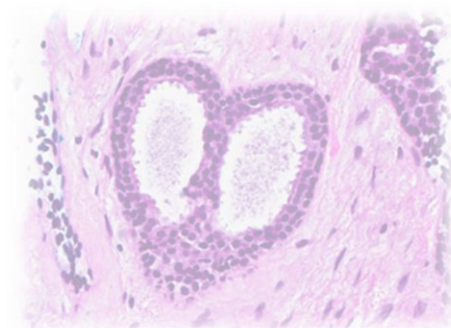
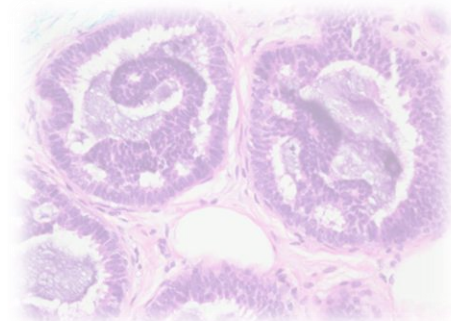
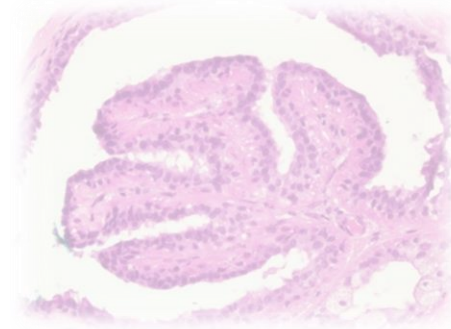
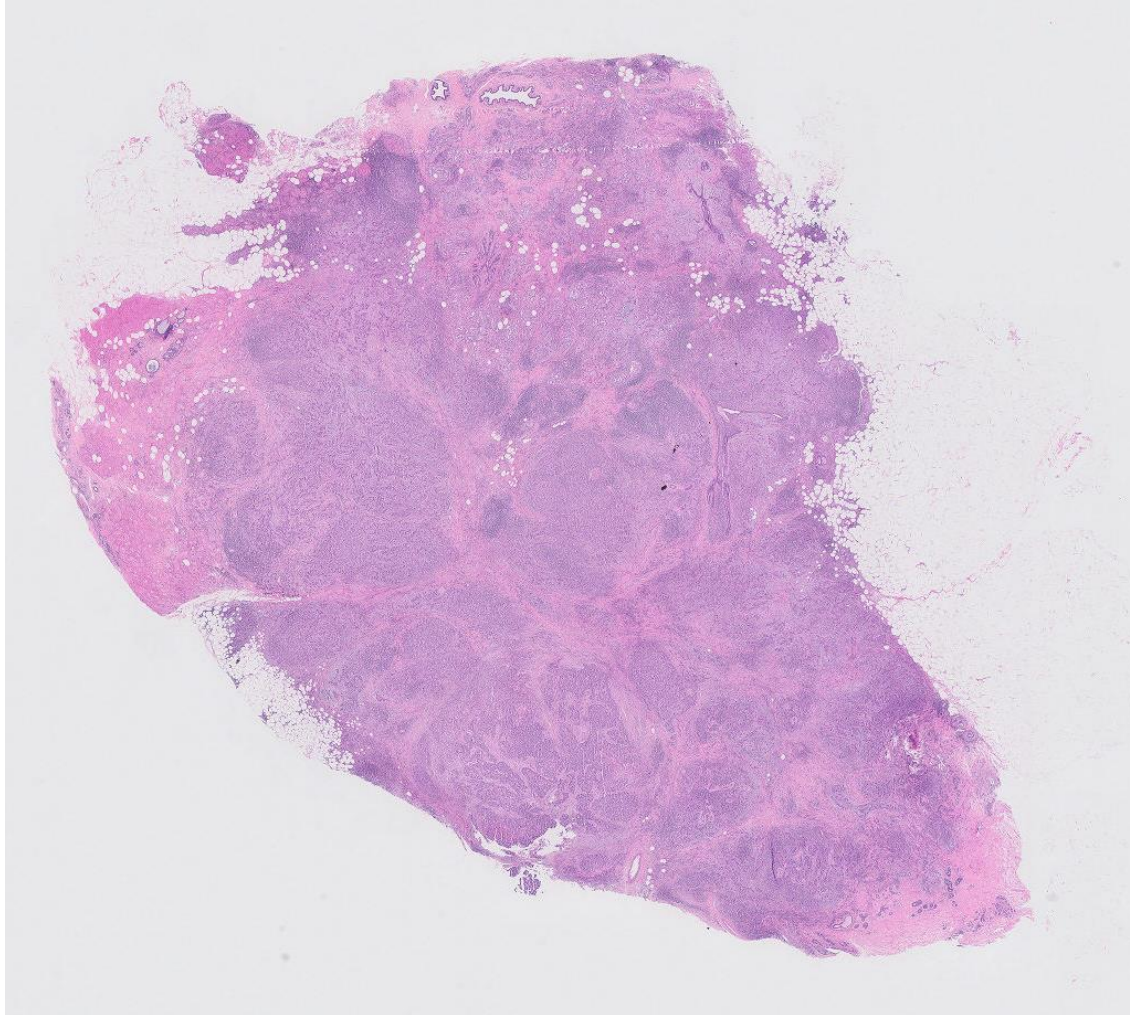


## Case 3

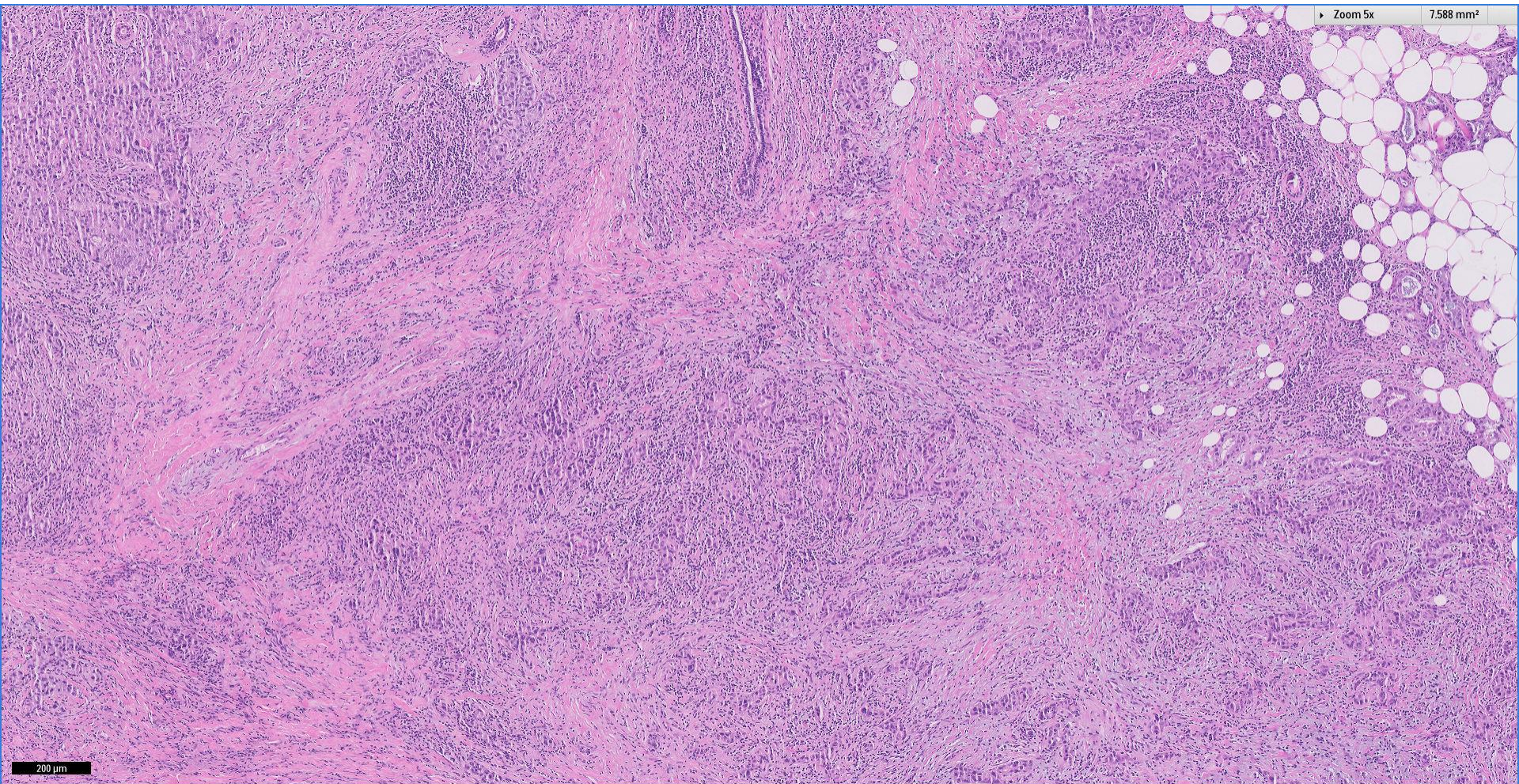
48 year old Indonesian female.  
Materials of a breast tumour  
submitted for histological review.

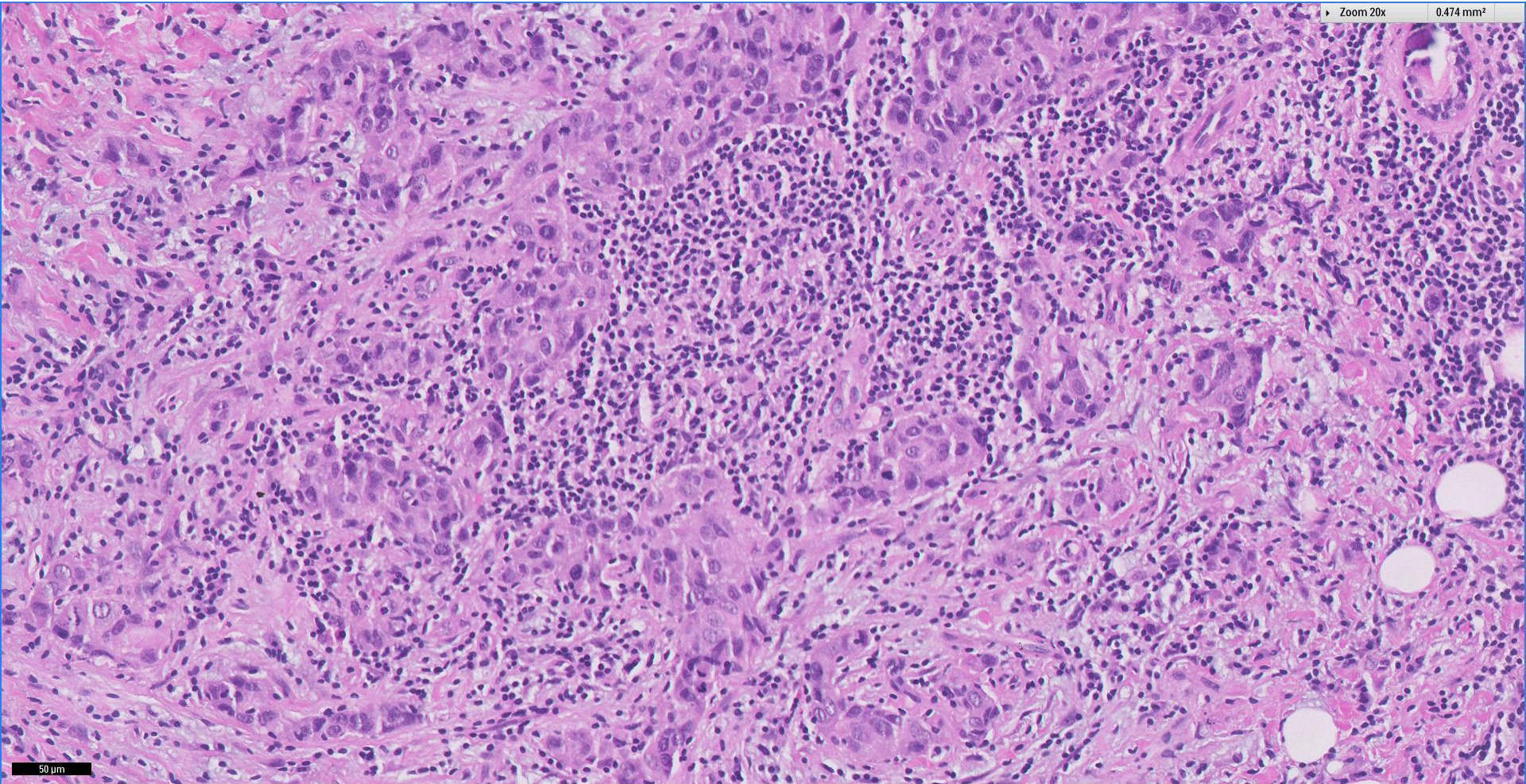


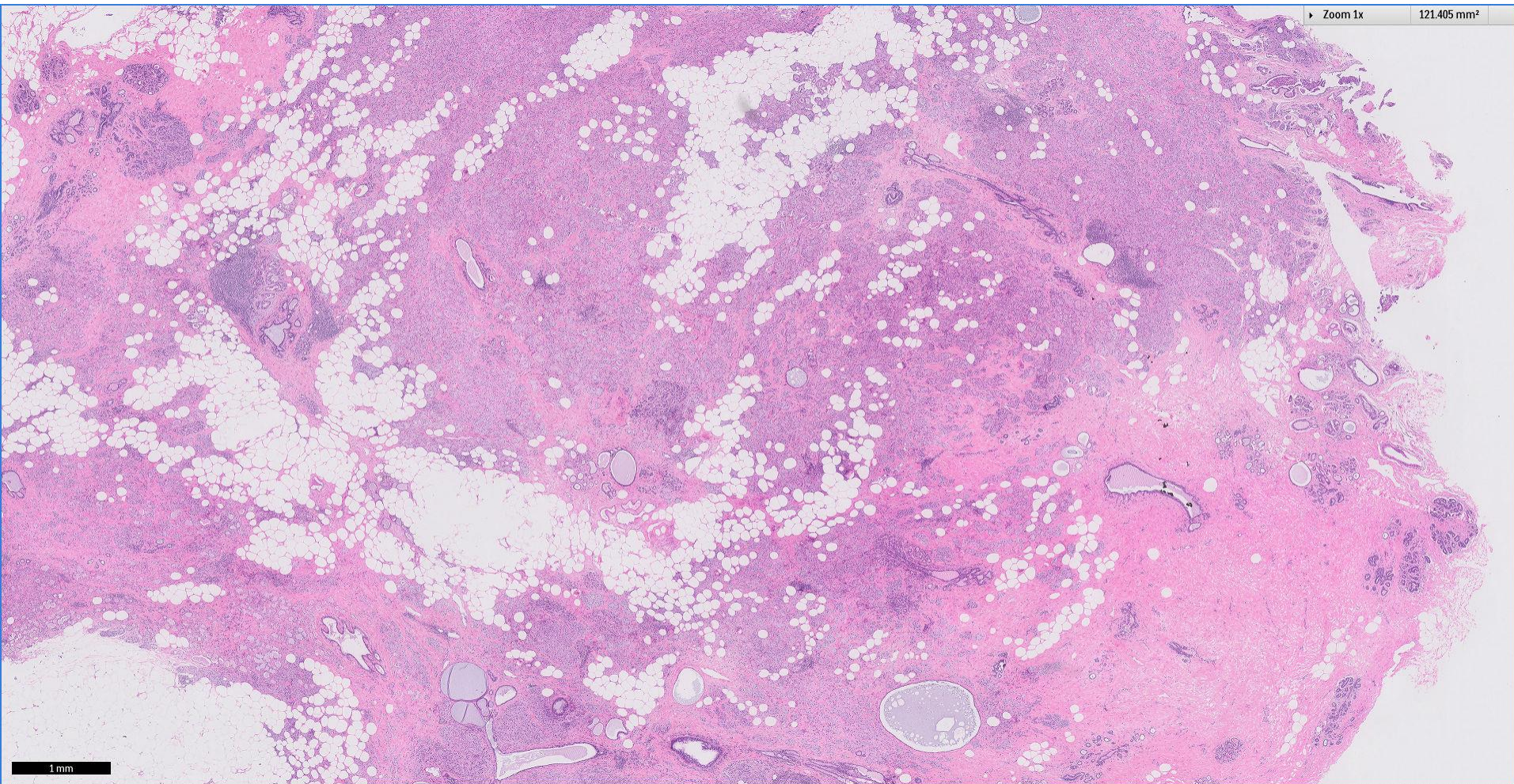


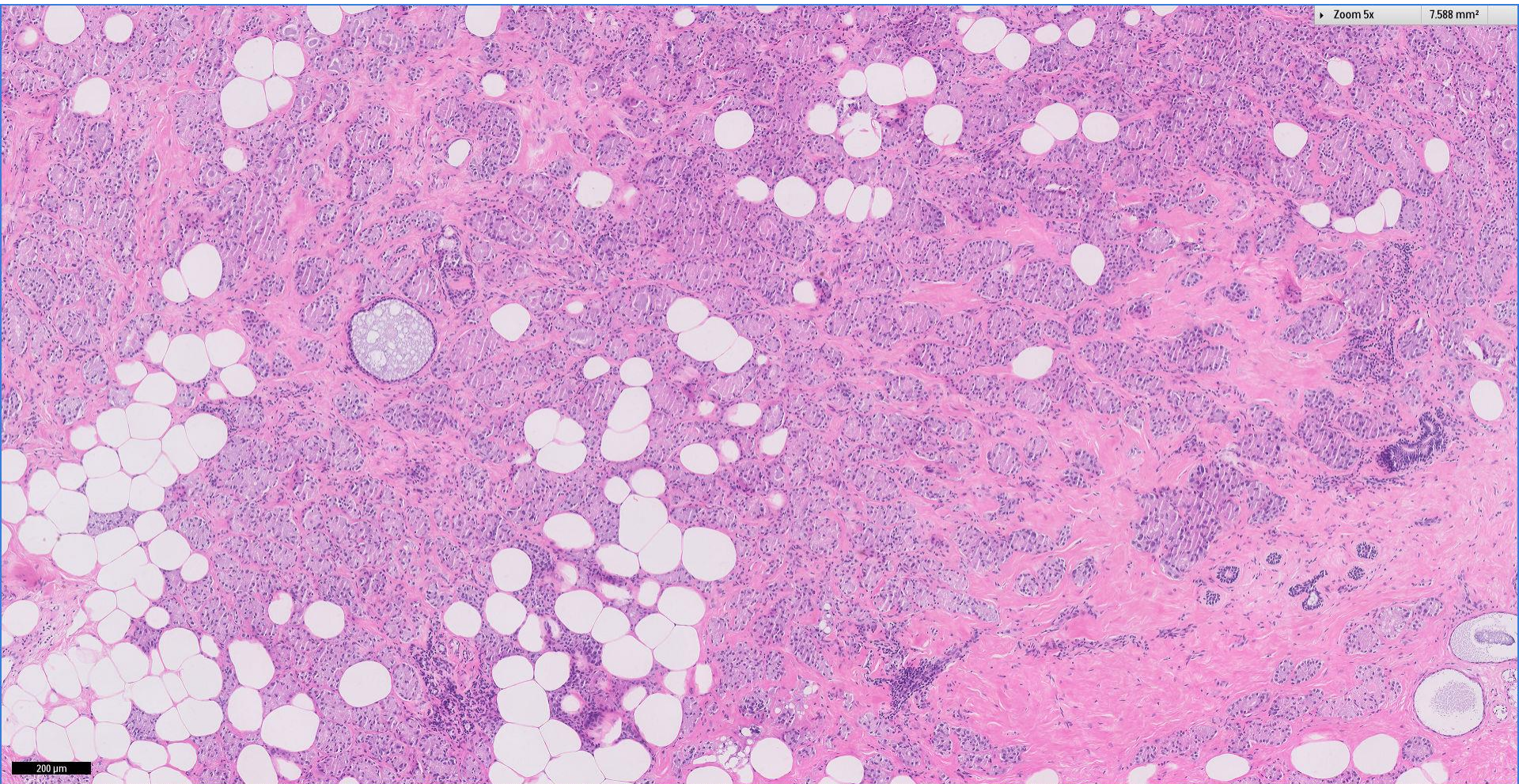
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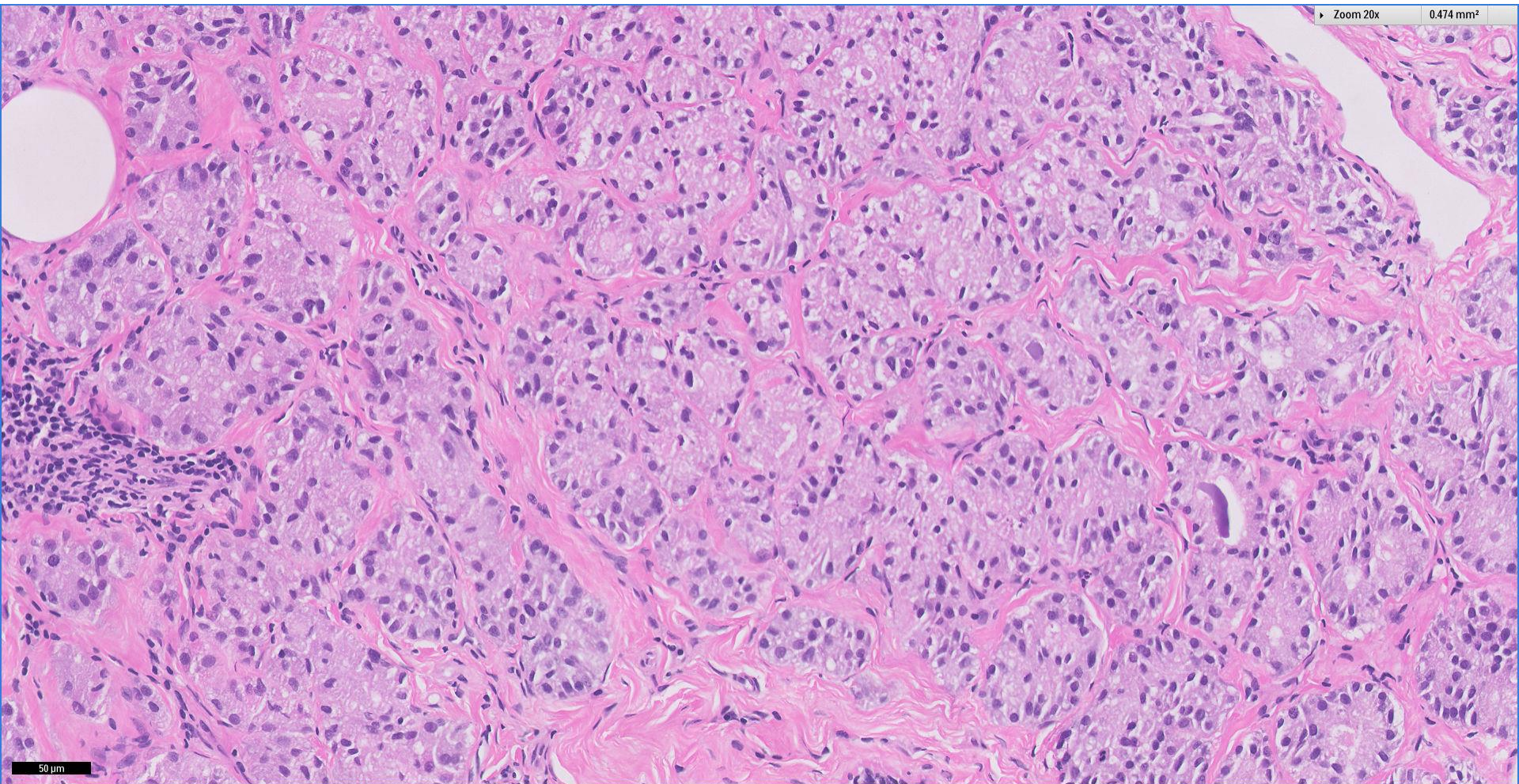


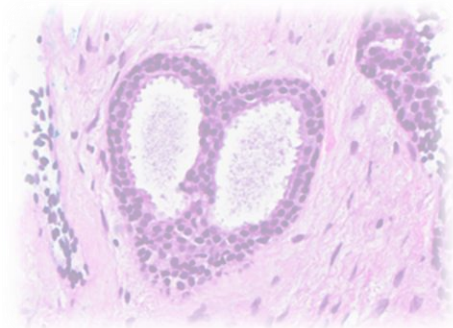
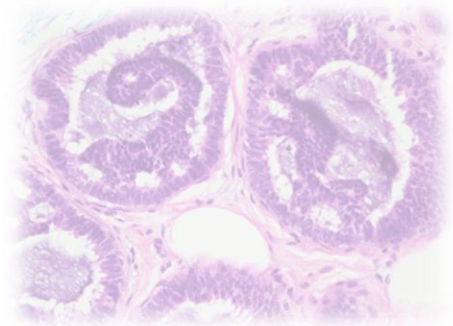
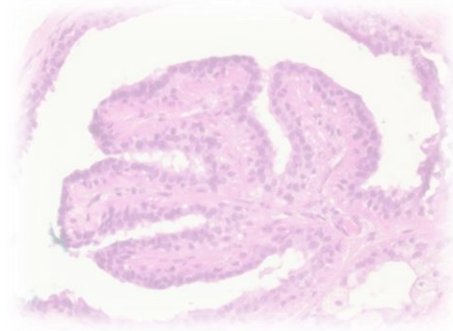






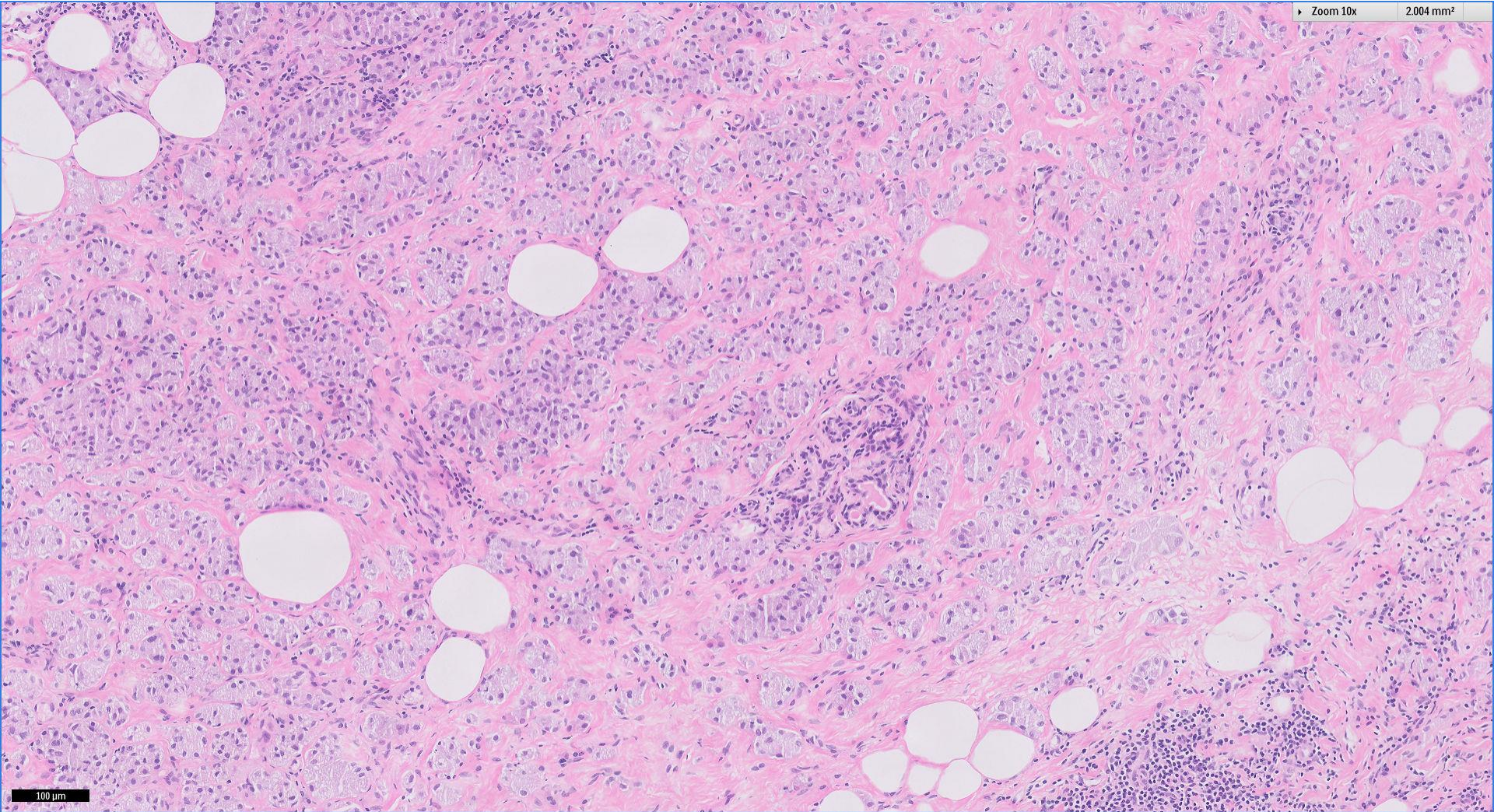






# *Additional pictures*

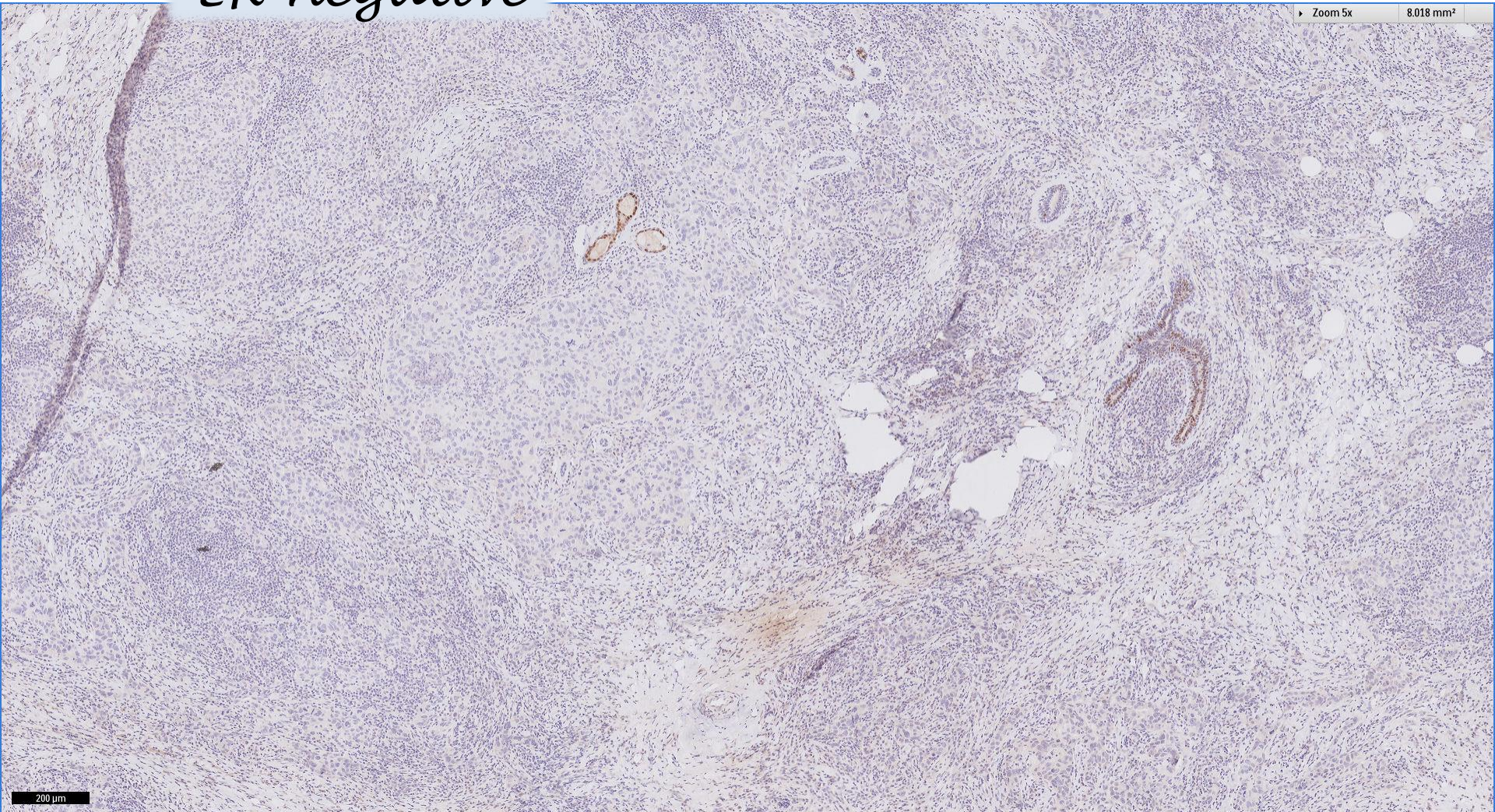




100 μm

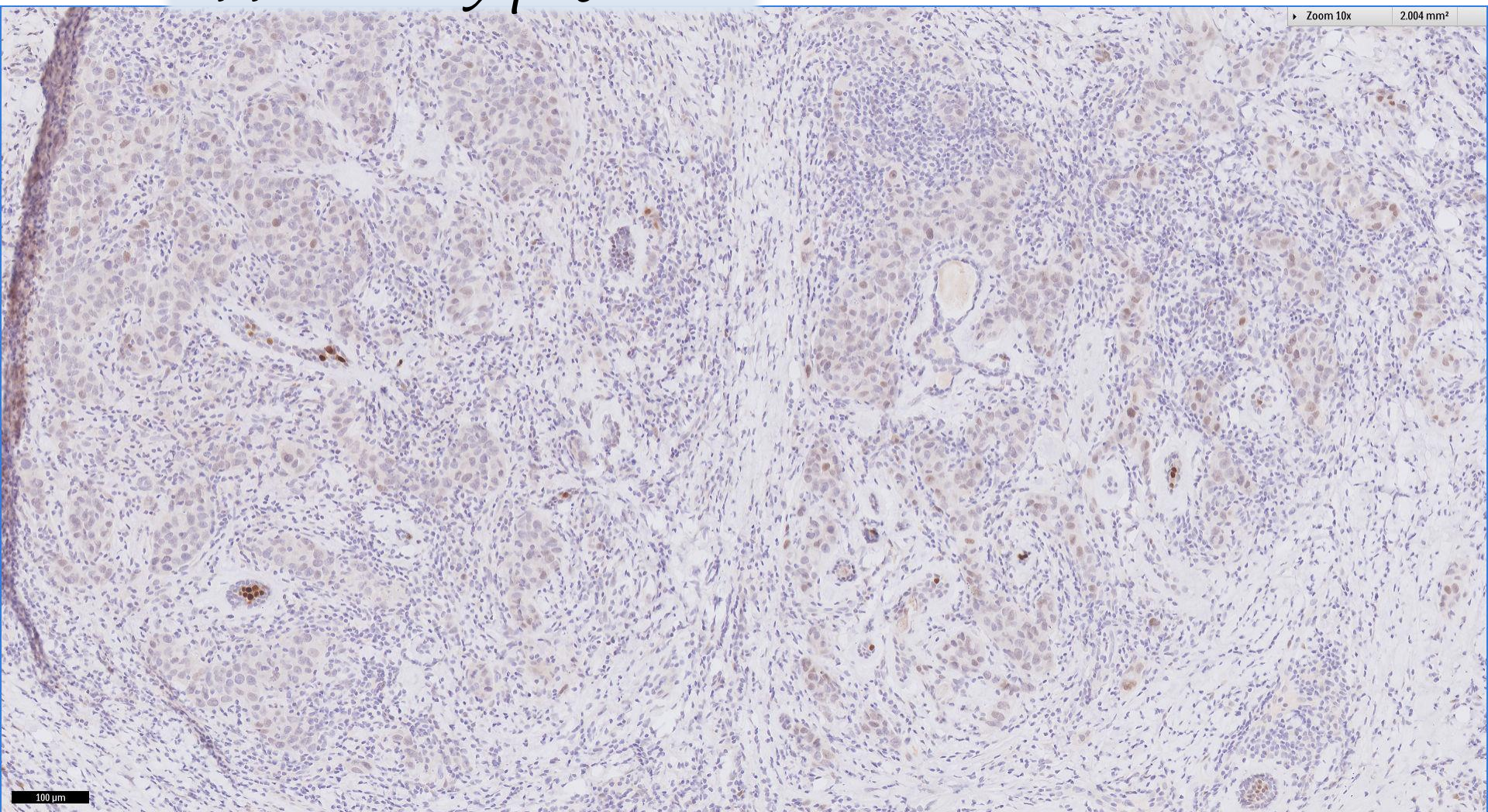
ER negative

Zoom 5x 8.018 mm<sup>2</sup>



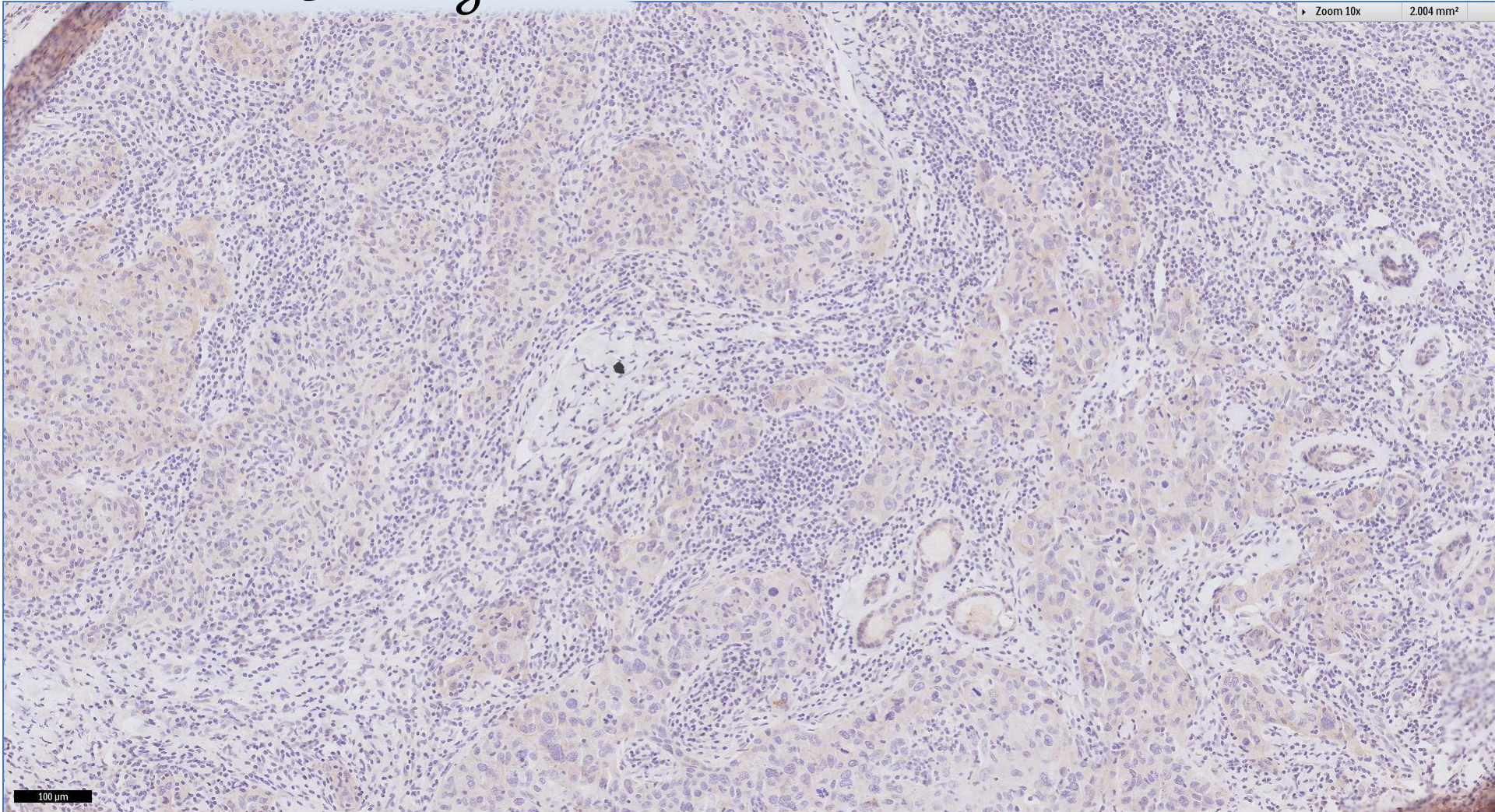
200 µm

*PR weakly positive*



*cerbB2 negative*

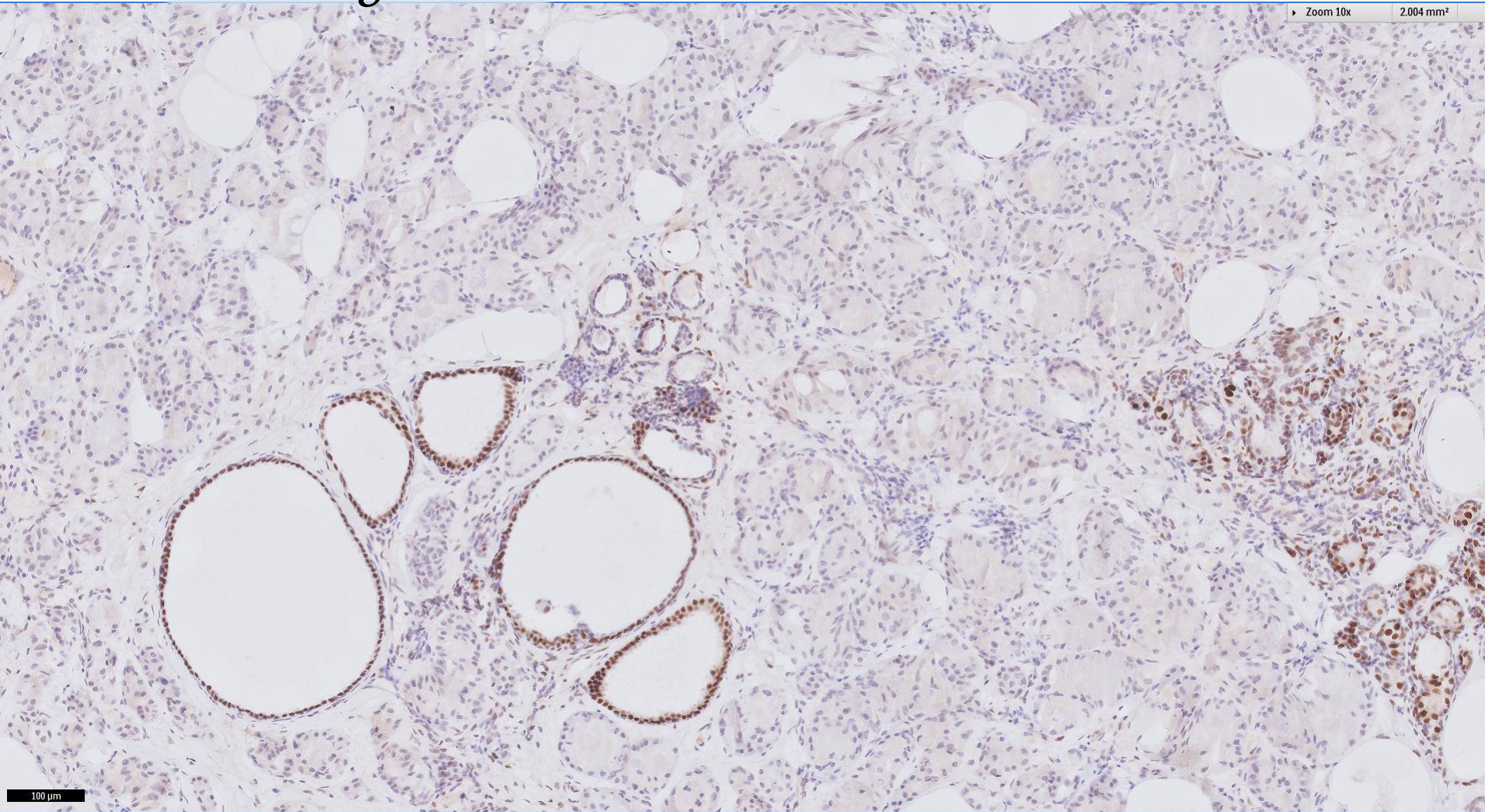
Zoom 10x 2.004 mm<sup>2</sup>



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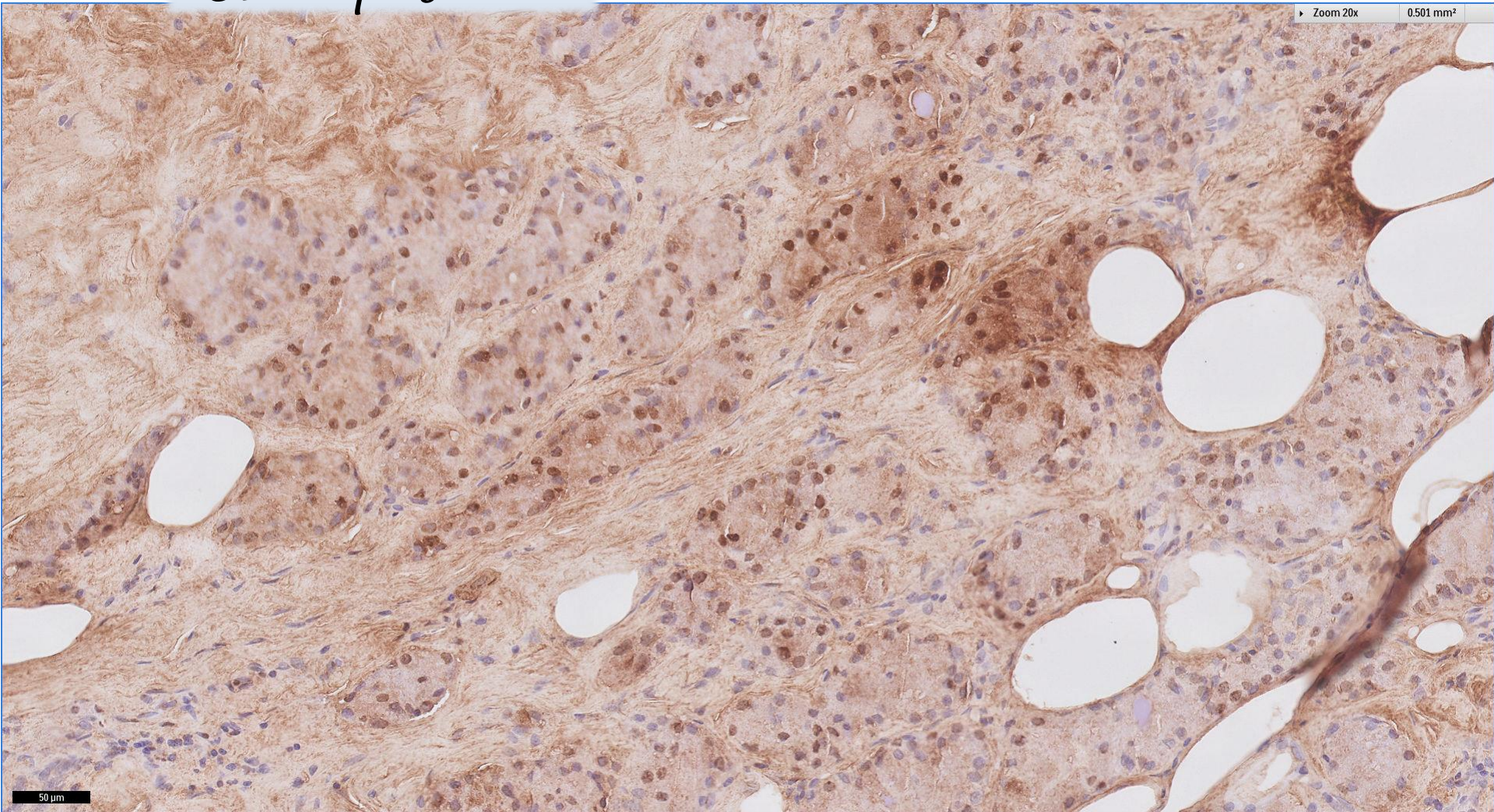
# AR negative



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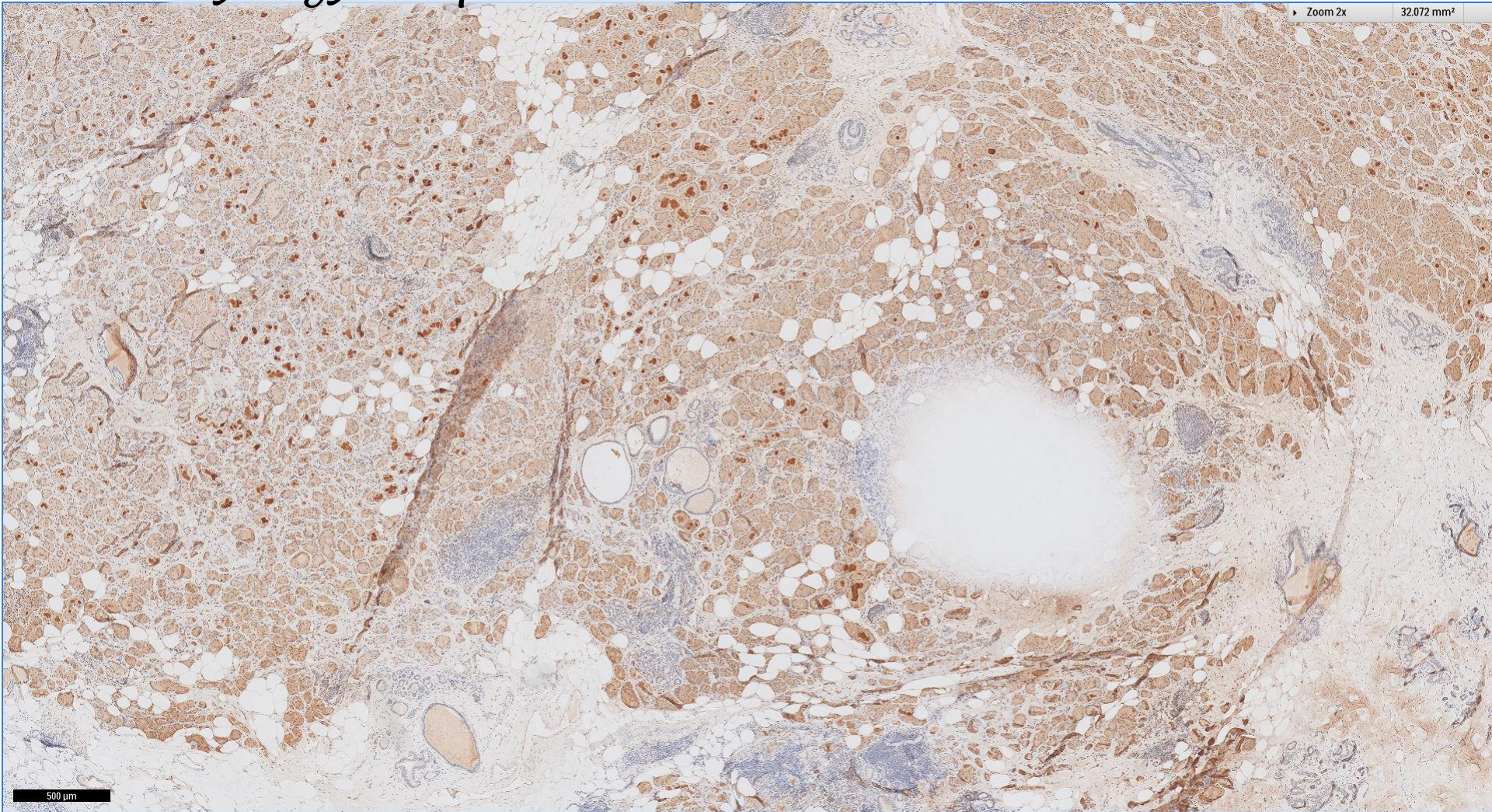


*S100 positive*



# Lysozyme positive

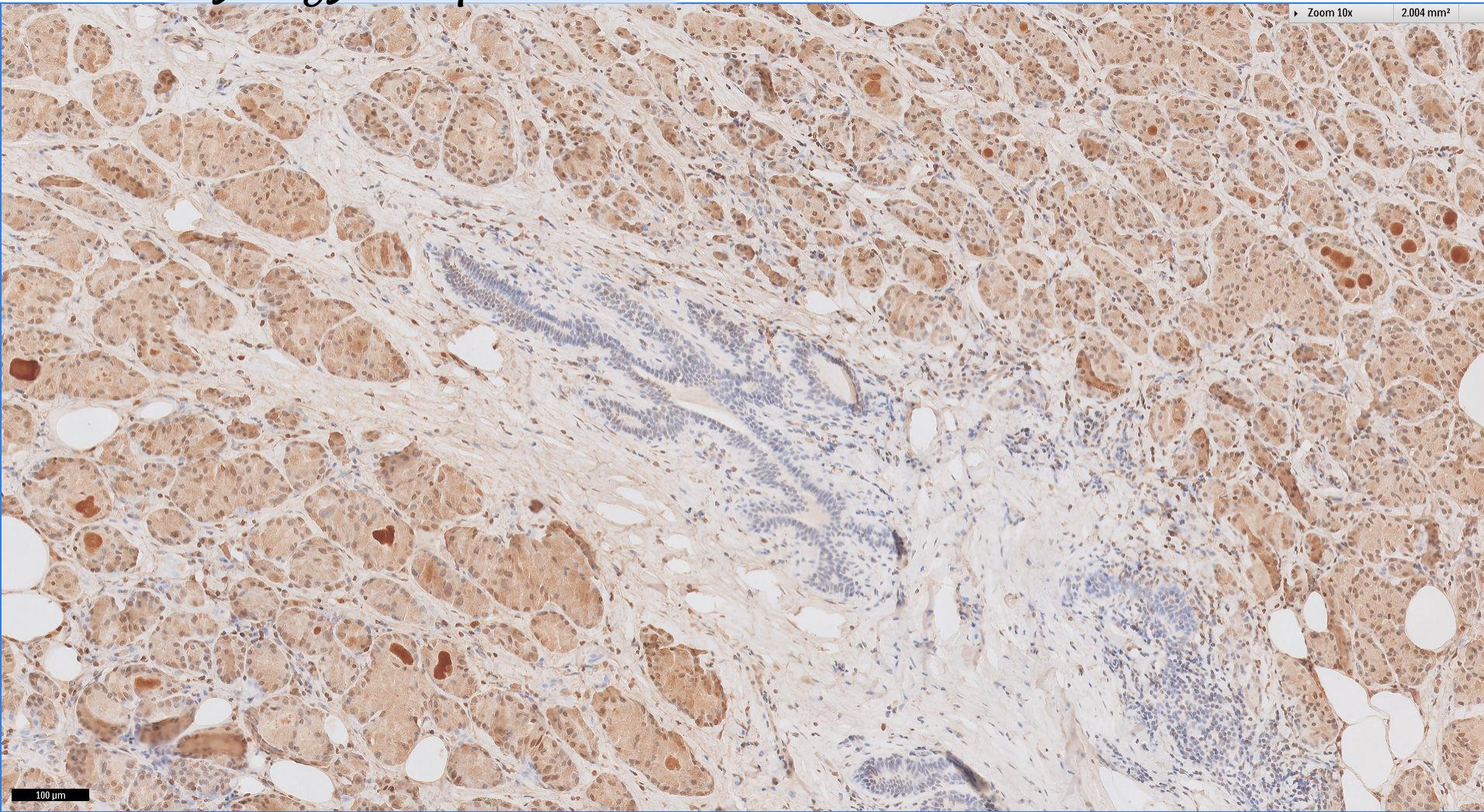
Zoom 2x 32.072 mm<sup>2</sup>



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# Lysozyme positive



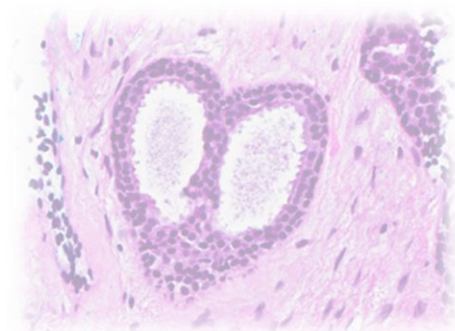
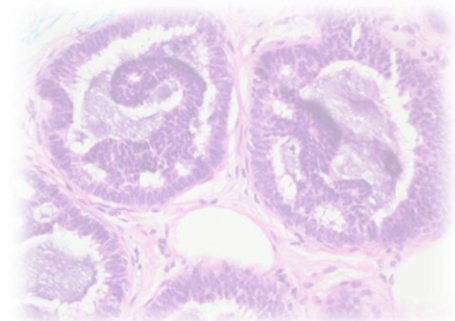
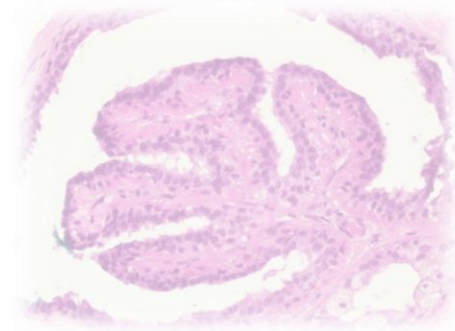
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# Diagnosis, case 3

- Submitted materials, breast tumour, laterality not specified:  
Invasive carcinoma with mixed ductal and acinic cell features, grade 3.  
ER negative, PR weakly positive (1+, 10%), cerbB2 negative.



# *Acinic cell carcinoma*

- Definition ~

Malignant epithelial neoplasm composed of clear and granular epithelial cells, some of which contain intracytoplasmic zymogen granules, arranged in microglandular and solid patterns.

**WHO 2019**

# Acinic cell carcinoma

WHO 2019

- **Localisation** ~
  - Any breast quadrant, with no site predilection.
- **Clinical features** ~
  - Adult women (aged 20–80 years).
  - A single case affecting the male breast has been reported.
  - Clinical presentation is similar to that of IBC-NST.
- **Epidemiology** ~
  - Rare subtype of invasive breast carcinoma.
  - Originally described by Roncaroli et al in 1996.
  - Subsequently better delineated by Damiani et al in 2000.
  - Thereafter, fewer than 50 cases have been described in the literature.
- **Etiology** ~
  - Unknown.

# Acinic cell carcinoma

WHO 2019

- **Pathogenesis** ~

- Breast glands can show acinic-like differentiation that can explain the development of acinic cell carcinoma.
- One case arose in a BRCA1-mutated patient.
- DNA copy-number and mutation landscape similar to that of triple-negative breast carcinomas of conventional histology or diagnosed in association with microglandular adenosis.
- Mutations of *TP53*, *PIK3CA*, *KMT2D*, *ERBB4*, *ERBB3*, *NEB*, *BRCA1*, *MTOR*, *CTNNB1*, *INPP4B*, and *FGFR2*.
- Mutation profiles differ from those of acinic cell carcinomas of the salivary glands, suggesting that these are not related entities, as opposed to most salivary gland-like tumours of the breast.

# *Acinic cell carcinoma*

WHO 2019

- **Macroscopy** ~
  - Same as that of invasive breast carcinoma NST.
  - Characterized by infiltrative nodules, hard in consistency, and ranging in size from 11 to 50 mm.
  - Report of one case arising within a fibroadenoma.

# *Acinic cell carcinoma*

WHO 2019

- **Microscopy** ~

- Great variety of architectural patterns.
- Range from a microglandular proliferation to solid areas often centred on necrosis.
- Two architectural patterns frequently merge together.
- Diagnosis is based on recognition of the cytological features.
- Neoplastic cells have abundant, variably eosinophilic and basophilic granular cytoplasm, imparting a variegated appearance.
- PASD staining reveals intracellular, large, coarse eosinophilic granules.
- Intracytoplasmic granules are clearly evident on ultrastructural examination.
- The cytoplasm is sometimes clear.
- The nucleus is centrally located and atypical, with a prominent nucleolus.
- Neoplastic cells show various degrees of atypia.
- Cellular atypia and mitotic figures are more prominent in the solid areas.
- Ductal carcinoma in situ of high nuclear grade can be present.

# *Acinic cell carcinoma*

WHO 2019

- **Immunohistochemistry** (positive stains) ~
  - Lysozyme
  - $\alpha$ 1-antichymotrypsin
  - S100
  - EMA
  - Low-molecular-weight cytokeratins
  - Focal positivity for GCDFP-15

# Acinic cell carcinoma

WHO 2019

- **Differential diagnosis:**
  - Wide range of breast tumours, including high-grade invasive carcinomas and secretory carcinoma.
  - Distinction based on cell features, especially on the presence of intracytoplasmic granules and markers of serous acinar differentiation.
  - Tumours with bland nuclear morphology can raise suspicion of secretory carcinoma of the breast, but ***acinic cell carcinoma lacks the  $t(12;15)$  ETV6-NTRK3 translocation that is typically present in secretory carcinoma.***



# *Acinic cell carcinoma*

WHO 2019

- **Cytology** ~
  - Hypercellular, as seen in breast carcinomas NST.
  - Intracytoplasmic coarse granules are useful for correct diagnosis.
- **Diagnostic molecular pathology** ~
  - Consistently negative for ER and PR.
  - ERBB2 (HER2) amplification has not been demonstrated.
  - AR immunoreactivity has been documented.

# *Acinic cell carcinoma*

WHO 2019

- **Essential & desirable criteria ~**

Essential:

- Neoplastic cells with eosinophilic and basophilic granular cytoplasm and PASD-positive intracytoplasmic granules.
- Immunohistochemical positivity for EMA and markers of serous acinar differentiation.

# Acinic cell carcinoma

- **Staging**

WHO 2019

According to TNM system.

- **Prognosis & prediction**

Prognostic information is still limited.

Available data indicate that acinic cell carcinoma is a triple-negative carcinoma with intermediate aggressive potential.

In one review, axillary node metastases were present in 9 of 30 cases, and 3 patients developed metastases to the liver, bone, and lung, leading to death in 2 cases {*Pathology. 2017 Feb;49(2):215–27*}.

Most patients are alive with no evidence of recurrence 6–184 months after the (mean: 42 months).

Most patients underwent chemotherapy and radiotherapy in addition to surgery. Available molecular evidence may support the contention that acinic cell carcinoma could be the precursor of more-aggressive forms of triple-negative breast carcinomas.

*Thank You*