.g. 'Cannot confirm with digital image').

Slides scanning, image hosting and viewing software:

A complete set of tissue slides from all control and high dose animals and target tissues from mid- and low-dose animals were scanned by Flagship Biosciences on an Aperio ScanScope® XT scanner. The slides were scanned at 20x magnification and placed on a secure Flagship server. Peer review pathologists were granted access to images via web-based viewing software (SlidePath Digital Image Hub), and were provided a guide for use of the software.

Data Generation:

Pathologists were to conduct the digital peer review and provide concordance opinions on the study worksheets. The pathologists were also to provide subjective opinions on the digital peer review process via a questionnaire. The study sought to determine both the ability to recognize and evaluate tissue lesions, and the use of digital media in the process.

Results

Subjective data on the use and potential utility of remote digital peer review is presented. Concordant data from the digital peer review will be presented in subsequent presentations.

Peer review pathologists were located in the 2 US and China. All study pathologists used a PC-based operating system and either Windows XP or Windows 7. A single monitor was used and ranged from a standard laptop screen to a 26-inch monitor. High speed cable was the internet connection used most often, with one pathologist also using a hotel connection (Asia) and a DSL connection (US). The time of day for internet connectivity was only a negative issue in Asia when, during the work day (after 9 am) and weekends (after 10 am), the connectivity was markedly slower.

Results (con't)

Pathologists ranked a series of subjective evaluation criteria on a scale of '1' (easy/good) to '5' (difficult/problematic).

	Average Score	Range of Scores
Accessing Web-based viewing system	1.7	1-2
Maneuvering within the viewing system	2.7	2-3
Use of viewing system	3.0	1-5
Accessing of folders and images	2.7	1-5
Overall experience with Data/Viewer interface	3.0	2-4
Magnification of images (20x)	2.3	1-4
Image quality	2.3	1-4
Image refresh rate affecting workflow	4.7	4-5

The web-based viewing (SlidePath Digital Image Hub), the magnification of the images and the image quality all ranked as easy or good, while the refresh rate for the images ranked as difficult and problematic. One pathologist noted that the refresh rate 'was the worst aspect of the system'. The use of the viewing system, the accessing of images and the overall experience of using the viewer interface ranged widely from easy to difficult among all peer review pathologists. Magnification at 20x was sufficient in most cases.

All pathologists commented negatively on slide presentation and sequencing of images within their respective folders, and would like to have them follow the block order.

Pathologist's comments:

'It was great to be able to work on the project in multiple different locations without having to transport a microscope and glass slides around the world. I would have had to cancel my vacation, spend more time in the office, and rearrange my schedule if this had been a conventional peer review project'

'I see digital imaging of more use for individual specific situations than for use in peer review. Like many things in the IT world, I think that it will take a generation of pathologists who 'grow-up' with this sort of technology to make it viable.'

'I firmly believe that digital pathology is the future. However, ...I could not survive economically using the current system. When the problems with speed are resolved, I will be happy to try again.'

Discussion

The use of current applications in digital pathology has its positive aspects as well as its limitations. Peer review pathologists on this study all agree that some form of digital pathology lay ahead for our profession, but current software lacks in such crucial areas as image refresh rate when accessing from remote servers. The image presentation and placement in folders was problematic for each pathologist, and can be easily resolved with image presentation customized to meet individual peer review pathologists' preferences. Pathologists ranked high the ability to conduct peer review from remote locations and the potential time and cost savings in reduced travel. The balance between the current accessibility of digital images versus travel time and costs must be weighed by each pathologist and on each study. The consensus was that current software is better suited for small, focused, investigative studies than a large preclinical toxicology study.