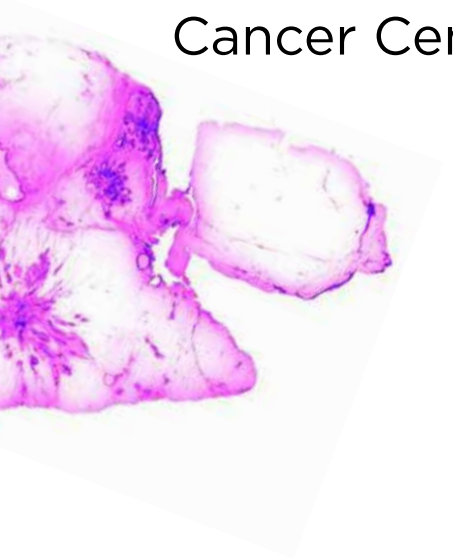
WARREN ALPERT CENTER'S DIGITAL IMAGING LABORATORY

At Memorial Sloan Kettering Cancer Center



The Warren Alpert Foundation Center for Digital and Computational Pathology, Department of Pathology, MSK

Memorial Sloan Kettering Cancer Center

WELCOME MESSAGE

Dr. Yagi's Digital Imaging Laboratory focuses on the development and validation of new technologies in digital imaging. Our lab allows us to work with other researchers and physicians to explore and evaluate the correlation between pathology imaging and other imaging modalities, such as OCT, Surgical and molecular imaging.

Our current research initiatives include:

Multispectral imaging: We have published papers and presentations in this area using MSI for "digital staining", decision support, stain and color standardization.

Automated tissue sectioning systems and decision support systems: we have been fortunate to work with several companies in this area. Automated tissue sectioning will be important in the full automation of the histology lab.

Other areas include a combination of pathology imaging and the imaging of other modalities, such as whole slide imaging, OCT, MRI, ultrasound, and visualization technologies.

Mobile Digital Pathology and Simulations.

Digital Pathology in Biomarker development and evaluation.

Standardization and calibration of digital imaging in a clinical and research setting.

Single cell to whole organ 3D imaging.

We are grateful for the ongoing support and collaboration from our colleagues here at MSK and external collaborators that support our mission and research as we explore the new and exciting things in the field of digital pathology. A special thanks to The Warren Alpert Foundation for their generous donation to help further advance our research. We are proud and excited to share an overview of our 2017 research projects with you and look forward to the new year.

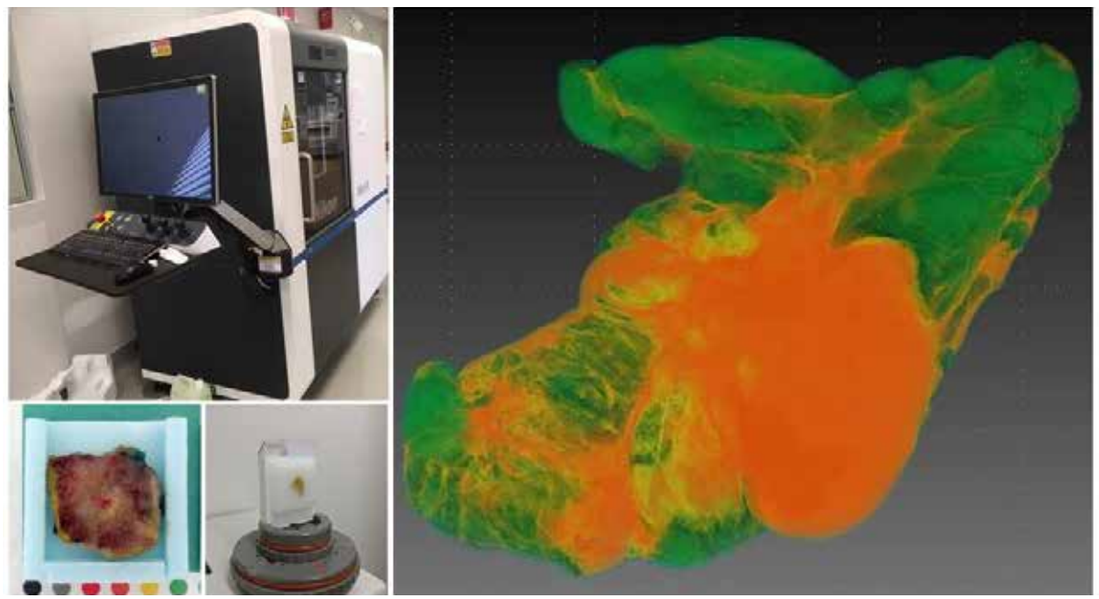
Warm Regards,

Yukako Yagi

Yukako Yagi, PhD
Director of Pathology
Digital Imaging

MICRO-COMPUTED TOMOGRAPHY IN SURGICAL PATHOLOGY

Micro-computed tomography (micro-CT) is an emerging technology within the biomedical field and holds great promise for imaging pathology specimens for reconstruction, modeling, and three-dimensional (3D) analysis. The capacity of micro-CT to create high-resolution 3D models of ex vivo tissue, therefore, creates a unique opportunity to correlate micro-CT image data with other imaging modalities and bring additional information for diagnosis into the future of Pathology. The objectives of this research are 1) to evaluate micro-CT in tissue specimens in pathology, 2) to develop a scanning protocol and workflow specific to the tissue specimens.

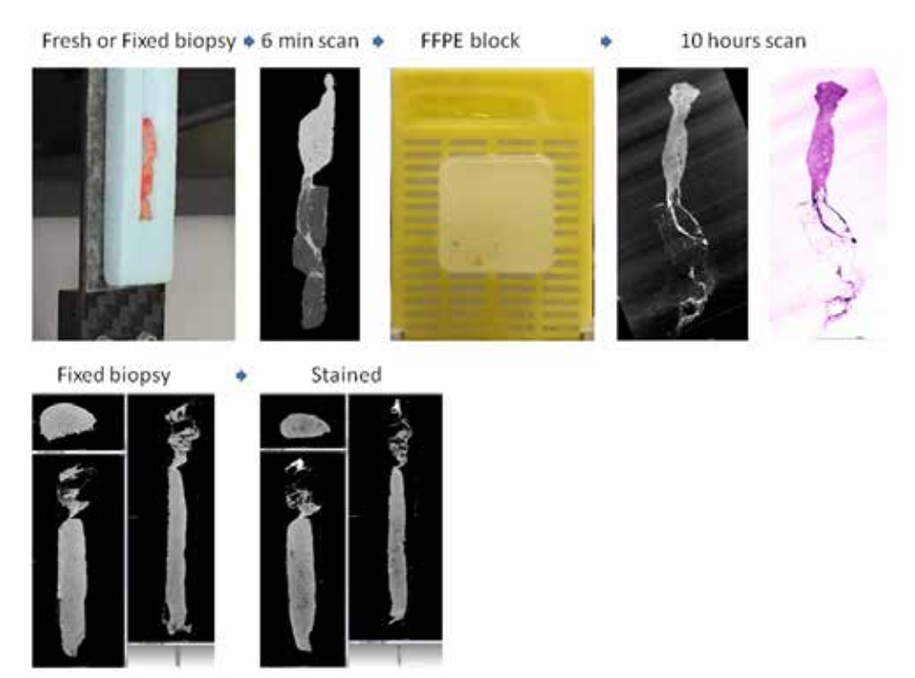


PROJECT WITH

Fu Xiujun, Michael H. Roehrl, MD, PhD, Peter Ntiamoah, Qing Chen, John L. Humm, PhD, Sahussapont Joseph Sirintrapun, MD, Melissa Murray, DO, Jinru Shia, MD, William D. Travis, MD, Meera R. Hameed, MD, Kazuhiro Tabata, MD, and Alexei Teplov

CORRELATING MICRO-COMPUTED TOMOGRAPHY OF SUSPICIOUS BREAST LESION (BI-RADS 4 OR 5) CORE BIOPSY SPECIMENS WITH HISTOPATHOLOGY

Micro-CT technology offers high resolution images at the microscopic level (up to a resolution of less than 10 microns), and can allow to identify different components such as fibroglandular tissue and adipose tissue in the breast specimen. In this pilot study we will explore the utility of micro-computed tomography in a clinical setting for the evaluation of breast surgical specimens along with histopathologic correlation /validation. Scanning with the micro-CT is completed within 5 minutes, making it suitable for rapid evaluation of fresh surgical specimens without a substantial delay in fixation. The use of micro-CT, could potentially enhance the definition of the tumor spatial distribution, in particular with regard to tumor multifocality. It could also guide selective sampling of the tumor areas, reducing the number of tissue sections/block and workload in the pathology laboratory. We expect this approach to improve the accuracy of breast tissue assessments e.g. lymph nodes status, especially in axillary lymph node dissection.

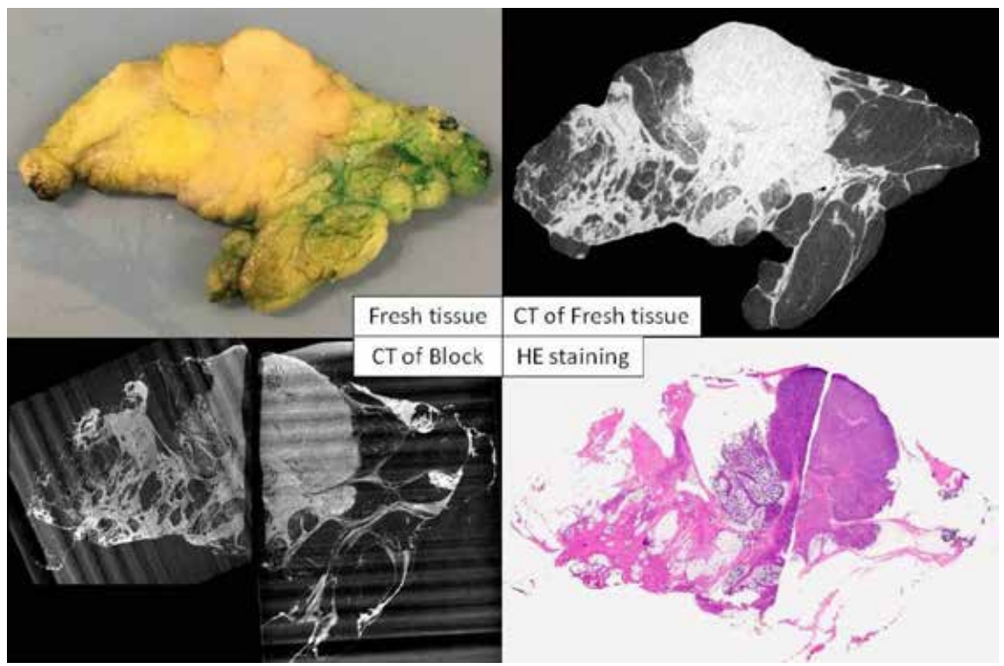


PROJECT WITH

Hanna Y. Wen, MD, PhD, Melissa P. Murray, DO,
Anne Grabenstetter, MD, Kant Matsuda, MD

THE ROLES OF MICRO-COMPUTED TOMOGRAPHY (CT) IN BREAST PATHOLOGY

It is established that breast cancer spreads by contiguous stromal invasion and also by intraductal proliferation with possible noncontiguous invasion. Intra-operative frozen section evaluation of the surgical margin is advocated by some investigators to accelerate detection of margin involvement and reduce the re-excision rate and local recurrence, but sampling error or skipped lesions may limit the assessment. Micro-computed tomography (micro-CT) enables the study of the three-dimensional structure of the tissue and does not require any tissue sectioning or loss of the sample. We evaluate micro-CT images of fresh breast tissue and lymph nodes and compare the findings with those in micro-CT images of formalin-fixed paraffin embedded (FFPE) tissue blocks with available hematoxylin and eosin (H&E) stained sections.

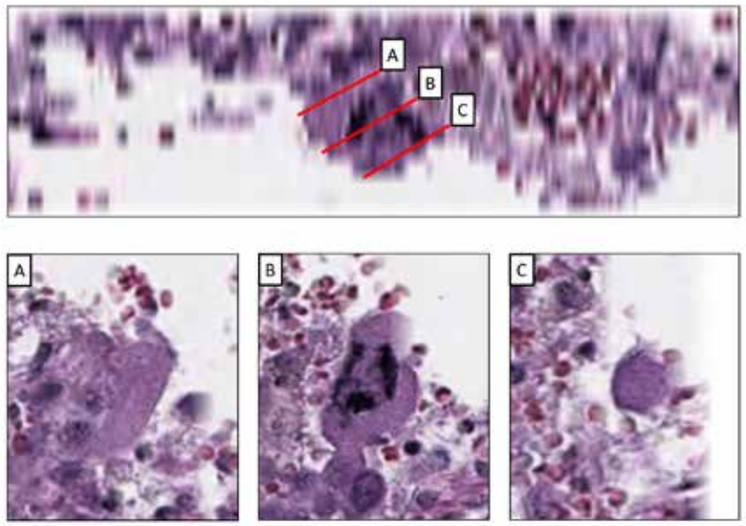


PROJECT WITH

Michael Roehrl, MD, PhD, Meera R. Hameed, MD, Kant Matsuda, MD,
Melissa Murray, DO, Edi Brogi, MD, Kazuhiro Tabata, MD, Alexei Teplov

MITOTIC COUNTING AND CLASSIFICATION STUDY

Supervised image analysis algorithms are only as good as the ground-truth on which they are trained. The most practical ground-truth for training an algorithm is a pathologist's assessment on whole slide images (WSIs). Inter-observer variability may affect the reliability of the algorithm. Annotations from WSIs are subject to other limitations such as the inability to focus on nearby planes of a section (as may occur on a microscope). In this work, we conducted a preliminary feature analysis study detecting mitoses with WSI and a microscope. This study provides candidate mitoses for a larger study to be conducted on a 14-head microscope. Data from the larger study will be used to evaluate the performance of an automated mitosis detection algorithm. Detecting and quantifying mitoses is an important pathology task when evaluating tumors in many organs; it is also challenging and burdensome to pathologists. Because such a task is likely to be impacted by scan quality, we also investigate its suitability for evaluating image quality.

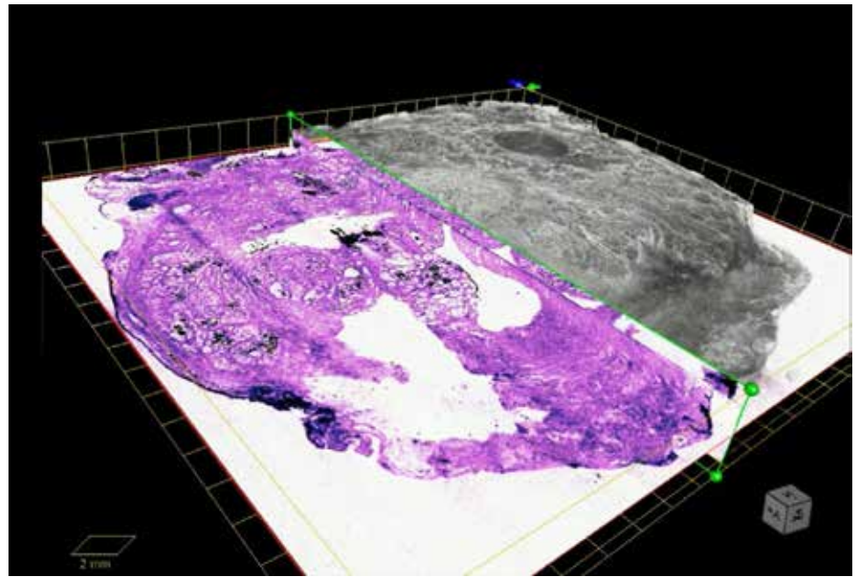


PROJECT WITH

Brandon D. Gallas, PhD, Jamal K. Benhamida, MD, Qi Gong, Matthew Hanna, MD, Partha Mitra, PhD, Sahussapont Joseph Sirintrapun, MD, Meera R. Hameed, MD, David S. Klimstra, MD, Naohiro Uraoka, MD, Kazuhiro Tabata, MD

WHOLE BLOCK IMAGING IN PROSTATE CANCER

Traditional histologic methods are hindered by glass slide creation through tissue sectioning, staining, and additional scanning. Traditional sectioning microscopy also only provides two-dimensional (2D) image representations of 3D structures. Micro-computed tomography (micro-CT) opens a disruptive imaging opportunity, not only in obviating the need for sectioning and tissue staining but in potentially rendering 3D images useful for new morphologic insights. Recently micro-CT has become high performance in image acquisition and volume processing. We have applied micro-CT in rendering 3D images of prostate whole mounted paraffin embedded slices.

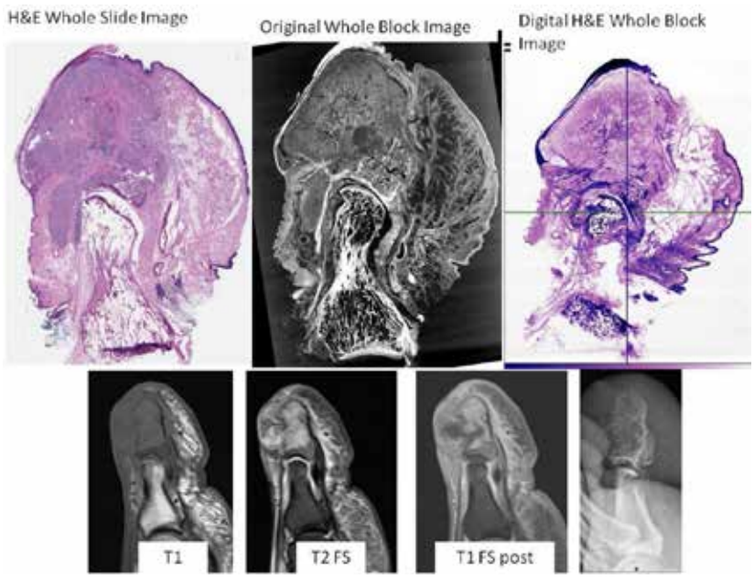


PROJECT WITH

Sahussapont Joseph Sirintrapun, MD, Anuradha Gopalan, MD, Hikmat A. Al-Ahmadie, MD, Ying-Bei Chen, MD, PhD, Samson W. Fine, MD, Satish K. Tickoo, MD, Victor E. Reuter, MD, Alexei Teplov, Kazuhiro Tabata, MD

WHOLE BLOCK IMAGING IN BONE TUMOR

In Orthopedic Pathology, correlation of imaging characteristics to histopathology is important for a meaningful and accurate diagnostic interpretation. This traditional practice has provided many insights on tumor characteristics such as growth pattern, relationship to adjacent normal bone, matrix production, tumor aggressiveness, etc. In Radiology, three-dimensional (3D) reconstruction of digital images is an easily available technique whereas traditional Pathology provides only a 2D image of 3D anatomical structures albeit with much higher resolution than radiological images. Although 3D histological reconstruction is possible, it requires automated sectioning of hundreds of slides with 3D reconstruction using appropriate software. 3D Whole block imaging (WBI) by micro-computed tomography provides a new imaging modality to create 3D reconstruction of tissue sections with microscopic level resolution, potentially up to 10x without the need for tissue sectioning.

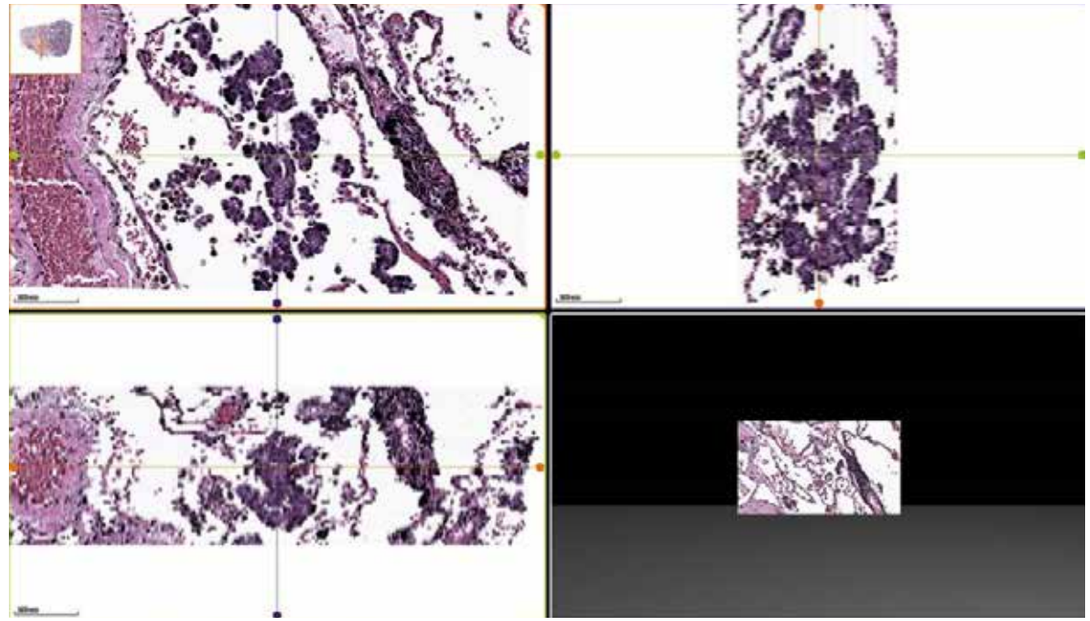


PROJECT WITH

Sinchun Hwang, MD, Meera R. Hameed, MD,
Kazuhiro Tabata, MD, Alexei Teplov

THREE-DIMENSIONAL ASSESSMENT OF SPREAD THROUGH AIR SPACES IN LUNG ADENOCARCINOMA: INSIGHTS AND IMPLICATIONS

Tumor spread through air space (STAS) is a newly recognized form of invasion in lung adenocarcinoma and squamous cell carcinoma that growing evidence shows is associated with recurrence and survival. The observation that tumor STAS clusters/nests, or single cells, within air spaces on two-dimensional hematoxylin and eosin slides raised the question: “How could these cells survive within air spaces without a vascular supply?” This, in turn, has led some to speculate that STAS is an artifact. Herein, we perform the high-resolution high-quality three-dimensional reconstruction and visualization of normal lung and tumor in a lung adenocarcinoma to investigate the invasive pattern of STAS.

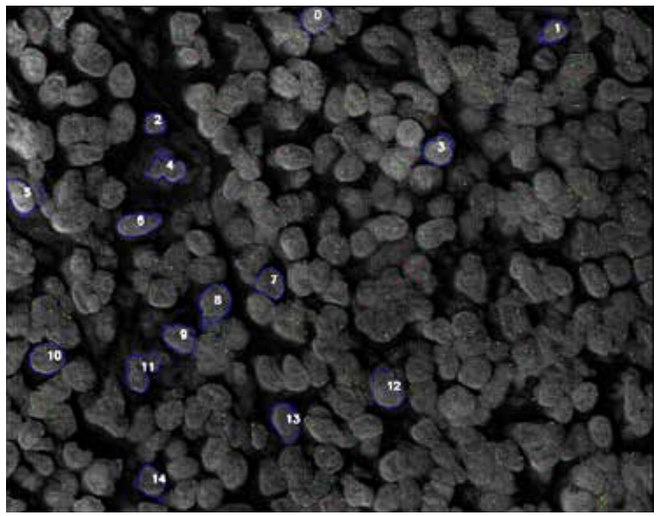


PROJECT WITH

Kazuhiro Tabata, MD, Natasha Rekhtman, MD, Takashi Eguchi, MD,
Xiujun Fu, MD, Joseph Montecalvo, MD, Prasad Adusumilli, MD, Katia Manova, PhD,
Meera Hameed, MD and William D. Travis, MD

AUTOMATED FFPE FISH SIGNAL SCORING USING CONFOCAL SCANNER

The Automated FFPE FISH Signal Scoring using Confocal Scanner project intends to fully automate the process of scan data access, nuclear segmentation, fluorescence spot detection and statistical classification of nuclei according to MYC break-apart sorting criteria. Previous analysis was semi-automated, relying on manual methods to generate z-stack image data from confocal scan data and for nuclear segmentation using CaseViewer and Imaris, respectively. The automated system utilizes the OpenCV computer vision framework and skimage image processing library in conjunction with the python programming language to segment and classify nuclei, count spots, and generate summary statistics based on the clinical scoring system. Reports will be automatically generated by the system and statistics will persist in a relational database management system dedicated to the project.

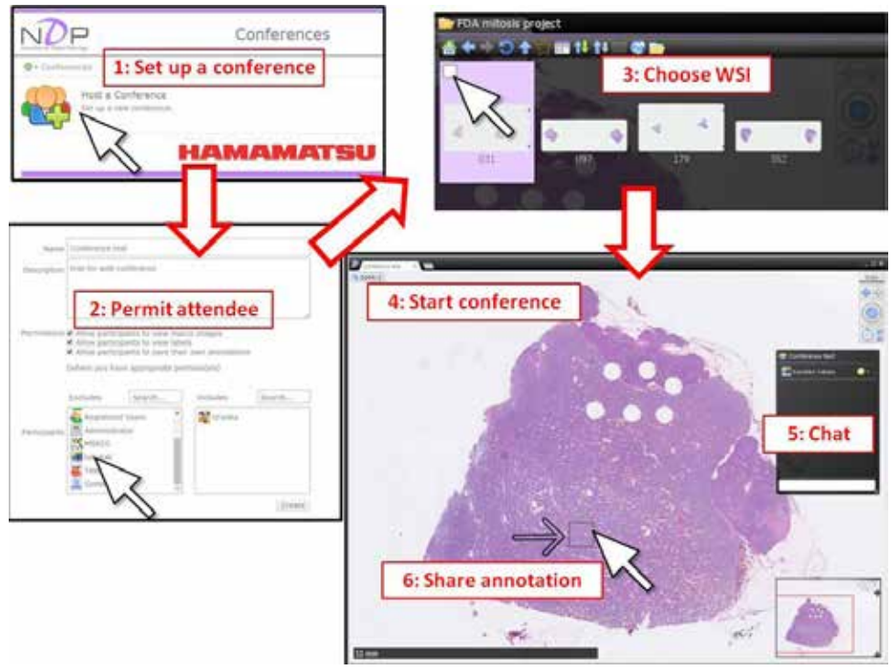


PROJECT WITH

Meera R. Hameed, MD, Lu Wang, MD, PhD, and Yanming Zhang, MD,
Travis Hollmann, MD, PhD, Paul Matises, Naohiro Uraoka, MD

WHOLE SLIDE IMAGE BASED ON-LINE CONFERENCING

Digital pathology systems facilitate telepathology, including consultation. After testing the telepathology web conference capabilities of multiple vendors, we analyzed the merits and demerits of each. Our NDP server 3.0 software (Hamamatsu photonics, Hamamatsu, Shizuoka, Japan) is a digital pathology system that makes in-network consultation and conferences easy and accessible in a clinical and educational settings.



PROJECT WITH

Kazuhiro Tabata, MD and Naohiro Uraoka, MD

OTHER PROJECTS IN SUPPORT OF CLINICAL OPERATIONS

Cytology Evaluation and Validation Study
Project with Oscar Lin, MD, PhD, Paul Matises, Naohiro Uraoka, MD

Technical and Clinical Standardization for Digital Pathology
Dr. Yagi's Digital Imaging Laboratory

Emphasis on developing and integrating useful technologies in digital pathology to enhance clinical workflows and operations.

SPECIAL THANK YOU

Thank you to the Department of Pathology, Radiology and Medical Physics , the Josie Robertson Surgical Center, the Warren Alpert Center for Digital and Computational Pathology, Nikon and all of our research partners and supporters.