Application Note: Whole-Mount Slide Imaging in Traumatic Brain Injury Research

Introduction

Traumatic Brain Injury (TBI) is a significant health issue with neuroscience underlying its management and treatment. In the United States alone, there are approximately 2.5 million new cases each year, and about 5.3 million people living with long term disabilities as a result of TBI. In 2014, President Obama hosted the first summit on *Healthy Kids and Safe Sports* to raise awareness for sports-related concussions, while U.S. organizations committed over $70 million to researching and raising awareness for TBI. The public is growing to understand the long term risks for youth who play contact sports and other groups who often suffer from concussions, such as soldiers. In clinical management of these cases, non-invasive imaging techniques such as CT and MRI are used to monitor patients and the extent of injury. These techniques also allow researchers to study the effects of TBI on cognitive tasks. However, non-invasive techniques are limited by the resolution they're able to provide. On the other hand, histology images tissue at a much higher resolution, and can validate results from other modalities, but only postmortem. Therefore, methods like MRI and CT have to be combined with postmortem histology to further our understanding of the brain. Of the technologies available for histology, whole-mount slide imaging such as Huron Digital Pathology's TissueScope™ solution provides researchers with the opportunity to effectively map the entire brain, and link detailed cytoarchitectural maps with functional imaging data.

Whole-mount slide imaging enables innovative processes and outcomes for brain research. Because the TissueScope can fit slides of up to 6x8", an entire slice of the human brain can be scanned at once, making a precise 3D reconstruction of the whole brain possible. Unlike traditional microscopy, sections do not have to be excluded, so a global image is more easily obtained. A procedure for reconstructing the brain from histology slides involves thinly slicing the brain along one axis. Although there are thousands of slides to be scanned, the TissueScope images whole slides in minutes. Additionally, accessories such as the TissueSnap™ improve throughput by offloading pre-processing and preview scanning, so that the main scanner operates at maximum speed, running without interruption. A tiling algorithm can be used so that for each slice of the brain thousands of uniformly spaced scans are taken at a high resolution. With the TissueScope, this resolution can reach up to 0.25µm at 40x magnification, or lower resolutions of 0.50µm at 20x, or 1µm at 10x. This provides researchers with a detailed, cellular mapping of the brain, with the potential to clarify uncertainties present in lower resolution in-vivo imaging modalities. Through software, brain slice images can be compiled into a 3D volume. Huron offers 3D histology software to provide volumetric reconstruction of whole-mount slides, so that hundreds of sections can be processed and viewed in minutes. Additionally, volumetric images from confocal and optical z-stacks can be read, visualized, and explored. From here, researchers can count cells, measure volume of specific regions, and more.

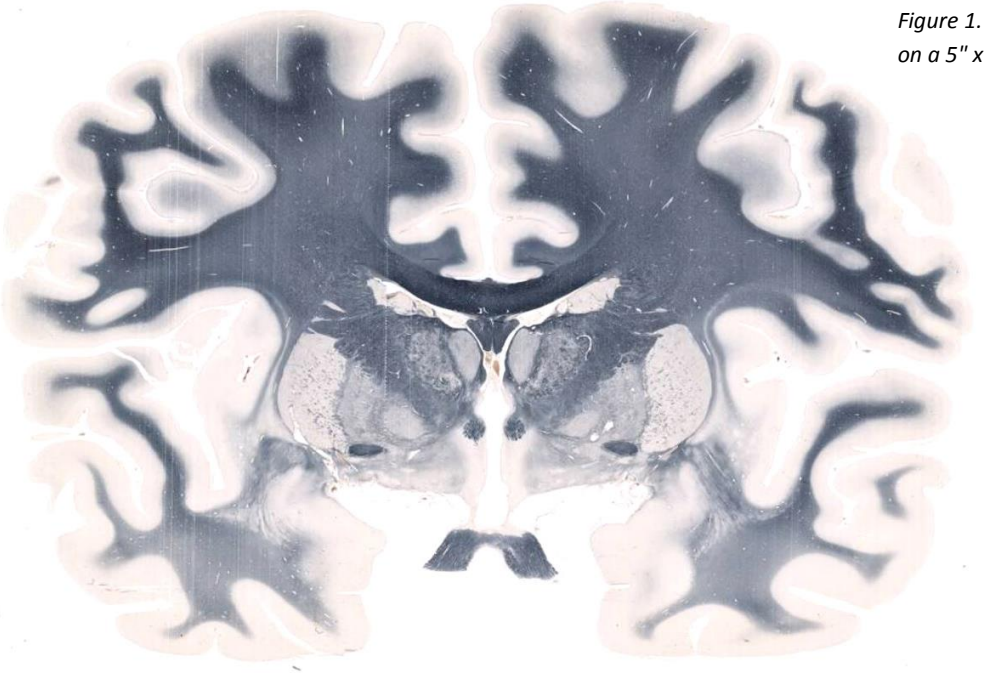

Figure 1. Whole-mount Brain scanned on a 5" x 7" slide at 20X resolution

HURON Digital Pathology

Huron Digital Pathology
550 Parkside Dr. Unit B6
Waterloo, ON Canada N2L 5V4
T 519.886.9013 **F** 519.886.5300
Email: info@hurondigitalpathology.com
www.hurondigitalpathology.com

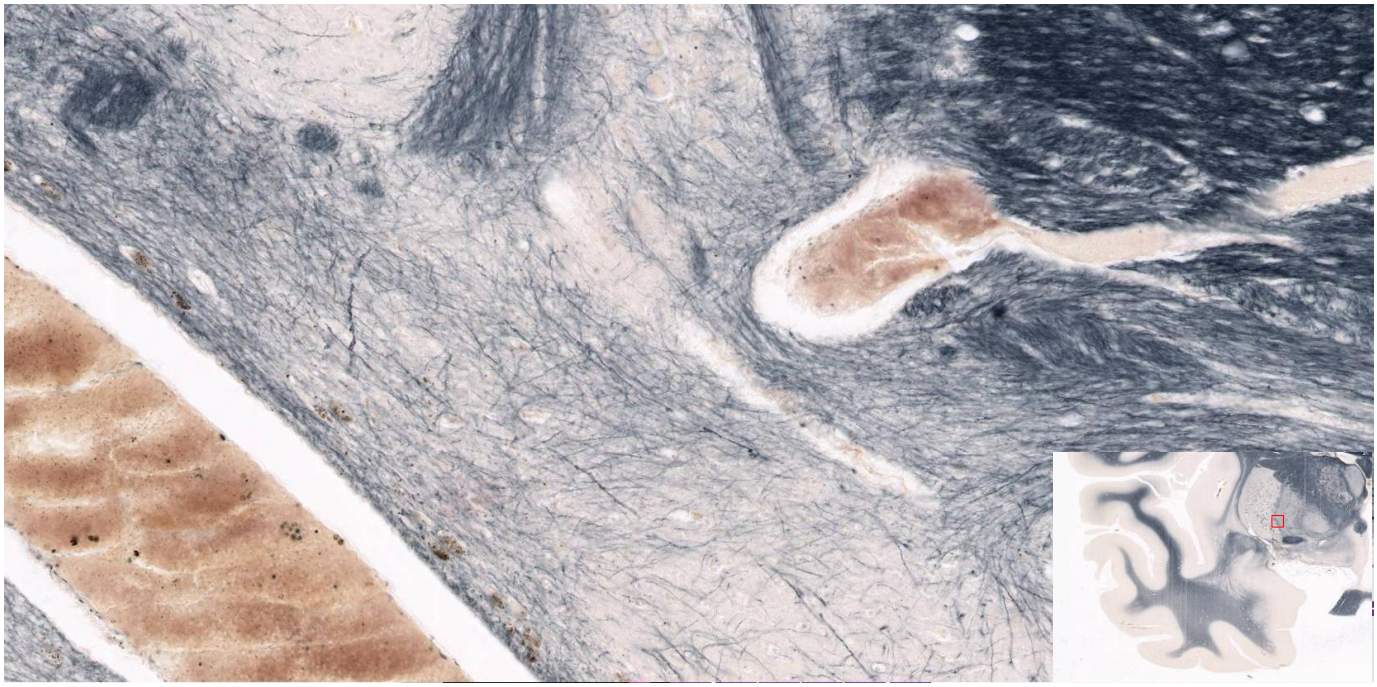

Figure 2. The brain in figure 1 magnified to highlight regions of interest in the left hemisphere.

Because the whole-mount method allows for high resolution, 3D reconstruction, it enables new insights in itself and also when combined with other modalities. In historically significant, long term cases, studies performed with non-invasive techniques like MRI or CT can be put into greater context in comparison to whole-mount histology imaging. In patients with TBI, whole-mount imaging can reveal diffuse pathology in the brain's deep white matter, and allow the boundaries of lesions or injury to be more precisely determined. Acquiring this high-resolution reference, further studies can lead to insight on neural circuits used in perceptual tasks and how those are affected by TBI. By combining whole-slide imaging with molecular methods, the effect that TBI has on global brain connectivity can be better understood.

Overall, a microscopic map of the brain has the opportunity to be linked to a variety of other structural and functional data. Histological study can validate the results of non-invasive MR-based imaging, improving the methods used in treating traumatic brain injury, ultimately to improve patient outcomes.

Huron Digital Pathology has already supported a variety of human brain research through the acquisition of high resolution, whole-brain images. Want to see more? Visit Huron's image gallery.

Figure 3. The 5x7" slide of a human brain on Huron's whole-mount slideholder.

HURON Digital Pathology

Huron Digital Pathology
550 Parkside Dr. Unit B6
Waterloo, ON Canada N2L 5V4
T 519.886.9013 **F** 519.886.5300
Email: info@hurondigitalpathology.com
www.hurondigitalpathology.com