

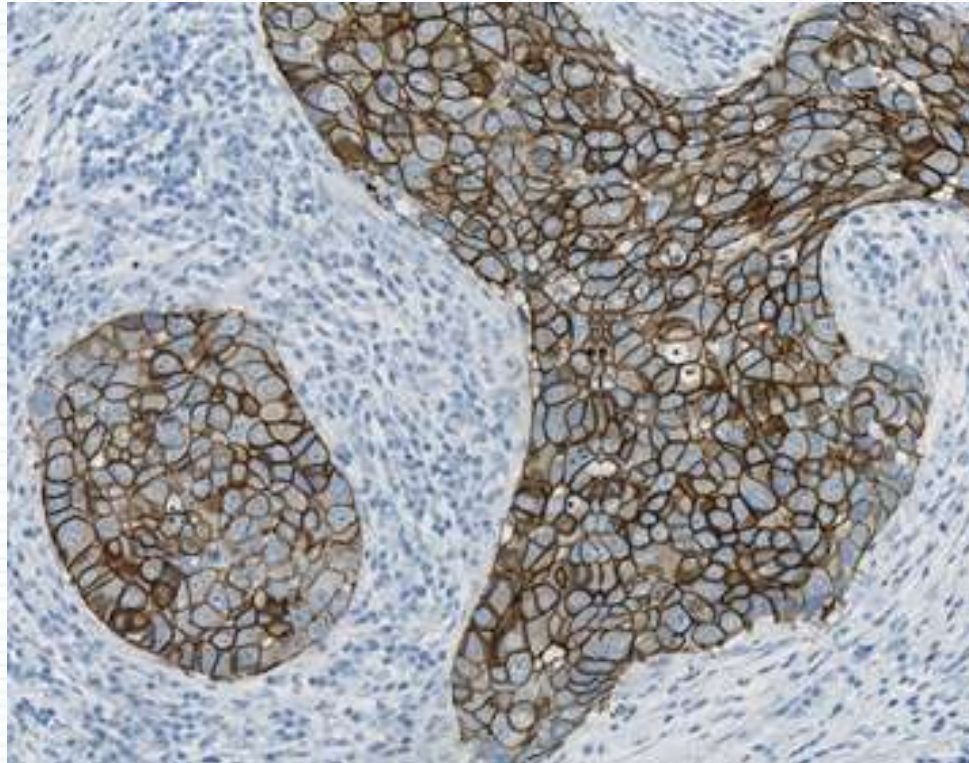
Disclaimer:

The following slides were presented at the TIGA Workshop, and are enclosed in the PP "show" format (*.pps) in order to include all presented details.

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1st European Workshop on Tissue Imaging and Analysis
Heidelberg Feb 13-14 2009 at Copenhagen University LIFE

Quantitative Histomorphometry of Whole Slide Digital Images of Tumor Tissue



Michael Grunkin & Niels T. Foged

Visiopharm A/S: A brief company introduction



- **Founded in 2001.**
- **HQ in Copenhagen. Subsidiary in US**
- **Business focus: Automated quantitative microscopy**
- **Products: Advanced software for histomorphometry**
- **Customers: Scientists in universities/hospitals & biotech/pharma**
- **Increasing requests: Pathologists and teachers**

**Products: Software modules for automated:
imaging, data base management, image analysis and stereology**



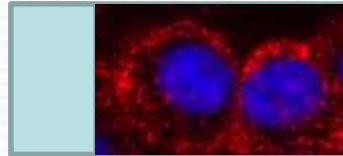
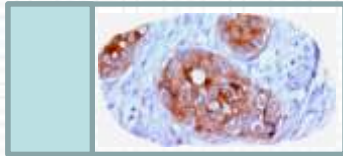
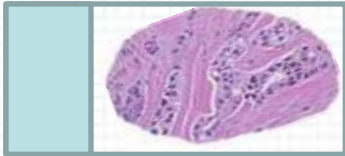
- **Software handles "all" types of image files.**
- **Visiopharm software users can easily switch between traditional microscopy and slide scanning.**
- **Visiopharm is expanding from life science to clinical applications**

Collaboration projects in (breast) cancer pathology

Malignancy grading H&E

Primary Tumor IHC

Proximity ligation IHC

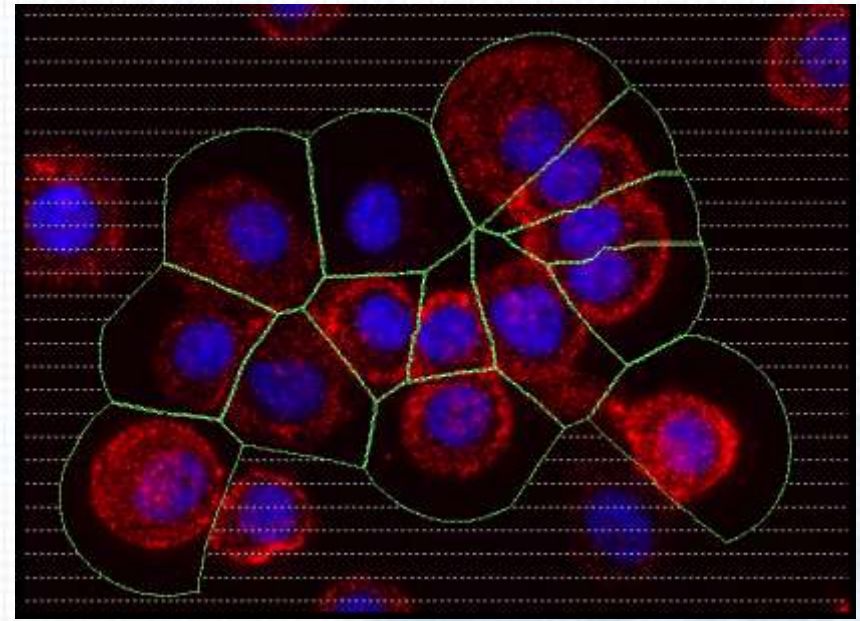
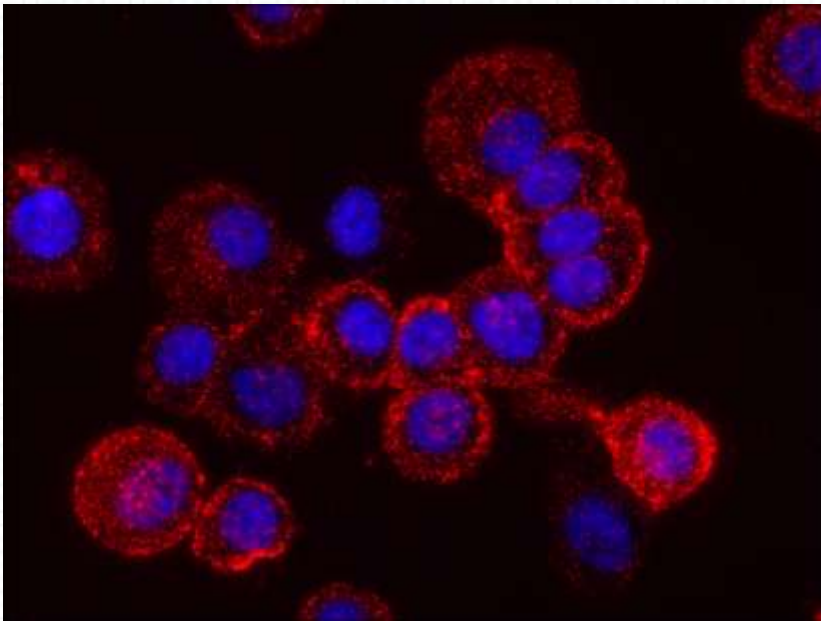


- Tubularity
- Nucl. pleomorph.
- Mitotic grade

- ER/PR IHC
- HER-2 IHC
- TIMP-1 IHC



Proximity Ligation Assay (PLA)



Dual antibody-based immunohistochemistry, e.g. HER-2/3 dimers

"Blob"-signals by Rolling Circle Amplification

Quantification of signals per cell by Visiomorph™ software module

Collaboration projects in (breast) cancer pathology

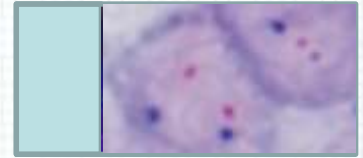
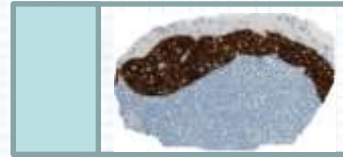
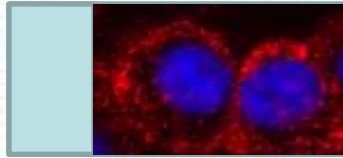
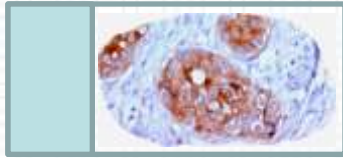
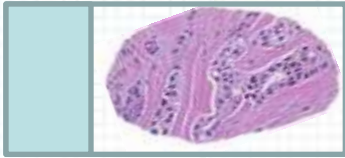
Malignancy grading H&E

Primary Tumor IHC

Proximity ligation IHC

Sentinel node IHC

Chromosomal FISH/CISH



- Tubularity
- Nucl. Pleomorph.
- Mitotic grade



- HER2 FISH/CISH
- TOP2A FISH/CISH
- TIMP-1 FISH/CISH

- ER/PR IHC
- HER-2 IHC
- TIMP-1 IHC

- SLN metastasis:
 - Presence
 - Vol./stereology

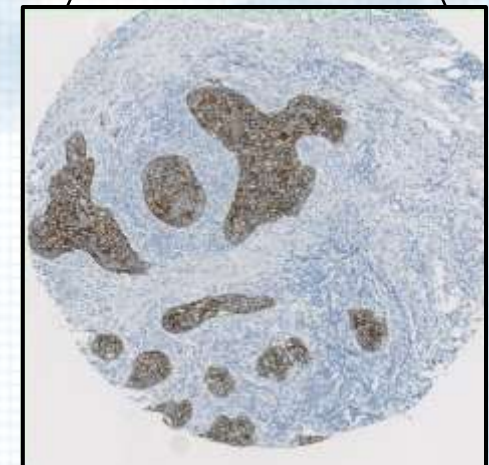
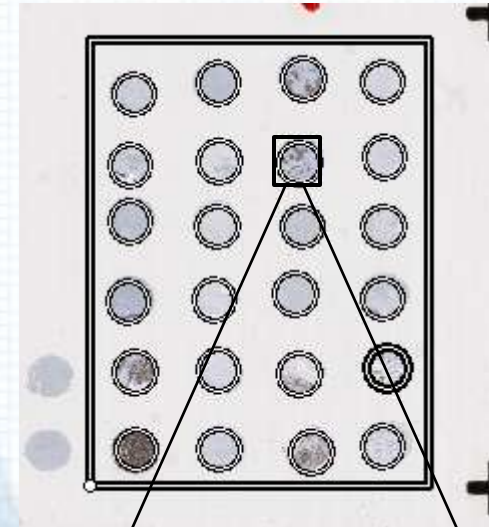
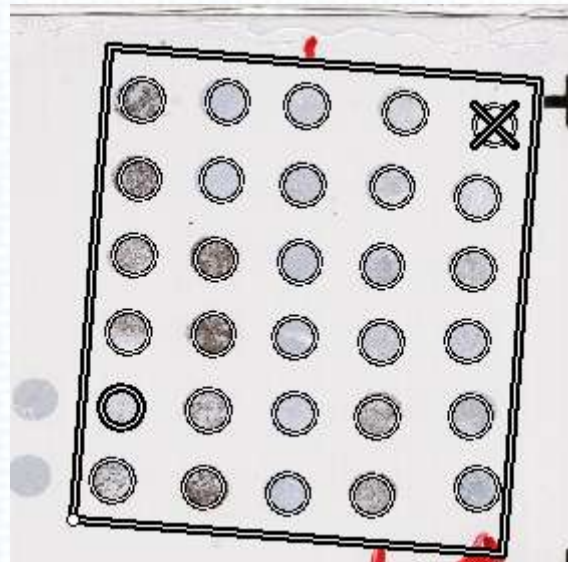
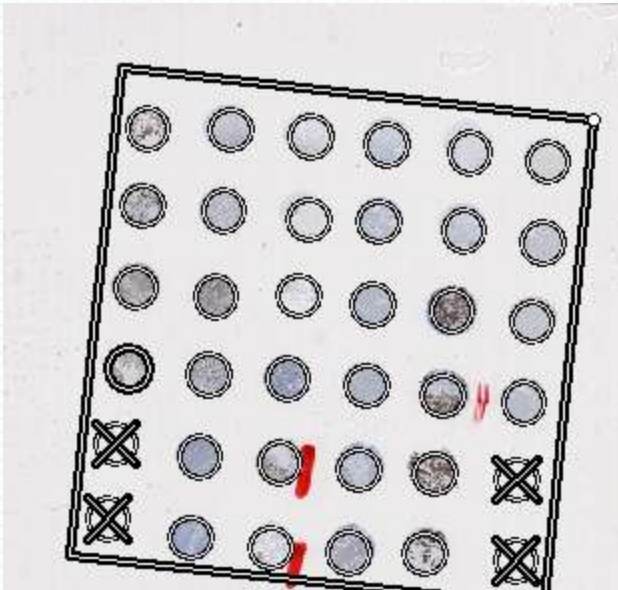
Individual grading and staging of cancer



Today's focus:
HER-2 Immunohistochemistry

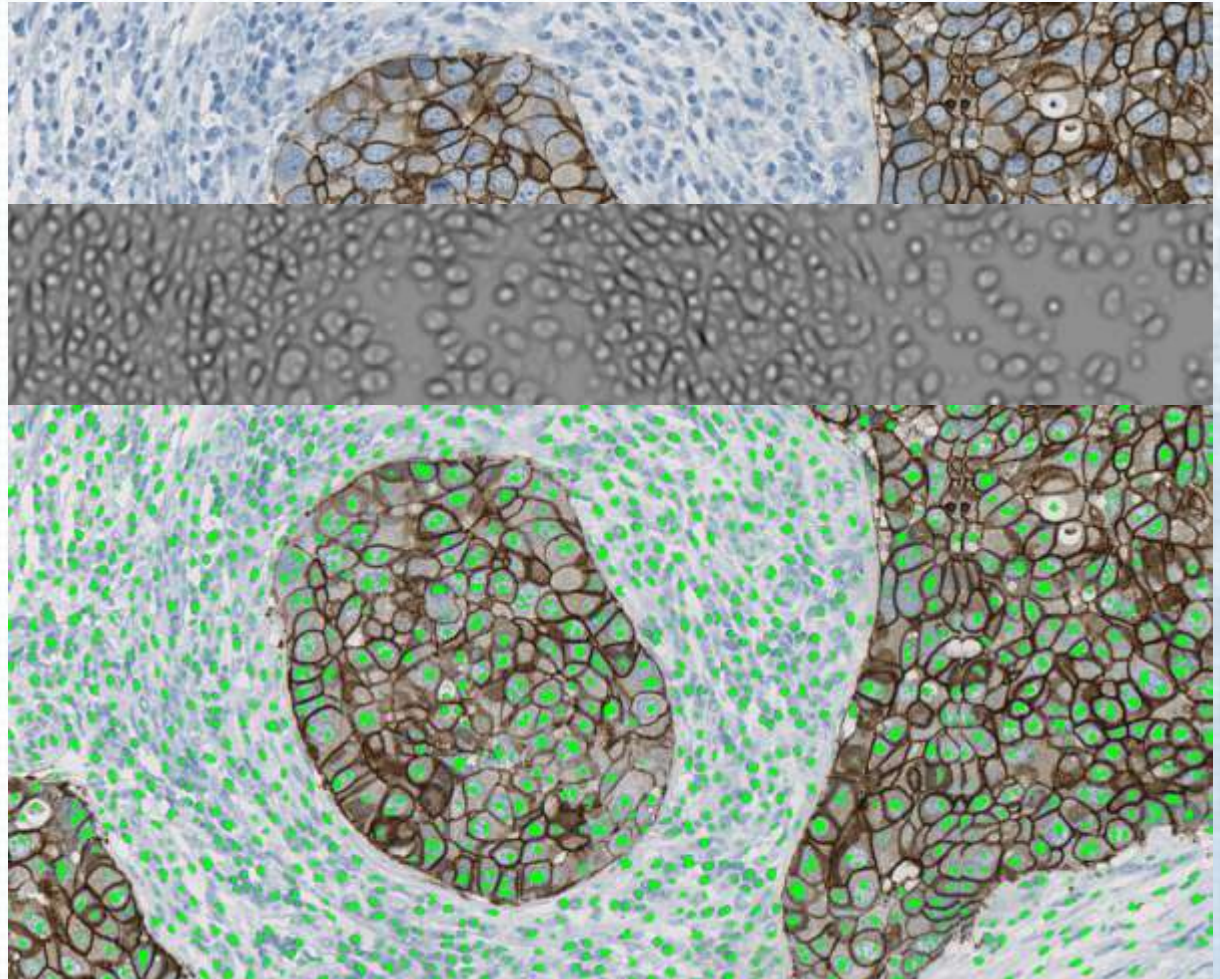
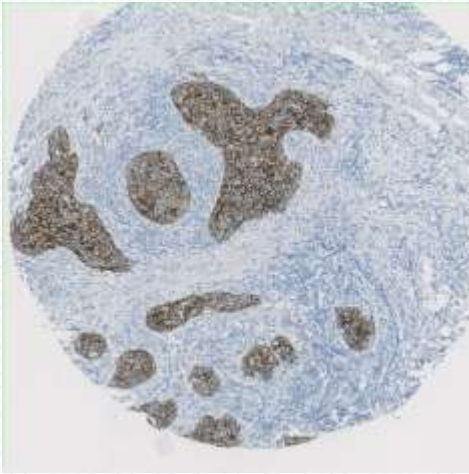
HER-2 IHC Algorithm: **Work in progress**

Clinical collaboration study with Mogens Vyberg, NordiQC (Aalborg Hospital)

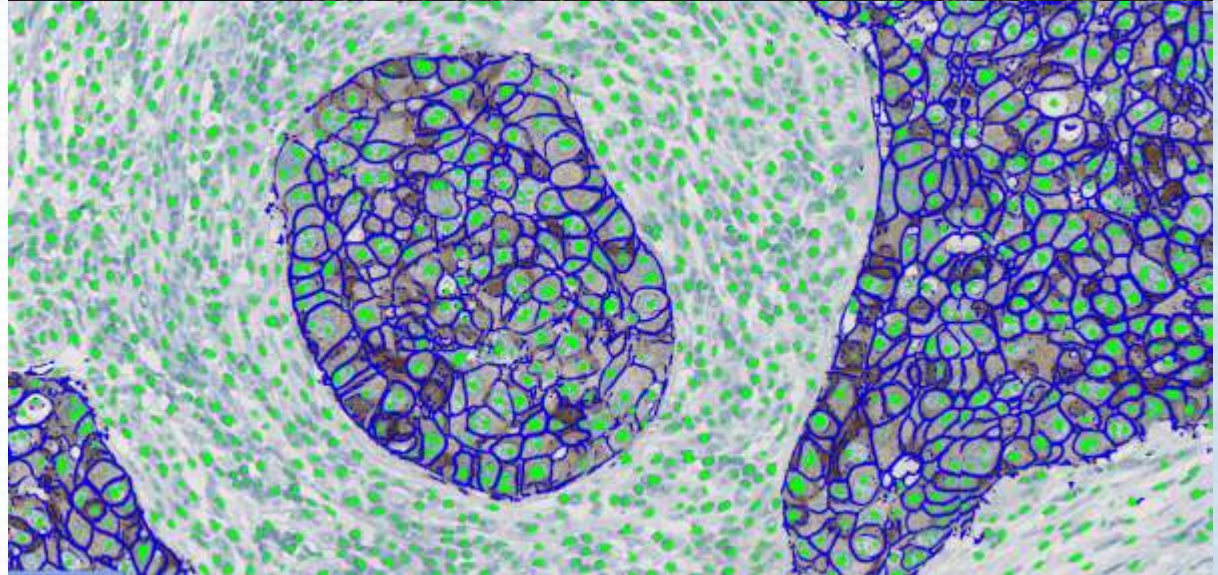
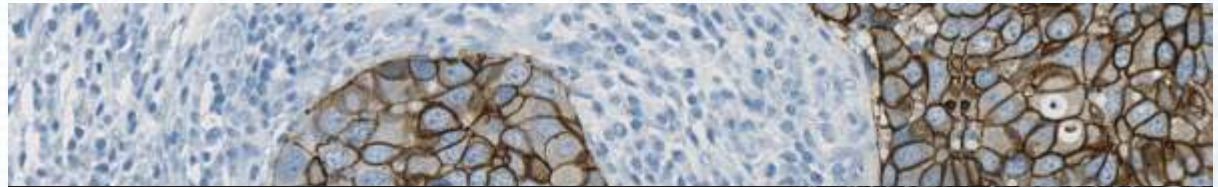
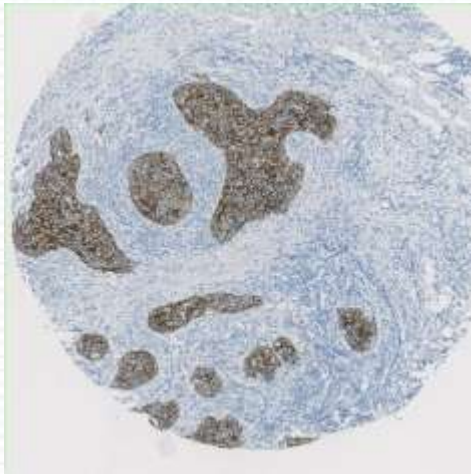


- Tumor tissue from 75 breast cancer patients
- Three TMA's stained with the Herceptest™ (Dako)
- Adjudicated consensus scores by a panel of expert pathologists
- Scanned with Nanozoomer @ x20
- Visiopharm proprietary software used for feature extraction

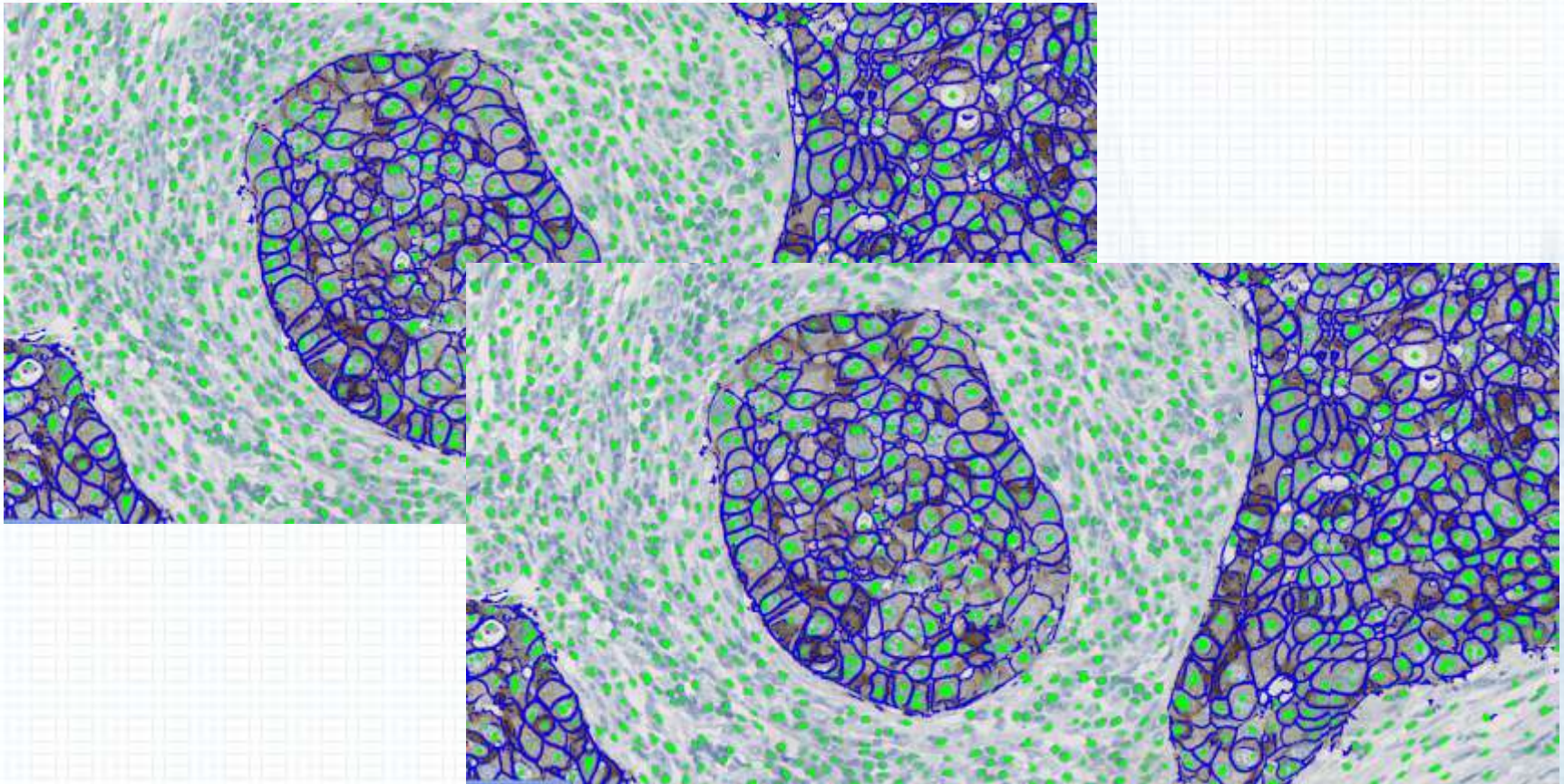
ENHANCING STAINED NUCLEI (BLUE) USING A SPECIAL FILTER



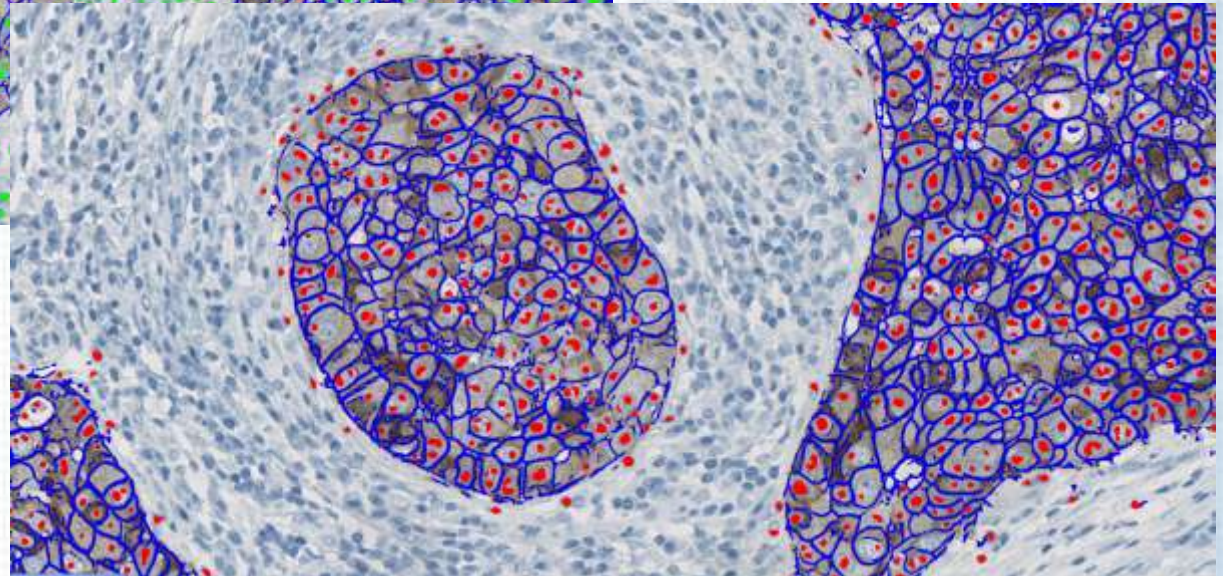
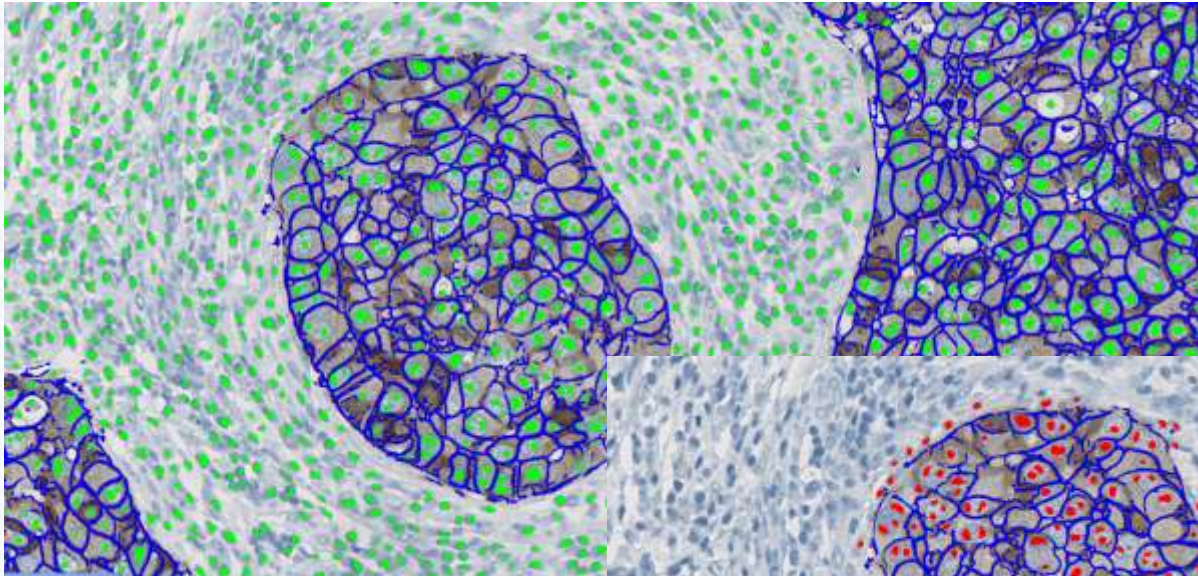
ENHANCING STAINED MEMBRANES (BROWN) USING A SPECIAL FILTER



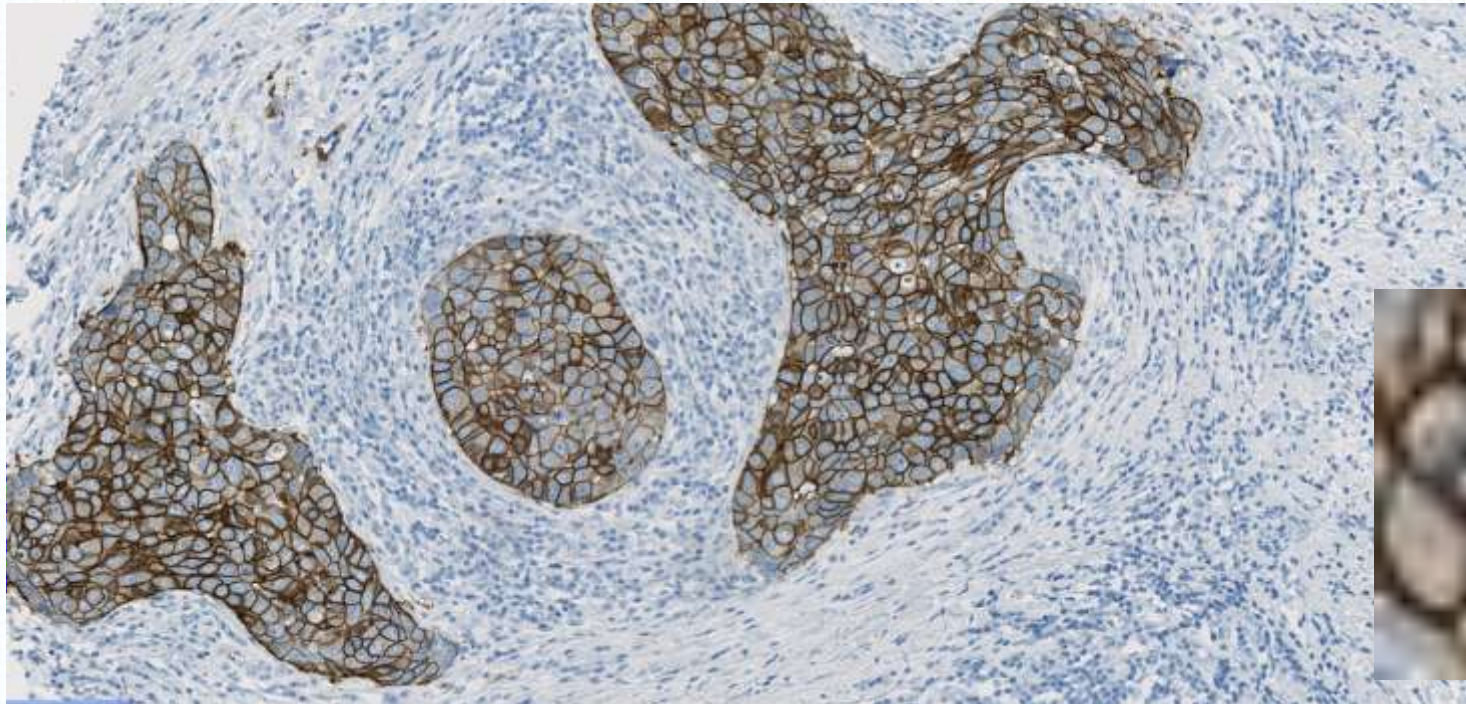
POST PROCESSING STEP1: Remove (too) small nuclei & membrane objects



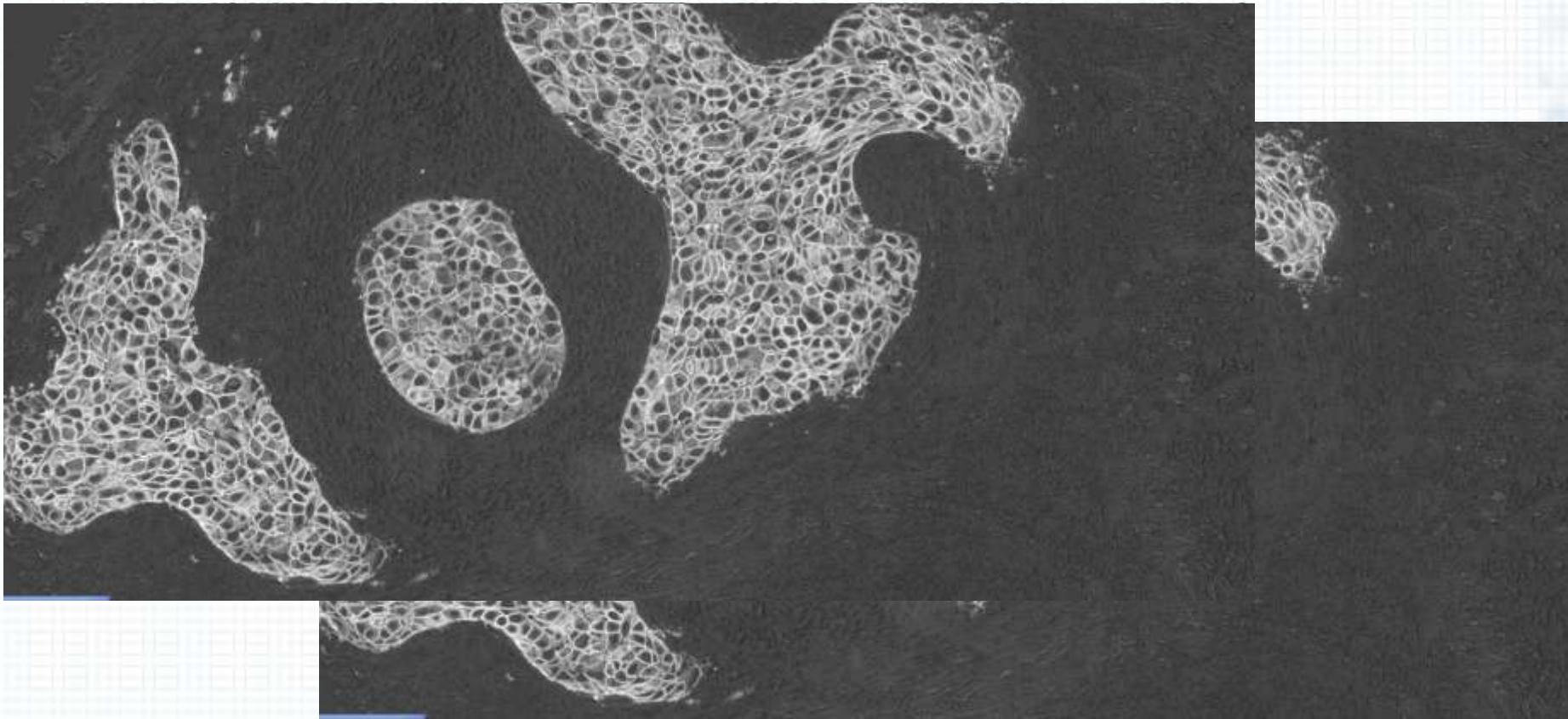
POST PROCESSING STEP2:
Remove nuclei without a membrane and
membrane structures without a nucleus



FINAL SEGMENTATION

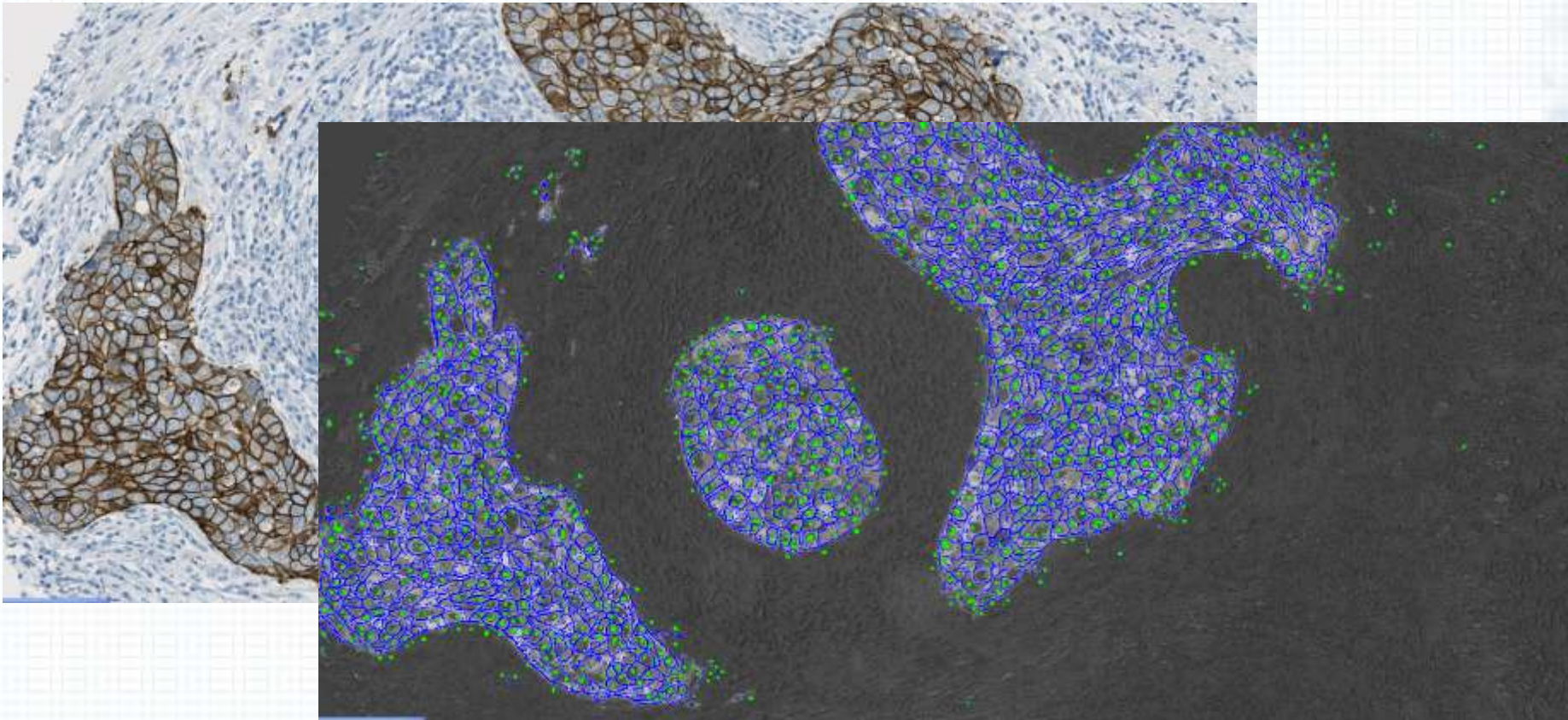


MEASURING STAINING INTENSITY



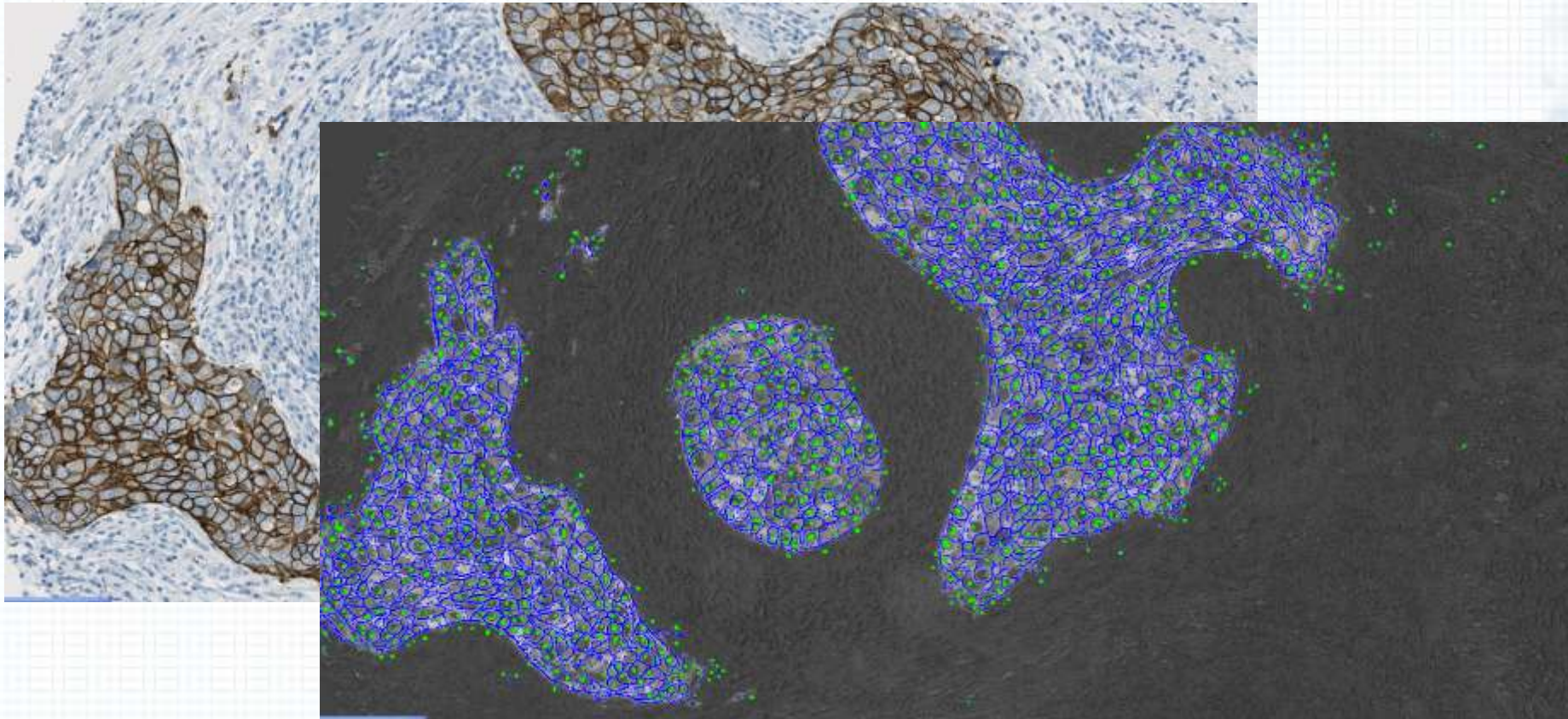
Using a special algorithm quantifying brown

MEASURING STAINING INTENSITY



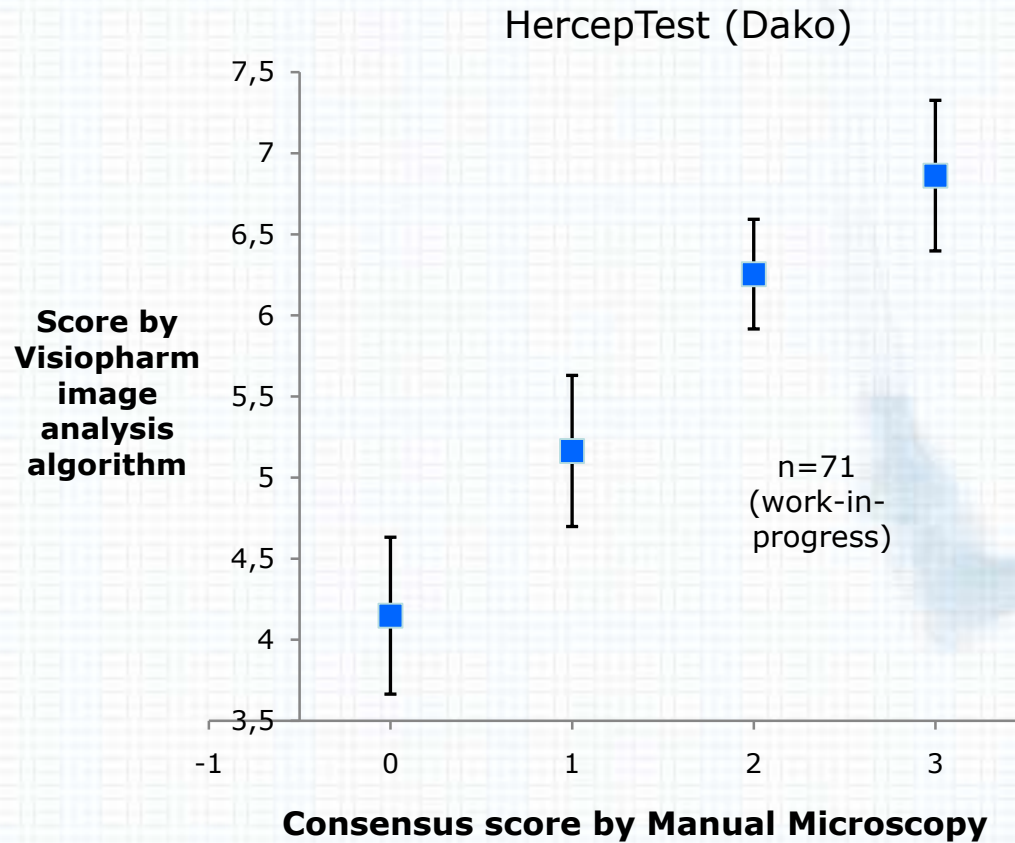
Measuring average staining intensity (i.e. brown)
below the identified membrane label

PLANIMETRIC FEATURES



Measuring area of membrane, number of nuclei, and average amount of membrane per identified nucleus.

Preliminary results of comparison to consensus scores obtained by manual microscopy



**Please feel free to visit the Visiopharm booth
for further discussions and a live demo
by Jakob Raundahl, PhD**