Use of Telepathology for Pathology Peer Review in Multinational Studies

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Introduction

Pathology peer review of toxicologic pathology findings in safety assessment studies of drugs, food additives and agrochemicals is commonly done prior to submission of test results to regulatory authorities. Following completion of pathology evaluation of preclinical toxicity studies, histopathology slides are often shipped to the peer review pathologist (PRP), or the PRP would travel to the study pathologist (SP) facility to review the histopathology slides with the SP using a double headed microscope.

The purpose of our study was to determine if new telepathology technologies can effectively be used for the peer review aspect of the preclinical study, and thus reduce need for travel and logistic expense.

Materials

A novel telepathology system (Augmentiqs™) (Siegel et al. 2017) becomes an integrated component of the pathologist's existing microscope by being placed in the optical path above the nose piece and below the eyepieces (Figure 1). The pathologist continues to view the optical plane of the tissue through the microscope eyepiece, while an embedded image sensor within the telepathology system captures a live feed of the tissue on the microscope stage. Without the use of whole slide scanning, the telepathology system enables remote parties to view and discuss a live image that is of high digital-pathology grade, and similar to the dimensions of the tissue as seen within the microscope eyepiece.

Multiple remote parties are able to view the live telepathology session from their own computer after downloading a client viewing software. All participants may save digital-pathology grade images of the tissue directly to their computer. The dynamic nature of the telepathology technology allows remote parties to perform and view all annotations or morphometric calculations during the slide evaluation phase of the telepathology session. The audio part of the live discussion may be conducted using a regular telephone or using communication programs such as Skype.

Figure 1

Figure 1. Optical module installed on microscope.

Methods

Following completion of the pathology evaluation of preclinical toxicity studies at contract laboratories located in the U.S. and Europe, histopathology slides are shipped to the PRP located in Israel. The PRP then utilizes the novel telepathology system from his existing microscope in order to discuss histopathology diagnoses and reach a consensus, and thereby avoiding the need to travel to the SP situated at the contract laboratories.

Experimental Design

Three recent examples of pathology peer review were carried out using this novel system for telepathology.

The slides chosen for the peer review were those which had lesions which the PRP questioned or did not agree with the classification of the lesions provided by the SP.

The two pathologists would work to obtain a consensus while simultaneously viewing and discussing the selected slides as they were under the microscope. The PRP with the novel telepathology system would work normally, including the use of moving the mechanical stage, changing focal planes, and switching objectives as needed for increased magnification.

Results

Within a timeframe ranging from 1-2 hours, multiple selected slides were reviewed. Participants could see the actual slides projected from the microscope of the PRP, discuss the lesions, annotate, and save high resolution images on their computers.

Upon completion of the slide review, the PRP prepared a "*Live Telepathology Review Report*" which documented the procedure of the review of slides, use of the live telepathology technology, and representative photos of all microscopic fields of the slides which were shared. This unofficial report served as study notes and was sent from the PRP to the SP.

Eventually, the SP and PRP signed a *Formal Peer Review* Statement indicating that the revised report reflects the consensus achieved by the pathologists during the telepathology session. This document was eventually included in the formal study report that was submitted to FDA.

Examples of photos, which include annotations and morphometric data, taken by the Augmentiqs live-telepathology system from other unrelated studies, are demonstrated in Figure 2 A -D.

Peer Review	Number of Slides Shipped	Number of Slides Reviewed Via Novel Telepathology System	Length of Online Peer Review
1	900	11	1 hour
2	700	15	1 hour
3	400	40	2 hours

References

Siegel G, Regelman D, Maronpot R, Rosenstock M, Nyska A. (2017).New Technologies: Real-time Telepathology Systems-Novel Cost-effective Tools for Real-time Consultation and Data Sharing. Toxicol Pathol. 45(8):1039-1042.

Figure 2

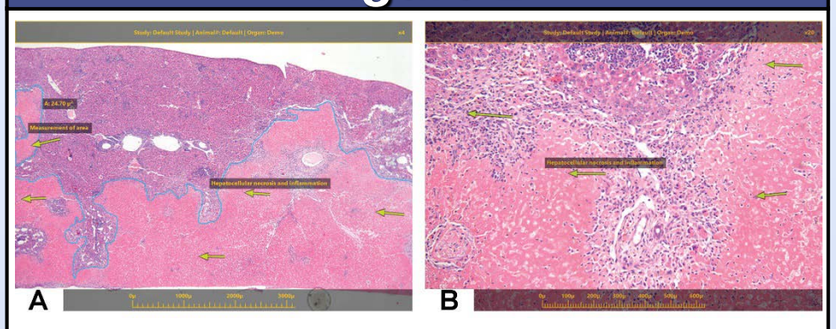

Figure 2 (A and B). The objective of this study was to assess the safety of an anti-cancer therapeutic modality in mice, following intravenous (IV) single administration. Histopathological evaluation indicated extensive hepatocellular necrosis and inflammation (Figures A and B). **The live telepathology technology helped in instantly sharing the microscopic findings with the study director and the sponsor, adding annotations and measurements (i.e., area of the necrosis), and documentation.**

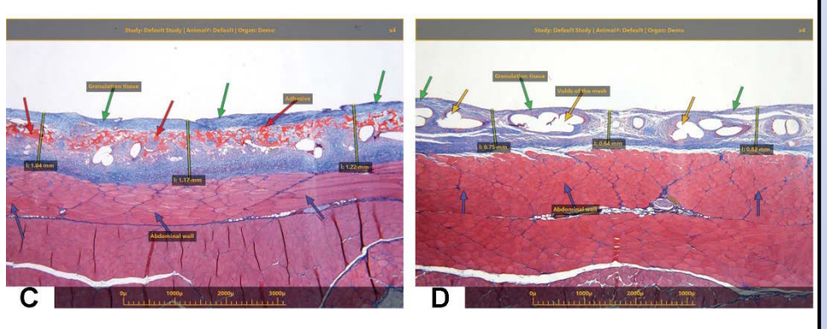

Figure 2 (C and D). The objective of this study was to assess the biodegradability and local effects of the Test Item, a medical device with a biodegradable (Figure C) and non-degradable component (Figure D), following intra-peritoneal (IP) implantation on the abdominal wall in SD rats over the course of 2 weeks. The tissue reaction related to the presence of the biodegradable component (Figure C) is characterized by the presence of mild granulation tissue, which was of uniform thickness along the entire implantation site, and intimately surrounded the device. The tissue reaction related to the presence of the Reference device (i.e., without non-degradable component) (Figure D) is characterized by the presence of mild granulation tissue, which was not of uniform thickness along the entire implantation site. **The live telepathology technology helped in instantly sharing the microscopic findings with the study director and sponsor, adding annotations and measurements (i.e., thickness of the granulation tissue), and documentation.**

Conclusion

The novel telepathology system connected to an existing microscope presents a feasible, cost-effective, and practical method of consultation and peer review in biomedical research and preclinical studies. The technology further acts as a viable alternative to travel of pathology experts and can facilitate more informed decision making relating to study results and strategic business steps in a shorter period of time.

In addition, the Augmentiqs telepathology technology facilitates good science by conveniently supporting informal and formal consultation and pathology peer review consistent with best pactices of toxicologic pathology

Impact Statement

Based upon our experience, telepathology showing the region of interest live from the microscope can be used for peer review, other GLP-compliant review applications, or for simple informal consulting. New technologies which offer true cost and time saving benefits, while maintaining best-use standards, will play a more prominent role in the development of new drugs and treatment modalities. Greater transparency and more open communications between pathologists, CROs and sponsors is expected to increase with the adaptation of real-time telepathology, and the novel Augmentiqs system in particular. We believe that more data will accumulate from peer review sessions, pathology working groups and other applications that will enrich the science that can be supported by this telepathology technology.