Digital HER2 IHC-evaluation is equal to the semi-quantitative method
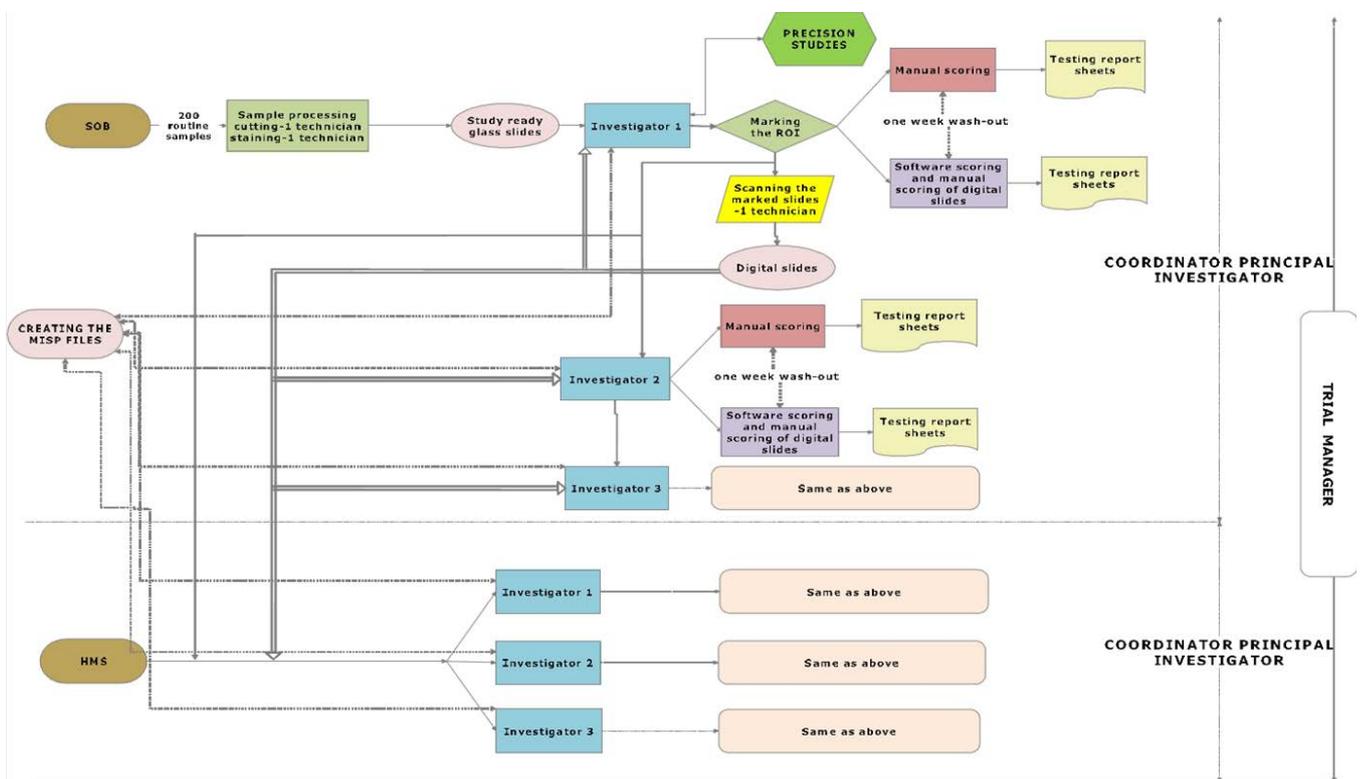
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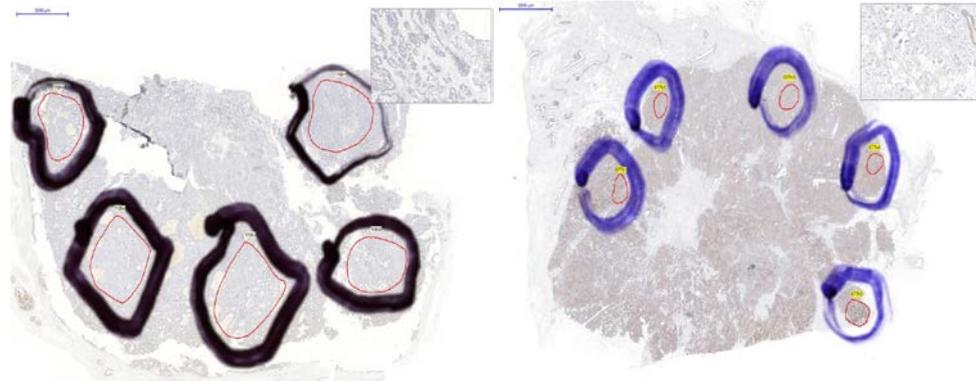
Objective

Quantification of HER2 expression of breast cancer became an inevitable part of the histopathological report which determines patient selection for targeted anti-HER2 therapy. Perfect targeting of trastuzumab therapy needs precise and standardized evaluation and documentation, for which purpose the digital pathology offers effective software support tools. Our objective was to validate digital evaluation in a retrospective study on numerous cases using digitized and glass slides.

Methods

HER2 immuno-slides of 186 breast cancer cases with 1 to 5 regions of interest (marked ROI on glass slides and annotations on digitized slides) were evaluated manually on glass slides and semi-automated on digitized slides in parallel by 3 pathologists and then compared by calculating Cohen's kappa (CK) and Quadratic weighted kappa (QWK) in each interobserver (between pathologists) and intermethod (manual versus semi-automated) setting.

Region of interest were marked with markers on glass slides and with free-handed annotations on digitized slides.

Results

HER2 interobserver (between pathologists) Cohen's kappa (CK) with manual reading ranged 0,712-0,779 and Quadratic Weighted Kappa (QWK) ranged 0,925-0,942. HER2 interobserver CK with semi automated reading ranged 0,698-0,722 and QWK ranged 0,912-0,916. HER2 intermethod (manual vs semi-automated)CK comparing manual and semiautomated reading ranged 0,579-0,820 and QWK ranged 0,876-0,951.

	P1 Manual	P1 Semi-automated	P2 Manual	P2 Semi-automated	P3 Manual	P3 Semi-automated
P1 Manual		0.820 (0.788-0.852)	0.779 (0.744-0.813)	0.698 (0.659-0.736)	0.712 (0.674-0.750)	0.670 (0.631-0.710)
P1 Semi-automated			0.692 (0.654-0.730)	0.722 (0.684-0.760)	0.597 (0.556-0.639)	0.712 (0.674-0.750)
P2 Manual				0.634 (0.593-0.674)	0.725 (0.687-0.763)	0.596 (0.554-0.637)
P2 Semi-automated					0.599 (0.558-0.641)	0.698 (0.659-0.736)
P3 Manual						0.579 (0.538-0.621)
P3 Semi-automated						

Table 7. Comparison of different HER2 slide assessments using Cohen's kappa.
Legend: P=pathologist. Cells highlighted with grey denote agreements between the manual assessments (i.e. gold standard).

	P1 Manual	P1 Semi-automated	P2 Manual	P2 Semi-automated	P3 Manual	P3 Semi-automated
P1 Manual		0.951 (0.942-0.961)	0.942 (0.930-0.953)	0.915 (0.901-0.929)	0.925 (0.913-0.937)	0.904 (0.889-0.919)
P1 Semi-automated			0.917 (0.904-0.930)	0.917 (0.902-0.933)	0.892 (0.877-0.907)	0.916 (0.902-0.930)
P2 Manual				0.901 (0.886-0.916)	0.936 (0.925-0.947)	0.884 (0.869-0.901)
P2 Semi-automated					0.876 (0.856-0.895)	0.912 (0.897-0.928)
P3 Manual						0.876 (0.858-0.894)
P3 Semi-automated						

Table 8. Comparison of different HER2 slide assessments using quadratic weighted kappa.
Legend: P=pathologist. Cells highlighted with grey denote agreements between the manual assessments (i.e. gold standard).

Conclusions

Our data validated that evaluation of membranous HER2 immunostaining on glass and digitized slides resulted the same data without any adverse effect of digitization, but offering more convenient and flexible working method. This data will gain increasing importance with the continuous improvement of digitization platforms using fully-automated evaluation algorithms.