Breast Pathology Course 2018

Case 27

51 year old female.
Left breast suspicious 2:00 nodule 1.1 x 1.6 x 0.8 cm, 4 cm from nipple. Hard on elastography.
Core biopsy followed by excision performed.

Case contributed by Dr Mihir Gudi, Singapore

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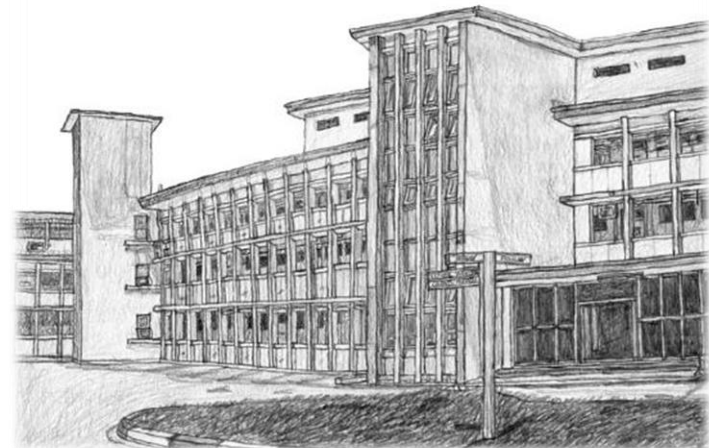
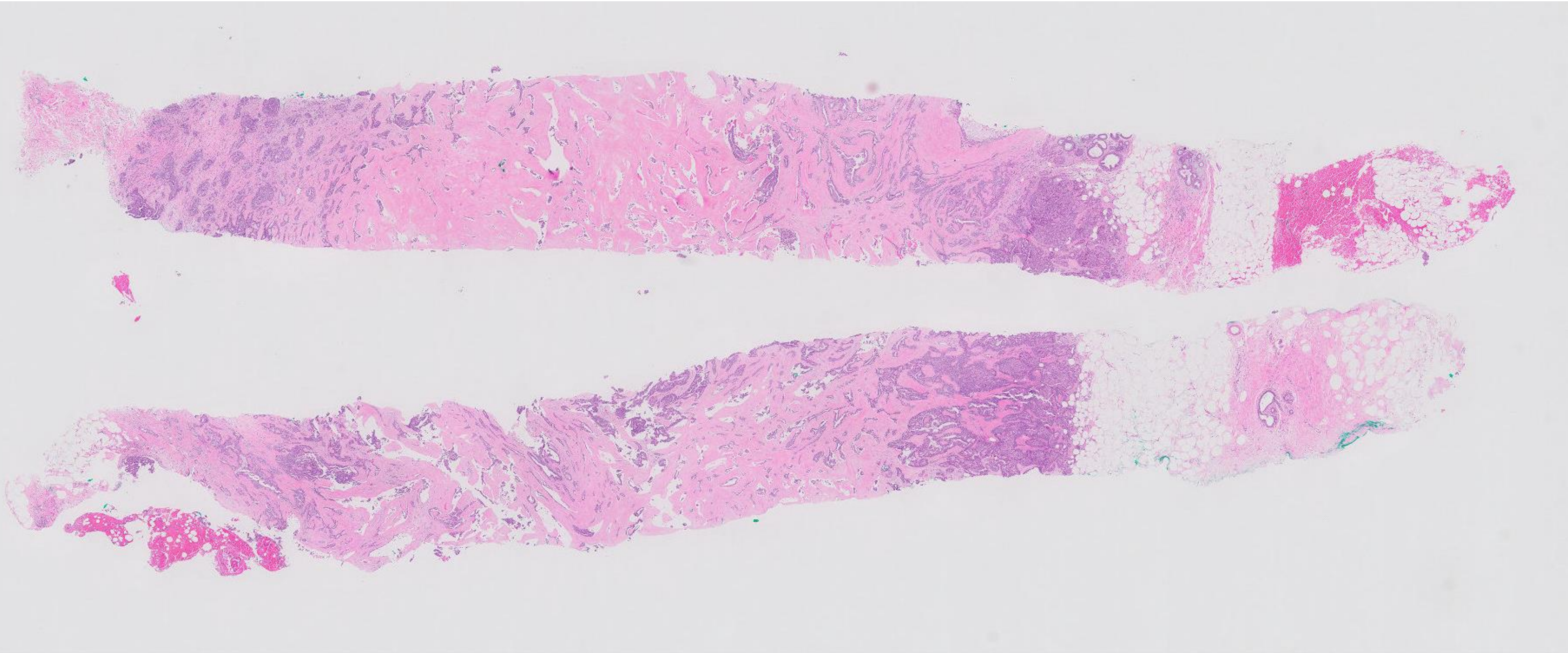
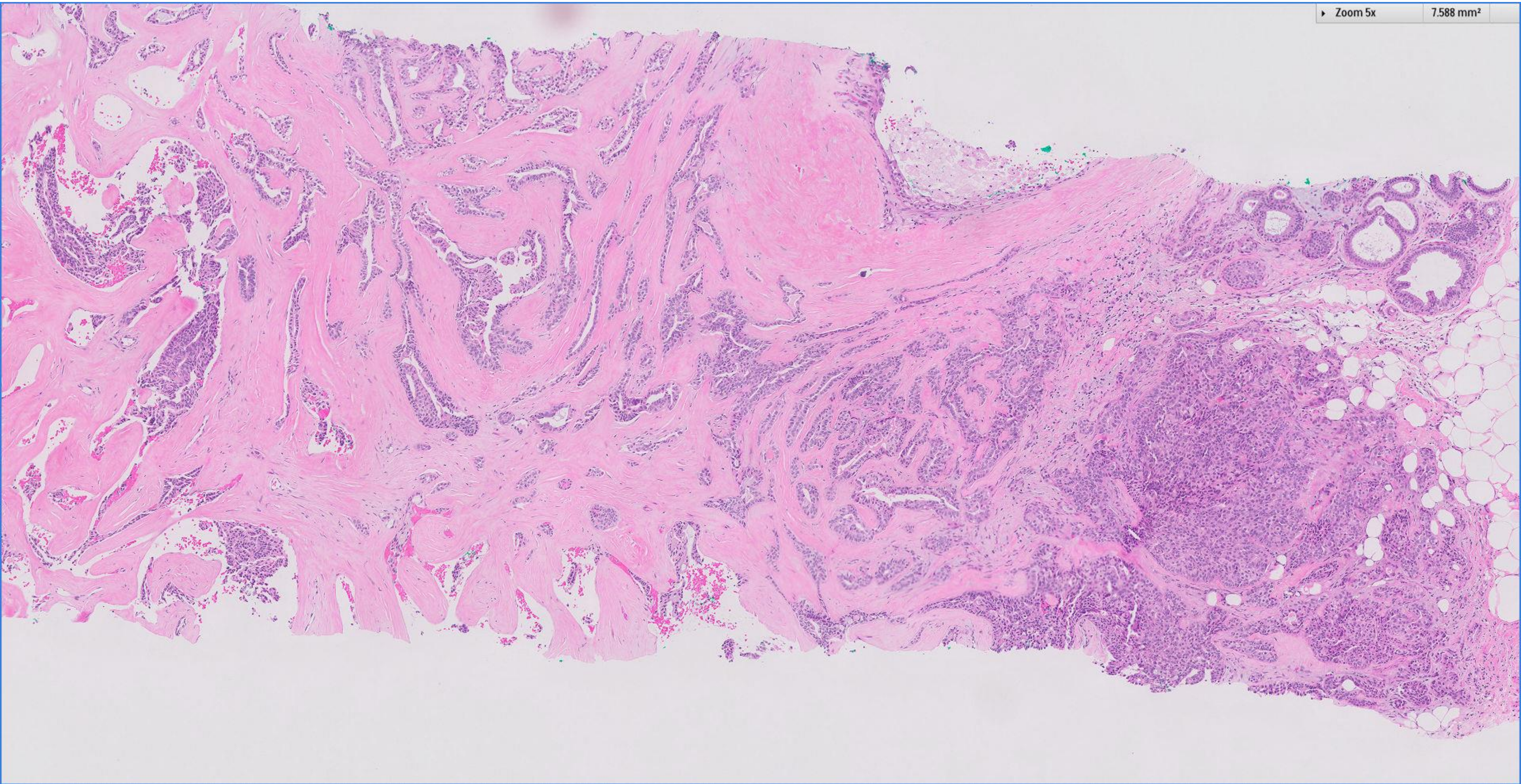


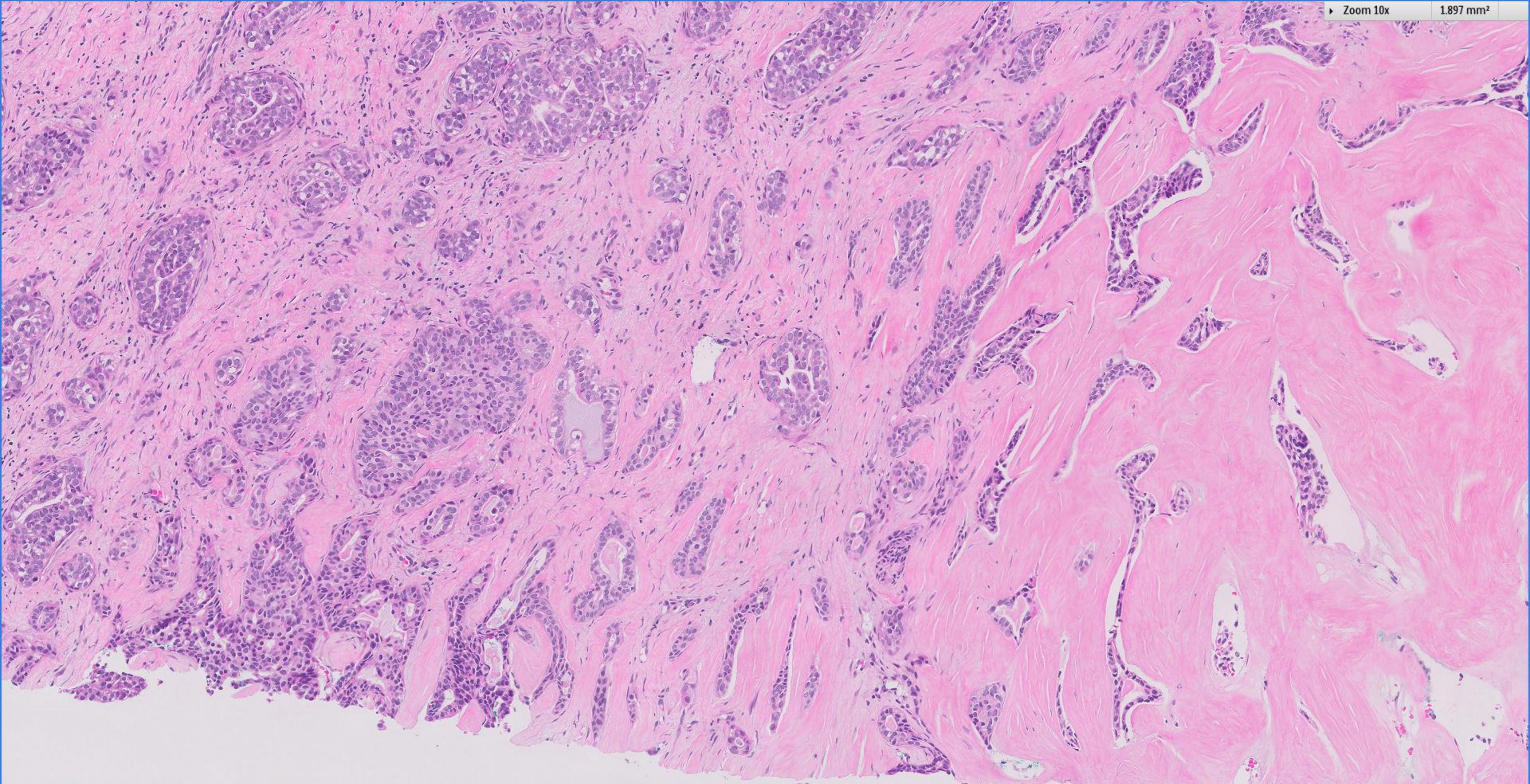
Core biopsy



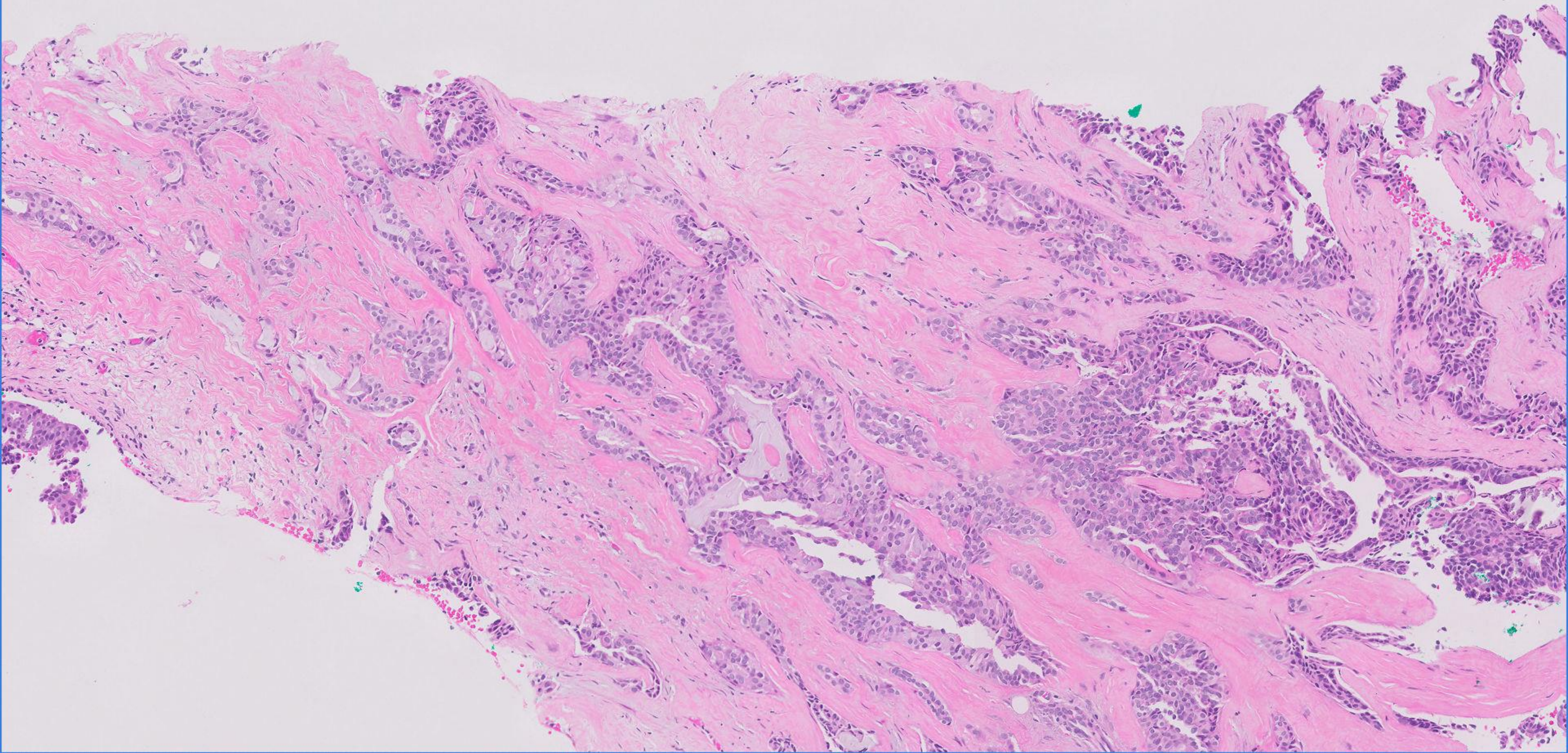
Core biopsy



Core biopsy



Core biopsy



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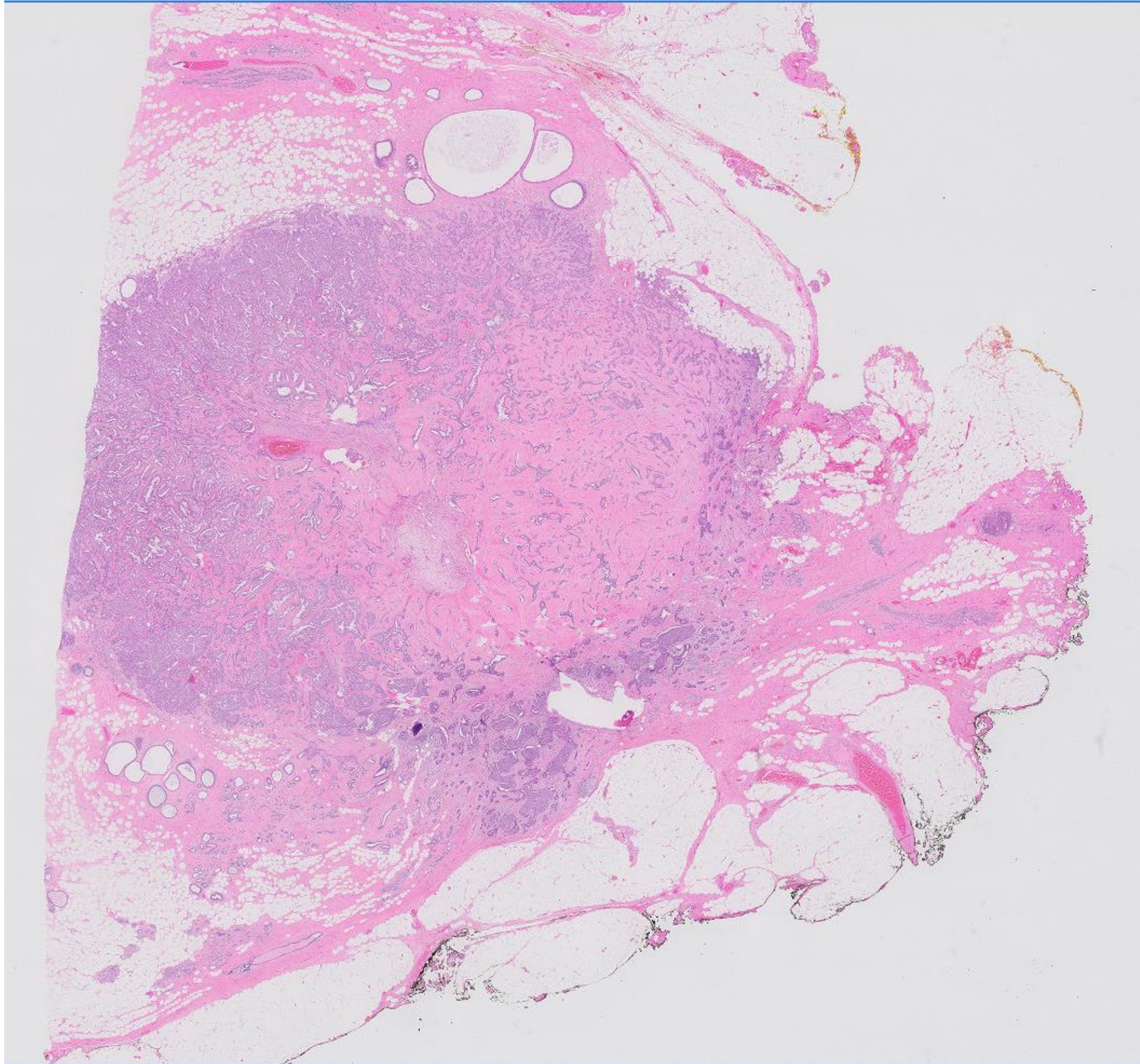

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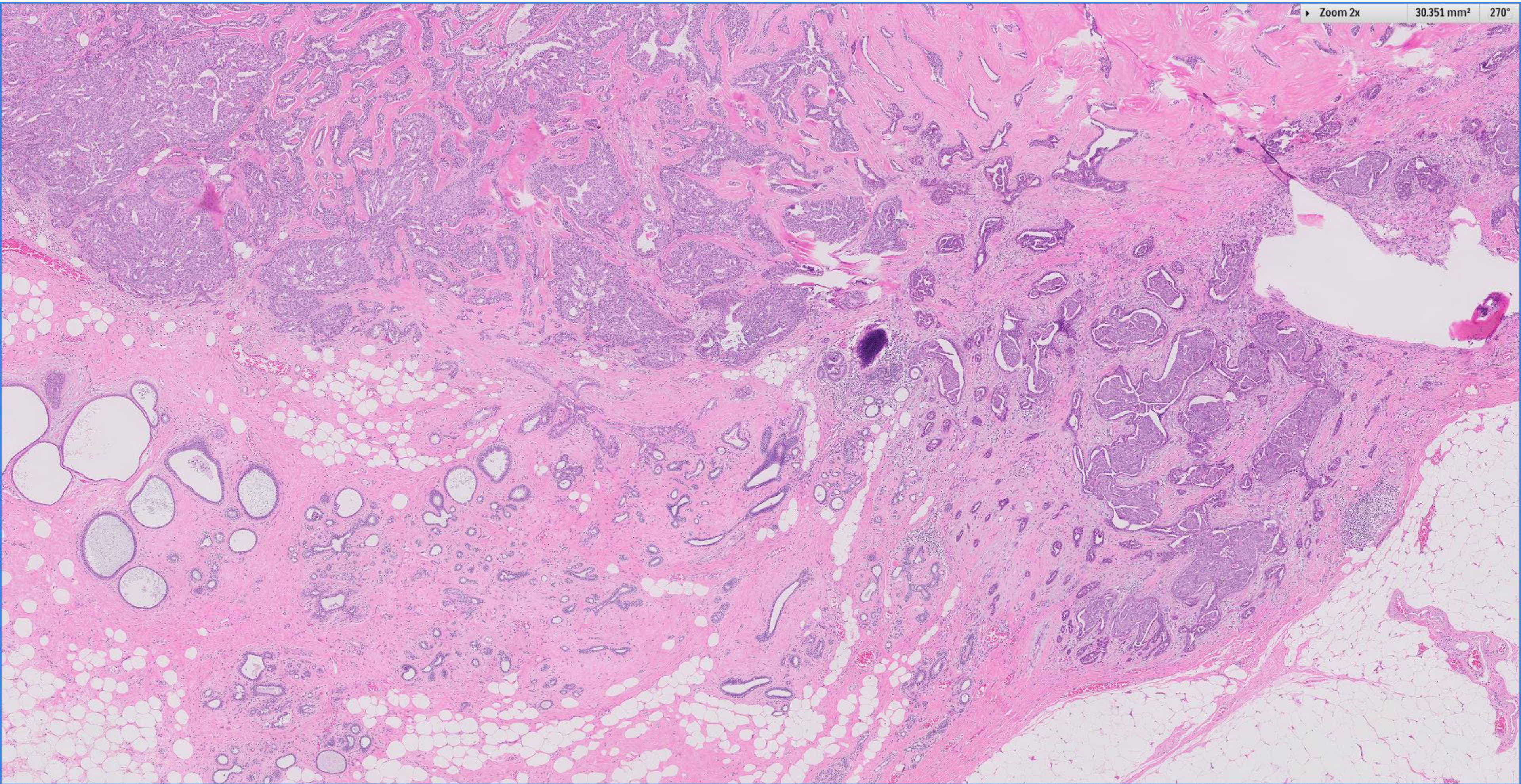

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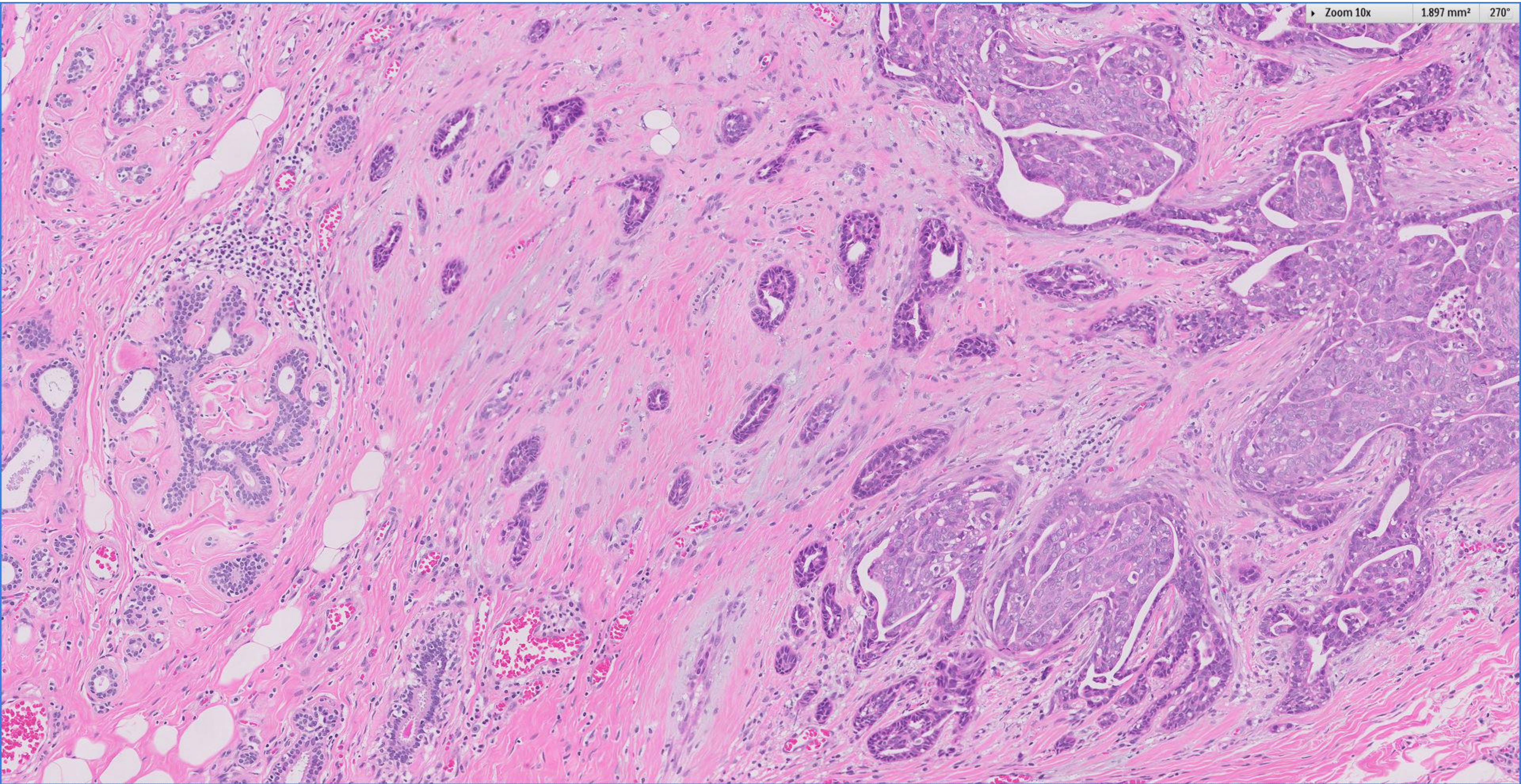

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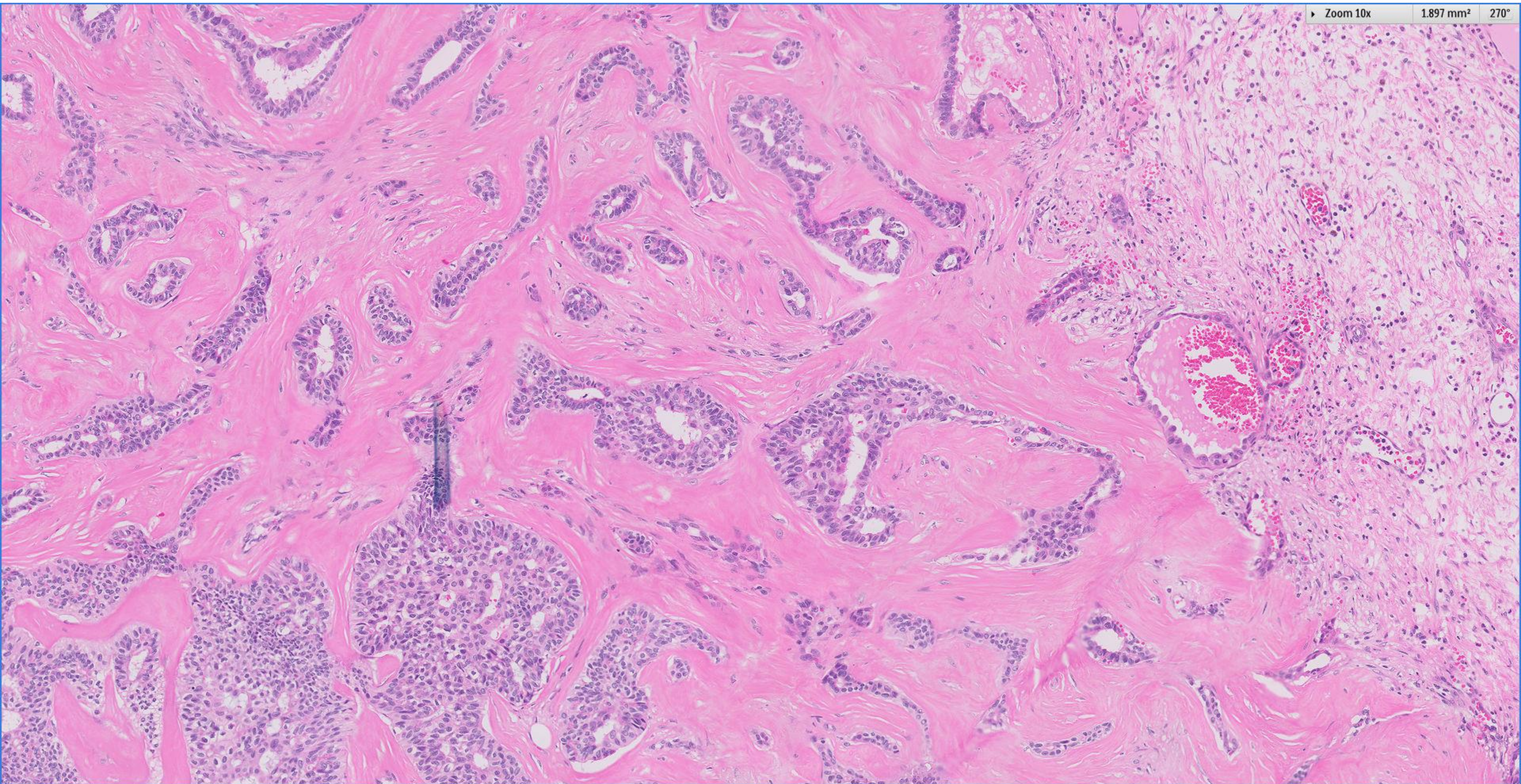

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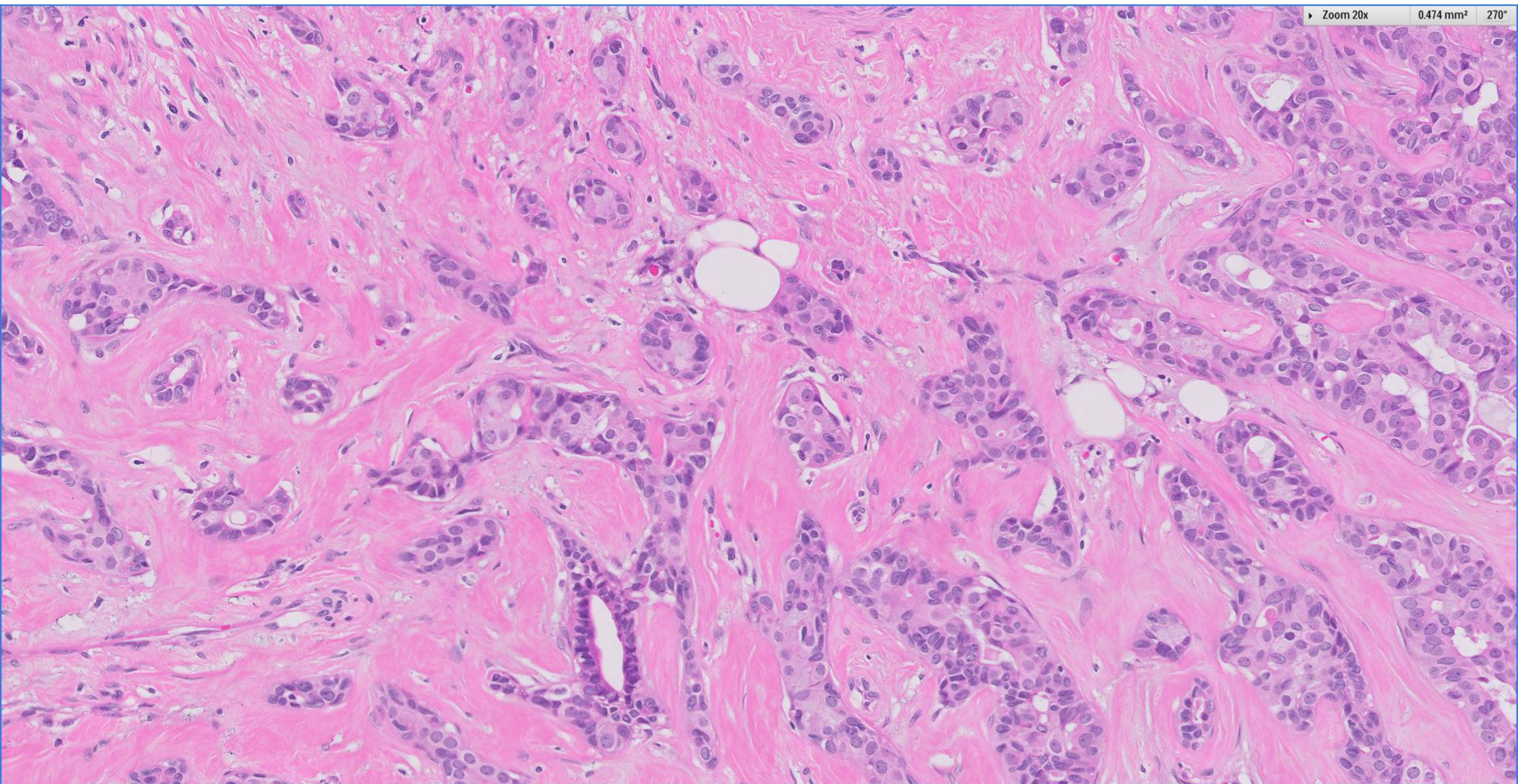
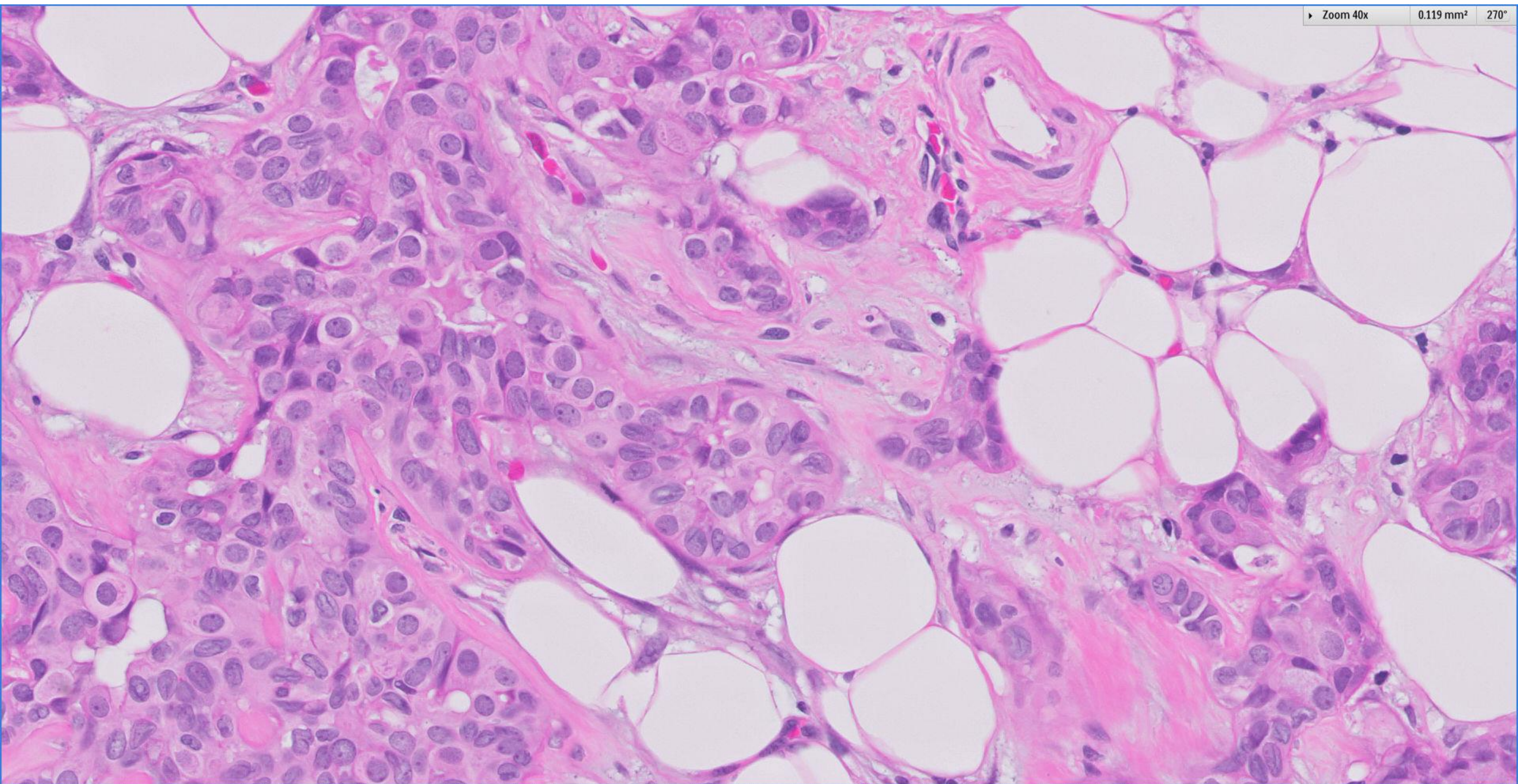


Excision



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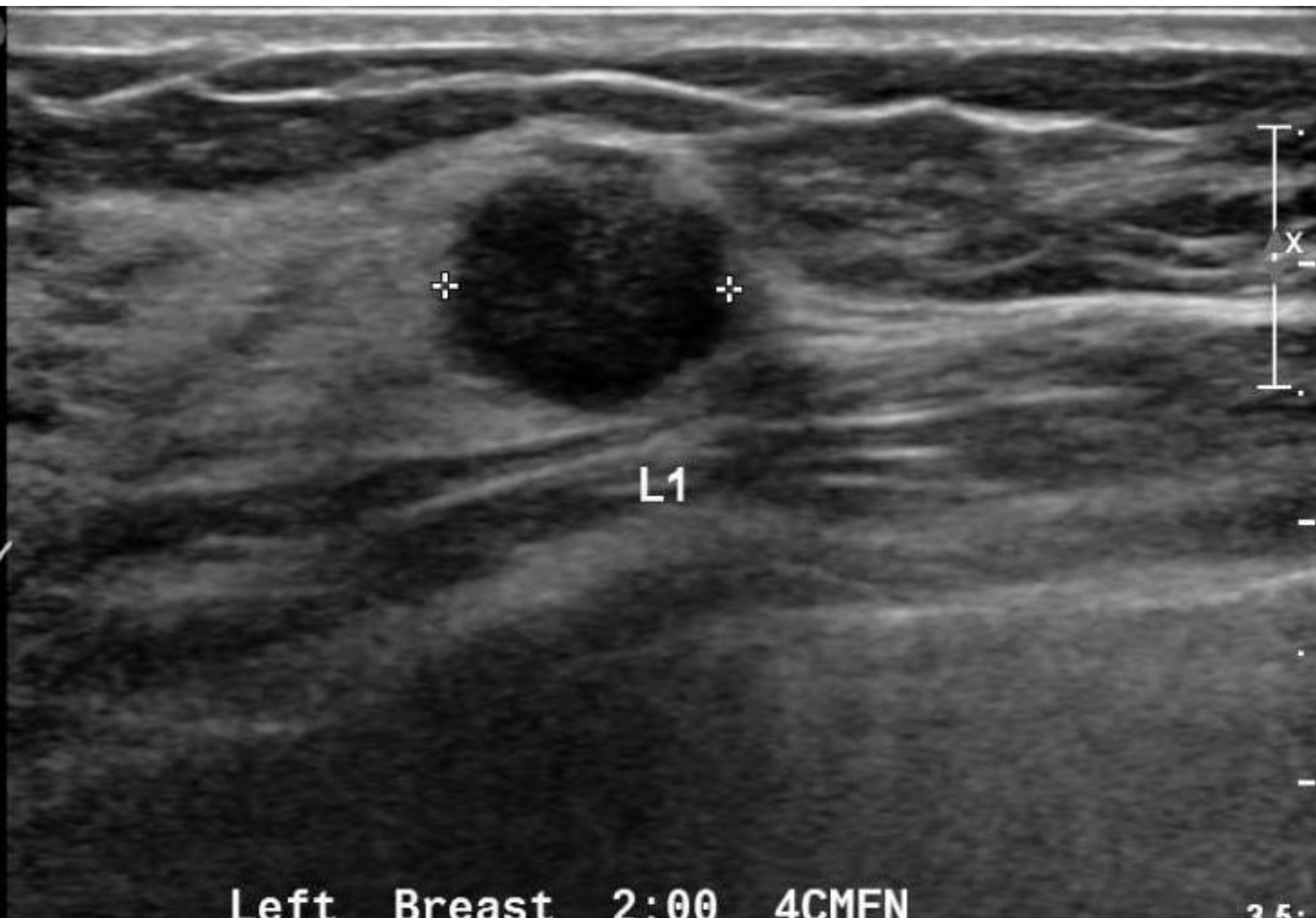
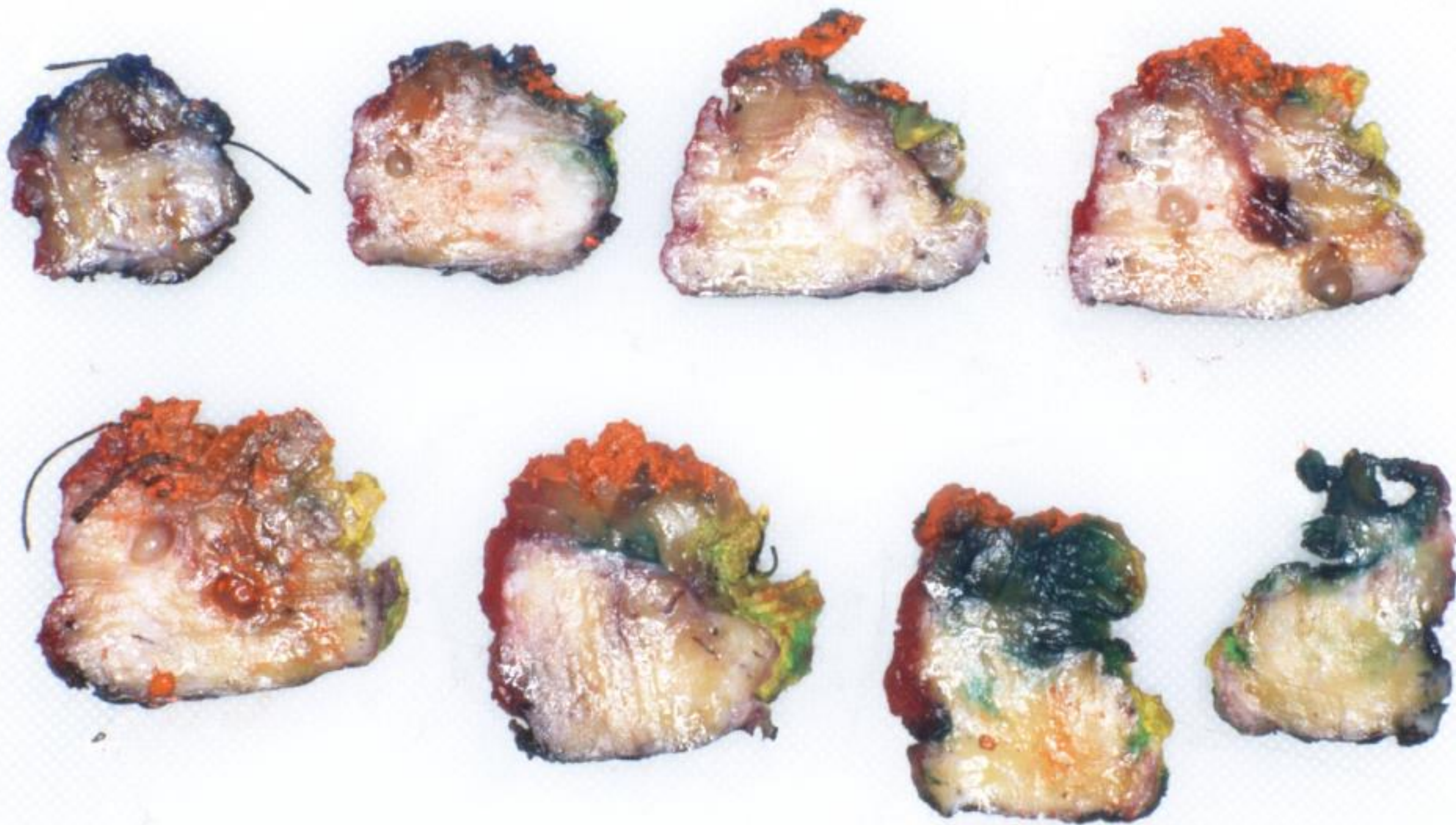
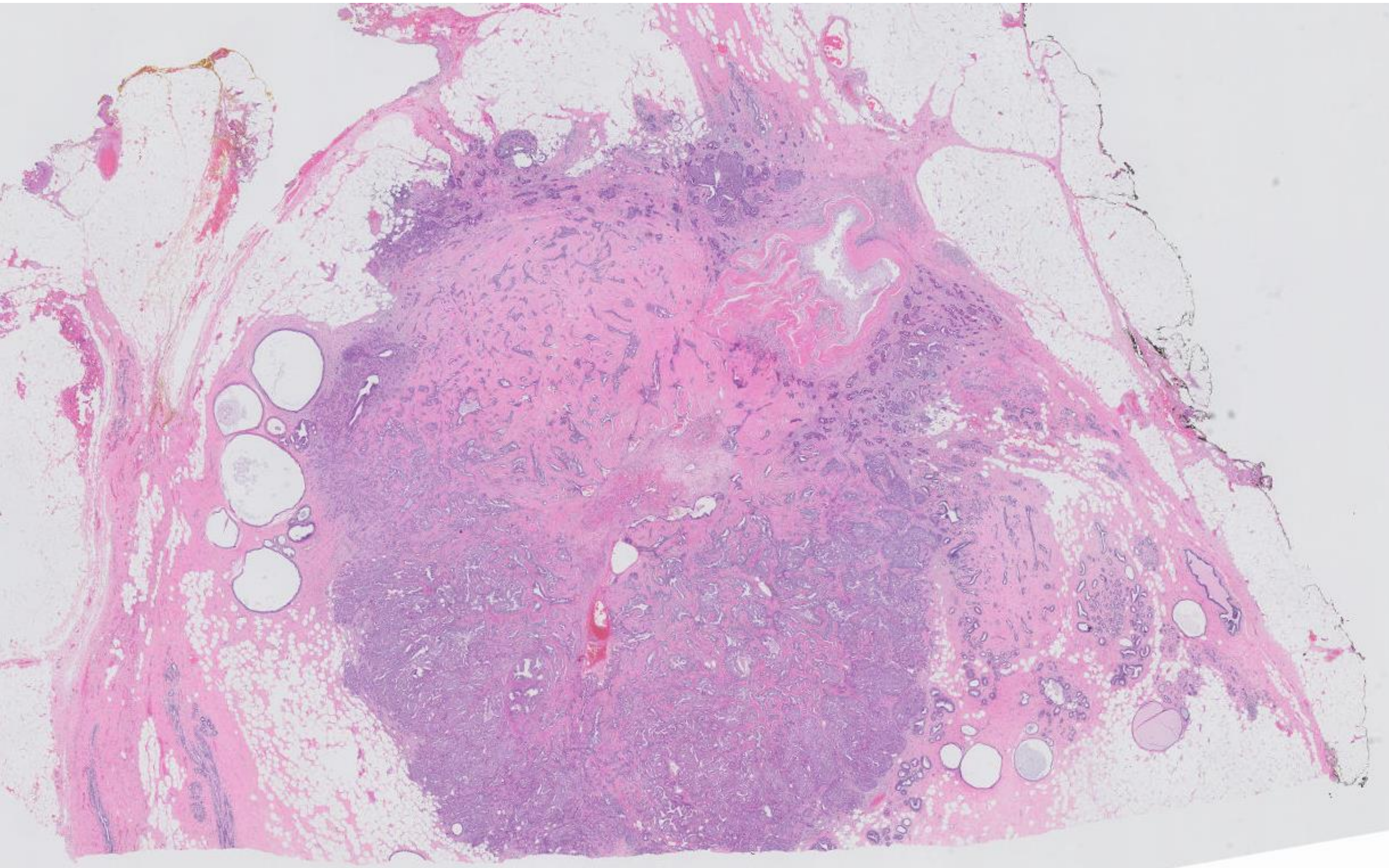
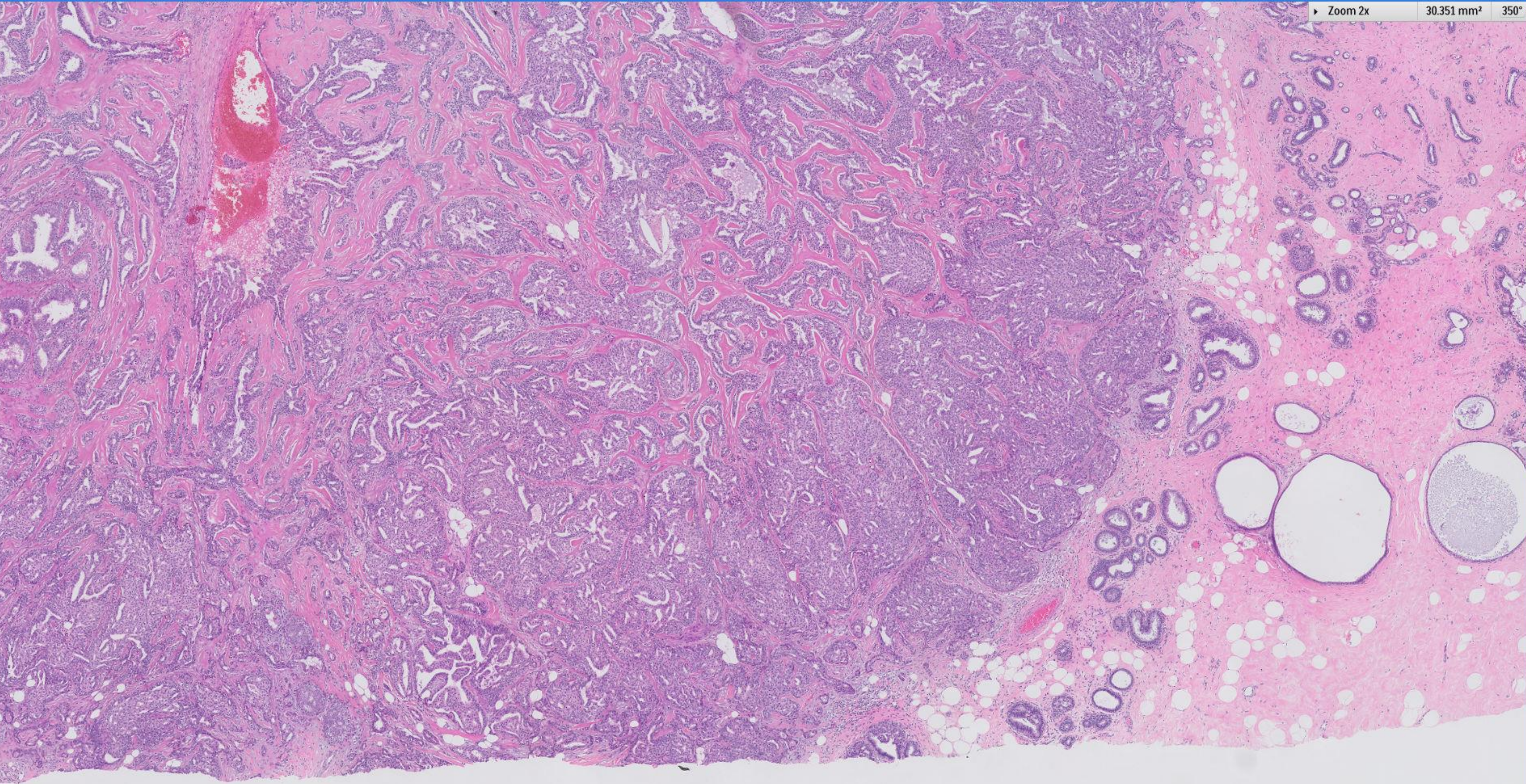
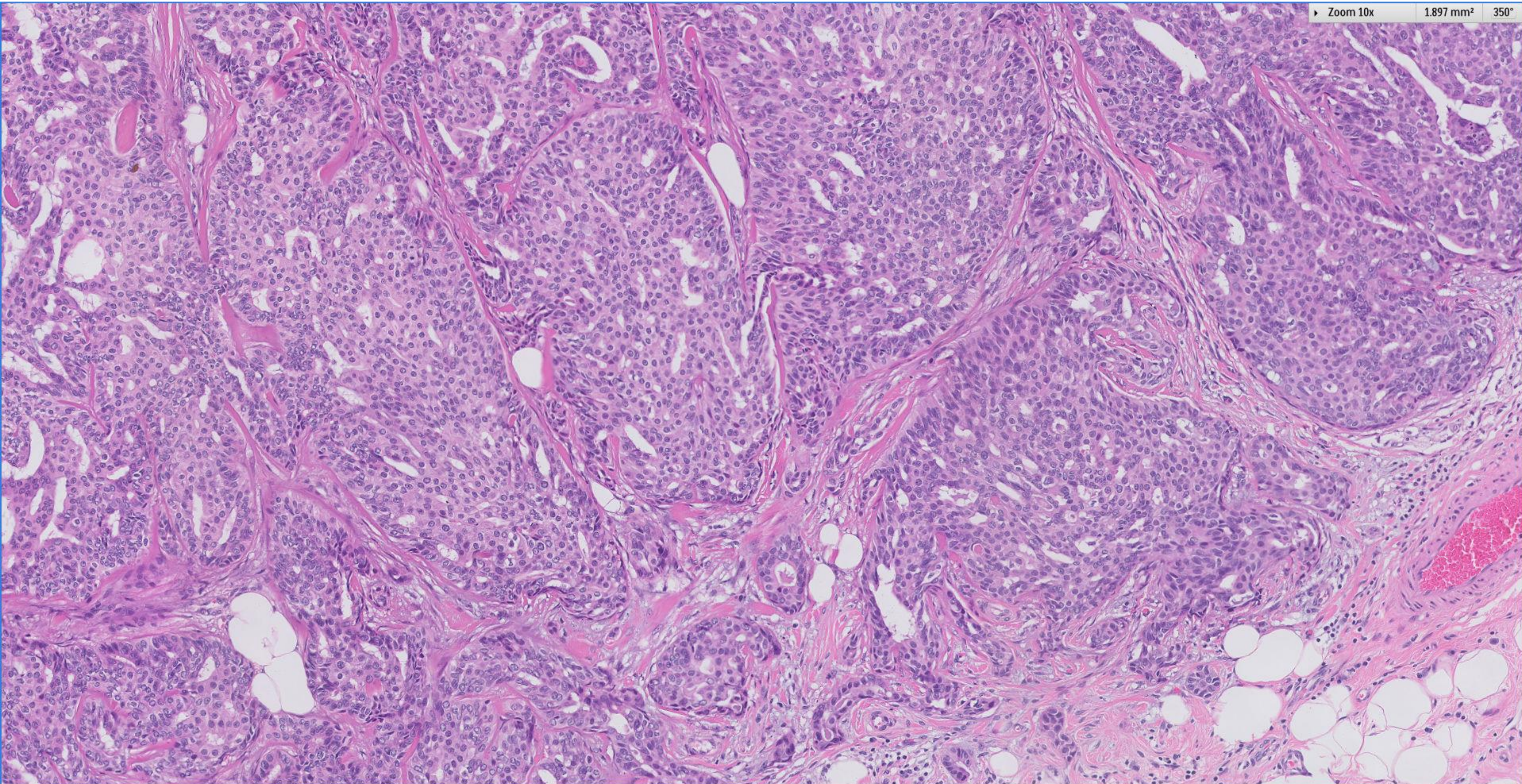
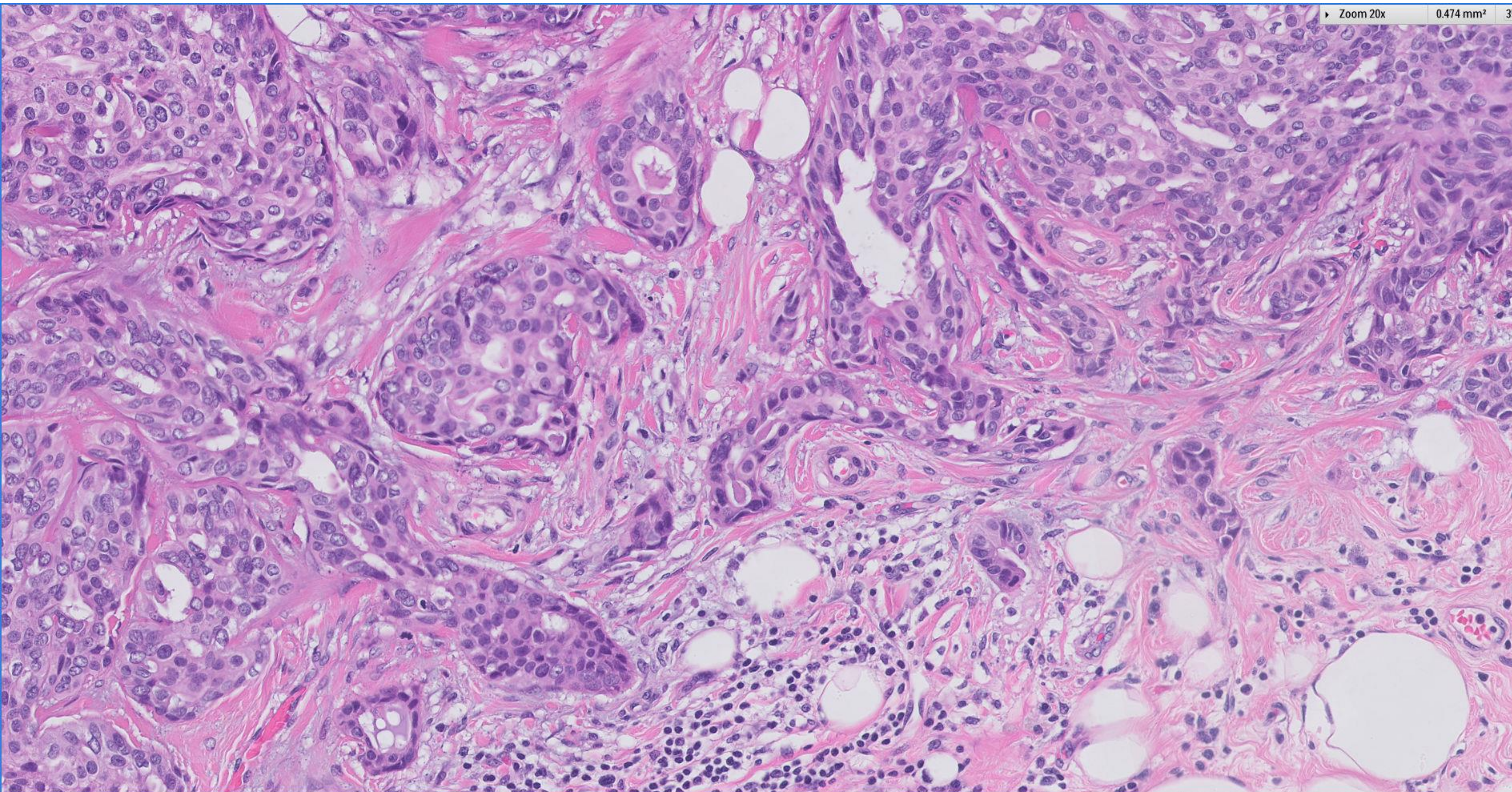

55%
C 66
P Med
Res
L1
9
3
Left Breast 2:00 4CMFN
3.5
Dist 1.09 cm

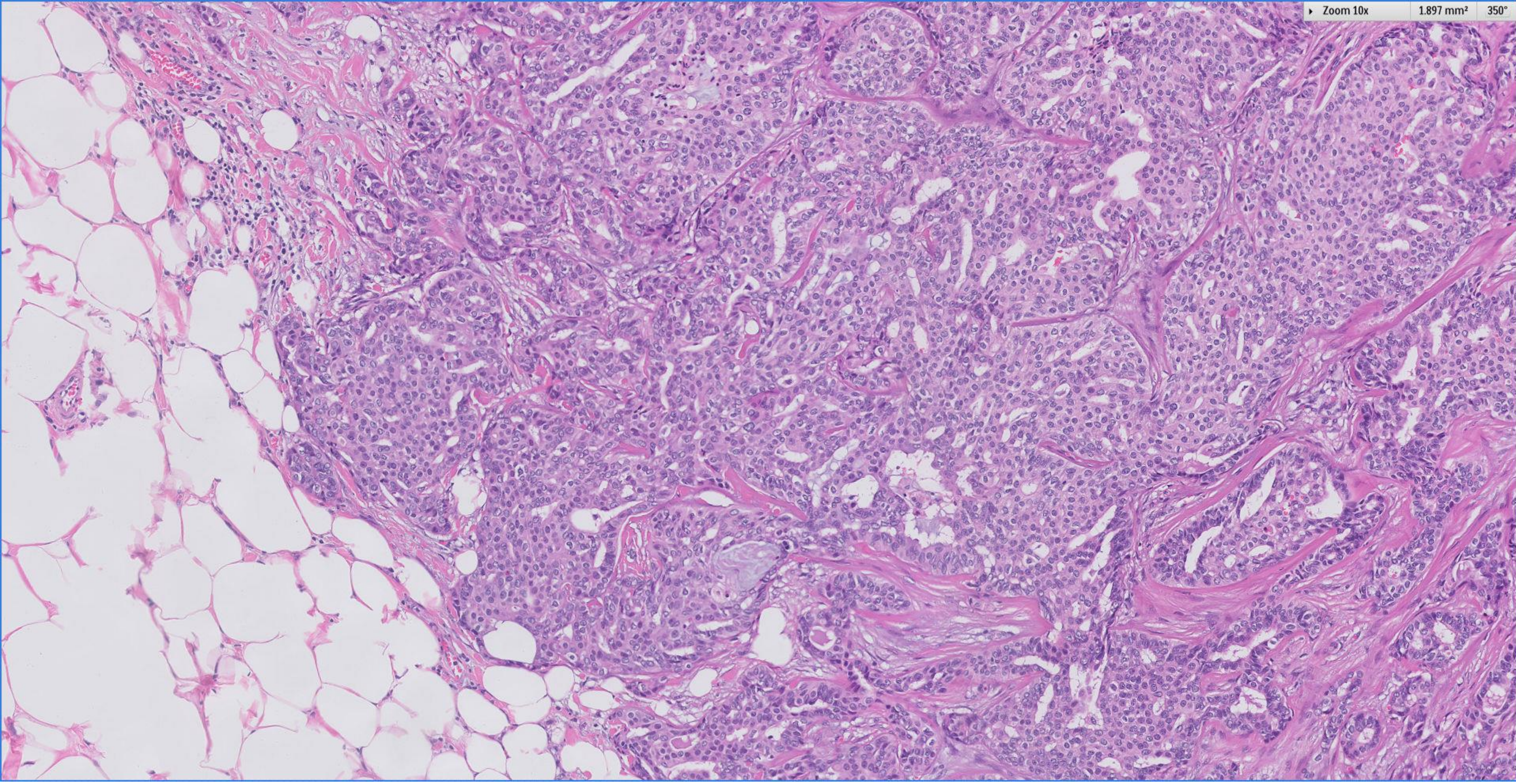

20 mm

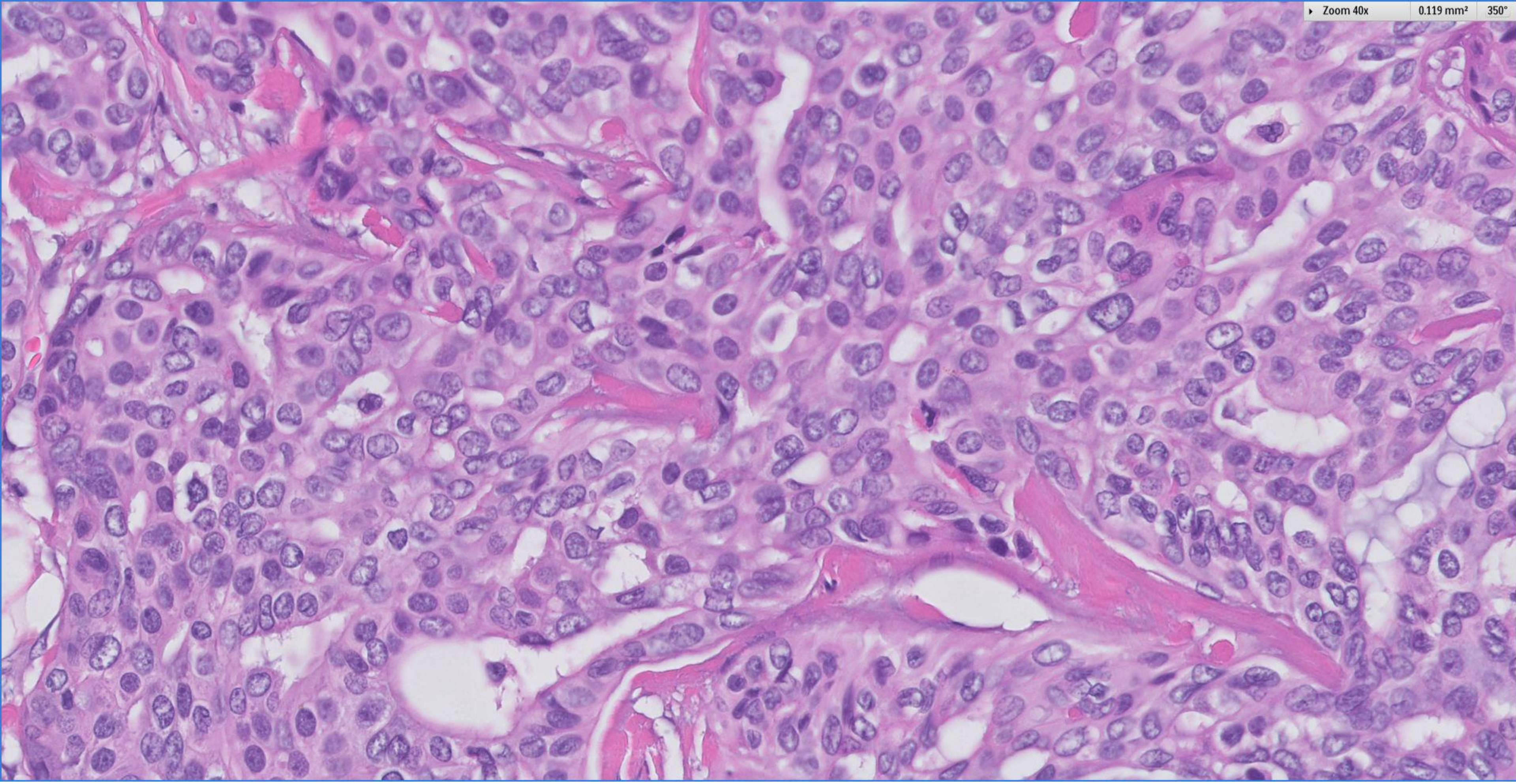



Zoom 2x
30.351 mm²
350°

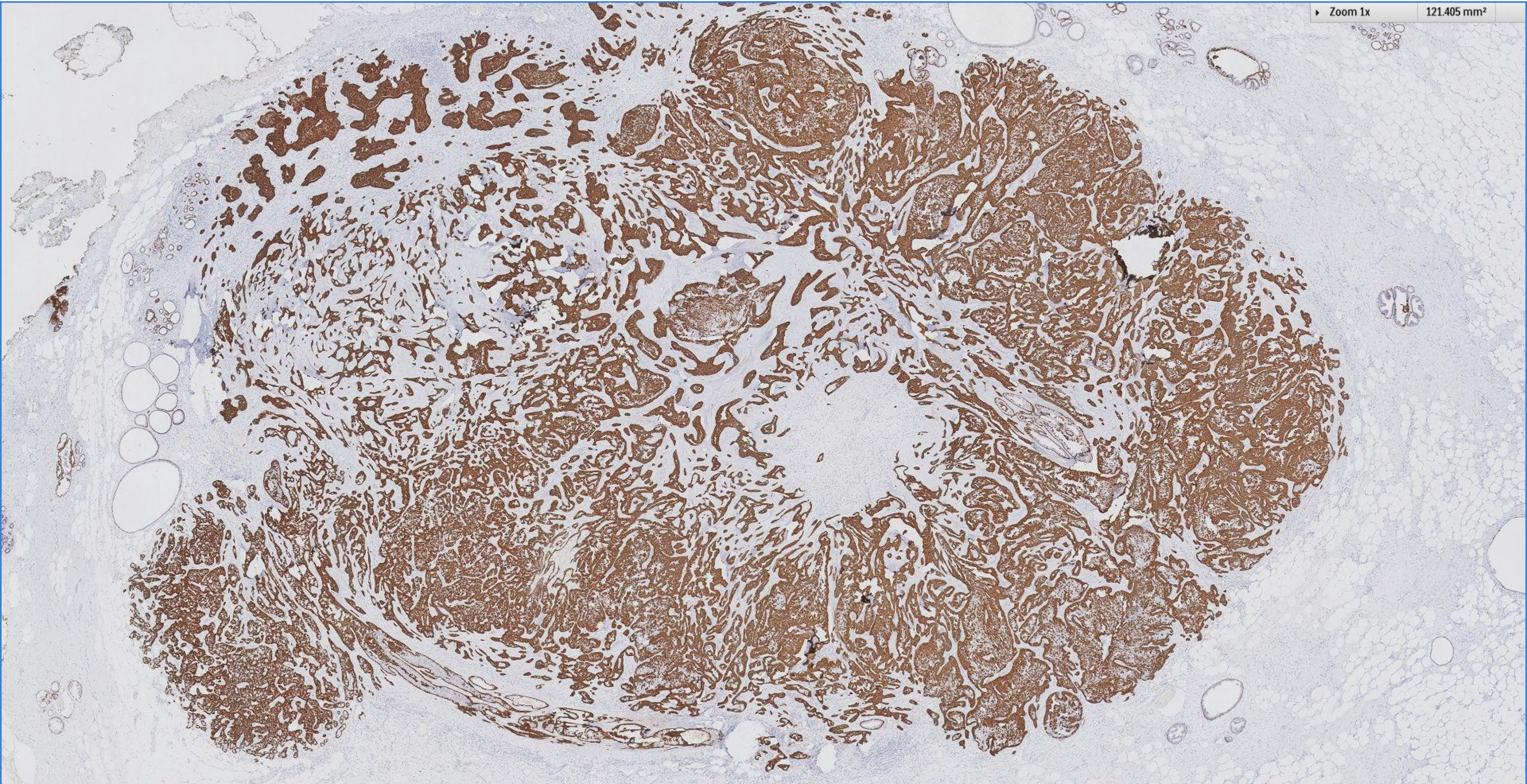

Zoom 10x
1.897 mm²
350°


Zoom 20x
0.474 mm²

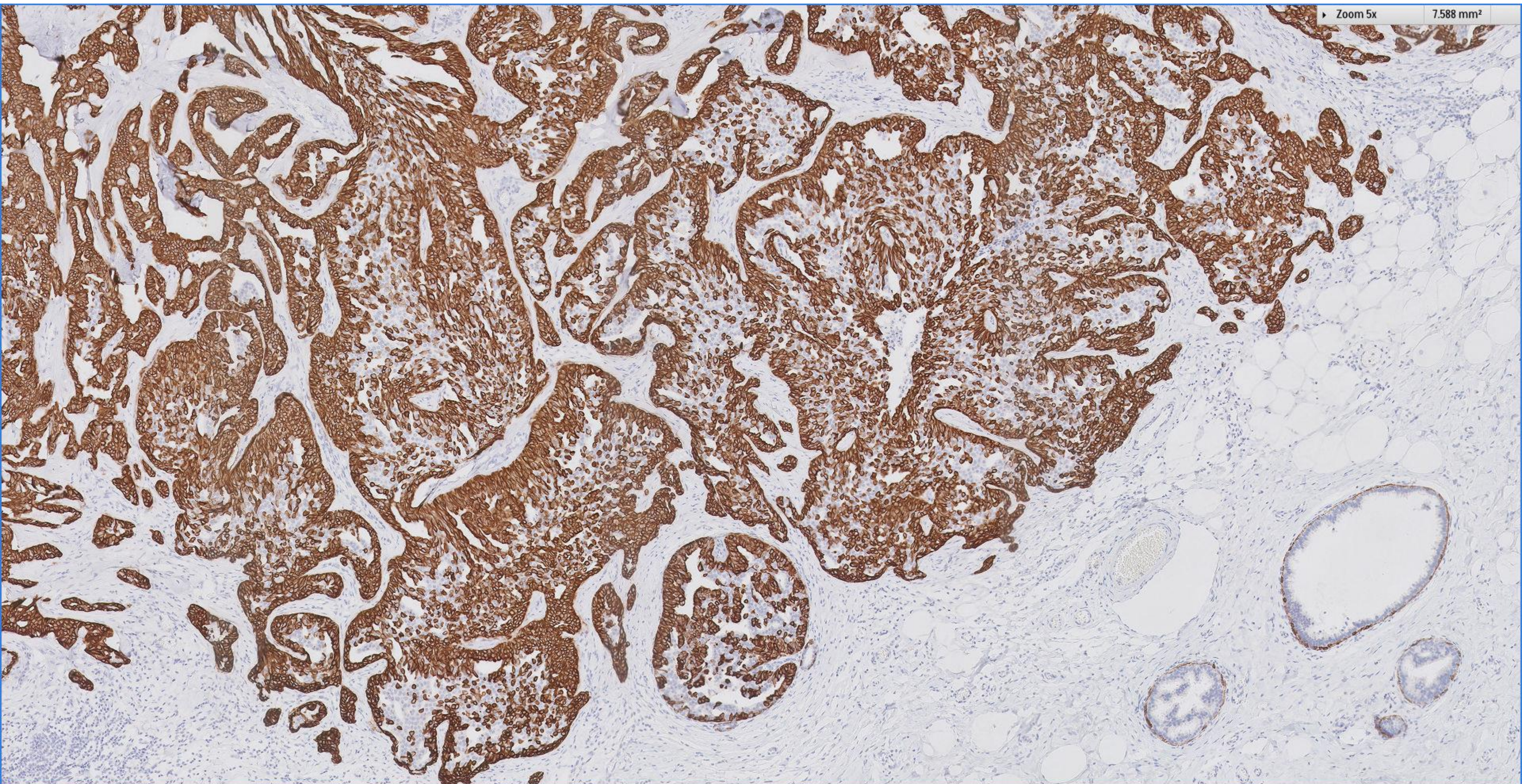

Zoom 10x
1.897 mm²
350°


Zoom 40x
0.119 mm²
350°

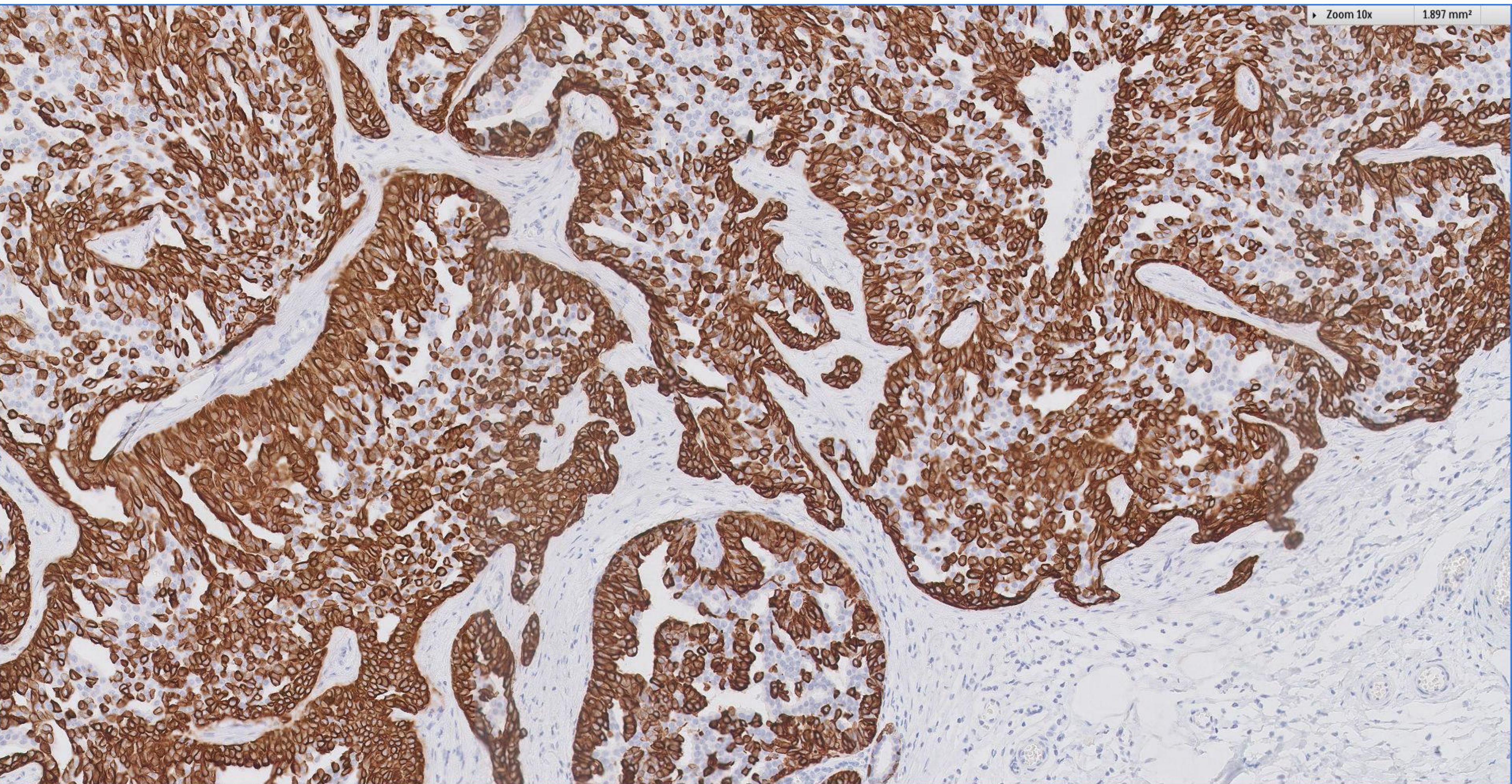
CK14



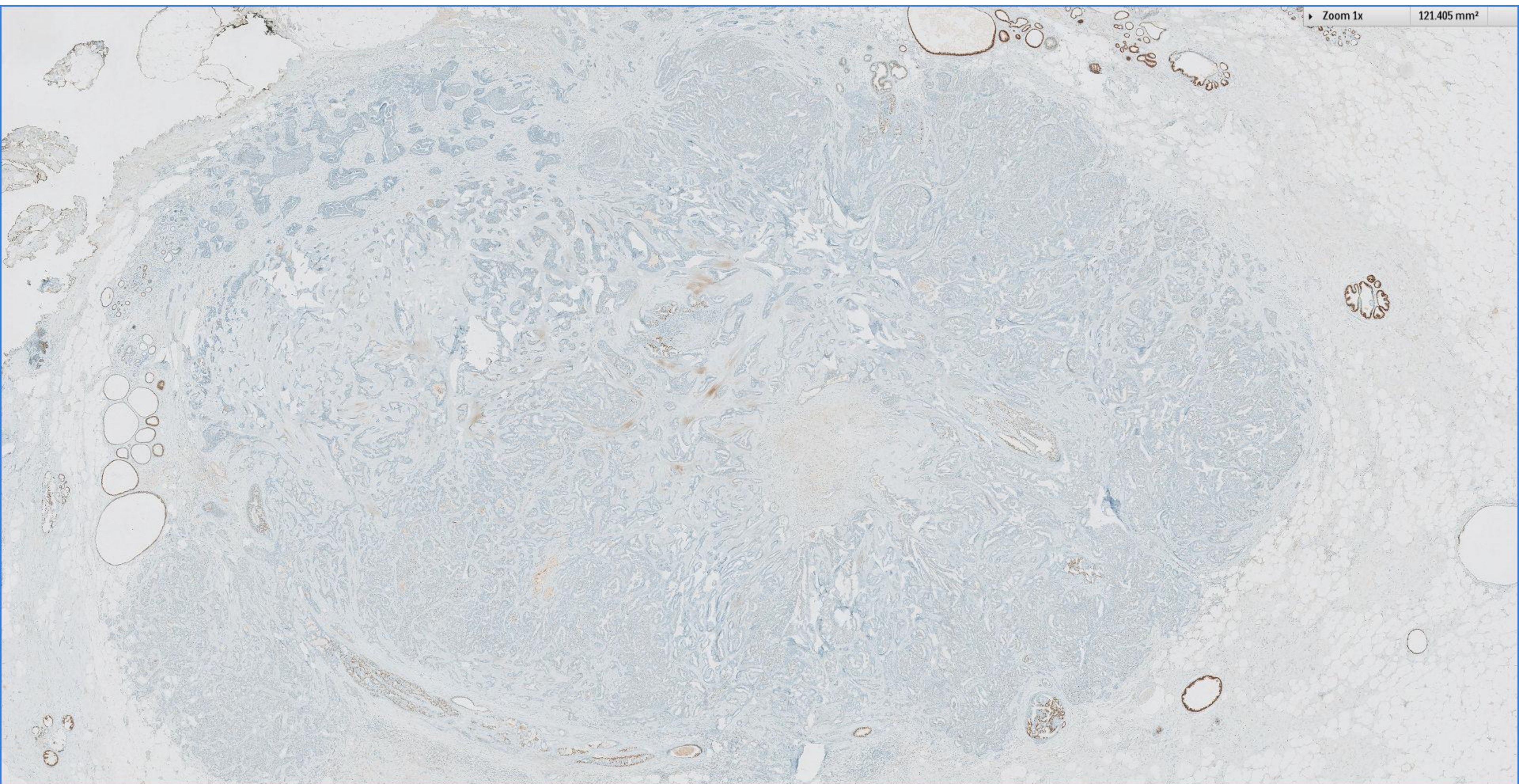
CK14



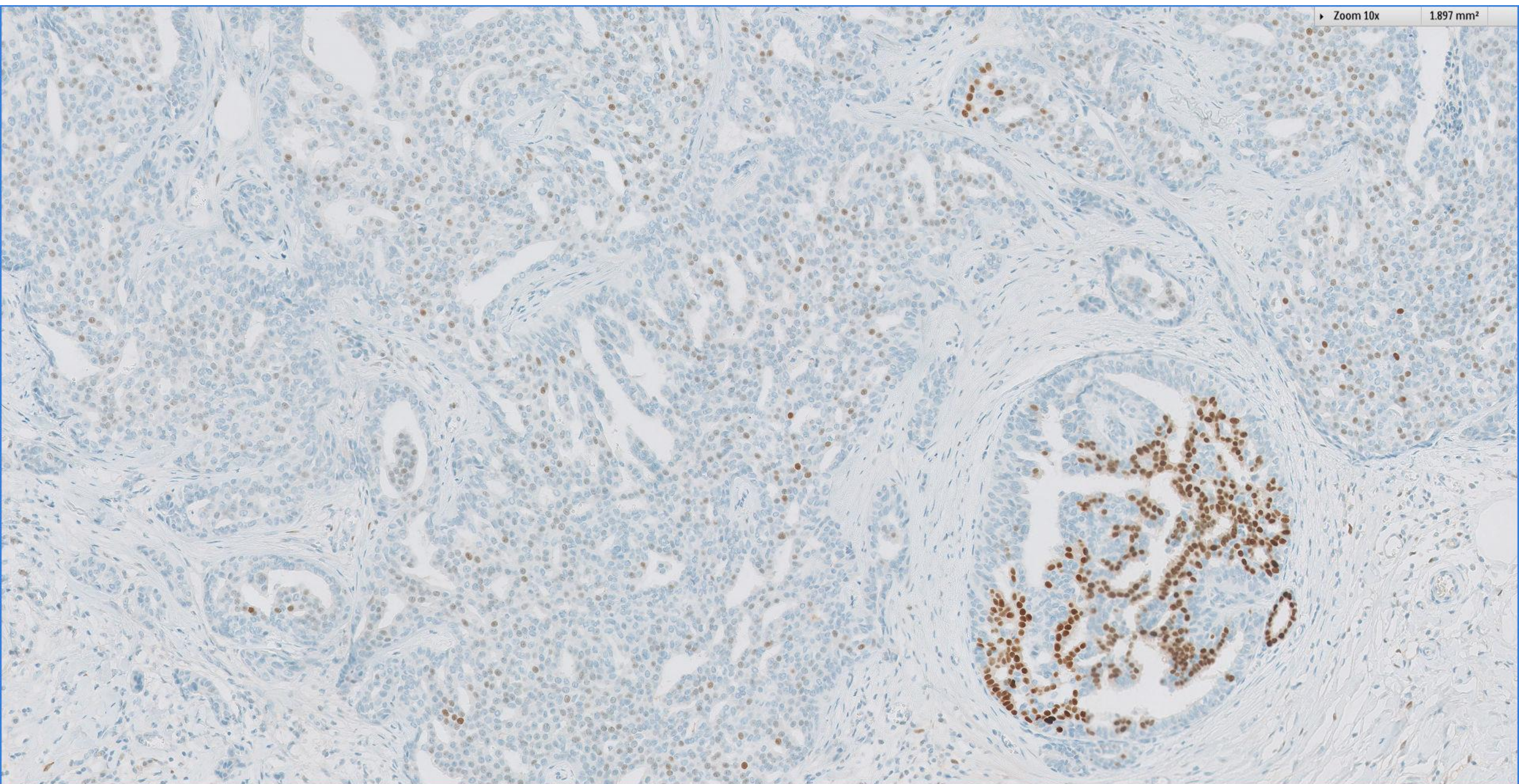
CK14



ER



ER



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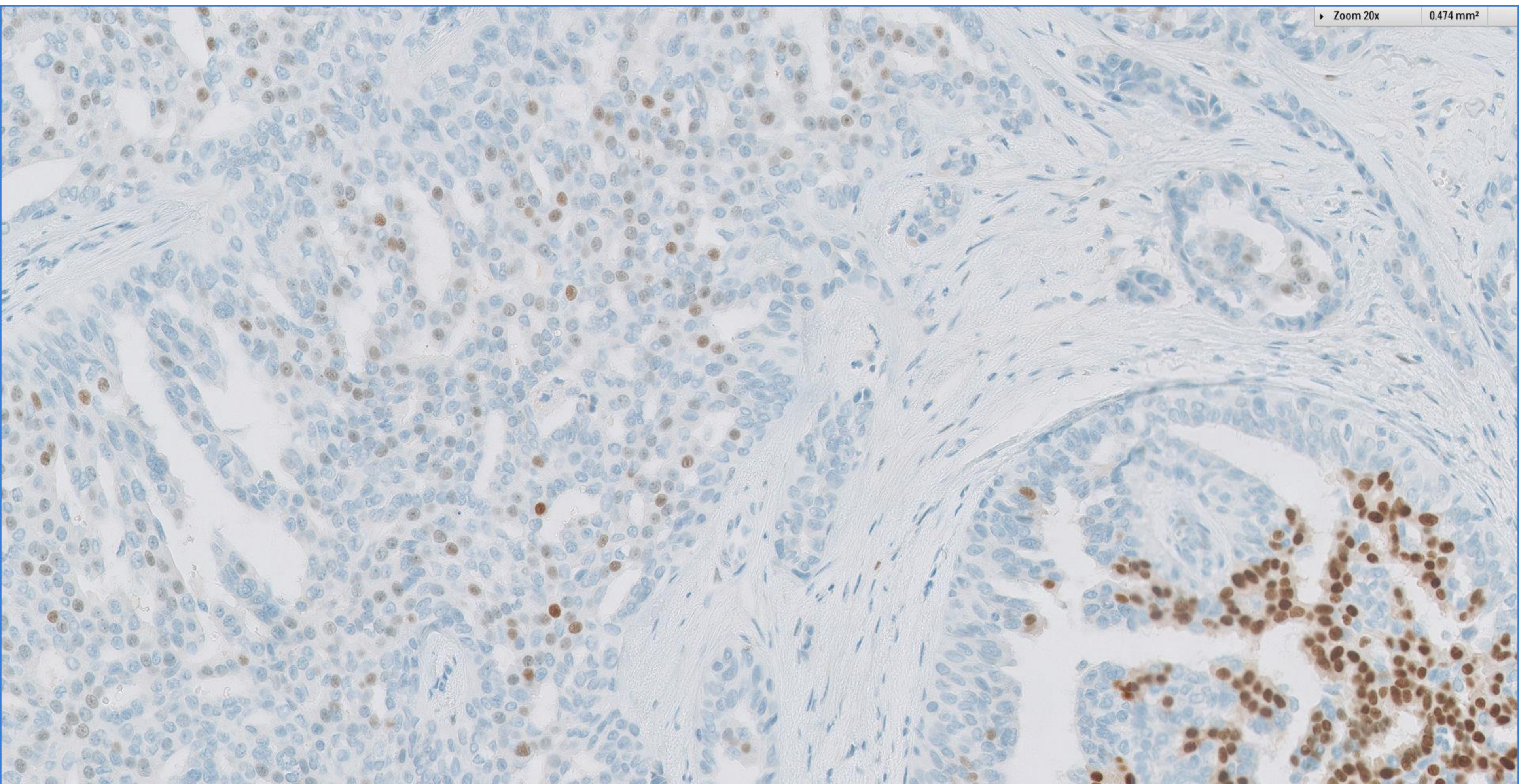

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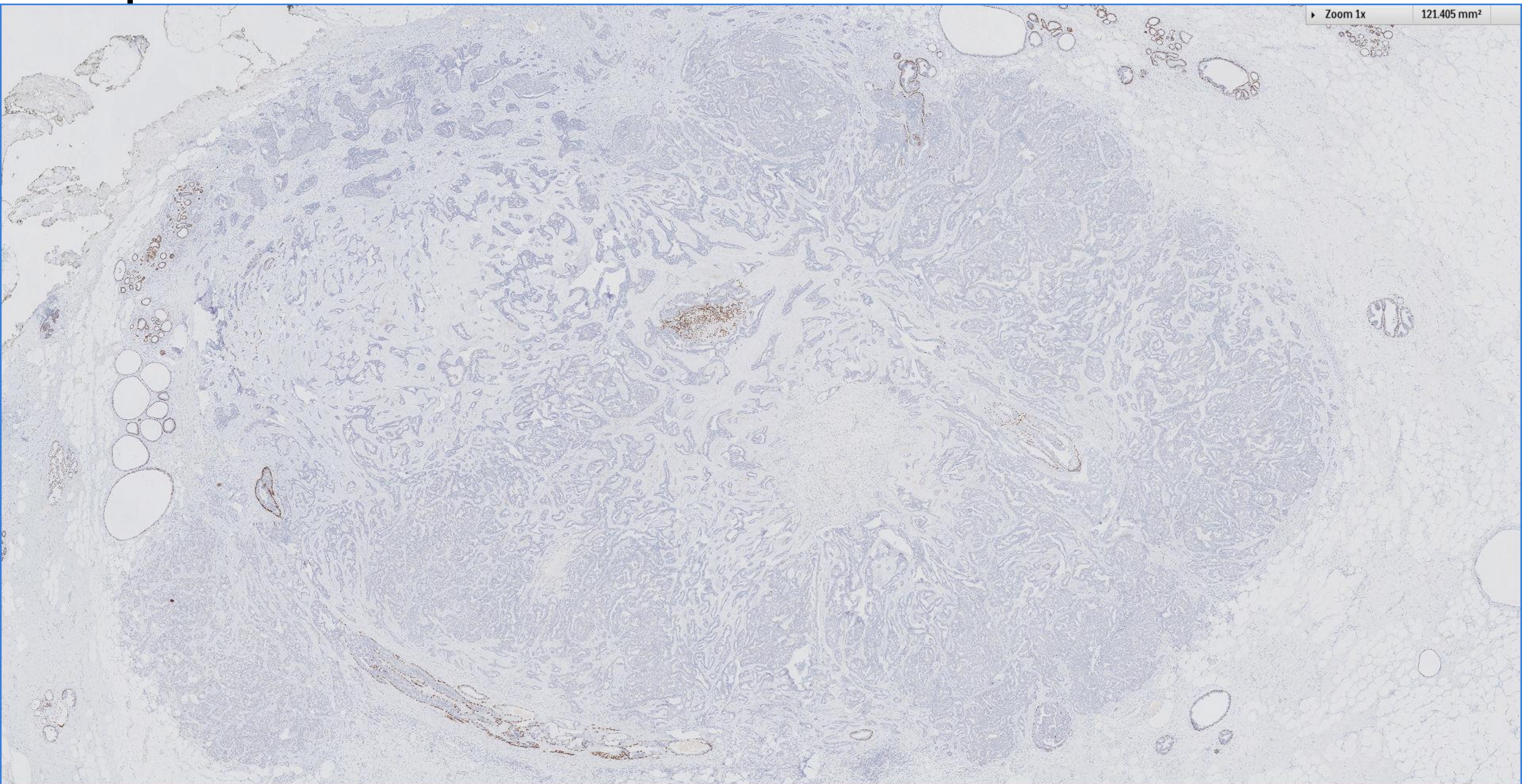

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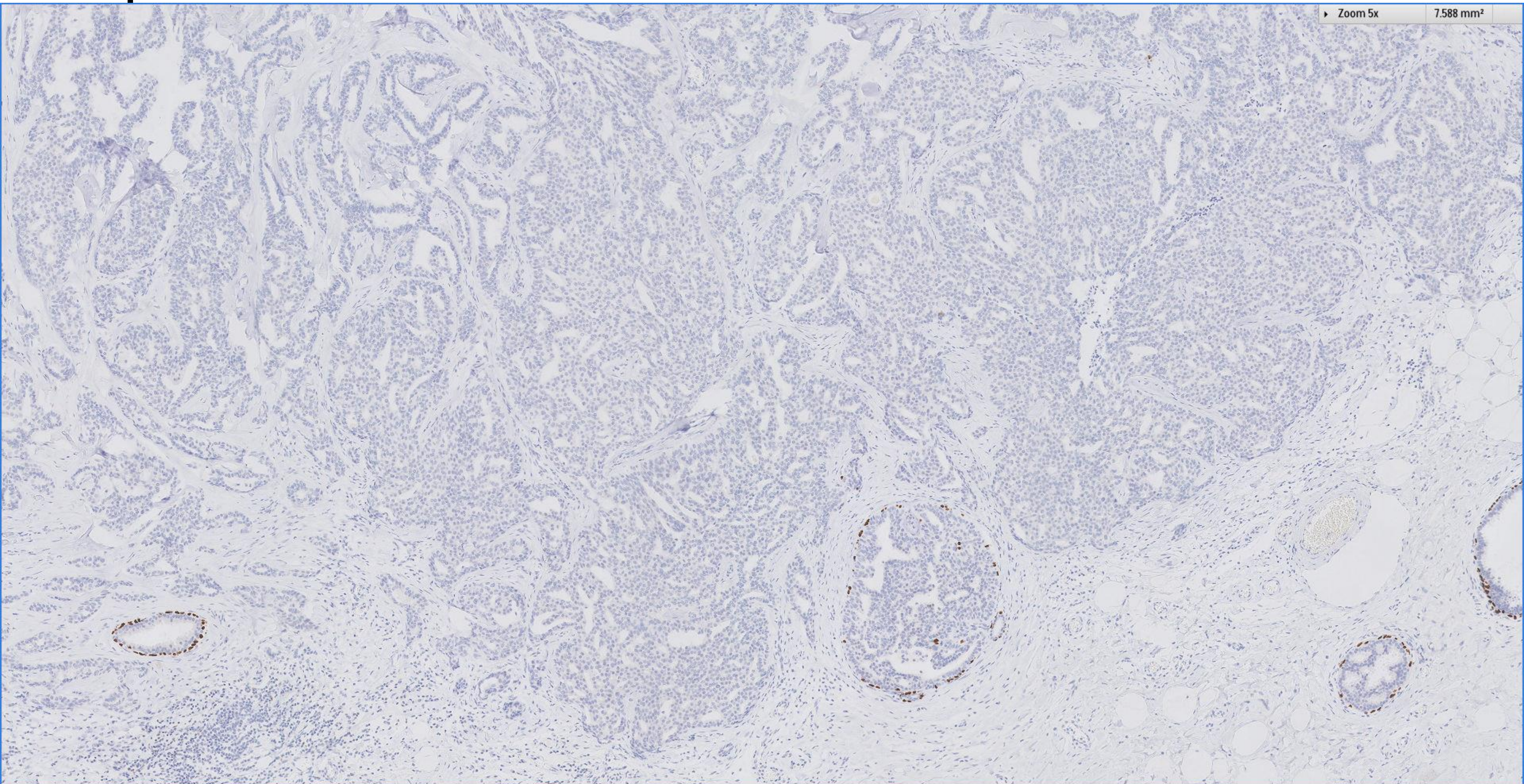

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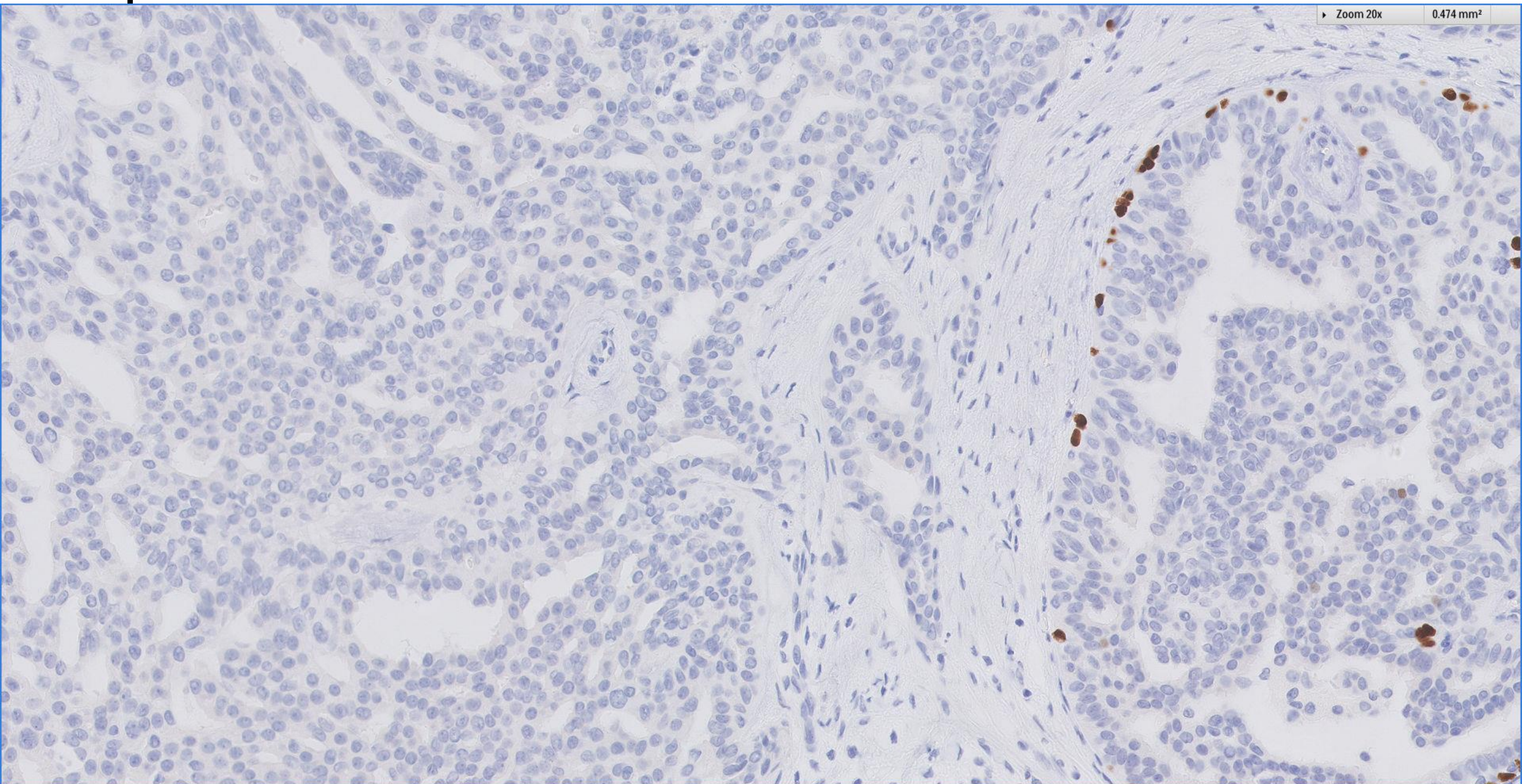
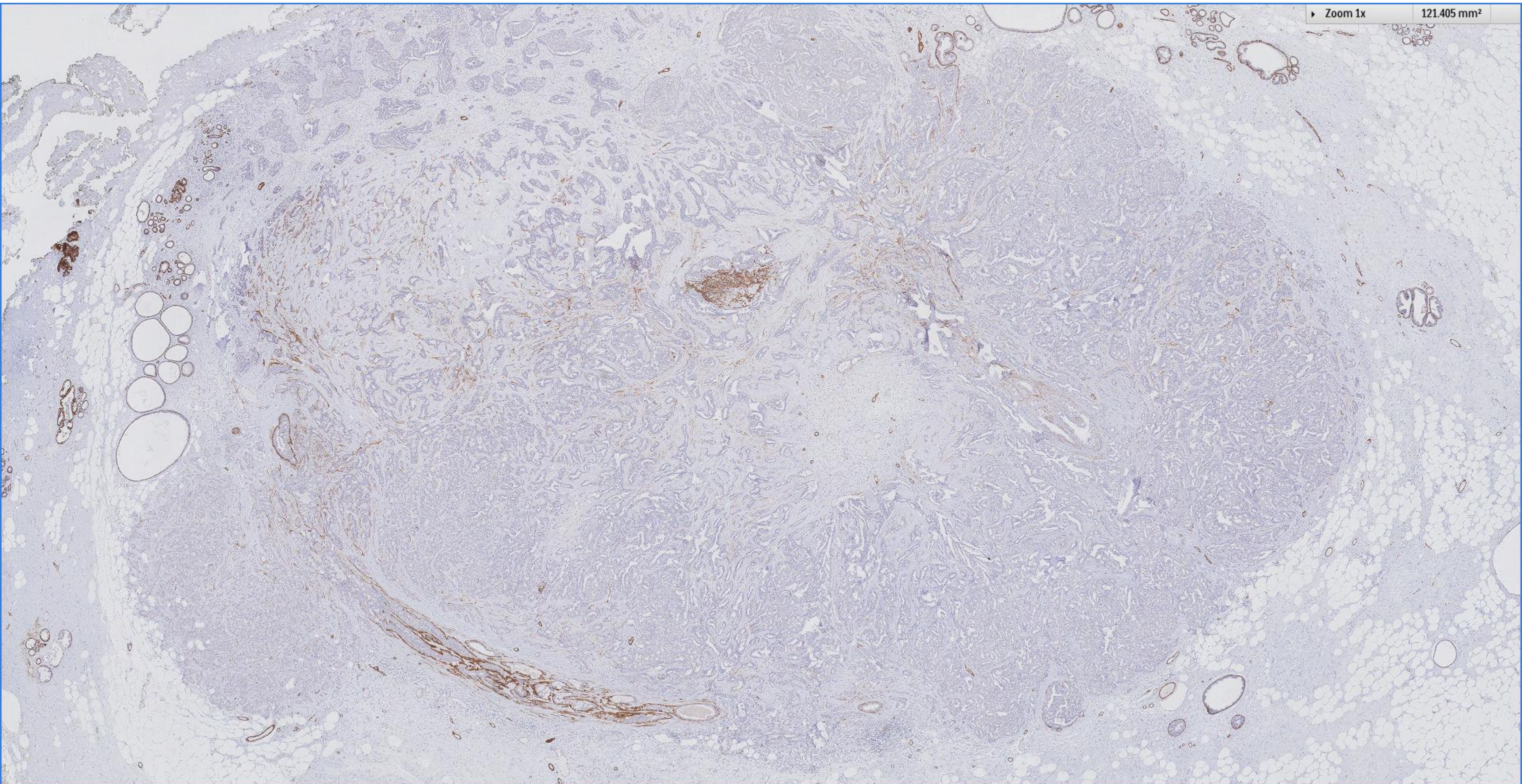


SMMS



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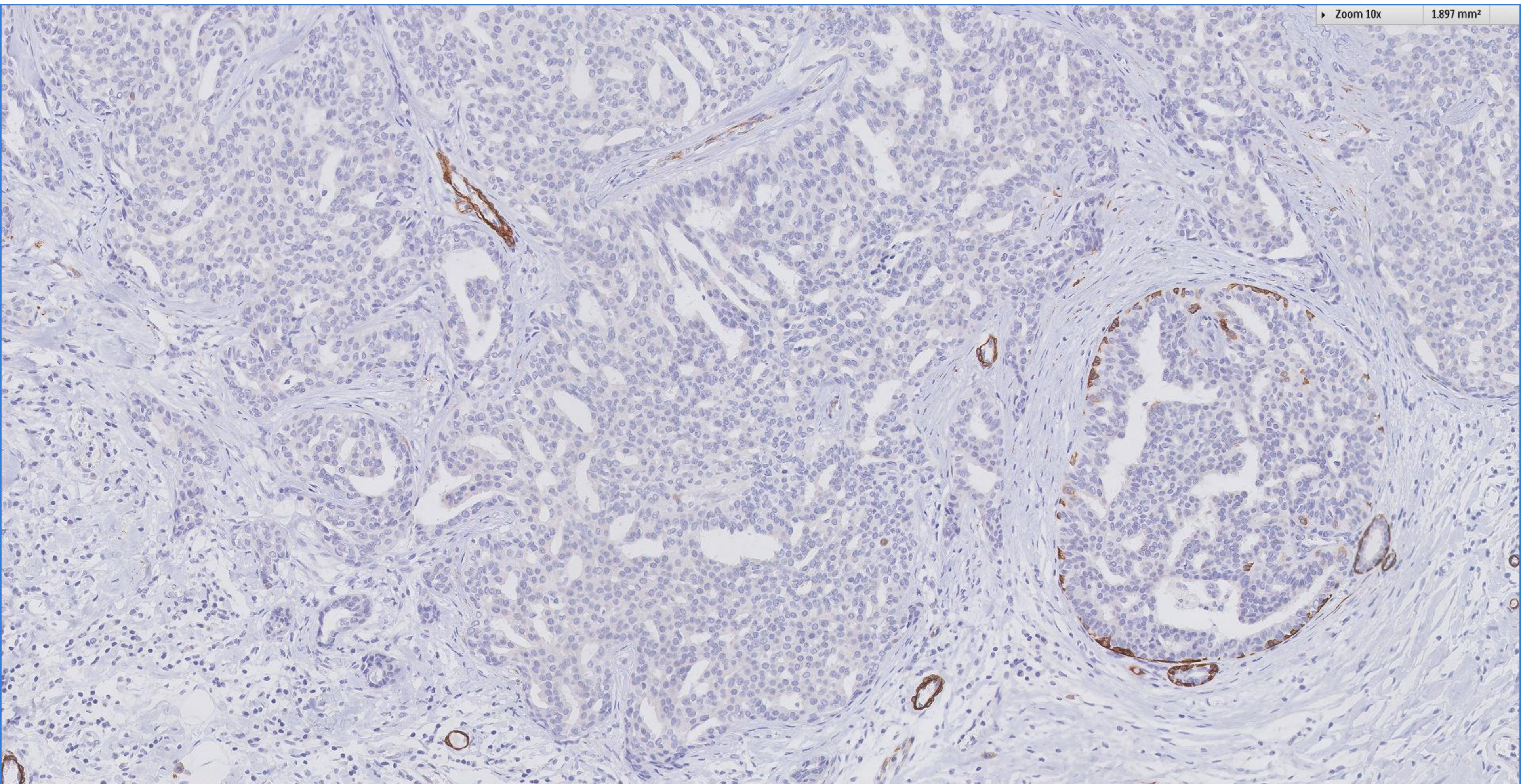

Breast Pathology Course 2018

Diagnosis

Infiltrating epitheliosis

(in consultation with Dr Ian Ellis and Dr Emad Rakha)

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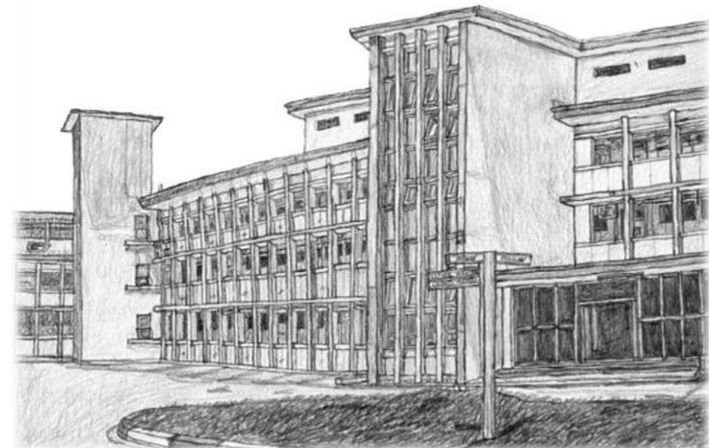

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Infiltrating epitheliosis of the breast: characterization of histologic features, immunophenotype and genomic profile

Carey A Eberle[1], Salvatore Piscuoglio[1], Emad A Rakha[2], Charlotte KY Ng[1], Felipe C Geyer[1,3], Marcia Edelweiss[1], Rita A Sakr[4], Britta Weigelt[1], Jorge S Reis-Filho[1], and Ian O Ellis[2]

AIMS—Infiltrating epitheliosis is a rare complex sclerosing lesion of the breast, characterized by infiltrating ducts immersed in a scleroelastotic stroma and filled with cells having architectural and cytological patterns reminiscent of those of usual ductal hyperplasia. Here we sought to define the molecular characteristics of infiltrating epitheliosis.

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METHODS AND RESULTS—Eight infiltrating epitheliosis, adjacent breast lesions (one usual ductal hyperplasia, one papilloma, one micropapillary ductal carcinoma *in situ* and one low-grade adenosquamous carcinoma), and corresponding normal breast tissue from each case were microdissected and subjected to massively parallel sequencing analysis targeting all coding regions of 254 genes recurrently mutated in breast cancer and/or related to DNA repair. Mutations in components of the PI3K pathway were found in all infiltrating epitheliosis samples, seven of which harbored *PIK3CA* hotspot mutations, while the remaining case displayed a *PIK3R1* somatic mutation.

CONCLUSIONS—Somatic mutations affecting PI3K pathway genes were found to be highly prevalent in infiltrating epitheliosis, suggesting that these lesions may be neoplastic rather than hyperplastic. The landscape of somatic genetic alterations found in infiltrating epitheliosis is similar to that of radial scars/complex sclerosing lesions, suggesting that infiltrating epitheliosis may represent one end of this spectrum of lesions.

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Infiltrating epitheliosis

- Term first introduced by Azzopardi in 1979.
- Often used synonymously with ‘sclerosing adenosis with pseudoinfiltration’, ‘sclerosing papillary proliferation’.
- Classification is controversial.

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Infiltrating epitheliosis

- Histological features (Eusebi & Millis) ~
  - Predominantly florid usual ductal hyperplasia proliferation with focal squamoid features.
  - Diffuse scleroelastotic stromal alterations.
  - Desmoplastic stroma with keloid-like fibrous bands.
- Involved ducts have jagged and irregular edges.
- Proliferating epithelium ‘flows out’ into adjacent stroma.
- Nuclear pseudoinclusions similar to those seen in UDH can be present.
- Papillary component may be encountered.
- Often classified with radial sclerosing lesions.
- Infiltrative appearance mimics invasive disease.
- Absent to discontinuous peripheral myoepithelial layer compounds the resemblance to invasive cancer.
- Immunophenotypic abnormalities in myoepithelial cells in the majority of cases of infiltrating epitheliosis.

Infiltrating epitheliosis

- PIK3CA and PIK3R1 mutations identified, suggesting neoplasia rather than hyperplasia.
- PIK3CA activating mutations are also seen in radial sclerosing lesions, implying that infiltrating epitheliosis may be the most proliferative end of the same disease spectrum.
- CK5/6 positive & heterogeneous; ER can be negative.
- Current management approach is similar to that for complex sclerosing lesions.

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Infiltrating epitheliosis ~ differential diagnosis

- Radial sclerosing lesion ~
  - Fibroelastotic changes in the centre of the lesion
- Florid usual ductal hyperplasia ~
  - Lacks the infiltrative edges
- Solid papillary carcinoma with reverse polarity/breast tumour resembling the tall cell variant of papillary thyroid carcinoma
- Invasive carcinoma ~
  - Lacks UDH type appearance

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Infiltrating epithelioisis & breast tumour resembling papillary thyroid carcinoma

'Continuum between infiltrating epitheliosis and BTRPTC, and they may represent a spectrum of papillary lesions with infiltrating epitheliosis at the sclerosis-rich/epithelial-poor end and BTRPTC at the epithelium-rich/stroma-poor end of the spectrum.'

Bhargava et al. Am J Clin Pathol April 2017;147:399-410

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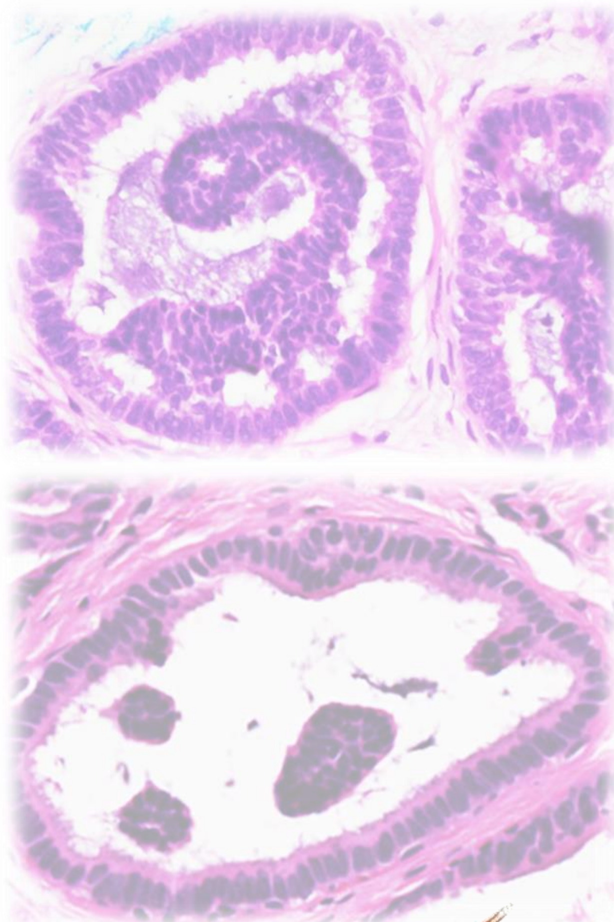

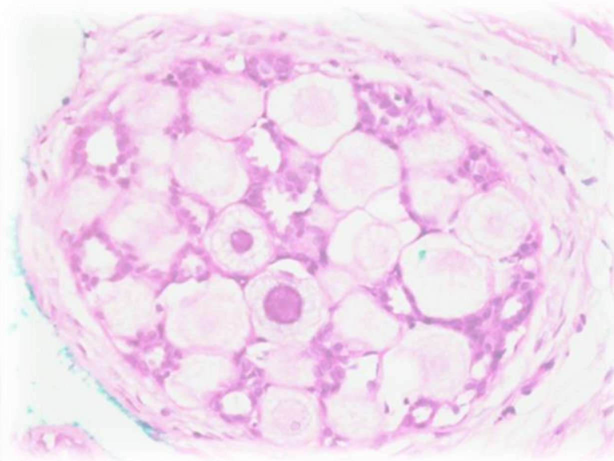

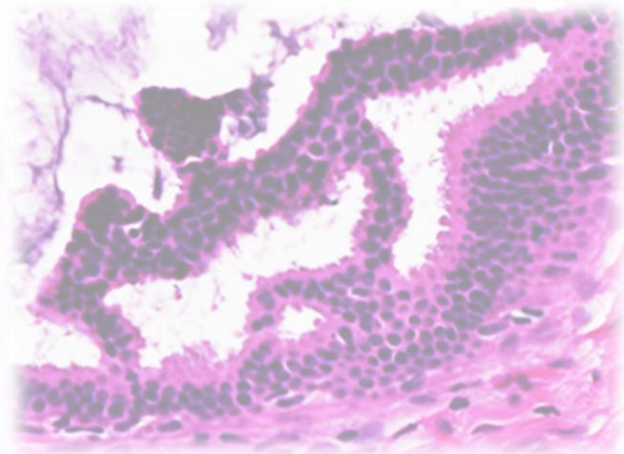

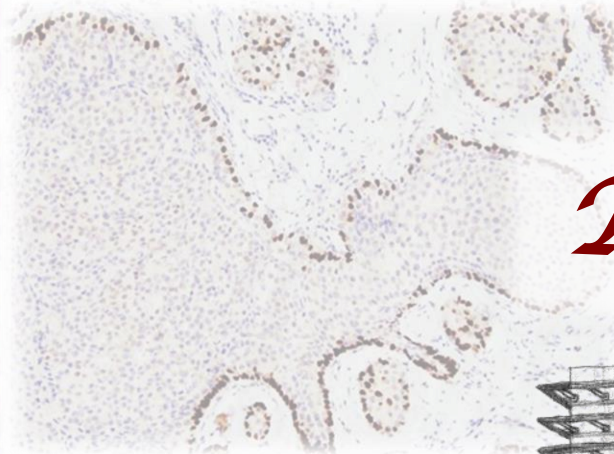

Thank you!