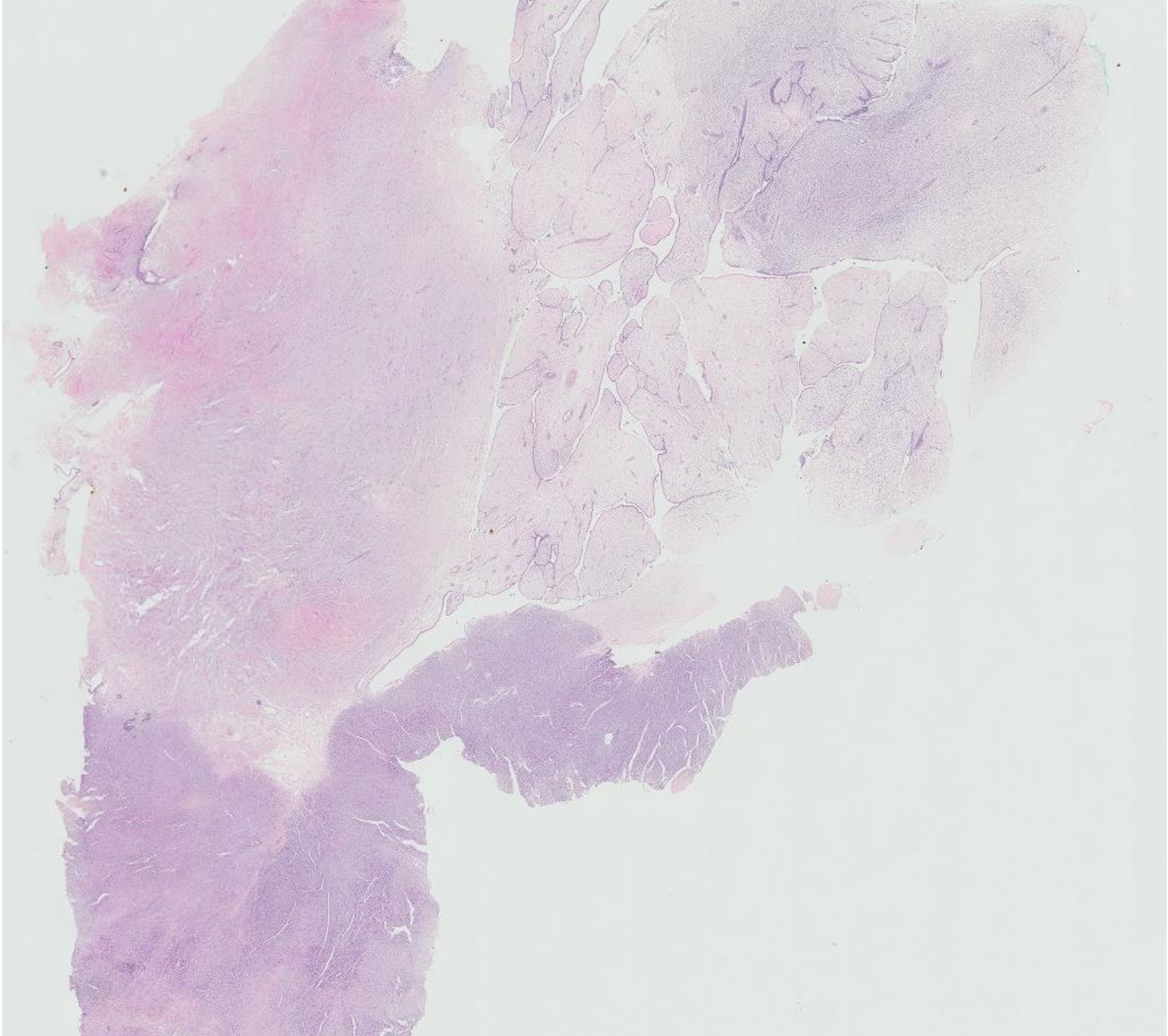
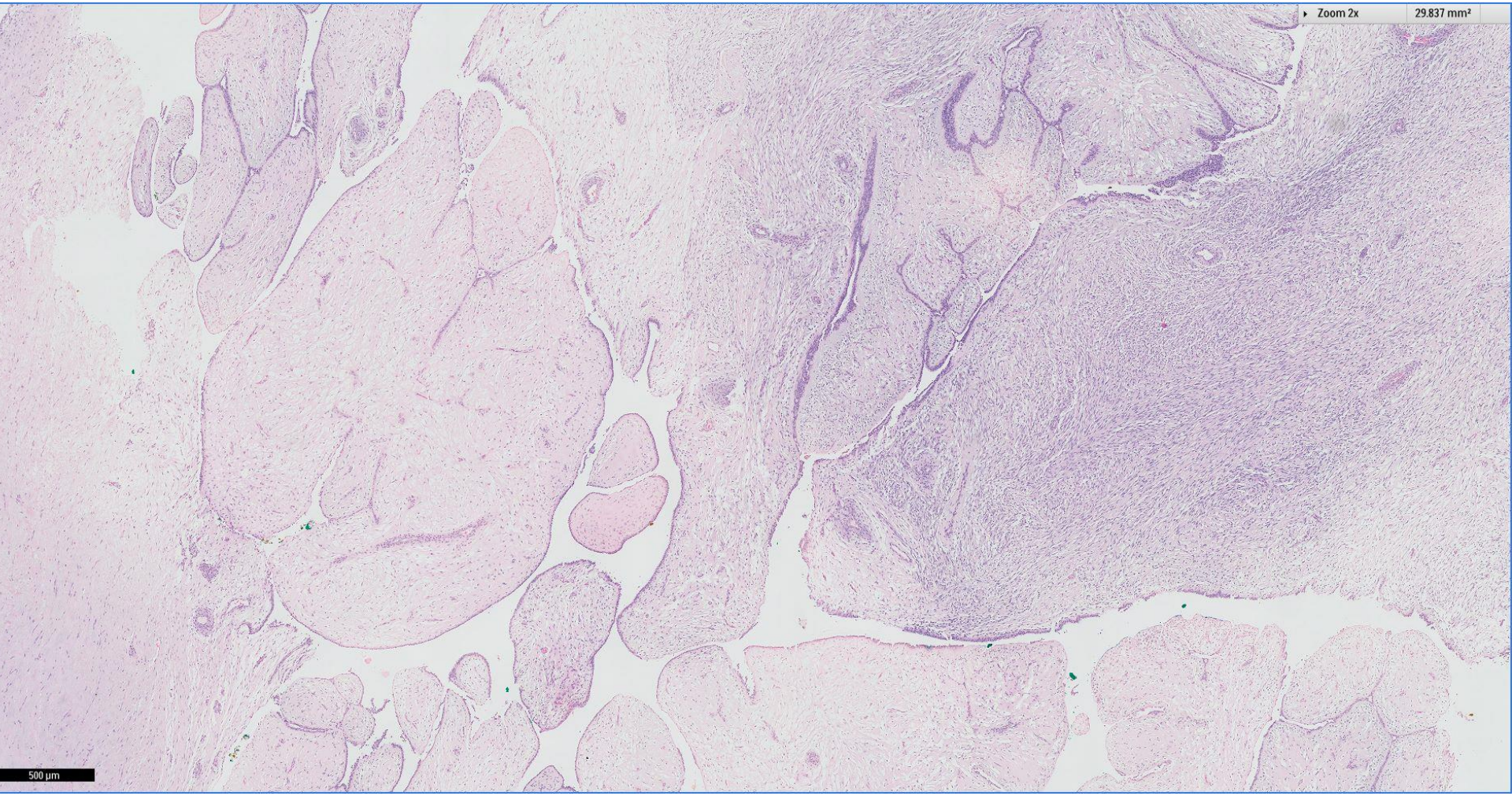
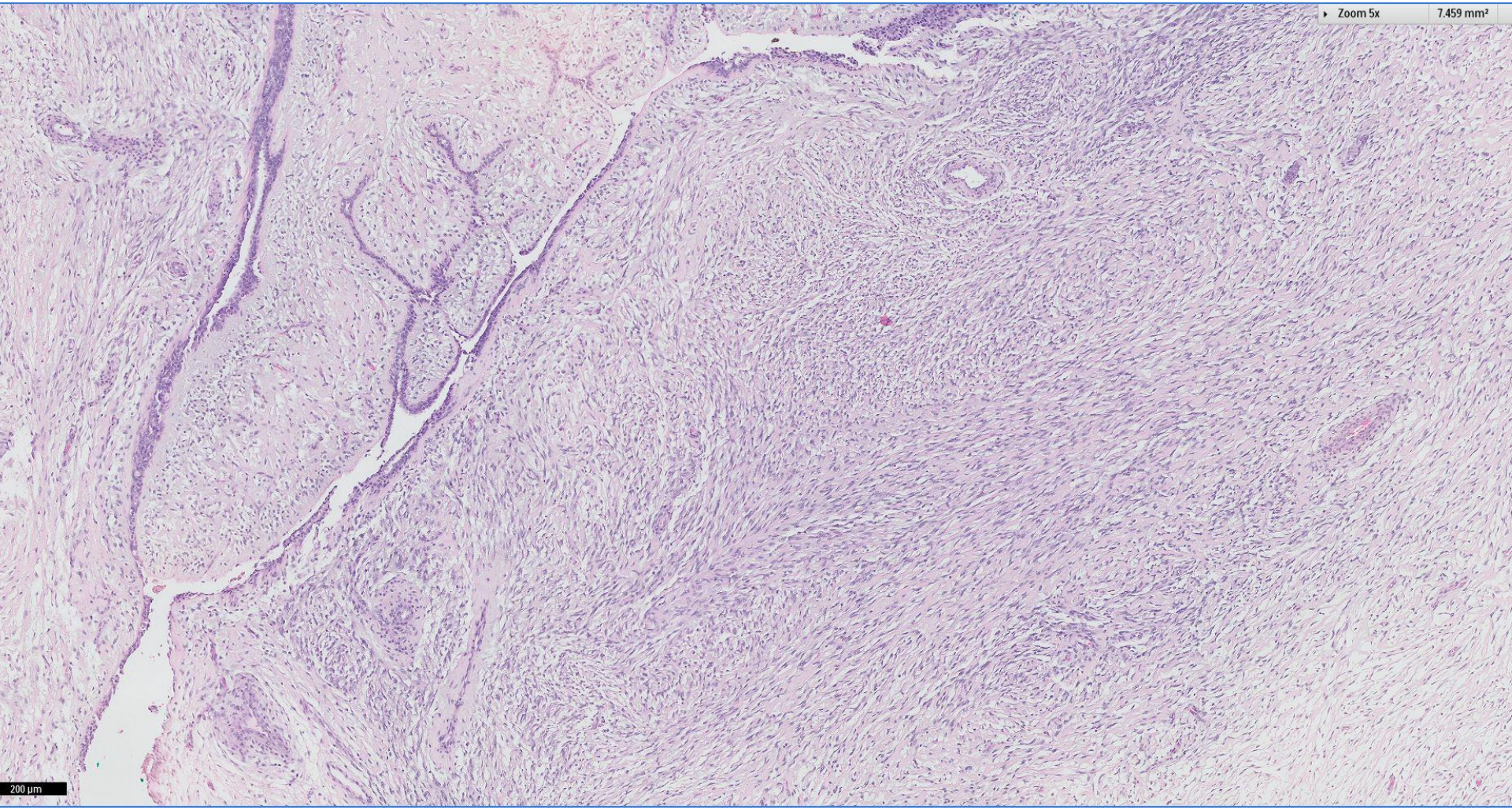
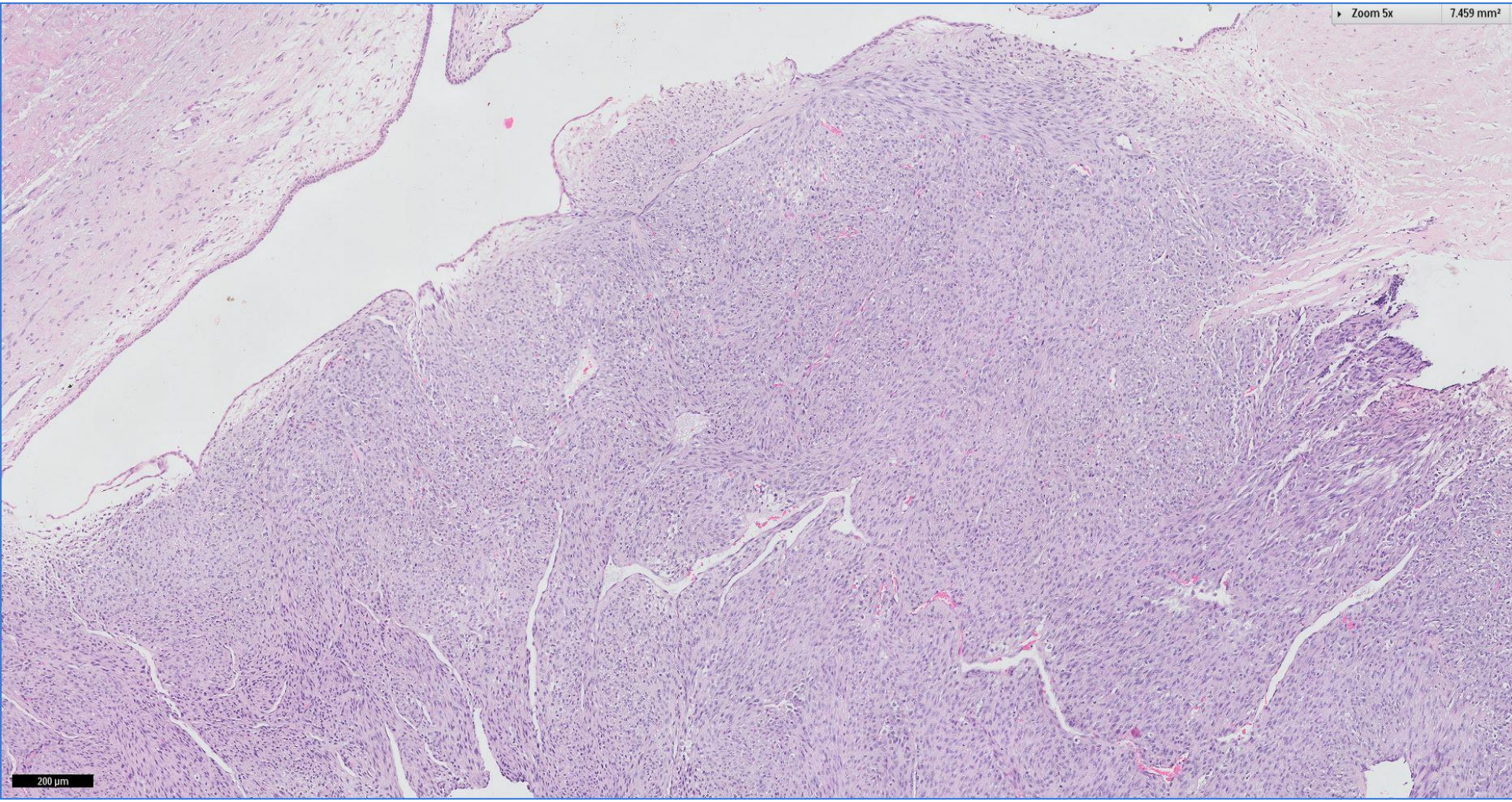
Case 11

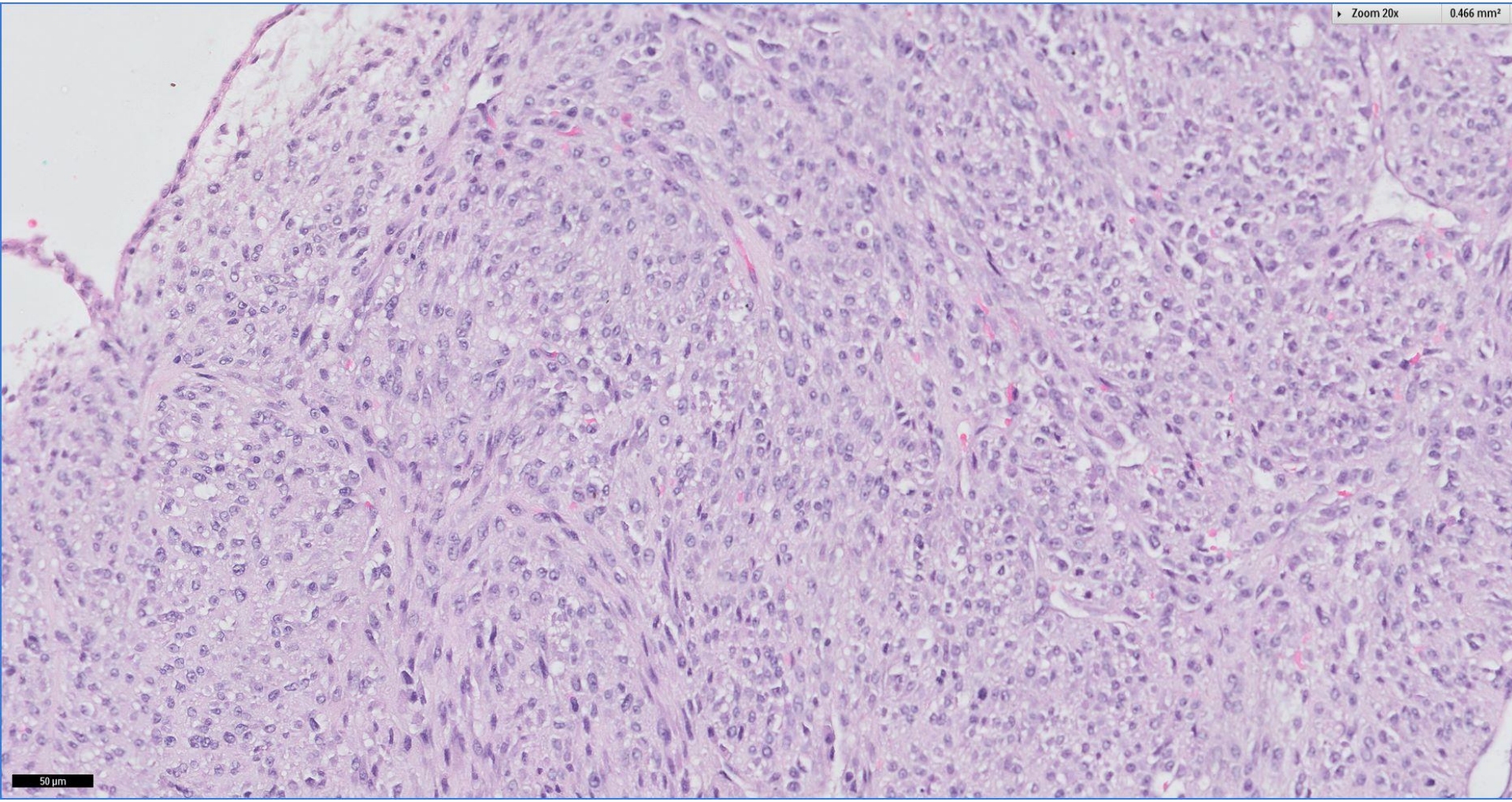
53 year old woman underwent mastectomy
for a large breast mass.
Previous core biopsy reported malignancy.

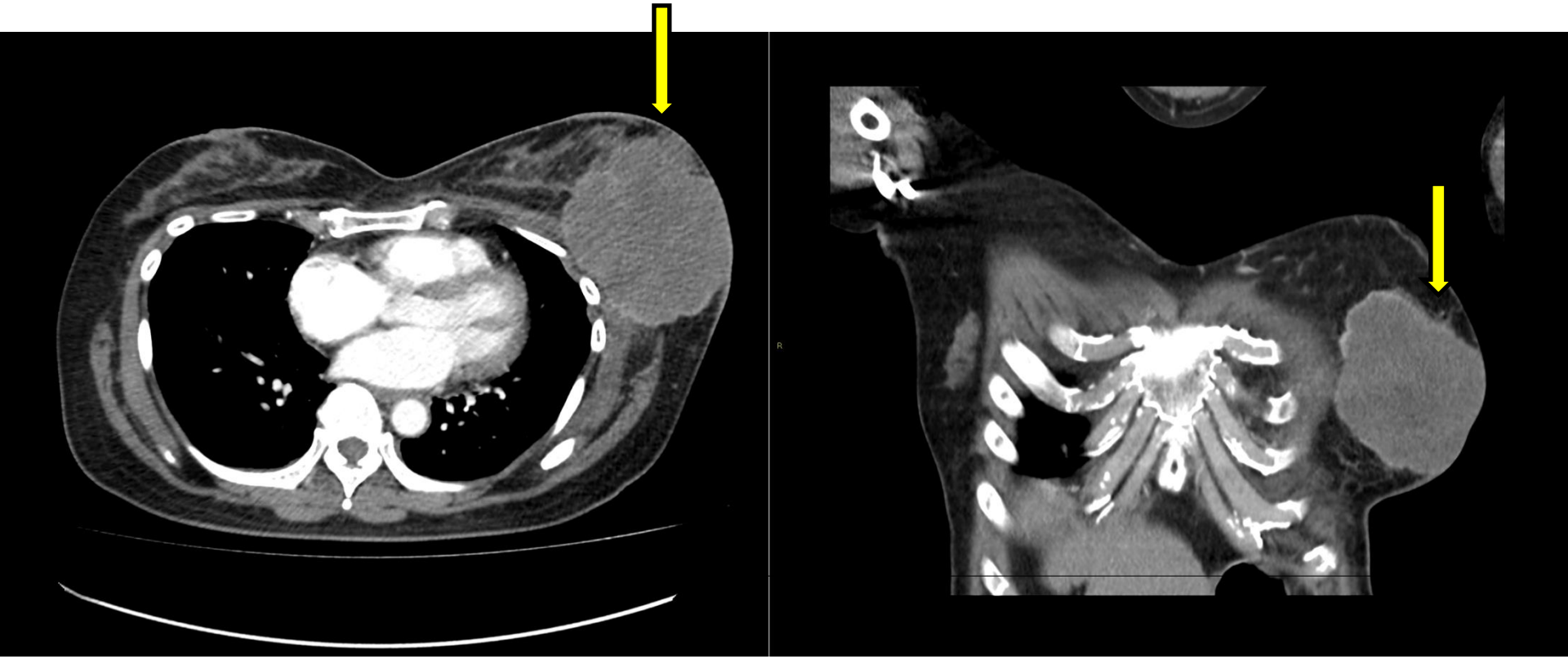



Zoom 2x
29.837 mm²
500 µm

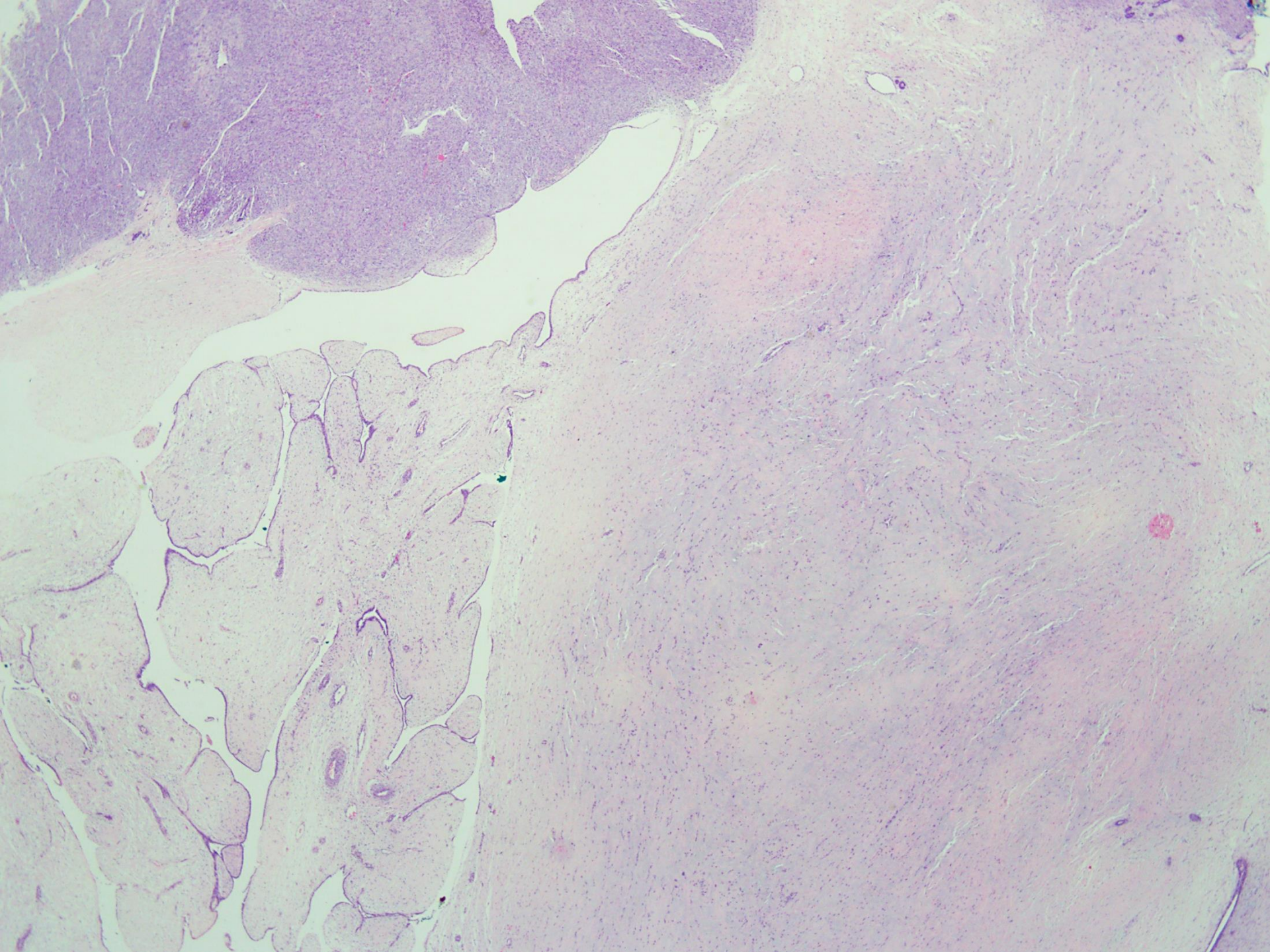

Zoom 5x
7.459 mm²
200 µm

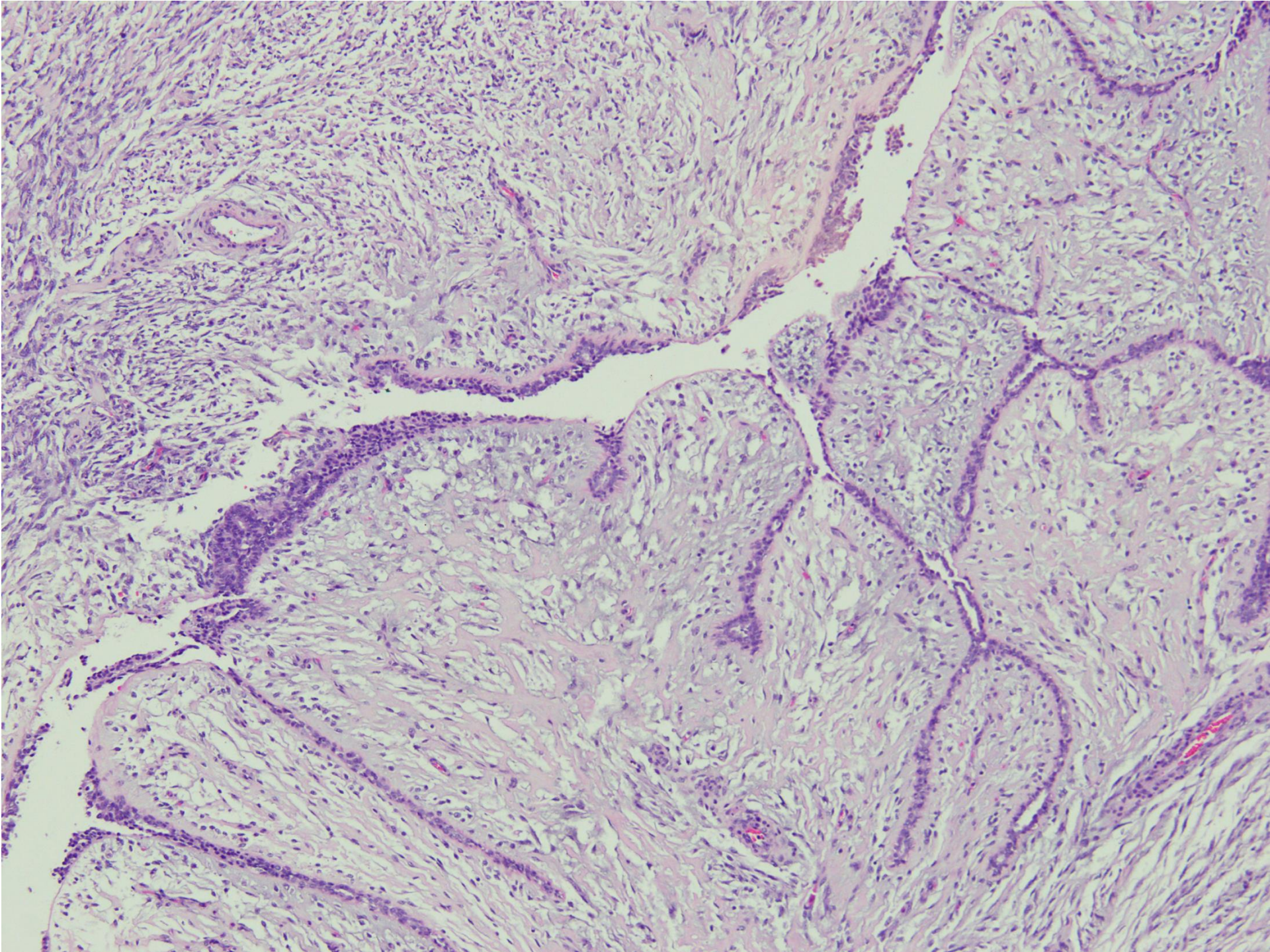

Zoom 5x
7.459 mm²
200 µm

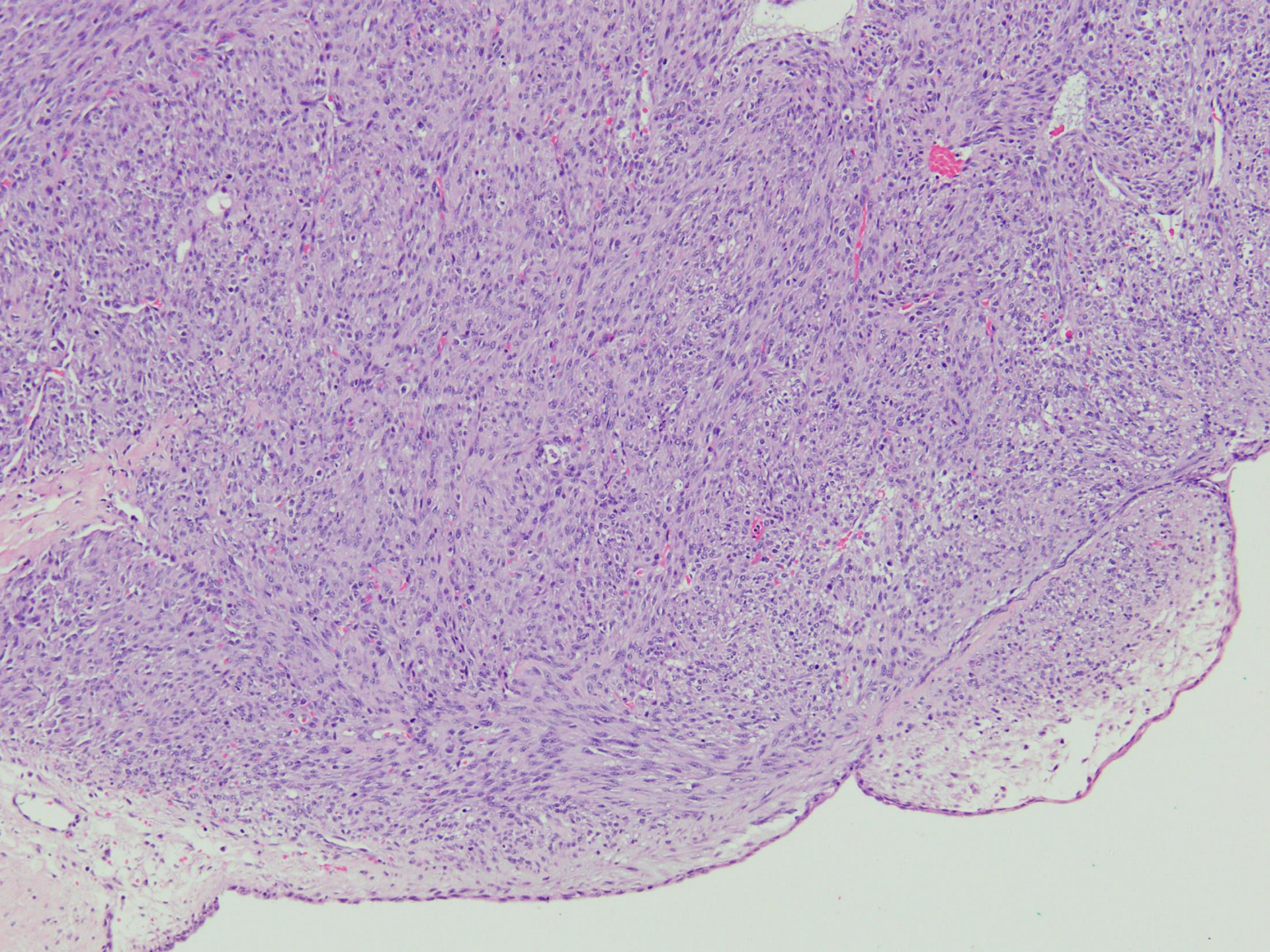

Zoom 20x
0.466 mm²
50 µm

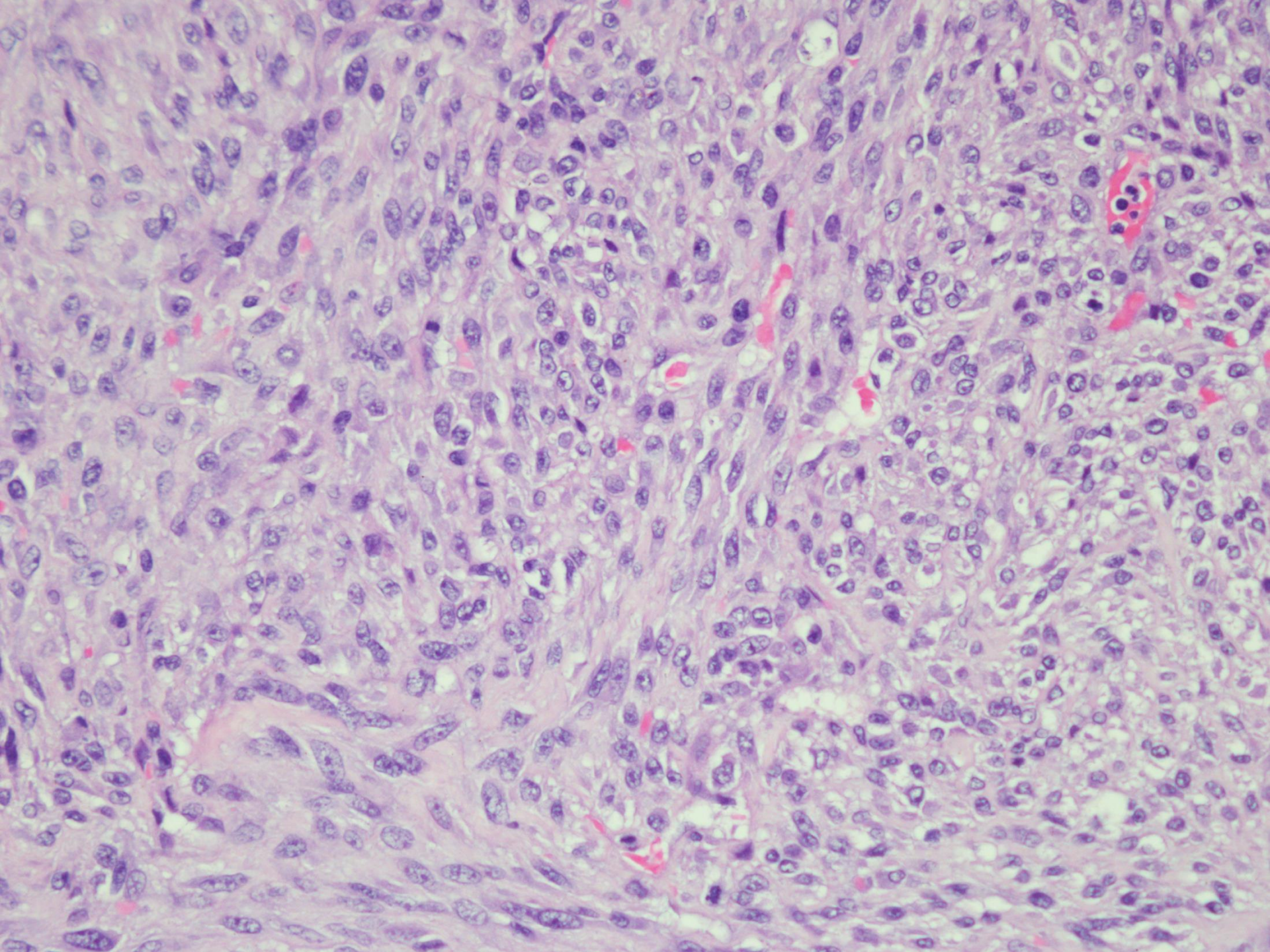


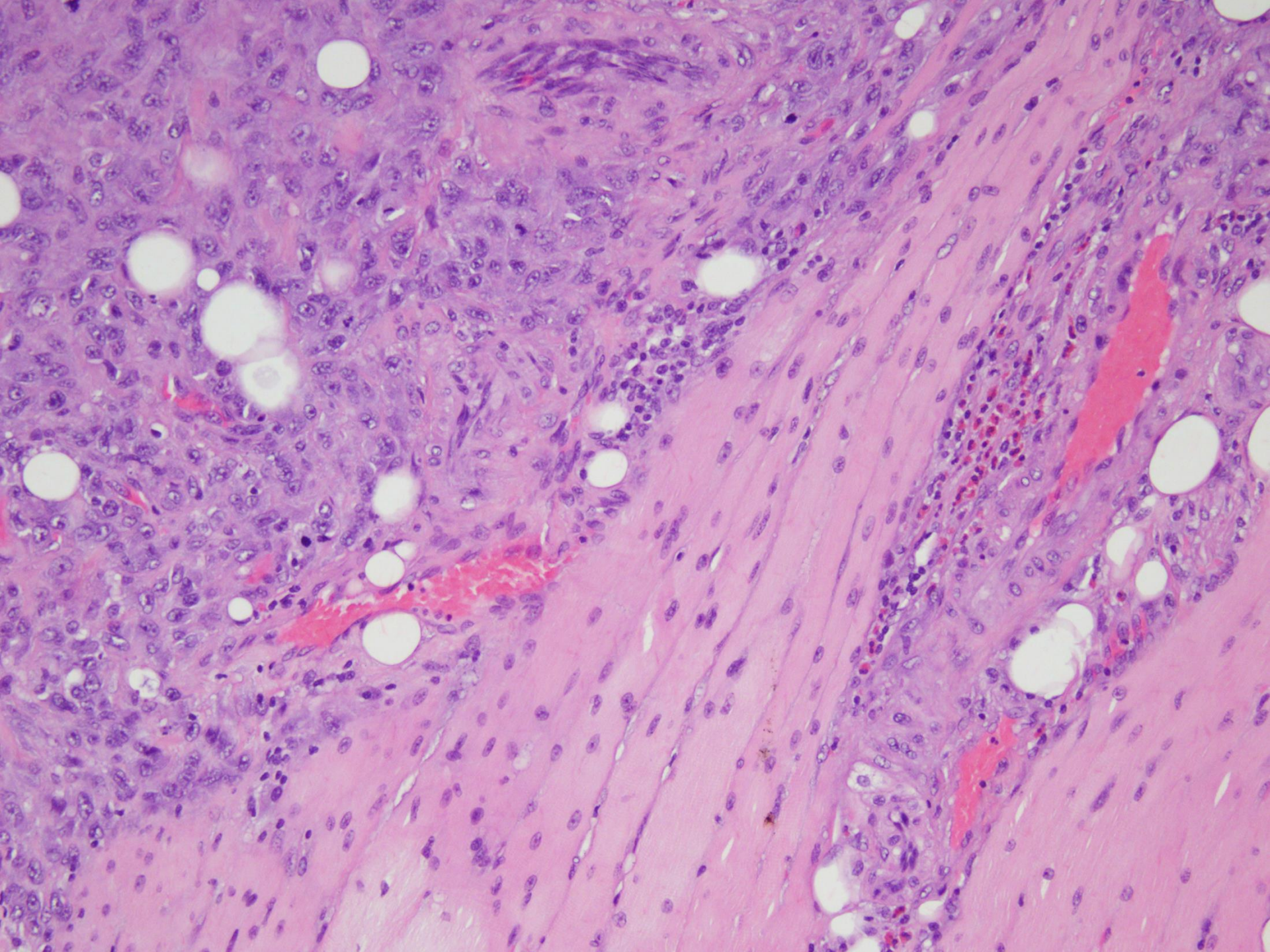
CT scans











Diagnosis
Simple mastectomy:
Malignant phyllodes tumour

~ Marked stromal hypercellularity

~ Marked stromal atypia

~ Brisk mitoses (31 per 10 hpf)

~ Stromal overgrowth

~ Permeative borders

Malignant spindle cell tumour

- Malignant phyllodes tumour

  vs

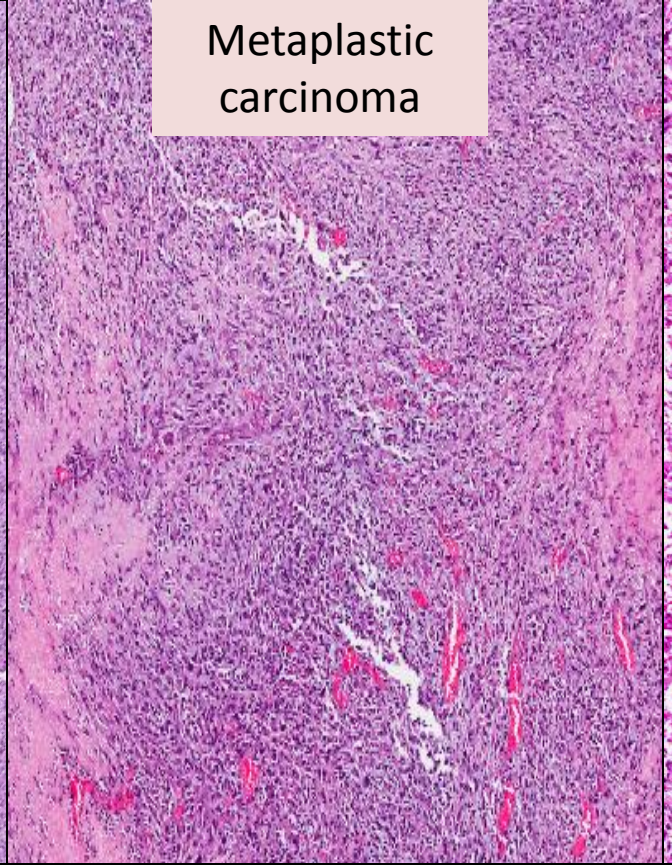
- Metaplastic breast carcinoma

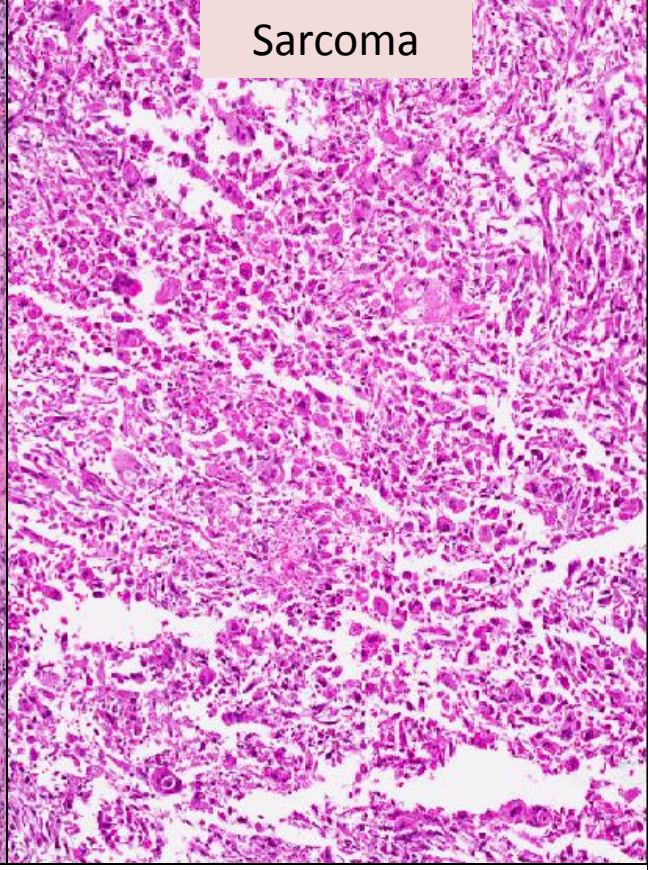
  vs

- Sarcoma

Metaplastic carcinoma may be subjected to neoadjuvant chemotherapy & sentinel lymph node biopsy


Phyllodes tumour, malignant


Metaplastic carcinoma


Sarcoma

Immunohistochemical panel

	Malignant phyllodes tumour (spindle cell component)	Metaplastic carcinoma (spindle cell component)	Primary sarcoma
MNF116	-	+	-
AE1/3	-	+	-
Cam 5.2	-	+	-
34βE12	-	+	-
p63	-	+	-
CD34	+/-	-	-
bcl2	+/-	-	-

?

Practical points

- Thorough sampling for histology.
- Search for:
  - Epithelium lined fronds – phyllodes tumour.
  - In situ or invasive carcinoma – metaplastic carcinoma.
- Use of immunohistochemistry:
  - Cytokeratin panel including basal-type keratins.
  - p63.
  - CD34.

Keratins in differential diagnosis of phyllodes, sarcoma and metaplastic carcinoma

A word of caution……

Table 8 Immunohistochemical expression of keratins in phyllodes tumours, spindle cell sarcoma NOS, spindle cell components of metaplastic carcinoma and low-grade spindle cell lesions of the breast

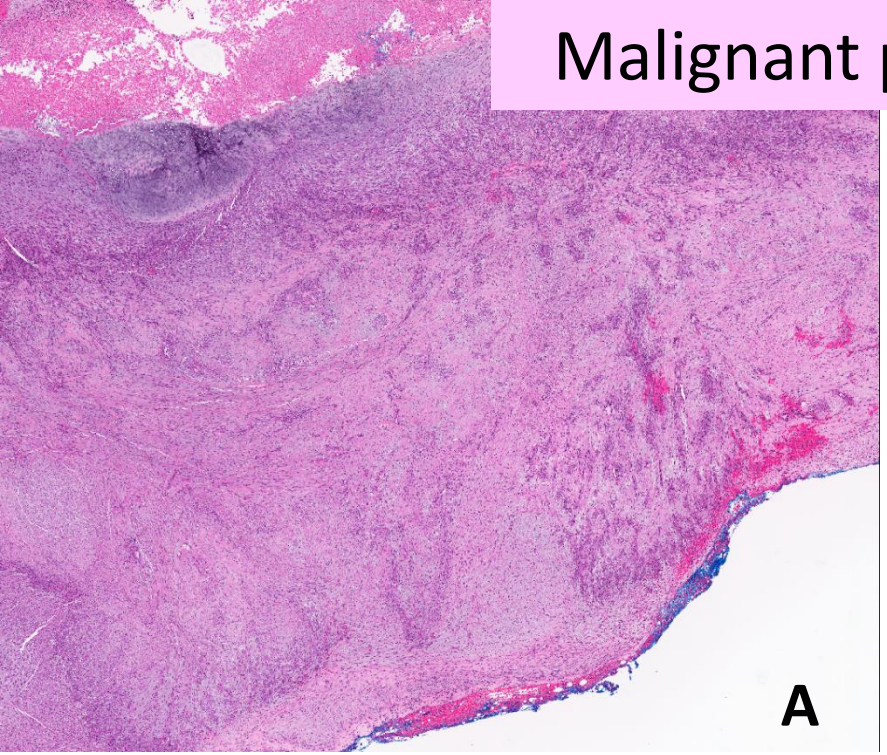
Diagnosis	Total no of cases	AE1/3 positive	CK14 positive	Cam5.2 positive	CK7 positive	34βE12 positive	MNF 116 positive
Phyllodes tumour	109	9/109 (8.3%)	2/109 (1.8%)	2/109 (1.8%)	31/109 (28.3%)	24/109 (21.8%)	13/109 (11.8%)
Benign	70	4/70 (5.7%)	0/70 (0%)	0/70 (0%)	20/70 (28.6%)	11/70 (15.7%)	6/70 (8.6%)
Borderline	30	3/30 (10.0%)	2/30 (6.7%)	1/30 (3.3%)	9/30 (30.0%)	9/30 (30.0%)	4/30 (13.3%)
Malignant	9	2/9 (22.2%)	0/9 (0%)	1/9 (11.1%)	2/9 (22.2%)	4/9 (44.4%)	3/9 (33.3%)
Spindle cell sarcoma	8	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Spindle cell component of metaplastic carcinoma	8	5/8 (62.5%)	8/8 (100%)	6/8 (75.0%)	3/8 (37.5%)	2/8 (25.0%)	7/8 (87.5%)
Low-grade spindle cell lesions	13	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

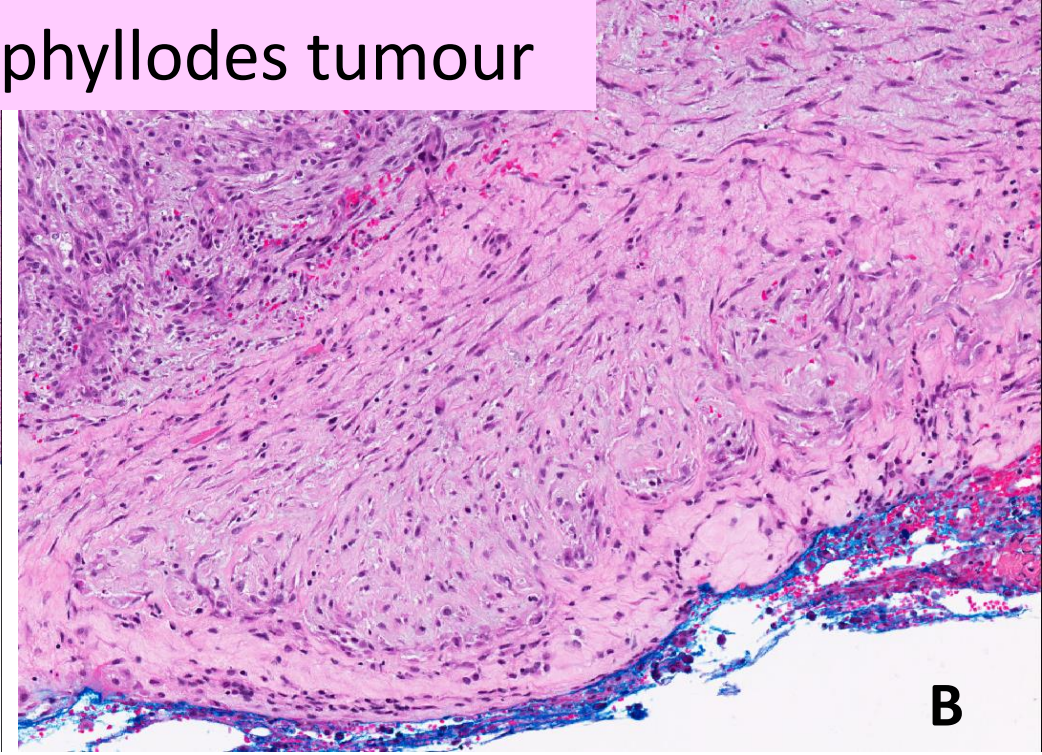
NOS, not otherwise specified.

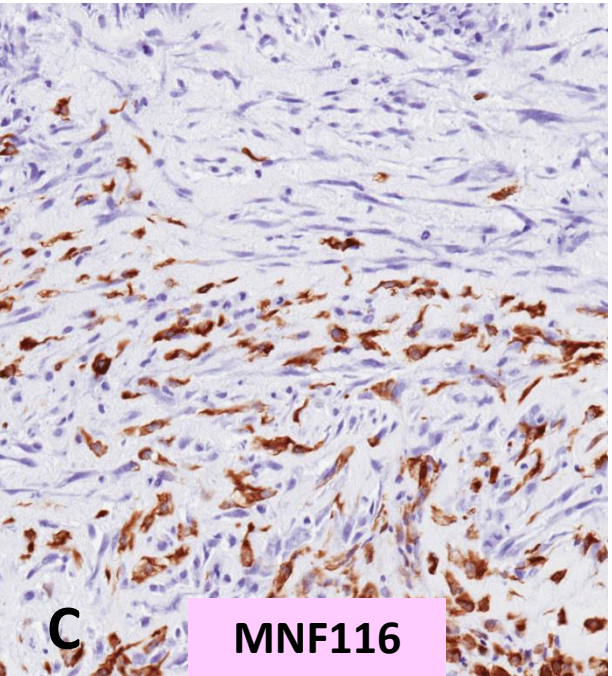
Chia Y et al. J Clin Pathol. 2012 Apr;65(4):339-47.

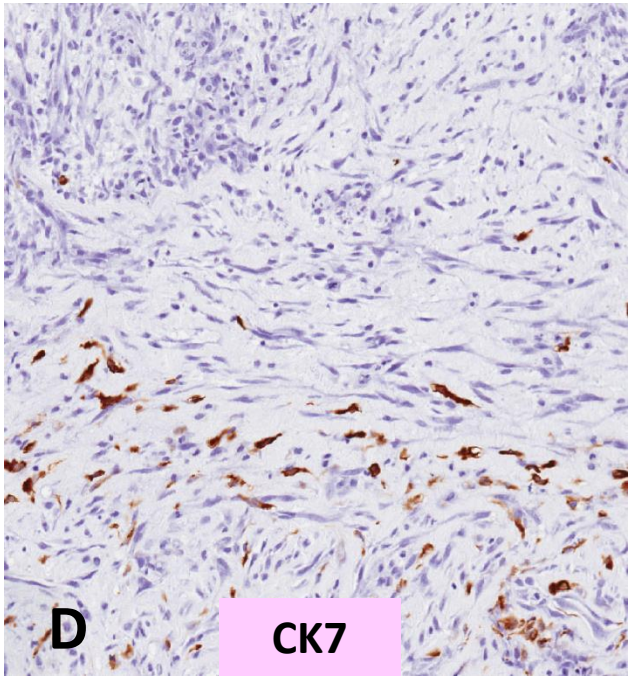
Note: Staining in phyllodes tumours is focal (less than 5% of stromal cells) and patchy.

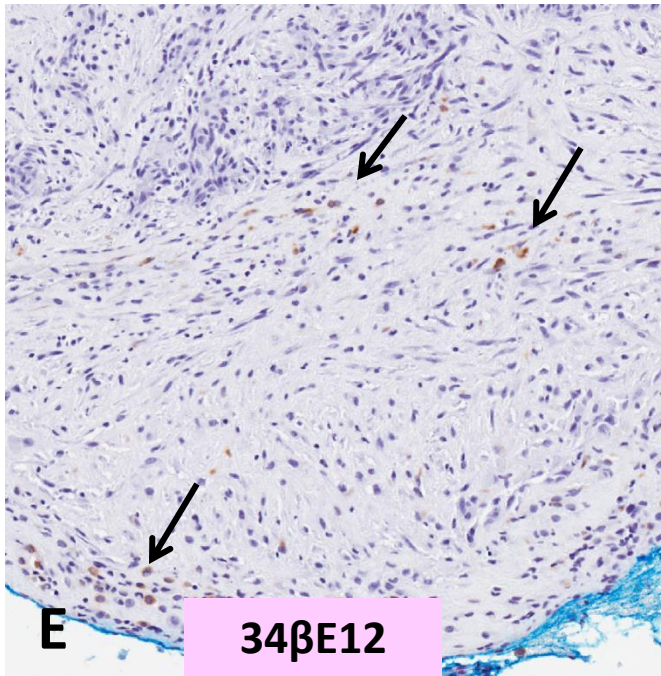
Malignant phyllodes tumour



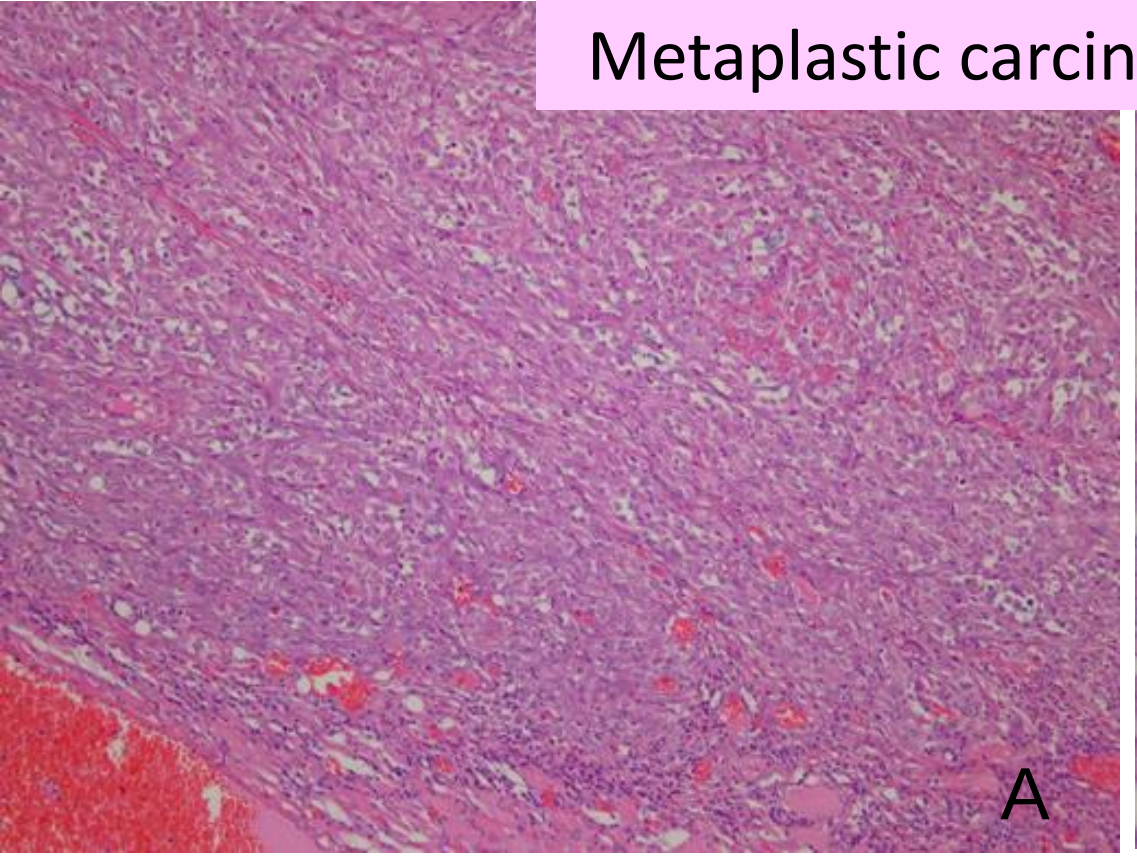


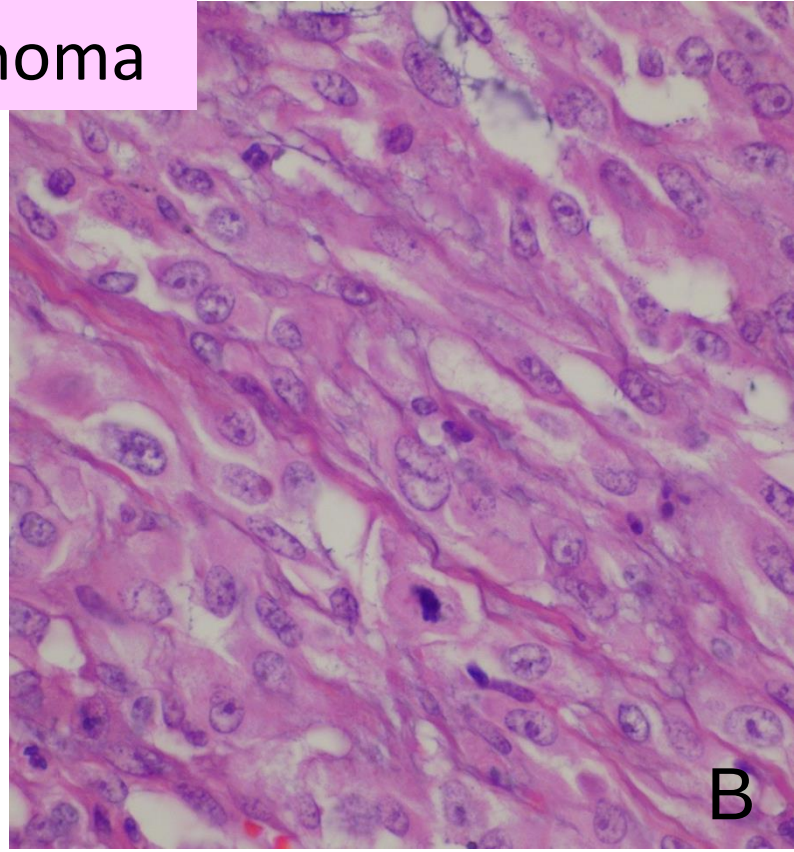


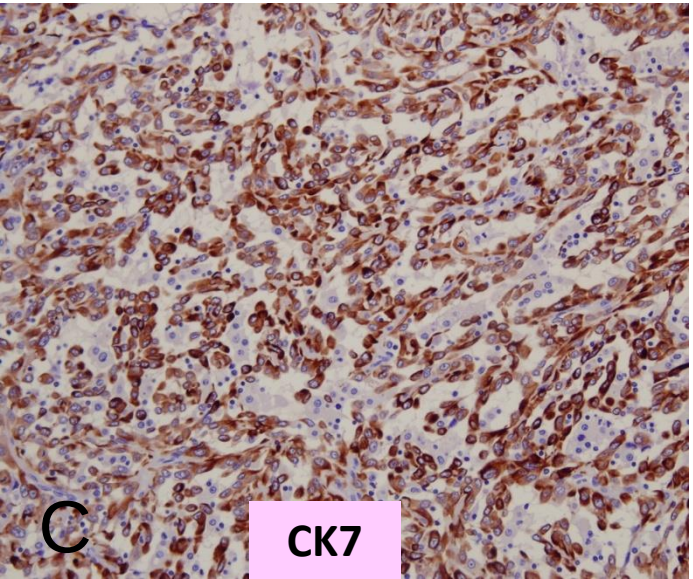


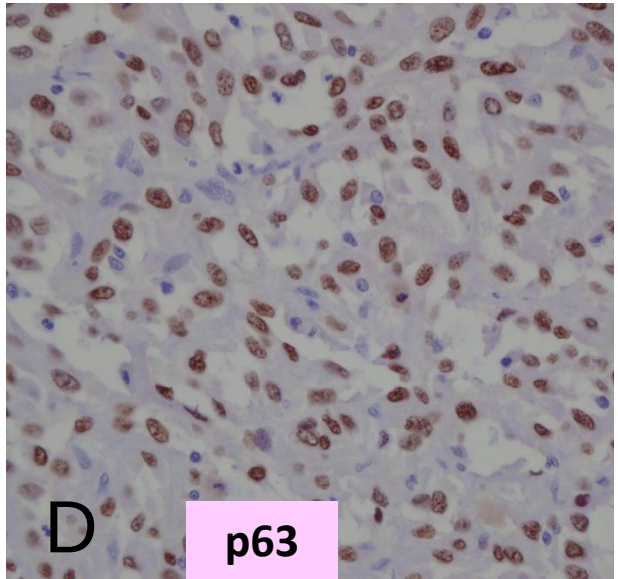


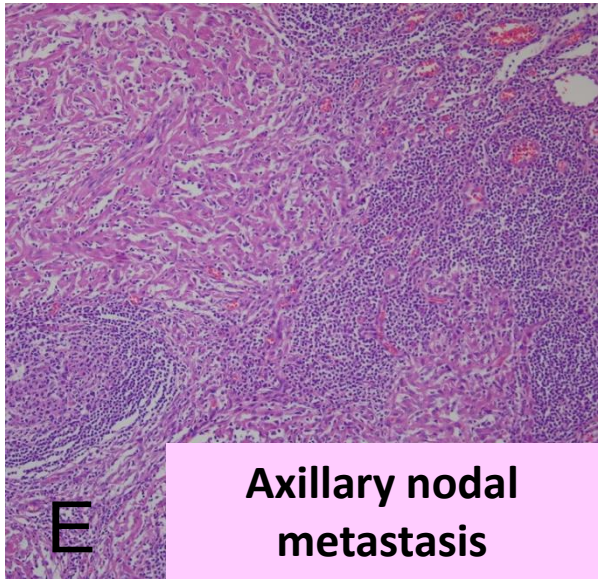
Metaplastic carcinoma











Keratin immunohistochemistry in metaplastic carcinoma

Table 7 Immunohistochemical staining results of the spindle cell component of metaplastic breast carcinomas

Case	p63	CD34	34βE12	MNF116	CK7	CK14	Cam 5.2	AE1/3
1	−	−	−	+	+	+	+	+
2	−	−	−	−	−	+	+	+
3	−	−	−	+	+	+	+	−
4	−	−	−	+	−	+	−	−
5	+	−	−	+	−	+	−	+
6	−	−	−	+	−	+	+	+
7	−	−	+	+	−	+	+	+
8	+	−	+	+	+	+	+	−

Chia Y et al. J Clin Pathol. 2012 Apr;65(4):339-47.

Keratins in differential diagnosis of phyllodes, sarcoma and metaplastic carcinoma

Take-home messages

- Phyllodes tumours of the breast may express keratins in stromal cells on immunohistochemistry, albeit focal and patchy in distribution.
- CD34 stromal staining is associated with phyllodes tumour grade, with benign tumours showing a higher proportion of positivity.
- None of the phyllodes tumours display stromal p63 reactivity.
- On limited material such as core biopsies, focal keratin expression of a spindle cell breast tumour needs to be interpreted with caution, and should not be immediately concluded as a tumour of metaplastic origin.

Chia Y et al. J Clin Pathol. 2012 Apr;65(4):339-47.

p63 and p40 in breast phyllodes tumours

A Subset of Malignant Phyllodes Tumors Express p63 and p40

A Diagnostic Pitfall in Breast Core Needle Biopsies

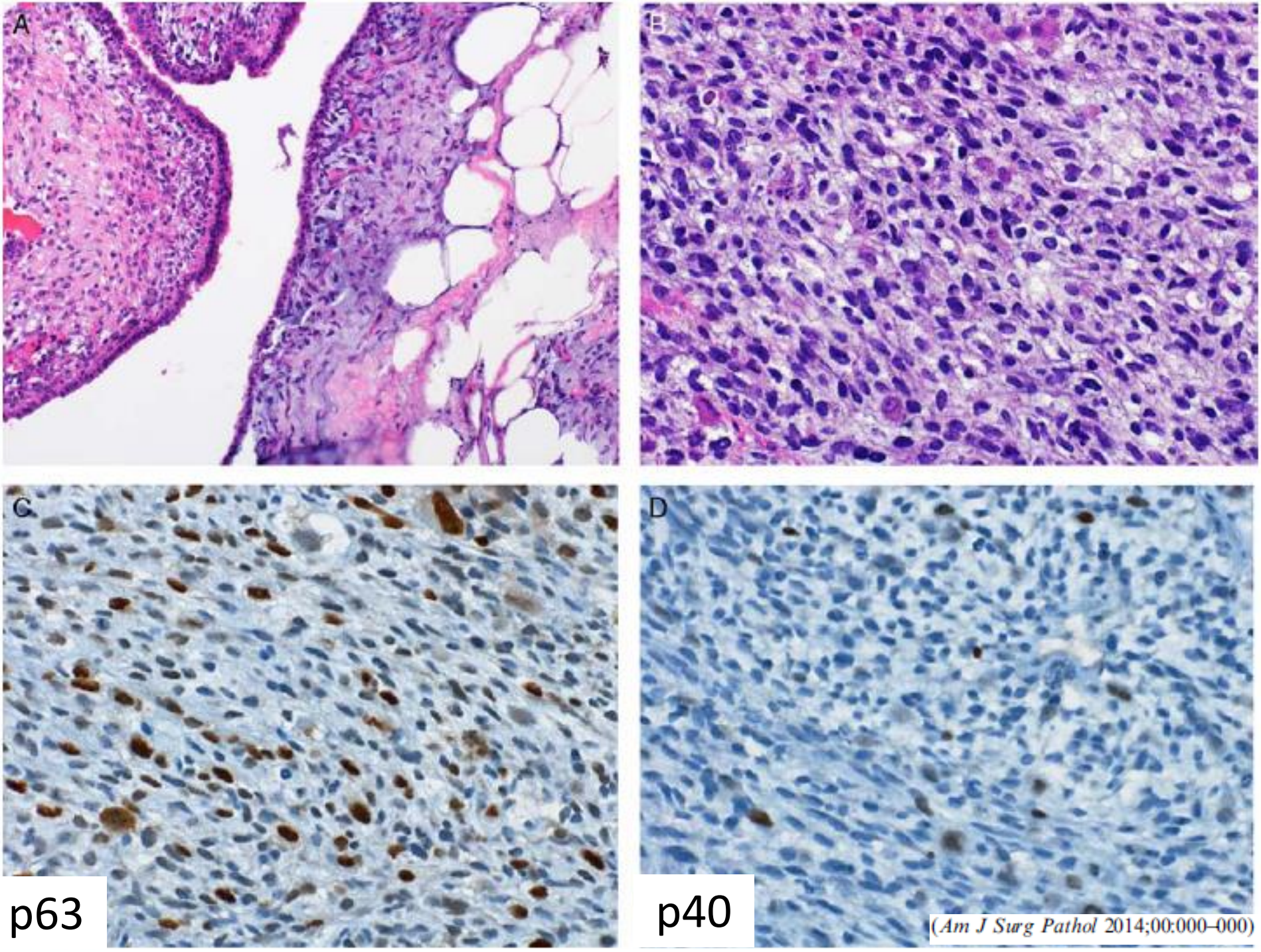
Ashley Cimino-Mathews, MD, Rajni Sharma, PhD, Peter B. Illei, MD, Russell Vang, MD, and Pedram Argani, MD

(*Am J Surg Pathol* 2014;00:000–000)

TABLE 3. IHC Labeling for p63, p40, Cytokeratins, and CD34 in Breast SCs, PTs, and FAs

Tumor Type	Total Number	p63 Positivity (n [%])	p40 Positivity (n [%])	Cytokeratin Positivity (n [%])	CD34 Positivity (n [%])
SC	13	8 (62)	6 (46)	13 (100)	0 (0)
MP	14	8 (57)	2 (14)	3 (21)	8 (57)
BLP	10	0 (0)	0 (0)	0 (0)	10 (100)
Benign Phyllodes	10	0 (0)	0 (0)	0 (0)	10 (100)
FA	10	0 (0)	0 (0)	0 (0)	10 (100)

p40 is an isoform of p63 and is believed to be a more specific marker of squamous or sarcomatoid differentiation


A
B
C
D
p63
p40
(Am J Surg Pathol 2014;00:000–000)

Take home messages

- Core biopsies of malignant spindle cell tumours:
  - Look for histologic clues.
  - Be aware of pitfalls of keratin, and p63/p40 immunohistochemical staining.

Follow-up

- Patient underwent postoperative radiation therapy.
- Last clinical follow-up on 14 August 2014.
- She was well and disease free.
- CT chest done revealed no abnormalities.

Breast Pathology Course 2014