

The role of pathologists in clinical research

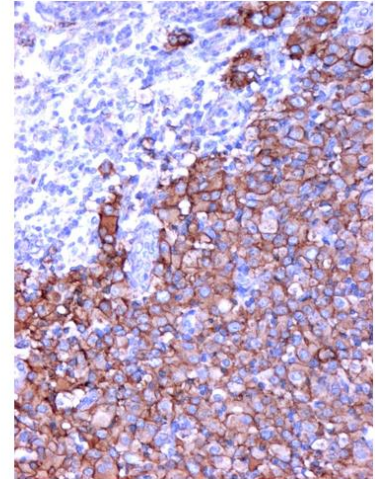
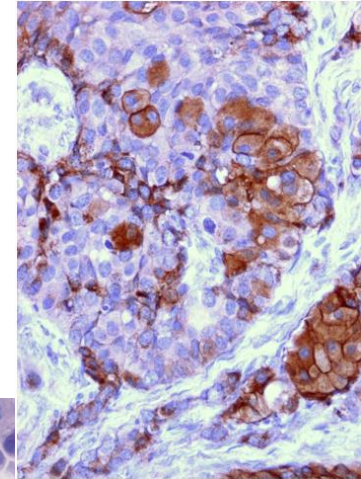
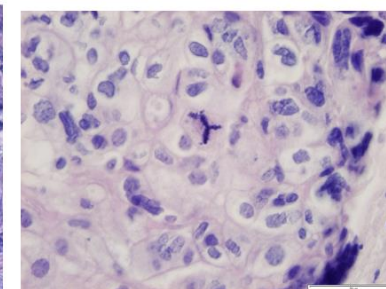
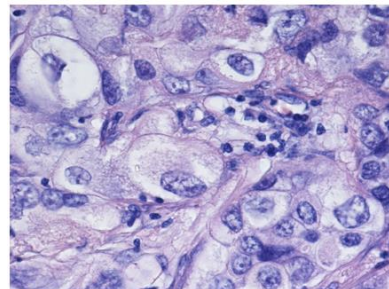
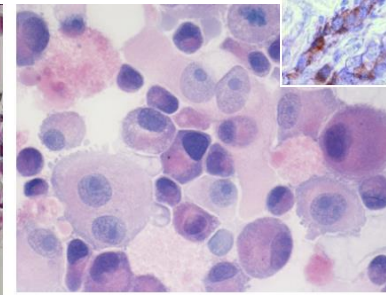
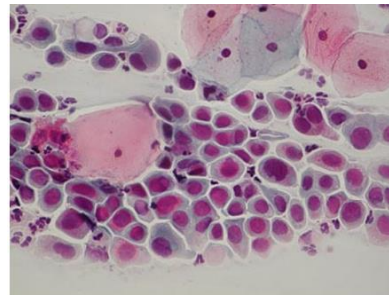
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Content:

- Legal aspects of pathology (briefly 😊)
- Pathology in practice – methods step by step
 - Analytics
 - Diagnostic pathology
 - Molecular pathology (in brief)
 - Praeanalytics
 - Postanalytics
- Special issues concerning clinical trials



Legal aspects of pathology

- EN ISO 15189 Medical laboratories — Requirements for quality and competence
 - The same in all EU countries
- Request form
- Final report
- Personal responsibility
- EQA program
- Internal quality control system

- Regular audits (once per two years) by independent authority

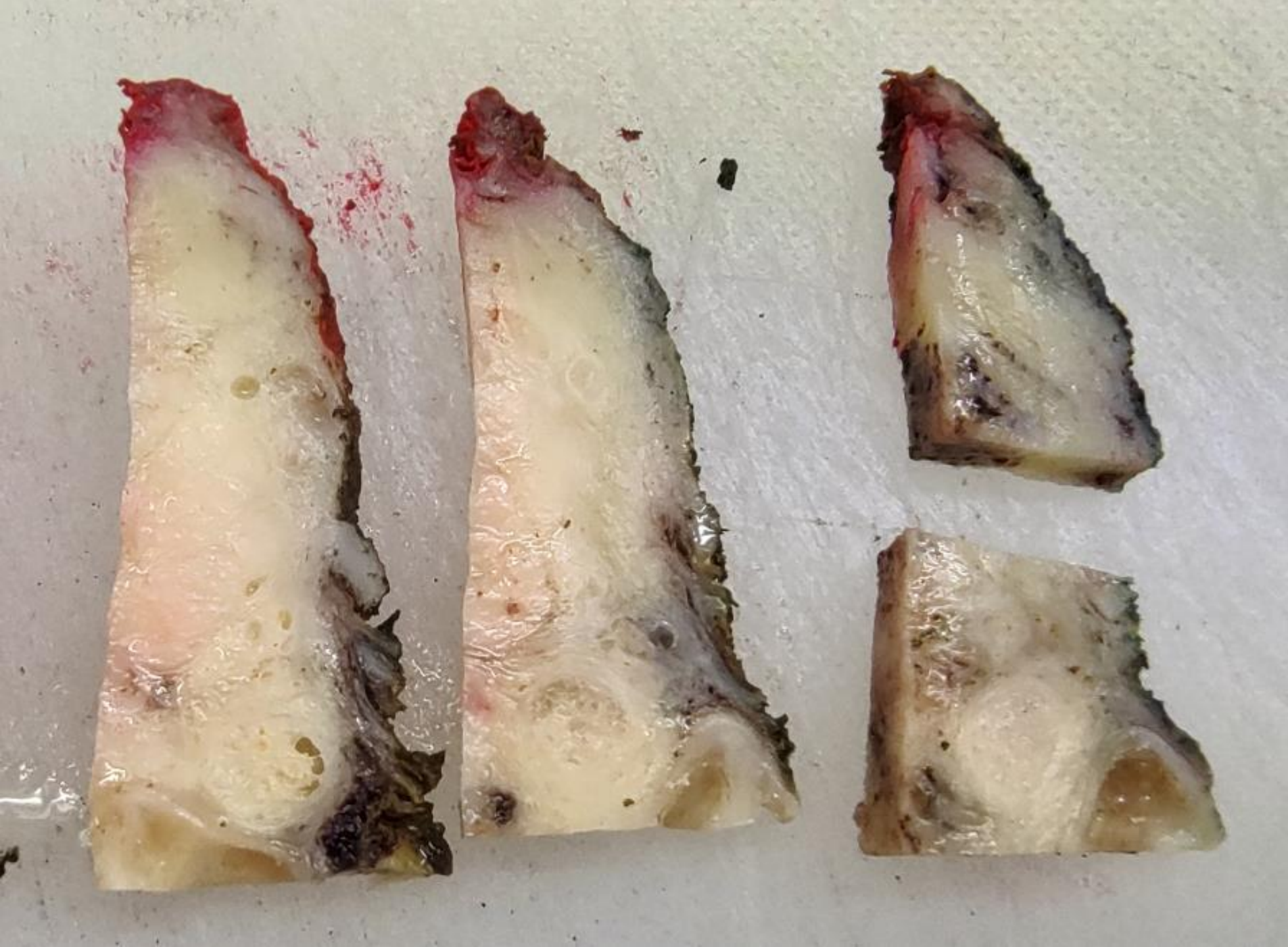


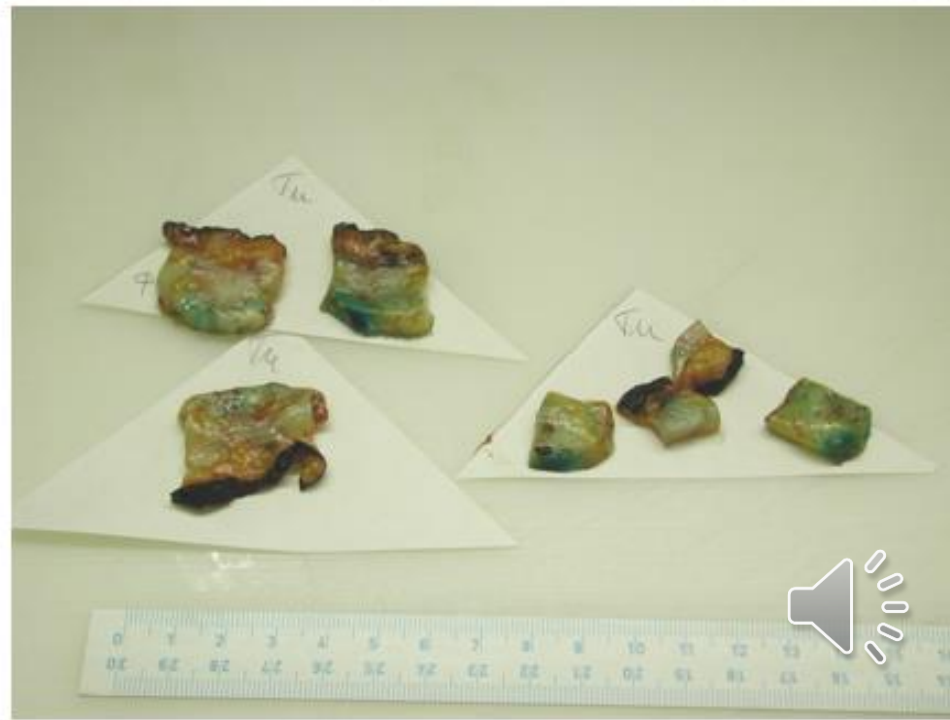
„Analytical phase“ in the pathology lab

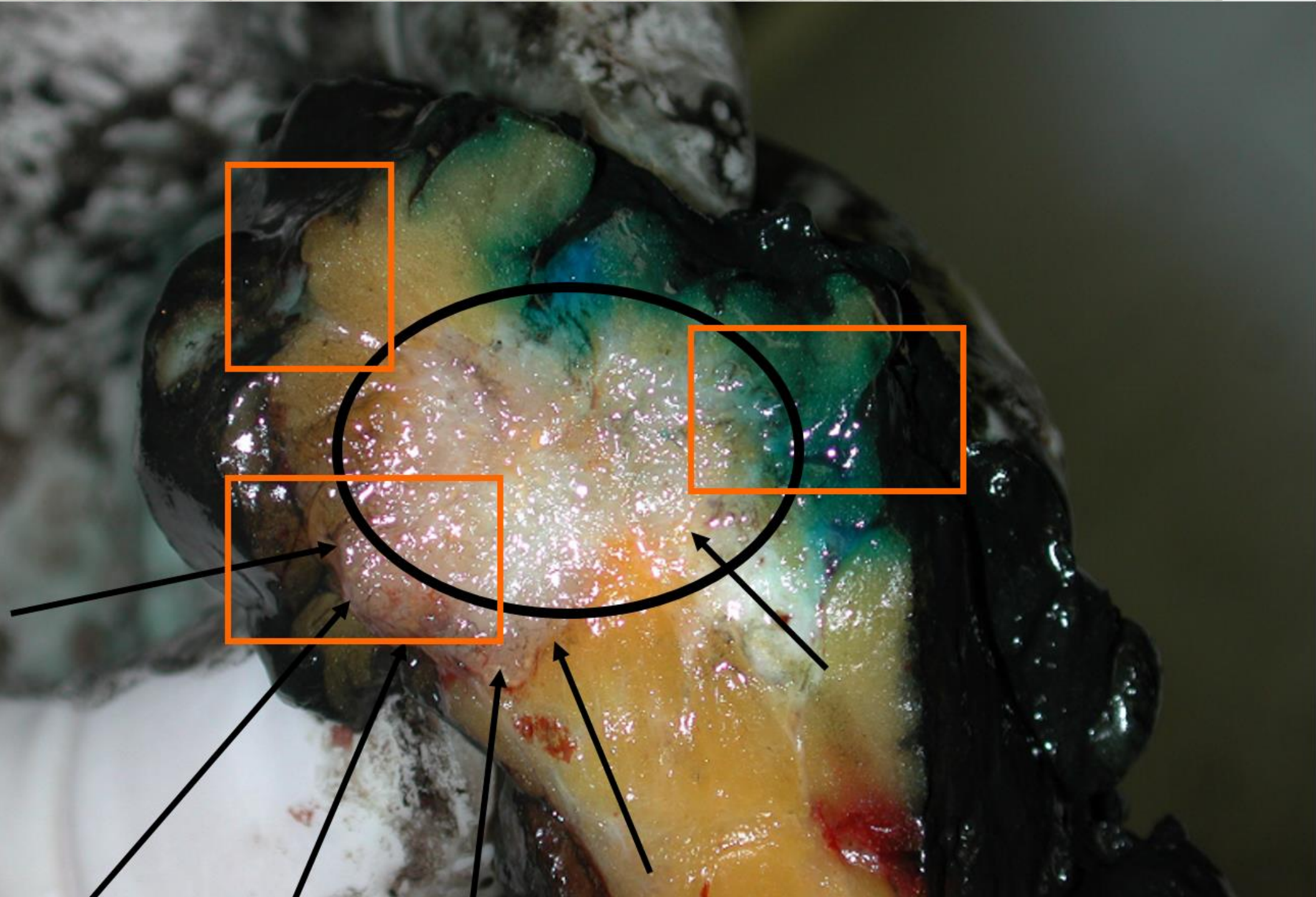
- Images of raw tissue, sampling blocks of blocks with tissue, numbered...

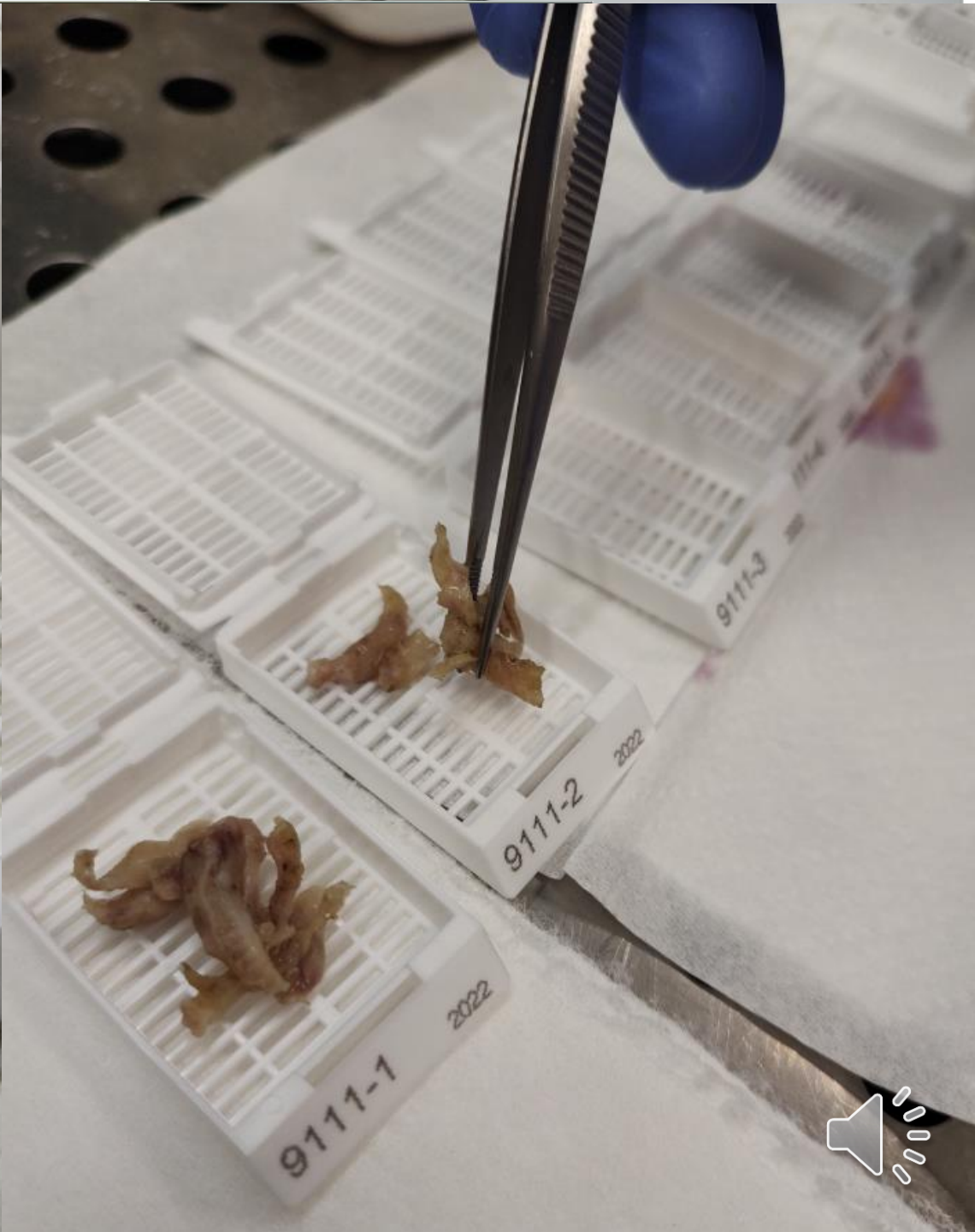
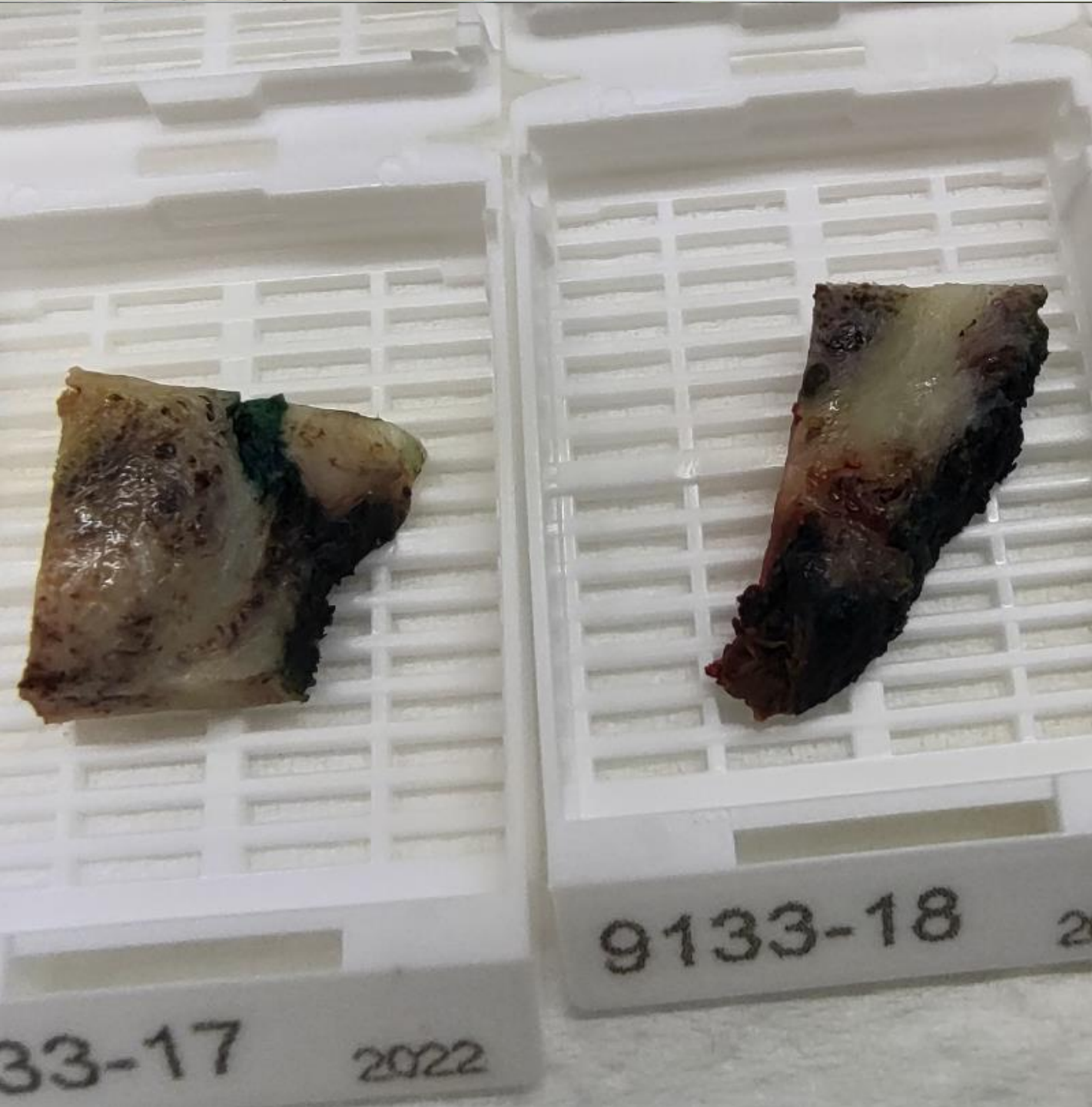


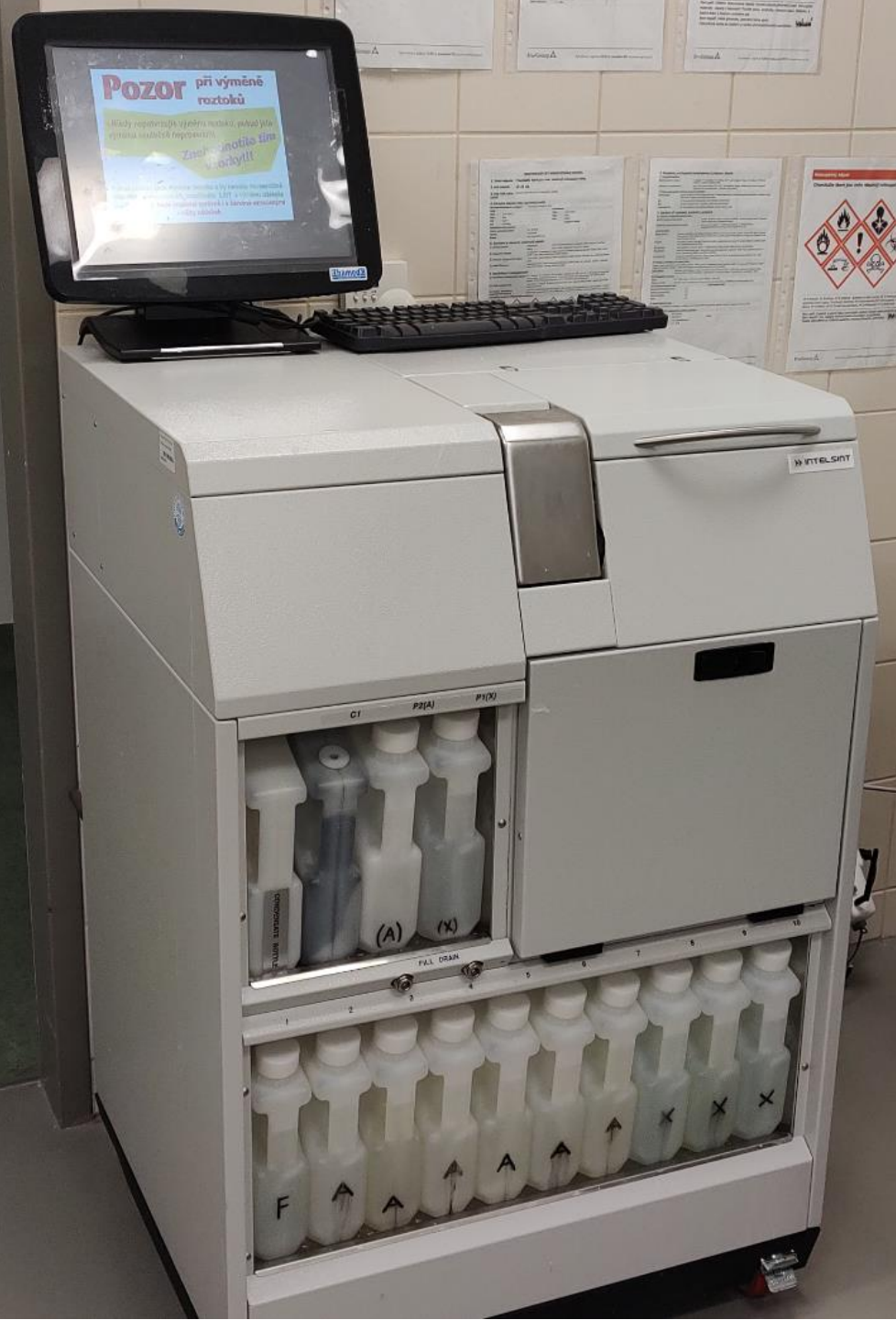


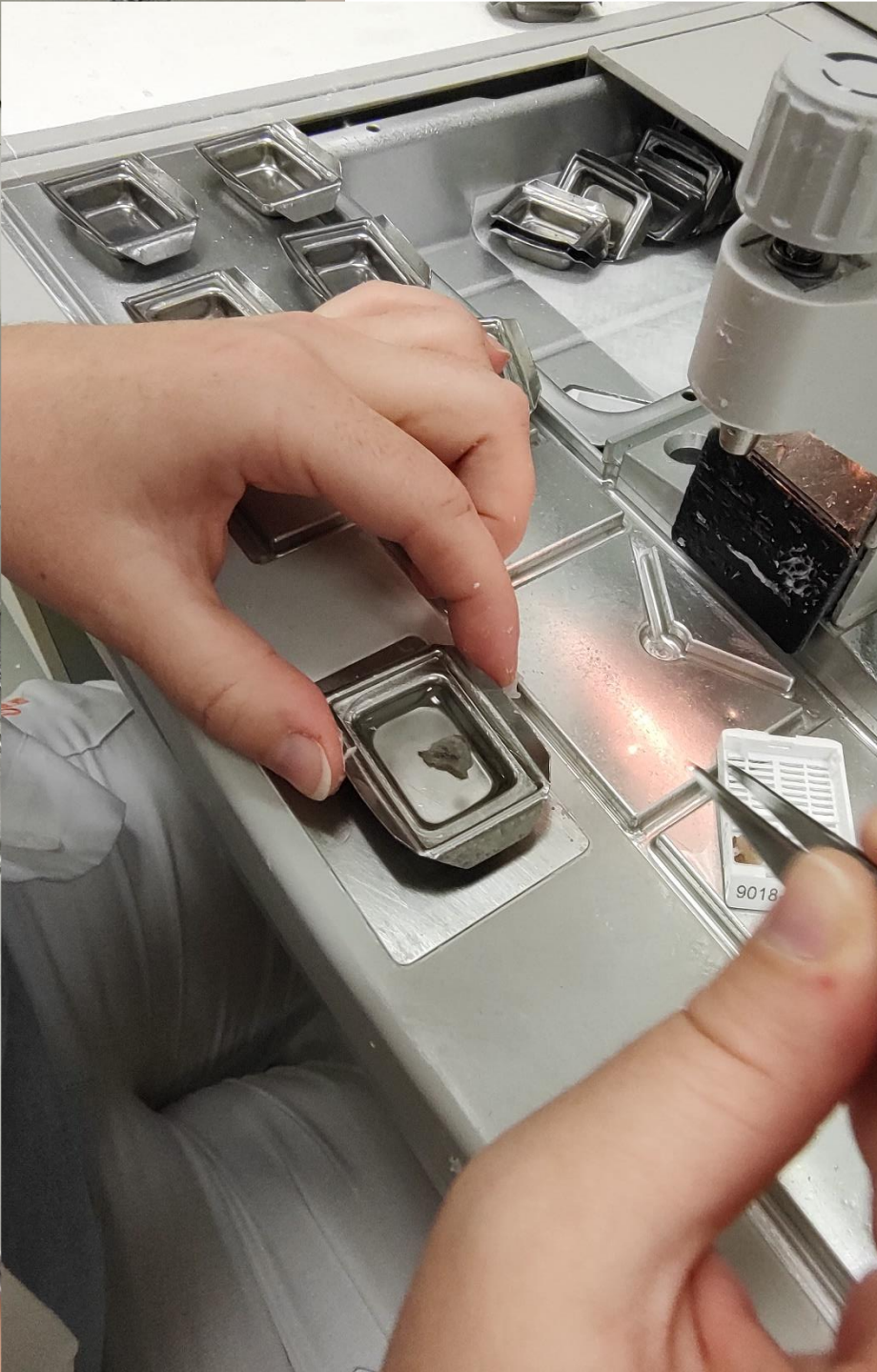


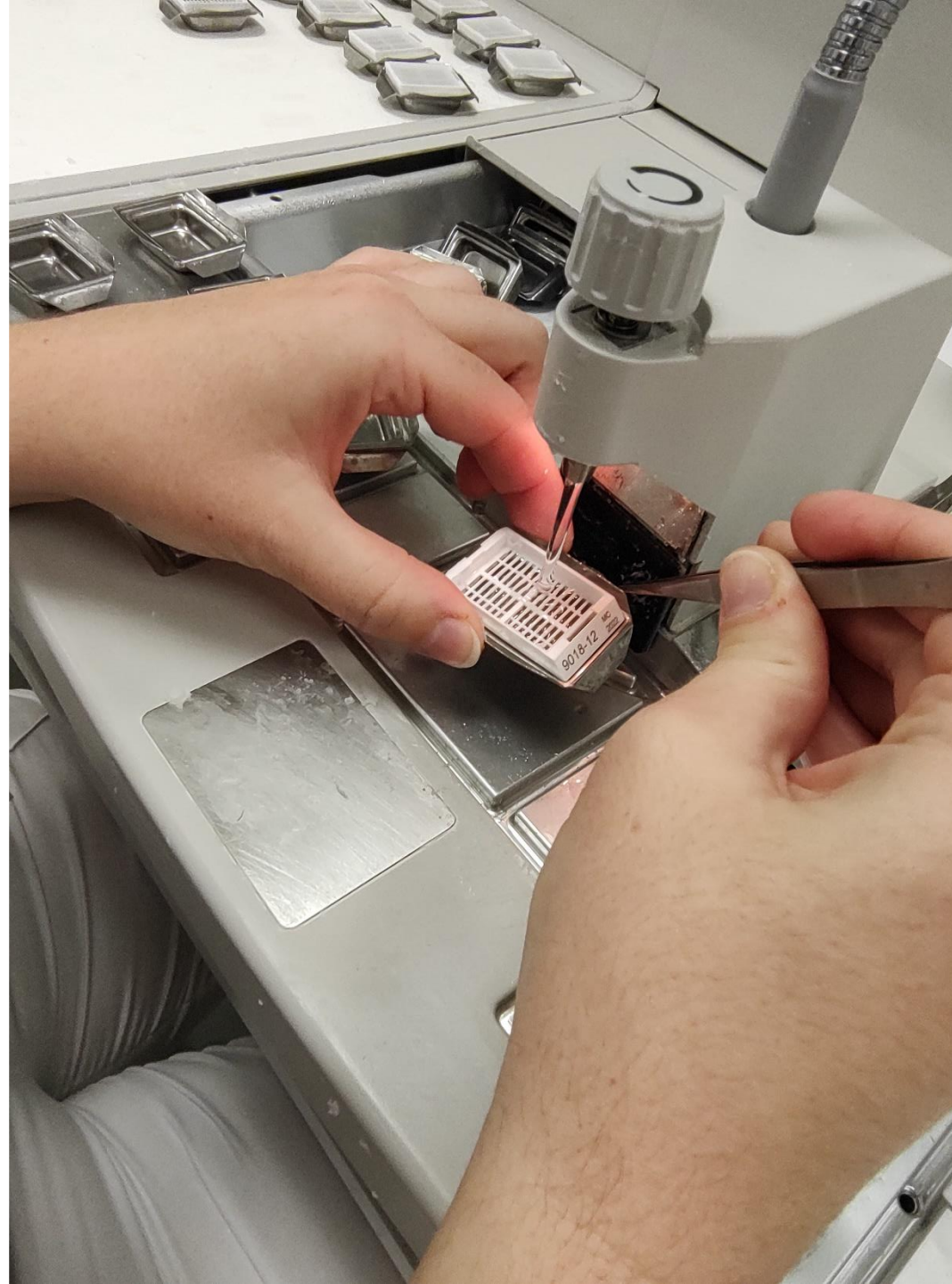












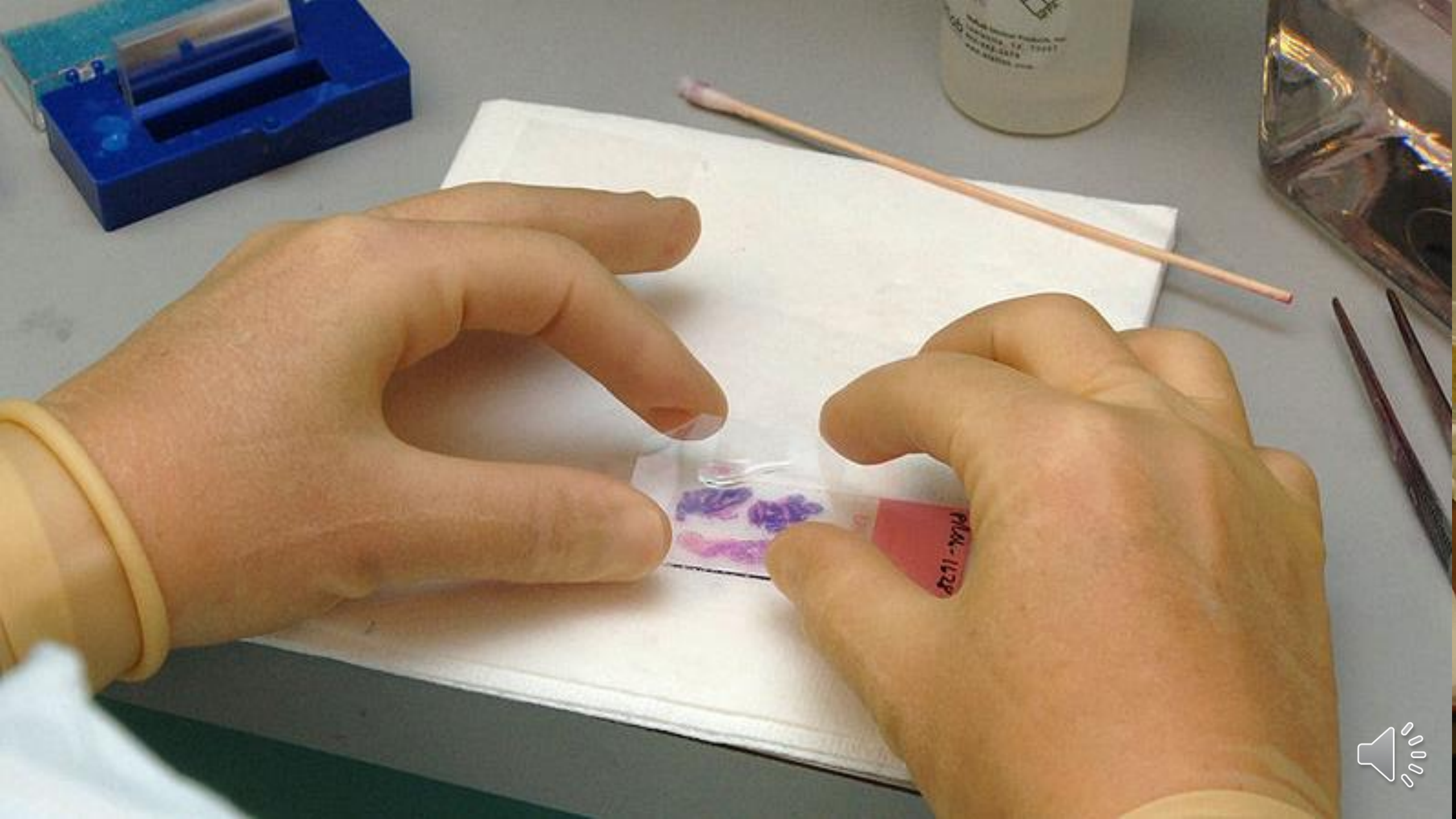




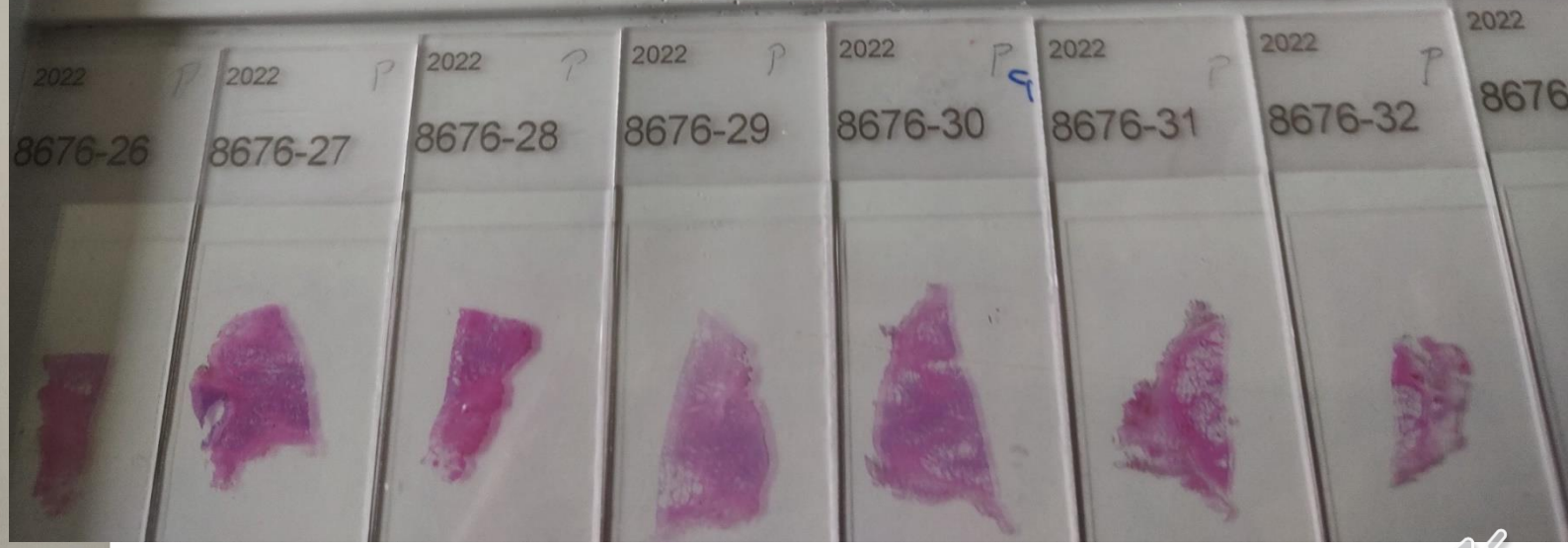










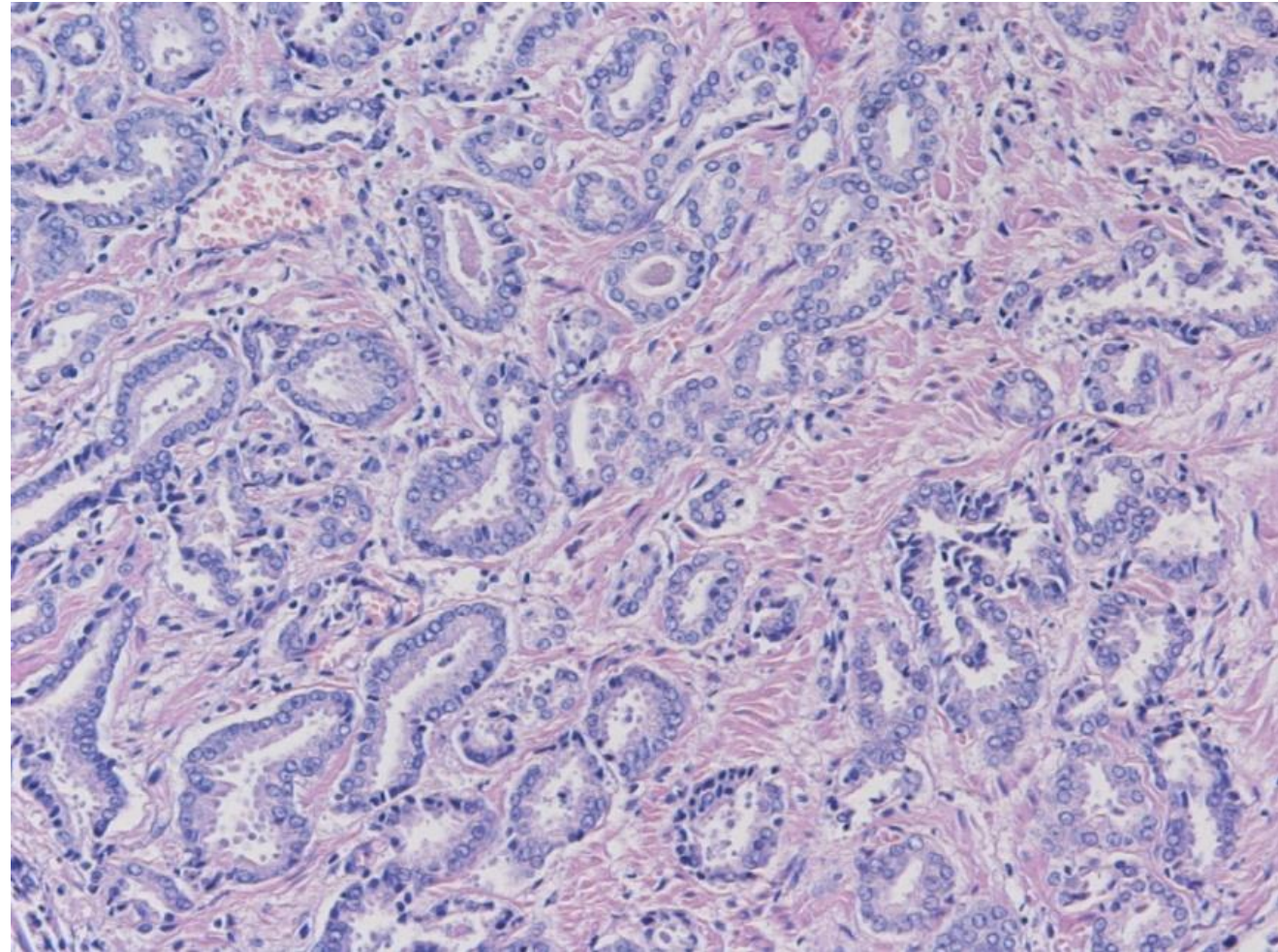


Finonit: 27.10.2022
8676
F/S

Číslo na: 27.10.2022, hospitalizace v době vzniku šlávniny; OUIRO [27.10.22 10.21]
Předmět vyšetření a lokalizace: 1) Prostata s vstřik
2) Hrdlo měchýře - sterální odtok
Klinická diagnóza (popř. stručný klinický průběh): Ačinnými adenokarcinomem prostaty, v obou lžících. Gleasonův skóre 7(3+4) WHO grade group 2, 4+7(4), 2+7 (4). cT2aN0M0, PSA 6.52
MORCC LN# 6%
IEF# 4 23, EPIC 4-0-0-0-0
dky



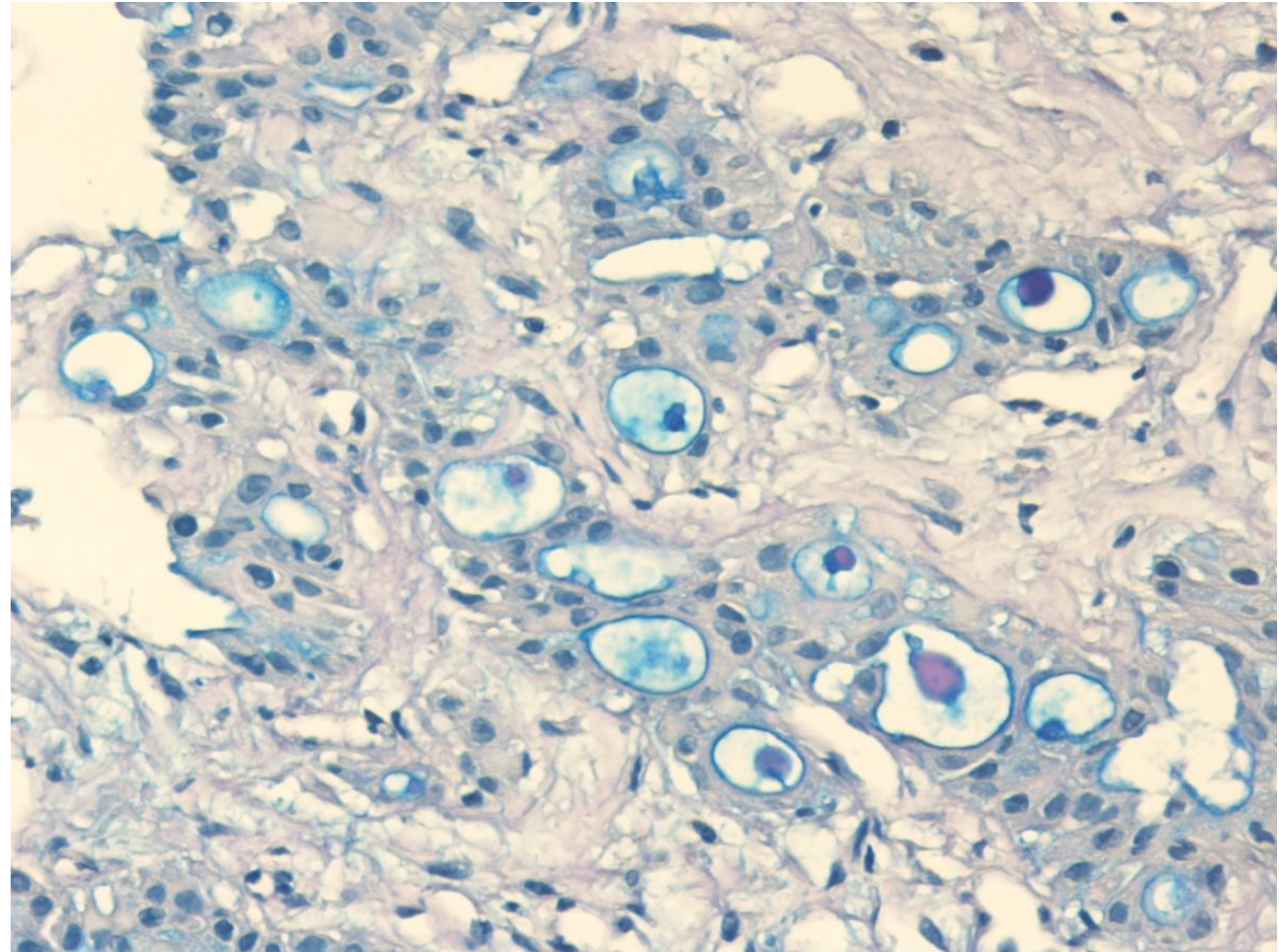
- HE slide
 - Final diagnosis
 - OR:
 - Further work required
 - Special staining methods
 - Immunohistochemistry (IHC)
 - FISH
 - Other (generally: DNA analysis)



- HE slide
 - Final diagnosis

 - OR:

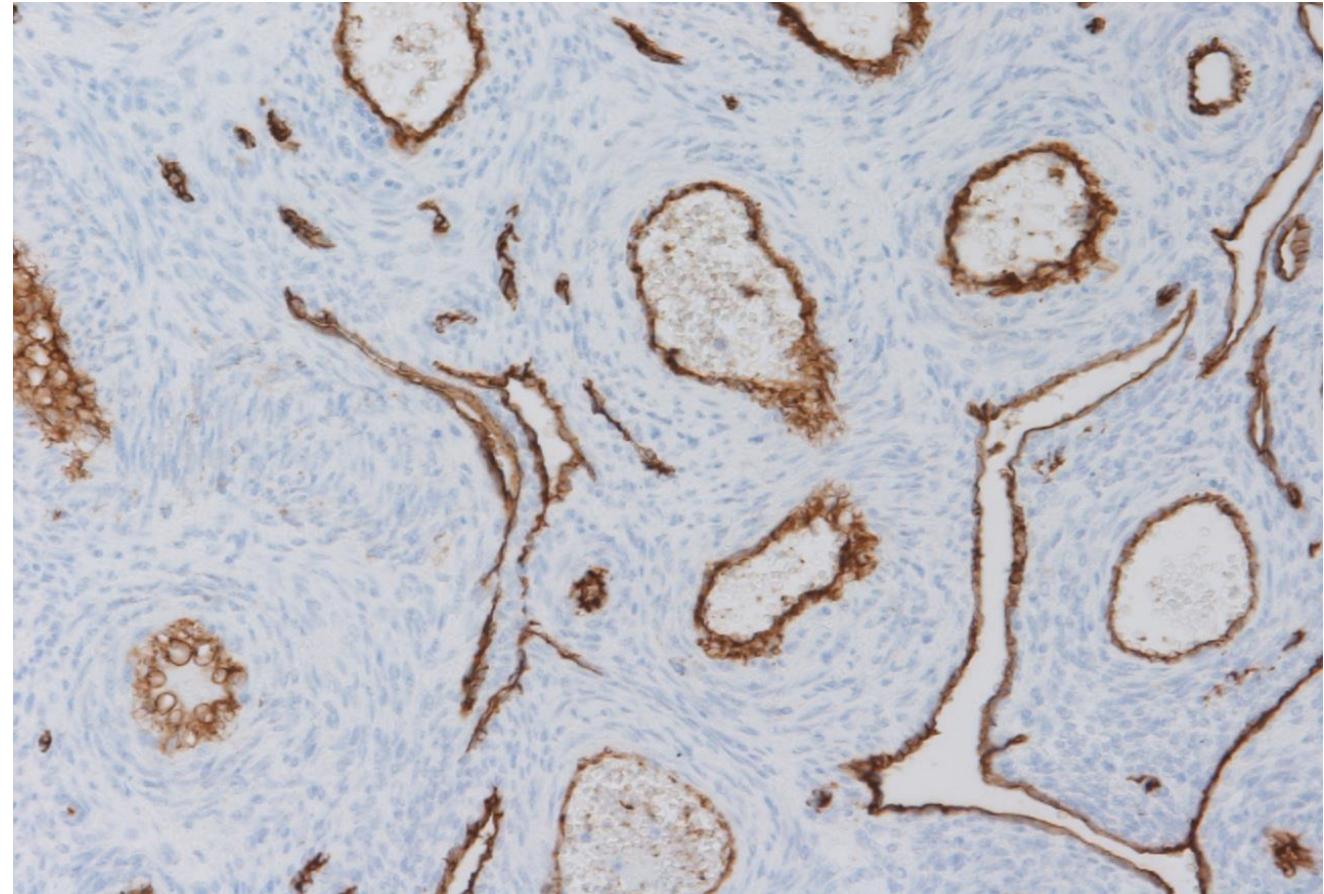
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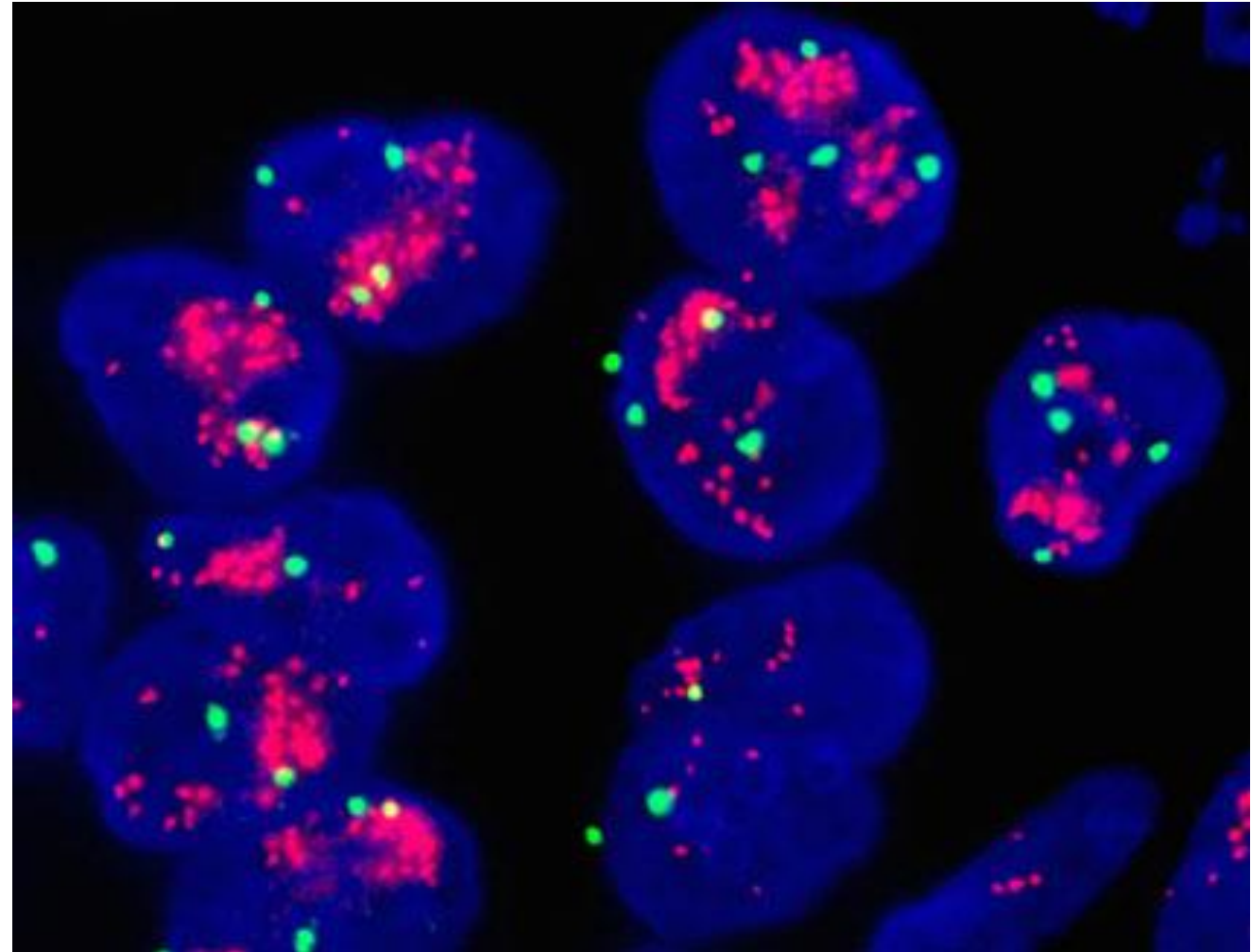
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 - OR:

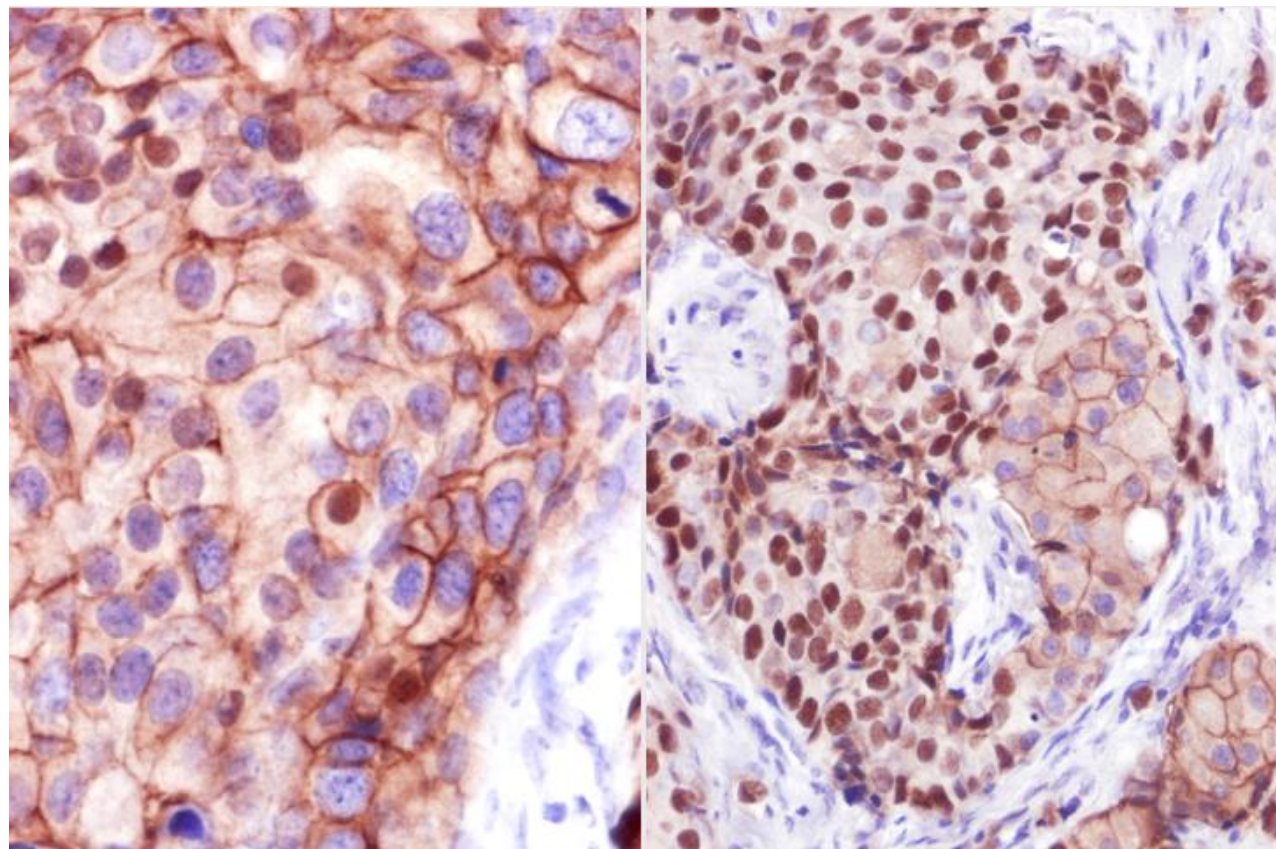
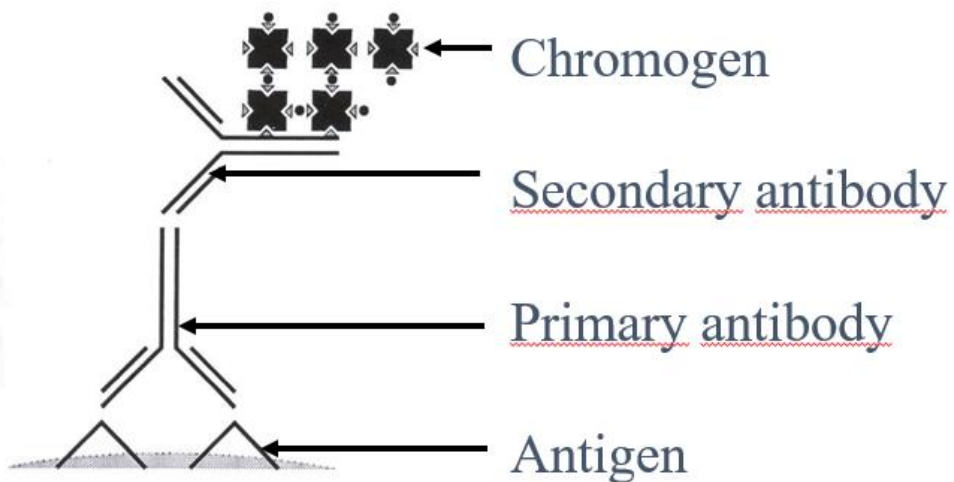
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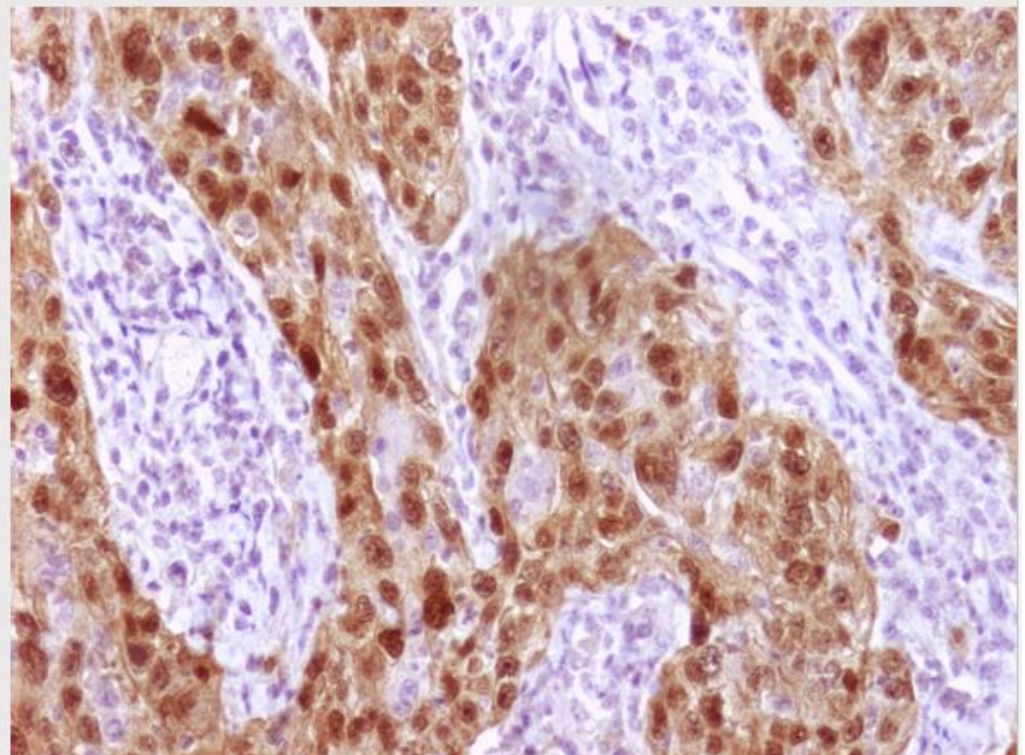
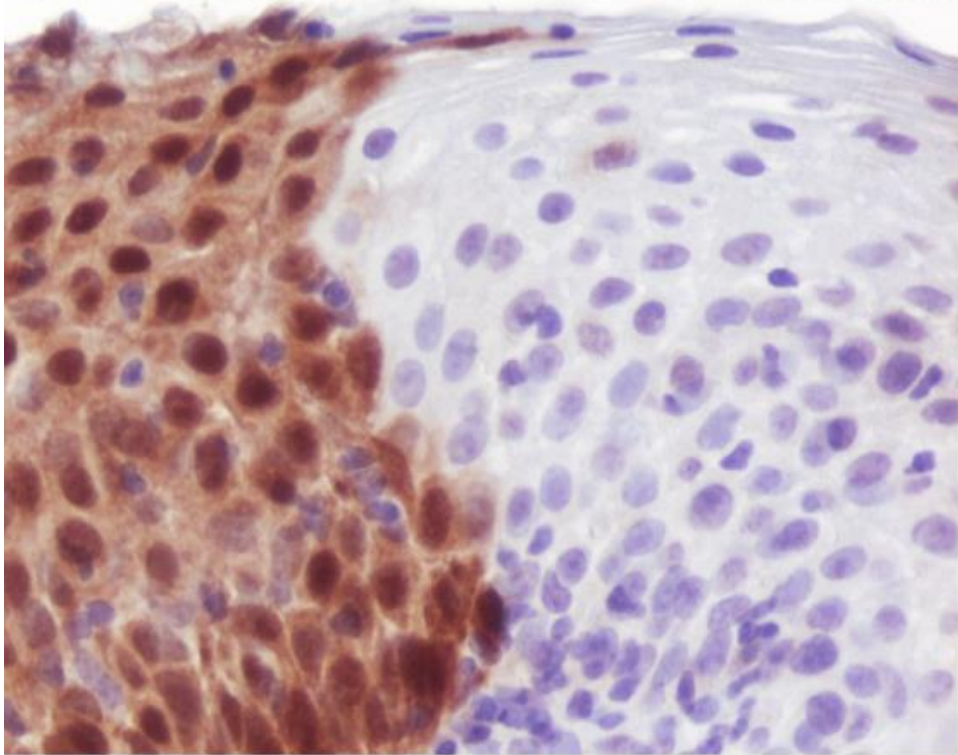
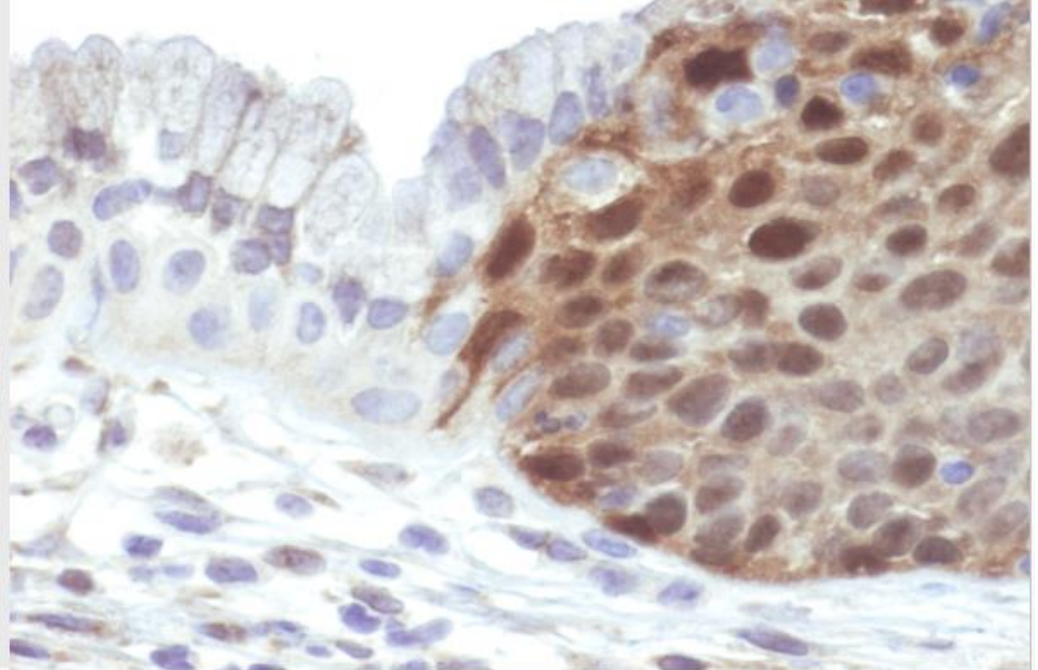
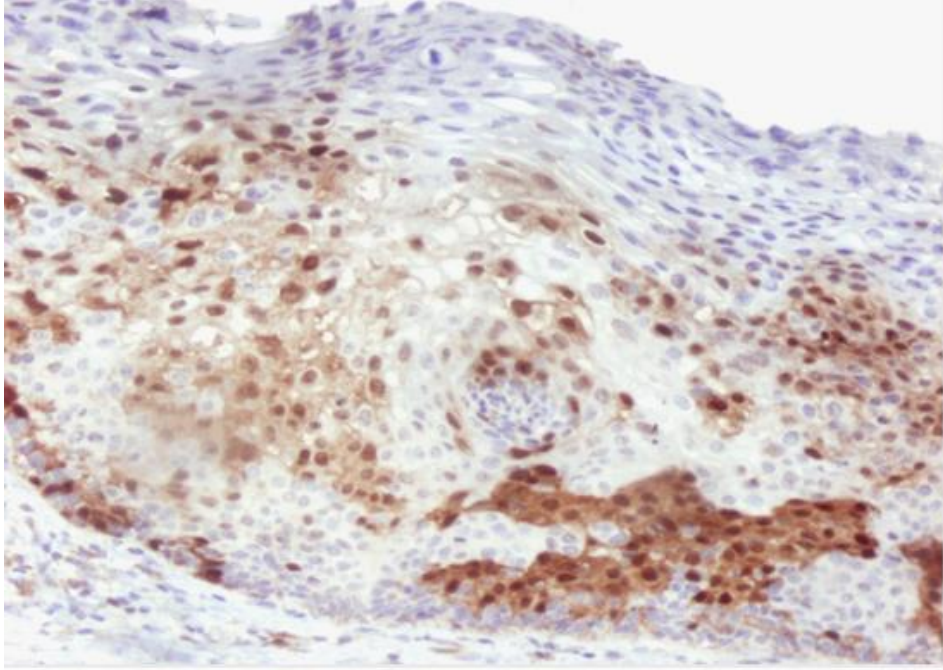
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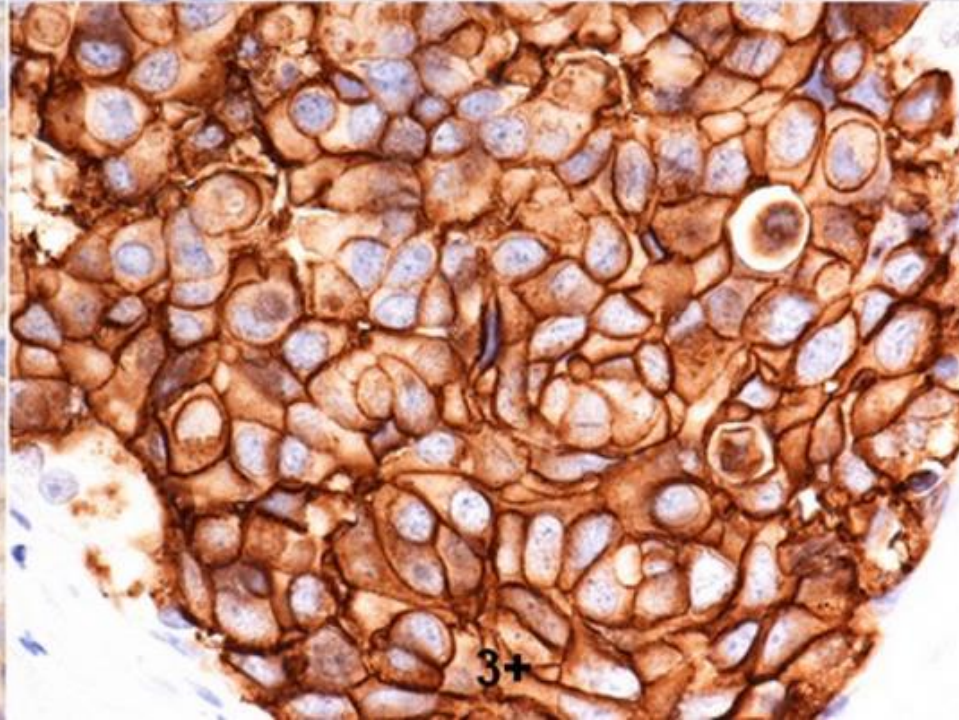
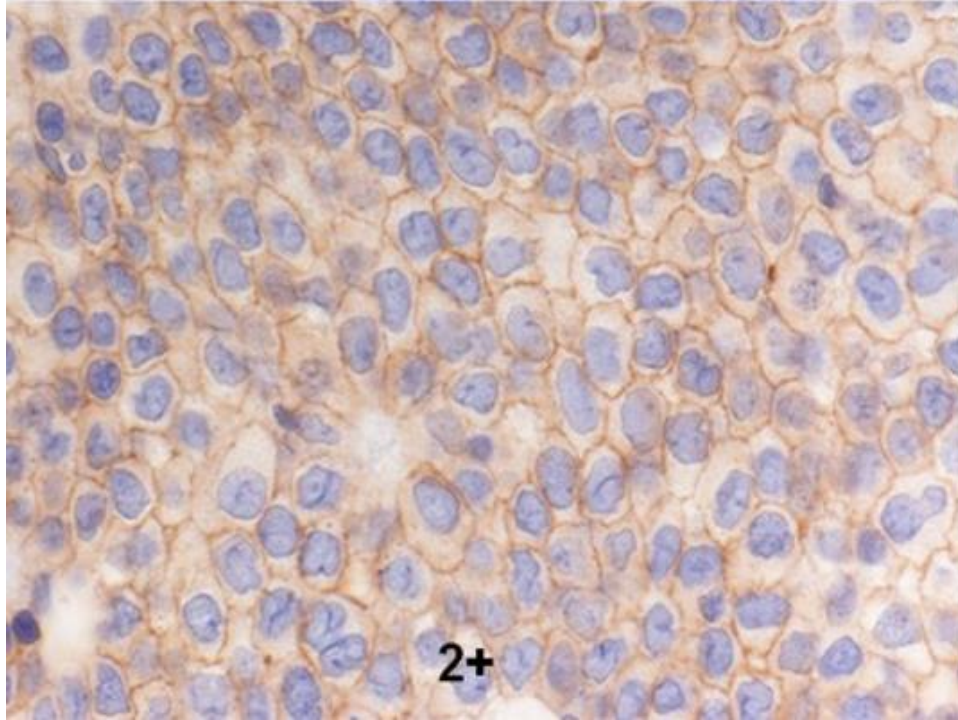
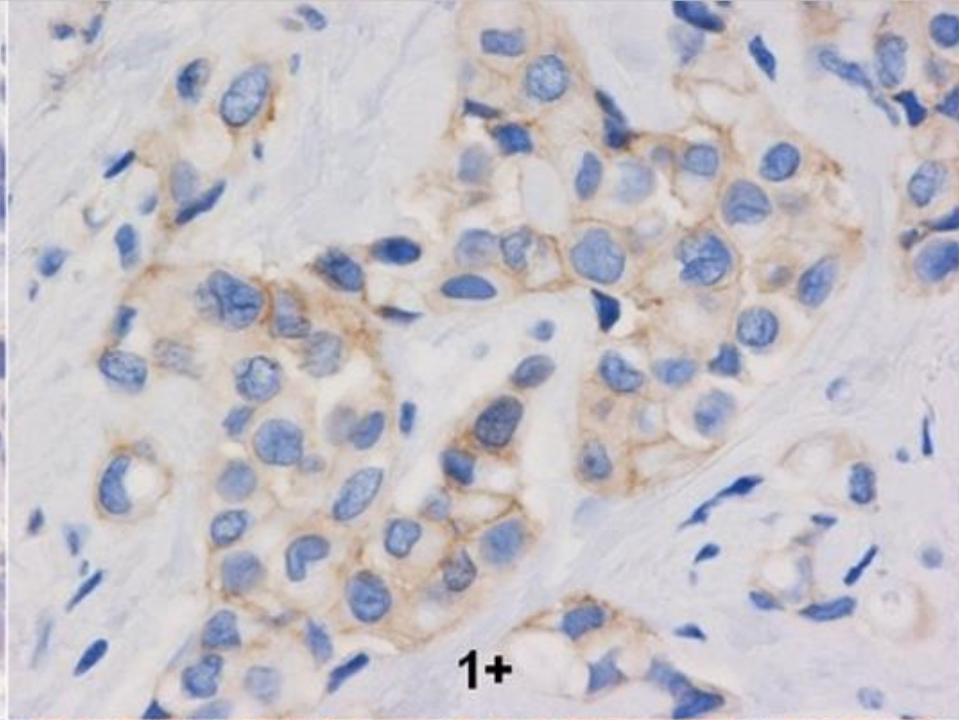
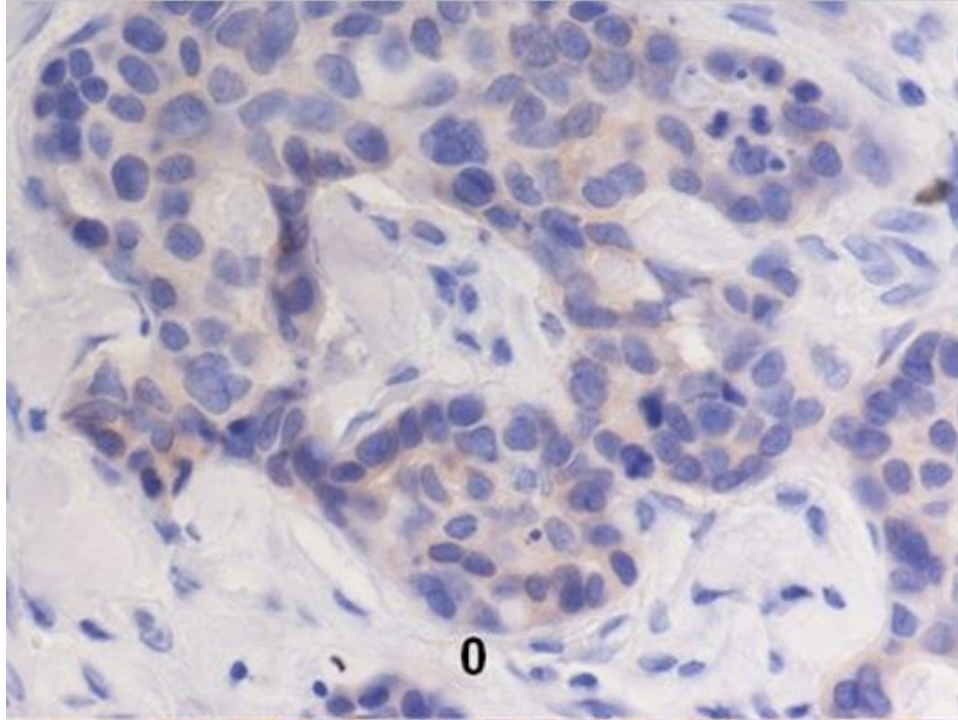


Immunohistochemistry





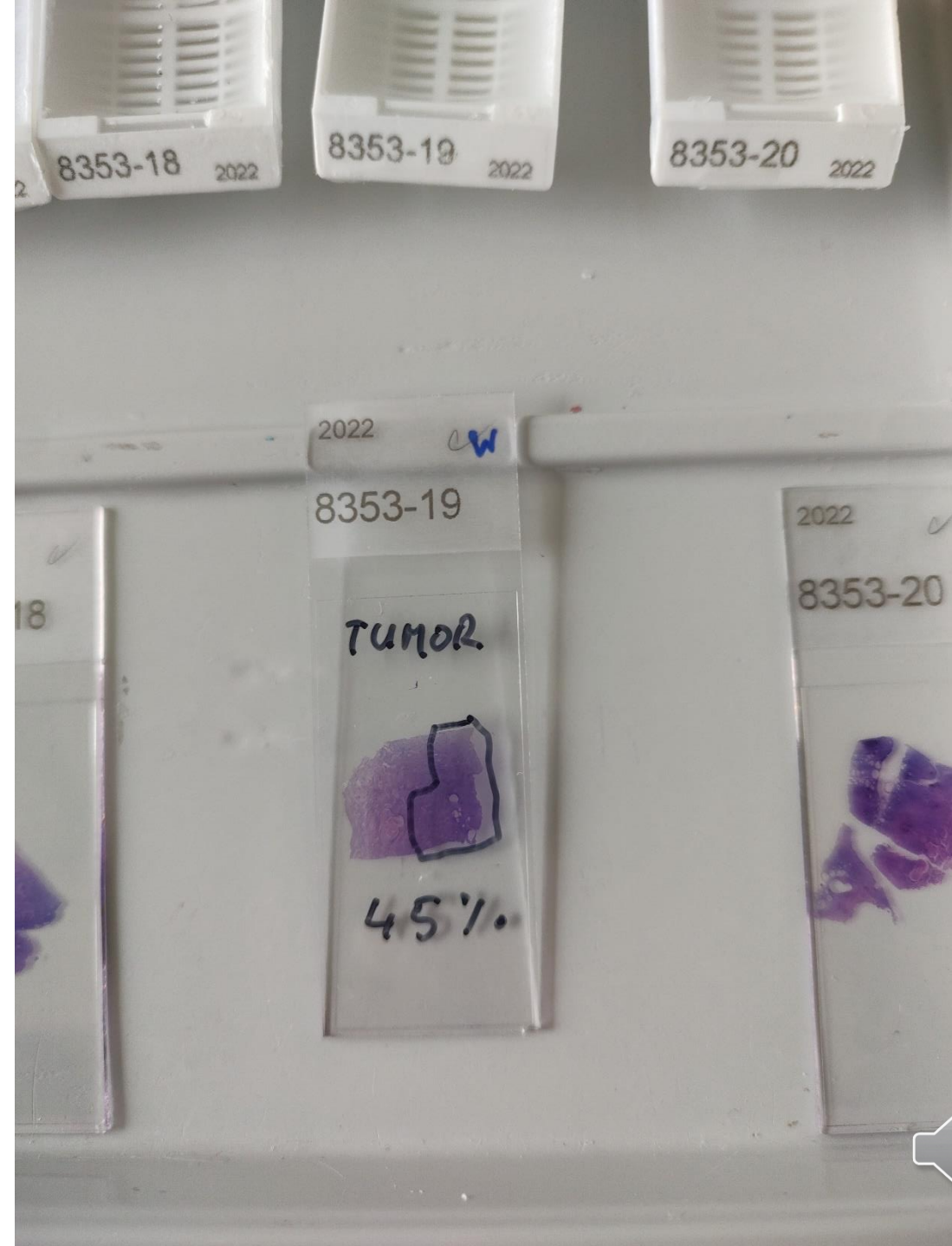




Molecular pathology

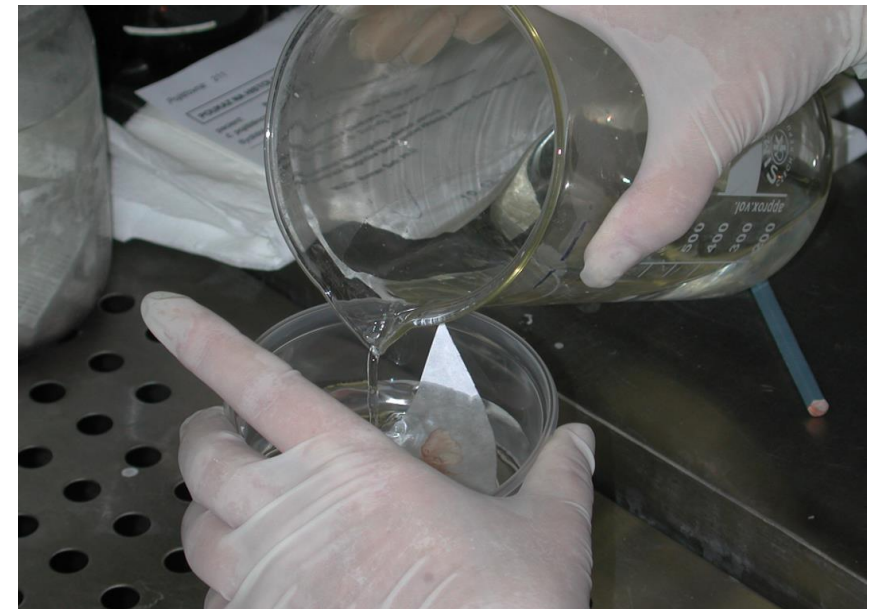
- Methods based on PCR, NGS and others
- Diagnostic
 - Specific DNA alteration (mutation, translocation) is a diagnostic feature of a particular tumor entity (e.g. c-kit mutation for GIST, EWS-FLI-1 translocation for Ewing's sarcoma, FOXL-2 mutation for adult granulosa cell tumor etc).
- Predictive
 - Specific DNA alteration is predictive for treatment response with a particular drug / compound (e.g. Her-2 amplification is predictive for trastuzumab efficacy in breast cancer patients).





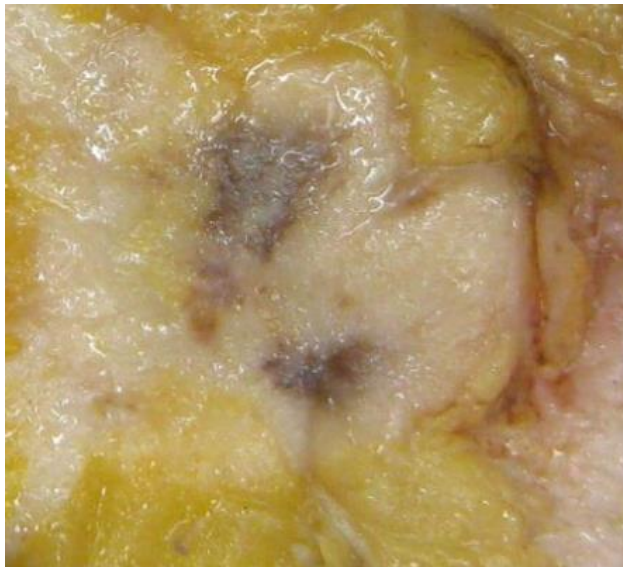
Praeanalytics

- All that happens **before** the specimen arrives at the pathology laboratory
- 1) Fixation
 - Coumpound (neutral buffered 10% formalin)
 - Time (not too long, not too short)



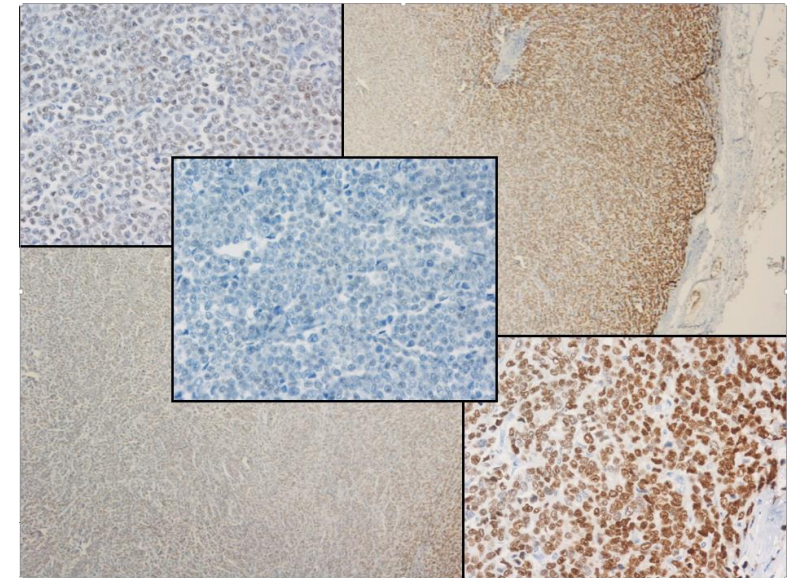
Praeanalytics

- All that happens **before** the specimen arrives at the pathology laboratory
- 2) Cold ischemia time
 - „cold ischemic time, which is the time between tissue removal and the initiation of formalin permeation of the tissue...“



Imperfect fixation
in the tumor centre

Zonal ER positivity
in the tumor tissue
(false negative
estrogen receptor
status in the tissue
with long cold
ischemia)



Praeanalytics

- Date of paraffin embedding
 - After fixation is done, the paraffin processing begins and the date of paraffin embedding is usually one day after „material receiving date“.
 - But not allways and consultation with a study pathologist is adequate

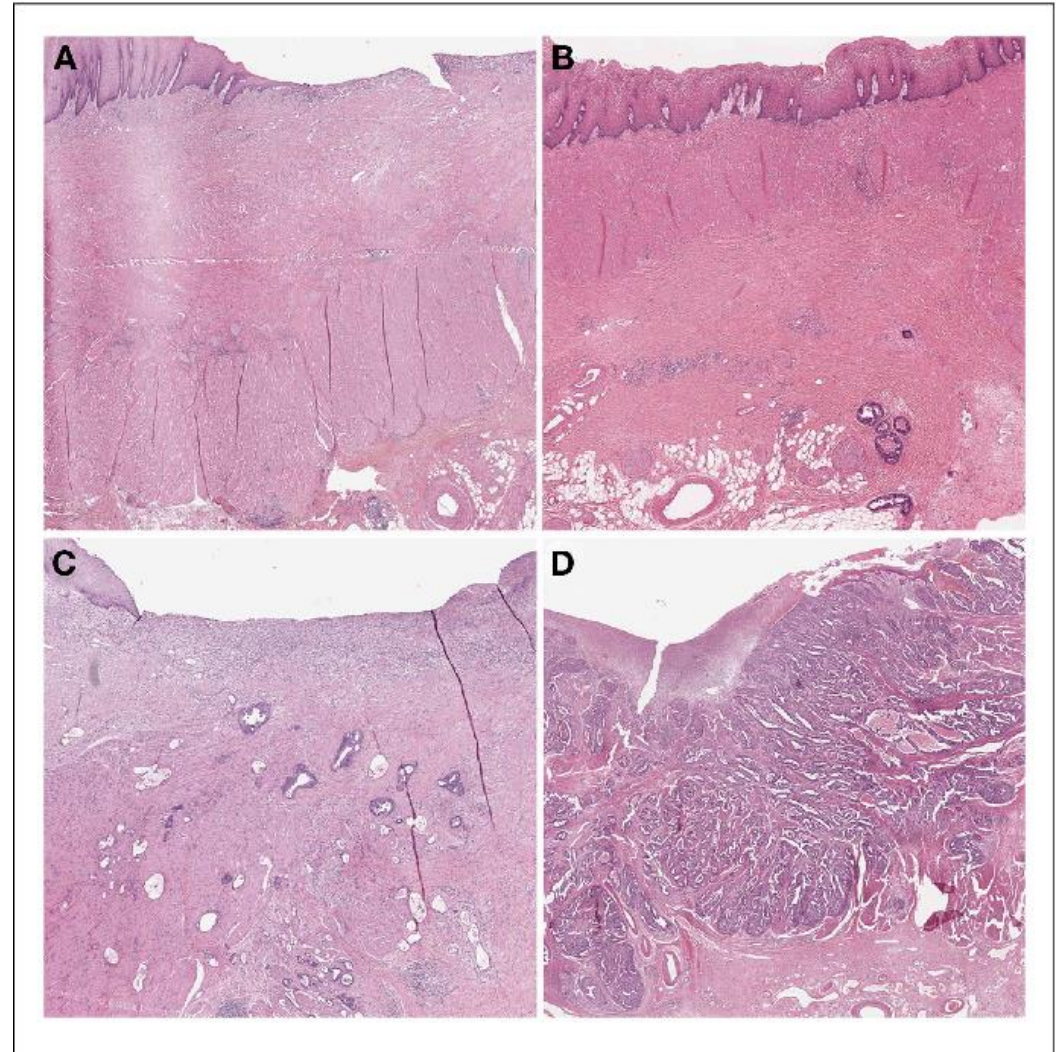


Postanalytics – formal informations

- Report should contain a lot of „technical“ informations, not only the tissue description and a final diagnosis.
 - Material receiving date / time
 - Result release date / time
 - Responsible persons
 - Other – comments on inappropriate fixation, insufficient specimen identification etc.

Postanalytics – tumor regression grade

- TRG (tumor regression grade) reflects the changes in tumor tissue **after** the neoadjuvant therapy
- Should be a constant part of the pathology report
- There are many systems (most of them are „organ specific“), usually are named according to their own inventors (Mandard, Dworak, Chevallier etc.)



Postanalytically – tumor regression grade-examples

TRG Mandard

- 1 complete regression
- 2 some tumor cells
- 3 fibrosis prevailing
- 4 tumor prevailing
- 5 no regression

TRG Chevallier

- 1 complete regression (including lymph nodes)
- 2 DCIS only
- 3 regression present, not quantified
- 4 regression nearly absent

Postanalytics – alphanumerical coding

- ICD-10 diagnosis
 - C 50.9 = malignant breast tumor (irrespective of the tumor type)
 - C 43.9 = malignant skin tumor
- ICD-O 3.2
 - T = topography C 50.9 = Breast
 - C 44.9 = Skin (topography C 43 does not exist!!!)
 - M = morphology .. 8520/39 = invasive lobular carcinoma
 - /0 = benign
 - /2 = carcinoma in situ (praemalignant)
 - /3 = malignant (primary tumor)
 - /6 = malignant (metastasis)
 - /9 malignant, unknown
 - /3X – tumor grading (if exists)

Postanalytics – alphanumerical coding

- TNM classification
 - T = tumor
 - N = (regional lymph) nodes
 - M = (distant) metastasis
- Clinical (cT cN cM) or pathological (pT pN) – sometimes identical, sometimes very different
- Specific system for each organ, based on different principles
 - In hollow organs - the deepest level of the organ wall infiltration
 - Or on largest diameter (measured in mm)
 - Or permeation into adjacent organs
 - Or combination of these principles...and others
- Additional information like vascular invasion (L0/1), clear resection margins (R0/1)



Postanalytics – alphanumerical coding

- Numerical codes carry many (if not all) the important informations about the tumor, so that is very usefull to be familiar with this systems.
- T C50.1 M 8520/31 pT1c pNo(sn)

Postanalytics

- Pathological report may contain the molecular results
 - „Must be“ in case of diagnostic molecular pathology
- Or these may be reported separately

- Some of these molecular tests results are extremely long and complex, so the short and clear clinical interpretation is advisable

Thank you for your attention!

