AI-Enabled Digital Pathology: Lessons Learned From Utilization of PathAI's HER2 Algorithm

Dr. Roshanak Derakhshandeh, MD

Agilent USCAP Seminar

March 25, 2024

MedStar Health

MEDSTAR GEORGETOWN UNIVERSITY HOSPITAL

PathAI

AIM HER2

Background

Human Epidermal Growth Factor Receptor 2 (HER2) is a prognostic and predictive factor in the management of breast cancers

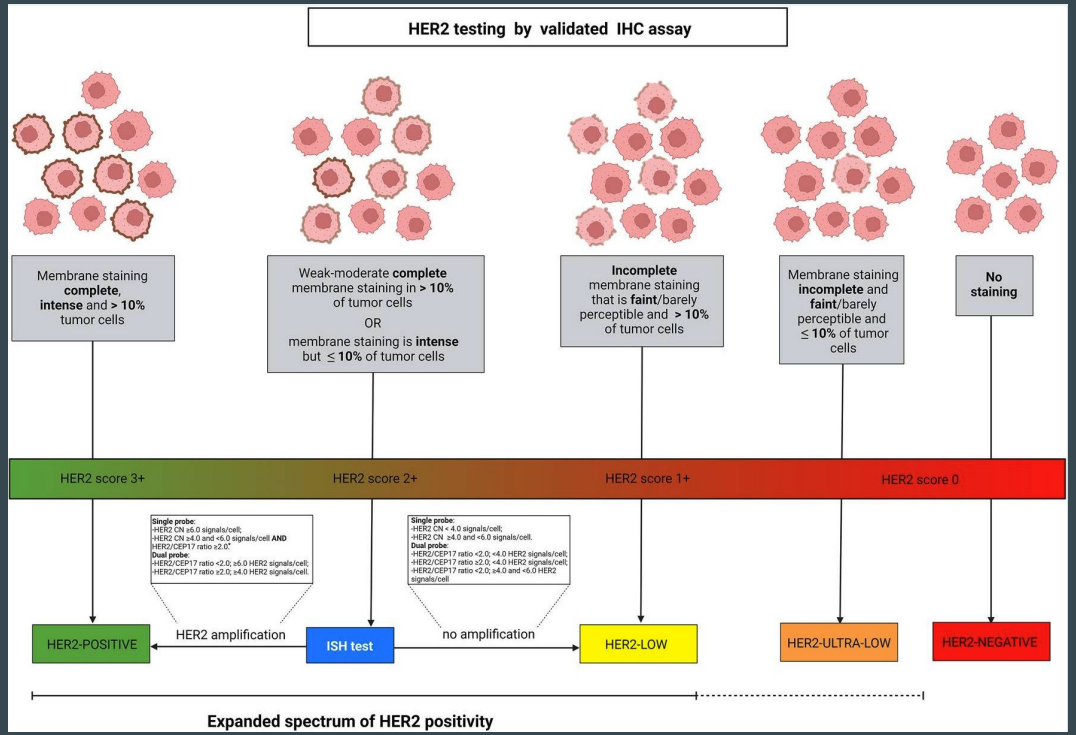
Table 12
Treatment Effects in Study 5 as a
Function of HER2 Overexpression or Amplification

HER2 Assay Result	Number of Patients (N)	Relative Risk[b] for Time to Disease Progression (95% CI)	Relative Risk[b] for Mortality (95% CI)
CTA 2+ or 3+	469	0.49 (0.40, 0.61)	0.80 (0.64, 1.00)
FISH (+)[a]	325	0.44 (0.34, 0.57)	0.70 (0.53, 0.91)
FISH (–)[a]	126	0.62 (0.42, 0.94)	1.06 (0.70, 1.63)
CTA 2+	120	0.76 (0.50, 1.15)	1.26 (0.82, 1.94)
FISH (+)	32	0.54 (0.21, 1.35)	1.31 (0.53, 3.27)
FISH (–)	83	0.77 (0.48, 1.25)	1.11 (0.68, 1.82)
CTA 3+	349	0.42 (0.33, 0.54)	0.70 (0.51, 0.90)
FISH (+)	293	0.42 (0.32, 0.55)	0.67 (0.51, 0.89)
FISH (–)	43	0.43 (0.20, 0.94)	0.88 (0.39, 1.98)

[a] FISH testing results were available for 451 of the 469 patients enrolled on study.
[b] The relative risk represents the risk of progression or death in the Herceptin plus chemotherapy arm versus the chemotherapy arm.

FDA: Herceptin Package Insert

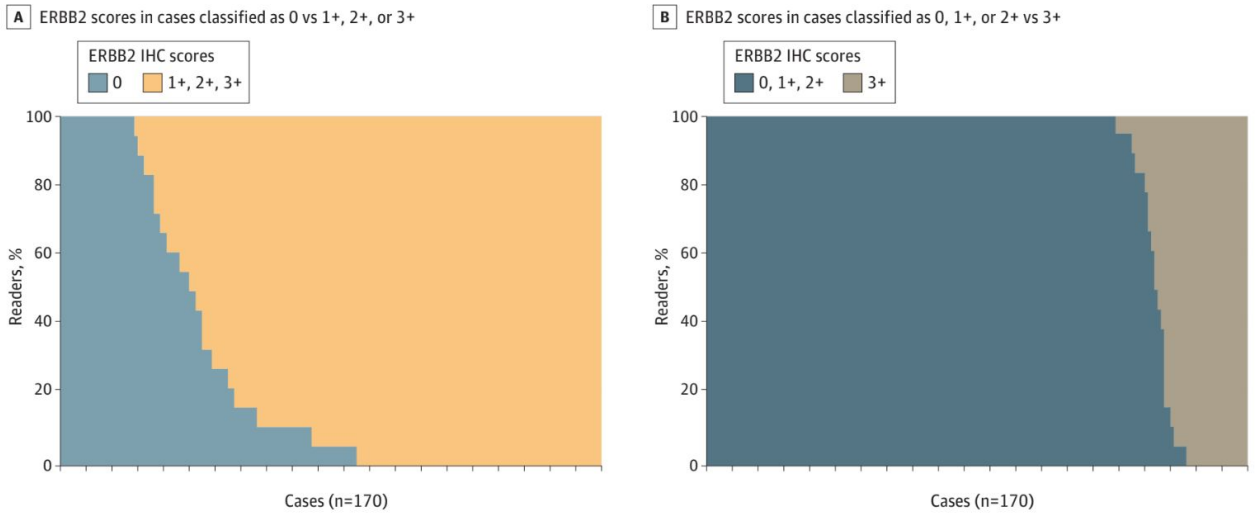
Equivocal HER2 (2+) results by immunohistochemistry (IHC) present a significant diagnostic challenge, and require FISH adjudication



Venetis *et al.* HER2 Low, Ultra-low, and Novel Complementary Biomarkers: Expanding the Spectrum of HER2 Positivity in Breast Cancer. Front Mol Biosci. 2022.

HER2 1+ cases also feature significant inter-pathologist variability: Only 26% of cases have >90% agreement (0 vs 1+) across 18 pathologists

Figure. Distribution of ERBB2 Immunohistochemistry (IHC) Scores in 170 Cases Read by 18 Pathologists/Readers of Whole Tissue Sections in the Yale Cohort



A, Each case (on the x-axis) is shown as the percentage of observers who called the case ERBB2 0 vs ERBB2 1+, 2+, or 3+. B, Each case (on the x-axis) is shown as the percentage of observers who called the case ERBB2 3+ vs ERBB2 0, 1+, or 2+.

Fernandez AI, *et al.* Examination of Low ERBB2 Protein Expression in Breast Cancer Tissue. JAMA Oncol. 2022.

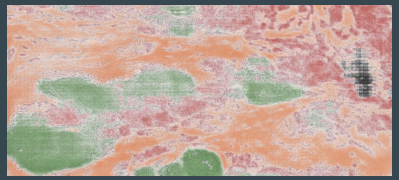
AIM-HER2 Breast Cancer (PathAI) is an AI-powered tool for scoring HER2 immunohistochemistry, available via AISight™ Image Management System[1]

Attribute		Description
Input(s)	Tumor Type(s)	Primary or metastatic breast cancer
	Collection Type(s)	Biopsies, resections
	Stain(s)	HER2 (Dako HercepTest or Ventana 4B5)
	Scanner(s)	Aperio AT2, Aperio GT450, Hamamatsu S360
Output(s)	Key Result	ASCO/CAP HER2 score (0, 1+, 2+, 3+)
	Supporting Results	Area of invasive carcinoma (mm^2) aMIL scoring heatmaps
Training Data[2]		• >157,000 annotations • ~12,000 slide-level HER2 scores • ~4,000 slides • 65+ board-certified breast pathologists
Workflow		AI-assisted read on AISight™
Regulatory Status		Research Use Only

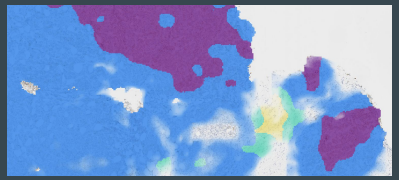
Sub-models work together to generate scores

Artifact Model
Detect and remove all artifact (e.g., folds, blur)

Tissue Model
Identify and classify stroma, necrosis, and invasive cancer



Scoring Model
Calculate slide-level scores (per 2018 ASCO / CAP guidelines)



[1] AIM-HER2 Breast Cancer and AISight™ are for Research Use Only. Not for use in diagnostic procedures.
[2] Shanis *et al.* Accurate quantification of slide-level HER2 scores in breast cancer using a machine-learning model, AIM-HER2 Breast Cancer. SABCS 2023.

Methods

To assess feasibility of AI-based workflows, AIM-HER2 and FISH results were compared on 101 retrospective equivocal (2+) HER2 cases

Cohort Attribute	Value
Tumor Site	Primary and metastatic breast cancer
Number of Cases	101
Sign-out Date	March 2022 – April 2023
HER2 IHC Score	2+ (n=101)
Scanner	Hamamatsu NanoZoomer

Results

AIM-HER2 and pathologist score were concordant for 87% (88/101) cases; 46% (6/13) of discordances were acceptable based on FISH adjudication

AI vs Pathologist Score
(All Cases, n=101)

		Pathologist			
		0	1+	2+	3+
AI	N/A *	–	–	1 (1%)	–
	0	–	–	1 (1%)	–
	1+	–	–	4 (3%)	–
	2+	–	–	88 (87%)	–
	3+	–	–	7 (7%)	–

AI vs FISH Result
(Discordant AI vs Pathologist Cases, n=13)

		FISH	
		Negative	Positive
AI	N/A *	1 (8%)	–
	0	–	1 (8%)
	1+	3 (23%)	1 (8%)
	2+	–	–
	3+	4 (31%)	3 (23%)

Concordance | Acceptable Discordance | Unacceptable Discordance | N/A

* AIM-HER2 returns N/A if <0.1 mm^2 invasive cancer is detected.

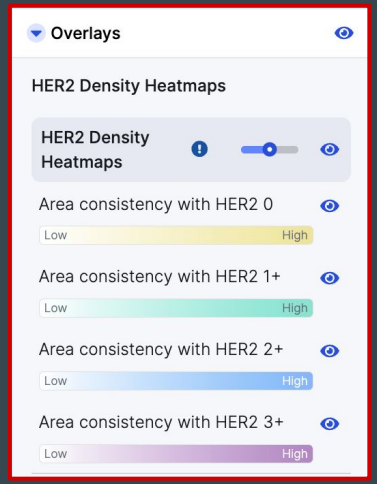
AIM-HER2 is deployed on a whole slide image within the AISight™ Image Management System, and automatically identifies on-slide control tissue*

* AIM-HER2 and AISight™ are for Research Use Only. Not for use in diagnostic procedures.

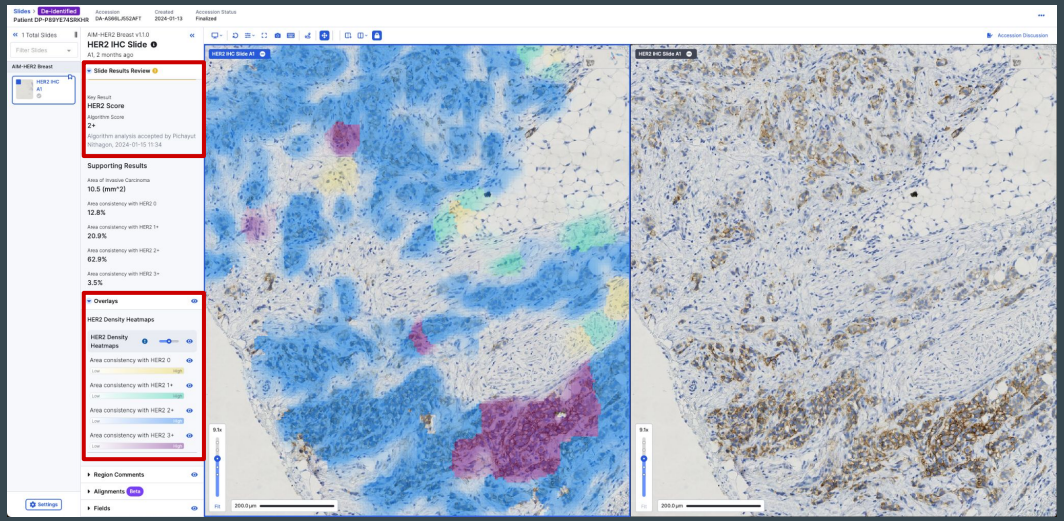
Case DA-AS66LJ552AFT

AIM-HER2 provides supporting measures and overlays which can be used to localize staining patterns and highlight intra-tumoral heterogeneity

AI score (2+) is accepted by pathologist.

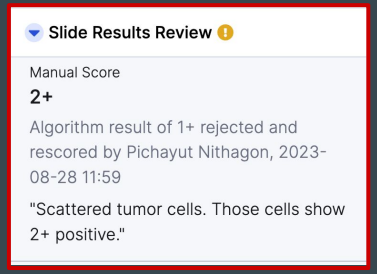


HER2 density heatmaps localize staining patterns.

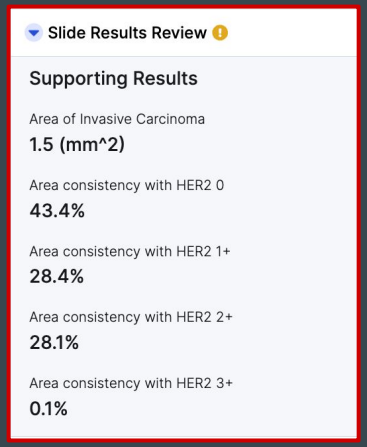


AI results are displayed side-by-side with the whole slide image (Case DA-AS66LJ552AFT).

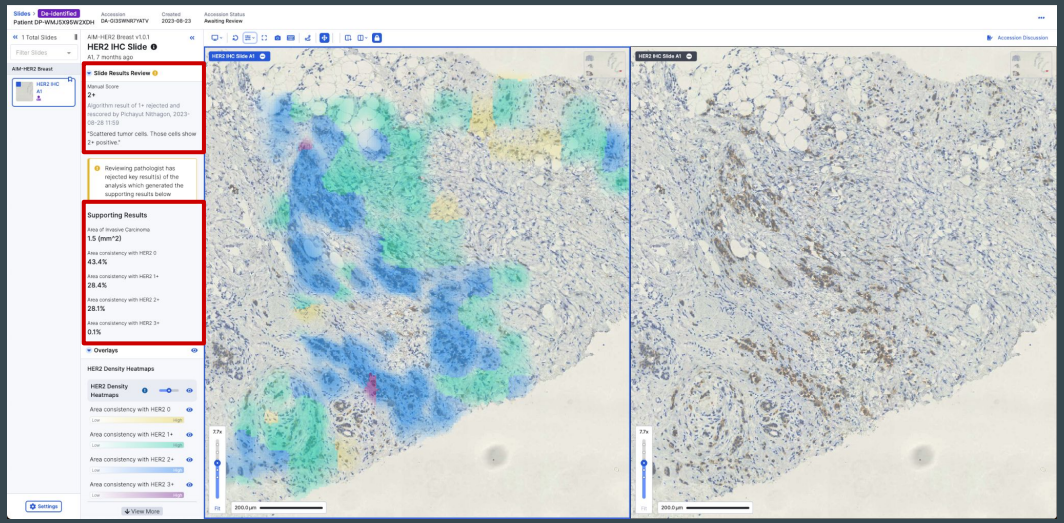
AIM-HER2 provides supporting measures and overlays which can be used to interrogate borderline cases



AI score (1+) is rejected by pathologist (2+), with rationale.



"Area consistency" results highlight this is a borderline 1+/2+ case. Some discordances were in cases with minimal invasive carcinoma detected.



AI results are displayed side-by-side with the whole slide image (Case DA-GI3SWNR7YATV).

Discussion

Conclusions

- In 88/101 cases, AIM-HER2 and the pathologist agreed on the HER2 IHC scoring.
- AI has potential as a screening tool for HER2 IHC, including for equivocal (2+) cases.
- Pathologist oversight is necessary in “AI-assisted pathologist” workflows, especially in cases with minimal residual disease.
- In the era of novel ADC therapies for HER2-low patients, AI has the potential to improve the reproducibility of HER2 low (1+) IHC scoring.

Q & A