COLLEGE of AMERICAN PATHOLOGISTS

Ex-Vivo Microscopy:

A Promising Next-Generation Digital Microscopy Tool for Surgical Pathology Practice

Savitri Krishnamurthy, MD, FCAP

April 11, 2019

Savitri Krishnamurthy, MD, FCAP

- Professor, Deputy Division Head of Pathology and Laboratory Medicine
- Director of Clinical Trials Research and Development at The University of Texas MD Anderson Cancer Center in Houston, TX
- Member of the In Vivo Microscopy Committee

Disclaimer

- **The CAP does not permit reproduction of any substantial portion of the material in this Webinar without its written authorization. The CAP hereby authorizes attendees of the CAP Webinar to use the PDF presentation solely for educational purposes within their own institutions. The CAP prohibits use of the material in the Webinar – and any unauthorized use of the CAP's name or logo – in connection with promotional efforts by marketers of laboratory equipment, reagents, materials, or services.**

Disclaimer

- **Opinions expressed by the speaker are the speaker's own and do not necessarily reflect an endorsement by the CAP of any organizations, equipment, reagents, materials, or services used by participating laboratories.**

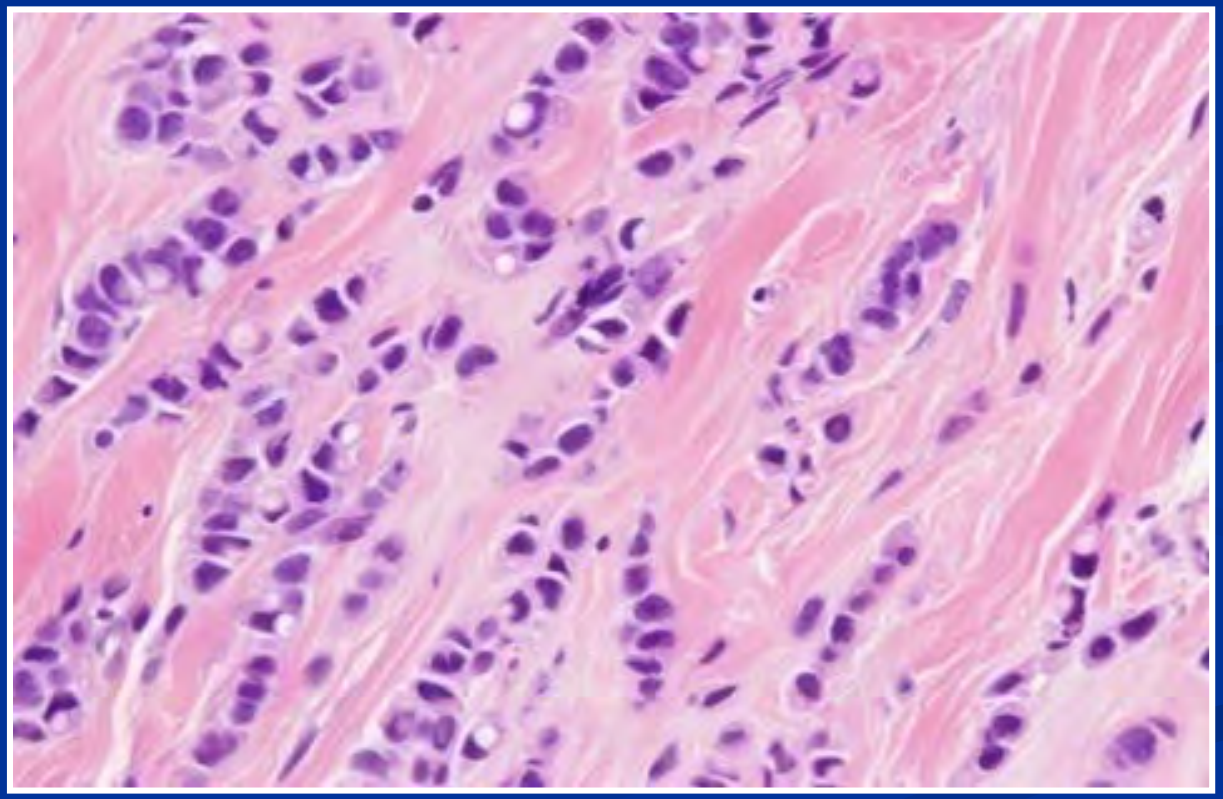
Disclosures

- I do not have financial interests in the products or companies covered in the webinar.
- My research with optical imaging modalities is supported by funding from MD Anderson Cancer Center, NIH, Sheikh Khalifa Bin Zayed Al Nahyan Institute for Personalized Cancer therapy AND Sponsored Research grant from Caliber Imaging Inc. Rochester, NY.

Anatomic Pathology

Image based diagnosis of stained tissue sections

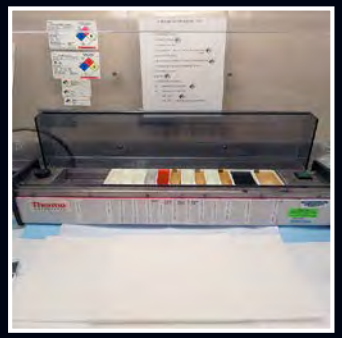
TISSUE HISTOPATHOLOGICAL DIAGNOSIS



COLLEGE of AMERICAN PATHOLOGISTS

Surgical Pathology

FROZEN SECTION



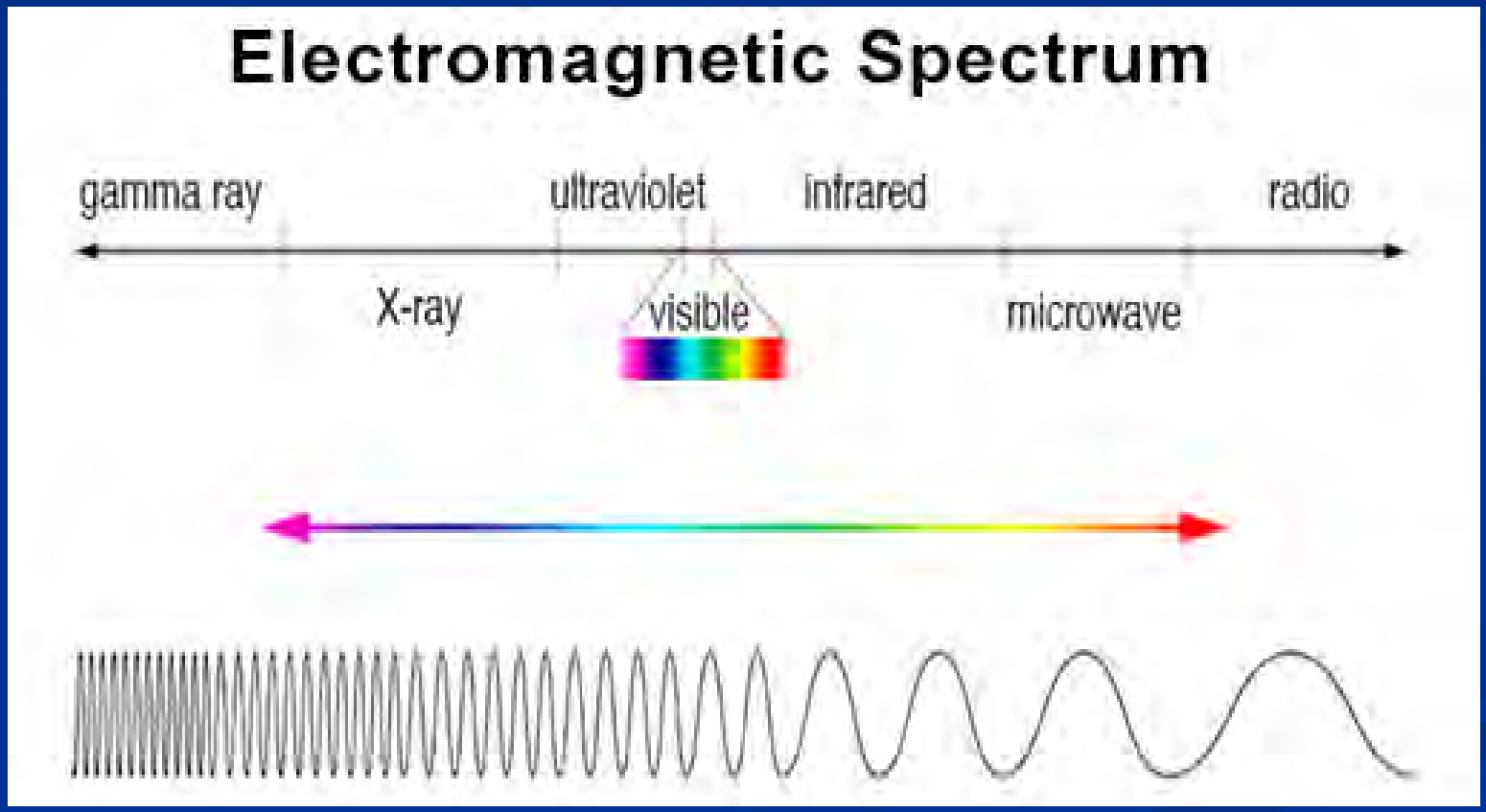
HISTOPATHOLOGICAL EVALUATION

FFPE TISSUE SECTIONS

COLLEGE of AMERICAN PATHOLOGISTS

Optical Imaging

Utilizes light in the visible and adjacent spectrum
Techniques for noninvasive imaging of tissues



Ex-Vivo Tissue Optical Imaging

EX-VIVO OPTICAL IMAGING PLATFORMS

Optical principle

Pathology studies conducted
Overall performance

Advantages and Limitations

Suitability for Surgical Pathology practice

PATHOLOGIST'S PERSPECTIVE

COLLEGE of AMERICAN PATHOLOGISTS

Ex-vivo Tissue Optical Imaging

Optical Principle

- Confocal Microscopy (CM)
- Optical Coherence Tomography (OCT)
- Full-field optical coherence tomography (FF-OCT)
- Microscopy using Ultraviolent Surface Excitation (MUSE)
- Structured illumination microscopy (SIM)
- Light Sheet Microscopy (LSM)
- Stimulated Raman Scattering Microscopy (SRS)
- Nonlinear Microscopy (NLM)

Ex-vivo Tissue Optical Imaging

Optical Principle

Without using extrinsic Contrast /Labeling Agents

Confocal reflectance microscopy

Optical Coherence Tomography (OCT)

Full-field Optical coherence Tomography (FF-OCT)/ Dynamic FF-OCT

Stimulated Raman Scattering Microscopy (SRS)

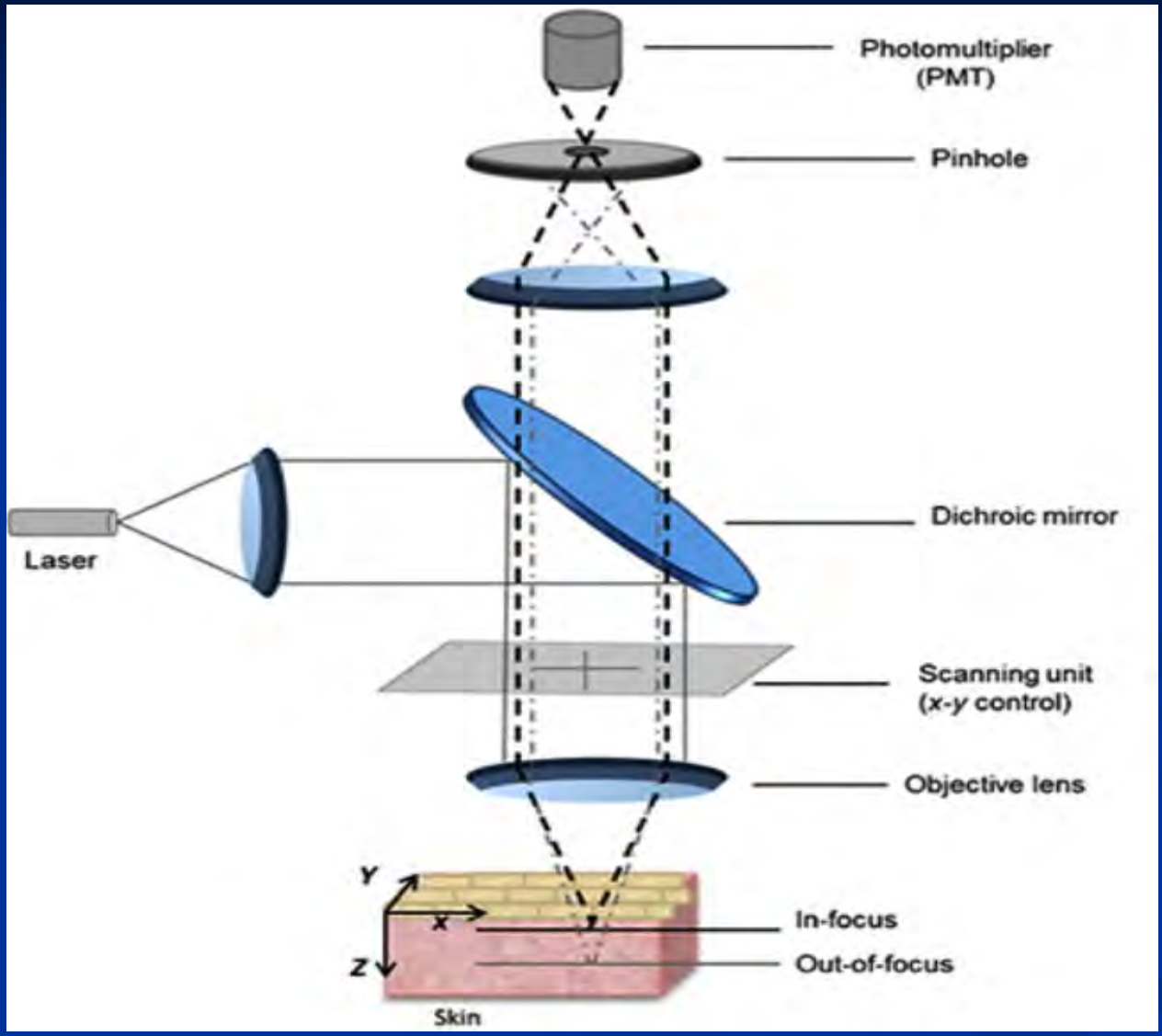
Ex-vivo Tissue Optical Imaging

Optical Principle

With Contrast/Labeling Agents : Fluorescent dyes

- Confocal Fluorescence Microscopy (CFM)
- Structured Illumination Microscopy (SIM)
- Light Sheet Microscopy (LSM)
- Microscopy using UV surface excitation (MUSE)
- Non Linear Microscopy (NLM)

CONFOCAL MICROSCOPY

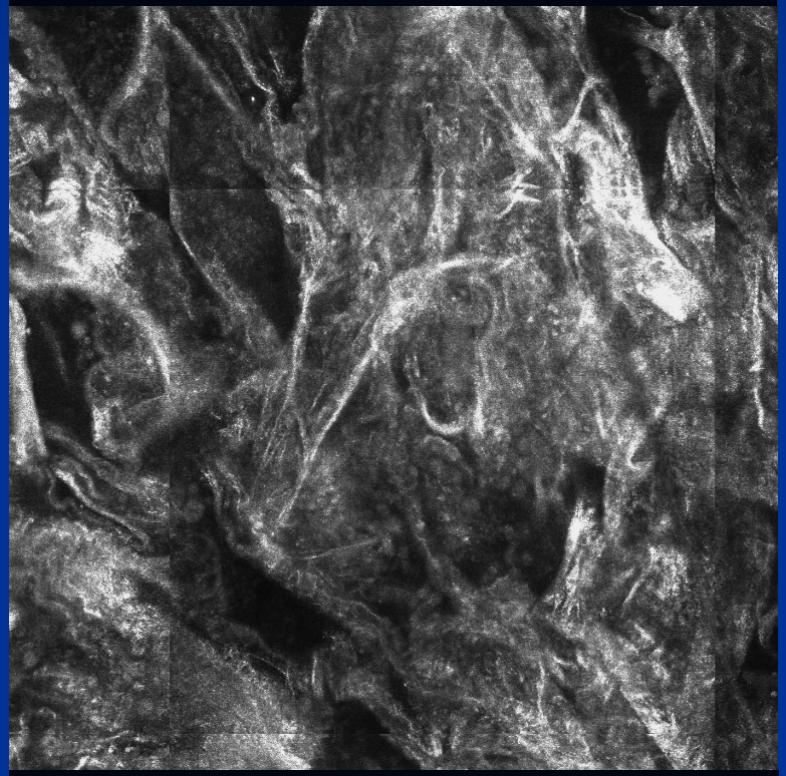


COLLEGE of AMERICAN PATHOLOGISTS

Rossetti CF et al. Confocal Laser Microscopy, 2013

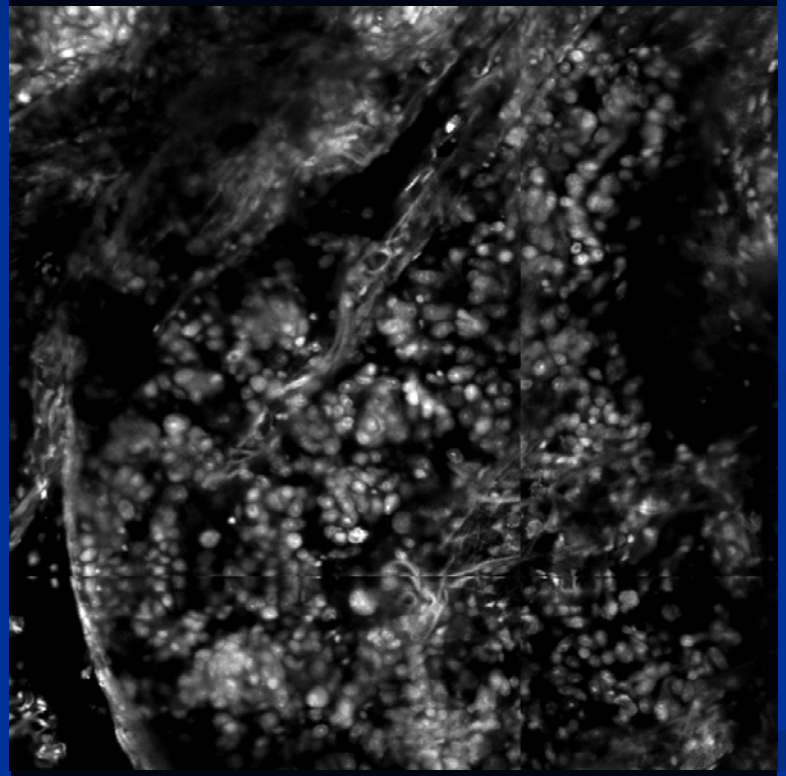
CONFOCAL MICROSCOPY

Reflectance:
Tissue autofluorescence



785 nm

Fluorescence:
With contrast agents



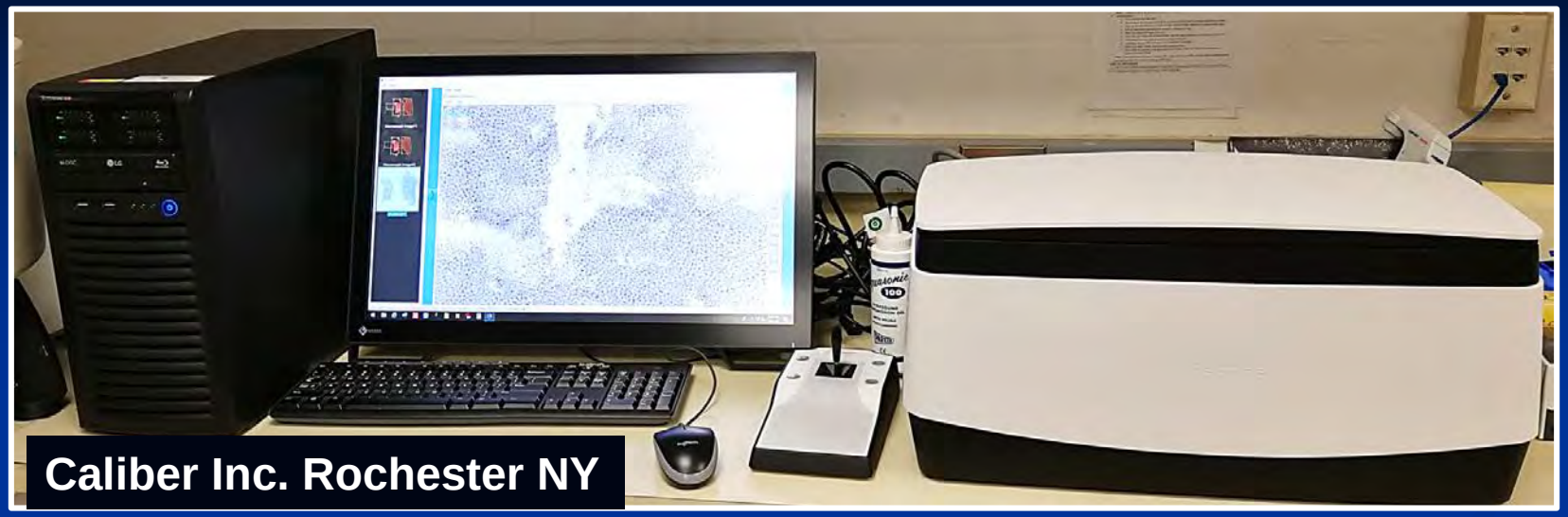
Acridine orange : 488 nm

COLLEGE of AMERICAN PATHOLOGISTS

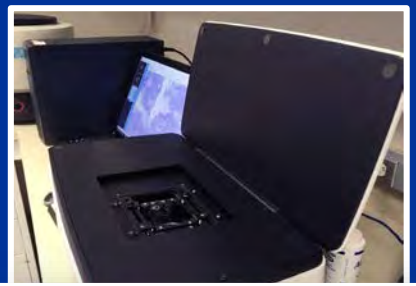
Fluorescent agents and laser wavelengths for excitation

Fluorescent Dye	Wavelength (nm)
Proflavine	488
Acridine Orange	488
Cresyl Violet	561
Fluorescein	488
Indocyanine Green	780
Methylene Blue	638
Toluidine Blue	638
Acriflavine Hydrochloride	488

CONFOCAL MICROSCOPE



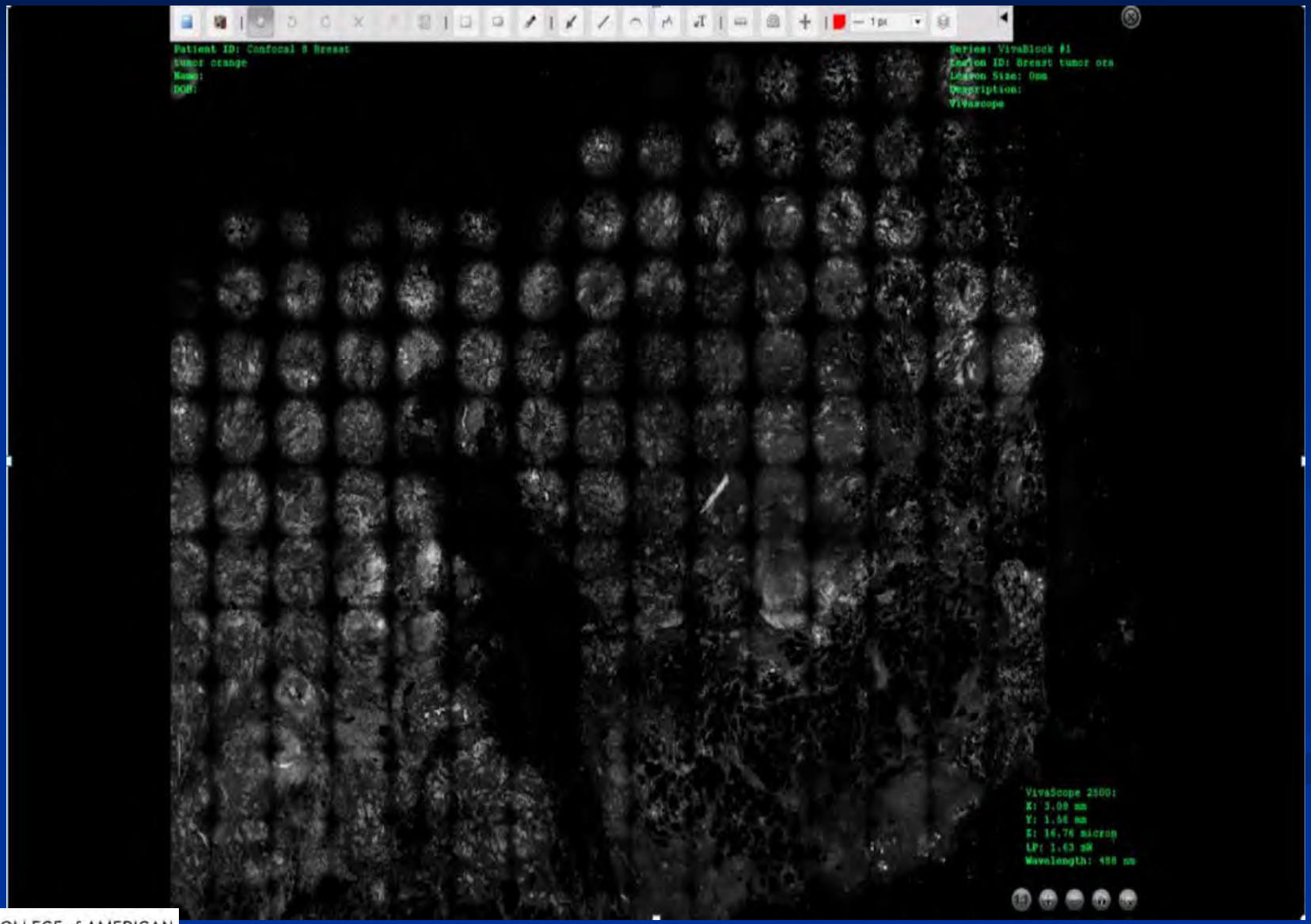
Caliber Inc. Rochester NY



- Lateral resolution : 1 µm
- Axial resolution : 5.0 µm
- Field of view : 2.0 cm
- Depth of imaging : 250-300 µm
- Frame rate: 9 frames/sec
- Image resolution: 1000 x 1000 pixels
- Operating wavelength : 488 nm, 785 nm, 830 nm

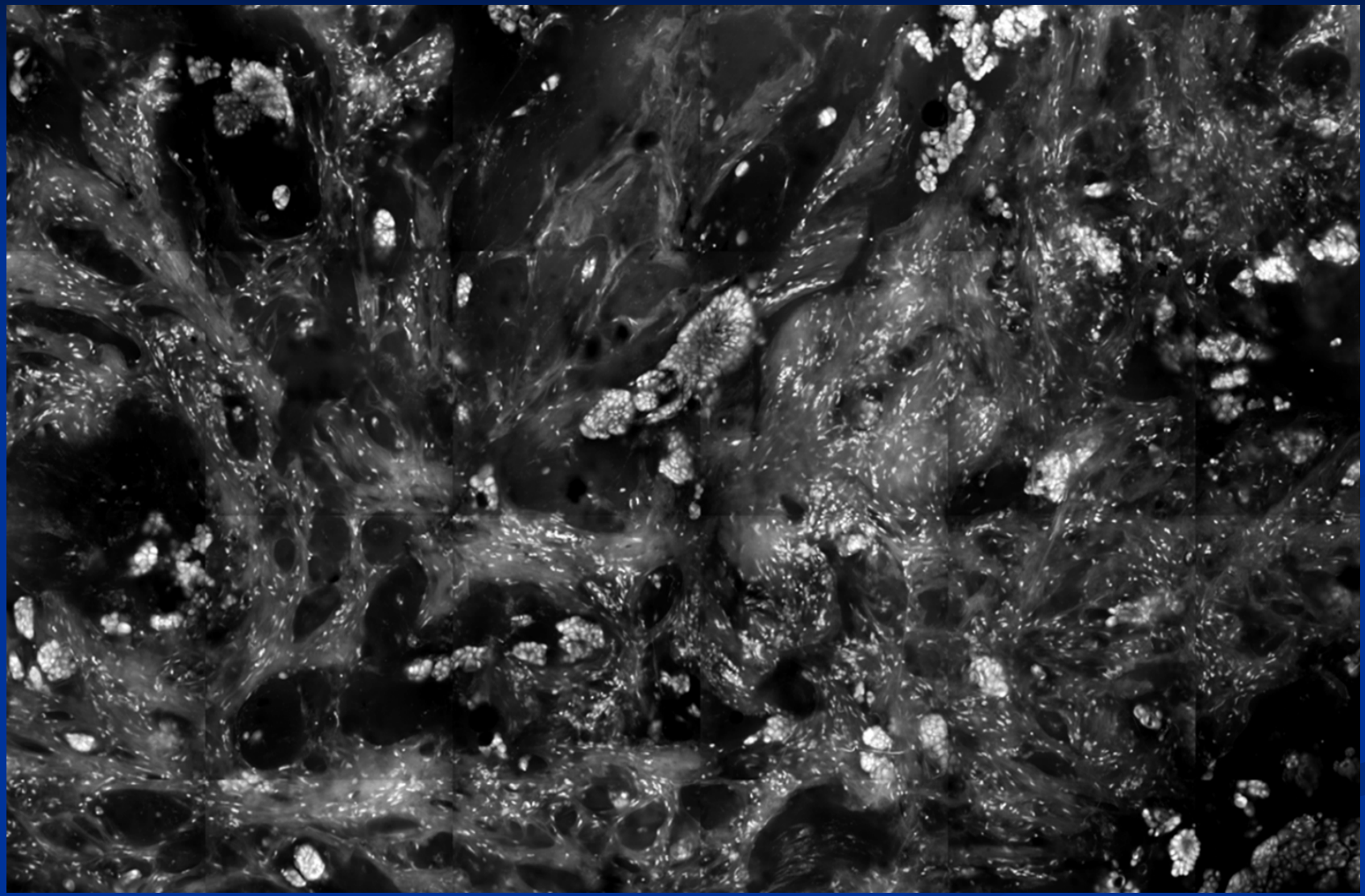
COLLEGE of AMERICAN PATHOLOGISTS

MOSAIC OF FLUORESCENCE CONFOCAL MICROSCOPY IMAGES

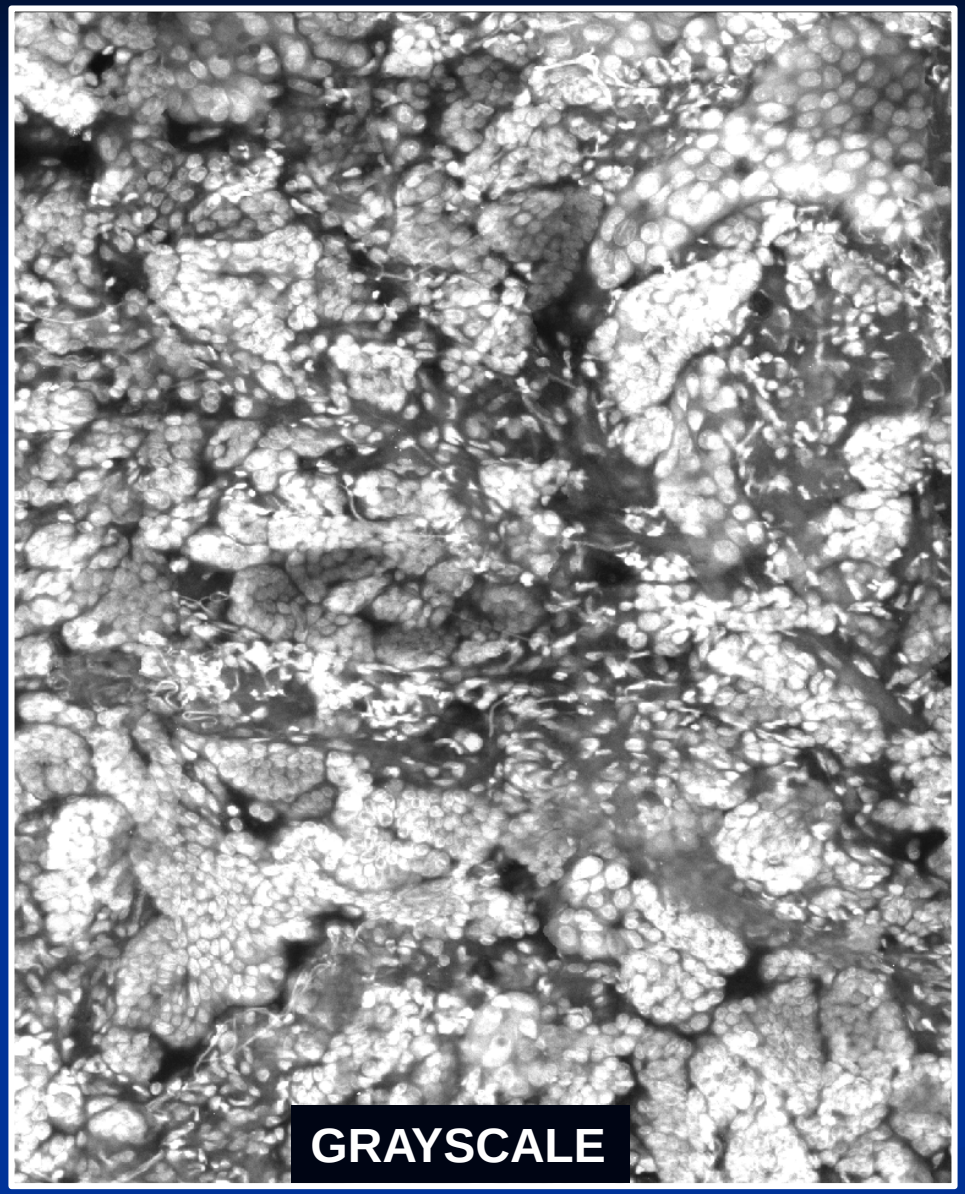


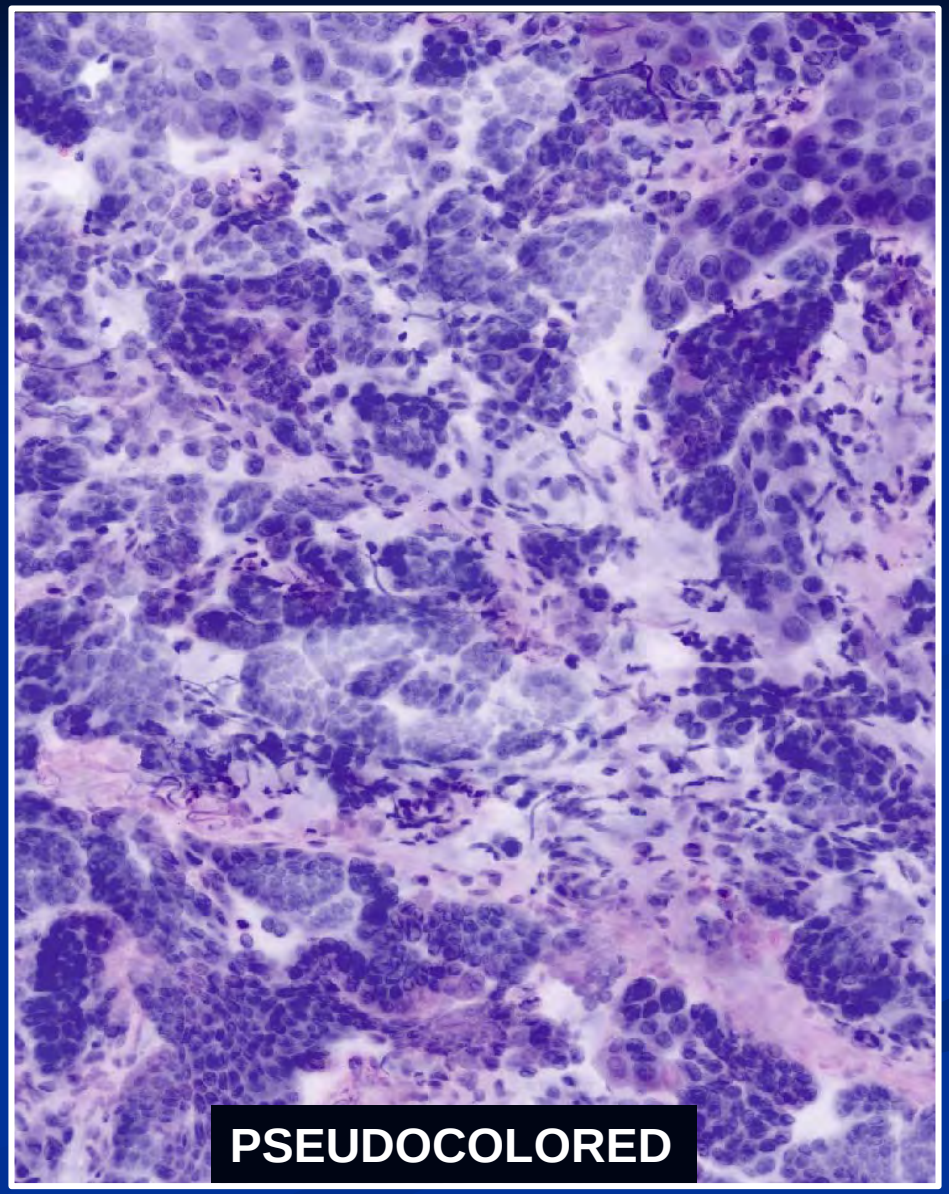
COLLEGE of AMERICAN PATHOLOGISTS

Fluorescence confocal microscopy (FCM) Image of Invasive Ductal Carcinoma of Breast



FLUORESCENCE CONFOCAL MICROSCOPY (FCM)





FLUORESCENCE CONFOCAL MICROSCOPY (FCM)

Most Frequently Used in Studies Related to Ex vivo Tissue Imaging

Skin Specimens	Non-skin specimens from
Moh's Surgery	almost all organs
Basal Cell Carcinoma	Tissue Recognition
Diagnosis	Specific Diagnosis
Margin Assessment	

Sensitivity	~ 96%	~ 96%
Specificity	~ 99%	~ 97%

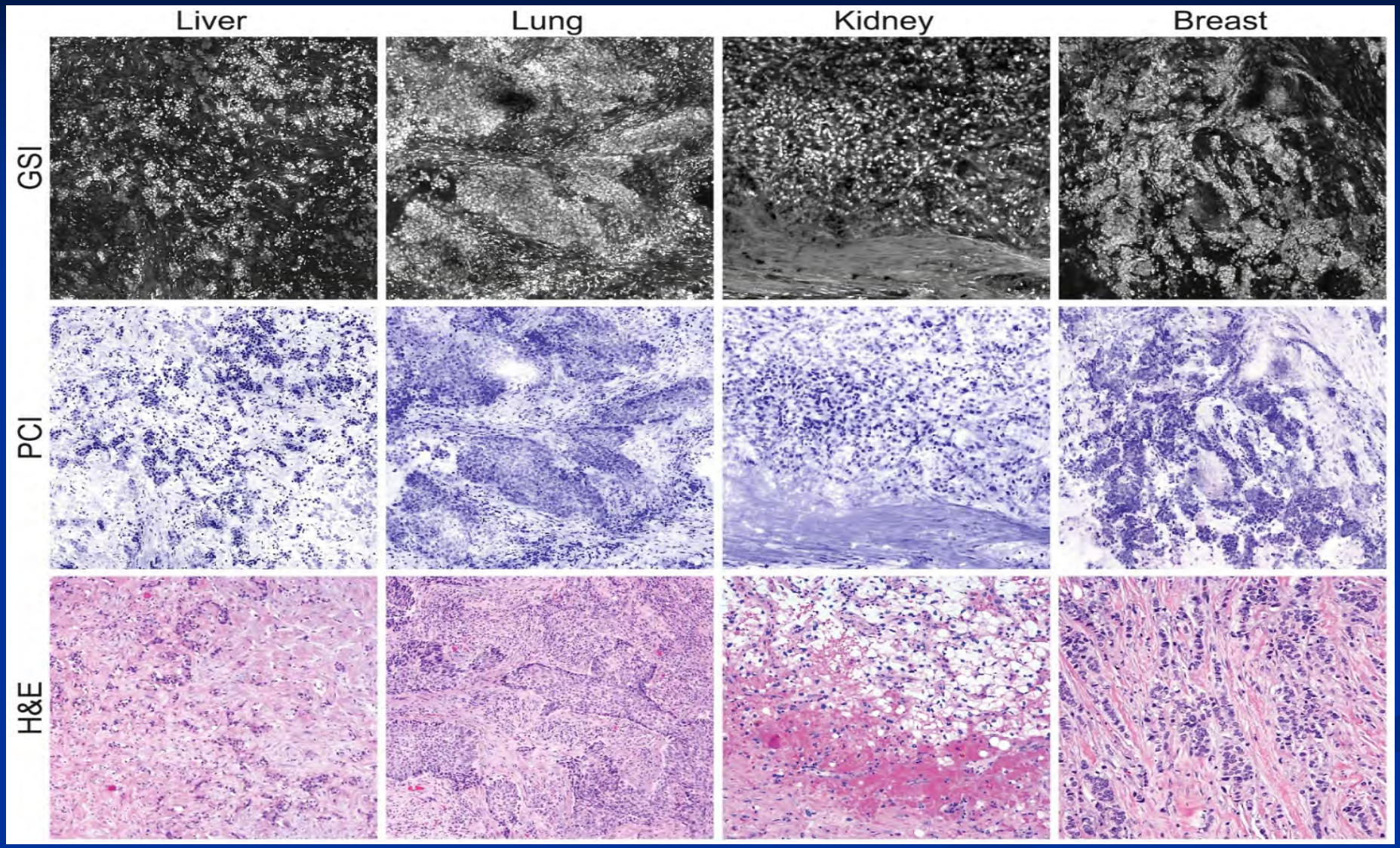
Imaging platform: Custom built or commercially available platform (Vivascope 2500, Caliber Inc. Rochester, NY)

Majority of studies investigated the role of FCM for evaluation of skin specimens with BCC

COLLEGE of AMERICAN PATHOLOGISTS

Longo C et al. Br J Dermatol. 2018
Krishnamurthy S et al Archives of Pathol Lab Medicine 2018
Puliatti S et al. BJU 2019

FLUORESCENCE CONFOCAL MICROSCOPY (FCM)



COLLEGE of AMERICAN PATHOLOGISTS

Krishnamurthy S et al Archives of Pathol Lab Medicine 2018

FLUORESCENCE CONFOCAL MICROSCOPY (FCM)

Quality of the images

1 - 20% of recognizable tissue
2 - 20-50% of recognizable tissue
3 - >50% recognizable tissue

96% tissue image of score 3

SENSITIVITY	-	95.5%
SPECIFICITY	-	97.3%
PPV	-	95.5%
NPV	-	97.3%

Even flattening of tissue for imaging can be a problem

Irregular contrast uptake resulting in dark areas

Issues do not impact overall recognition of tissue

COLLEGE of AMERICAN PATHOLOGISTS

Krishnamurthy S et al Archives of Pathol Lab Medicine 2018

FLUORESCENCE CONFOCAL MICROSCOPY (FCM)

544 skin specimens,

525 FCM images

Time to generate images 5.17 min

Sensitivity 73%

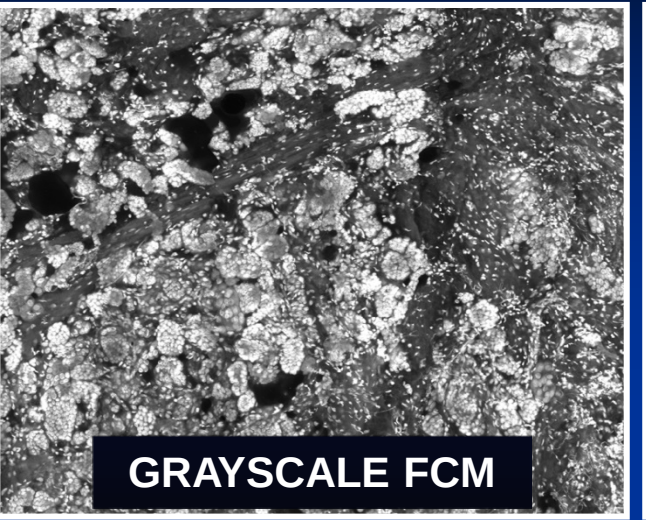
Specificity 96%

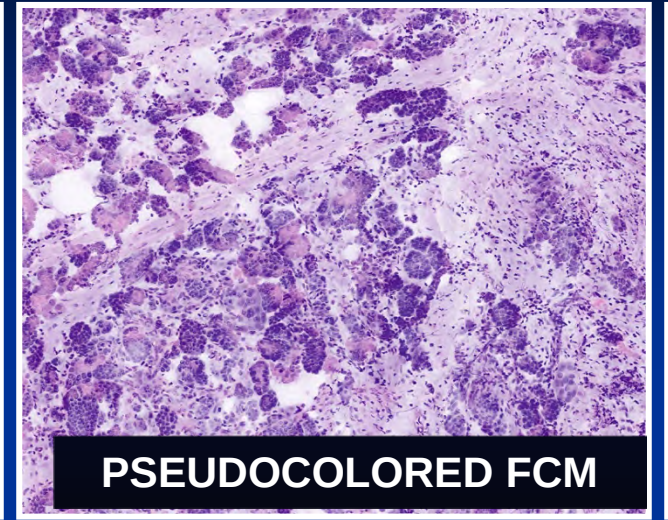
Histolog Scanner, SamanTree Medical SA

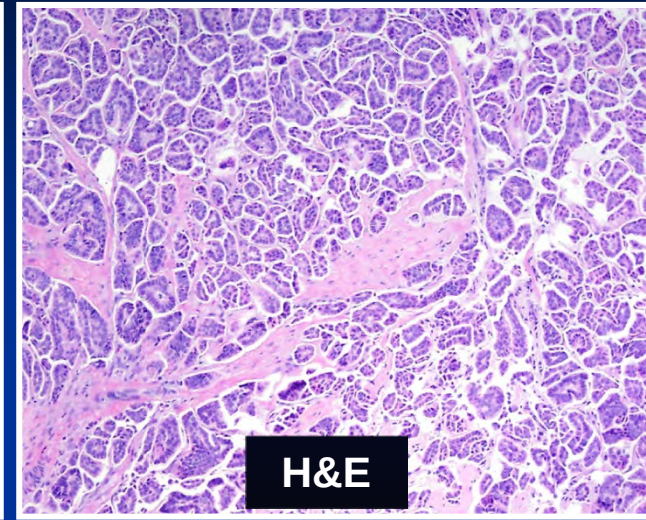
Peters N et al. European Acad. of Dermatology and Venereology 2019

COLLEGE of AMERICAN PATHOLOGISTS

FLUORESCENCE CONFOCAL MICROSCOPY (FCM)





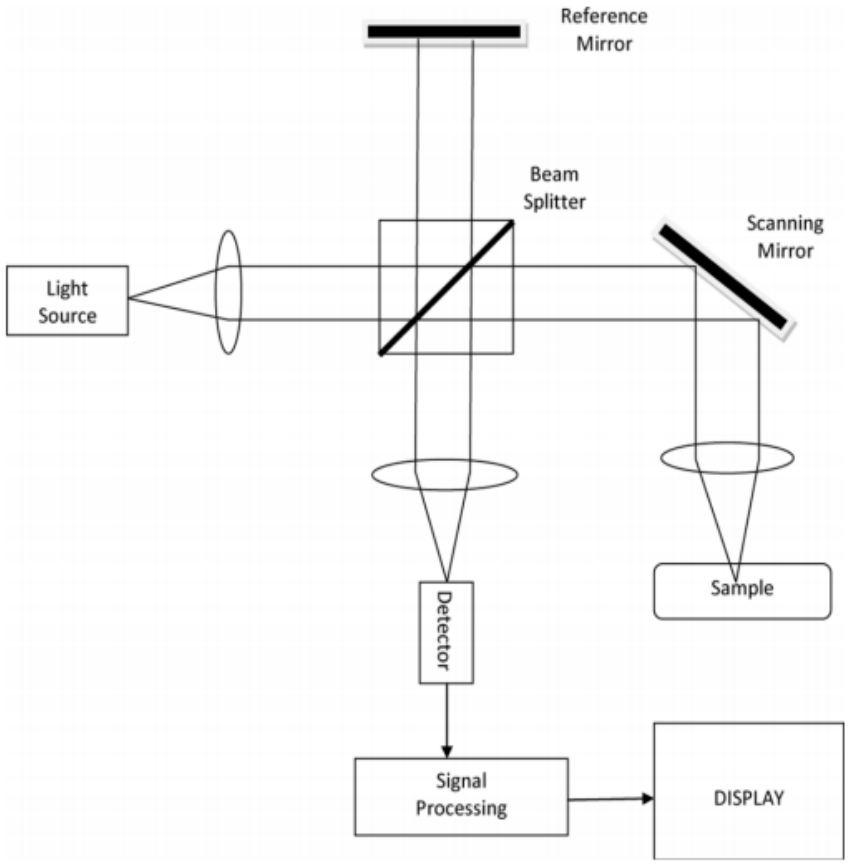


- FCM can be used for real-time tissue evaluation of small fragments of tissue : core biopsies, endoscopic biopsies and tissue fragments that are prepared as frozen sections for intraoperative evaluation.

- Margin assessment of small skin specimens such as those obtained from Moh's surgery, small skin excisions, neurosurgical specimens, small surgical excisions can be performed.

COLLEGE of AMERICAN PATHOLOGISTS

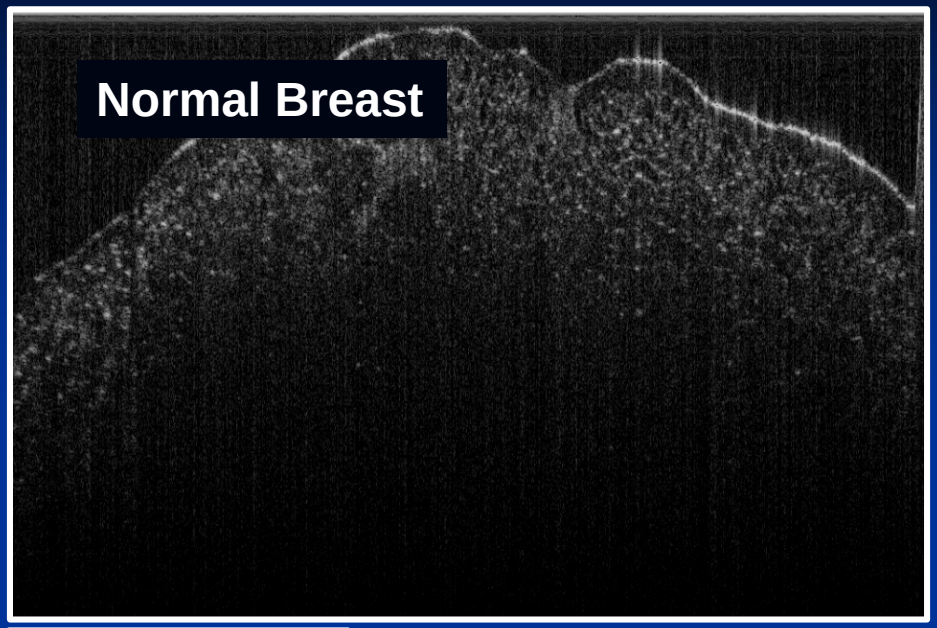
OPTICAL COHERENCE TOMOGRAPHY (OCT)

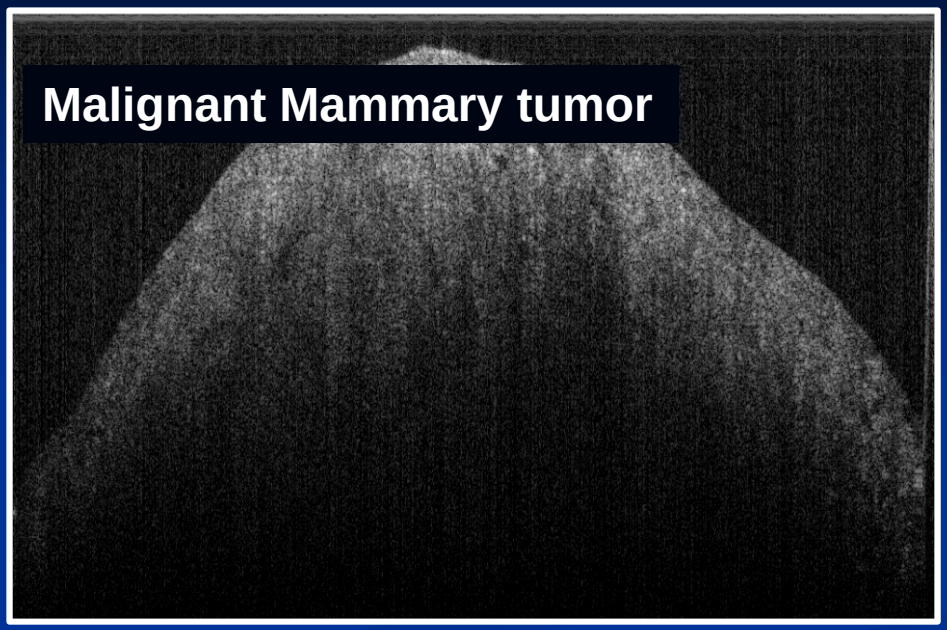


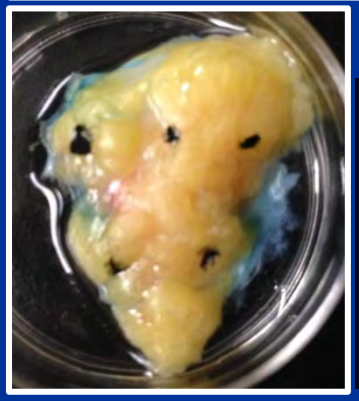
- Analogous to ultrasound but uses light to achieve higher resolution
- Measures the echo time delay and intensity of backscattered light by comparing it to light that has traveled a reference path length
- The optical backscattering through a cross section of tissue is displayed as grayscale/false colored image

Dhawan AP et al. IEEE Rev Biomed Eng. 2010

OPTICAL COHERENCE TOMOGRAPHY (OCT)







Enables visualization of tissue architecture
Cellular details cannot be appreciated
Contrast arises from scattering within tissue
Image resolution: 1-15 µm
Imaging depth : 2-3 mm

COLLEGE of AMERICAN PATHOLOGISTS

OPTICAL COHERENCE TOMOGRAPHY
OTIS (Perimeter Medical Imaging, Toronto)

Margin assessment of breast specimens

Interpretation of 90 OCT image atlas by Radiologists, surgeons, pathologists

Sensitivity : 80%
Specificity : 87%
Accuracy : 87%

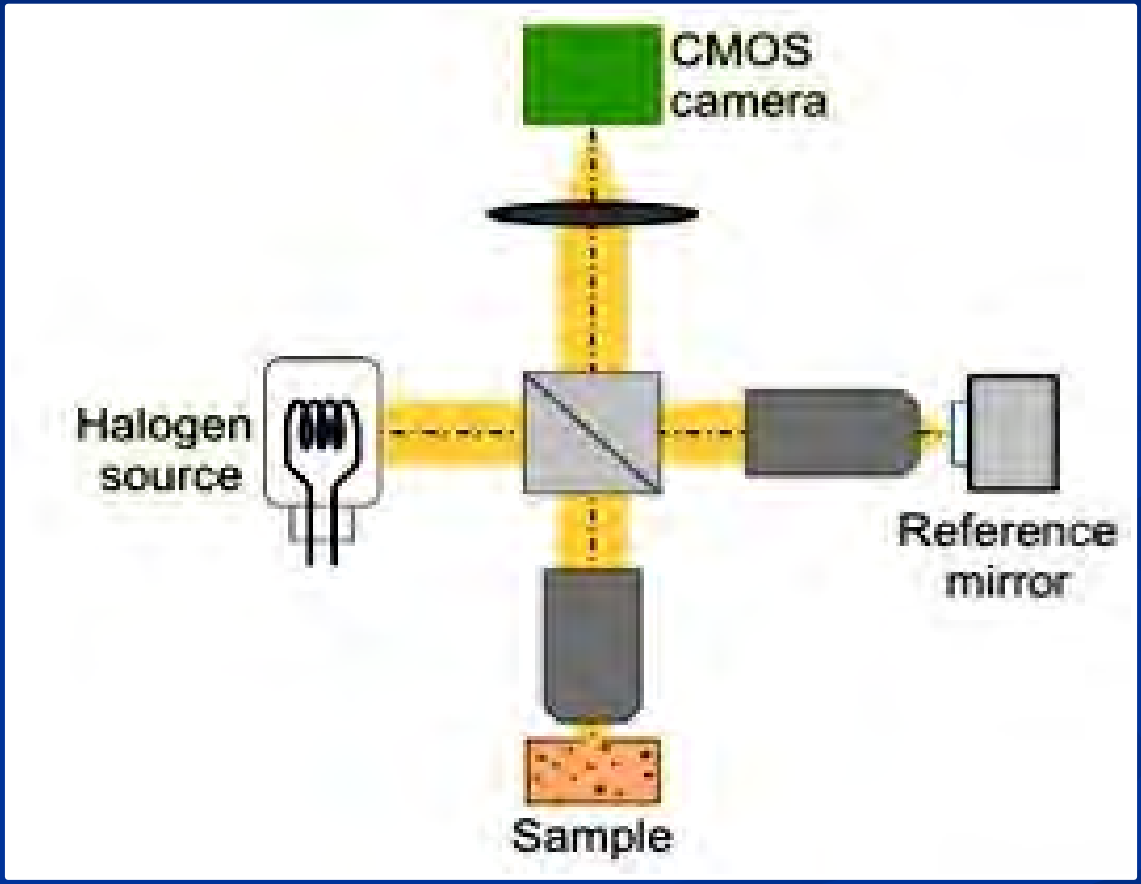
Ongoing prospective clinical studies

Ha R et al. Acad Radiol. 2018

COLLEGE of AMERICAN PATHOLOGISTS

FULL-FIELD 0PTICAL COHERENCE TOMOGRAPHY (FF-OCT)

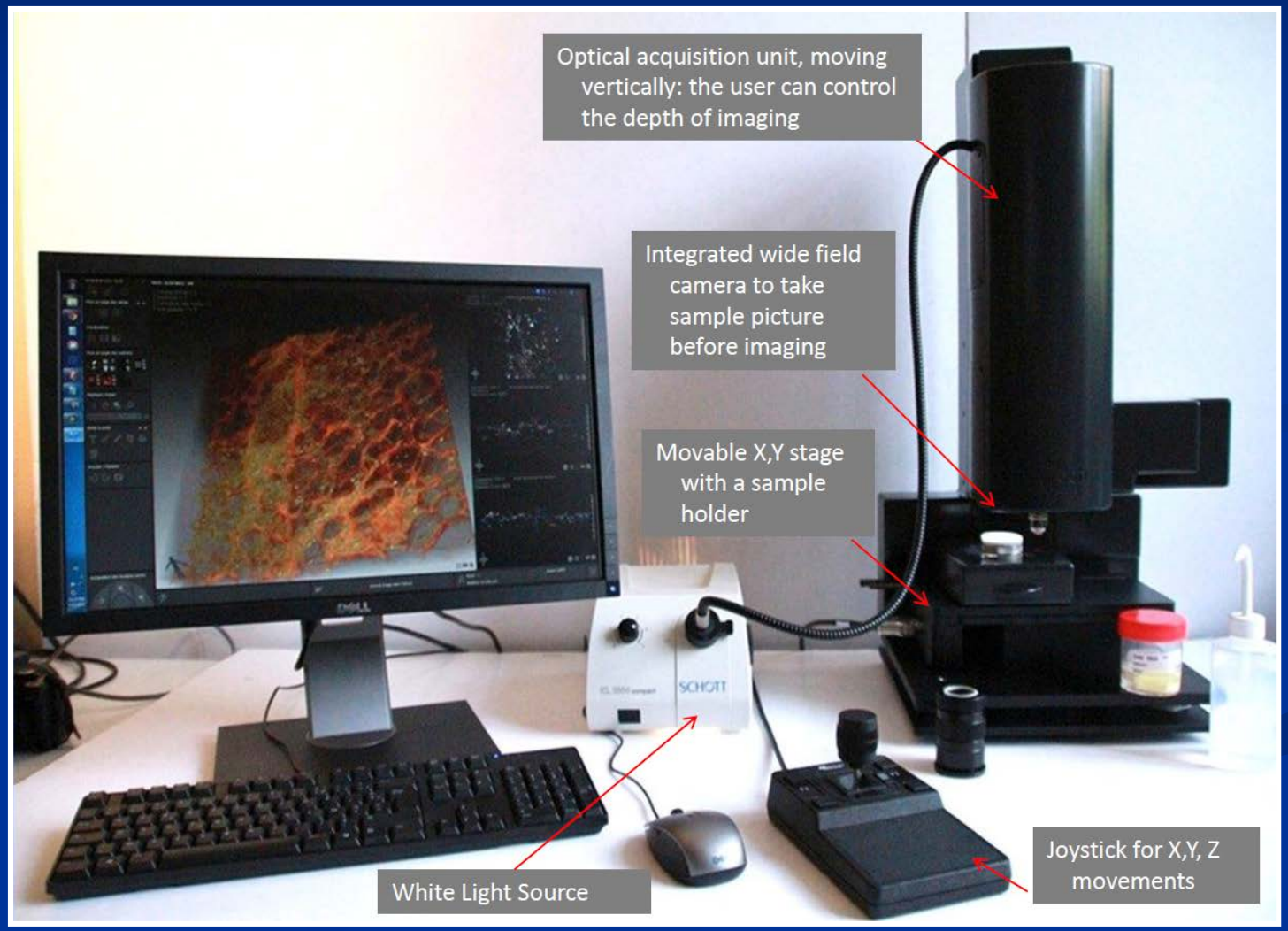
Interference microscope: Regular microscope with a reference arm
Noninvasive high resolution optical sectioning



COLLEGE of AMERICAN PATHOLOGISTS

http://www.lltechimaging.com/products-applications/ffoct

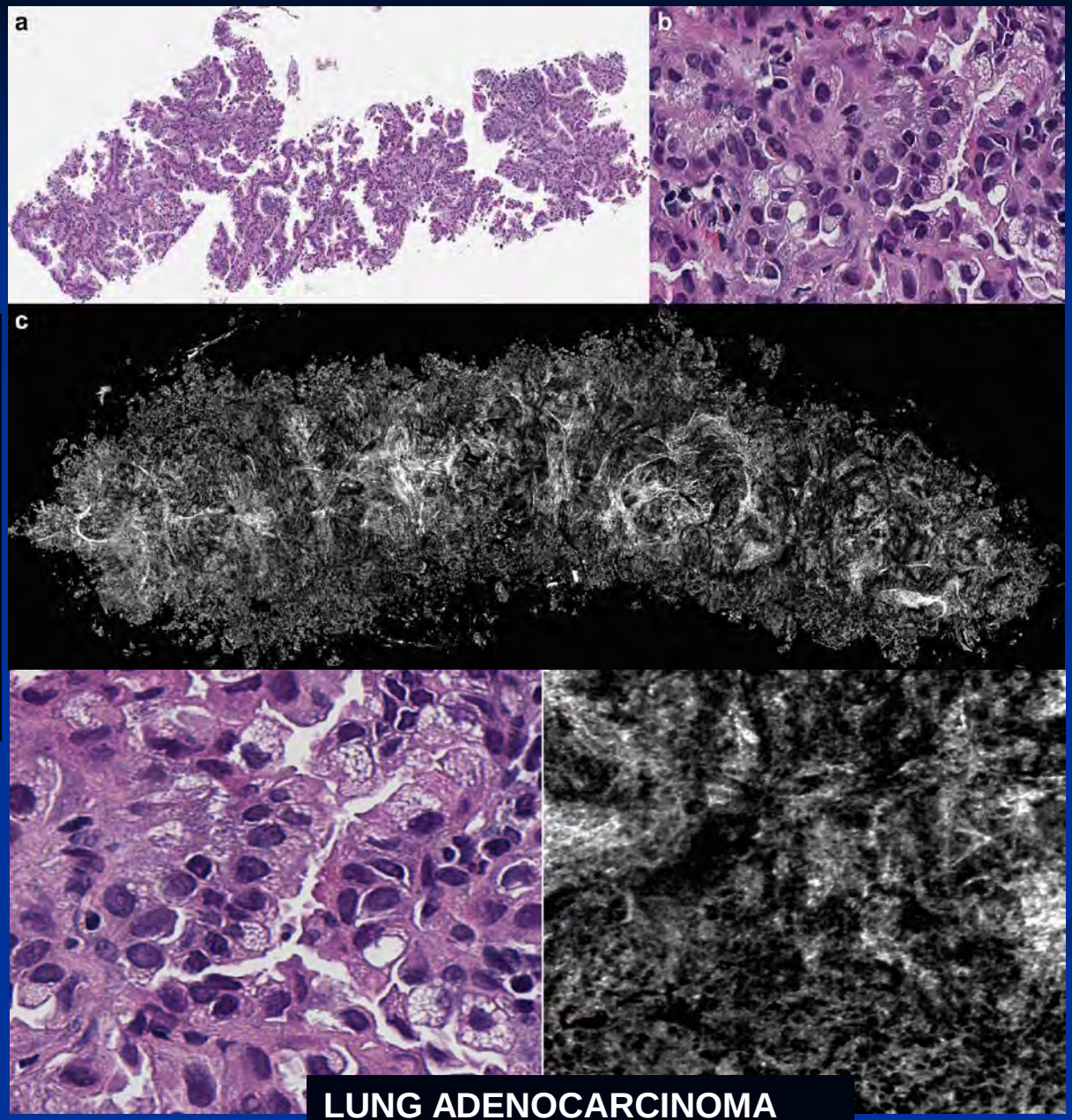
FULL-FIELD 0PTICAL COHERENCE TOMOGRAPHY (FF-OCT) Light CT Scanner (LLTech Paris)



COLLEGE of AMERICAN PATHOLOGISTS

FULL-FIELD 0PTICAL COHERENCE TOMOGRAPHY (FF-OCT)

Axial resolution
1 µm
Transverse resolution
1.5 µm
Depth of penetration
200 µm to 1mm
Field of view
25 mm



LUNG ADENOCARCINOMA

COLLEGE of AMERICAN PATHOLOGISTS

FULL-FIELD 0PTICAL COHERENCE TOMOGRAPHY (FF-OCT)

Ex Vivo imaging of unprocessed and unlabeled tissue

Tissue measuring up to 2.0 x 2.0 cm can be imaged in 10 minutes

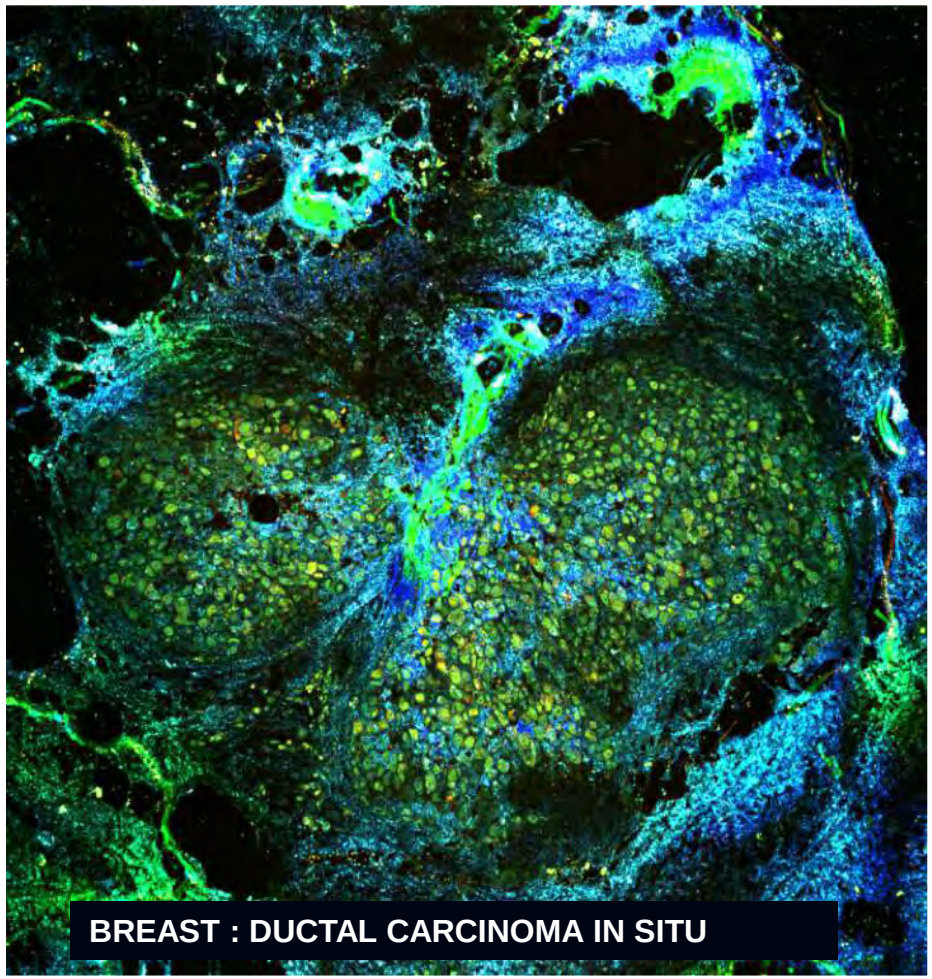
Several studies using FF-OCT :
Tissues from a variety of organs:
Lung, Kidney, Breast, Brain, Pancreas, skin
Sample size : 13-100
Sensitivity : 72% to 94%
Specificity: 73% to 79%

Prostate core biopsy : 119 cores
Sensitivity : 63%
Specificity : 74%

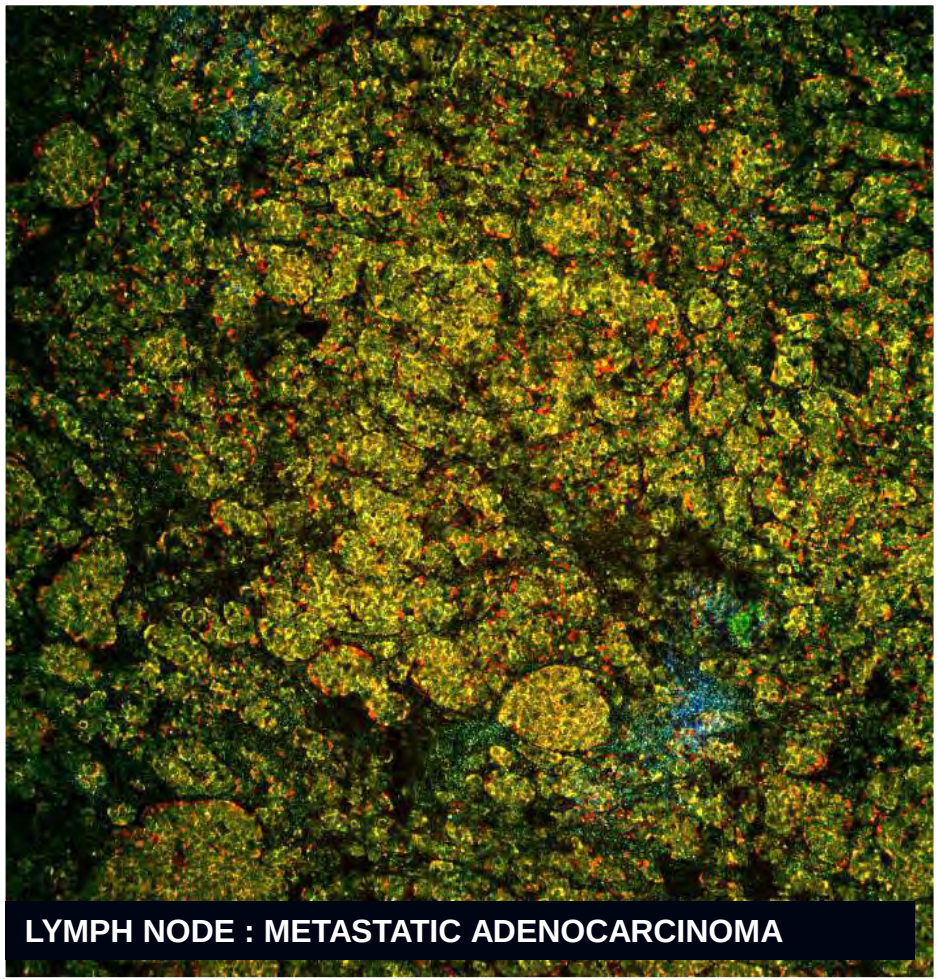
COLLEGE of AMERICAN PATHOLOGISTS

Lopater J et al. World J Urol. 2016
Assayag O et al. TCRT Express 2013
van Manen L et al PLOS ONE 2017

DYNAMIC FULL-FIELD OPTICAL COHERENCE TOMOGRAPHY (D-FFOCT)



BREAST : DUCTAL CARCINOMA IN SITU

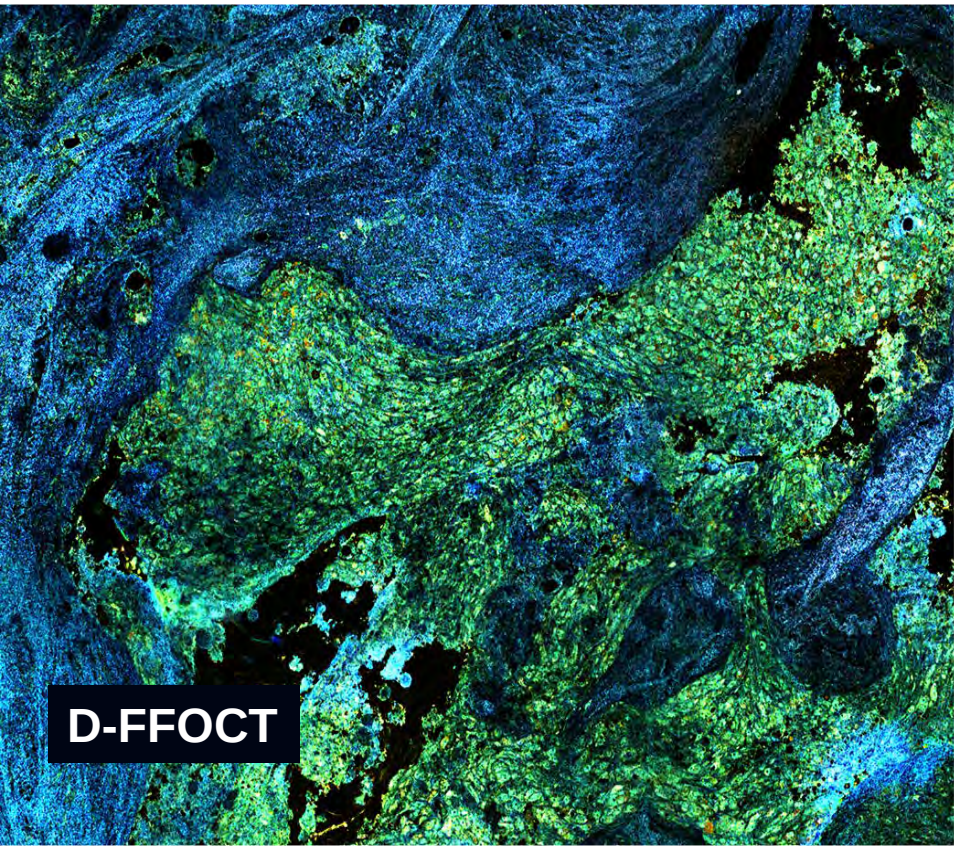


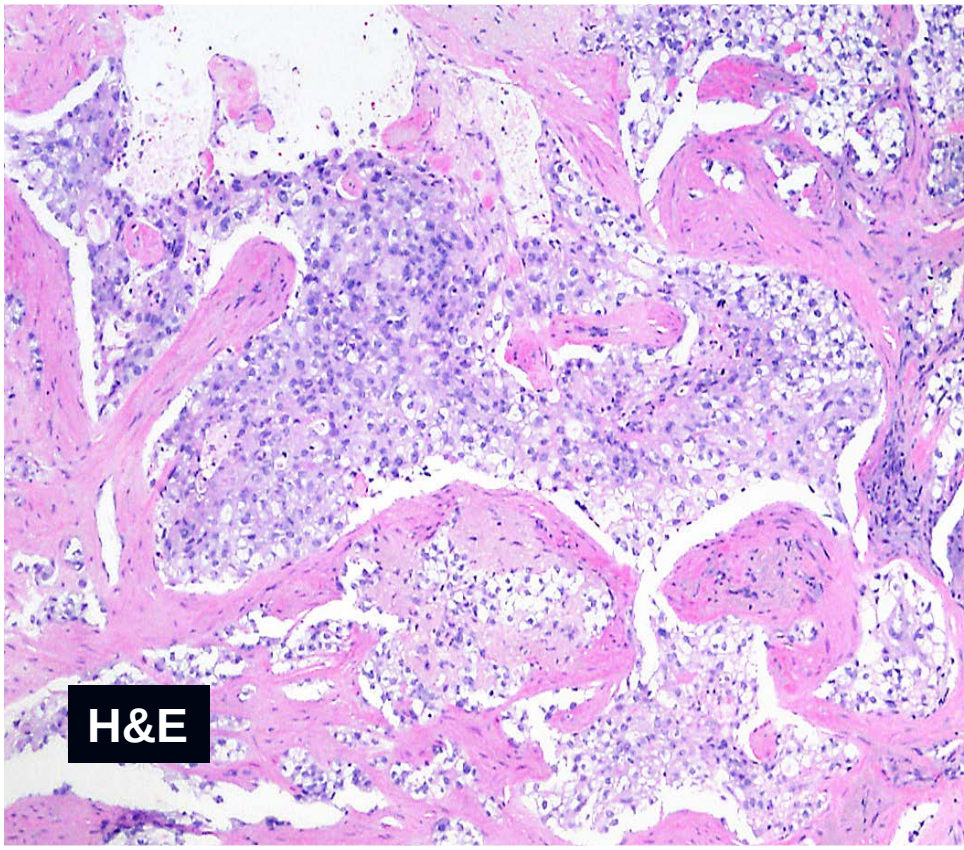
LYMPH NODE : METASTATIC ADENOCARCINOMA

COLLEGE of AMERICAN PATHOLOGISTS

Apelian C et al. Biomed Opt Express 2016

DYNAMIC FULL-FIELD 0PTICAL COHERENCE TOMOGRAPHY (D-FFOCT)





COLLEGE of AMERICAN PATHOLOGISTS

Invasive Ductal carcinoma

STIMULATED RAMAN SCATTERING MICROSCOPY (SRS)

- Imaging based on intrinsic vibrational properties of molecules such as lipids and proteins

  Coherent anti-Stokes Raman scattering microscopy
  Stimulated Raman scattering microscopy

- Chemical contrast created by the vibrational properties of lipids and proteins

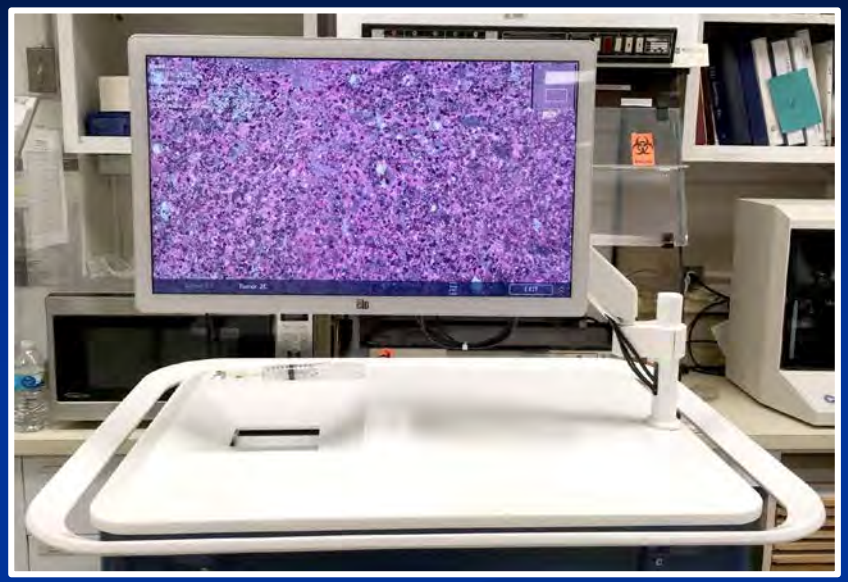
- Optical sectioning by nonlinear excitation

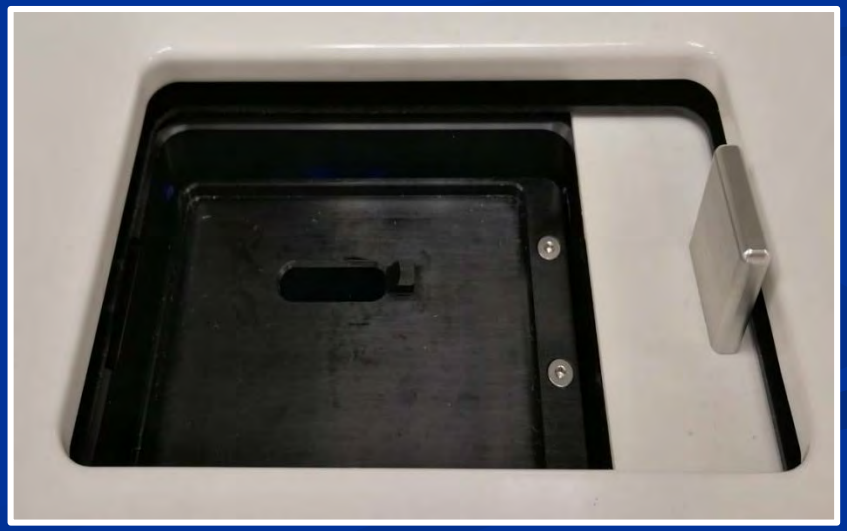
- Tissue imaging without adding extrinsic labeling agents

- Image processing to create virtual pseudocolored images resembling H&E – Stimulated Raman Scattering histology (SRH)

COLLEGE of AMERICAN PATHOLOGISTS

STIMULATED RAMAN SCATTERING MICROSCOPY (SRS)





InVenio Imaging Inc. Santa Clara, CA

COLLEGE of AMERICAN PATHOLOGISTS

STIMULATED RAMAN SCATTERING MICROSCOPY (SRS)

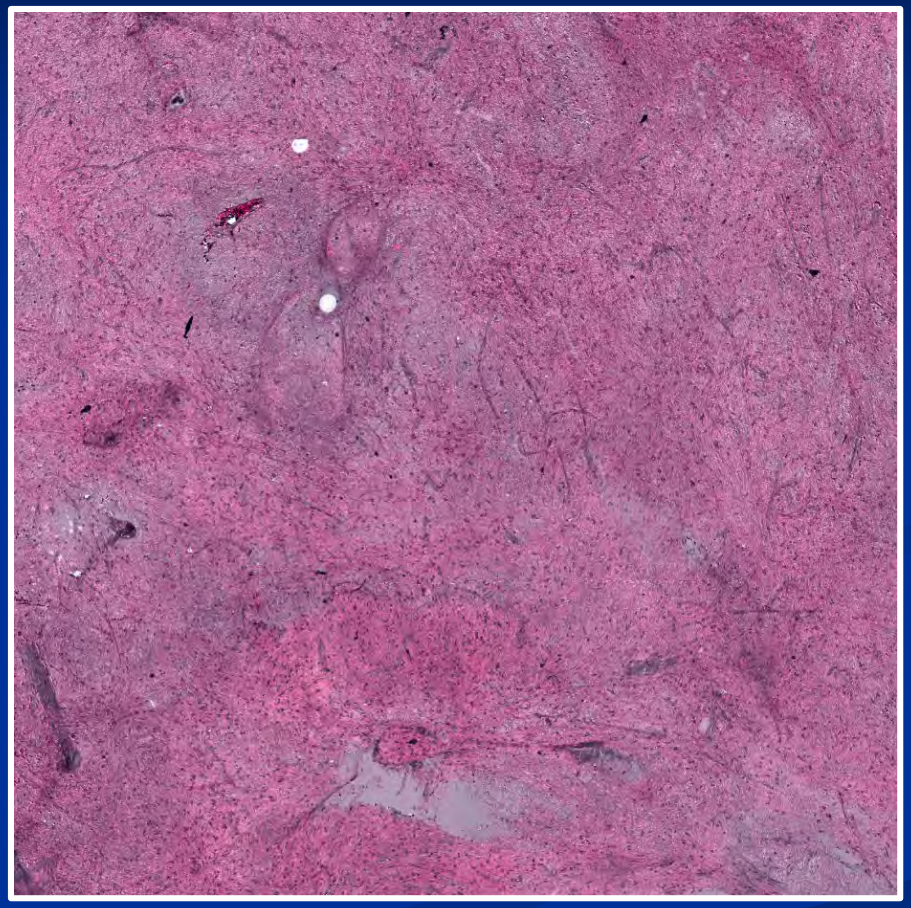
- 101 neurosurgical specimens studied in Neurosurgery operating room using a portable fibre-laser based SRS microscope
- Image processing to create images resembling H&E- stimulated Raman histology (SRH)
- Virtual H&E stained slides revealing essential diagnostic features
- 92 % concordance of SRH and conventional histology
- Supervised machine learning algorithm enabling automated tissue diagnosis based on quantified SRH image attributes
- Brain tumor subtypes predicted with 90% accuracy
- Study of 33 pediatric brain tumors : 96% concordance of SRH with conventional histology
- Machine learning algorithm for distinction of benign from malignant tumors : Prediction with 100% accuracy.

COLLEGE of AMERICAN PATHOLOGISTS

Orringer DA et al Nat Biomed Eng. 2017
Hollon T et al Neurosurg Focus 2016

STIMULATED RAMAN SCATTERING MICROSCOPY (SRS)

Meningioma

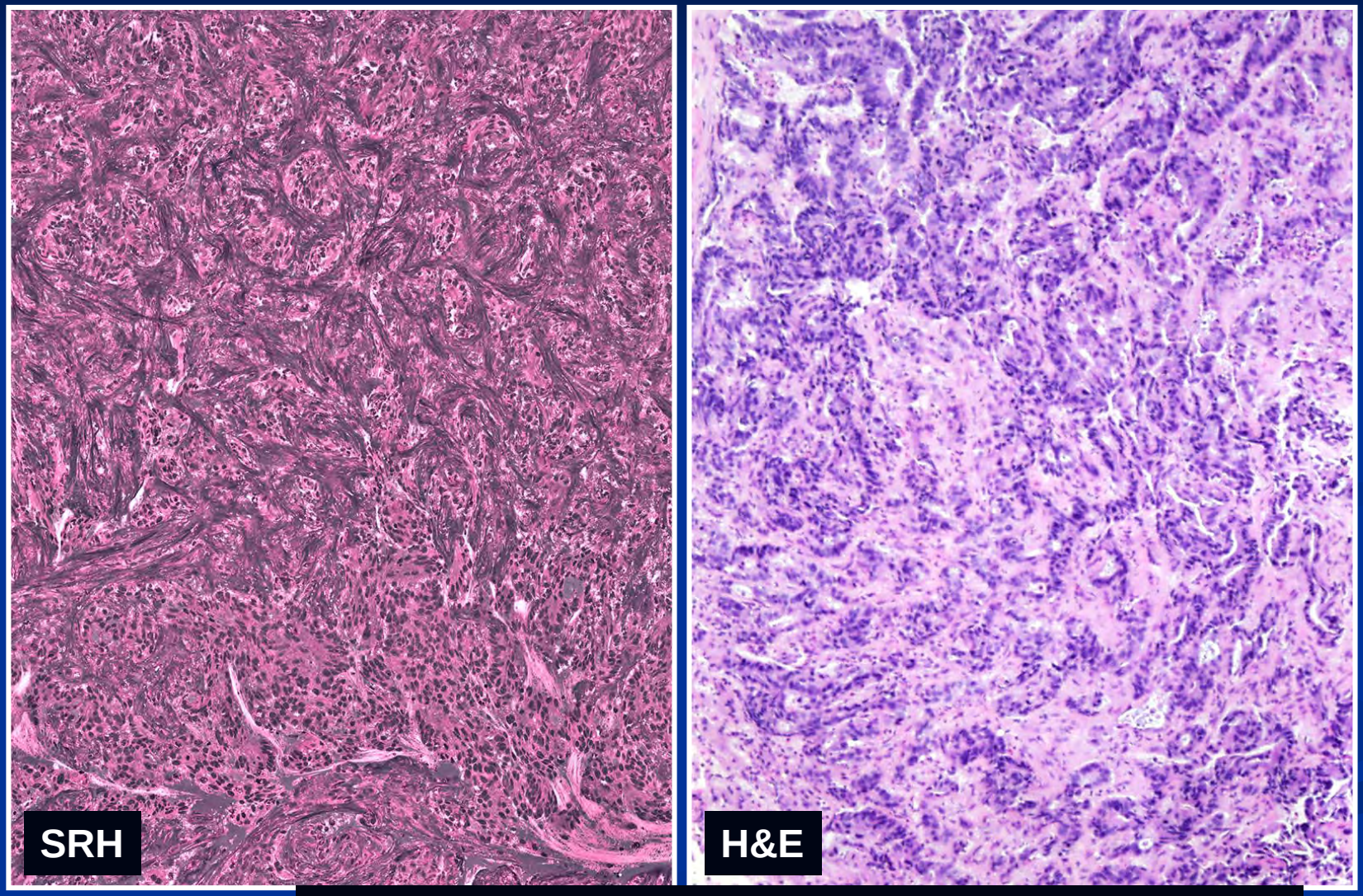


Pilocytic Astrocytoma

COLLEGE of AMERICAN PATHOLOGISTS

Image donated by Invenio Imaging Inc.

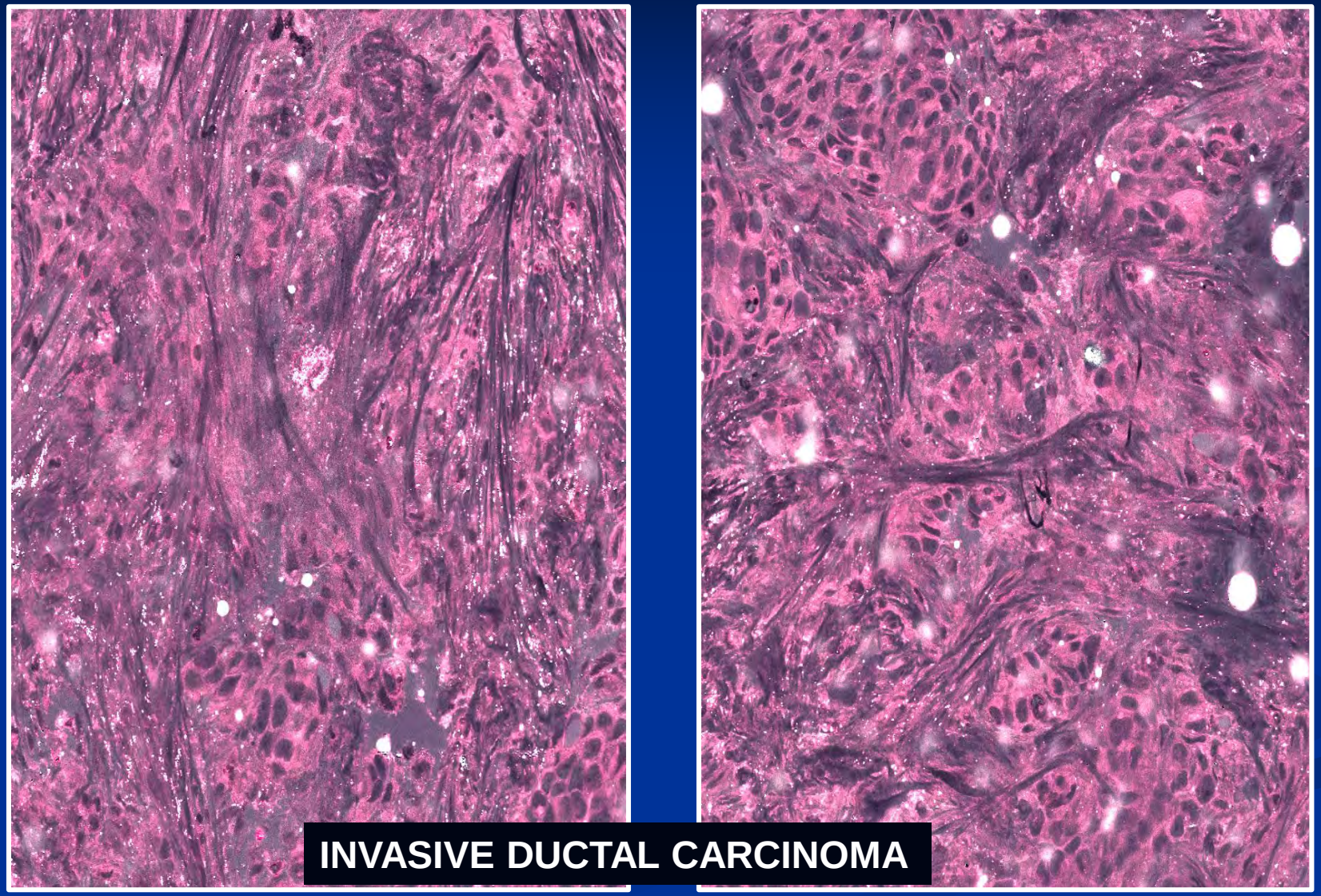
STIMULATED RAMAN SCATTERING MICROSCOPY (SRS)



Liver : Metastatic Adenocarcinoma from GI Primary

COLLEGE of AMERICAN PATHOLOGISTS

STIMULATED RAMAN SCATTERING MICROSCOPY (SRS)



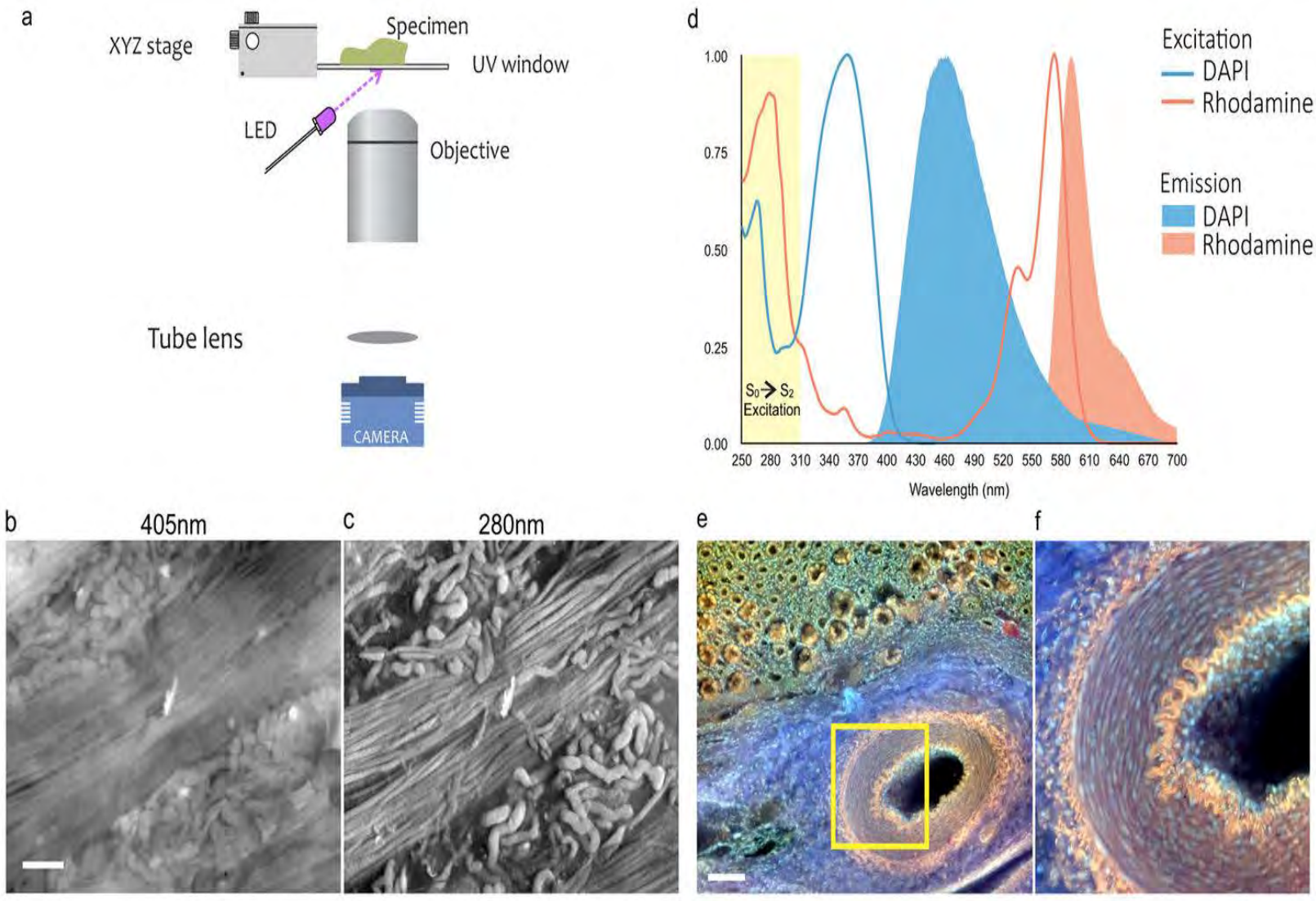
INVASIVE DUCTAL CARCINOMA

STIMULATED RAMAN SCATTERING MICROSCOPY (SRS)

- Effective tissue imaging using SRS microscope and acquisition of SRH images requires the tissue to be less than 25µm in thickness
- Tissues that are soft in consistency allow good compression thereby aiding in the acquisition of good quality SRH images for interpretation
- The commercially available SRS microscope (Invenio Imaging Inc. Santa Clara, CA) is currently available for intraoperative diagnosis of tissues obtained from neurosurgical procedure
- Utility of SRS microscope for non-neurosurgical specimens not yet investigated

COLLEGE of AMERICAN PATHOLOGISTS

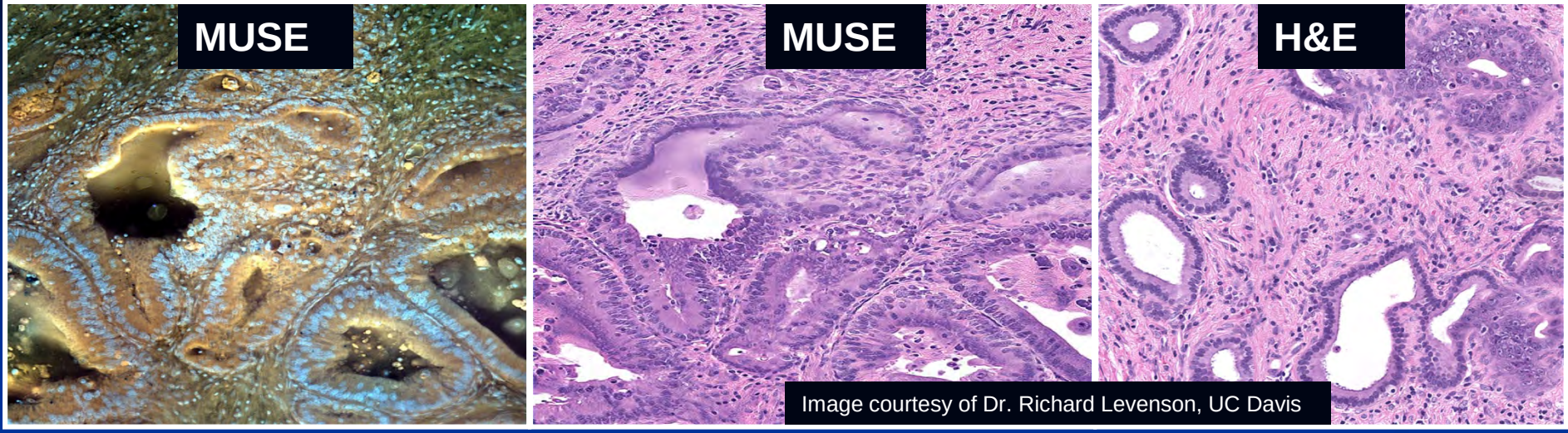
MICROSCOPY USING ULTRAVIOLET SURFACE EXCITATION (MUSE)



COLLEGE of AMERICAN PATHOLOGISTS

Fareidouni F et al Nat Biomedical Eng. 2017

MICROSCOPY USING ULTRAVIOLET SURFACE EXCITATION (MUSE)



LIMITED FEASIBILITY STUDIES

66 fresh and fixed normal and neoplastic tissues from ovary, lung, kidney, breast and Brain stained with Rhodamine and Hoechst

15 mm x 15 mm tissue imaged in 2-3 minutes

93% concordance in interpretation with conventional H&E sections

Evaluation of skin and breast surgical margins after staining the tissue with Propidium iodide and eosin

COLLEGE of AMERICAN PATHOLOGISTS

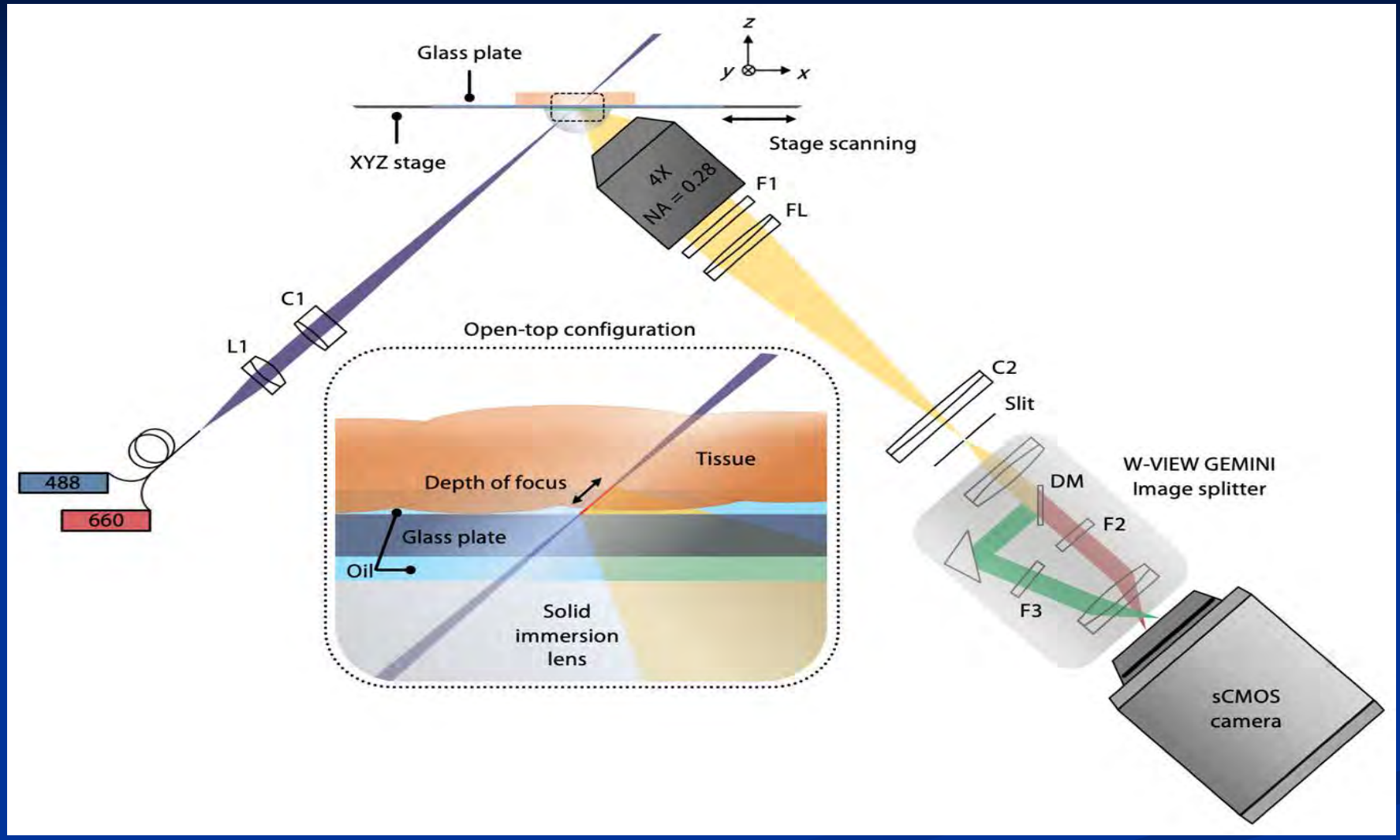
Fareidouni F et al. Nat Biomed Eng. 2017
Yoshitake T et al. Sci Rep. 2018

MICROSCOPY USING ULTRAVIOLET SURFACE EXCITATION (MUSE)

Rapid evaluation of fresh and fixed tissues stained with fluorescent dyes

Ex-vivo imaging of small fragments such as core biopsy/endoscopic biopsy and larger resection specimens for margin assessment

OPEN TOP LIGHT SHEET MICROSCOPE



COLLEGE of AMERICAN PATHOLOGISTS

Chen Y et al. Biomed Opt Express 2019

LIGHT SHEET MICROSCOPY

- 25 large human prostate slices measuring 3.5 cm in maximum dimension stained with acridine orange and imaged using an open top LSM in 10 min/slice
- A large slice of breast tissue 2.0 cm in maximum dimension
- Prostate core biopsy, optically cleared overnight, stained with DRAQ 5/Eosin imaged in 14 min. allowing volumetric analysis.

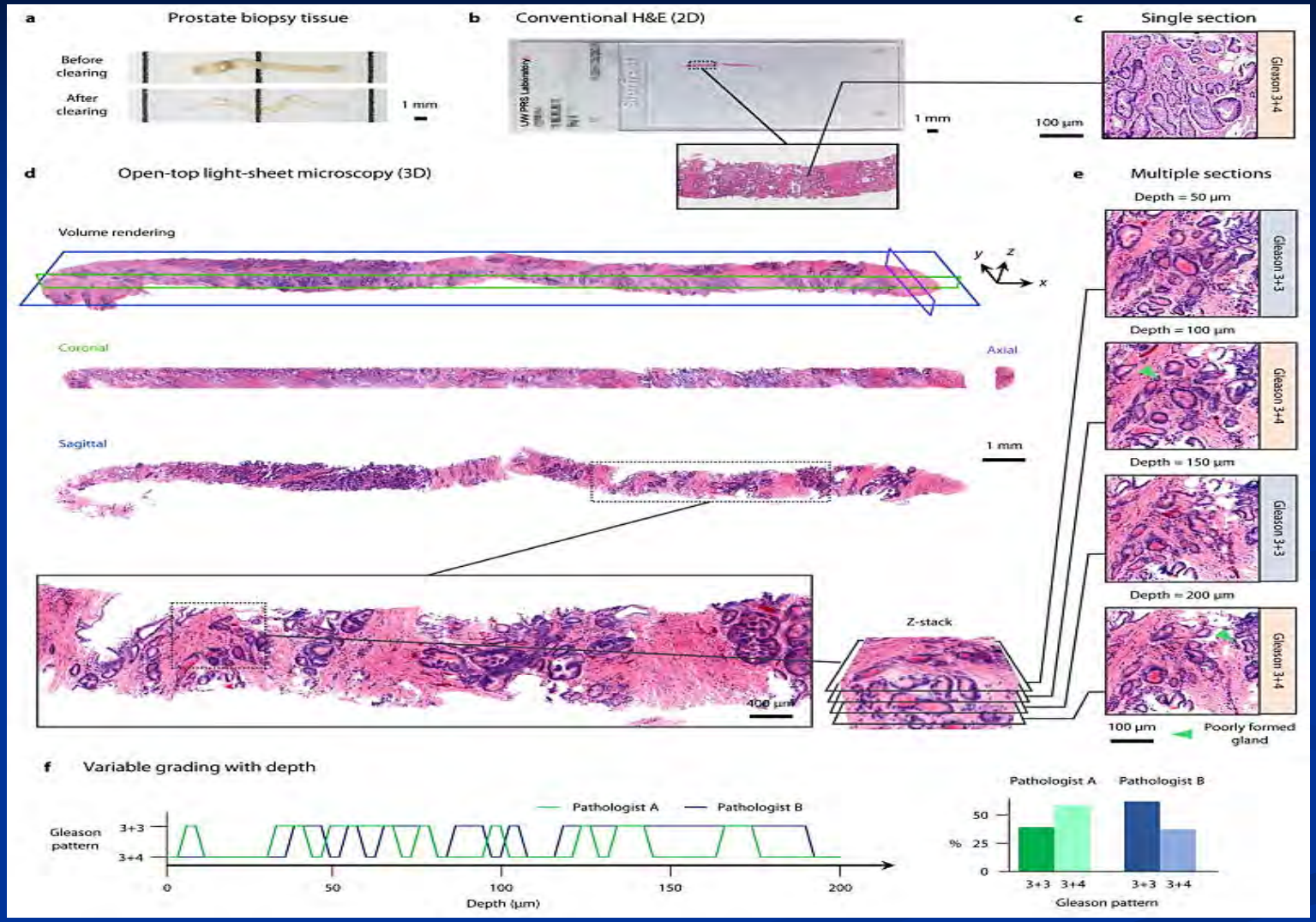
- Three dimensional imaging of 26 optically cleared sections of pancreas for morphological evaluation and localization of CK19 in pancreatic parenchyma

- Volumetric analysis of FFPE skin specimens

Glaser AK et al. Nature Biomed Eng 2017
Abadie S et al. Skin Res Technol 2018
Noe M et al. Am J Pathol 2018

COLLEGE of AMERICAN PATHOLOGISTS

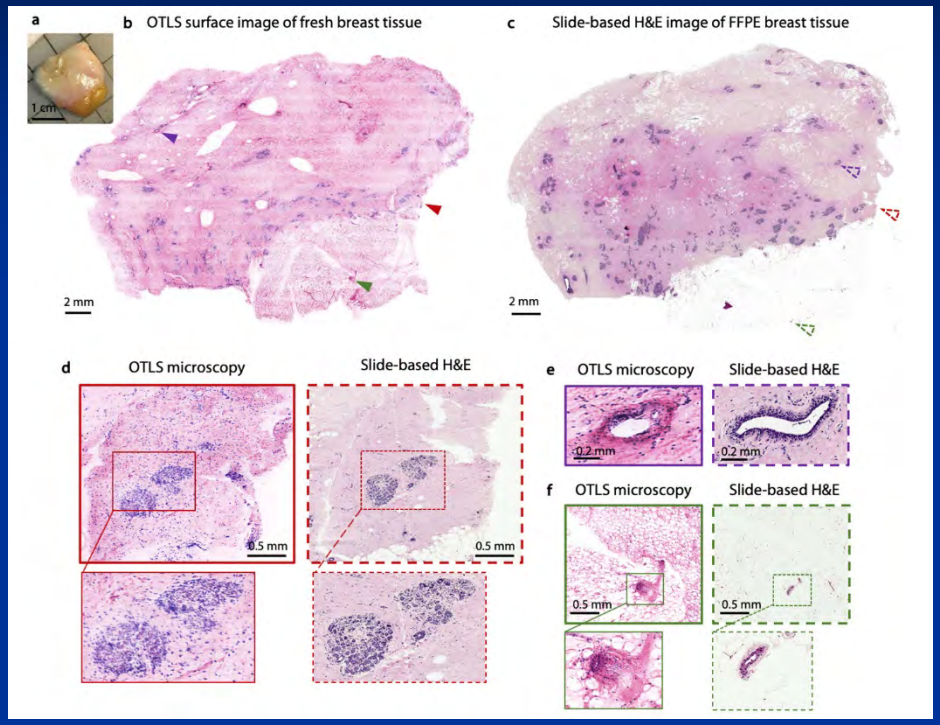
OPEN TOP LIGHT SHEET MICROSCOPY(OTLS)

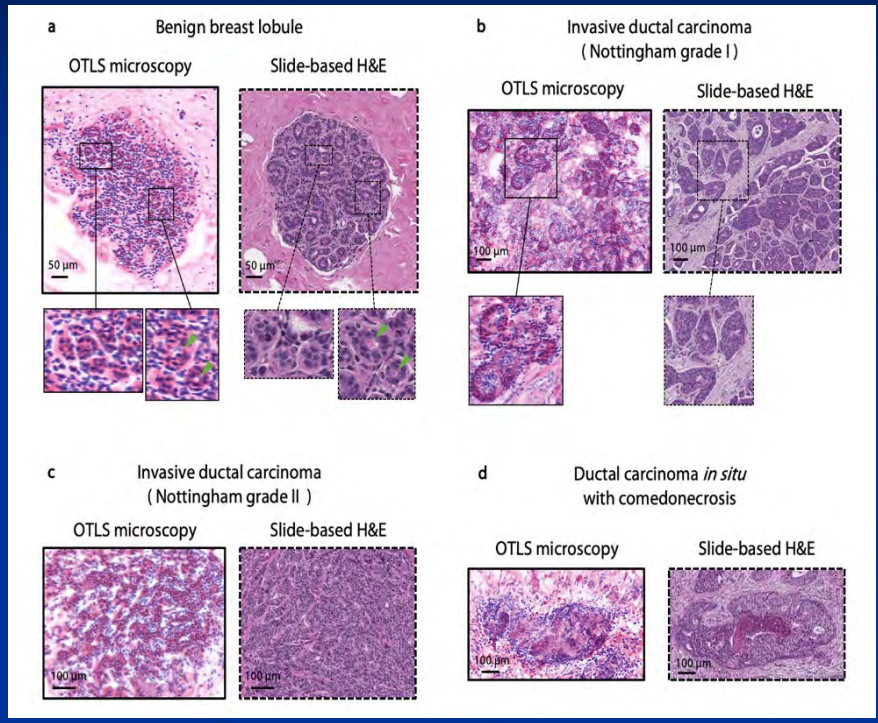


Glaser AK et al. Nat Biomed Eng. 2017

COLLEGE of AMERICAN PATHOLOGISTS

OPEN TOP LIGHT SHEET MICROSCOPE (OTLS)





OTLS for Breast lumpectomy margin evaluation
Fluorescent stains: SYBR Gold / ATT0655 NHS ester
Imaging speed: 1.5 cm^2/min

COLLEGE of AMERICAN PATHOLOGISTS

Chen Y et al Biomed Optic Express 2019

LIGHT SHEET MICROSCOPY

- LSM can be used for rapid surface microscopy of tissues of any size stained with contrast agents

- LSM can be used for volumetric imaging of optically cleared tissues that are stained with contrast agents

- LSM is a versatile Ex-Vivo microscopy tool

COLLEGE of AMERICAN PATHOLOGISTS

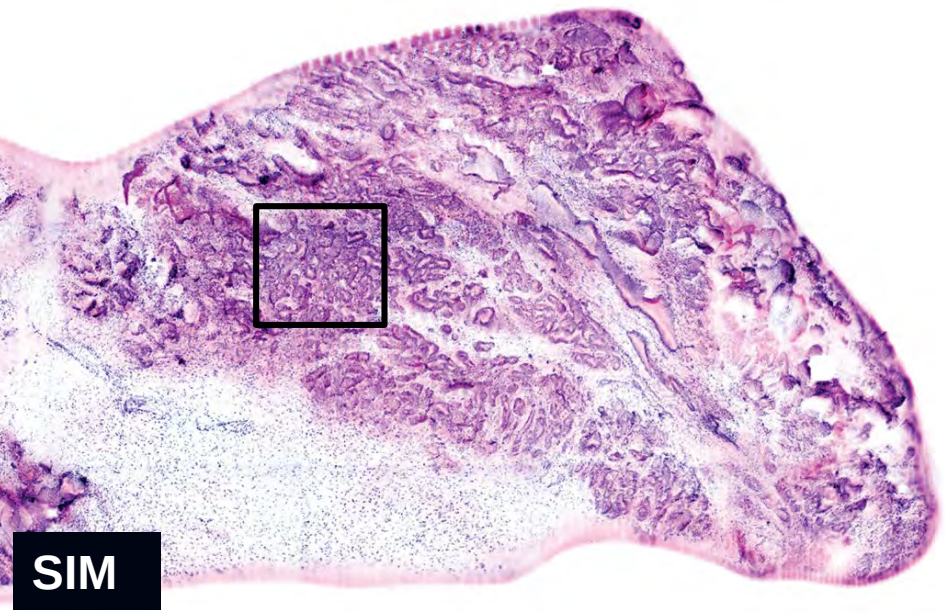
STRUCTURED ILLUMINATION MICROSCOPY (SIM)

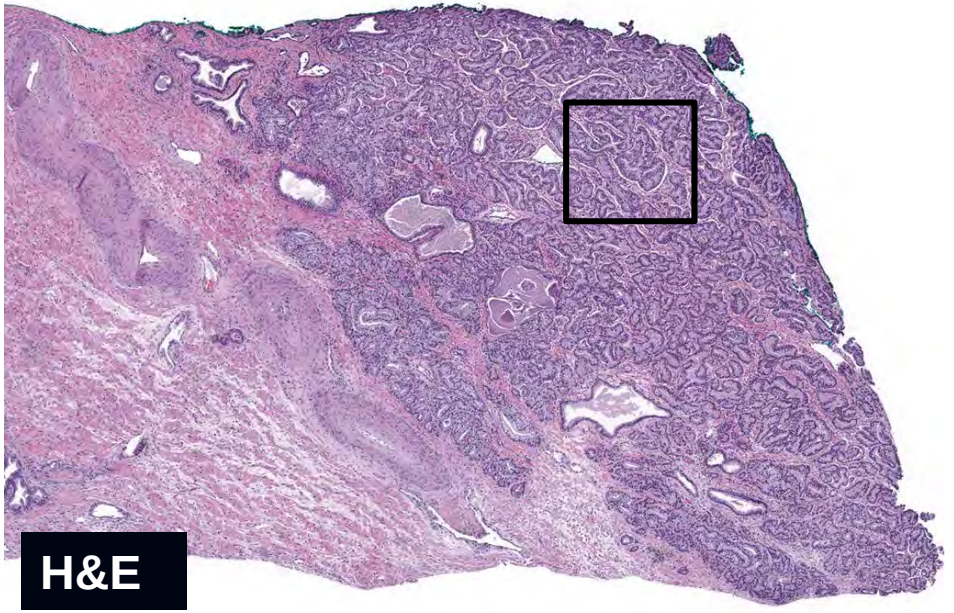
- Patterned illumination to preferentially modulate and retain the in-focus object information separately from the out-of-focus background.

- Parallel pixel acquisition : Overall pixel scaling frequency correlates with the pixel count of the detector rather than the pixel exposure time.

- The speed of imaging is decoupled from the field of view because all pixels are acquired in parallel and the pixel resolution is determined by the camera specifications

STRUCTURED ILLUMINATION MICROSCOPY (SIM)





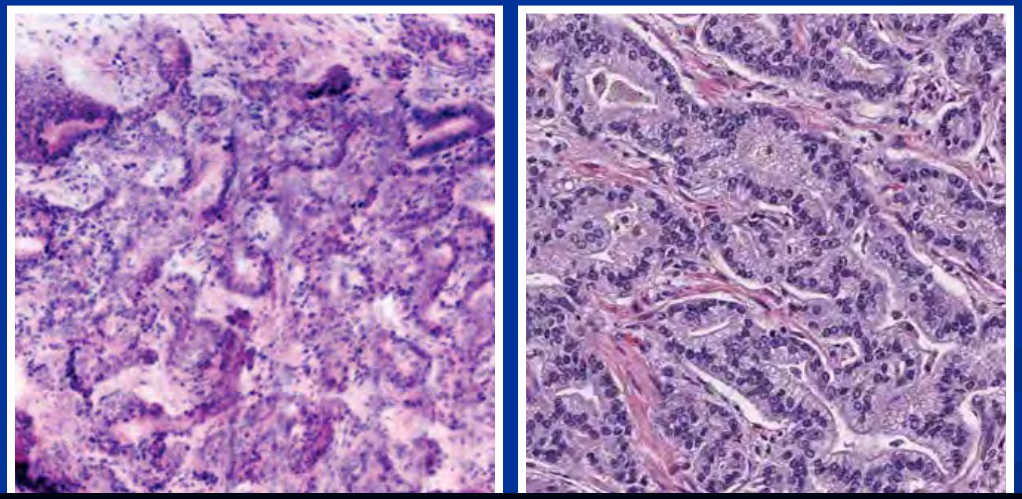


Image courtesy of
Dr. David Tulman,
Dr. Mei Wang,
Dr. Jonathan Quincy Brown
Tulane University

COLLEGE of AMERICAN PATHOLOGISTS

Punch Biopsy of Prostate Adenocarcinoma

STRUCTURED ILLUMINATION MICROSCOPY (SIM)

- 34 unfixed and uncut 5 mm punch biopsy of prostate obtained from radical prostatectomies stained with acridine orange.

- High quality greyscale mosaic images of prostate biopsies obtained in seconds mosaicking microscopy of 4.4 cm/minute with 1.3 µm lateral resolution.

  Sensitivity 63% to 88%
  Specificity 78% to 89%

- Margin assessment of 19 intact prostatectomy specimens
- 4 circumferential prostate margins imaged in an hour
- Gigapixel panorama images of prostate surface with relevant contrast and subcellular details
- VR-SIM confirmed positive margins in 3 out of 4 prostatectomy specimens

Wang M et al. Cancer Res 2015
Wang M et al. Sci Rep. 2016

STRUCTURED ILLUMINATION MICROSCOPY (SIM)

- **DRAQ5/Eosin established as the dual component fluorescent stain analogous to H&E staining for Video - rate SIM tissue imaging**

- **65 kidney biopsy specimens 18 G in size**
  Stained with DRAQ5/Eosin, imaged with SIM
  Sensitivity: 79.2%
  Specificity: 95.1%

Elfer KN et al. PLoS One 2016
Liu J et al. Urology 2016

COLLEGE of AMERICAN PATHOLOGISTS

STRUCTURED ILLUMINATION MICROSCOPY (SIM)

- SIM is a light efficient wide-field technique for rapid ex-vivo tissue evaluation of small sized fragments and large resection specimens

- SIM can be used for surface microscopy but has limited ability to obtain high quality optical sections deep into the tissue.

- High quality images of large tissue surfaces can be obtained to resemble light microscopic images of H&E tissue sections

COLLEGE of AMERICAN PATHOLOGISTS

NONLINEAR MICROSCOPY

- Nonlinear microscopy
  Multiphoton, two-photon and second harmonic generation microscopy
- High resolution imaging in optically scattering tissues
- NLM can be useful for surface microscopy and for imaging deeper into tissues
- Imaging depth is better than FCM but less than OCT
- NLM has ability to use both intrinsic and extrinsic contrast enabling visualization of nuclear size, shape and morphological changes such as reorganization of collagen

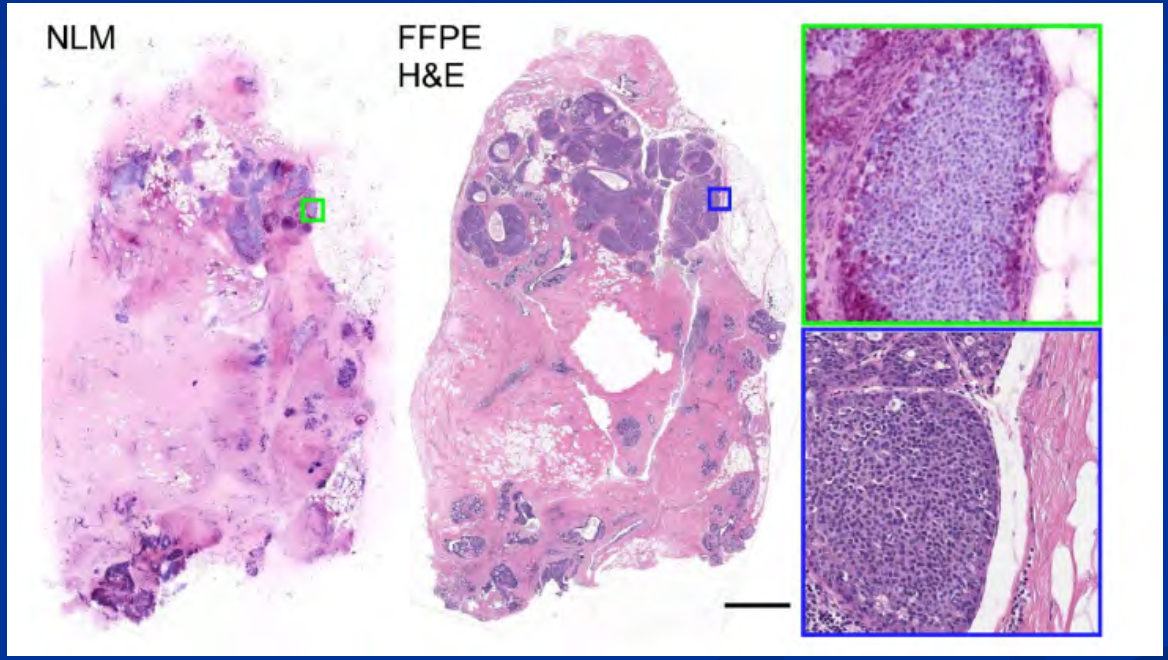
NONLINEAR MICROSCOPY (NLM)

50 breast specimens stained with acridine orange and sulphorhodamine 101 and imaged using a multiscale NLM microscope

Specimens imaged at 1030 nm using a custom multiscale NLM system with Ti:sapphire laser

Margins could be imaged at cellular resolution

Potential for margin assessment



Giacomelli MG et al Biomed Opt Express 2018

COLLEGE of AMERICAN PATHOLOGISTS

MULTIPHOTON MICROSCOPY

- **Nonlinear laser-based imaging technique that can generate high-resolution images resembling images of H&E stained sections**

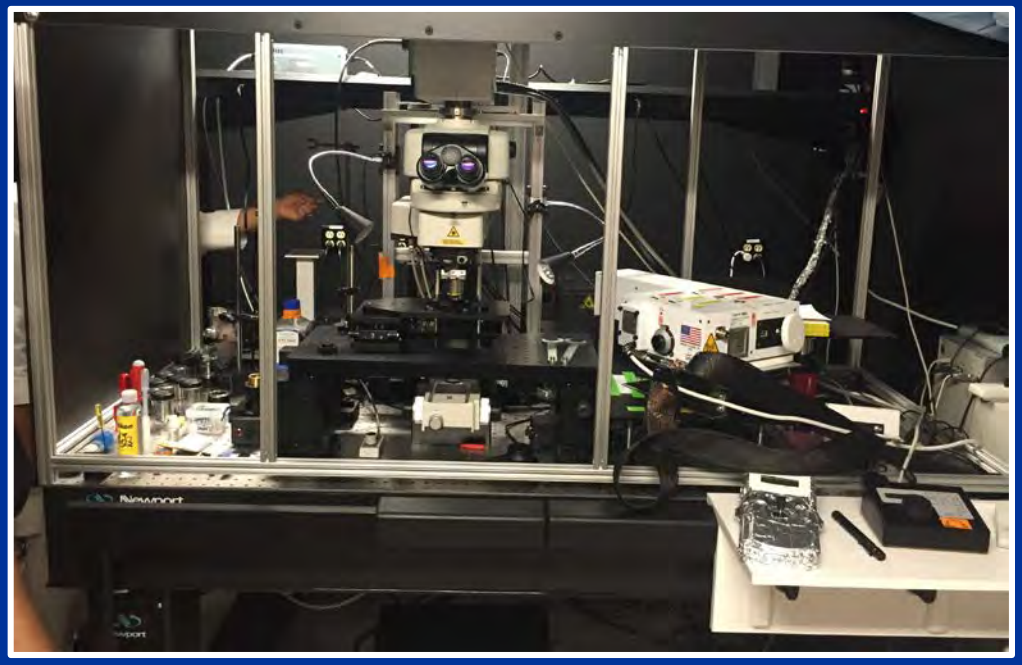
- **Image generation based on :**
  Short-wavelength autofluorescence in the wavelength range of 420-490 nm that captures the emission signals derived from reduced NADH and lipofuscin

  Long-wavelength autofluorescence in the range of 550-650nm capturing signals derived from FAD, NADH, lipofuscin and iron

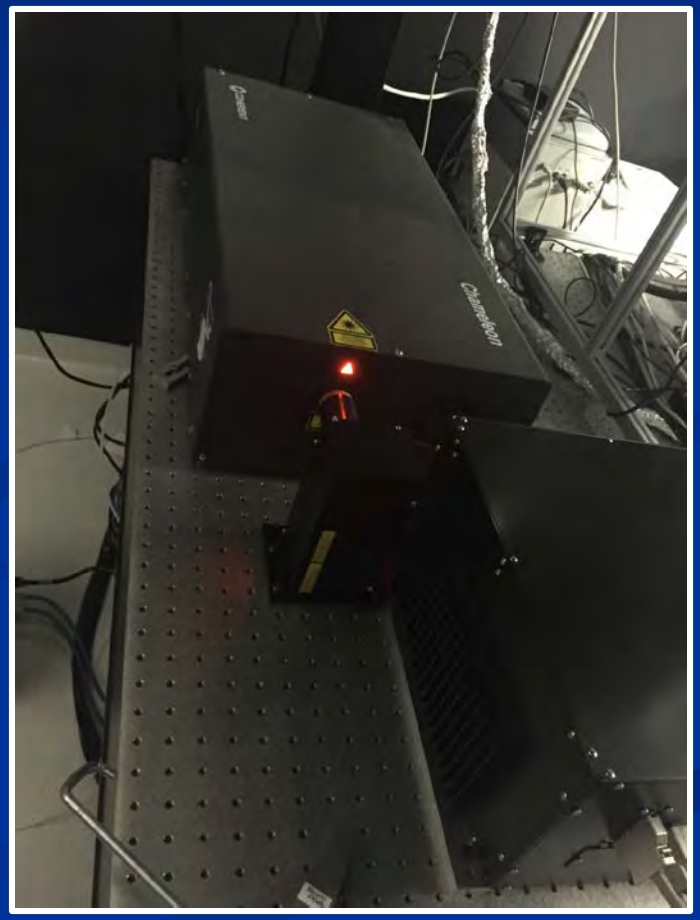
  Second harmonic generation in the range of 360-400nm capturing signals from collagen

MULTIPHOTON SYSTEM

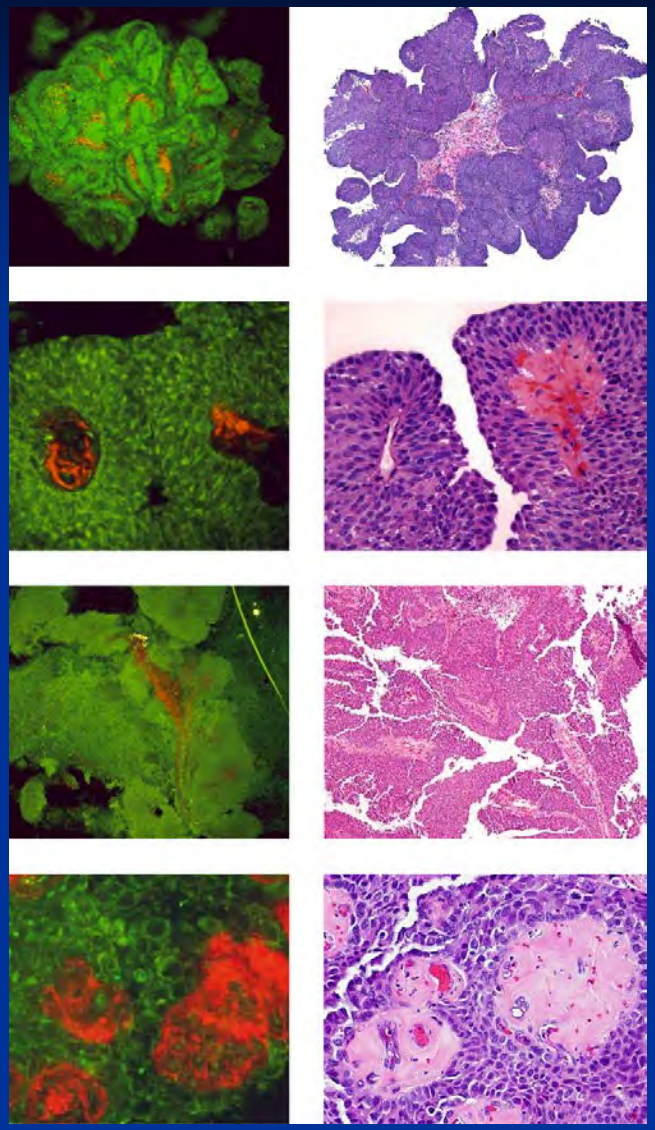
Multiphoton Microscope



Laser System



MULTIPHOTON MICROSCOPY



PAPILLARY UROTHELIAL CARCINOMA: Low grade shows papillary nature of the lesion (complex papillae with thin fibrovascular cores)

PAPILLARY UROTHELIAL CARCINOMA: Cytological features of low grade tumor

PAPILLARY UROTHELIAL CARCINOMA: High grade shows papillary nature of the lesion (complex papillae with thin fibrovascular cores)

PAPILLARY UROTHELIAL CARCINOMA: Cytological features of high grade tumor

COLLEGE of AMERICAN PATHOLOGISTS

Jain M et al. Archives of Pathol Lab Med 2012

Ex Vivo Microscopy

POTENTIAL APPLICATIONS

Real time bedside tissue qualification of core needle biopsy, endoscopic biopsy

Intraoperative evaluation of small fragments of tissues

Intraoperative evaluation of margins of surgical resection specimens

Procuring high quality tissue for biobanking

COLLEGE of AMERICAN PATHOLOGISTS

Suitability of Ex Vivo Tissue Imaging Platforms for Potential Applications in Surgical Pathology Practice

Commercially Available Platforms

Optical Technique	Labeled	Un-Labeled	H & E Like Images
Fluorescence Confocal Microscopy	√	x	√
Dynamic Full-field Optical Coherence Tomography	x	√	√
Stimulated Raman Scatterings Microscopy	x	√	√
Optical Coherence Tomography	x	√	x

Suitability of Ex Vivo Tissue Imaging Platforms for Potential Applications in Surgical Pathology Practice

COMMERCIALLY AVAILABLE PLATFORMS

Optical Technique	Evaluation of Core Biopsy Endoscopic Biopsy	Adjunct to Intraoperative Frozen Section Analysis	Surgical Margin Evaluation		Biobanking
			Moh's Surgery / Small Excision	Non-Skin Larger Specimen	
Fluorescence Confocal Microscopy	√	√	√	x	√
Dynamic Full-field Optical Coherence Tomography	√	√	√	X	√
Stimulated Raman Scattering Microscopy	X	√ (Neuropathology specimens)	X	X	√
Optical Coherence Tomography	X	X	X	√	X

COLLEGE of AMERICAN PATHOLOGISTS

Suitability of Ex Vivo Tissue Imaging Platforms for Potential Applications in Surgical Pathology Practice

Not Yet Commercially Available

Optical Technique	Labeled	Un-Labeled	H & E Like Images
Microscopy Using Ultraviolet Surface Excitation	√	x	√
Light Sheet Microscopy	√	x	√
Structure Illumination Microscopy	√	x	√
Non-Linear Microscopy	√	x	√

Suitability of Ex Vivo Tissue Imaging Platforms for Potential Applications in Surgical Pathology Practice

Not Yet Commercially Available

Optical Technique	Evaluation of Core Biopsy Endoscopic Biopsy	Adjunct Intraoperative to Frozen Section Analysis	Surgical Margin Evaluation		Biobanking
			Moh's Surgery / Small Skin Excursion	Non-Skin Larger Specimen	
Microscopy Using Ultraviolet Surface Excitation	√	√	√	√	√
Light Sheet Microscopy	√	√	√	√	√
Structure Illumination Microscopy	√	√	√	√	√
Non-Linear Microscopy	√	√	√	√	√

Ex-Vivo Tissue Optical Imaging

Optical sectioning microscopy techniques

- Evaluation of tissues requiring minimal or no tissue preparation

Entirely digital images

- Digital images can be viewed at the site of procurement or remotely
- Digital images can be stored, retrieved, and integrated into electronic health records
- Digital images amenable to machine learning

COLLEGE of AMERICAN PATHOLOGISTS

Ex-Vivo Microscopy in Surgical Pathology Practice

- Promising potential for different applications in
- surgical pathology practice

- Feasibility studies

- Recognition of strengths and limitations

- Need for prospective clinical studies

NEXT GENERATION DIGITAL MICROSCOPY TOOLS

COLLEGE of AMERICAN PATHOLOGISTS

Ex-Vivo Microscopy in Surgical Pathology Practice

NEXT GENERATION DIGITAL MICROSCOPY TOOLS

Feasibility

Clinical studies

Standard of Care

Useful Adjunct

CURRENTLY INVESTIGATIONAL

COLLEGE of AMERICAN PATHOLOGISTS

Acknowledgements

Pathology
Stanely Hamilton, M.D
Michael Riben M.D
Yun Wu MD PhD
Lei Huo MD PhD

Interventional Radiology
Michael Wallace MD
Marshal Hicks MD
Sharjeel Sabir MD
Kamran Ahrar MD
Sanjay Gupta MD
Ravi Murthy MD
Alda Tam
Rahul Sheth

Sheikh Khalifa Bin Zayed Al Nahyan Institute for Personalized Cancer Therapy
Kechan Ban
Andrea Cortes
Kenna Shaw PhD
Gordon Mills MD PhD

Rice University
Rebecca Richards-Kortum PhD
Jessica Dobbs PhD

Diagnostic Imaging
Wei Yang MD

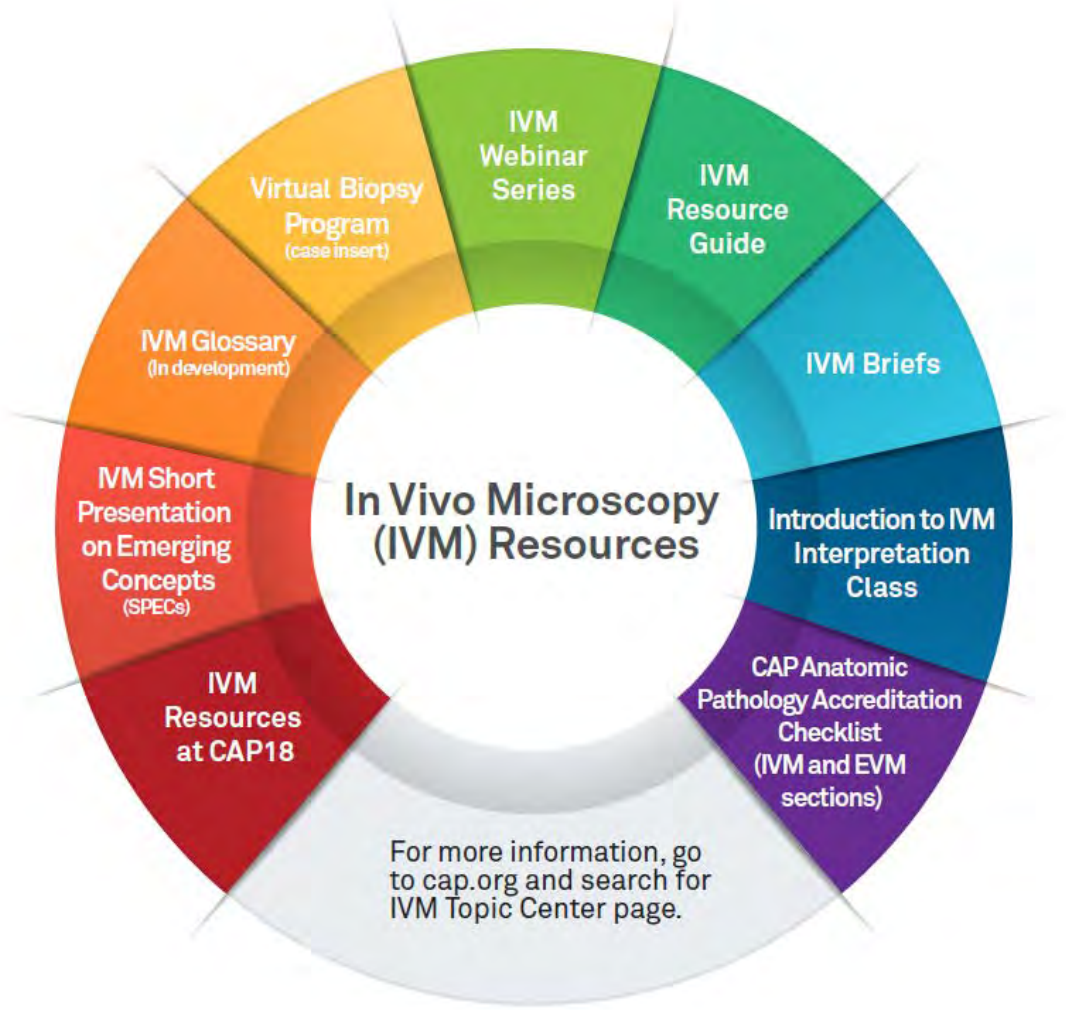
Breast Surgical Oncology
Henry Kuerer MD PhD

FUNDING

The state of Texas grant for rare and aggressive cancers
The Morgan Welch Inflammatory breast cancer Research Program
Susan G Komen for the cure
NIH/NCI SBIR
IPCT
MDACC
Caliber Inc.
PSI Inc.

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

IVM Resources at CAP



Upcoming IVM Webinars

Date	Topic	Speaker
June 17, 2019	Functional Requirements	Sharad Mathur, MD, FCAP

Register for these upcoming webinars as well as archived webinars:
cap.org > Calendar > Webinars

The CAP In Vivo Microscopy Resource Guide – see handout

- **The IVM resource guide highlights current IVM articles and other resources that assist in understanding and potentially adopting IVM and EVM**
  - **Printed guides are available for members ($39) and non-members ($69)**
  - **The digital copies of all four Resource Guides are a complimentary member benefit**
  - **Access them www.cap.org > Resources and Publications**

IVM Short Presentations on Emerging Concepts (SPECs) – see handout

- **IVM SPECs are:**
  - **Short PowerPoints, created for pathologists**
  - **Useful for educating colleagues about IVM and GI specialist on the role and value of pathologists in IVM**
- **IVM SPEC Topics:**
  - **In Vivo Microscopy (IVM): A New Role for Pathologists**
  - **IVM of the GI Tract**
  - **Ex Vivo Microscopy (EVM): A New Tool for Pathologists**
  - **Access them www.cap.org > Resources and Publications**

IVM Topic Center Page on CAP.ORG

- **Check the IVM Topic Center for continued updates and for all your IVM resources**

  www.cap.org > Search for “IVM Topic Center”

THANK YOU!

Thank you for attending our webinar "Ex-Vivo Microscopy: A Promising Next Generation Digital Microscopy Tool for Surgical Pathology Practice" by Savitri Krishnamurthy, MD, FCAP

For comments about this webinar or suggestions for upcoming webinars, contact ivminfo@cap.org

NOTE: There is no CME/CE credit available for today's complimentary webinar. The pdf of the presentation will be sent out in about 1 week.

COLLEGE of AMERICAN PATHOLOGISTS