

Case 28

47 year old Chinese woman.

Core biopsy (A) of a left breast 4 o'clock lump, diagnosed as fibroadenoma with stromal giant cells.

Opted for surveillance, but one year later, underwent excision (B) after the lesion was found to have grown in size to 3.5cm.



Singapore
General Hospital

SingHealth

Division of Pathology

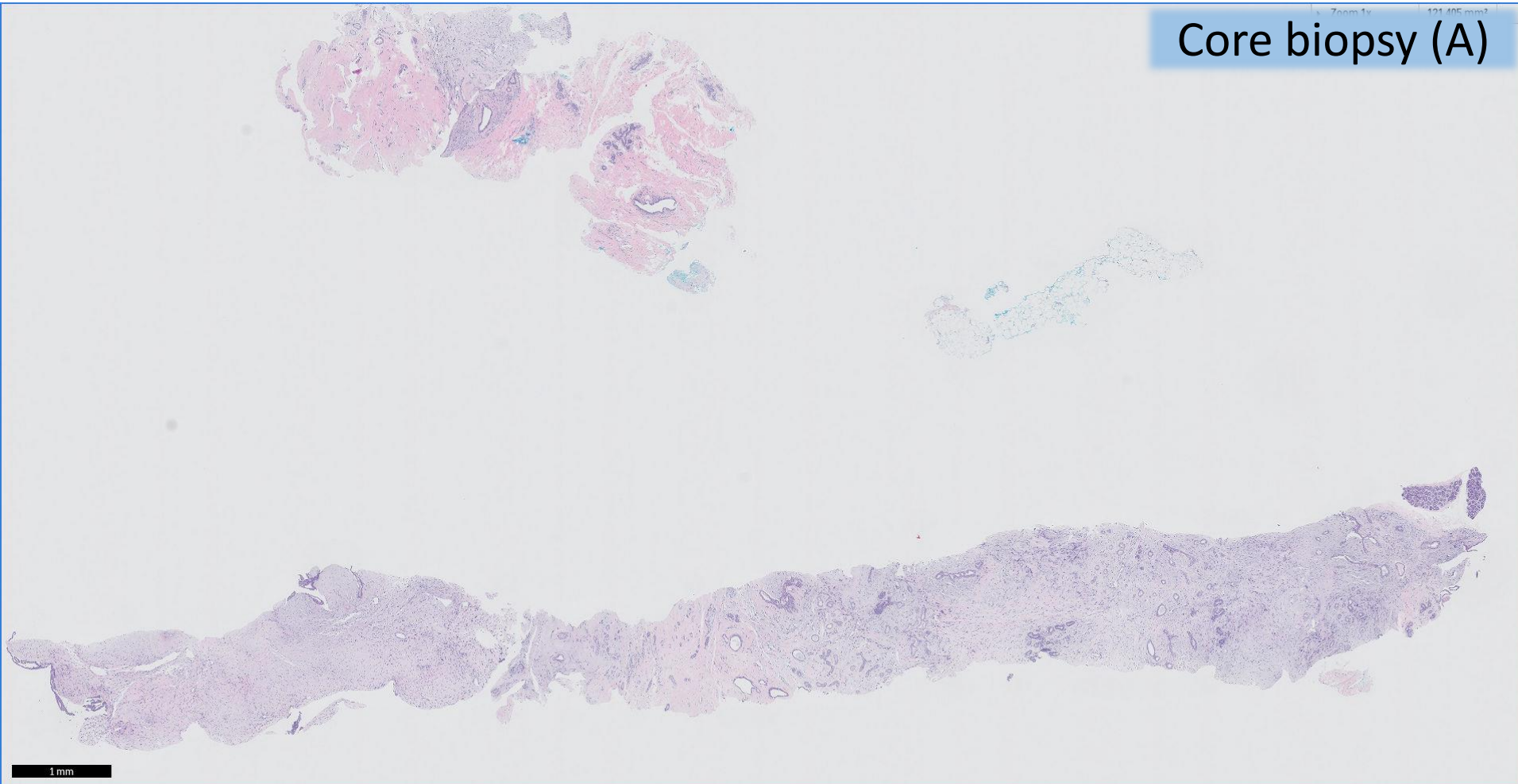


PATHOLOGY

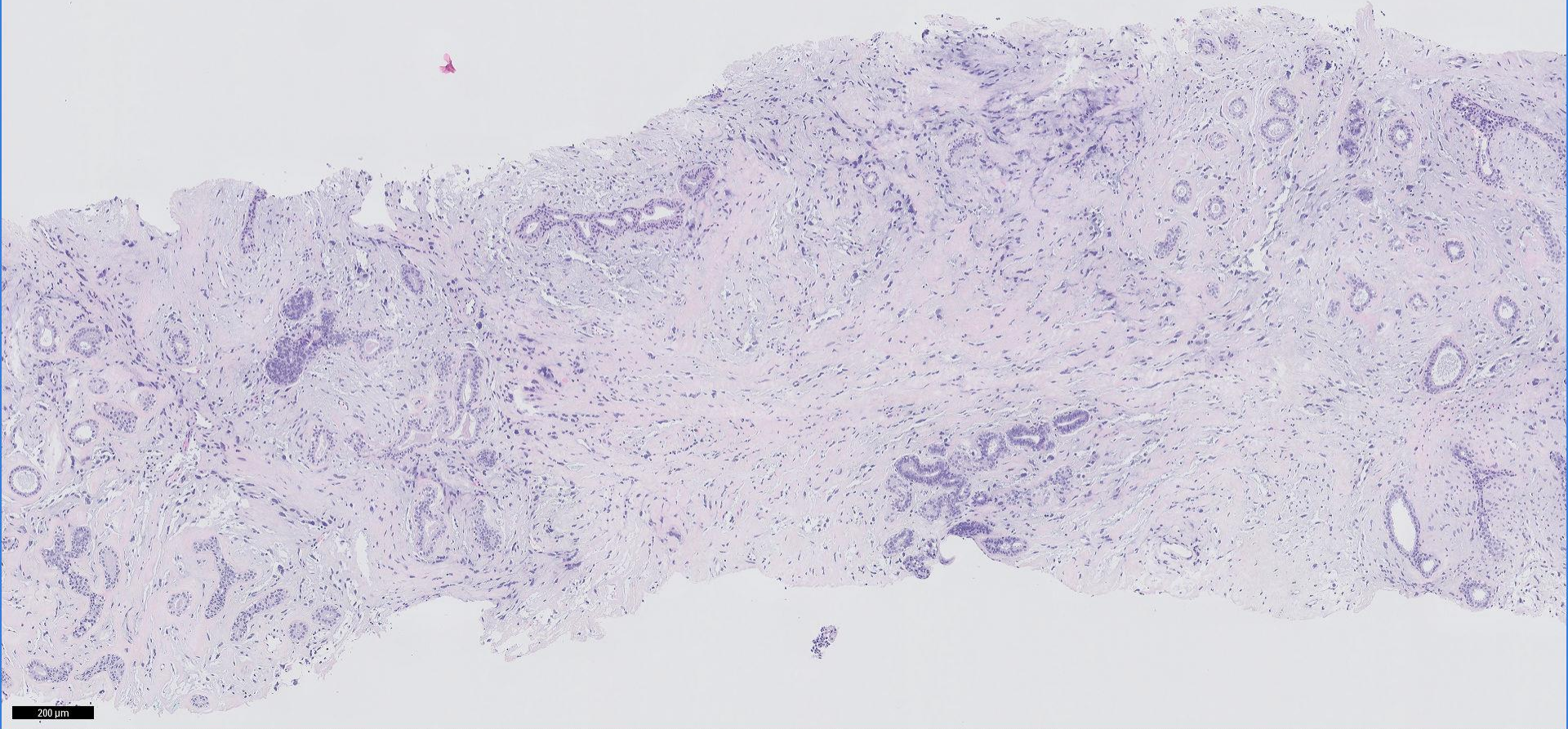
IAP

International Academy of Pathology
Singapore Division

7mm 1x 121 105 mic3
Core biopsy (A)

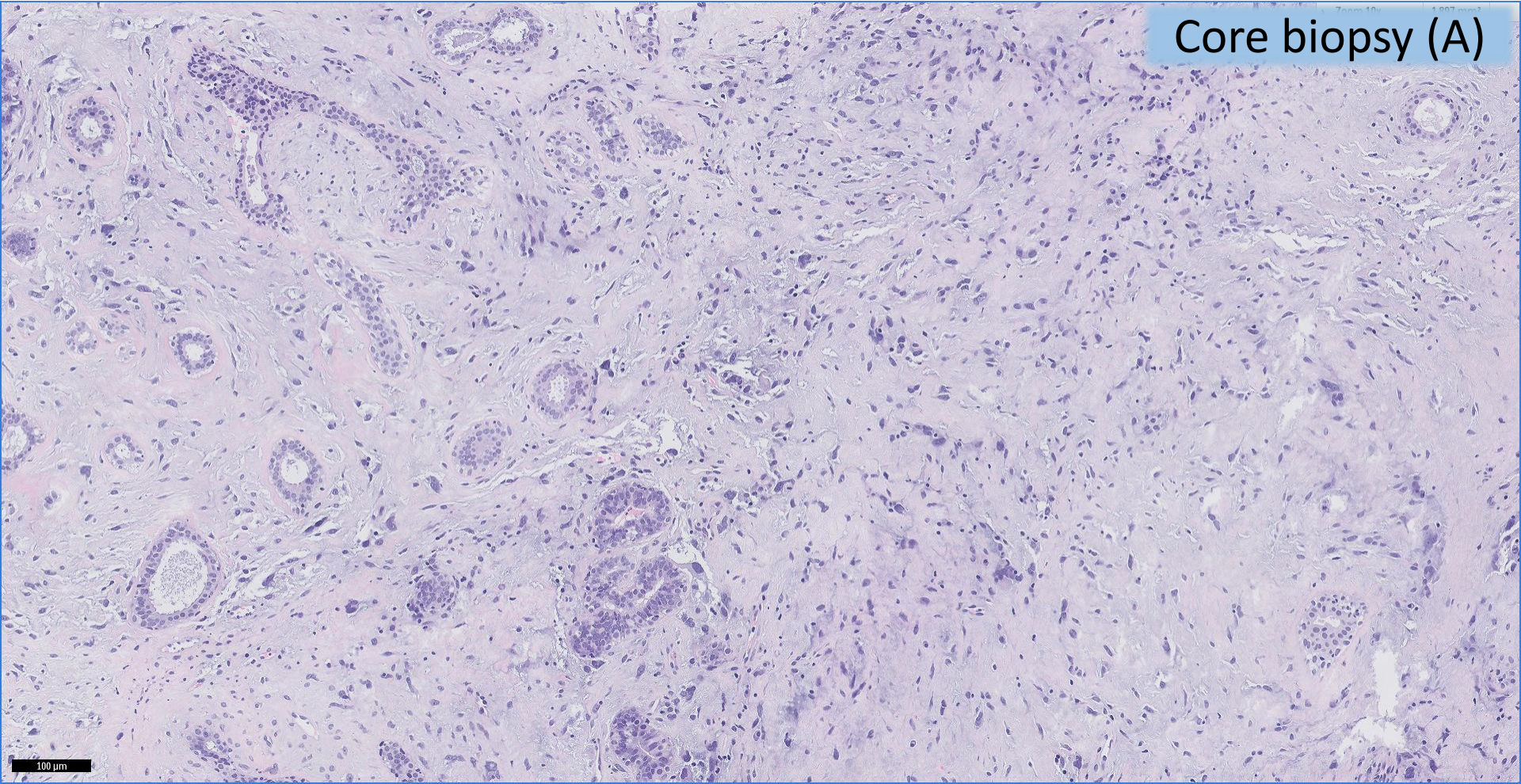


Core biopsy (A)



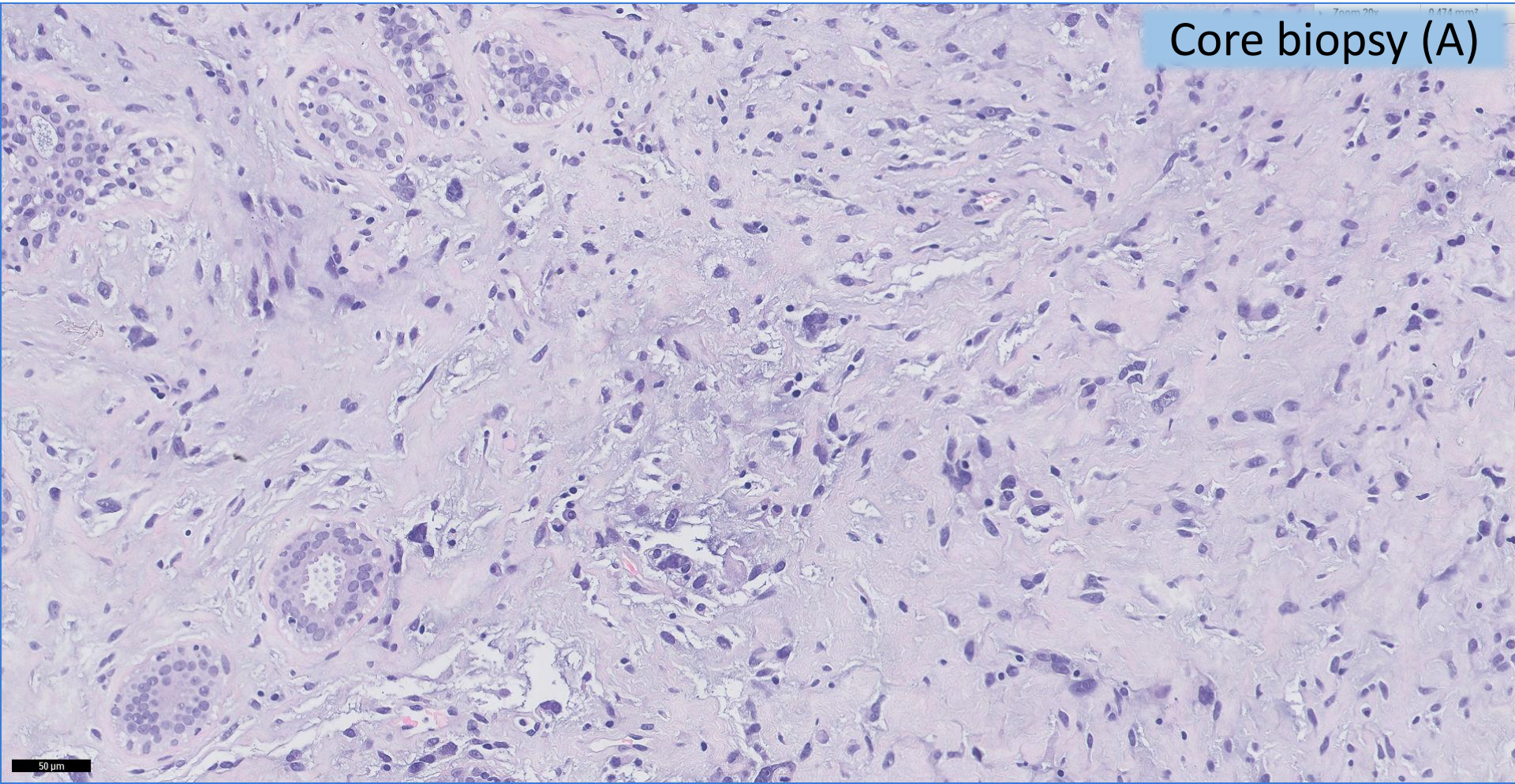
200 μ m

Core biopsy (A)



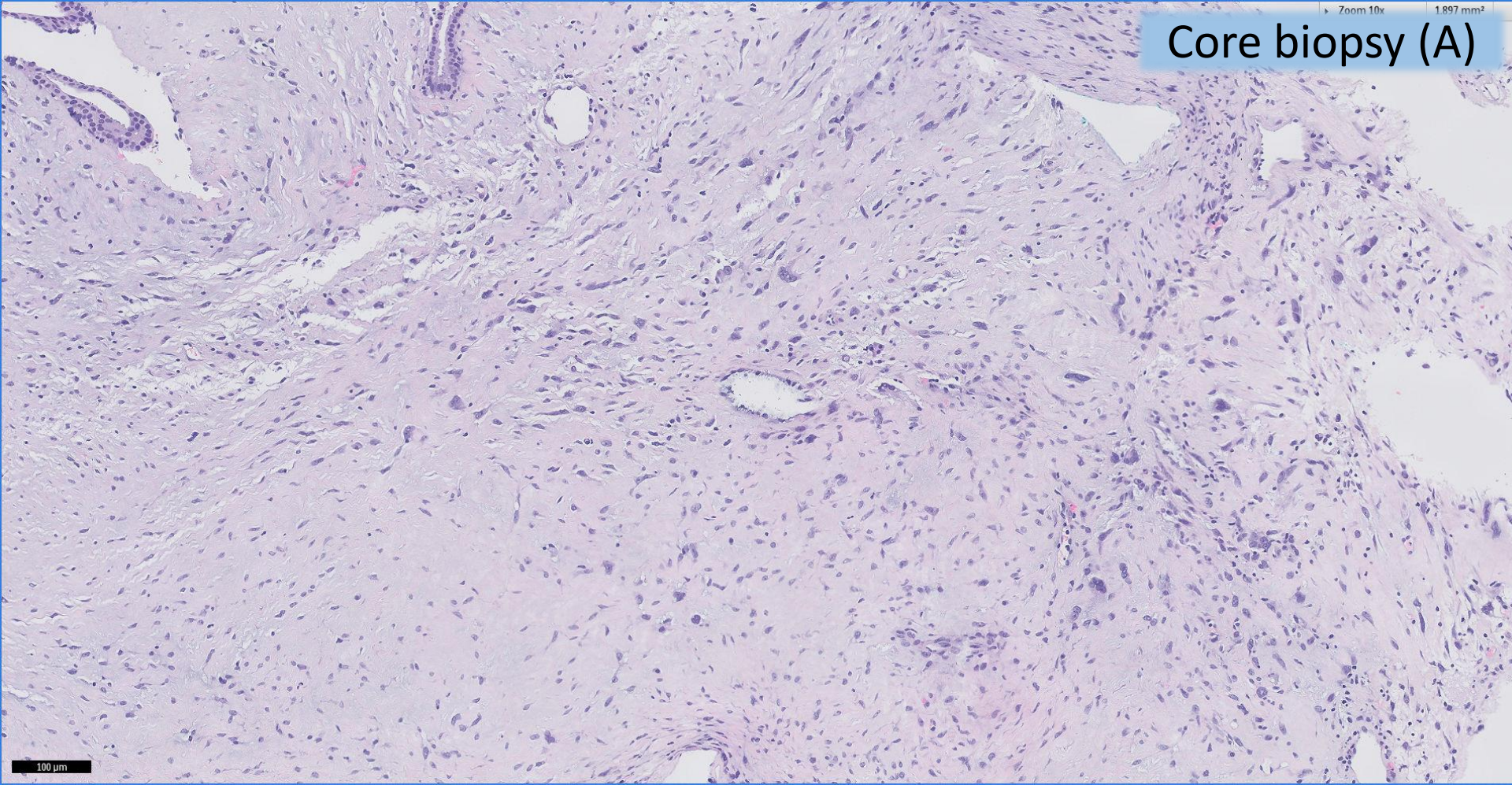
100 μ m

Zoom 20x 0.174 mm²
Core biopsy (A)

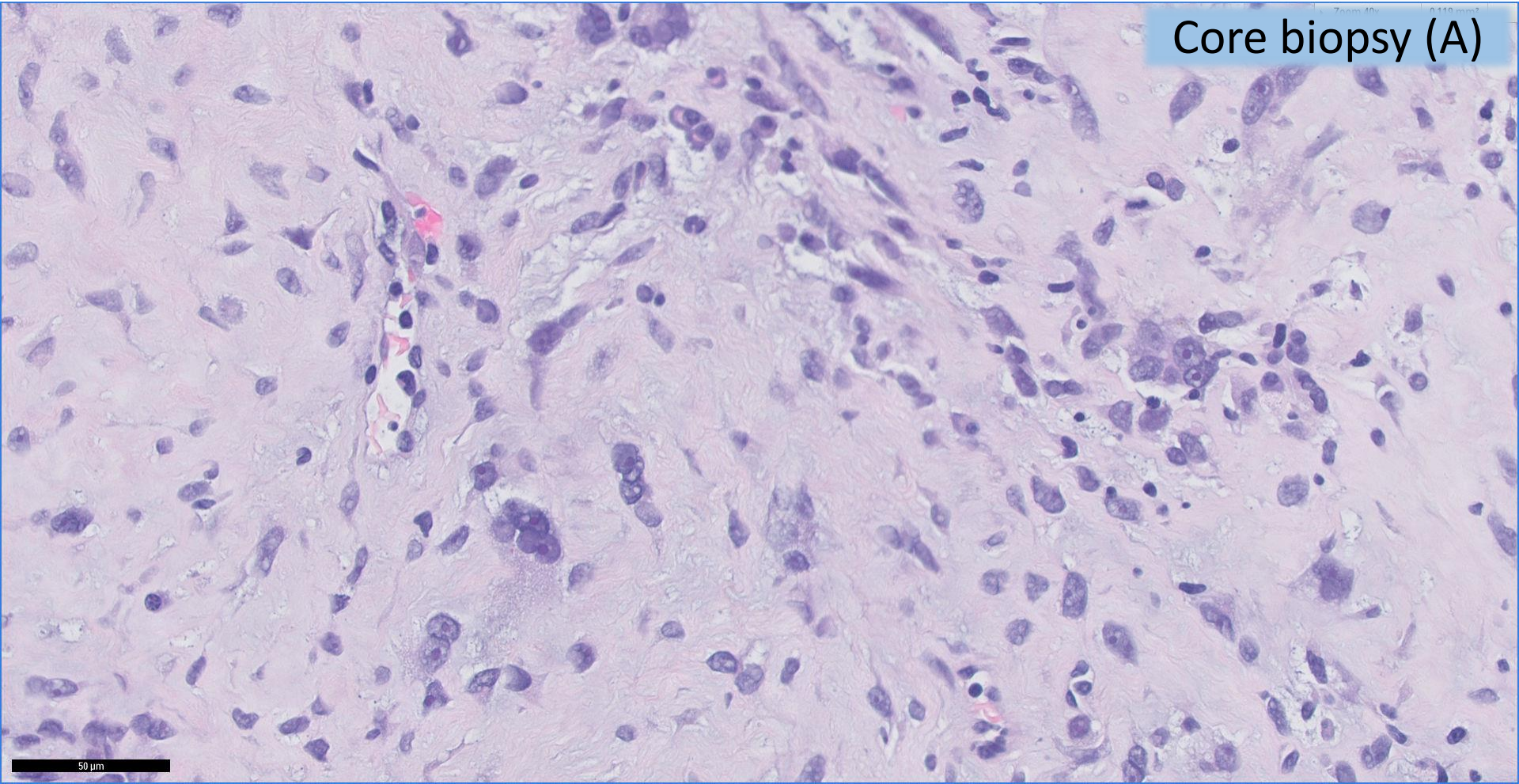


50 μm

Core biopsy (A)

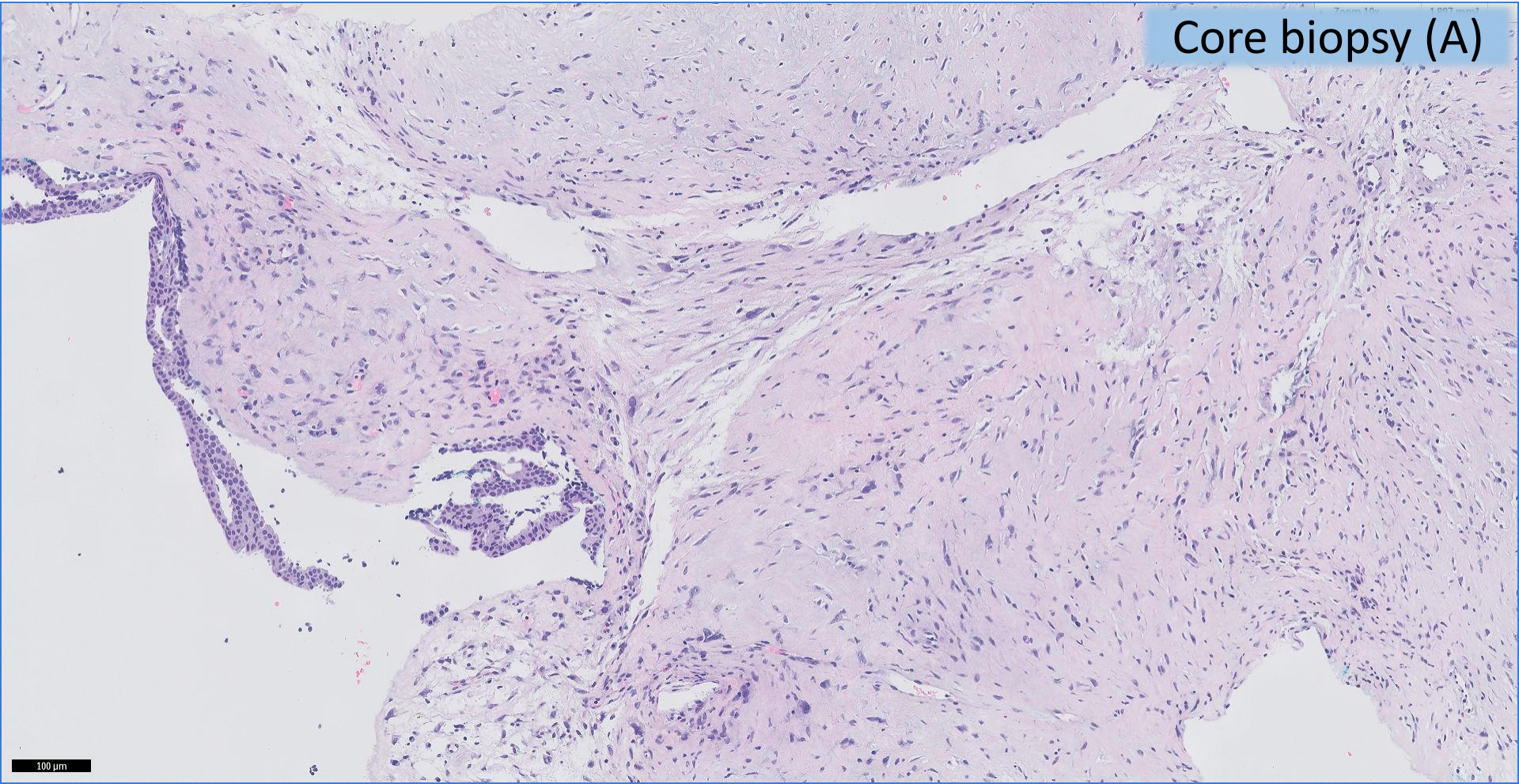


Core biopsy (A)



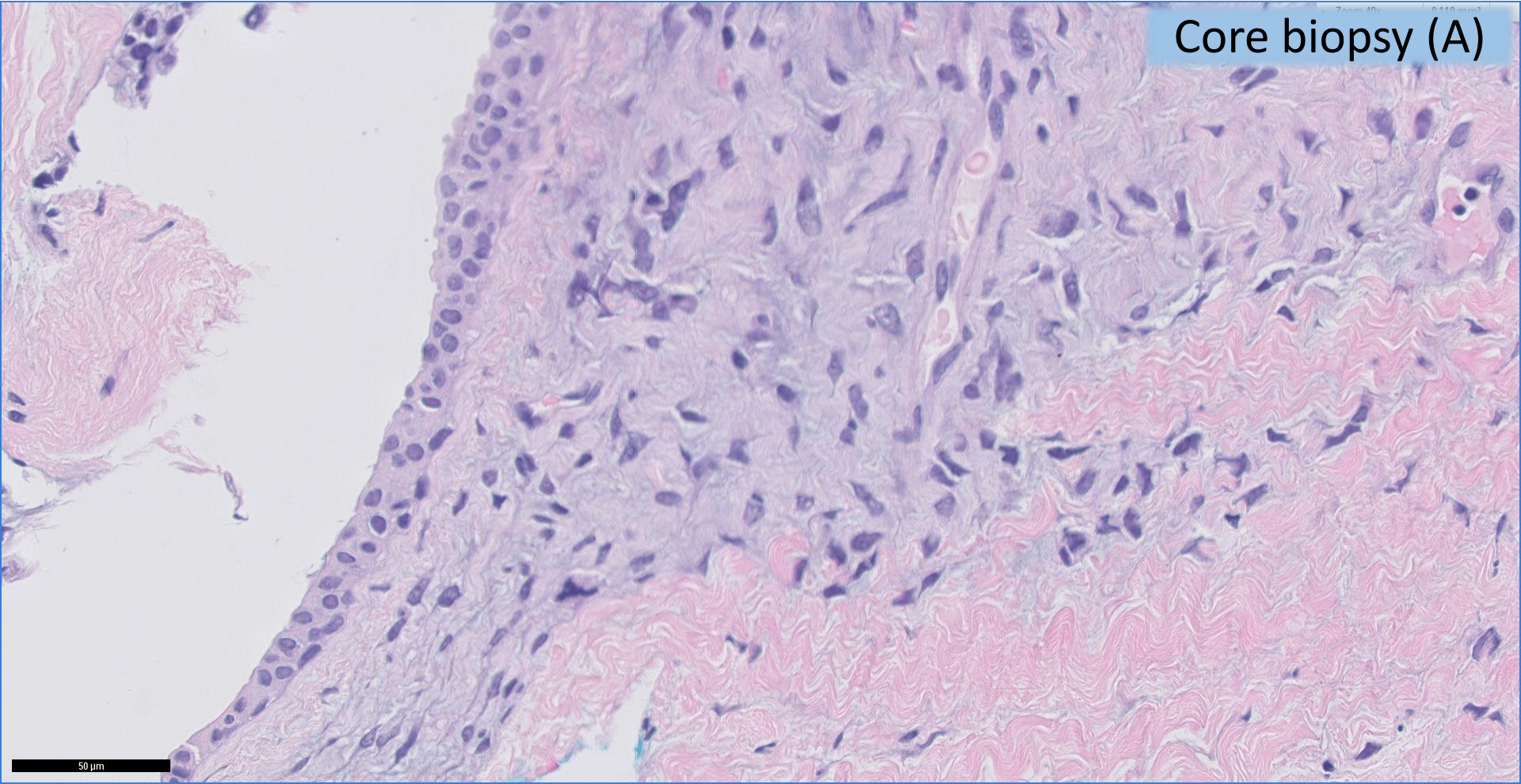
50 μ m

Core biopsy (A)



100 μ m

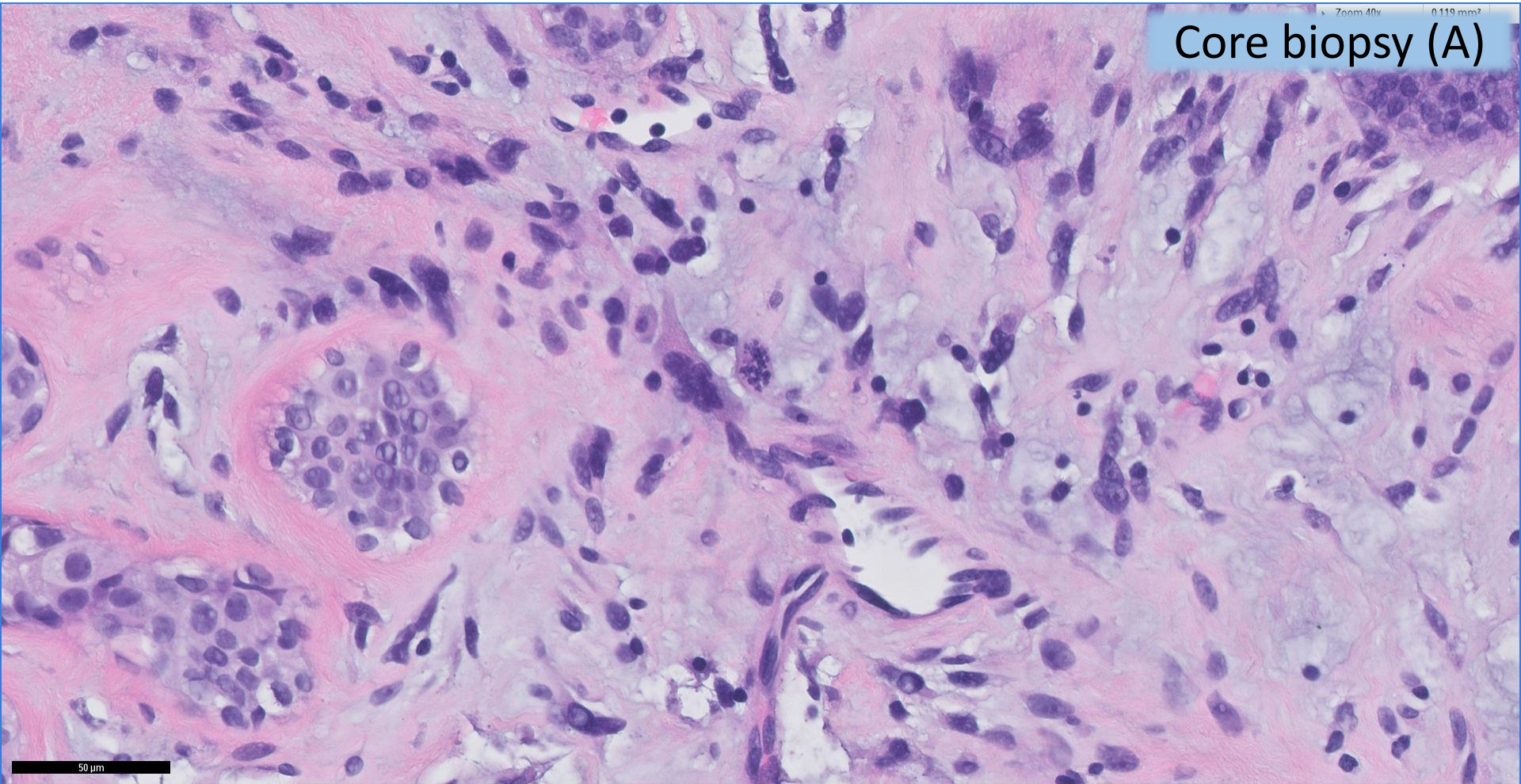
Core biopsy (A)



50 μm

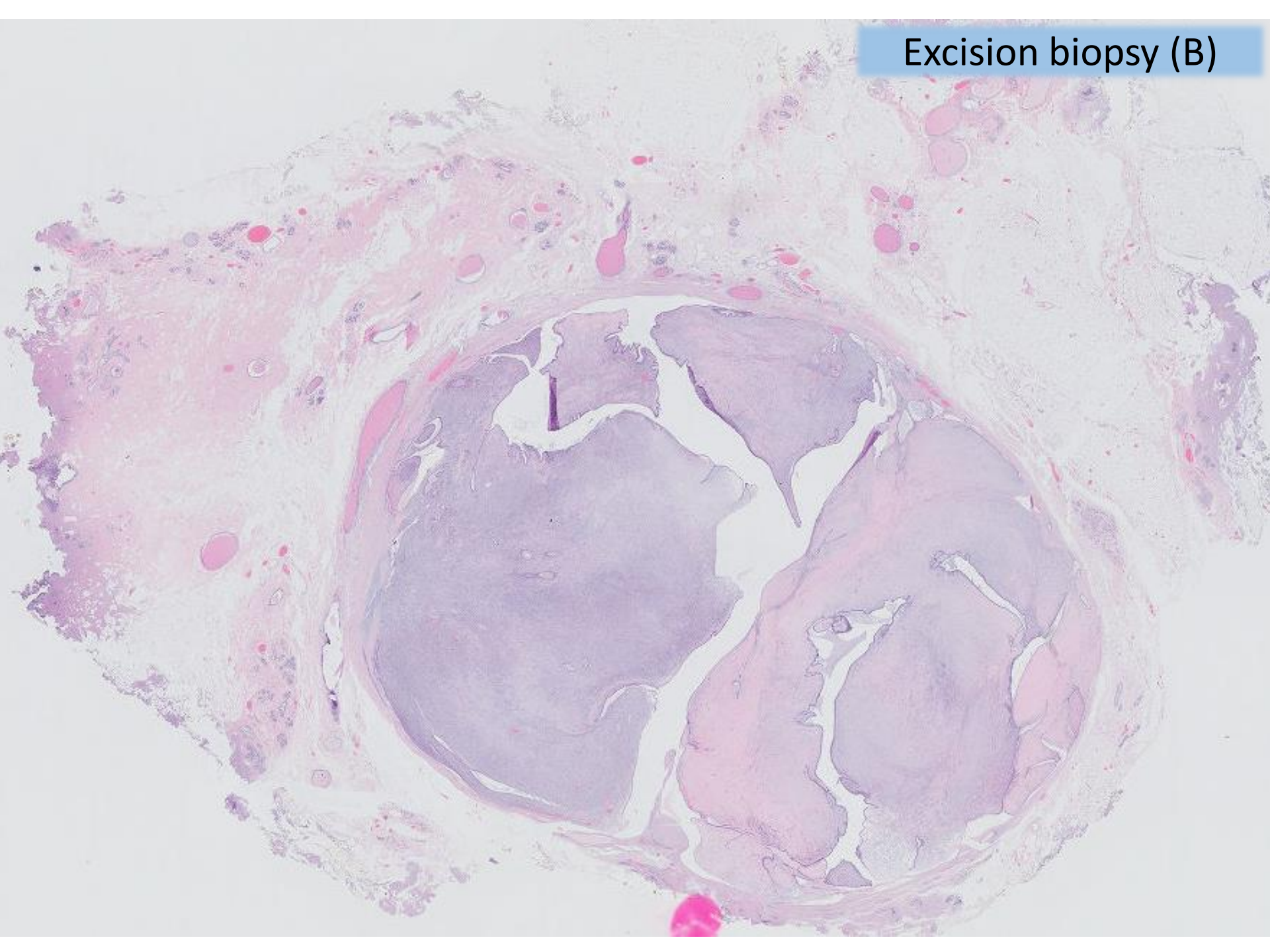
Zoom 40x 0.119 mm²

Core biopsy (A)

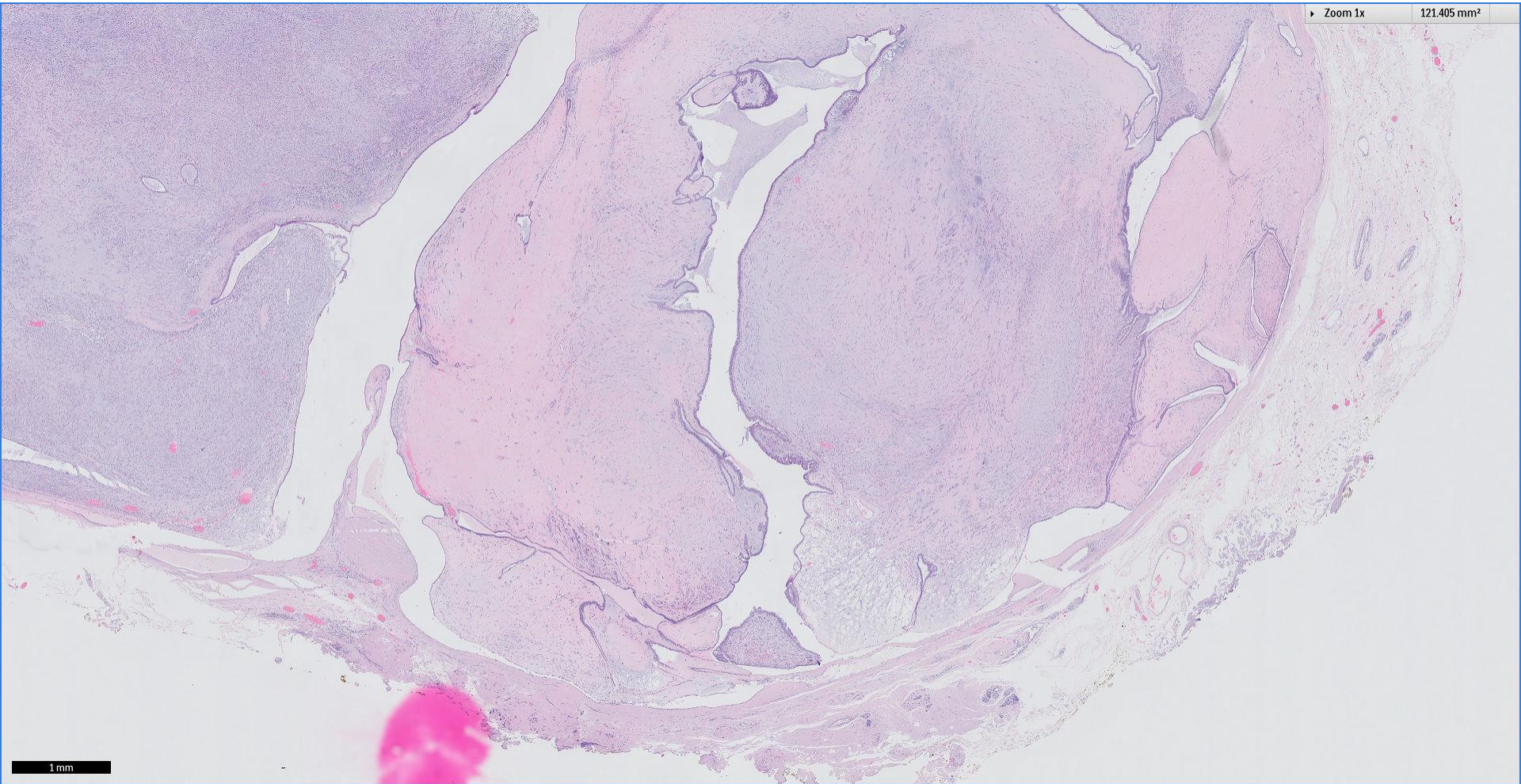


50 μ m

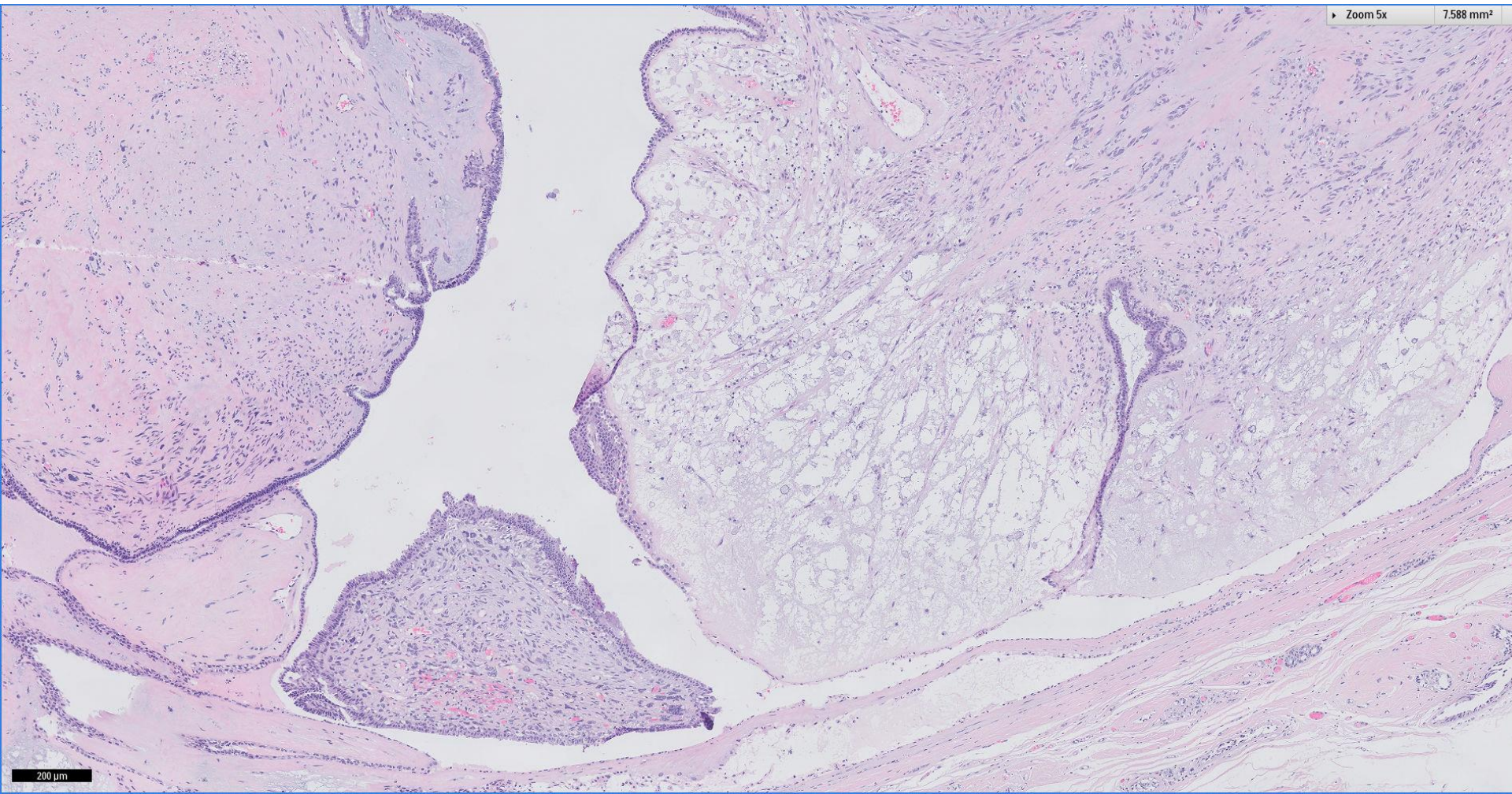
Excision biopsy (B)



Excision biopsy (B)



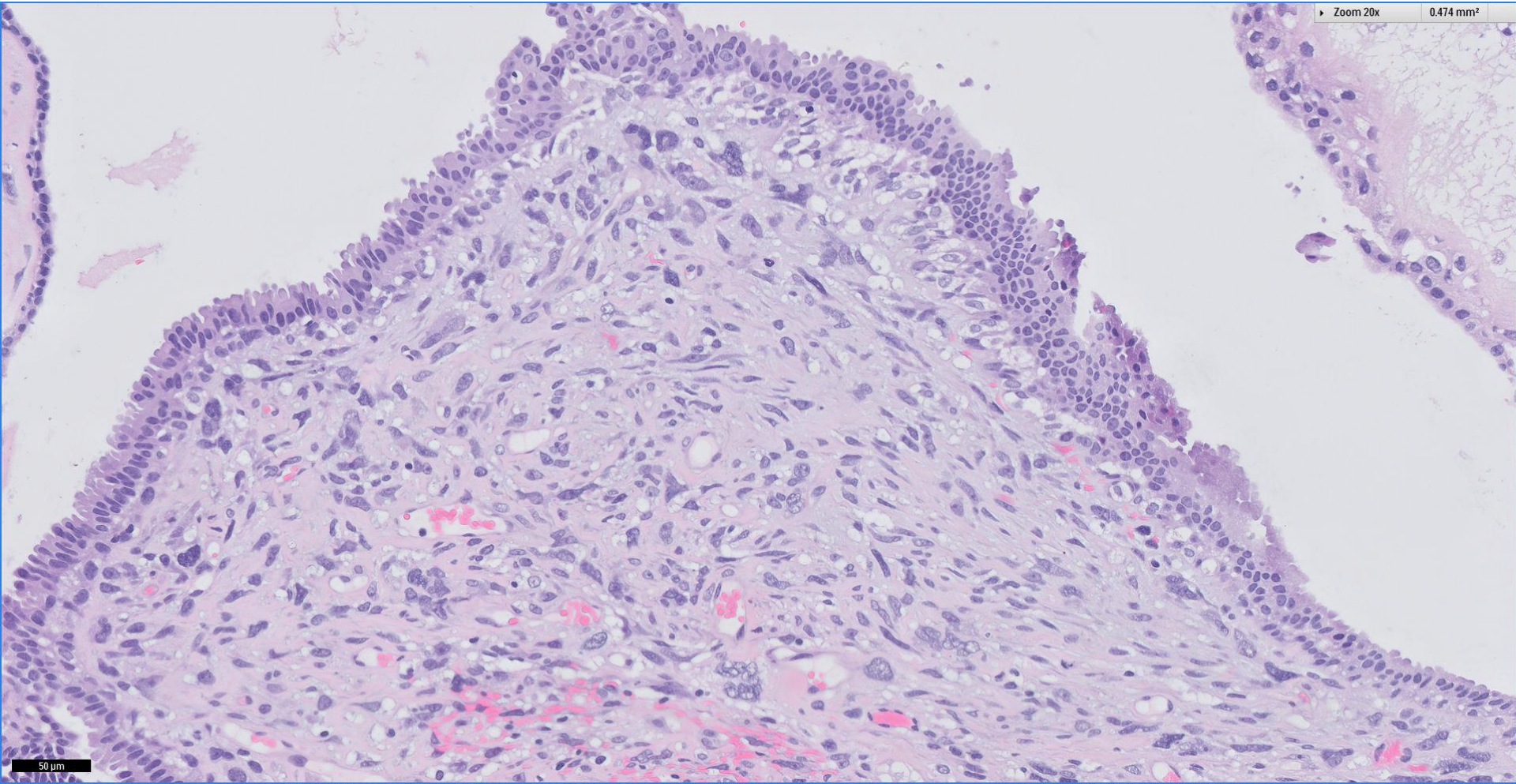
Excision biopsy (B)



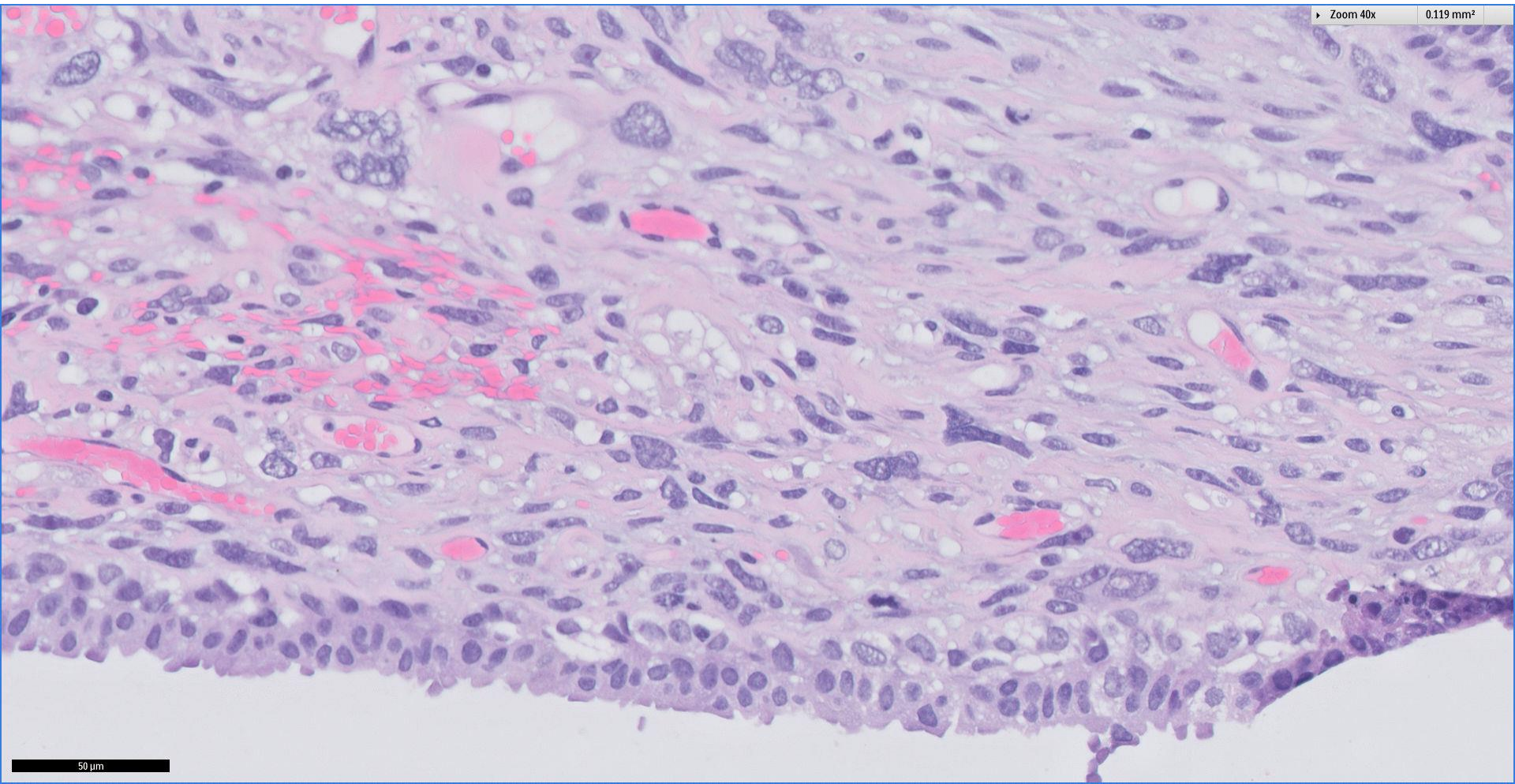
Zoom 5x 7588 mm²

200 μm

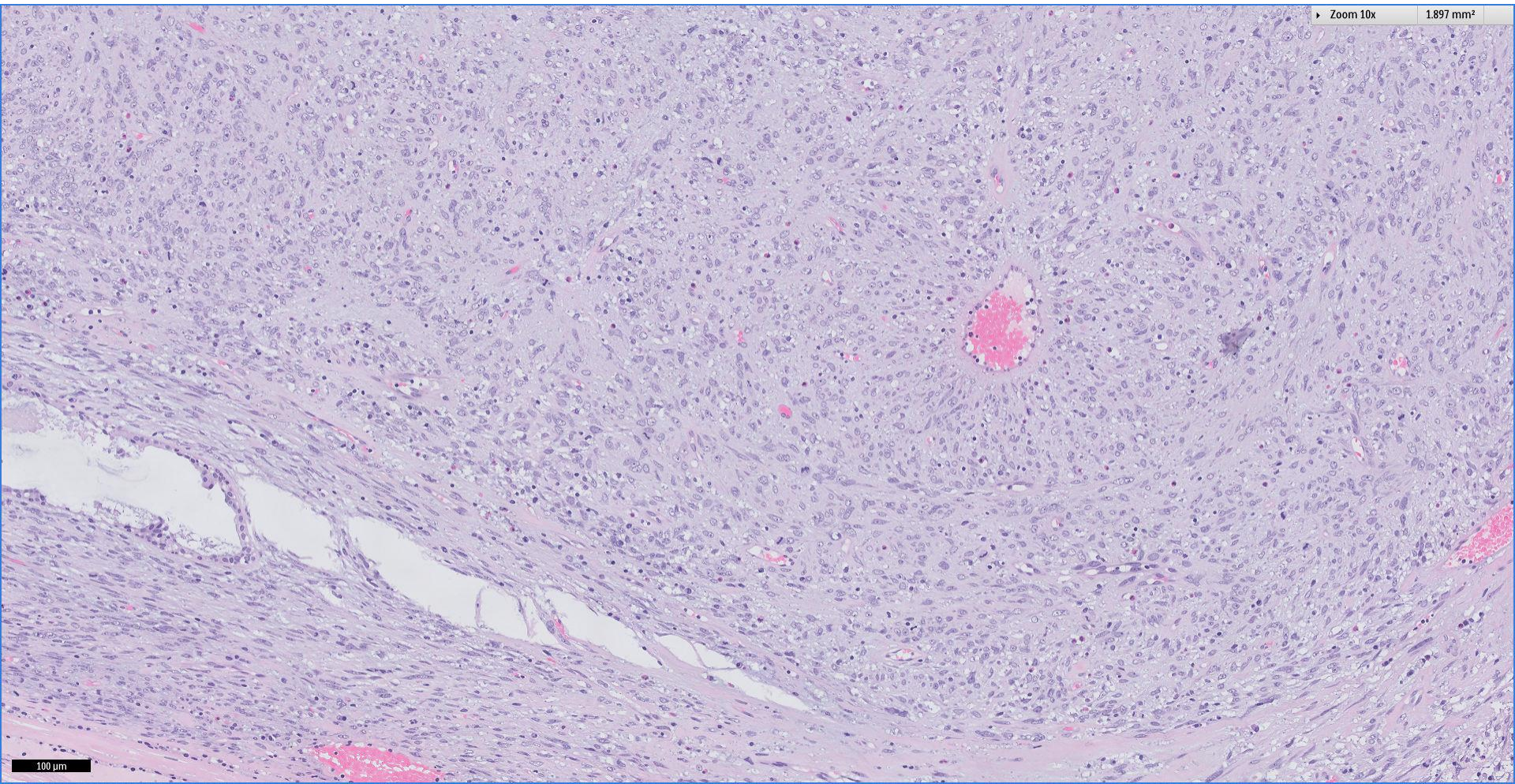
Excision biopsy (B)



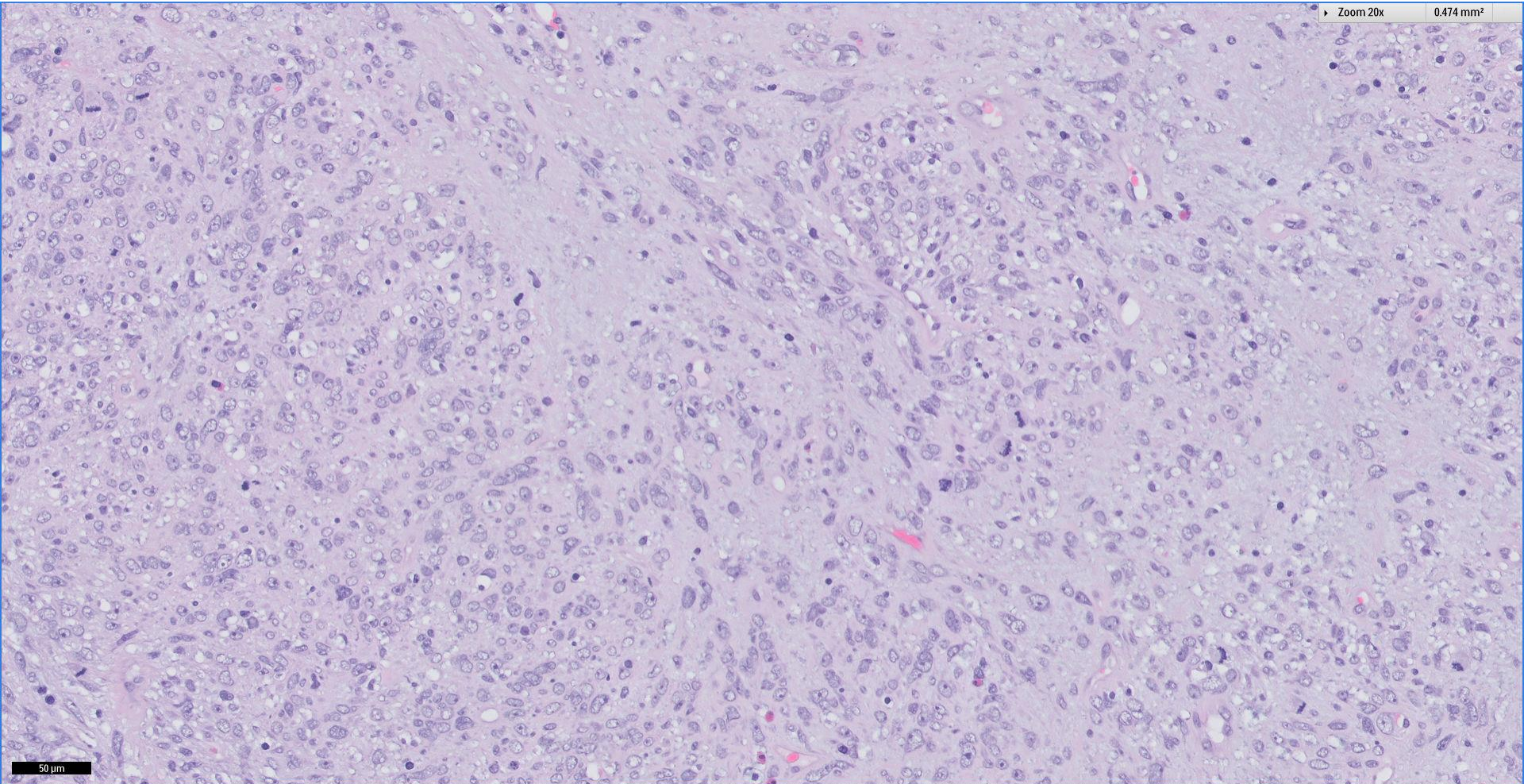
Excision biopsy (B)



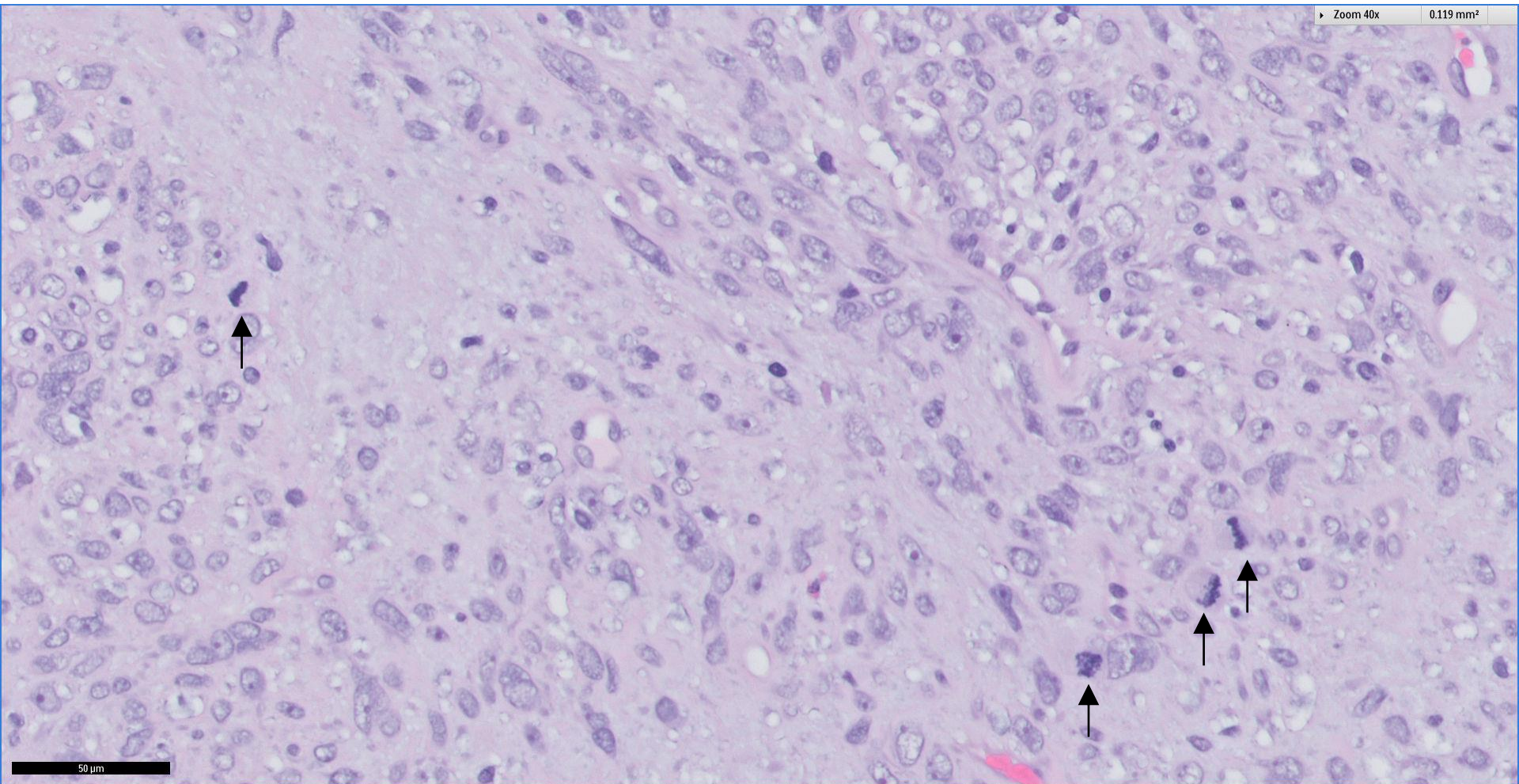
Excision biopsy (B)



Excision biopsy (B)

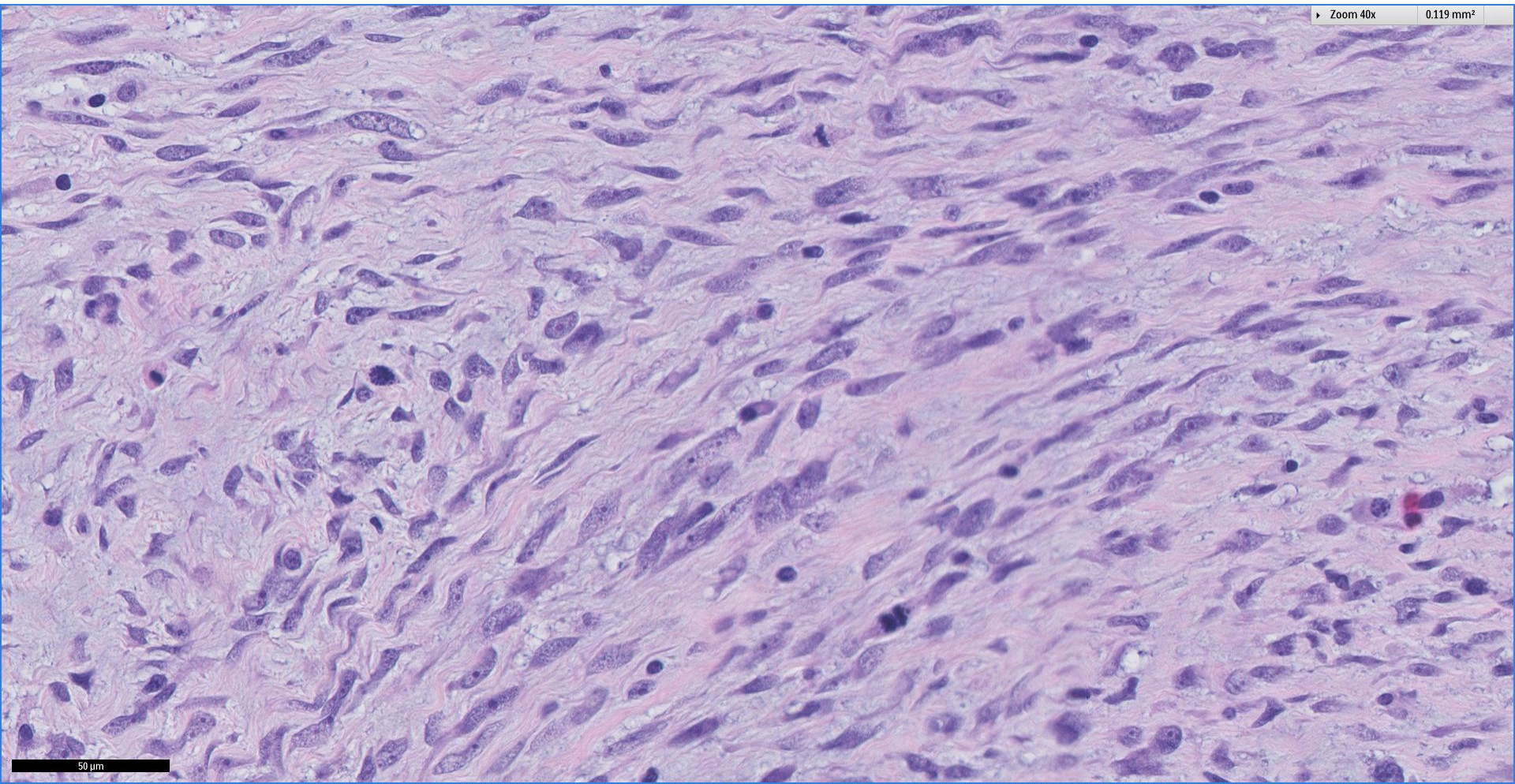


Excision biopsy (B)

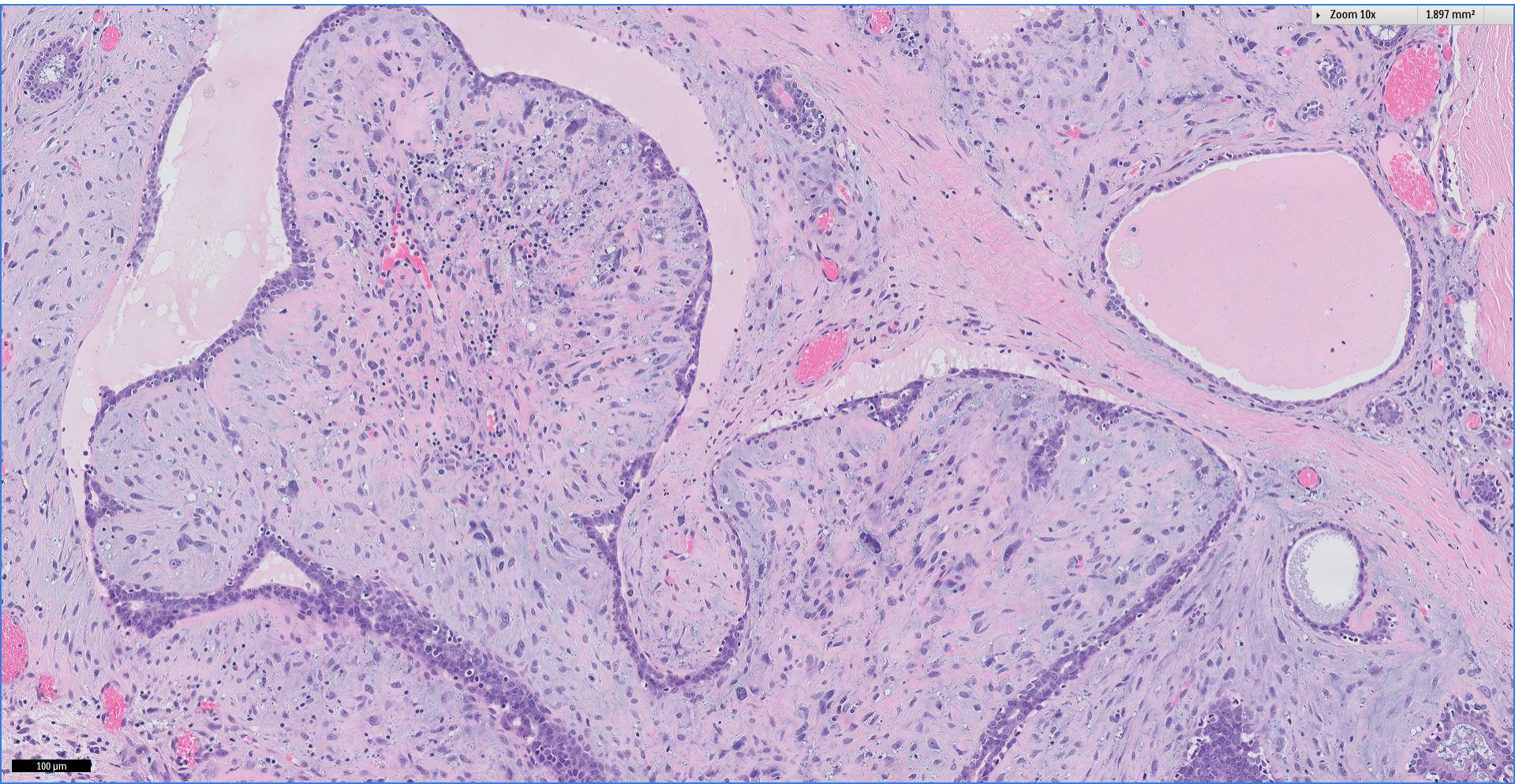


34 mitoses per 10 high power fields

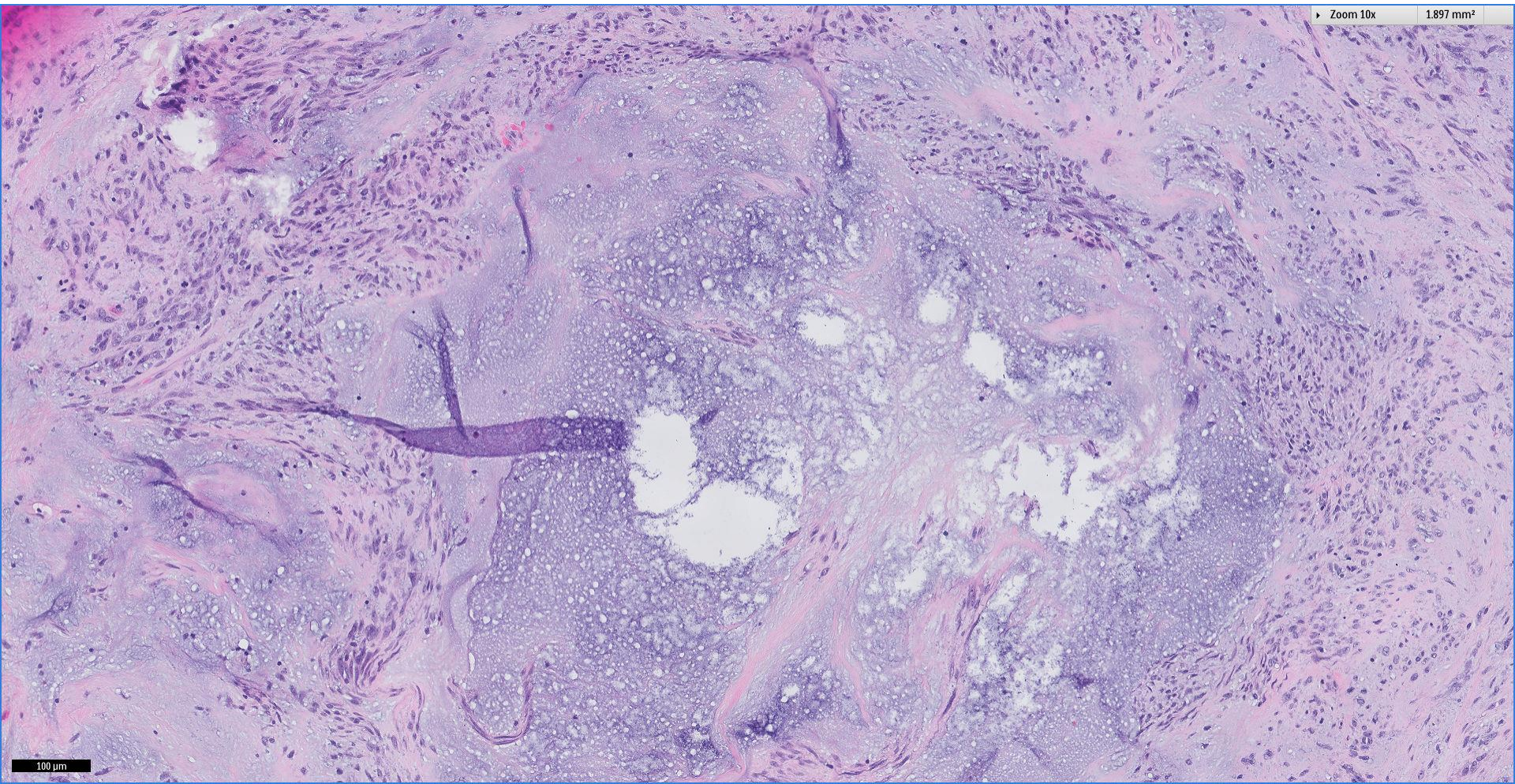
Excision biopsy (B)



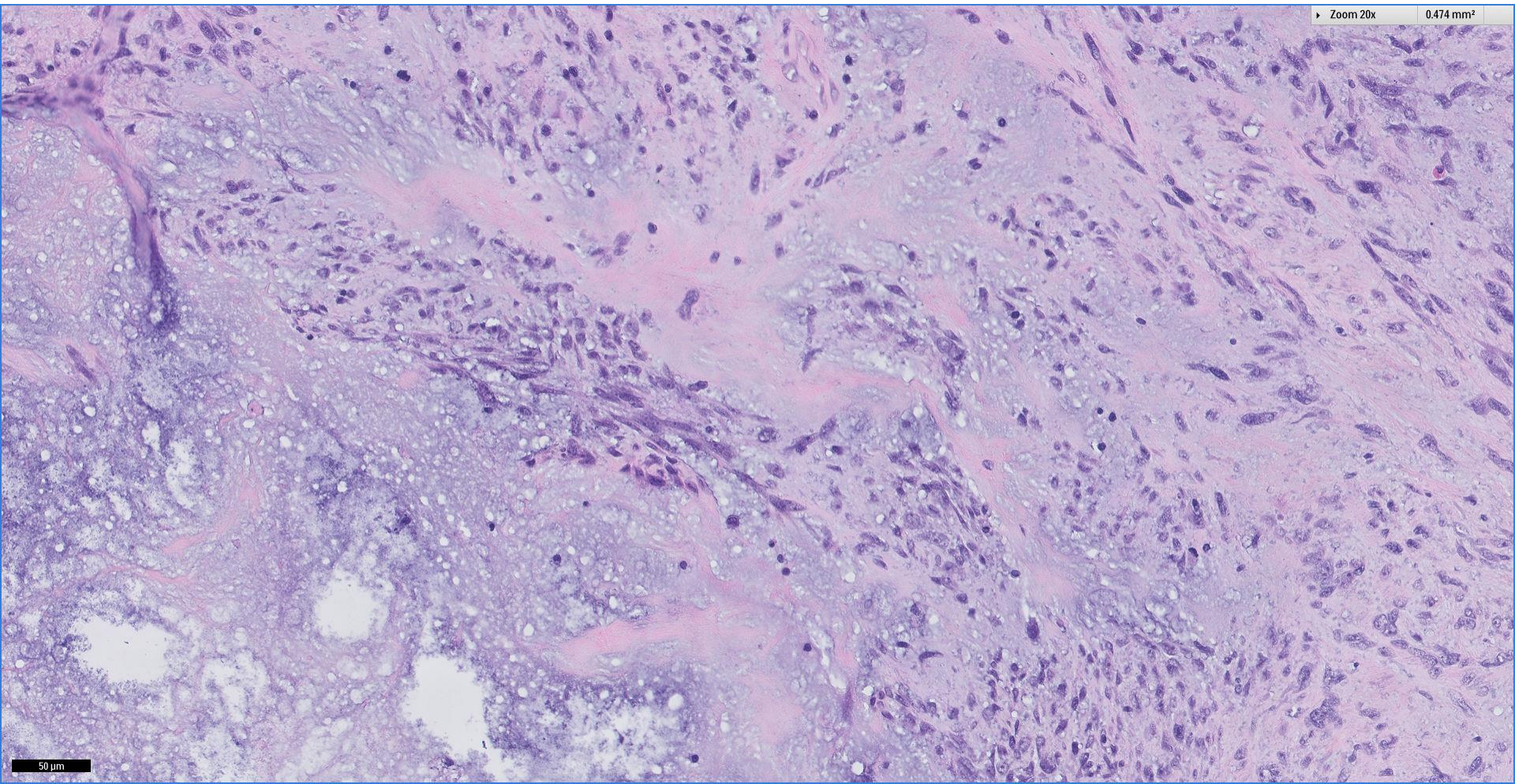
Excision biopsy (B)



Excision biopsy (B)



Excision biopsy (B)



Diagnosis

Left breast lump ~

(A) Core biopsy ~ Cellular fibroepithelial lesion with atypical stromal cells.

(B) Excision biopsy ~ Malignant phyllodes tumour.



Singapore
General Hospital

SingHealth

Division of Pathology



SingHealth DukeNUS
ACADEMIC MEDICAL CENTRE

PATHOLOGY



IAP

International Academy of Pathology
Singapore Division

Malignant phyllodes tumour

- Malignant grade based on ~
 - Moderate to marked increase in stromal cellularity.
 - Moderate to markedly atypical stromal cells.
 - High mitotic rates averaging about 34 per 10 high power fields, including occasional atypical tripolar mitoses.
 - Stromal overgrowth.
- No malignant heterologous elements are present.
- Tumour size 27mm.



Singapore
General Hospital

SingHealth
Division of Pathology



SingHealth DukeNUS
ACADEMIC MEDICAL CENTRE

PATHOLOGY



IAP

International Academy of Pathology
Singapore Division

Phyllodes Tumour Recurrence Risk Assessment

Welcome to the Singapore General Hospital's Department of Pathology risk assessment tool for estimating a person's recurrence free likelihood following a histologic diagnosis of breast phyllodes tumour.

This tool is based on a study undertaken at the Singapore General Hospital ([Tan PH et al. J Clin Pathol. 2012 Jan;65\(1\):69-76.](#))

This tool was designed for use by healthcare professionals. If you are not a healthcare professional, you are encouraged to discuss the results with your doctor. Please read the [SGH Nomogram Terms of Use](#) before proceeding with this tool.

Detailed information on this risk assessment tool is available [[Definitions for nomogram](#)].

Risk assessment tool

Does the tumor show stromal cytologic atypia

None or mild ⓘ

Moderate ⓘ

Marked ⓘ

How many mitoses are visible per 10 high powered fields? ⓘ

Mitoses per 10 hpf



Is there stromal overgrowth seen? ⓘ

Absent

Present

Are the margins histologically involved (positive)?

Negative ⓘ

Positive ⓘ

Nomogram Score : 46

Based on the data you have provided above, the following estimates of outcomes can be inferred

At 1 year, the recurrence free probability is estimated as 94%, with a 95% confidence interval between 89% to 96%.

At 3 years, the recurrence free probability is estimated as 79%, with a 95% confidence interval between 68% to 87%.

At 5 years, the recurrence free probability is estimated as 70%, with a 95% confidence interval between 55% to 81%.

At 10 years, the recurrence free probability is estimated as 63%, with a 95% confidence interval between 46% to 76%.

Validation of the SGH nomogram

- Japanese cohort of 45 patients with phyllodes tumours (2 excluded due to death from other causes), Shikoku Cancer Center, Matsuyama Japan.
- Median age 45 years; follow-up 4.7 to 309.9 months (median 129 months); median time to recurrence 113.3 months.

Factor	No of events/ No of patients	HR (95% CI)	p-value
Mitotic activity	6/43	0.89 (0.53, 1.50)	0.665
Stromal overgrowth			
Absent	4/38	Reference	
Present	2/5	3.60 (0.66, 19.79)	0.115
Surgical margins			
Negative	0/25	Reference	
Positive	6/18	-	0.0006
Stromal atypia			
Mild	6/37	Reference	
Moderate	0/6	-	0.287

Validation of the SGH nomogram

- Japanese cohort.

	HR (95% CI)	P-value	Concordance index
Nomogram	1.11 (1.02, 1.20)	0.0005	0.904

High concordance index indicates the ability of the SGH nomogram to accurately predict the recurrence likelihood of the Japanese cohort of patients.

Nishimura et al. J Clin Pathol. 2014 Aug;67(8):748-50.

Validation of the SGH nomogram

- Australian cohort of 34 patients with phyllodes tumours from Liverpool Hospital Sydney Australia.
- Median age 54 years; follow-up of up to 9 years (median 1.7 years); median time to recurrence 7.4 years.

Factor	No of events/ No of patients	HR (95% CI)	p-value
Mitotic activity	5/33	1.21 (1.04, 1.4)	0.0039
Stromal overgrowth			
Absent	1/18	Reference	
Present	5/16	6.00 (0.69, 52.49)	0.0589
Surgical margins			
Negative	2/14	Reference	
Positive	4/20	1.03 (0.17, 6.23)	0.9763
Stromal atypia			
Mild	0/17		
Moderate	4/14	0.11 (0.01, 1.27)	0.0020
Marked	2/3	Reference	

Concordance index 0.933

Validation of the SGH nomogram

(Data from the Kandang Kerbau Women's and Children's Hospital, Singapore)

Table 1: Univariable analysis of RFS

Factor	No of events/No of patients	HR (95% CI)	P-value
Mitoses	13/258	1.15 (1.07, 1.23)	<0.0001
Overgrowth			0.0454
Negative	10/238	reference	
Positive	3/21	3.74 (1.03, 13.62)	
Margin			0.0007
Negative	2/188	reference	
Positive	11/71	13.48 (2.99, 60.91)	
Atypia			0.1581
Mild	10/227	Reference	
Mod	1/19	0.99 (0.13, 7.79)	
Marked	2/13	4.44 (0.96, 20.57)	
Diagnosis			0.2446
Benign	9/211	Reference	
Borderline	2/30	1.28 (0.28, 5.92)	
Malignant	2/18	3.77 (0.80, 17.73)	
Nomogram	13/258	1.08 (1.04, 1.11)	<0.0001

259 cases
C-index 0.863

USCAP 2017 abstract

C-index for nomogram is 0.866, which reflects a good concordance between predicted and actual recurrences.

Validation of the Singapore Nomogram For Outcome Prediction in a US-Based Population of Women with Breast Phyllodes Tumors (PT)

1. Camilla Cristando MD¹, 2. HuiHua Li, Phd², 3. Mathilde Almekinders MD³, 4. Puay Hoon Tan², 5. Edi Brogi MD, PhD¹ and 6. Melissa Murray DO¹.

Table 1: Univariable analysis of RFS

concordance index of 0.84

USCAP 2017 abstract

Factor	No. of patients n=76 (%)	No. of events n=9	HR (95% CI)	P-value
Diagnosis				0.0139
Benign	45 (59)	2	Reference	
Borderline	15 (20)	2	3.23 (0.45, 23.01)	

Conclusion: Analysis of a US-based cohort of women with PT using the Singapore Nomogram yielded a concordance index of 0.84. Our findings support the utility of the PT Singapore Nomogram to estimate the RFS in US women.

Factor	No. of patients n=76 (%)	No. of events n=9	HR (95% CI)	P-value
Atypia				0.0001
Mild	48 (63)	1	Reference	
Moderate	18 (24)	3	8.75 (0.91, 84.12)	
Marked	10 (13)	5	28.65 (3.32, 247.26)	
Mitoses	76 (100)	9	1.08 (1.04, 1.13)	<0.0001
Margin				0.92
Negative	61 (80)	7	Reference	
Positive	15 (20)	2	1.08 (0.22, 5.21)	
Nomogram	76 (100)	9	1.06 (1.02, 1.11)	0.0007

Stromal multinucleated cells in phyllodes tumour

- Stromal multinucleated cells similar to those observed in fibroadenomas, that do not contribute to grading assessment, may be encountered in phyllodes tumours.
- These however, need to be distinguished from abnormal stromal cells with multilobated and bizarre nuclei that reflect stromal atypia, as in this case.
- Helpful to assess non-multinucleated stromal cells and other histological parameters used in grading.



Singapore
General Hospital
SingHealth
Division of Pathology



Stromal multinucleated cells in phyllodes tumour

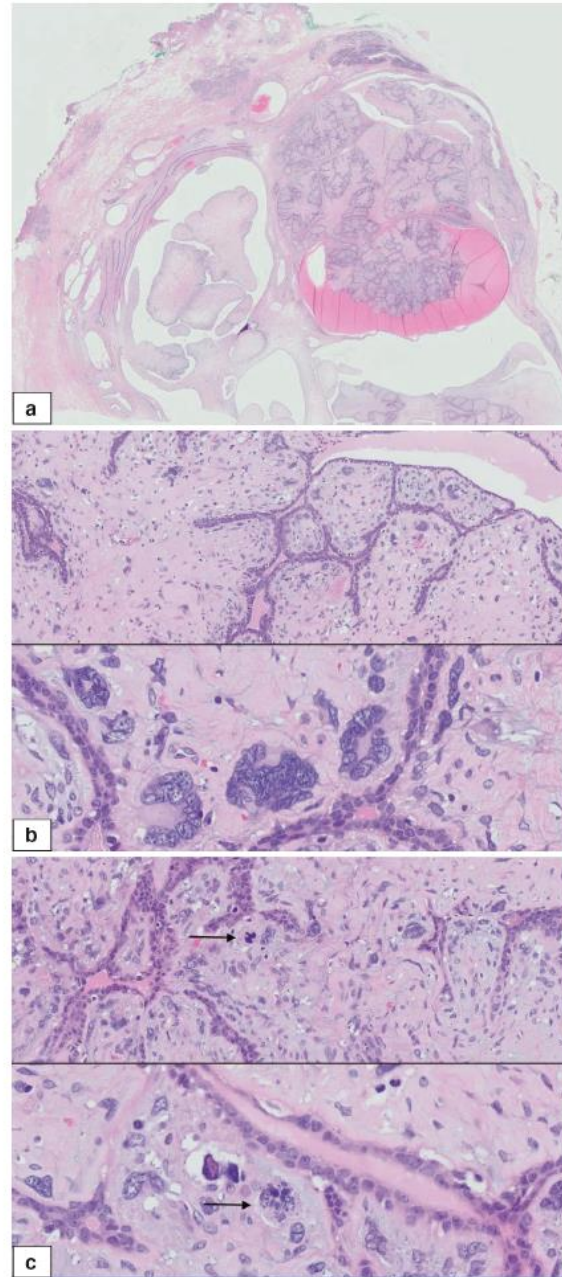
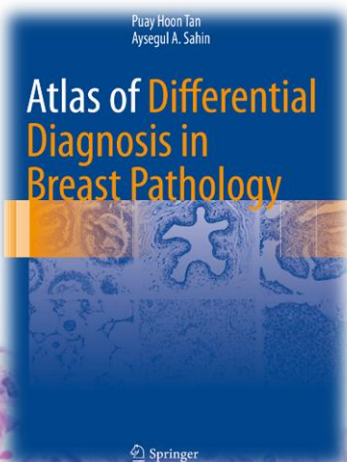
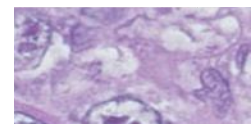


Fig. 3.65 Phyllodes tumour with stromal atypia and bizarre multinucleated giant cells. (a) Low magnification, broad stromal fronds project into cystic spaces. (b) Medium and high magnification shows bizarre multinucleated giants cells with polylobated nuclei. Moderate nuclear atypia is present in surrounding stromal cells. (c) Mitoses are present

(arrows) including a tripolar mitosis (*upper field*). The tumour was initially classified as a benign phyllodes tumour, but due to the stromal atypia and mitotic activity, the tumour would be better classified as borderline. No stromal overgrowth or permeative border was seen.



 Breast
Pathology
Course 2017

