Non-Clinical Uses of a Digital Pathology System in an Academic Training Program

Douglas J. Hartman, MD
December 13, 2019
Disclosures

• Up-To-Date – Ongoing royalties for educational content creation

• Philips – one time payment for educational presentation
Overview – The Side Items

• Education
• Consultation
• Tumor Boards
• Quality Assurance
• Image Analysis
• Research
Education

- Medical Student
- Resident
- Junior faculty/Competency Assessment
- Foreign institutions
- Training cytotechnologists/ advanced professionals
Use Case Breakdown #1

• Medical Student
  – Within a broader curriculum
  – “Classic” cases; focused review of subject matter
  – General pressure to reduce pathology presentation within curriculum
  – Great pressure to provide unlimited resources
  – Same material used year after year
Digital Pathology for Education

• Nearly all medical schools teach pathology with WSI
• Anatomic pathology residency revolves around learning glass slides
• Residents in pathology still get minimal exposure to WSI
Use Case Breakdown #2

- Resident
  - Fundamental knowledge
  - Mixture of “bread and butter” as well as “zebra” cases; comprehensive review of subject matter
  - Pressure to provide unlimited resources and reduce work hours
  - More frequent updates required
Resident Education

• Weekly didactic lectures with associated 6-10 slide sets
• Study sets by subject matter
• Board review material
• Daily “routine” cases
• Other demands on resident time
Study set
Resident Weekly Unknown Conference

Weekly Unknown Conference – AP Didactic

Clinical history: 47-year-old female with abnormal bleeding and fibroids.
Use Case Breakdown #3

• Junior Faculty /Competency Assessment
  – Competency assessment for certain biomarkers
  – Certain diagnostic subject matters have high interobserver variability
  – With volume of cases reviewed, comes experience
Several organizations have moved toward using digital imaging for proficiency testing

- American Board of Pathology – a subset of the slides for histologic review are now digital slides

- Virtual Biopsy Program (VBP) from the College of American Pathologists – exclusively uses digital slides in order to run the program
Competency Assessment
Use Case Breakdown #4

• Foreign Institutions
  – Slide sets are often components of requests to outside invited speakers
  – Crossing systems/requires coordination ahead of visit
Use Case Breakdown #5

• Training Cytotechnicians/cytopathologists
  – Year long training in order to satisfy certification
  – Training often done by other cytotechs
  – High power microscopy is a must
Main Layout
• 10 Modules
• 42 Submodules
• Just the first six weeks worth of class material.
Tests

• Currently one Practice Test
• Has not been used for grading purposes yet with students.
• Haven’t had a chance to see results accumulate.
• Would eventually like for this to replace glass unknown slide sets and exams.

Challenges

• Cannot select and preview a single question. Must click through entire test to preview a specific question.

Courtesy of Karyn Varley
Education – Digital Pathology Benefits

- Numerous copies of digital slides can be made without damaging the original material
- No physical slide is required (no geographic restriction in order to access material)
- Whole slide images provide the entire slide (rather than snapshots of slides) for educational purposes
Education – Digital Pathology Cons

– No reimbursement for the creation of content
– Few platforms to host content
– Education alone does not support the business case of digital pathology
– Value of the resource dependent on the quality of the source
Academic Hospital Rotations

Children’s Hospital

Shadyside Hospital

Veteran’s Hospital

Presbyterian

Montefiore

Magee Women’s

Clinical Laboratory Building

Slide Courtesy of Dr. N. Barasch
Consultation

• Routine practice to get second opinion for diagnostic work
• Two components
  – Sending out
  – “In-sourcing”
External Consultation

• When sending out glass slides, there can be issues
  – Breakage
  – Time
  – Multiple opinions
  – Return
“In-Sourcing”

- Current Telepathology Portals at UPMC
  - ISMETT
  - Direct (ad-hoc)
  - KingMed (China)
  - Qingdao (China)
  - Xinxiang (under development)
Data Entry
### Clinical Data

Required fields are marked with *

<table>
<thead>
<tr>
<th>Field</th>
<th>Description</th>
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<td>* Organ</td>
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<td>Clinical History</td>
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<tr>
<td>Pre-op Diagnosis</td>
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<td>Post-op Diagnosis</td>
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<td>Procedure</td>
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<td>Gross Description</td>
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### Division

Please select a division where you would like this request directed. You should also select a specific physician you would like to perform the consultation, or select "First Available."
Data Entry – Cont’d (2)

Please select a division where you would like this request directed. You should also select a specific physician you would like to perform the consultation, or select "First Available."

<table>
<thead>
<tr>
<th>Division</th>
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<tbody>
<tr>
<td>AUTOPSY/INFECTIONAL PATHOLOGY</td>
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<tr>
<td>BONE-SOFT TISSUE PATHOLOGY</td>
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<tr>
<td>BREAST/GYNECOLOGIC PATHOLOGY AND CYTOPATHOLOGY</td>
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<tr>
<td>CARDIAC PATHOLOGY</td>
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<tr>
<td>CYTOPATHOLOGY NON-GYNECOLOGICAL</td>
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<tr>
<td>DERMATOPATHOLOGY/HIF</td>
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<td>ENDOCRINE PATHOLOGY</td>
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<td>EYE PATHOLOGY</td>
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<td>GENITOURINARY PATHOLOGY</td>
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<td>GI PATHOLOGY</td>
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<td>HEAD AND NECK PATHOLOGY</td>
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<td>HEMATOLOGY</td>
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<td>INFORMATICS</td>
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<td>KIDNEY/EM</td>
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<td>LIVER AND TRANSPLANT PATHOLOGY</td>
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<td>MALIGNANT MELANOMA</td>
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<td>NEUROPATHOLOGY</td>
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<td>PERINATAL PATHOLOGY</td>
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<td>THORACIC PATHOLOGY</td>
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Finalized Report
Multidisciplinary Conferences

• Conference that meets to discuss patient care
• Multiple medical disciplines present findings
• Radiology and Pathology are foundation plus clinical group
Multidisciplinary Sample from UPMC

<table>
<thead>
<tr>
<th>2nd Monday of Month</th>
<th>7:30 AM</th>
<th>Complete Anorexy Conference</th>
<th>PACCOM Conference Room, MA 421, MLH</th>
<th>30 min</th>
<th>Mary Folkerts, B.A., Office Mgr.</th>
<th>412.600.2150</th>
<th><a href="mailto:mfolkert@upmc.edu">mfolkert@upmc.edu</a></th>
<th>Dr. Bari Younssi</th>
<th>Thoracic Fellows (set to learn Patient &amp; Thoracic Fellows)</th>
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<tbody>
<tr>
<td>TUE 8/18 7:30-10 AM</td>
<td>UPMC UPMC Thoracic Oncology Tumor Board</td>
<td>UPMC Shadyside Hospital, Wool Wing Classroom 408</td>
<td>8 hrs</td>
<td>Dr. Rasesh Oza, MBA</td>
<td>412.456.3205</td>
<td><a href="mailto:raza@upmc.edu">raza@upmc.edu</a></td>
<td>Dr. Jose/Thoracic Fellows</td>
<td>(set to learn Patient &amp; Pulmonary to pull slides)</td>
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<tr>
<td>11:30 AM-12:30 PM</td>
<td>Dr. Faber Conference</td>
<td>PVH-4416.1 (Multi-headed Scope Room)</td>
<td>5 hrs</td>
<td>Dr. Christine Pate</td>
<td>412-600-2710</td>
<td><a href="mailto:faber@upmc.edu">faber@upmc.edu</a></td>
<td>Staff Pulmonologists</td>
<td>(entrance to Transplant Board)</td>
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<tr>
<td>Noon</td>
<td>Pathology Case Conference #31</td>
<td>PVH-N412 Large Multi-headed Scope Room</td>
<td>3 hrs</td>
<td>Diana Wentz</td>
<td><a href="mailto:wentz2@upmc.edu">wentz2@upmc.edu</a></td>
<td>alp@jnu, Fellows, Residents invited</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4:30 PM</td>
<td>Liver Conference, Additive</td>
<td>Transplant Pathology Conference Room 1010.1004</td>
<td>2-3 hrs</td>
<td>Anthony J. Demetris, MD</td>
<td>412.600.5367</td>
<td><a href="mailto:coudias@upmc.edu">coudias@upmc.edu</a></td>
<td>(case list sent to Jaapkep Behar, Jessica Balls, Elizabeth Kielam, Vini Jayaram, Diane Wentz, Nicole A. Amy Schulten) (ent into pulls slides)</td>
<td></td>
<td></td>
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<tr>
<td>1st Tuesday of Month</td>
<td>Noon</td>
<td>Heart Case Conference</td>
<td>Transplant Pathology Conference Room 1010.1004</td>
<td>1 hr</td>
<td>Sibtech Coudias</td>
<td><a href="mailto:coudias@upmc.edu">coudias@upmc.edu</a></td>
<td>Anthony J. Demetris, MD</td>
<td>(ent into pulls slides)</td>
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<td>2nd Tuesday of Month</td>
<td>6:30 am</td>
<td>Colpos Conference</td>
<td>MAH - Room 2131</td>
<td>3 hrs</td>
<td>E. Ehrman, MD</td>
<td>OB/GYN Residents</td>
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<table>
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<tr>
<th>TUESDAY</th>
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<tbody>
<tr>
<td>Schedule changes (Item A)</td>
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| 8:00-10 AM | Thyroid/Cytology Conference | PUMC-N412 Large Multi-headed Scope Room | 3 hrs | Lisa Silver | 412-456-4343 | silver@upmc.edu | Dr. Chelsie Silver | Tissue to the med
| 10:00-10 AM | Tissue Education Day (Int. Tissue Tumor Pathology) | PUMC Watson Education Ctr., Room G-300 | 6 hrs | Angela Kostas, Project Coordinator | 412.268.2418 | kostas@upmc.edu | Staff Pathologists on Thoracic (include thoracic Fellowship) (case list sent to Clara Wurtz) who forwards to whom who supports pathologist on Thoracic Board |
Elements of Multidisciplinary Conference

• Location
• Transition between presenters
• Summarize findings/decisions
• Preparation
Solutions for Multidisciplinary

- Sectra
- Inspirata
- Proscia
- Corista
- PathPresenter

*NB – many commercial and opensource offerings (incomplete list)
Quality Assurance

- Post-Signout review
- Pre-Signout review
- CAP PIP slides
Post-Signout Review

• At UPMC, we perform ~12% post-signout QC
• Single pathologist ~100 miles from central site
• Using hybrid scanner, we have been able to perform post-signout QC
Post-Signout Review Experience

• With the introduction of hybrid scanners, the devices that have been deployed for remote intraoperative consultation can now also be used for other purposes.
• We found that using digital slides for post signout review shortened the average review time per case by nearly 3 months.
• For the sending site, the digital method was more convenient and secures the integrity of the slides.
• Multiple use cases can help to add to the return on investment of a hybrid scanner.
Pre-Signout QC at UPMC

- Since 2010, we have routinely performed “Pre-Signout” QC
- Available personnel
Using Hybrid Scanner for Pre-Signout QC

- Consolidation within the community division
- Hybrid scanner supports subspecialty intraoperative consultation
- Scanner can also be used for Pre-signout QC
College of American Pathologists – Professional Improvement Program (PIP)

• 10 cases with glass slides
• Quarterly distributed
• CAP now offering Virtual Biopsy program (VBP) which is digital slides
Image Analysis

• Suggested to be a Driver for digital pathology adoption
• Can provide detail/reproducibility not available by conventional microscopy
• May assist with rare event detection (improve quality)
• Reimbursement already present for Breast Biomarkers
Image Analysis
Outcome Data based on Univariate Analysis (n=74)

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<tr>
<th>Mann-Whitney test</th>
<th>n</th>
<th>Tumor Density</th>
<th>Margin Density</th>
<th>Stromata Density</th>
<th>Entire Section Density</th>
<th>Total Density (Tumor + margin + stroma)</th>
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<td></td>
<td></td>
<td>Median</td>
<td>U</td>
<td>P value</td>
<td>Median</td>
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<td>256.5</td>
<td>425.0</td>
<td>0.614</td>
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<td>687.0</td>
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<td>372.1</td>
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<td>0.001</td>
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Survival based on Density of CD8 cells

The survival distributions for the two entire section density groups were statistically significantly different (Chi square = 11.413, p = 0.001), demonstrating that the overall survival of patients with high-density entire section cellularity was significantly longer than patients with low-density section cellularity. The median survival (the smallest time at which the survival probability drops to 50%) was 18 years for the high-density section group (95% CI 9.1-26.9 years), compared to 5 years for the low-density section group (95% CI 0.6-9.4 years). The Kaplan-Meier survival curves shown below demonstrates that patients with low-density section cellularity were at a greater risk of earlier death than patients with high-density section cellularity.

Utility of CD8 score by automated quantitative image analysis in head and neck squamous cell carcinomas

Oral Oncology 86 (2018) 278–287

Presence of the low section density shows a trend of significantly lower survival in relation to high-density section cellularity. Low section density, n = 37; died, 27; censored (alive as of last follow-up), 10; median, 5 years. High section density, n = 37; died, 11; censored (alive as of last follow-up), 26; median, 18 years.
Take Home Message

• We have successfully cross-validated quantitative IHC image analysis with quantitative fluorescence (AQUA)
• For a cohort of 74 oropharyngeal cases a density above 136 cells/mm² was associated with a mean survival of 18 years
• We are ready to expand quantitative image analysis for more indications and need cases with outcome data in order to provide this for clinical care
Research

• External to Department Consultations
  – Other departments within University
  – Industry

• Image Data as a new field of data analysis
Conclusions

✓ Evaluating Institutional needs during acquisition process is more likely to lead to success implementation

✓ Full utilization of digital pathology will likely require capabilities outside of the digital pathology solution

✓ Many opportunities exist to maximize the use of a digital pathology platform
Questions and Answers

Douglas J. Hartman MD

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