Virtual Microscopy: Express Surgical Pathology Consultation

Mercè Jordà, University of Miami, Florida
Telepathology versus Virtual microscopy (Digital Pathology)
Telepathology

- Use of telecommunications technology to share real-time pathology images between two or more locations
  - Frozen Section
  - Internal Consultation
  - Second opinion
  - First cancer diagnosis
  - QA in surgical pathology
  - External Consultation
Digital Pathology

It is an image-based environment that enables the acquisition, management and interpretation of anatomic pathology information generated from a digitized glass slide obtained through whole slide scanning, also called “virtual microscopy”
Virtual Microscopy

- Use of computer technology to convert analog microscopic images into digital images
- Whole slide imaging, digital imaging, virtual slides, virtual microscopy
- Real-time usage is optional
Virtual Microscopy Ingredients

- Microscope
- Camera
- Scanner
- Computer
- Monitor
- Software
- Internet connection
- And of course, glass slides!
Virtual Microscopy: Ingredients

Conventional optical microscope

- Mechanical scanner
- Light source
- Imaging optics
- Digital image sensor
- Image processed with software
- Computer display
- Image files (computer data)
Virtual Microscopy: Solutions

ACIS (Dako)
Applied Imaging Ariol (Genetix)
Bliss HD (Bacus Labs/Olympus America)
Dotslide 2.0 (Olympus)
DX-40 (Dmetrix)
iScan (Biolimagene)
MIRAX Scan (3DHistech / Zeiss)
Nanozoomer (Hamamatsu)
ScanScope (Aperio)
SNC400 (Leica)
Vassalo/Toco (Claro)
Others: A. Menaniri Diagnostics

Viewers and platforms:
Digital SlideBox (SlidePath)
mScope (Aurora MSC)
Omnyx (GE)
Philips (Integration)
PathPACS® (Apollo)
Virtual Microscopy: Applications

- Primary Diagnosis (?)
- Education
- Research
- Image analysis
- Archival and retrieval
- Laboratory information system
- Secondary diagnostic consultations and virtual slide sharing


UHealth | UNIVERSITY OF MIAMI MILLER SCHOOL of MEDICINE Pathology
Virtual Microscopy: Legal Status

- Federal Drug Administration (FDA) evaluated DP
- Safety and cost effectiveness were compared with conventional light microscopy
- Up to date, FDA has not yet approved DP for routine first line AP diagnosis to replace conventional light microscopy.

J Pathol Inform. 2: 36, 2011
Lack of FDA approval for use as primary diagnostic tool

- Multi-Center Clinical Trials
- Subsequent mass adoption
Many vendors are currently looking into different market economies, such as Europe, where health policies are looser and better integrated.

U.S. government takes a more incremental approach to health policies than European countries.
Virtual Microscopy – Prime Time

Pathology Labs Replace Microscopes with Digital Imaging

http://www.labmedica.com/lab_technology/articles/294738658/pathology_labs_replace_microscopes_with_digital_imaging.html
Virtual Microscopy – Prime Time

- Microscopes are being replaced with digital imaging in southern Sweden
- The system will be possibly the largest and among the first of its kind in the world
- New workflow management system will manage both the preanalytical and analytical stages

http://www.labmedica.com/lab_technology/articles/294738658/pathology_labs_replace_microscopes_with_digital_imaging.html
Virtual Microscopy – Prime Time

- 4 laboratories
- 400,000 glass slides / year
- 14 total scanners
- Real-time status of each sample, slide, and case
- Digital slides stored remotely in Japan in multiple locations (increased security) for at least 20 years

http://www.labmedica.com/lab_technology/articles/294738658/pathology_labs_replace_microscopes_with_digital_imaging.html
Virtual Microscopy – Prime Time

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http://www.labmedica.com/lab_technology/articles/294738658/pathology_labs_replace_microscopes_with_digital_imaging.html
Virtual Microscopy

- Many studies assessing reproducibility when using WSI versus conventional microscopy
- Results are showing that virtual slides are as useful as conventional slides for diagnosis
- Differences are presumed to be due to the pathologists’ lack of experience using the virtual microscope.

Arch Pathol Lab Med, 137: 518-524, 2013
APMIS, 120: 298-304, 2011
Seminars in Diag Path 27, 160-166, 2010
Human Pathology, 41, 1770–1776, 2010
J Pathol Inform. 1: 16, 2010
Is Virtual Microscopy Ready For The Prime Time?
A Comparison With Conventional Microscopy

C Reyes, M Nadji, O Ikpatt, R Cote

Histologic diagnoses of breast core biopsies compared between CM and WSI
Aim

To investigate the possibility of whole slide imaging being used for first line diagnoses of breast core biopsies

Materials and Methods

- 103 needle breast biopsies
- Each slide was scanned at 20X
- Three pathologists
- 1st CM  WSI  2nd CM
Diagnostic categories included:
- FCC with or without DH
- ADH
- DCIS
- IDC

The intra-pathologist reproducibility was recorded for CM vs WSI

Variation between the first CM and the second CM was used as control
Slide Review (CM # 1)

1 week

Slide Review (CM # 2)

CM vs CM

Whole Slide Image (WSI)

CM vs VM

Intra-Observer Agreement
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<td>1&lt;sup&gt;st&lt;/sup&gt; CM vs WSI</td>
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\( p \) value < 0.3
All intra-pathologist diagnostic disagreements (CM vs CM and CM vs WSI) were DH and ADH.

There were no intra-observer disagreements in the diagnosis of benign versus malignant disease.
The intra-observer variability in the dx of breast core biopsies by WSI is at least same as CM

WSI could replace CM in the diagnosis of breast core biopsies
Validation of Whole Slide Imaging For First Line Diagnosis Of Prostate Biopsies

J Zeitouni, M Jorda, C Reyes, M Nadji

Histologic diagnoses of prostate core biopsies compared between CM and WSI
Virtual Microscopy – Prostate Core Bx

- **Aim**
  - To investigate the possibility of whole slide imaging being used for **first line** diagnoses of breast core biopsies

- **Materials and Methods**
  - 103 needle breast biopsies
  - Each slide was scanned at 20X
  - Three pathologists
  - 1\textsuperscript{st} CM \quad WSI \quad 2\textsuperscript{nd} CM
Virtual Microscopy – Prostate Core Bx

- Diagnostic categories included:
  - BPT
  - HGPIN
  - PCa Gleason 6
  - PCa Gleason 7
  - PCa Gleason >7
- The *intra-pathologist reproducibility* was recorded for CM vs WSI
- Variation between the first CM and the second CM was used as control
Slide Review (CM # 1)

Slide Review (CM # 2)

Whole Slide Image (WSI)

CM vs CM

CM vs VM

Intra-Observer Agreement
# Virtual Microscopy – Prostate Core Bx

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$ p $ value < 0.3
All intra-pathologist diagnostic disagreements (CM vs CM and CM vs WSI) were between Gleason grades 6 and 7.

There were no intra-observer disagreements in the diagnosis of benign versus malignant disease or for the Gleason >7 category.
The intra-observer variability in the diagnosis of prostate biopsies by whole slide imaging (WSI) is the same as glass slide microscopy.

Our results suggest that WSI could be used as an alternative to CM for the first line diagnosis of prostate core biopsies.
In sum, UM message.....

Our results suggest that.....

WSI could be used as an alternative to CM for first line diagnosis breast & prostate core biopsies
Virtual microscopy does not compromise, but might improve, the accuracy of grading in prostate needle biopsies.”
Novel Quantitative Method to Evaluate Globotriaosylceramide Inclusions in Renal Peritubular Capillaries by Virtual Microscopy in Patients With Fabry Disease

Laura Barisoni, MD*; J. Charles Jennette*, MD; Robert Colvin*, MD; Sheela Sitaraman, PhD; Alexander Bragat, BSc; Jeff Castelli, PhD; Dan Walker, BA; Pol Boudes, MD

Arch Pathol Lab Med. 2012;136:816–824

Conclusions.—BLISS is a simpler and more sensitive scoring system compared to the semiquantitative approach. The virtual microscopy–based methodology increases accuracy and reproducibility; moreover, it provides a permanent record of retrievable data with full transparency in clinical trials.
Virtual Microscopy: Education

- PDF clinical history
- Digital slides
- Digital IF images
- Digital EM images
- PDF report

- Review of cases with instructor
- Independent review of cases
- Annotation of specific features for review
- Annotation of specific features for testing
Virtual Microscopy – Clinical Trials
Neptune: Use of Virtual Microscopy
Virtual Microscopy

- Wider adoption of WSI will require
  - full integration with the LIS
  - continuous automated scanning
  - high-large storage capacity
  - interfaces.
Virtual Microscopy: Other than 1st line diagnosis

- case consultation
- legal cases
- multidisciplinary conferences
- can also assist in keeping records of slides to be sent out or destroyed by ancillary testing

Poses multiple controversial issues:
- Licensing
- Liability
- Security
- Reimbursement
- Scanning quality and its validation.

Regulations and standardization are not yet in place

Controversies of Virtual Microscopy Consultation Services

**Major Challenges**

- Network connectivity and firewall configurations when linking two separate organizations
- Information technology regulations for each organization
Controversies of Virtual Microscopy Consultation Services

Solutions vary in type of user.....

- **occasional user:**
  - asynchronous upload is recommended

- **custom/client**
  - telepathology portal with capacity of large volume
  - imaging streaming method: provides real-time consultation

Disadvantages

- implementation cost is higher
- requires high level of connectivity between original and consulted institution
Advantages of Virtual Microscopy Consultation Services

- Facilitates rapid, efficient communication between subspecialty pathologists and generalist pathologists
- 2\textsuperscript{nd} opinion on challenging cases
- Fine-tuning of diagnostic interpretation
Advantages of Virtual Microscopy Consultation Services

- Overnight shipping/mailing charges/costs can be avoided
- Loss of slides and international costumes for transferring human tissues are not anymore a concern
- Results are delivered via secure website, which expedite consultation response improving client’s satisfaction and patient treatment.

Potentially faster patient diagnosis and treatment decreasing healthcare cost
Advantages of Virtual Microscopy

- Data can be encrypted for online transmission via “https” (Hypertext Transfer Protocol Secure)

- HIPAA guidelines are adhered to by receiving institution
Advantages of Virtual Microscopy

- Variety of virtual microscopy image formats currently utilized:
  - *.jp2
  - *.svs
  - *.vms
  - *.vmu
  - *.mrxs
  - *.ndpi
Virtual Microscopy and File Upload Time

- File upload time is dependent on file size and internet connection speed
- Most institutions have “high-speed” internet connections
Virtual Pathology Consultative Services