

Application Note MMI-CS-001 – Tissue Scanning

Whole Slide Imaging on a Microscope

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Abstract

Whole Slide Imaging is becoming increasingly popular in digital pathology as well as in clinical and basic research. The MMI CellScan system has been developed to combine whole slide imaging with all functional flexibility of a research microscope.

In this study, we show that the MMI CellScan is a *bona fide* slide scanner. With the sensitive CMOS MMI camera and the fast microscopy stage, the MMI CellScan is able to scan a 15 mm x 15 mm section using the 20 x objective in less than 1 min. We demonstrate how the MMI CellScan can be applied for whole slide imaging applications.



Figure 1: MMI CellScan system on the Nikon Ts2R inverted microscope. The system is compatible with many microscope brands and models and can be combined with all MMI cell isolation systems for various research applications.

Introduction

Whole slide imaging (WSI) - also known as virtual microscopy – is a rather young technology to digitally scan and archive slides in high resolution. Scanners take images of each field of view across the entire microscopy slide. The pictures are then stitched together to generate a single digital image in high resolution.

The technology of whole slide imaging developed rapidly over the last decade, as storage of large datasets, barcoding and file tracing as well as data exchange were improving tremendously. Thus, telepathology workflows emerged and enabled pathologists to send image files to their colleagues from all over the world in order to discuss non-obvious cases or to consult experts on specific tissue types or diseases.

Moreover, digital slides are advantageous over tissue sections as color changes or degradation issues due to long-term storage conditions may compromise the quality of the physical tissue slides. Researchers thus aimed to digitally archive tissue slides in order to maintain quality over time and to be able to analyze the tissue after years and decades.

The MMI CellScan is a whole slide imaging system based on standard research microscopes. Thus, it also can utilize all functionalities of the research microscope

making this system highly versatile, flexible, and upgradeable. Scanning is not limited to one resolution, but changing objectives or switching between brightfield and fluorescence imaging modes can be performed with just one mouse click (if installed on a fully motorized microscope such as the Nikon Ti2E or the Olympus IX83). The MMI CellScan, in addition to standard microscopy slides, is compatible with various sample formats such as MMI Membrane Slides for laser microdissection as well as well plates and dishes.

Here, we present the new MMI CellScan whole slide imaging system using standard tissue sections. Digital images are saved in the open file format called BigTIFF which is compatible with our free MMI CellViewer as well as many other slide viewer and image analysis software packages.

Material and Methods

A FFPE tissue section was mounted onto an MMI Membrane Slide and covered with a standard microscope slide. The slide was placed into the 4-slide holder on the stage of an inverted microscope outfitted with the MMI CellScan module.

Using the Preview Scan function, the slide was first scanned at a magnification of 4 x. The software automatically identified the regions

where tissue was present and then scanned those areas at 20 x magnification. A focus map can be automatically assigned or applied manually. The image was automatically saved as BigTIFF and was analyzed using the free MMI CellViewer software.

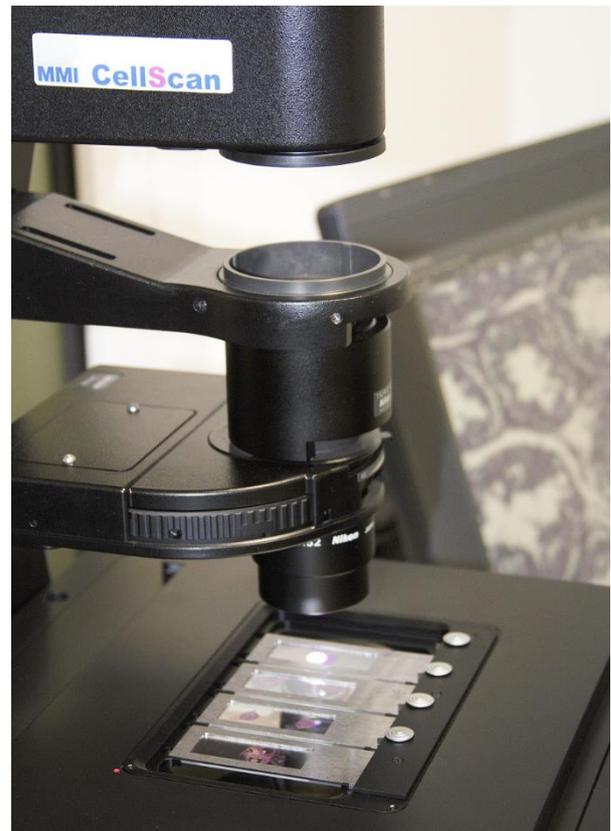


Figure 2: The MMI CellScan is installed on a Nikon Ts2R microscope and can scan four slides at a time.

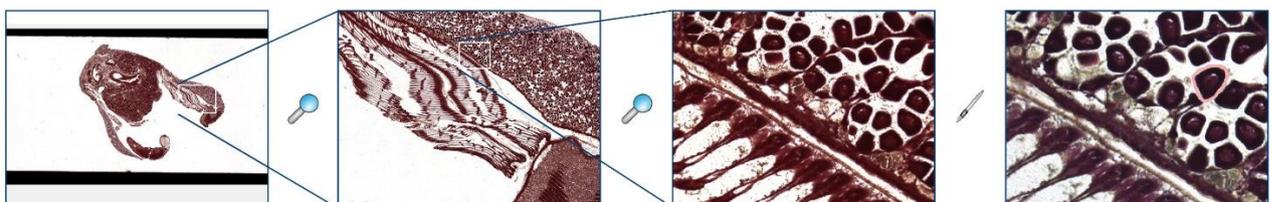


Figure 3: Image analysis using the free MMI CellViewer. The image opens in low resolution to fit the window size. Seamless and rapid zooming down to the full resolution is enabled by a binning algorithm. Areas of interest and single cells can be marked and annotated.

Results

The MMI CellScan is a flexible microscope-based slide scanner with various applications in clinical and basic research. Here, we demonstrate that the MMI CellScan fulfills all the needs of a standard slide scanner and can be employed to scan full resolution slides in a medium-throughput setting.

The MMI CellTools software offers different features and parameter settings to efficiently scan one or several slides automatically providing optimal image quality. The autofocus function automatically sets reference points in the z-dimension to optically flatten uneven samples. Thus, the resulting image is in focus at every position and allows for detailed and automatic image analysis.

To test the performance of the MMI CellScan, a tissue slide was digitally archived as a full resolution image file. With the sensitive CMOS MMI camera and the fast microscopy stage, the MMI CellScan is able to scan a 15 mm x 15 mm section using the 20 x objective in less than 1 min. The image was then automatically saved in a pyramid BigTIFF file format and was loaded in the free MMI CellViewer software for image analysis.

The binning algorithm implemented in the MMI CellViewer enables rapid loading of large image files and allows for a fast and seamless zooming to full resolution. Easy navigation tools enable fast screening through the sample file. In addition, the software provides several functions to mark, measure, and annotate regions of interest as well as single cells.

Discussion

In this study, we demonstrate that the MMI CellScan is a high performance slide scanner able to scan full resolution images with the highest image quality. We showed that the MMI CellScan, in addition to standard microscopy slides, can scan tissue mounted on MMI Membrane Slides dedicated for Laser Microdissection. Interestingly, the MMI CellScan can be integrated on the MMI CellCut system to uniquely and seamlessly combine whole slide imaging and laser microdissection.

Since the MMI CellScan is a microscope-based scanning system, it offers full flexibility of a research microscope and can additionally be employed for standard microscopy applications. To scan images, the MMI CellScan can use all objectives and works both with brightfield and fluorescence.

This combination makes the MMI CellScan a highly versatile scanning system offering many features and parameter settings for optimal scanning of any sample type.

MMI - your partner providing unique competence in microdissection – micromanipulation - imaging. We offer

- Capillary-based selective isolation of single cells from suspension (CellEctor)
- PicoCut laser microdissection to isolate cells in tissue (CellCut)
- Microscopy-integrated Whole Slide Imaging (CellScan)
- Optical tweezers to quantify biological forces (CellManipulator)

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