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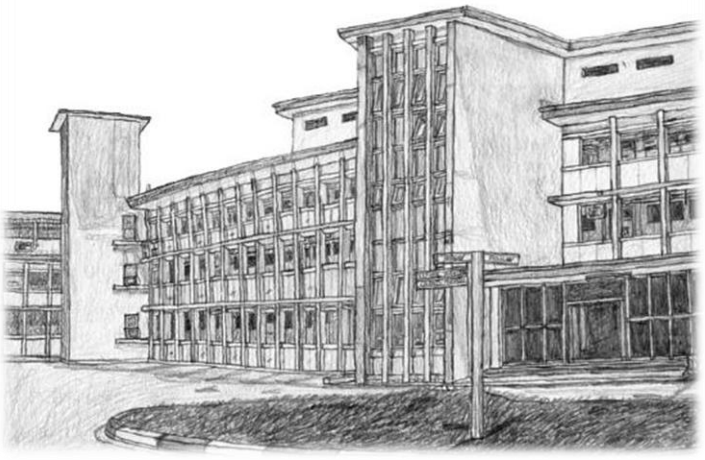
Case 19

39 year old female.
Left breast upper inner quadrant mass, 3cm, firm and movable, for one year; no axillary lymph nodes.
Ultrasonography revealed a solid-cystic multilobulated mass measuring 4 x 2cm.

Case contributed by Dr Lu Kim, Vietnam



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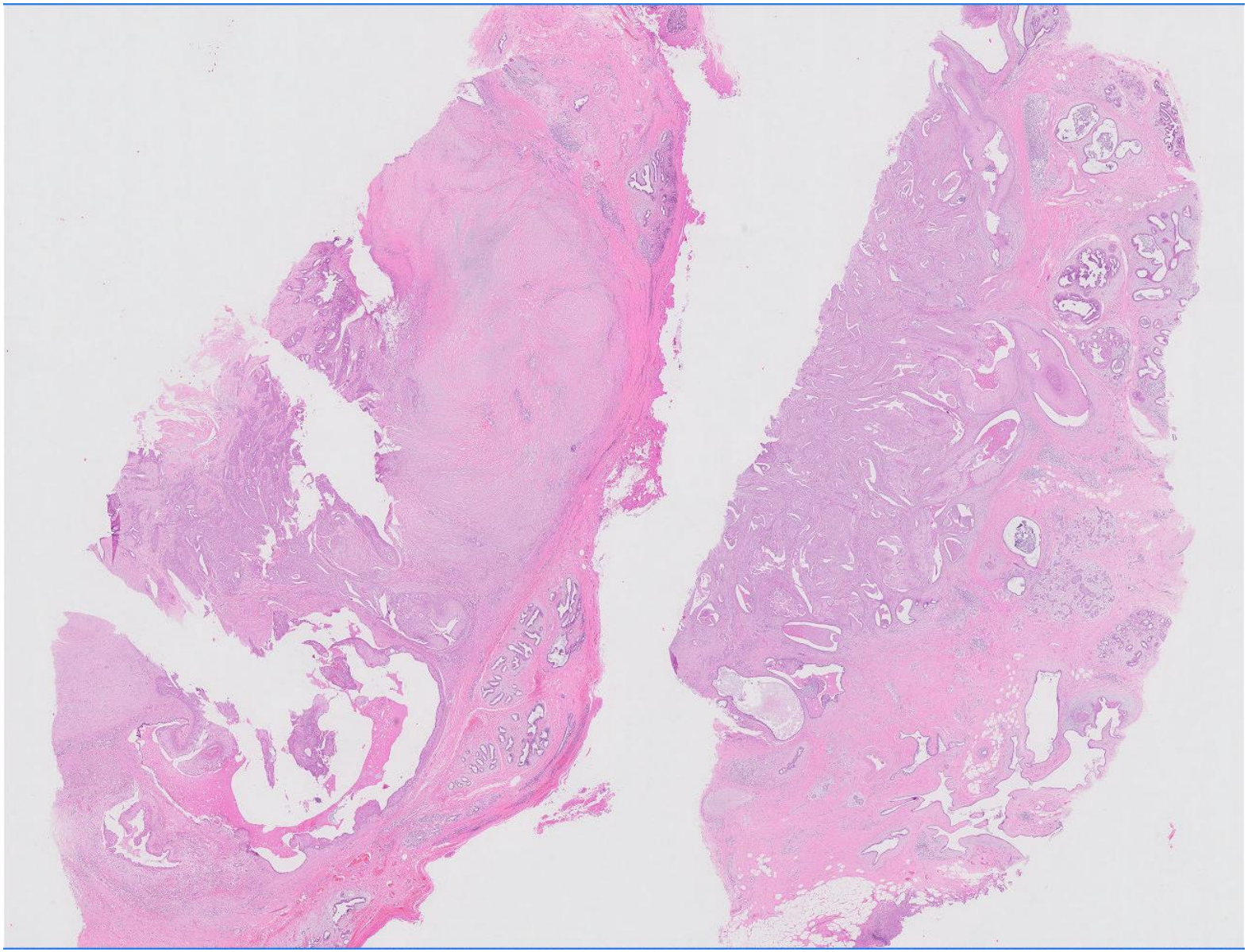

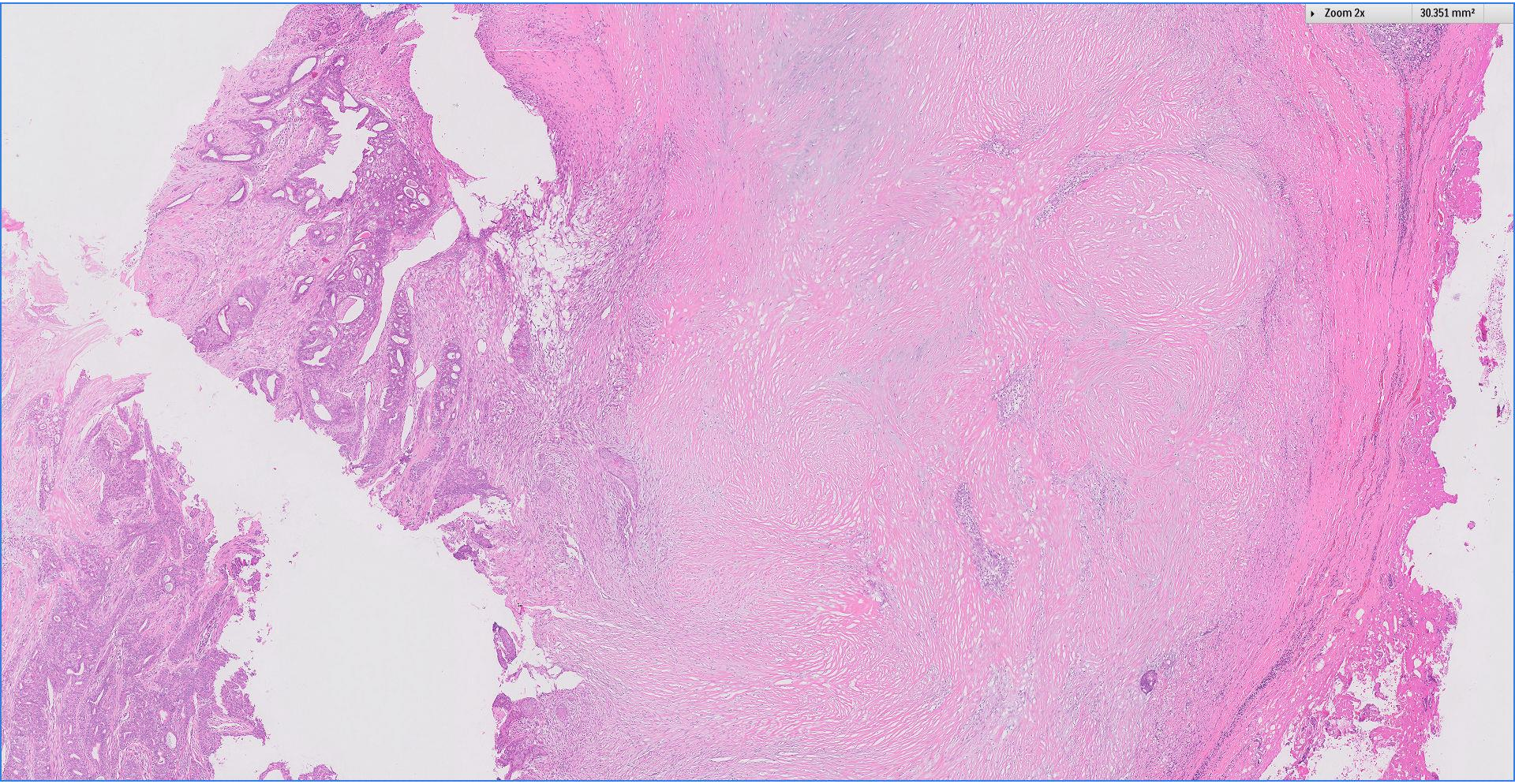
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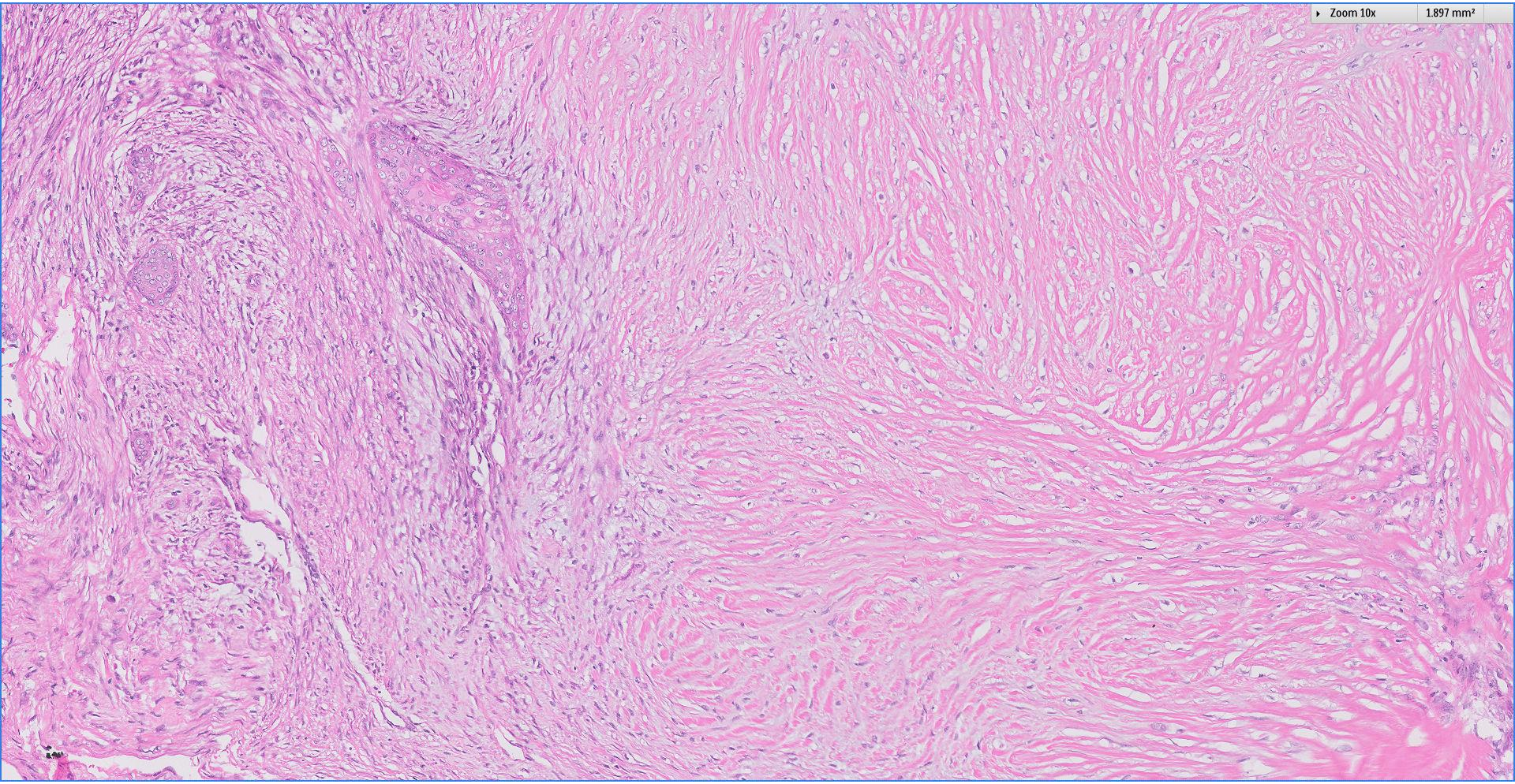
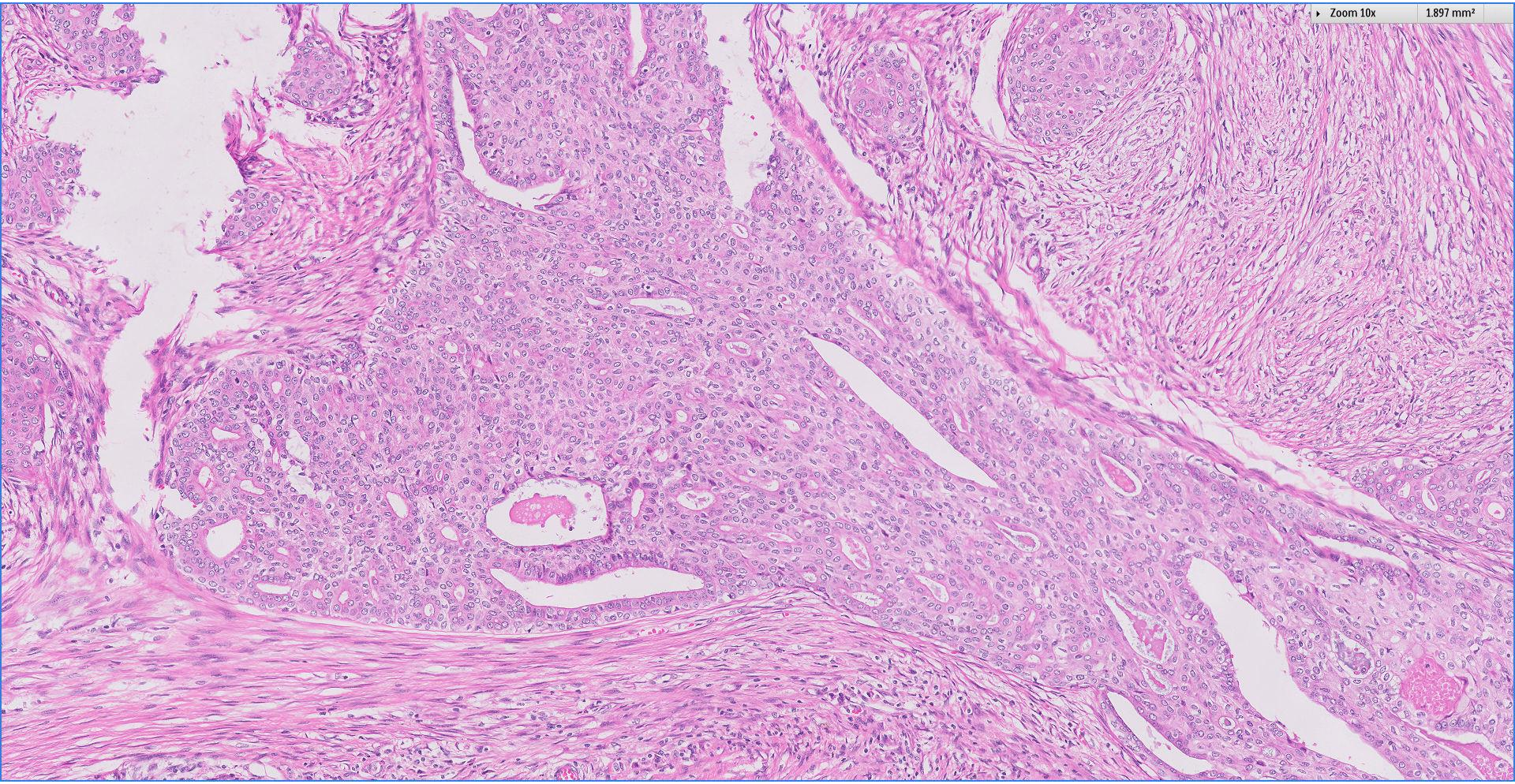

Zoom 10x
1.897 mm²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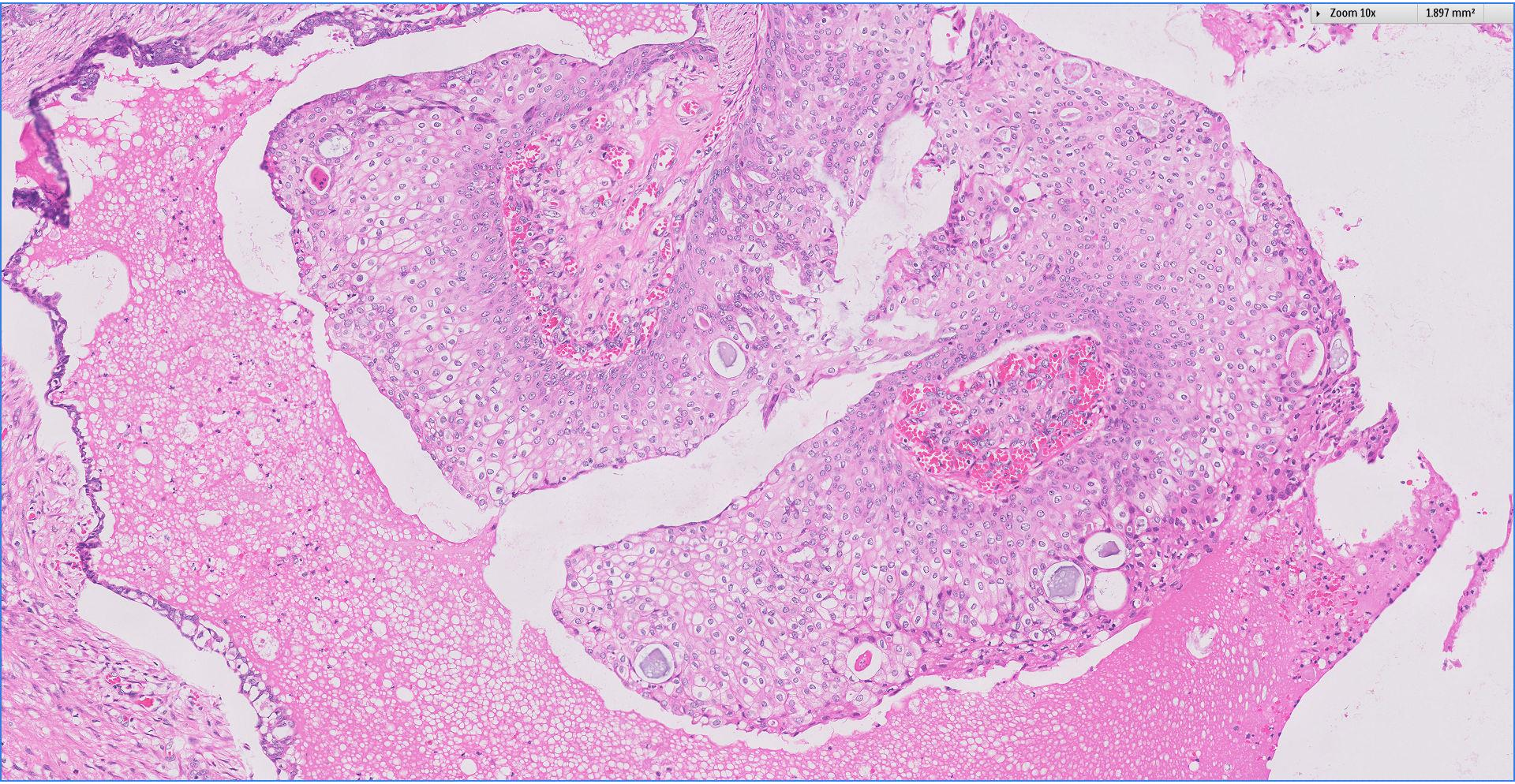
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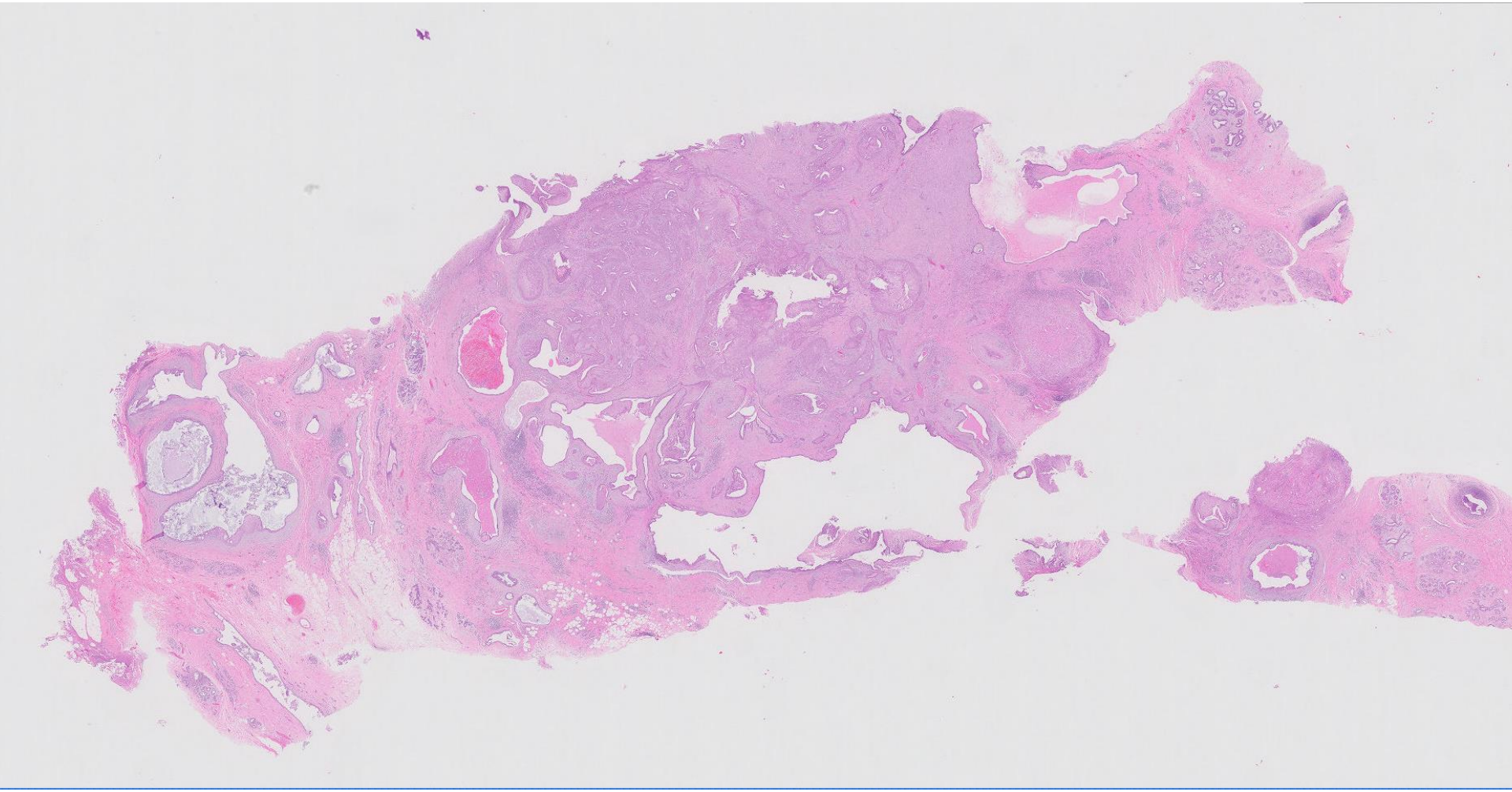

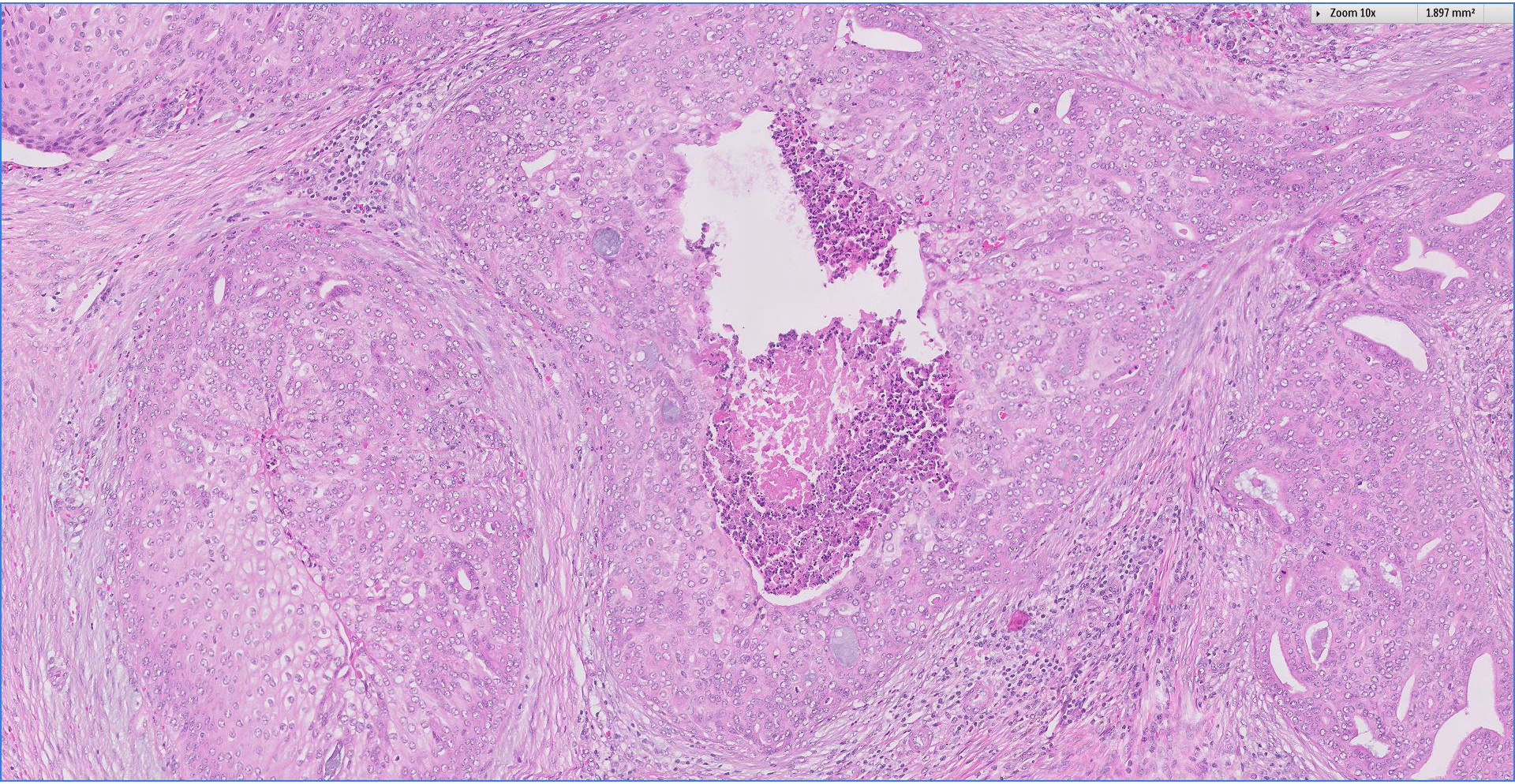
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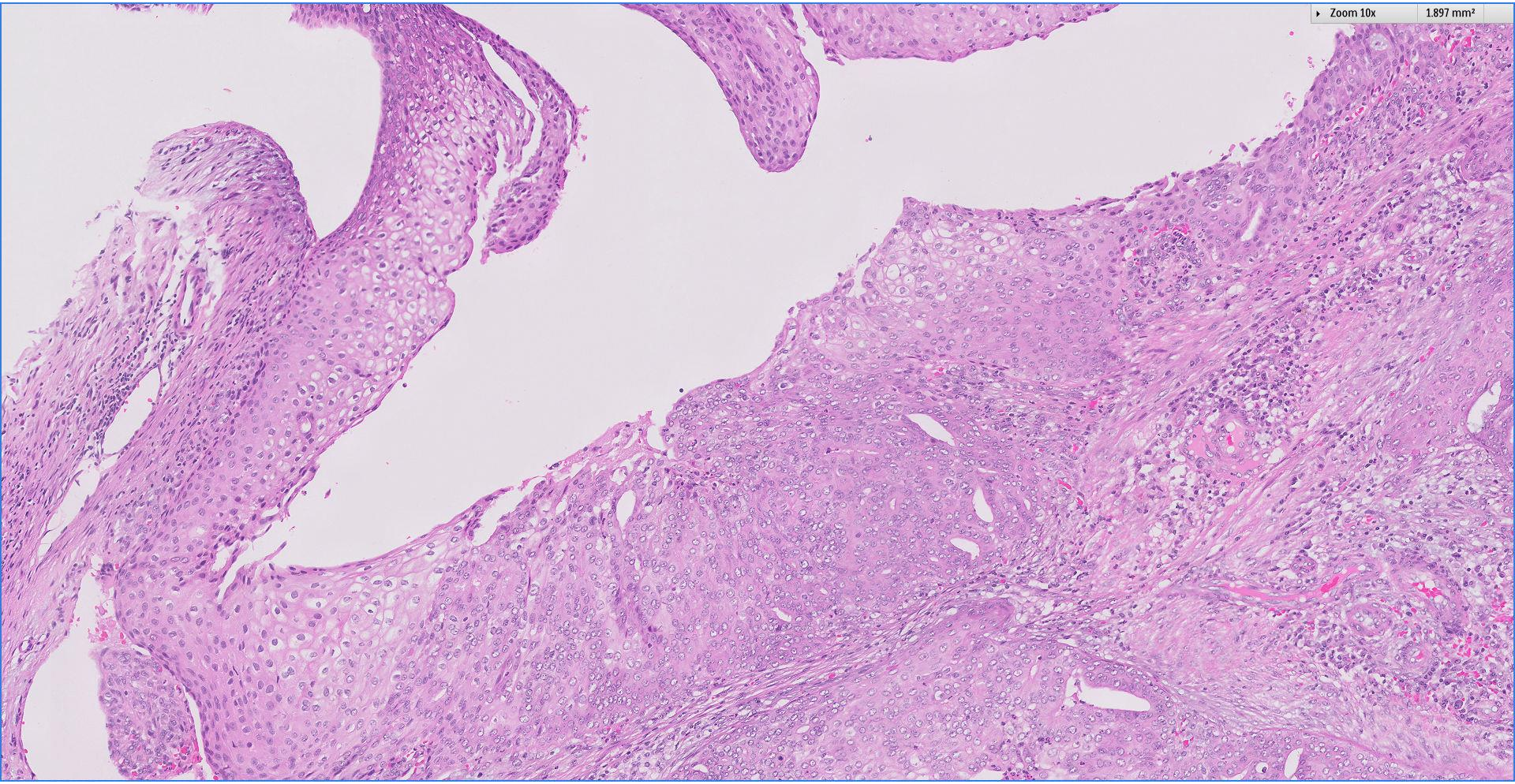
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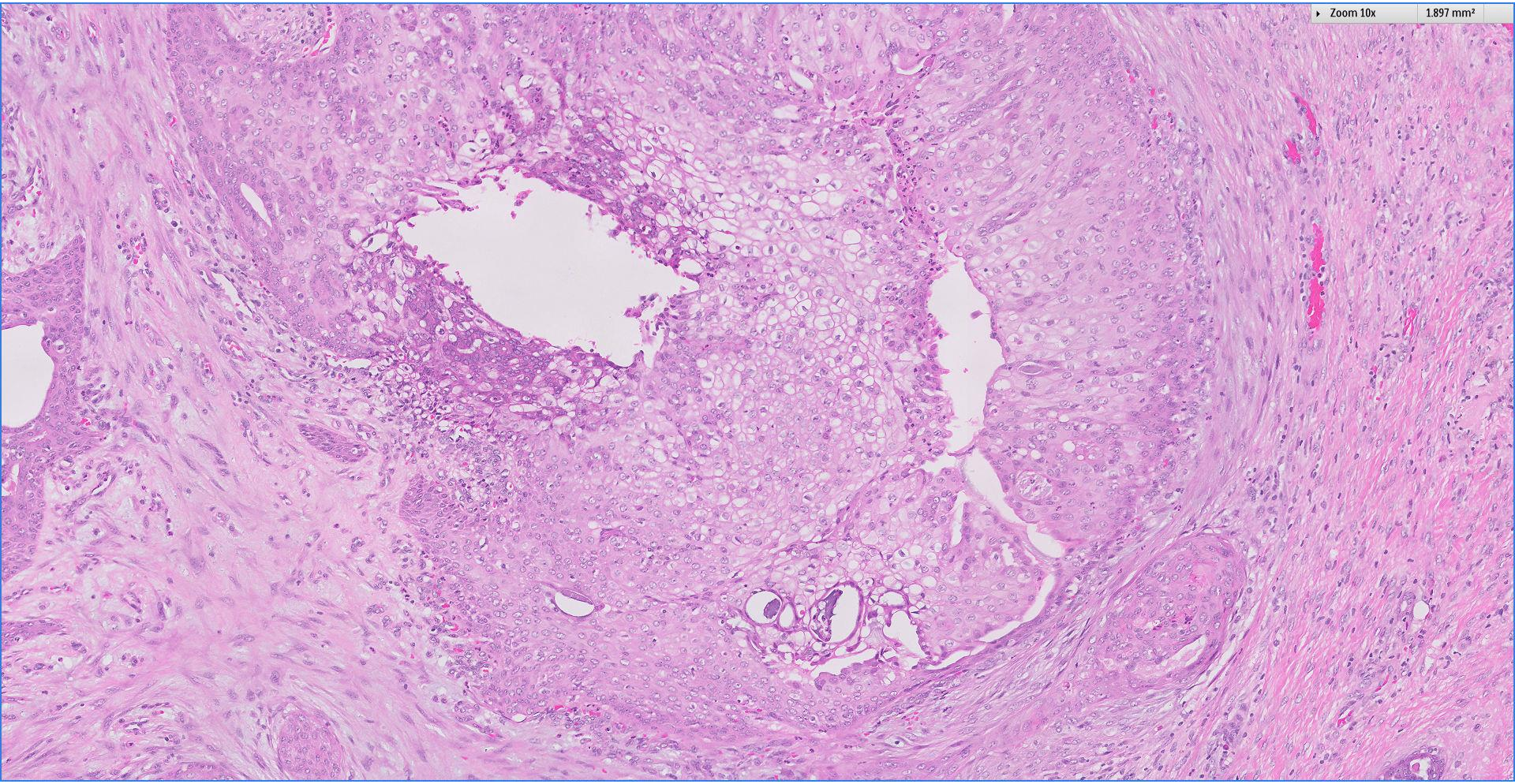
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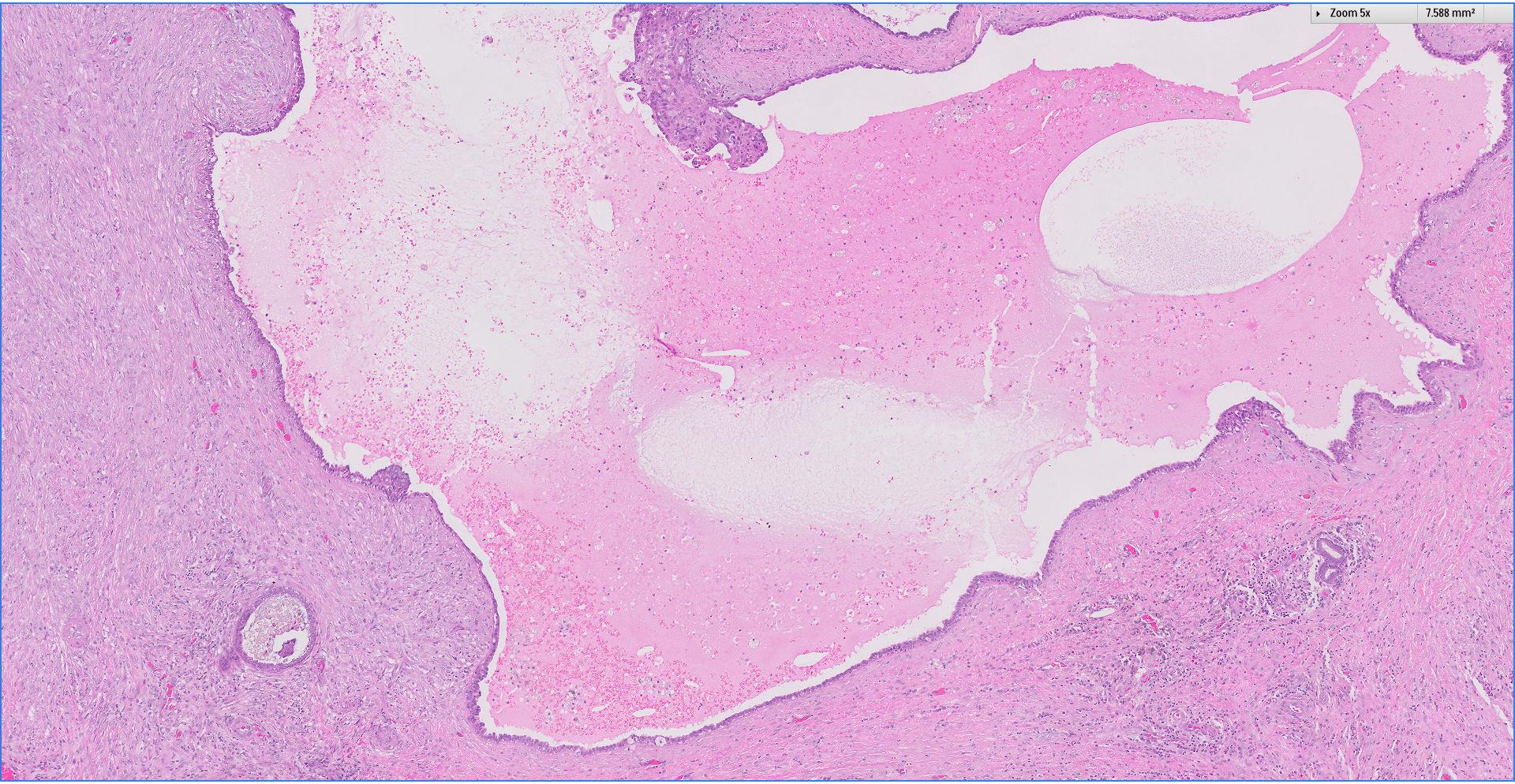
Zoom 5x
7.588 mm²

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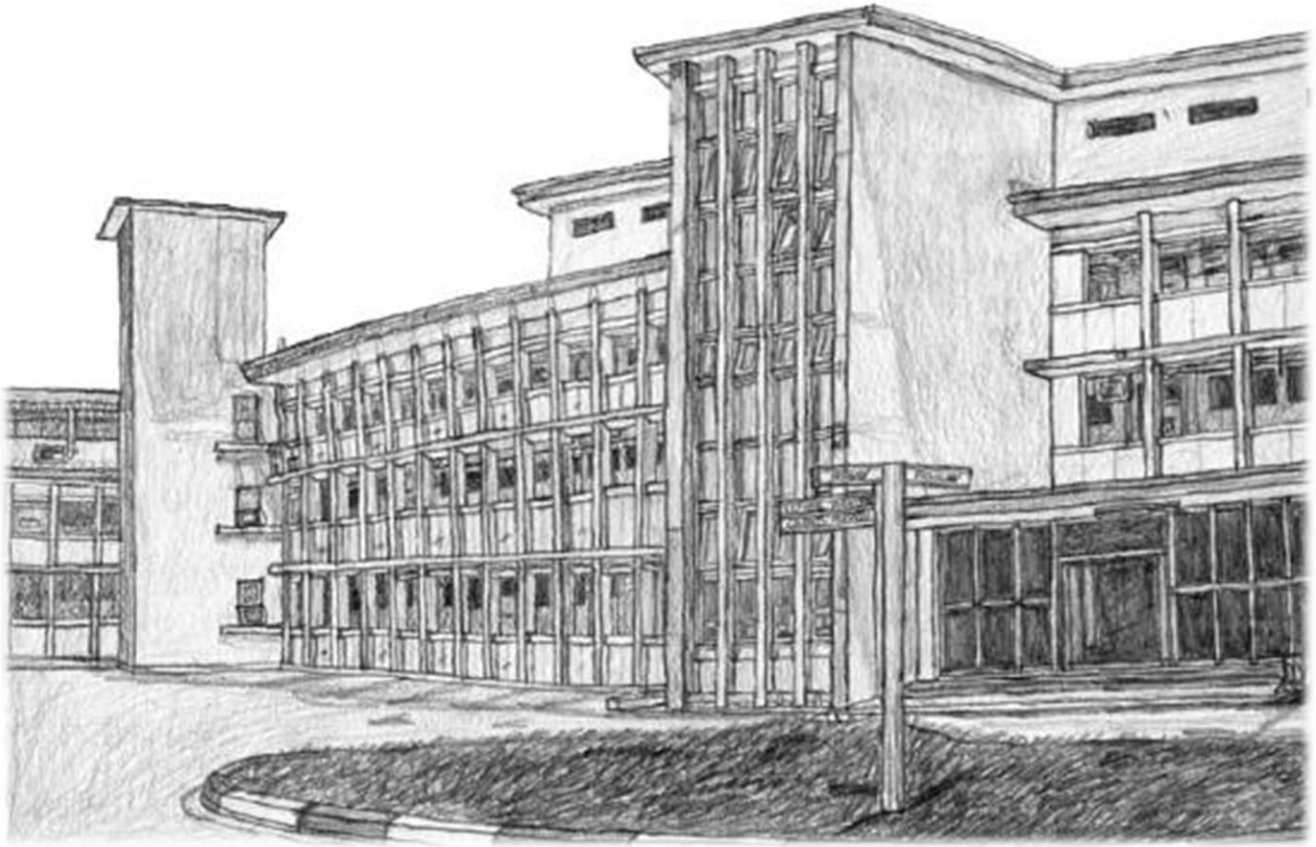

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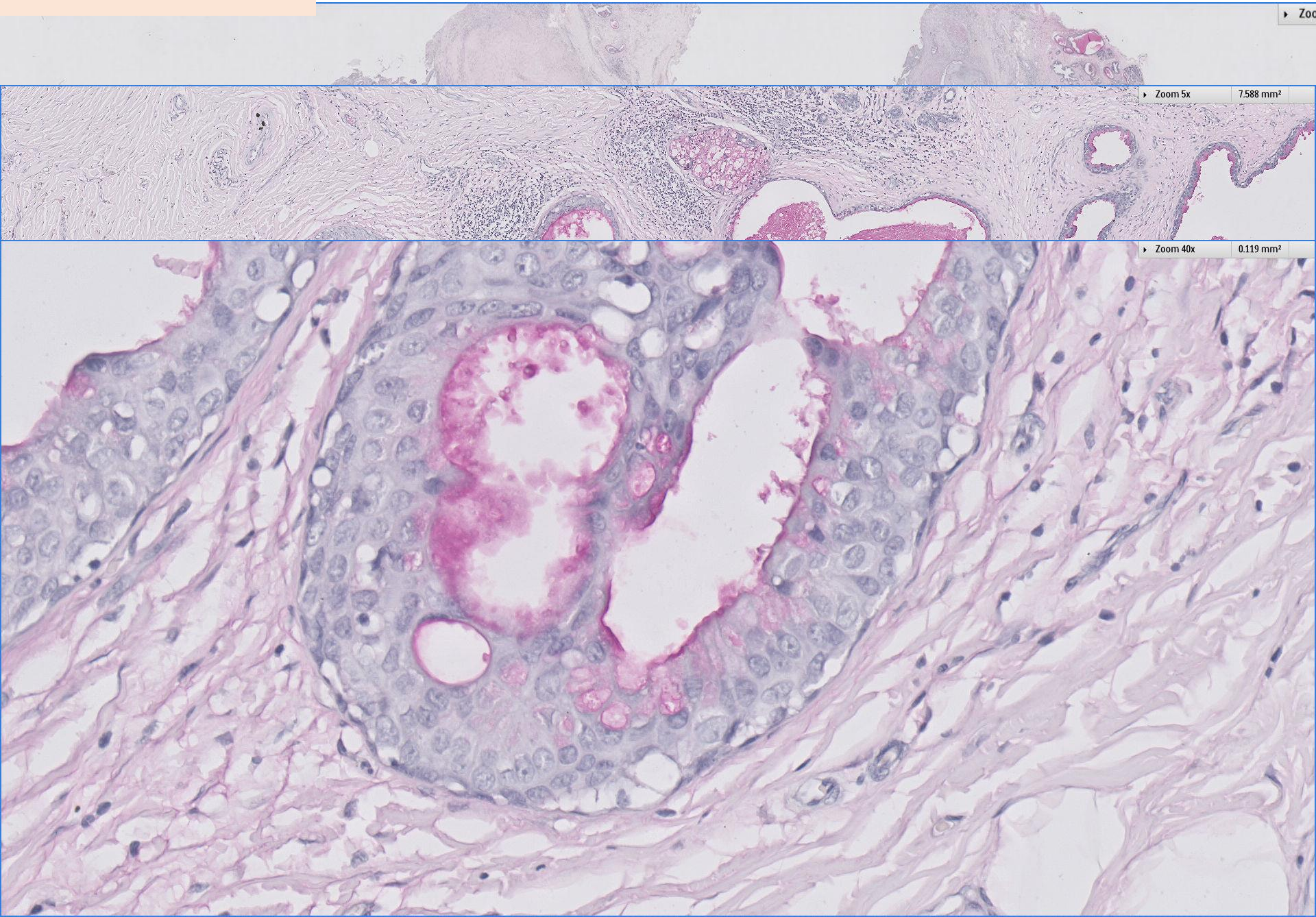
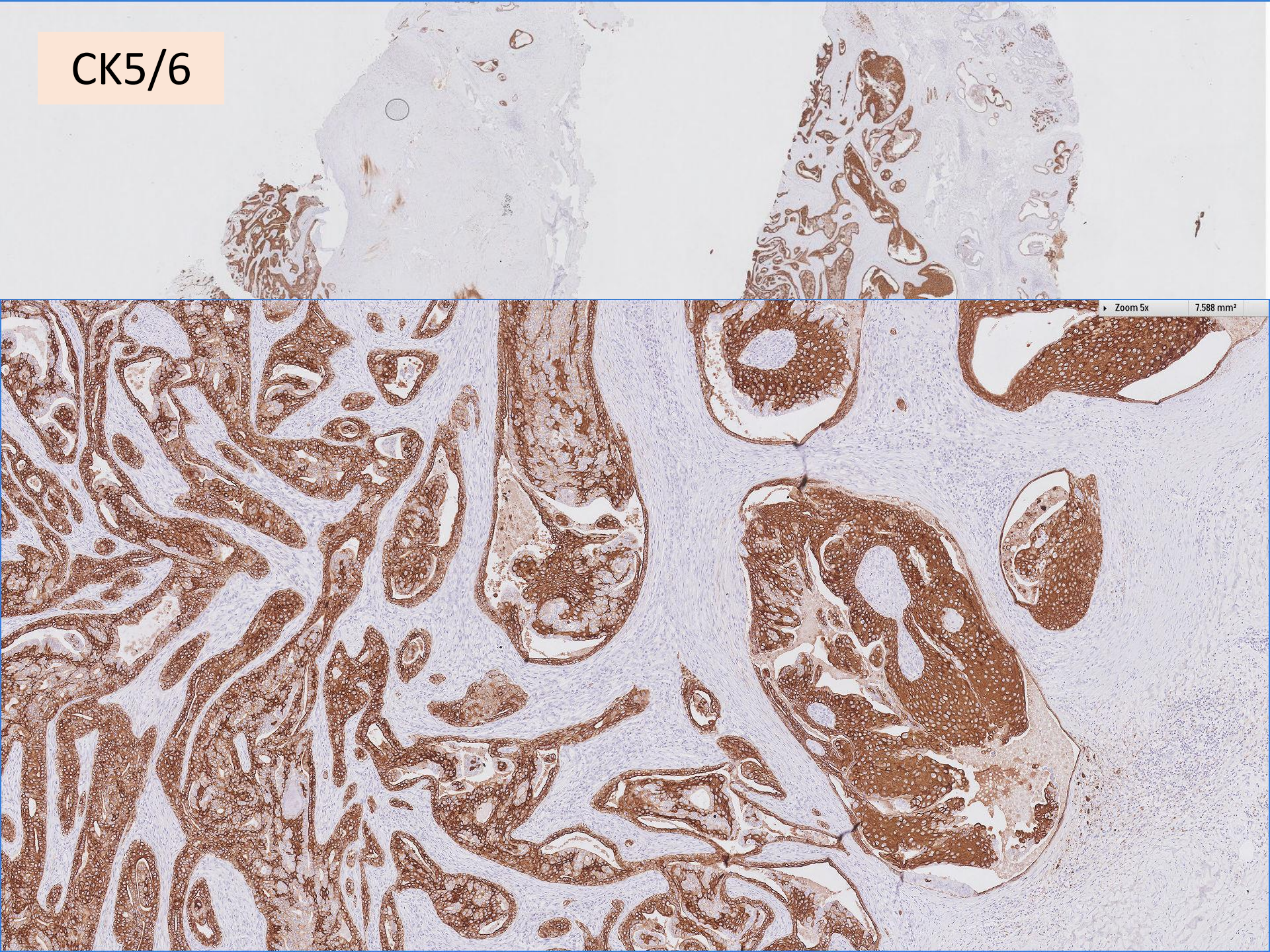
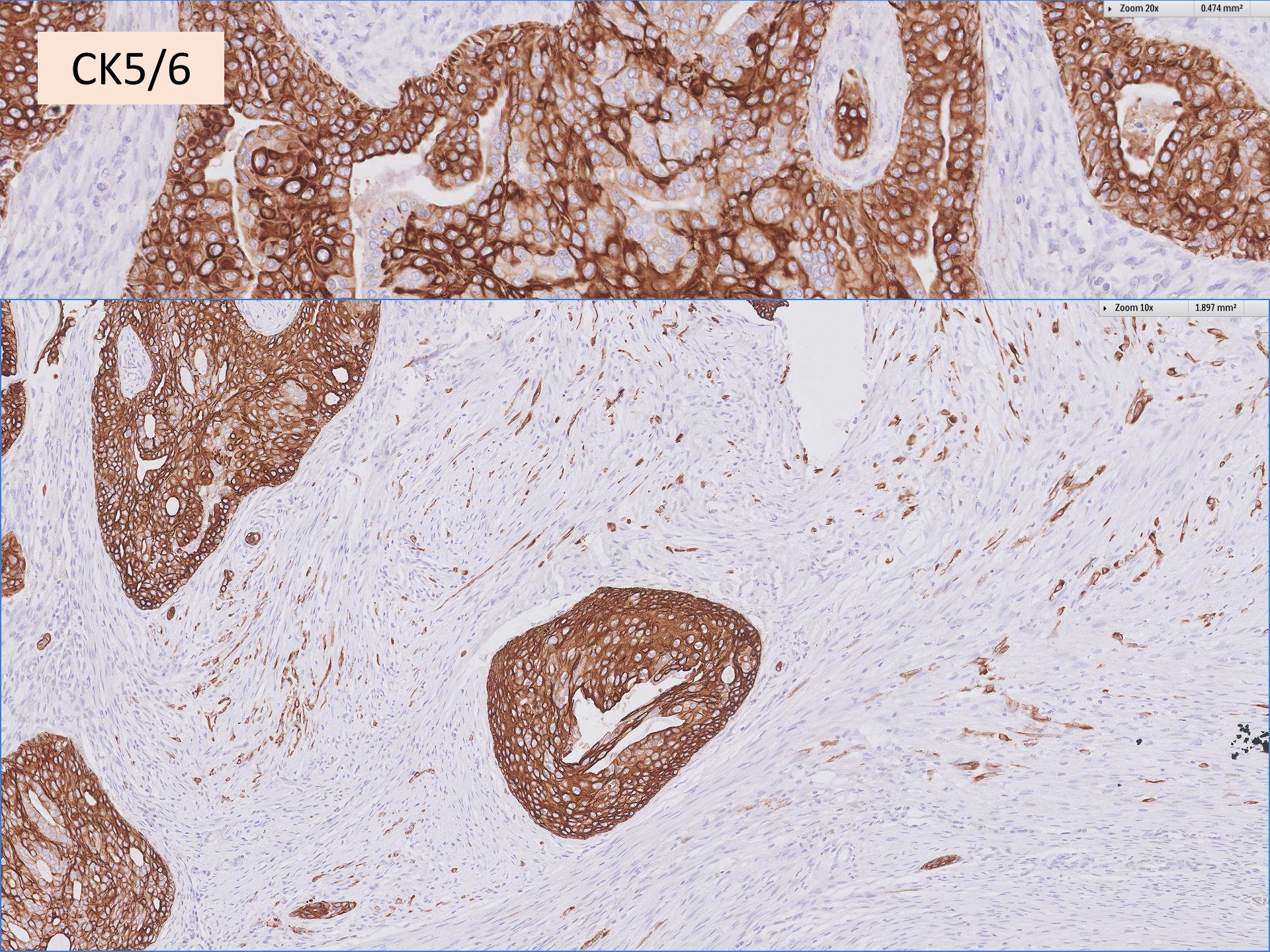
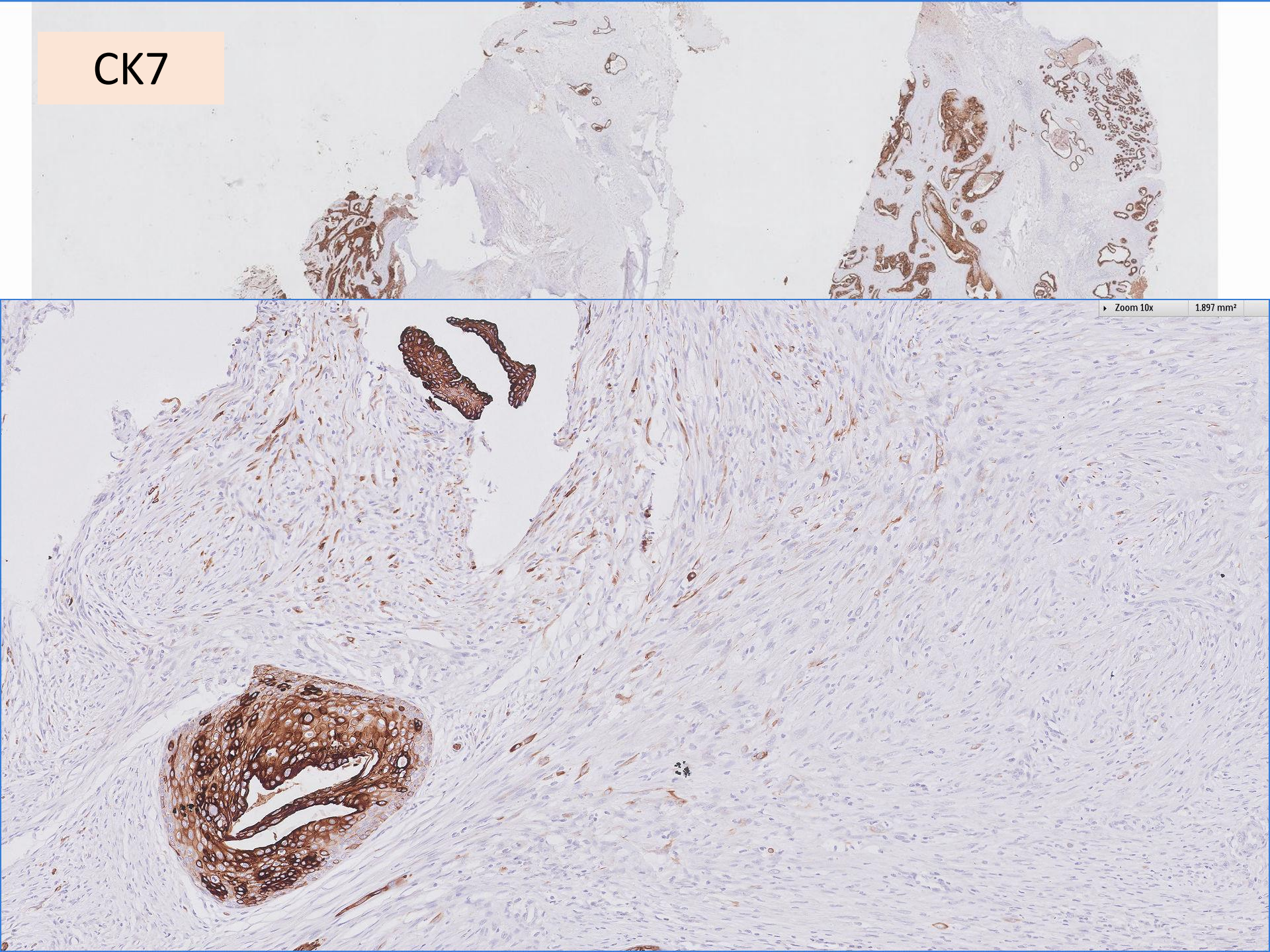
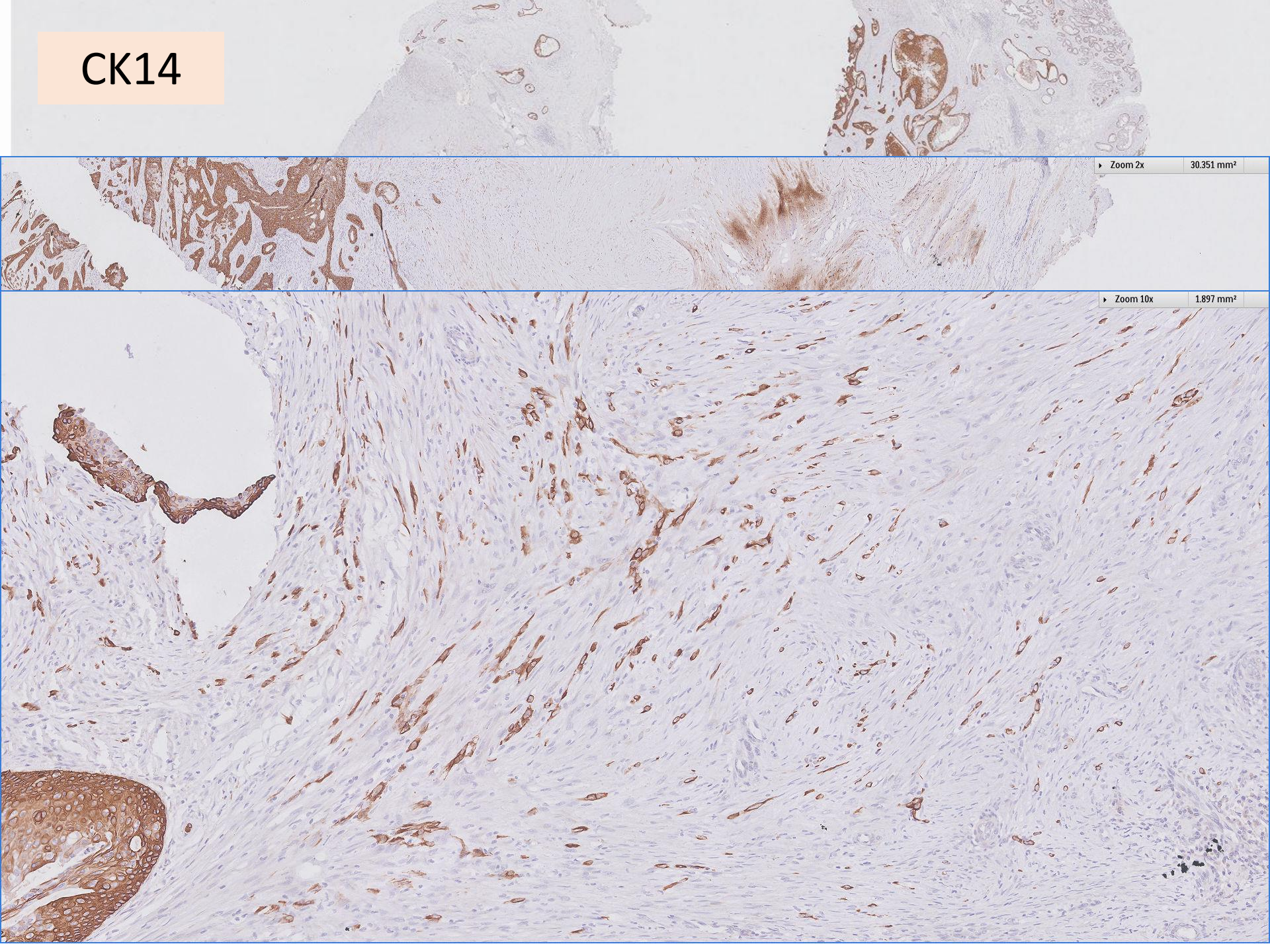
Mucicarmine

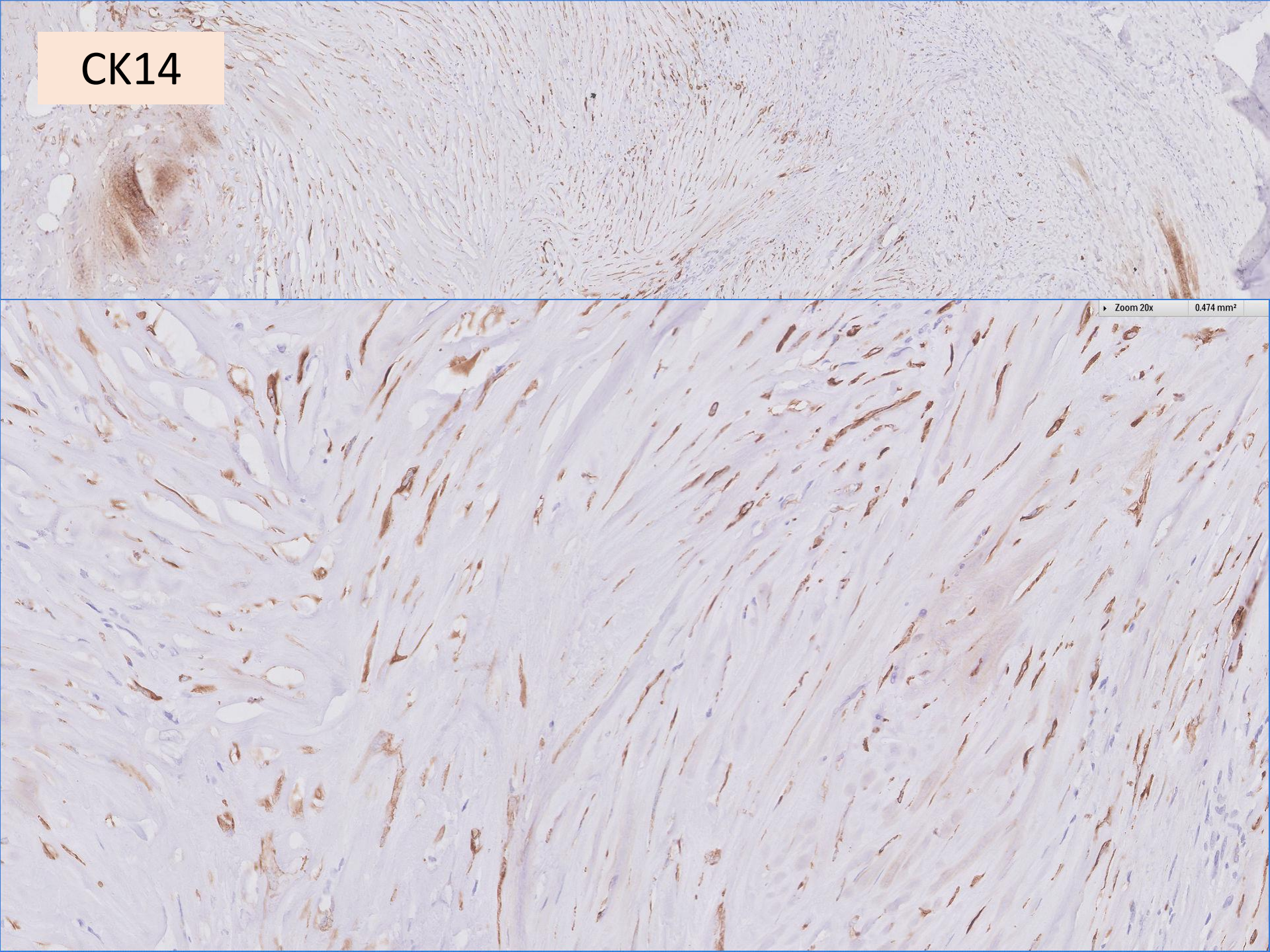



CK5/6
Zoom 5x
7.588 mm²

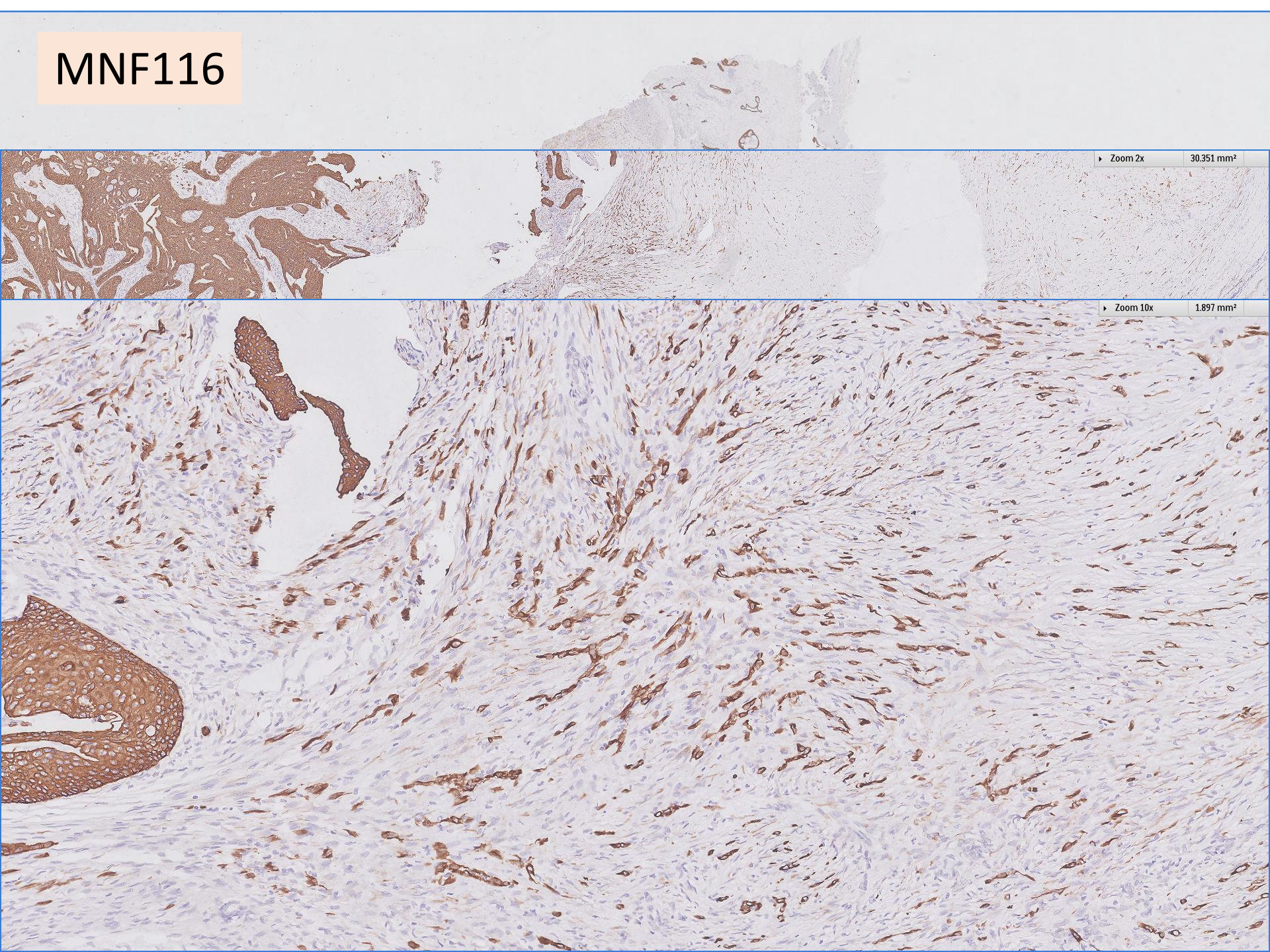

CK5/6
Zoom 20x
0.474 mm²
Zoom 10x
1.897 mm²


CK7
Zoom 10x
1.897 mm²

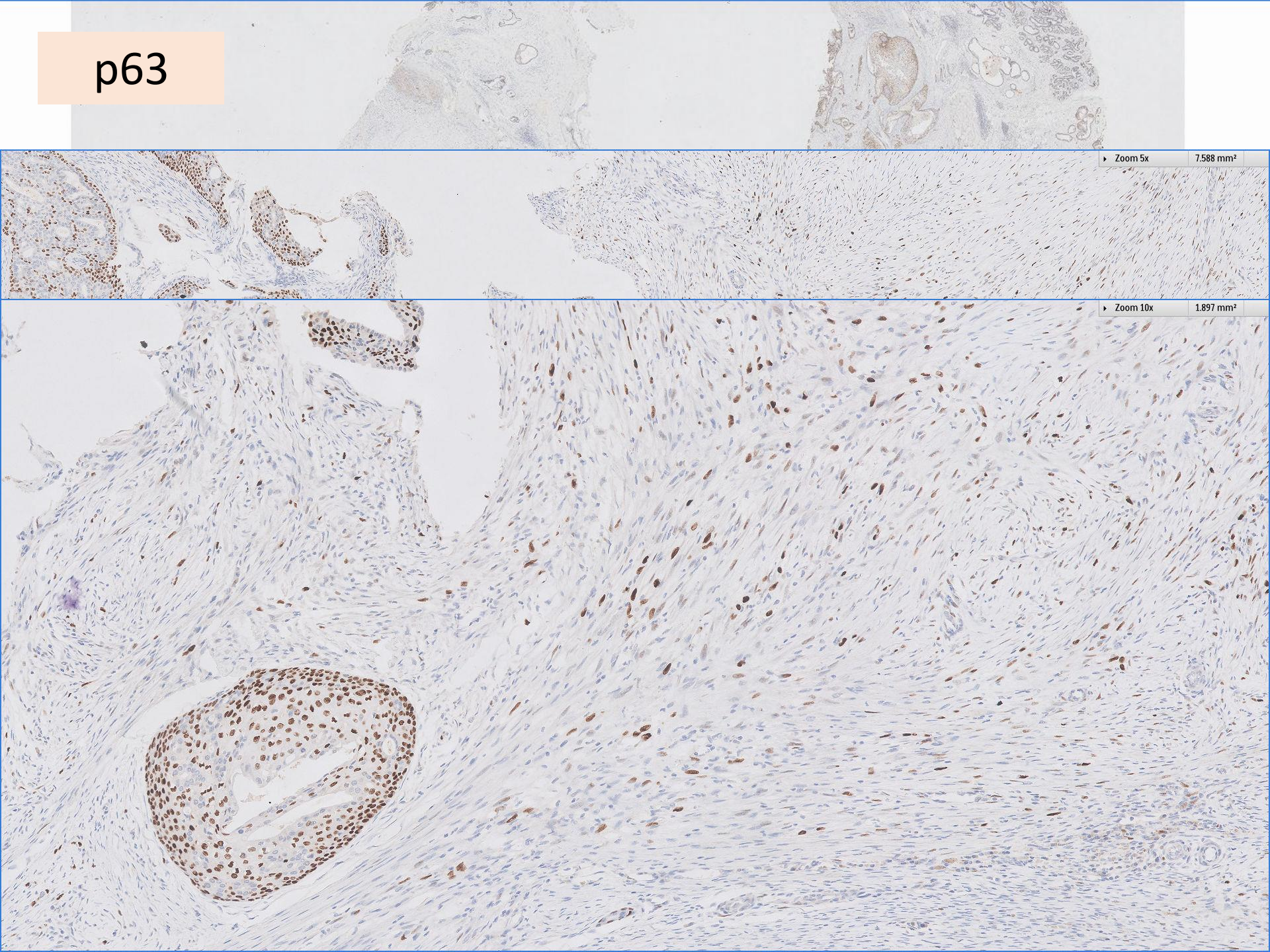

CK14
Zoom 2x
30.351 mm²
Zoom 10x
1.897 mm²

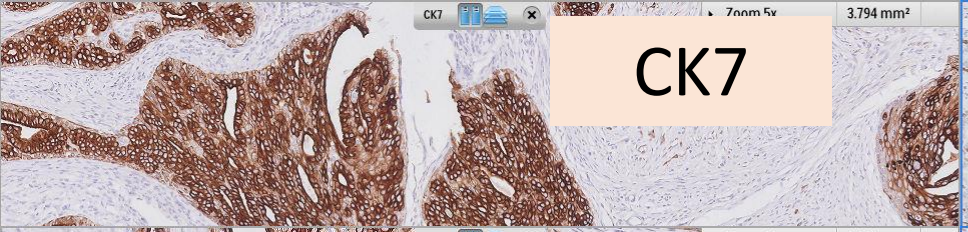

CK14
Zoom 20x
0.474 mm²

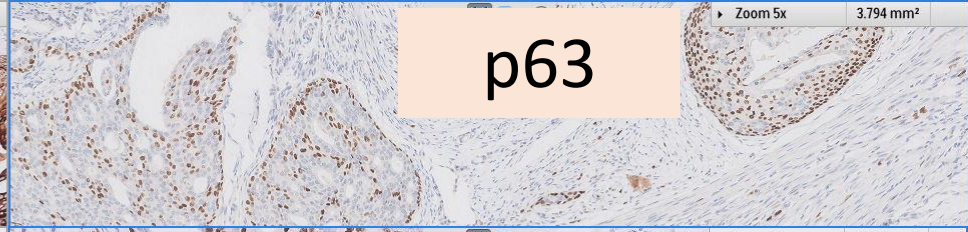
MNF116



p63




CK7
Zoom 5x
3.794 mm²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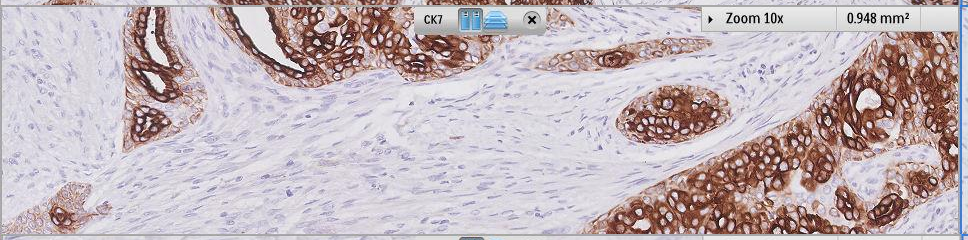
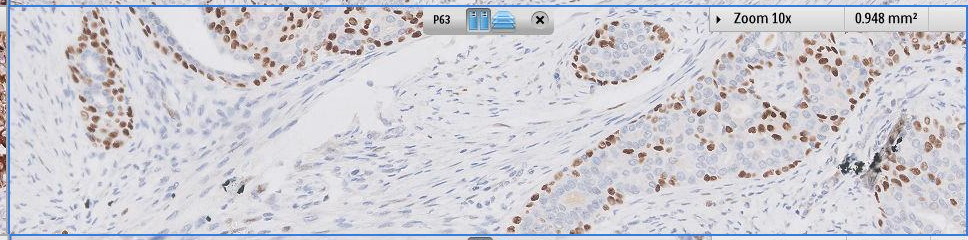
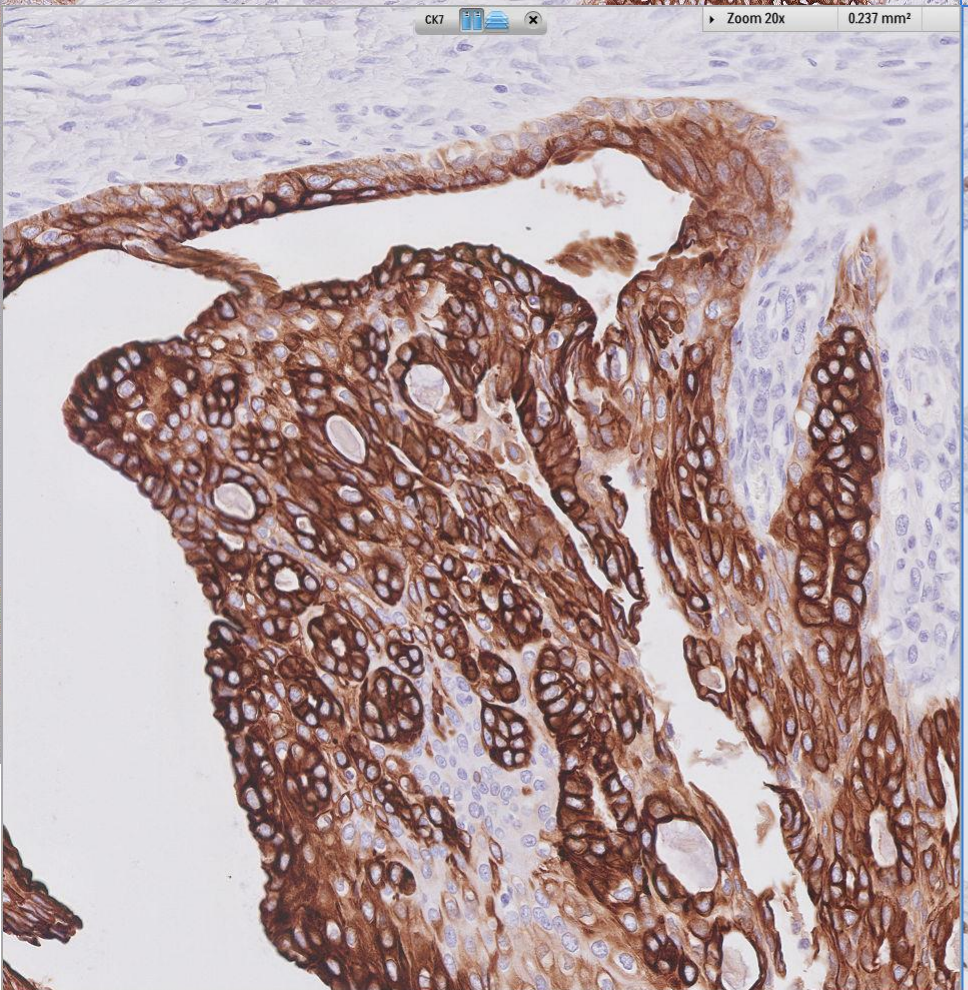
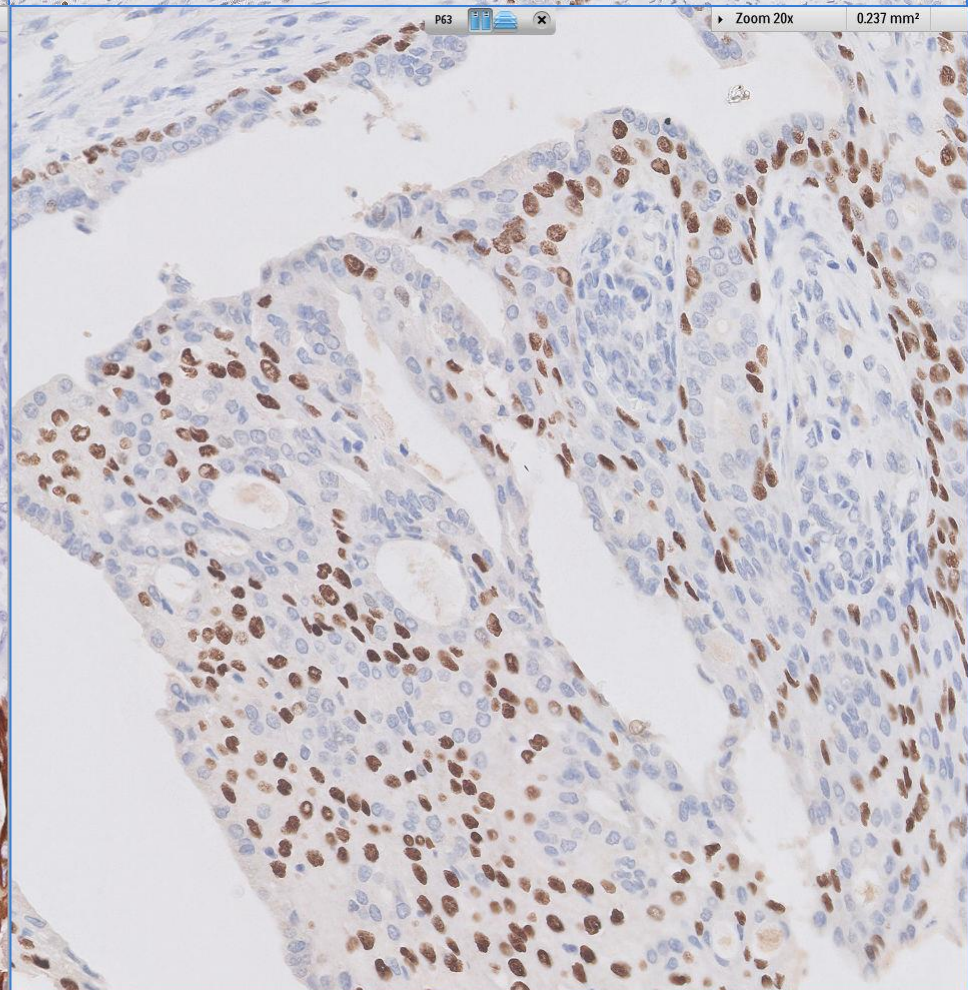
Zoom 5x
3.794 mm²


CK7
Zoom 10x
0.948 mm²


P63
Zoom 10x
0.948 mm²


CK7
Zoom 20x
0.237 mm²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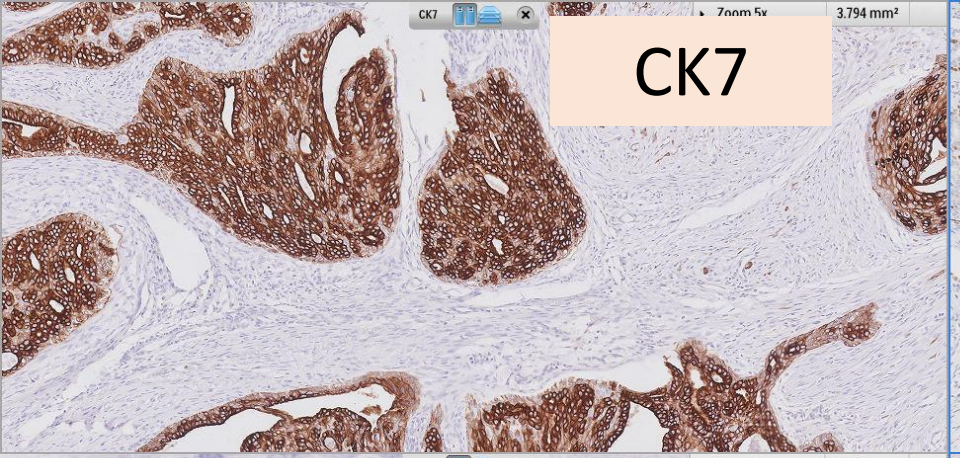
Zoom 20x
0.237 mm²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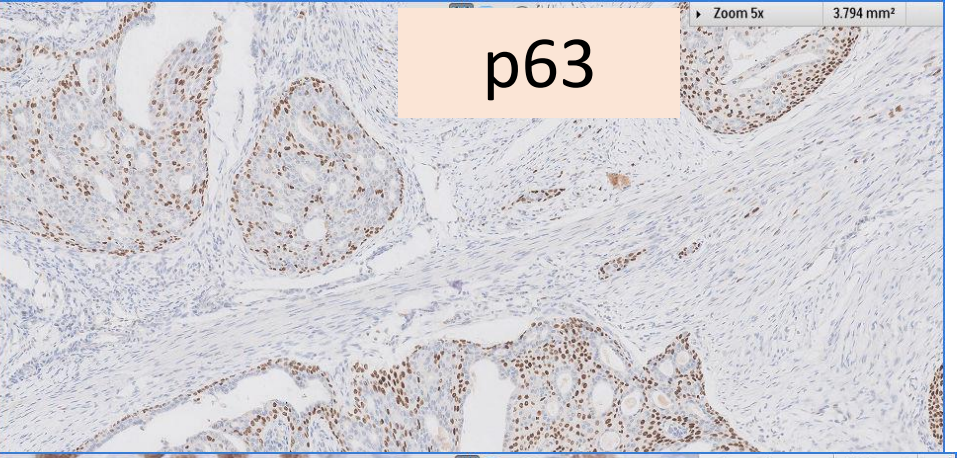
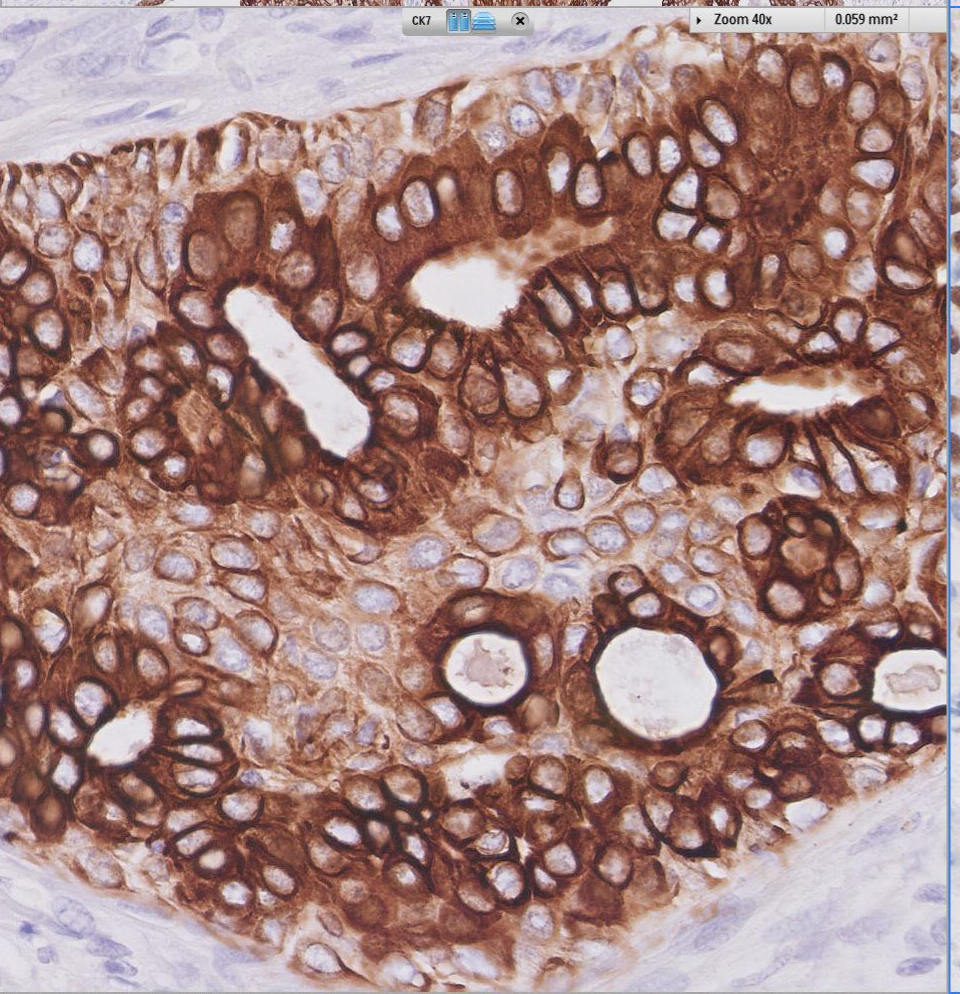
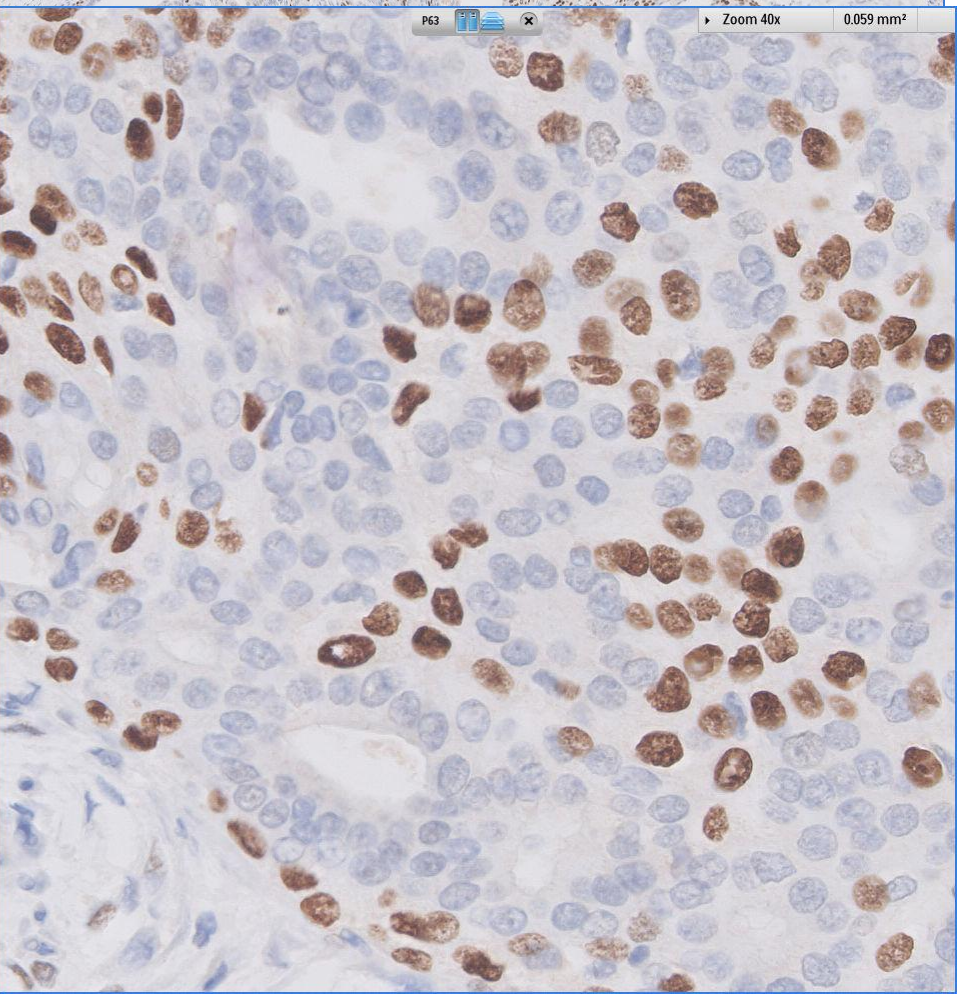
3.794 mm²


p63
Zoom 5x
3.794 mm²


CK7
Zoom 40x
0.059 mm²


P63
Zoom 40x
0.059 mm²

Summary of histological features

- Solid-cystic tumour.
- Papillary component
- Epithelial-myoepithelial appearance.
- Squamoid foci.
- Mucin and possible mucinous cells.
- Dense fibrocollagenous-like paucicellular spindle cell zone with keratin and p63 positivity.

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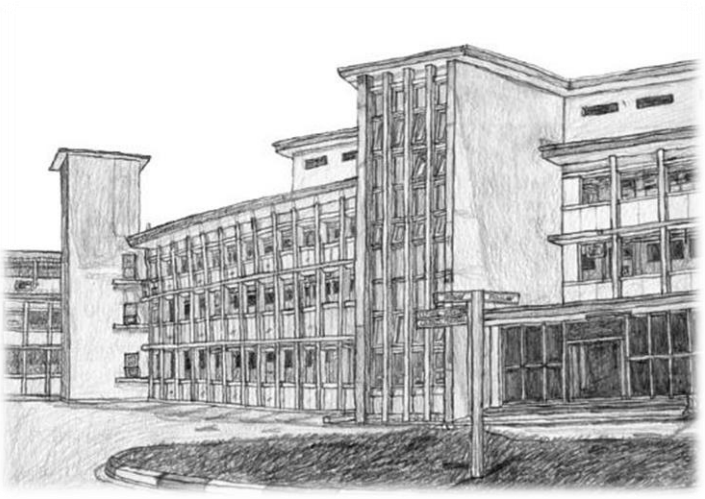
Diagnosis

Adenomyoepithelial tumour with suggestion of mucoepidermoid component and low grade fibromatosis-like metaplastic carcinoma.



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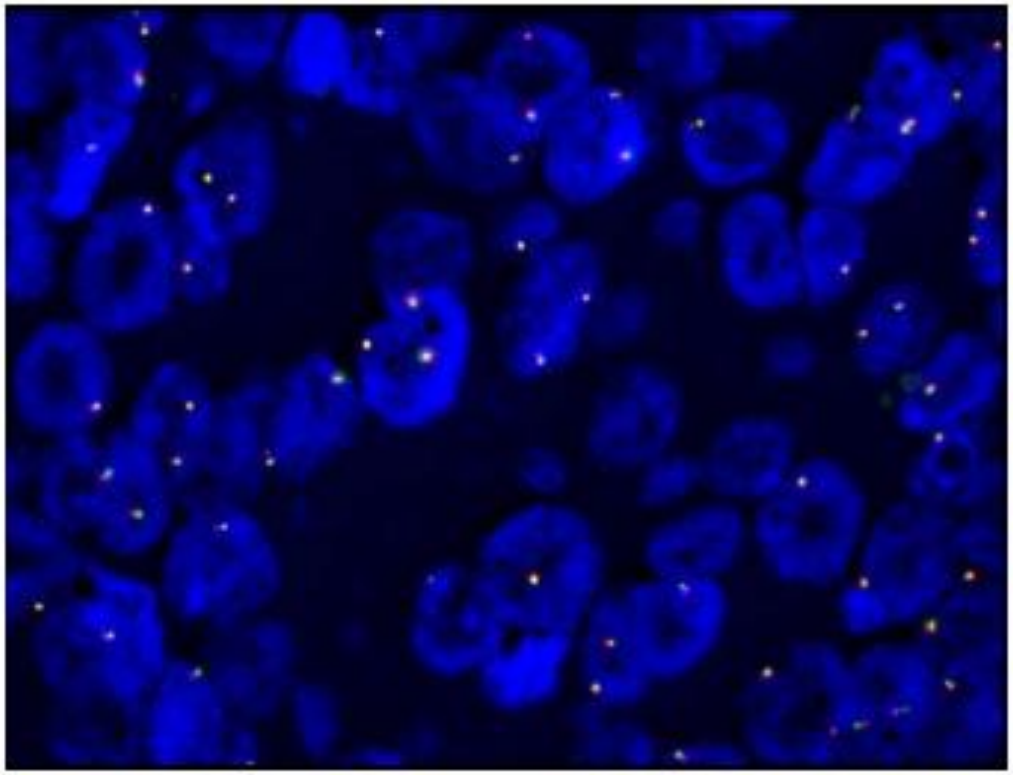
Mucoepidermoid carcinoma of breast

- Rare tumour in the breast, resembling its counterpart in the salivary gland, with basaloid, intermediate, epidermoid and mucinous cells.
- Most are low grade with a prevalence of mucous cells.
- High-grade tumours are rare, generally solid, and contain predominantly intermediate and squamous cells.
- True keratinization with formation of squamous pearls should exclude mucoepidermoid carcinoma and favour the diagnosis of metaplastic carcinoma with squamous differentiation.

Mucoepidermoid carcinoma of breast

- MAML2 rearrangements are described, similar to those in the salivary gland.
- In this case, MAML2 rearrangements were not identified.

Case No: A6464
FISH Probe: MAML2 Break Apart



The MAML2 dual color break apart probe consists of two direct labeled probes hybridized to 11q21 band. The green fluorohrome direct labeled probe hybridizes distal to the MAML2 gene and the orange fluorochrome direct labeled probe hybridizes proximal to the gene.

100% of 200 nuclei scored showed two normal fusion signals indicating absence of MAML2 gene rearrangement.

Title: *CRTC1-MAML2* Fusion in Mucoepidermoid Carcinoma of the Breast

Authors: Gregory R Bean[1], Gregor Krings[2], Christopher N Otis[3], David A Solomon[2], Joaquín J García[4], Annemieke van Zante[2], Sandra Camelo-Piragua[5], Jessica Van Ziffle[2], Yunn-Yi Chen[2]

Histopathology epub

Aims Mucoepidermoid carcinomas (MEC) are the most common malignant neoplasms of salivary glands but are uncommon in other sites. Salivary gland MEC are most frequently associated with *CRTC1-MAML2* translocations. Exceedingly rare MEC of the breast demonstrate a basal-like and often triple (estrogen and progesterone receptor, HER2) negative immunophenotype, with a single case previously reported to show *MAML2* rearrangement, although the fusion partner was not known. Comprehensive genomic studies of breast MEC are lacking. In this study, we analyzed the immunophenotype and molecular landscape of two breast MEC to elucidate the pathogenesis of these rare tumors.

Methods and Results Two breast MEC were subjected to capture-based next-generation DNA sequencing of 479 cancer-related genes. The presence of the *CRTC1-MAML2* fusion transcript was interrogated by reverse-transcriptase polymerase chain reaction. In addition, the immunoprofiles of breast MEC were compared to salivary gland MEC. Both breast MEC harbored *CRTC1-MAML2* fusions. In contrast to most triple-negative breast carcinomas of no special type, the mutational burden of MEC was very low, with one case demonstrating only an inactivating *SETD2* mutation, and the other harboring no somatic variants in genes on the panel. No copy number alterations were identified. The immunoprofiles of breast and salivary gland MEC were overlapping but not identical.

Conclusions The findings highlight MEC as a breast cancer subtype more closely related to its salivary gland counterpart than to basal-like/triple-negative breast cancers of no special type.

Table 2: Morphologic mimics of breast mucoepidermoid carcinoma.

Differential diagnosis	Features that may overlap with MEC	Features helpful in differential diagnosis
Simple cysts	Macrocystic architecture with one to few cell layers; mucoid material alone on limited sampling	Radiologic-pathologic correlation against simple cysts in MEC; presence of mucinous cells in MEC; negative SMM/calponin around cysts of MEC
UDH	Heterogeneous cell population with bland cytology and irregular microcystic spaces; strong positive CK5/6	Presence of mucinous and epidermoid cells in MEC; ER patchy positive in UDH and ER negative in MEC
DCIS, cribriform pattern	Rounded ductal contours with microcystic/cribriform architecture; well-defined cellular borders	Lack of nuclear polarization around spaces in MEC; positive CK5/6 and negative ER in MEC; negative CK5/6 and diffuse strong ER in DCIS
Metaplastic SCC	Squamoid tumor cells with overlapping immunophenotype (triple negative, positive CK5/6 and p63)	Circumscribed nodules of MEC versus infiltrative growth of SCC; multiple cell types in MEC; lack of true keratinization in MEC
Secretory carcinoma	Prominent cystic components; PASD-positive secretory material; cytologically bland tumor cells with overlapping immunophenotype (triple negative, positive mammaglobin and MUC4)	Positive p63 in MEC; positive S100 in secretory carcinoma; positive *MAML2* break-apart FISH in MEC; positive *ETV6* break-apart FISH in secretory carcinoma

Abbreviations: MEC – mucoepidermoid carcinoma; UDH – usual ductal hyperplasia; DCIS – ductal carcinoma in situ; SCC – squamous cell carcinoma; PASD – Periodic acid-Schiff, diastase; FISH – fluorescence in situ hybridization

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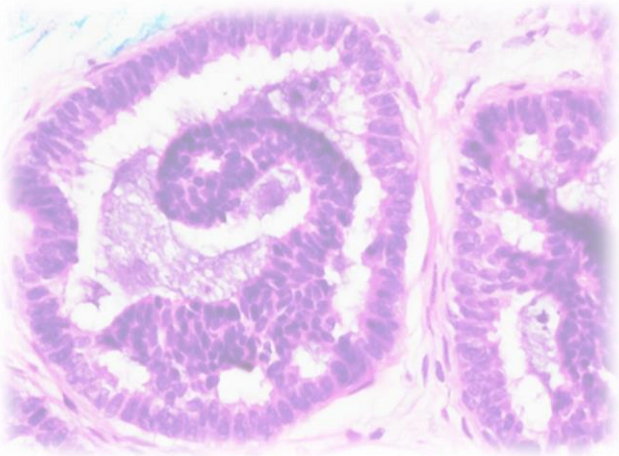
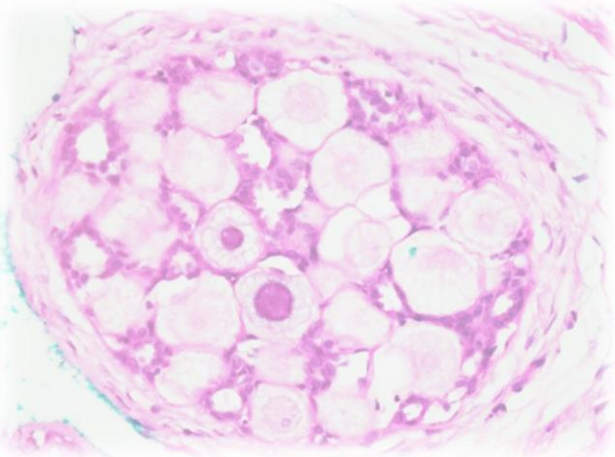
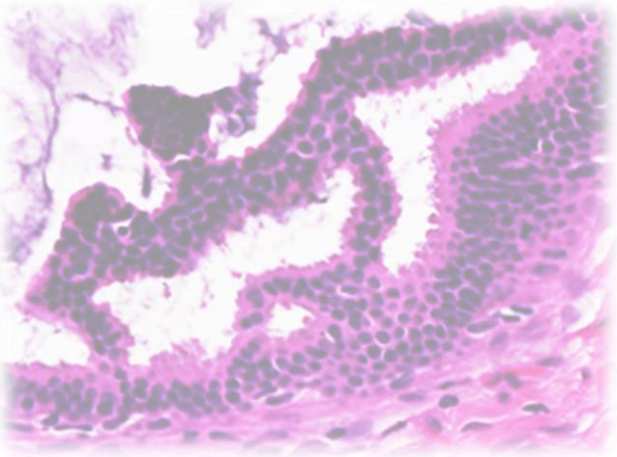
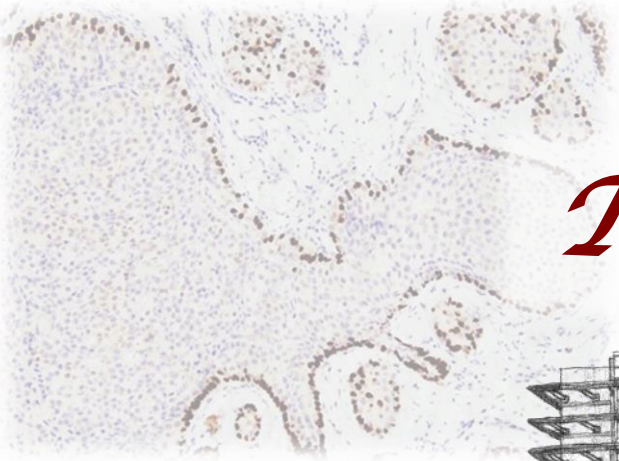

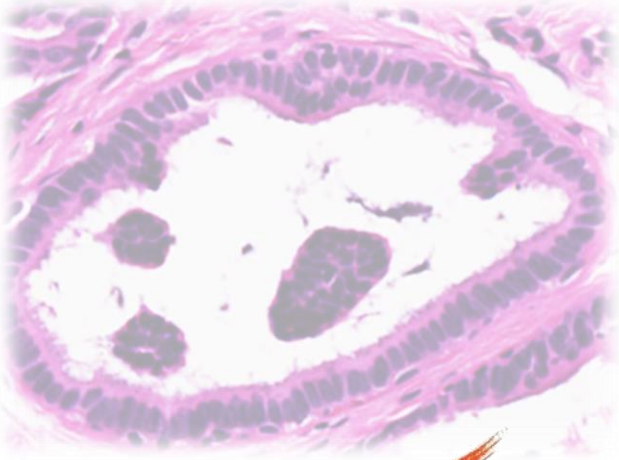

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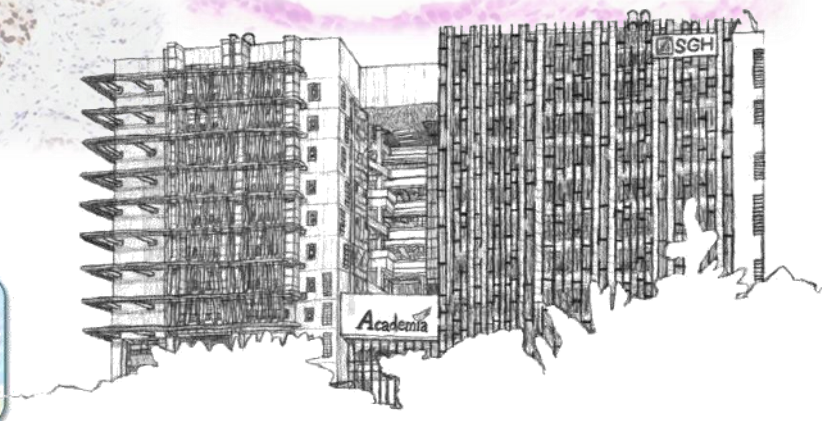

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