OPTIMIZING HER2 DIAGNOSTIC PATHWAYS: AI ASSISTANCE ENRICHES GENE AMPLIFIED CASES IN EQUIVOCAL CATEGORY AND REDUCES TURNAROUND TIME

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BACKGROUND

- HER2 expression is a key prognostic and treatment-influencing factor in breast cancer and is assessed routinely in all patients diagnosed with invasive breast carcinoma (BC)
- As with all immunohistochemistry (IHC) staining, visual interpretation of HER2 expression is subjective, which leads to intra- and inter-pathologist variability[1-3]

OBJECTIVE

To evaluate the clinical utility (accuracy and efficiency) of artificial intelligence (AI)-based HER2 scoring solution on whole slide digital images of HER2 IHCs of breast samples

METHODS

Observational two-arm multi-reader study on 2,300 biopsies and excisions including diverse BC subtypes from primary and metastatic tumors

- N=2181 HER2 IHC-stained breast cancer slides
- 14 clinical laboratories from US, EU, Brazil, and UK
- 28 pathologists
- 8 different scanners from 5 manufacturers

- 28 pathologists scored HER2 IHCs according to the 2023 ASCO/CAP guidelines[4] unassisted and supported by AI HER2 solution (Ibex Breast HER2®)
- Each HER2 IHC slide was reviewed independently by two pathologists
- Both study arms were compared to ground truth score (GT), established as the majority HER2 score of three breast pathologists who scored the slides manually

Age	Invasive Carcinoma Type				Procedure			Local HER2 score				
Mean (±Std)	IDC	ILC	IDC+ ILC	Other/ missing	Biopsy (%)	Excision (%)	Other/ missing	0	1+	2+	3+	Missing
62.8 (±14.3)	1,638 (75%)	271 (12%)	20 (1%)	252 (12%)	1,613 (74%)	433 (20%)	135 (6%)	645 (29%)	673 (31%)	408 (19%)	280 (13%)	175 (8%)

Table 1 | Cohort characteristics

- 119 slides were excluded from analysis – due to poor technical quality, lack of invasive tumor in the slide, or unsupported cancer types (papillary or micropapillary histology)
- 2,181 slides included in the study analysis

HER2 AI algorithm

- A fully automated AI-based solution for HER2 scoring according to the 2023 ASCO/CAP guidelines
- Classifies tissue regions as invasive carcinoma, ductal carcinoma in situ (DCIS) and other morphologies and provides HER2 score based on the staining pattern of cells in the invasive areas
- The AI was trained using >3M images collected from multiple labs and scanners with 405,000 annotated cells[5]

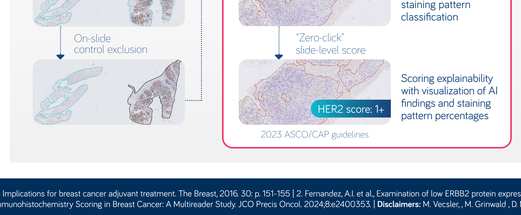


Figure 1 | Overview of the algorithm

RESULTS

HER2 Low and UL Accuracy

Improved overall accuracy with AI

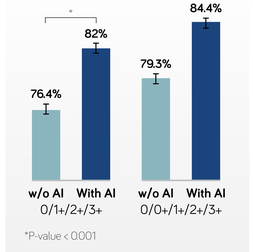


Figure 2 | Pathologists agreement with GT for HER2 low (Left) and UL/Null (Right) classification

57% improvement in the accurate detection of HER2 Low and UL expression

57% of false HER2 0 null classifications corrected to HER2 UL/1+ with AI assistance (97 false reads w/o AI; 55 reads corrected with AI)



HER2 2+ Accuracy

35% less cases classified as HER2 2+ with AI (16% vs. 10%)

Number of cases classified as HER2 2+ by reader pathologists

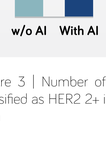


Figure 3 | Number of cases classified as HER2 2+ in each arm

Pathologists' supported by AI were 53% more accurate in HER2 2+ assessment (29% vs. 19% correct reads)

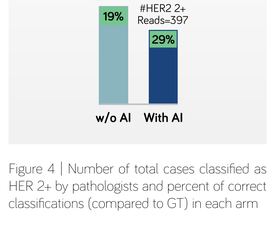


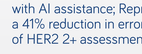
Figure 4 | Number of total cases classified as HER 2+ by pathologists and percent of correct classifications (compared to GT) in each arm

Improved Accuracy and Efficiency of HER2 Positive Assessment

- Analysis of HER2 Negative (0/1+/2+ FISH negative) vs. HER2 positive (2+ FISH positive/3+)
- AI assistance resulted in 66% less error rate in HER2 positive classification (35 false HER2 positive classifications w/o AI vs. 11 with AI; Table 2)

AI reduced unnecessary FISH testing and improved efficiency of HER2 assessment

Patients misclassified as HER2 positive w/o AI



59% of reads classified as 2+ w/o AI were classified as 0/1+ with AI assistance; Represents a 41% reduction in error rate of HER2 2+ assessment

w/o AI

GT	HER2 Neg	HER2 Pos
HER2 Neg	2836	35
HER2 Pos	20	653

AI-assisted

GT	HER2 Neg	HER2 Pos
HER2 Neg	2989	11
HER2 Pos	25	660

Table 2 | Confusion matrix of readers' HER2 positive classification vs. GT w/o and with AI assistance. AI decreased "false" HER2 positive scoring by 66% (N=35 w/o AI vs. 11 with AI assistance)

Pathologists Feedback

How do you feel about your scoring accuracy when assisted by the application, in comparison to routine practice (microscope/digital review)?

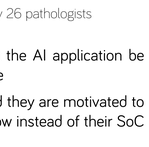


Figure 5 | User survey completed by 26 pathologists

- 100% of pathologists report the AI application be useful in their clinical practice
- 83% of pathologists reported they are motivated to continue using the AI workflow instead of their SoC workflow

Examples of slides with borderline HER2 scores and AI utility

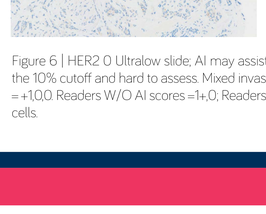


Figure 6 | HER2 0 Ultralow slide; AI may assist in identifying slides when the % of stained cells is below the 10% cutoff and hard to assess. Mixed invasive ductal and lobular carcinoma biopsy. GT HER2 scores = +1,0,0. Readers W/O AI scores =1+,0, Readers with AI scores = 0+,0+, AI = 6.35% faint complete stained cells.



Figure 7 | HER2 Low slide; AI may assist in distinguishing between 1+ and 2+ slides. Invasive ductal carcinoma (IDC) biopsy. GT HER2 scores = 1+,2+,1, Readers w/o AI scores = 1+,2+, Readers with AI scores = 1+,1+; AI = 22.57% faint incomplete, 6.47% moderate incomplete and 0.34% moderate complete stained cells.

CONCLUSION

This international multi-center study demonstrates the clinical utility of AI-based HER2 scoring

Pathologists supported by AI showed improved accuracy for HER2 scoring, including HER2 0 subclassification, HER2 low, and HER2 positive classification

AI-assisted review reduced equivocal (HER2 2+) classifications, enriched HER2 gene amplification status in cases classified as HER2 2+, potentially enabling faster diagnostic turnaround

AI solutions could be used as decision-support tools for pathologists, enhancing the accuracy and efficiency of HER2 scoring, thus enabling optimal treatment pathways and better patient outcomes

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