Oil and Fluorescent Digital Pathology Services

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Abstract

At Nationwide Children's Hospital, the Biomedical Imaging Team (BIT) is part of the Biopathology Center at The Research Institute of Nationwide Children's Hospital specializing in digital pathology services and high resolution whole slide imaging. The BIT department provides various imaging services for the pathologic purpose of enhancing biomedical research. The services provided by the team include whole slide digital scanning, digitized tissue microarrays, image storage, image analysis, and an automated pathology review application. Whole slide digital images provide researchers with high quality digital images obtained scanning with either brightfield or immunofluorescent stained slides. These whole slide images are available 200 times or 400 times normal image size as well as 1000 times through the use of an oil immersion scanner. The oil immersion scanner produces high quality whole slide digital images at 1000 times the original tissue size. The oil immersion scanner produces this high resolution image by having oil placed above the tissue on the slide, allowing for the image to be digitized with oil immersion optics. The fluorescent scanner aims to produce high quality images at 200 times the original tissue size while decreasing the possibility of photobleaching the tissue, made possible by having auto-exposure and autofocusing capabilities. The camera within the fluorescent scanner also has monochrome image capturing capabilities as well as having a filter set, allowing for up to four different color channels to be used. Scanning provides a high resolution whole-slide image. Image storage is optimal due to the reduction of the cost of physical slide storage and offers a solution for long term sample preservation. The Virtual Imaging for Pathology, Education, and Research (VIPER) application is an in-house developed web-based application which facilitates the automated pathology digital review of normal and diseased tissues. As technology continues to progress, the BIT will continue adding tools to allow researchers to automate processes and further reduce computational time.

Background

The Biopathology Center (BPC) located in Columbus, OH, functions as a biorepository under guidance of The Research Institute at Nationwide Children's Hospital in collaboration with The Ohio State University Wexner Medical Center. The fundamental purpose of the BPC is acquisition and storage of cancerous, normal, and diseased biospecimens. The Biomedical Imaging Team (BIT) is a multidisciplinary team within the BPC which provides imaging services to enhance biomedical research for several national organizations.

In the last decade, whole slide imaging and virtual microscopy have seen tremendous growth in functionality and utility of their services due to the demand for more expedient pathology review. The basic workflow for digital pathology begins with a glass slide and ends with the completed pathology review of a high resolution whole slide image. An important educational tool and capable of image sharing with a quick turnaround time, virtual microscopy has appealed to clinicians and researchers alike.[1,2,3,4]

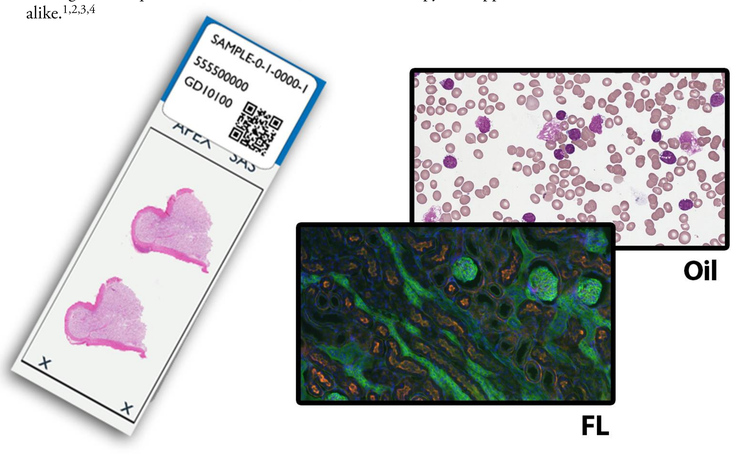

Figure 1. Left image is an example of a pathology glass slide which is used for scanning. Examples of digital glass slide images from oil and fluorescent slides with their varying degrees of magnification to the right.

Methods

Whole-slide image preparation begins with receiving specimen glass slides from internal and external healthcare institutions. The slides then undergo a cleaning process where the slides are first checked for any excess mounting media or protruding coverslips. Once the check is complete, the slides are cleaned using alcohol pads and Kimwipes® to remove any debris off the slides, which are now ready for imaging.[1,2,3,4]

Oil whole-slide digital scanning is achieved through the use of a high-capacity, slide-scanning oil immersion robot and provides researchers with high resolution digital images. The BIT lab has an Aperio ScanScope OS scanning robot in which provides users with hematopathology and microbiological whole-slide images at 100x magnification using oil immersion, allowing users to evaluate the cellular details electronically (Figure 2). The digital images are produced by placing oil above the tissue on the slide and scanning using the robot. The robot uses a high numerical aperture oil immersion lens, allowing for the resulting images to mirror the detailed image one views under a microscope (Figure 1).[1,4,5]

Fluorescent whole-slide digital scanning is achieved through the use of a high-capacity, slide-scanning fluorescent robot and provides researchers with high resolution digital images. The BIT lab has an Aperio ScanScope FL scanning robot in which provides users with fluorescent stained whole-slide images at 20x magnification, allowing users to evaluate the fluorescent cellular details electronically (Figure 2). The digital images are produced by scanning the fluorescent stained slide using the robot (Figure 1). The robot captures the fluorescent cellular detail, while decreasing the possibility of photobleaching the tissue, by allowing for auto-exposure, autofocus, and advanced illumination. The Aperio FL scanning robot allows for one or multiple fluoresced colors in a single image through the use of the scanner's monochrome image capturing or multi-band pass filter set where up to four color channels can be applied.[1,4,6]

Digital asset management allows for digital storage of the images captured by the scanning robots. Image storage is available to reduce the cost of physical slide storage or potential transportation damages and helps long term sample preservation for future research use. After each image is reviewed for quality purposes, the images are transferred to and stored at the Ohio Supercomputer Center (OSC) digital slide repository.

Automated pathology review application allows for the review of normal and diseased tissues for quality control purposes using an in-house developed web-based application called Virtual Imaging for Pathology, Education, and Research (VIPER). Through the use of VIPER, pathologists have the ease of accessing images and provide their expertise on the available images and related pathology data from anywhere in the world.

Multiple image analysis tools allow for analysis of normal and diseased tissues.

Figure 2: Aperio ScanScope FL scanning robot to the left and the Aperio ScanScope OS scanning robot to the right.

Results

The workflow for digital pathology includes all steps necessary for slide preparation, high resolution whole-slide imaging (Figure 3). Images are evaluated for resemblance of the tissue on the slide, they are then transferred to the Ohio Supercomputer Center and are assigned to pathologists through the automated pathology review application. The Ohio Supercomputer Center has currently stores 184,217 whole-slide images utilizing 68 terabytes of storage.[4]

Pathologists review these digital images using VIPER as a means of rapid pathological review. This allows for one to quickly assign, QC, and review cases when authorized to do so. There are currently 132 registered users for VIPER and a count of 6468 cases.[4]

Acknowledgements

BPC Leica Ohio Supercomputer Center An OH·TECH Consortium Member

Discussion

Growing with technology, digital pathology is playing a vital role for research and educational purposes and has been approved by the FDA.[7] The whole-slide imaging allows pathologists and researchers to share images world wide electronically. To further understand the function and structure of the different cellular components, using digital pathology can provide the capability of interacting and focusing on many portions of the slides for easier analysis. In the future, the next generation of digital pathology may branch out to regular clinical uses. Despite there being no current FDA approval for clinical use, approval for whole-slide imaging via digital pathology is being researched and considered.

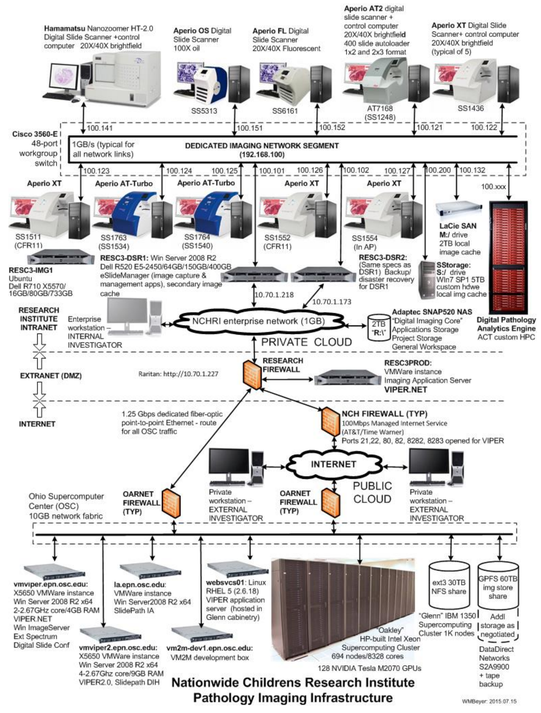

Figure 3. This graphic shows the workflow and infrastructure of the digital imaging process.

References

1. Abhange, S., Hobensack, A., Barr, T., Ramirez, N. "Integrated Workflow for Digital Pathology in a Biospecimen Repository Environment." Impact and Public benefits of Biorepositories. 15 May 2011.
2. "Digital Imaging-Utilization in a Children's Comprehensive Health Care Institute." Digital Pathology Healthcare Seminar. May 2011.
3. http://www.nationwidechildrens.org/biomedical-imaging-team
4. Jones, M., Rarmirez,N., Barr, T., *et al.* "Next Generation Digital Pathology Services." Nationwide Children's Research Institute Research Retreat. Nov. 2016.
5. http://www.leicabiosystems.com/digital-pathology/aperio-digital-pathology-slide-scanners/products/aperio-cso/
6. http://www.leicabiosystems.com/digital-pathology/aperio-digital-pathology-slide-scanners/products/aperio-fl/
7. Pantanowitz, L. "Digital Images and the Future of Digital Pathology." *Journal of Pathology Informatics* 1 (2010): 15. *PMC.*