

Trainable IHC HER2 Image Analysis System for Dako HercepTest and Ventana PATHWAY HER2

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Background

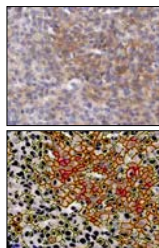
Multiple reagent manufacturers provide Immunohistochemistry (IHC) Human Epidermal Growth Factor Receptor 2 (HER2) reagents, each expressing different staining characteristics.

The American Society of Clinical Oncology (ASCO) and the College of American Pathologists (CAP) provide HER2 guidelines recommending laboratories show 95% concordance with another validated test.

Aperio Technologies Inc. provides trainable IHC HER2 Image Analysis that allows adaptation to the staining characteristics of different reagents and correlates the analysis results to a scoring standard.

IHC HER2 Image Analysis

The IHC HER2 image analysis analyzes the HER2 slide in the same way as pathologists according to HER2 assay instructions and provides an intuitive and detailed assessment in terms of the HER2 score, the underlying percentages of cells, and a comprehensive overlay image.



HER2 Score: 2+

3+ Cells:	7.3%
2+ Cells:	39.6%
1+ Cells:	52.5%
0 Cells:	0.6%

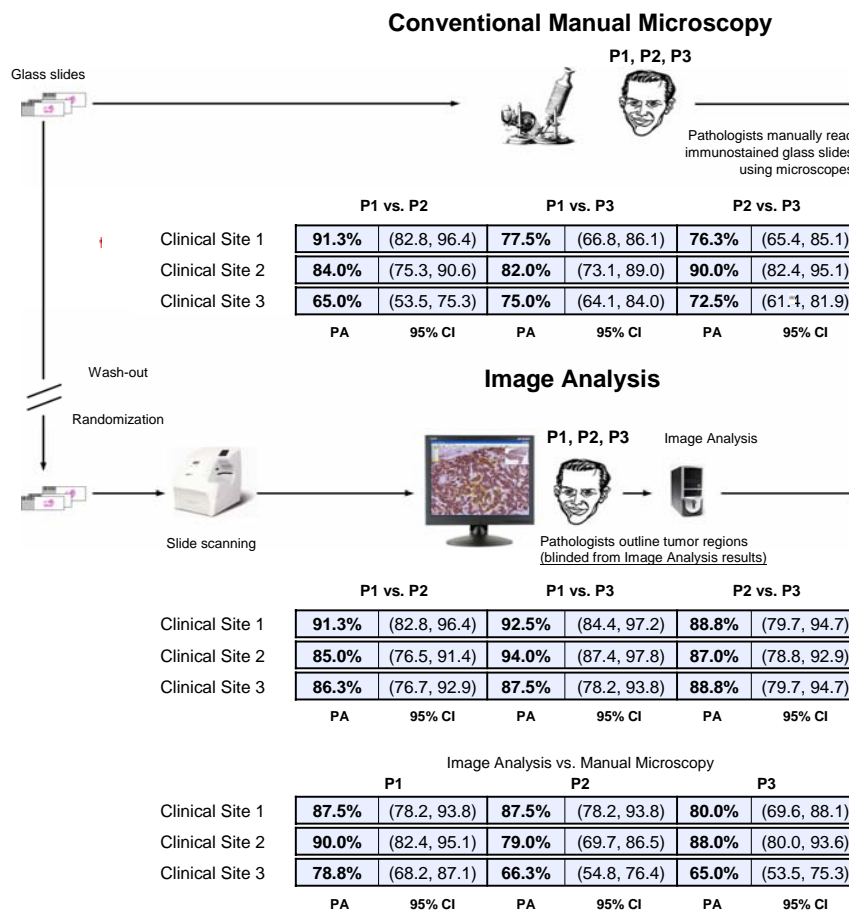
Image Analysis Results

With the image analysis reporting the percentages of 3+ cells, pathologists can use it according to the ASCO/CAP HER2 guidelines, calling HER2 slides positive when more than 30% of the cells are 3+.

Automatic Training

Pathologists outline the tumor regions for analysis on the digital slides and provide the scores for a representative set of slides the same way as is done manually. The algorithm then automatically calculates the optimum intensity thresholds for the HER2 scoring scheme.

A Multi-Site Performance Study using 260 HER2 Stained Breast Specimens



Design

A multi-site performance study was conducted at Emory University Hospital, Quest Diagnostics Nichols Institute, and Medical Laboratory Associates. Aperio Technologies Inc.'s trainable IHC HER2 Image Analysis was compared to conventional manual microscopy using different IHC reagents.

260 formalin-fixed, paraffin-embedded breast tissue specimens from 3 clinical sites were assayed; 80 specimens with almost equal HER2 score distribution from clinical site 1 and 100 routine specimens from clinical site 2 were stained with Dako HercepTest™, and 80 specimens with almost equal HER2 score distribution from clinical site 3 were stained with Ventana PATHWAY HER2.

At each site, 20 representative slides with scores from 3 pathologists were used to automatically train the image analysis algorithm.

At each site, 3 pathologists performed a blinded read of the glass slides using their microscopes, and reporting the HER2 score (0, 1+, 2+ or 3+) for each slide. The glass slides were then scanned using a 20X objective and randomized. After a wash-out period of over one week the same 3 pathologists outlined a representative set of tumor regions to be analyzed by image analysis. The image analysis reported the HER2 score for each of the 3 pathologists for each of the slides.

The image analysis itself was run in batch mode blinded from the pathologists to avoid influencing the pathologists in their choice of the tumor regions.

Result

Each of the methods: manual microscopy and image analysis were evaluated separately and comparatively between methods using Percent Agreement (PA) along with an exact 95% Confidence Interval (CI) of a trichotomous categorization of the HER2 scores combining 0 and 1+ and leaving 2+ and 3+ uncombined.

The image analysis show overall higher percent agreement values than manual microscopy, and comparable percent agreement values between image analysis and manual microscopy.

Conclusion

This performance study has demonstrated that Aperio Technologies Inc.'s trainable IHC HER2 Image Analysis, when used with Dako HercepTest or Ventana PATHWAY HER2 can improve the consistency of the IHC HER2 test results.