2nd European Workshop on Tissue Imaging and Analysis
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Use of tissue micro array (TMA) in routine clinical analysis

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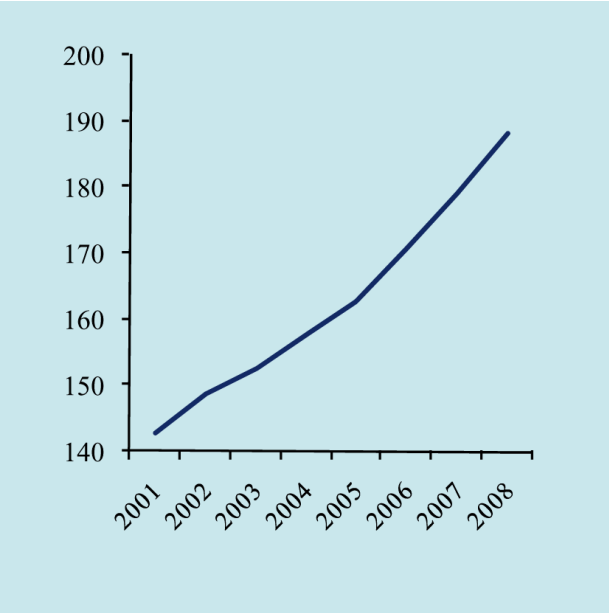
Cancer and cancer-related treatment

Figure. Number of persons, received a cancer or cancer related treatment, 2001 – 2008, 1.000



CHALLENGE:

- Financial crisis
- Increasing proportion of population will be in cancer treatment
- New medical treatments
- National integrated cancer pathways (waiting time and survival rates)
- Implementing molecular analysis of biomarkers

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Denmark

- Population 5.5 millions
- Jutland, Funen, Zealand
- Health service is financed by a national 8% tax
- 1/3 of the Danish population is living in the capital (Copenhagen) or in the suburbs of Copenhagen

Figure. Map of Denmark with the 6 national CancerBiobank key hospitals

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Danish CancerBiobank

- Danish CancerBiobank is funded by the government (www.danskcancerbiobank.dk)
- Danish CancerBiobank is archiving cancer tissue and blood samples from patients
- All patients are asked to enroll
- Based on unique national Danish, social security number

Figure. Map of region H

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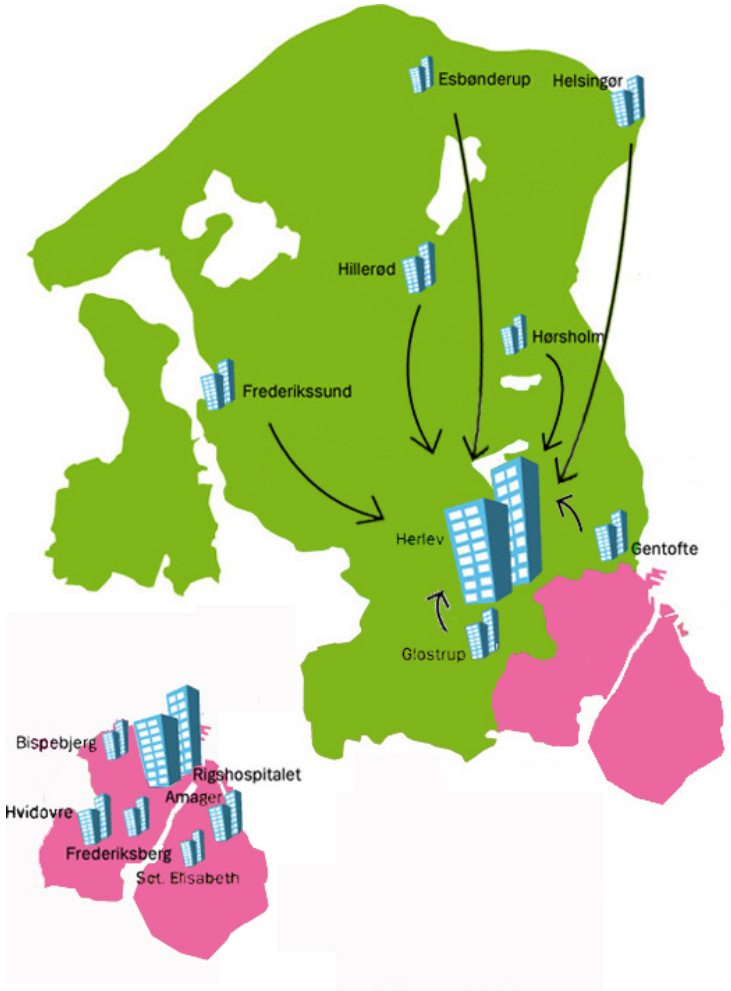
Central Danish CancerBiobank

- Hospitals get paid by the government per sample sent to the Danish CancerBiobank
- The Danish National Board of Health, is collecting journals of all persons in contact with the Danish health care system and all newly diagnosed cancer patients
- Herlev Hospital is home of the Danish CancerBiobank



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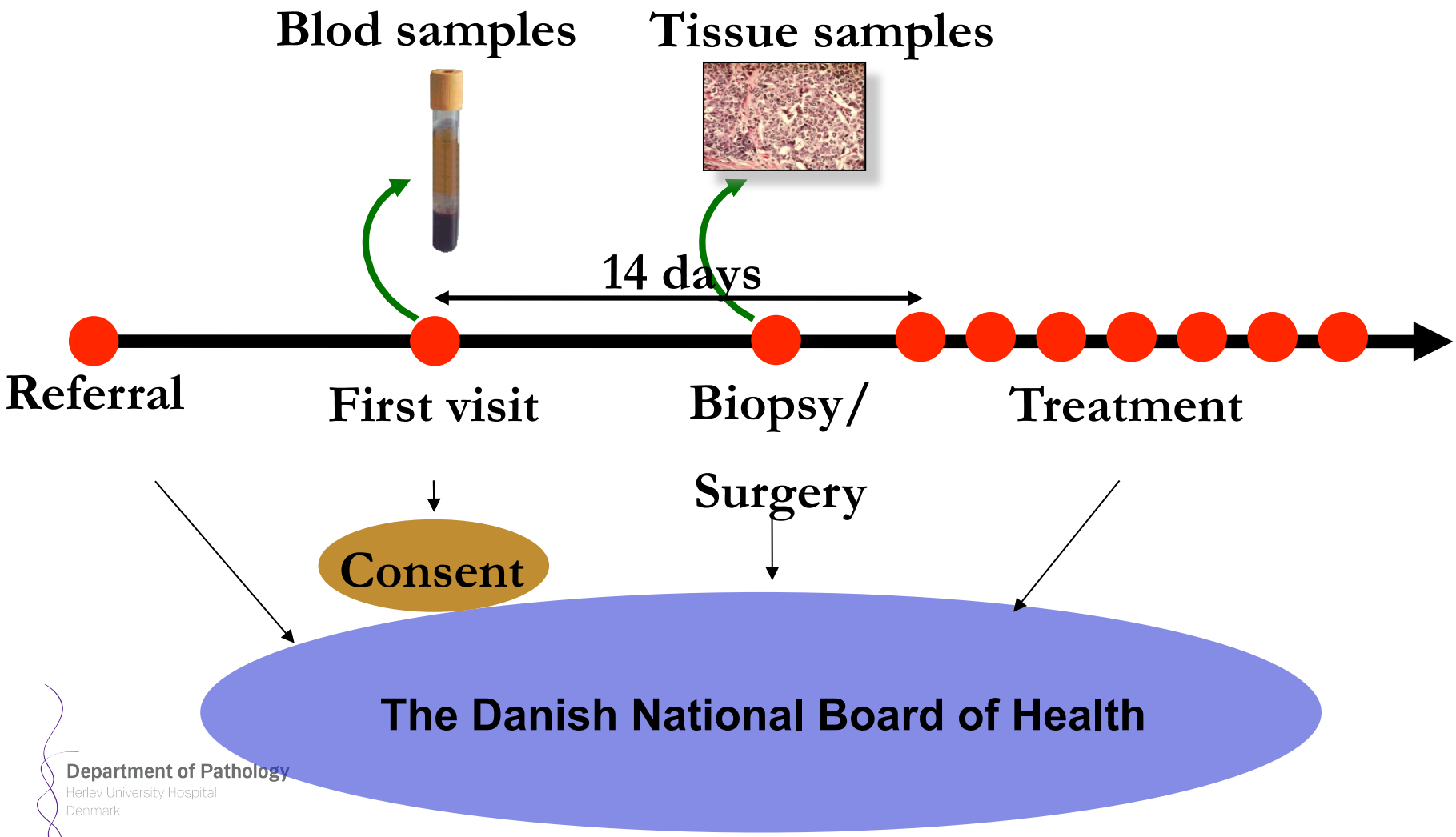
Central Danish CancerBiobank



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Collecting all cancers cases

BioBank center	preparations
Copenhagen	3.484
Herlev	3.433
Naestved	2.263
Odense	4.475
Aarhus	4.574
Aalborg	2.344
Total	21.573

Cancer	
Skin	1.250
Colon	4.000
Lung	4.000
Mama	4.500
Prosteta	3.500
Other	4.000
Total	21.500

Selection of cancer area

- Examine H&E staining
- Select the right tumor area for tissue micro array (TMA)
- Prepare TMA block(s) two times per week
- Today on slide - in future on digital image

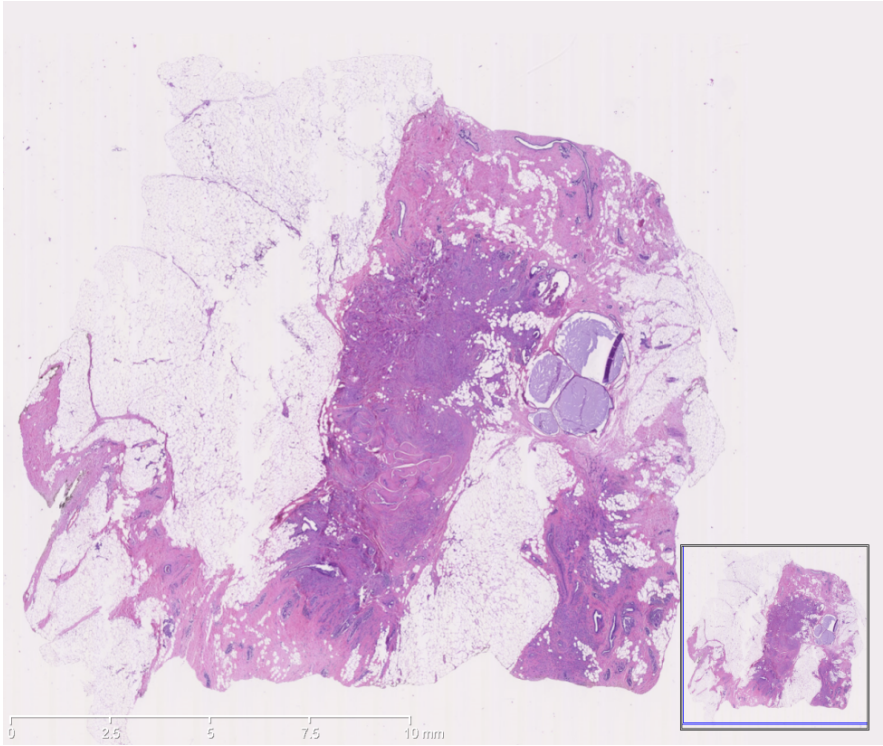

Figure. Digital image of H&E staining of a breast cancer section, captured on a NanoZoomer 2.0

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Present: Tissue micro array

- High throughput
- Formalin fixed paraffin embedded (FFPE) blocks
- Core punches diameter 2 mm
- Fast
- Manuel paper work

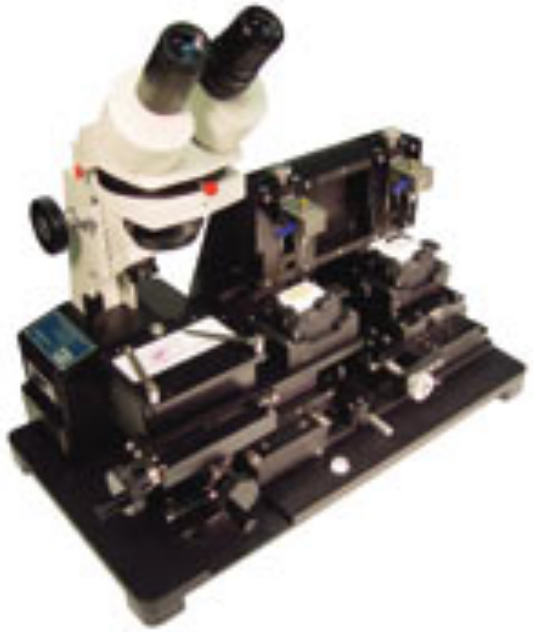

Fig. ATA-100 TMA, reliable old fashion

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Coming: Tissue micro array

- Electronic documentation
- Walk away
- 26 cores per TMA
- QC

Fig. ATA-27 TMA, from Beecher with a transfer capacity of 26 cores from different donor blocks to each recipient block.

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Use of Tissue micro array

- Whole slide: typically one (1) patient sample per slide
- TMA: Current method 25 patient samples per slide
- This will lower the price per test ~20x

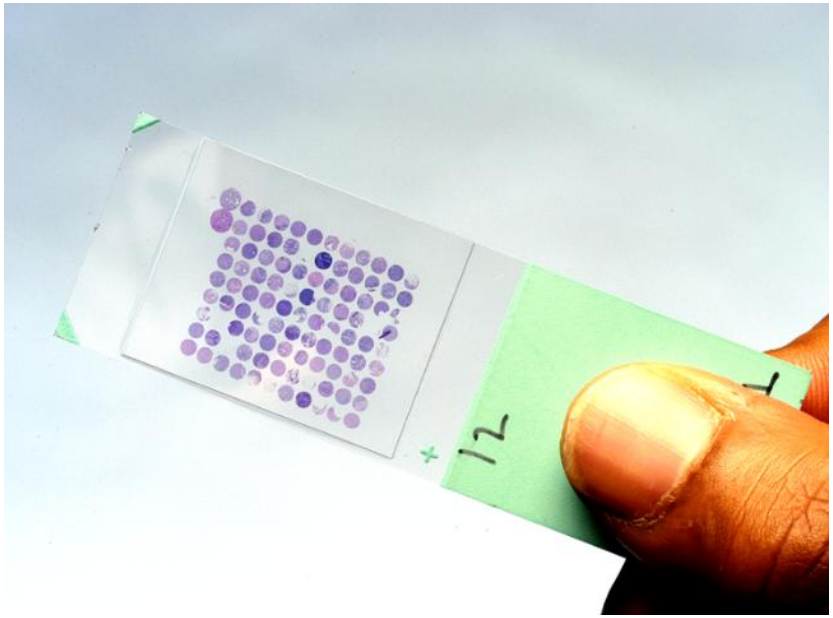

Figure. Slide with 99 different cancer tissue

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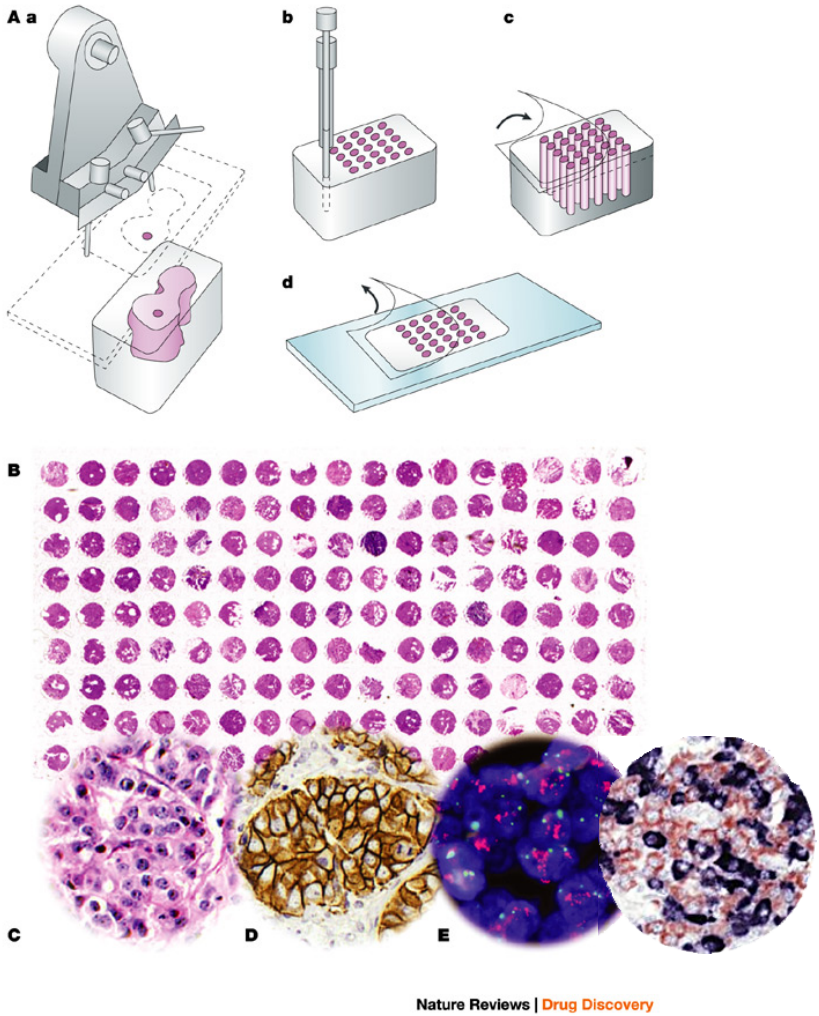
Multiple use of TMA slides

- TMA can be used for a range of molecular analyses:

- H&E
- IHC
- FISH
- ISH

- Typically used for analysis of biomarkers



Nature Reviews | Drug Discovery

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Mamma panel

- HER2 IHC (Herceptin)
- ER IHC (Hormonal therapy*)
- PGR IHC (Hormonal therapy*)
- KI-67 IHC (Prognostic)
- TOP2A FISH (Anthracyclin)
- ERRB2 FISH (Herceptin)

*Tamoxifen or aromatase inhibitors

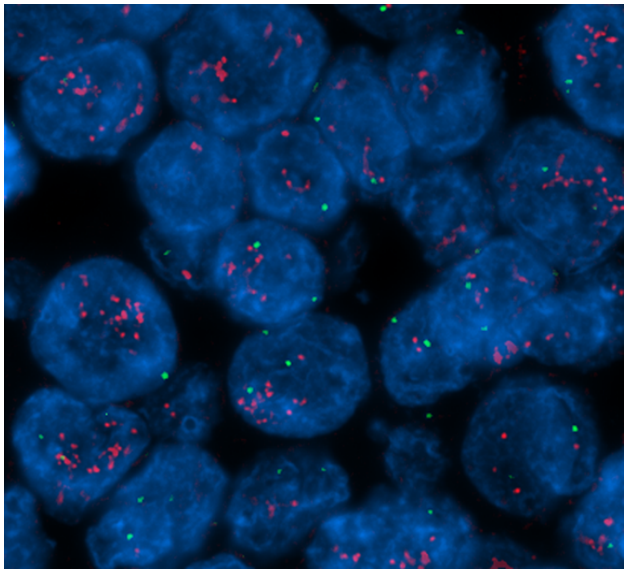

Figure. Breast canncer tissue with biomarker HER2 gene copy number change. Treatment with herceptin is only effective in amplified cases. Only 20% of all breast cancers are HER2 amplified.

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Image capturing

- Fluorescence image capturing (Mirax Scan)
- Brightfield image capturing (Nanozoomer)

Mirax scan 150 / Panoramic

NanoZoomer 2.0

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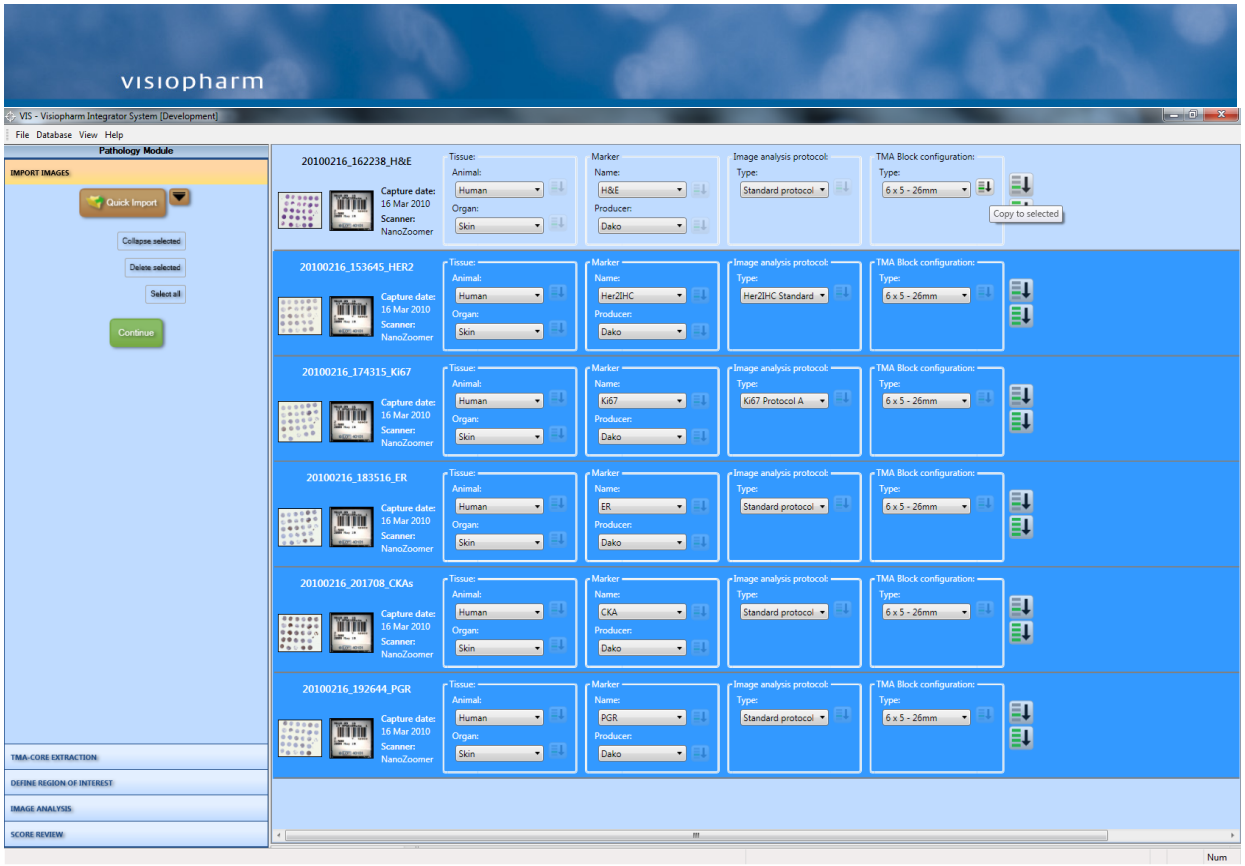
Analysis of the digital images

- Process digital files
- Select analysis protocol
- Define TMA configuration
- Define tissue type

or

- Include all information in TMA file and bar code.



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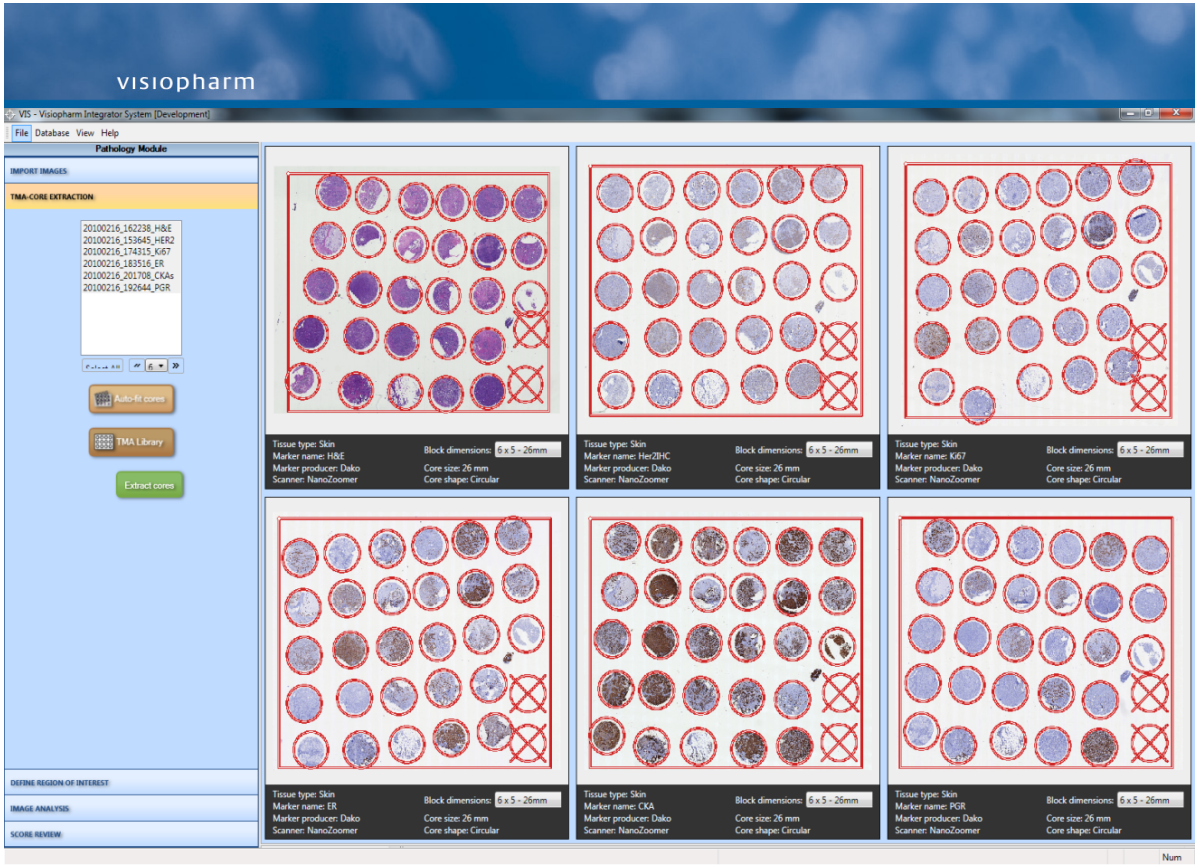
Analysis of the digital images

- Process digital files
- Extract each core
- Run the different image analysis protocols



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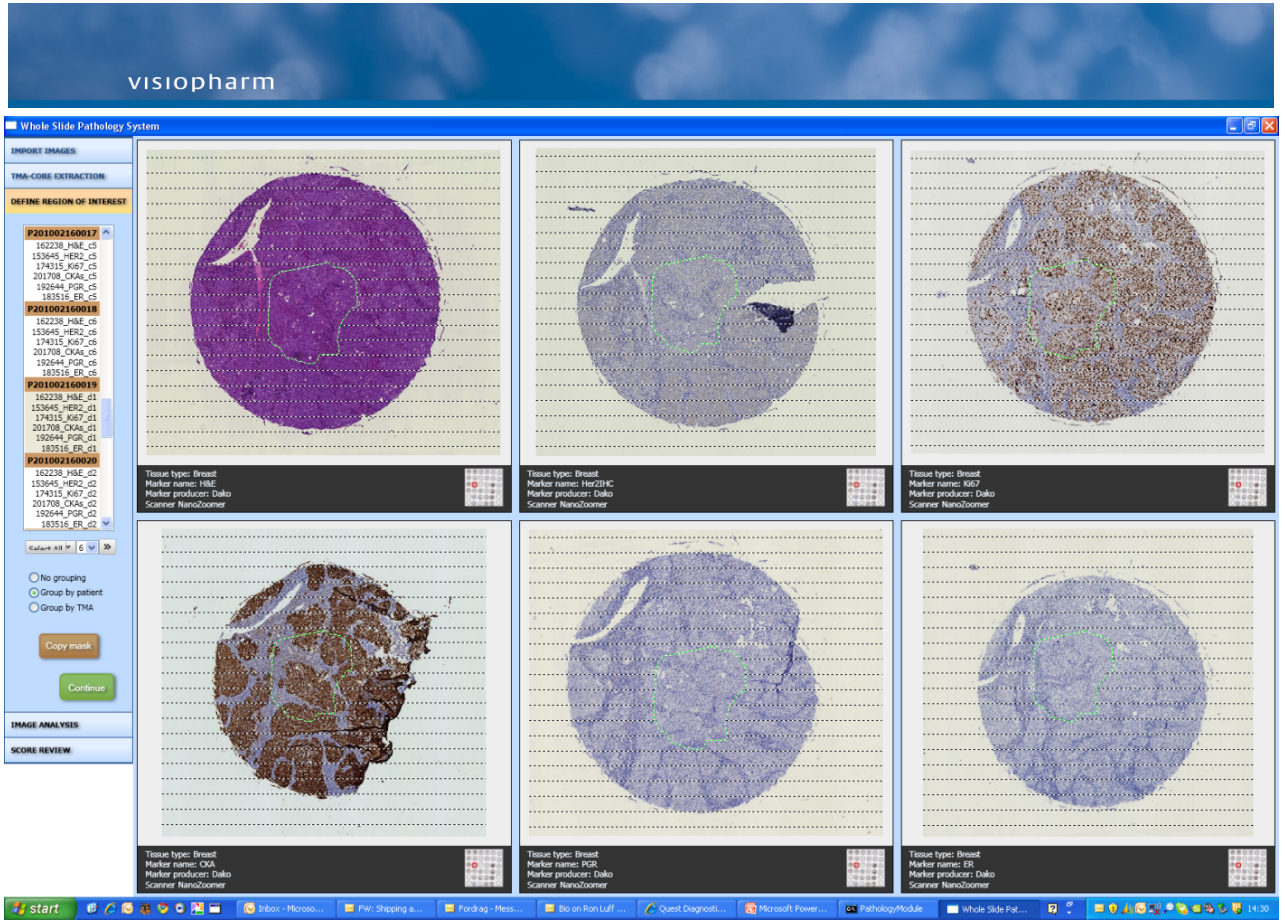
Analysis of the digital images

- Select patient
- Automatically retrieve all cores from this patient
- Mask region of interest in one core (e.g., H&E or CKA)
- Automatically align ROI in other cores



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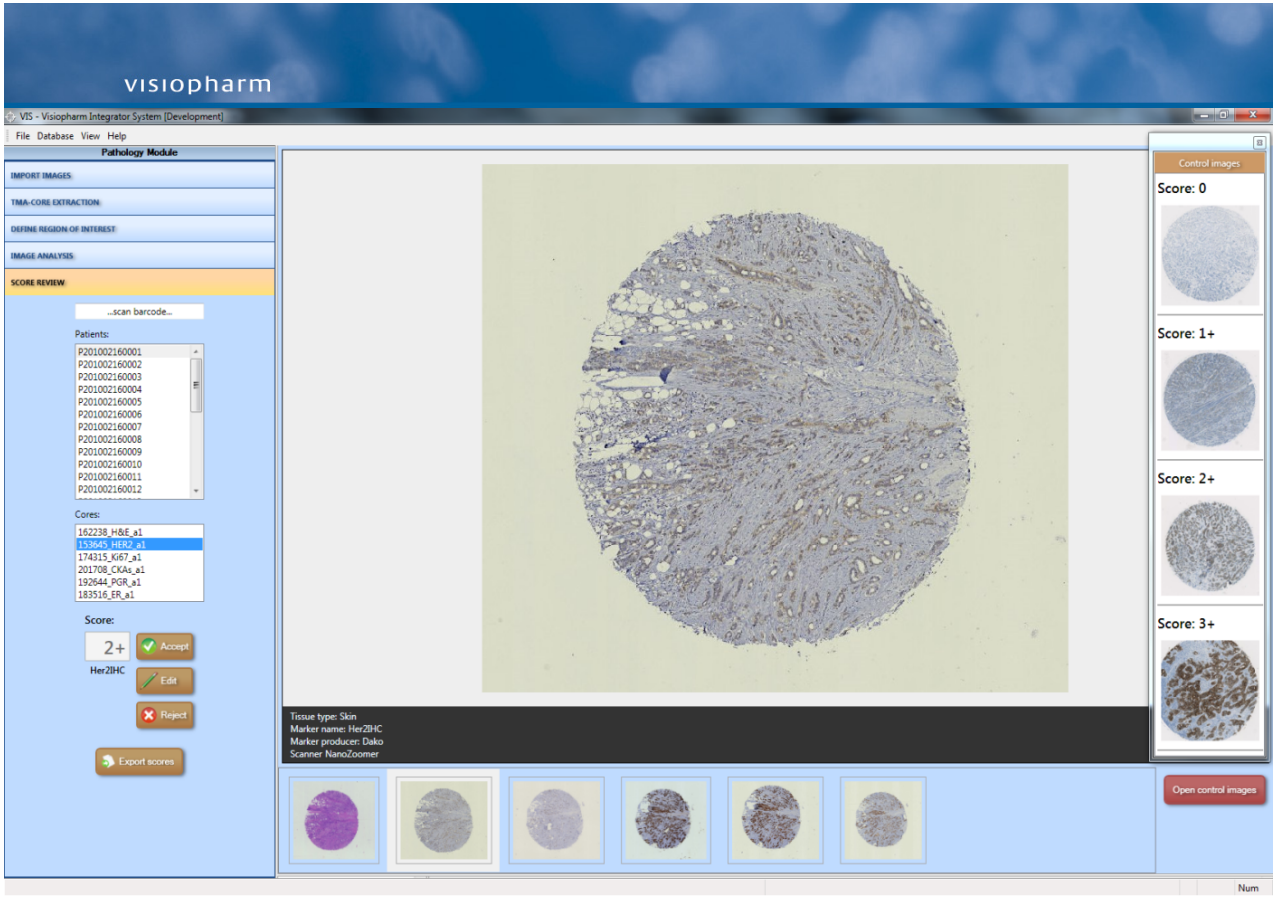
Analysis of the digital images

- Evaluate the results from the selected protocols
- IHC
- FISH
- ISH

Link results to the patient record and consult the oncologist



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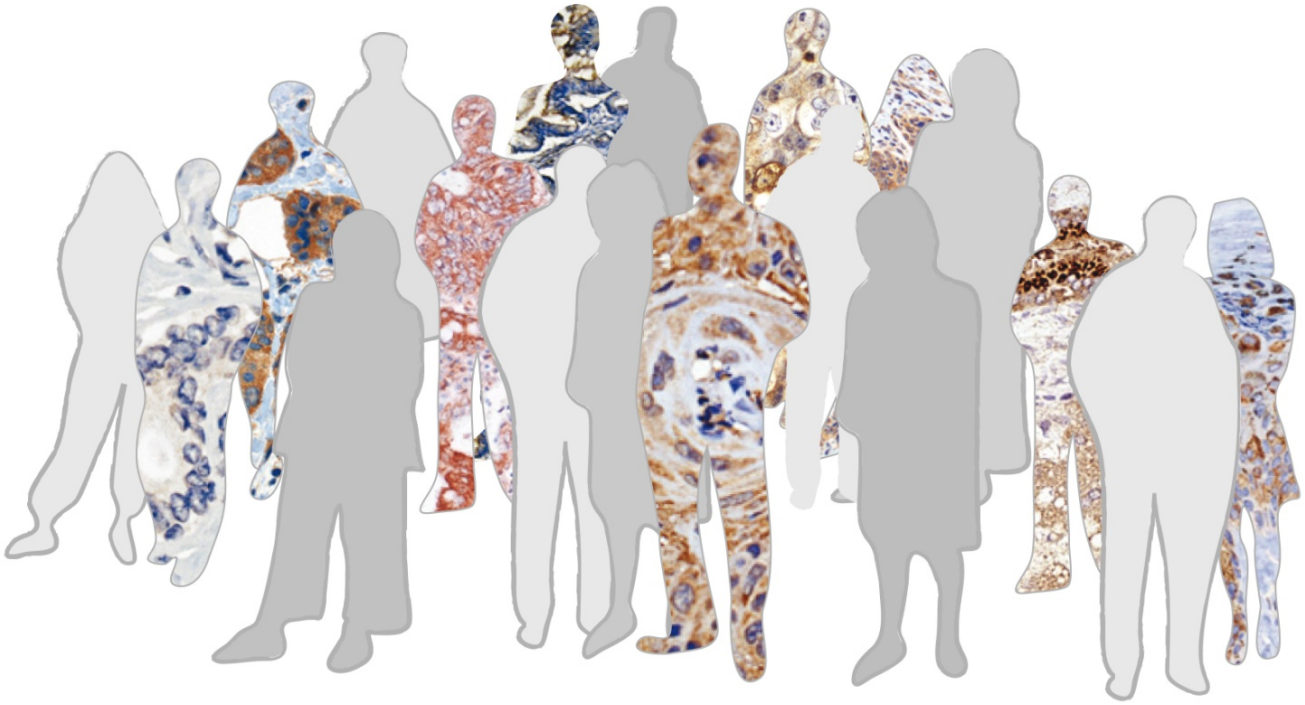
Personalized Medicine

Select the right patients for the right treatment



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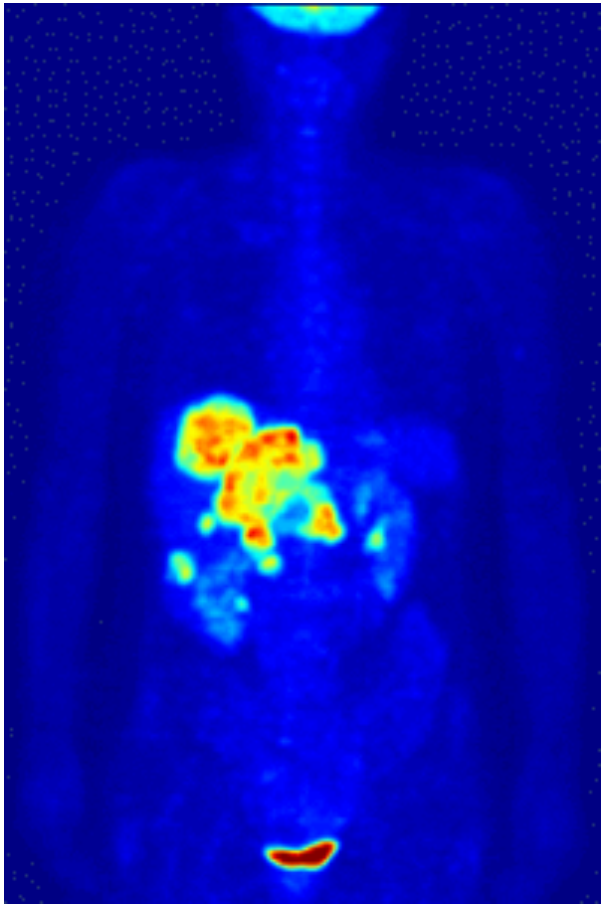
Future non invasive follow up

- PET/CT with FDG for follow up on treatment
- Fine needle biopsy for diagnose



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Speciel thanks!

- Public Welfare Technology (ABT-fonden) (ATA-27)
- Herlev Hospital (Mirax Scan)
- Hamamatsu/DE (NanoZoomer Scan)
- Nordic BioSite (FISH assay)
- Visiopharm (Image analyse software)

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