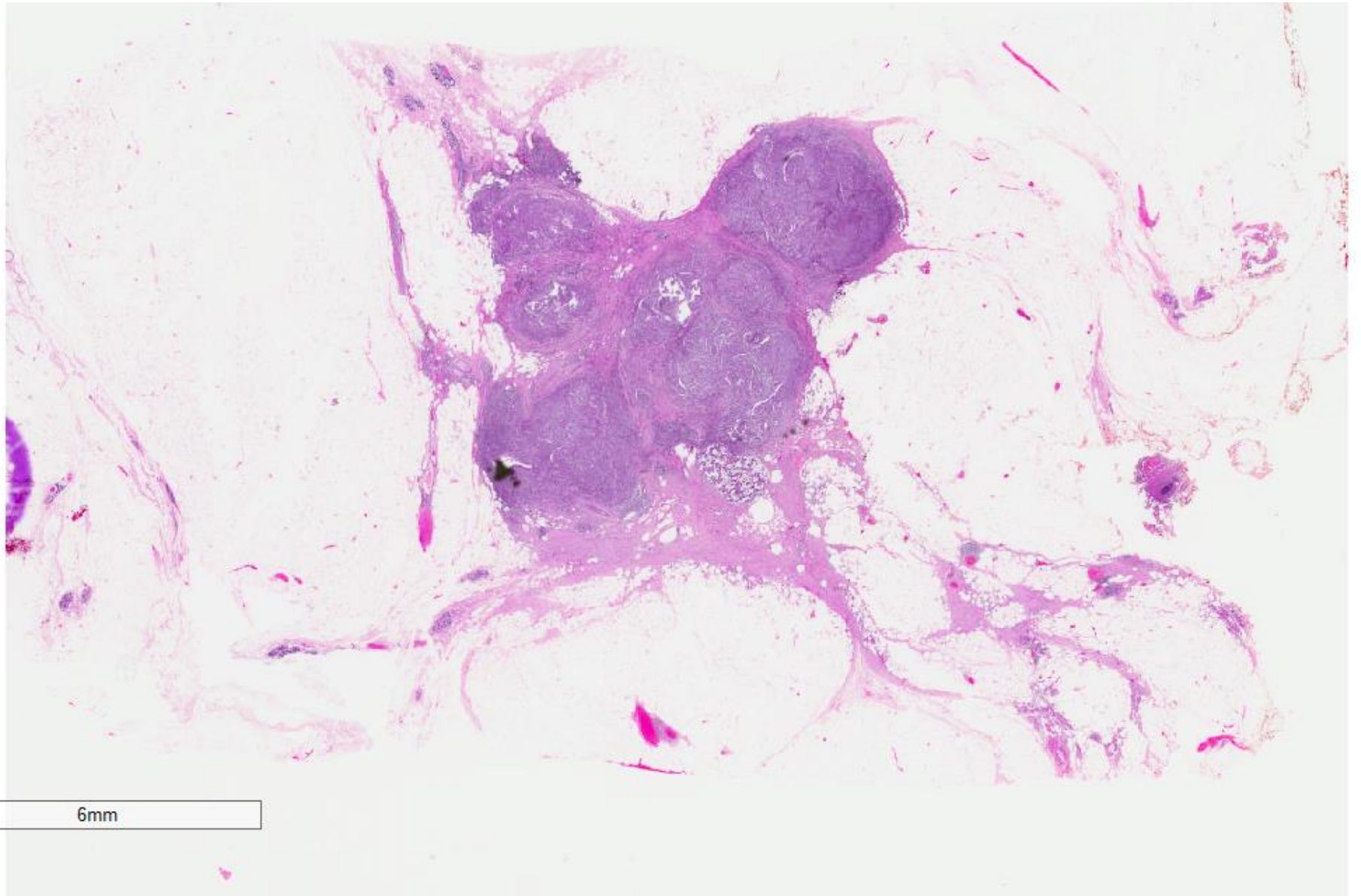
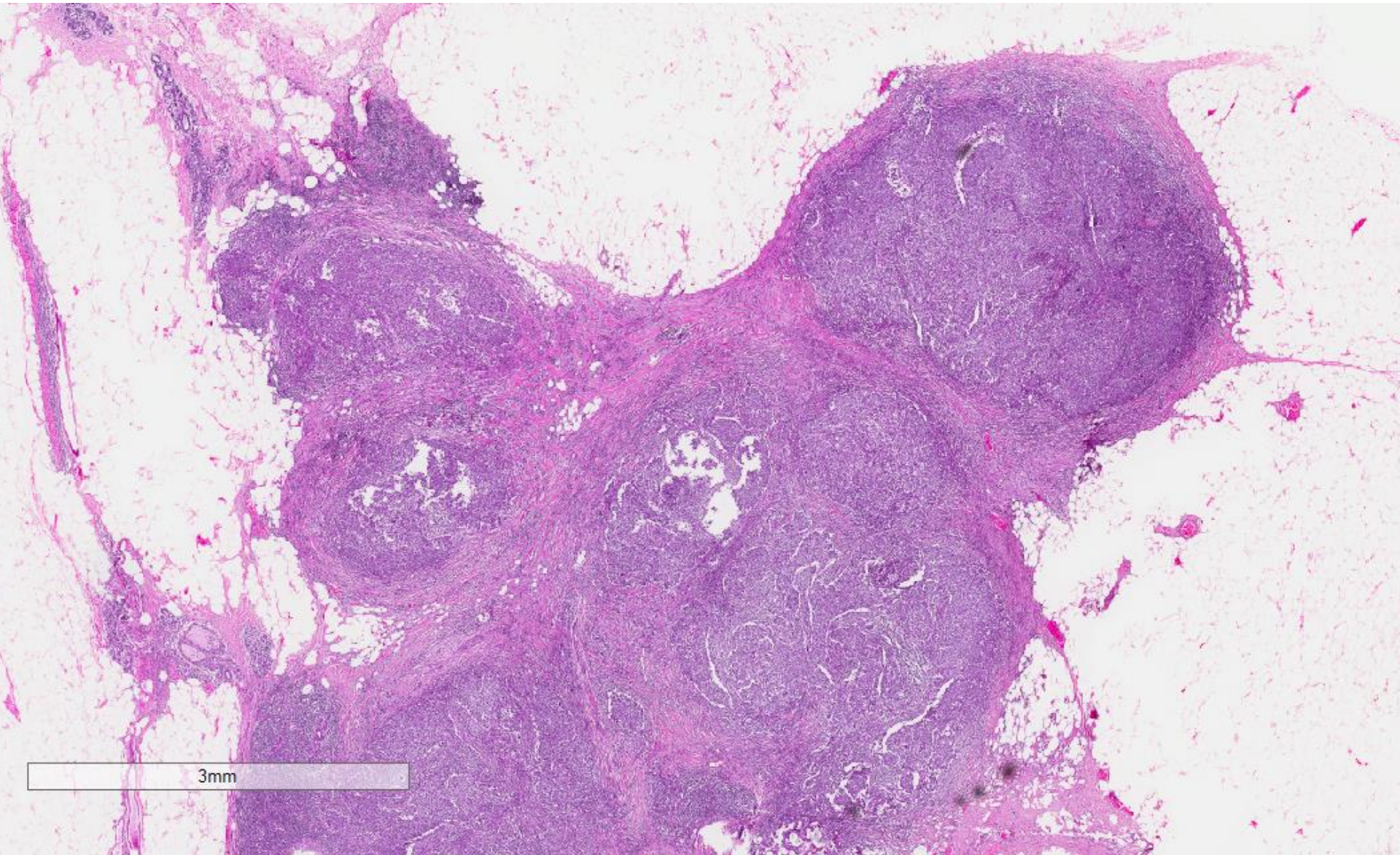


Case 26

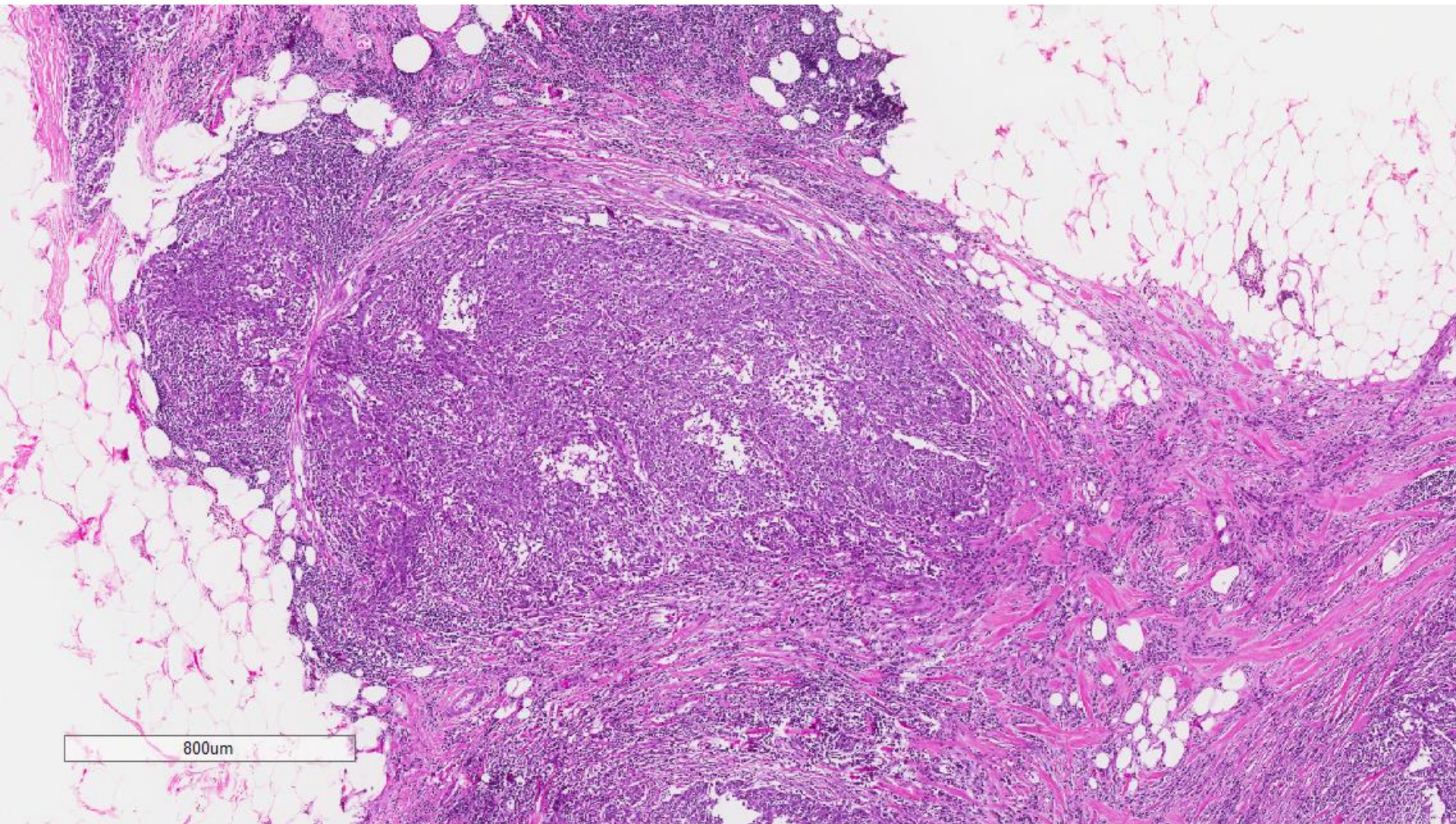
48 year old lady underwent excision
of a left breast lesion.



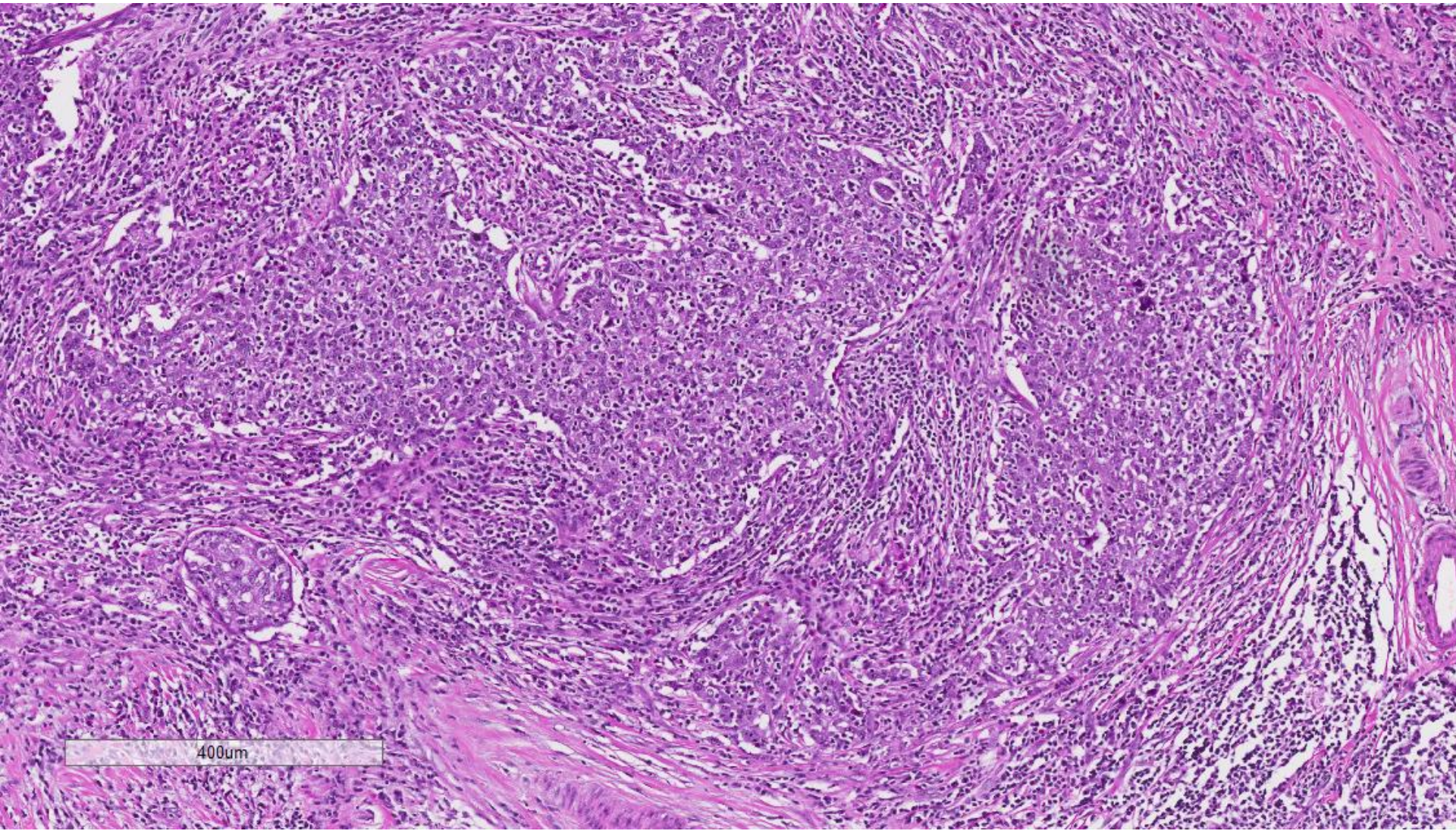
6mm



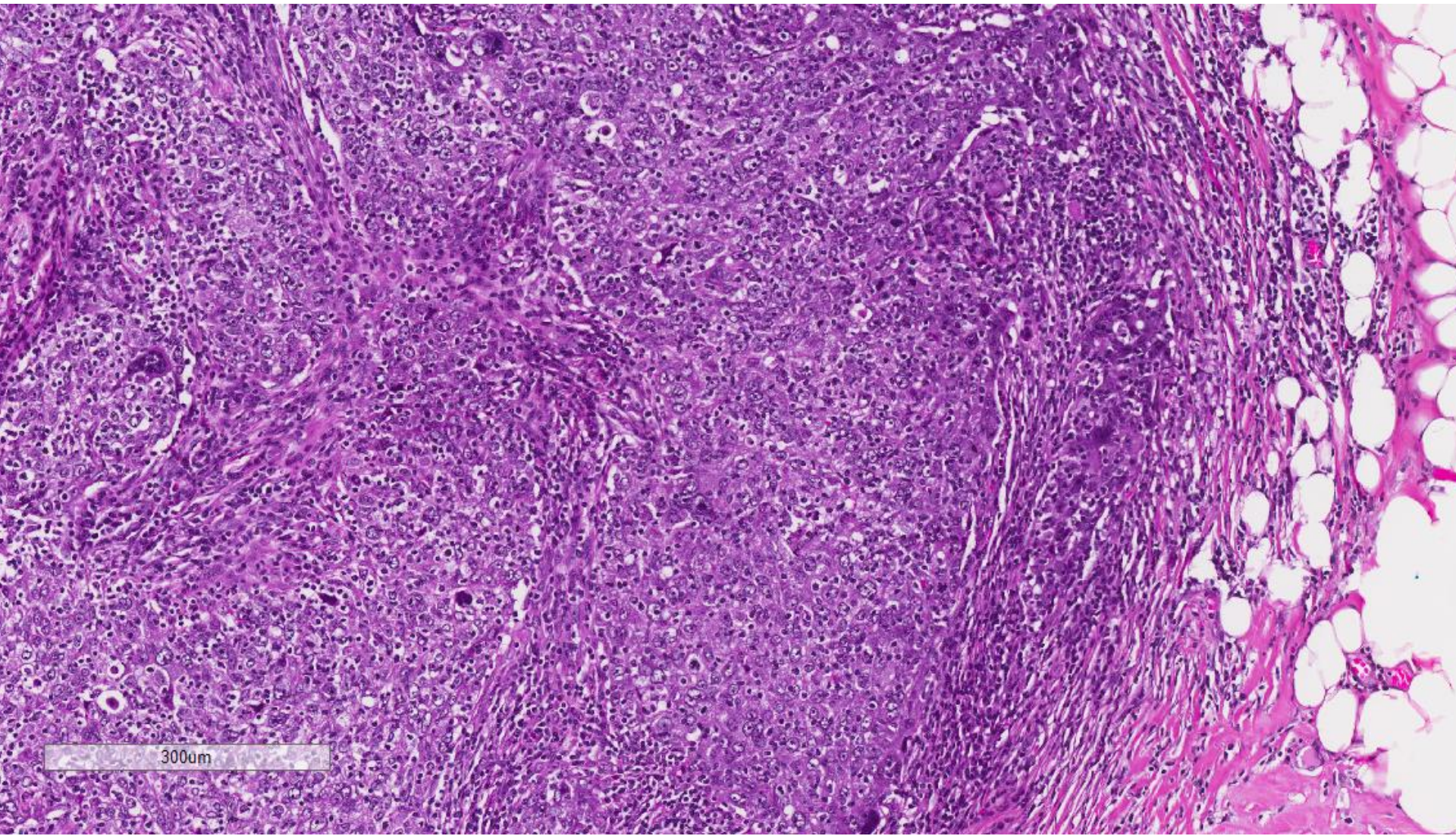
3mm



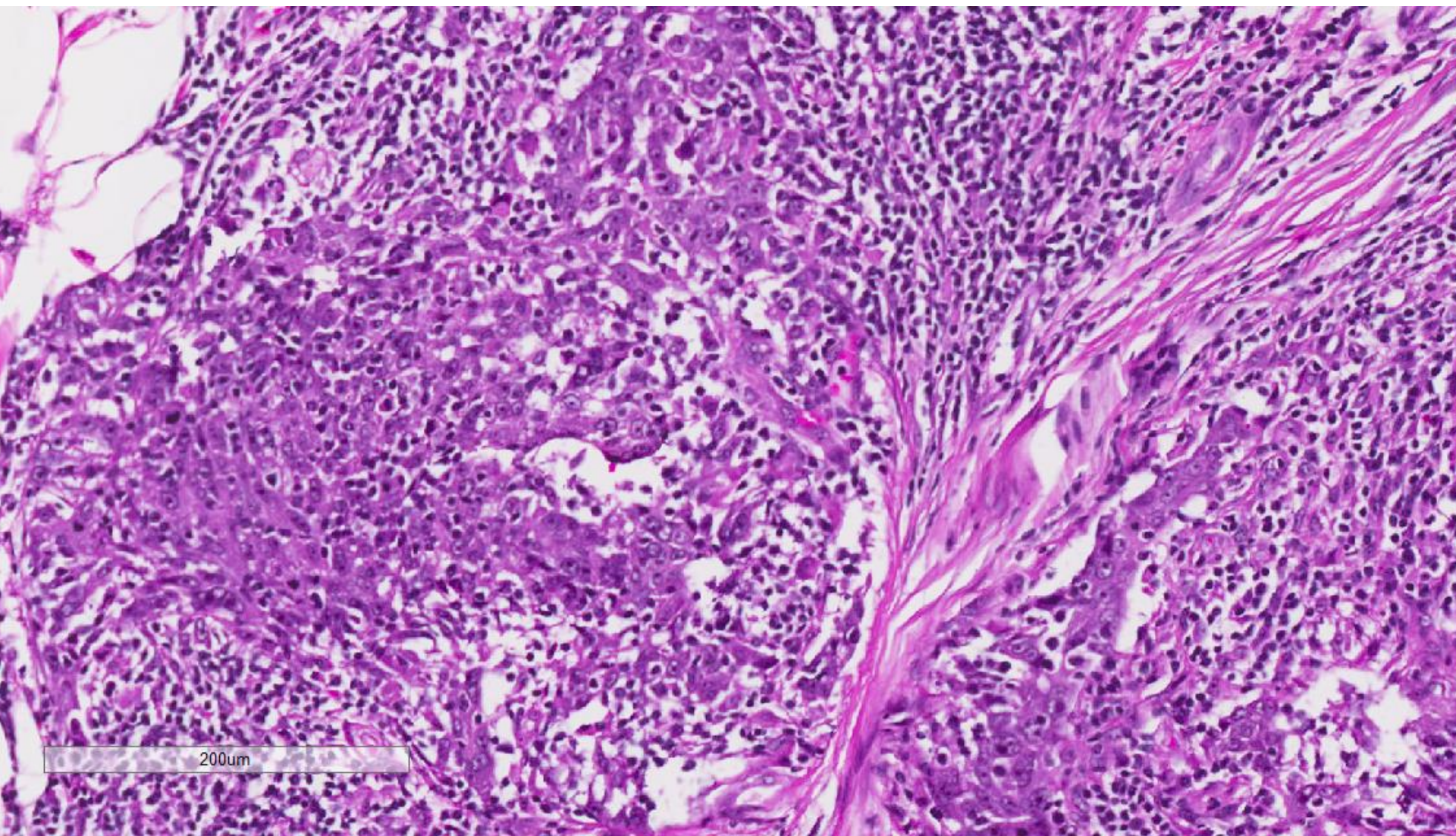
800um



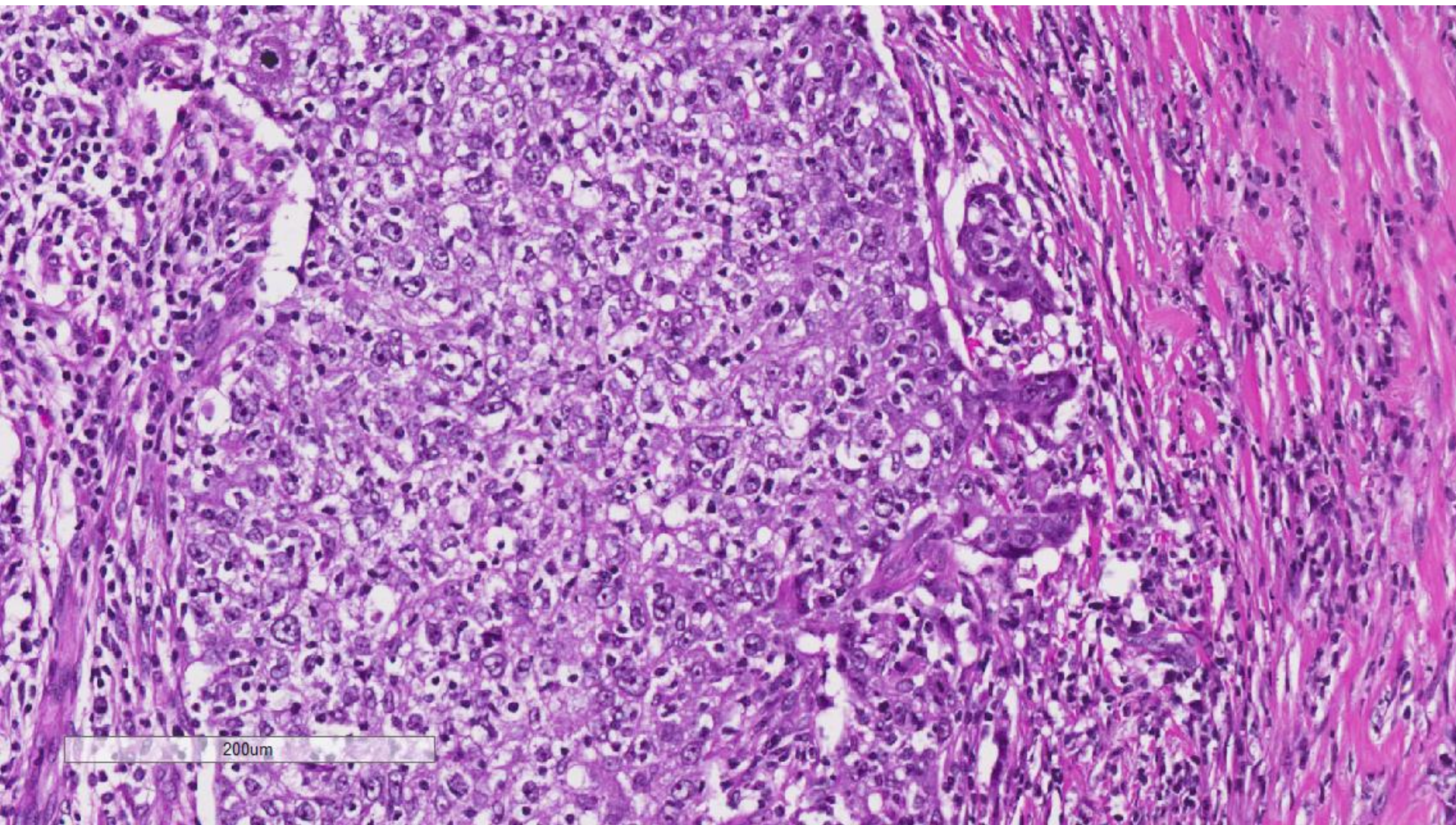
400µm



300um

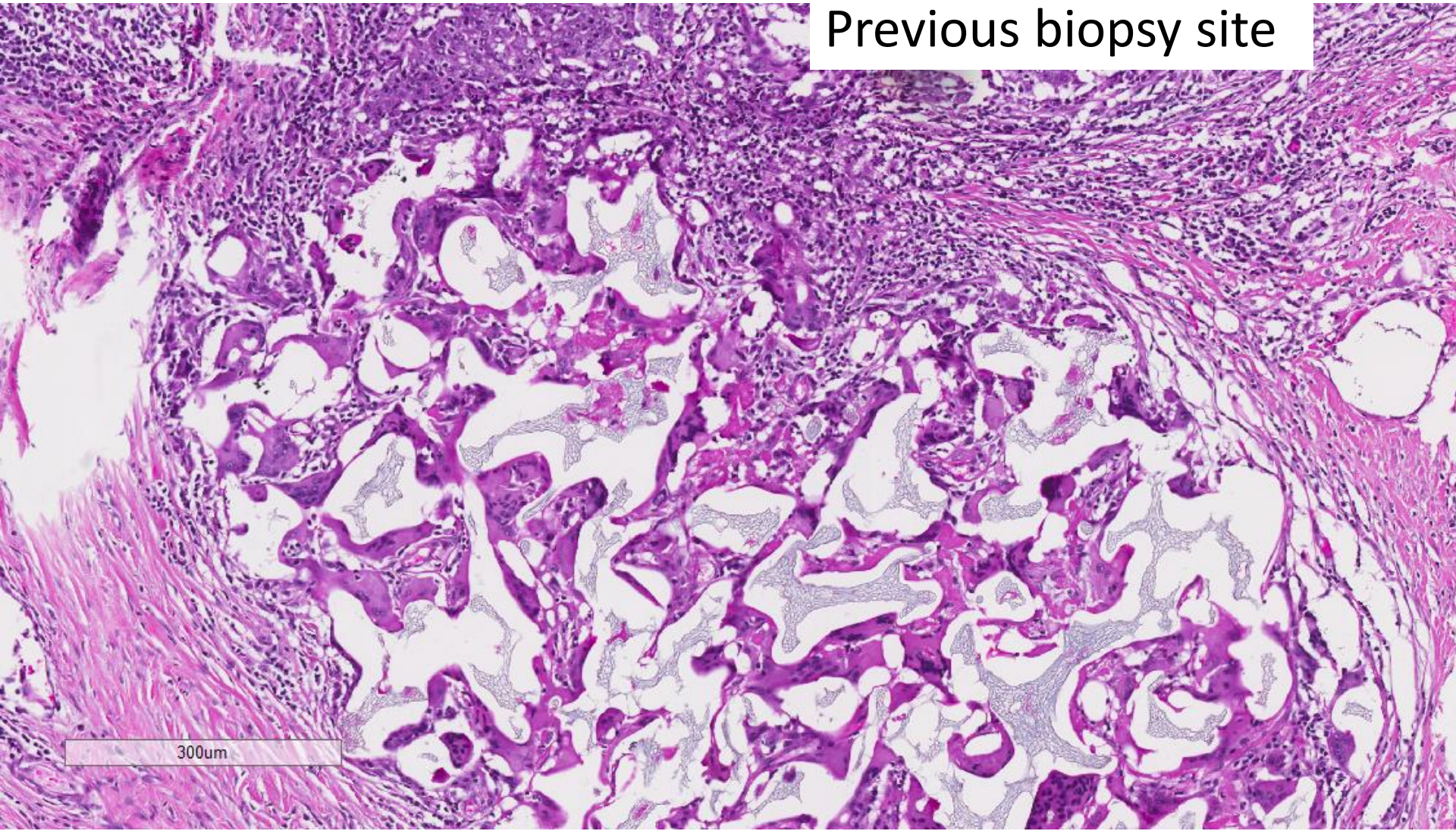


200µm



200um

Previous biopsy site



300um

Invasive carcinoma with medullary-like features

ER negative, PR negative, cerbB2 negative

Carcinomas with medullary differentiation

- Medullary carcinoma
- Atypical medullary carcinoma
- Invasive carcinoma of no special type with medullary-like features

Medullary carcinoma

- Classical criteria:
 - Syncytial architecture in $> 75\%$ of tumour mass.
 - Histological circumscription with pushing margins.
 - Lack of tubular differentiation.
 - Prominent and diffuse lymphoplasmacytic infiltrate.
 - High grade pleomorphic nuclei with brisk mitoses.

Carcinomas with medullary differentiation

- Atypical medullary carcinoma
- Carcinoma with medullary-like features
 - *Refer to tumours that do not fulfil all histological criteria.*
- Difficulty in applying diagnostic criteria.
- Poor interobserver reproducibility.

Table 3.01 Comparative immunohistochemical profiles (% of cells expressing the given marker)

Immunohistochemical markers	Typical medullary breast cancer {634}	Invasive carcinoma with medullary features {1194}	Invasive carcinoma, grade 3 {1135}
Nielsen Basal profile (ER-negative/HER2-negative and keratin 5/6-positive and/or EGFR-positive)	Not evaluated for this signature	62.9%	18.9%
ER-negative	<div style="border: 1px solid black; padding: 5px; display: inline-block;"><i>Triple negative</i></div>	89.5%	38.5%
PR-negative		48.7%	34%
HER2-negative		97.7%	76.2%
Keratin 5/6-positive	<div style="border: 1px solid black; padding: 5px; display: inline-block;"><i>Basal-like</i></div>	54.8%	17.9%
P-cadherin-positive		65.6%	7.9%
p53-positive		69.3%	31.6%
Ki67 > 50%		54.5%	63.2%
Cyclin E		31.4%	26.2%
P-cadherin-positive/Ki67 > 50% HER2-negative/p53-positive		54%	0%

EGFR, epidermal growth factor receptor; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor.

Carcinomas with medullary features

- Medullary carcinoma considered to have a favourable prognosis compared with grade-matched invasive cancer NST.
- 10 year distant relapse free survival rate of 94.9% vs 77.5% for invasive cancer NST (*Vu-Nishino et al. Int J Radiat Oncol Biol Phys 62: 1040-41, 2005*).
- Low reproducibility limits reliance on study results.
- Current practice of treating carcinomas with medullary features as basal-like triple negative disease with aggressive therapy.

Carcinomas with medullary features

- Prognostic importance of lymphoplasmacytic infiltrates.
- Expression levels of immune response genes are independent predictors of outcome in both ER positive and ER negative breast cancers with high proliferative activity.
- Improved clinical behaviour of medullary cancer may be related to the prominent lymphoplasmacytic infiltrates.

Carcinomas with medullary features: *implications of 'new' classification*

- Acknowledges the low reproducibility of original criteria of medullary carcinoma.
- Allows widening the spectrum of these tumours with similar biological features:
 - Triple negativity.
 - Basal-like expression.
 - Hereditary breast cancer.