Recommendations for Validating Whole Slide Imaging Systems for Diagnostic Purposes in Pathology*

October 10, 2012

Presented by John Sinard on behalf of the Expert Panel

* Pending final CAP Approval
Digital Pathology Validation Expert Panel
Convened June 2010

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What needs to be done to “validate” a whole slide digital imaging system for diagnostic purposes before it is placed in clinical service?

Panel addressed: Intended use, preparation types, number of cases, equipment, personnel, and process
Systematic Review Results

- Literature search was conducted; 767 studies met the search term requirements; 27 underwent data extraction for evidence evaluation.
- Panel met 8 times to develop draft recommendations
- Open Comment Period: July 2011; 132 respondents; 531 comments
- Panel met 10 additional times to review feedback, make revisions to recommendations, and assess strength of evidence supporting the 12 final recommendations
Quality Assessment and Grading of Evidence

• **Strength of evidence:** level of evidence, quantity, size of the effect, statistical precision and, quality assessment (risk of bias) of included studies.

• Also taken into account were the study components of consistency, clinical impact, generalizability, and applicability to WSI when determining the strength of evidence score.
## Quality Assessment and Grading of Evidence

<table>
<thead>
<tr>
<th>Grade of recommendation</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>Body of evidence can be trusted to guide practice</td>
</tr>
<tr>
<td>B</td>
<td>Body of evidence can be trusted to guide practice in most situations</td>
</tr>
<tr>
<td>C</td>
<td>Body of evidence provides some support for recommendation(s) but care should be taken in its application</td>
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<tr>
<td>D</td>
<td>Body of evidence is weak and recommendation must be applied with caution</td>
</tr>
<tr>
<td><strong>Expert Opinion</strong>*</td>
<td><strong>Insufficient or conflicting body of evidence</strong>*</td>
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*CAP definition
• All pathology laboratories considering the implementation of WSI technology for clinical diagnostic purposes should carry out their own validation study.

Grade: Expert Opinion
• Validation should be appropriate for and applicable to the intended clinical use and clinical setting of the application in which WSI will be employed. Validation of WSI systems should involve specimen preparation types relevant to intended use (e.g., formalin-fixed paraffin-embedded tissue, frozen tissue, IHC stains, cytology slides, hematology blood smears).

  Note: If a new intended use for WSI is contemplated, and this new use differs materially from the previously validated use, a separate validation for the new use should be performed.

Grade: Recommendation, Level A
The validation study should closely emulate the real-world clinical environment.

Grade: Recommendation, Level A
#4

- The validation study should encompass the entire WSI system.
  
  Note: It is not necessary to validate separately each individual component (e.g., computer hardware, monitor, network, scanner) of the system nor the individual steps of the digital imaging process.

Grade: Recommendation, Level B
• Re-validation is required whenever a significant change is made to any component of the WSI system.

Grade: Expert Opinion
#6

- A pathologist(s) adequately trained to use the WSI system must be involved in the validation process.

Grade: Recommendation, Level B
• The validation process should include a sample set of at least 60 cases for one application (eg, HE, FS, cytology, hematology) that reflects the spectrum and complexity of specimen types and diagnoses likely to be encountered during routine operation.

  o Note: The validation process should include another 20 cases for each additional application (eg, IHC, special stains).

Grade: Recommendation, Level A
The validation study should establish diagnostic concordance between digital and glass slides for the same observer (i.e., intraobserver variability).

Grade: Expert Opinion
• Digital and glass slides can be evaluated in random or non-random order during the validation process.

Grade: Recommendation, Level A
#10

- A washout period of at least 2 weeks should occur between viewing digital and glass slides.

Grade: Recommendation, Level B
#11

• The validation process should confirm that all of the material present on a glass slide to be scanned is included in the digital image.

Grade: Expert Opinion
#12

- Documentation should be maintained recording the method, measurements and final approval of validation for the WSI system to be used in the clinical laboratory.

Grade: Expert Opinion
Conclusion

• Validation of WSI is necessary to ensure that a pathologist using this technique to view digitized glass slides can consistently make the same clinical interpretation as they would from viewing the glass slides using a traditional bright field microscope.

• Validation should address both technical and interpretative components, and must be specific for the intended clinical use.