Digital Pathology Consultation: A Decade of Experience at UPMC

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No Conflicts of Interest
Objectives

1. Review the different modes available for telepathology.
2. Share UPMC experience with each teleconsultation method.
3. Review lessons learned from our telepathology service.
Telepathology Definition

- The practice of pathology at a distance, transmitting macroscopic &/or microscopic images via telecommunication links for:
  - Remote interpretations (telediagnosis)
  - Second opinions or consultations (teleconsultation)
  - Educational purposes (teleconferencing)
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Telepathology Applications

- **Anatomical Pathology**
  - Intraoperative consultation (frozen sections)
  - Surgical pathology (2nd opinions, immunostains)
  - Telecytology (eg, on-site evaluation)
  - Ultrastructural pathology

- **Clinical Pathology**
  - Telehematology (eg, blood smears)
  - Microbiology (eg, parasites)
  - Chemistry (eg, gels)
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  o Chemistry (eg, gels)
Telepathology Modes

- **Static (store & forward)**
  - Examination of pre-captured still image(s).
  - Sent via e-mail or stored on a shared server.
  - Telemicroscopy (microscope mounted digital camera)

- **Dynamic (live)**
  - Examination of images in real-time.
  - Video or robotic microscopy.

- **Hybrid (whole slide imaging)**
  - Dynamic viewing of a digitized slide.
  - Selected areas viewed at higher magnification.
Telepathology at UPMC

• Our health system operates 20 geographically diverse hospitals with partners located in distant states (Indianapolis, Indiana) and countries (Italy, China).
• Academic Centers of Excellence (COE) subspecialty model.
• Telepathology has been employed at our institution for over a decade to provide remote subspecialty expertise at local, national and international sites.
UPMC Technology Timeframe

1998 - Image management using Xippix from Image Life Cycle Solutions
2000 - Static telepathology for transplant pathology service in Italy
2001 - Live microscopy conferencing using VTEL & PictureTel videoconferencing products
2002 - Nikon digital network (intranet) camera for telecytology
2003 - Aperio scanner with images stored on a network DVD Juke Box
- Nikon Coolscope digital microscope unit for FS telepathology
2004 - Aperio scanner with images stored directly on network servers
2005 - iPath telemedicine platform tried for global teleconsultation
2006 - Trestle 4 & 50 whole slide scanner for telepathology
2007 - Olympus DP digital cameras with microsuite & cellSens net cam module for live microscopy (hematology & cytology)
2008 - Hamamatsu nanozoomer for educational scanning
2009 - Zeiss & Mirax scanners for educational scanning + Omnyx
2010 - Zeiss robotic telepathology system for FS
- Telepathology digital portal
2011 - Citrix desktop virtualization of telepathology applications
Live Video/TV Microscopy

2004, Totten Conference room, Sony DXC-970MD 3CCD on Olympus Scope connected to a VTEL Galaxy, sharing LIVE microscope image over video conference, 384k ISDN

2004, Presbyterian Hospital Pathology sign-out room, Sony DXC-970MD 3CCD on Olympus Scope connected to a VTEL, sharing LIVE microscope image over video conference, 384k ISDN
Digital Network Cameras

Sony DXC-970MD 3CCD on Olympus Scope connected to a VTEL, sharing LIVE microscope image over video conference, 384k ISDN. Nikon DN100 Digital Network Camera on the same scope, accessing the same image using a web browser.

Remote view of a live scope image using the DN100 Digital Network Camera
Hardware Solutions

Software Solutions

Welcome to MyApp

Main > Laboratory > Telepathology

- Coolscope SHY-FRZ
- CytoPath Netcam
- Hemepath NetCam
- MedMicroscopy
- Mobile NetCam - PUH
- OncologyPath Netcam
- PathConsult
Static Telepathology
UPMC Transplant Pathology

• **Clinical Need:**
  - Rapid & accurate interpretation of allograft biopsies influences outcome after organ transplantation.
  - Expert histopathologic interpretation determines whether a donor organ should be used for transplantation or disposed.

• **System Architecture:**
  - Telepathology system requires coverage 24 hours a day, 7 days a week.
  - Communication limited to a private network between Italy (host) & and UPMC (consulting pathologists).
  - Static-image architecture supporting both real-time interactive sessions & capacity to run in a store-and-forward mode.

• **Telepathology Outcome:**
  - Static teleconsultation enhanced the transplantation pathology practice.
  - Concordance: Full agreement in 67/78 (86%) cases (1999-2000).
  - Deferrals: 4 cases slides/blocks were requested.
  - Discrepancies: 11 (14%) cases with 8 minor & 3 clinically significant.
**Digital Transplant Pathology Evolution**

- **ISMETT consultations:**
  - Mediterranean Institute for Transplantation and High Specialization Therapies
  - Located in Palermo, Italy
  - Founded in 1997
  - Teleconsultation from 1999
- **12 years involving 3000 cases**
- **Evolution of telepathology:**
  - **1st generation**: Static images (TPIS email-centric system)
  - **2nd generation**: Dynamic robotic microscopy (Nikon Coolscope streaming)
  - **3rd generation**: Hybrid rapid virtual microscopy (Trestle live viewing)
  - **4th generation**: WSI ultra-rapid virtual microscopy (Mirax Midi since 2009)
Store- & Foreword Transplant Telepathology Client-Server System

Pioneering Benefits

- Early & continued adoption has provided:
  - Experience in Digital Pathology & improved workflow (fewer bottlenecks)
  - Resources (facilitated funding for equipment, IT infrastructure & staff)
- Multiplex-stained WSI permits brightfield + fluorescence microscopy & image analytics

Example: WSI of kidney allograft

*Isse et al. AM J Transplant 2012: 12:27-37*
UPMC Telehematology

• **Clinical Need:**
  - Rapid & accurate interpretation of peripheral blood differentials.
  - Expert hematopathologist interpretation required for difficult cases (eg, blasts in leukemia) at remote hospitals.

• **System Architecture:**
  - CellaVision™ automated digital system to locate, pre-classify, store & transmit WBC, RBC & platelet images.
  - Technologist confirms/edits images & emails them to Hematopathologist.

• **Telepathology Outcome:**
  - The device correctly classified up to 94% of cells, with reduced accuracy for immature granulocytes (*Rollins-Raval et al. JPI 2012; 3:29*).
  - Opportunity to incorporate digital images into the EMR.
CellaVision Analyzer & Remote Review System
Possible immature cells, high n/c ratio, nucleoli
Video Microscopy
Dynamic Video Microscopy System

Adapted from Sinard JH. Practical Pathology Informatics. Springer 2006.
## Telecytology Options

<table>
<thead>
<tr>
<th>Telepathology Mode</th>
<th>Current Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Static</td>
<td>Most Published</td>
</tr>
<tr>
<td>Dynamic (Video)</td>
<td>Most Practical</td>
</tr>
<tr>
<td>Dynamic (Robotic)</td>
<td>Impractical</td>
</tr>
<tr>
<td>WSI (Hybrid)</td>
<td>Investigational</td>
</tr>
</tbody>
</table>

At UPMC, live video streaming has remained the mode of choice for providing immediate adequacy assessment of cytology specimens by telecytology.
UPMC Telecytology

- Web-based streaming for FNA rapid on-site evaluation (ROSE)
Comparative performance

Parameters:
- Tissue adequate
- High Case Complexity
- Good Image Quality
- Lack of obscured features
- High Diagnostic confidence
- Correct diagnosis

Comparisons:
- Optical Microscope
- Web Based Streaming System
Time taken per case (average)

<table>
<thead>
<tr>
<th></th>
<th>Seconds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optical Microscope</td>
<td>50</td>
</tr>
<tr>
<td>Web Based Streaming System</td>
<td>94</td>
</tr>
</tbody>
</table>
Robotic Telepathology
Robotic Telepathology

Frozen Section Diagnoses by Robotic Telepathology


<table>
<thead>
<tr>
<th>Year</th>
<th>Primary author</th>
<th>Accuracy (%)</th>
<th>Deferral (%)</th>
<th>Time (min/slide)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991</td>
<td>Nordrum [9]</td>
<td>100</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>1995</td>
<td>Oberholzer [10]</td>
<td>90.3</td>
<td>6(^a)</td>
<td>20-40</td>
</tr>
<tr>
<td>1999</td>
<td>Della Mea [12]</td>
<td>100</td>
<td>NA</td>
<td>4.5</td>
</tr>
<tr>
<td>2005</td>
<td>Sukal [16]</td>
<td>NA(^b)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>2005</td>
<td>Hitchcock [18]</td>
<td>95.3</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>2006</td>
<td>Hutarew [14]</td>
<td>97.9</td>
<td>0</td>
<td>10.7</td>
</tr>
<tr>
<td>2007</td>
<td>Horbinski [7]</td>
<td>95.5-96.9</td>
<td>12-20</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviation: NA indicates not available.

\(^a\) These reports did not provide deferral rates but rather the percentage of cases during which technical problems were encountered.

\(^b\) This report did not provide diagnostic accuracy data but concluded that TP was a useful adjunct in Mohs surgery.
• Clinical Need:
  o Neuropathology Center of Excellence (COE) model at one location includes remote intraoperative consultations.

• System Architecture:
  o Zeiss (previously Trestle) robotic microscopes & network accessible software (MedMicroscopy).
  o Dynamic system does not require transfer of large images across networks, so bandwidth demand is low.

• Telepathology Outcome:
  o >10 years intrainstitutional experience.
  o Expanded our practice to cross state lines (interinstitutional) with a financially separate medical center.
  o Implementation of technology was less of a hurdle than administrative & legal issues.
Neuropathology Frozen Section Rate


YEAR

Number of Cases

- telepathology
- conventional

YEAR

2002 2003 2004 2005 2006 2007 2008 2009

(13%)  (15%)  (20%)  (31%)  (28%)  (18%)  (21%)  (21%)
Robotic Telepathology System

Robotic (motorized) microscope (1-4 slides)

Digital/video camera

Networked PC (server software)

Remote Microscope Controls (Viewing software required)
Robotic Telepathology System

Remote Microscope Controls
(Viewing software required)

Digital/video camera

Networked PC
(server software)

Robotic (motorized) microscope
(1-4 slides)
SL-4 Slide Loader System
Microscope Site
(4 systems at UPMC)
Standard PC
Internet Connection
Microscope
Motorized Stage & Focus Control
Digital Camera
Digitizer

SL50 Slide Loader System
Microscope Site (3 systems at UPMC)
Standard PC
Internet Connection
Microscope
Motorized Stage & Focus Control
Digital Camera
Digitizer

Viewer Site
Standard PC
Internet Connection

MedMicroscopy Application

UPMC FIREWALL

Java-based viewer from the Internet through UPMC Citrix

DSS Server on IIS attached to SAN. Pulls images from SL-4 and SL-50, serves for local and public

Java-based viewer for the Internet

http://dpiq.upmc.com
Diagnostic Outcomes

Horbinski & Wiley Neuropathol 2009; 29:655-663

- Telepathology deferral rates (19.7%) varied & higher than conventional FS cases (10%)
- Good telepathology vs conventional FS concordance
- Discrepancy & deferral rate differences not statistically different

2002-2006
Conventional FS = 1227
Telepathology FS = 402

2007-2008
Conventional FS = 547
Telepathology FS = 262
### Technical problems that occurred during intra-operative consultations

<table>
<thead>
<tr>
<th>Problem</th>
<th>Number of occurrences</th>
<th>Resolution</th>
<th>Implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>VPN did not connect</td>
<td>3</td>
<td>Changed computers or resolved password expiration</td>
<td>Delayed intra-operative consult</td>
</tr>
<tr>
<td>Wrong call back number on pager</td>
<td>2</td>
<td>Recognized error immediately or received phone call through administration</td>
<td>Delayed intra-operative consult</td>
</tr>
<tr>
<td>Diffuculty scanning slide</td>
<td>2</td>
<td>Re-booted host computer</td>
<td>Delayed intra-operative consult</td>
</tr>
<tr>
<td>Scanned slide upside down</td>
<td>1</td>
<td>Reloaded slide after recognizing problem</td>
<td>Delayed intra-operative consult</td>
</tr>
<tr>
<td>Scope would not focus</td>
<td>2</td>
<td>Re-booted host computer</td>
<td>Delayed intra-operative consult</td>
</tr>
<tr>
<td>No slide overview seen</td>
<td>1</td>
<td>Re-scanned slide</td>
<td>Delayed intra-operative consult</td>
</tr>
<tr>
<td>Internet down</td>
<td>1</td>
<td>-</td>
<td>Abandoned attempt to perform consult, discussed with local pathologist differential</td>
</tr>
</tbody>
</table>
### Time requirements for single block frozen sections

Evans AJ et al. Human Pathology 2009; 40:1070-1081

<table>
<thead>
<tr>
<th># FS</th>
<th>Slide preparation time (min)</th>
<th>Slide interpretation time (min)</th>
<th>Total TAT (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 350</td>
<td>10.33 (9-42)</td>
<td>9.65 (&lt;1-25)</td>
<td>19.98 (11-45)</td>
</tr>
<tr>
<td>N = 633</td>
<td>12.26* (8-20)</td>
<td>3.42**, b (&lt;1-10)</td>
<td>15.68* (9-35)</td>
</tr>
</tbody>
</table>

- Robotic microscopy system = Leica TPS2
- Hybrid whole slide scanner = Aperio ScanScope CS
WSI scanners
WSI Telepathology
Digital Pathology Consultation Portal

UPMC Digital Pathology Consultation Portal

Now it’s easier than ever to send your slides electronically and let UPMC Pathology experts be your second set of eyes for diagnosis and treatment.

The UPMC Digital Pathology Consultation Portal gives you a valuable second opinion necessary to be accurate and efficient in both diagnosis and treatment.
Web-Based Digital Consultation Portal

- Web-based tool for digital pathology 2nd opinion consultation.
- Outside entities can enter case data & upload digital files (static & WSI).
- Consulting pathologists view requests & submit diagnoses securely at their PCs.
Case ID Number: DC11-00312

Current Status: Processing  Assigned To: William Cable

Clinical Data

<table>
<thead>
<tr>
<th>Specimen Case Number(s):</th>
<th>12546578</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical History:</td>
<td>Complains of discomfort</td>
</tr>
<tr>
<td>Organ:</td>
<td>lower intestine</td>
</tr>
<tr>
<td>Pre-op Diagnosis:</td>
<td>blockage</td>
</tr>
<tr>
<td>Post-op Diagnosis:</td>
<td>scope</td>
</tr>
<tr>
<td>Specimen Submitted/Procedure:</td>
<td>scope</td>
</tr>
</tbody>
</table>

Save Draft  Preview Final Report  Submit Diagnosis
Web-Based Digital Consultation Portal

System Design (web tool technology & features):

• **Clients:** Offers secure login to submit patient data, upload images, check status, view & print 2nd opinion reports.

• **Host Pathologist:** Hosts the diagnosis tool where pathologists can view images using a Java applet (supports multiple WSI formats), annotate & capture static image snapshots, view clinical data, & submit diagnoses.

• **Host Consultation Services:** Allows managers to triage requests, monitor workflow, & maintain personnel data.

• **Host Transcriptionist:** Contains data entry fields for diagnoses dictated through the current dictaphone system.
Web-Based Digital Consultation Portal

Portal Outcome

• The submission tool can:
  o Accept large image files (format-agnostic for key vendors).
  o Capture clinical information for consultation (while protecting patient privacy).
  o Remain robust & user-friendly for clients & consultants.

• Streamlined workflow & training ensures prompt turn-around time & buy-in by institute pathologists.
## Different Telepathology Portals

<table>
<thead>
<tr>
<th>General Portal</th>
<th>Client-Specific Portal</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Simple and cheaper (no IT-level client set up required)</td>
<td>• Configurable (customized access to WSI stored at client site)</td>
</tr>
<tr>
<td>• Image transfer required (for small slide volumes) with possible delays</td>
<td>• No need for image transfers (supports large consult volumes)</td>
</tr>
<tr>
<td>• Supports multiple WSI vendor formats</td>
<td>• Customized to run only the client’s desired WSI format</td>
</tr>
<tr>
<td>• WSI files organized by folders (file name is unimportant)</td>
<td>• Files organized by scanner software (indexed by file name)</td>
</tr>
<tr>
<td>• Customers enter PHI into the portal tool (more user intervention needed)</td>
<td>• No transmission or storage of PHI (prohibited in China; only DOB &amp; gender)</td>
</tr>
<tr>
<td>• Built-in billing component</td>
<td>• Flat fee per case (contractual)</td>
</tr>
</tbody>
</table>
UPMC Portal Server

UPMC Portal Monitors NDP.Serve via Web Service for New Scanned Images, Notifies Pathology When Images are Available

UPMC Pathology Reviews Scanned Images

Submission of Telepathology Case to UPMC Portal

(1) Hamamatsu NDP.Serve
(2) Query WebService
(3) NiceLabel SW (Barcode)

Completed Scan Copied to NDP.Serve

Hamamatsu NanoZoomer PC

Scanning

NanoZoomer Scanner

Barcode Printer

Barcoded Slides Sent to Scanner
Preliminary Portal Data

- All cases were surgical pathology specimens, most commonly breast/female genital tract & soft tissue.
- WSI (average 11 slides/case) received include H&E, histochemical & immunohistochemistry slides.
- Mean turnaround time for 22 consulting pathologists was 40 hours (range 2-152 hours).
- Delayed cases were due to network outage problems.
- Post-launch feedback resulted in customization to:
  - Incorporate transcription services
  - Peer-to-peer review for consultants
  - Provision for issuing addenda/amendments
  - Improved WSI viewing experience.
## Practical Considerations

<table>
<thead>
<tr>
<th>Factor</th>
<th>Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>Direct (hardware, software) &amp; Indirect (staff, storage)</td>
</tr>
<tr>
<td>Distance</td>
<td>Time zones &amp; downtime (close enough to be on-site for a failure)</td>
</tr>
<tr>
<td>Education</td>
<td>FS surgeon expectations &amp; acceptable downtime for malfunction</td>
</tr>
<tr>
<td>Networks</td>
<td>Bandwidth limitation, firewalls &amp; security</td>
</tr>
<tr>
<td>Computers</td>
<td>Compatibility with enterprise OS &amp; antiviral software</td>
</tr>
<tr>
<td>Maintenance</td>
<td>Timely vendor support, IT staff &amp; clinical availability (eg, 24hrs/day)</td>
</tr>
<tr>
<td>Images</td>
<td>Formats (proprietary), LIS integration &amp; storage (retention policy)</td>
</tr>
<tr>
<td>Metadata</td>
<td>Access to clinical information ± relevant lab data (eg, LIS, EMR)</td>
</tr>
<tr>
<td>Workflow</td>
<td>Handling tissue (eg, FS ± smear), # slides, &amp; multiple specimens</td>
</tr>
<tr>
<td>Regulations</td>
<td>Validation, QA (eg, CAP telepathology checklist), &amp; billing</td>
</tr>
<tr>
<td>Medicolegal</td>
<td>Credentialing, licensing, &amp; malpractice coverage</td>
</tr>
<tr>
<td>Human factor</td>
<td>Professional reluctance, training &amp; monitoring performance</td>
</tr>
</tbody>
</table>
• Era of digital pathology consultation spanned a decade. All modes of telepathology have been successfully utilized at our institution during this time to exploit subspecialty expertise & compete for pathology services.

• Technology has become more cost effective. Accuracy and turnaround time improved with advancing technology, as well as user training and experience.

• Early & continued adoption has promoted digital pathology resources (facilitated funding for equipment, IT infrastructure & staff).

• Telepathology is not as easy as it looks! Comfort in use is acquired with hands-on practice. Technological issues are often easier to overcome than administrative, contractual and legal challenges.
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