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Whole Slide Imaging/ Digital Pathology

Historical Perspective
Advantages
Obstacles
Experience from our Demonstration Project
Disclosures

No financial relationship with any digital pathology company including Philips.

Member of the team evaluating the Philips Image Management System as part of a demonstration project with Sonora Quest Laboratories and Banner Health System.
And for you Dodger Fans!

I set my DVR to record 'The Biggest Loser' and it keeps recording Dodger games.

someecards user card
Objectives

• Review the historical time line/ evolution of digital pathology.

• Describe the advantages of whole slide imaging.

• What are the key elements/ obstacles for implementation.

• Knowledge gained from Philips-Banner-SQL Demonstration Project.
100 year span

Leitz Lantern Slide Camera, circa 1910

Bausch and Lomb Lantern Slide Projector, circa 1908

Morrison and Gardner: Arch Pathol Lab Med. 2015;139:1558
Enter the 1930-1960s

1935

1945

1956

1961
Enter the 1950-60s

photo by William Day, copyright 2007
Enter the 1980’s

Morrison and Gardner: Arch Pathol Lab Med. 2015;139:1558
Enter the late 1990’s
Enter the 21 century

Patient A BAL fluid

Proof of Lung origin

CK7

TTF-1/ Napsin
Advantages to Whole Slide Imaging

Rapid availability of scanned images to the pathologist.

Eliminate courier time and cost for labs with multiple remote sites.

Evaluation of multiple slides and regions simultaneously.

Rapid and easy measurement: depth of invasion, area, cell size.

Telepathology: Frozen sections, internal and external consults

Image analysis and application of deep learning tools.

Real time consultation and collaboration

Considerations in Implementation

Barriers to the Adoption of Whole Slide Imaging for Clinical Use

Cost: hardware, software, information technology support/infrastructure and maintenance

Pathologist perception of inferior performance compared to microscopy

Lack of standards and/or best practice guidelines

Barriers to the Adoption of Whole Slide Imaging for Clinical Use

Regulatory issues: lack of US FDA approval (prior to late 2017)

Medicolegal liability, licensure, and credentialing issues

Absence of defined professional billing codes or business models

Considerations: Implementing WSI for Diagnosis

Cost: hardware, software, information technology support/infrastructure and maintenance
Pathologist perception of inferior performance compared to light microscopy
Lack of standards and/or best practice guidelines
Regulatory issues: lack of US Food and Drug Administration approval in the United States
Medicolegal liability, licensure, and credentialing issues
Absence of defined professional billing codes or business models

Considerations: Implementing WSI for Diagnosis

Applications of WSI in patient care: where to start and how to assemble an implementation team: all slides; IHC, sp. stains etc.

Strategy for selecting a WSI scanner

Resources required to operate and maintain a clinical digital pathology program

Validation of the system to be used

Strategies to encourage adoption of WSI by pathologists

What to expect after going live, based on the experience of early adopters

**Considerations: Implementing WSI for Diagnosis**

| Applications of WSI in patient care: where to start and how to assemble an implementation team |
| Strategy for selecting a WSI scanner |
| Resources required to operate and maintain a clinical digital pathology program |
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| Strategies to encourage adoption of WSI by pathologists |
| What to expect after going live, based on the experience of early adopters |

Pathologist Discomfort with WSI

Lack of training or experience with the technology
Time required to review cases by WSI such that confident diagnoses are rendered
Fundamental mechanical and ergonomic differences between WSI and light microscopy
Concern that WSI will introduce unfamiliar digital artifacts over and above those generated by routine histologic processing
Lack of US Food and Drug Administration approval to use WSI for primary diagnosis in the United States

Considerations: Implementing WSI for Diagnosis

Applications: WSI

Aperio - upper left: View up to 4 slides

Hamatsu: upper right
Cytology

Vision Tek-Sakura
Multiple slides - modalities

14 month randomized, blinded study using cases intended for routine surgical pathology diagnosis.

1992 cases read across 4 institutions and 16 pathologists

Philips Intellisite Pathology Solution: 15,292 reads

4 week washout period before re-read using alternative method (digital vs microscopy and vice versa)

73% of slides were HE, 27% IHC and histochemical test slides.

Am J Surg Pathol Volume 42, Number 1, January 2018
Whole Slide Imaging Philips Study

Study Design: non-inferiority
Verified by Enrollment Pathologists

Reference standard

Determined by Adjudication Pathologists

Major discordance rate WSI vs. Reference standard

Determined by Adjudication Pathologists

Major discordance rate Microscopy vs. Reference standard

Primary Analysis
Confidence interval WSI-Microscopy <4%

Diagnosis by WSI

Made by Reading Pathologists

Diagnosis by Microscopy

Made by Reading Pathologists

Am J Surg Pathol Volume 42, Number 1, January 2018
Digital slides were read in batches of 20.

Mean read time: microscopy: 74 seconds; digital: 84 sec

94% slides scanned adequately on first scan; 98.5% by 2 scans. Maximum # scans utilized was 5.

Reference standard: Original sign out Dx by microscopy.

Major discrepancy rate with ref. standard: 4.6% by microscopy and 4.9% by WSI.
Differences by Organ System:

<1% WSI discordance > microscopy: Stomach, skin, brain, colorectal and prostate.

>1% WSI discordance: GYN (1.2), bladder (1.3), neopl. Kid (1.5); endocrine (1.8%)

<1% microscopy discord > WSI: Breast, respiratory, LN’s

>1% microscopy discord > WSI: liver/biliary, salivary, perianal

No difference: peritoneal, appendix, gallbladder, soft tissue

Am J Surg Pathol Volume 42, Number 1, January 2018
7 week evaluation of the Philips Intellesite Scanner and Image Management System (IMS): Sonorq Quest Labs; Banner Health

Scanned IHC, recut and special stain slides in first 4 weeks and then added selected up front HE slides

2 Pathologists at independent sites reading their own cases in parallel with glass slides, in no particular order, though usually digital slides first.

Not intended as a validation of the system or individual pathologists
Slides scanned at the central SQL location into server on site.

IMS system application installed on each pathologist’s current workstation and their current monitor was used.

The FDA approved workstation was intended for use but could not be installed in time for each pathologist. Available for demonstration, training and additional exploration at the central location, as time allowed.

As of 4/2/18, number of cases and slides imaged and read per pathologist: 450 cases/1575 slides.
38 yo: abnl vaginal bleeding and ovarian mass
Granulosa cell tumor

SMA

CD99

inhibin

CD56
60 year old with pulmonary consolidation - BAL
60 year old with pulmonary consolidation - BAL

S-100

Melan A

CK 5/6

p40
Metastatic Melanoma and SCCA - BAL

S-100

Melan A

CK 5/6

p40
Inflammatory myofibroblastic tumor

Bronchial biopsy

Bronchial wash CB
IMT: ALK IHC images exported

Bronchial biopsy

Bronchial wash CB
Comparing levels: images exported

Bronchial biopsy - metastatic breast carcinoma 5X
Comparing levels: images exported

Level 1

Level 3

Level 2
Bronchial biopsy- metastatic breast carcinoma- 10X
5.45 mm lateral margin
0.2924 mm (292.4 um) depth
Measurements

0.395 mm depth
H. Pylori
Endometrial CA MMR, 0.5X

MLH1  Aligned slides  MSH6

MSH6  PMS2
<table>
<thead>
<tr>
<th>MLH1</th>
<th>Aligned slides</th>
<th>MSH6</th>
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<tbody>
<tr>
<td><img src="image1" alt="MLH1 Image" /></td>
<td><img src="image2" alt="Aligned Slides Image" /></td>
<td><img src="image3" alt="MSH6 Image" /></td>
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<tr>
<td>MSH6</td>
<td>PMS2</td>
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</tbody>
</table>
Endometrial CA MMR, 20X

MLH1  Aligned slides  MSH6

MSH6  PMS2
Next level small fragments out of focus
Selecting the appropriate implementation team is critical.

IT support is paramount: ensuring proper bandwidth and workstations and troubleshooting.

WSI is a powerful tool with equivalence to glass slide reading for diagnosis in routine surgical pathology. Cytology, frozen sections, hematopathology smears not yet FDA approved.

Some lag time and minimal image quality issues exist versus the optimized FDA approved workstation (not prohibitive for proof of concept in the project).

Rare out of focus issue with very small fragments of tissue.
Philips- Demonstration Project Team!

**Project Manager:** William Desalvo, SQL

**SQL Management:** Anthony Cerullo, Joseph Berryhill, Ida Male, Sandra Bambulas, Susan Schmidt

**SQL Histology:** Tamara Stahn, Dawn Stapley, Nelly Melendez Rosario and Steven Stubblefield.

**SQL and Banner IT:** Calley McCoy, Bart Mika, Khai Dao, Diane Blasko

**Philips Corporation:** Cynthia Marr, Steve Sorenson, Nora Mansoorian and Lisa Cuomo.

**Banner Lab Managers:** Gabrielle Siciliano (BTMC) and Denise Waltrip (BDMC)

**Pathologists:** Holly McDaniel (BDMC) and Richard Eisen (BTMC).


THE END