



IMAGING INFORMATICS & TELEPATHOLOGY

CHRIS GARCIA, M.D. 05/22/2017



★ Notice of Faculty Disclosure

In accordance with ACCME guidelines, any individual in a position to influence and/or control the content of this ASCP CME activity has disclosed all relevant financial relationships within the past 12 months with commercial interests that provide products and/or services related to the content of this CME activity.

The individual below has disclosed the following financial relationship(s) with commercial interest(s):

Christopher A. Garcia, MD

Philips DPS Consultant Consulting Fees

WHAT IS THIS PRESENTATION ABOUT?

- Advances in imaging, computing, and networking allow for a changes in workflow, organizational structure, and business models
- **Imaging informatics** and **telepathology** are crucial in achieving and maximizing these changes
- This presentation covers the **basics** of imaging modalities, imaging systems, and image management

- Imaging Informatics
 - Imaging modalities
 - Still Photography
 - Whole Slide Imaging
 - In Vivo Microscopy
 - Imaging Informatics Systems
 - Image Based Workflow Systems
 - Image Analysis
 - Computer Aided Diagnostic Tools
- Telepathology
 - Basics
 - Known Applications



**IMAGING
INFORMATICS**
& TELEPATHOLOGY

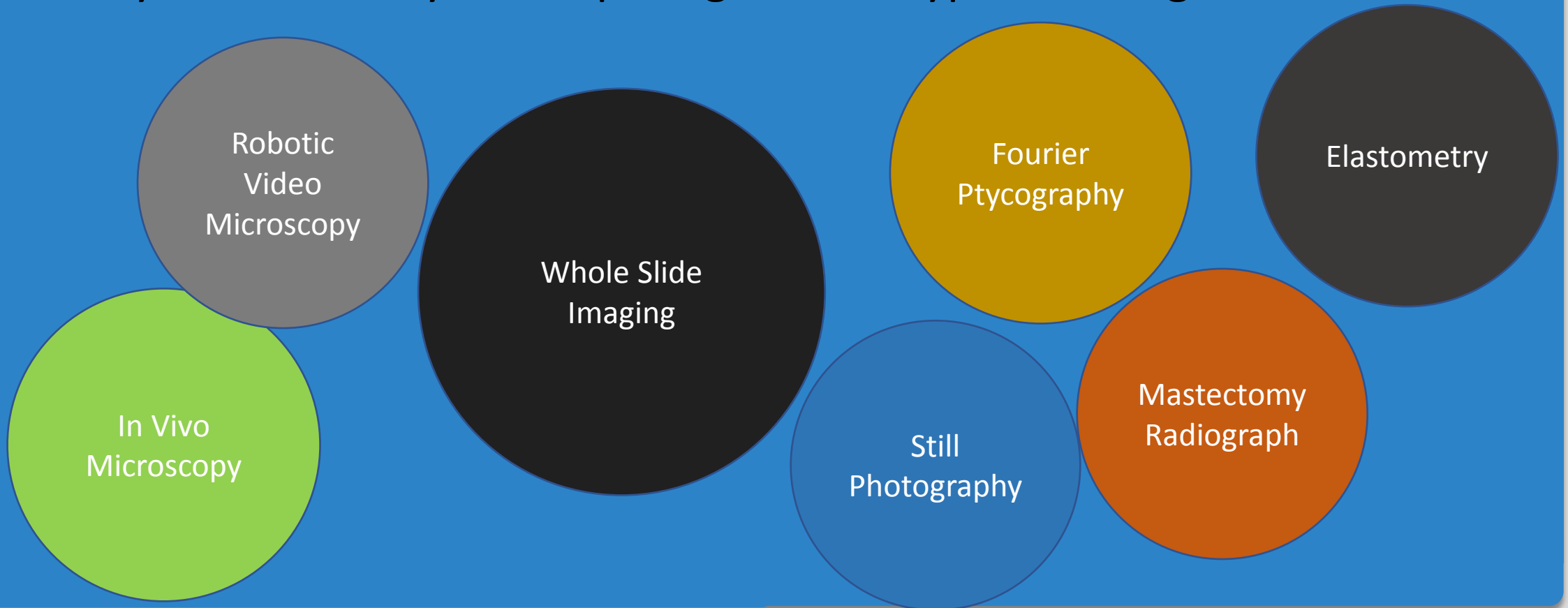
IMAGING INFORMATICS

IMAGING INFORMATICS

- “How Medical Images are used and exchanged throughout complex healthcare systems”
 - American Board of Imaging Informatics
- When people use the term “IMAGING INFORMATICS”, most people think of Radiology
- As digital images become more integrated into the daily practice of Pathology, it will become more common in our literature and

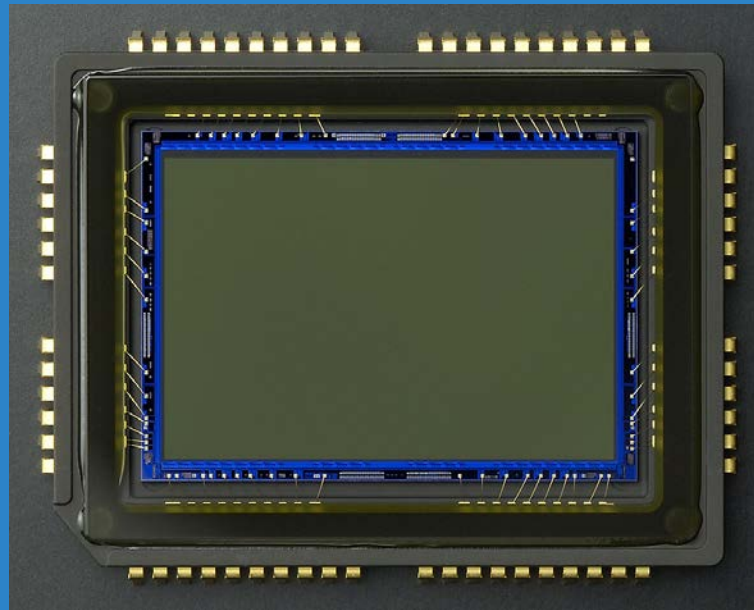
PATHOLOGY IMAGING MODALITIES

- Many different ways of acquiring various types of images



Digital Still Photography

- Use of an image sensor and a computer to capture and create a static digital image



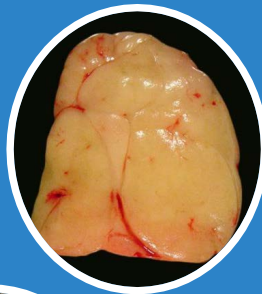
Digital Still Photography

- **Applications**

- Clinical Pictures



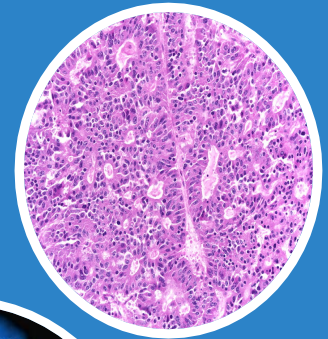
- Gross Photography



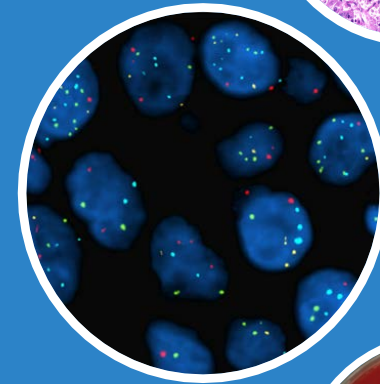
- Case Tracking



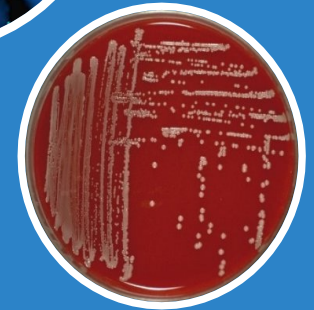
- Case Documentation



- FISH images



- Microbiology images



Digital Still Photography

- **File type**

- Single file
- Many different files
- Size varies depending on need
 - 2 – 30 mb

- **Viewer**

- Most operating systems can open all of these file types



Digital Still Photography

- **File and Workflow Management**

- Can be scattershot and poor
- Few practices have centralized still image management
- Sometimes captured and stored into OS folders



Digital Still Photography

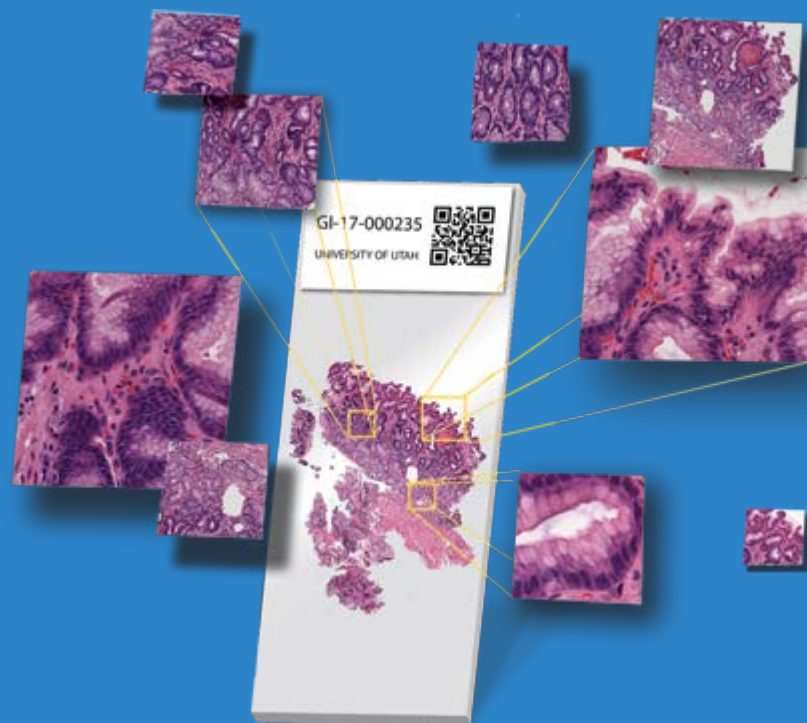
- **Regulation**

- No firm regulation
- Must associate images with case identifiers for utility and safety

- **Reimbursement**

- There is no reimbursement for the capture or use of a still image in Pathology

WHOLE SLIDE IMAGING



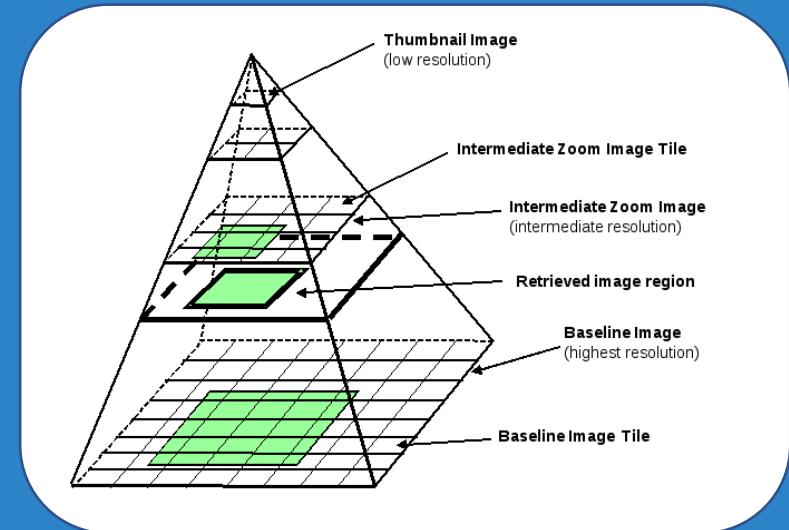
WHOLE SLIDE IMAGING

- The use of scanning technology and imaging software to create a virtual slide



WHOLE SLIDE IMAGING

- **File type**
 - Organized image “tiles” arranged in pyramids
- **The files are fairly large**
 - Up to 30 GB per slide
 - After compression, around 700 MB-1 GB for one slide
- **View example [here](#)**



WHOLE SLIDE IMAGING



- **File and workflow management**
 - WSI file management for clinical purposes is different than for education or research
 - Most are currently tied to proprietary systems
 - Many lessons to learn from Radiology
 - Interface with LIS is important
 - A well managed workflow system allows for successful integration of computer aided analysis

WHOLE SLIDE IMAGING

Regulation

The screenshot displays the official website of the U.S. Food & Drug Administration (FDA). The header includes the U.S. Department of Health and Human Services logo, the FDA logo, and the text "U.S. FOOD & DRUG ADMINISTRATION". A search bar labeled "Search FDA" is positioned on the right. Below the header is a navigation menu with links to Home, Food, Drugs, Medical Devices, Radiation-Emitting Products, Vaccines, Blood & Biologics, Animal & Veterinary, Cosmetics, and Tobacco Products. The main content area features a "News & Events" section with a breadcrumb trail: Home > News & Events > Newsroom > Press Announcements. The headline of the news release is "FDA allows marketing of first whole slide imaging system for digital pathology". Below the headline are social media sharing buttons for Facebook, Twitter, LinkedIn, Pinterest, Email, and Print. The release date is "April 12, 2017". The text of the release states: "The U.S. Food and Drug Administration today permitted marketing of the Philips IntelliSite Pathology Solution (PIPS), the first whole slide imaging (WSI) system that allows for review and interpretation of digital surgical pathology slides prepared from biopsied tissue. This is the first time the FDA has permitted the marketing of a WSI system for these purposes." On the right side of the page, there are sections for "Inquiries" (Media contact: Stephanie Caccamo, 301-348-1956; Consumers contact: 888-INFO-FDA) and "Related Information" (links to FDA: Medical Devices and FDA: Office of In Vitro Diagnostic and Radiological).

U.S. Department of Health and Human Services

FDA U.S. FOOD & DRUG ADMINISTRATION

A to Z Index | Follow FDA | En Español

Search FDA

Home Food Drugs Medical Devices Radiation-Emitting Products Vaccines, Blood & Biologics Animal & Veterinary Cosmetics Tobacco Products

News & Events

Home > News & Events > Newsroom > Press Announcements

FDA News Release

FDA allows marketing of first whole slide imaging system for digital pathology

[f SHARE](#) [t TWEET](#) [in LINKEDIN](#) [p PIN IT](#) [e EMAIL](#) [p PRINT](#)

For Immediate Release April 12, 2017

Release

The U.S. Food and Drug Administration today permitted marketing of the Philips IntelliSite Pathology Solution (PIPS), the first whole slide imaging (WSI) system that allows for review and interpretation of digital surgical pathology slides prepared from biopsied tissue. This is the first time the FDA has permitted the marketing of a WSI system for these purposes.

Inquiries

Media

✉ Stephanie Caccamo
☎ 301-348-1956

Consumers

☎ 888-INFO-FDA

Related Information

- FDA: Medical Devices
- FDA: Office of In Vitro Diagnostic and Radiological

WHOLE SLIDE IMAGING

Regulation

The “systems” are defined by anything that creates, processes, or displays a pixel



WHOLE SLIDE IMAGING

Regulation

The screenshot displays the CAP website's header and main content area. The header includes the CAP logo, navigation links (ABOUT THE CAP, CALENDAR, NEWS & MEDIA, CAREERS AT THE CAP, SHOP, CONTACT & SUPPORT), a search bar, and a 'LOG IN' button. Below the header, a secondary navigation bar lists 'Get Involved', 'Laboratory Improvement', 'Learning', and 'Resources & Publications'. The main content area features a large purple banner with the title 'VALIDATING WHOLE SLIDE IMAGING FOR DIAGNOSTIC PURPOSES IN PATHOLOGY'. Below this banner, the 'Background' section begins with the text: 'The CAP's evidence-based guideline, "VALIDATING WHOLE SLIDE IMAGING FOR DIAGNOSTIC PURPOSES IN PATHOLOGY," serves as a practical guide for pathologists and laboratories to confirm the accuracy and concordance of their own whole slide imaging (WSI) systems for diagnostic work while ensuring the digital tool is being used'. To the right of the 'Background' section is a purple box with the text 'Feedback on Recommendations'.

COLLEGE of AMERICAN PATHOLOGISTS

LOG IN

ABOUT THE CAP CALENDAR NEWS & MEDIA CAREERS AT THE CAP SHOP CONTACT & SUPPORT

Q Search

Get Involved Laboratory Improvement Learning Resources & Publications

VALIDATING WHOLE SLIDE IMAGING FOR DIAGNOSTIC PURPOSES IN PATHOLOGY

Background

The CAP's evidence-based guideline, "**VALIDATING WHOLE SLIDE IMAGING FOR DIAGNOSTIC PURPOSES IN PATHOLOGY**," serves as a practical guide for pathologists and laboratories to confirm the accuracy and concordance of their own whole slide imaging (WSI) systems for diagnostic work while ensuring the digital tool is being used

Feedback on Recommendations

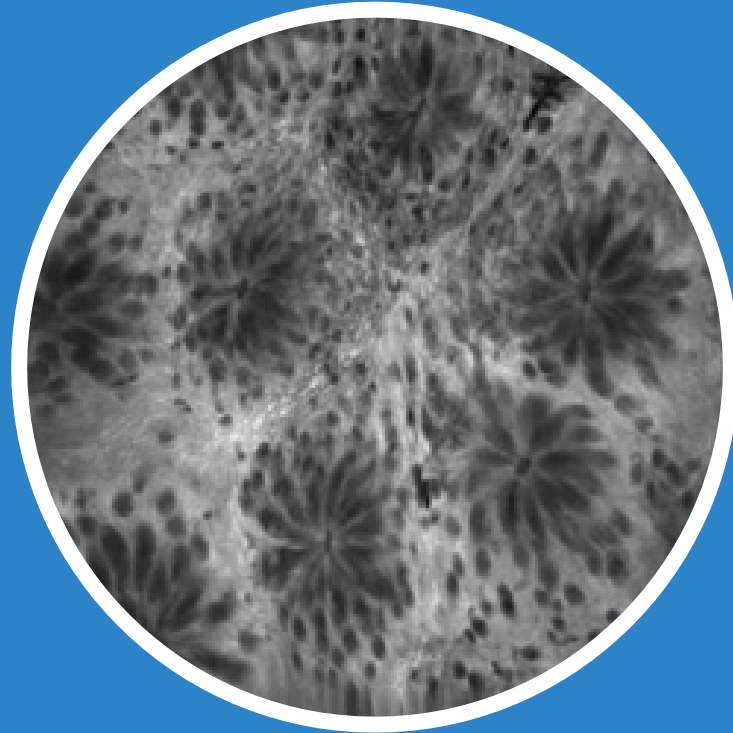
WHOLE SLIDE IMAGING

- Reimbursement

| CPT CODE(S) | DESCRIPTION | DIGITAL PATHOLOGY APPLICATION |
|---------------------|---|---|
| 88300-88309 | Accession, examination, and reporting of gross and microscopic | Primary Diagnosis preformed on whole slide images* |
| 88321 | Consultation and report on referred slides prepared elsewhere | Second opinion consultations preformed on whole slide images |
| 88323 | Consultation and report on referred material requiring preparation of slides | Second opinion consultations on whole slide images |
| 88329, 88331, 88332 | Pathology consultation during surgery, frozen section | Frozen section consultation preformed via live telepathology or on whole slide images |
| 88360, 88361 | Morphometric analysis, tumor immunohistochemistry (eg. Her-2/neu, ER/PR), quantitative or semiquantitative, each antibody, manual or using computer assisted technology | Manual or computer- assisted analysis of HER2, ER/PR, Ki-67, p53, etc** |
| 88365, 88367, 88368 | In situ hybridization (eg. FISH), morphometric analysis (quantitative or semi-quantitative), manual or using computer assisted technology for each probe | Manual or computer assisted analysis of FISH* |

[Digitalpathologyassociation.org/healthcare-faqs](https://digitalpathologyassociation.org/healthcare-faqs)

IN VIVO MICROSCOPY



IN VIVO MICROSCOPY

- **Definition**

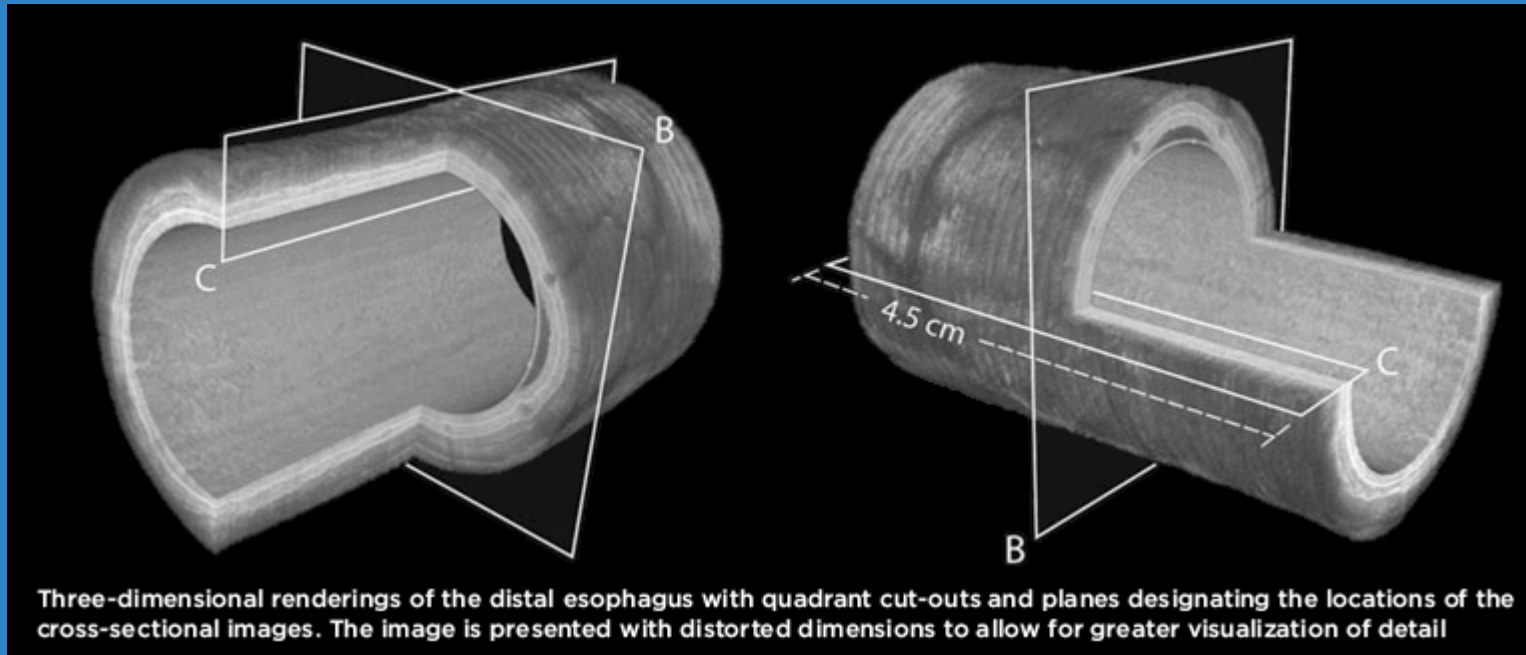
- Microscopic images are obtained real-time, in a nondestructive manner

- **Basic Concepts**

- Miniaturization of the microscope with microelectromechanical technology
 - Use of fiber optic bundles with instruments on the proximal end
 - Spectrally-encoded endoscopy
 - Ultraminiature endoscopy that encodes each spatial location on the sample with a different wavelength
 - And more....

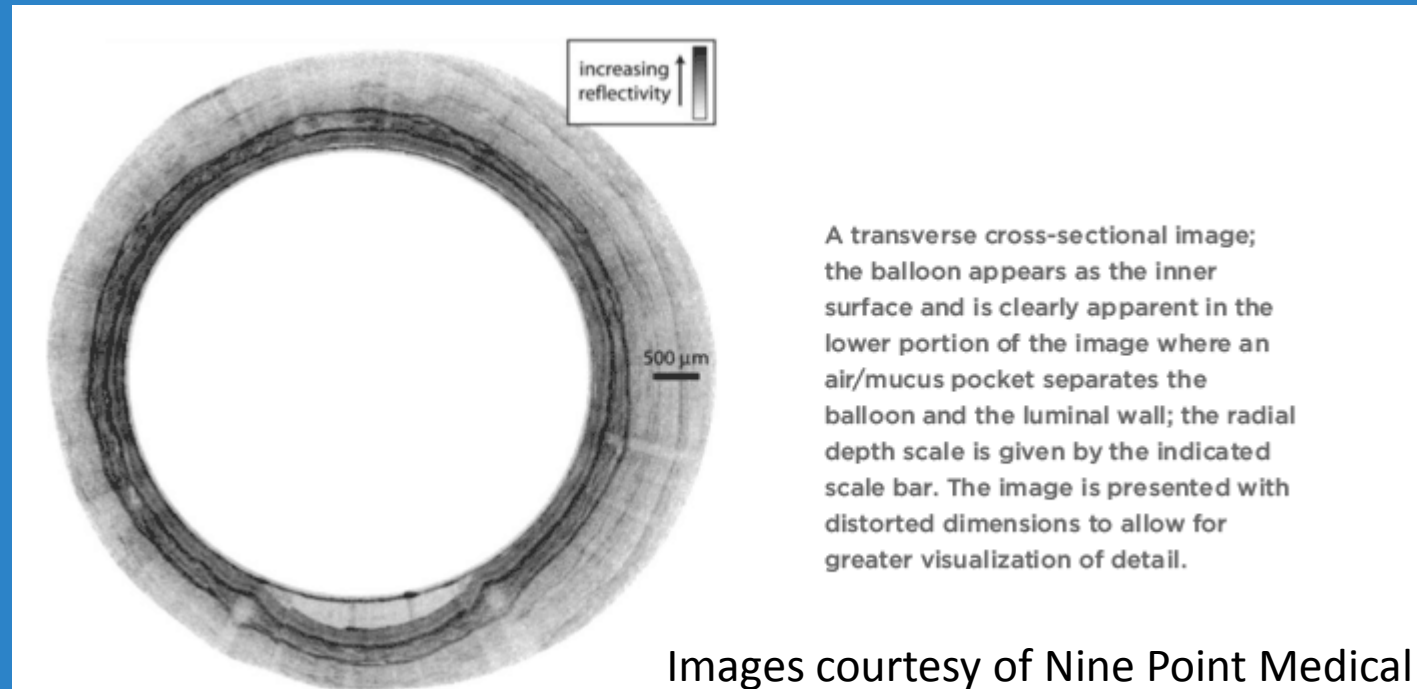
IN VIVO MICROSCOPY

- **Optical Coherence Tomography (OCT)**
 - Enables micron scale and 3D imaging of microstructure found in biological tissues in situ and real time



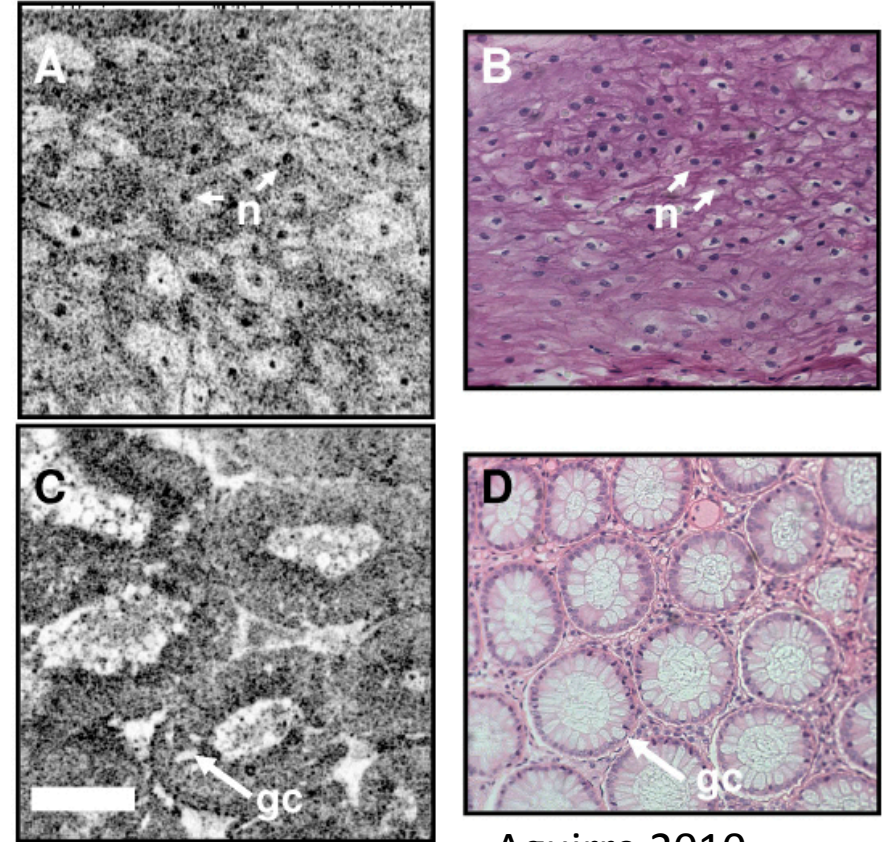
IN VIVO MICROSCOPY

- **Optical Coherence Tomography (OCT)**
 - Microstructure imaging with 1-10 micrometer resolutions and 1-2mm penetration depths
 - “Optical biopsy”



IN VIVO MICROSCOPY

- **Optical Coherence Microscopy (OCM)**
 - Combines confocal microscopy with OCT to achieve cellular resolution imaging in the en face plane



Aguirre 2010

IN VIVO MICROSCOPY

- **Files and Workflow management**

- Obtained in a manner similar to ultrasound
- Greyscale
- Video and still images
 - Size ranges from 2 mb to 400 mb
- Obtained usually by a non-Pathologist clinician
 - Pathology services similar to “Intraoperative consultation”

- **Systems**

- Proprietary, on-hardware
- Images are not usually managed in Pathology
- Cases are logged in LIS



IN VIVO MICROSCOPY

- **Regulation**

- Multiple FDA approved devices

- **Reimbursement**

- CPT 88375 “Optical microscopic image, interpretation, and report”
 - Separate CPT codes for “Optical Biopsies” in different organs
 - CPT 43252 “EGD with optical microscopy”





**IMAGING
INFORMATICS**
& TELEPATHOLOGY

SYSTEMS

LABORATORY INFORMATION SYSTEM (LIS)



- The main legacy workflow system in pathology
- Many LIS vendors provide an image management module
 - Consists of separate server
 - Integrated into current system

• Pros

- Use one system for workflow
- Everyone with access to LIS has access to images

• Cons

- User experience can be lacking
- Workflow is not designed around images
- Varied experiences in handling WSI

PATHOLOGY PACS



- PACS = Picture Archiving and Communication System
- Specialized system built for storing and sharing images
- Not always all inclusive (WSI vs Still image vs video)

• Pros

- May offer workflows that benefit from prior Radiology PACS experience
- Can integrate with LIS, EHR, etc
- Can be a scalable solution

• Cons

- No Dominant Architecture
 - Currently undergoing change
- Usually Vendor Specific
- Can be monolithic
 - Traditional vs deconstructed

VENDOR NEUTRAL ARCHIVE



- VNA
- Is an enterprise solution for management, storage, retrieving, and querying images in healthcare
- Mostly a Radiology solution, but is rapidly moving into Pathology space

• Pros

- Vendor agnostic
- Can interface with multiple systems at multiple institutions
- Can be shared infrastructure with Radiology, Dermatology, etc

• Cons

- Limited adoption in Pathology Currently
- Governance / Turf wars
- Poorly defined, undergoing change



**IMAGING
INFORMATICS**
& TELEPATHOLOGY

IMAGE ANALYSIS

IMAGE ANALYSIS



- **Not new**
 - Multiple vendors have 510(k) clearances for quantitative analysis of ER,PR, HER2/neu, Ki-67, p53 in breast
- **Great potential**
 - Augmenting quality/consistency
 - Many excellent vendors
 - Very interesting applications using machine vision, machine learning, etc.
- **Workflow**
 - Currently fairly separated
 - Integration with clinical digital pathology system should be thoughtfully constructed

IMAGE ANALYSIS

- **Gaining momentum**
 - Watch this space
- **Excellent research**
- **Many good workshops**
 - Path Informatics Summit
 - Pathology Visions

Detecting Cancer Metastases on Gigapixel Pathology Images

Yun Liu^{1*}, Krishna Gadepalli¹, Mohammad Norouzi¹, George E. Dahl¹,
Timo Kohlberger¹, Aleksey Boyko¹, Subhashini Venugopalan^{2**},
Aleksei Timofeev², Philip Q. Nelson², Greg S. Corrado¹, Jason D. Hipp³,
Lily Peng¹, and Martin C. Stumpe¹

{liuyun,mnorouzi,gdahl,lhpeng,mstumpe}@google.com

¹Google Brain, ²Google Inc, ³Verily Life Sciences,
Mountain View, CA, USA

Abstract. Each year, the treatment decisions for more than 230,000 breast cancer patients in the U.S. hinge on whether the cancer has metastasized away from the breast. Metastasis detection is currently performed by pathologists reviewing large expanses of biological tissues. This process is labor intensive and error-prone. We present a framework to automatically detect and localize tumors as small as 100×100 pixels in gigapixel microscopy images sized $100,000 \times 100,000$ pixels. Our method leverages a convolutional neural network (CNN) architecture and obtains state-of-the-art results on the Camelyon16 dataset in the challenging lesion-level tumor detection task. At 8 false positives per image, we detect 92.4% of the tumors, relative to 82.7% by the previous best automated approach. For comparison, a human pathologist attempting exhaustive search achieved 73.2% sensitivity. We achieve image-level AUC scores above 97% on both the Camelyon16 test set and an independent set of 110 slides. In addition, we discover that two slides in the Camelyon16 training set were erroneously labeled normal. Our approach could considerably reduce false negative rates in metastasis detection.

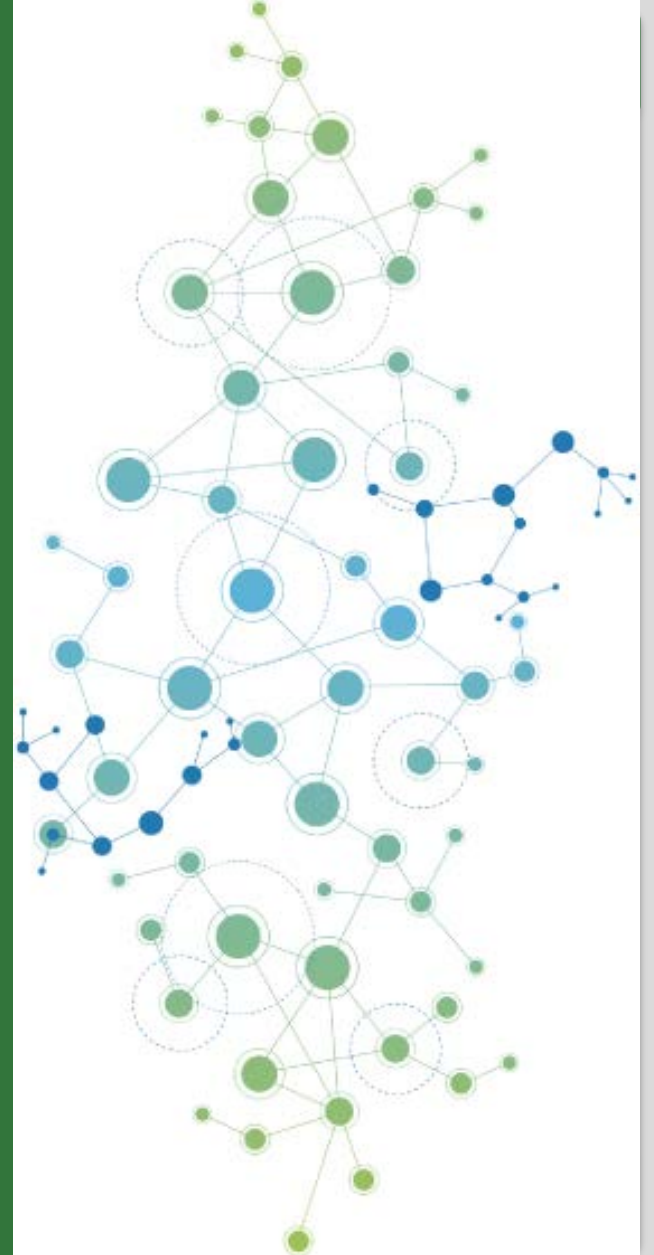


**IMAGING
INFORMATICS**
& TELEPATHOLOGY

TELEPATHOLOGY

TELEPATHOLOGY

- “The practice of pathology at a distance”
 - Ron Weinstein, M.D. 1986
- A subspecialty of “Telehealth”
 - Culmination of networking, digital capture, and systems
- Not limited to WSI
 - Currently is largely comprised of live video microscopy and static image sharing



TELEPATHOLOGY



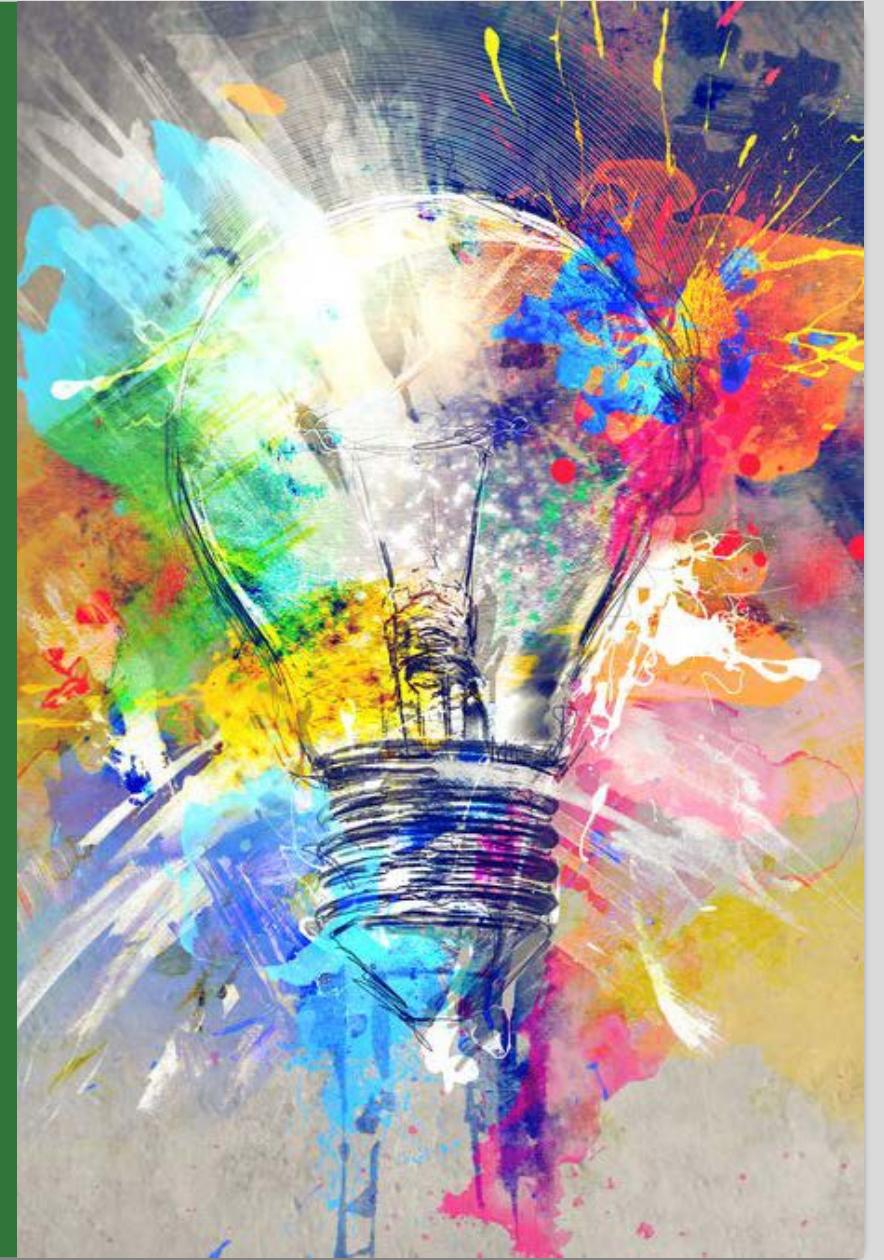
Clinical Guidelines for Telepathology

Table of Contents

| | |
|---------------------------------------|----------|
| Preamble | 5 |
| Scope | 6 |
| Introduction | 6 |
| Clinical Guidelines for Telepathology | 8 |
| Technology | 8 |
| Technical Specification | 8 |

TELEPATHOLOGY

- Applications
 - Primary Diagnosis
 - Intraoperative consultation and/or Rapid On Site Evaluation
 - Attitudes on FDA regulation may be changing
 - Please stay aware of regulations
 - Secondary Consultation
 - Education
- Stay aware of regulations
 - State licensing restrictions, reimbursement
 - FDA
 - Security is key



- Imaging Informatics
 - Imaging modalities
 - Still Photography
 - Whole Slide Imaging
 - In Vivo Microscopy
 - Imaging Informatics Systems
 - Image Based Workflow Systems
 - Image Analysis
 - Computer Aided Diagnostic Tools
- Telepathology
 - Basics
 - Known Applications

THANK YOU



REFERENCES

- Aguirre AD, Sawinski J, Huang SW, Zhou C, Denk W, Fujimoto JG. High speed optical coherence microscopy with autofocus adjustment and a miniaturized endoscopic imaging probe. Opt Express. 2010 Mar 1;18(5):4222-39.
- Colby R. VNA: An Unavoidable Investment? Radiol Manage. 2015 Mar-Apr;37(2):13-5.
- College of American Pathologists Press. Digital Pathology Resource Guide, 2015.
- College of American Pathologists Press. In Vivo Microscopy Resource Guide, 2015.
- Digital Pathology Association. FAQs. (n.d.). Retrieved May 10, 2017, from <https://digitalpathologyassociation.org/healthcare-faqs>
- Pantanowitz L, Dickinson K, Evans AJ, Hassell LA, Henricks WH, Lennerz JK, Lowe A, Parwani AV, Riben M, Smith CD, Tuthill JM, Weinstein RS, Wilbur DC, Krupinski EA, Bernard J. American Telemedicine Association clinical guidelines for telepathology. J Pathol Inform. 2014 Oct 21;5(1):39.
- Pantanowitz, Liron, J M. Tuthill, and Ulysses J. Balis. *Pathology informatics : theory & practice*. Chicago, Ill: American Society for Clinical Pathology Press, 2012. Print.

Please fill out the Post-
Workshop Survey

<http://tinyurl.com/mcrya2l>

