Welcome to the PHC Webinar Series

This lecture on “How Whole Slide Imaging (WSI) Can Improve Your Pathology Practice” is given by Kenneth Bloom, MD, FCAP

Your host is Jill Kaufman, PhD. For comments about this webinar or suggestions for upcoming webinars, please contact Jill Kaufman at jkaufma@cap.org

THE WEBINAR WILL BEGIN MOMENTARILY. ENJOY!
Kenneth Bloom, MD, FCAP

- Chief Medical Officer of Clarient a GE Healthcare company, Medical Director of Clarient Diagnostic Services and President of Clarient Pathology Services

- Specializes in pathology with a special interest in breast disease and esoteric testing including immunohistochemistry, fluorescence in-situ hybridization and molecular analysis

- More than two decades serving in leadership and advisory roles for hospitals, medical schools and industry

- Prolific researcher and lecturer in the fields of pathology, cancer, telemedicine and informatics
How Whole Slide Imaging (WSI) Can Improve Your Pathology Practice

Kenneth J. Bloom, MD, FCAP
Chief Medical Officer, CLARIENT Inc., A GE Healthcare Company
Clinical Professor of Pathology, Keck School of Medicine

June 8, 2011
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Disclaimer

- I work for Clarient, a GE Healthcare company
- I am an Advisory Board Speaker for Genentech
- I was an expert witness for Wyrth
What is WSI

- **Scan glass slide to create a virtual copy that exists as an image file in a computer system.**
  - Overcomes shortcomings of traditional glass slides including: time consuming archival and retrieval, breakage, loss, costly transport, inability to make optimal comparisons
  - Images can be shared anytime, anywhere
  - Facilitates education, research, consultation
Common Uses of WSI

- Remote Frozen Sections
- Expert review/consultation
  - Intrapractice, Interpractice, International
- Improve productivity
- Improve storage and retrieval
  - Facilitates access to previous slides, conferences, research, publications
- Provide access to digital image analysis tools.
Remote Frozen Section

- No need to travel for occasional frozen section
- Rapid second opinion when necessary
- Ability to obtain specialty expertise, neuropath, transplantational path, etc.
Expert Consultation

- **Intrapractice** consultation allows sharing of cases without getting up from your desk or microscope. Includes sharing slides with colleagues at a remote site.

- **Interpractice** consultation allows sharing of pathologist knowledge within a community. For example, practice “A” hires a neuropathologist and practice “B” hires a transplant pathologist and both practices benefit from the resulting in-house expertise.

- **Expert** consultation allows access to national and international experts within seconds.
Improving Traditional H&E/IHC Workflow

IHC Biomarker Ordered

• Take pictures
• Sign Out Report

Block Pulled & Slides Sectioned

Pathologist Review & Interpretation

IHC Stain Performed

Slides Collated & Delivered To Pathologist
Improved Productivity: WSI Workflow

- Pathologist Review & Interpretation
- Incorporate Images Into Reports
- Image Analysis
- Off-Site Review
- Consultation Review/Tumor Board & Presentations QA/QC Review
- Educational/Research

Virtual Microscopy
Improve Productivity

- Expert Second Opinion

Local Pathologist reviews complex tumor. Needs to order special studies

Sent via local courier + airlines

Stains performed and scanned

Local Pathologist reviews case on PathSite. Orders consultation

Report returned

Stains performed and scanned

Local Pathologist releases results to clinician

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Improve Storage and Retrieval

• **Previous Slides:** Access to previous material when reviewing a patient sample is critical. Not infrequently slides from an outside institution are reviewed and sent back prior to the patient’s definitive procedure.

• **QA:** Easy access to random or directed slides for QA review.

• **Conferences:** Slides need to be retrieved for tumor board, etc.

• **Research:** Need rapid access to slides to qualify patients for clinical trials.

• **Publications:**
**Education**

- **Single slide set for Medical Students:** Everyone reviews exactly the same slides with exactly the same features; Costs are dramatically reduced since no slide boxes need to be maintained; Tissue requirements virtually non-existent to become a teaching case because only one slide set needs to be prepared.

- **No need for resident slide sets:** Residents create virtual slide decks of interesting cases. No more recuts for personal collections. Everyone can have a copy of key illustrative cases.

- **Competency assessments:** Assessments can be carried out easily with no issues of slide to slide variation. Easy to pull random cases for review.
Access to Analysis Tools

- **Quantitative IHC**: ER, PR, HER2, KI67
- **Obtain measurements easily**: Accurate assessment of tumor size, margin distances, etc.
- **Find rare events**: DCT, CTC, viral inclusions, etc
- **Nextgen tools**: Aid in predicting response to therapy and overall outcome.
- **View distributions easily**
Image Analysis Viewer

**Raw Image**

**Brown Threshold**
This defines pixels that correspond to chromagen (shown in red).

**Blue Threshold**
This defines pixels that correspond to nuclear counterstain (shown in blue).
Image Analysis Report

Patient Name: ERT HT42, Breast - Scopena
DOB: 1976-03-22
Gender: Female
Medical Record #: 03-20-03-497
Tumor Size (cm): 2

IHC Report

Breast Tissue: 53456
10% Neutral Buffered Formalin / 6-48 hrs

H&E

Estrogen Receptor

Progestrone Receptor

Her-2/new

Methodology:
The ERT slides were incubated with the SP11 monoclonal anti-ErbB-2 antibody from Novocastra at a 1:1000 dilution for 2 minutes following heat induced epitope retrieval in citrate buffer. Visualization was achieved with Vision Biosystem Novolink Polv-AP detection system. The slides were then counterstained with Dako hematoxylin for 1 minute.
The TRK slides were incubated with the PAb1801 monoclonal anti-TRK antibody from Dako at a 1:5000 dilution for 2 minutes following heat induced epitope retrieval in citrate buffer. Visualization was achieved with Vision Biosystem Novolink Polv-AP detection system. The slides were then counterstained with Dako hematoxylin for 1 minute.
Increasing index value -> decreasing DFS

Subject 289, Alive, Survival = 263.4 months, IDX = -337.486

Subject 241, Dead, Survival = 27.4 months, IDX = -233.819

Subject 154, Dead, Survival = 10.5 months, IDX = 1506.037

Key
- High Index
- Medium Index
- Low Index
WSI offers a number of benefits and spans a wide range of applications.

- Eliminating inefficiencies of “snapshot” imaging
- Sharing slides across distances
- Access to experts, irrespective of patient location
- Ability to share cases among multiple peers simultaneously
- Integrating the workflow of pathologists with EMR
- Reduces/eliminates slide couriers/filers
- Immediate access to archived images

Why Whole Slide Imaging?
WSI Challenges

Challenges to WSI¹

(N = 20)

<table>
<thead>
<tr>
<th>Challenge</th>
<th>No. of Respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>12 (60%)</td>
</tr>
<tr>
<td>IT</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>Storage</td>
<td>9 (45%)</td>
</tr>
<tr>
<td>Integration of Work Flow</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>Reimbursement</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>Education</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>Regulations</td>
<td>2 (10%)</td>
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</tbody>
</table>

¹(N = 20)
## WSI Opportunities

Significant challenges exist that will need to be overcome to fully integrate WSI into a clinical setting.

<table>
<thead>
<tr>
<th>Cost</th>
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<tbody>
<tr>
<td>• Initial costs (both direct and indirect) of setting up a digital system – scanner, IT resource requirements, integration into workflow, informatics, FTEs – is non trivial.</td>
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<tr>
<td>• Scanner is still very expensive and digital images are expensive to store.</td>
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<thead>
<tr>
<th>Information Technology</th>
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<tbody>
<tr>
<td>• IT infrastructure is a limitation — very high speed is required to transfer a large amount of data related to digital slides.</td>
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<tr>
<td>• Protecting patient privacy over the internet is a concern.</td>
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<table>
<thead>
<tr>
<th>Regulations</th>
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<tr>
<td>• Presently there are no regulations in place governing quality and storage of slide images.</td>
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<tr>
<td>• FDA is looking into WSI and FDA involvement may help promote/demote the technology.</td>
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<tr>
<th>Storage</th>
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<td>• Digital images occupy considerable space on servers; it will be difficult to store and manage volumes of images.</td>
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<th>Reimbursement</th>
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<tr>
<td>• Reimbursement and valuation models require alterations to drive adoption among pathologists.</td>
</tr>
<tr>
<td>• Unclear return on investment will preclude heavy investment in the technology.</td>
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<tr>
<th>Integration of Work Flow</th>
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<tbody>
<tr>
<td>• Integration between LIS (Laboratory Information Systems) and image scanners / WSI process will be required to streamline workflow and abide by existing operational requirements/processes.</td>
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<tr>
<td>• Digital workflow is slower compared to analog workflow (short-term).</td>
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<thead>
<tr>
<th>Education</th>
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<tbody>
<tr>
<td>• Pathologists should be acquainted with the benefits of the technology to help them overcome potential negative perception of WSI.</td>
</tr>
<tr>
<td>• Pathologists need to be educated to ensure that they provide reliable results.</td>
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<thead>
<tr>
<th>Equipment Speed</th>
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<tr>
<td>• The slow speed of scanners is a significant challenge for a digital pathology model that aims to incorporate scanning at every step of the pathology workflow.</td>
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## Issues with WSI

<table>
<thead>
<tr>
<th>Feature</th>
<th>Problem</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Image acquisition</td>
<td>Too expensive</td>
<td>$0.91 per slide</td>
</tr>
<tr>
<td>Throughput</td>
<td>Too slow</td>
<td>6-7 minutes at 20x</td>
</tr>
<tr>
<td>Quality</td>
<td>Good enough for diagnosis?</td>
<td>Excellent at 20X</td>
</tr>
<tr>
<td>Storage</td>
<td>Too expensive</td>
<td>1.00 per slide per 30 days</td>
</tr>
<tr>
<td>Viewing</td>
<td>Too cumbersome, lack of standards</td>
<td>Real-time virtual microscope</td>
</tr>
</tbody>
</table>
## WSI Challenges

<table>
<thead>
<tr>
<th>Awareness</th>
<th>• Inform pathologists about benefits of WSI and remove their fear about adoption.</th>
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<tbody>
<tr>
<td>Education</td>
<td>• Develop the required WSI skill set by educating pathologists.</td>
</tr>
<tr>
<td>Guidelines/Standards</td>
<td>• Provide WSI guidelines to pathologists.</td>
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<tr>
<td></td>
<td>• Work with FDA and other government bodies to formulate, review, and communicate standards.</td>
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<td></td>
<td>• Ensure that legal implications for WSI do not pose a hurdle to adoption.</td>
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<tr>
<td>Collaborate with other associations</td>
<td>• Partner with other pathology associations to publish whitepapers to help develop a culture of digital pathology.</td>
</tr>
<tr>
<td>Reimbursement</td>
<td>• Incentivize research and offer grants for continuous development of the technology.</td>
</tr>
<tr>
<td></td>
<td>• Act as the spokesperson of American pathologists, in case of financial and legal issues.</td>
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WSI: Impact on US Pathologists

% of Respondents (N = 1,028)

Whole Slide Imaging will lead to significant outsourcing of slide interpretation to low-cost providers overseas

Disagree: 31%  
Neither Agree nor Disagree: 24%  
Agree: 46%

Whole Slide Imaging will lead to significant insourcing of slide interpretation to US pathologists from overseas

Disagree: 40%  
Neither Agree nor Disagree: 34%  
Agree: 26%
How Can WSI Improve Your Pathology Practice?
Apply Basic Business Strategy

• Strategies based on disruptive innovations have the highest chance of creating growth.
• Introduce benefits such as
  • Simplicity
  • Convenience
  • Ease of use
  • Lower price
The Disruptive Playbook

- **Scratch an unscratched itch**
  - Make it easier to get an important job done

- **Make an ugly business attractive**
  - Find a way to prosper at the low end of established markets by providing a good enough solution at low prices

- **Democratize a limited market**
  - Expand the market by removing barriers such as lack of skills or access
Applied Economic Implications of WSI

- **Make it easier to get an important job done**
  - Quantitative assessment
  - Find rare events
  - Obtain measurements easily
  - Simplify and improve access to second opinions

- **Make an ugly business attractive**
  - Reduce Fed Ex costs
  - Absorb specimens from rest of world

- **Democratize a limited market**
  - Centralize complex/difficult immunostains
  - Eliminate the need for to obtain space, people and equipment
Manpower/Resource Issues Potentially Addressed by WSI

- Shortage of qualified histotechnologists
- Potential shortage of subspecialty expertise
- High priced equipment without adequate volume – Stepwise growth
- Lack of space
- Competing resources
- More residents being trained in advanced technology but those technologies not available to them in the job market
What problem are you trying to solve?

- **Universities**
  - Reduce need for medical school slide sets
  - Reduce need for resident recuts
  - Keep permanent record of outside slide review
  - Provide support for outlying hospitals
  - Improve departmental reproducibility
What problem are you trying to solve?

- **Reference laboratories**
  - Reduce fed-ex costs
  - Improve turnaround time
  - Allow for 24 x 7 operation
  - Reduce need workforce requirements
  - Attract new customers
What problem are you trying to solve?

- **Small to Medium size laboratories**
  - Access second opinion
  - Frozen section outreach
  - Increase revenues
Who understood the problem space?
Motorola Lost Despite Winning its problem space

- Better
- Faster
- Cheaper

Today there are more texts than phone calls. Email, Apps, Web, etc…
Tumor sample from patient 37
ER(-), AR(-), p53(+) red, Her2(+) white,
keratin (green), actin (yellow),
nucleus (blue)
Increasing index value -> decreasing DFS

Key

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(dead with disease)
Issues for Another Day

• Picking Hardware
• Picking Software
• Project Manager
• Facilities
• IT
• Billing
• Contracting
Next in the Series of Free PHC Webinars

- **Next Generation Sequencing for the Clinical Laboratory, Wednesday, July 20th, 11:00-12:00 pm CT**
  - Karl Voelkerding, MD, FCAP

- Go to [www.cap.org/institute](http://www.cap.org/institute) For All Upcoming Webinars!

- Past Webinars Available Now Online at [www.cap.org/institute](http://www.cap.org/institute)
  - Accountable Care Organizations
  - Whole Genome Analysis as a Universal Diagnostic
  - How to Build and Fund a Financially Viable Molecular Lab
  - Cancer: The Critical Role of Pathology
  - Molecular Markers in Breast Cancer
  - Bethesda System: Integrating Cytology and HPV Molecular Testing
  - Molecular Diagnosis for Lung Cancer Patients
  - Molecular Diagnosis for Colorectal Cancer Patients
CAP Events of Interest

• Don’t Forget to Register for CAP’11 – THE Pathologists’ Meeting – September 11 – 14, 2011 held at the Gaylord Texan in Grapevine, Texas!

—Go to www.cap.org/CAP11 or call 1-800-967-4548. International attendees please call 1-847-996-5891.
6:30-7:45 am on Tuesday, Sept 12th:

**TP120 Breakfast Workshop – Hot Topics in Pathology: What Every Community Pathologist Should Know About Clinical Requests for Molecular Tests**
Panelists--Samuel K. Caughron, MD, FCAP
   Frederick L. Kiechle, MD, PhD, FCAP
   Michael S. Brown, MD, FCAP

8:00-11:30 am on Wednesday, Sept 13th:

**ST111 What’s in It for Me? Using Technology to Become a Diagnostic Hero**
Faulty--Kenneth J. Bloom, MD, FCAP
   John W. Turner, MD, FCAP

8:00-9:00 am on Wednesday, Sept 13th:

**ST110 Direct-to-Consumer Genetic Testing: Staying Ahead of Patients in This Current Trend**
Faulty--Nazneen Aziz, PhD
   Elizabeth A. Mansfield, PhD