Breast Pathology Course 2017

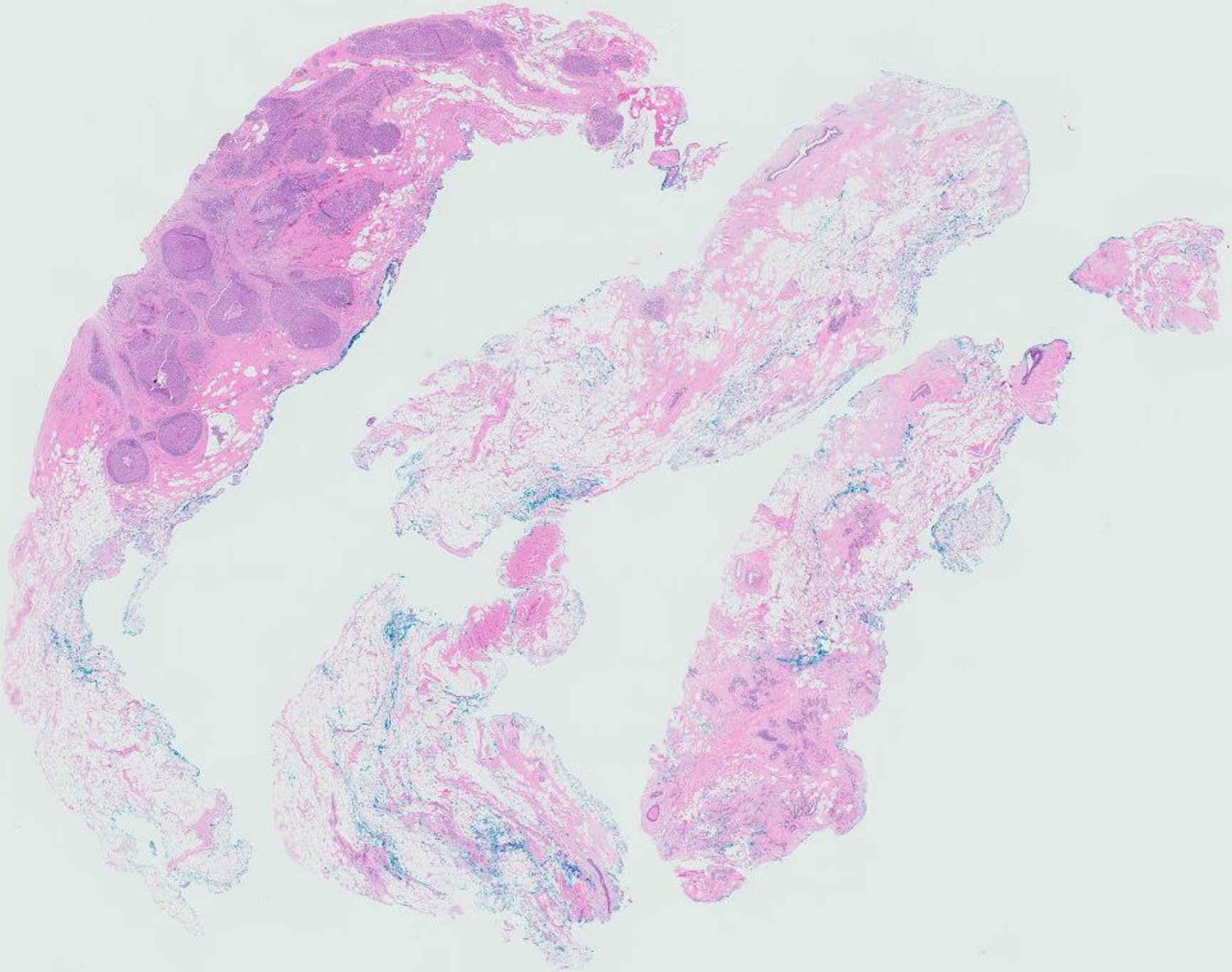
Case 4

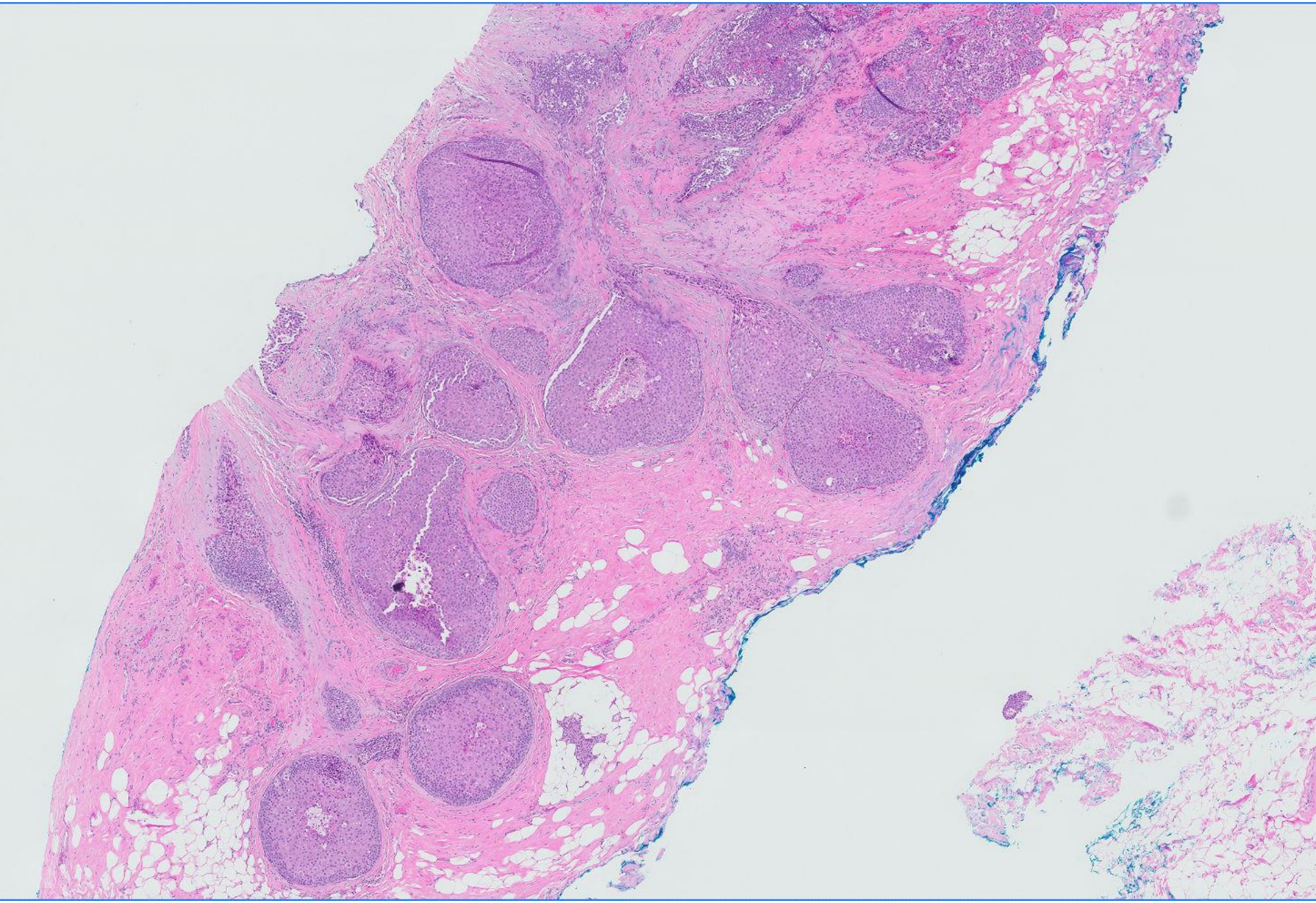
59 year old Malay female.

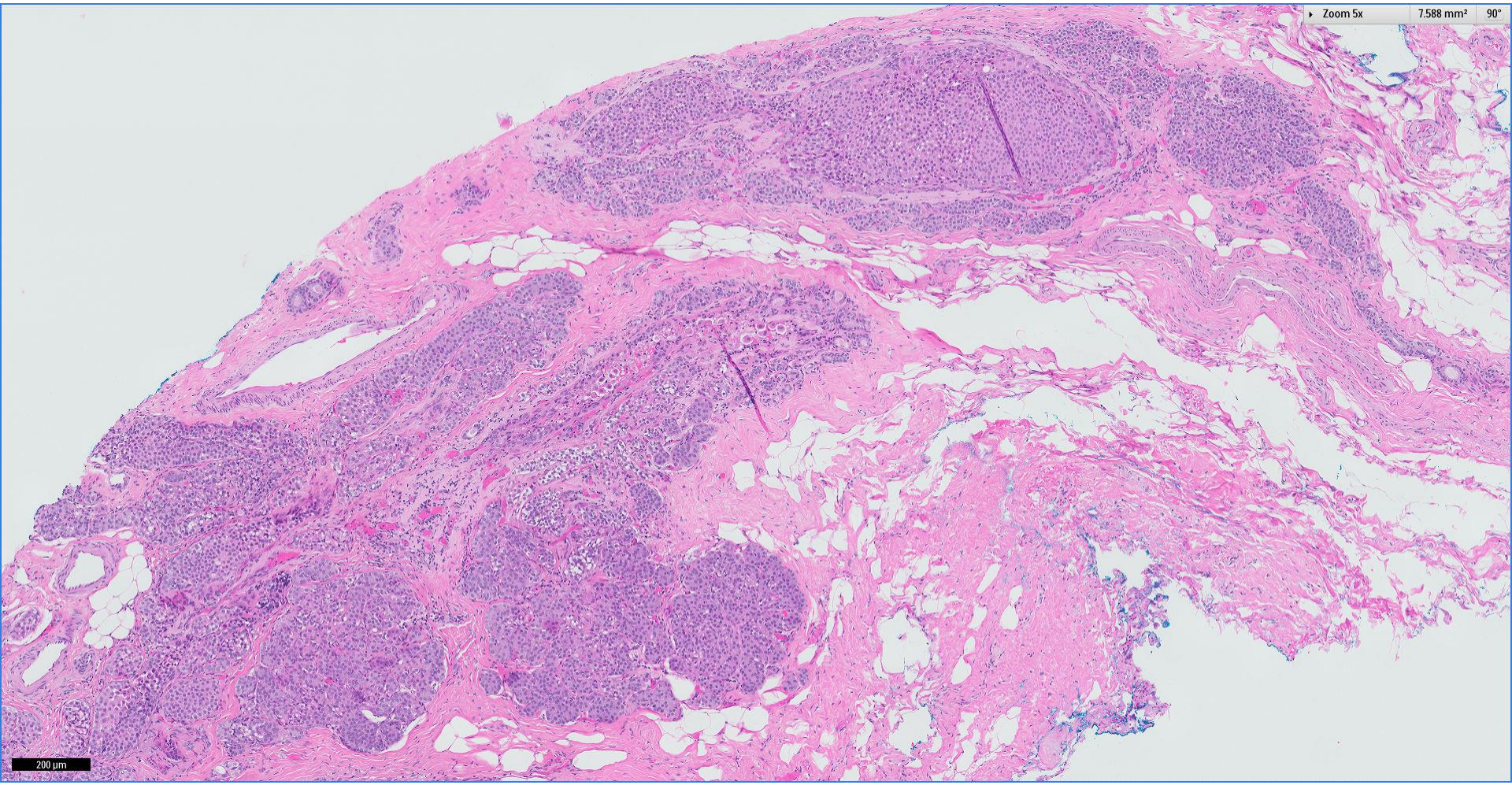
Past history of right breast cancer status post-mastectomy in 2006.

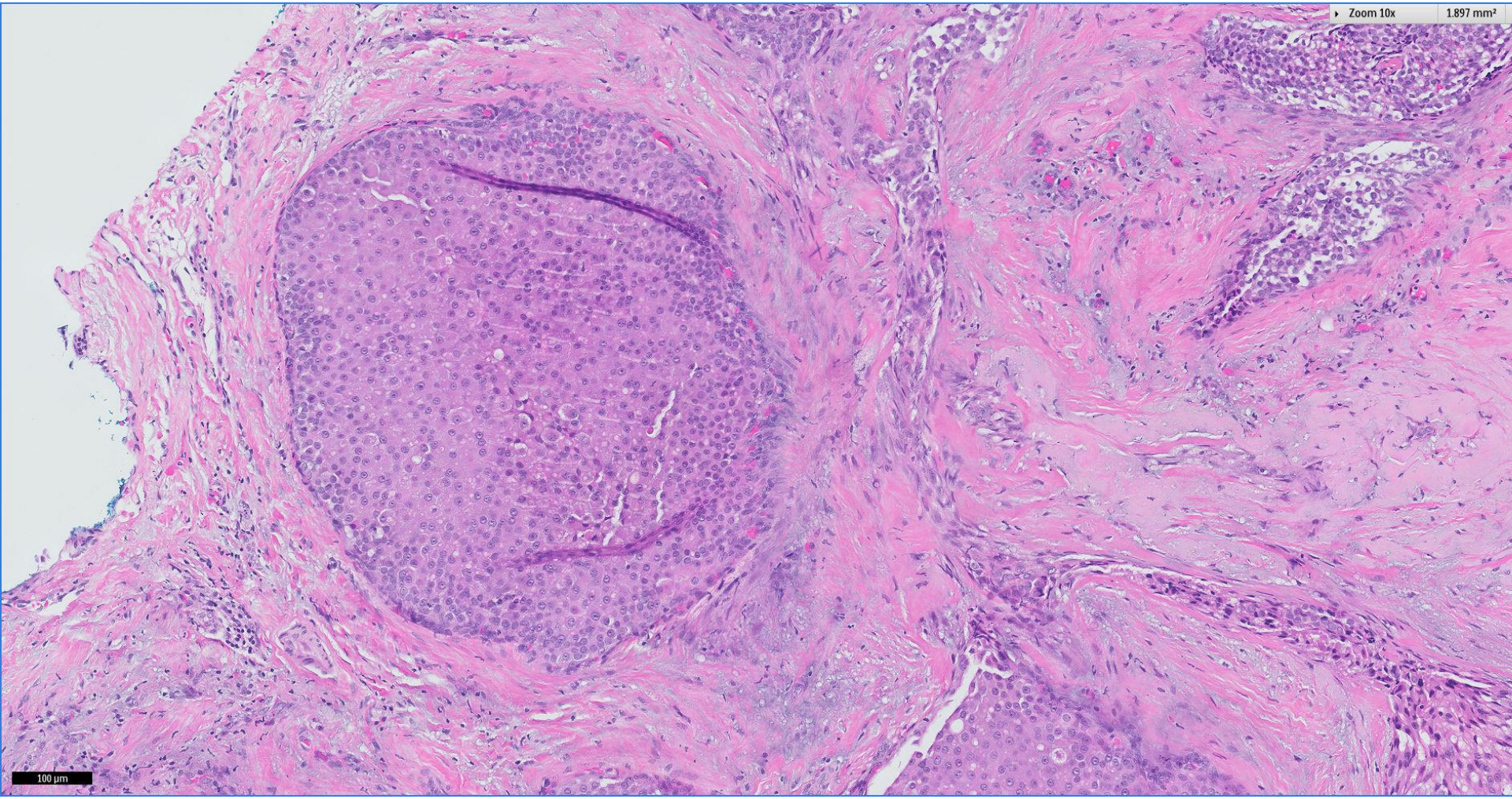
Currently discovered on radiology to have a cluster of microcalcifications in the left breast outer central region.

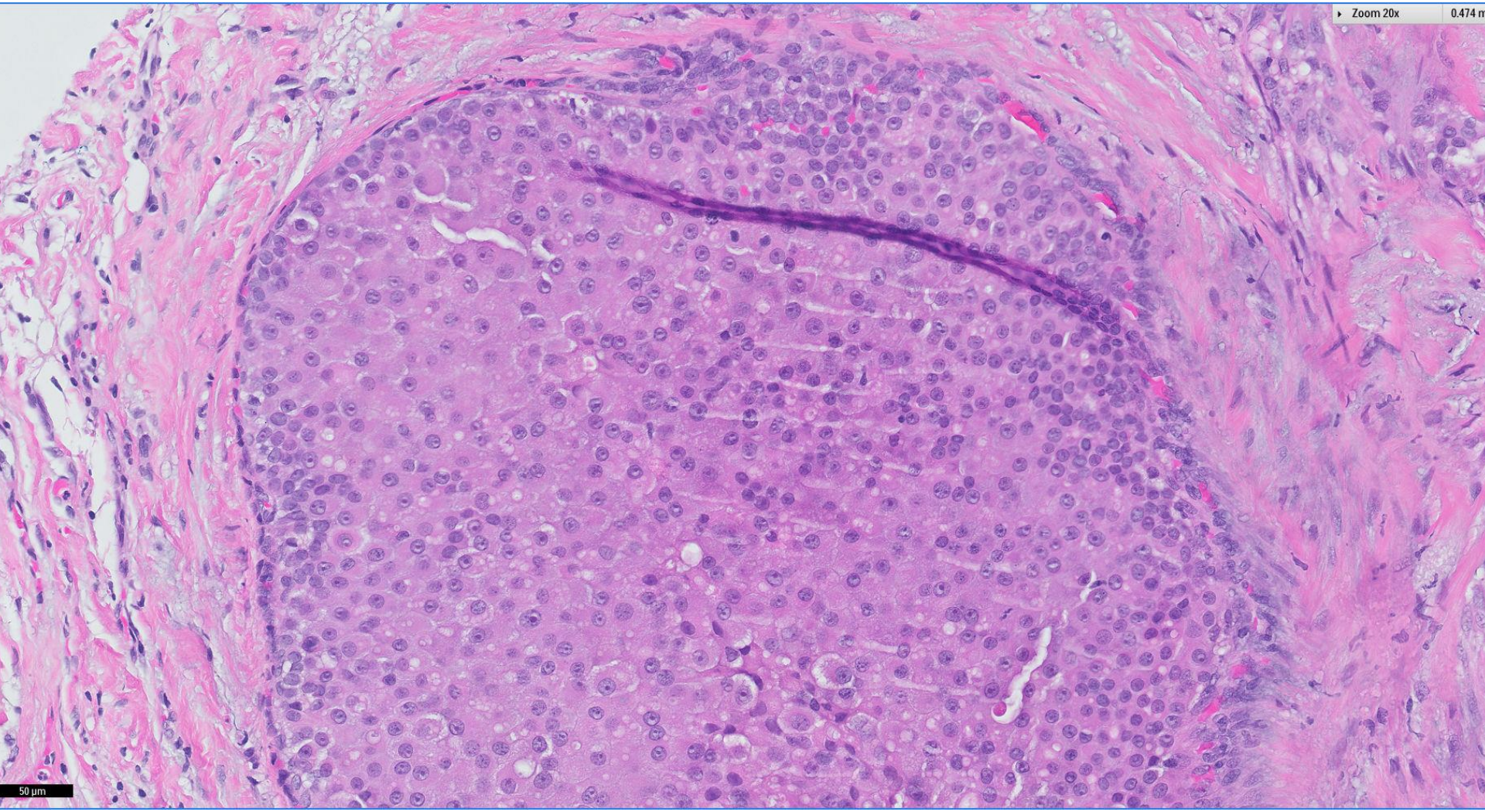
Stereotactic vacuum assisted biopsy of the left breast microcalcifications performed.

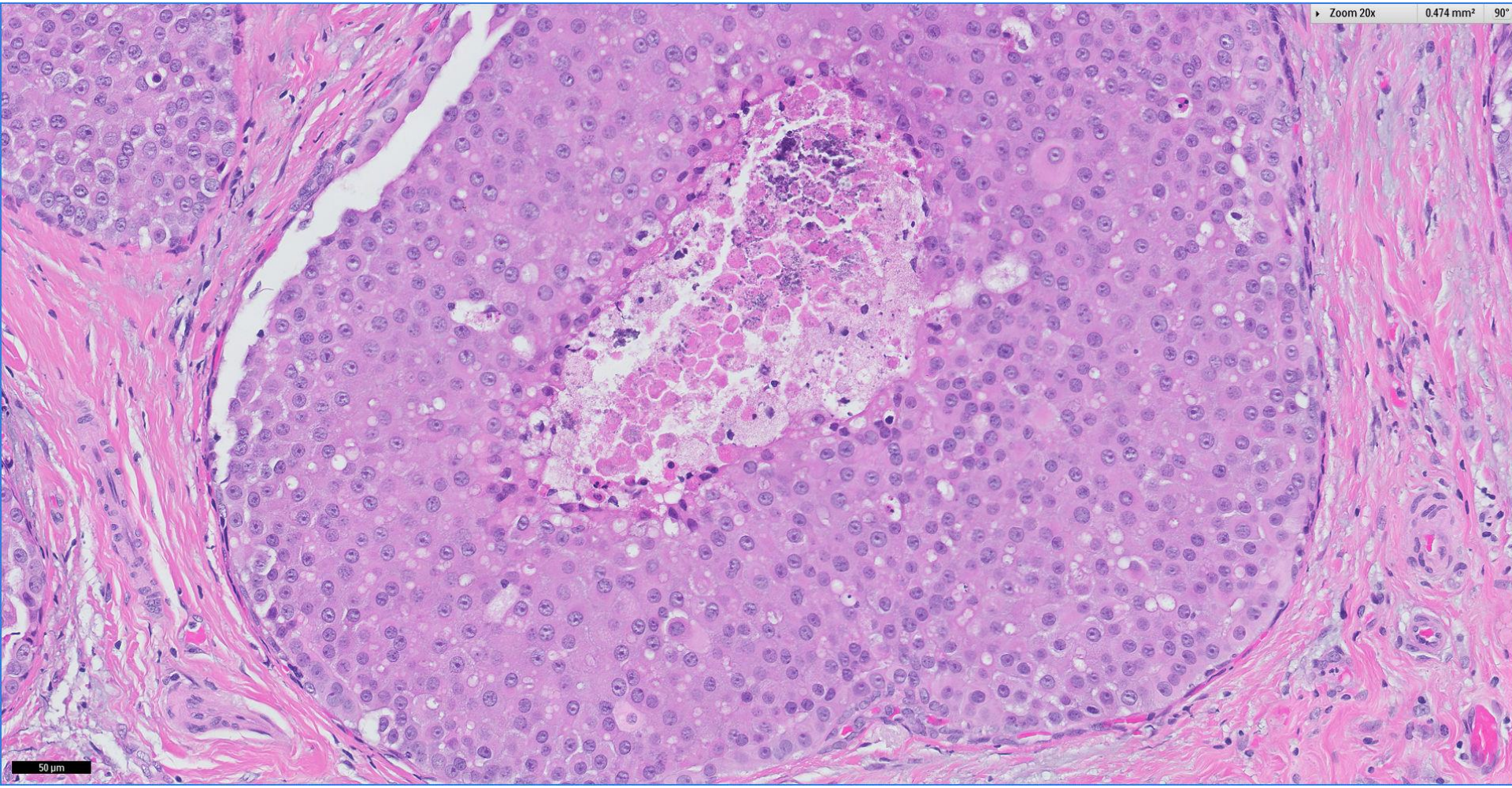


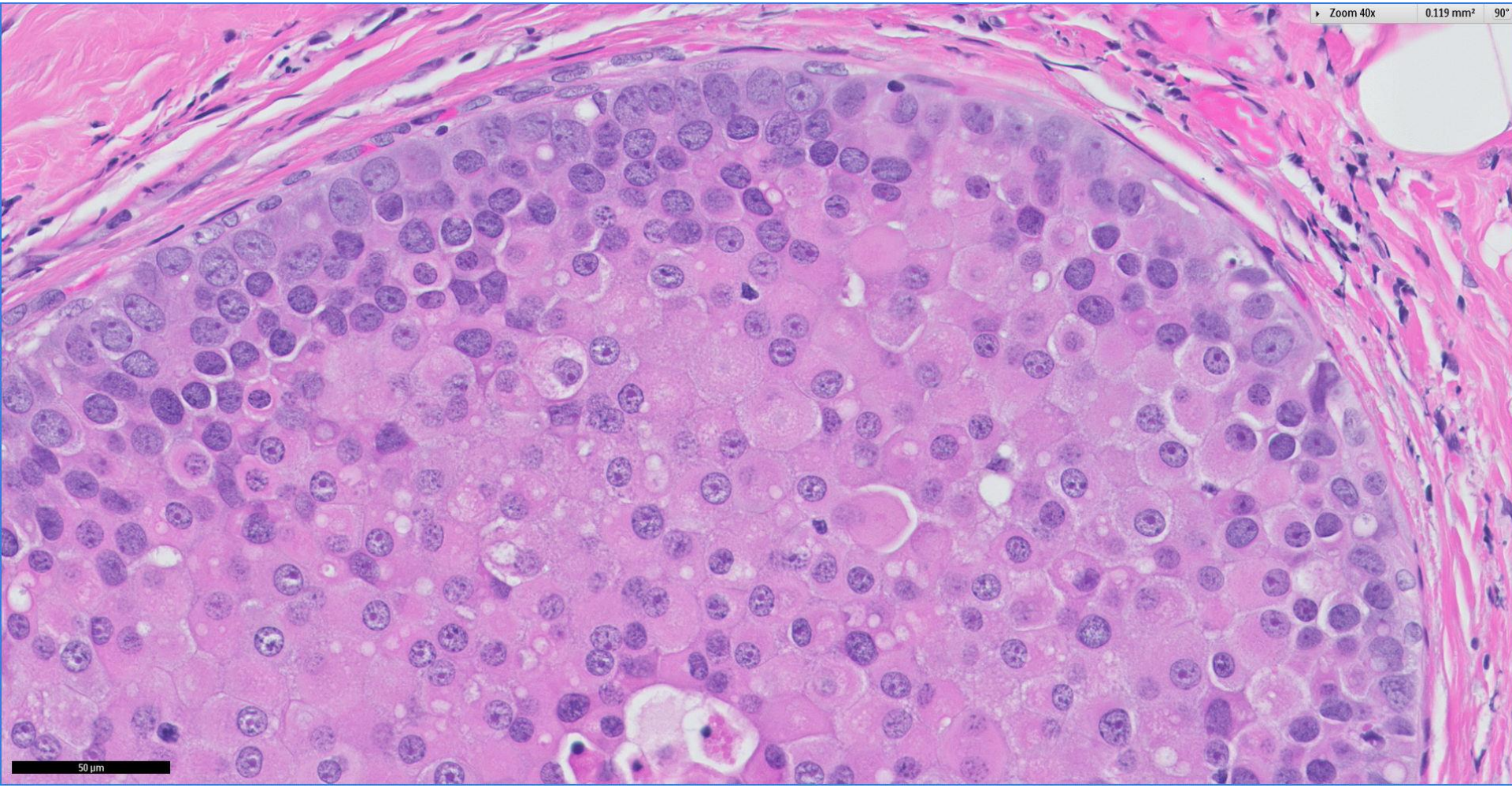


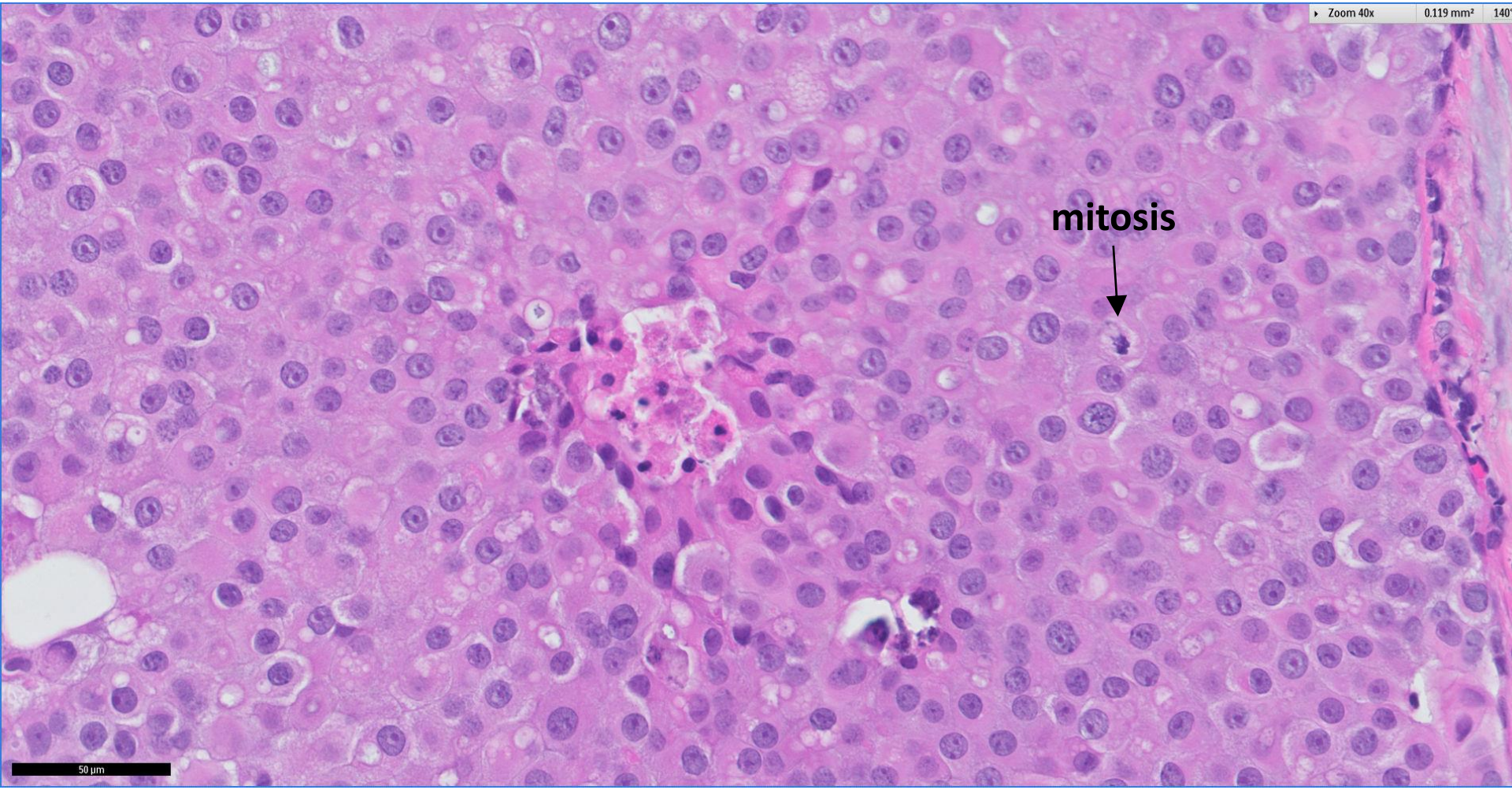

Zoom 5x
7.588 mm²
90°
200 µm

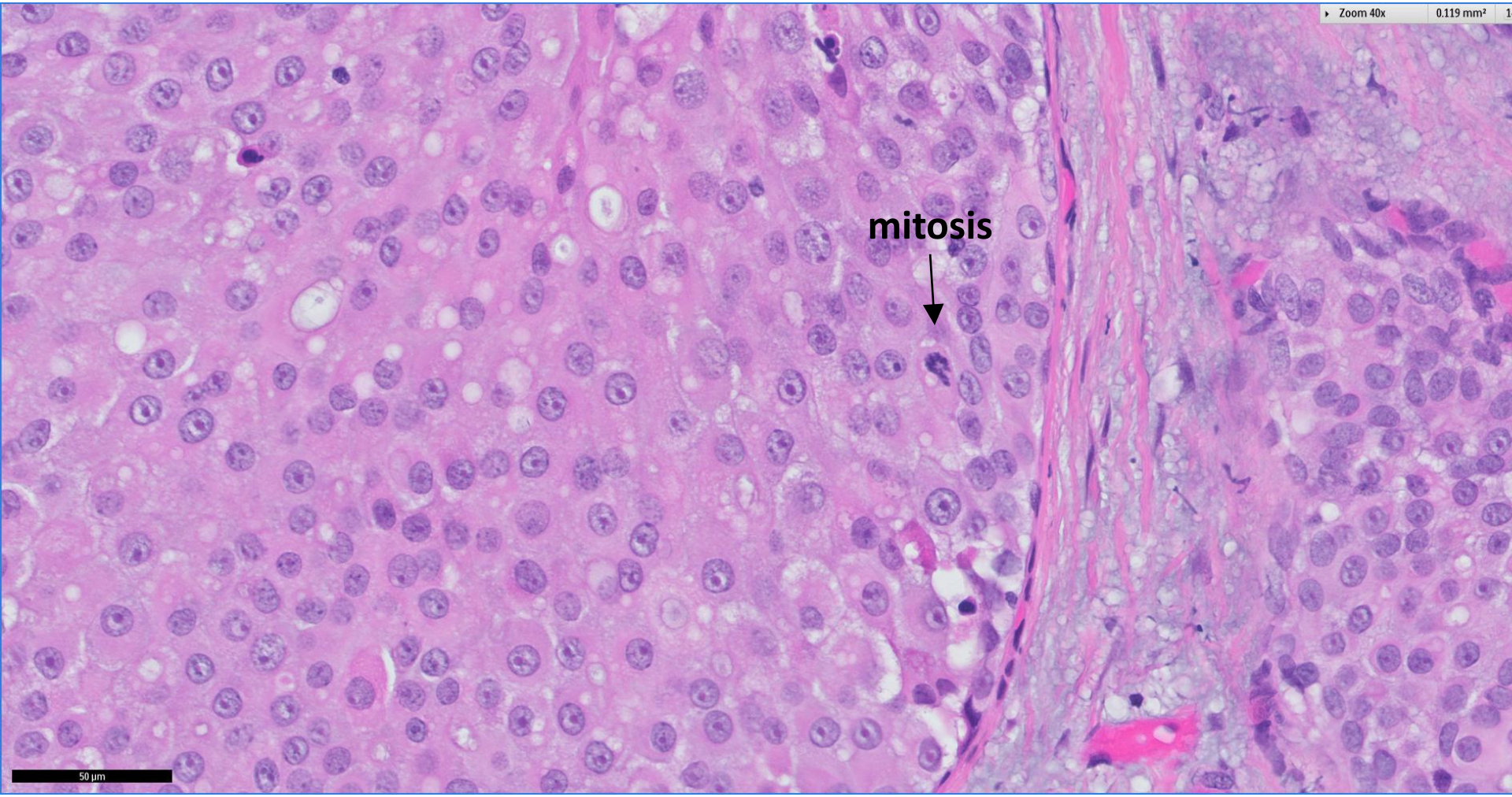

Zoom 10x
1.897 mm²
100 µm


Zoom 20x
0.474 m
50 µm

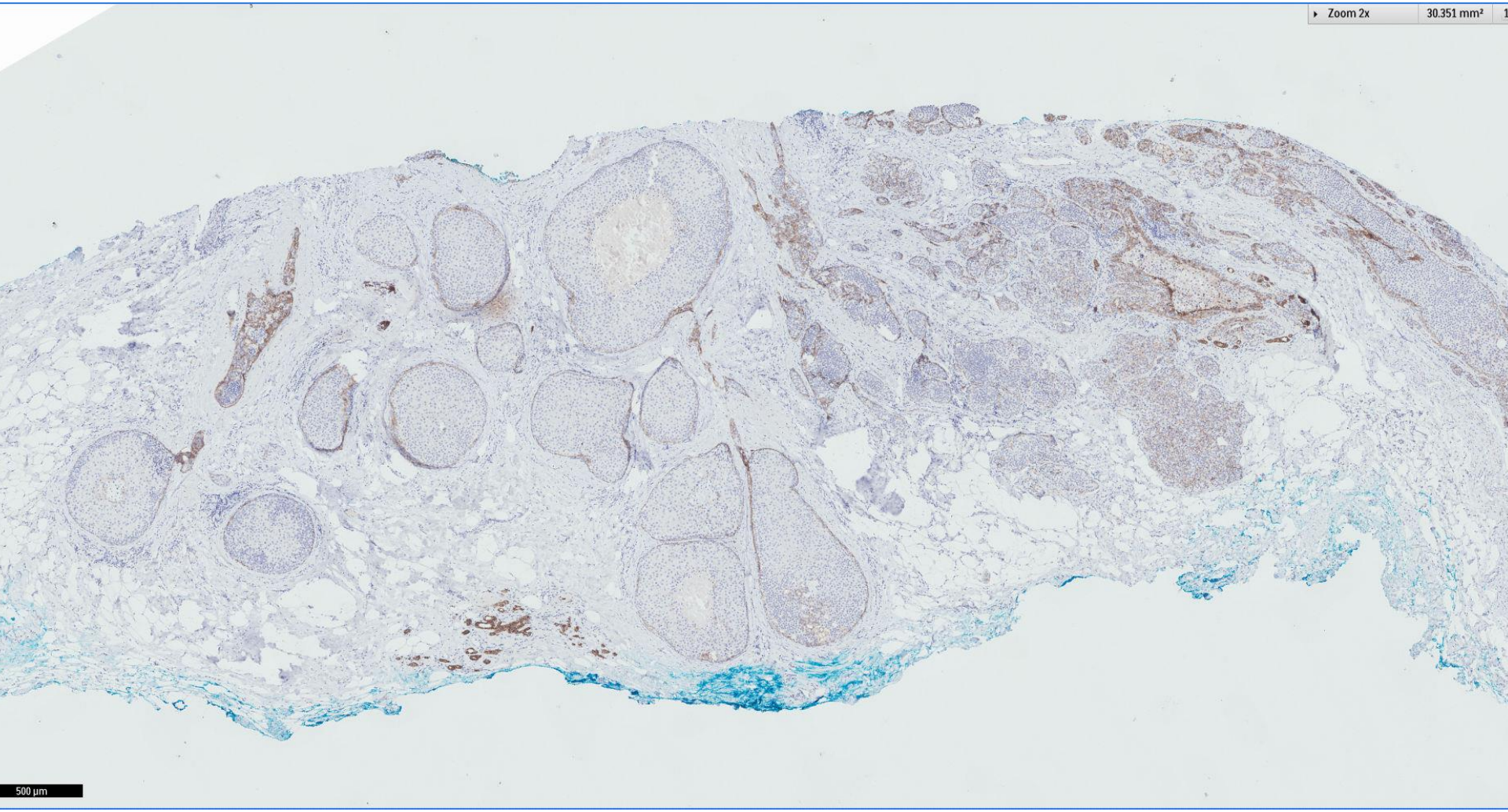

Zoom 20x
0.474 mm²
90°
50 µm


Zoom 40x
0.119 mm²
90°
50 µm

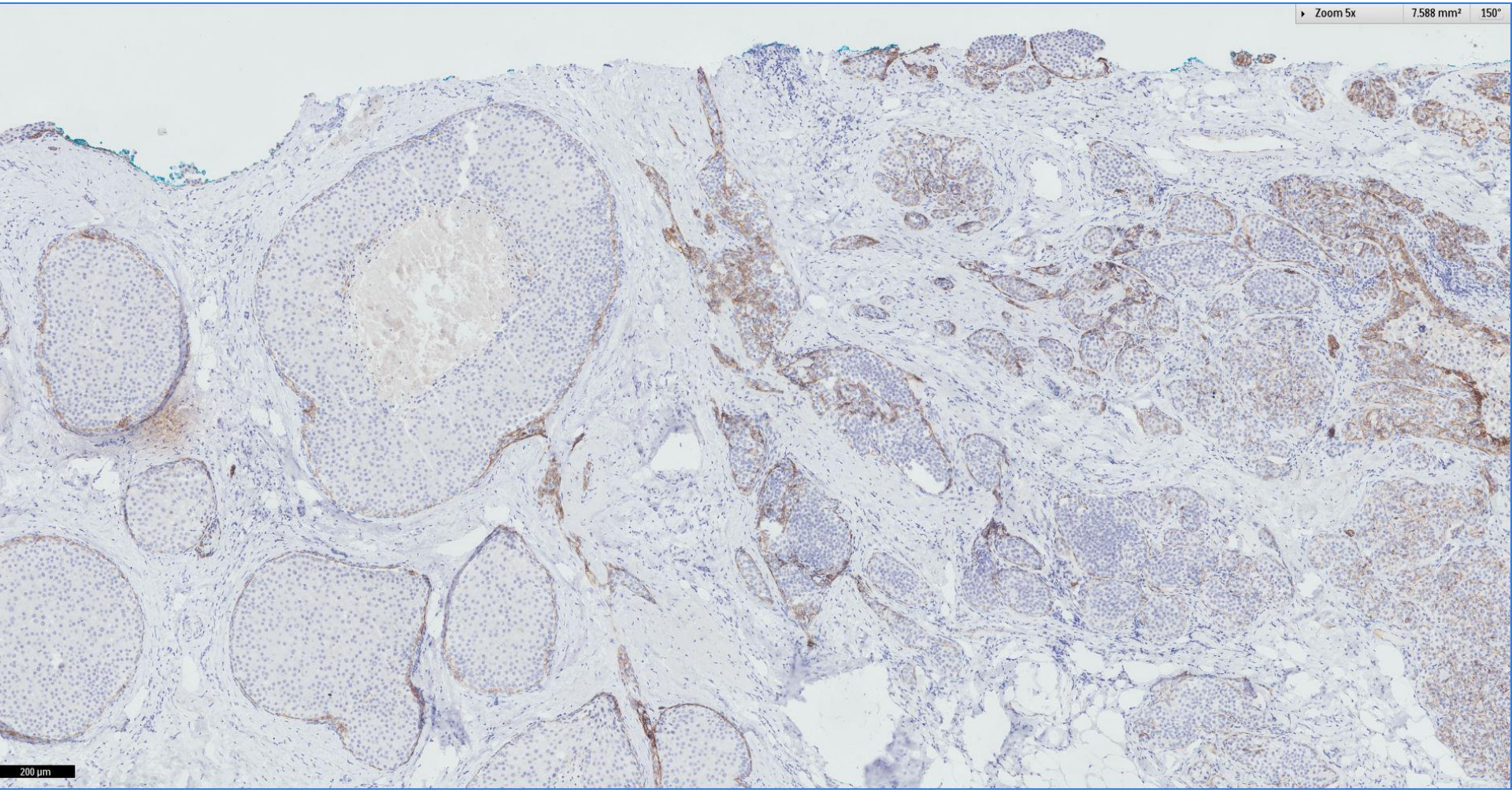

Zoom 40x
0.119 mm²
mitosis
50 µm


Zoom 40x
0.119 mm²
mitosis
50 µm

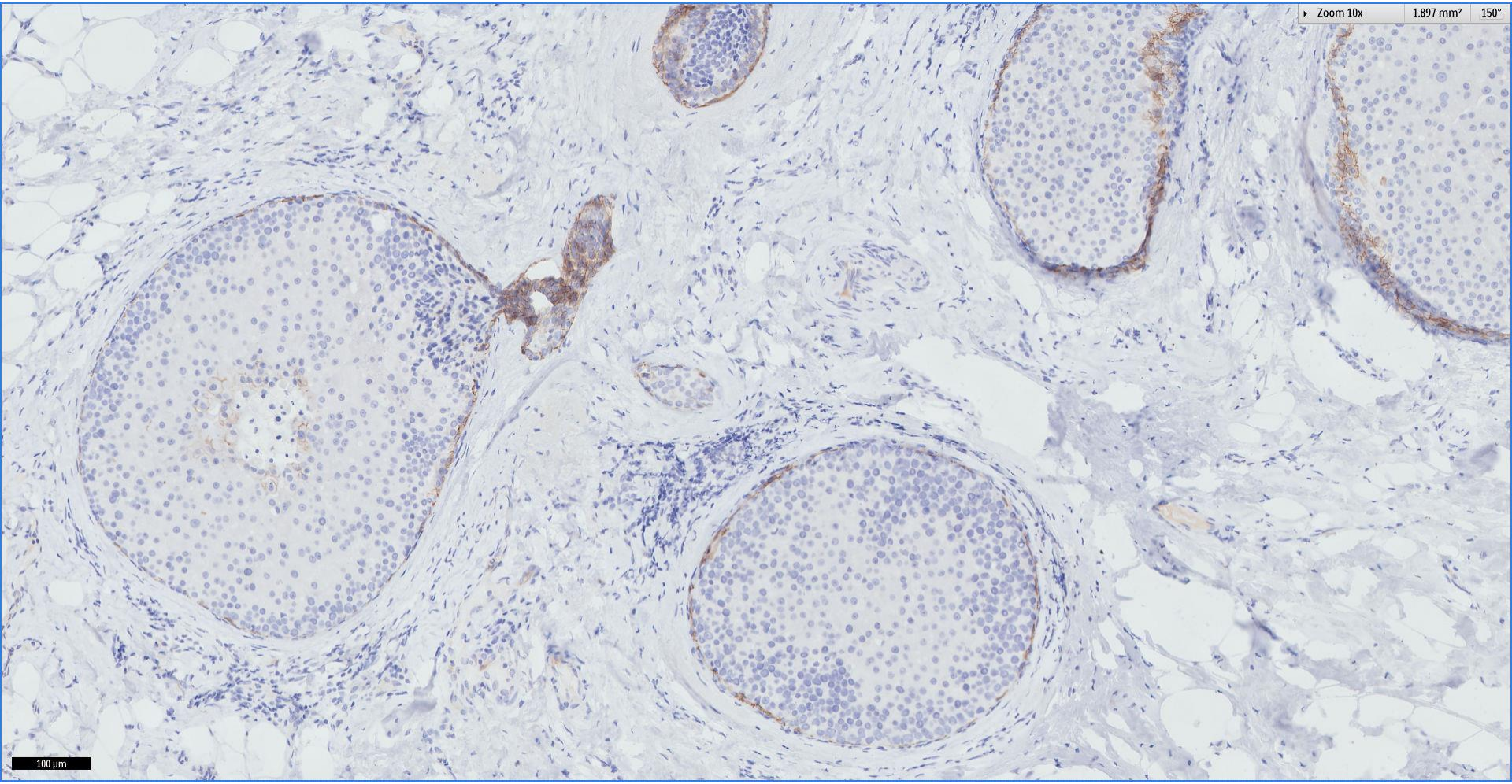
E-cadherin



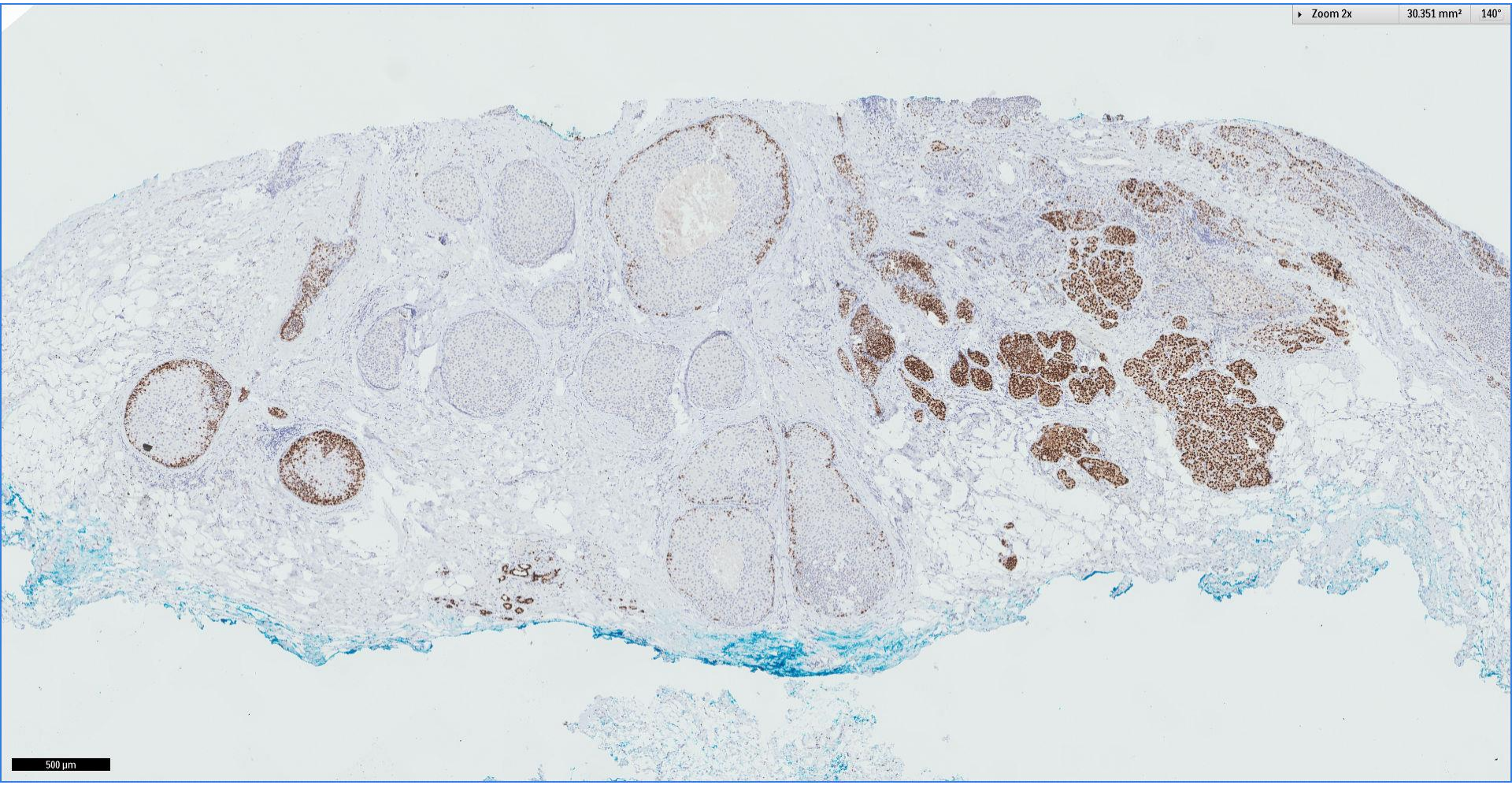
E-cadherin



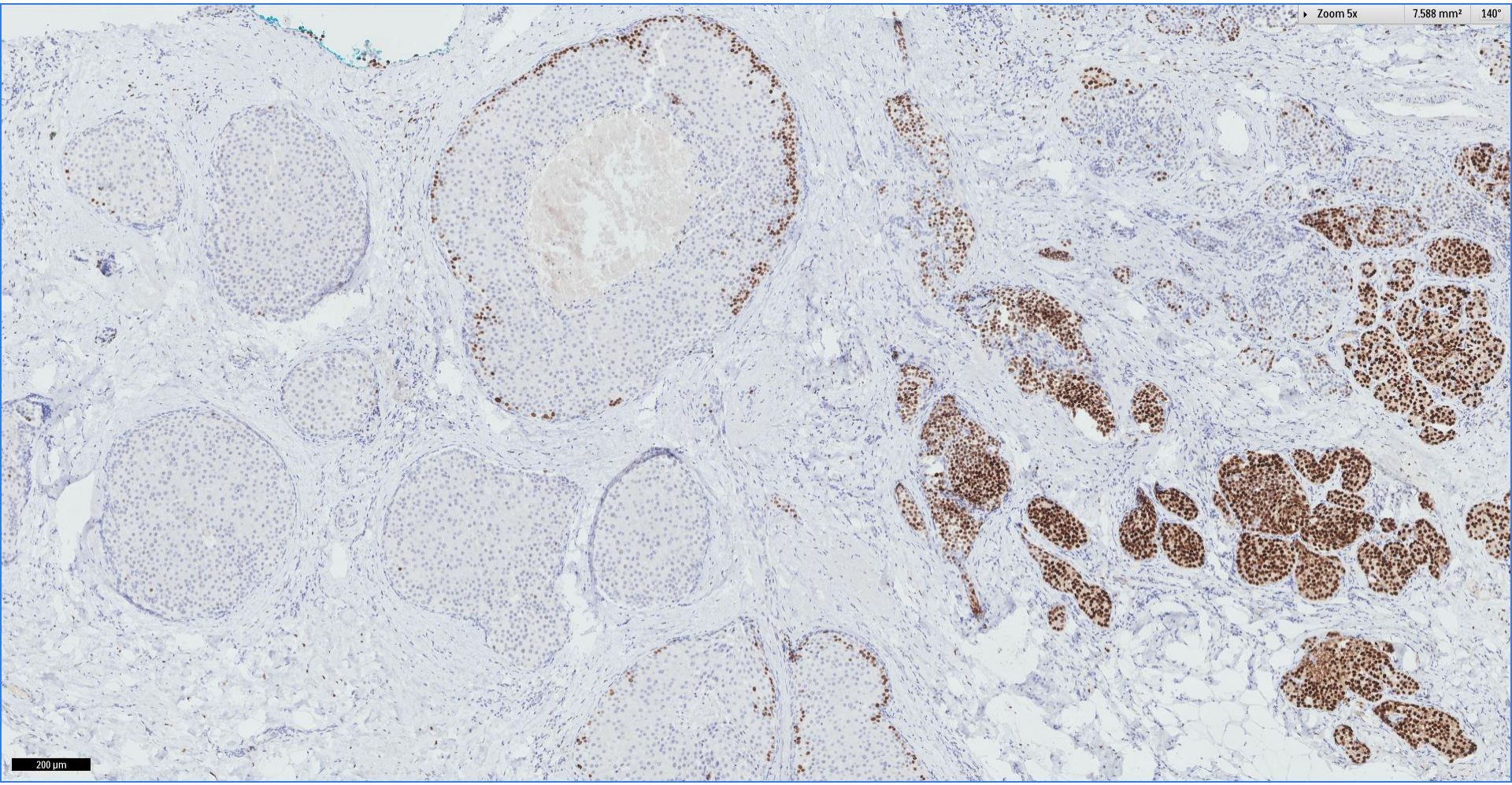
E-cadherin



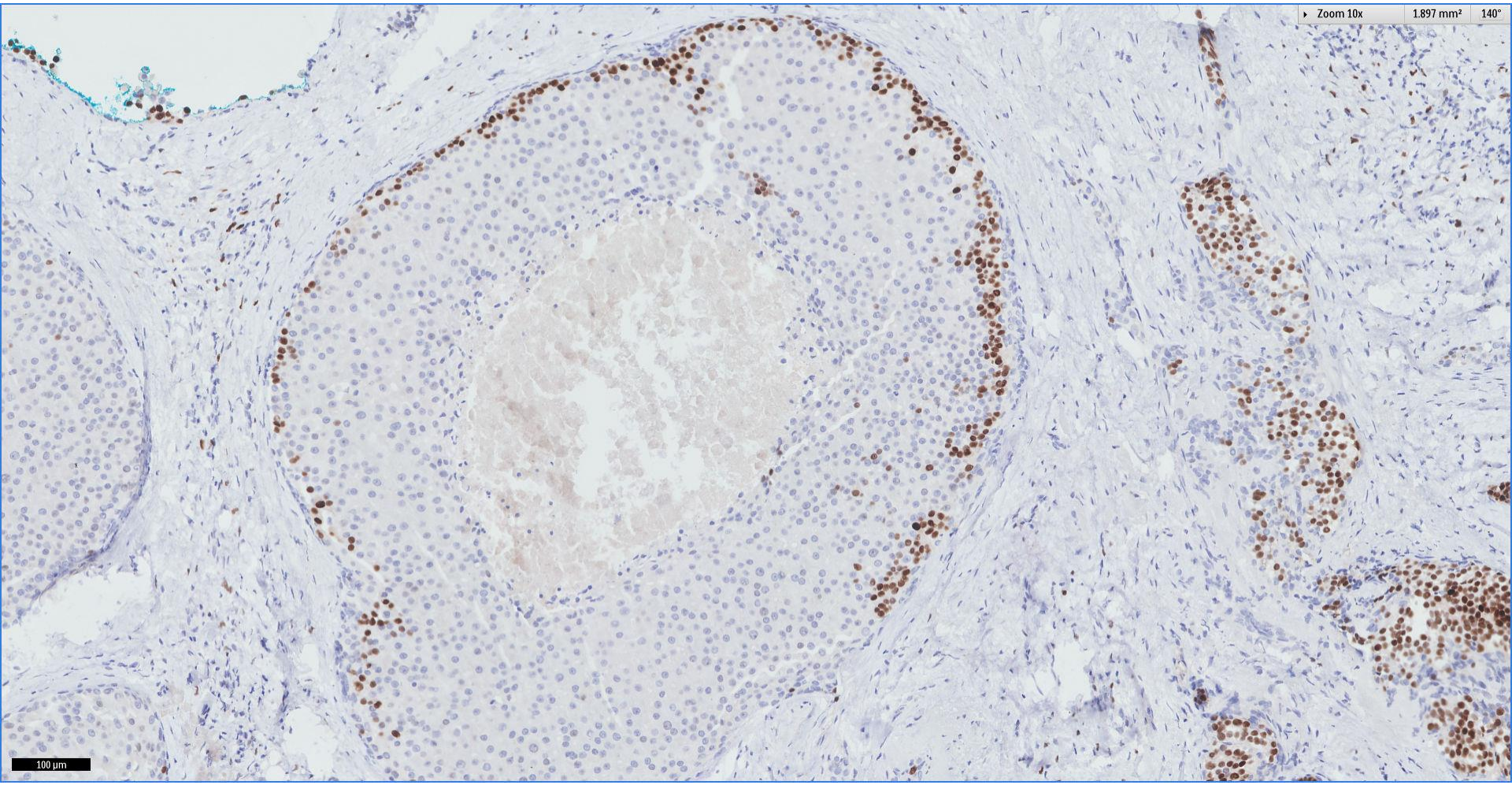
ER

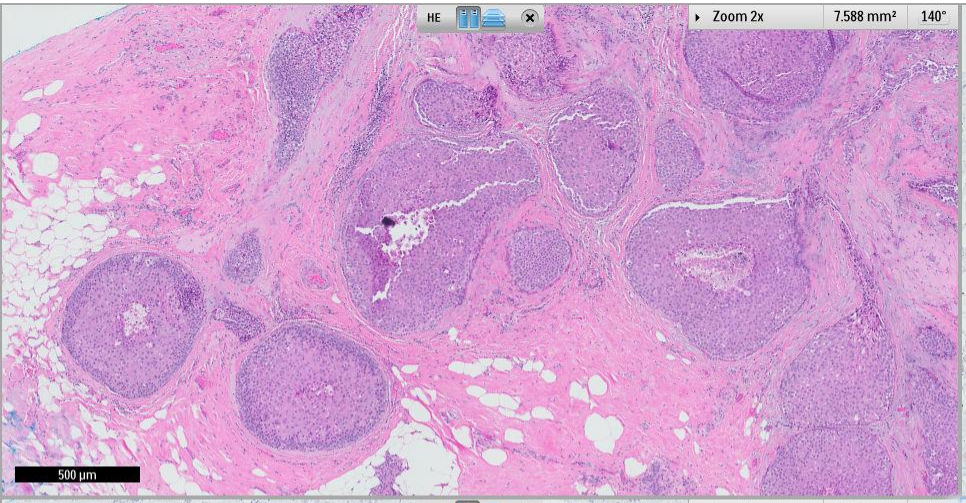


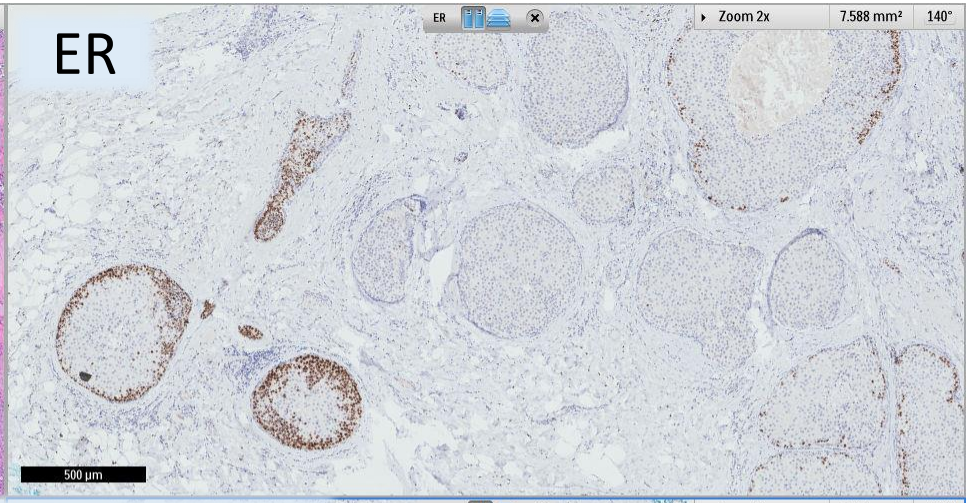
ER

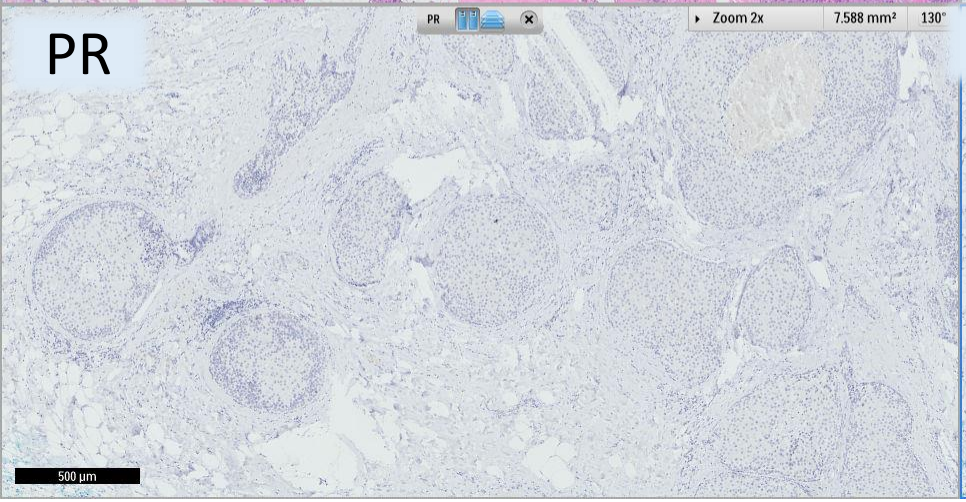


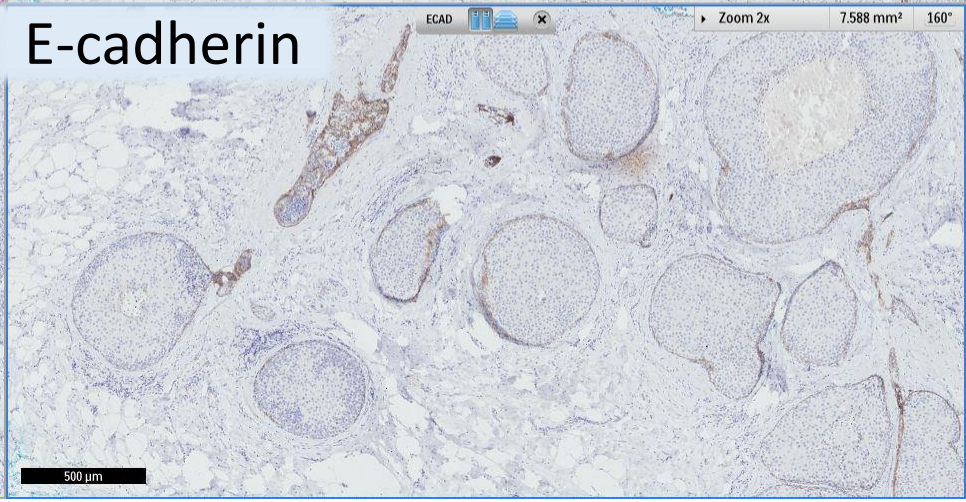
ER

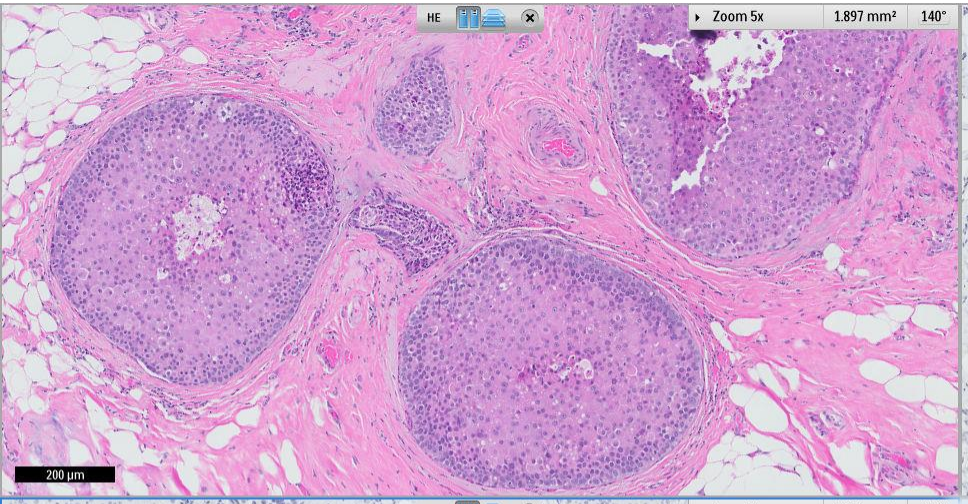


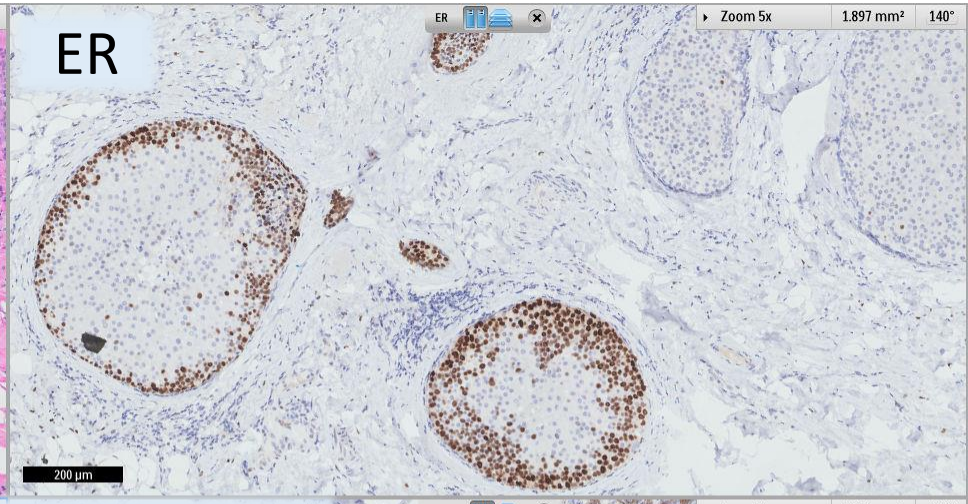

HE
Zoom 2x
7.588 mm²
140°
500 µm

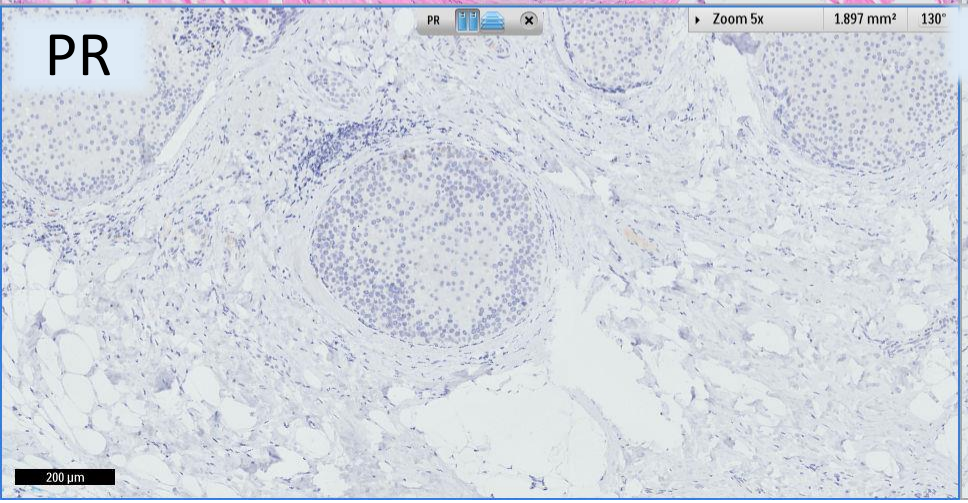

ER
ER
Zoom 2x
7.588 mm²
140°
500 µm

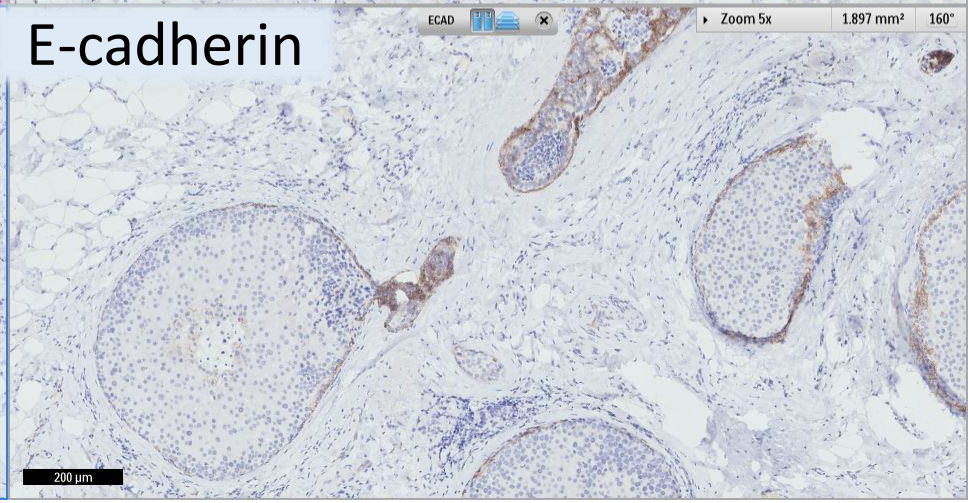

PR
PR
Zoom 2x
7.588 mm²
130°
500 µm

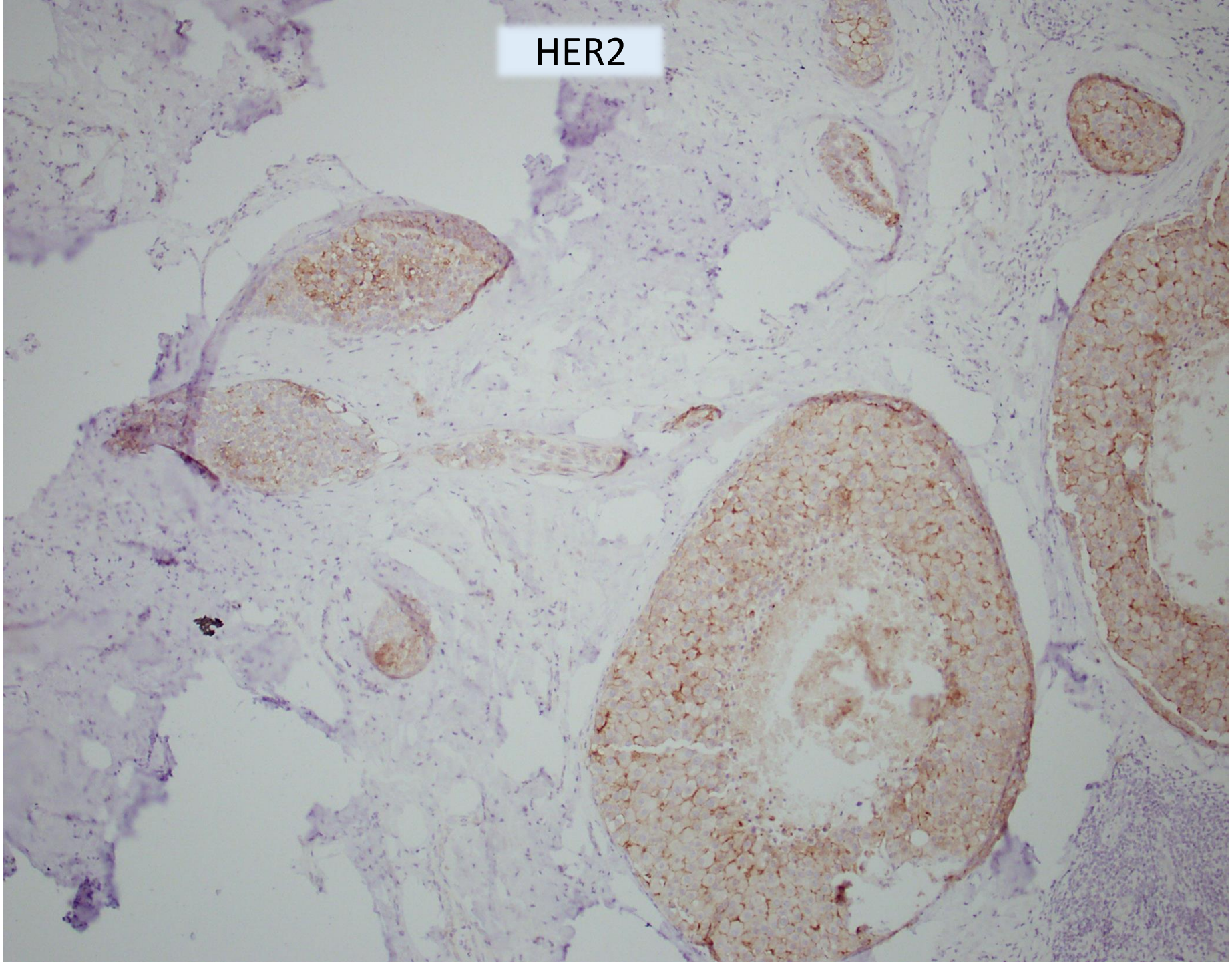

E-cadherin
ECAD
Zoom 2x
7.588 mm²
160°
500 µm

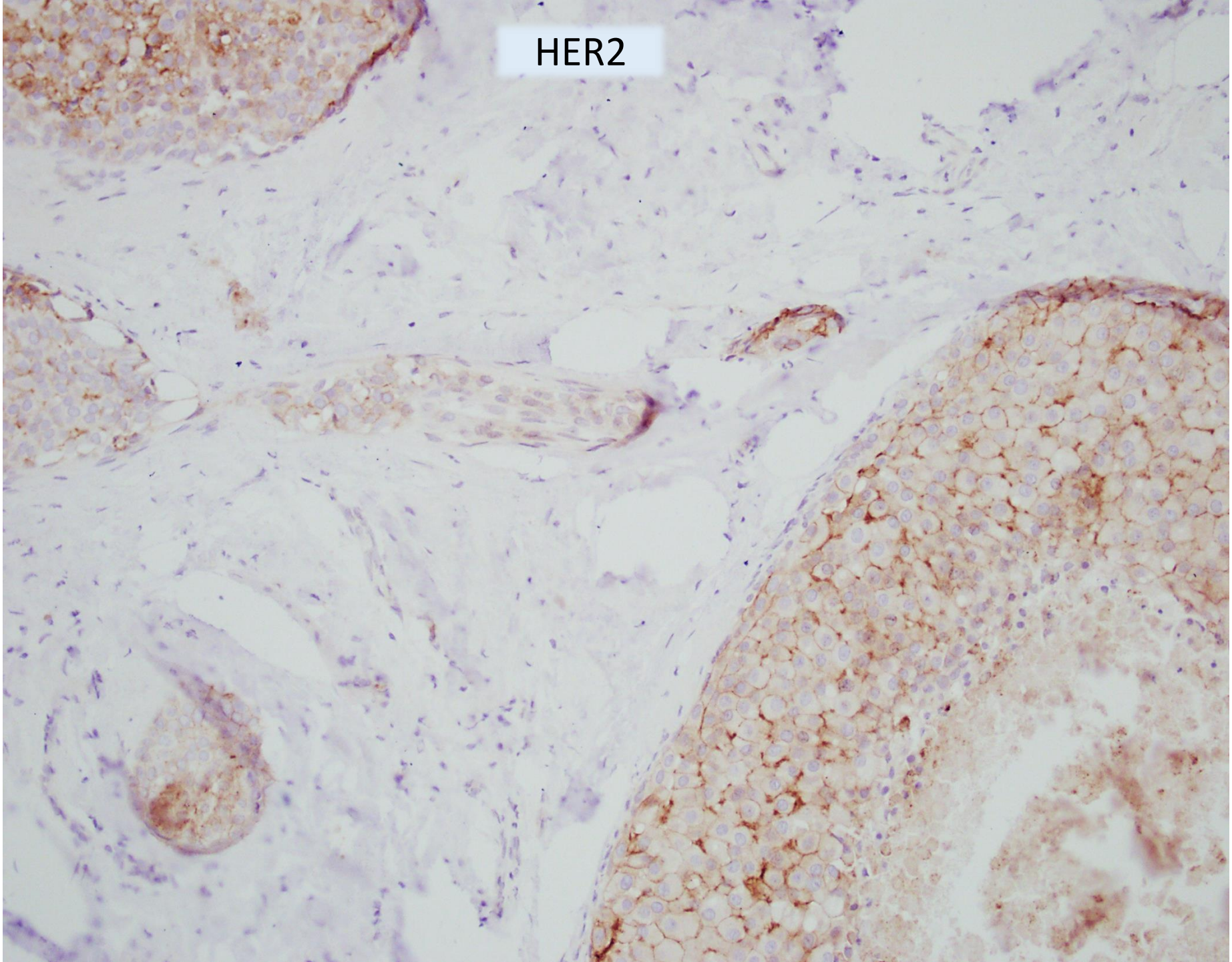

HE
Zoom 5x
1.897 mm²
140°
200 µm

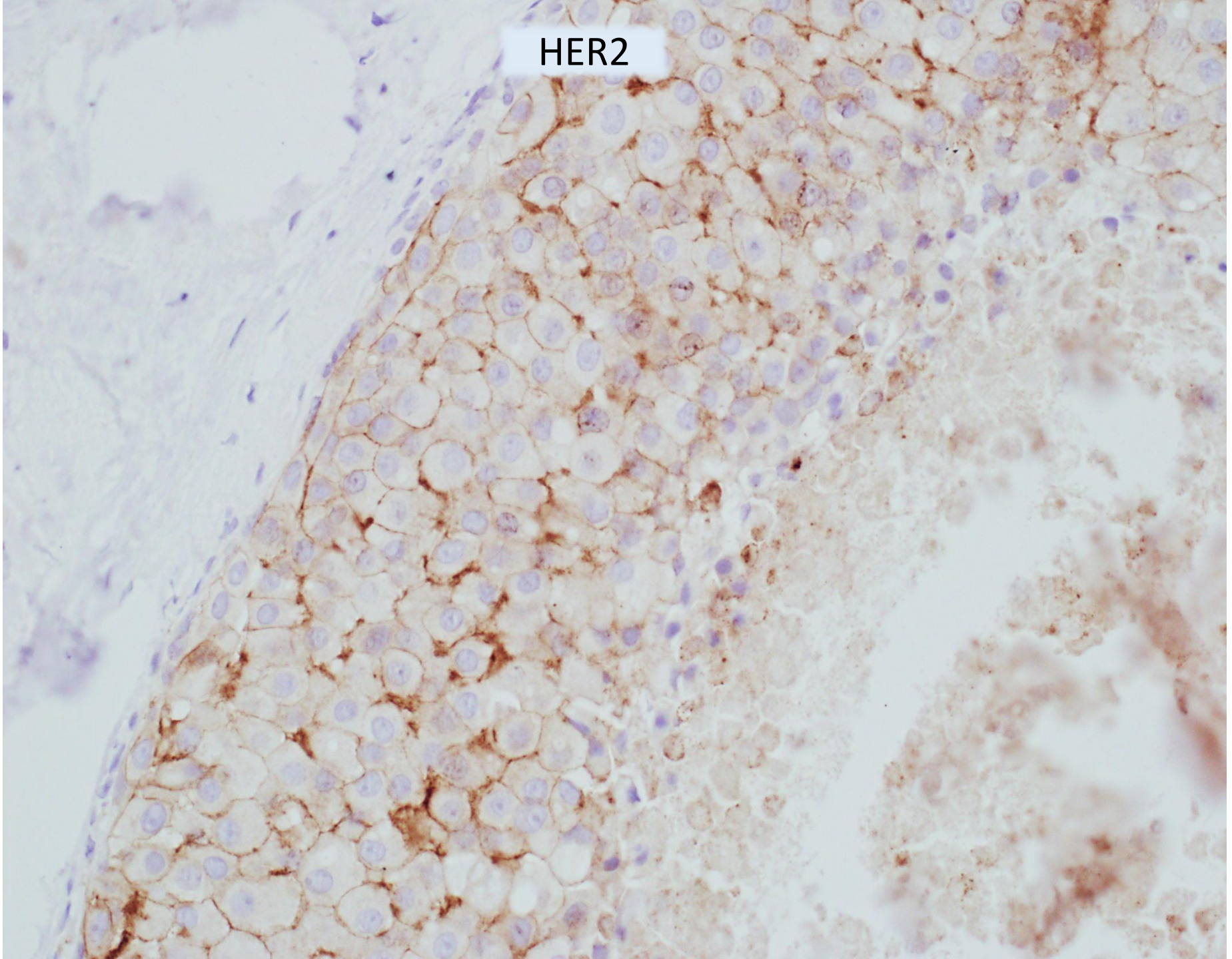

ER
ER
Zoom 5x
1.897 mm²
140°
200 µm


PR
PR
Zoom 5x
1.897 mm²
130°
200 µm


E-cadherin
ECAD
Zoom 5x
1.897 mm²
160°
200 µm


HER2


HER2


HER2

Breast Pathology Course 2017

Diagnosis:

Stereotactic vacuum assisted biopsy, left breast upper outer quadrant ~

Lobular carcinoma in situ, pleomorphic (apocrine) and classical forms

Singapore General Hospital
SingHealth
Division of Pathology

SingHealth DukeNUS
ACADEMIC MEDICAL CENTRE
PATHOLOGY

IAP
International Academy of Pathology
Singapore Division

Lobular neoplasia

- Encompasses both atypical lobular hyperplasia and lobular carcinoma in situ.
- Non-invasive, abnormal proliferation of discohesive cells within the lobule.
- Lobular neoplastic cells are characterised by aberration of the E-cadherin gene leading to a dysfunctional E-cadherin protein, an intercellular adhesion molecule.
- Lobular neoplasia usually features cells with uniform, rounded morphology referred to as type A cells, but it may also be composed of type B cells with moderate nuclear variation.

Lobular neoplasia

- Encountered in up to 4 % of breast core biopsies, often in premenopausal women.
- Usually an incidental lesion discovered during histologic evaluation of biopsy specimens and excisions performed for other clinicoradiological indications.
- No specific clinical or radiological characteristics of lobular neoplasia per se.
- Unusually, lobular neoplasia may be mass forming, resulting in clinical or radiological detection.
- Occasionally it can be associated with necrosis and calcifications leading to mammographic discovery.

Lobular neoplasia

- Lobular neoplasia can coexist with ~
  - columnar cell lesions
  - flat epithelial atypia
  - atypical ductal hyperplasia
  - low-grade invasive carcinoma

"*low nuclear grade neoplasia family*" of breast lesions

Lobular neoplasia

- Marked nuclear pleomorphism, often with apocrine cytomorphology, is sometimes seen in LCIS and is referred to as the ***pleomorphic*** *variant.*
- Necrosis and calcifications may be found in pleomorphic LCIS, but they can also be observed in classic forms of the disease.
- Lobular neoplasia with type B cells should not be diagnosed as pleomorphic LCIS.
- When required, E-cadherin immunohistochemistry can be used to confirm a lobular phenotype, displaying negative staining of the lobular neoplastic cells.
- It is important to be familiar with aberrant E-cadherin staining patterns.
- Other immunohistochemical markers include p120 catenin and β-catenin, which show cytoplasmic rather than membrane localization of staining.

Pleomorphic LCIS

- Lesions that show marked nuclear pleomorphism (equivalent to that seen in high-grade ductal carcinoma in situ, with or without apocrine features and comedo necrosis.
- Bi- and multinucleation (Am J Clin Pathol. 2015 Nov;144(5):722-6.)
- Lacks E-cadherin expression and displays genomic alterations by array-based comparative genomic hybridization (CGH) typical of lobular lesions (16q losses and 1q gains).
- More likely to be negative for ER, particularly in the apocrine variant, positive for HER2 and p53 and to have a higher Ki67 proliferative index.

Core biopsy diagnosis of LCIS

- Excision should be performed for the following ~
  - classical LCIS with comedo necrosis
  - bulky mass-forming LCIS lesions
  - pleomorphic LCIS
- Management of patients with ALH and classical LCIS when diagnosed on needle-core biopsy is controversial.
- Reported rates of upgrade to a worse lesion on excision vary widely due to variations in study design.
- There is consensus that excision should be performed if there is another lesion which by itself would warrant excision or if there is pathological-mammographic discordance.
- In cases where ALH or LCIS on core biopsy is a completely incidental finding, radiological–pathological correlation is recommended for determining further management.

High Nuclear Grade DCIS Versus Pleomorphic Lobular Carcinoma In Situ

- Pleomorphic LCIS is not infrequently mistaken for high nuclear grade DCIS with both lesions often showing comedonecrosis and calcifications.
- Clues to pleomorphic LCIS ~
  - cellular discohesion
  - presence of classic LCIS as well as atypical lobular hyperplasia.
- An apocrine cytomorphology is commonly associated with pleomorphic LCIS although apocrine features can also be found in high nuclear grade DCIS.
- Immunohistochemistry for E-cadherin can help make the distinction, though in many institutions, pleomorphic LCIS is often managed in a similar manner to DCIS.

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