Breast Pathology Course 2017

Case 16

67 year old Chinese woman underwent right mastectomy and sentinel lymph node biopsy for an invasive breast carcinoma with ductal features, diagnosed on prior core biopsy.

Apart from the grade 3 invasive ductal carcinoma found in the mastectomy, a separate 0.8cm lesion was found located 0.8cm from the main tumour.

Section is from the 0.8cm lesion.

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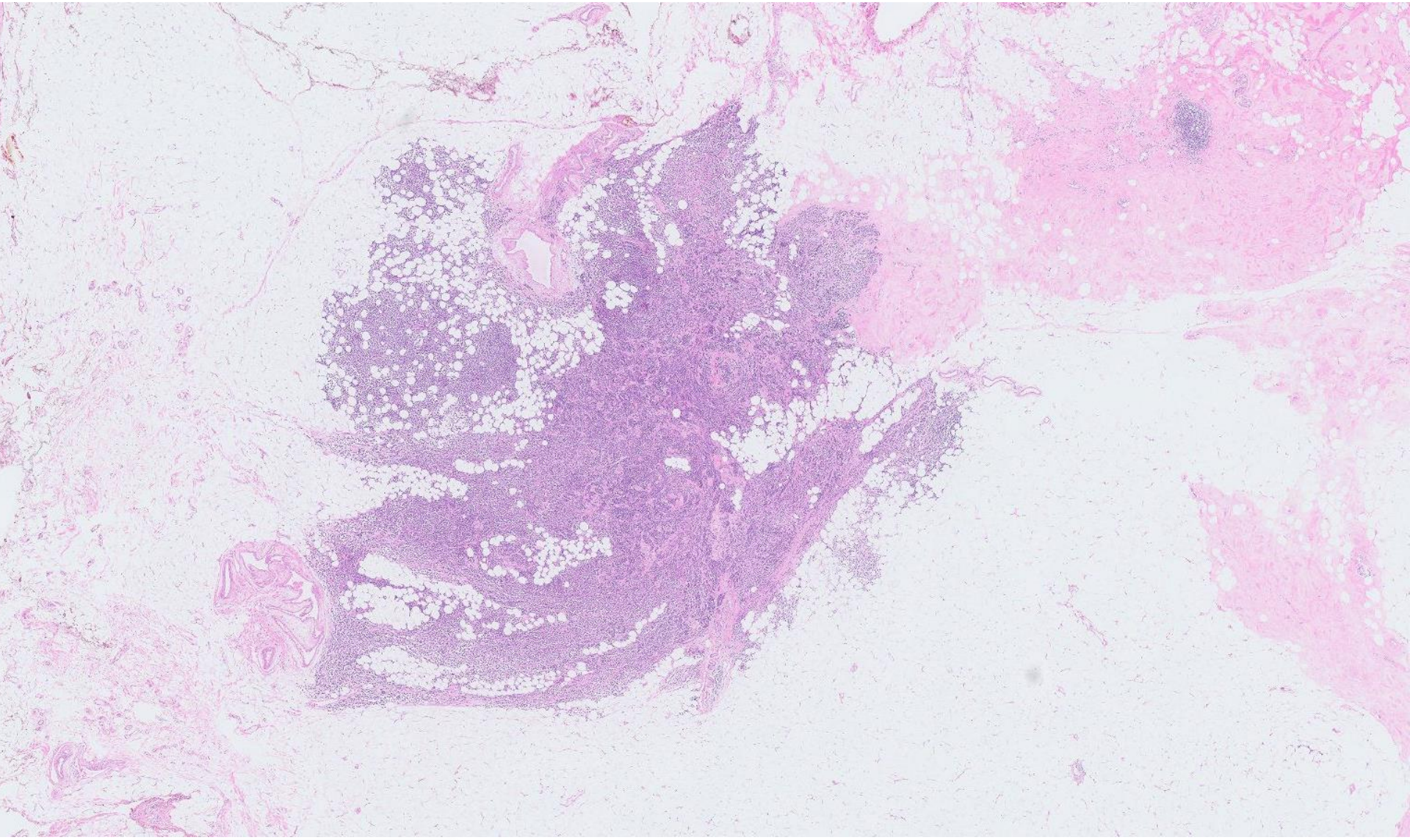
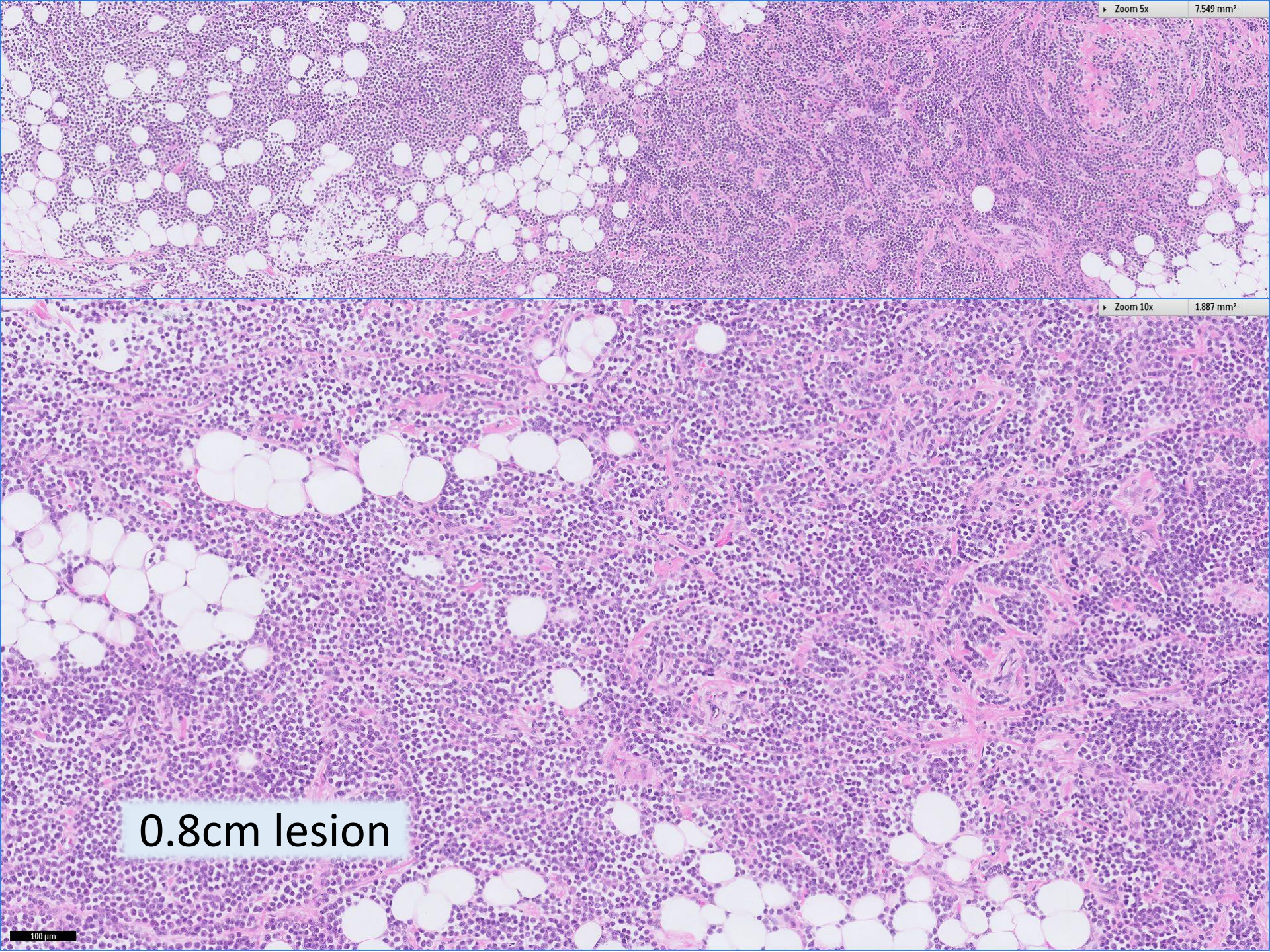
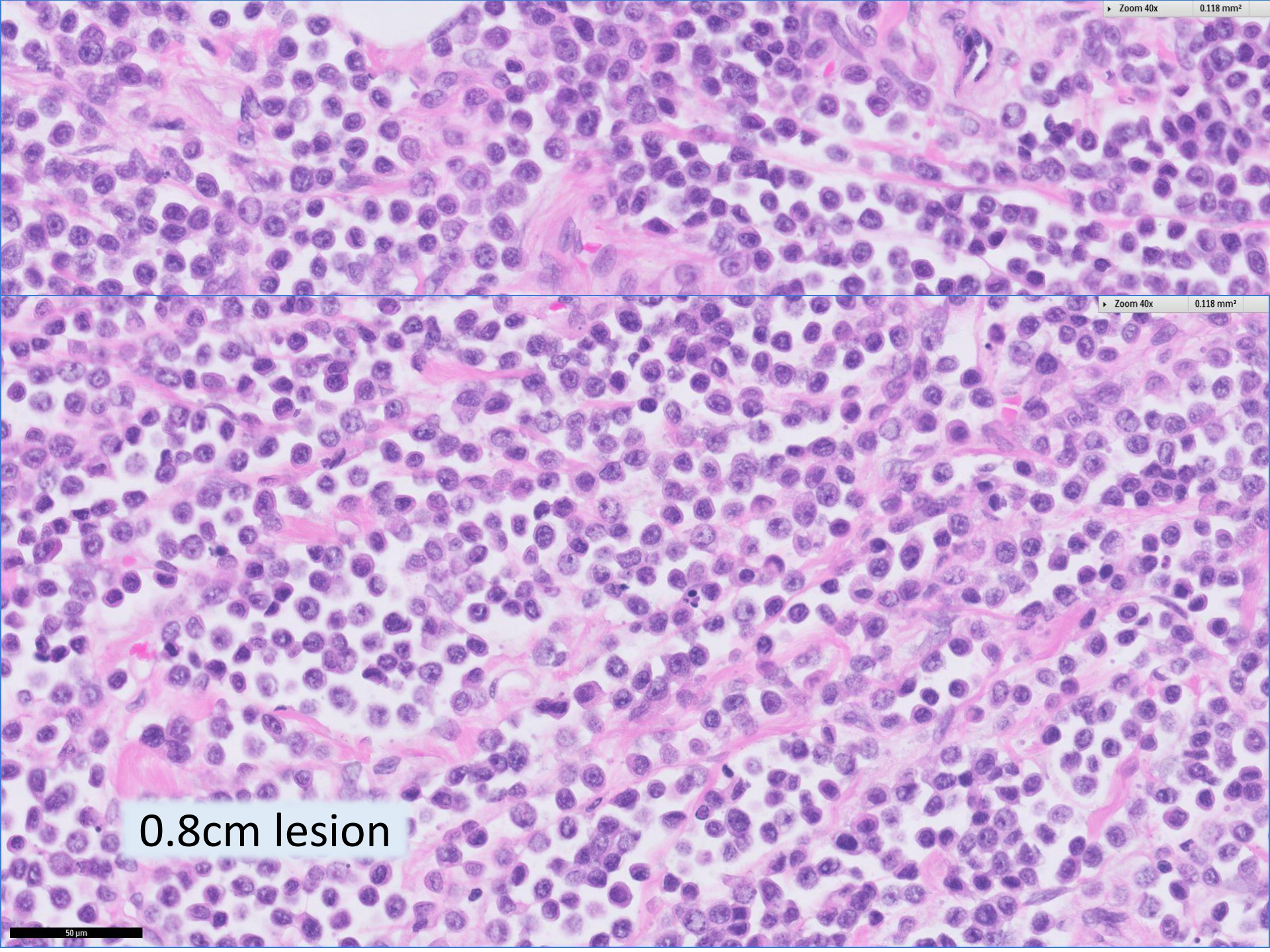
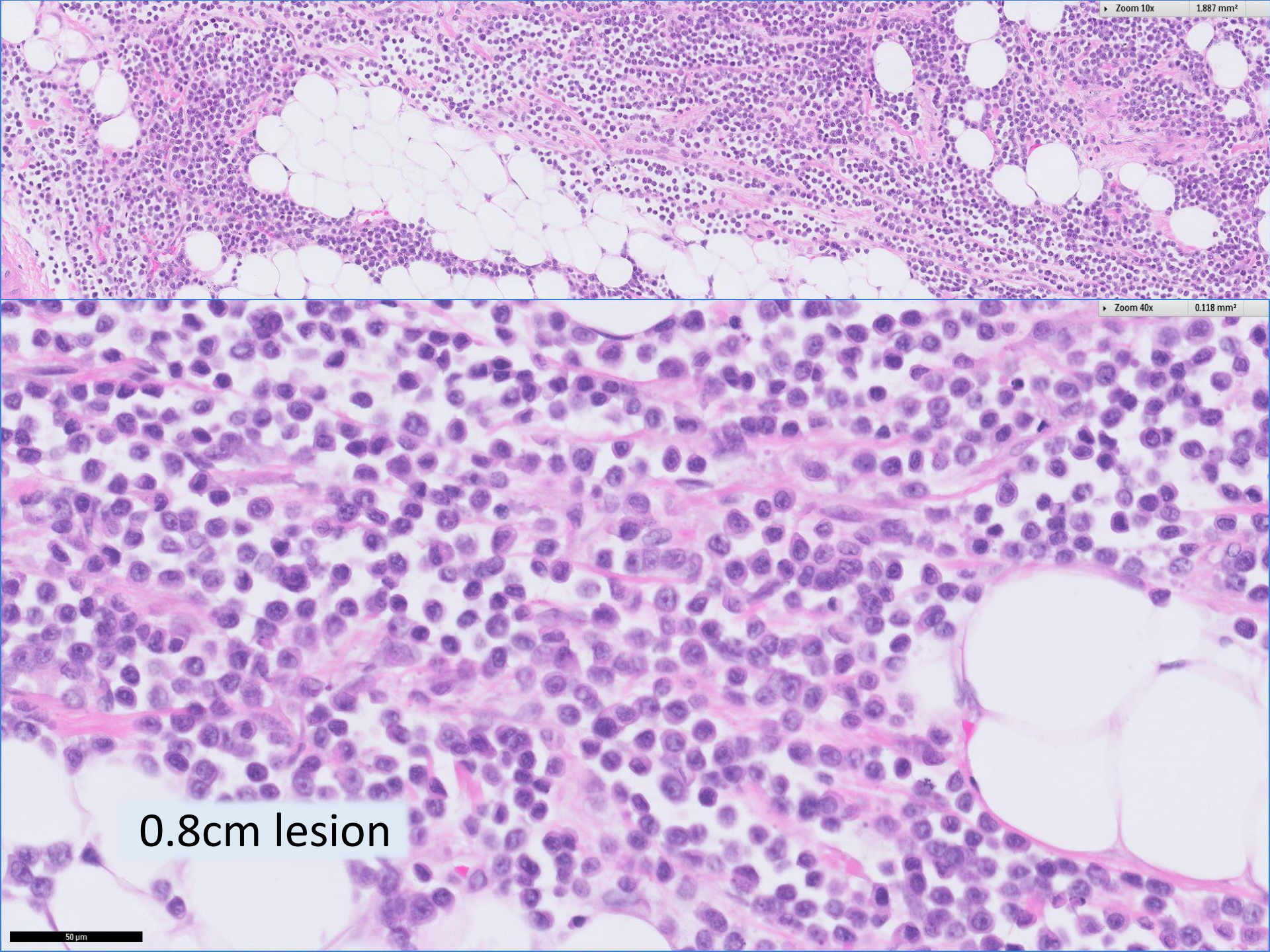
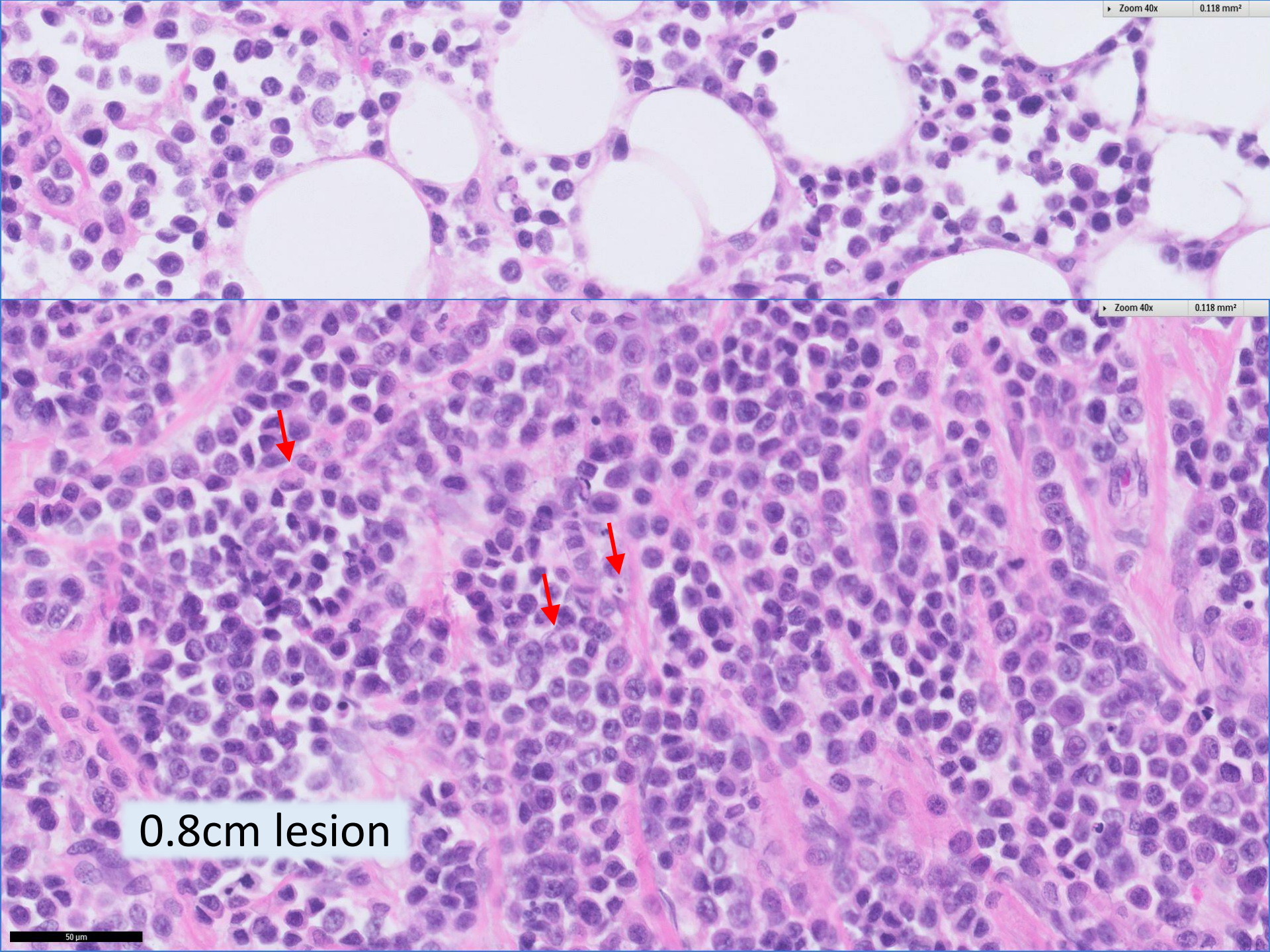


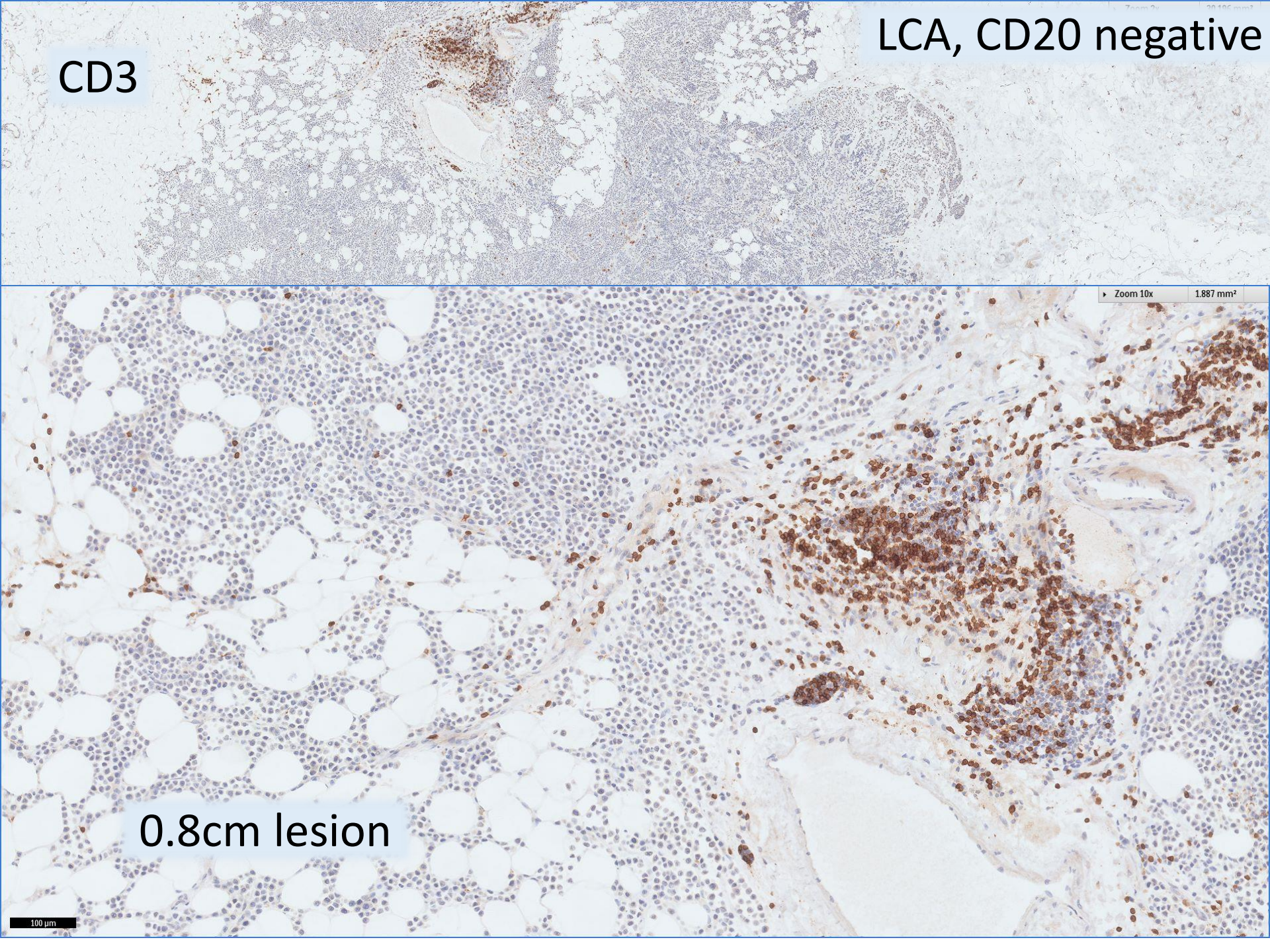
0.8cm lesion

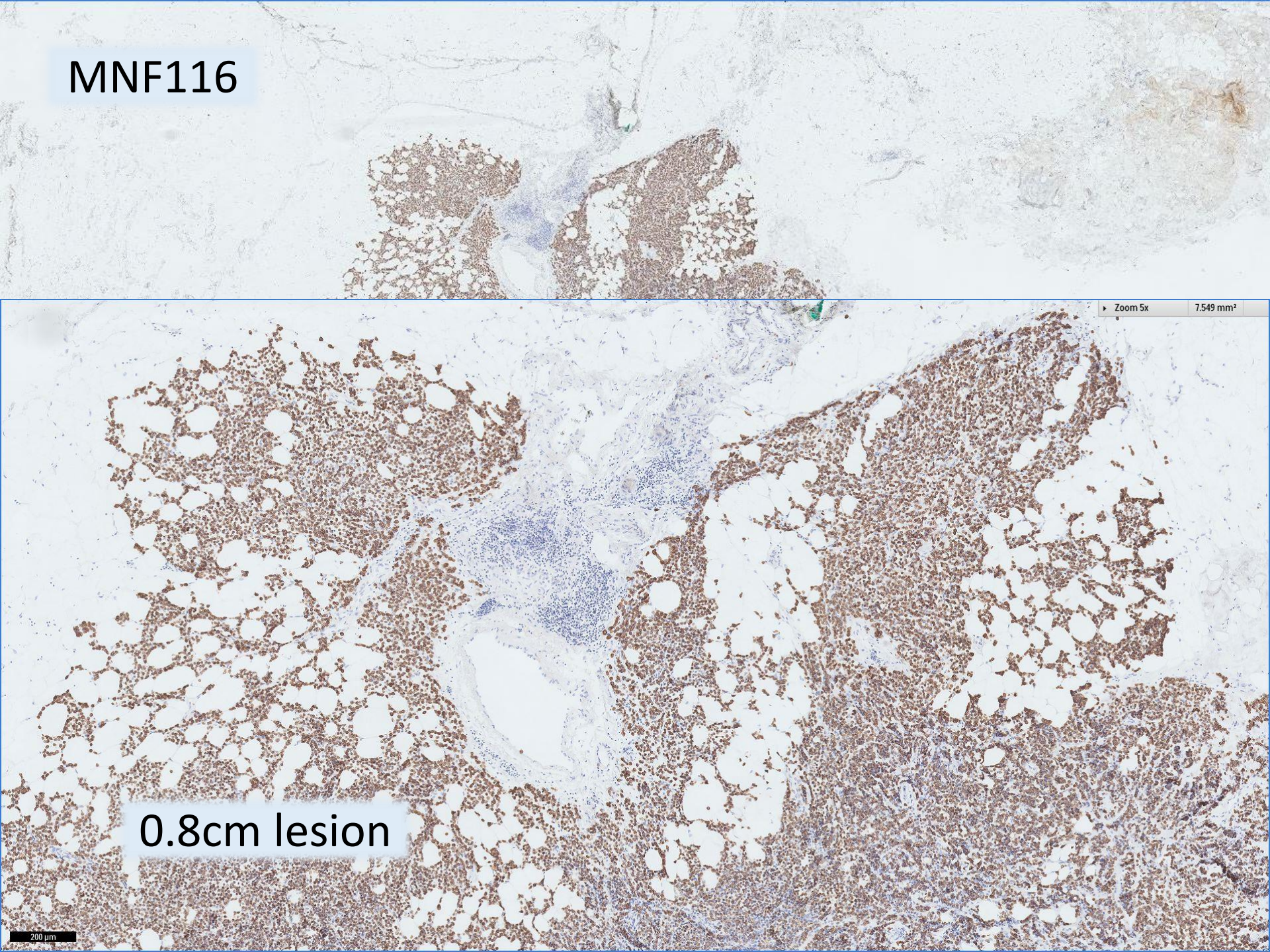

Zoom 5x
7.549 mm²
Zoom 10x
1.887 mm²
0.8cm lesion
100 µm

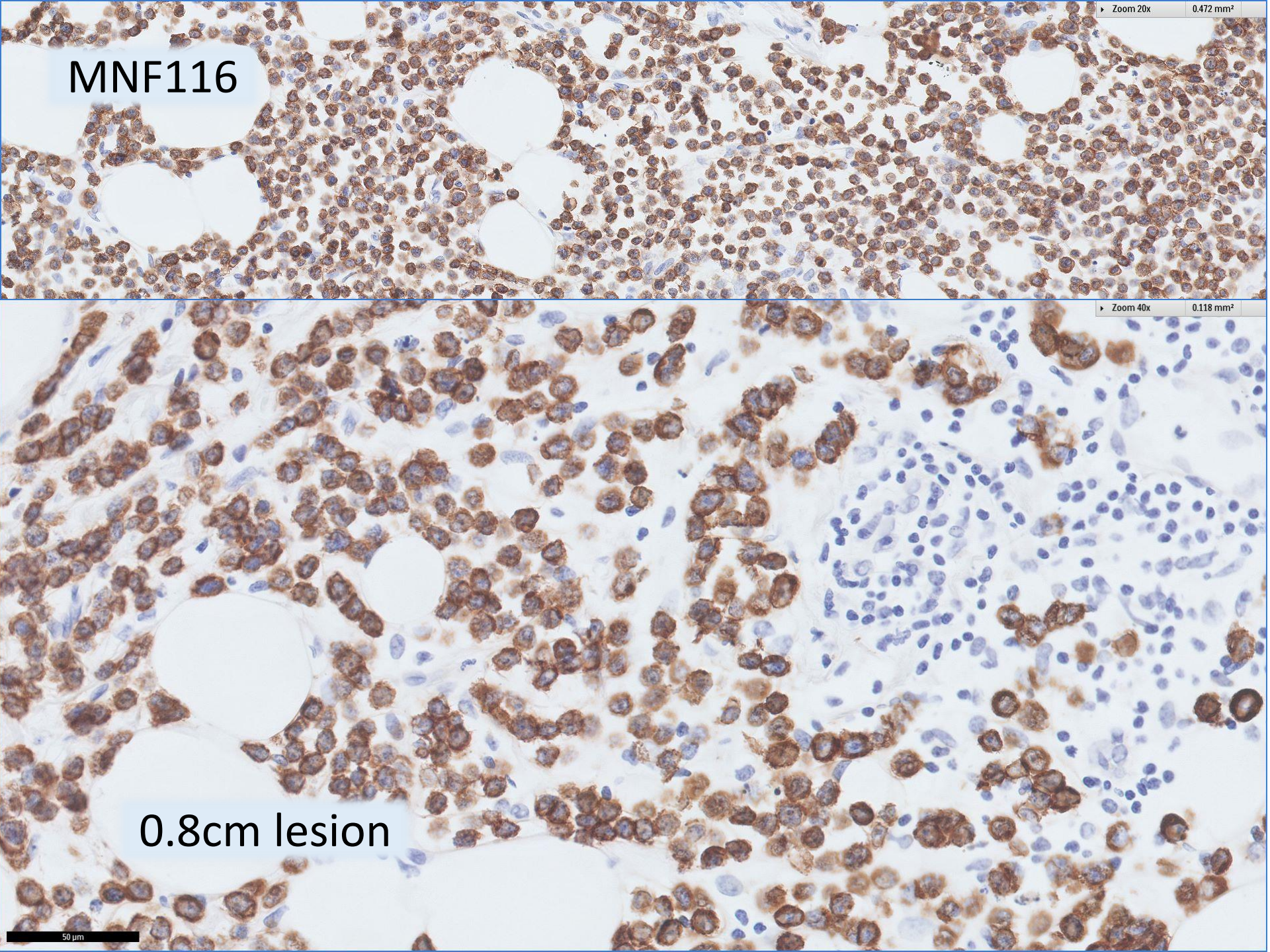

Zoom 40x
0.118 mm²
Zoom 40x
0.118 mm²
0.8cm lesion
50 µm


Zoom 10x
1.887 mm²
Zoom 40x
0.118 mm²
0.8cm lesion
50 µm

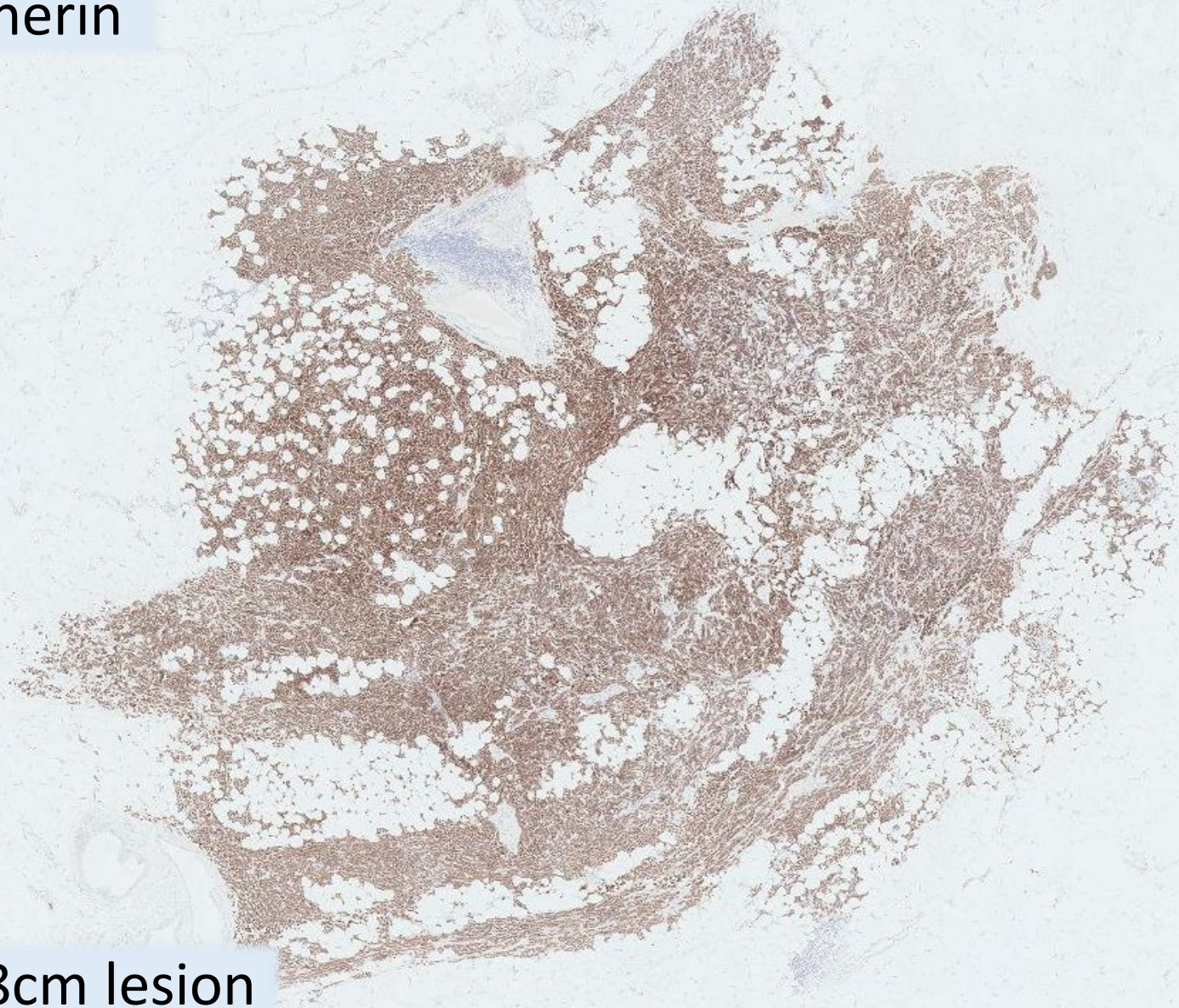

Zoom 40x
0.118 mm²
Zoom 40x
0.118 mm²
0.8cm lesion
50 µm


CD3
LCA, CD20 negative
Zoom 10x
1.887 mm²
0.8cm lesion
100 µm

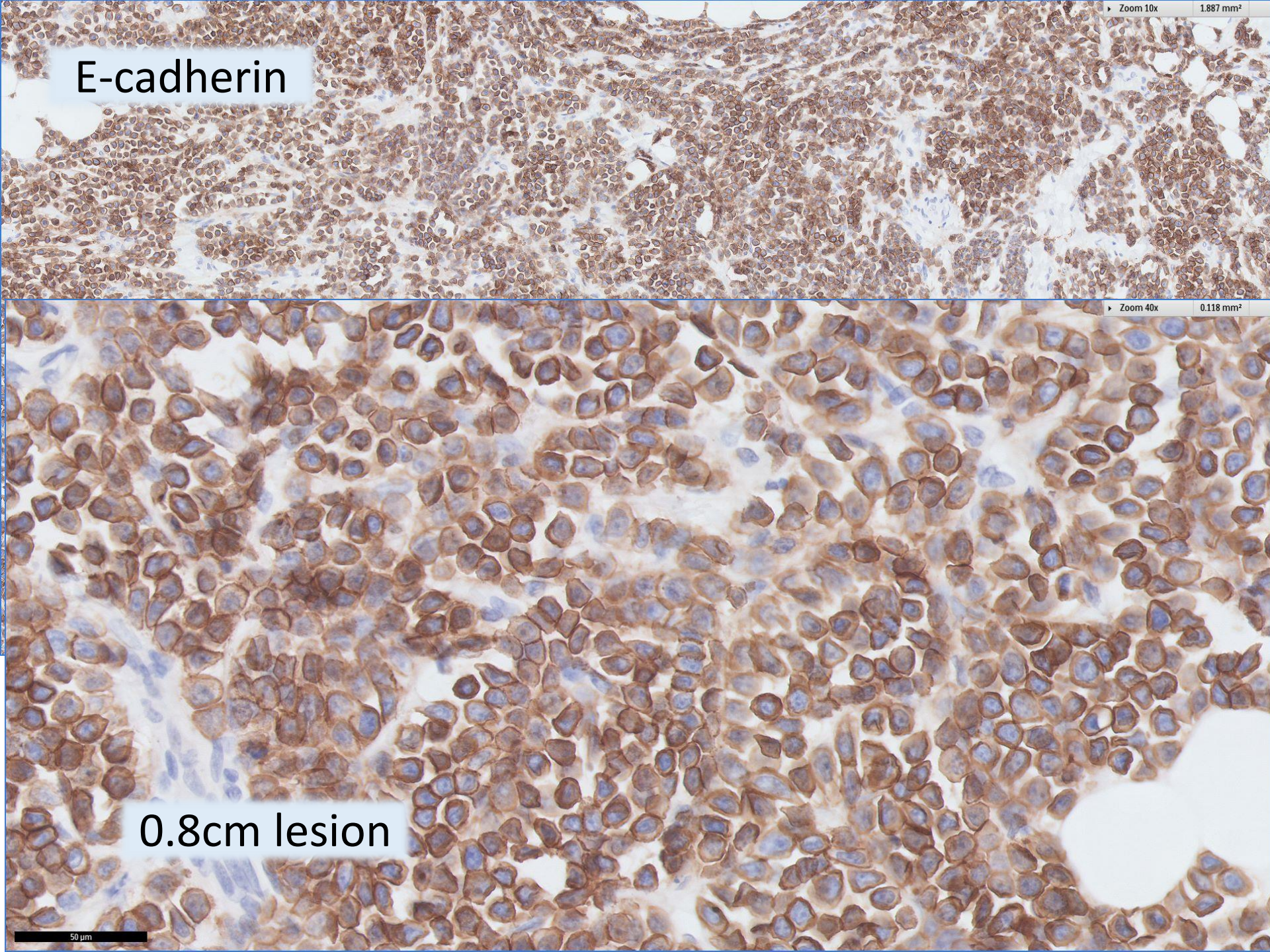

MNF116
Zoom 5x
7.549 mm²
0.8cm lesion
200 µm


MNF116
Zoom 20x
0.472 mm²
Zoom 40x
0.118 mm²
0.8cm lesion
50 µm

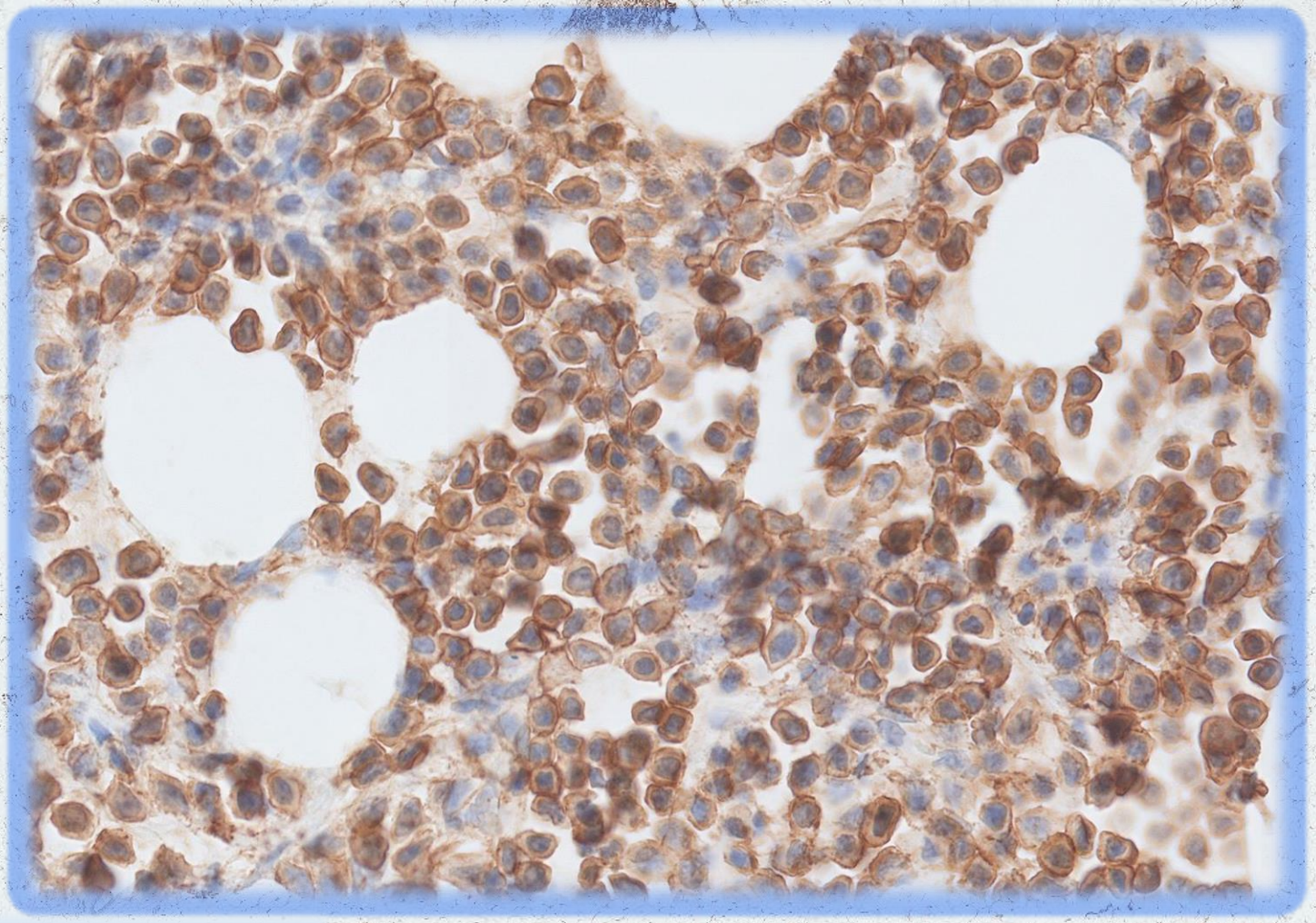
E-cadherin



0.8cm lesion

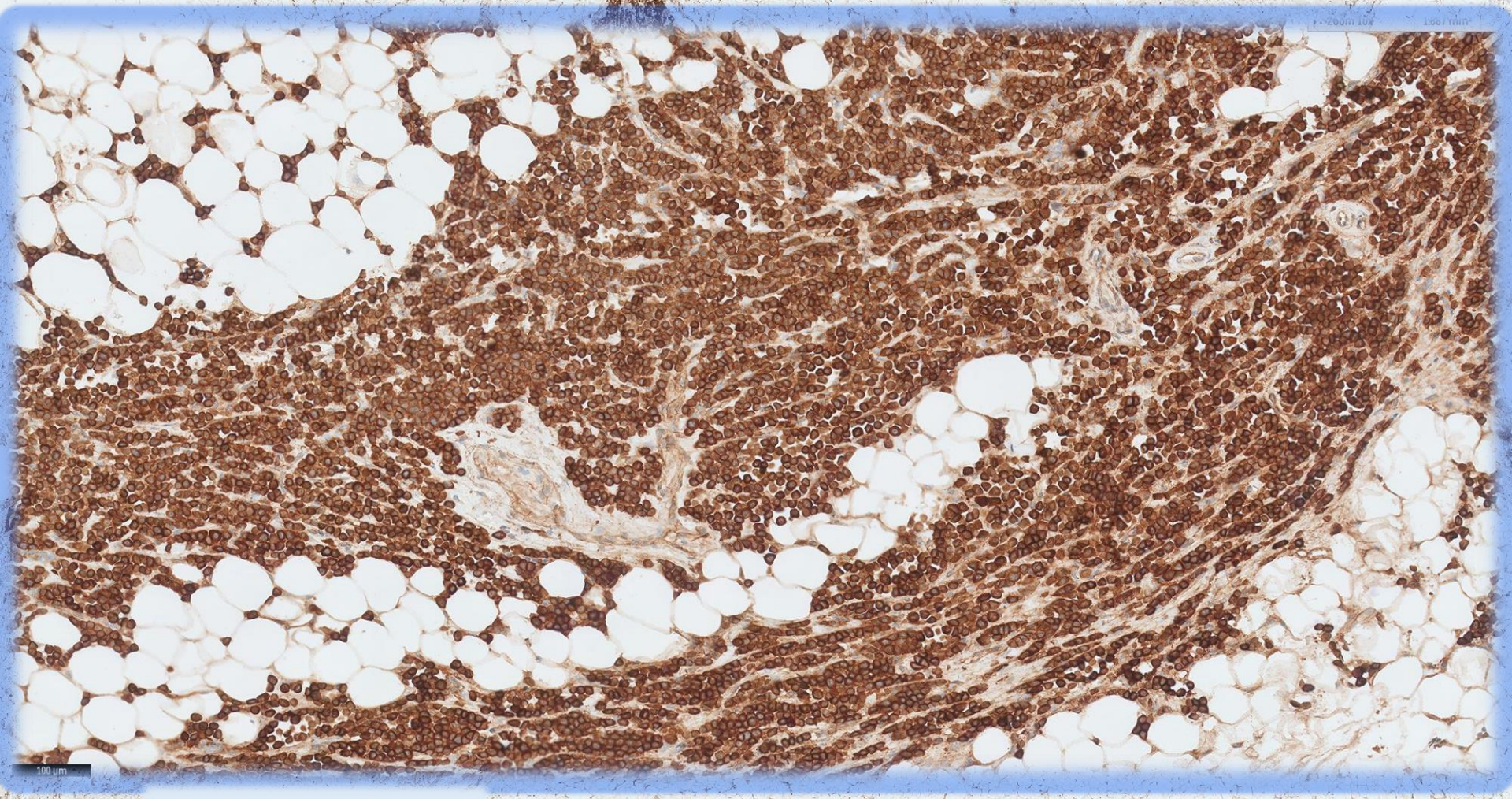

E-cadherin
Zoom 10x
1.887 mm²
Zoom 40x
0.118 mm²
0.8cm lesion
50 µm

Beta catenin

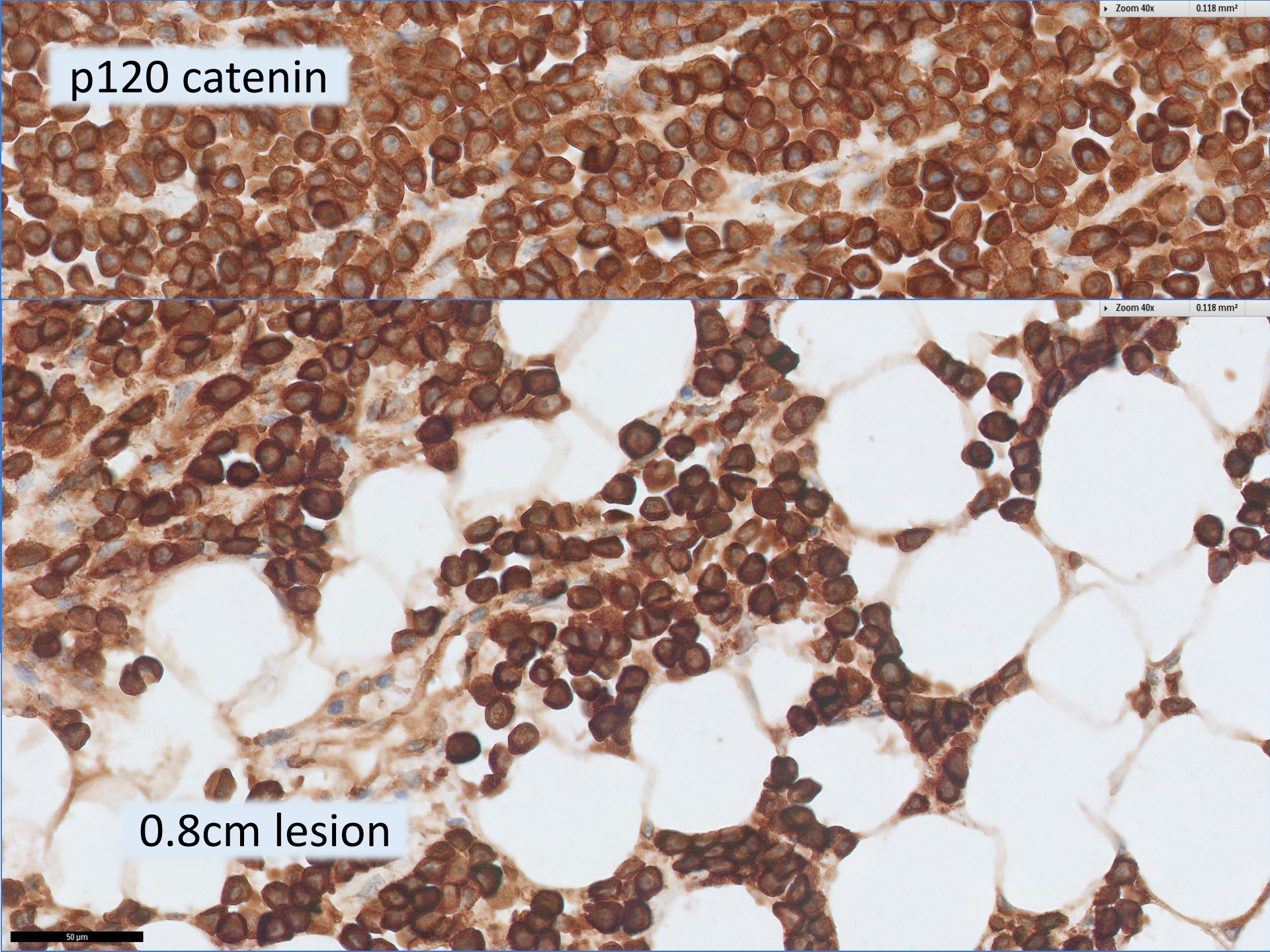


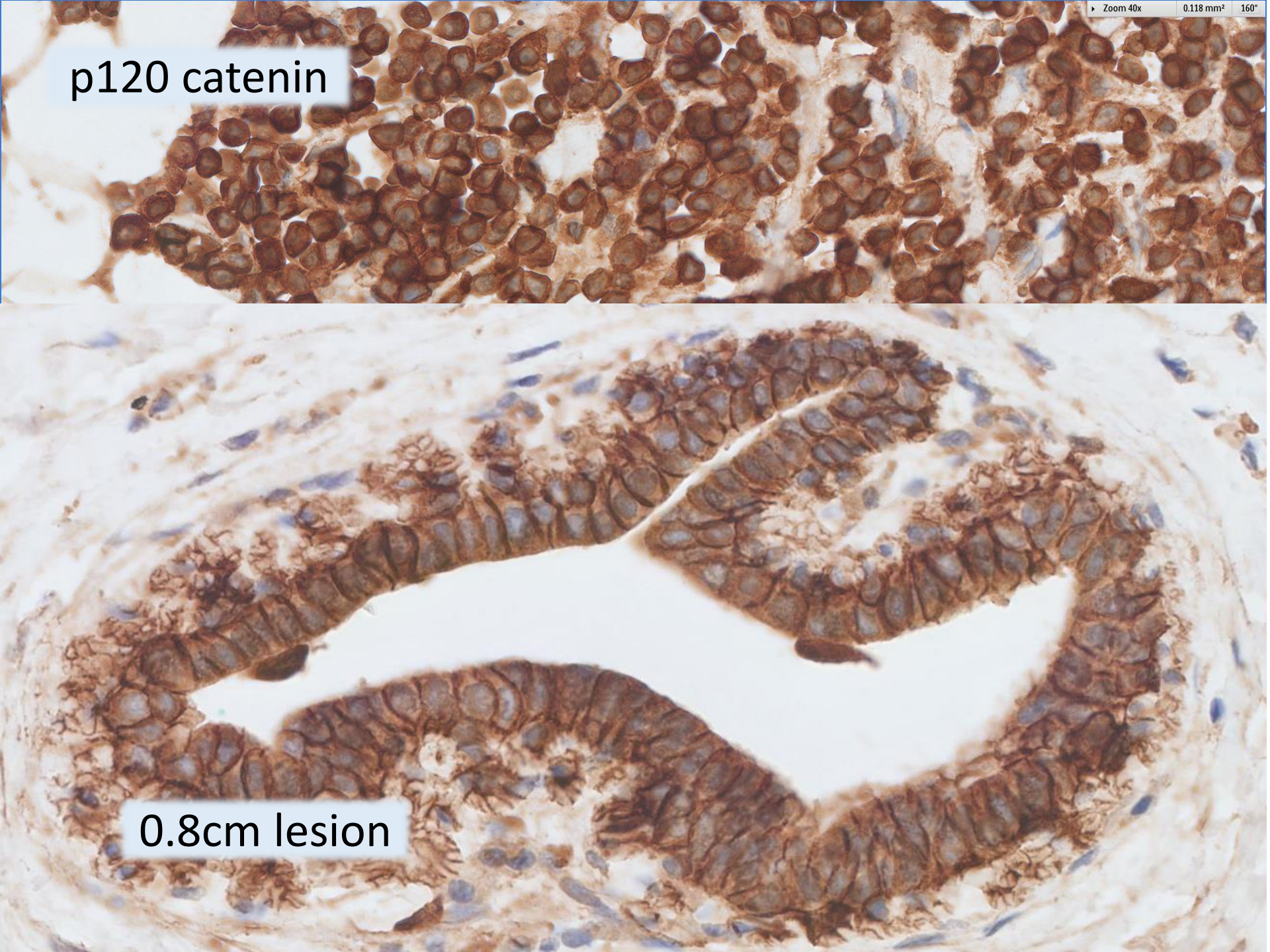
0.8cm lesion

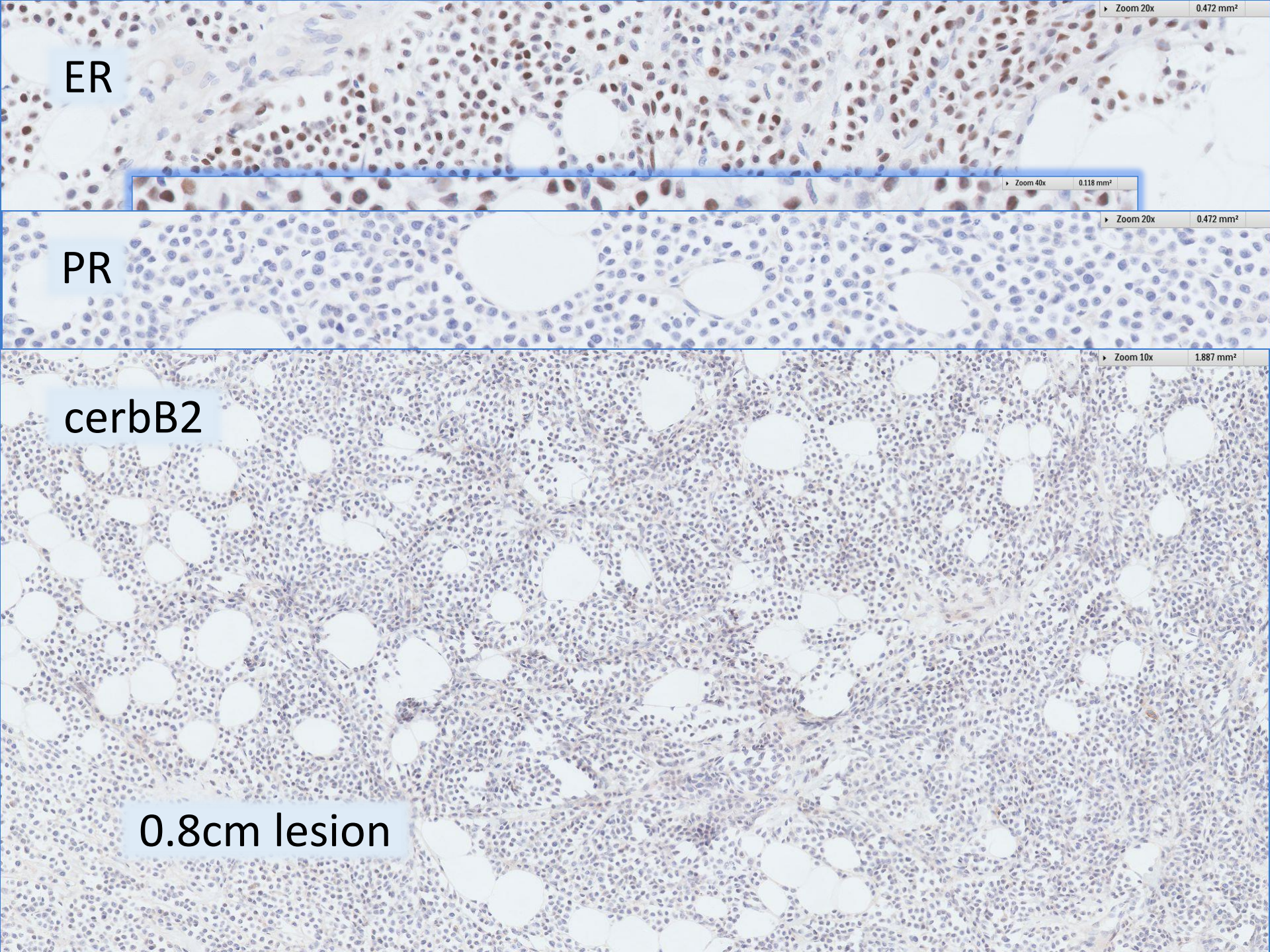
p120 catenin



0.8cm lesion

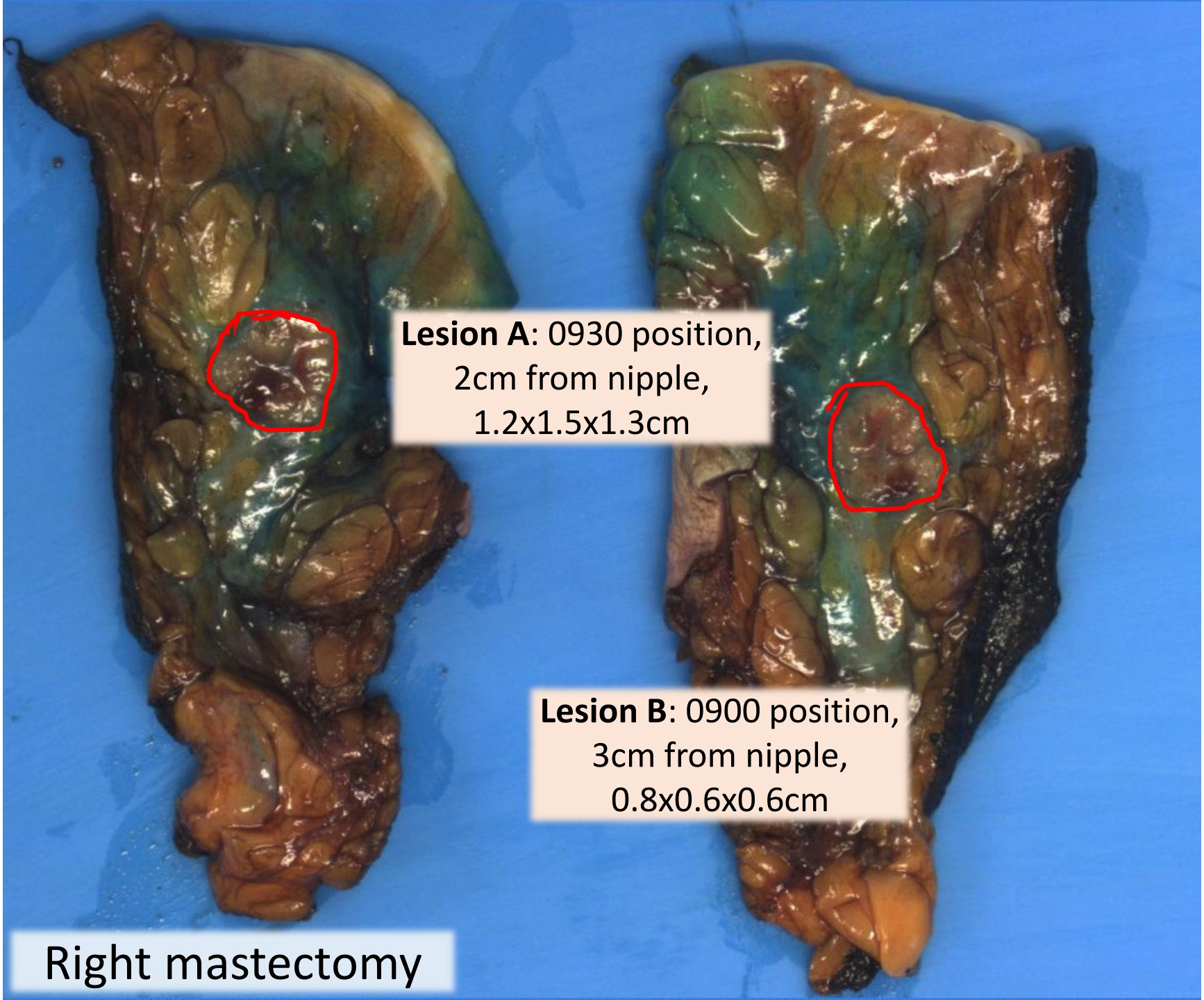

p120 catenin
Zoom 40x
0.118 mm²
Zoom 40x
0.118 mm²
0.8cm lesion
50 µm

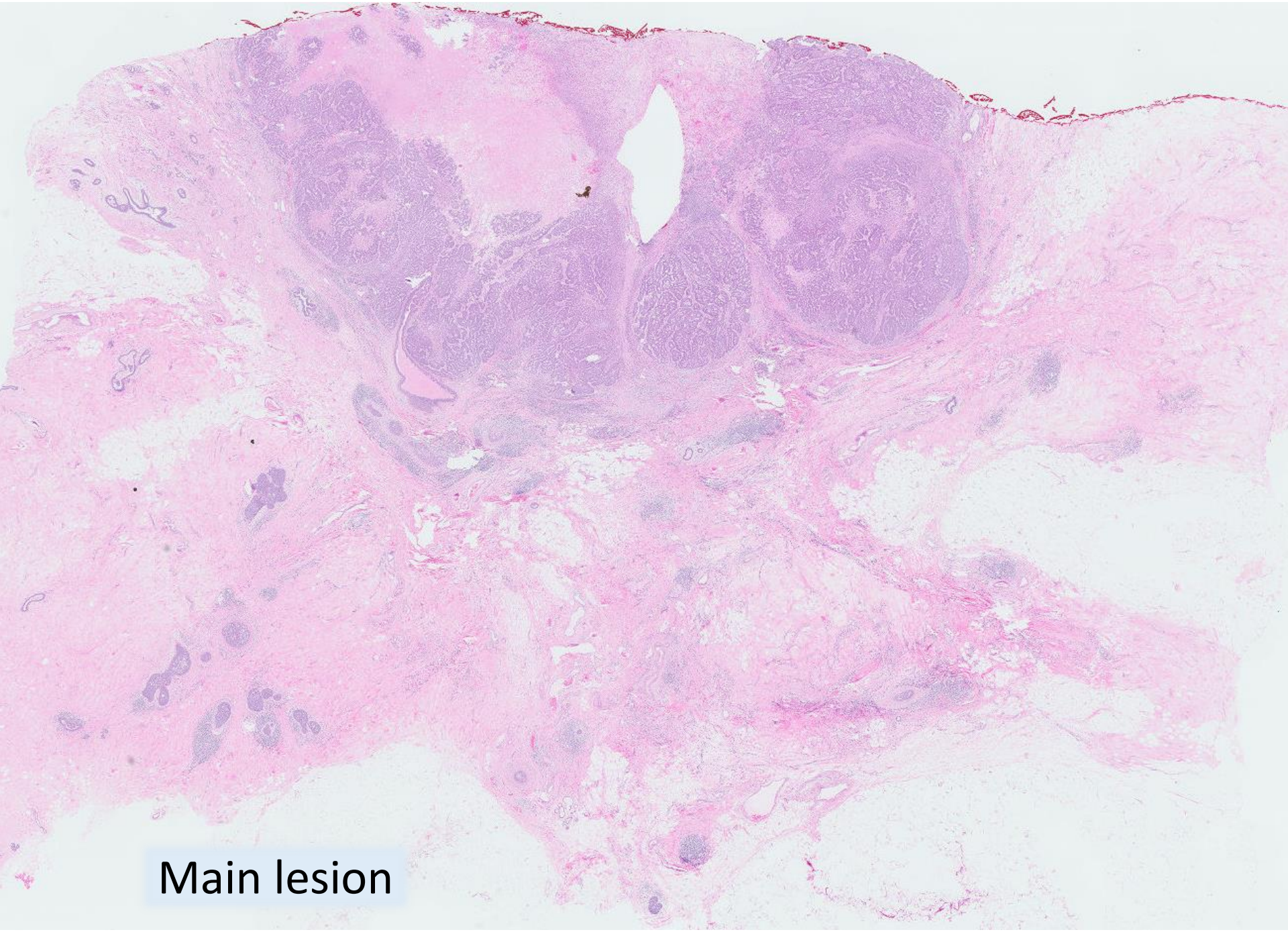

Zoom 40x
0.118 mm²
160°
p120 catenin
0.8cm lesion

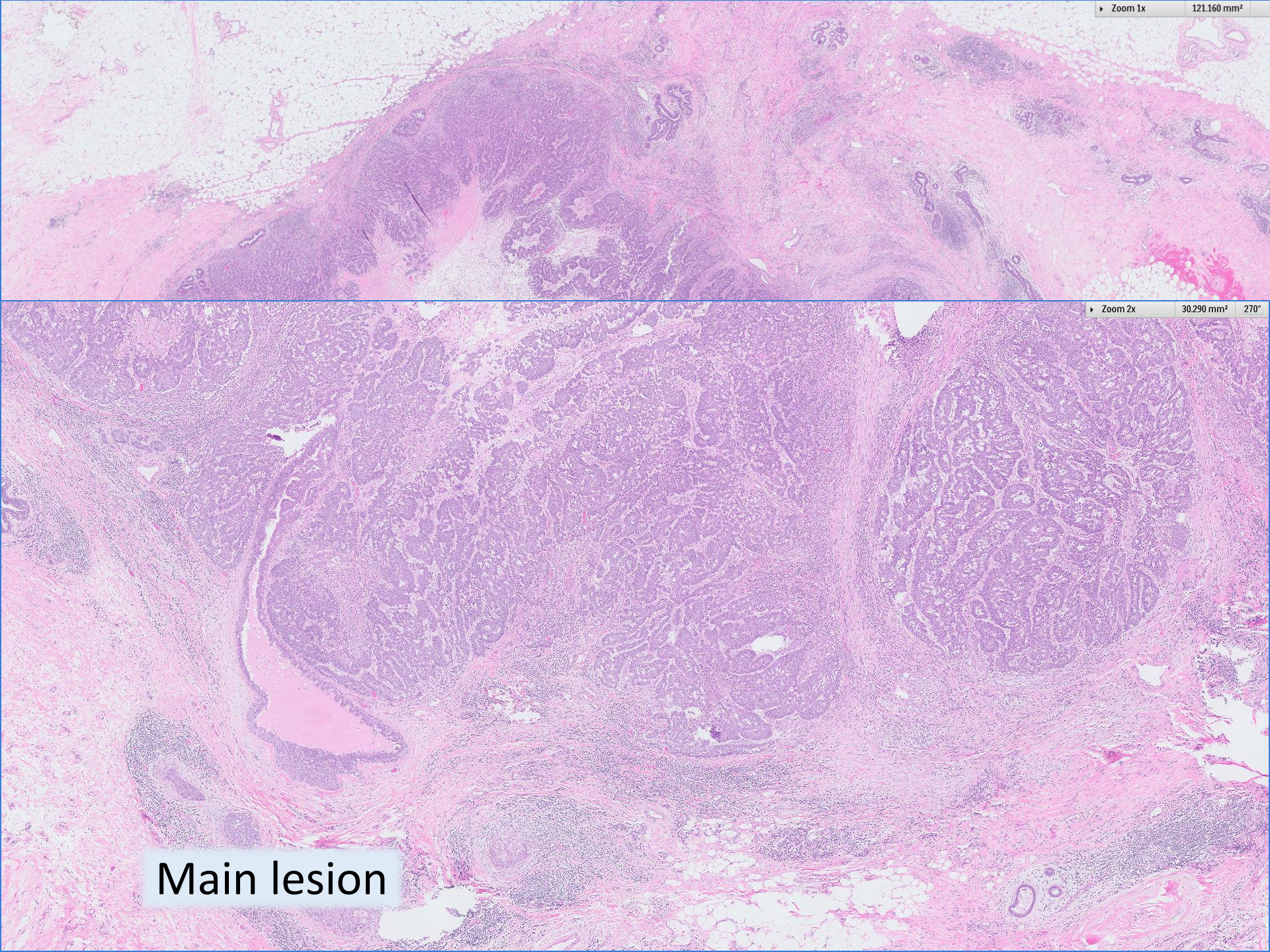

ER
Zoom 20x
0.472 mm²
Zoom 40x
0.118 mm²
PR
Zoom 20x
0.472 mm²
cerbB2
Zoom 10x
1.887 mm²
0.8cm lesion

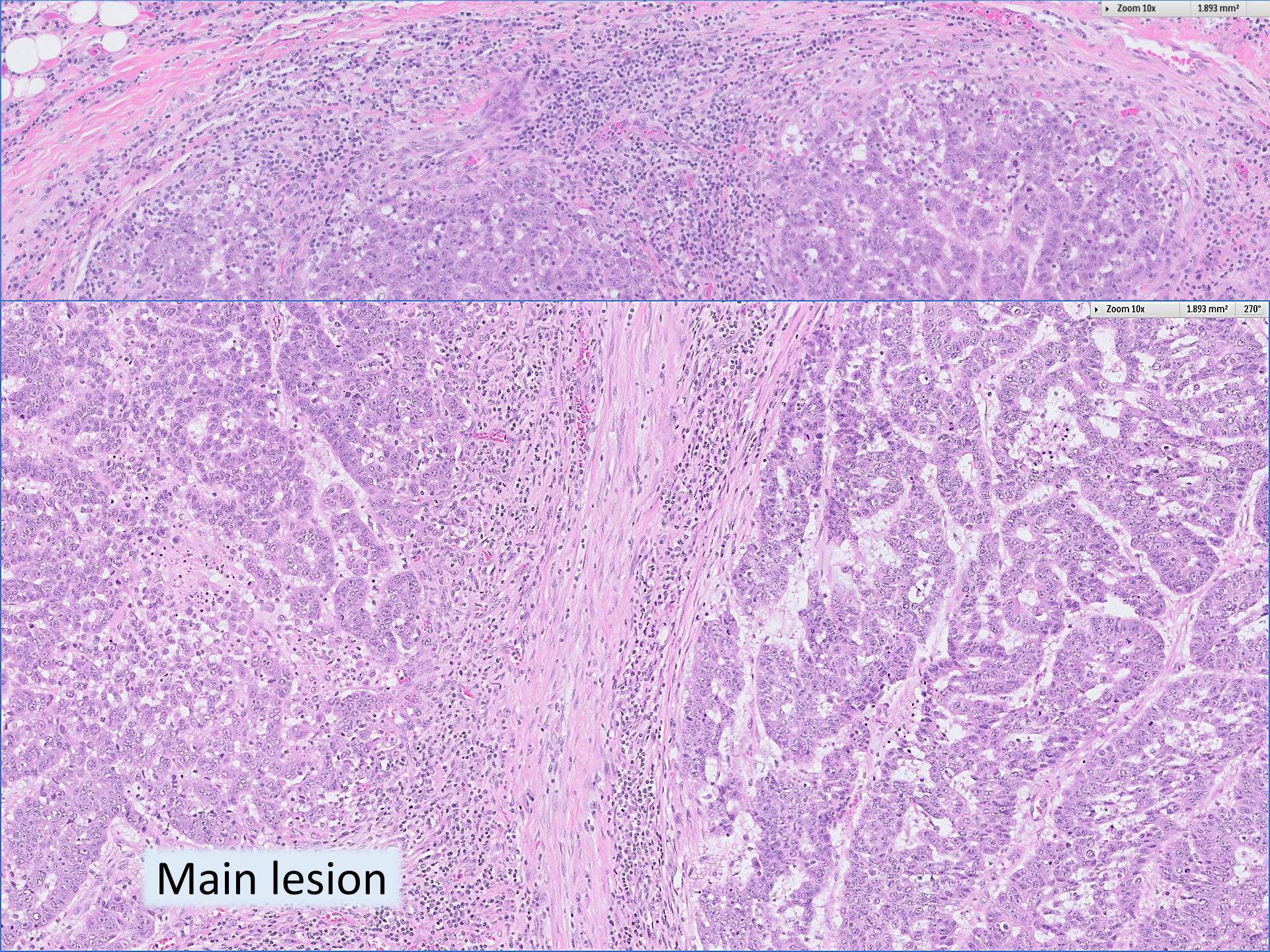
Right breast, 0.8cm lesion

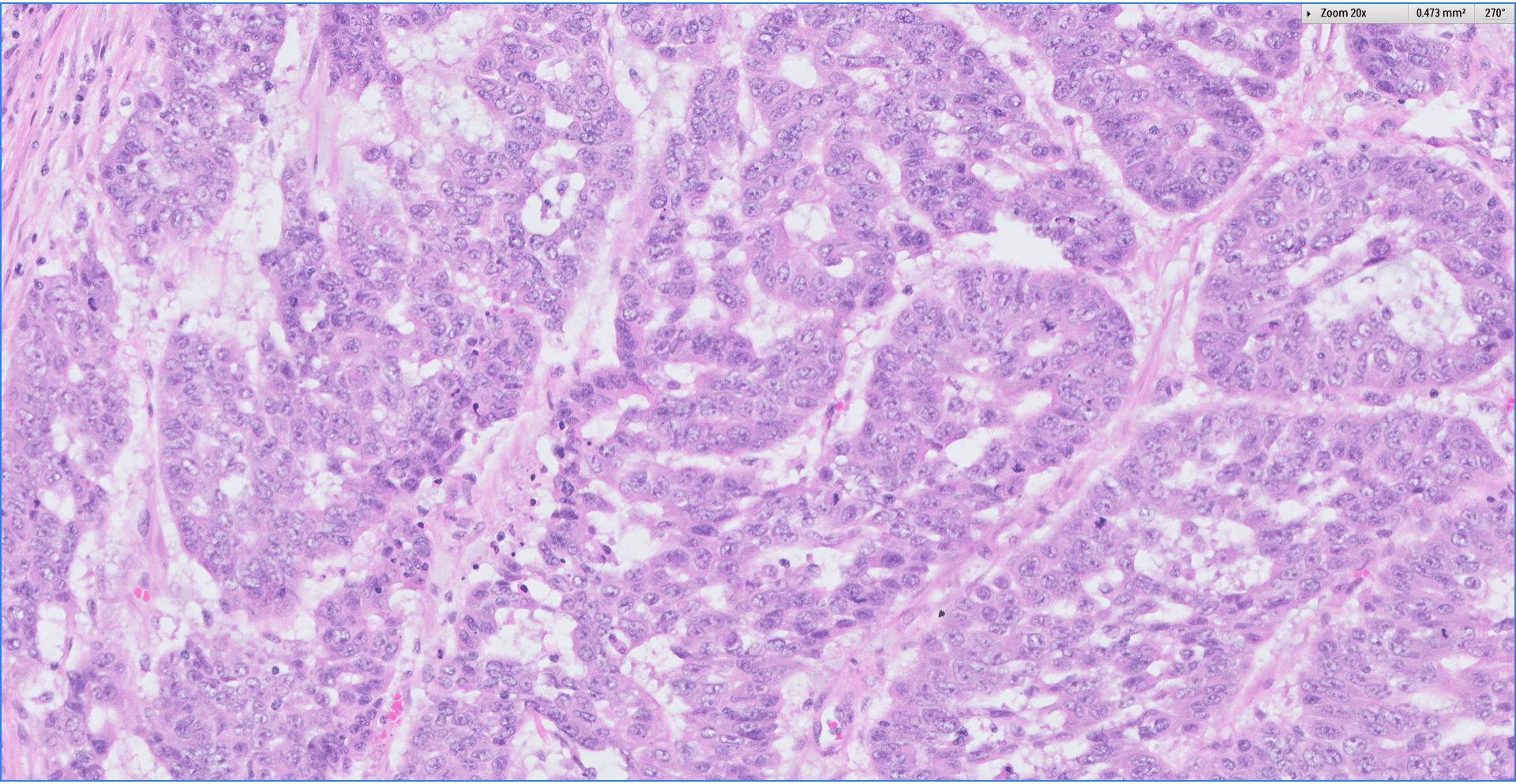
- Invasive lobular carcinoma, grade 1, 0.8cm.
- ER positive, PR negative, cerbB2 negative.


Lesion A: 0930 position,
2cm from nipple,
1.2x1.5x1.3cm
Lesion B: 0900 position,
3cm from nipple,
0.8x0.6x0.6cm
Right mastectomy


Main lesion


Zoom 1x
121.160 mm²
Zoom 2x
30.290 mm²
270°
Main lesion


Zoom 10x
1.893 mm²
Zoom 10x
1.893 mm²
270°
Main lesion



Main lesion

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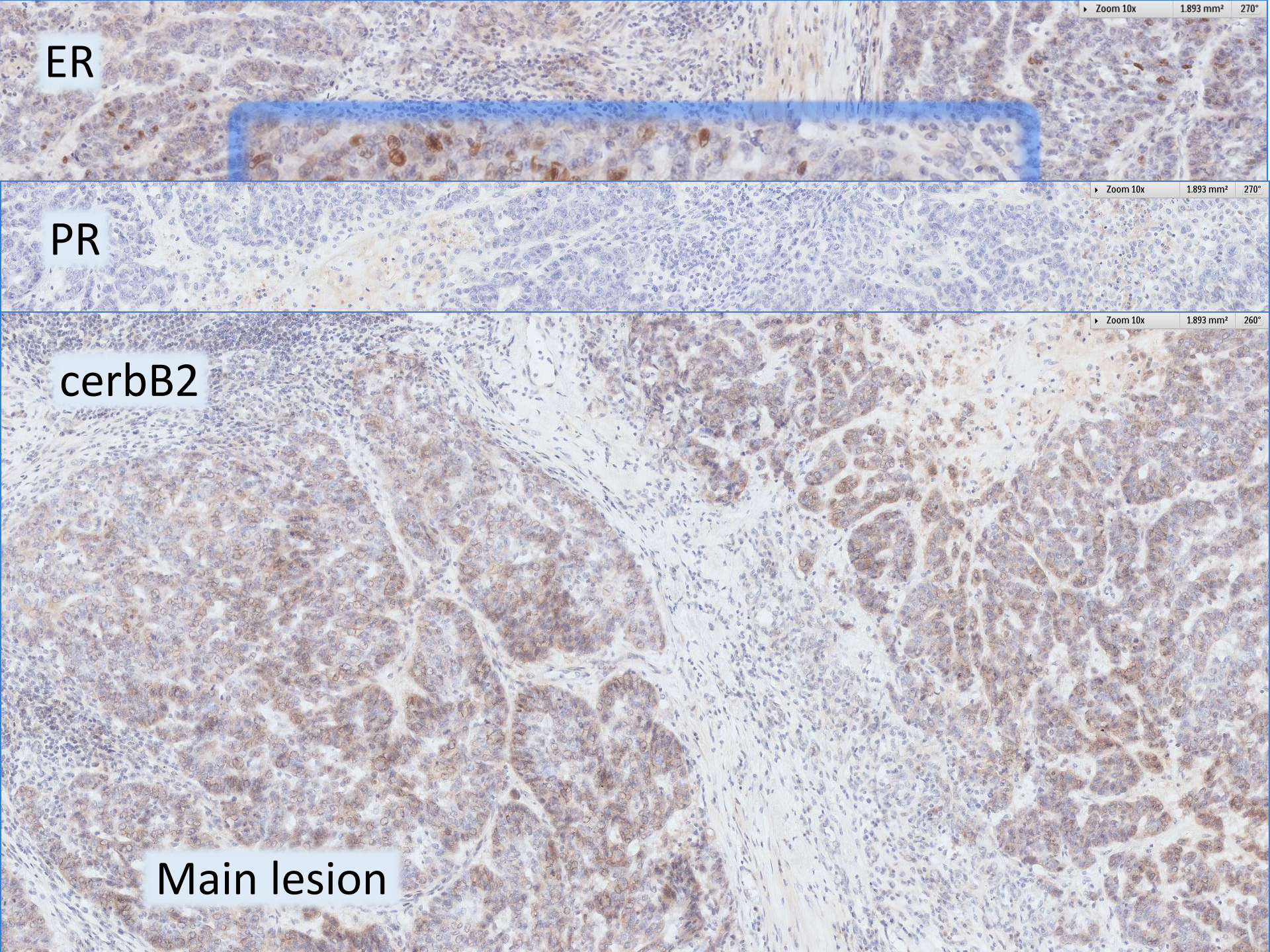

ER
Zoom 10x 1.893 mm² 270°
PR
Zoom 10x 1.893 mm² 270°
cerbB2
Zoom 10x 1.893 mm² 260°
Main lesion

Right breast, main lesion

- Infiltrative ductal carcinoma, grade 3, 1.5cm.
- ER positive, PR negative, cerbB2 negative.

Right breast, 0.8cm lesion ~ differential diagnosis

- Lymphoma
- Plasmacytoma
- Invasive lobular carcinoma

Invasive lobular carcinoma

- 1st described with lobular carcinoma in situ in 1941 by Foote and Stewart.
- Desmoplastic stromal reaction.
- Linear arrangement of tumour cells.
- Targetoid growth pattern.
- Accounts for < 5% to 14% of invasive breast cancer.
- Incidence increases since 1980s, attributable to increased used of hormone replacement therapy.
- Median age at diagnosis between 57 to 65 years.
- Contralateral tumours, including synchronous tumours, in 5% to19% of cases.

Invasive lobular carcinoma: Pathology

- Microscopic subtypes:
  - Classical
  - Variants:
    - Trabecular
    - Alveolar
    - Solid
    - Tubulolobular
    - Pleomorphic, histiocytoid, myoid

Invasive lobular carcinoma: Immunoprofile

- 80% -95% ER positiivity.
- 60% -70% PR positivity.
- Rate of ER positivity highest (100%) in alveolar and lowest (10%) in pleomorphic ILC.
- HER2 amplification and overexpression is rare, though evident in some pleomorphic ILCs.
- Proliferation rate, measured by MIB1/Ki67 labelling, is generally low in ILC, although higher in the variants.
- E-cadherin loss, but 15% of ILC can express E-cadherin, often in an aberrant manner.

(Absent) E-cadherin staining in invasive lobular carcinoma

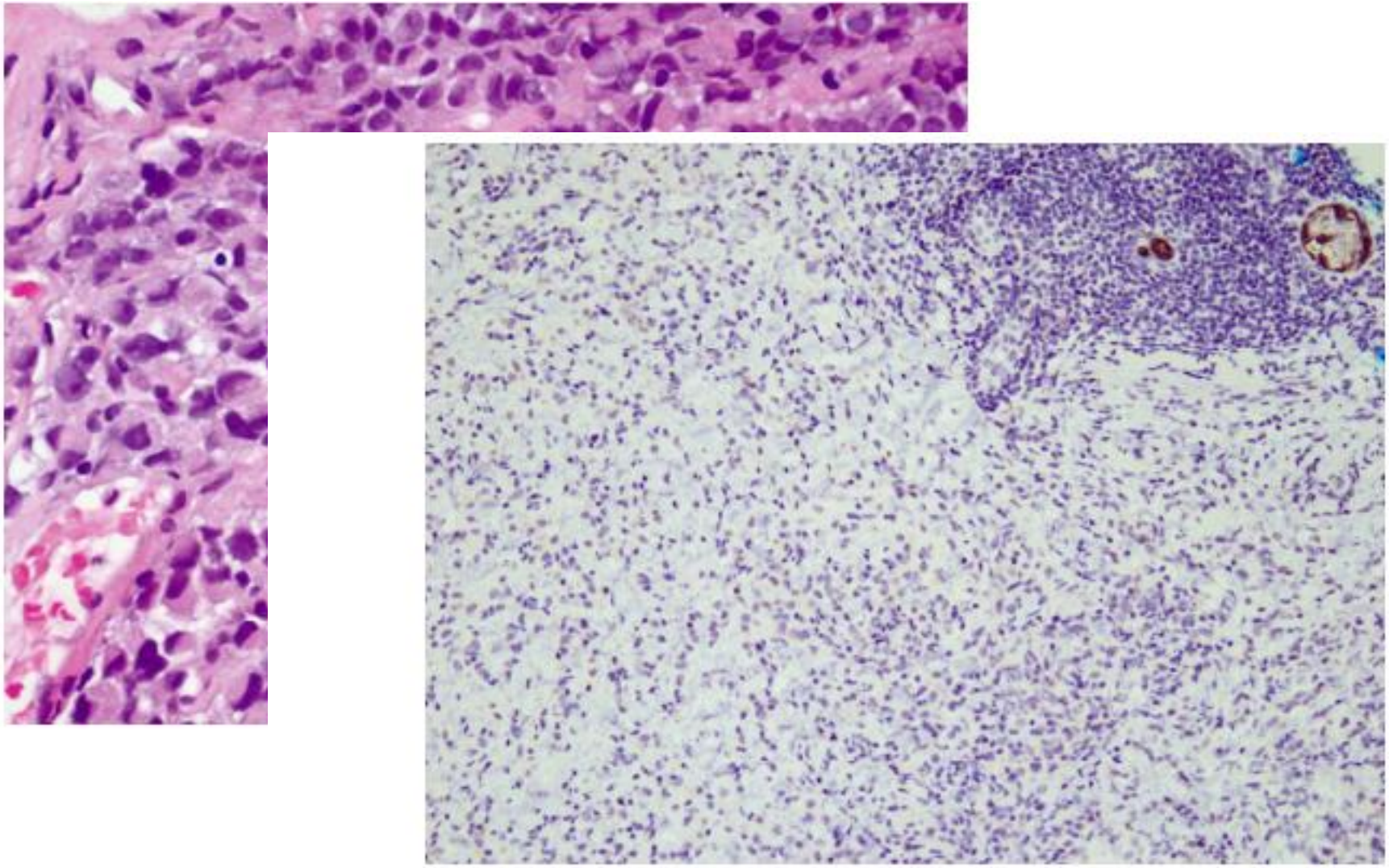


Fig. 10.78 Invasive lobular carcinoma. E-cadherin immunohistochemistry shows negative staining of tumour cells, with resident benign ducts displaying positive staining

Aberrant E-cadherin immunostaining

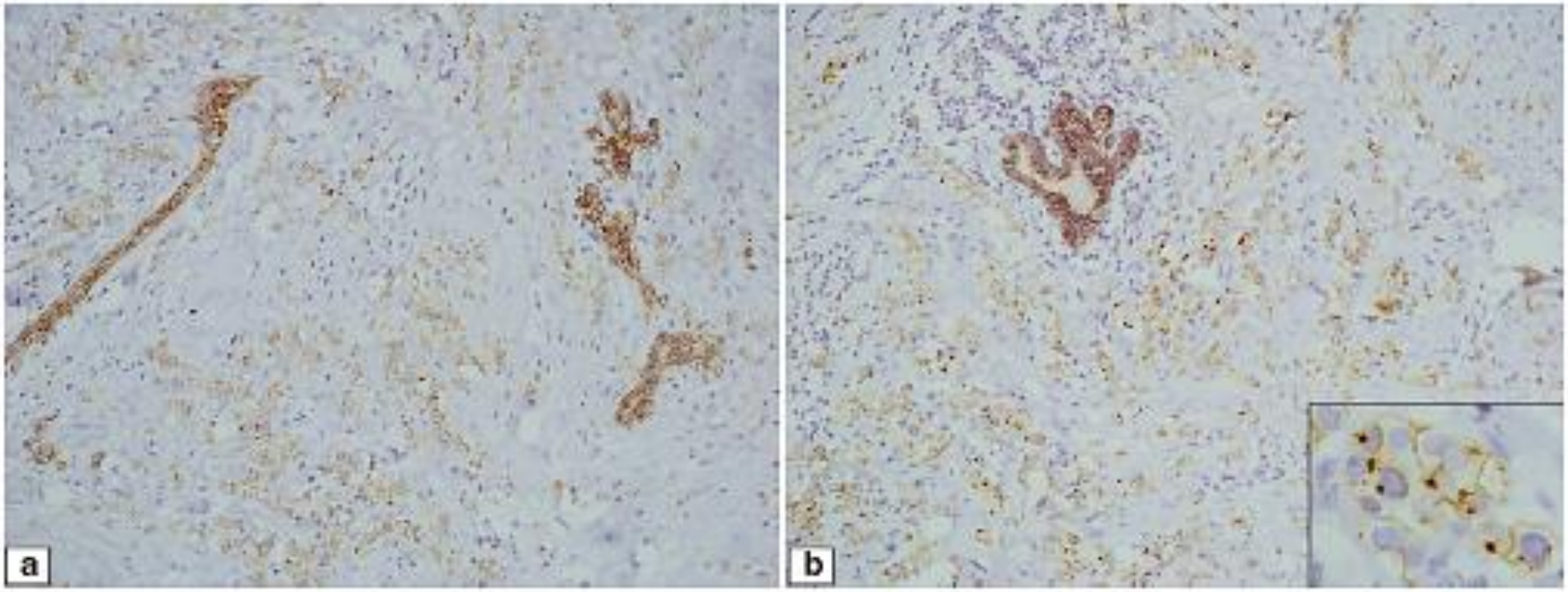
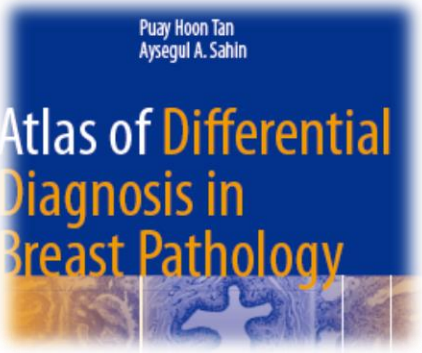


Fig. 10.37 Aberrant E-cadherin staining. (a) Invasive lobular carcinoma cells show diminished intensity and incomplete membrane staining for E-cadherin, contrasting against the benign ducts and acini, which disclose more intense membrane reactivity of epithelial cells. (b) A globular, dot-like staining is seen in the cytoplasm of invasive lobular carcinoma cells. Inset shows paranuclear globular staining for E-cadherin of lobular carcinoma cells



Aberrant E-cadherin immunostaining

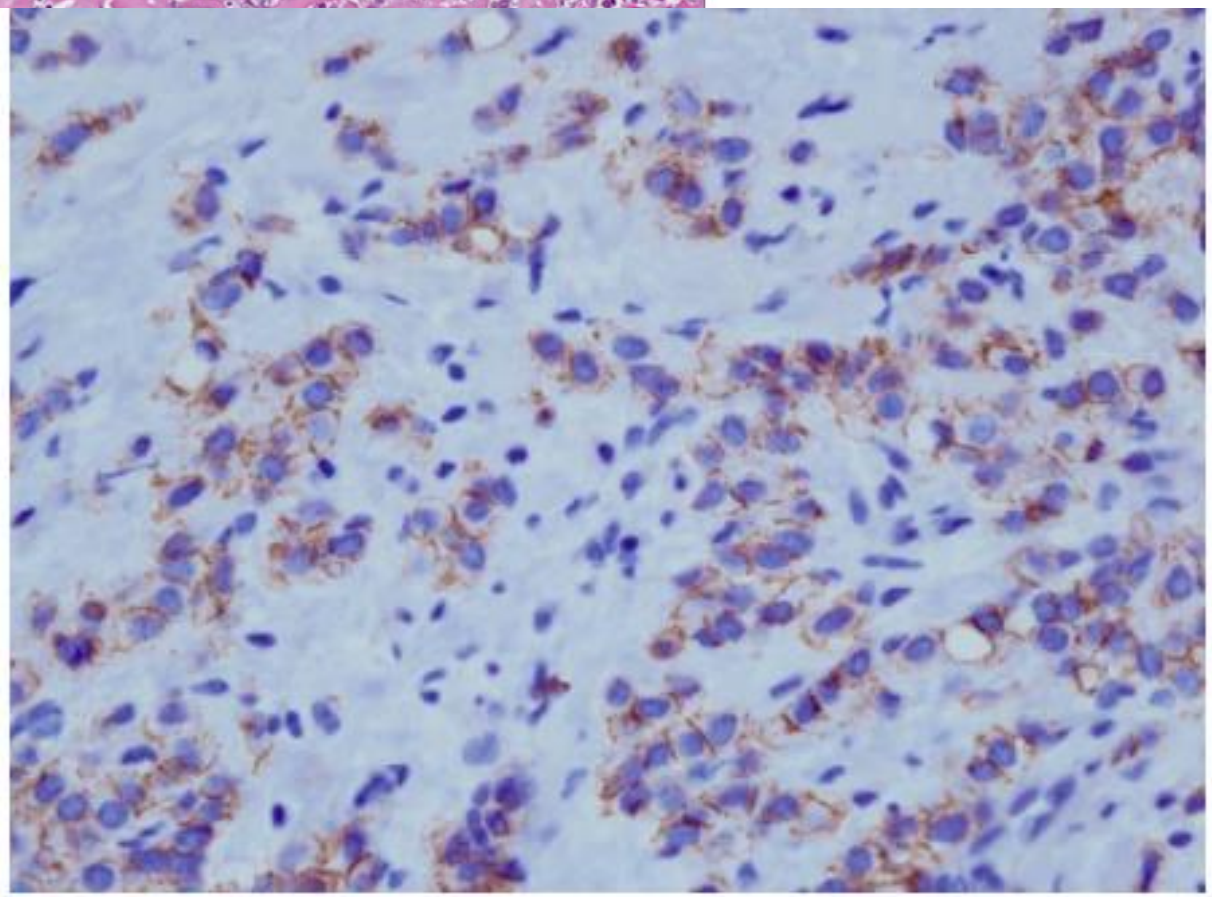


Fig. 10.86 Invasive tu

Fig. 10.87 Invasive tubulolobular carcinoma. E-cadherin immunohistochemistry shows diminished and incomplete membrane staining of the tumour cells. Some reports of tubulolobular carcinoma have documented retention of E-cadherin cytoplasmic membrane positivity, suggesting that this subtype may be of ductal rather than lobular phenotype, but the WHO classification of 2012 [1] classifies it within the spectrum of invasive lobular carcinomas

Aberrant E-cadherin immunostaining

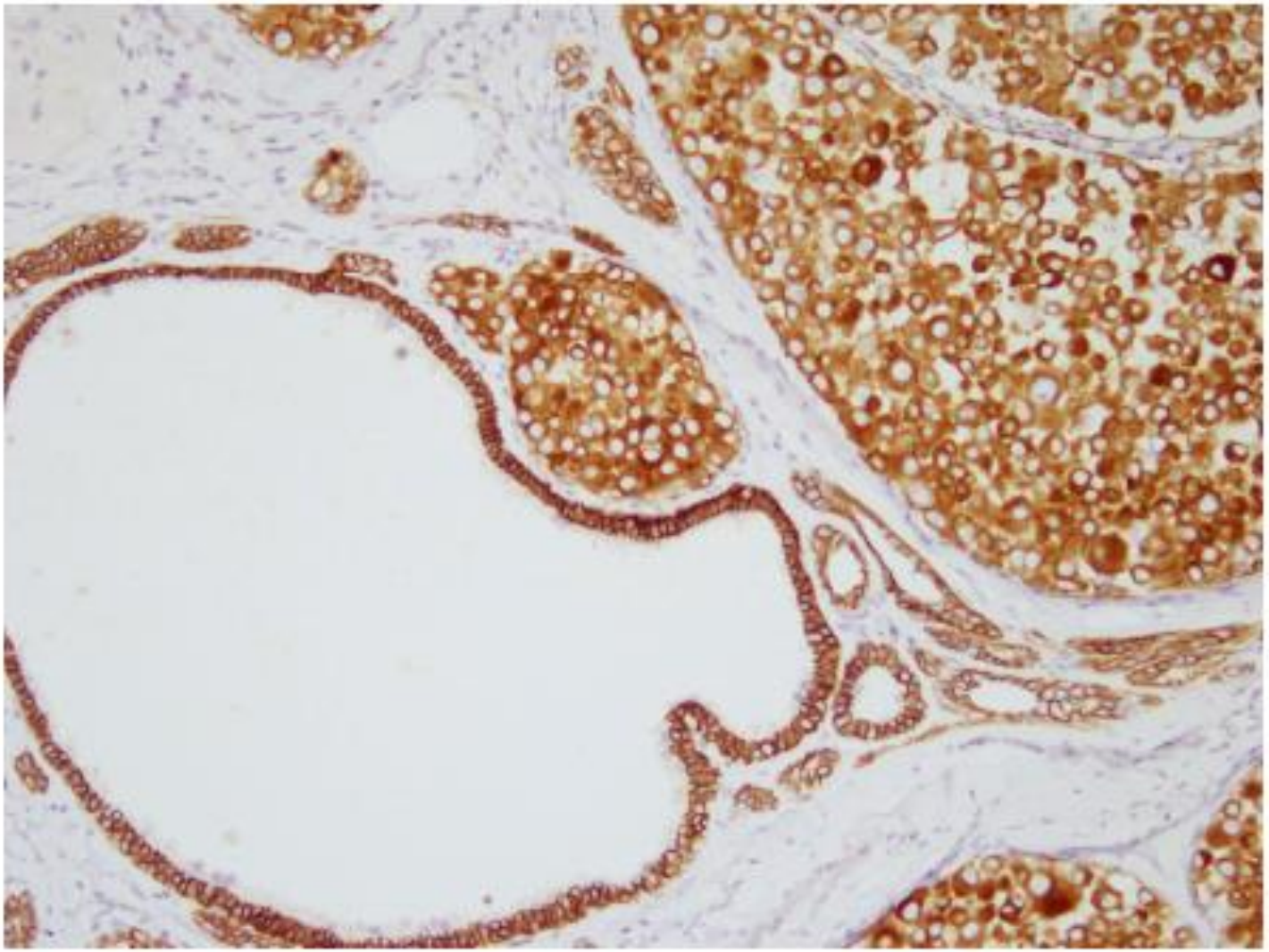


Fig. 10.36 Aberrant E-cadherin staining in LCIS shows cytoplasmic rather than membrane staining, contrasting against the membrane localisation of E-cadherin in the adjacent ducts

p120 catenin immunostaining

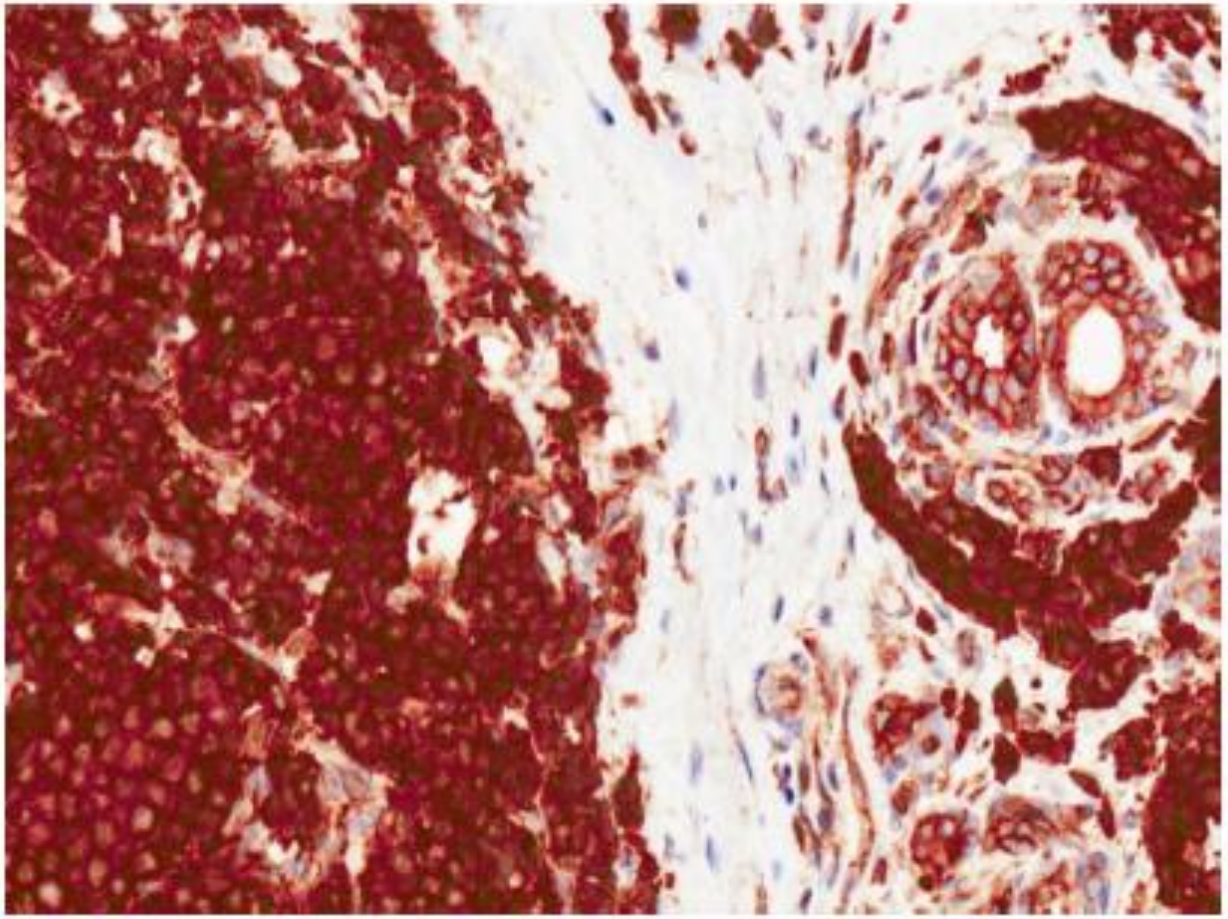


Fig. 10.85 Invasive lobular carcinoma, solid type. Immunohistochemistry for p120 catenin shows cytoplasmic staining; in comparison, benign ducts show cytoplasmic membrane staining

Invasive lobular carcinoma: Genetics

- Diploid in about 50% of cases on flow cytometry.
- Alterations in DNA copy number:
  - Loss of chromosomal arm 16q.
  - Gain of material on 1q and 16p.
- Pleomorphic ILCs exhibit similar alterations, but in addition contain amplifications at loci such as 8q24, 17q12 and 20q13, which are characteristic of high-grade ductal carcinomas.
- Inactivation of E-cadherin is the most commonly identified genetic alteration in ILC, occurring as an early event in oncogenesis.
- Most frequently classified as luminal A-type molecular tumours, but they can also be classified as luminal B, HER2, normal-like or basal-like.

Invasive lobular carcinoma: Prognosis

- Several studies have reported a more favourable outcome for ILC than IDC, whereas others found no significant differences or a worse prognosis for ILC.
- Patients with ILC have a better or similar outcome to those with IDC in the first 10 years following diagnosis; but long-term prognosis for ILC is worse than IDC.
- Favourable outcome for classical type than for variants, such as pleomorphic and solid.
- Higher frequency of metastases to bone, gastrointestinal tract, uterus, meninges, ovary and serosa.

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Differential diagnoses

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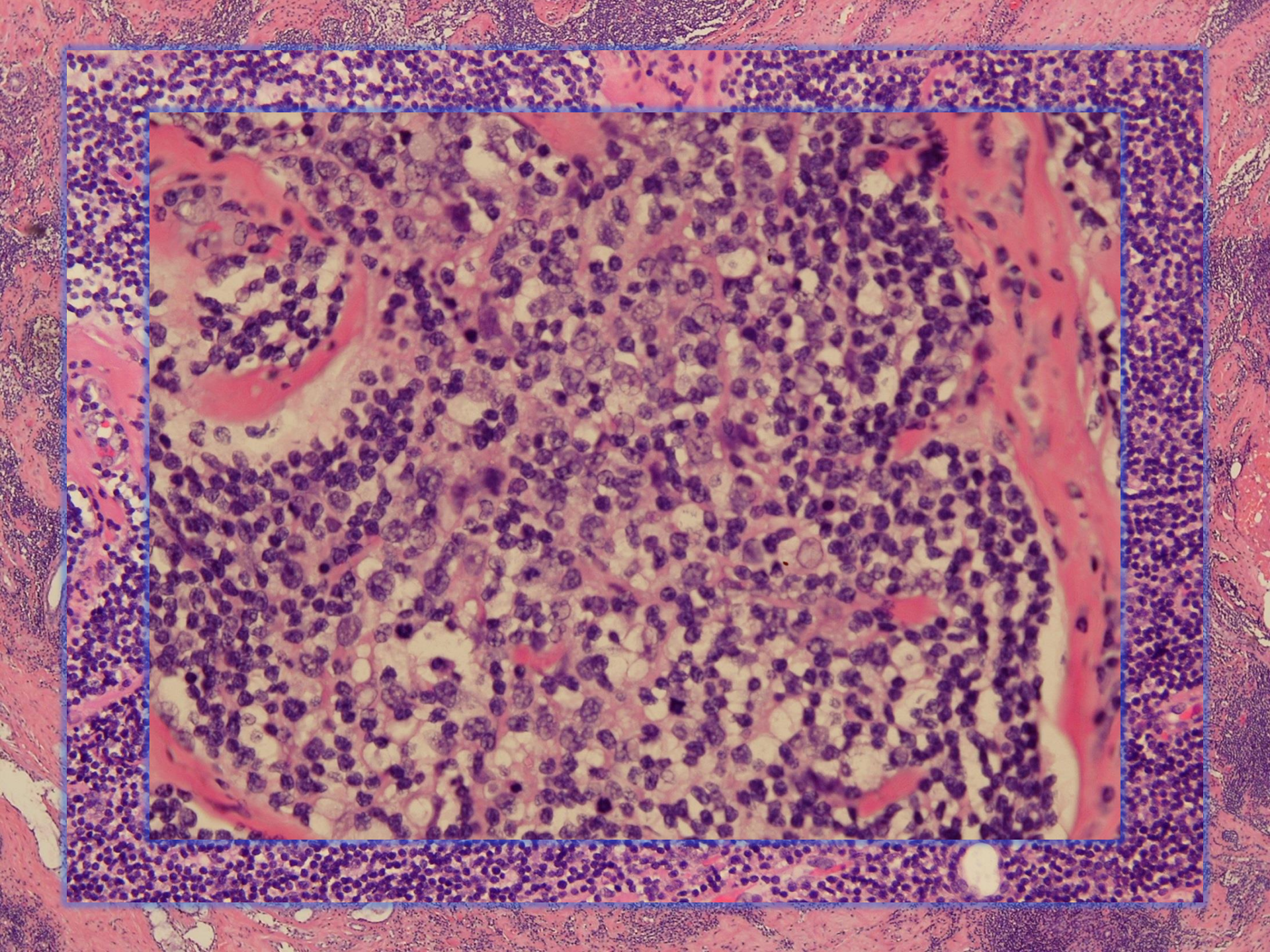
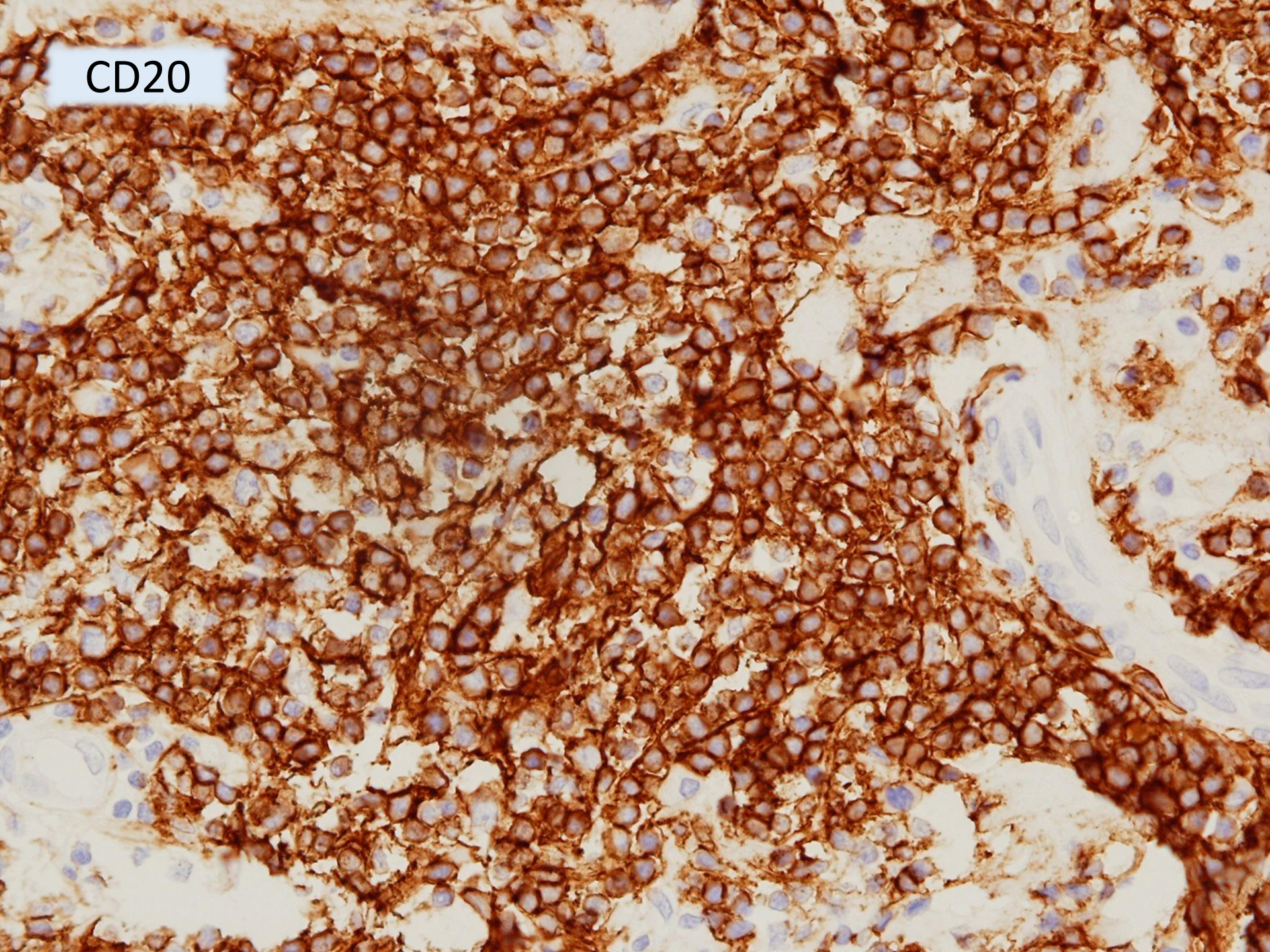
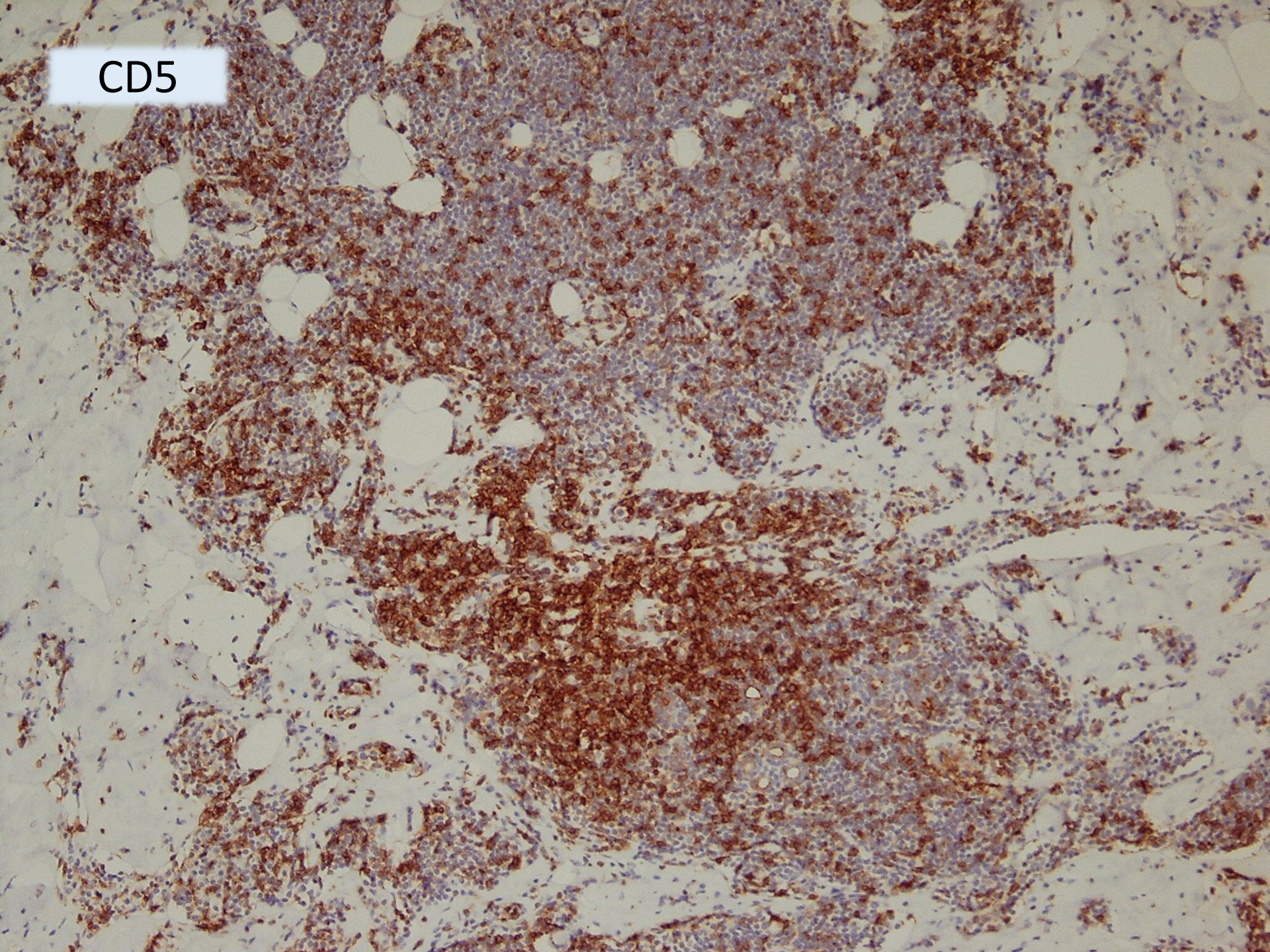
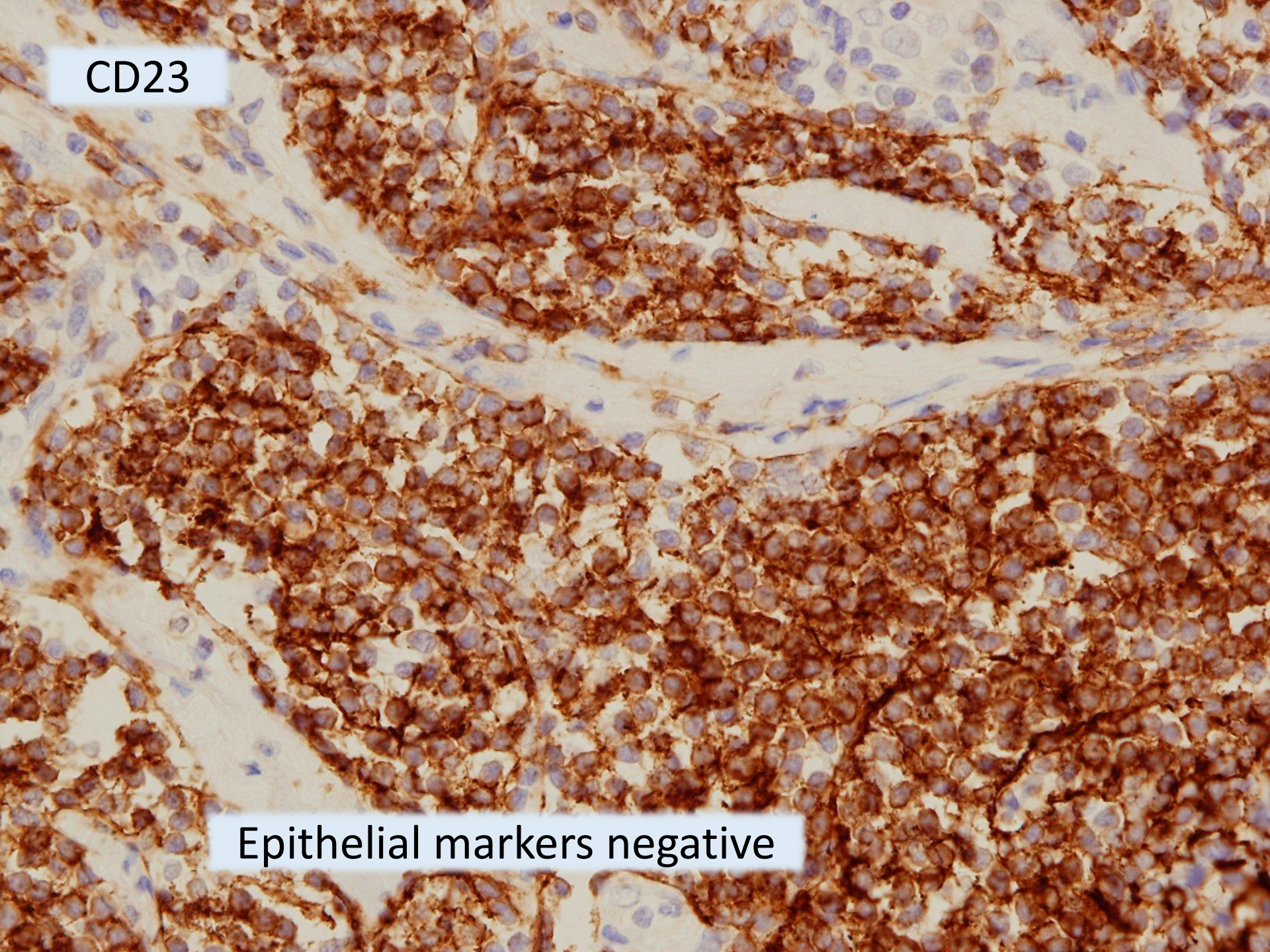



CD20


CD5


CD23
Epithelial markers negative

Diagnosis

Low grade B cell lymphoma

Breast plasmacytoma

Arch Pathol Lab Med. 2001;125:1078–1080

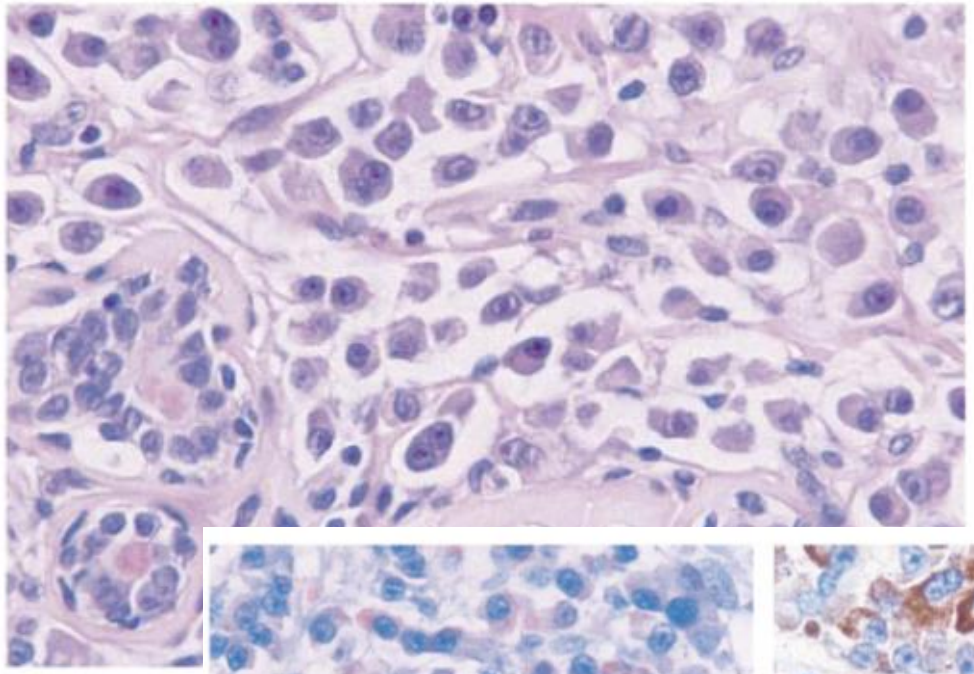


Figure 2. *Th*
surrounding n

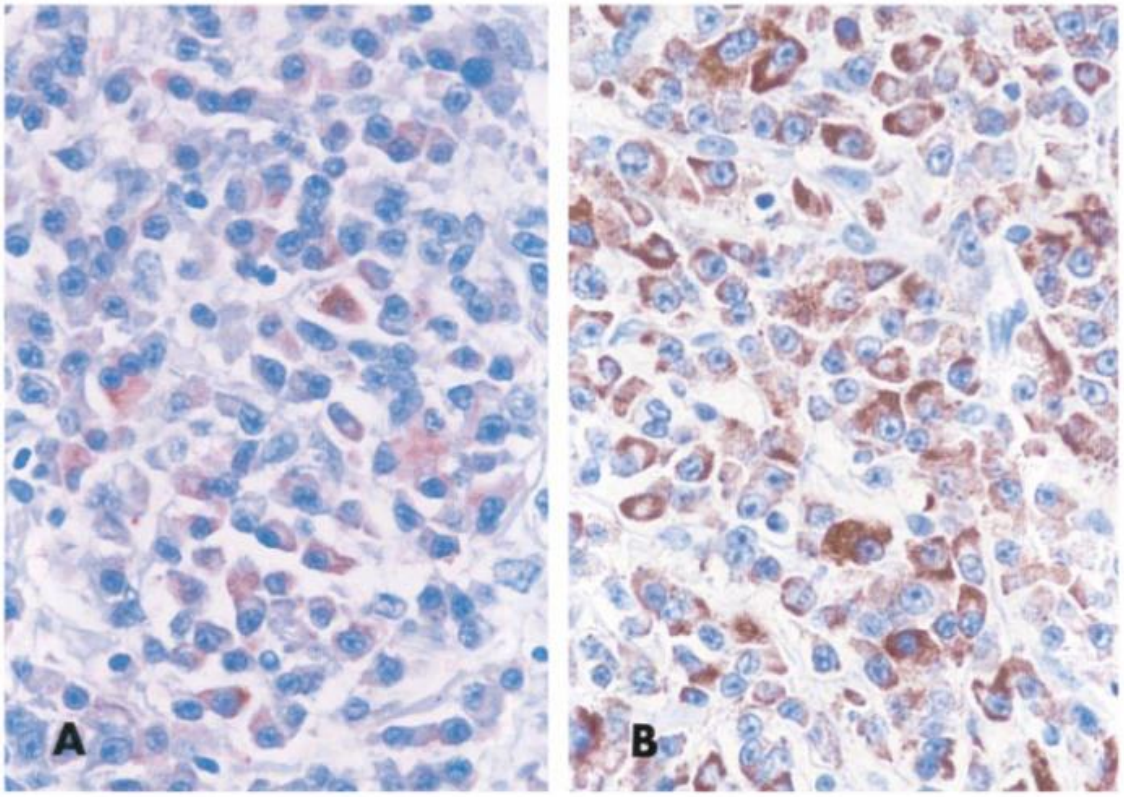


Figure 3. *The plasma cells are diffusely and strongly positive for IgA (A) and κ light chains (B) (original magnification ×20).*

Summary

- Invasive lobular carcinoma with ‘small cells’, mimicking lymphoma & plasmacytoma.
- E-cadherin immunostaining patterns.
- p120 catenin immunohistochemistry.

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