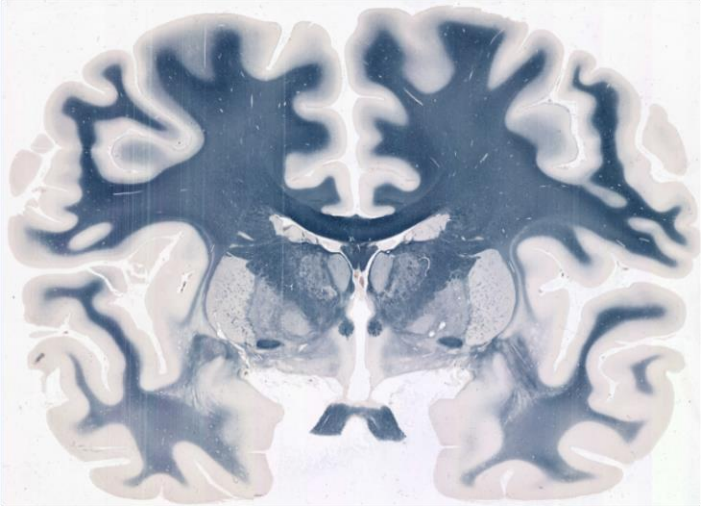
Application Note: Whole Mount Human Brain Imaging

Introduction

Current research in neuroimaging for human subjects cannot be adequately understood without knowing the anatomy of the brain. Studying the structural and functional organization of the human brain requires the integration of several imaging modalities such as MRI, fMRI, DWI and CT. These modalities are steadily increasing in resolution and accuracy, yet postmortem imaging of actual brain tissue remains the gold standard. To produce accurate representations of the human brain (ideally represented in a probabilistic, cytoarchitectonic atlas of the human brain) cross-sections need to be imaged using macroscopy and microscopy techniques, gross anatomical landmarks should be established and corresponding inter-subject variability including those of microstructural organization must be known.

Furthermore, a better understanding of neurological disease states necessitates that images viewed (or measured) with MRI and DWI be reconciled with follow-up neuropathology reports. MRI-neuropathology correlations are therefore critical for full understanding of the brain by building digital histological maps of the brain, combined with 3-D models representing anatomical relationships. Also, the development of higher resolution maps with associated inter-connectivity allows for the visualization of structural changes in neurological and psychiatric disorders.



Investigating global relationships in the cortex at 10x magnification with 1 micron resolution

Limitations of Traditional Microscopy in Human Brain Imaging

1. **Limited glass slide sizes available for imaging:** Entire cross sections of human brain tissue cannot fit onto standard (1”x3”) microscope-slides. Instead, brain samples must be divided into numerous sections and placed on several glass slides which are then individually imaged, tiled and stitched. This produces a “checker-board” effect resulting from the overlap of tiled sections which produces significant artifacts in the image.

2. **Loss of sample integrity:** Cutting of human brain sections and pasting on separate microscope slides effectively reduces and distorts the integrity of the specimen sections for future use. Furthermore, since sampling is rarely informed by previous MRI, the true extent of damage in the brain could be overlooked and important features could be missed.

3. **Limited automation and workflow enhancements:** The process by which each sample is prepared, loaded, imaged and reviewed is manual in nature and time consuming. Automated processes for a large number of samples are restricted to operator speeds for systems not specifically designed for the workflow associated with large specimen imaging.

4. **Limited objective lens field-of-view**: While MRI provides low resolution images of neuropathogenetic phenomena in the whole brain; traditional postmortem neuropathological microscopy only provides evidence from few and very small pieces of tissue. Traditional microscope objectives are limited in their field-of-view. Their use requires a tremendous amount of processing power and speed to scan (at sufficient magnification) each tile and to stitch the final image together in a reasonable time.

5. **Prohibitive processing time and costs:** Processing of images of large numbers of sample which adequately represent an entire human brain (with accompanied tiling and stitching) is grossly prohibitive given the amount of time, the number of systems required, labor and overhead expenses.

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Huron Digital Pathology's Large Specimen Imaging Solution

Huron Digital Pathology's TissueScope™ digital slide scanner has overcome the limitations of traditional microscopy for imaging large specimens like whole human brain slices. The TissueScope digital slide scanner provides key advantages for imaging large specimen, such as whole mount human brain images. These include:

- A proprietary laser-scan lens and optical configuration allows for the imaging of samples with a wide field-of-view (scanning strips 10mm wide at 20X magnification). Imaging both small and large specimen slides (ranging from 1"x3" up to 6"x8") significantly reduces scanning times by allowing the entire cross-section of a human brain to be produced without tiling and stitching. Postmortem examination of the whole brain allows for examination of distal effects of local features that are correlated based on anatomical and functional connectivity.

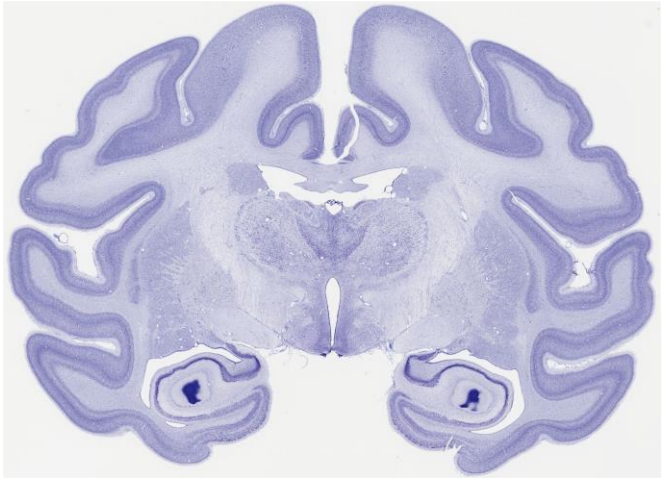
- An optional high-throughput Autoloader Module (TissueScope XT) enables fully automated scanning of a large quantity of slides of various sizes (300-1"x3" glass slides up to 25-6"x8" glass slides).

- The ability to scan samples at various magnifications (1X, 2X, 10X and 20X) using the same laser-scan lens enhances workflow and facilitates acquiring detailed images for analysis of areas of interest.

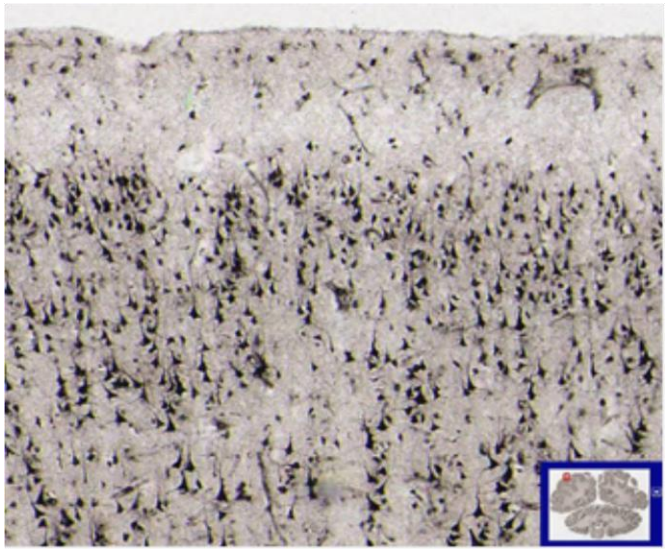
- Thick tissue sections can be imaged because of the long (3mm) laser-scan lens working distance. Proprietary optics in combination with a large working distance also facilitates imaging at specimen depths of up to 100µm as well as optical sectioning and Z-stacks.

- The images are produced in an open, non-proprietary TIFF file format and can be used with a wide variety of free or commercially available image analysis software.

Human Brain Cross-sectional Image Area: 35 inches2 (5"x7" glass slide)*	Time to Image
Using Traditional Microscopy	12 hours
Using TissueScope HS Digital Slide Scanner	12 minutes
*excluding preparation and setup time	



Nissil stain of human brain at 10X magnification using the TissueScope Digital Slide Scanner



Detailed zoom on 10x Magnification of human brain to highlight neuron density

Contact **Huron Digital Pathology** for your human brain section imaging applications!

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