Digital Image Analysis-Aided Assessment of HER2 Immunohistochemistry for External Proficiency Testing

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Disclosures: Rasmus Røge: None; Mélissande Cossutta: Employee, IMSTAR Dx; Heidi Lykke Kristoffersen: None; Ekaterina Tatarinova: Employee, IMSTAR Dx; Alexandre Papine: Employee, IMSTAR Dx; Françoise Soussaline: Employee, IMSTAR Dx; Søren Nielsen: None.

Background

NordiQC offers external proficiency testing for HER2 immunohistochemistry (IHC) in breast carcinoma (BC). The evaluation of the submitted results are conducted by an expert panel giving a consensus score for each slide evaluated. In NordiQC the HER2 results are assessed both concerning analytical accuracy and technical quality. The results are overall assessed as sufficient or insufficient. With an increased number of participants, we wanted to evaluate digital image analysis (DIA) as an un-biased supplement or alternative for the existing assessment method. We also wanted to evaluate the concordance of HER2 IHC scoring between the expert panel and DIA for all HER2 IHC categories (0, 1+, 2+ and 3+).

Design

105 slides from 6 NordiQC HER2 IHC runs were included. For each run, a new tissue microarray was used, containing 5 BCs with the critical reportable ranges (0-3+) of HER2 IHC expression. Of central importance each run included two IHC 2+ BCs; one with HER2 gene amplification and one without. The slides were selected to include both sufficient and insufficient results comprising both false positive and false negative results. In addition, insufficient results caused by technical issues as excessive counterstaining and cytoplasmic staining were included. All slides were scored by two methods; visually by the NordiQC expert panel giving a consensus score according to the 2018 ASCO/CAP guidelines and by DIA using an automated image analysis platform (IMSTAR PathoScan Tumor-Marker).

Results

A concordance of 94,3% was obtained comparing DIA and the NordiQC expert panel to separate the participants results as sufficient or insufficient. In five of the six discrepant cases, DIA gave a higher HER2 score and in one case a lower score compared to the panel with impact on final HER2 status. A concordance of 85% was obtained for all individual BCs categorizing these in the four IHC categories (see Fig. 1). The agreement for 3+ and 2+ results was 96% and 89%, respectively compared to 72% and 34% for 1+ and 0 .

		Digital Image Analysis				
	HER2 score	0	1+	2+	3+	Concordance
NordiQC Expert Panel	0	**15**	**29**	**0**	**0**	**34%**
	1+	**0**	**65**	**25**	**0**	**72%**
	2+	**0**	**10**	**154**	**9**	**89%**
	3+	**0**	**0**	**8**	**210**	**96%**
						85%

Fig. 1: Distribution of HER2 scores by NordiQC Expert Panel and DIA

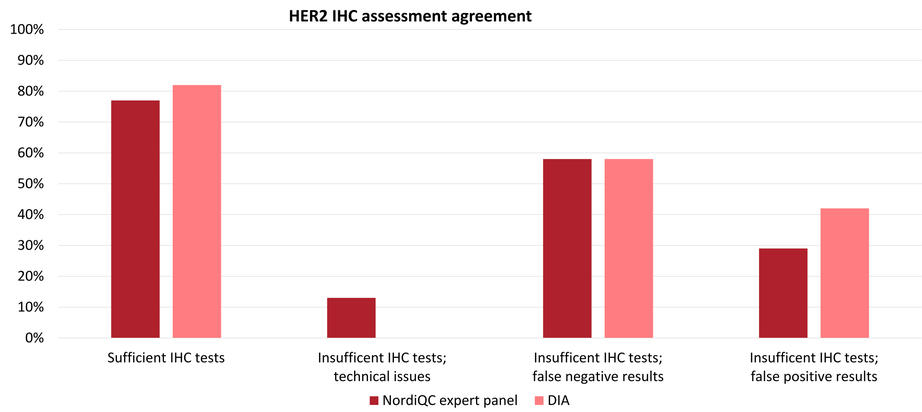

Fig. 2: Assessment agreement on HER2 IHC tests accuracy and technical quality

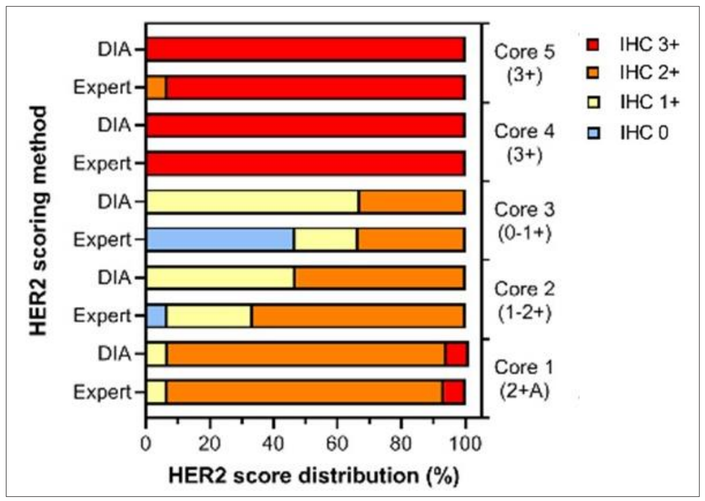

Fig. 3: Distribution of HER2 scores in 5 BCs included in one NordiQC HER2 IHC run (15 participants)

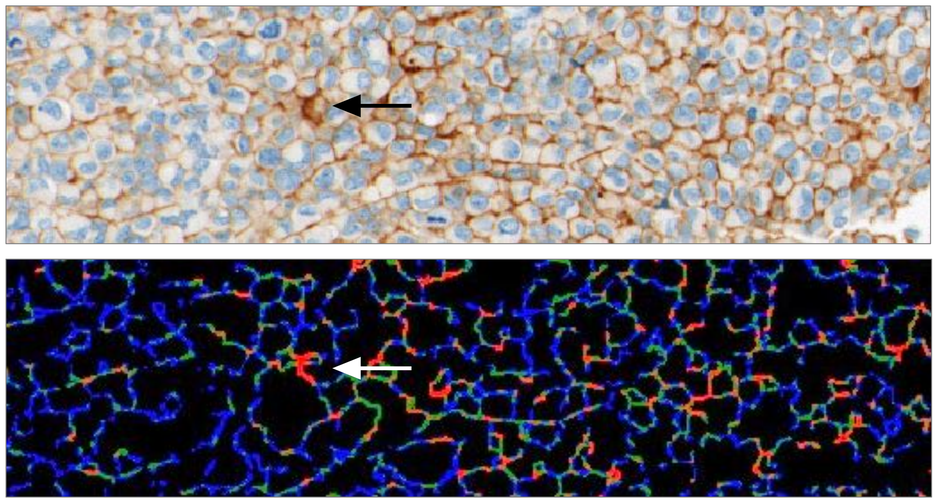

Fig. 4: Identification of 3 intensity levels of HER2 IHC staining by DIA: weak (blue), moderate (green) or strong (red) HER2 staining intensity

Conclusion

DIA was found to be similar effective to an expert panel to evaluate the participants IHC results as sufficient or insufficient. DIA was able to assess and categorize the HER2 IHC results despite different assays, counterstaining and chromogens were applied by participants. Due to the low scoring concordance for HER2 0 and 1+, more comparative studies must be performed to address this observation, being relevant for HER2 low expressing BCs and essential for HER2 IHC standardization and therapeutic decisions.