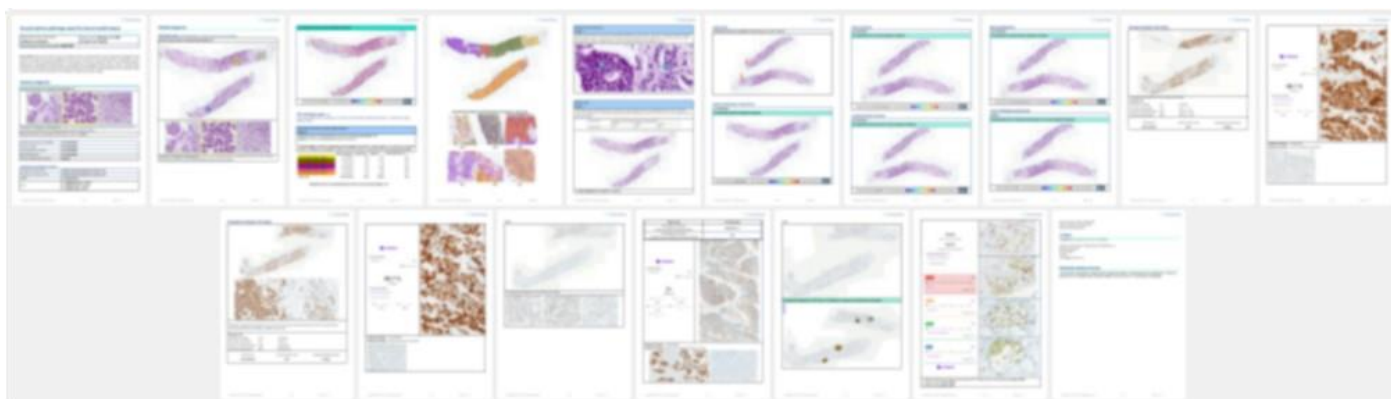


Main features of the detailed AI-supported TwiceView second opinion report of breast core needle biopsy

DISCLAIMER

This second opinion report is intended to support clinical decisions concerning patient management and should be considered as a part of diagnostic workup prior to treatment. If the second opinion is discordant in some aspects with primary histopathology report, as it may happen concerning subjective nature of many histopathological assessments, discordances should ideally be discussed with pathologists issuing primary report to provide clear information for treating physician before any treatment decisions are made. This second opinion is not intended for legal purposes and must not be used after the introduction of treatment at a given stage.

Sample report content



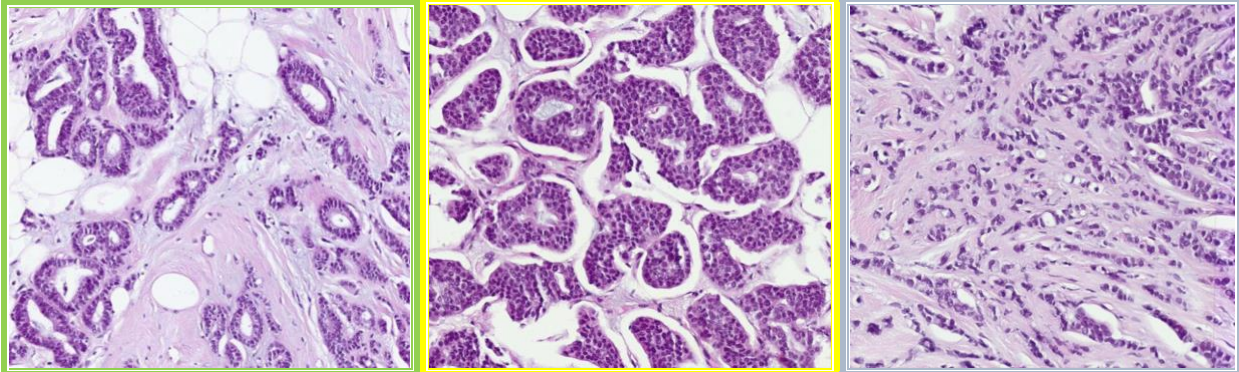
How we work to consult a case

- The case is analysed, reported and extensively image-documented by a consultant pathologist and then thoroughly reviewed by another consultant pathologist. Pathologists are supported by AI-based software.
- If required, especially in difficult or equivocal cases, additional pathologists will consult the case.
- Sometimes a preliminary report may be issued, which may suggest the need for additional stains (eg. immunostains) or technical steps to enhance the quality of slides which may be necessary to analyse the case with accordance to high standards.

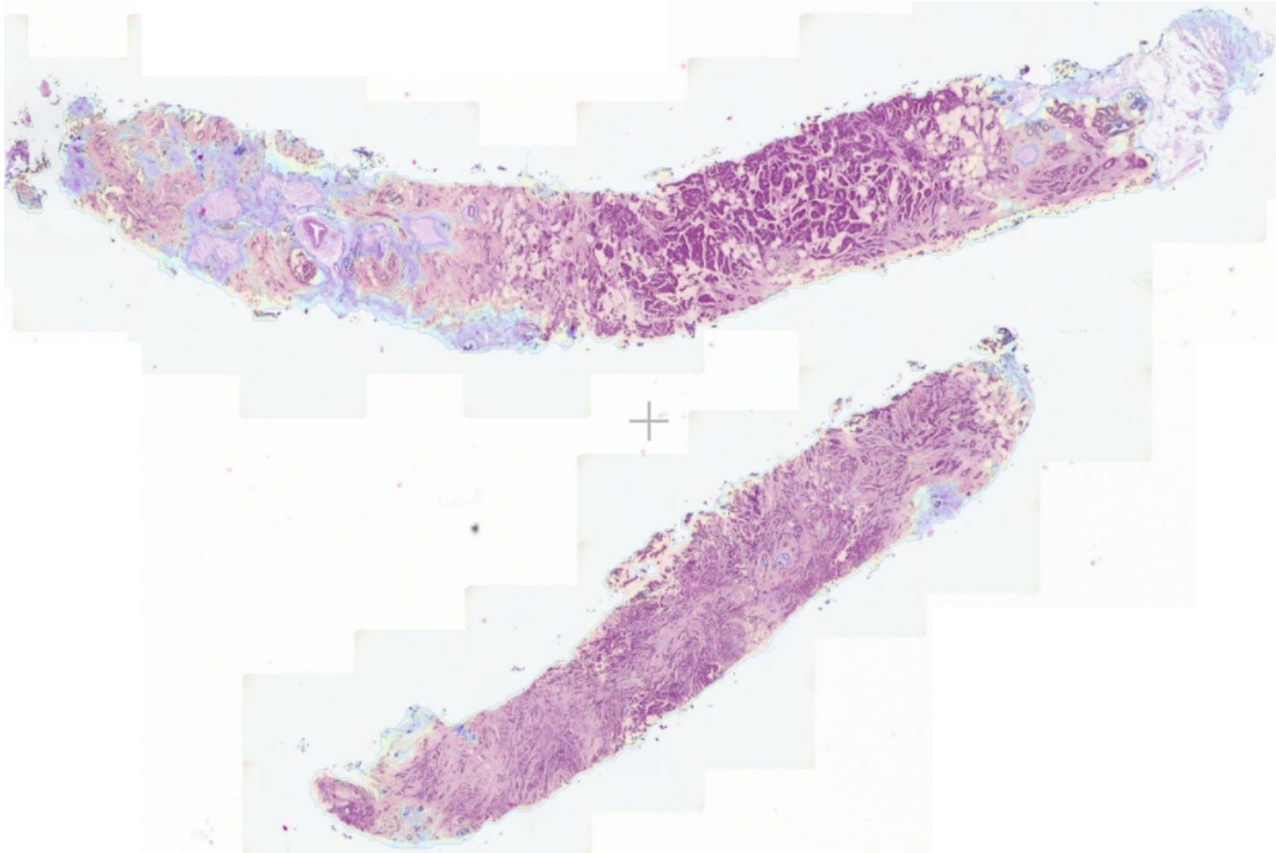
Main features of the report

1. Diagnosis of tumor type based on WHO classification with spatial characterization and photographic documentation of identified tumor subtypes. Support of artificial intelligence-based tool for the recognition of invasive cancer areas.

Invasive carcinoma of no special type (ductal), G1



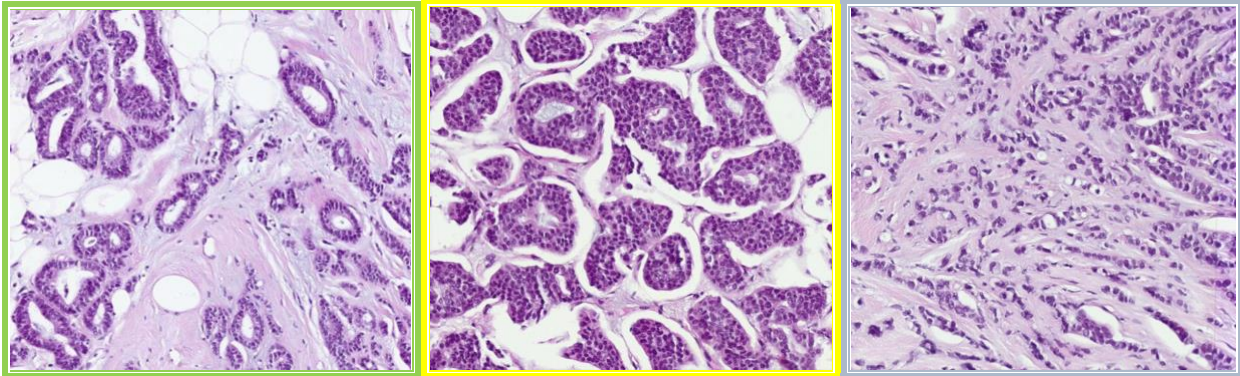
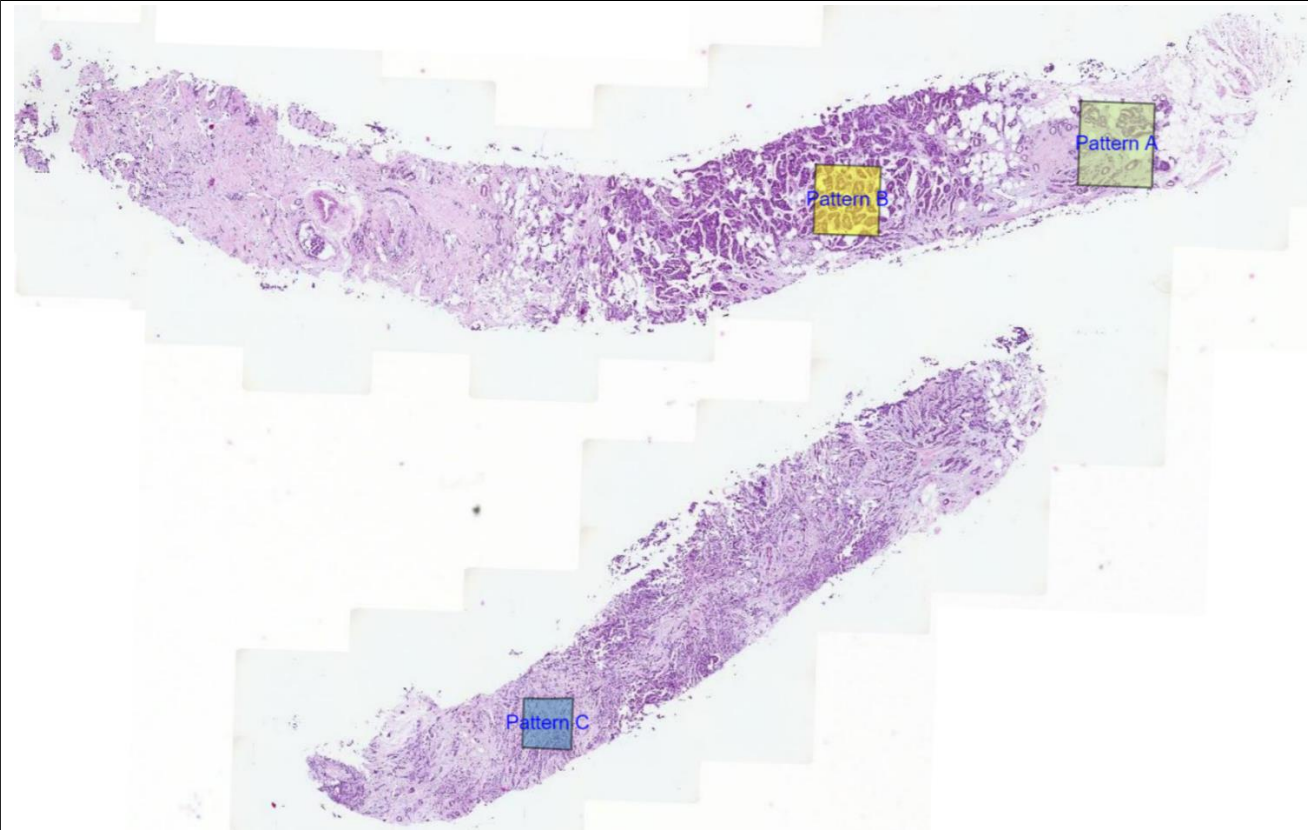
AI-supported invasive cancer detection heatmap



Active Heatmap: **Cancer** Low Probability  High Probability 

2. Characterization of tumor heterogeneity with spatial identification and photographic documentation of distinguishable patterns

Invasive carcinoma of no special type (ductal), G1



Intratumor histological heterogeneity: There is some histopathological heterogeneity observed within sampled tumor tissue and there are three distinguishable patterns (pictures above).

3. Digital image-empowered, precise tumor grading with strict and image-documented adherence to recommended criteria of Elston-Ellis modification of Bloom and Richardson grading classification (Nottingham Grading System)

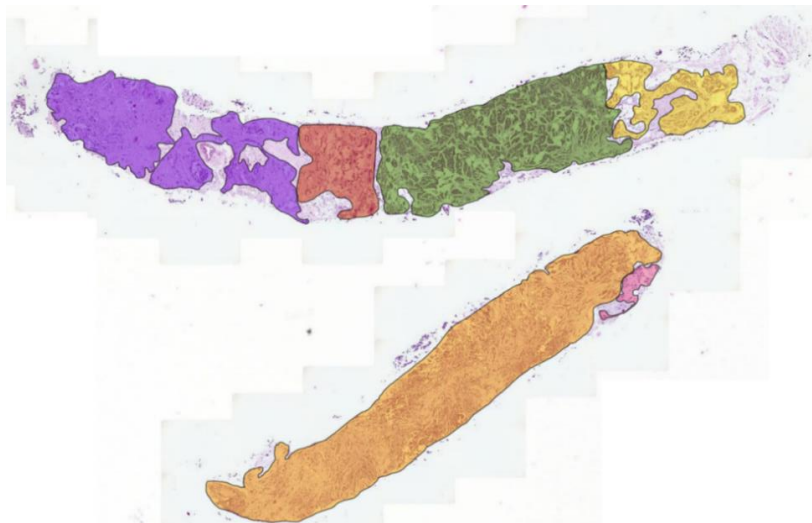
The percentage of tubular or glandular acinar spaces is estimated in several regions with distinctive morphology and fairly homogenous tubule/gland formation, and then the result is calculated as a weighted percentage.

Glandular (Acinar)/Tubular Differentiation **Score - 2**

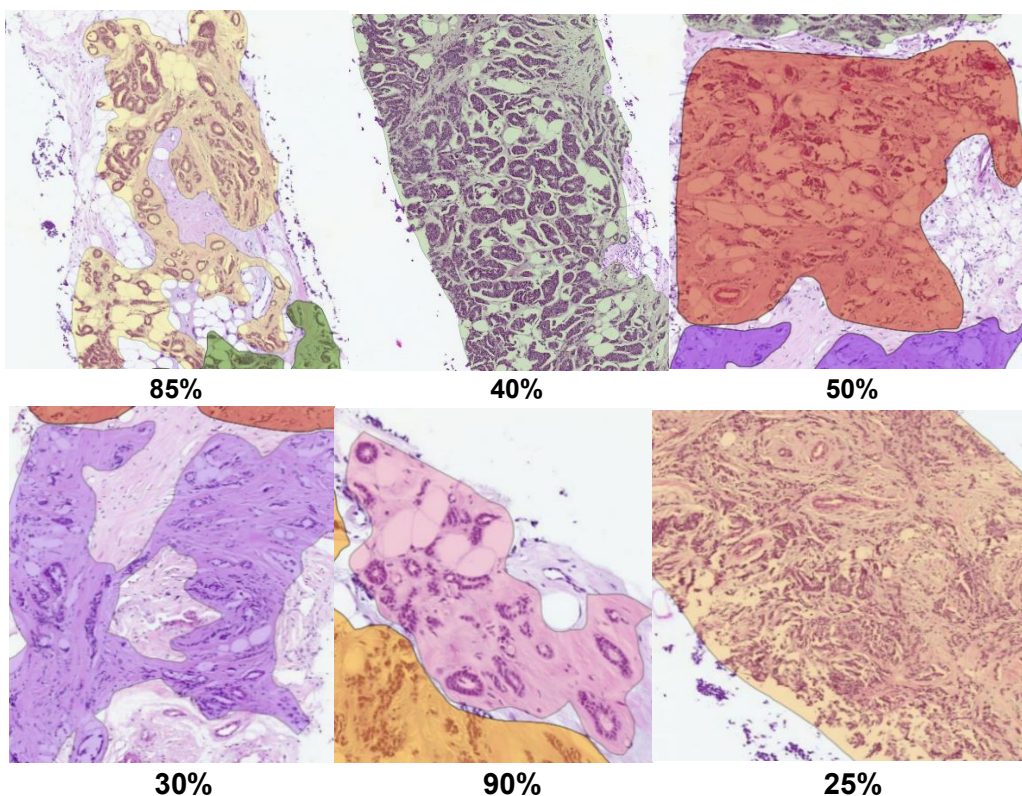
Weighted score for tubular/glandular (acinar) structures percentage: 37%

Score 2 [10-75% of tubular/glandular (acinar) structures]

The percentage of tubular or glandular acinar spaces is estimated in several regions with distinctive morphology and fairly homogenous tubule/gland formation, and then the result is calculated as an area-weighted percentage.



Estimated percentages of glandular/tubular structures in a given area

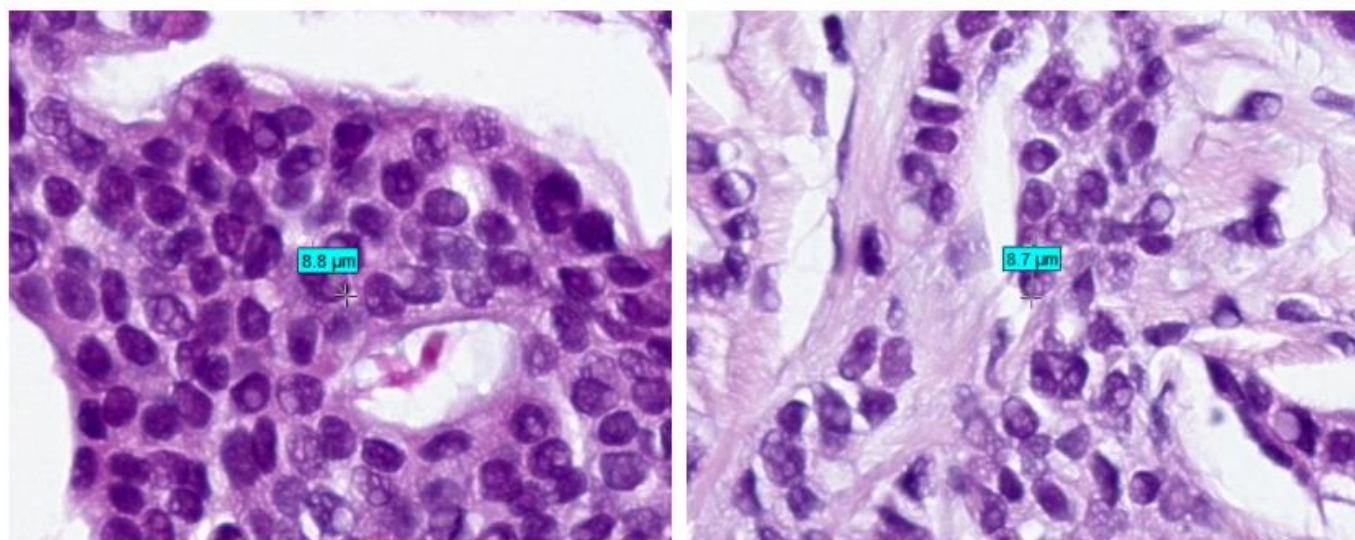


	Area (mm ²)	Share %	Tubular/glandular %
Tubular differentiation region 1	0,96	7,4%	85%
Tubular differentiation region 2	3,20	24,7%	40%
Tubular differentiation region 3	0,92	7,1%	50%
Tubular differentiation region 4	2,49	19,3%	30%
Tubular differentiation region 5	0,13	1,0%	90%
Tubular differentiation region 6	5,22	40,4%	25%
Tumor area	12,92	100,0%	37%

Nuclear pleomorphism assessment supported by measurements comparing tumor nuclei and nuclei of normal glandular structures or lymphocytes

Nuclear pleomorphism Score - 1

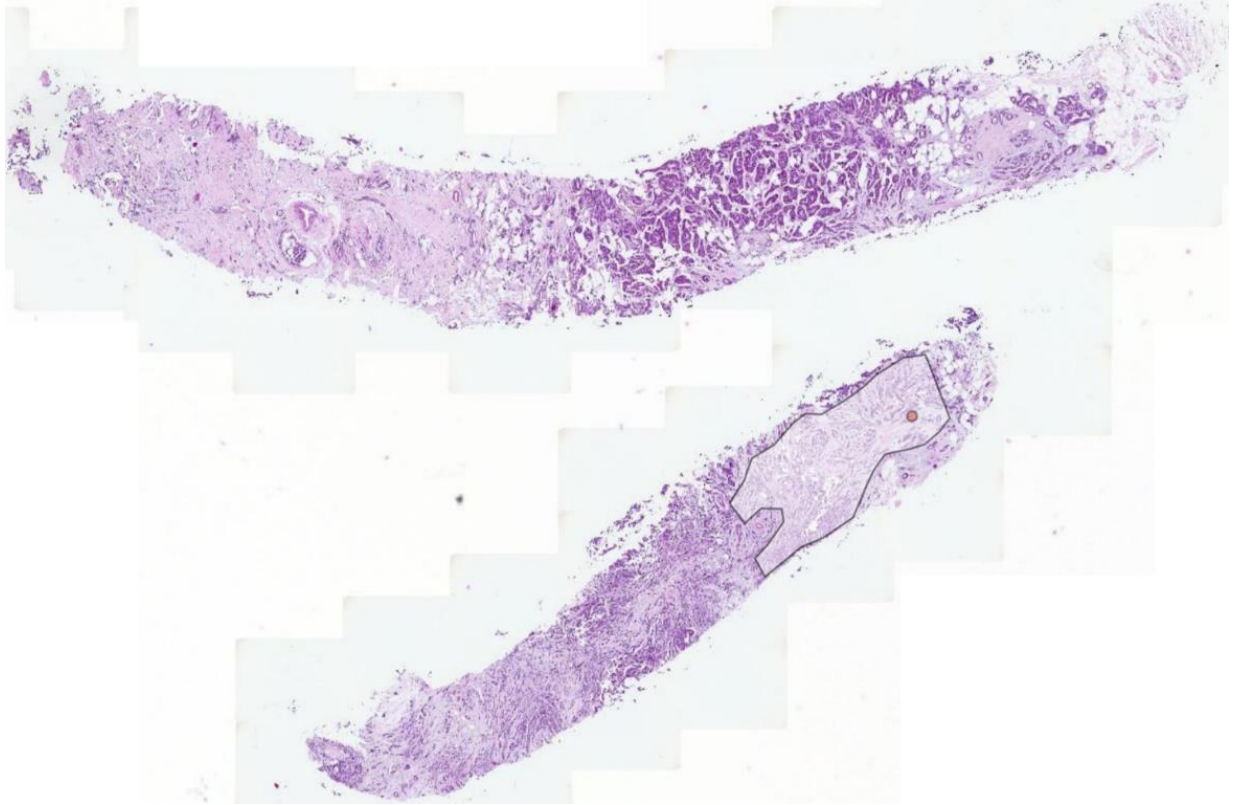
Nuclear pleomorphism scored in the least differentiated area of the tumor present in the sample. Nuclei small with little increase in size in comparison with normal breast epithelial cells (not larger than 1.5x of the size of a normal epithelial cell nucleus), regular outlines, uniform nuclear chromatin, little variation in size.



Mitotic rate Score - 1

The mitotic score is determined by the number of mitotic figures found in a predefined area of 1.25-1.32 mm², which corresponds to 10 consecutive high-power fields (measuring 0.125-0.132 mm²) in the most mitotically active part of the tumor.

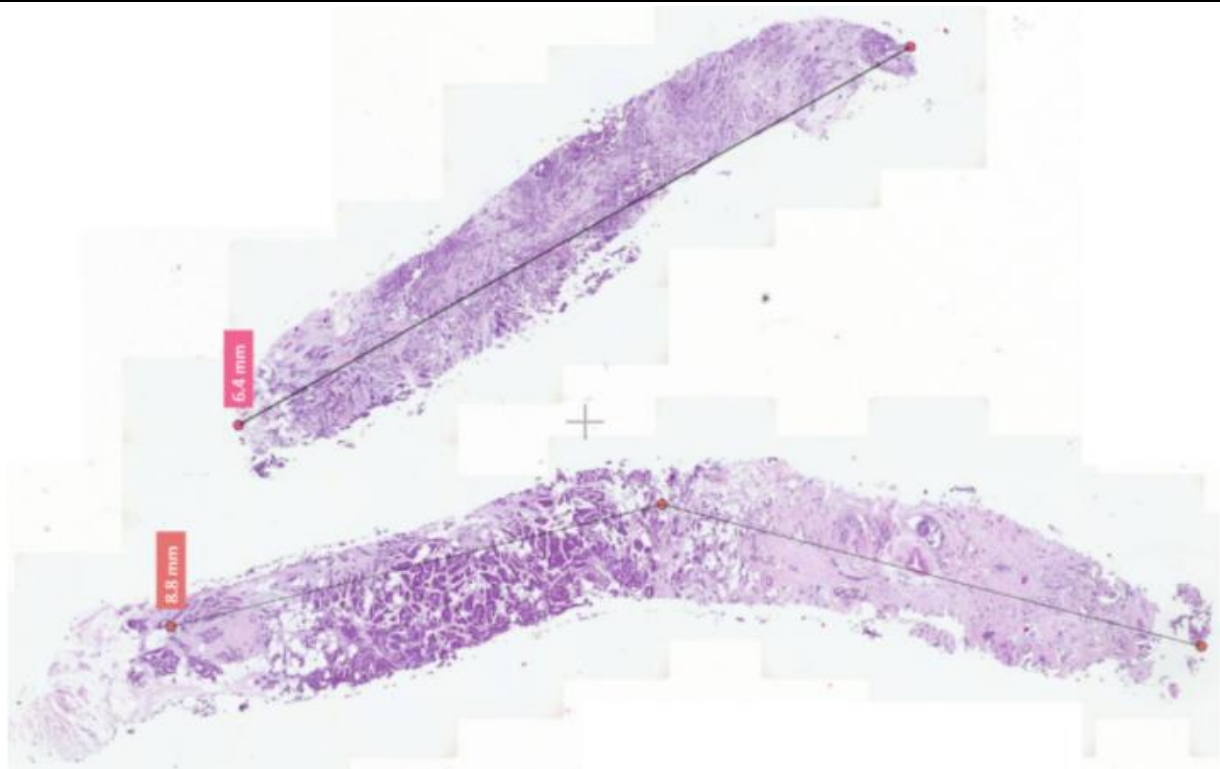
Area (mm ²)	Number of mitoses per 10 fields corresponding to:		
	Score 1	Score 2	Score 3
0.125-0.132	≤ 4	5-9	≥10



1 mitosis detected in an area of 1.32 mm²

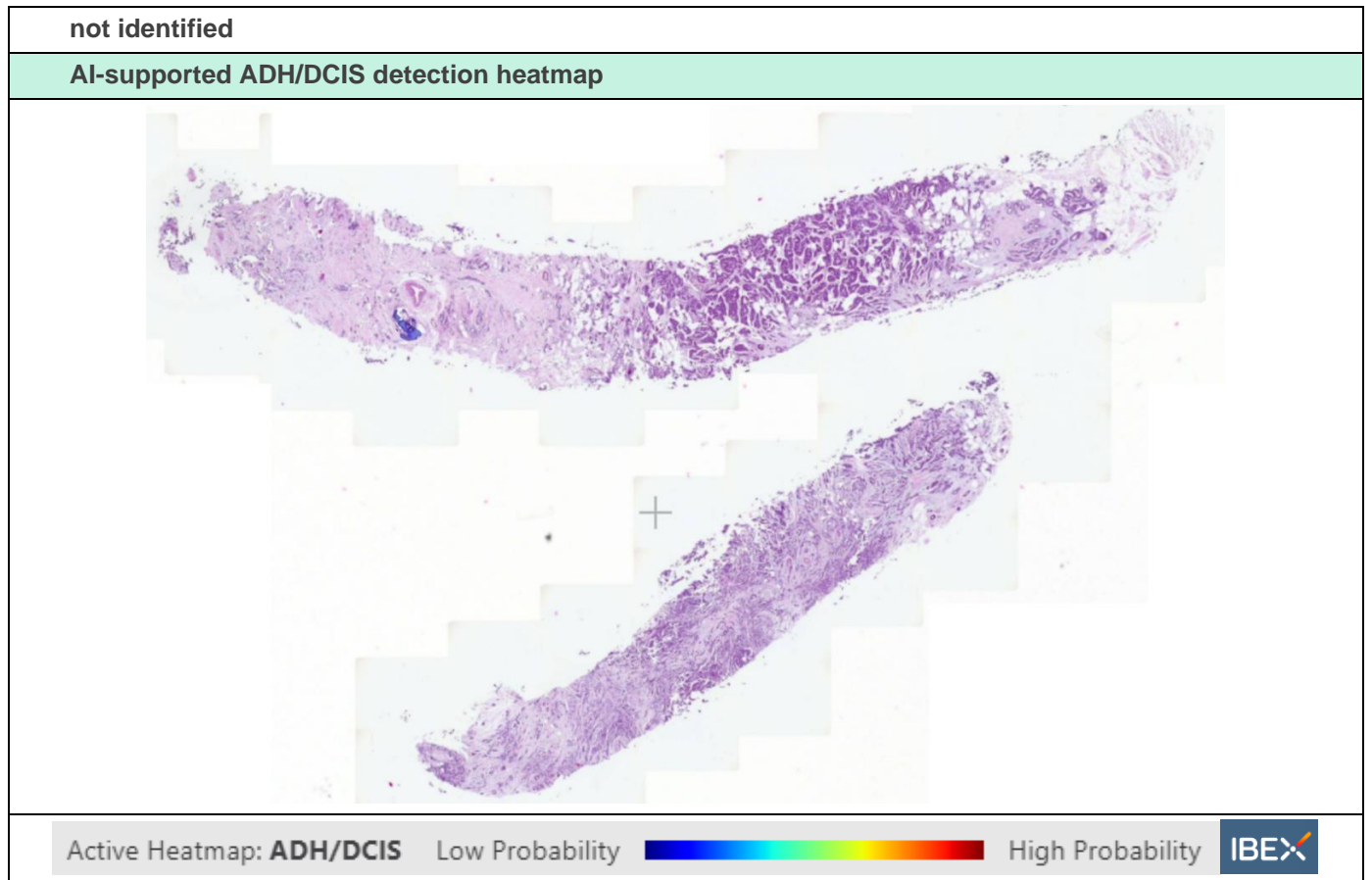
4. Precise tumor tissue size measurements

Greatest dimension of sampled invasive focus in a core – 8.8 mm

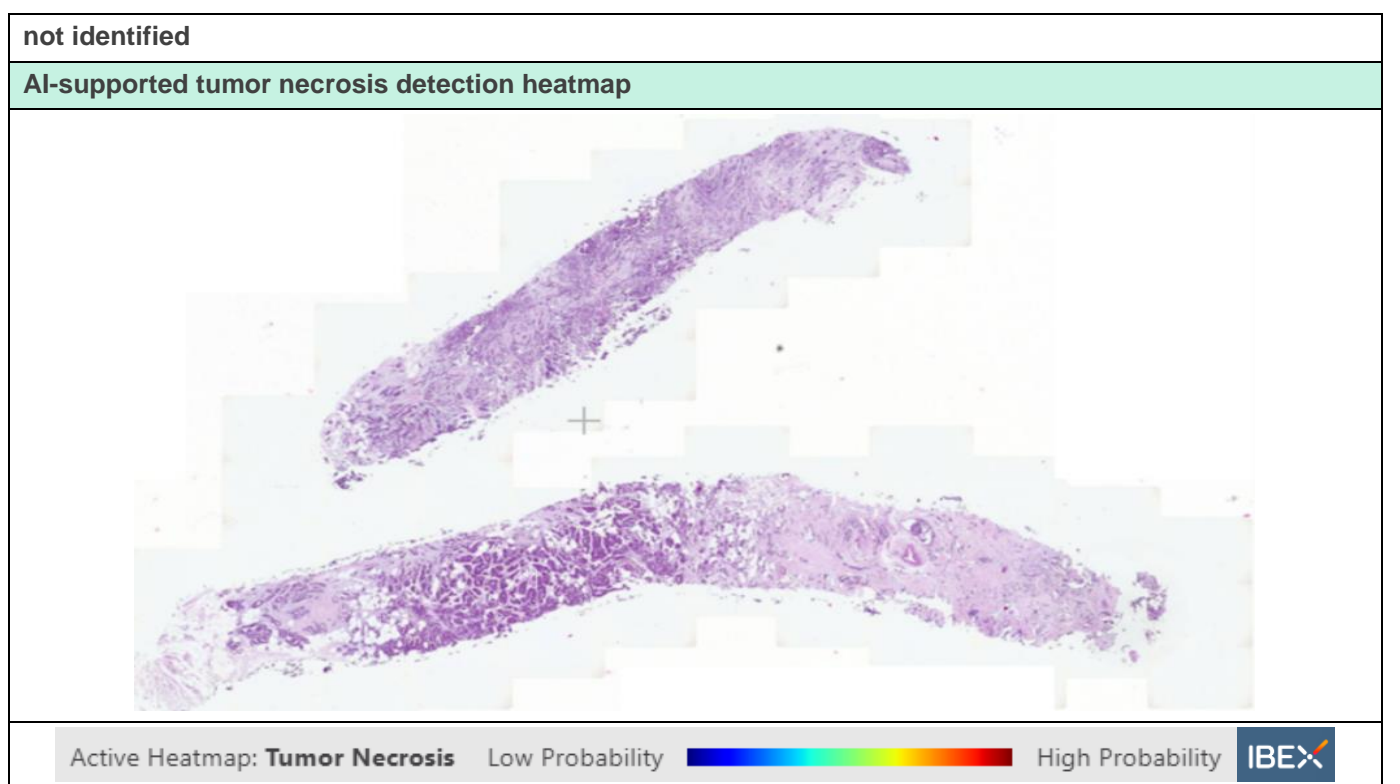


5. Clinically relevant sample characteristics detected with AI-based tool support

Ductal Carcinoma in Situ (DCIS)



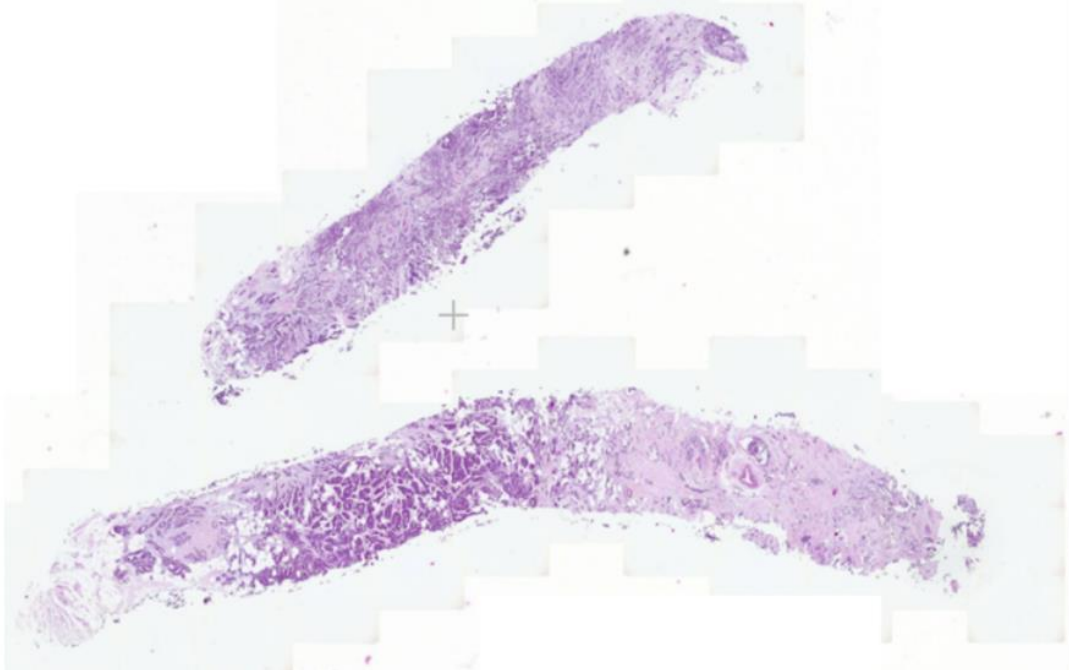
Tumor necrosis



Lymphovascular invasion

not identified

AI-supported lymphovascular invasion detection heatmap



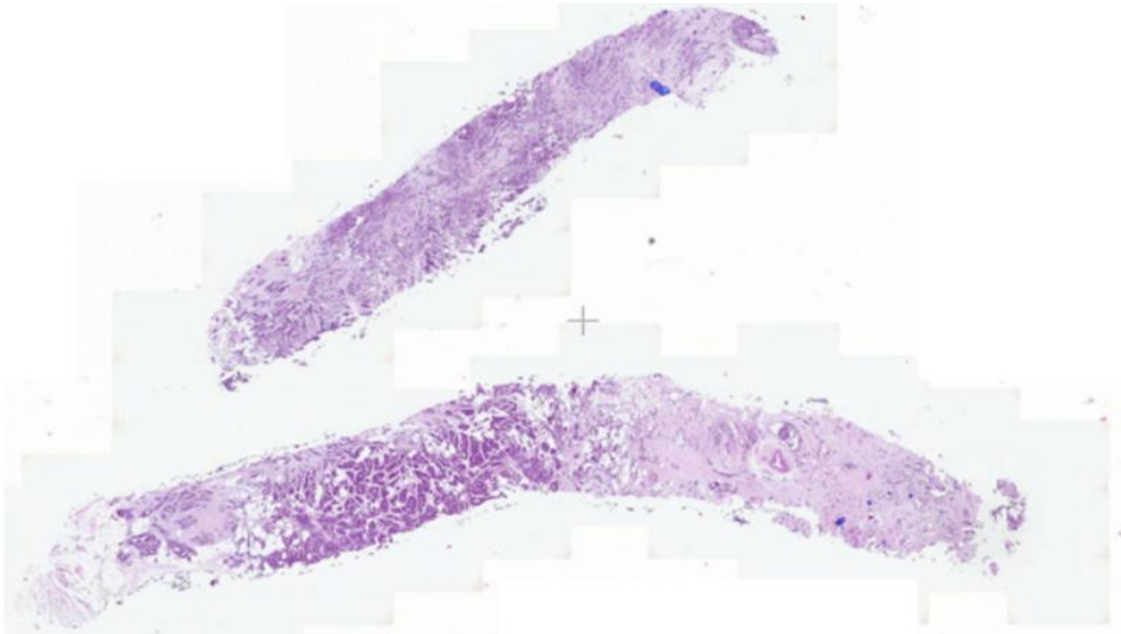
Active Heatmap: **ALI/LVI** Low Probability High Probability



Microcalcifications

not identified

AI-supported microcalcifications detection heatmap



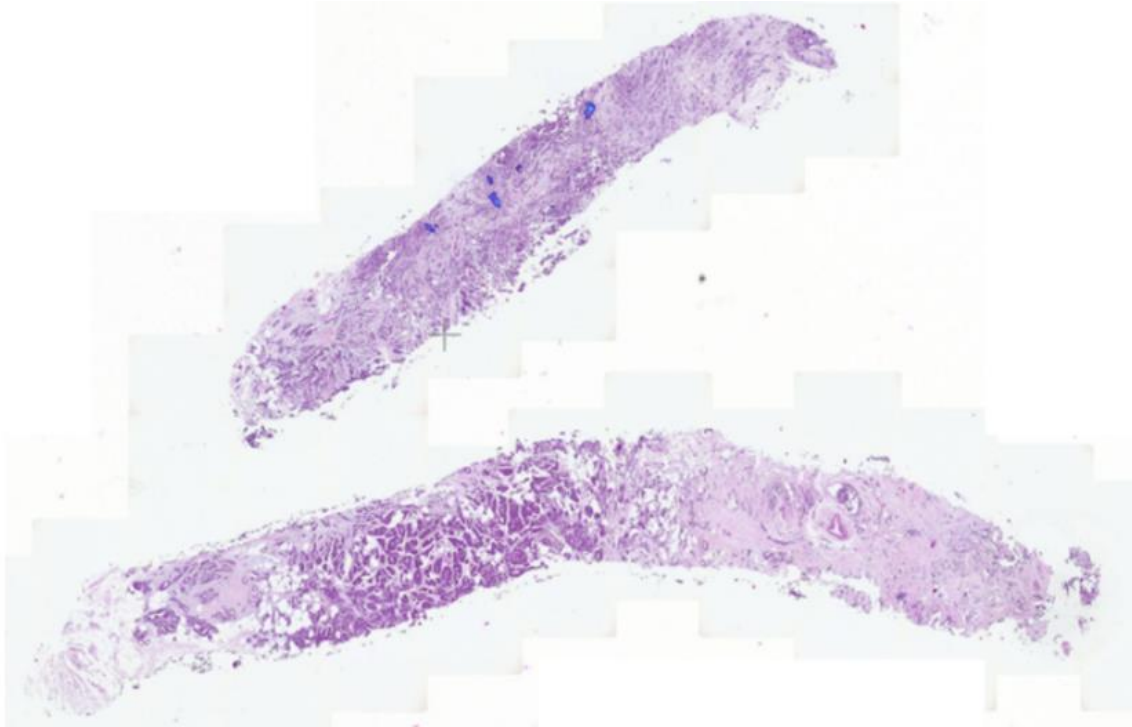
Active Heatmap: **Microcalcifications** Low Probability High Probability



Tumor infiltrating lymphocytes

absent

AI-supported tumor infiltrating lymphocytes (TILs) cancer detection heatmap



Active Heatmap: **TILs** Low Probability  High Probability




6. Estrogen receptor (ER) and Progesterone receptor (PR) status assessments

Automatic, AI-supported recognition of invasive tumor areas and automatic count of nearly all positive and negative invasive tumor cells (insignificant number of cells can be omitted or misclassified by an AI-based tool).

The results of AI-assisted assessment are supervised by reporting pathologist and can be fine-tuned, both in terms of sensitivity threshold as well as positivity and negativity of single cells or groups of cells.

Both Allred score and H-score are precisely calculated

Allred score	Positive cancer cells	Average staining intensity
8/8 (Positive)	98%	strong



AI Image Analysis

Breast ER ⓘ

CE-IVD marked

98.1 %

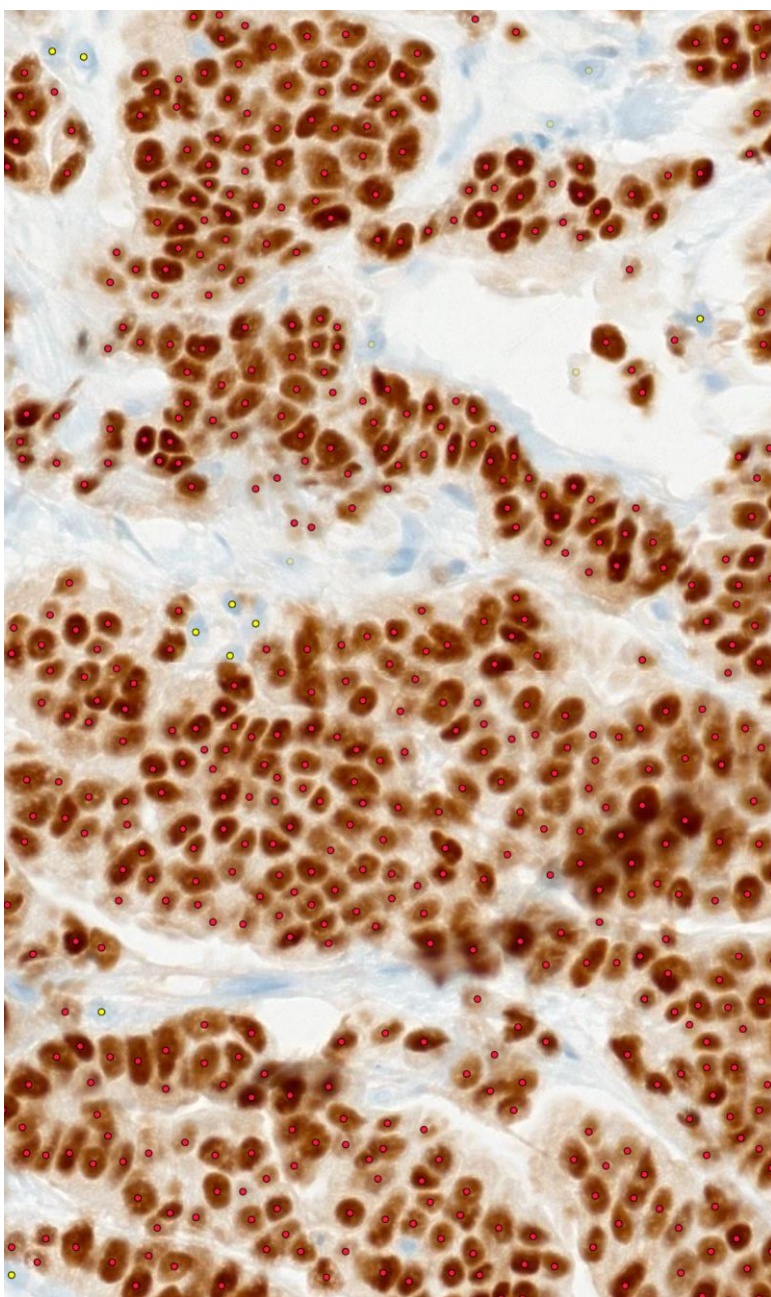
ER Score

Positivity threshold:

Reset threshold

● Tumor positive
14294

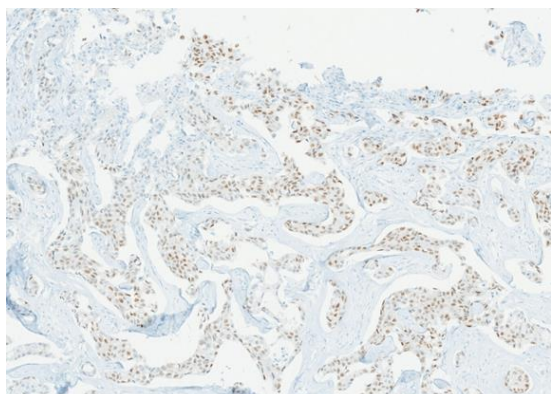
● Tumor negative
276



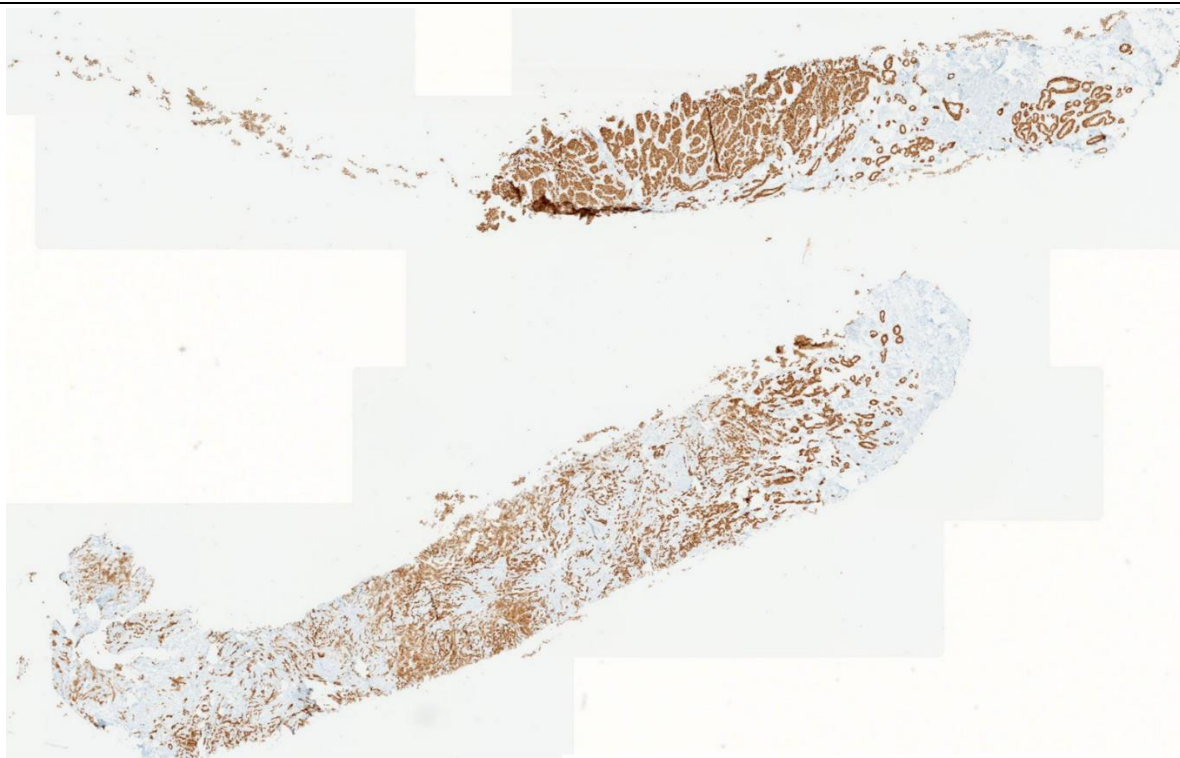
Presence of controls is reported in the assessed slides with interpretation and image documentation

Internal Controls – not identified

External Controls - present and stain as expected



Additionally, marker expression homogeneity/heterogeneity is described.



Homogenous expression over the whole tumor tissue.

H-Score: 251

Cells with no signal	2%	0% x 0 = 0
Cells with weak signal	5%	5% x 1 = 5
Cells with moderate signal	33%	34% x 2 = 66
Cells with strong signal	60%	60% x 3 = 180

Progesteron Receptor (PR) Status

Allred score	Positive cancer cells	Average staining intensity
8/8 (Positive)	90%	strong



AI Image Analysis

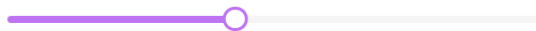
Breast PR ▼ ⓘ

CE-IVD marked

89.7 %

PR Score

Positivity threshold:



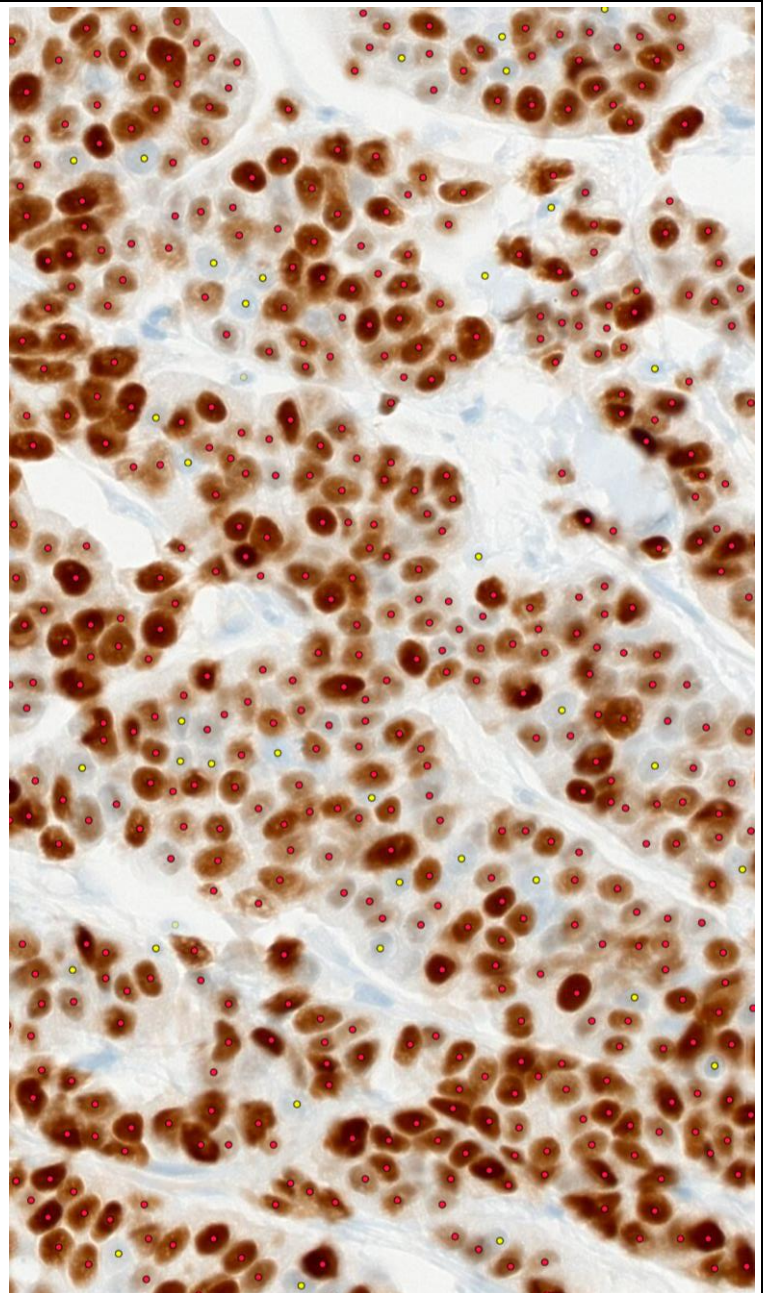
Reset threshold

● Tumor positive

31738

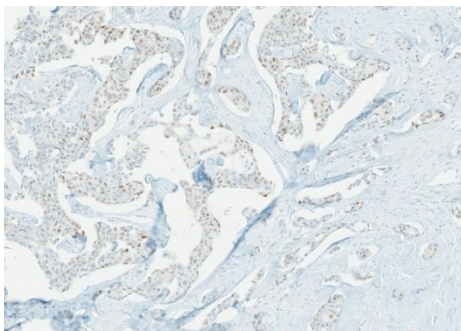
● Tumor negative

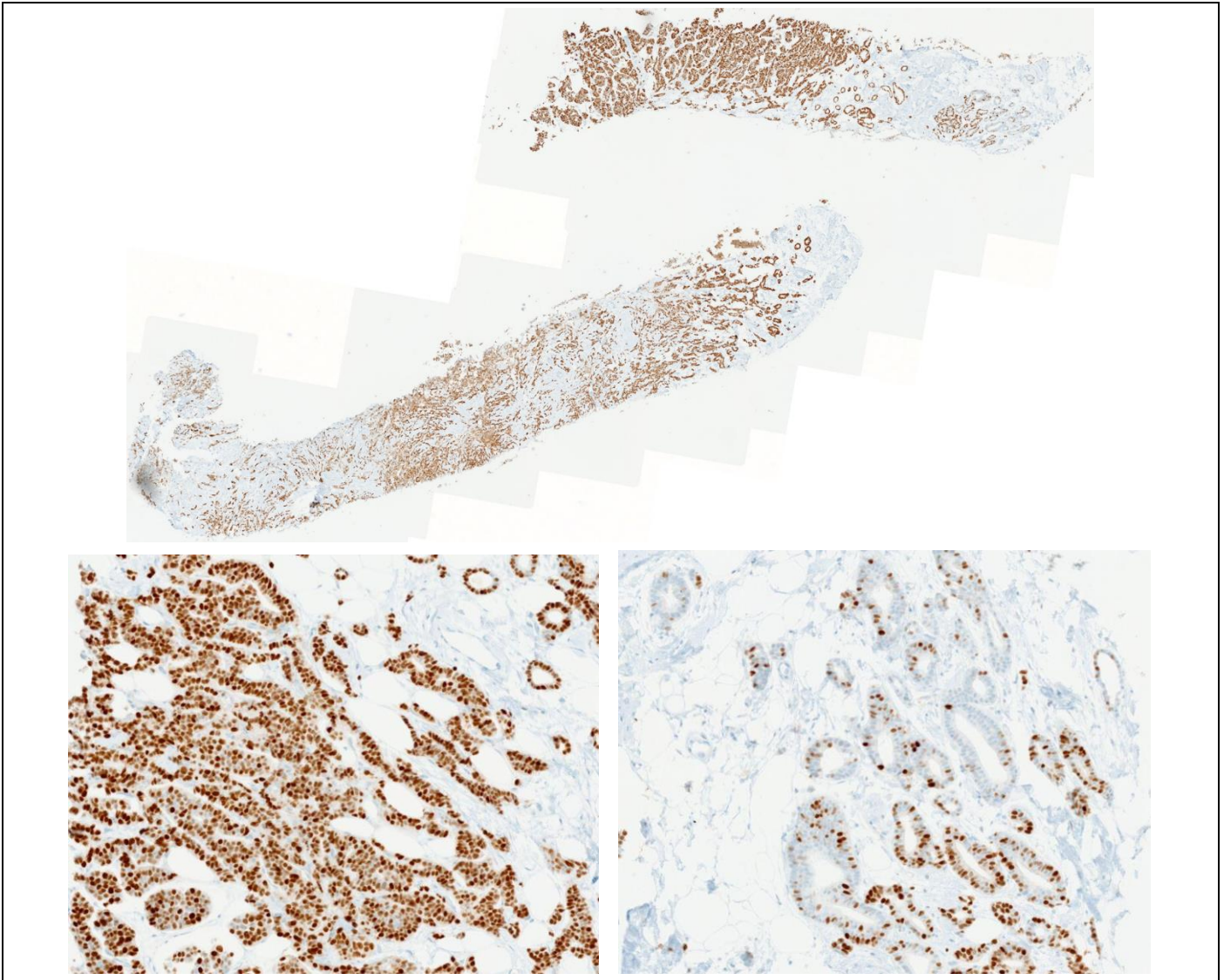
3658



Internal Controls – not identified

External Controls - present and stain as expected





Generally homogenous expression over the whole tumor tissue, with small area (ca. 5% of the tumor tissue) containing significant percentage of negative tumor cells.

H-Score: 230

Cells with no signal	10%	$10\% \times 0 = 0$
Cells with weak signal	5%	$5\% \times 1 = 5$
Cells with moderate signal	30%	$30\% \times 2 = 60$
Cells with strong signal	55%	$55\% \times 3 = 165$

7. HER2 assesment – automatic, AI-supported recognition of invasive tumor areas and automatic count of various categories of cells:

- negative invasive tumor cells
- partially stained invasive tumor cells
- completely weakly stained invasive tumor cells
- completely strongly stained invasive tumor cells
- unspecific tumor cells

The HER2 score produced by of AI-assisted assessment is supervised by reporting pathologist and can be fine-tuned by changing the status of single cells or groups of cells.

HER2 score	2+ (Equivocal)
Percentage of cells with intense complete membrane staining	Less than 1%
Percentage of cells with complete weak to moderate membrane staining	18%

AI Image Analysis

Breast HER2
▼
i

CE CE-IVD marked

2+

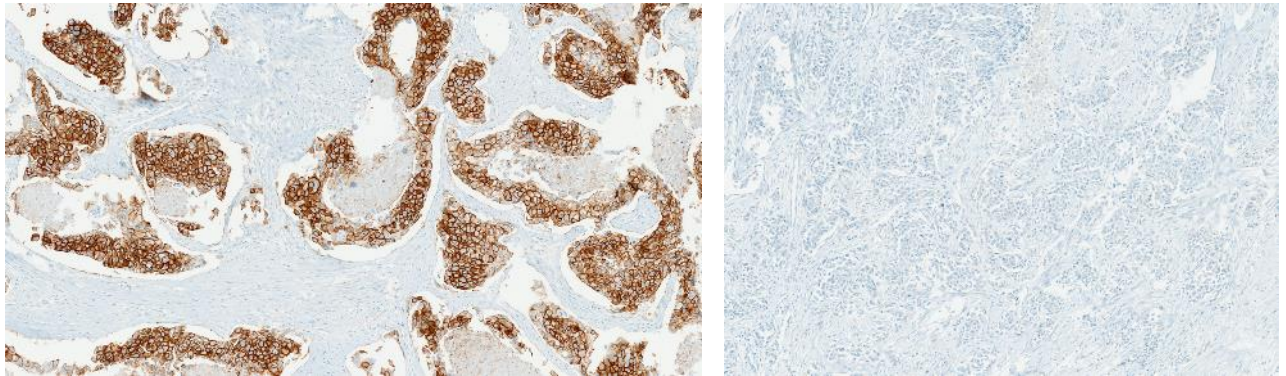
HER2 Score

● Negative tumor	● Partial tumor
10010	10393
● Complete weak tumor	● Complete strong tumor
3596	3
● Unspecific tumor	
0	

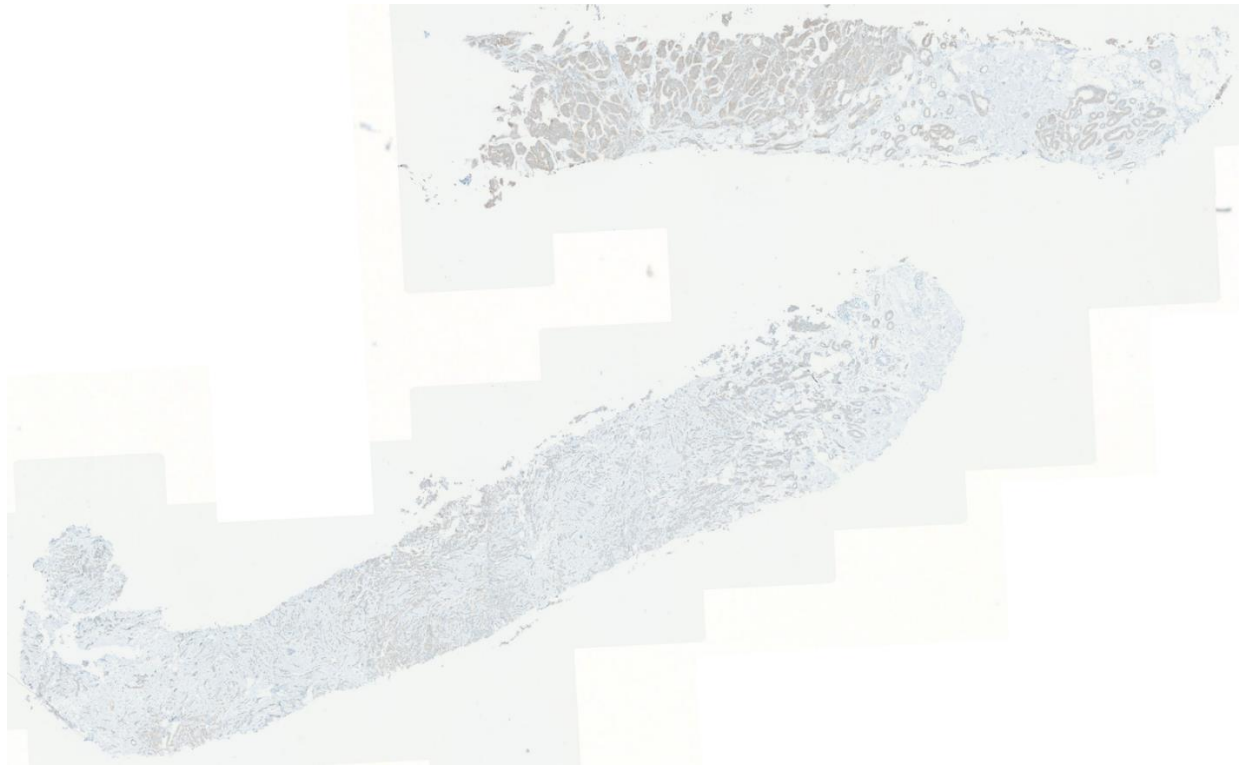
Presence of controls is reported in the assessed slides with interpretation and image documentation

Internal Controls – not identified

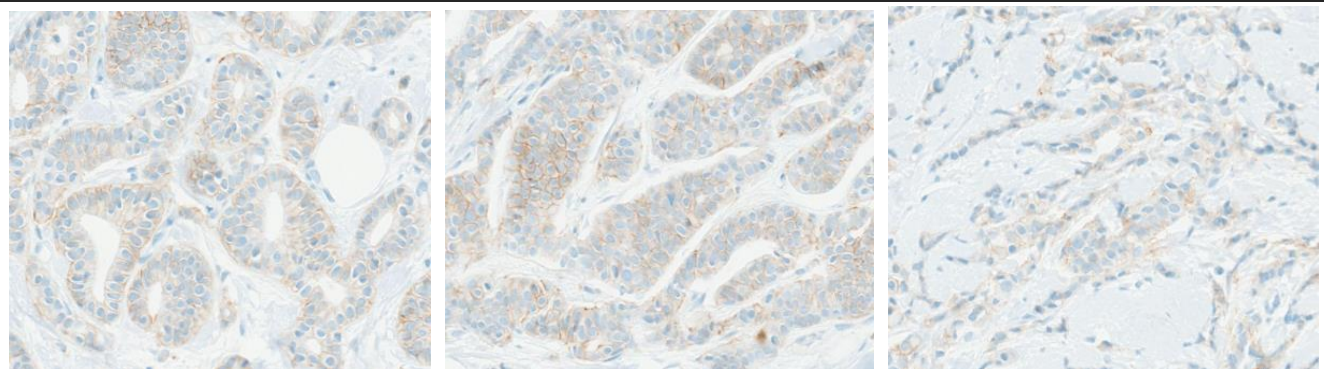
External controls: present, tumor tissue stained 3+, and 0+



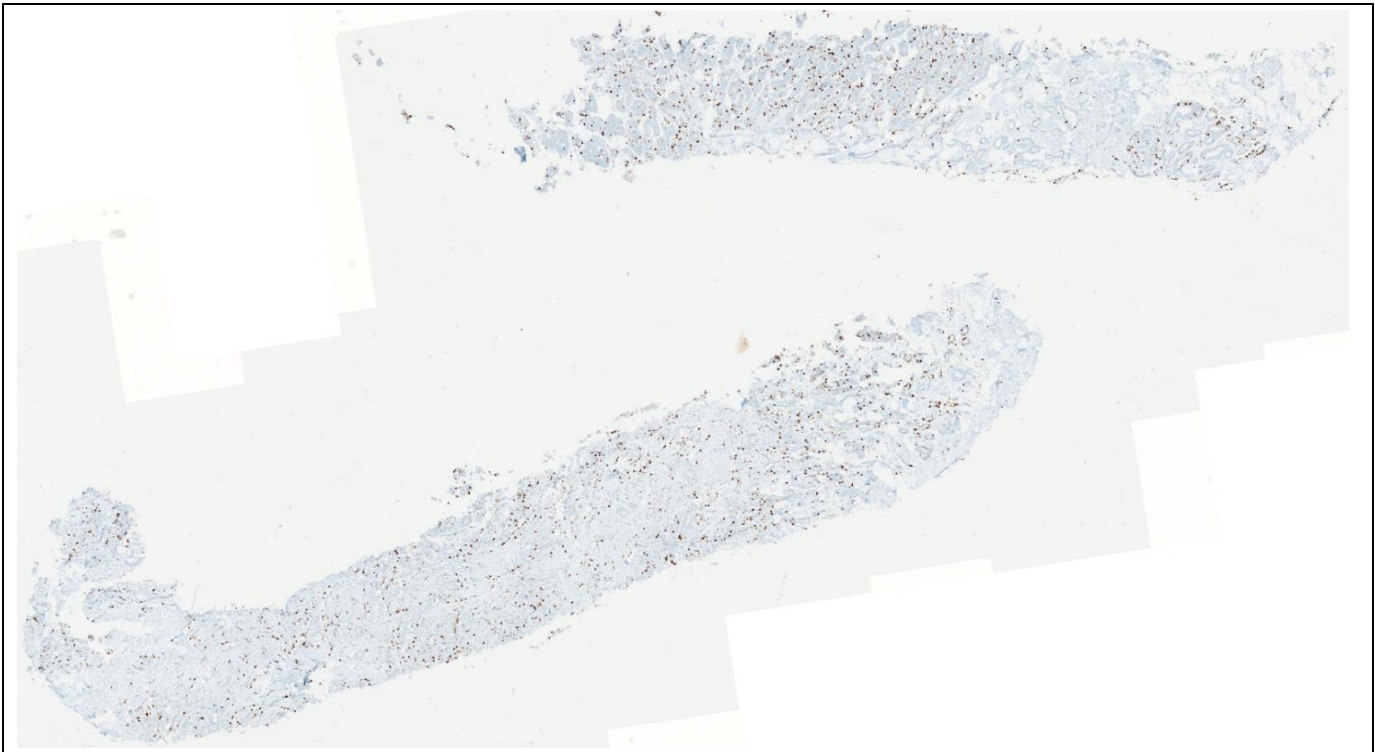
Additionally, marker expression homogeneity/heterogeneity is described.



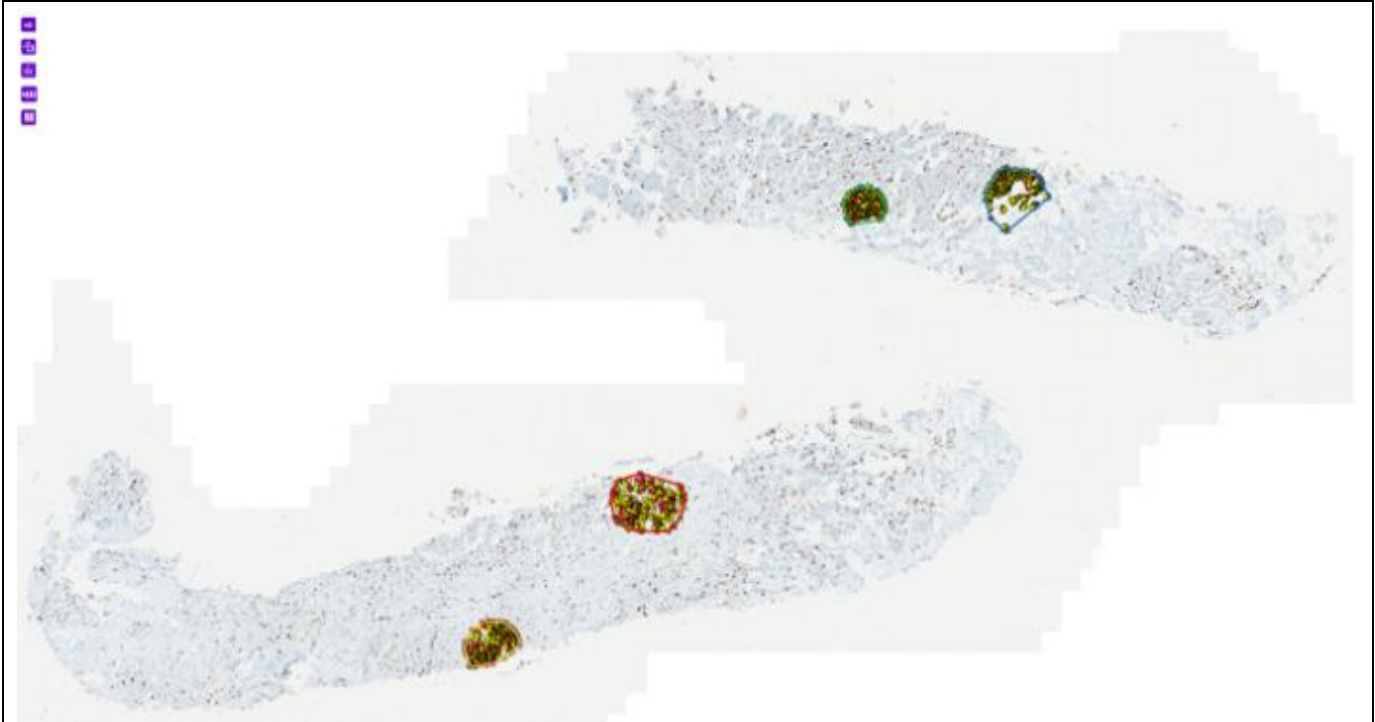
Homogenous expression over the whole tumor tissue.



8. AI-assisted reporting of Ki67 according to the method recommended by International Ki67 in Breast Cancer Working Group (4-region method). Additionally, global (average) score in the sample, as well as hotspot score are calculated and presented



AI-supported assesment of Ki67 stain with detection of regions with distinctive expression



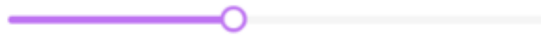
16.8%

Global Score (weighted)

18.0%

Global Score (unweighted)

Positivity threshold: 42%



Reset threshold

25.6%

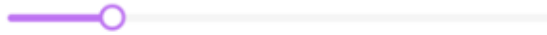
Tumor positive 103 Tumor negative 299



Weight 12%

21.8%

Tumor positive 88 Tumor negative 316



Weight 19%

17.2%

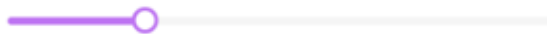
Tumor positive 69 Tumor negative 332



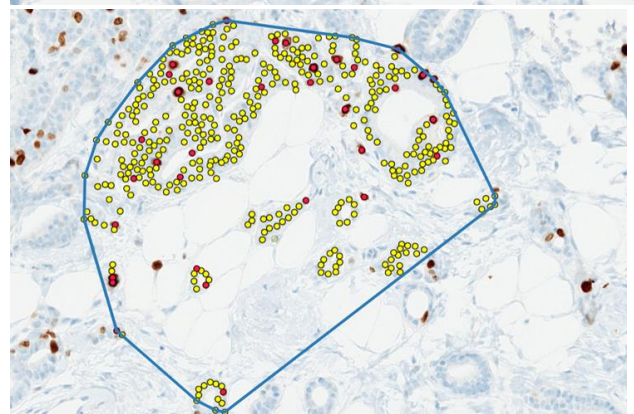
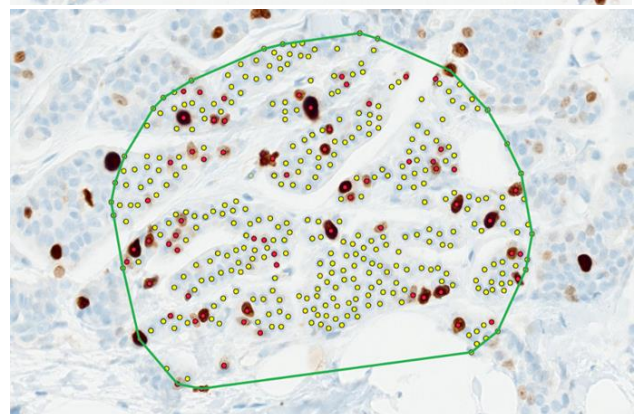
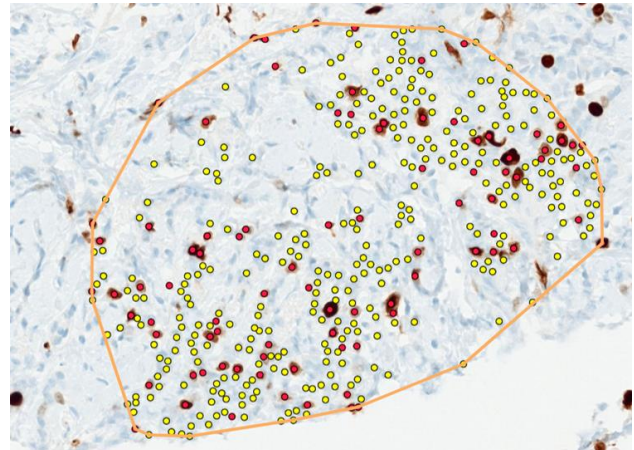
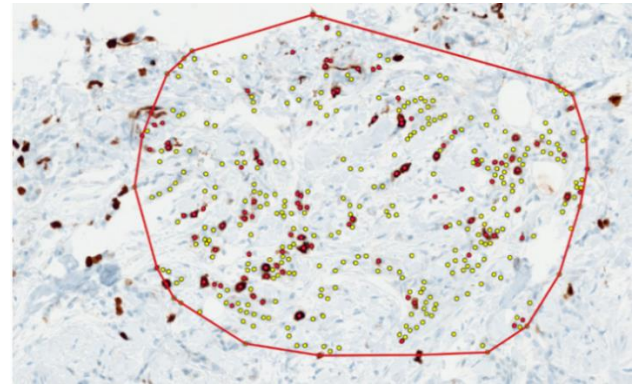
Weight 44%

8.0%

Tumor positive 34 Tumor negative 391



Weight 25%



1. Weighted Method (according to International Ki-67 in Breast Cancer Working Group), **score: 16,8%**
2. Hotspot method, **score: 25.6%**
3. Global method, **score: 18.0%**

Contact

TwiceView second opinion service is provided by:

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