

Commentary: Whole-slide Images – Good Enough for Primary Diagnosis?

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Commentary on Mukhopadhyay, *et al.* Whole Slide Imaging Versus Microscopy for Primary Diagnosis in Surgical Pathology. A Multicenter Blinded Randomized Noninferiority Study of 1992 Cases (Pivotal Study). *Am J Surg Pathol*.

SUMMARY

As advances in technology have brought digital images into so many aspects of our lives, some people wonder why diagnostic pathology has not become purely digital as was accomplished for radiology many years ago. There are many differences between digital radiology and pathology, but one factor that has limited the use of whole-slide images (WSIs) for primary diagnosis has been the suspicion that the quality of WSI might not measure up to that of the original glass microscope slides. Mukhopadhyay *et al.* recently published the results of a multicenter validation study intended to test whether or not the interpretation of digital, scanned microscope slides is inferior to the use of a microscope for making primary diagnoses in surgical pathology.^[1] Although several previous studies have demonstrated noninferiority,^[2-6] this study, designed in part after discussions with the US Food and Drug Administration and using only the Phillips IntelliSite Pathology Solution® scanning system, is one of the largest and most Comprehensive studies thus far completed.

Sixteen pathologists from four different institutions interpreted cases of variable complexity, from different organ systems using WSI or conventional light microscopy (LM), waited at least 4 weeks and then interpreted the same cases using the other method. An adjudication panel of pathologists classified the diagnoses as either concordant, major discordant, or minor discordant with respect to the original (reference) diagnosis. The results showed a major discordance rate of 4.9% for WSI and 4.6% for LM (not significantly different).

COMMENT

Because four pathologists interpreted each case using both WSI and LM, if a technical problem existed in WSI that would prevent the pathologist from reaching a correct diagnosis, that problem would have been identified by the combination of consistent major discordances between WSI and the reference diagnosis but concordant diagnoses between microscopic slide review and the reference standard on the same case. However, the study did not detect a single case where all four pathologists erred using WSI but made the correct diagnosis by LM. This consistency helps provide confidence in the reliability of the imaging technology for many different organ systems.

Unlike several previous studies,^[2,6] the pathologists in the Mukhopadhyay *et al.*'s study were not given the option of deferring a diagnosis as might be done in actual practice when a pathologist encounters a case outside his or her subspecialty. This might be one explanation for what seems like a relatively high rate of major discrepancies for both WSI and LM in some organ systems. Among prostate cases, for example, there was no significant difference in the rate of major discordances between LM or WSI, but major discordance rates of 11.3% between LM versus reference diagnosis, and 12% for WSI versus reference diagnosis suggests that the pathologists participating in the study might have interpreted cases that under normal circumstances would be further investigated with recuts, immunohistochemistry, or shared with a colleague or consultant. Therefore, the discordance rates reported in this study for either method should not be extrapolated to the practice of pathology in general.

Several previous studies have noted that neutrophils and eosinophils may be difficult to distinguish in WSI^[2,3] and that grading dysplasia may be a source of discrepancies.^[2,7-9] These issues might be improved by adjusting the monitor to improve the balance between the blue (hematoxylin) and pink (eosin).^[3,8] Not surprisingly, previous studies have also noted that high magnification scans may be needed to recognize bacteria, such as *Helicobacter*.^[3,4,8] While the Mukhopadhyay *et al.*'s manuscript describes the use of an "adjudication charter" to help classify cases, the details of that table are not readily available. So one wonders, for example, what exactly constituted a major versus a minor discrepancy, especially in these problematic areas such as the prostate. Similarly, it is not clear if differences in stage, based on completed College of American Pathologists (CAP) synoptic templates would be considered major or minor discrepancies. In contrast, at least one previous study has included numerous details describing the use and content of "synoptic discordance tables" as well as checklists from the CAP.^[6]

In the absence of the "adjudication charter," it is difficult for readers to develop their own opinion about the clinical significance or severity of discrepancies between the two methods. Nevertheless, it is important to recognize that the use of WSI in this study was not inferior to microscope slide interpretation, even for complicated cases that require staging and grading.

In summary, this large, prospective, multicenter study provides the most compelling evidence to date that WSI, at least using the hardware and software tested in this study, is not inferior to traditional LM for primary diagnoses in surgical pathology.

This seems applicable across multiple organ systems and practice settings.

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REFERENCES

- Mukhopadhyay S, Feldman MD, Abels E, Ashfaq R, Beltaifa S, Cacciabeve NG, *et al.* Whole slide imaging versus microscopy for primary diagnosis in surgical pathology: A Multicenter blinded randomized noninferiority study of 1992 cases (Pivotal study). *Am J Surg Pathol* 2018;42:39-52.
- Bauer TW, Schoenfield L, Slaw RJ, Yerian L, Sun Z, Henricks WH, *et al.* Validation of whole slide imaging for primary diagnosis in surgical pathology. *Arch Pathol Lab Med* 2013;137:518-24.
- Buck TP, Dilorio R, Havrilla L, O'Neill DG. Validation of a whole slide imaging system for primary diagnosis in surgical pathology: A community hospital perspective. *J Pathol Inform* 2014;5:43.
- Campbell WS, Lele SM, West WW, Lazenby AJ, Smith LM, Hinrichs SH, *et al.* Concordance between whole-slide imaging and light microscopy for routine surgical pathology. *Hum Pathol* 2012;43:1739-44.
- Houghton JP, Ervine AJ, Kenny SL, Kelly PJ, Napier SS, McCluggage WG, *et al.* Concordance between digital pathology and light microscopy in general surgical pathology: A pilot study of 100 cases. *J Clin Pathol* 2014;67:1052-5.
- Wack K, Drogowski L, Treloar M, Evans A, Ho J, Parwani A, *et al.* A multisite validation of whole slide imaging for primary diagnosis using standardized data collection and analysis. *J Pathol Inform* 2016;7:49.
- Ordi J, Castillo P, Saco A, Del Pino M, Ordi O, Rodriguez-Carunchio L, *et al.* Validation of whole slide imaging in the primary diagnosis of gynaecological pathology in a university hospital. *J Clin Pathol* 2015;68:33-9.
- Snead DR, Tsang YW, Meskiri A, Kimani PK, Crossman R, Rajpoot NM, *et al.* Validation of digital pathology imaging for primary histopathological diagnosis. *Histopathology* 2016;68:1063-72.
- Williams BJ, DaCosta P, Goacher E, Treanor D. A systematic analysis of discordant diagnoses in digital pathology compared with light microscopy. *Arch Pathol Lab Med* 2017;141:1712-8.

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