Computer-aided quantitative analysis as second opinion in the assessment of low HER2 IHC score in breast cancer – a pilot evaluation

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Background & Objectives

Digital review and quantitative analysis of immunohistochemical staining are gaining growing adoption, predominantly for diagnostic assessment, prognostic stratification of malignant lesions as well as therapeutic recommendation (1). Computer-aided methods for IHC analysis appear particularly useful for standardized scoring of HER2/neu expression, specifically in cases of low HER2 breast cancer for which inter-observer agreement is often limited (2), and recommendation for FISH testing (3) is not always consistent.

The aim of this pilot evaluation was to assess the potential usefulness of computer-aided quantitative analysis as a second opinion in the assessment of HER2 score in breast cancer cases.
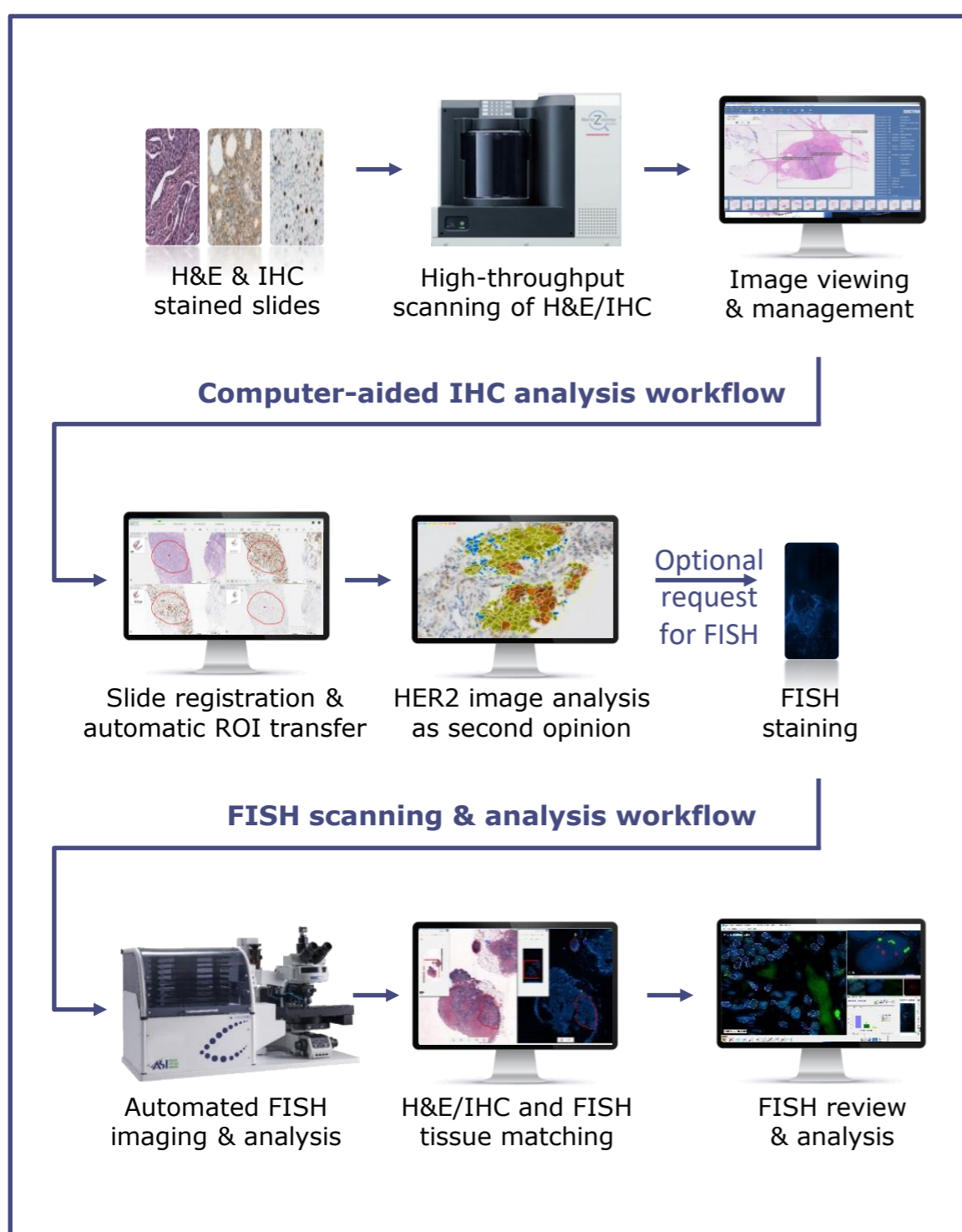

Figure 1: Illustrative example of IHC and FISH workflows

Methods

Core biopsy specimens from breast cancer patients were included in this pilot evaluation. Slides were prepared for each core and stained with hematoxylin-eosin (H&E) as well as a panel of immunohistochemical stains including ER, PR, Ki67 and HER2. All slides were scanned with the NanoZoomer S360 (Hamamatsu Photonics) at a 40X magnification.

Slides were examined by certified pathologists using a combination of conventional microscopy and digitalized images reviewed on the SECTRA viewing platform. The specimens were further analyzed using HiPath Pro digital pathology software (Applied Spectral Imaging). Regions of interest marked on the H&E slides were automatically transferred to the HER2 specimens following registration and tissue matching. Computer-aided quantitative analysis was performed using the HER2 biomarker and results were compared to the manual pathology reports (Figure 1). Equivocal cases were further analyzed with HER2 FISH.

Results

Nineteen core biopsy specimens from fourteen patients were included in this pilot evaluation. Ten patients had invasive ductal carcinoma (IDC), 3 had invasive lobular carcinoma (ILC) and one had mucinous carcinoma. Pathology reports indicated that all patients were ER positive (3+), 10 patients were PR positive (3+), 3 patients were PR (2+), and one patient was PR negative. Ki67 was above 15% in all except 4 cases. Finally, eight cases were scored HER2 (0) negative, five cases were scored HER2 (1+), three cases HER2 (2+) and three cases HER2 (3+). Further evaluation with fluorescence in situ hybridization (FISH) was recommended for the three patients with equivocal HER2 (2+) score.

Manual results were compared to the computerized scores obtained with the HER2 quantitative biomarker. Concordance between manual and computer-aided quantitative analysis was found in 14 out of 19 slides (11 patients) (Figure 2). 5 slides (3 patients) were manually reported as HER2 negative (0) or (1+) while the computerized system yielded positive (2+) scoring (Figure 3). A second manual review of these inconsistent results was performed by the pathologist in order to confirm the diagnosis with enhanced confidence.
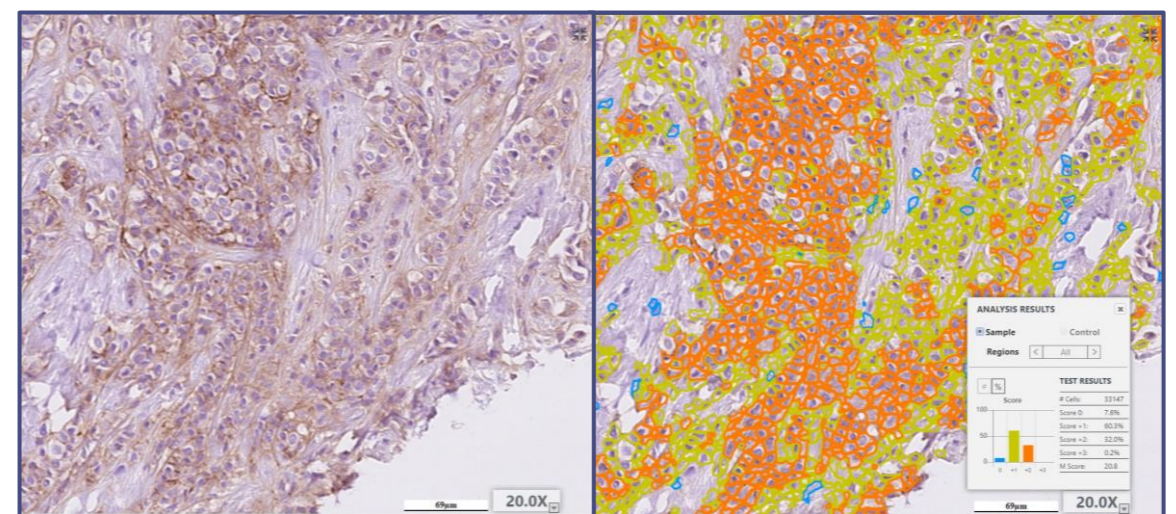

Figure 2: Representative example of concordant HER2 case featuring IHC staining (left image) and computer-aided analysis (right image)
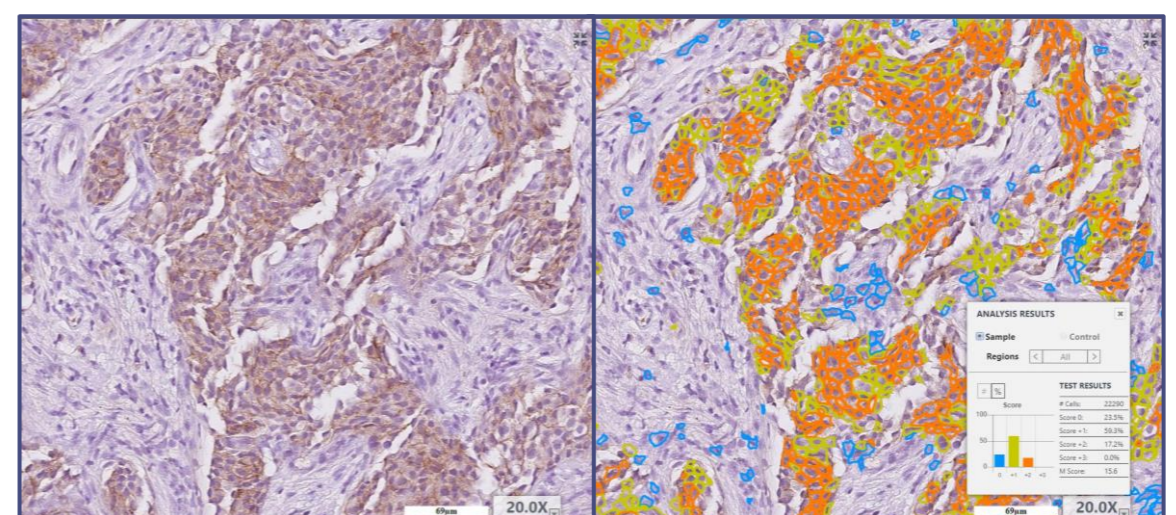

Figure 3: Representative examples of discrepant HER2 cases featuring IHC staining (left images) and computer-aided analysis (right images)

Conclusion

This evaluation exemplifies the potential usefulness of computer-aided quantification as a second opinion for the assessment of HER2 scoring, especially in cases of equivocal or low HER2. Such digital technology may help identify cases that would benefit from additional scrutiny for more standardized recommendations of ISH testing and, in turn, more consistent patient management.

References

(1) Chong Y, Diagnostics 2021; 11:343
(2) Baez-Navarro X, Mod Pathol 2023; 36(1):100009
(3) Wilcock DM, Arch Pathol Lab Med 2023 Mar 15