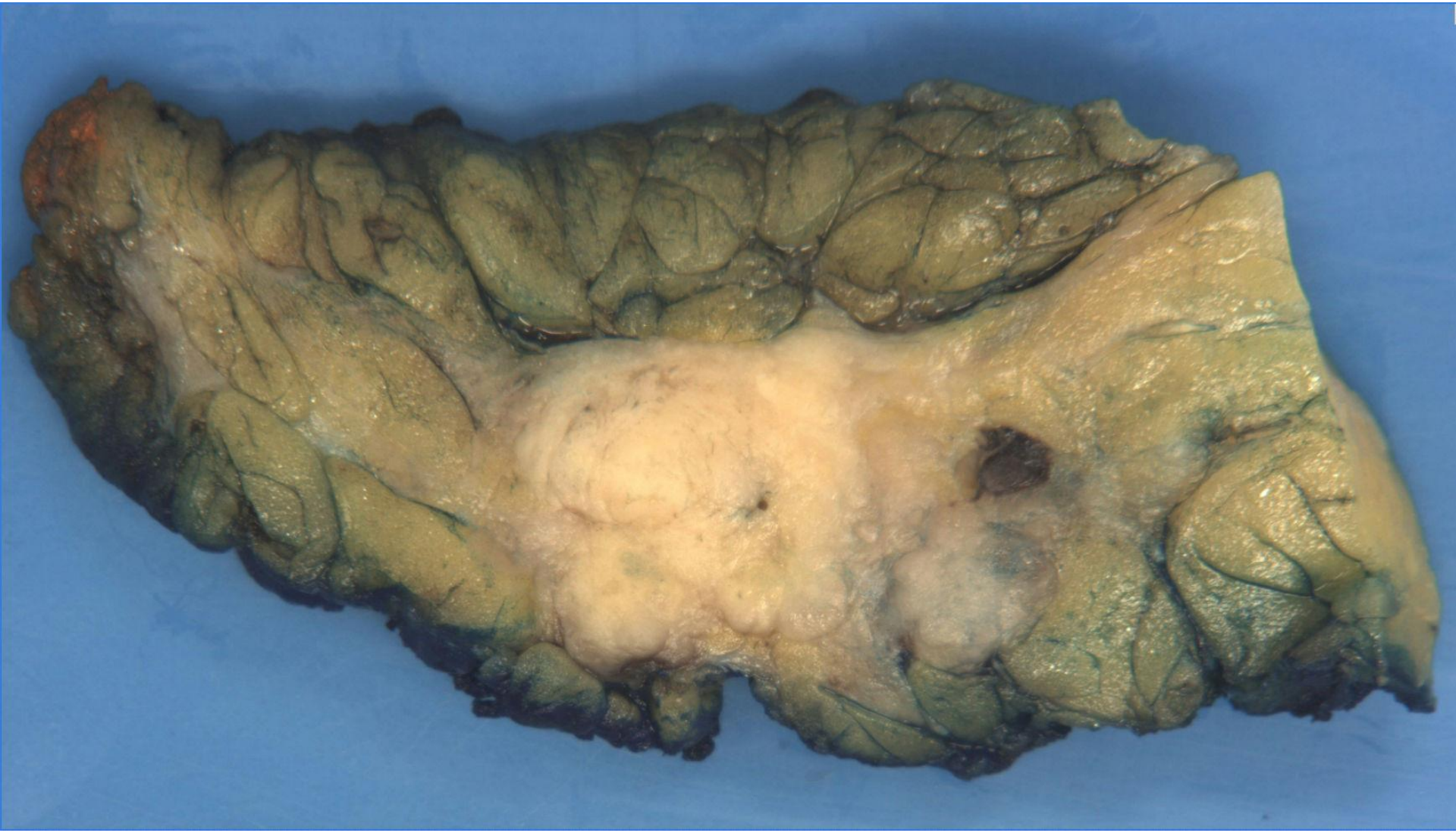
Breast Pathology Course 2017

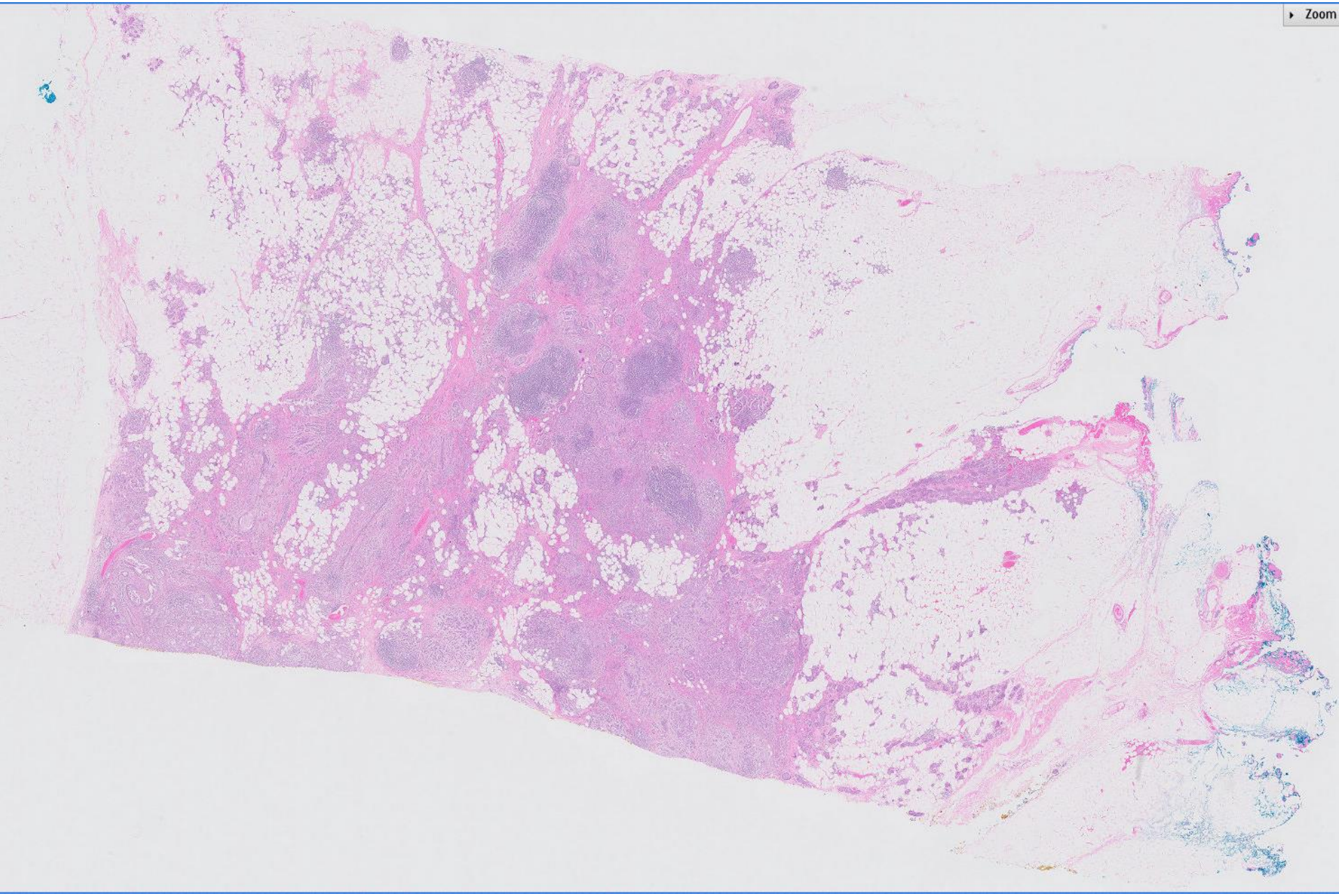
Case 25

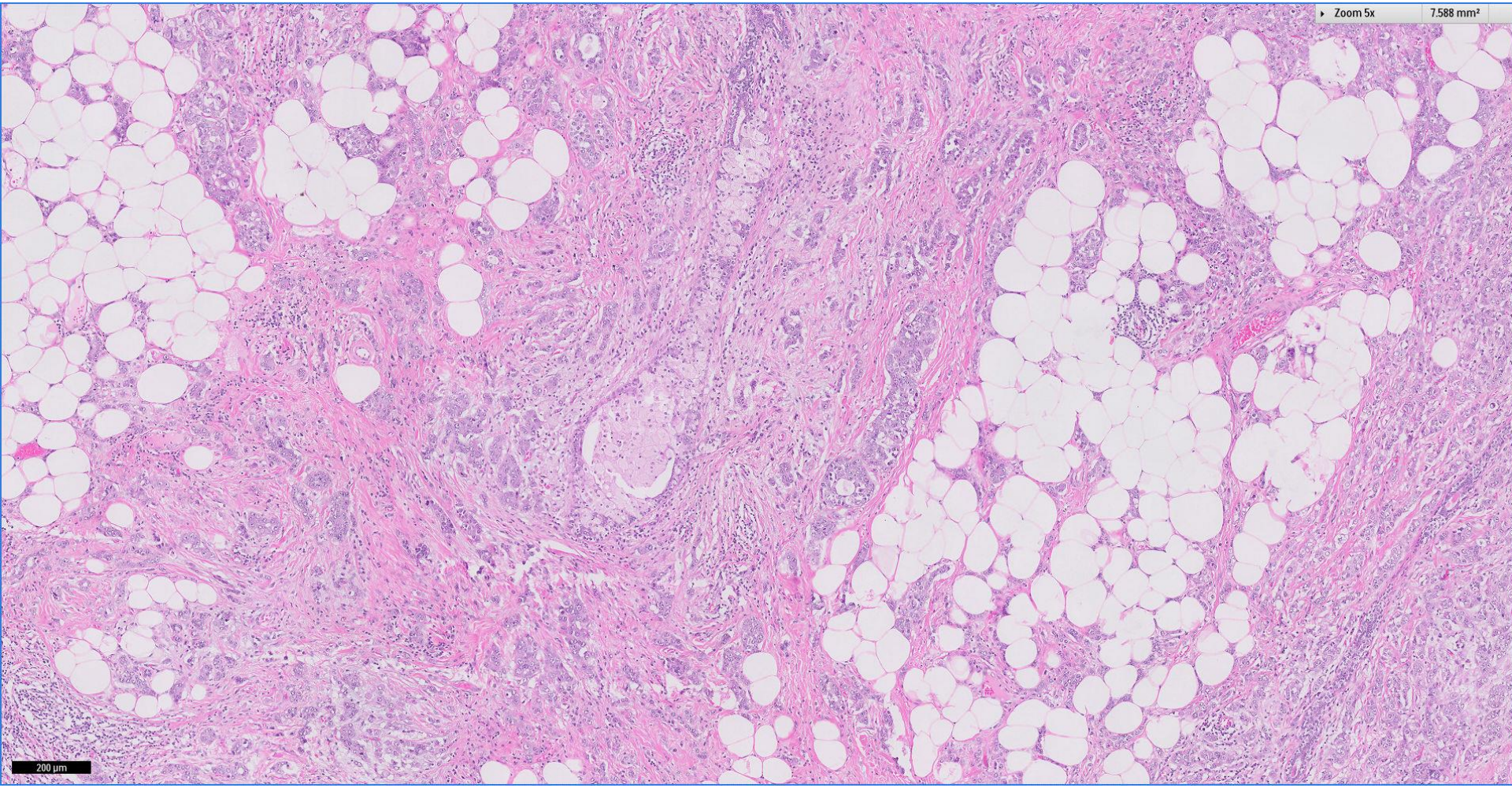
48 year old Chinese woman underwent right nipple sparing mastectomy and axillary clearance after a core biopsy of a right breast mass diagnosed an invasive carcinoma with ductal features.

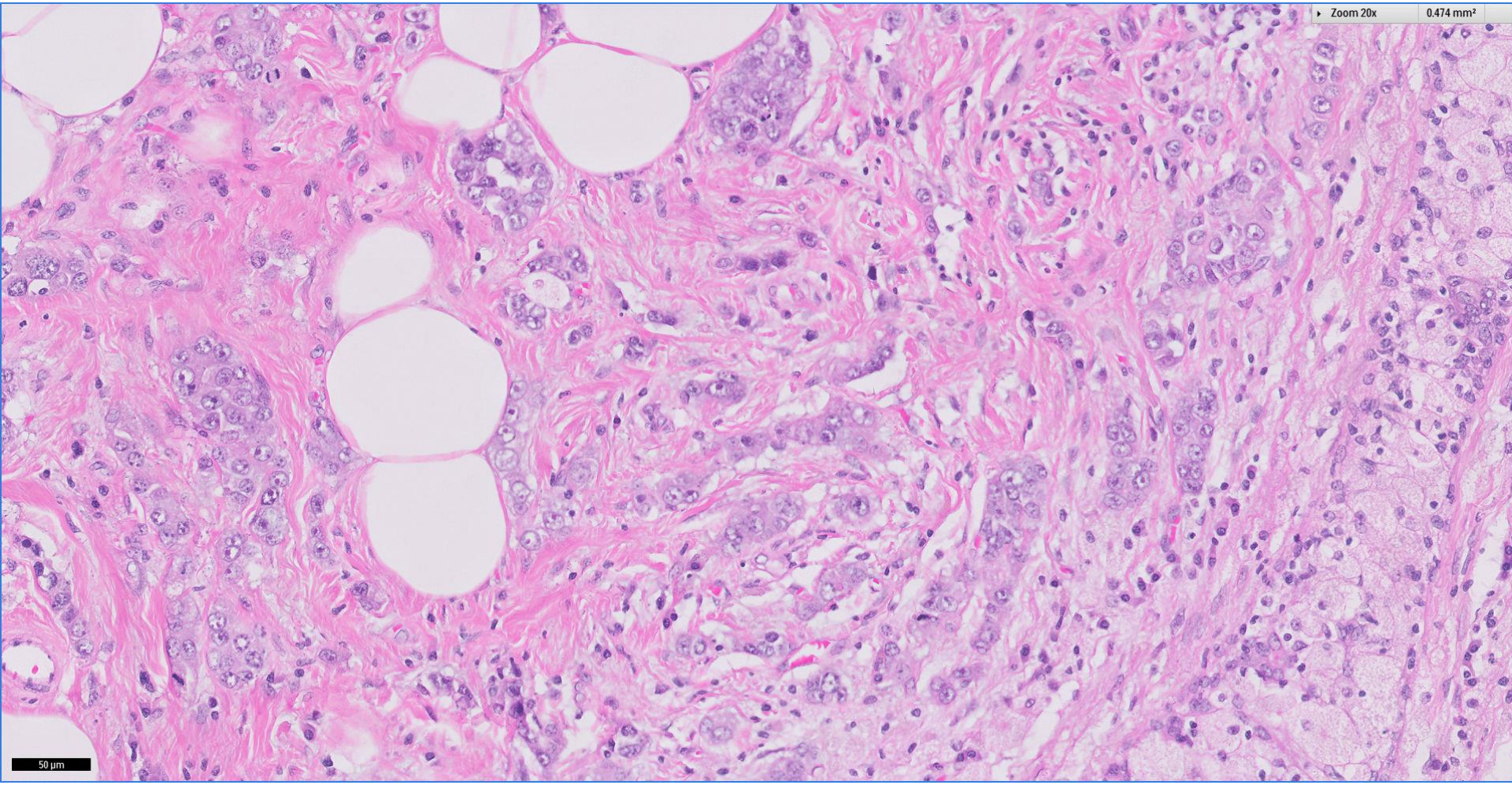
Sections from the right breast mass.

Singapore General Hospital
SingHealth
Division of Pathology
SingHealth DukeNUS ACADEMIC MEDICAL CENTRE
PATHOLOGY
IAP International Academy of Pathology Singapore Division




Zoom


Zoom 5x
7.588 mm²
200 µm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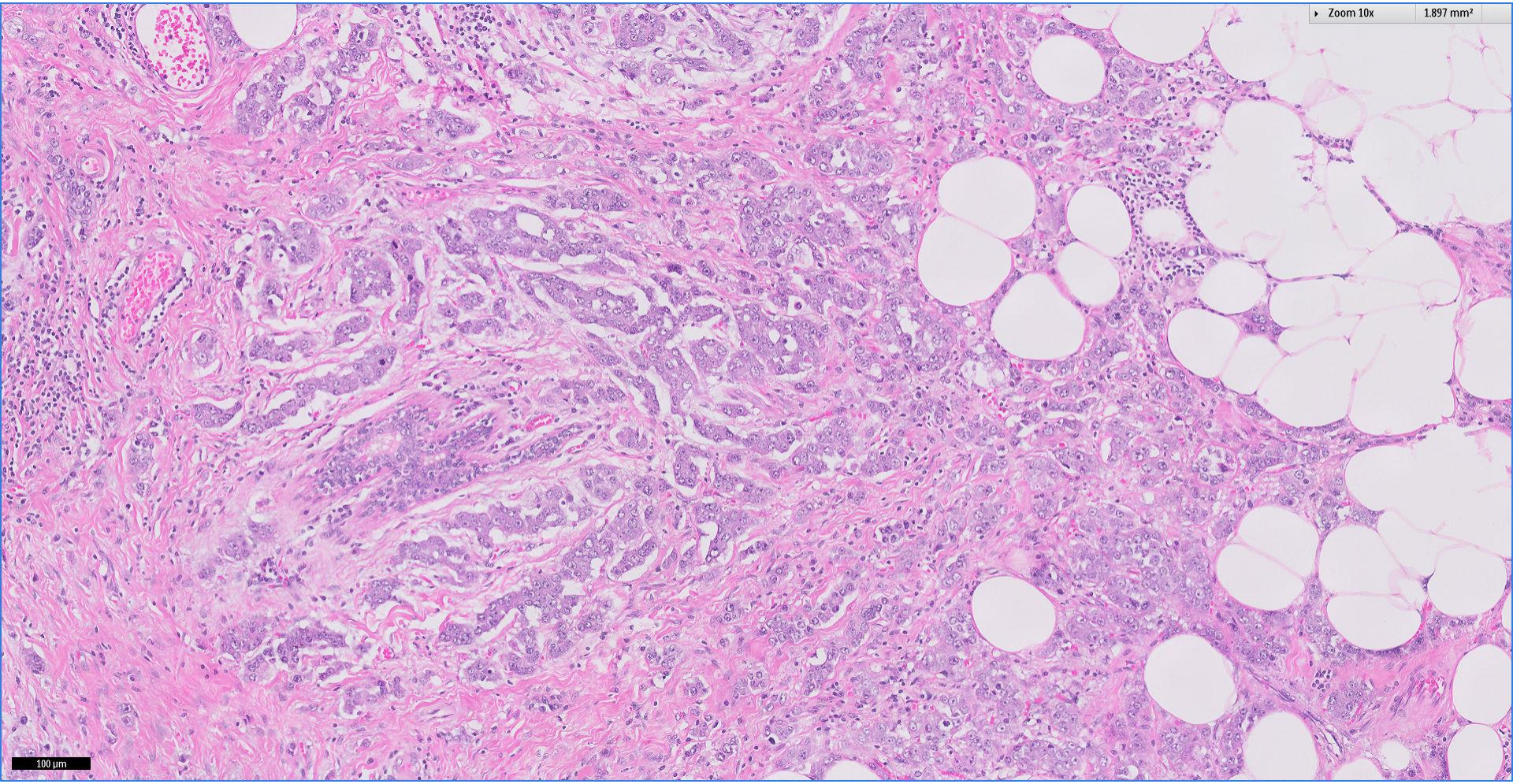
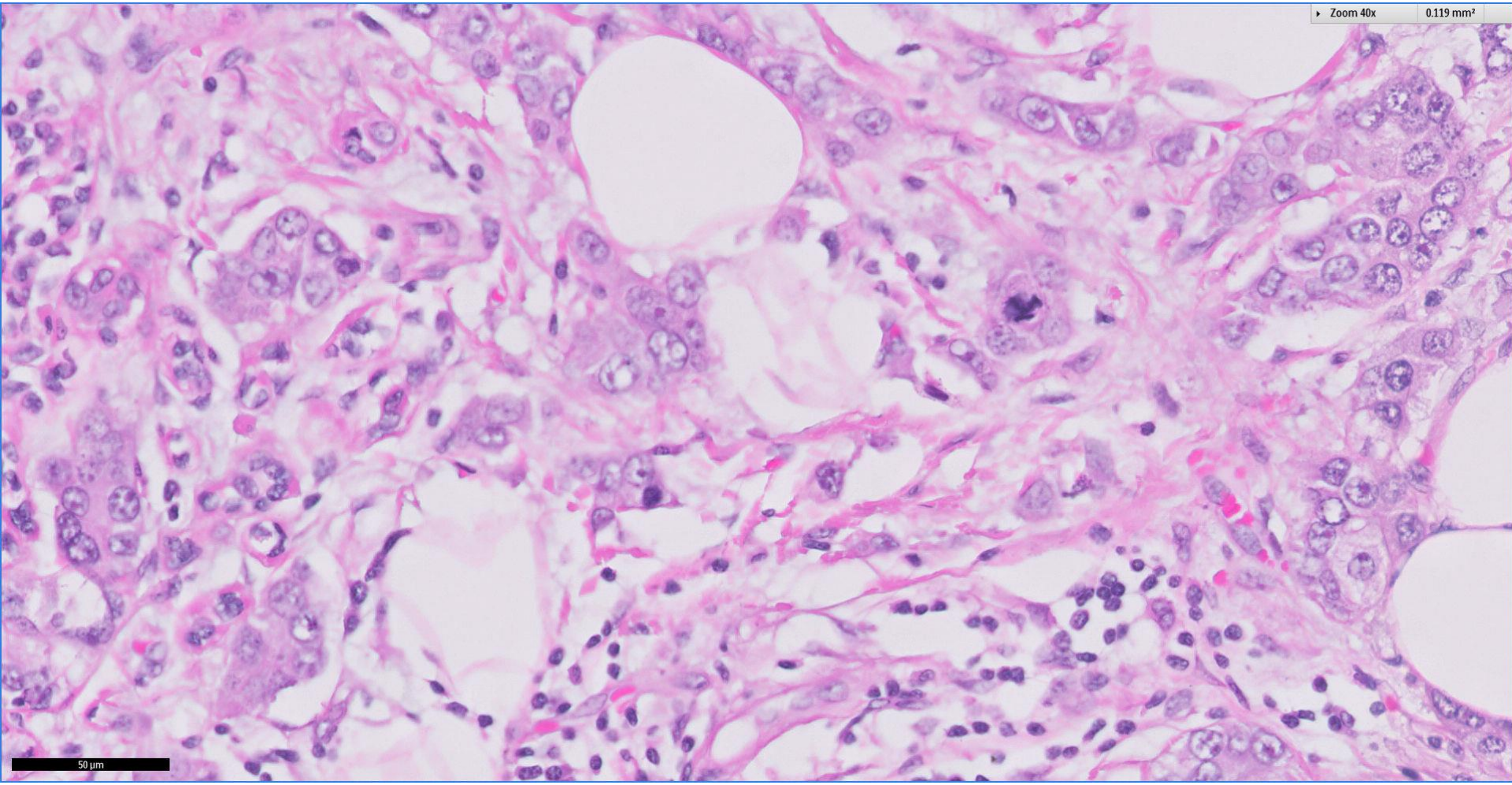

Zoom 10x
1.897 mm²
100 µm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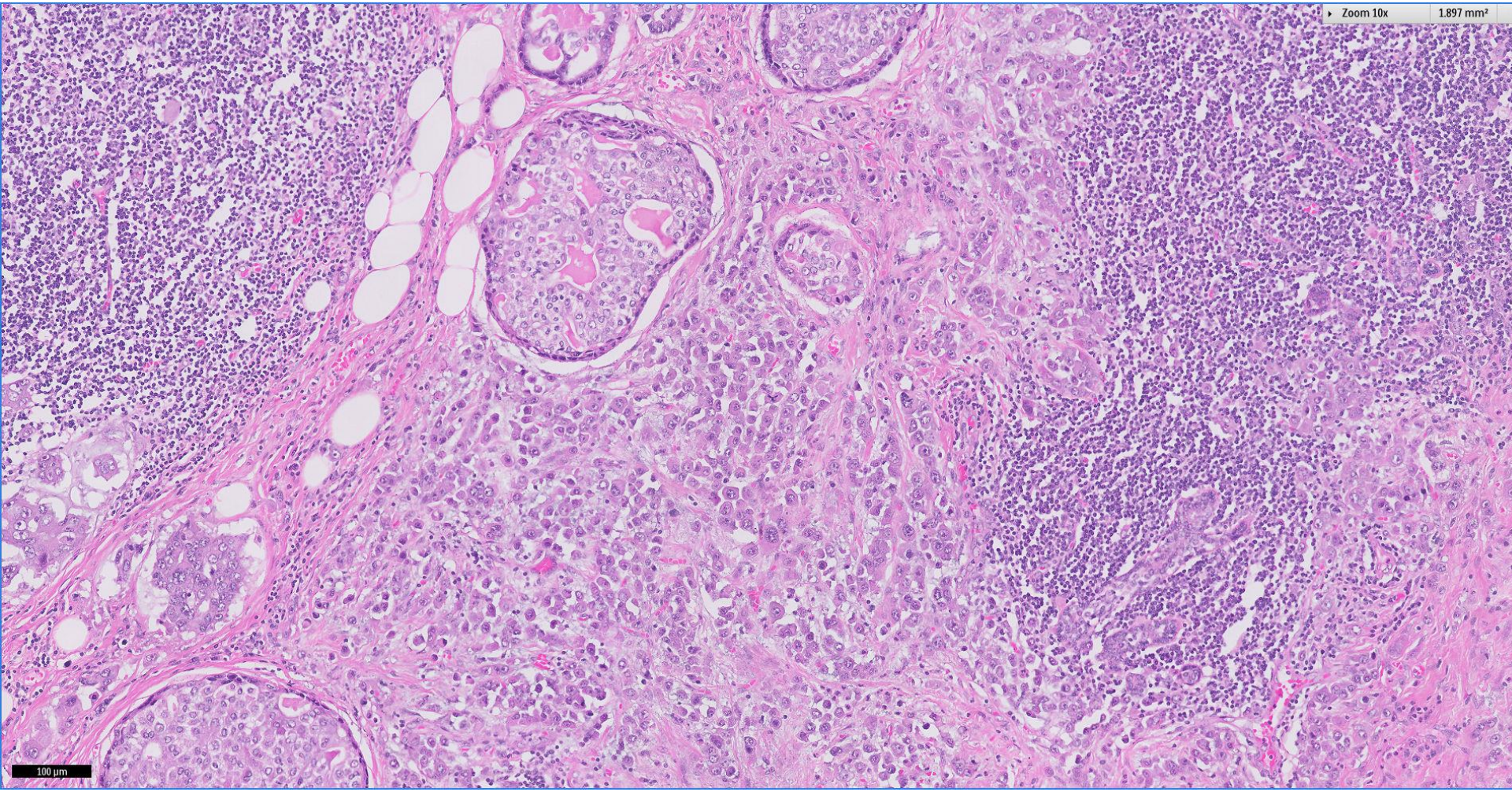
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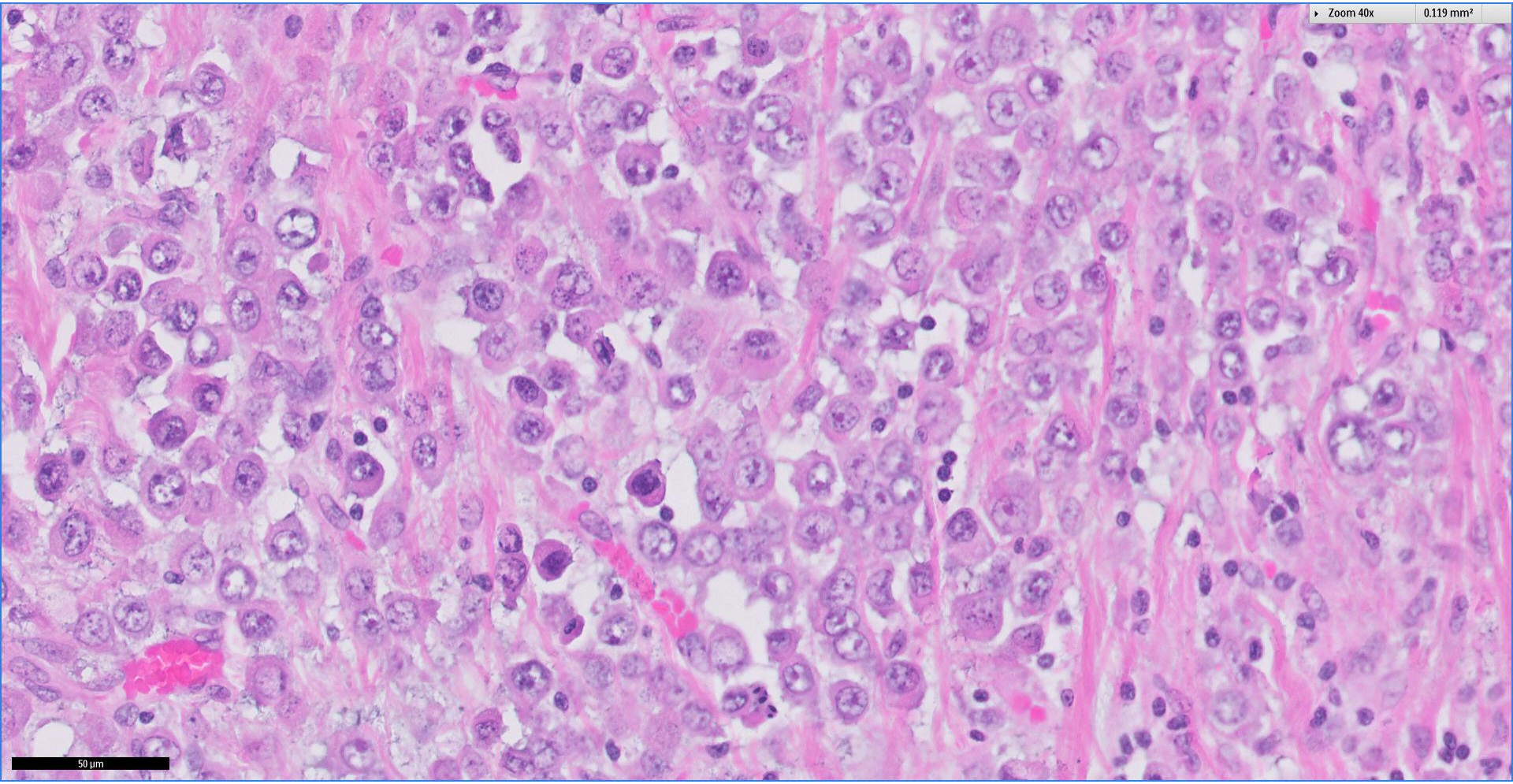
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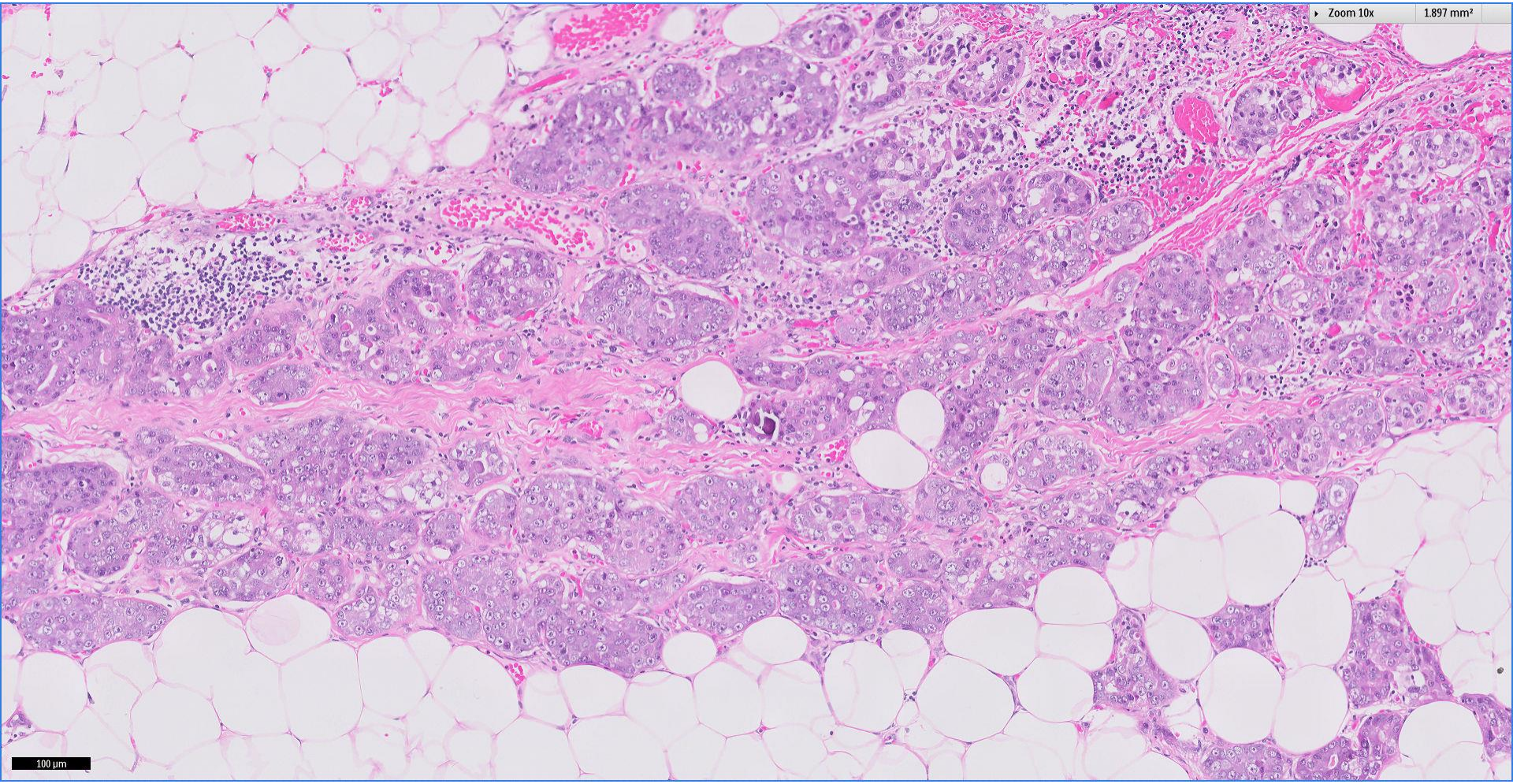
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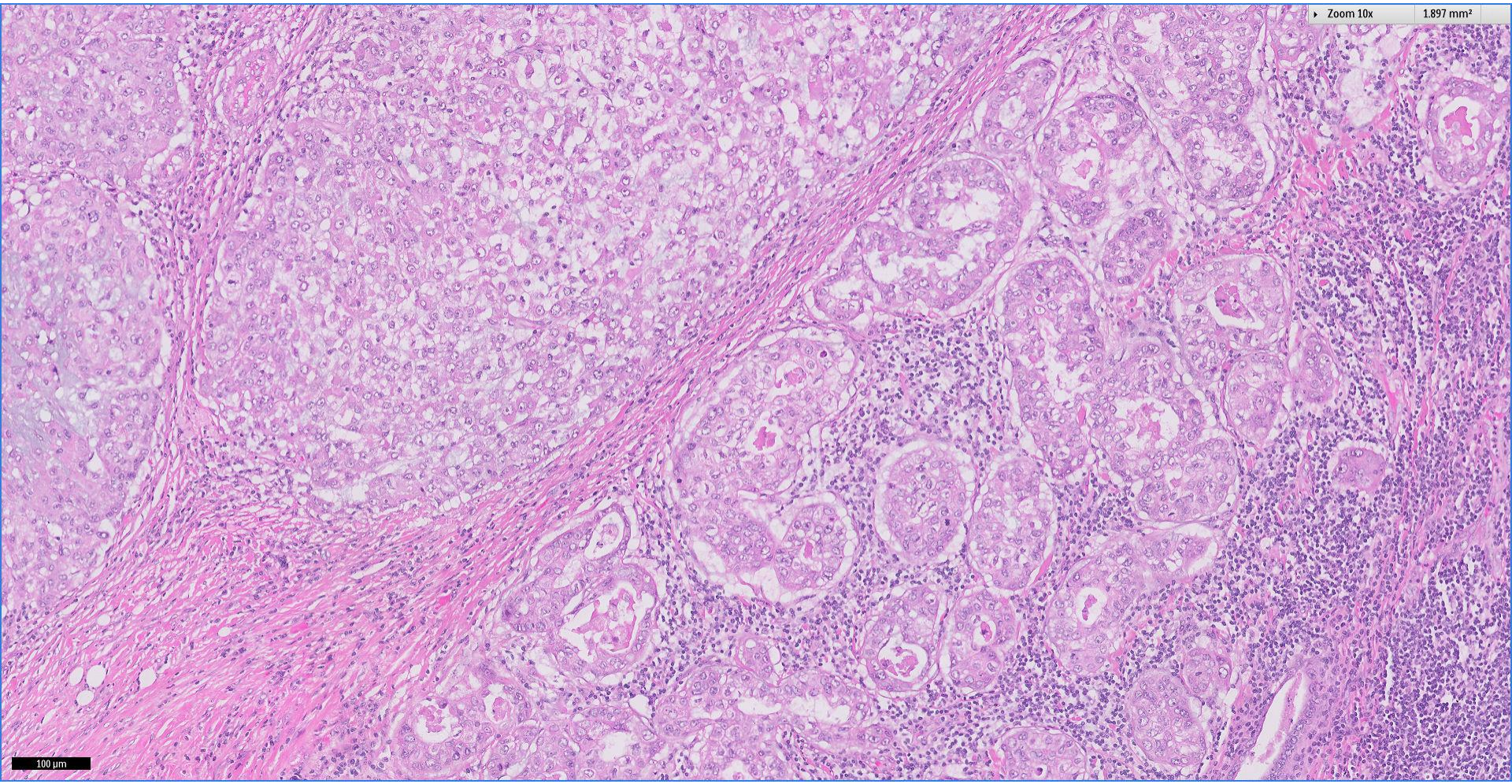
100 µm


Zoom 10x
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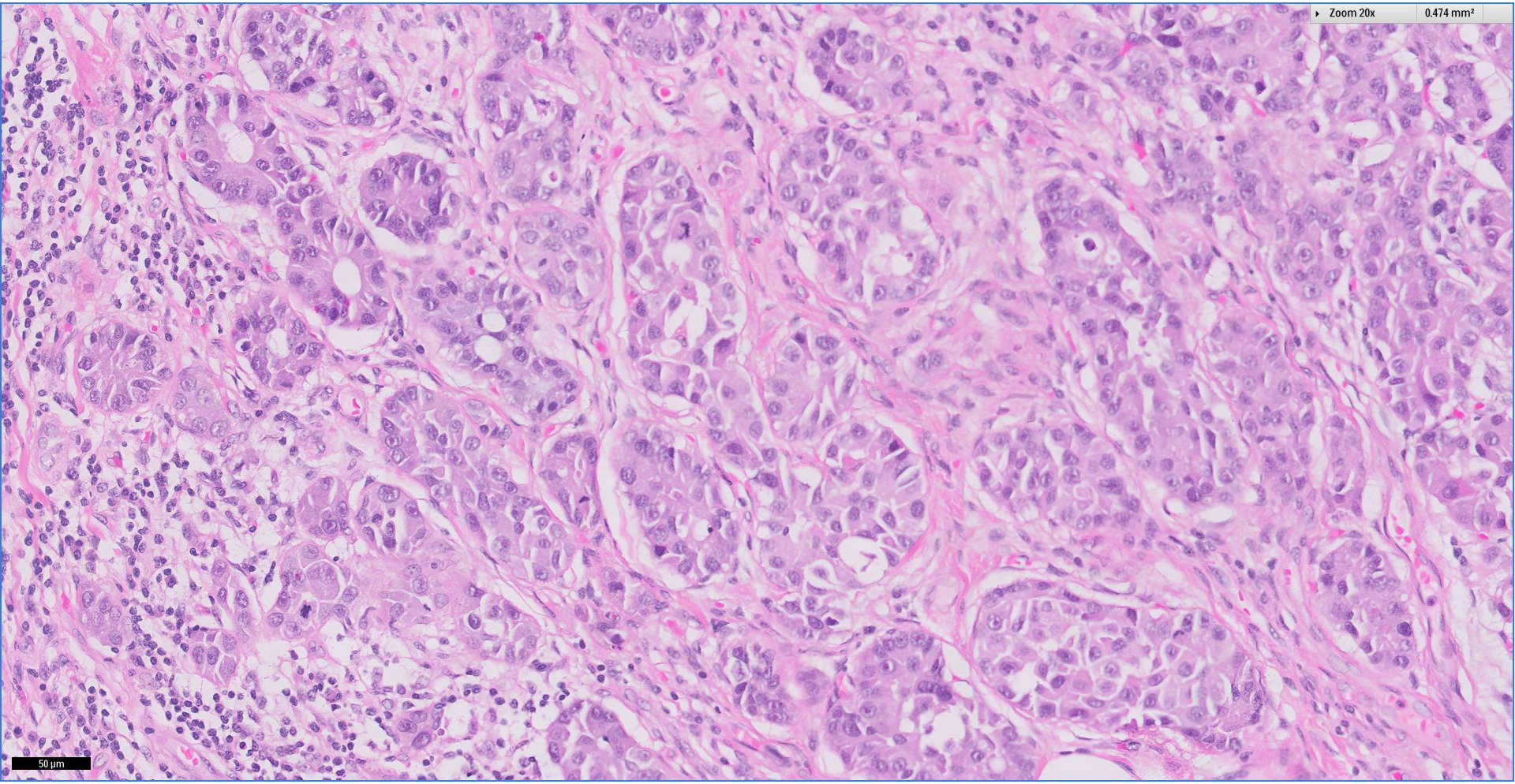
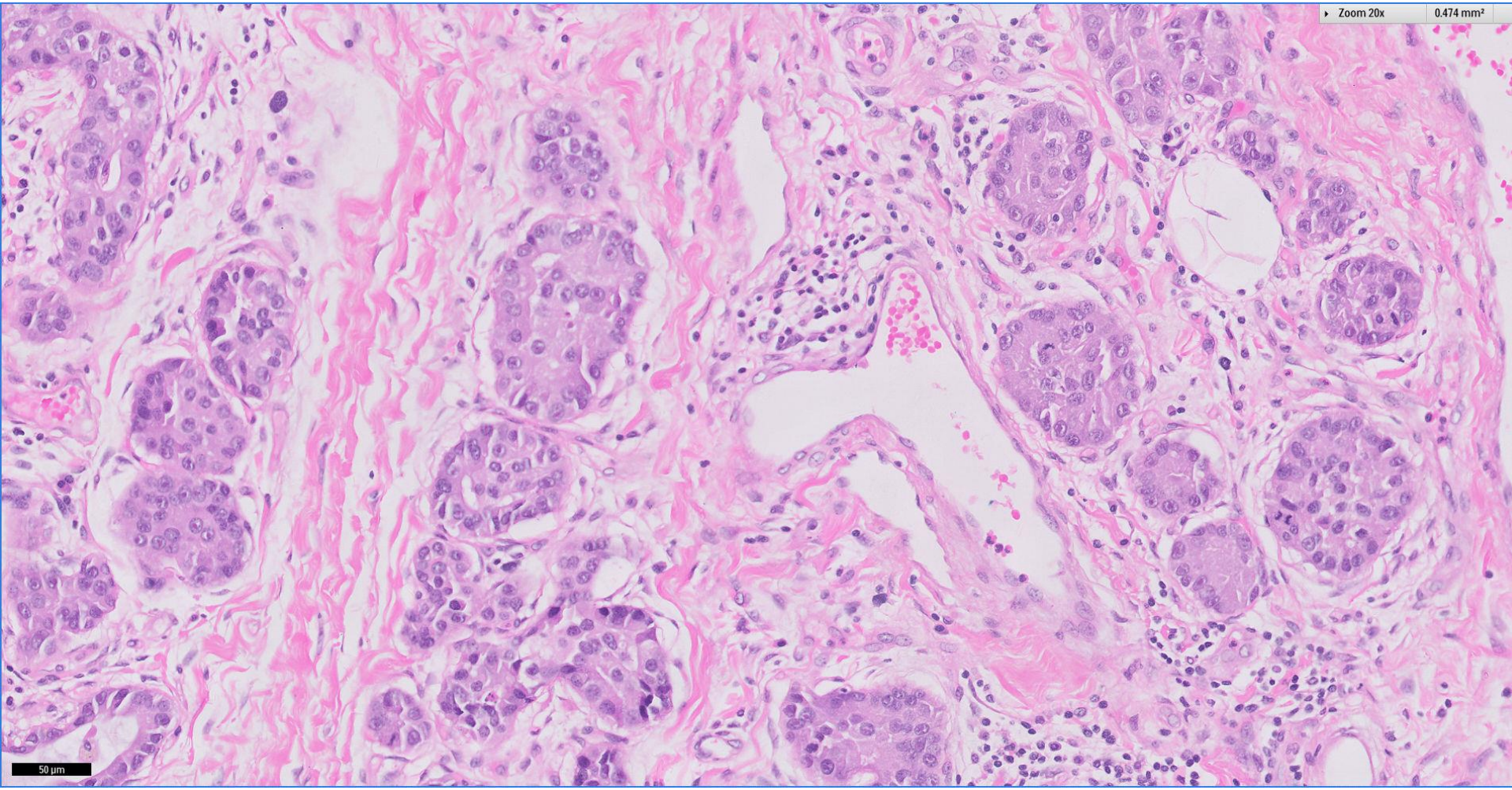
100 µm


Zoom 20x
0.474 mm²
50 µm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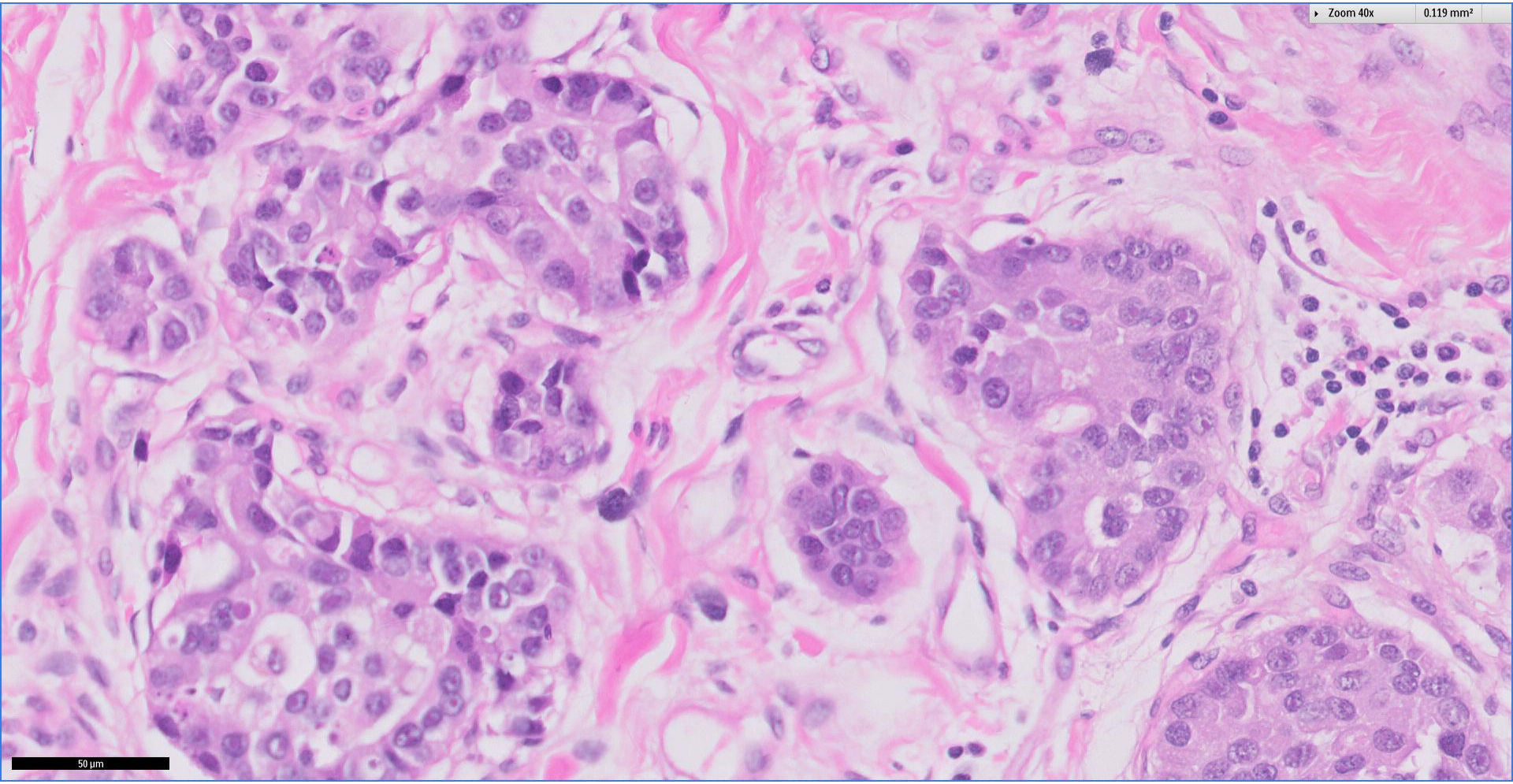
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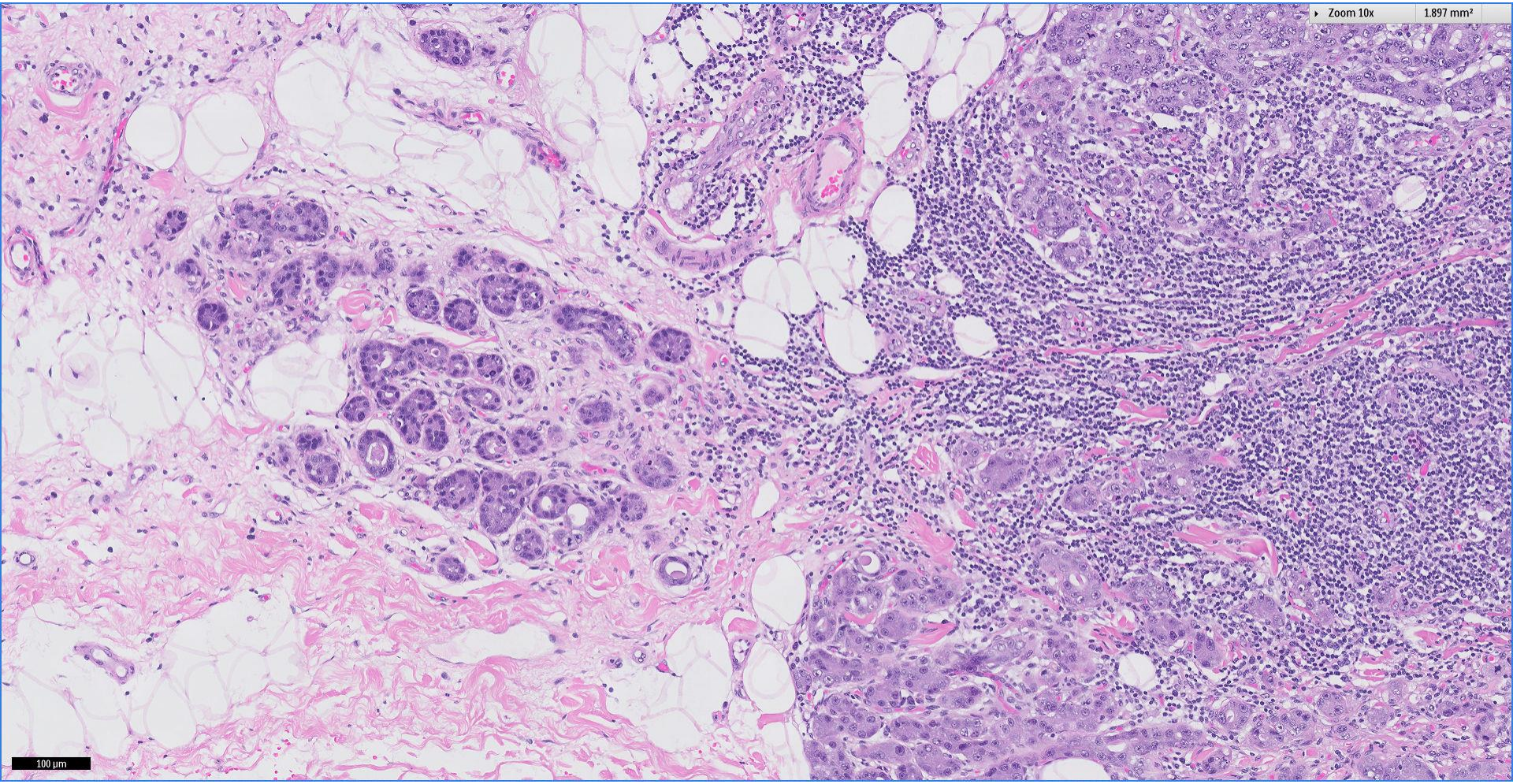
0.119 mm²
50 µm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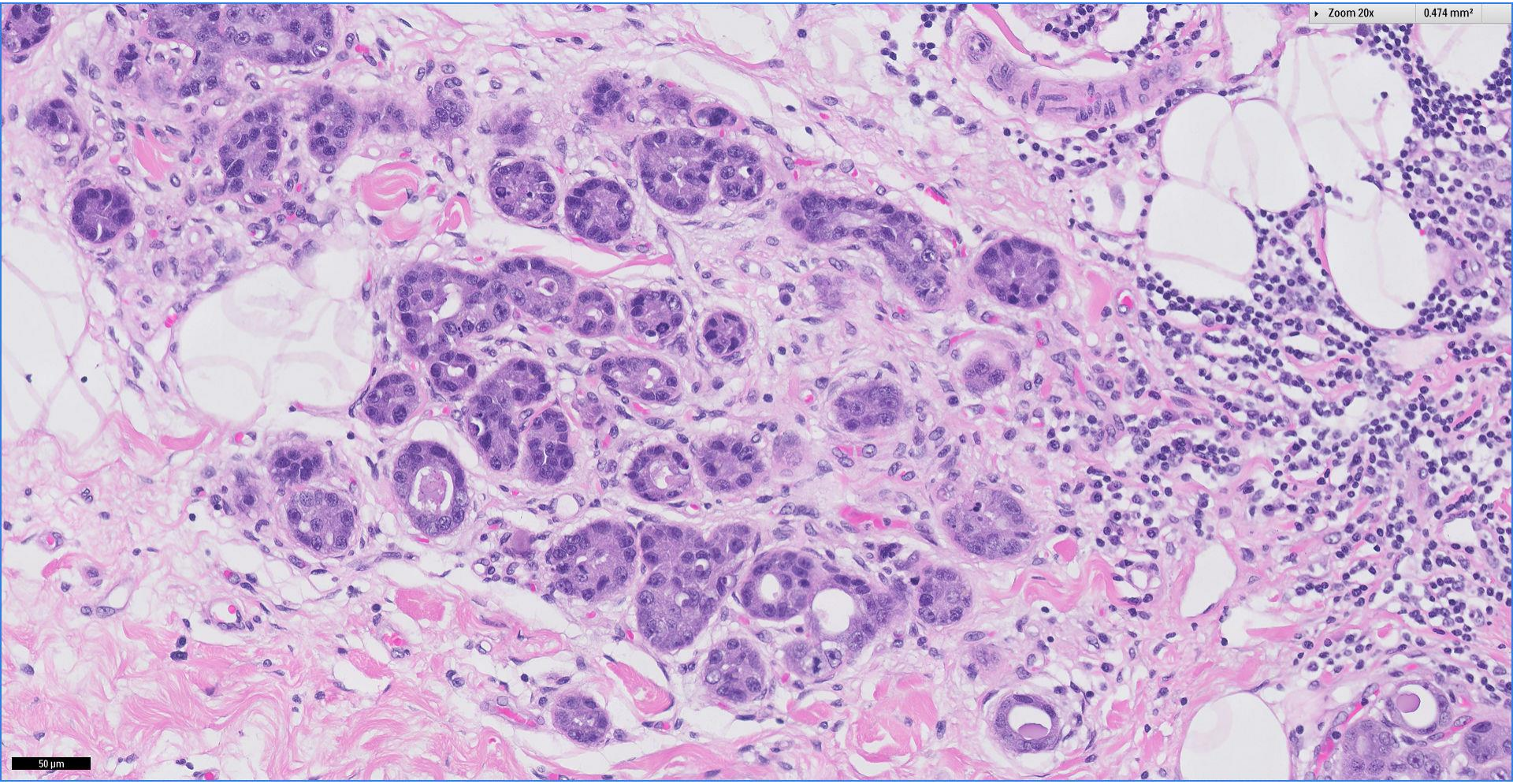
1.897 mm²
100 µm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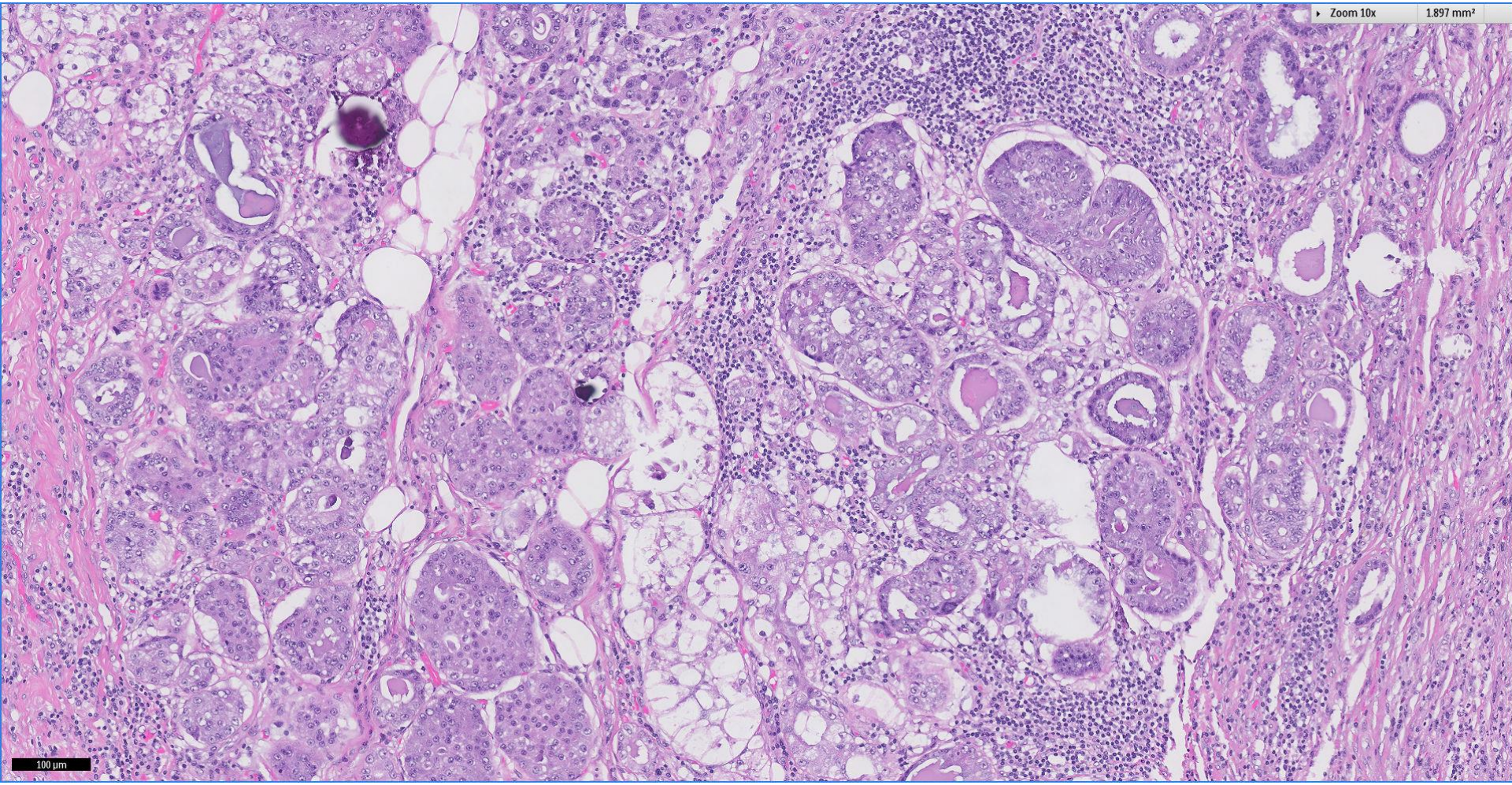
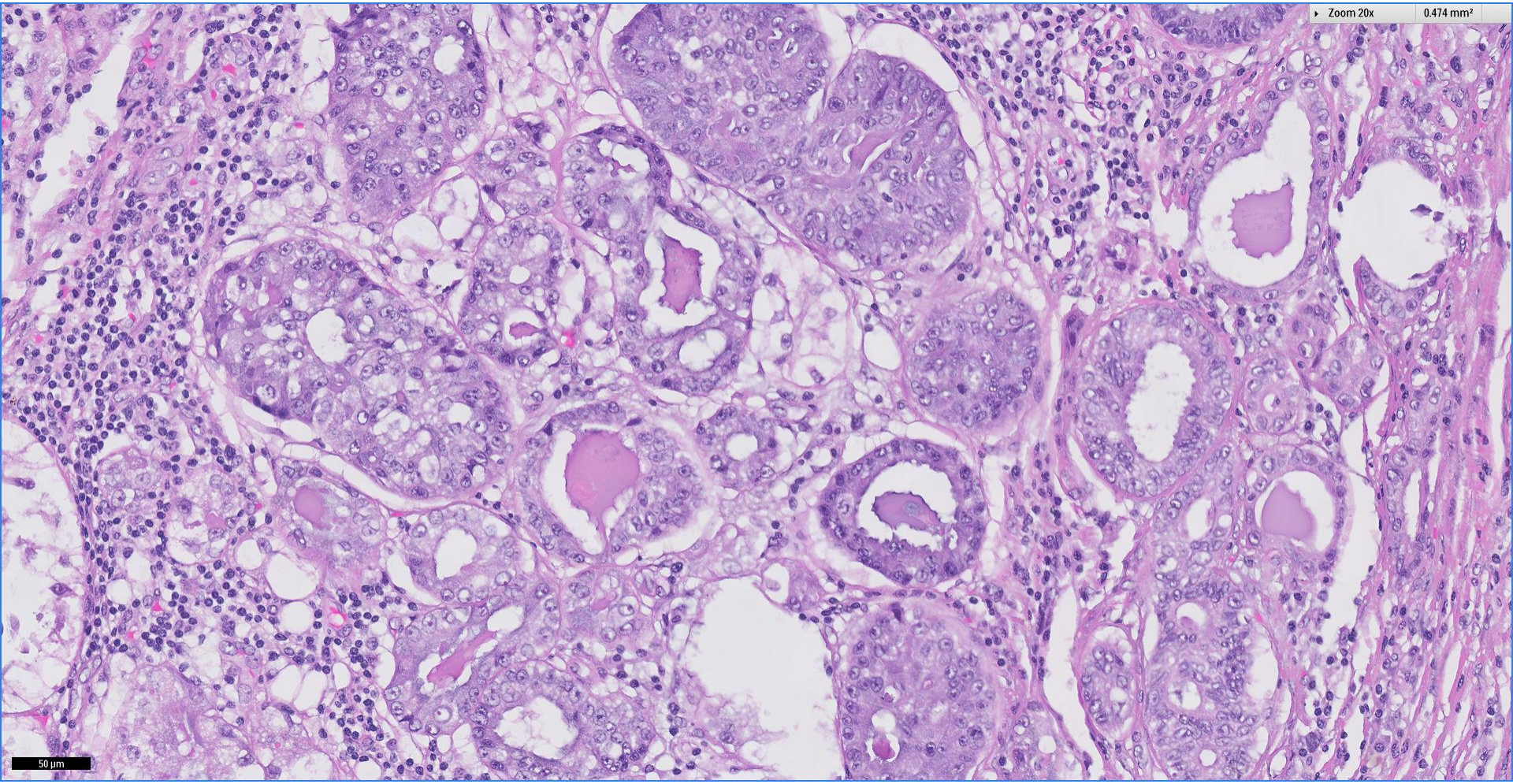
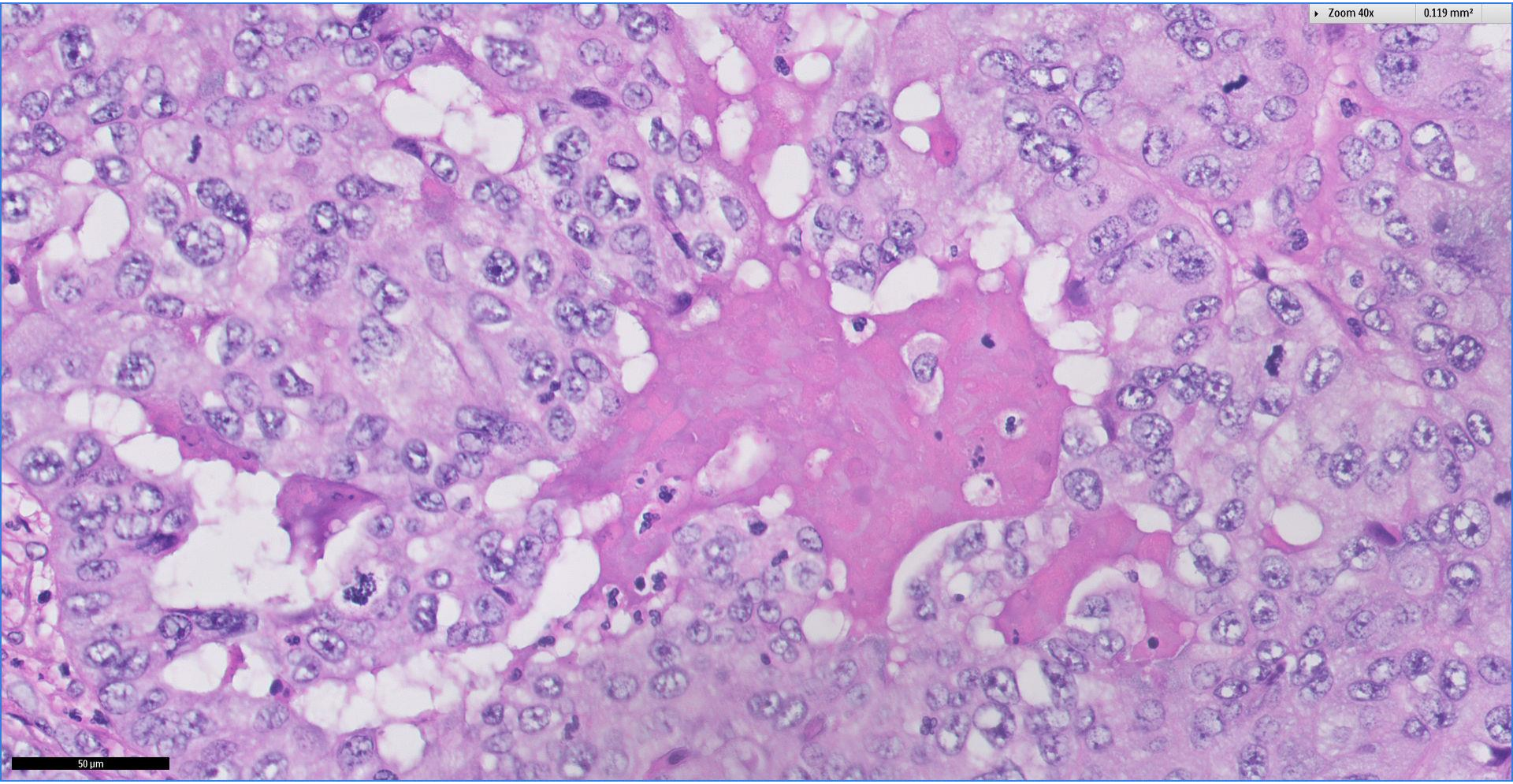
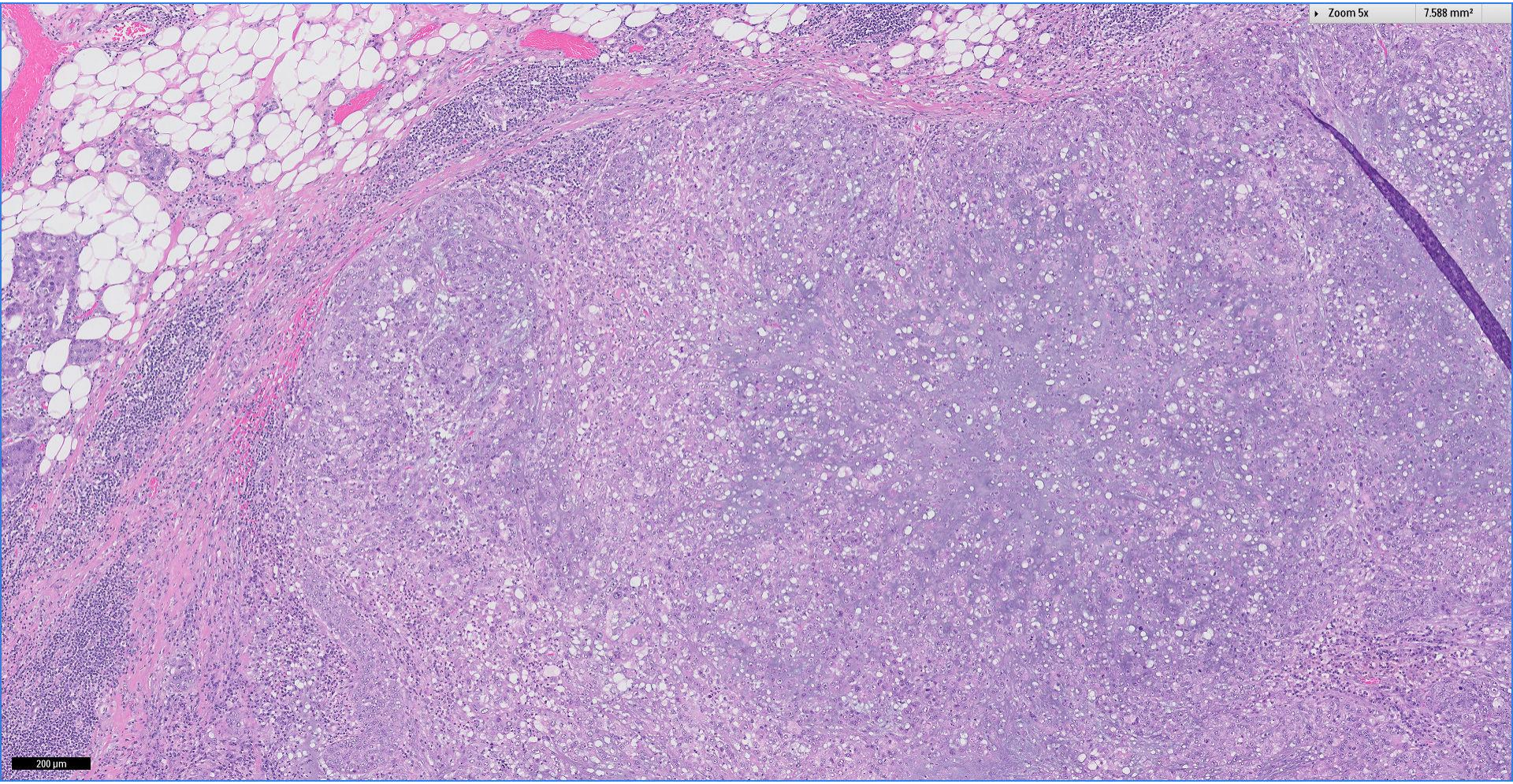
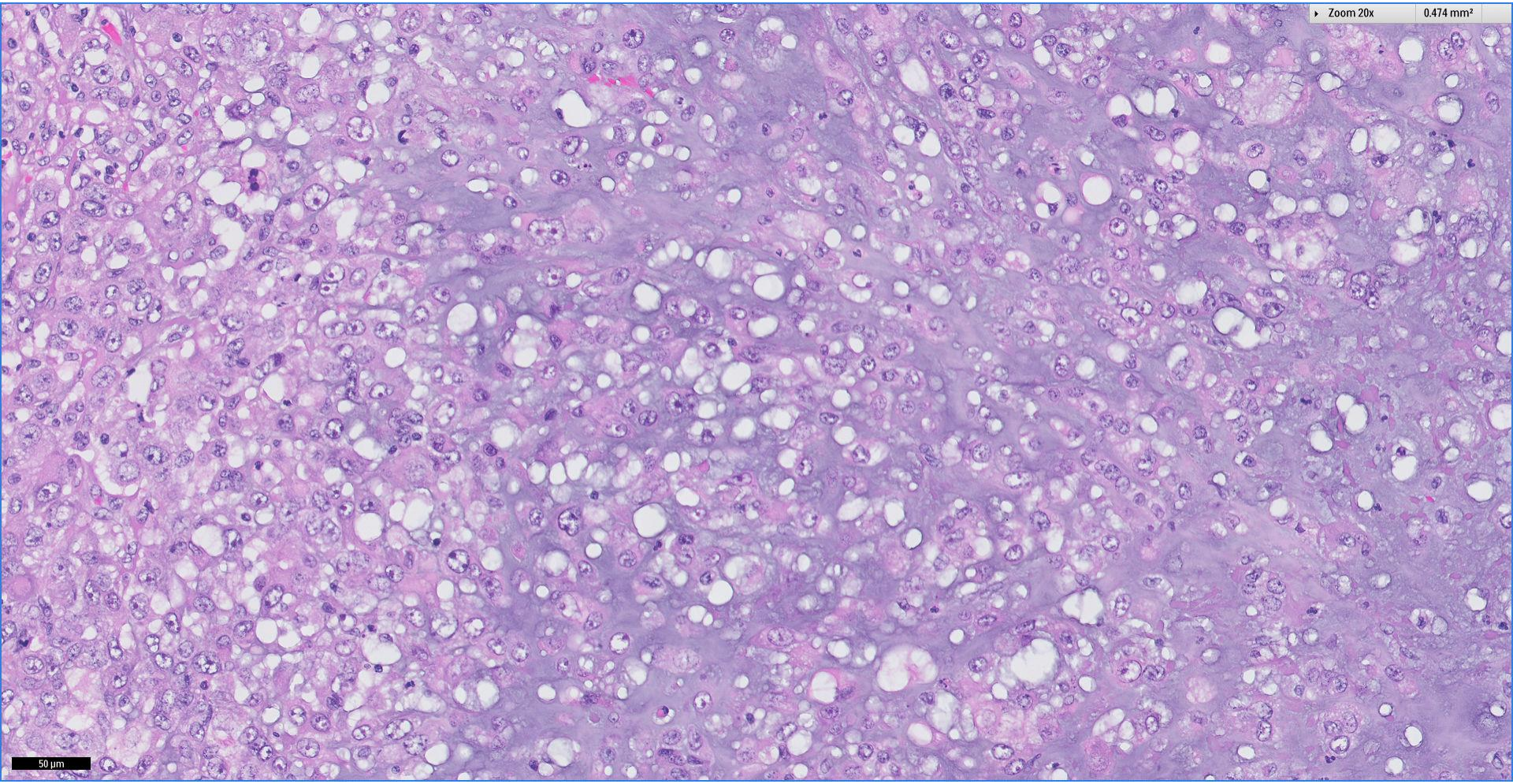
0.474 mm²
50 µm


Zoom 10x
1.897 mm²
100 µm


Zoom 20x
0.474 mm²
50 µm


Zoom 40x
0.119 mm²
50 µm


Zoom 5x
7.588 mm²
200 µm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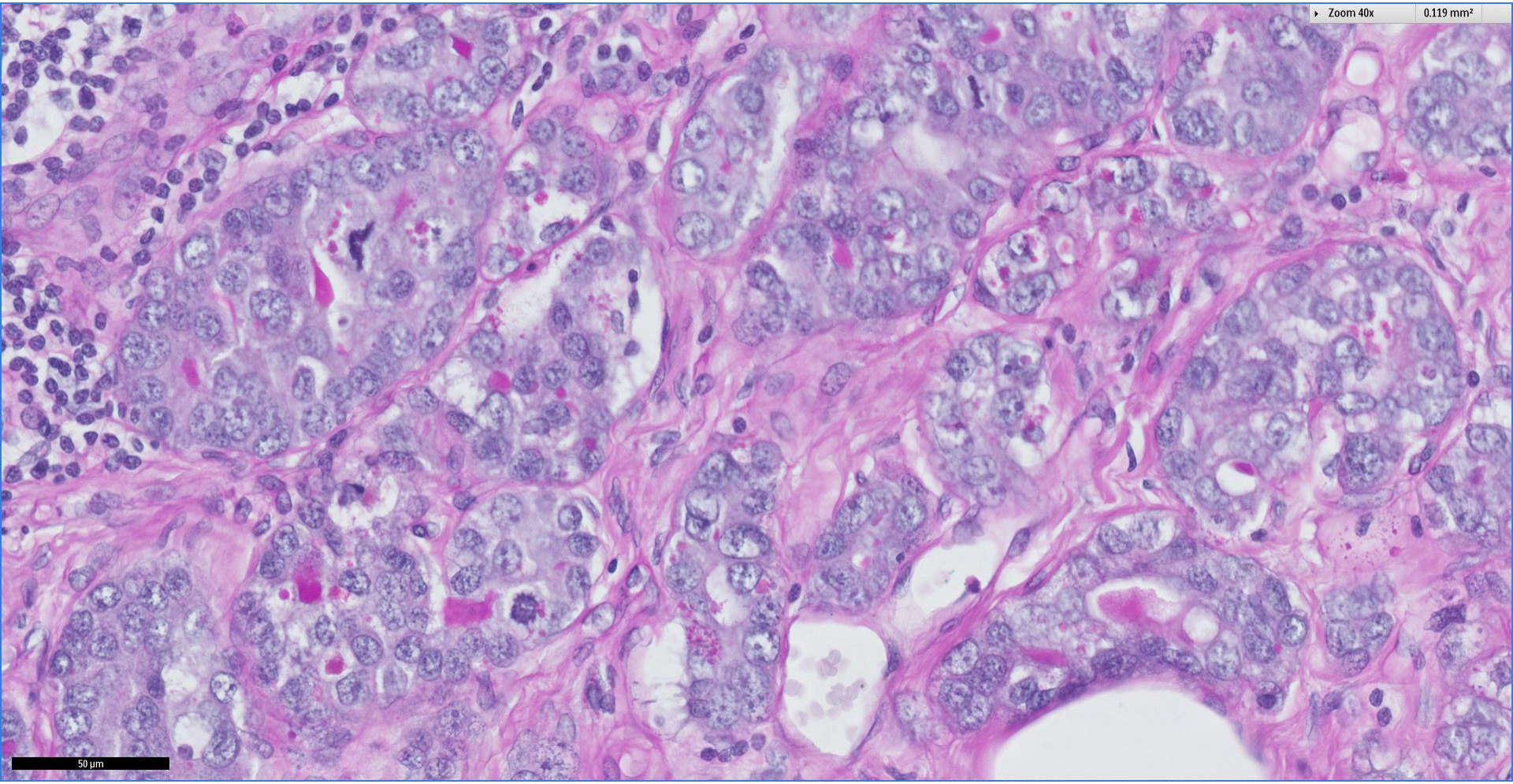
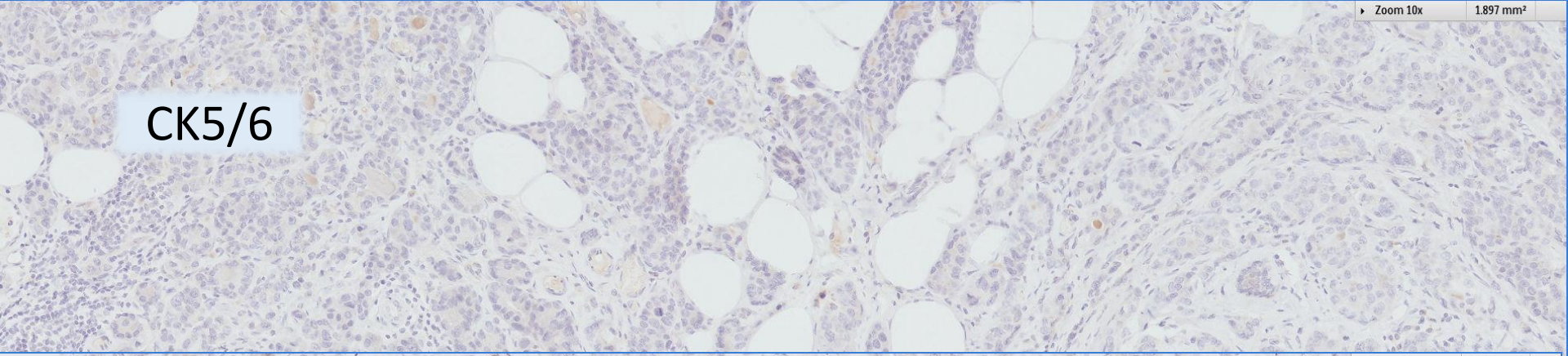
0.474 mm²
50 µm

PAS




Zoom 10x
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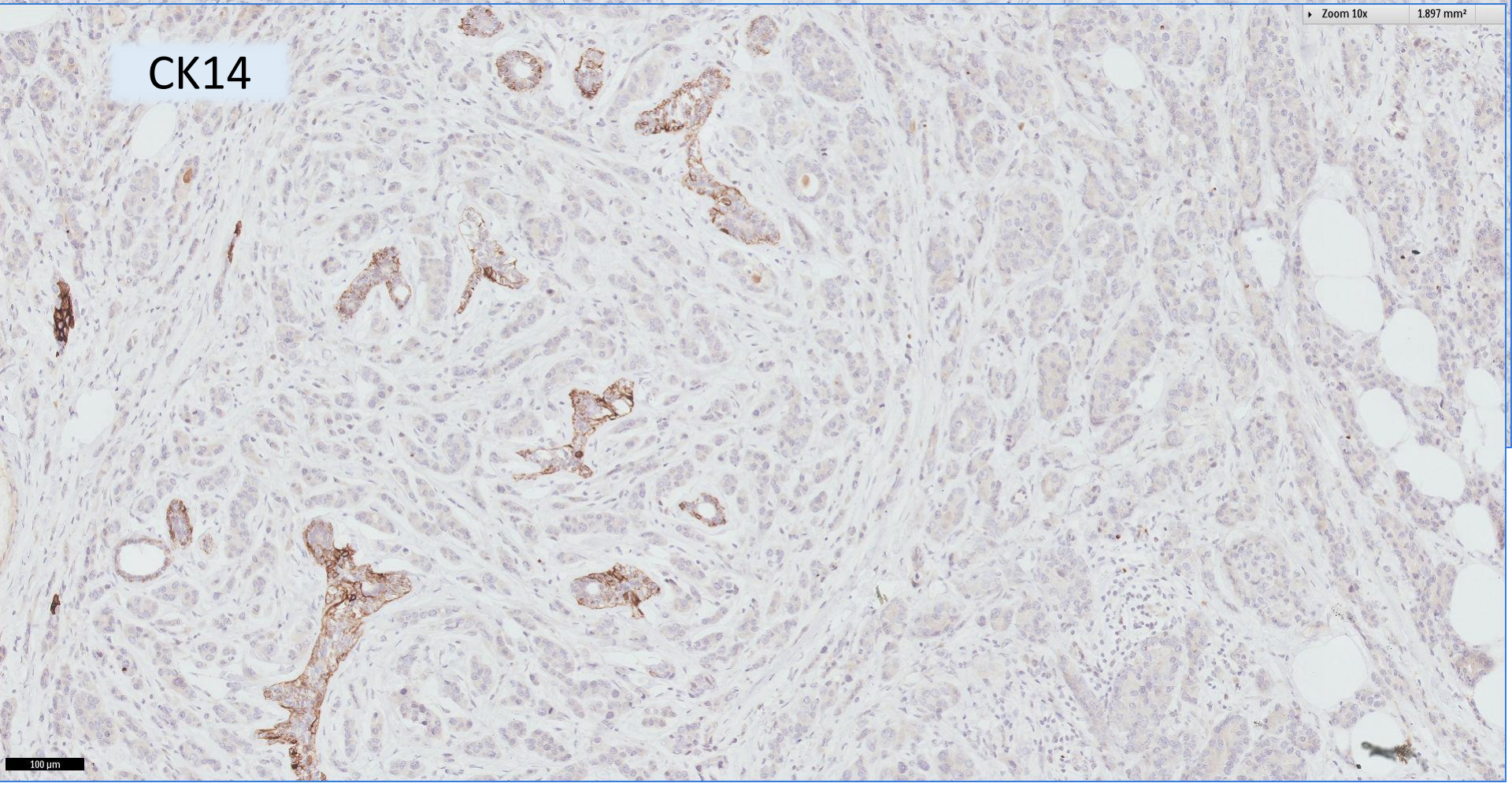
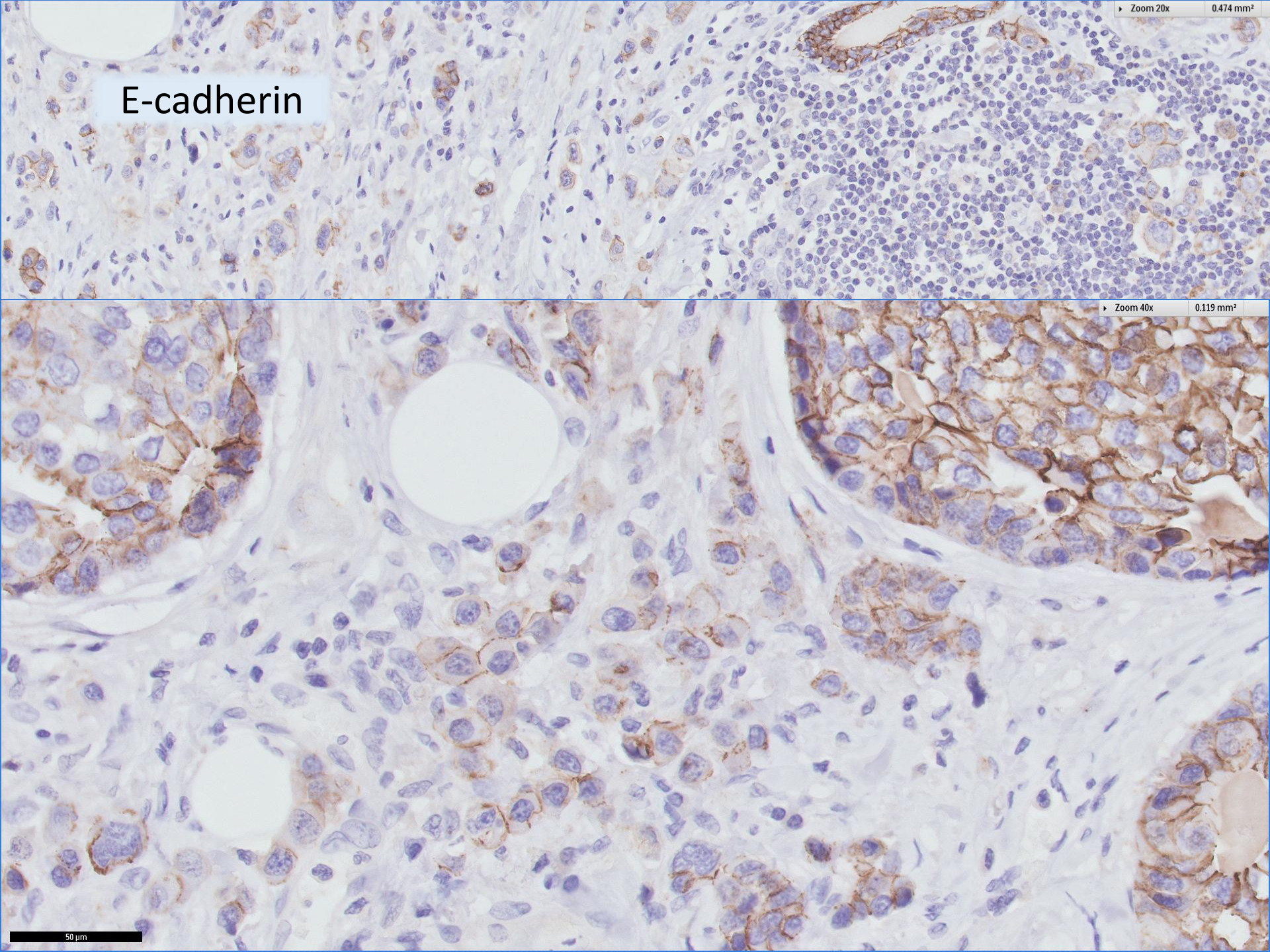
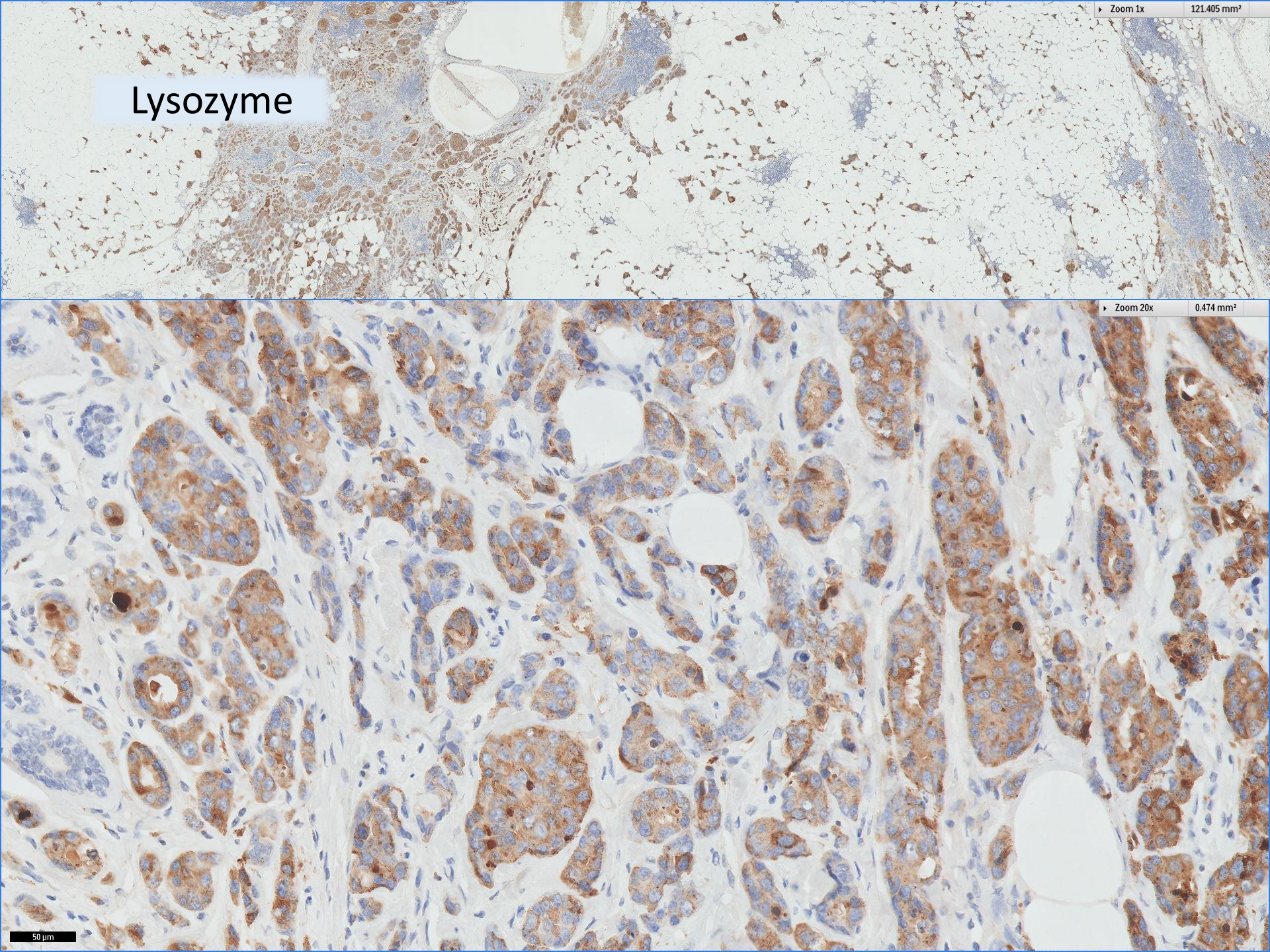
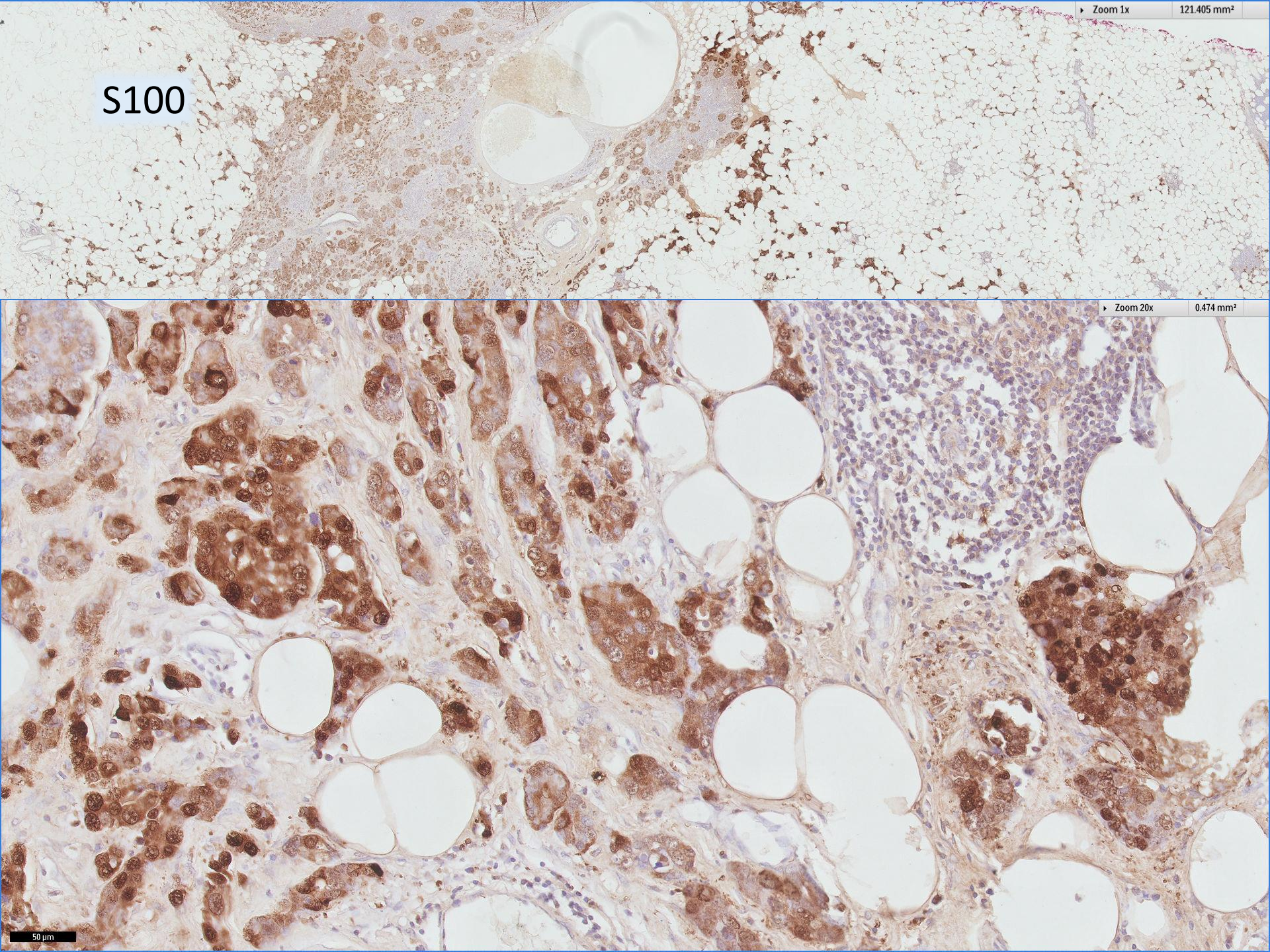
CK5/6


Zoom 10x
1.897 mm²
CK14
100 µm


E-cadherin
Zoom 20x
0.474 mm²
Zoom 40x
0.119 mm²
50 µm


Lysozyme
Zoom 1x
121.405 mm²
Zoom 20x
0.474 mm²
50 µm


S100
Zoom 1x
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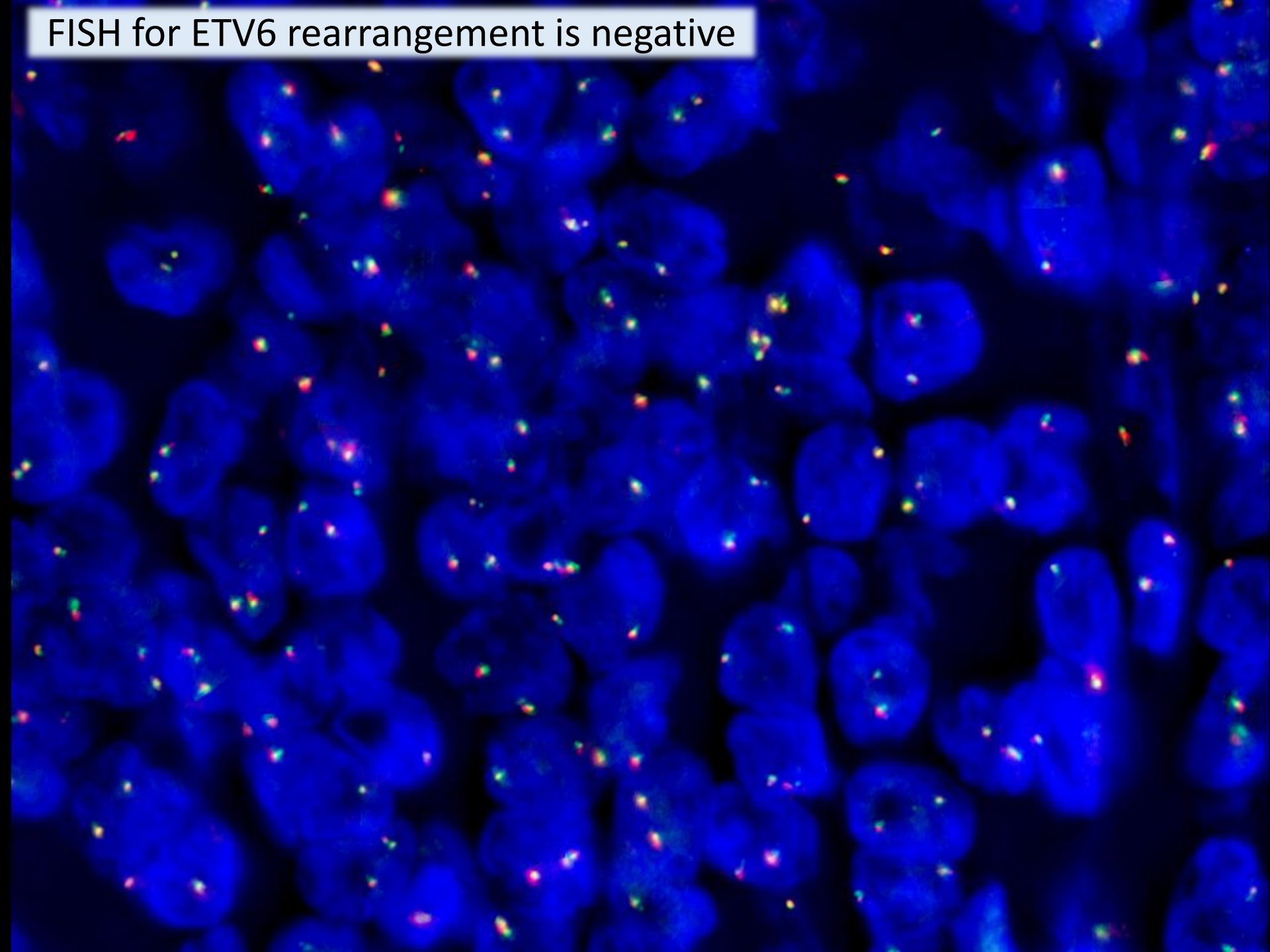
Zoom 20x
0.474 mm²
50 µm


FISH for ETV6 rearrangement is negative

Diagnosis

Right nipple sparing mastectomy and axillary clearance ~

Invasive carcinoma with metaplastic, acinic cell and lobular features, grade 3, 55mm.

ER negative, PR negative, cerbB2 negative (IHC equivocal, FISH negative).

Lymphovascular invasion.

Background atypical microglandular adenosis.

2 out of 14 axillary lymph nodes show metastases.

Acinic cell carcinoma

- Similar to acinic cell carcinoma of the parotid gland, showing serous differentiation with zymogen-type cytoplasmic granules.
- Consists of acini and solid nests of epithelial cells invading the stroma.
- Although the expression of S100, lysozyme, and amylase may be similar to secretory carcinoma, a key difference is the absence of the *ETV6- NTRK3* gene rearrangement in acinic cell carcinoma.

Acinic cell carcinoma

- Triple-negative (oestrogen receptor, progesterone receptor, and c-erbB-2 negative).
- Positive for lysozyme, alpha-1-antichymotrypsin, salivary gland amylase, EMA, and S100.
- On electron microscopy, cells show zymogen-like granules.
- Relationship with microglandular adenosis has been discussed, with a few reports of their coexistence.
- Several authors have suggested a histogenetic link, but others cite morphological, immunohistochemical, and ultrastructural differences that prevent a firm conclusion regarding their biological relationship.

Microglandular adenosis

- Can resemble the small acinar pattern of acinic cell carcinoma.
- In microglandular adenosis, however, the predominant appearance is of small, rounded tubules with luminal eosinophilic secretions, whereas acinic cell carcinoma tends to have more variable architecture, including solid nests and clear-cell aggregates.
- A basement membrane sheath may be observed around tubules of microglandular adenosis.
- Atypical microglandular adenosis shows cyto-architectural atypia.

Microglandular adenosis and metaplastic carcinoma

J Pathol Transl Med. 2017 Jul;51(4):418-421.

Metaplastic Carcinoma with Chondroid Differentiation Arising in Microglandular Adenosis. Kim GE, Kim NI, Lee JS, Park MH.

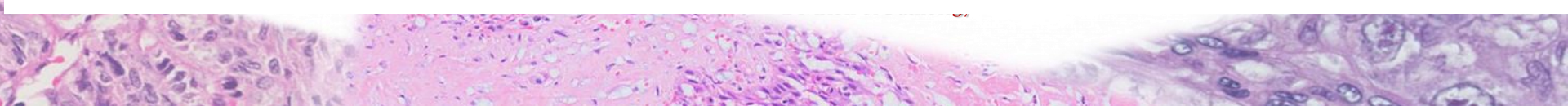
Microglandular adenosis (MGA) of the breast is a rare, benign proliferative lesion but with a significant rate of associated carcinoma. Herein, we report an unusual case of metaplastic carcinoma with chondroid differentiation associated with typical MGA. Histologically, MGA showed a direct transition to metaplastic carcinoma without an intervening atypical MGA or ductal carcinoma in situ component. The immunohistochemical profile of the metaplastic carcinoma was mostly similar to that of MGA. In both areas, all the epithelial cells were positive for S-100 protein, but negative for estrogen receptor, progesterone receptor, HER2/neu, and epidermal growth factor receptor. An increase in the Ki-67 and p53 labelling index was observed from MGA to invasive carcinoma. To the best of our knowledge, this is the first case of metaplastic carcinoma with chondroid differentiation arising in MGA in Korea. This case supports the hypothesis that a subset of MGA may be a non-obligate morphologic precursor of breast carcinoma, especially the triple-negative subtype.

Microglandular adenosis and metaplastic carcinoma

Int J Clin Exp Pathol. 2015 Jul 1;8(7):8568-72.

A case of matrix-producing carcinoma of the breast with micoglandular adenosis and review of literature. Liu LY, Sheng SH, Zhang ZY, Xu JH.

Matrix-producing carcinoma (MPC) of the breast is an extremely rare variant of metaplastic breast carcinoma that contains a mixture of epithelial and mesenchymal elements. As overt carcinoma with direct transition to a cartilaginous and/or osseous stromal matrix cells, MPC is of no spindle cells between those two elements. This is the case of a 43 year-old female patient with MPC which coexisted with microglandular adenosis (MGA), atypical MGA (AMGA) and carcinoma in situ arising in MGA (MGACA in situ). MGA is a rare, infiltrative, benign lesion of the breast with an indolent clinical course. Histological evidence of carcinoma arising from MGA has previously been documented. MPC arising in MGA is an extremely rare subtype of breast carcinoma and has been seldom detailed described in the previous studies. This report highlights one such case with cytomorphological and histopathological correlation, along with a review of pertinent literature and differential diagnosis.



Microglandular adenosis and metaplastic carcinoma

Int J Surg Pathol. 2000 Oct;8(4):303-315.

Carcinoma Arising in Microglandular Adenosis: An Immunohistochemical Analysis of 20 Intraepithelial and Invasive Neoplasms.

Koenig C, Dadmanesh F, Bratthauer GL, Tavassoli FA.

Microglandular adenosis (MGA) of the breast is an uncommon, benign lesion that may mimic invasive carcinoma and has recently been recognized as having significant premalignant potential. When carcinomas arise in MGA, there is often a transition from ordinary MGA to atypical MGA (AMGA) to carcinoma. Nineteen cases of carcinoma arising in MGA are reported: 7 invasive carcinomas, 7 intraductal carcinomas (DCIS), and 5 with both invasive and intraductal carcinoma. A single case of AMGA without carcinoma is also reported. The 20 patients ranged in age from 36 to 81 years (mean 52). The most common clinical presentation was either a palpable mass (13 patients) or a mammographic abnormality (4 patients). All 20 cases contained AMGA, and in some cases AMGA was the predominant lesion. In 18 of the 19 cases with carcinoma, there was a clear transition from AMGA to the carcinoma. Twelve cases contained ordinary MGA, but in only 2 cases was MGA a prominent component of the lesion. In contrast to ordinary MGA, the glands of AMGA were more irregularly shaped, closely packed, and cytologically atypical and tended to lack secretions. A solid, occlusive proliferation of cells in the tubules was seen in 10 cases. All 12 examples of in situ carcinoma were either grade 2 or 3 and typically showed a solid proliferation of severely atypical cells within the glands; a cribrifrom pattern was also present in 1 case.

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The invasive carcinomas were morphologically diverse and included 2 with a basaloid morphology and 2 metaplastic carcinomas. Various immunostains were performed, and each lesion (AMGA, in situ, and invasive carcinoma) was separately assessed for immunoreactivity. As expected, S-100 was positive in the vast majority of AMGA and in situ carcinomas and in all 12 invasive carcinomas. S-100beta was also positive in the majority of cases although the staining was weaker. Laminin and type IV collagen highlighted the basement membrane around the AMGA and in situ carcinoma and are useful stains in difficult cases. Except for a single case, ER and PR were negative in all lesions. Cytokeratin 7 (CK 7) was positive, while cytokeratin 20 (CK 20) was negative in all cases. Immunostains for CK903 showed no reactivity in any of the invasive carcinomas, in situ carcinomas, or atypical MGA but was focally present in the associated MGA in 2 of the 8 cases studied. Immunostains for MIB-1 and p53 were semiquantitatively assessed and both were positive in AMGA but tended to show a more intense staining in the carcinomas. Five cases were also studied for immunoexpression of alpha-1 antitrypsin (AAT), alpha-1 antichymotrypsin (ACTP), lysozyme, and salivary gland amylase. All 5 invasive carcinomas were positive for ACTP, though the staining was very focal in about 10% of the cells in a basaloid carcinoma.

Int J Surg Pathol. 2000 Oct;8(4):303-315.

Carcinoma Arising in Microglandular Adenosis: An Immunohistochemical Analysis of 20 Intraepithelial and Invasive Neoplasms.
Koenig C, Dadmanesh F, Bratthauer GL, Tavassoli FA.

The in situ carcinoma as well as the AMGA in 4 of the 5 cases were positive for ACTP. Three of the 5 invasive carcinomas were positive for AAT in 10% to 40% of the cells. The most intense positivity for AAT and ACTP was in cells with coarsely granular apocrine appearance evident in 2 of the 5 cases. Four of the 5 invasive carcinomas were positive for lysozyme in 10% to 50% of the cancer cells; the in situ carcinoma and the associated AMGA showed similar immunoreaction in each case. None of the 5 cases showed convincing positivity for salivary gland amylase. The MGA in all 5 cases was negative for AAT and ACTP; the MGA in 1 of the 5 cases was positive for lysozyme. This study confirms the potential of MGA to develop into an invasive carcinoma, more clearly defines the features of AMGA, highlights the importance of AMGA in the evolution of carcinoma from MGA, and expands our knowledge of the immunophenotype of AMGA and the carcinomas arising from it. The diagnostic criteria briefly noted previously for diagnosis of AMGA and carcinoma arising in MGA are expanded and formally proposed. Int J Surg Pathol 8(4):303-315, 2000

Breast Pathology Course 2017