



Cytology in the Digital Era: Challenges and Opportunities

David C. Wilbur, M.D.
Massachusetts General Hospital
Harvard Medical School
Boston, MA, USA



25 Ulusal Patoloji Kongresi
6. Sitopatoloji Kongresi

14 - 17 Ekim 2015 / Merinos AKKM - BURSA



Disclosures – David C. Wilbur

Scientific Advisory Boards

Corista LLC – no compensation

VisionGate – equity position

Massachusetts General Hospital Grants

Philips – no compensation



Pathology

Massachusetts General Hospital

Axioms and Hypotheses

- Digital pathology is already here
- We all use digital technology everyday
- Digital technology makes our lives easier
- The younger generation will embrace
- The younger generation will demand it

however.....

- There are still issues in routine use

Digital pathology is possible because ...

1) High resolution image capture – less expensive

2) Internet bandwidth has dramatically improved

- rapid transmission of images and information

- image compression technology speeds transmission without degradation of useful information

4) Computing power/storage dramatically increased

.....and.....

5) Advanced algorithm development will power advances

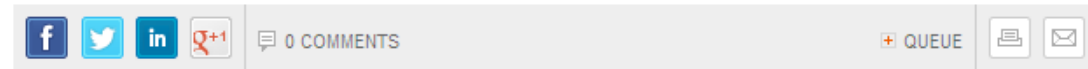
- machine decision-making, learning, and use of “big data”



1975 - Kodak invented the world's first digital camera. The prototype was the size of a toaster and captured black-and-white images at a resolution of 10,000 pixels (.01 megapixels).


2012 -- Kodak Files for Bankruptcy as Digital Era Spells End to Film

By Dawn McCarty & Beth Jinks - Jan 19, 2012 1:53 PM ET



Eastman Kodak Co. (EK), the photography pioneer that introduced the Brownie Camera more than a century ago, filed for bankruptcy after consumers embraced digital cameras, a technology Kodak invented and failed to commercialize.

The Rochester, New York-based company, which traces its roots to 1880, listed assets of \$5.1 billion and debt of \$6.8 billion in Chapter 11 documents filed in U.S. Bankruptcy Court in Manhattan.

 Enlarge image



"They were a company stuck in time," said Robert Burley, an associate professor at Toronto's Ryerson University who has photographed shuttered Kodak facilities in the U.S., Canada and France since 2005. "Their history was so important to them, this rich century-old history when they made a lot of amazing things and a lot of money along the way. Now their history has become a liability."

The company's credit deteriorated as revenue tumbled from traditional film, and the inventor of the Instamatic cameras was slow during the past decade to compete with Canon Inc. and Hewlett-Packard Co. in digital cameras and printers



Dell Projects Icahn Buyout Has \$3.9 Billion Funding Gap +



Japan's Floating Bullet Train Passes \$64 Billion Test +



Analog

24 or 36 pictures

Requires processing

Hours/days for pictures

Mail for transport

Non-reusable

Manipulation possible but difficult

? Better colors/resolution



Digital

10,800 pictures

No processing

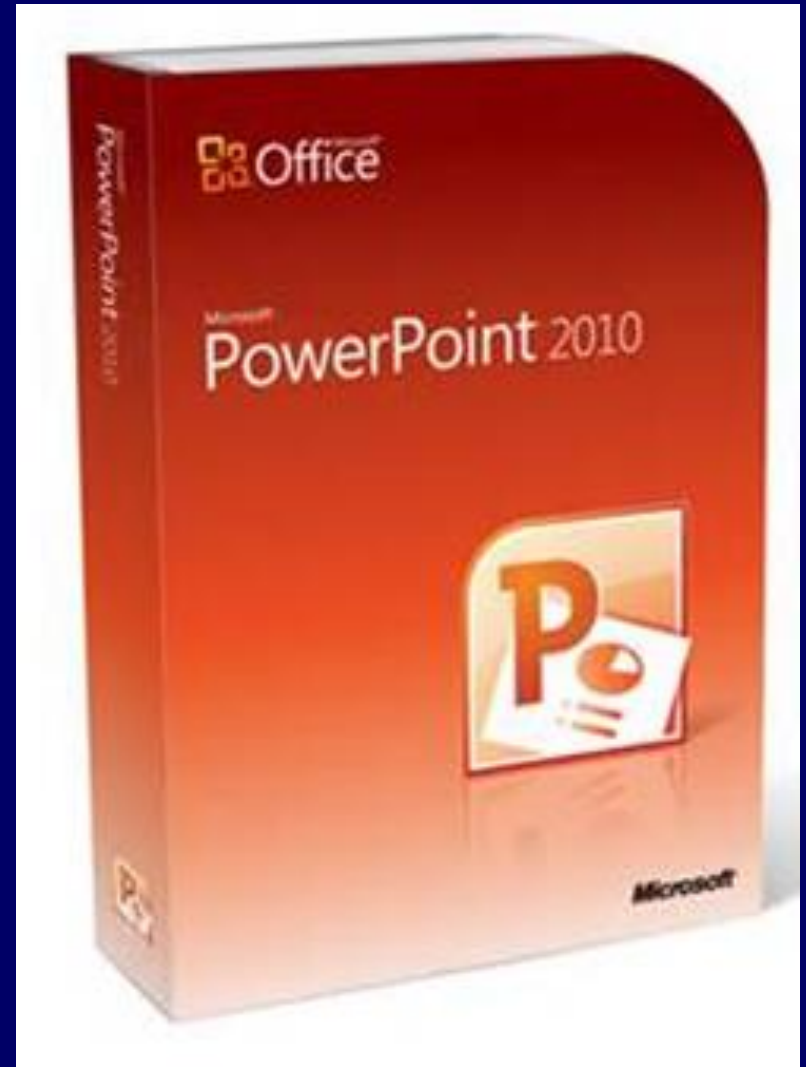
Pictures instantly

Instant internet delivery

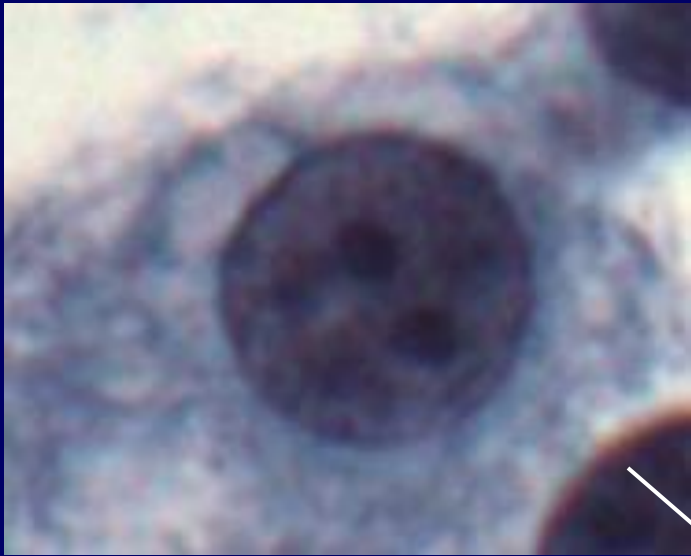
Reusable – 1000x

Manipulation easy

?????

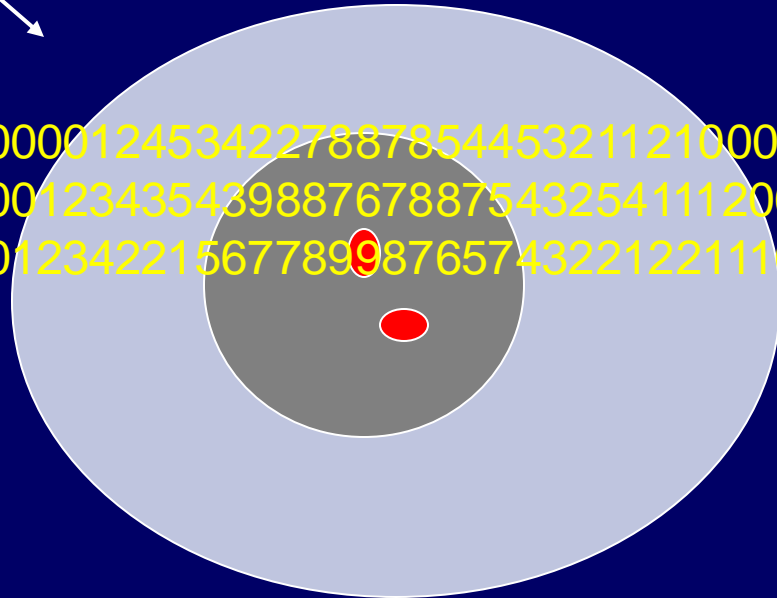


Then.....and.....Now



Digitization

000000000000124534227887854453211210000000000
00000000000123435439887678875432541112000000000
0000000000123422156778998765743221221110000000



** the smaller the pixels in a defined space (more pixels) the finer the resolution

Digital Cytology - Utility

- Teleconsultation
- Quality assurance
- Proficiency testing
- Continuing education
- Analytics
 - image/data mining

Telepathology

Telepathology – clinical services

- basic services to remote/uncovered areas
- night call from home
- rapid cytology/frozen sections
- expert consultative services to any area
- expert secondary opinions

Quality Assurance

- review of slides from remote sites
- by multiple people
- continuous monitoring
- teleconferencing – tumor boards

Proficiency Testing

- validated challenges
- given anywhere, anytime

Connect

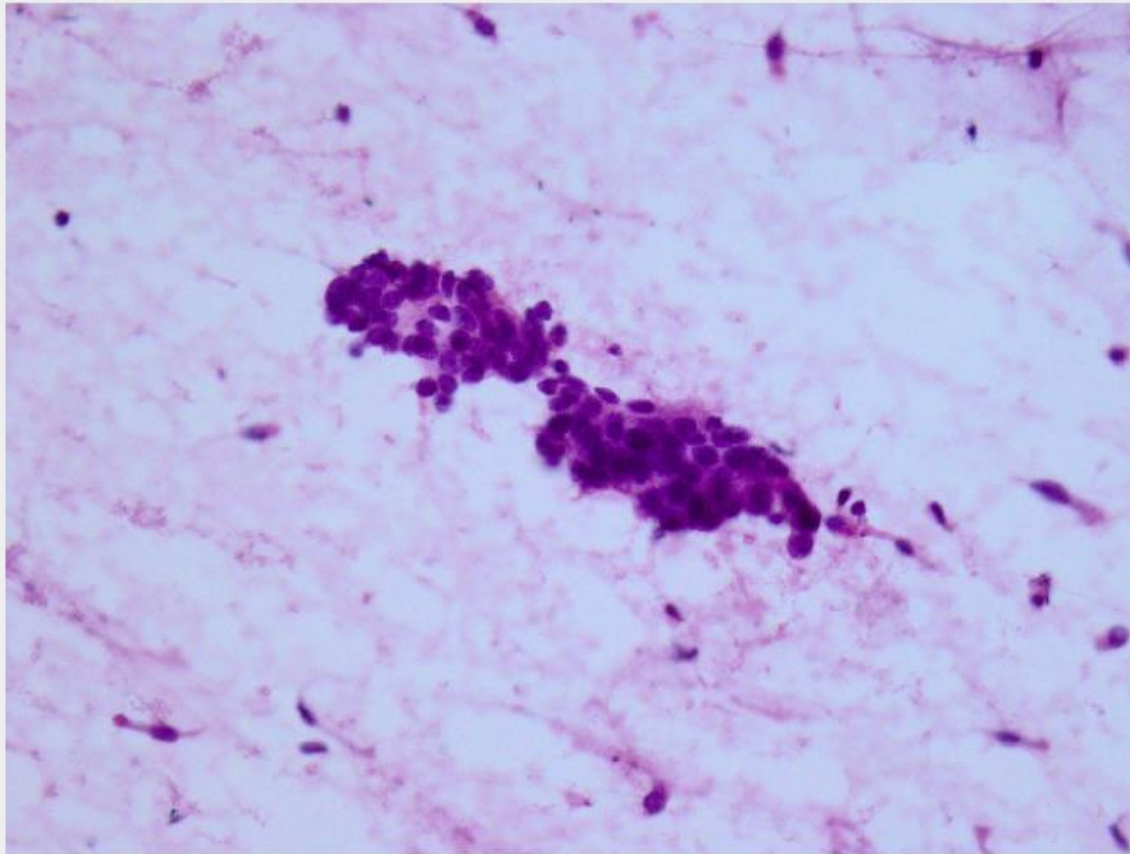
To connect to the NetCam Server, please press the "connect" button on this page below.

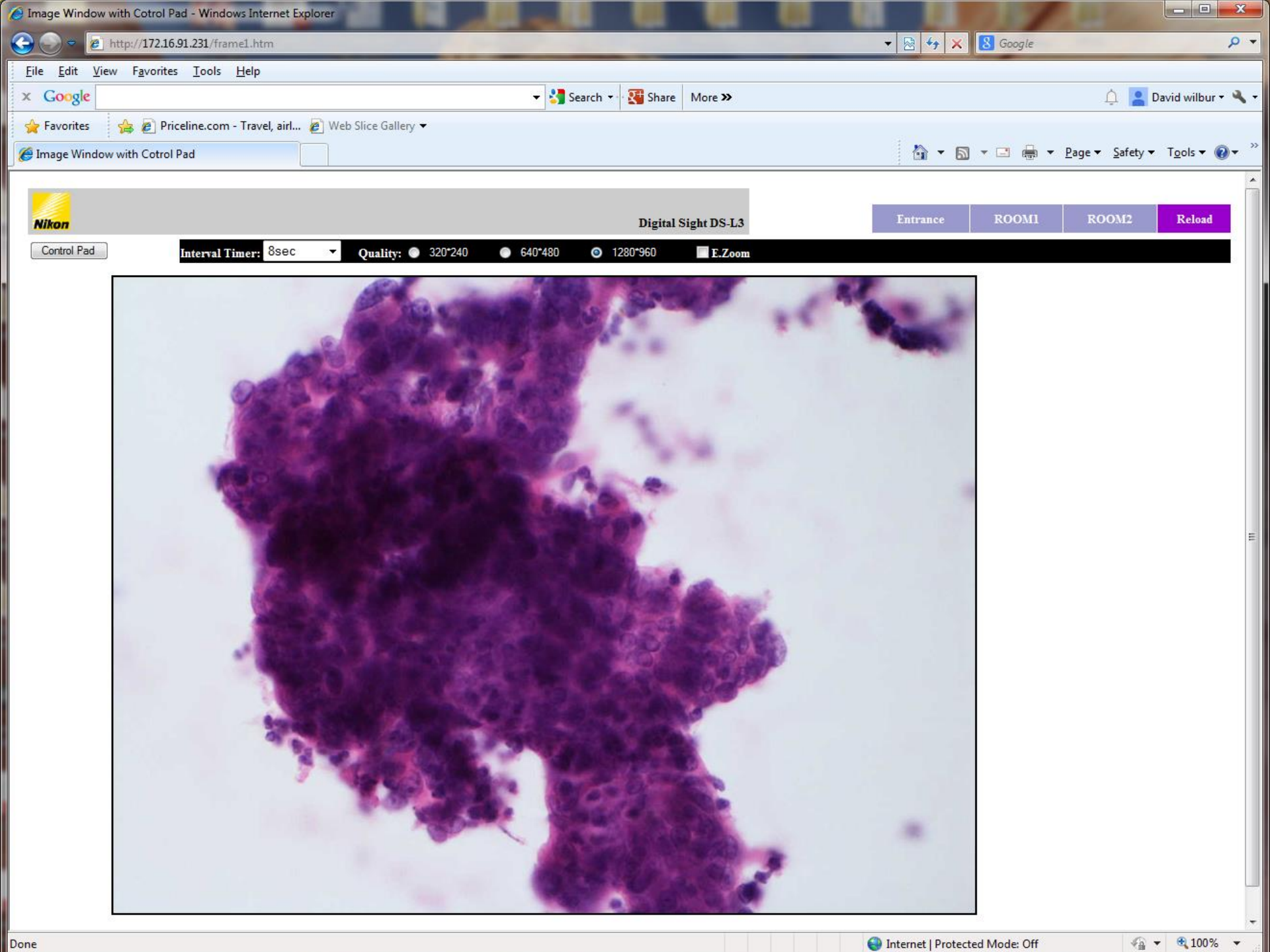
Back

Help

Connect

Disconnect





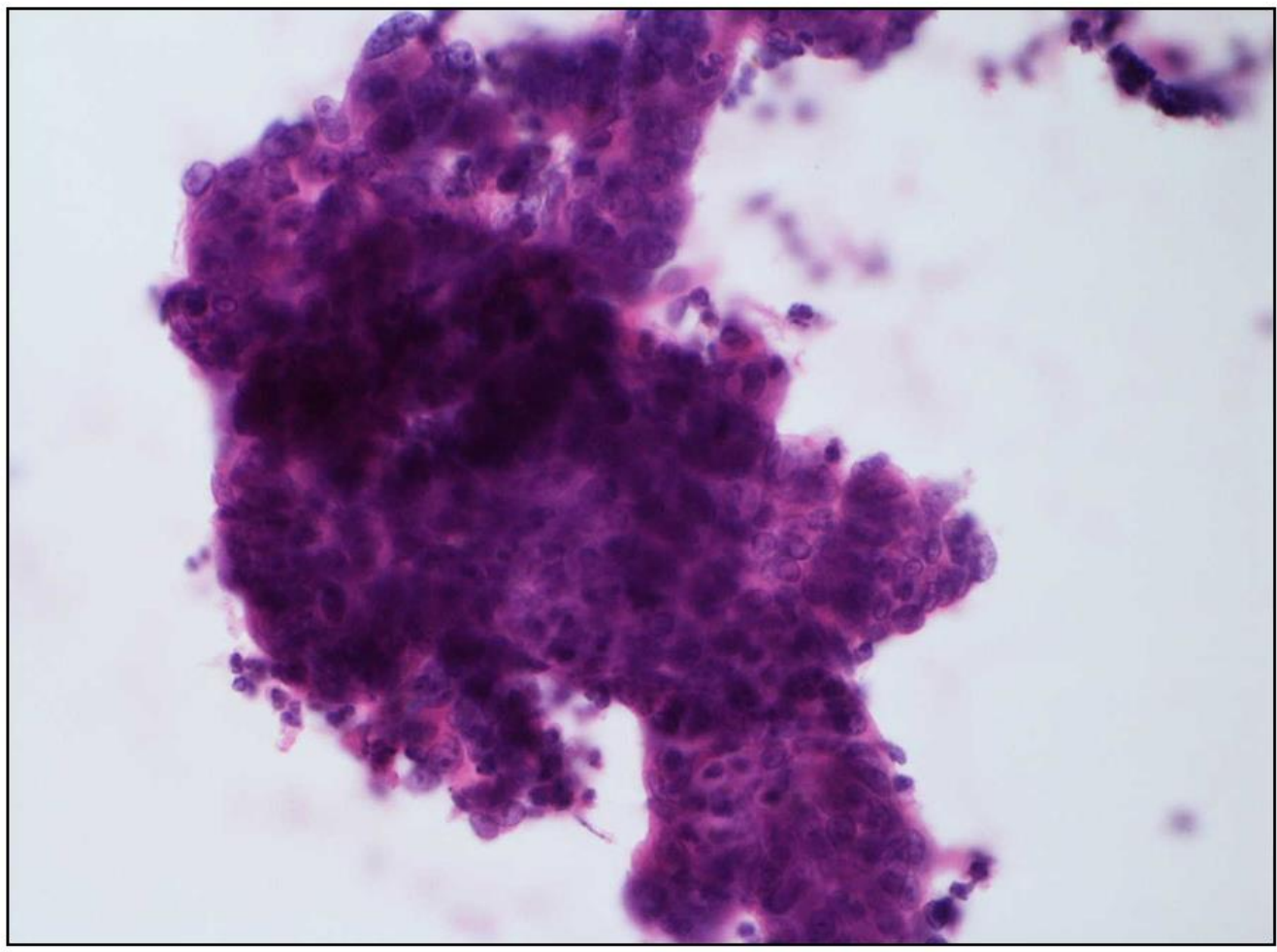
Digital Sight DS-L3

Entrance ROOM1 ROOM2 Reload

Control Pad

Interval Timer: 8sec

Quality: 320*240 640*480 1280*960 E.Zoom



My Computer, PanoptiqV, Set up applications, CopathLiv, Recycle Bin, Microsoft Outlook, amazon, Amazon Cloud Player, GoToMeet..., Visiongate CellGazer, Mozilla Firefox, Visiongate CellGazer, QCapture.exe, VLC media player, Dropbox, gosetup, Q-Capture Pro 7, CardMind, Google Chrome, ScanSnap Organizer

Image Window with Cotrol Pad - Windows Internet Explorer
http://172.16.91.231/frame1.htm

File Edit View Favorites Tools Help

Google

Image Window with Cotrol Pad

Nikon Digital Sight DS-L3

Entrance ROOM1 ROOM2 Reload

Control Pad Interval Timer: 8sec Quality: 320*240 640*480 1280*960 E.Zoom



Slide 33 of 40 "Office Theme"

Done Internet | Protected Mode: Off 100%

images, 29 Neuroendo...

Peru Teleconsultation – WebX Realtime

The screenshot displays a WebX Realtime teleconsultation session. The main window is titled "You are viewing: Nick Jones's Desktop" and shows a microscope image of a tissue sample. The image is displayed in a large window with a control panel on the left. The control panel includes sections for "Imaging Control", "Capture Control", "Camera Control", and "Capture Options".

Imaging Control: Includes buttons for "Remove", "Update", "Add", "White Balance", and "Area WB".

Capture Control: Includes a "Capture" button.

Camera Control: Includes sliders for "Exposure (ms)" (0 to 500, current value 1.174), "Average Intensity [0..255]" (Darker 206, Brighter), "Gain" (1 to 23.8154, current value 7.51563), and "Gamma" (0.01 to 5, current value 1.82). There is also a checkbox for "Enable camera cooling".

Capture Options: Includes "Time Lapse" and "Image Orientation".

The taskbar at the bottom shows the Start button, Google, and several open applications: "Inbox - Microsoft ...", "Microsoft Word", and "Microsoft...". A chat window is open in the bottom right corner, displaying a conversation:

Chat
to Nick Jones (privately):
LSIL
from Nick Jones to Everyone:
go
from Nick Jones to Everyone:
done
to Nick Jones (privately):
LSIL
from Nick Jones to Everyone:
go

The "Send to:" dropdown is set to "Nick Jo... (Host & Presenter)".

The system tray in the bottom right corner shows the time as 3:56 PM on 5/27/2011.

Peru Teleconsultation

The screenshot displays a GoToMeeting teleconsultation session. The main window shows a histology slide of a tissue sample, likely a Pap smear, with a central cluster of dark purple-stained cells. The interface includes a menu bar (File, Options, View, Help) and a toolbar with icons for screen sharing, audio, and chat. The right-hand side of the screen features a control panel with the following sections:

- Screen Sharing:** Now viewing cerviscusco's screen. Includes buttons for Show My Screen, Stop Showing Screen, Give Keyboard & Mouse, and Change Presenter.
- Attendee List (4 | Max 26):** A table listing participants:

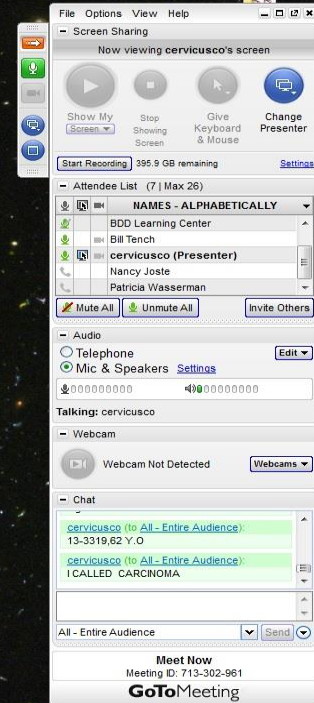
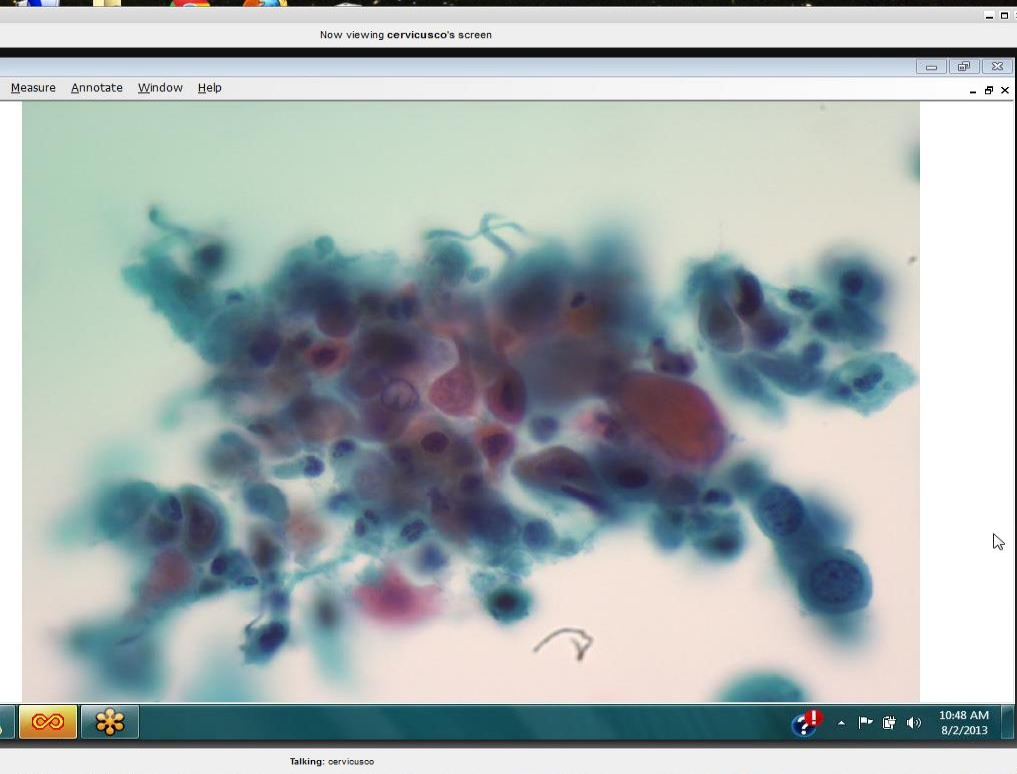
NAMES - ALPHABETICALLY	
Stephen Conley (Organizer, Me)	
Barbara K.	
bill tench	
cerviscusco (Presenter)	
- Audio:** Telephone (selected) and Mic & Speakers. Dial: +1 (267) 507-0016, Access Code: 133-412-833. Status: You are connected to audio.
- Webcam:** Webcam Not Detected. Webcams dropdown menu.
- Chat:** Messages from cerviscusco to All - Entire Audience: "13-11, Y.O ?" and "I CALLED LSL".
- Meet Now:** Meeting ID: 133-412-833, GoToMeeting logo.

The Windows taskbar at the bottom shows the Start button, taskbar icons for Internet Explorer, Windows Explorer, Skype, and GoToMeeting, and a system tray with the time 10:20 AM on 1/11/2013.

Peru Teleconsultation

The screenshot displays a GoToMeeting teleconsultation session. The main window shows a histology slide titled "INFINITY 2-2C-188039" with a menu including Database, Field, Adjust, Enhance, Measure, Annotate, Window, and Help. The slide content shows a microscopic view of cells stained with hematoxylin and eosin (H&E). The control panel on the right includes a "Screen Sharing" section with "Now viewing cervusco's screen", a "Start Recording" button (79.0 GB remaining), and an "Attendee List" (2 / Max 25) showing "IAMES - ALPHABETICALLY" with participants "Stephen Conley (Organizer, Me)" and "cervusco (Presenter)". The "Audio" section shows "Telephone" selected and "Mic & Speakers" as the active device. The "Webcam" section shows "Webcam Not Detected". The "Chat" section shows a message from "cervusco (to All - Entire Audience): 12-158,45 Y.O" and another from "cervusco (to All - Entire Audience): I CALLED HSIL". The "Meet Now" section shows "Meeting ID: 740-276-712" and the "GoToMeeting" logo. The Windows taskbar at the bottom shows the time as 10:34 AM on 11/30/2012, with icons for Start, GoToMeeting, and Microsoft Outlook.

Peru Teleconsultation



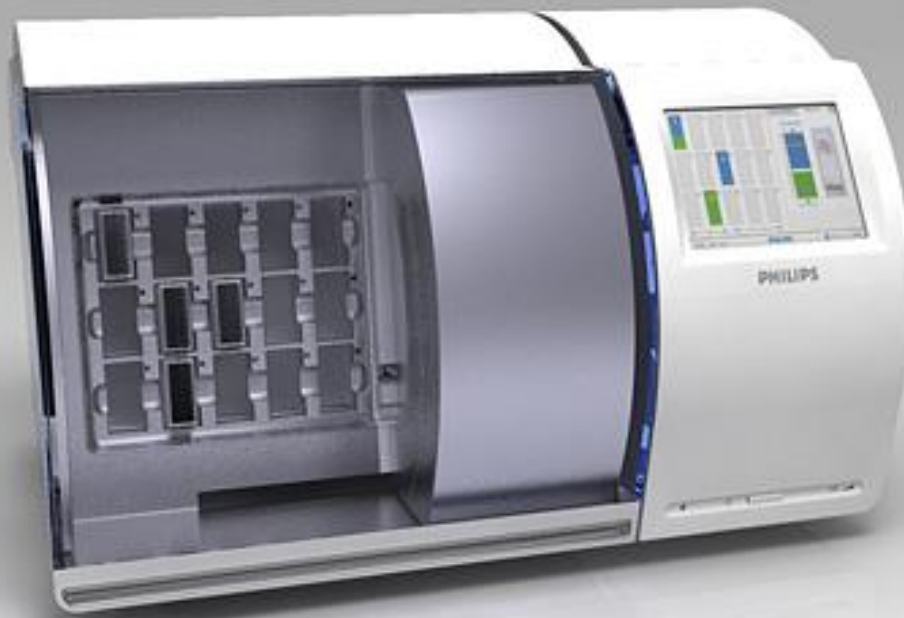
Over 1,150 interpretations over the past 4 years
Over 250 high-grade lesions and carcinomas have been identified
Cyto-histo correlation – 96% accuracy on initial review



WSI Facility at Holy Family Hospital, Rawalpindi with Massachusetts General Hospital, Boston
Supported by US State Department Development Grant



Supported by US Army Medical Research and Materiel Command PR033199



High volume – high speed scanner

Viewer

Corista - Mozilla Firefox

File Edit View History Bookmarks Tools Help

Corista

corista.partners.org/cases/87#slides-tab

HOME > N12-5271 > N12-5271 B1-1_20X.SWS

Assigned to Dr. David Wilbur 83 year old female, LILLIAN G. GAGLIARDI Dr. David Wilbur

Slides Annotations Consultations Diagnoses QA

Drag Annotation Measure Overview 10.0x Max

B. KIDNEY [CORE] BIOPSY, RIGHT

B. KIDNEY [CORE] BIOPSY, RIGHT
Taken On 2012-05-14

Description
B. KIDNEY [CORE] BIOPSY, RIGHT: Received in formalin, container labeled with patients name and MRN 0808971, is an aggregate of cylindrical soft tissue, measuring 0.6 x 0.5 x 0.2 cm. Entirely submitted in B1. D. KIDNEY [CORE] BIOPSY, RIGHT INTERPOLAR: Received in formalin, container labeled with patients name and MRN 0808971, is an aggregate of cylindrical soft tissue, measuring 0.8 x 0.6 x 0.2 cm. Entirely submitted in D1.

N12-5271 B1-1_20x.sws

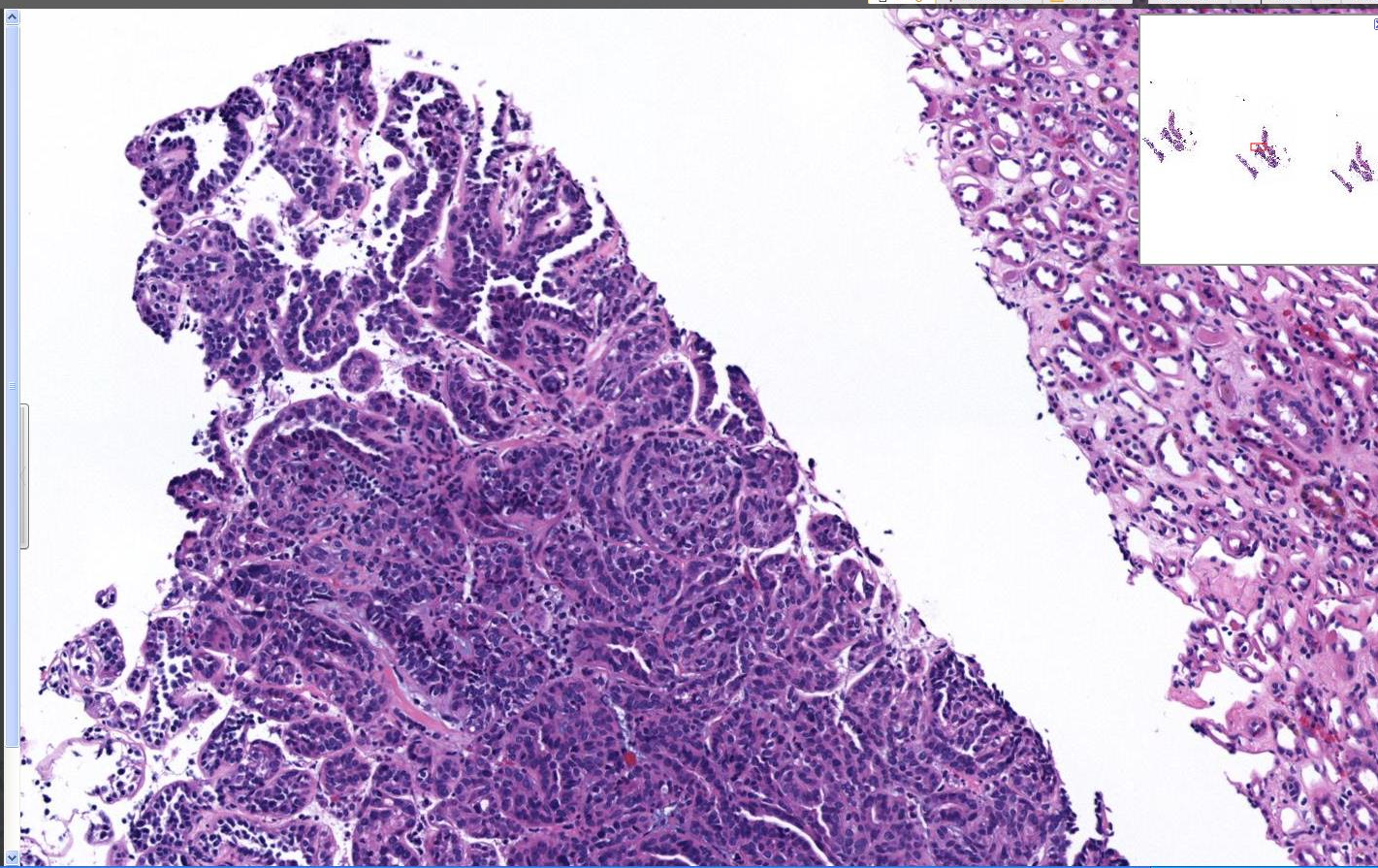
N12-5271 B1-2_20x.sws

D. KIDNEY [CORE] BIOPSY, RIGHT INTERPOLAR

D. KIDNEY [CORE] BIOPSY, RIGHT INTERPOLAR
Taken On 2012-05-14

Description
D. KIDNEY [CORE] BIOPSY, RIGHT INTERPOLAR: Received in formalin, container labeled with patients name and MRN 0808971, is an aggregate of cylindrical soft tissue, measuring 0.8 x 0.6 x 0.2 cm. Entirely submitted in D1.

N12-5271 D1-1_20x.sws



Viewer

Corista - Mozilla Firefox

File Edit View History Bookmarks Tools Help

Corista

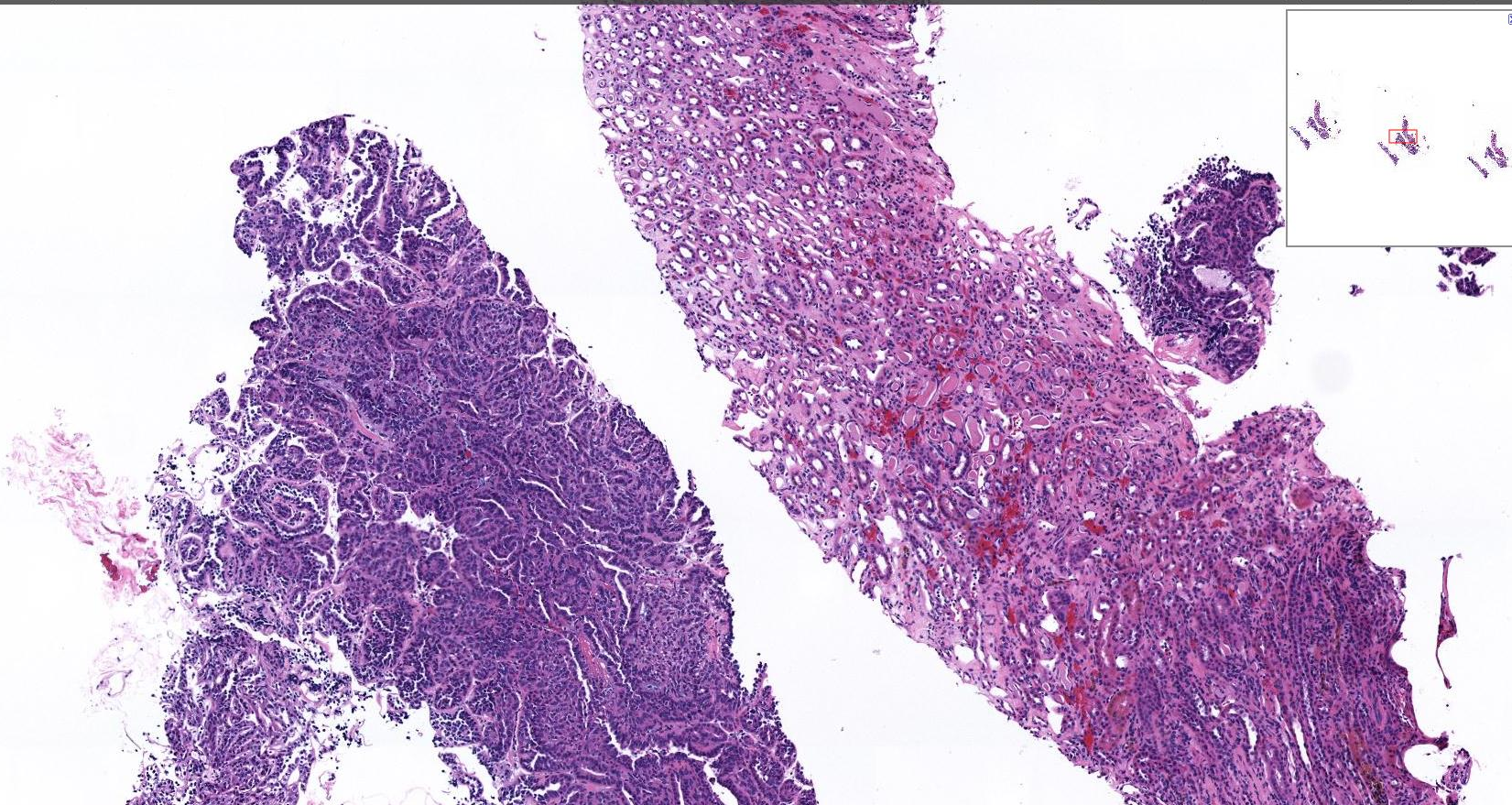
corista.partners.org/cases/87#slides-tab-270

Assigned to Dr. David Wilbur 83 year old female, LILLIAN G. GAGLIARDI Dr. David Wilbur

HOME > N12-5271 > N12-5271 B1-1_20X_SWS

Slides Annotations Consultations Diagnoses QA

Drag Annotation Measure Overview 5.0x Max



start

Inbox - Microsoft Out... CoPathPlus (copath) ... 4.6.0 Monday Dec ... Microsoft Word Microsoft PowerPoint ... Corista - Mozilla Firefox

2:39 PM

Consultation

File Edit View History Bookmarks Tools Help

http://mgh.meta.corista.6790/cases/304/specimens/5477/slide_id=973

New Bookmark MGH - Corista Portal DHMC - Corista Portal

corista Logged in as: Dr. David Wilbur

Home Logout

Lymph node

Enlarged hilar lymph nodes., for Button, Benjamin, 36 year old Male, taken from 2r 166 days ago, accessioned 166 days ago

0.6x

Consults Details Diagnosis Slides

New

Consultation with Dr. Ivan Chebib


On 11/29/2010 at 02:28 PM, dwilbur@mgh said:
Ivan - would you do special stains?

On 11/29/2010 at 02:30 PM, lchebib@mgh said:
No - I would just sign out as granulomatous

Invite

ok thanks

Delete



My Profile



[Upload New Photo](#)
[My Digital Slide Viewers](#)

General Information

* First Name:

* Last Name:

Email Address:

Contact Phone: (For ex - 1-234-567-8901)

User Type:

NPI Number:

Active Consultant:

Address 1: Public

Address 2:

City:

State:

Zip:

Speciality:

License Information:	License Number	License State
	Massachusetts	MA
	New York	NY
	Add License	

Outside U.S. Fee Schedule	Fee Schedule	Price	Processing Fee (50%)	Total
	Consult Fee (1 - 10 Slides)	<input type="text"/>	<input type="text"/>	<input type="text"/>

Potential Future Uses

- 1) Centralized pathology services in established networks
- 2) Specialty pathology services for underserved areas
- 3) Regional, national, international
- 4) Expansion to other image-based applications

Questions still to be addressed

- Is telepathology as accurate as slide interpretation
- Are errors similar to errors on glass slides
- Is telepathology less expensive
- Will telepathology increase consultation volume
- Will telepathology improve QA practice
- Will telepathology make CME more cost-effective
- Will pathologists readily adapt to the technology

Pilot Projects Done to Date

- WSI – Brazil pilot

Wilbur DC, Madi K, Colvin RB, Duncan LM, Faquin WC, Ferry JA, Frosch MP, Houser SL, Kradin RL, Lauwers GY, Louis DN, Mark EJ, Mino-Kenudson M, Misdraji J, Nielsen GP, Pitman MB, Rosenberg AE, Smith RN, Sohani AR, Stone JR, Tambouret RH, Wu CL, Young RH, Zembowicz A, Klietmann W. [Whole-slide imaging digital pathology as a platform for teleconsultation: a pilot study using paired subspecialist correlations](#). Arch Pathol Lab Med. 2009;133:1949-53.

- WSI – UMASS frozen section pilot

Fallon MA, Wilbur DC, Prasad M. [Ovarian Frozen Section Diagnosis: Use of Whole Slide Imaging Shows Excellent Correlation between Virtual Slide and Original Interpretations in a Large Series of Cases](#). Arch Pathol Lab Med 2010;134:1020-3.

- Dartmouth pilot – WSI

Pilot true subspecialty consult service

- Pakistan WSI consultation/education service

Pilot international static/dynamic/WSI service

- Cambridge Health Alliance consultation service

- Jones NC, Nazarian RM, Duncan LM, Kamionek M, Lauwers GY, Tambouret RH, Wu, C-L, Nielsen GP, Brachtel EF, Mark EJ, Sadow PM, Grabbe JP, Wilbur DC. Interinstitutional WSI Teleconsultation Service Development: Assessment using Internal Training and Clinical Consultation Cases. Arch Pathol Lab Med 2015;139:627-35.

Continuing Education

From anywhere to anywhere

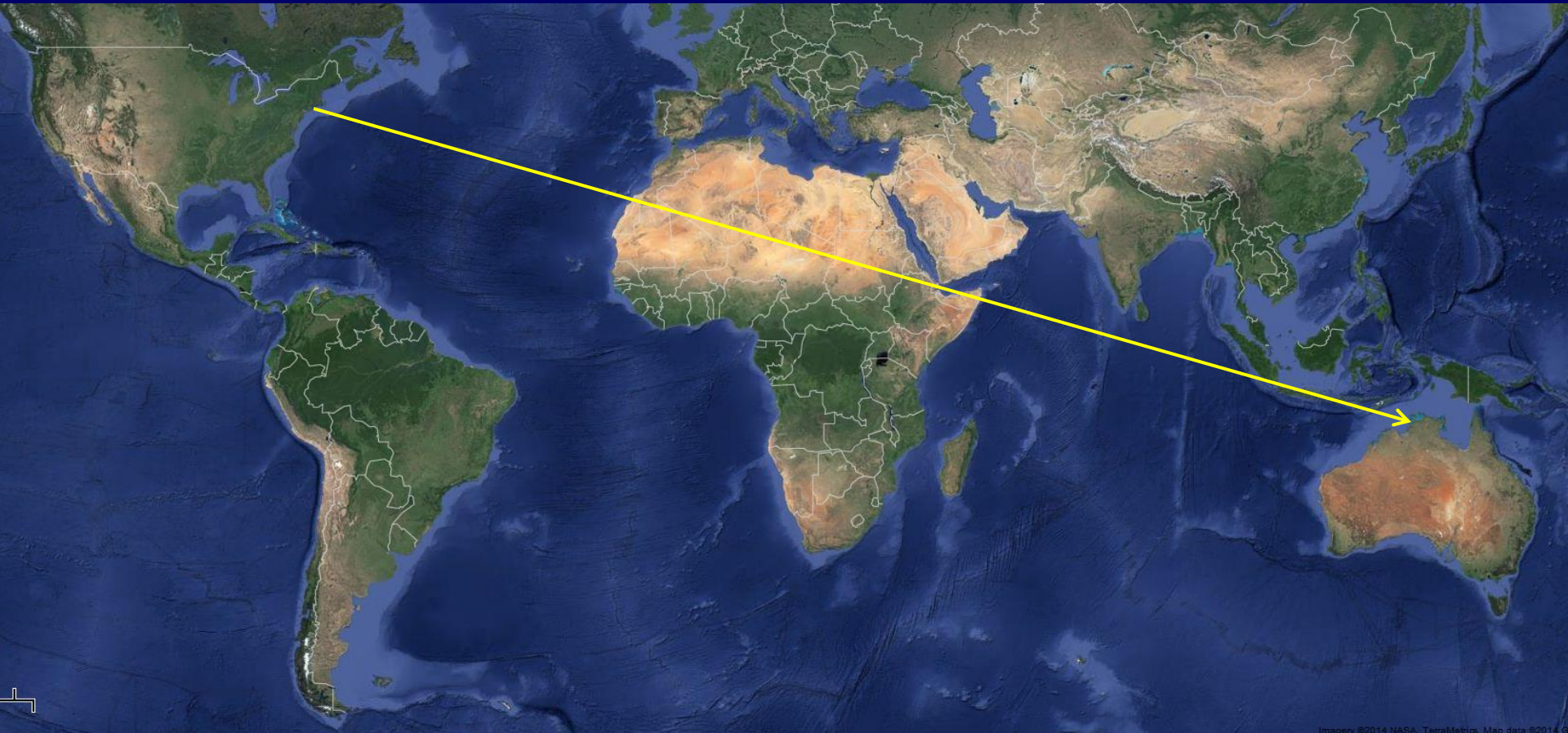
With any number of viewers

Cost – minimal

Speed – OK (you be the judge)

Virtual meetings – like the present

Archiving of live events

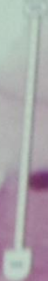


From Boston to Darwin – by telepathology link



LSI

38.0x



Stephen Conf...

Darwin Produ...



Case Of The Month

Presented by the Pathology Service at the Massachusetts General Hospital

MASSACHUSETTS
GENERAL HOSPITAL



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[Hematopathology](#) (3)

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[March 2009](#) (1)

[February 2009](#) (1)

[January 2009](#) (1)

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Archives for March, 2009

72 year-old male with a splenic mass

Posted by [Russell Ryan, M.D.](#) on Tuesday, March 3rd 2009

Clinical History

A 73 year-old man presented to the emergency room with severe, spontaneous abdominal pain. At laparotomy, he was found to have a hemoperitoneum and splenic rupture. A splenectomy was performed and the specimen was sent for pathological examination.

Three and a half years earlier, the patient had been diagnosed with chronic lymphocytic leukemia (CLL). An abdominal CT scan at that time revealed a 5 cm splenic mass with heterogeneous attenuation as well as periaortic and portocaval lymphadenopathy.



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DWILBUR@PARTNERS.ORG

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[72 year-old male with a splenic mass](#)

[Young Man with Finger Mass](#)

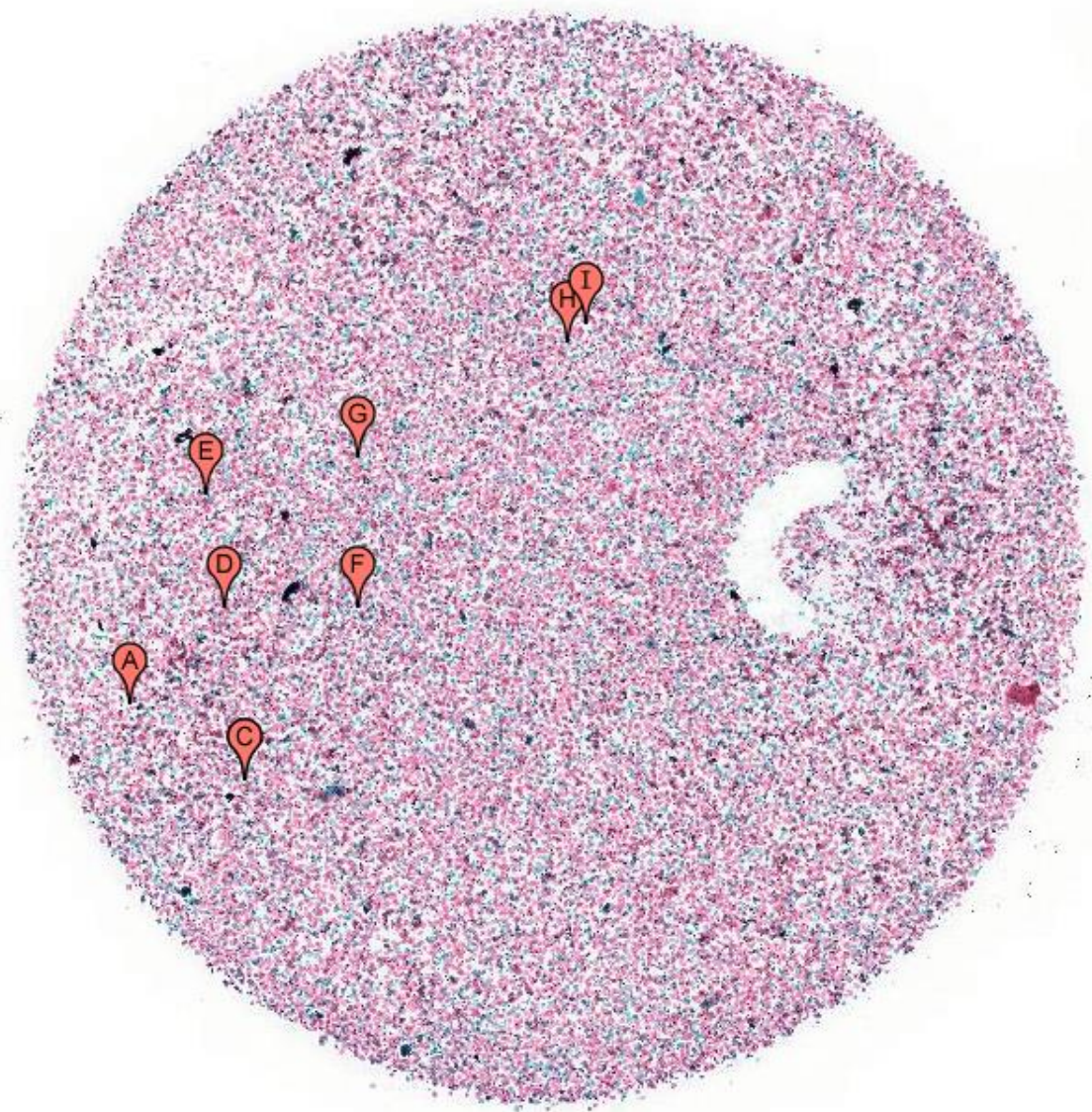
[Radiation Exposure](#)

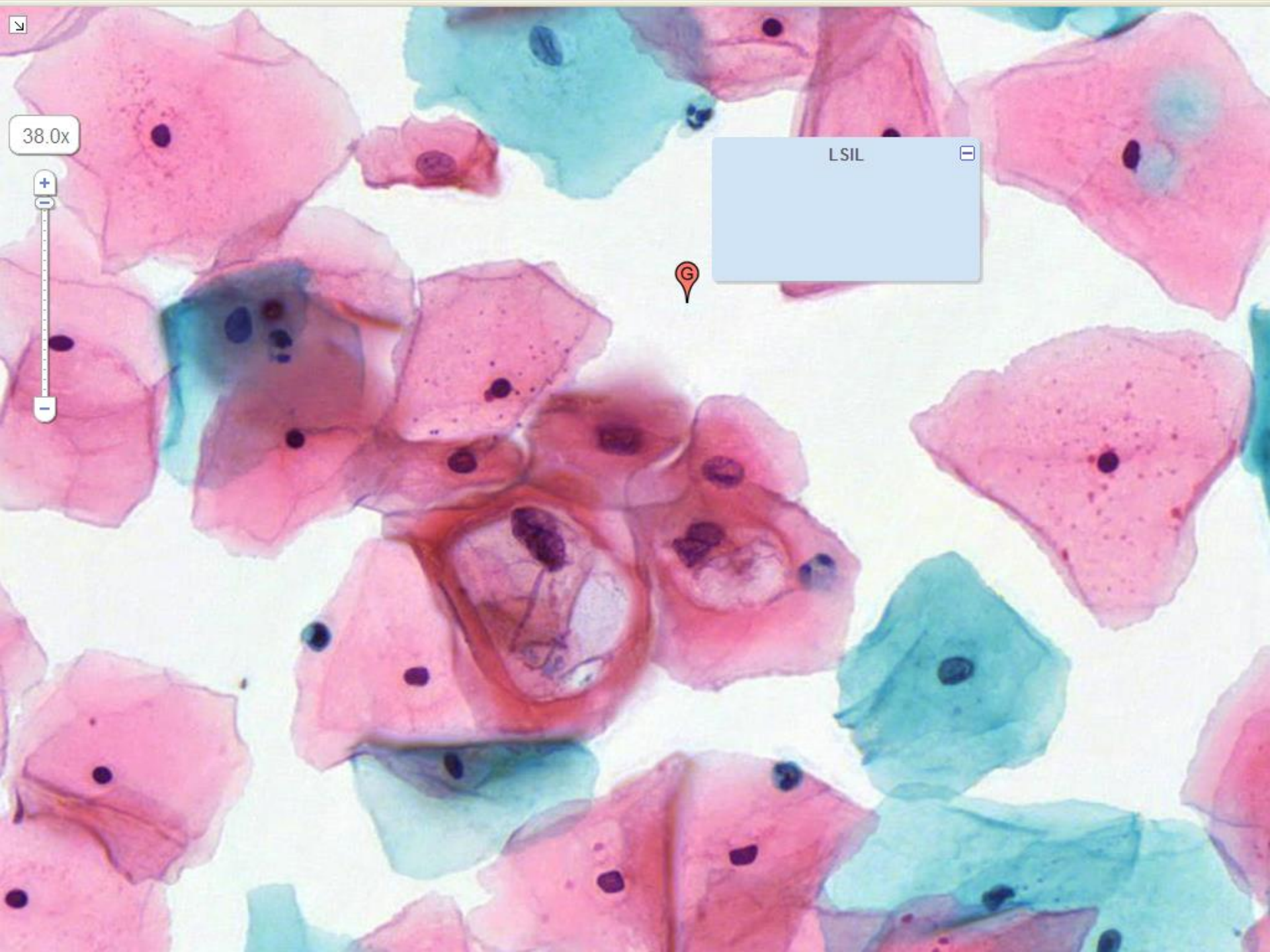


Slide Archiving – Digital Study Boxes



0.6x





LSIL

38.0x

+

0

1



Ariel D. Bravy

Impediments to Adoption

- Cost of scanning devices
- Device interface issues
- Information technology issues
- HIPAA (patient information confidentiality)
- Regulatory/FDA
- Medico-legal considerations

Challenges

Ergonomics

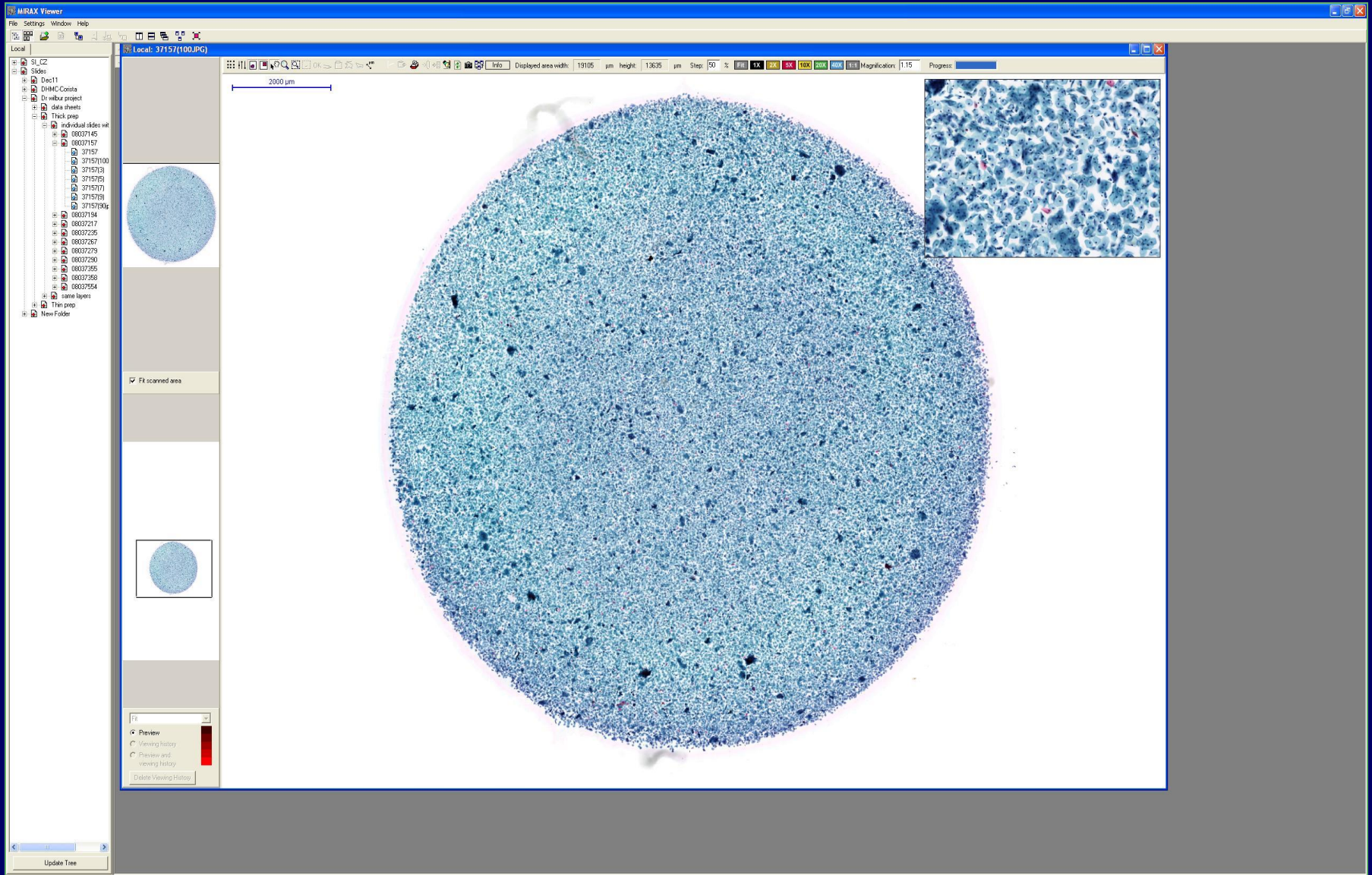
3-dimensionality

Slide areas large - thresholding

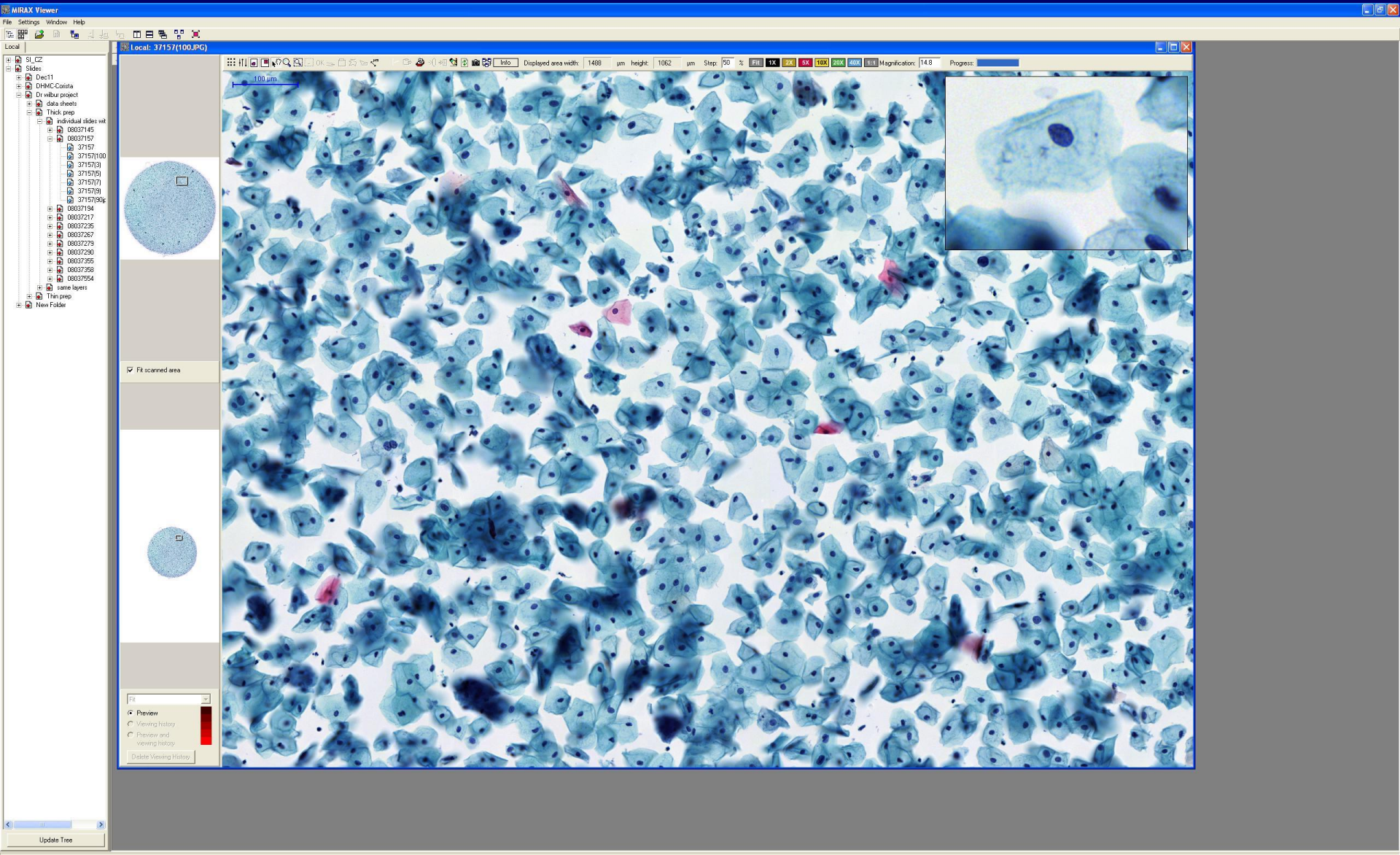
Analytics still developing

“Engineering problems”

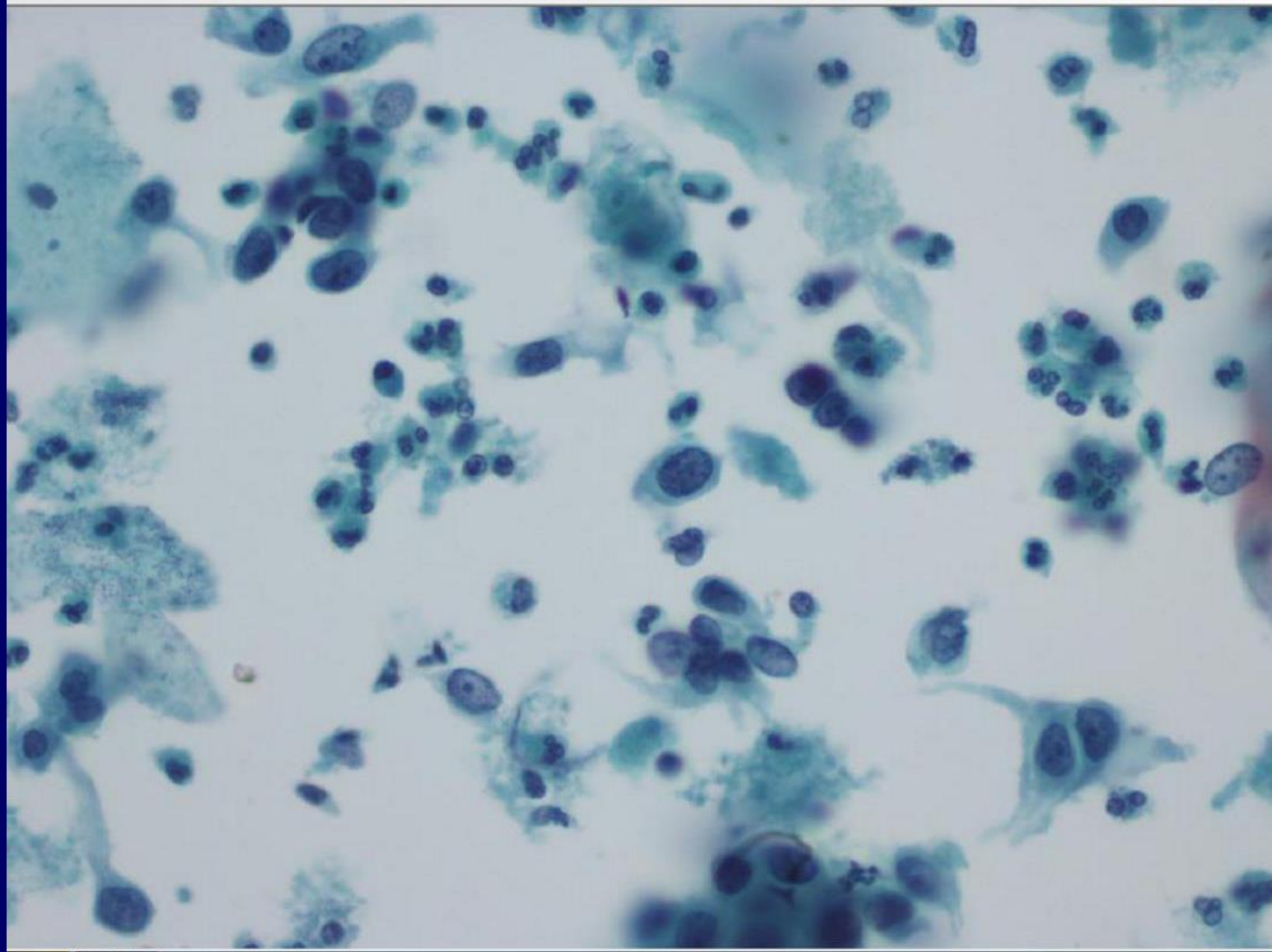
Cytology Specimen



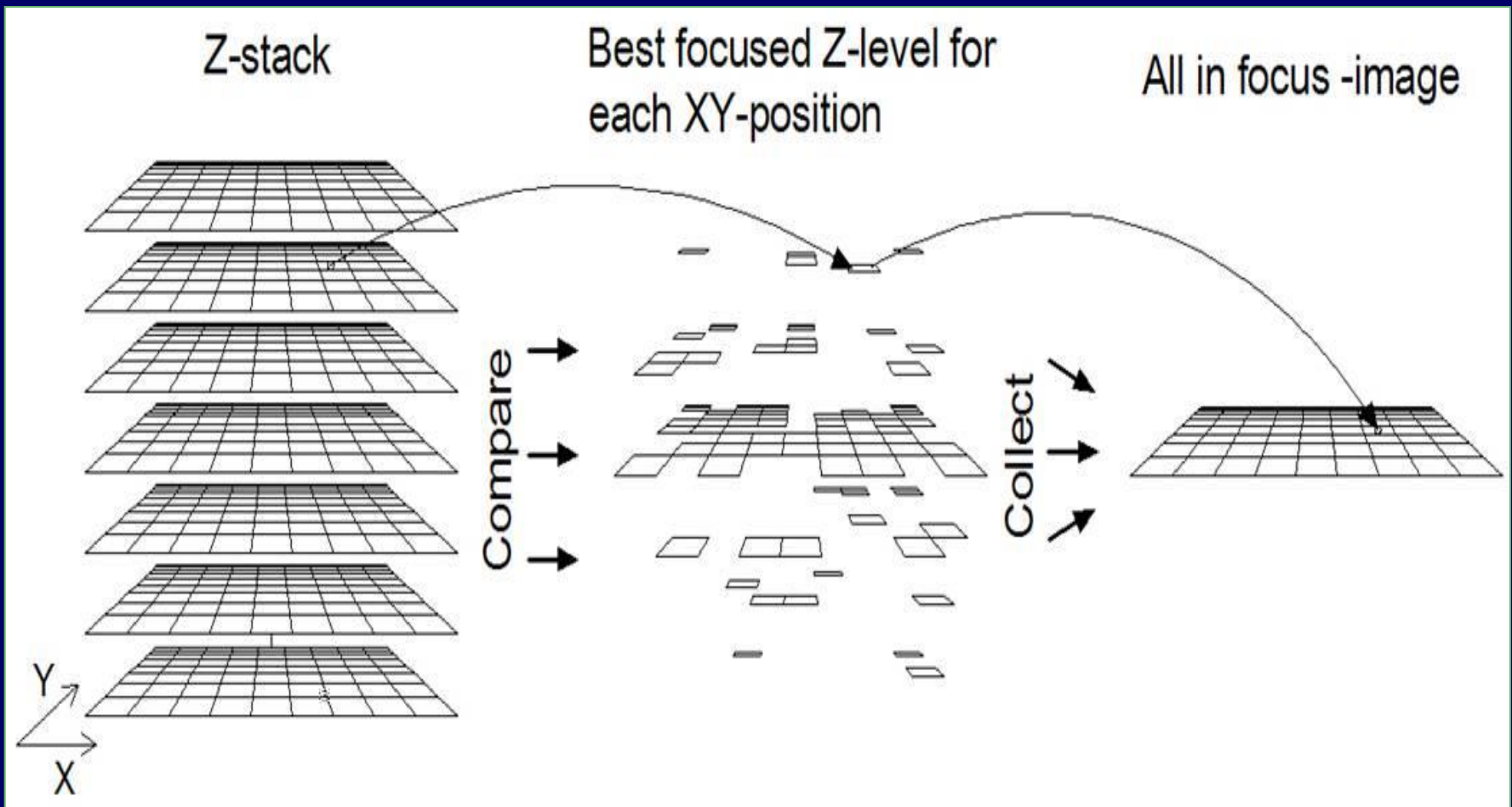
Cytology Specimen



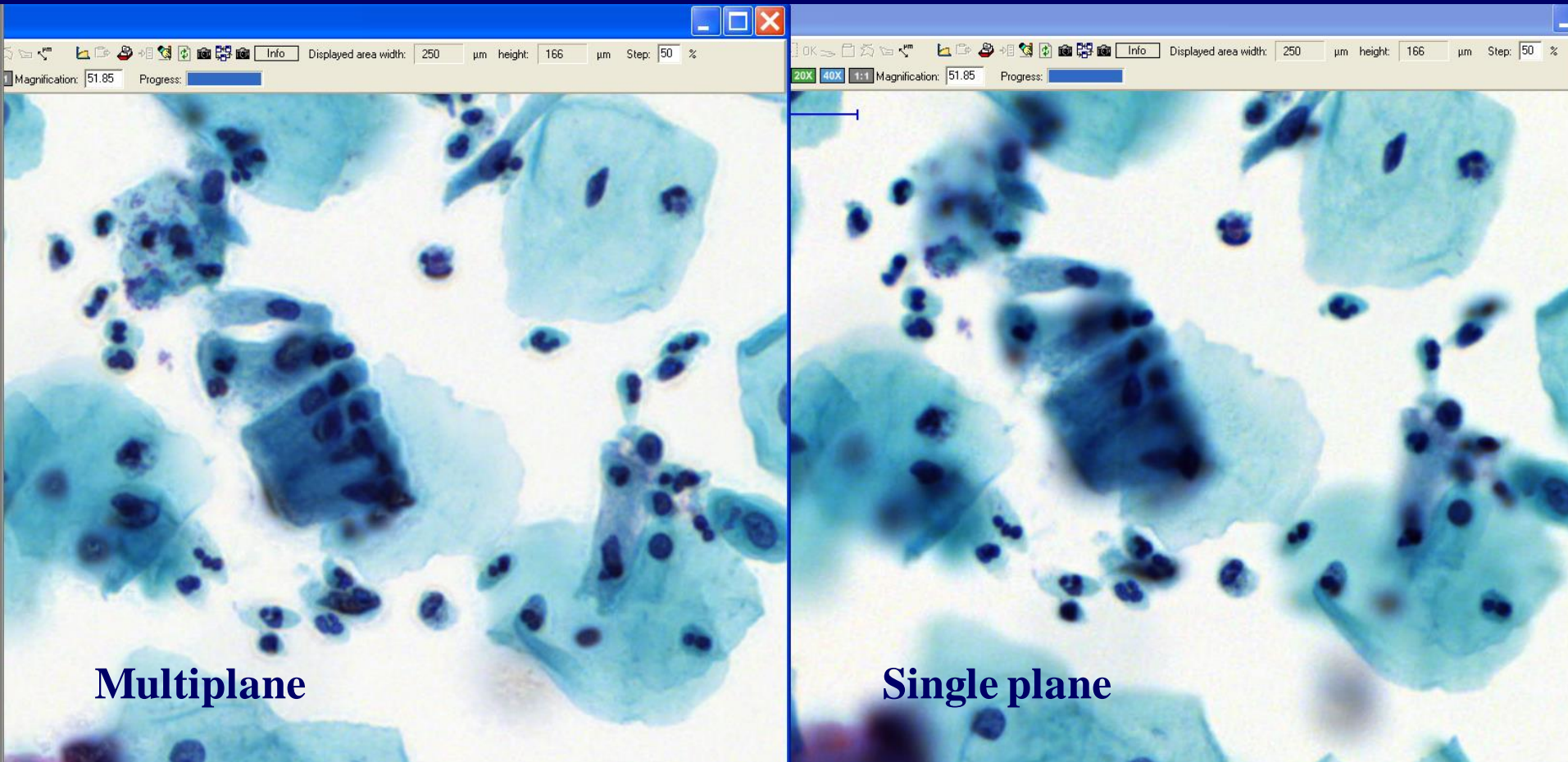
3-d \rightarrow Z-stacking or extended focus can help



Z-stack vs Extended focus



“Focused” cytology capture



Ergonomic solutions



Artificial Intelligence

- Image analysis with device decisions
- Feature extraction
- Image libraries
- Comparison of new cases



NEW
PAPNET™
Cytological Screening System

Scan Results

Cell Display

Screening Results

Significant Cells

3

4

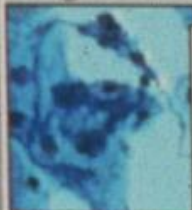
5

6

7

8

9



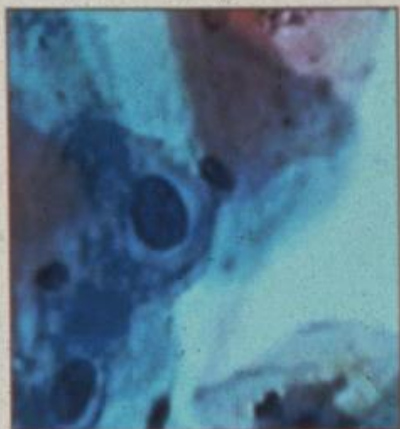
Represent



Sheets an

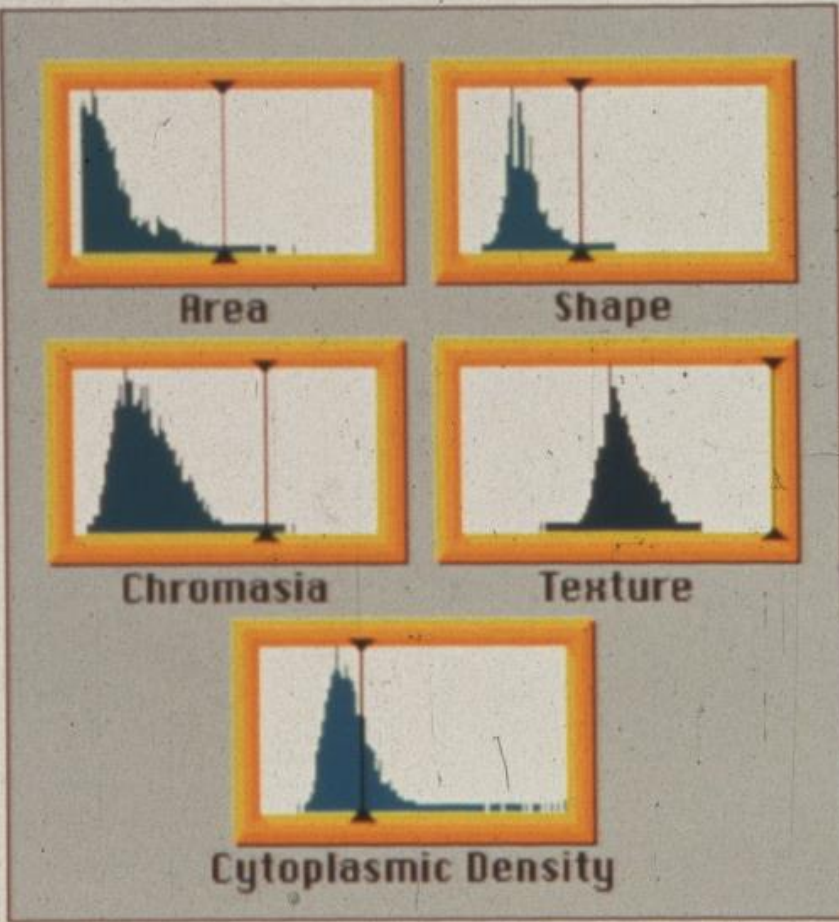


Significant Cell



Done

2x View



Check Lis

Endocervical Cells

Inflammation

Bacteria

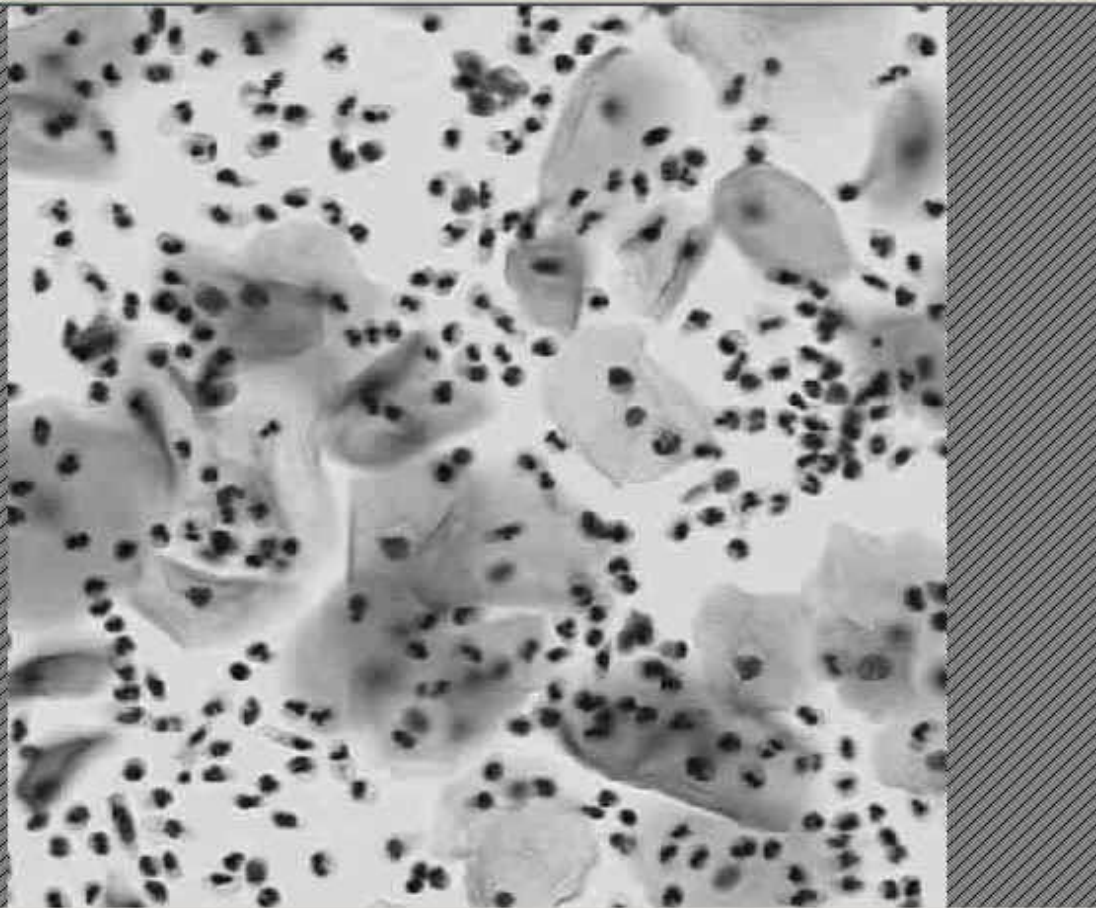
Trichomonas

Squamous Metaplasia

Repair

Candida

Cytolysis



LIS
 History
 Offset
 Track
 HotDot
 Help

Annotations:

Annotation Label: ASCUS
 User: bpreston
 Level: Cytotech
 Date: 6/21/2004 4:36:28 PM

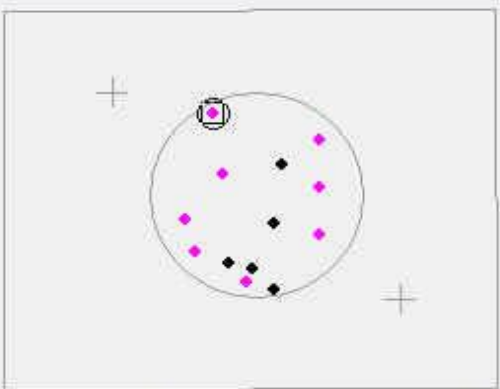
Annotation Label: Reactive Changes
 User: bpreston
 Level: QC Review
 Date: 6/21/2004 4:40:54 PM

Change Source Directory

Slide

Finish

Navigation icons: Home, Previous, Next, End



TRIPATH
care technologies™

SLIDEWIZARD® GS
microscope accessory

X Y

Phase 1 - Internet Screening Study

200 cases (ThinPrep/SurePath) – 6 observers
Appropriate Triage to ABNL (≥ 3 observers)

	<u>IS diagnosis</u>	<u>FDA trial (manual)</u>
ASC-US	5/6 = 83%	79% (ASC-US+)
ASC-H	3/3 = 100%	
LSIL	52/63 = 83%	85%
HSIL	17/18 = 94%	93%
AGC	2/5 = 40%	

CONCORDANCE = 86%

FP = 6%, FN = 12 %

SENSITIVITY = 88%, SPECIFICITY = 93%

Phase 2 Prospective Consented Patients

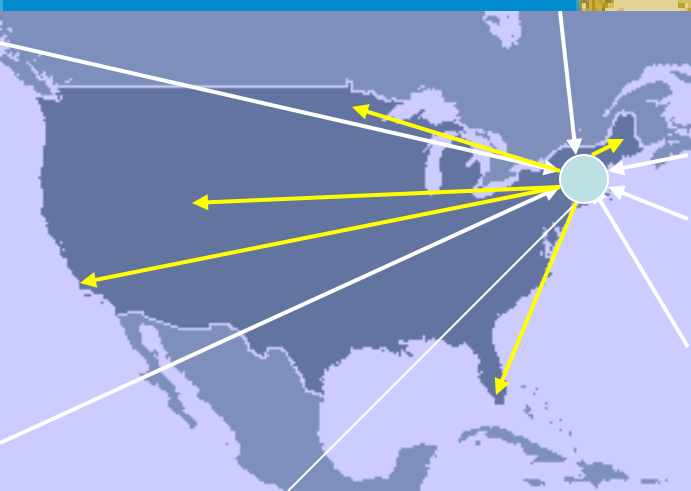
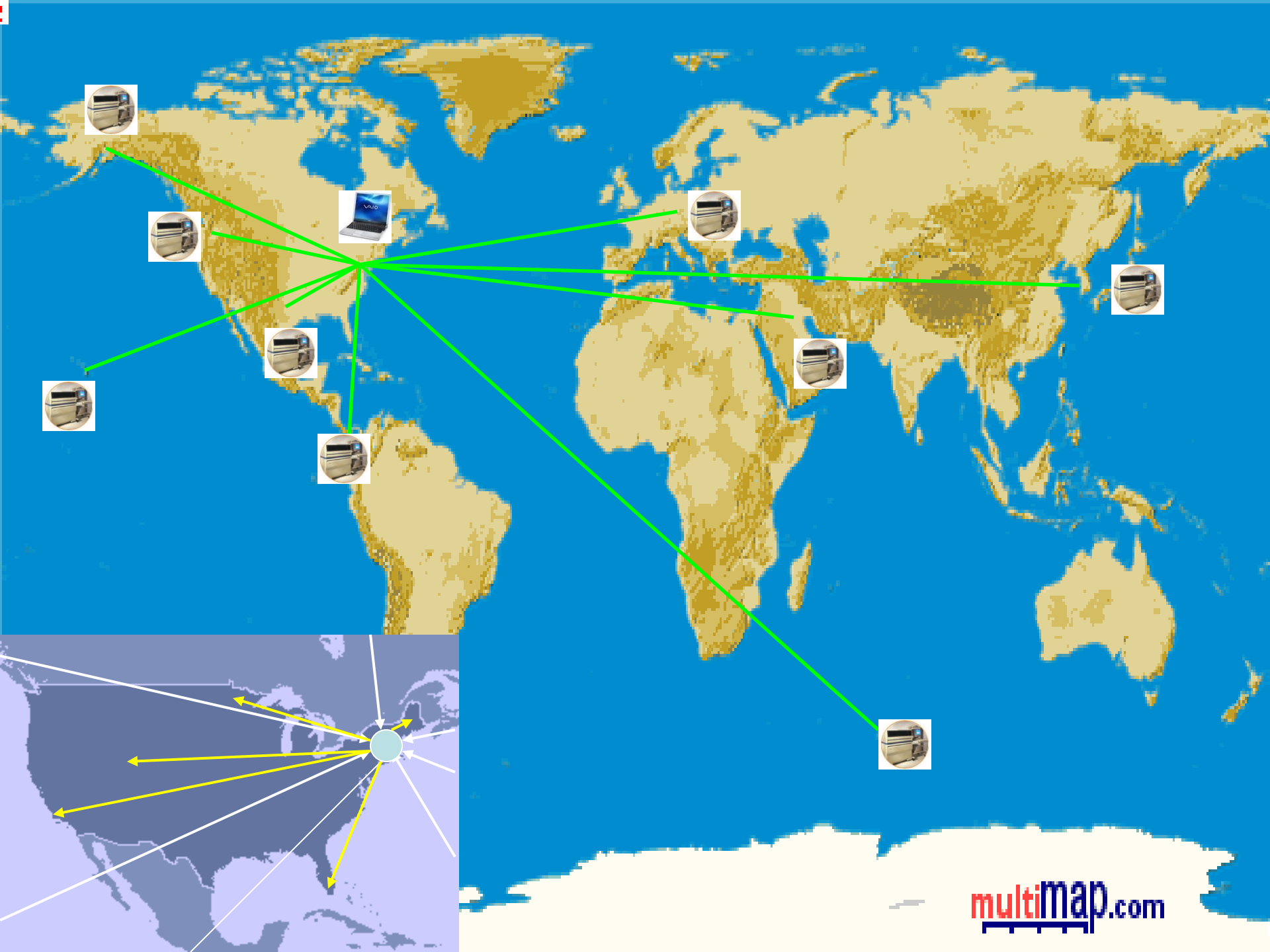
All Cases – SIL +
Single observer

LSIL+

TP	18
FN	2
Sens	90%

HSIL+

TP	4
FN	0
Sens	100%



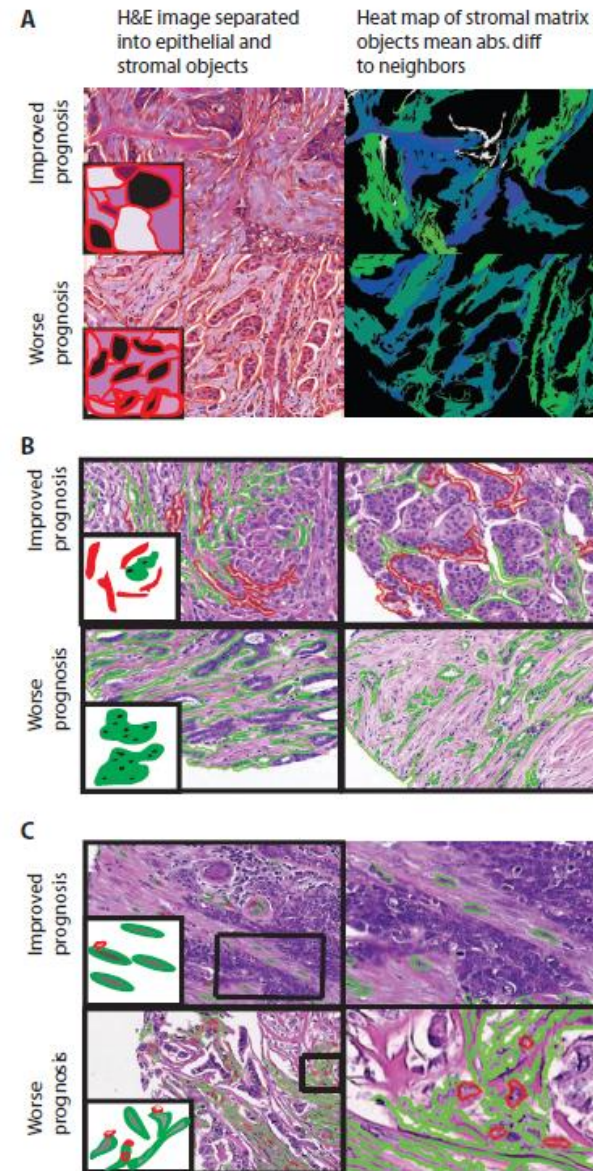
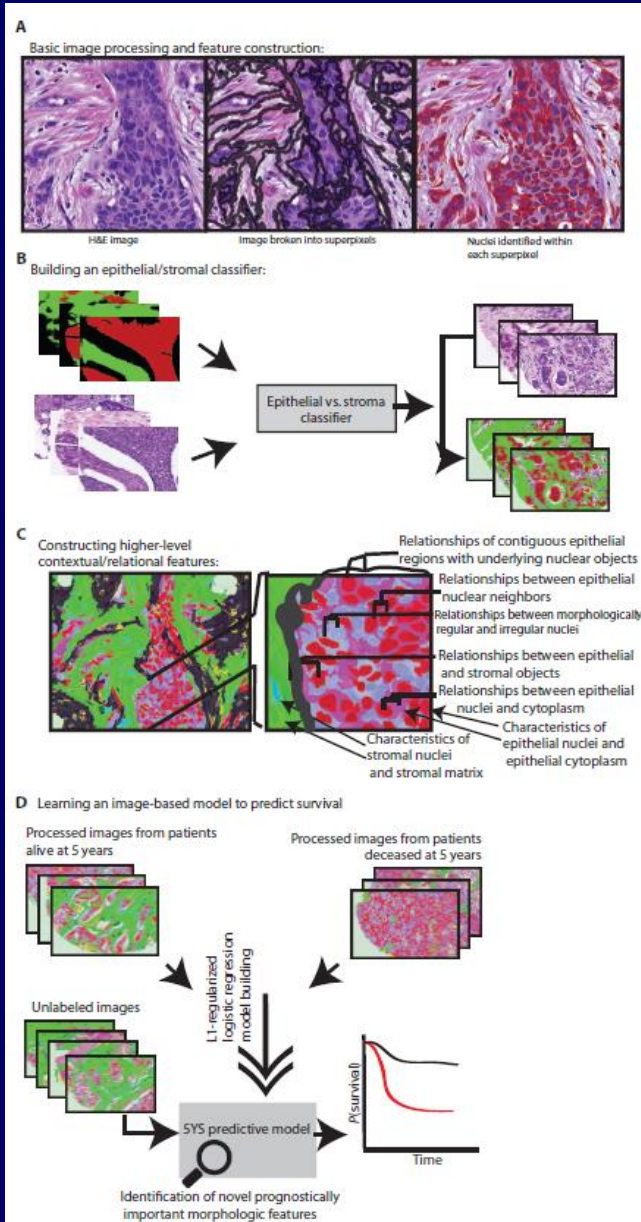
Internet Screening – Phase 3

- 3200 consecutive Pap cases screened in Korea (ThinPrep and Surepath)
- First pass on data (initial 1700 cases)
 - 85% sensitivity for all abnormalities
 - 79% for manual screening in FP clinical trial
 - 81% specificity
 - 100% sensitivity for HSIL+
 - 92% for manual screening in FP clinical trial

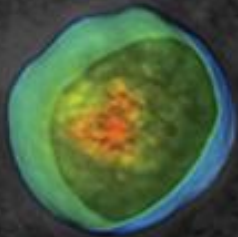
C-Path (Computational Pathologist)

- Breast cancer cases
- 6642 features in cancer epithelium and stroma
- Automatically quantitated
- Developed a “prognostic model score”
- Stromal morphologic structure features correlated strongly with survival
 - independent of clinical, pathologic, molecular
- “Watson-like visit to the Pathology Lab”

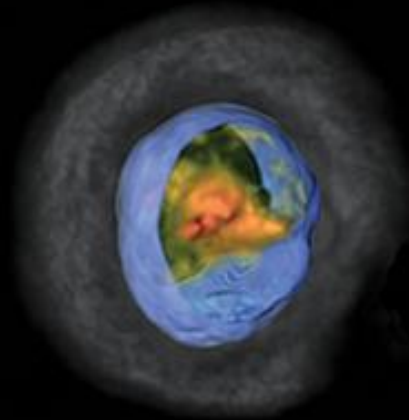
Analytics



Squamous Intermediate Cell

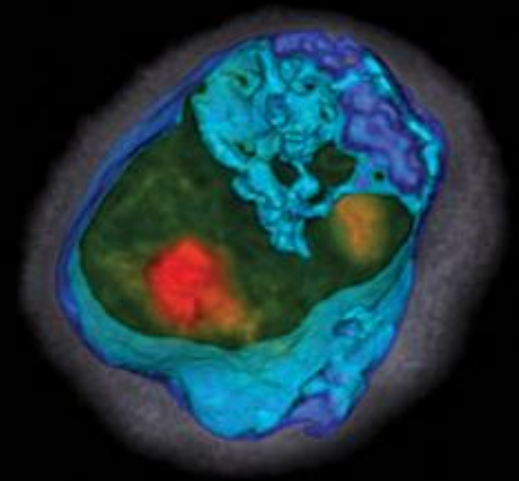


Moderate Dysplasia

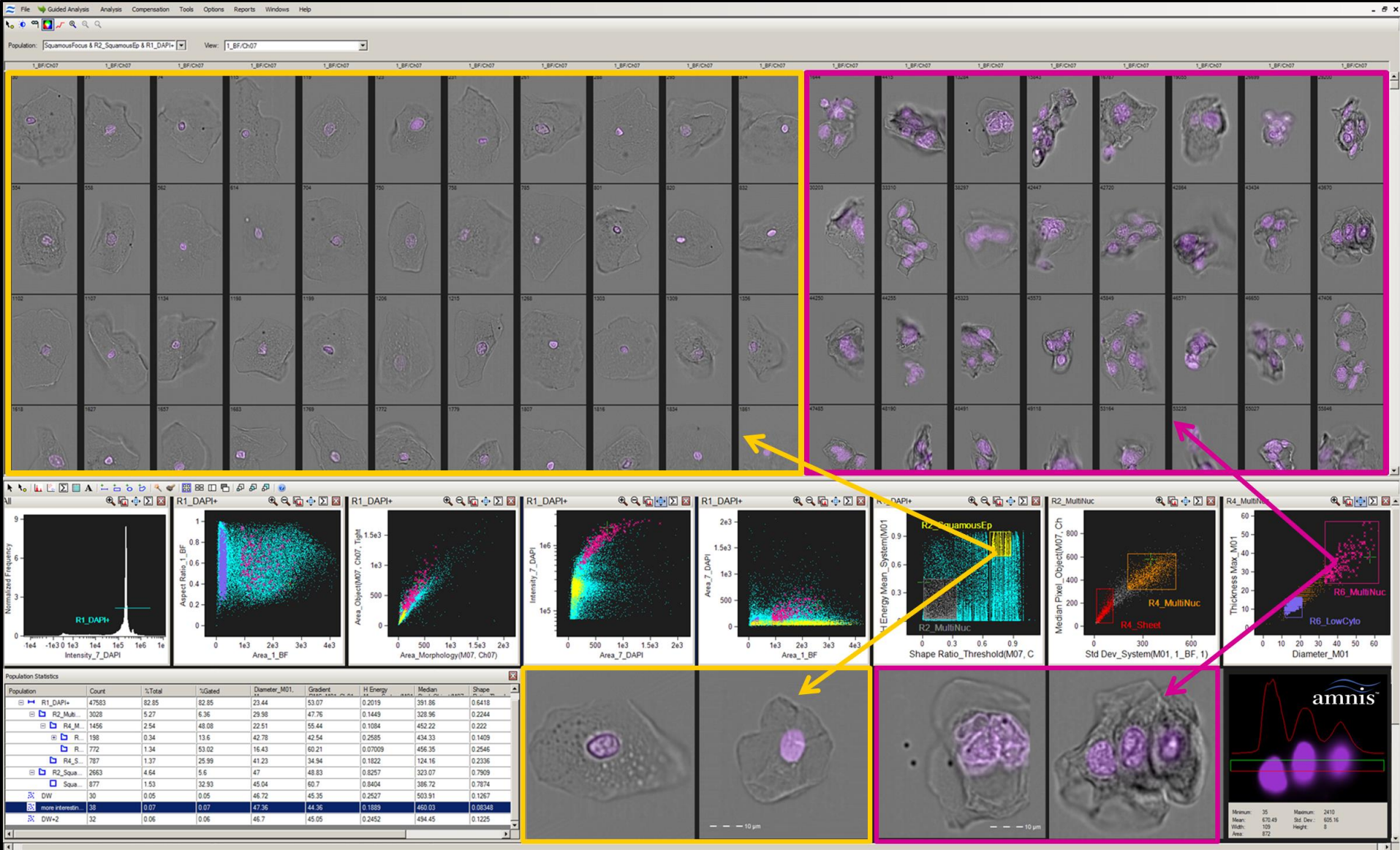


3μm

Squamous Cancer



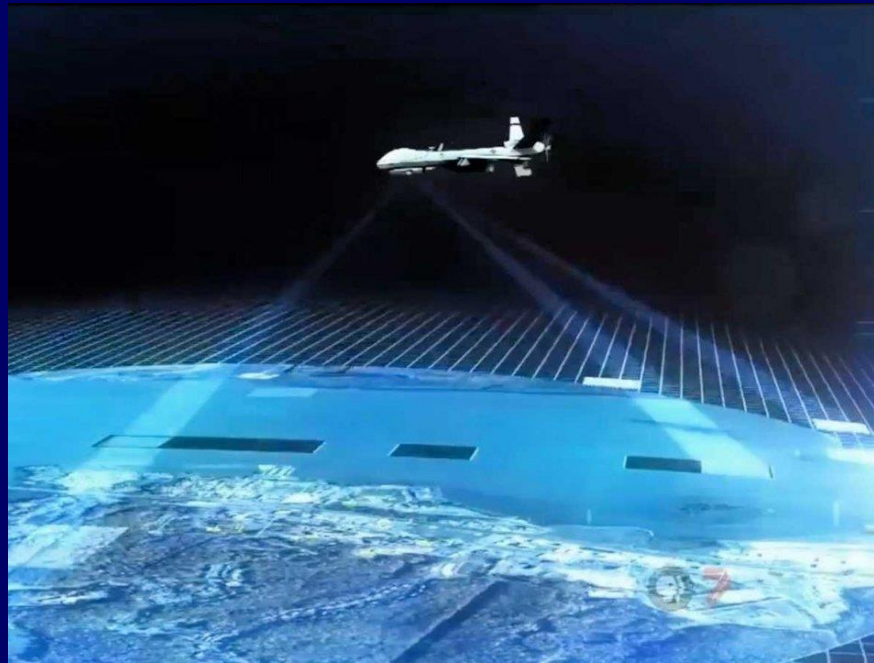
Cell-CT combined with analytics = increased diagnostic power



Flow cytometric imaging - increased speed – more cells = more diagnostic power

Faster and Higher Resolution

- DARPA ARGUS Camera
- 1.8 billion pixel camera – used on reconnaissance drones
- 1 million terabytes of data – everyday – all stored
- From 17,500 ft can image an entire city in HD



From PBS NOVA
“Rise of the Drones”



From PBS NOVA
“Rise of the Drones”

Cytology is the future of interventional medicine

Smaller specimens

Less trauma to obtain

Faster

Cheaper

Amenable to all molecular tests

Digital technology is the future of pathology/cytology

Anywhere, anytime

Archiving forever

Analytics





Thank You All Very Much