

Grundlaget for god digital patologi og digital billedanalyse

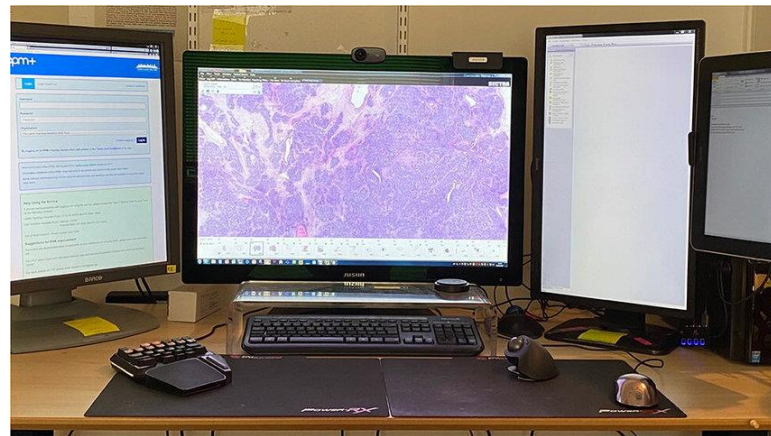
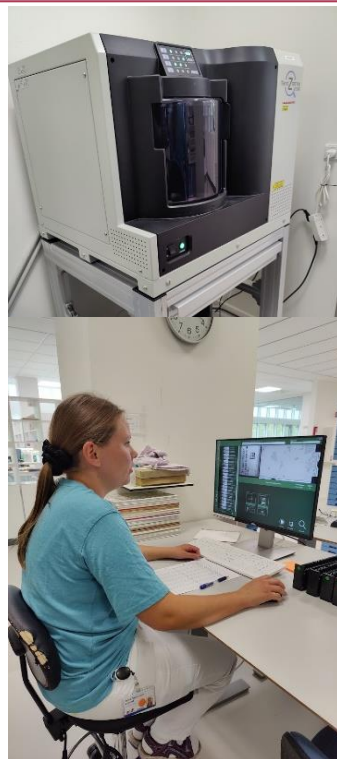
05-11-2022

Bioanalytiker

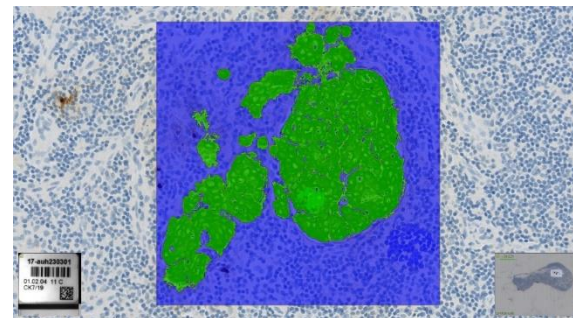
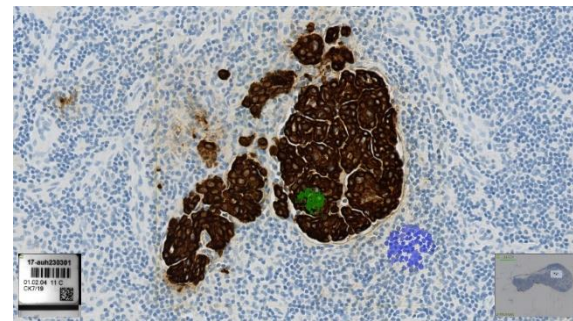
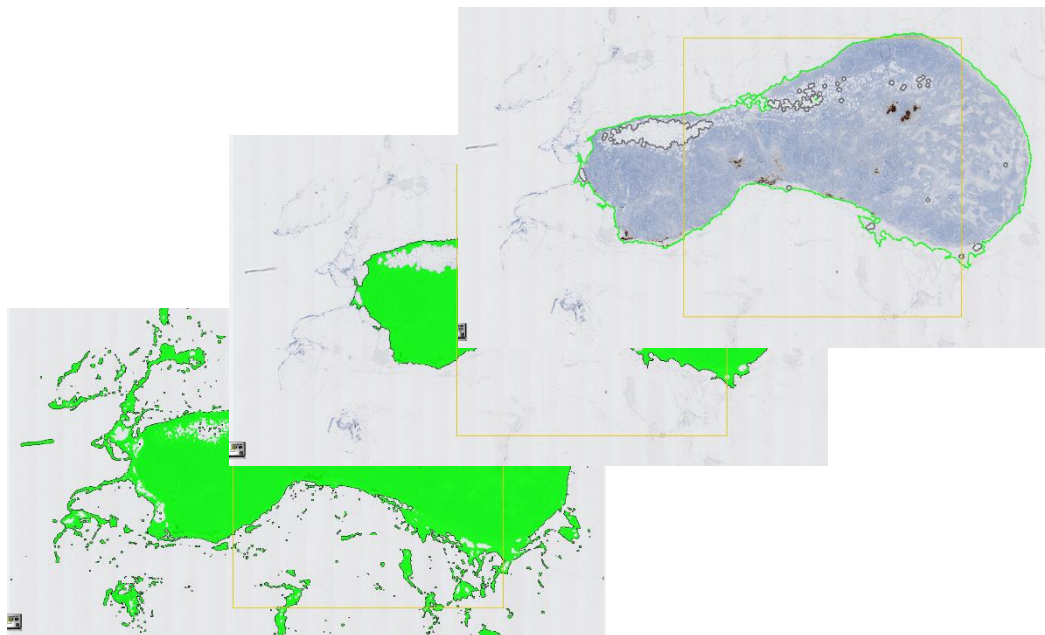
Kristina Lystlund Lauridsen

Patologi, Aarhus Universitetshospital

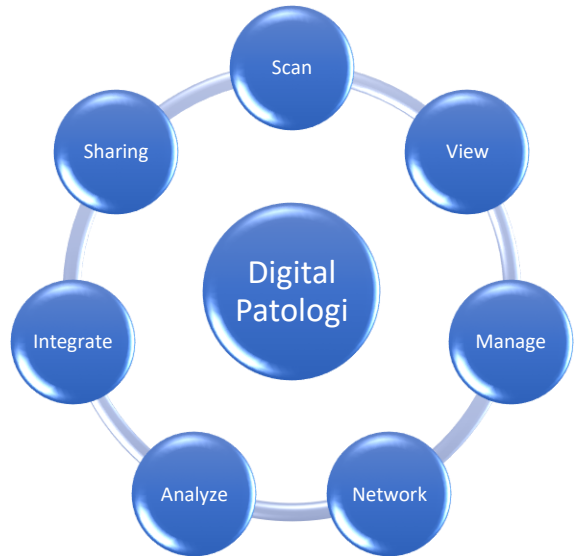
Digital patologi



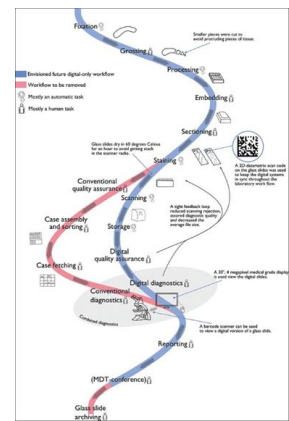
Et af målene: Digital billedanalyse



Samlet definition for digital patologi

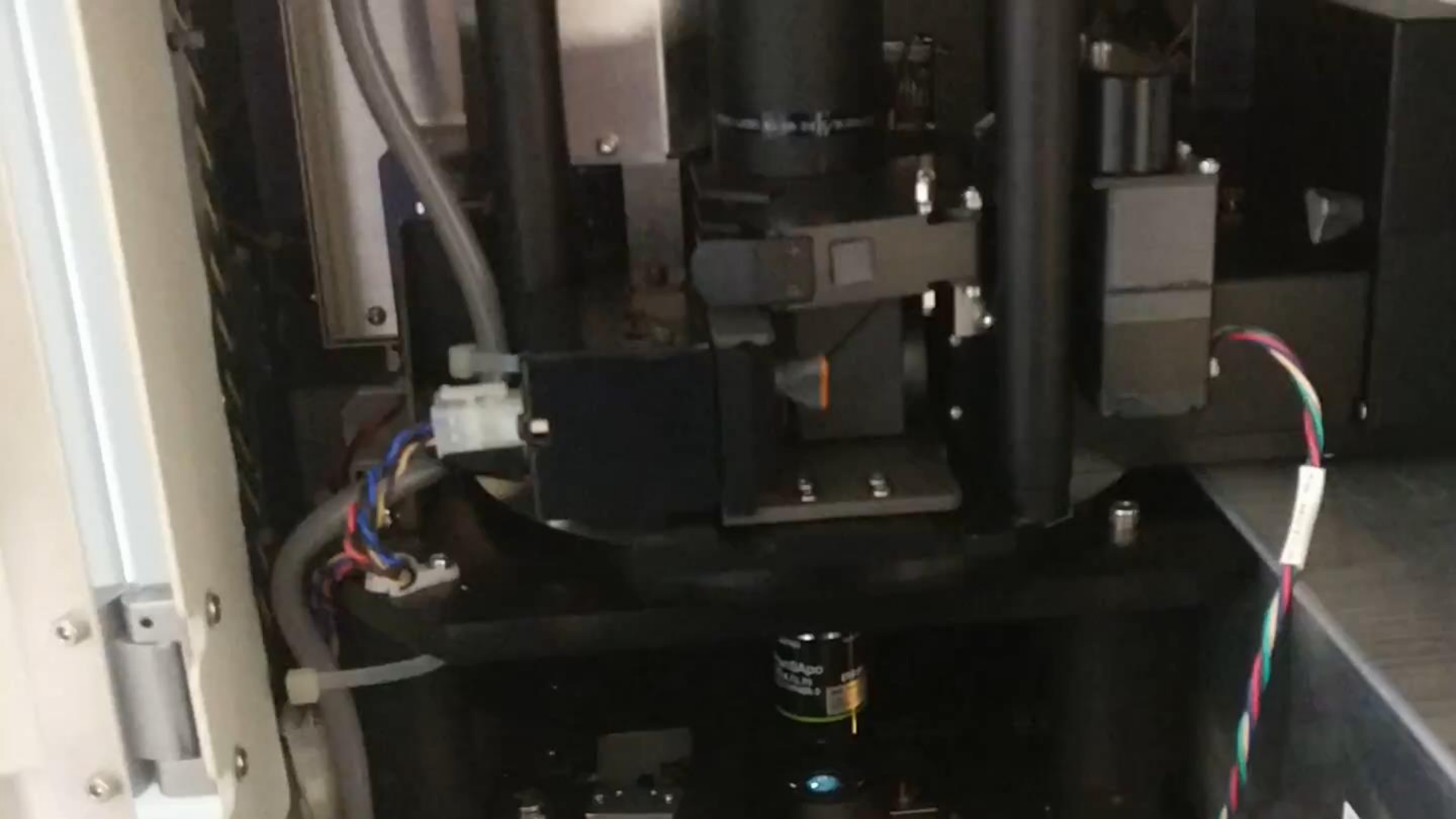


Den brede definition af digital patologi:



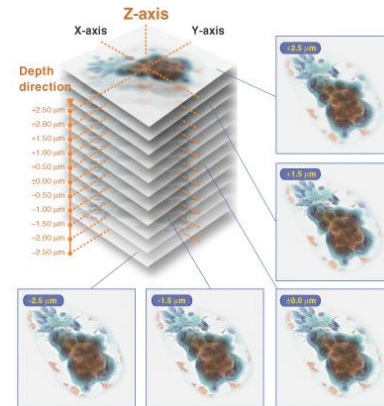
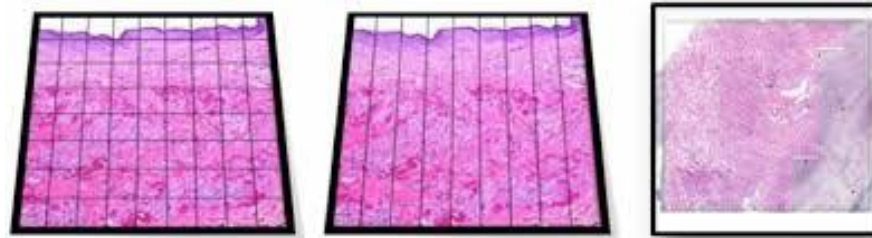
Thorstenson S, Molin J, Lundström
C. *J Pathol Inform* 2014

Skanneren



Skannertyper

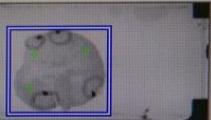

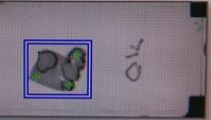

- Line- og tile-skannere
- Z-stacking



Rundt om skanneren I

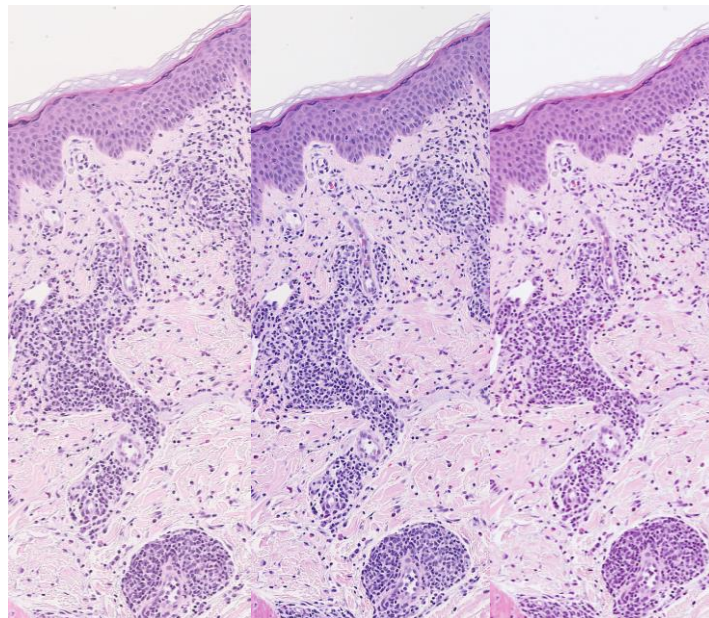
- Hastighed
 - Husk at se på total skantid
 - Rack eller holder
 - Tab af glas
- Kontinuert loading



	HT2.0			S360			
	Vævs størrelse	20x	40x	Vævs størrelse	20x	40x	
	Stor	563 MB 3,12 min	1,71 GB 5,32 min	Stor	718 MB 1,02 min	2,4 GB 1,03 min	
	Mellem	186 MB 1,22 min	588 MB 2,45 min	Mellem	259 MB 0,34 min	907 MB 0,34 min	
	Lille	24,9 MB 0,43 min	80,2 MB 1,2 min	Lille	33,3 MB 0,18 min	135 MB 0,18 min	

Rundt om skanneren II

- Kvalitet
 - Fejlrate
 - Farvegengivelse
- Opløsning/forstørrelse
 - Eksempel: Hamamatsu
Nanozoomer objektiv 20x/0,75NA



It is expected that within a single department, different scanners will be used for different purposes. One vendor may have the best high-throughput scanner for general histology, while another scanner is best for large or mega slides and yet another for cytology or fluorescence staining.

<https://medical.sectra.com/resources/supporting-digital-full-scale-primary-diagnostics-pathology/> Elin Kindberg

Rundt om skanneren III

- Semi og/eller fuldautomatisk skanning
- Oppetid
- Antal og størrelse glas
 - Mega slides
- Mulighed for service og support
- Filformater
- Cytologi?

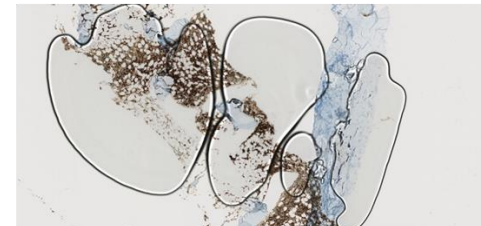
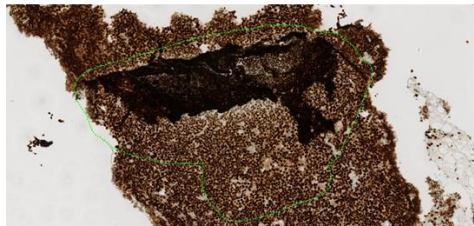
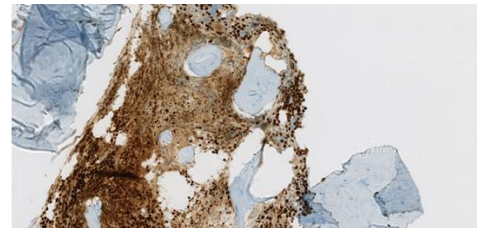


<https://argos-scanner.com/en/>

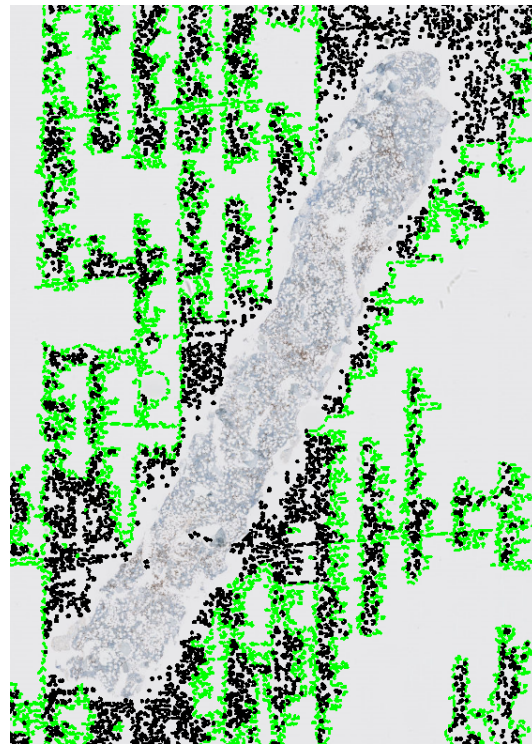
Forudsætninger for god skan-kvalitet

PROBLEMER

- Artefakter
 - Flydere
 - Ridser
 - Folder
 - Montering
- Tykkelse af vævssnit
- Fedtvæv/meget svagt farvet væv
- Skanneren



- **Hvad har i oplevet som et problem?**



Forudsætninger for god skan-kvalitet

PROBLEMER

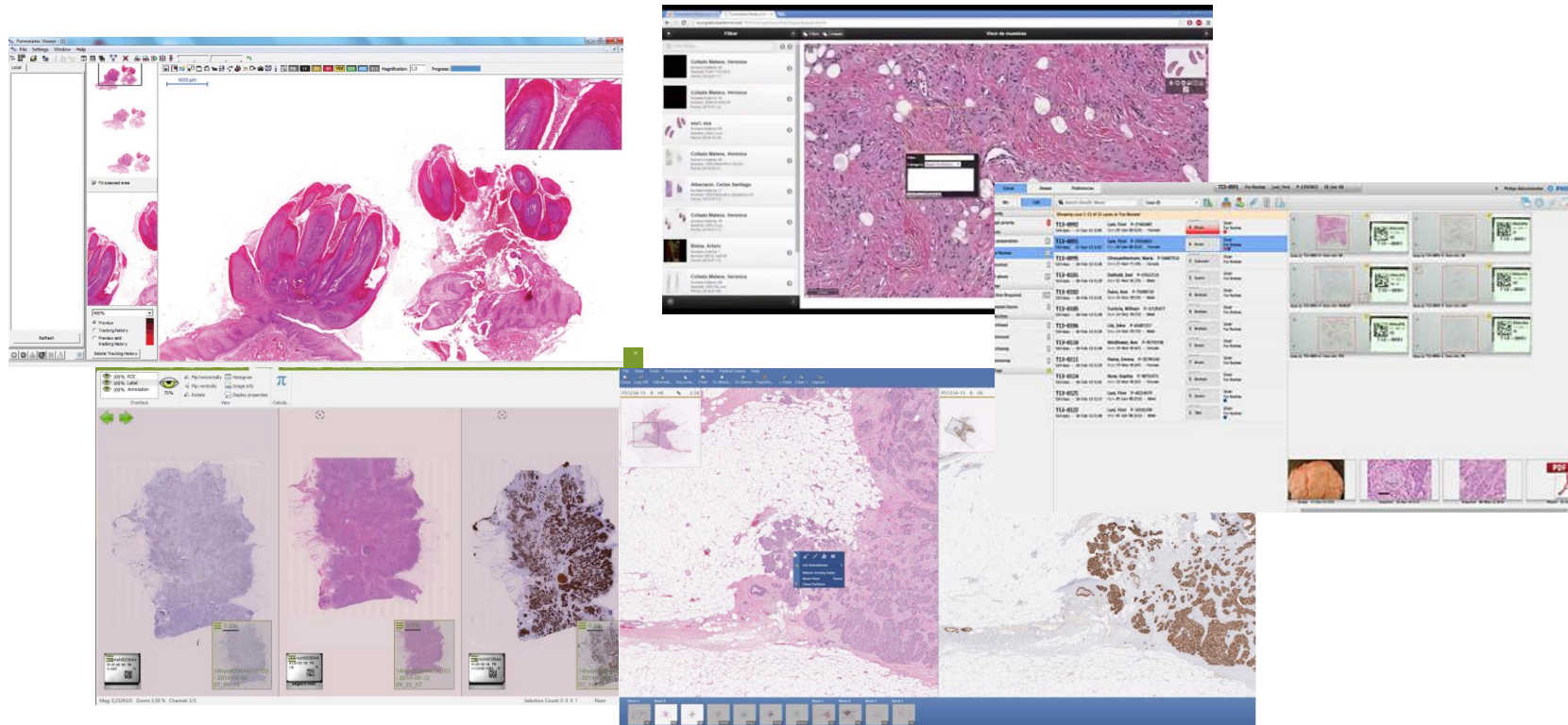
- Artefakter
 - Flydere
 - Ridser
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- Skanneren
- **Hvad har i oplevet som et problem?**

HVAD KAN VI GØRE?

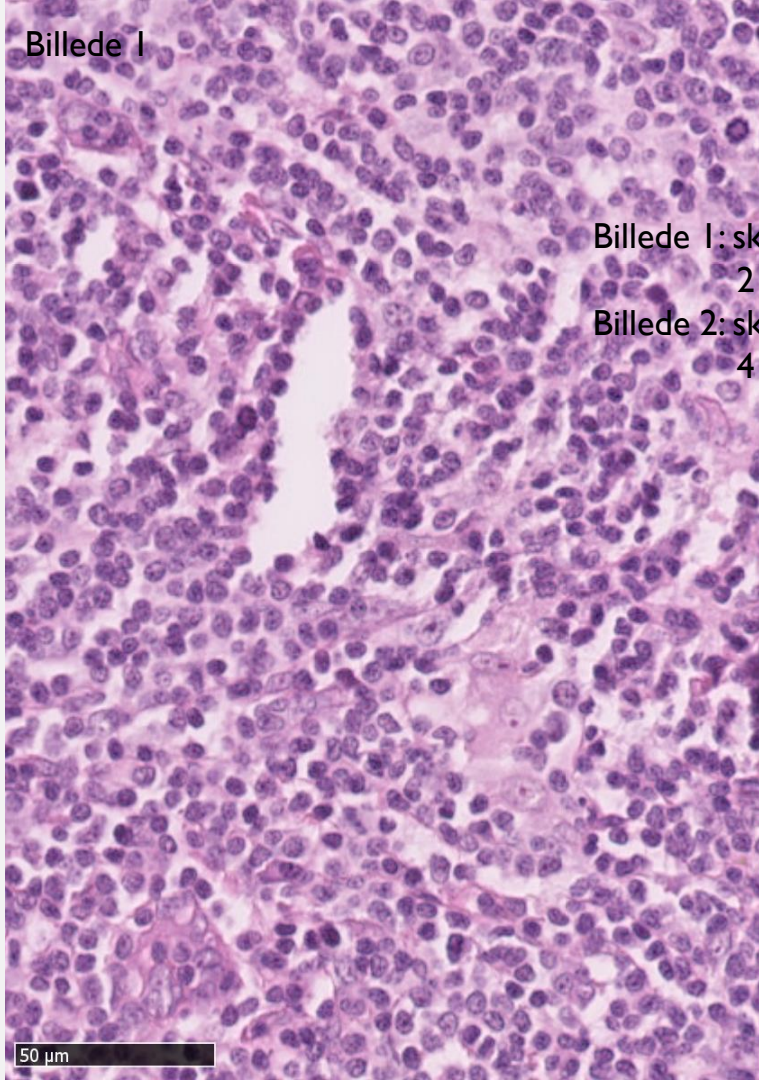
- Skift vandbad
- Tid til mikrotomi – ændring af fokus
- Snittykkelse
 - Mikrotomi-robotter
- Opmærksomhed på montering
- Kvalitetskontrol indbygget i skanneren
- Kalibrering
- Hvidbalance
- Rengøring
- **Har i andre løsninger?**



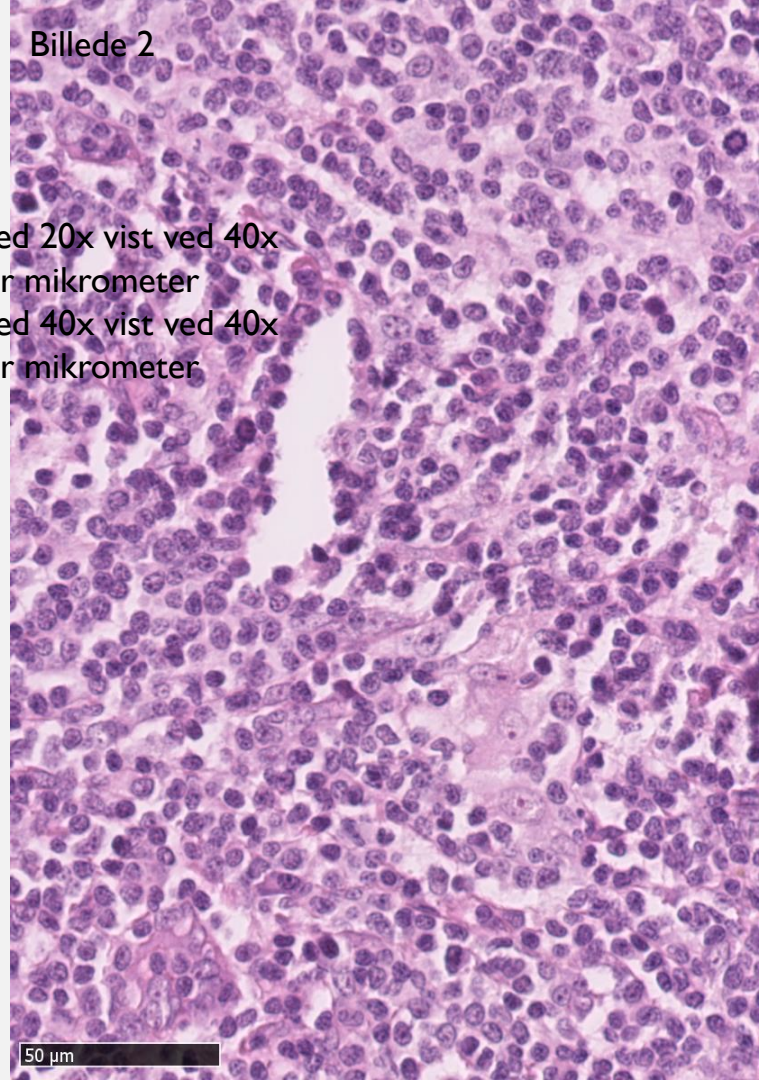
Viewer



Billede 1



Billede 2



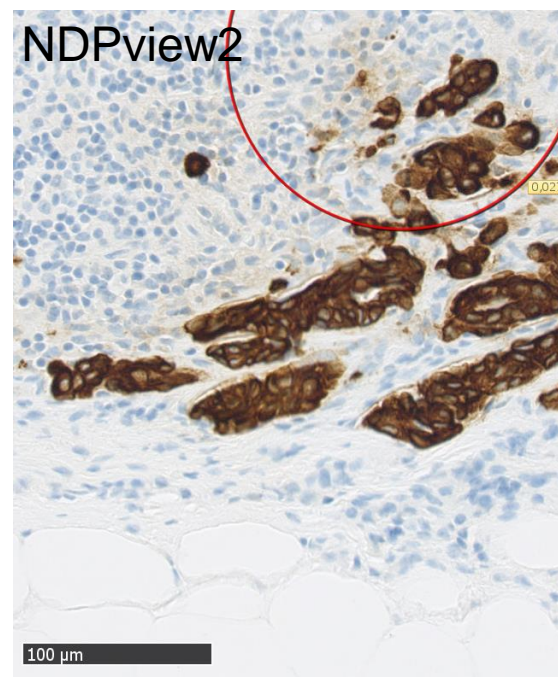
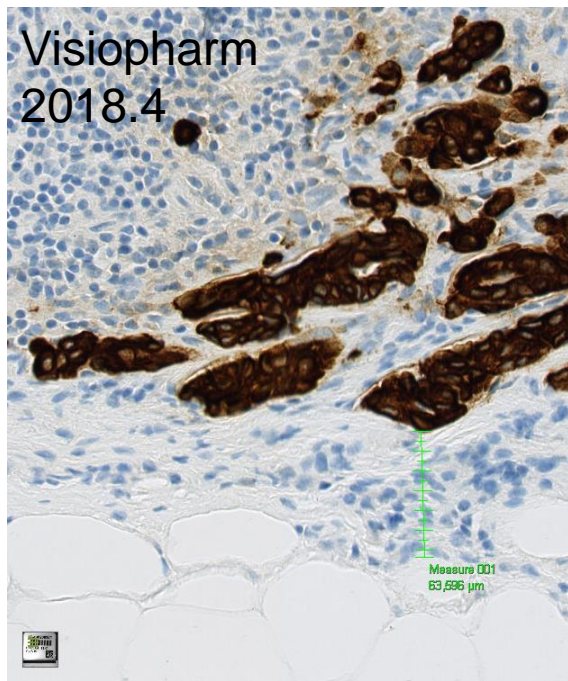
Billede 1: skannet ved 20x vist ved 40x
2 pixels pr mikrometer

Billede 2: skannet ved 40x vist ved 40x
4 pixels pr mikrometer

50 μm

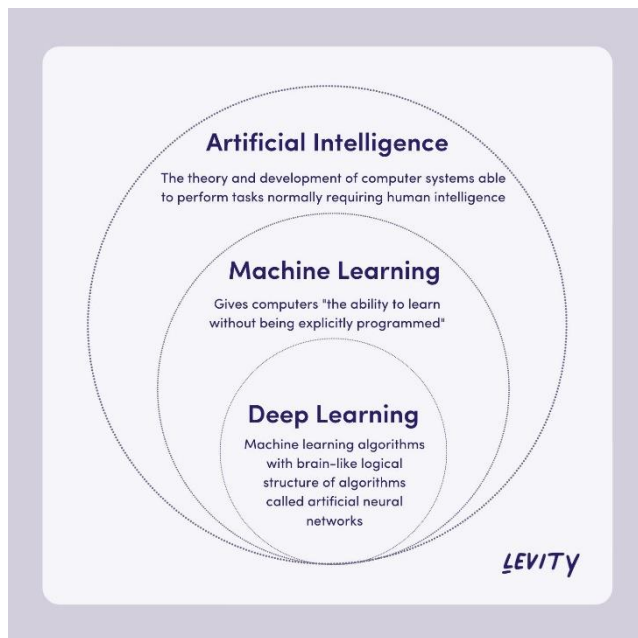
50 μm

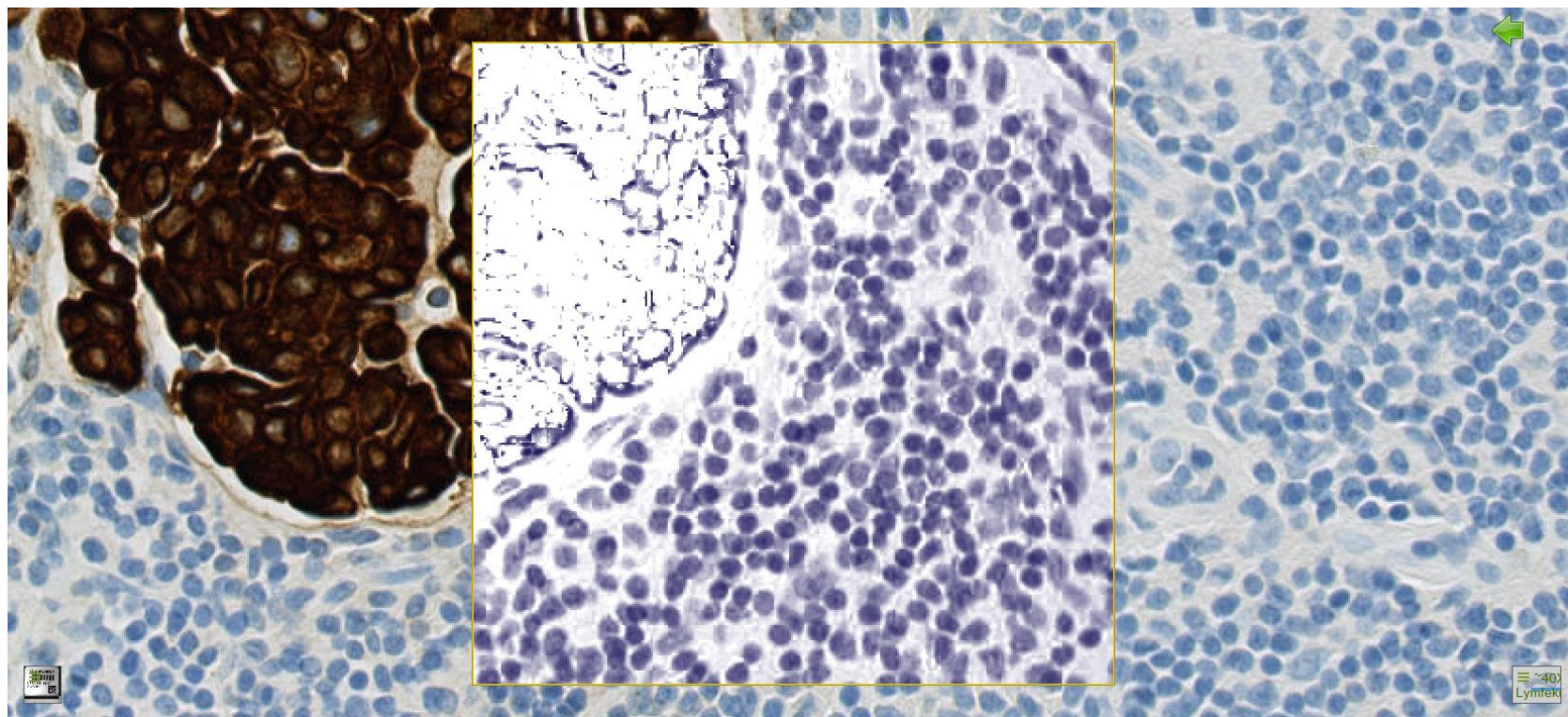
Viewer

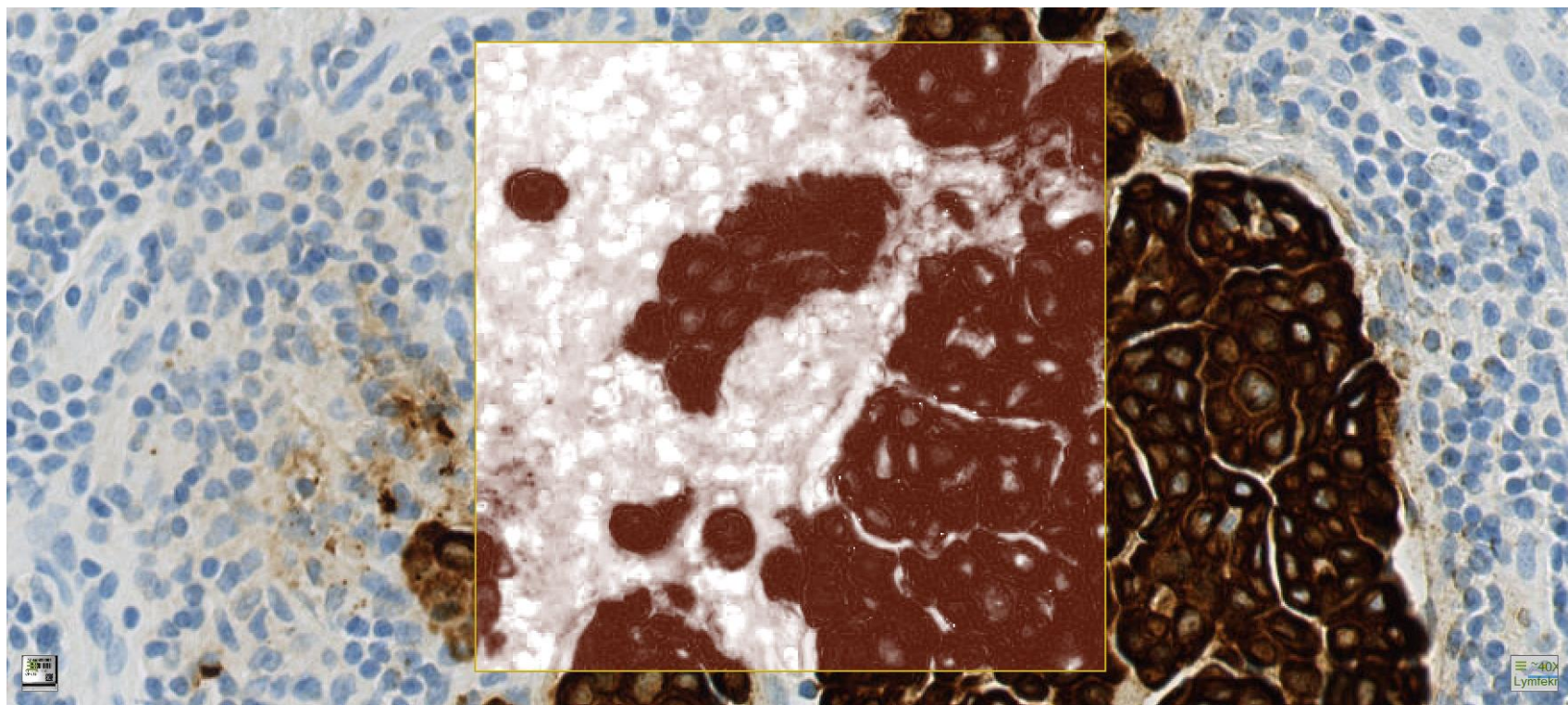


Digital billedanalyse

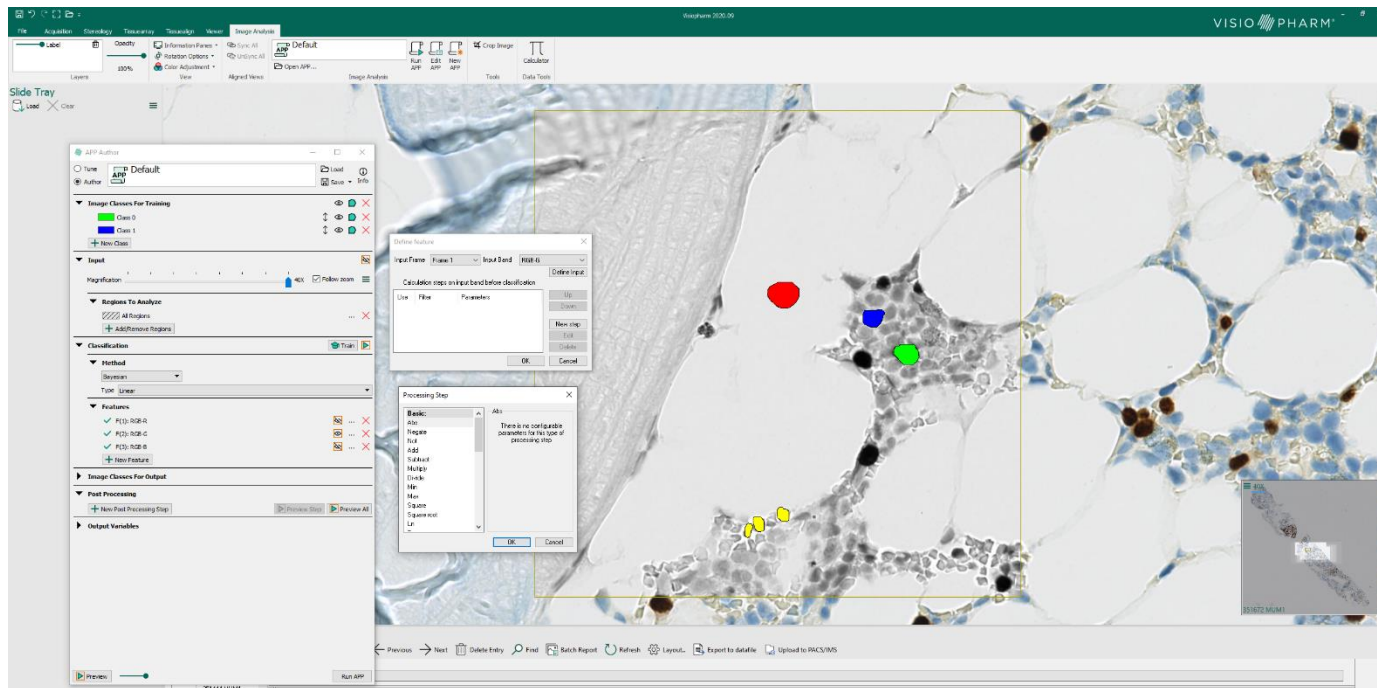
Ikke for dybt







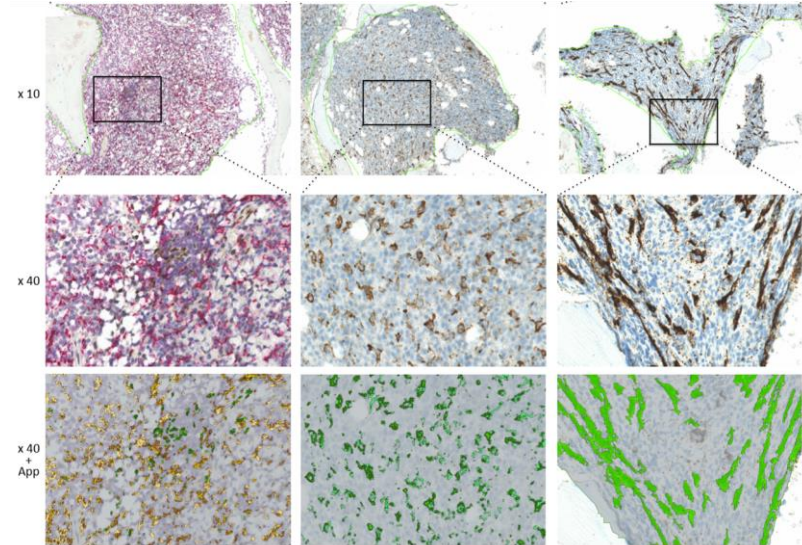
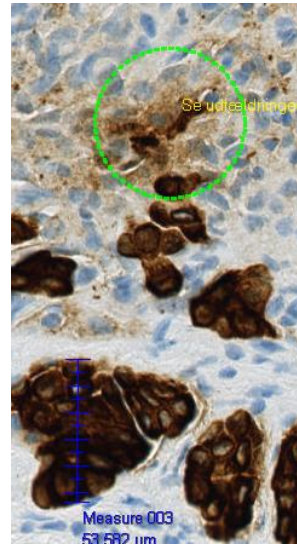
Træning af en billedanalyseprotokol (Machine learning)



Hvorfor er digital billedanalyse en del af fremtiden?

Hvorfor vil vi anvende digital patologi?

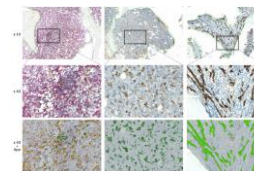
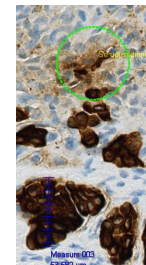
- Dokumentation
- Reproducerbarhed
- Objektivitet



Hvorfor vil vi anvende digital patologi?

- Dokumentation
- Reproducerbarhed
- Objektivitet

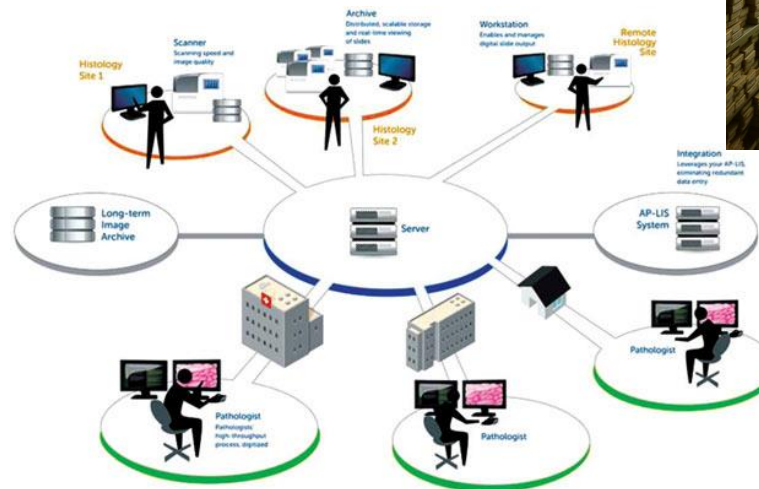
- Lad os udfordre det:
 - Data mængder
 - Hvad vil og skal vi gemme?
 - Men hvad hvis billedanalyse protokollen ændres?
 - Cloud-løsninger
 - Deep-learning – livslang læring
 - Hvad er det der er objektivt?
 - At bygge en algoritme



Hvorfor vil vi anvende digital patologi?

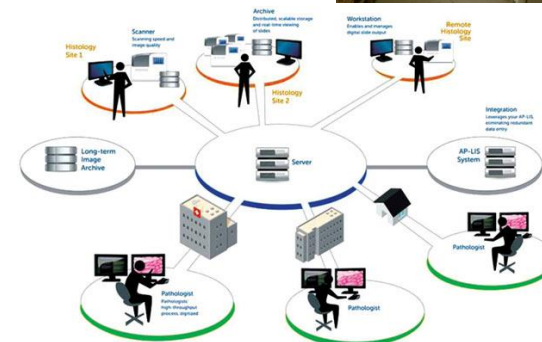
- Dokumentation
- Reproducerbarhed
- Objektivitet

- Multidisciplinære konferencer/arkivering
- Samarbejde nationalt og internationalt
 - Telepatologi
 - Undervisning



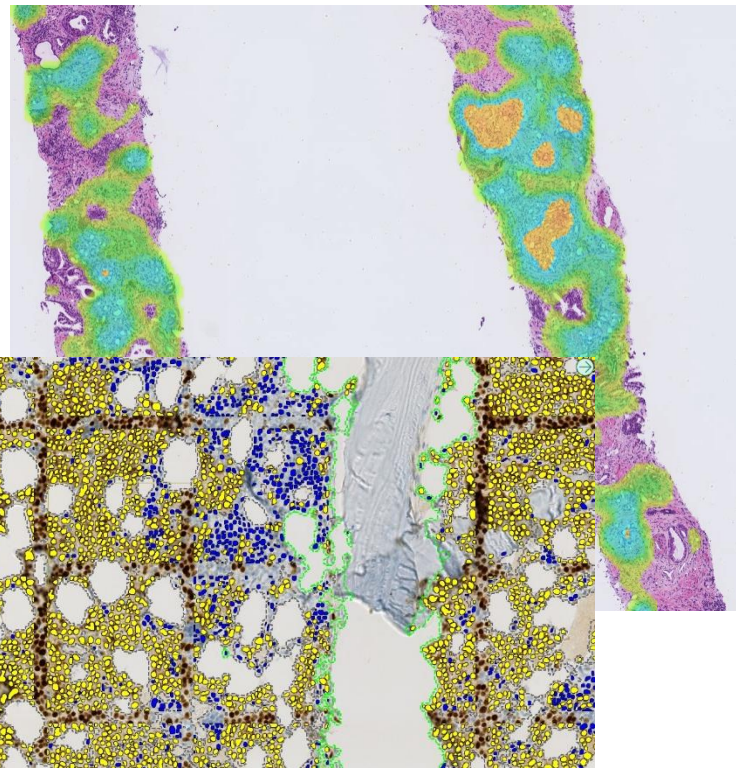
Hvorfor vil vi anvende digital patologi?

- Multidisciplinære konferencer/arkivering
- Samarbejde nationalt og internationalt
 - Telepatologi
 - Undervisning
- Lad os udfordre det:
 - Arkivplads
 - Vieweren
 - Forskellige skannere
 - Algoritmen



Hvorfor vil vi anvende digital patologi?

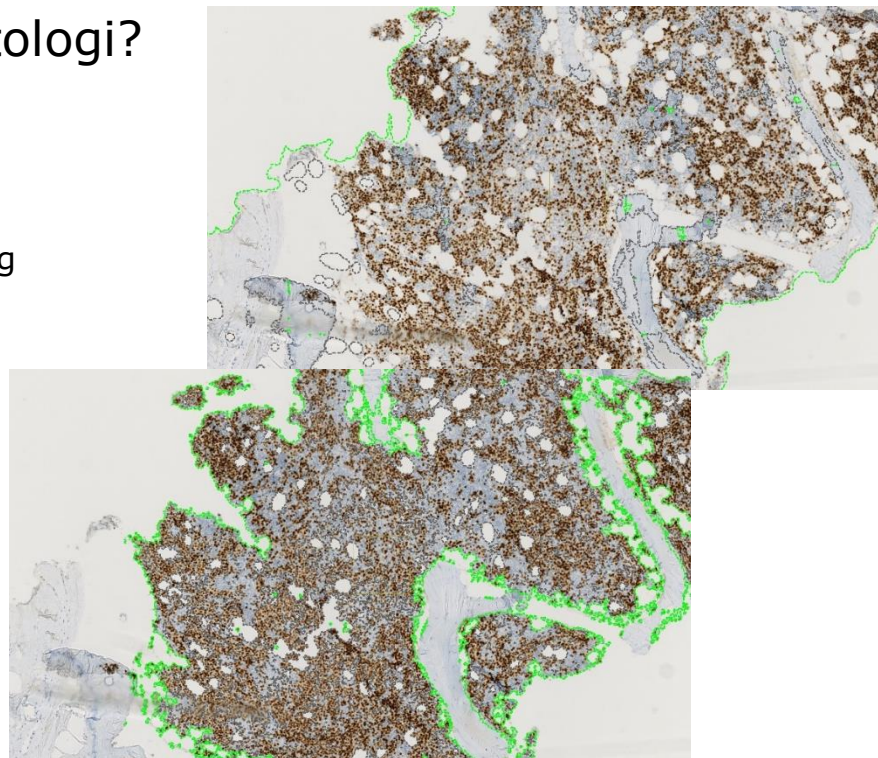
- Dokumentation
- Reproducerbarhed
- Objektivitet
- Multidisciplinære konferencer/arkivering
- Fordele arbejdsopgaver hensigtsmæssigt nationalt og internationalt
 - Telepatologi
 - Undervisning
- Opgaveglidning
- Tidsbesparende - triagering
- Kvalitetssikring
- Behandlingsbestemmende, prognostiske og diagnostiske analyser



Hvorfor vil vi anvende digital patologi?

- Opgaveglidning
- Tidsbesparende - triagering
- Kvalitetssikring
- Behandlingsbestemmende, prognostiske og diagnostiske analyser

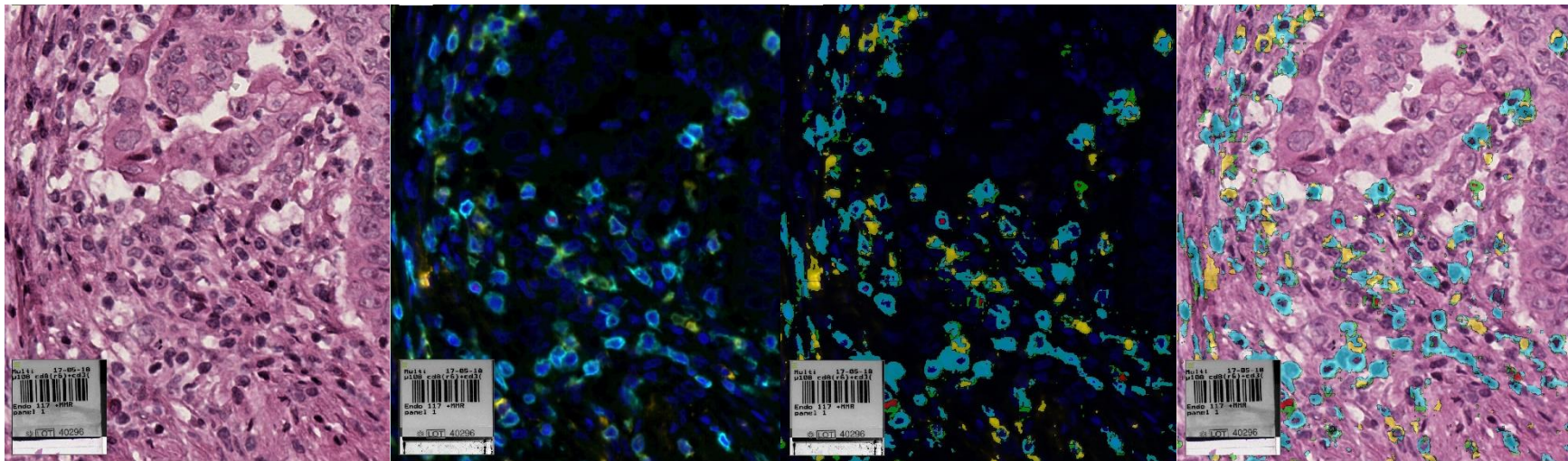
- Lad os udfordre det:
 - Region of Interest
 - Tidsbesparende?
 - Vi skal være kritiske – diagnostisk?
 - Hvordan passer det ind i flow i vores laboratorier



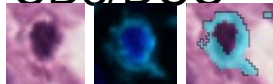
Hvorfor vil vi anvende digital patologi?

- Dokumentation
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- Behandlingsbestemmende, prognostiske og diagnostiske analyser

- Fluorescens og multiple kromogener
- Forskning



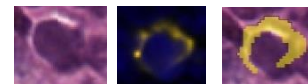
CD3/DCC



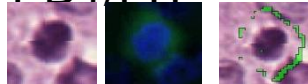
FOXP3/



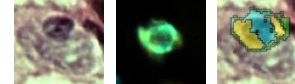
CD8/Rhodamin6



PD1/FIT



CD3/CD8/PD1



Hvorfor vil vi anvende digital patologi?

- Fluorescens og multiple kromogener
- Forskning

- Lad os udfordre det:
 - Skantider

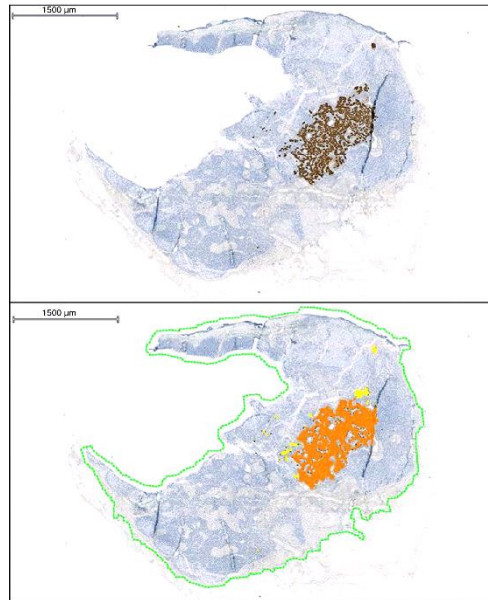
Et eksempel på digital billedanalyse

Application of automated image analysis reduces the workload of manual screening of sentinel lymph node biopsies in breast cancer

- Rigshospitalet
- Sygehus Sjælland
- Odense Universitetshospital
- Sentinel Lymph Node
- 135 pt – 900 glas
- 3 forskellige cytotokeratin immunhistokemiske farvninger
- Skannet centralt – 1 algoritme tilpasset de 3 immunhistokemiske farvninger

Henrik Holten-Rossing Maj-Lis Møller Talman Anne Marie Bak Jylling
Anne-Vibeke Lænkholm Martin Kristensson Ben Vainer

Application of automated image analysis reduces the workload of manual screening of sentinel lymph node biopsies in breast cancer



Skankvalitet blev undersøgt manuelt – ingen omtale af niveauet af behov for omskanning

Application of automated image analysis reduces the workload of manual screening of sentinel lymph node biopsies in breast cancer

Manual assessment	DIA		Total
	Negative	Positive	
Negative	524	237	761 (84.6%)
Positive	0	139	139 (15.4%)
Total	524 (58.2%)	376 (41.7%)	900
Percentage agreement			73.7%

Ingen falsk negative – sensitivitet på 100%

Reduktion i arbejdsmængde ca. 60%

Falsk positive

Ingen glas blev ekskluderet fra studiet pga. artefakter

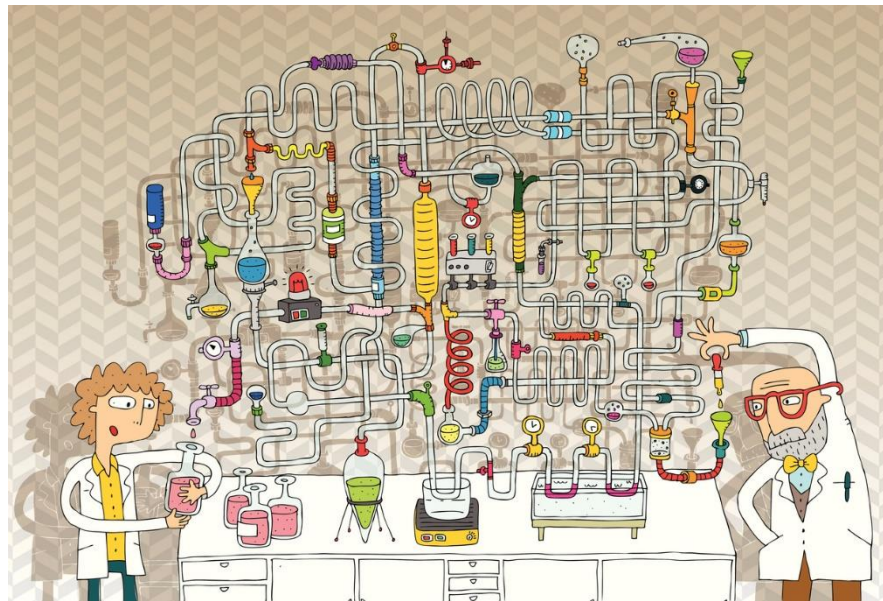
Application of automated image analysis reduces the workload of manual screening of sentinel lymph node biopsies in breast cancer

Time study, <i>n</i> = 12 (18 FFPE blocks)	Time/block
Total time spent (conventional microscopy):	76.0 min
Average time per block:	4.22 min
Average number of blocks per patient undergoing sentinel lymph node surgery	1.63
Average time spent on sentinel lymph node biopsy microscopy	6.88 min
Workload reduced to an average of:	2.88 min per patient

Rigshospitalet 2016:
580 pt med SN
Eksklusion af ca.
60% af
arbejdsbyrden
svarende til 39
timers arbejde.

Application of automated image analysis reduces the workload of manual screening of sentinel lymph node biopsies in breast cancer

Contaminating, CK-positive epithelial cells would result in a false-positive stain and, in a worst-case scenario, be misdiagnosed as positive for metastases. As such artefacts are unlikely to be excluded entirely, it is vital for the pathologist to assess the slides deemed to be positive by the digital algorithm, by using either a conventional microscope or the already scanned slides in a virtual or digital solution. Other artefacts, such as dirt, coverslip glue, hair, staining variation, and cross-reactions of the CK cocktails with endothelial cells or dendritic reticulum cells, also contributed to the large number of false-positive slides.



Tak og fortsat god lørdag!