Successful Validation of Virtual Microscopy for Surgical Pathology but Not Cytopathology: Application of the College of American Pathologists (CAP) Guidelines

Michael A. Arnold, M.D., Ph.D.[1]; Emily Chenever, MS, PA(AAPA; ASCPcm)[1], Peter B. Baker, M.D.[1]; Daniel Boue, M.D., Ph.D.[1]; Bonita Fung, M.D.[1]; Sue Hammond, M.D.[1]
Brett W. Hendrickson, M.D.[1]; Samir B. Kahwash, M.D.[1]; Christopher R. Pierson, M.D., Ph.D.[1]; Vinay Prasad, M.D.[1]; Kathleen K. Nicol, M.D.[1]; Thomas Barr, BS, MLT (ASCP)[2]
[1]Department of Pathology and Laboratory Medicine, Nationwide Children's Hospital, Columbus, OH; [2]Nationwide Children's Hospital, The Research Institute at Nationwide Children's Hospital, Columbus, OH

abstract

Background: Virtual microscopy (VM) is rapidly emerging as a key technology for transforming educational and diagnostic services. Recently, CAP published the first guidelines for validating the VM for diagnostic use. Herein, we report the findings of our VM validation study of surgical pathology and cytopathology specimens at our pediatric institution.

Design: The study included randomly selected cases, and cases specifically chosen to represent complex or less common diagnostic categories (Table 1). Surgical pathology specimens served as the primary modality (60 cases with 130 specimen parts) and cytopathology as the secondary modality (21 cases with 29 specimen parts). In total, the study included 627 slides. VM cases were reviewed by the 9 pathologists who had previously completed clinical evaluation of the glass slides, in accordance with the CAP guidelines. Digital slides corresponding to those ordered by the pathologist (special stains and immunohistochemical stains) and ancillary test results were available to the pathologist on request after initial VM review.

Results: Based on our previous experience, digital capture of cytospin slides and small biopsies was performed at 40x magnification. The remaining slides were captured at 20x magnification; all slides were imaged in a single plane. Low cellularity prevented digital capture of 2 cytology slides, precluding evaluation of one case. Of the surgical pathology cases, the final diagnoses were highly concordant with glass slide diagnoses; diagnostic discrepancies were seen in less than 2% of cases, and none altered patient management. Diagnoses for cytology specimens were significantly more discordant, with discrepancies or inadequate cytologic detail for confident review in 30% of cases.

Conclusion: Our results demonstrate that surgical pathology specimens representing the spectrum of pediatric pathology practice can be adequately reviewed using virtual microscopy. However, review of cytology specimens will require improved resolution, perhaps including Z-stacked images.

methods

Surgical Pathology Cases	
GI Biopsy, Random	8
GI Biopsy, Non-random	2
Heart Biopsy, Random	1
Heart Biopsy, Non-random	1
Liver Biopsy, Random	3
Lung Biopsy, Non-random	1
Neuropathology, Random	12
Other Surgical, Random	8
Other Surgical, Non-random	1
Placenta, Random	3
Skin, Non-random	5
Suction Rectal, Random	1
Tonsil, Random	5
Tonsil, Non-random	3
Tumor, Non-random	6

Cytopathology Cases	
BAL, Random	6
BAL, Non-random	1
CSF, Random	5
FNA, Random	3
FNA, Non-random	1
Marrow, Random	4
Pericardial, Random	1

Table 1: Case Selection for VM Validation
Cases selected for our VM validation study represented various areas of pediatric surgical pathology (left) and cytopathology (above). Cases were selected as either consecutive cases over 6 month period (Random), or were chosen to represent a specific diagnosis or specimen type (Non-random). All cases were previously reviewed as glass slides for clinical purposes prior to our VM validation study.

results

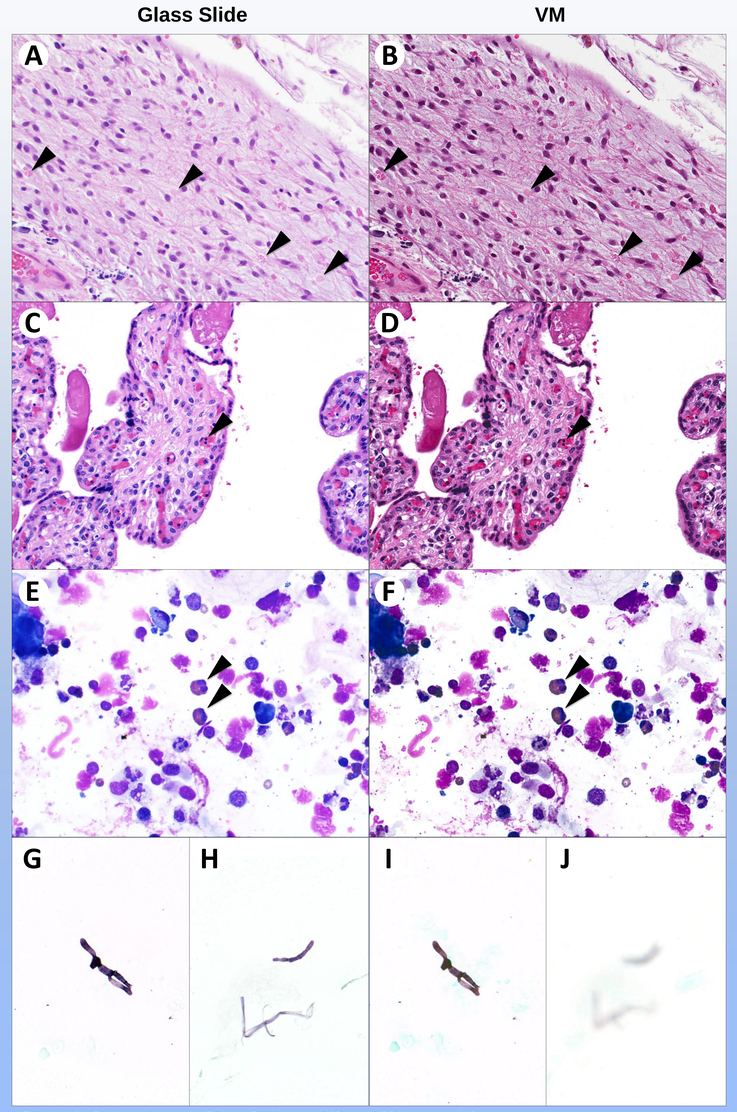

Figure 1: Comparison of Glass Slides and Virtual Microscopy Images
Comparisons of images taken from glass slides (left) with the VM slides (right) demonstrate subtle differences in the appearance of some histologic features, including eosinophilic granular bodies from a pilocytic astrocytoma (A and B, arrowheads), nucleated red blood cells in placental villi (C and D, arrowheads), and eosinophils in a cytospin specimen (E and F, arrowheads). G, H, I and J: Single plane image capture of cytospin specimens resulted in variable focus quality of the fungi in a GMS stained bronchoalveolar lavage.

results

	Surgical Pathology Diagnoses		Cytopathology Diagnoses	
	Concordant	Discordant	Concordant	Discordant
Cases	59	1	14	6
	98.3%	1.7%	70.0%	30.0%
Parts	127	3	26	8
	97.7%	2.3%	76.5%	23.5%

Table 2: VM Validation Study Concordance with Glass Slide Diagnoses
VM diagnoses for surgical pathology cases were highly concordant (98.3%) with the corresponding glass slide diagnoses. VM review of cytopathology cases resulted in a lower concordance rate (70%). Discordant cytopathology cases included 4 cases with inadequate image quality for confident review.

Surgical Pathology Discrepancies		
Major Surgical Pathology Differences	Cases	Parts
Brain tumor, Glioneuronal tumor (VM) vs. Pilocytic astrocytoma (glass)	1	3
Minor Surgical Pathology Differences	Cases	Parts
Liver, grading of inflammation or fibrosis	2	3
Colon, architecture change	1	2
Esophagus, chronic changes	1	1
Stomach, chronic inflammation	3	4
Placenta, inflammation and presence of nRBCs	1	1
Skin, architecture	2	4
Nerve, architecture	1	3
Heart, inflammation	2	2
Colon, eosinophils	1	4
Colon, architecture change and eosinophils	1	1
Total	**15**	**25**
Cytopathology Discrepancies		
Major Cytopathology Differences	Cases	Parts
Bronchial lavage, fungi not reported by VM	1	1
Bone marrow, lymphoblasts not reported by VM	1	3
Pericardial fluid (cytospin), inadequate VM detail	1	1
CSF (cytospin), inadequate VM detail	3	3
Total	**6**	**8**
Minor Cytopathology Differences		
Bone marrow, no differential count by VM	1	3
Bronchial lavage, rare bacteria not reported by VM	2	2
Total	**3**	**5**

Table 3: Observed Differences in VM and Glass Slide Diagnoses
Differences in VM review of surgical pathology review of cases resulted from difficulty in detecting specific features(see Figure 1). Discrepancies in cytopathology cases were most often associated with resolution of high magnification cellular detail or focus quality.

conclusions

- **We successfully implemented the CAP guidelines for VM validation using standard desktop computer resources and slide scanning capabilities with single plane imaging.**
- **Pediatric pathology surgical specimen VM review resulted in successful validation.**
- **Cytopathology specimen VM review was limited by resolution and focus plane selection.**
- **Pathologists should be aware of histologic features that appear different in VM slides.**
- **Image capture of cytology specimens can be limited by low cellularity.**
- **High resolution image capture (40x) is required to reliably identify cytologic detail, and capture in multiple image planes may be required for cytopathology specimens.**