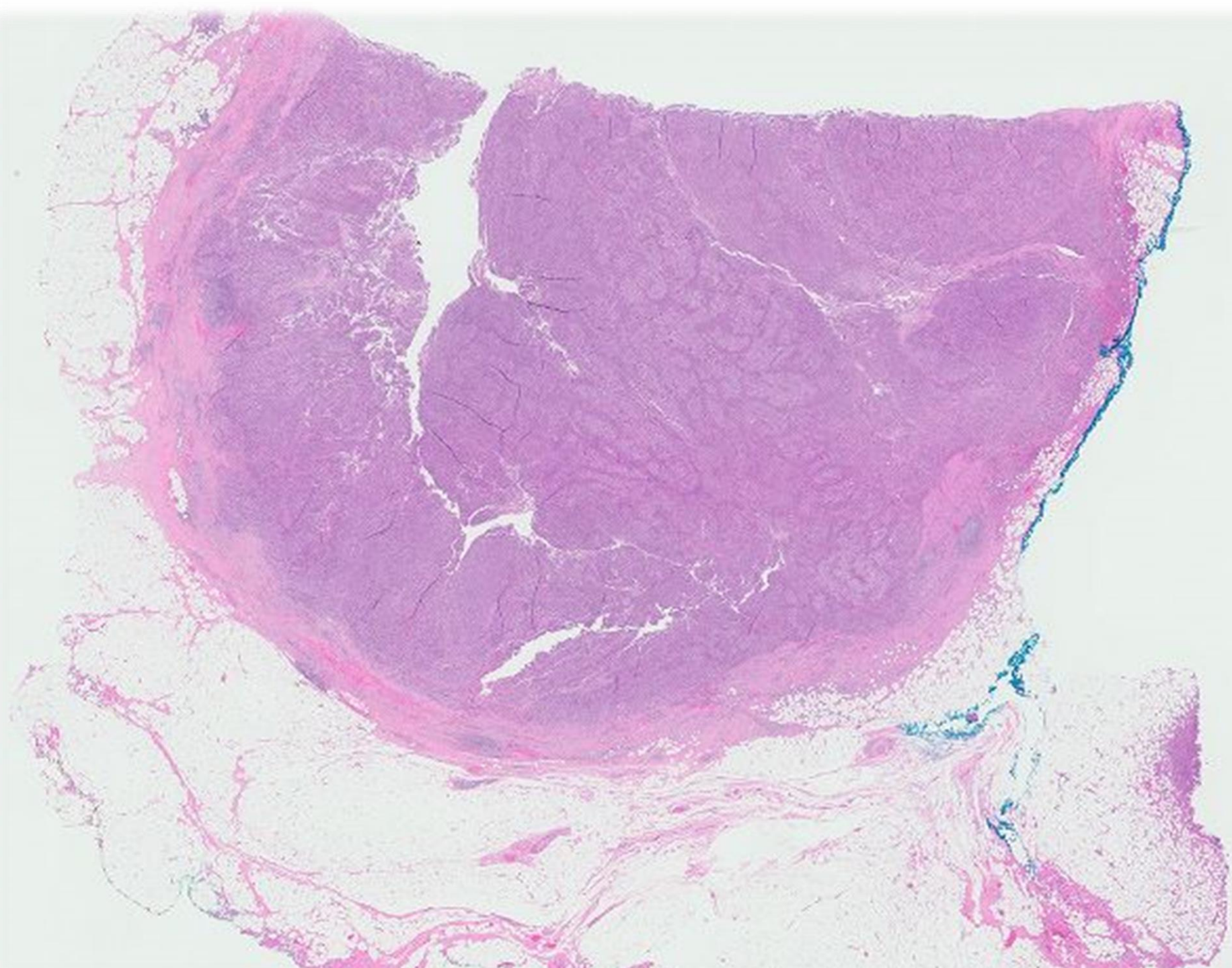


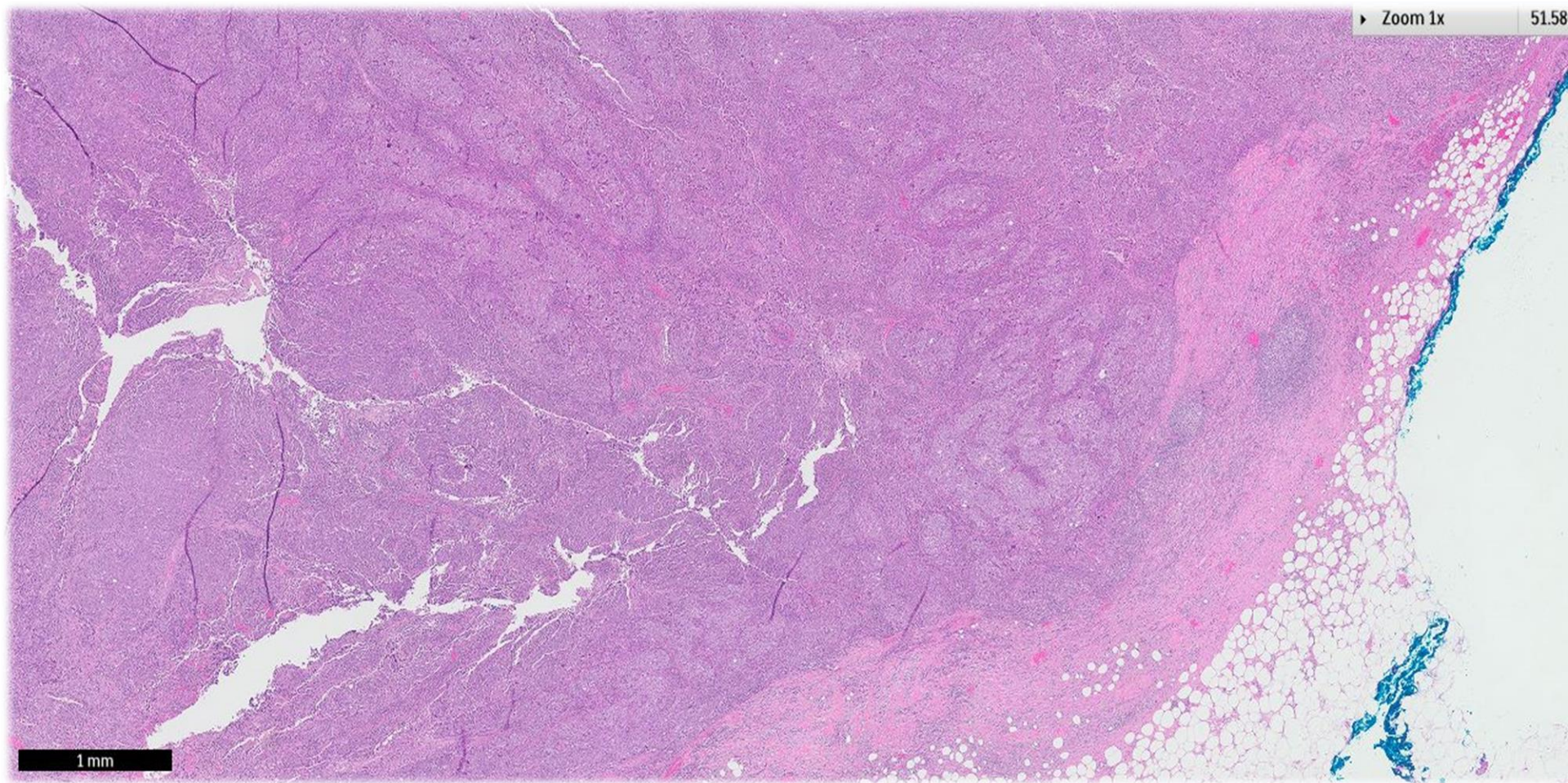
# Case 9

36 year old Indian lady underwent an excision biopsy for what was believed clinicoradiologically to be a fibroadenoma in the right breast.







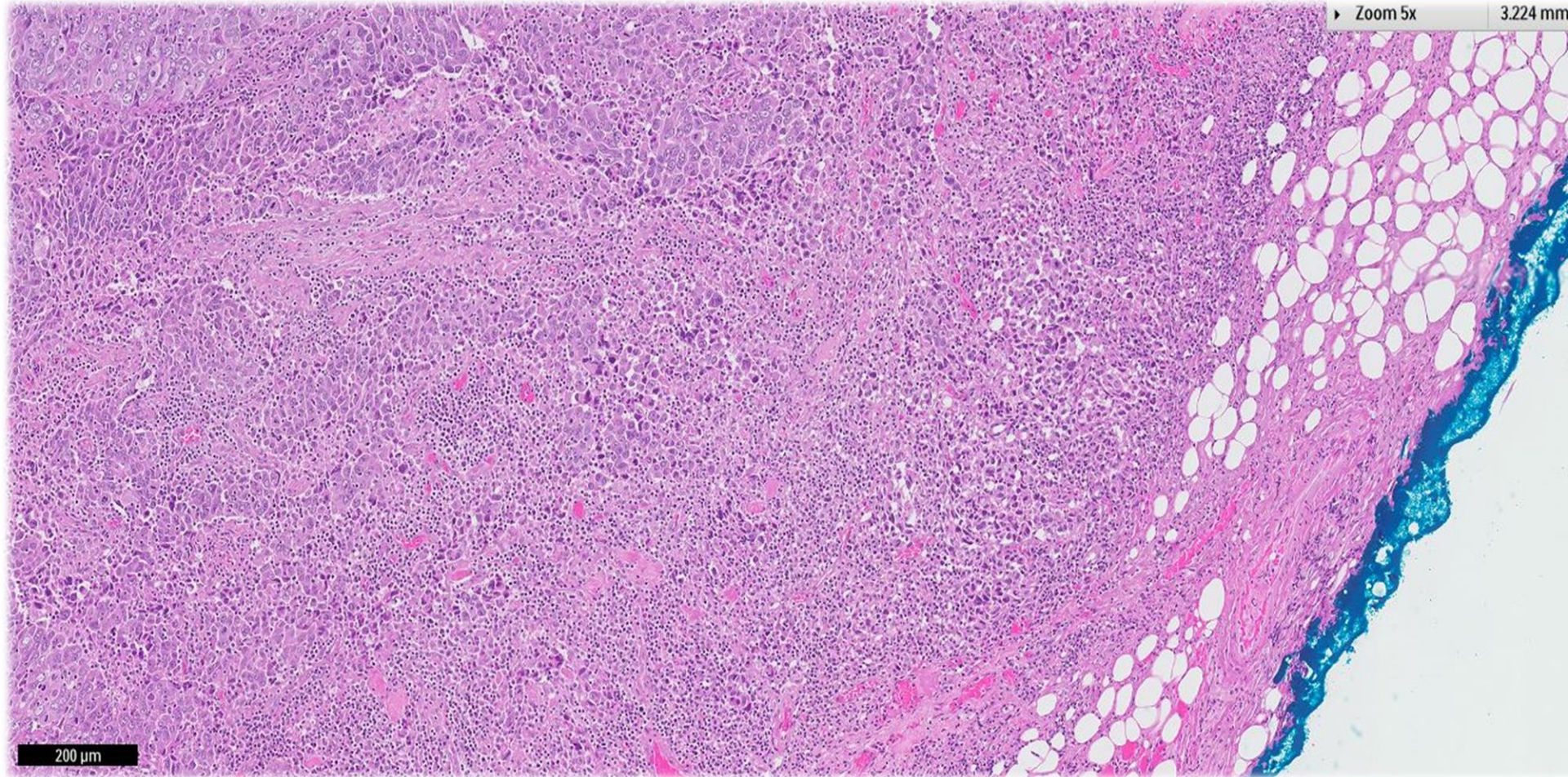


1mm



Zoom 5x

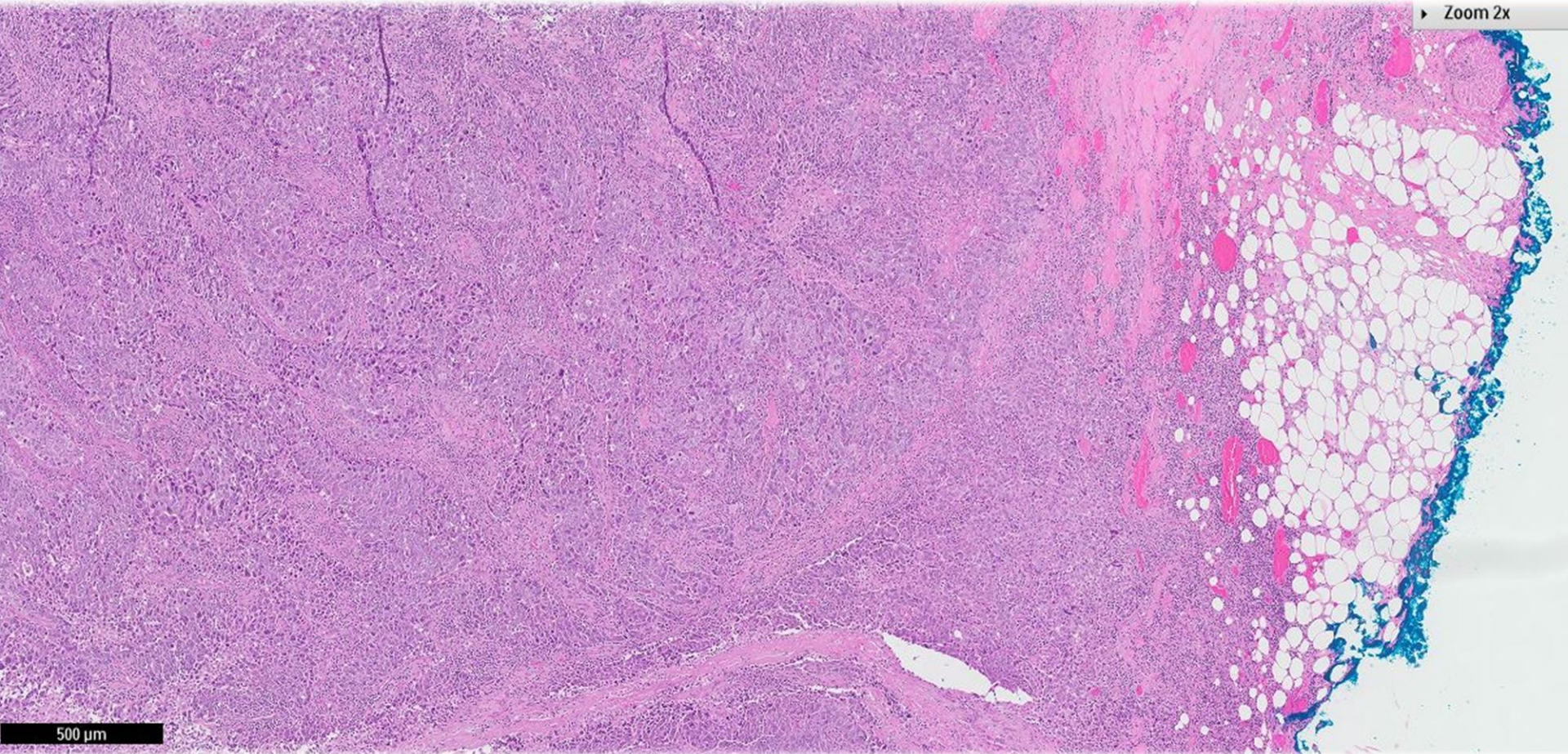
3.224 mm



200  $\mu$ m



▶ Zoom 2x

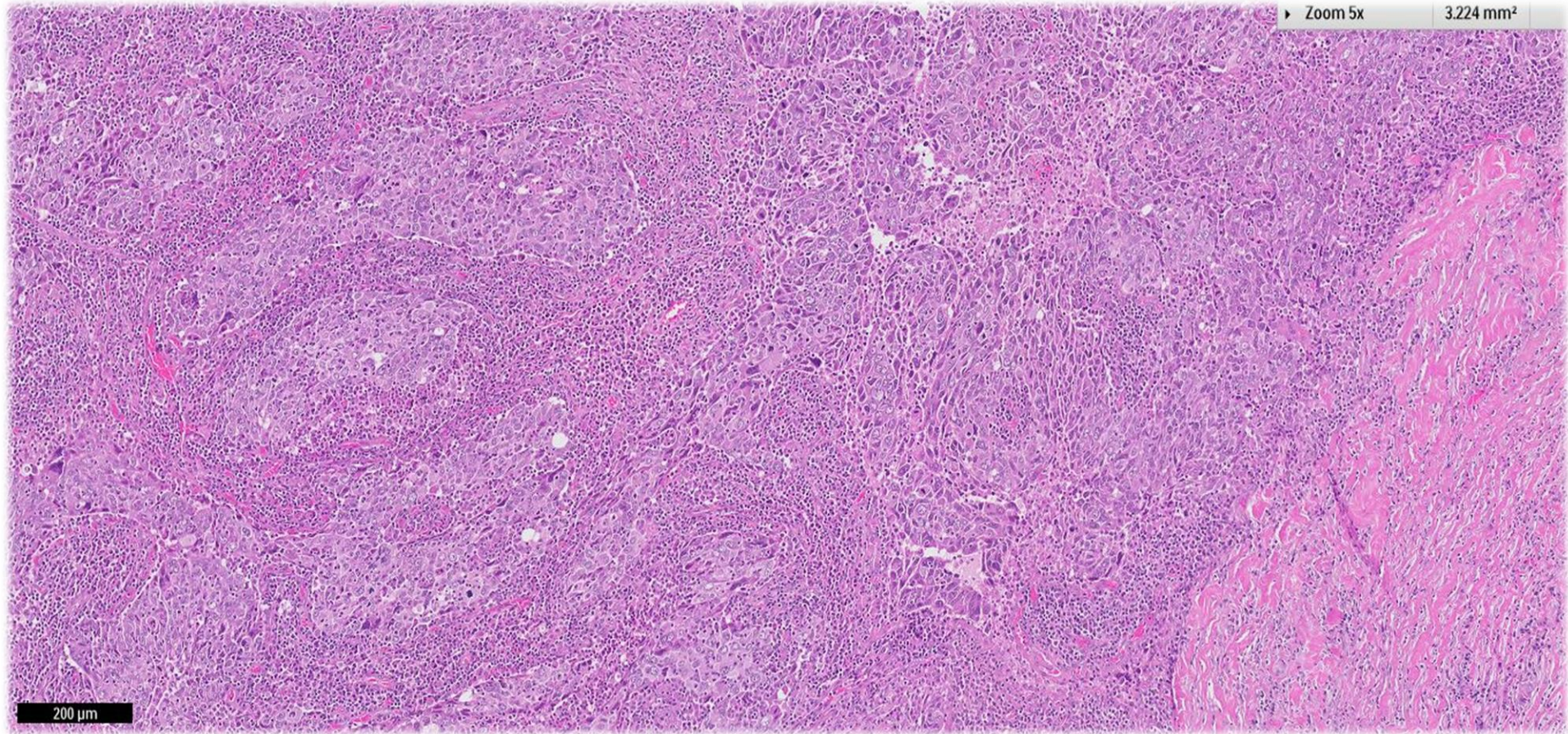


500  $\mu$ m



▶ Zoom 5x

3.224 mm<sup>2</sup>

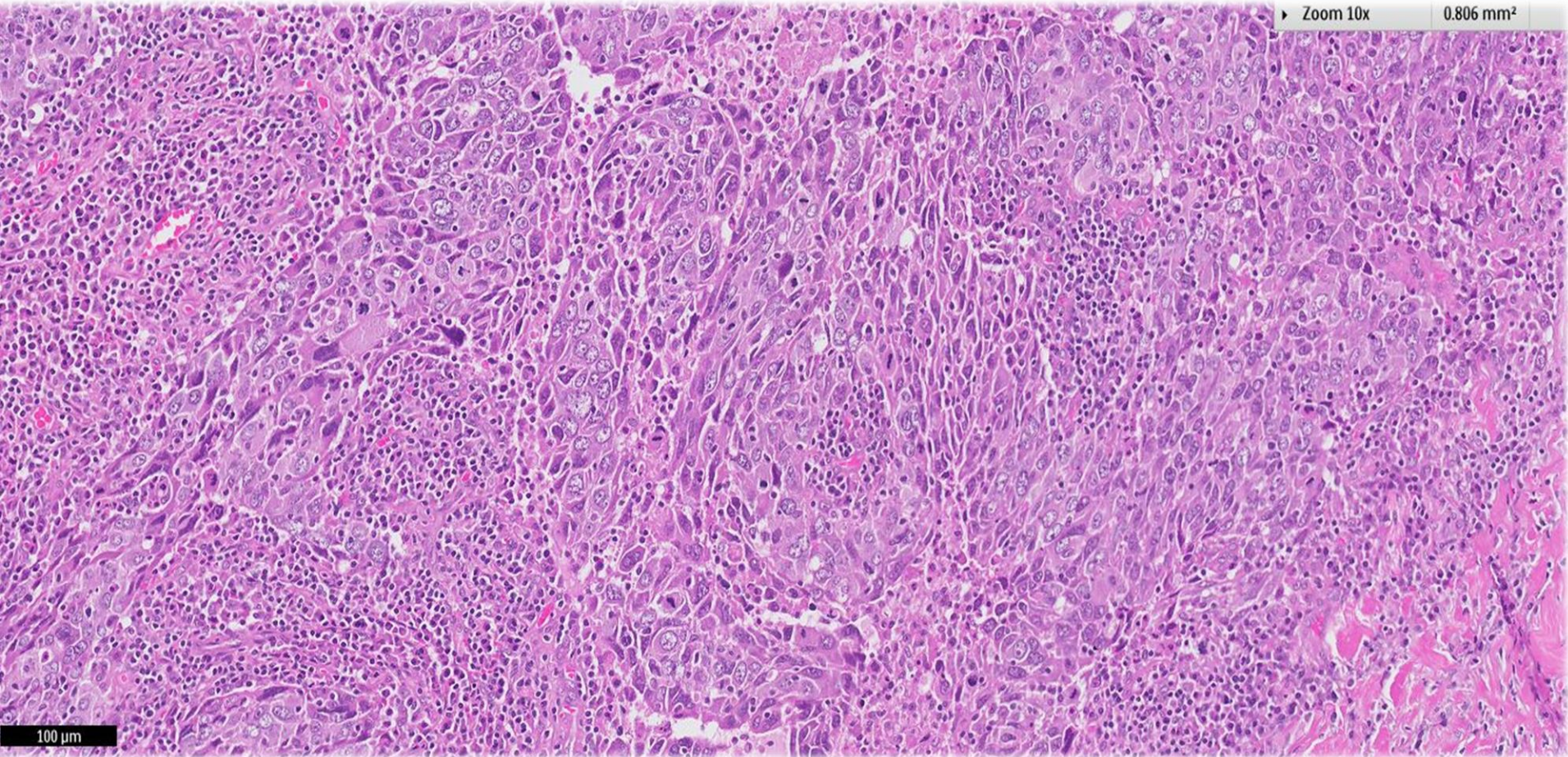


200 μm



Zoom 10x

0.806 mm<sup>2</sup>



100  $\mu$ m

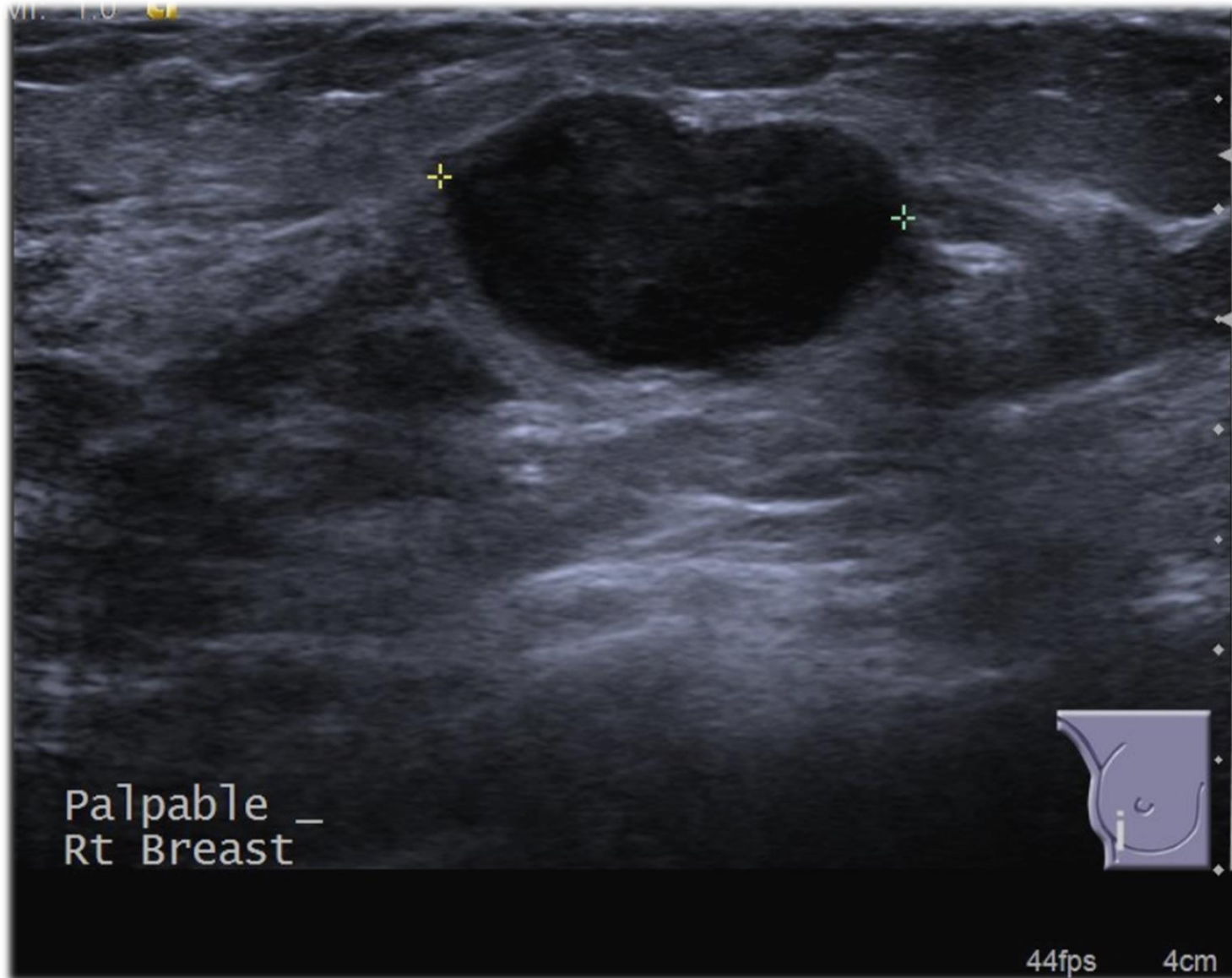


*Night view from One Fullerton, Singapore*





7/1/07



**SIEMENS**  
18L6 HD / \*Breast  
General  
2D \_\_\_\_\_ 100%  
GEN / 15.00 MHz  
0 dB / DR 65  
ASC 3 / DTCE M  
Map F / ST 3

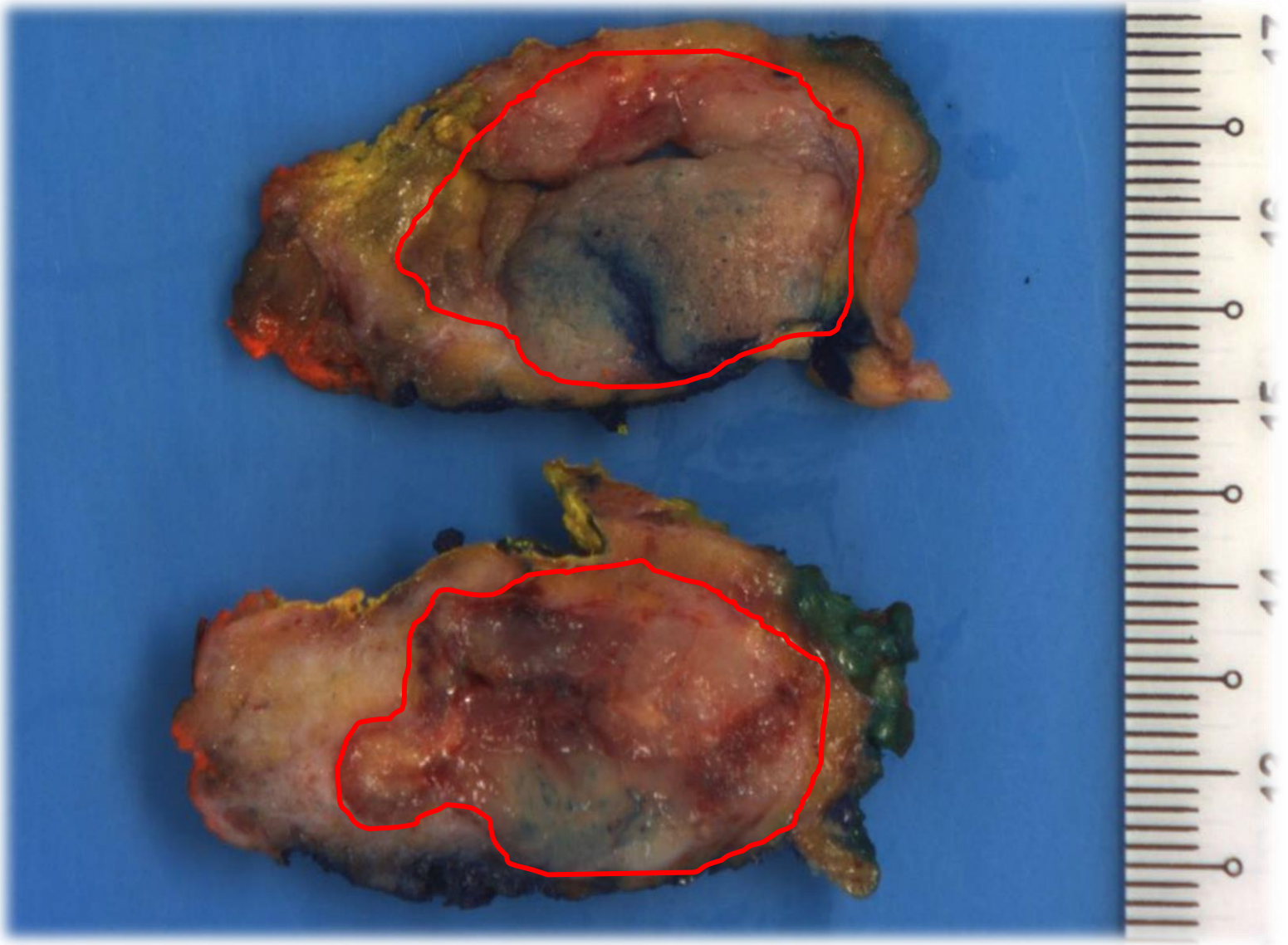
**D=21.6 mm**

Palpable \_  
Rt Breast

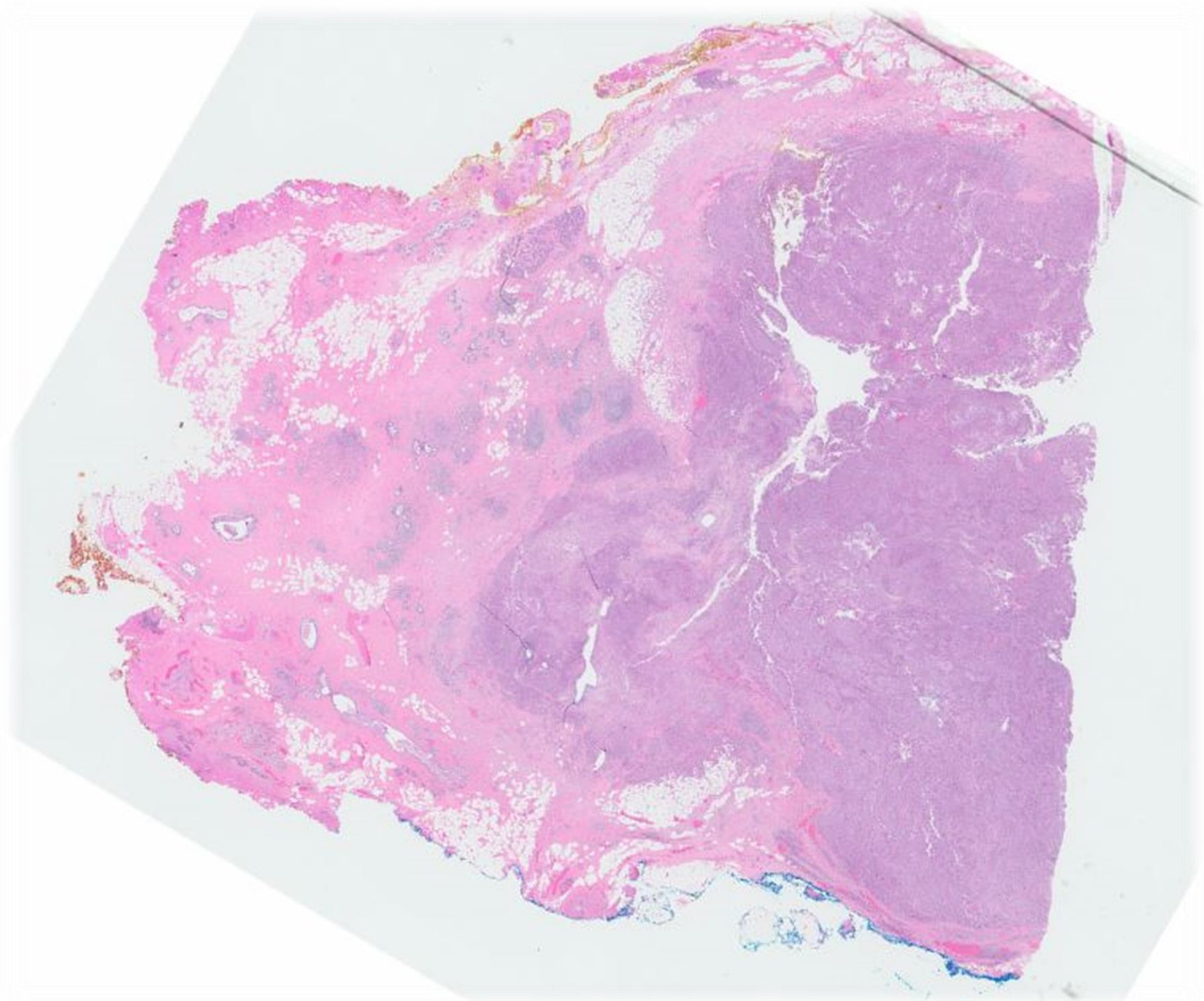
44fps 4cm

*Courtesy of Dr Lester Leong*

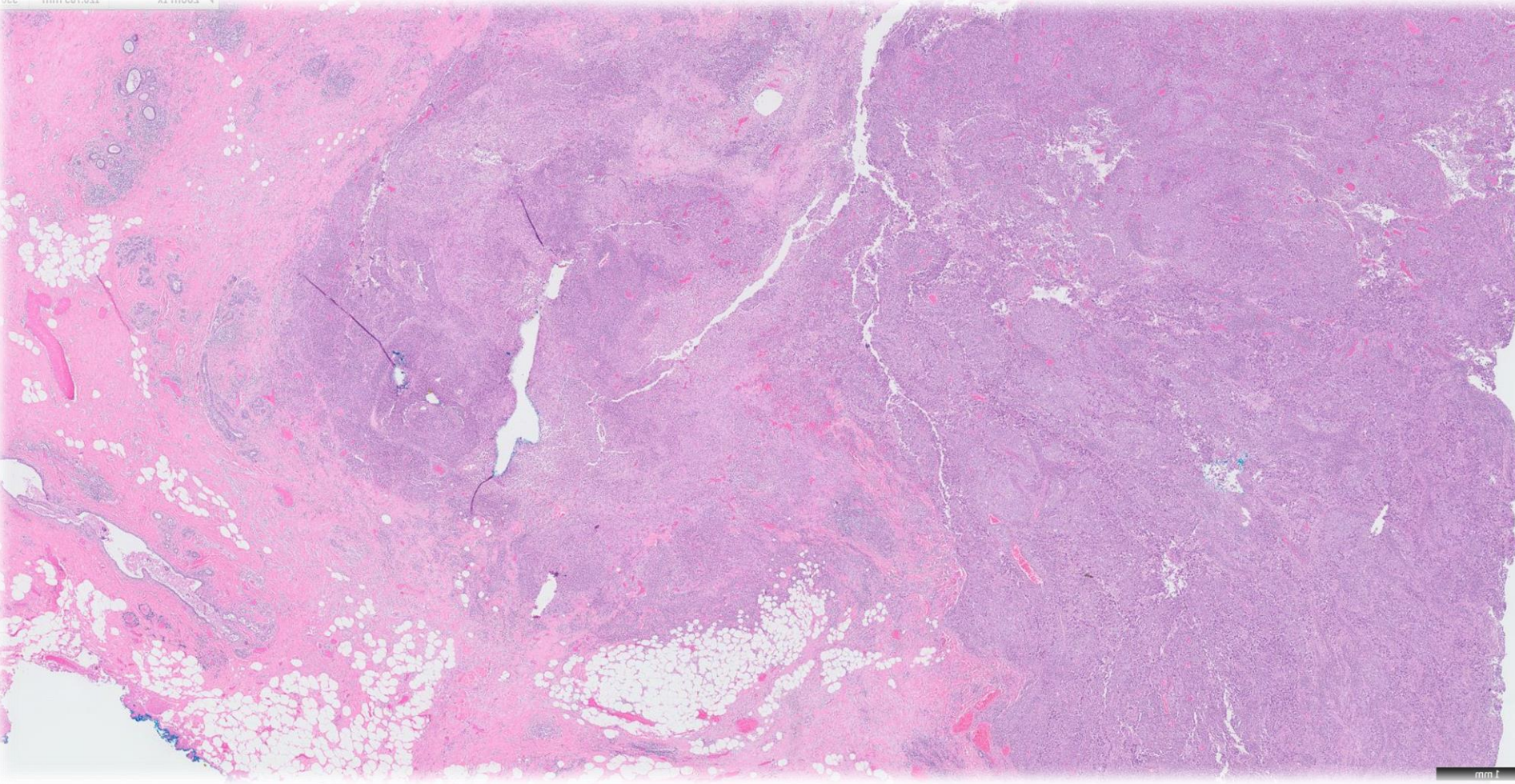




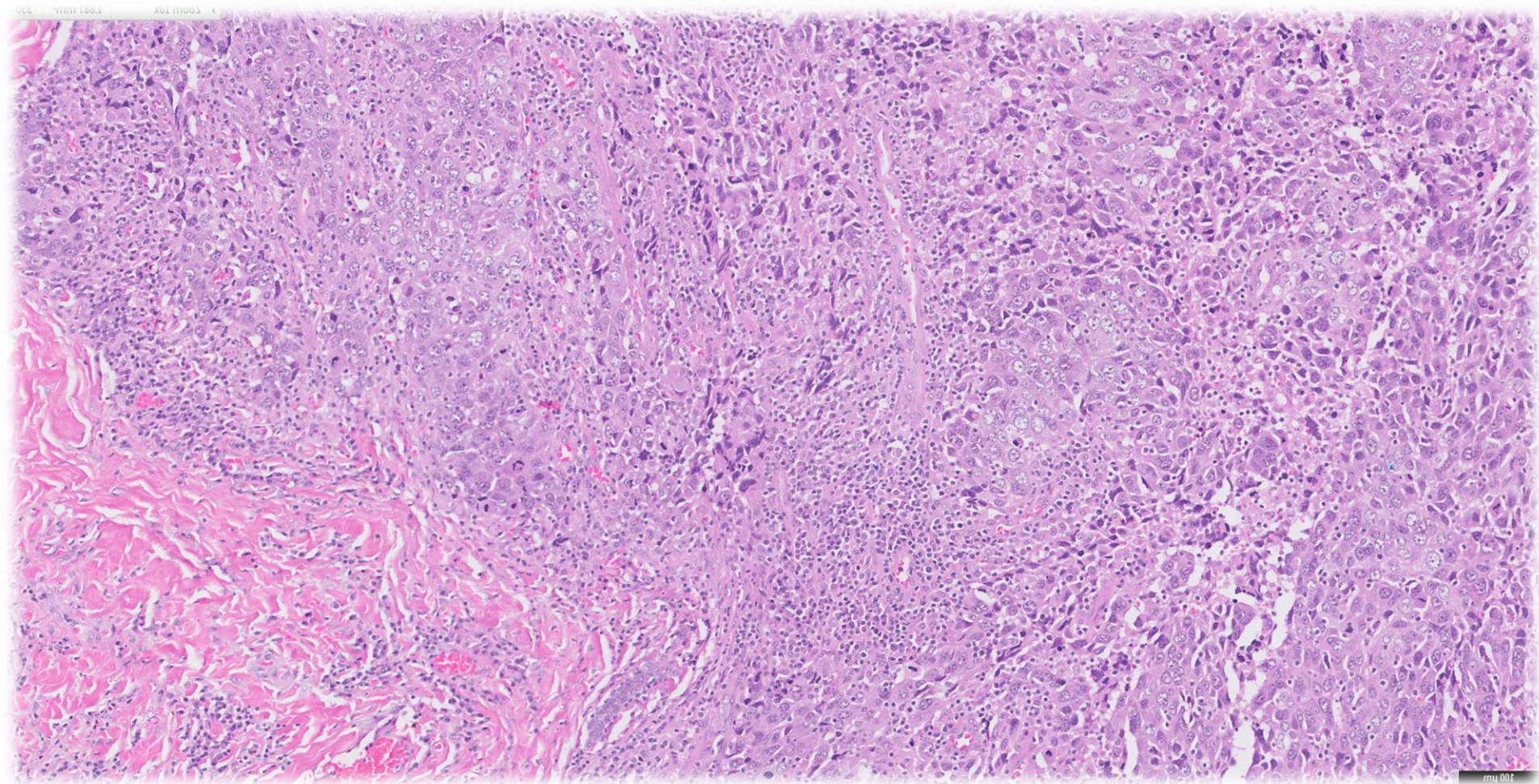




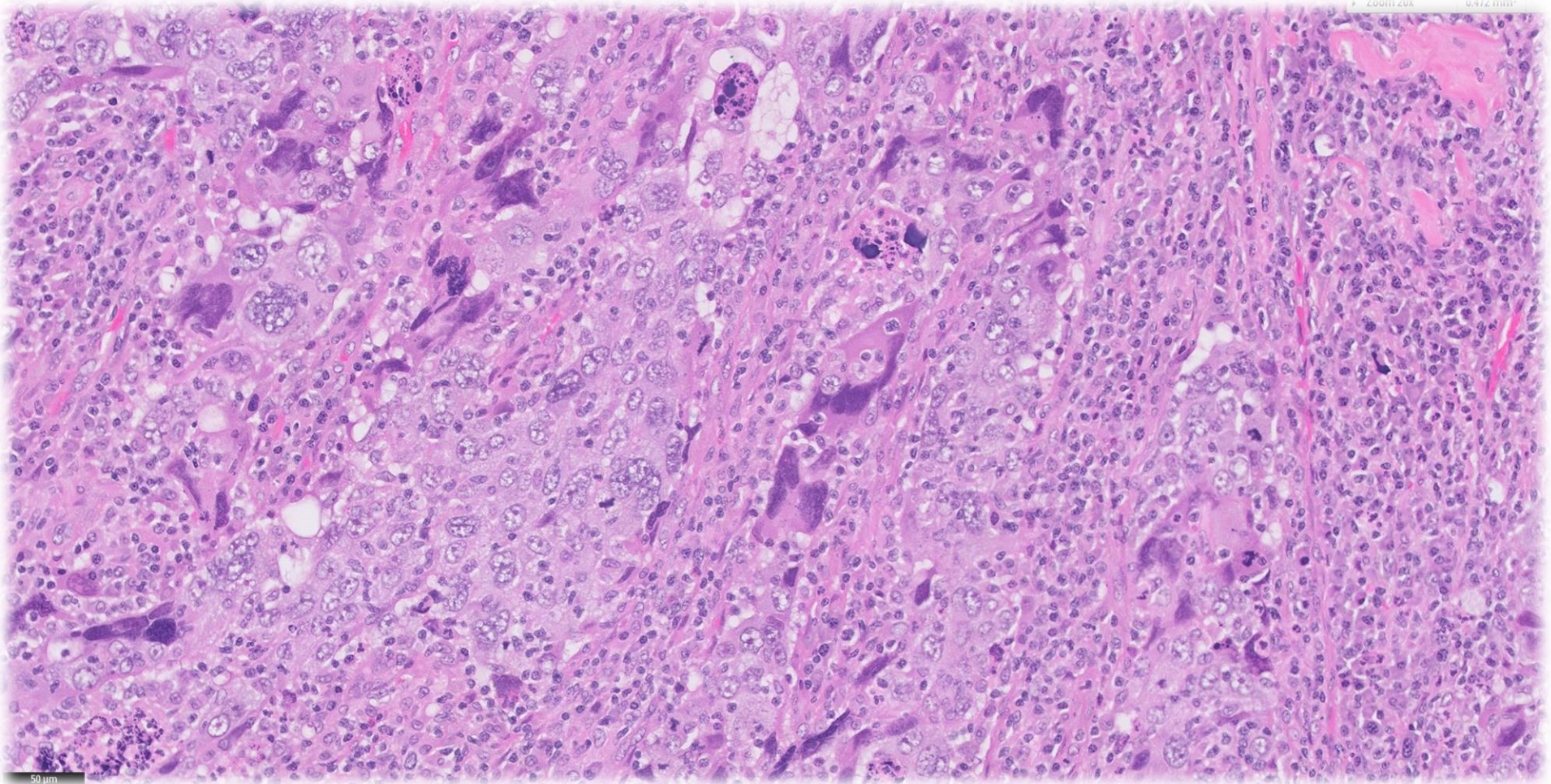




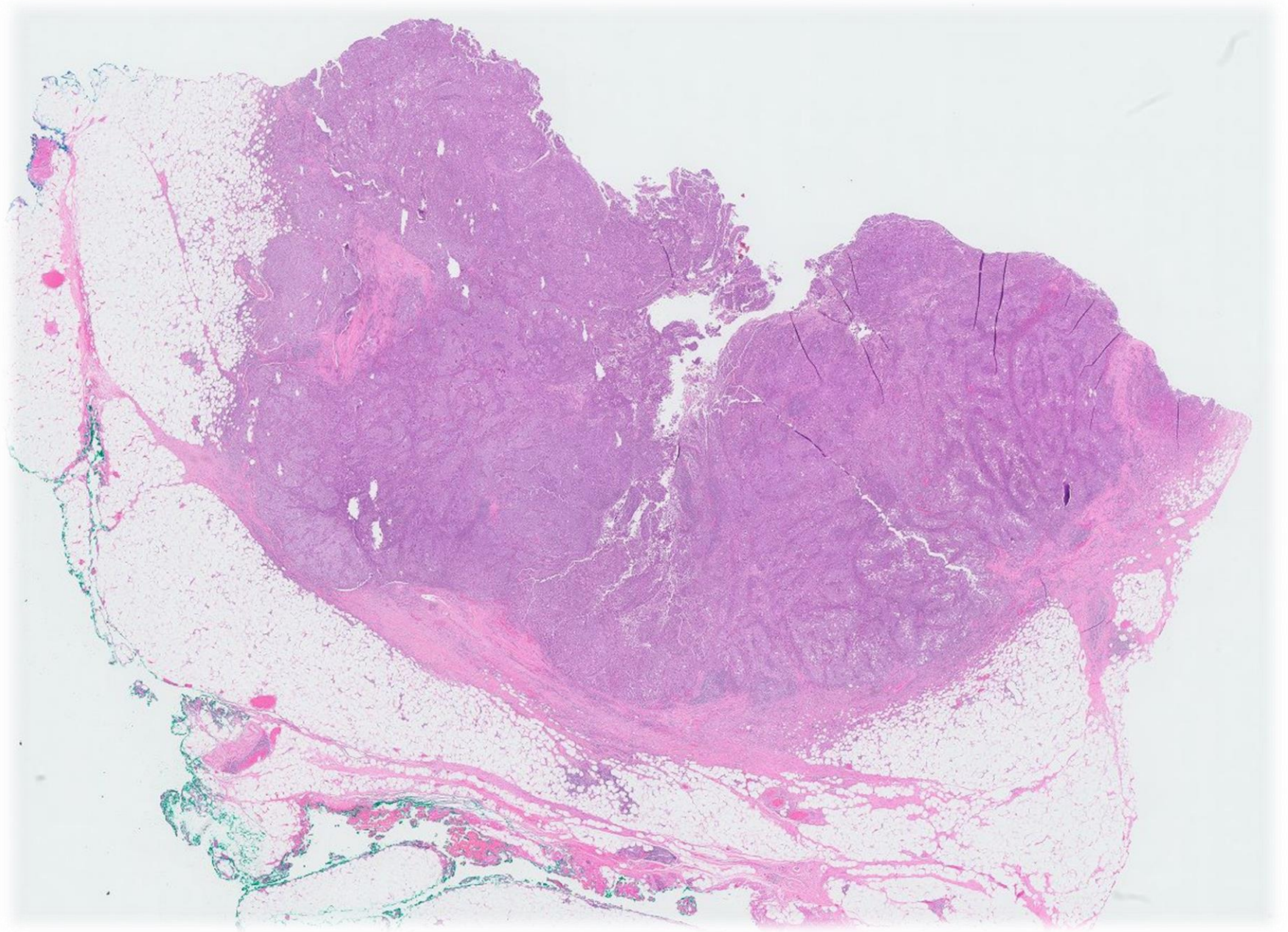




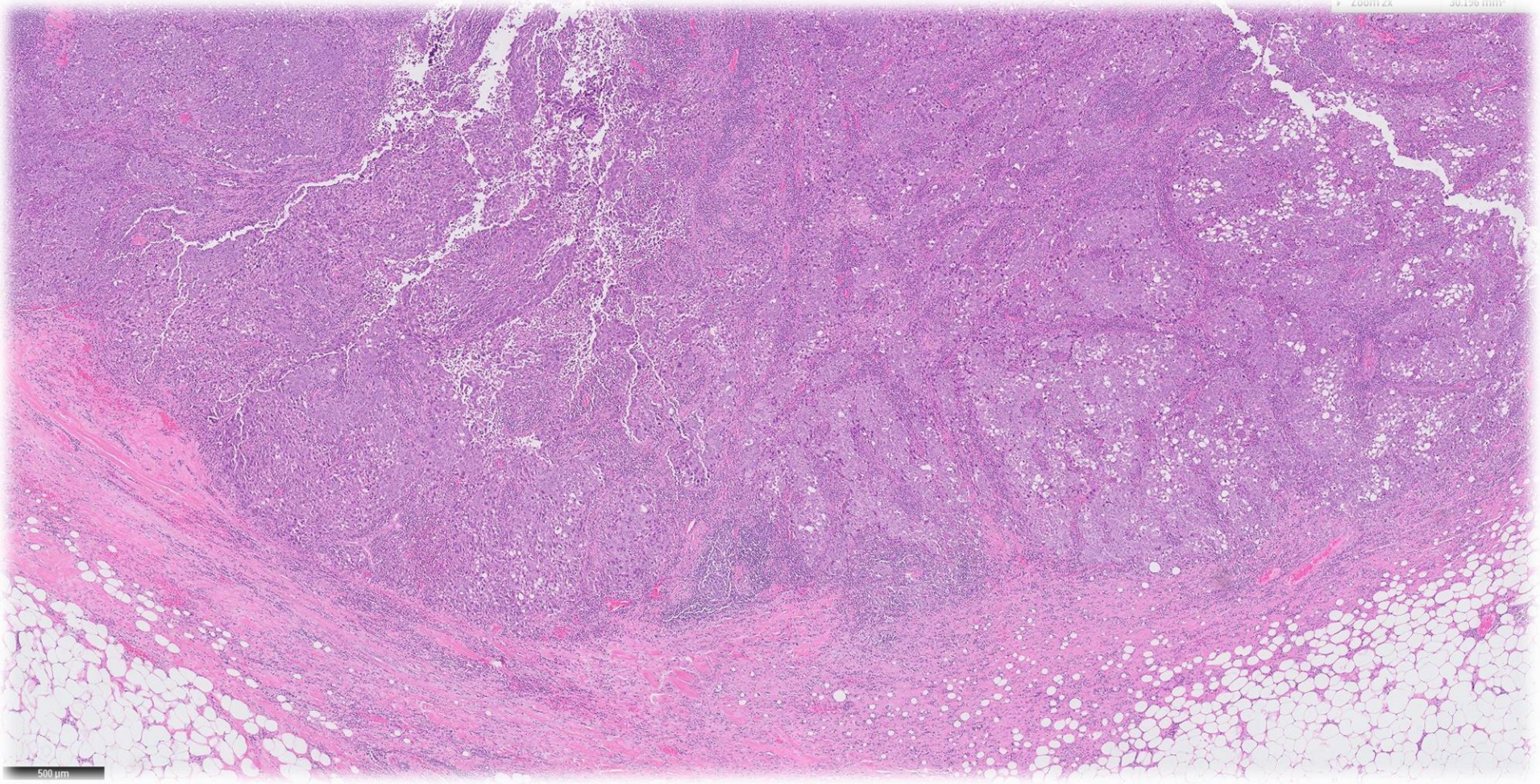




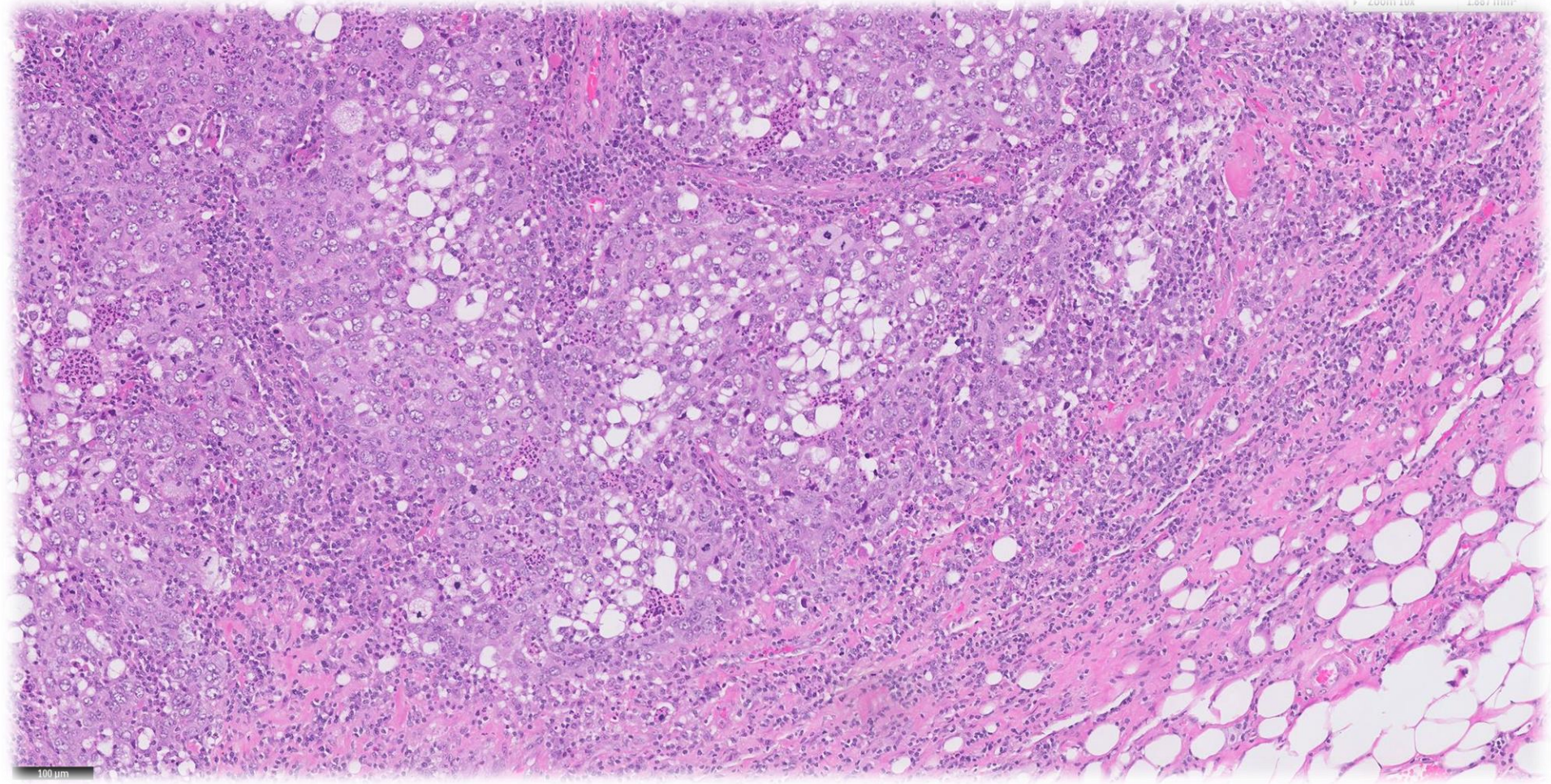






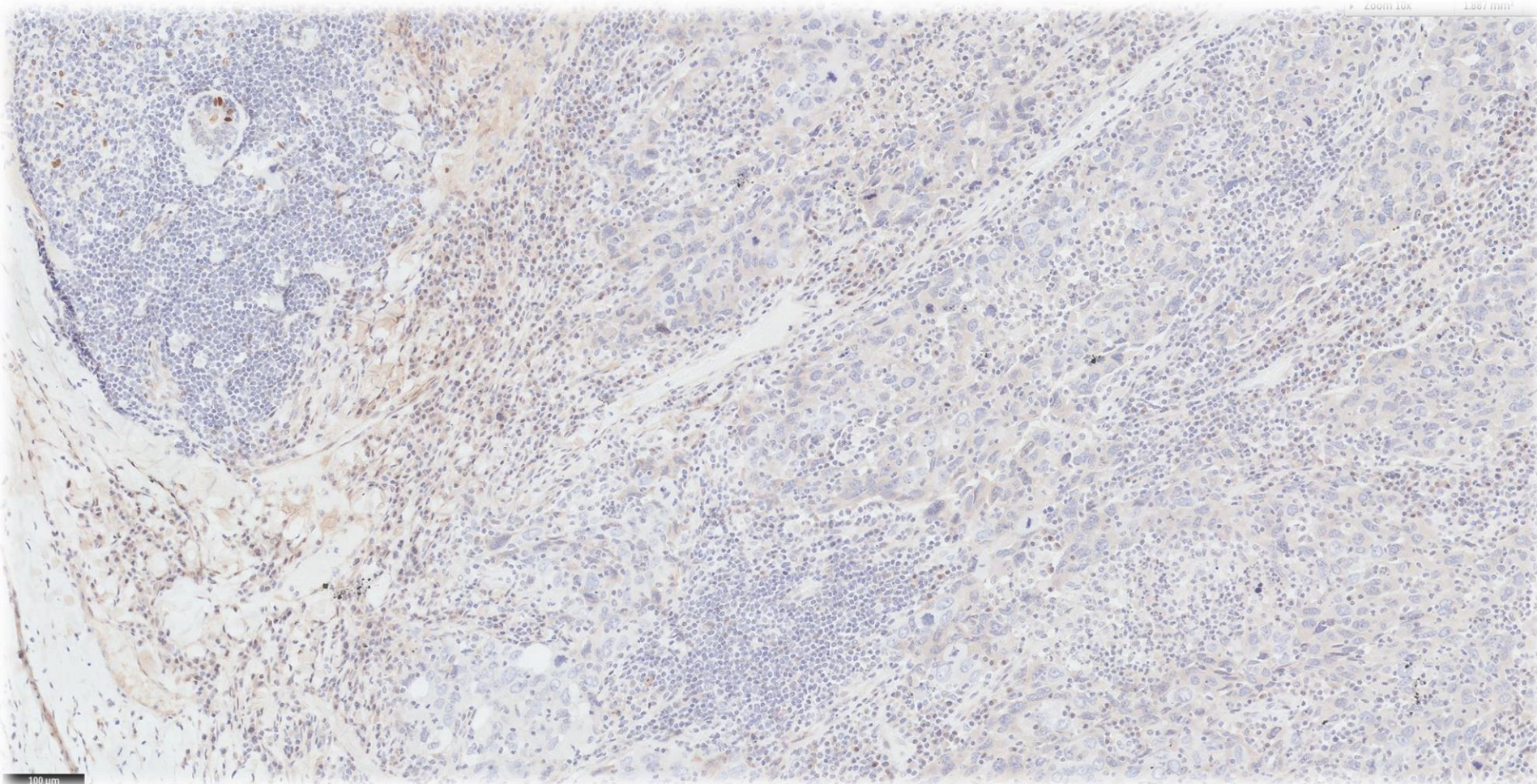








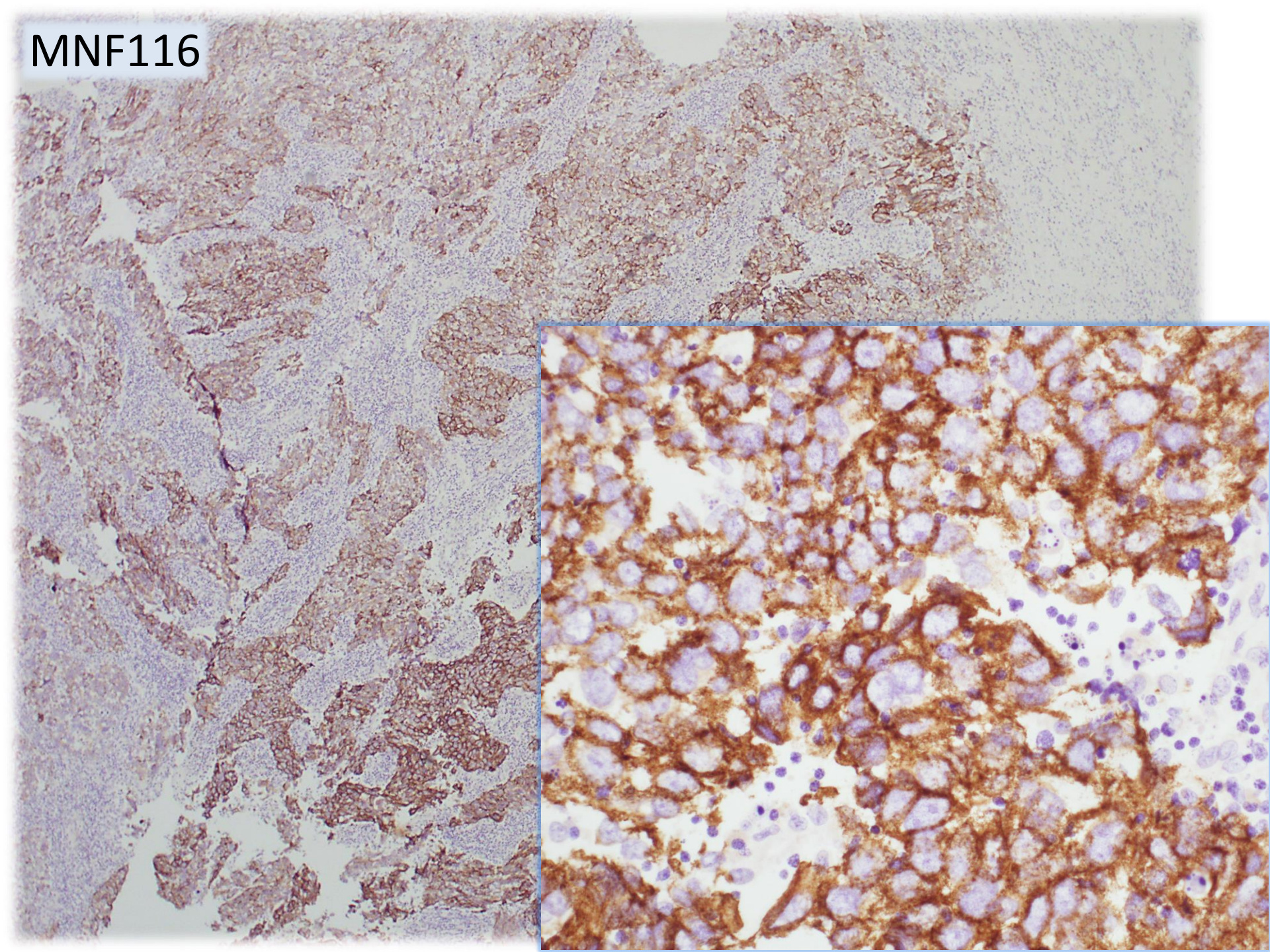
ER negative



PR, cerbB2 negative

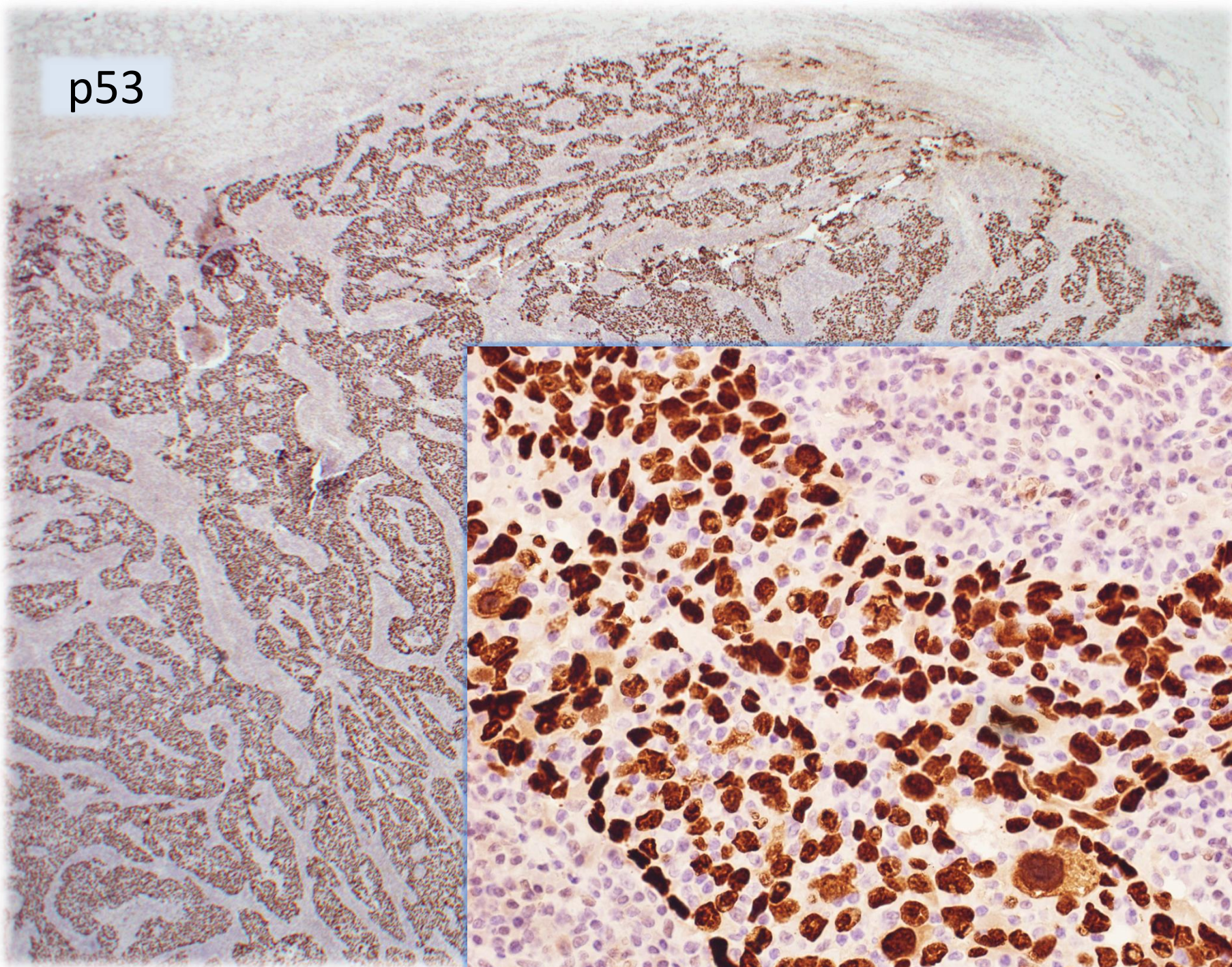


MNF116





p53





# Diagnosis

- Invasive carcinoma with atypical medullary features, grade 3, 30mm.
- ER negative, PR negative, cerbB2 negative (triple 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.



- 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	<i>Triple negative</i>	89.5%	38.5%
PR-negative		48.7%	34%
HER2-negative		97.7%	76.2%
Keratin 5/6-positive	<i>Basal-like</i>	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 the 'new' WHO 2012 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.



