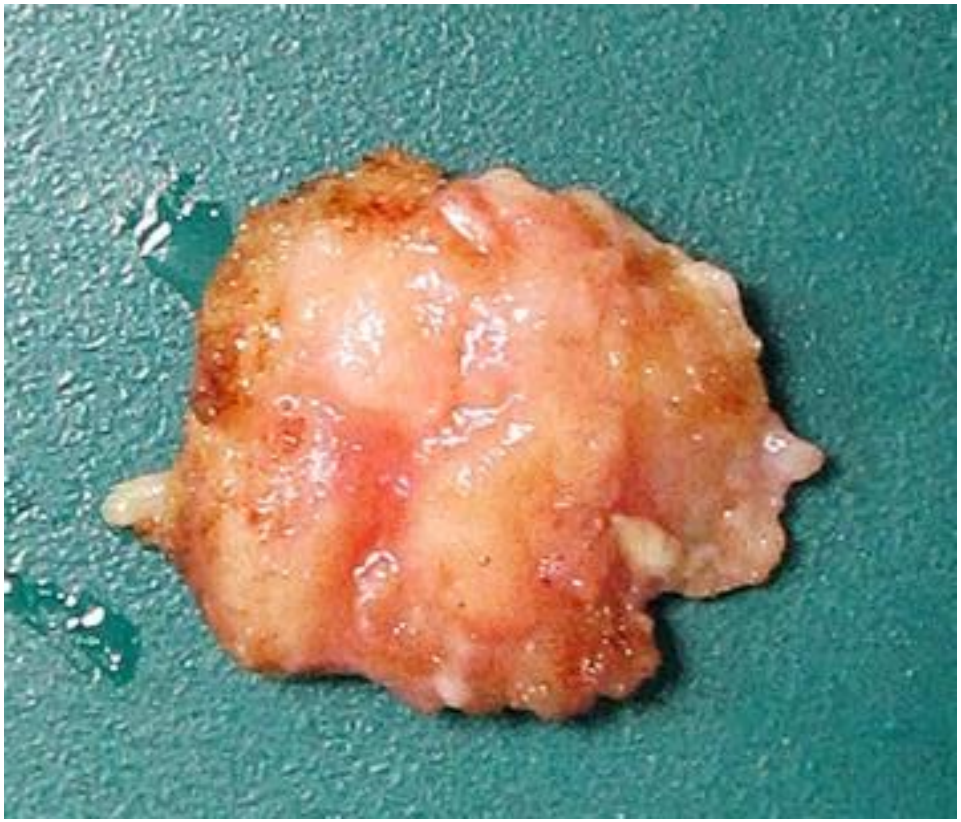
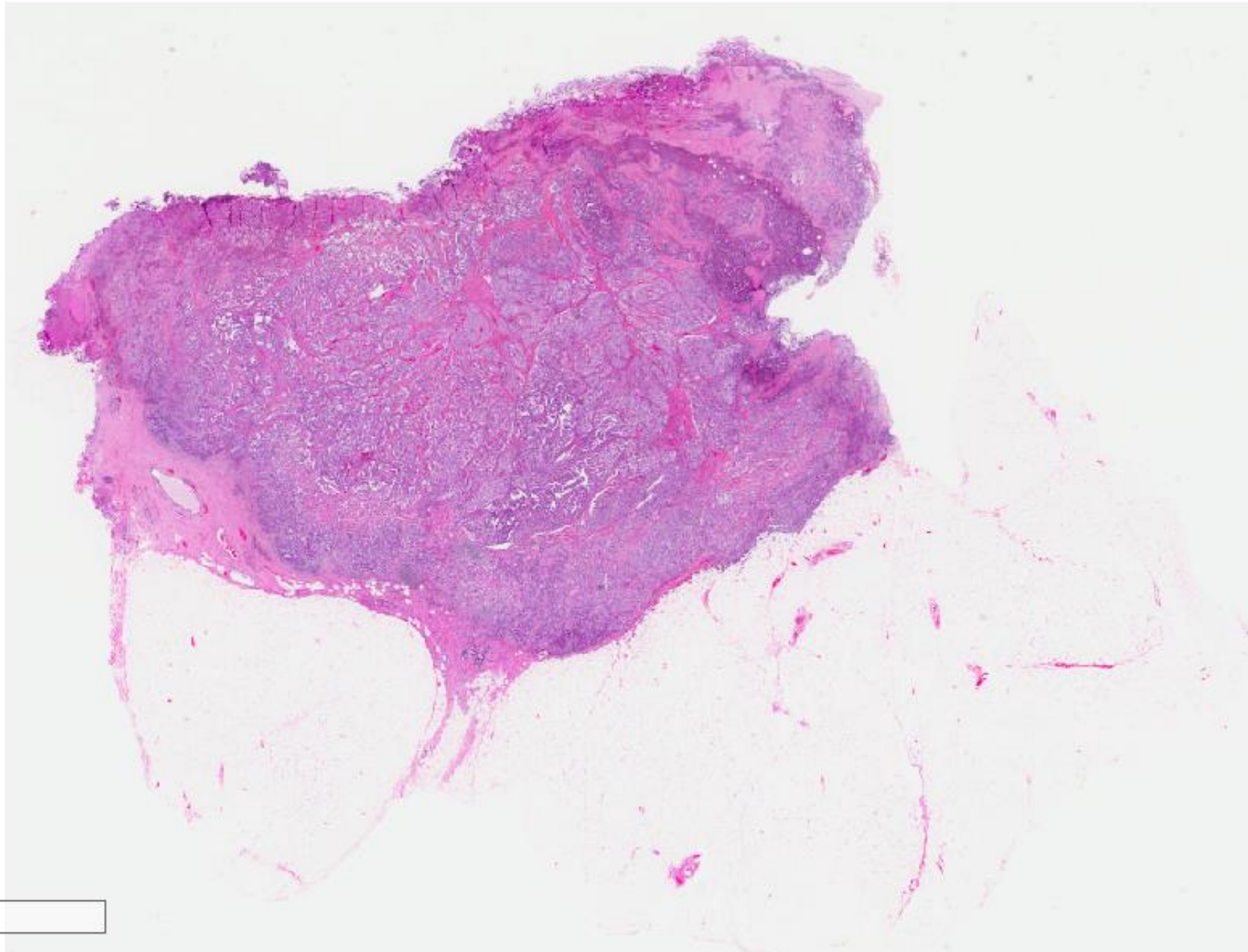
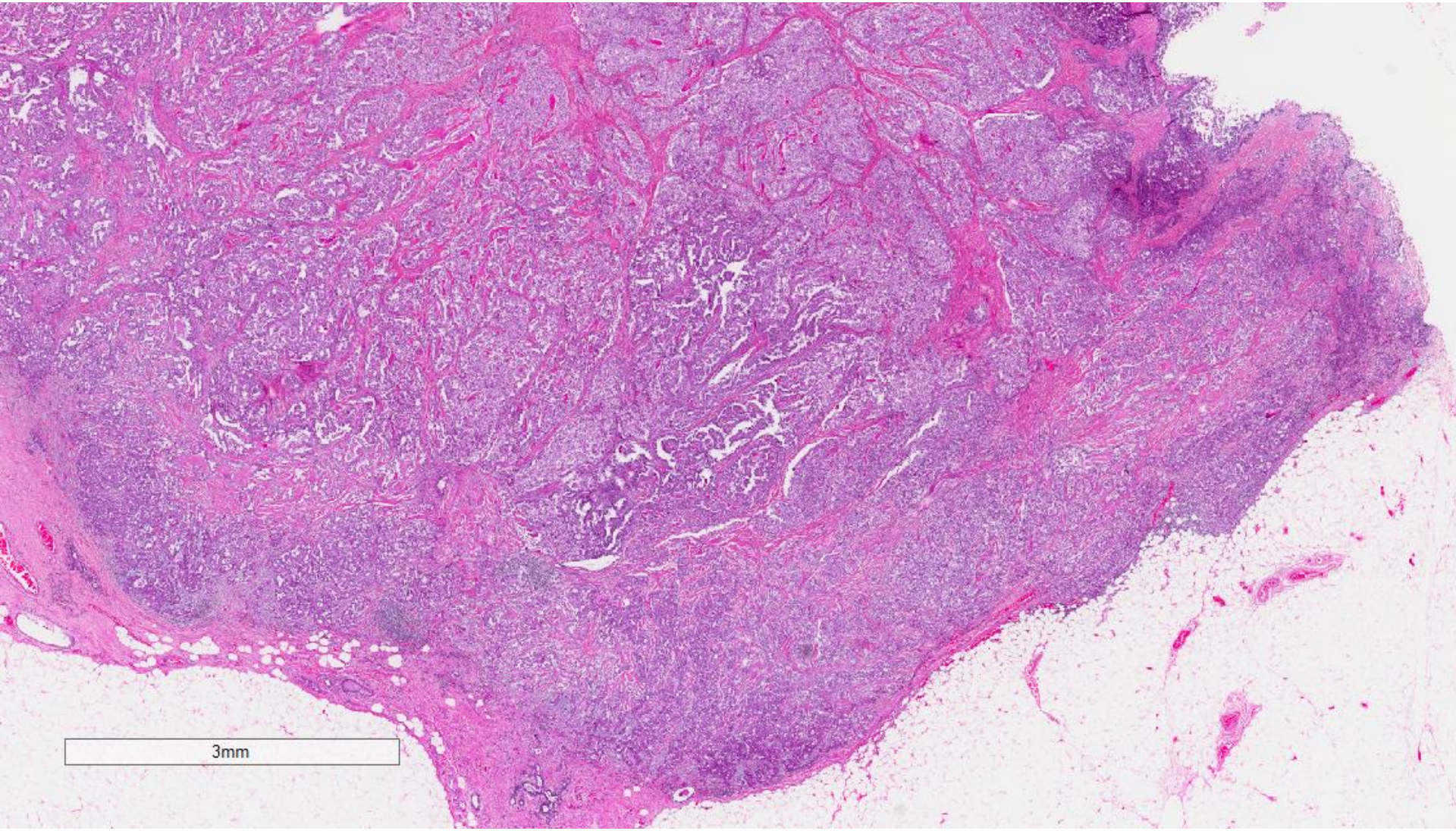
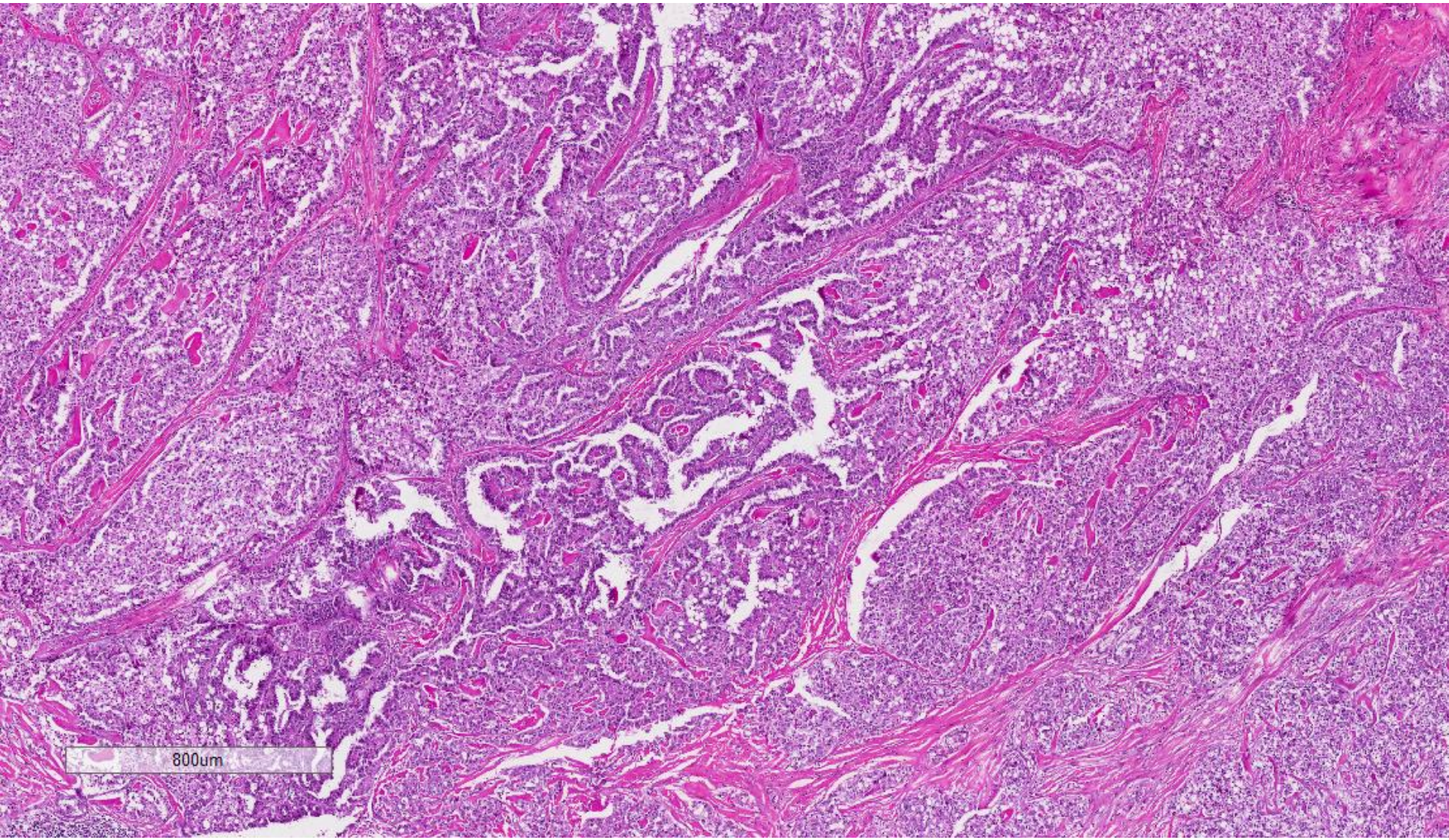
Case 48
62 year old lady underwent mastectomy for a right breast mass.

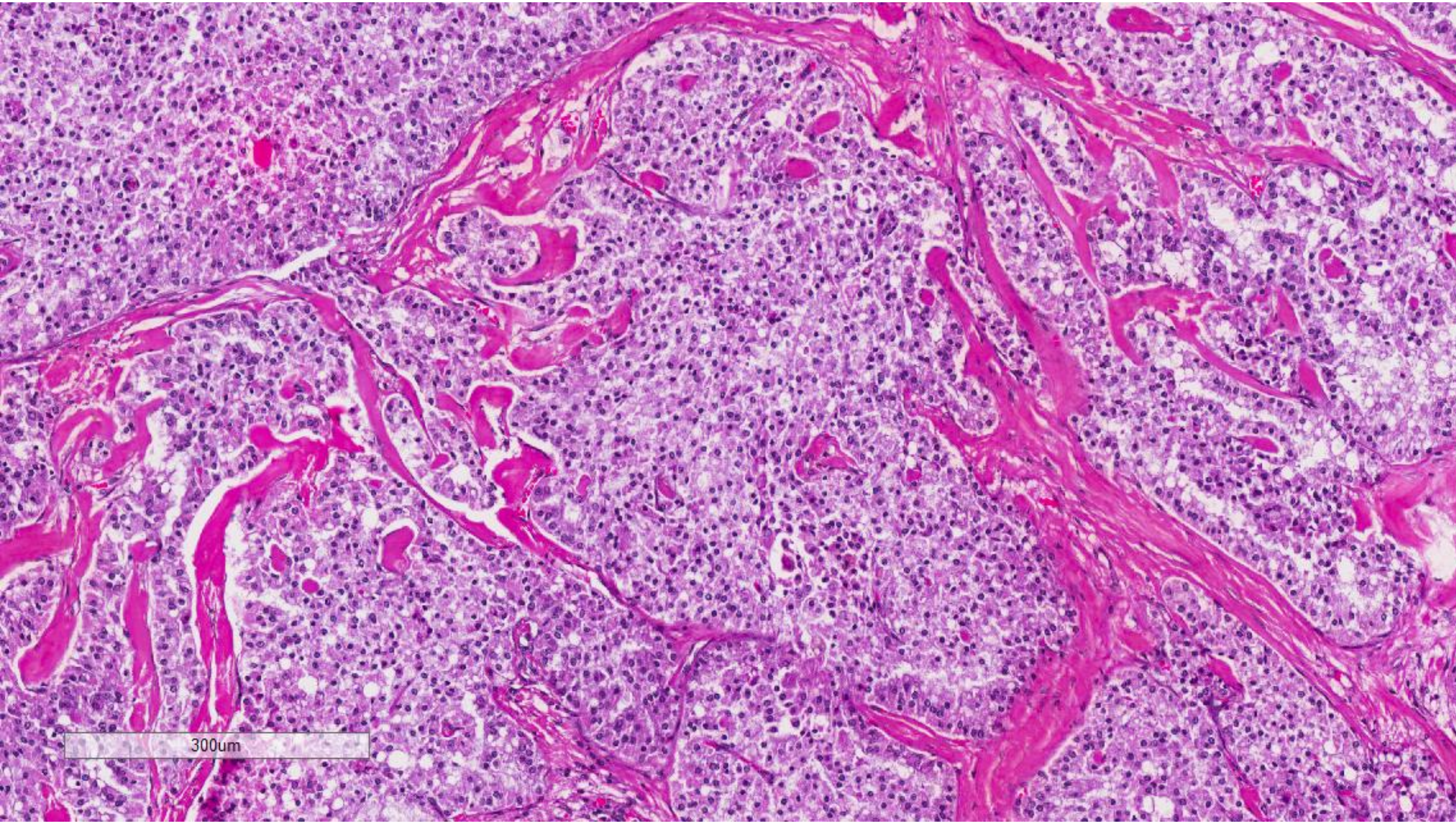
Right breast mass

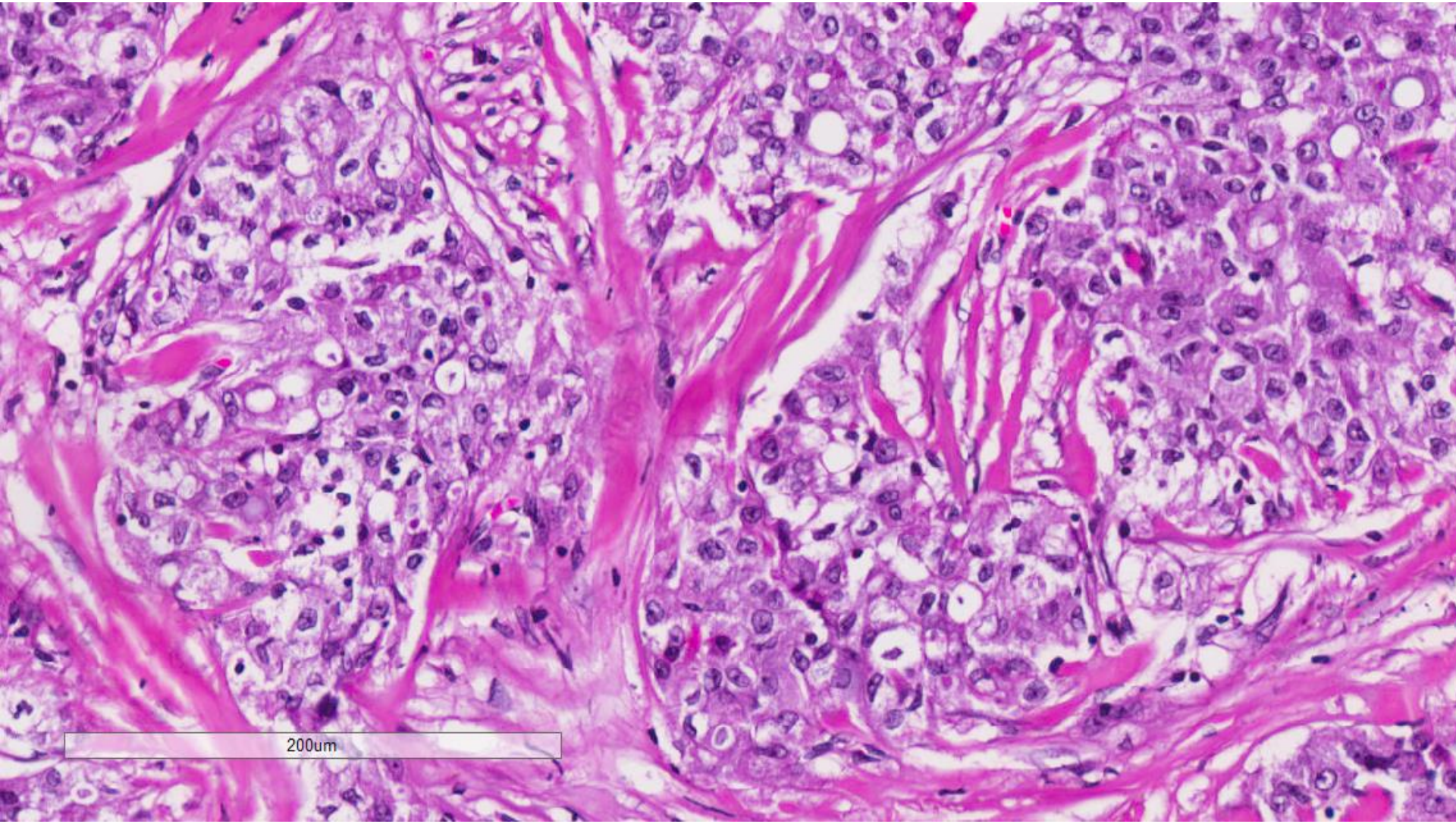



7mm


3mm


800um


300um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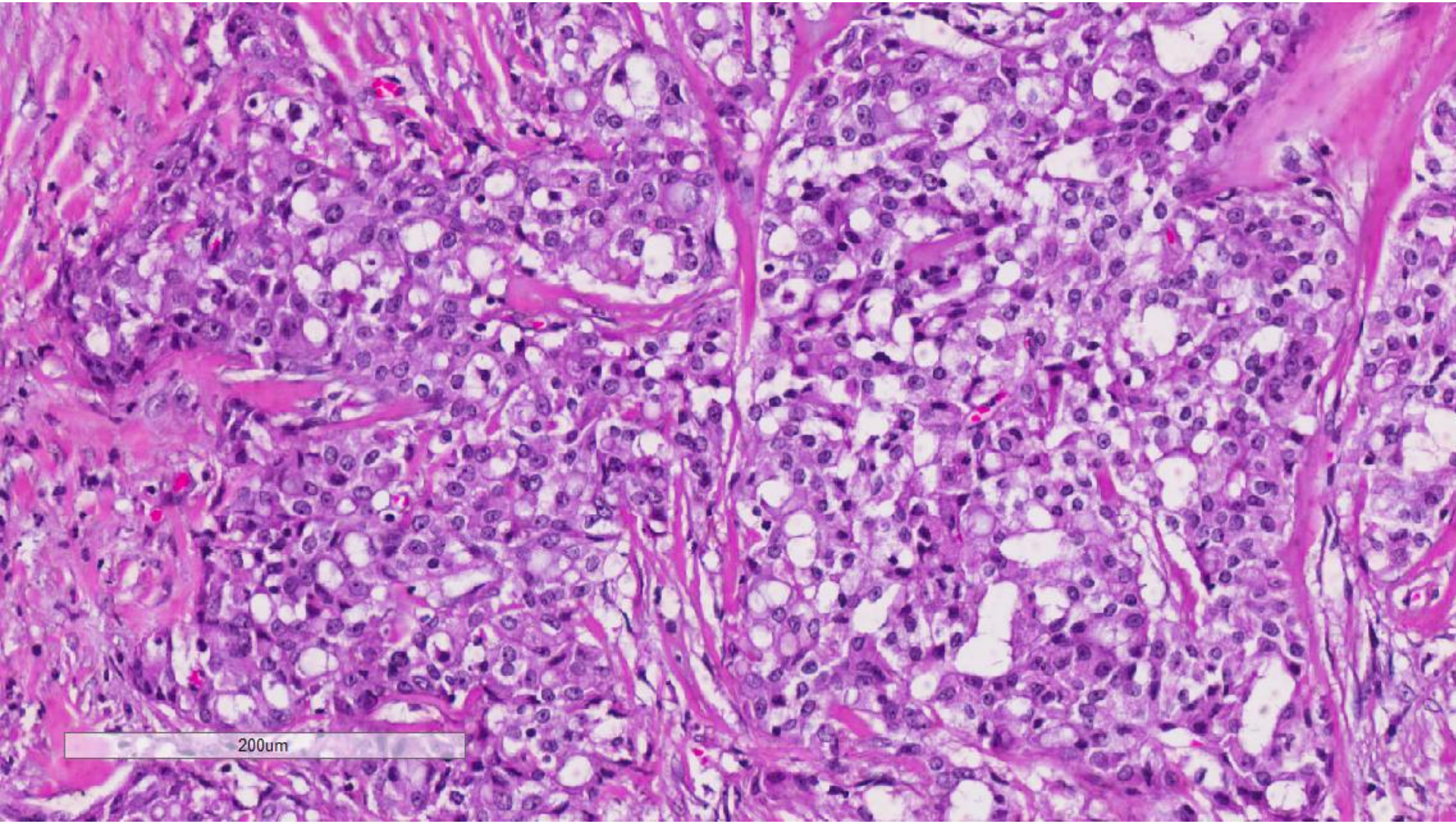
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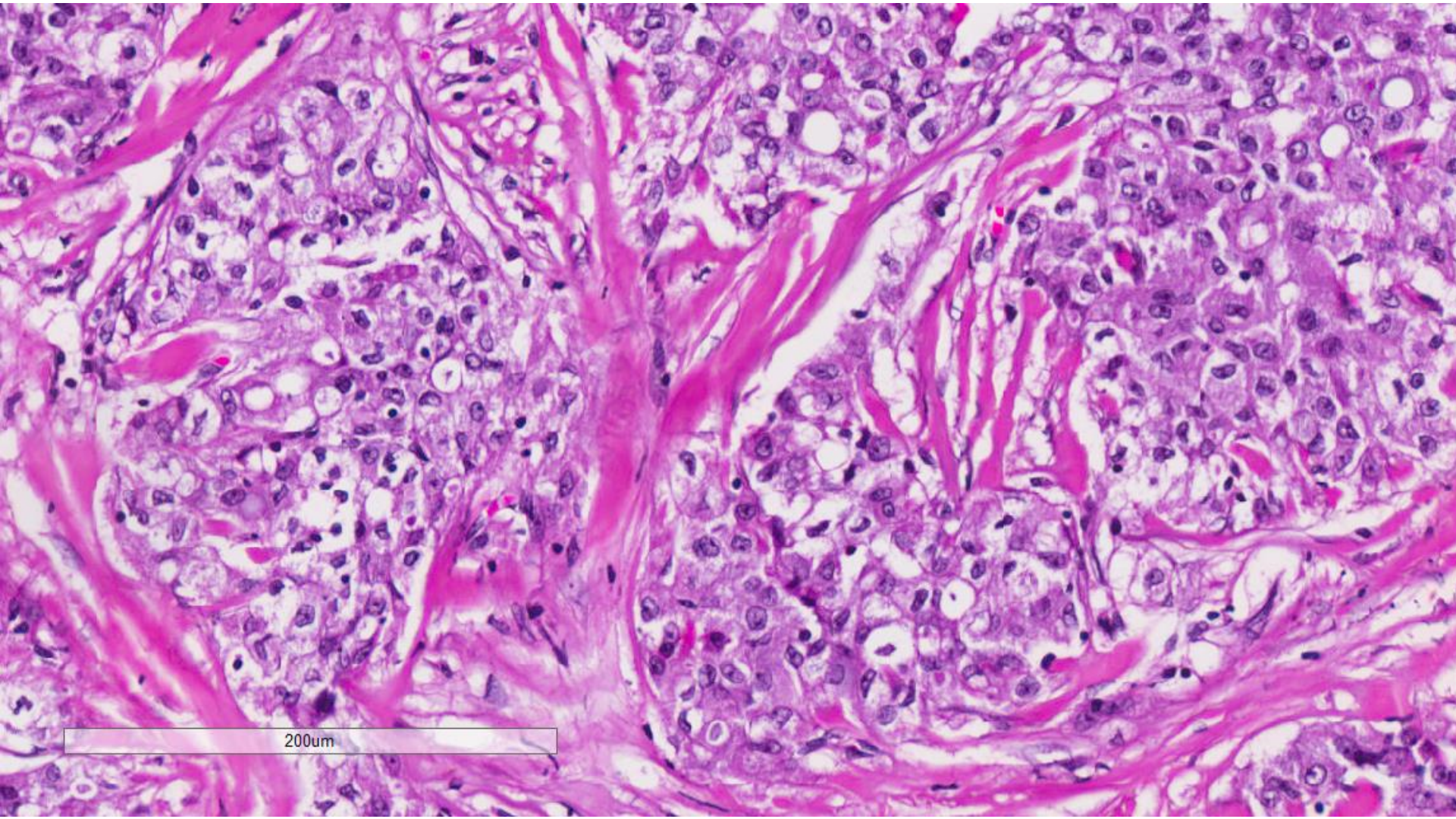
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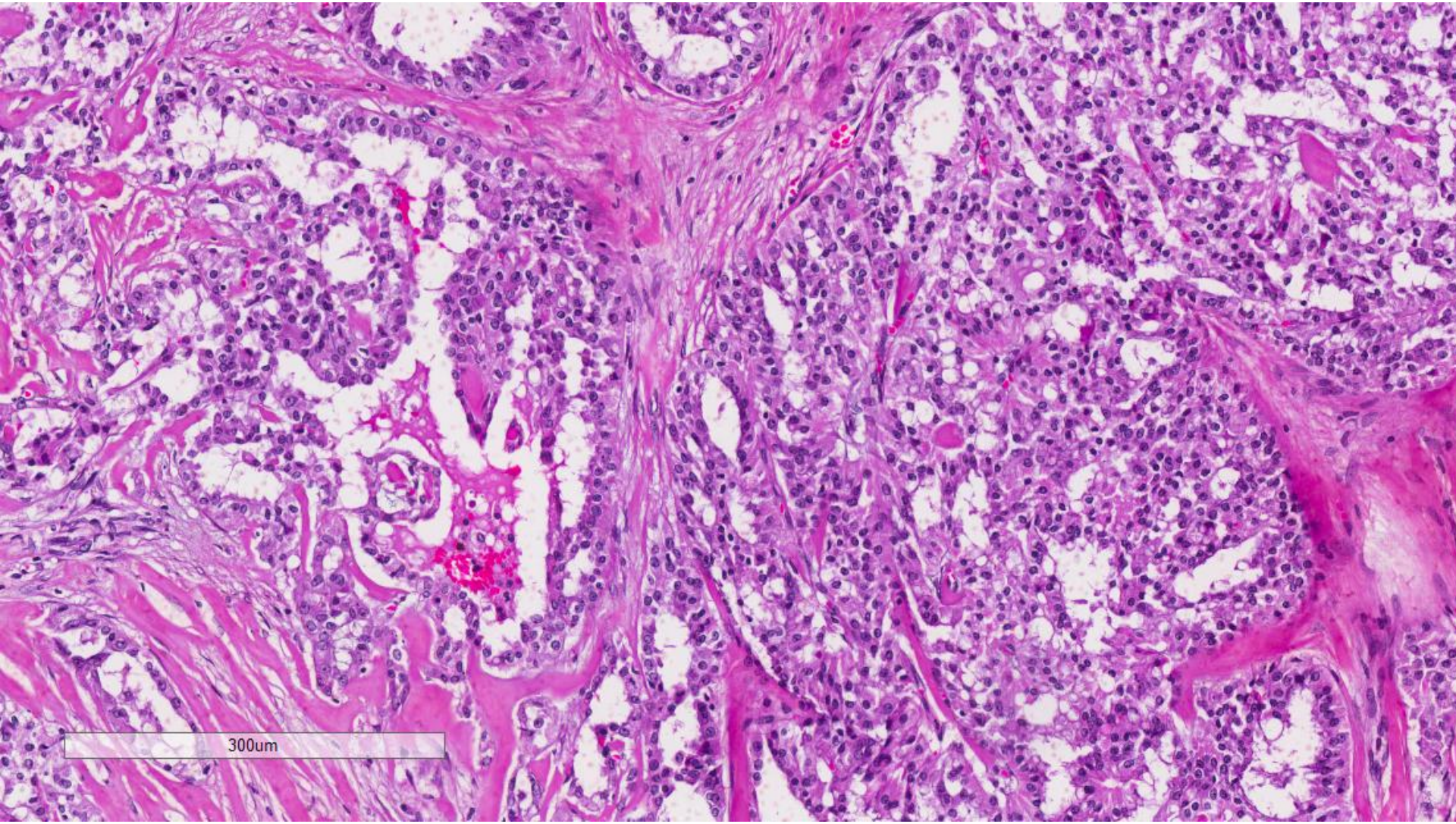
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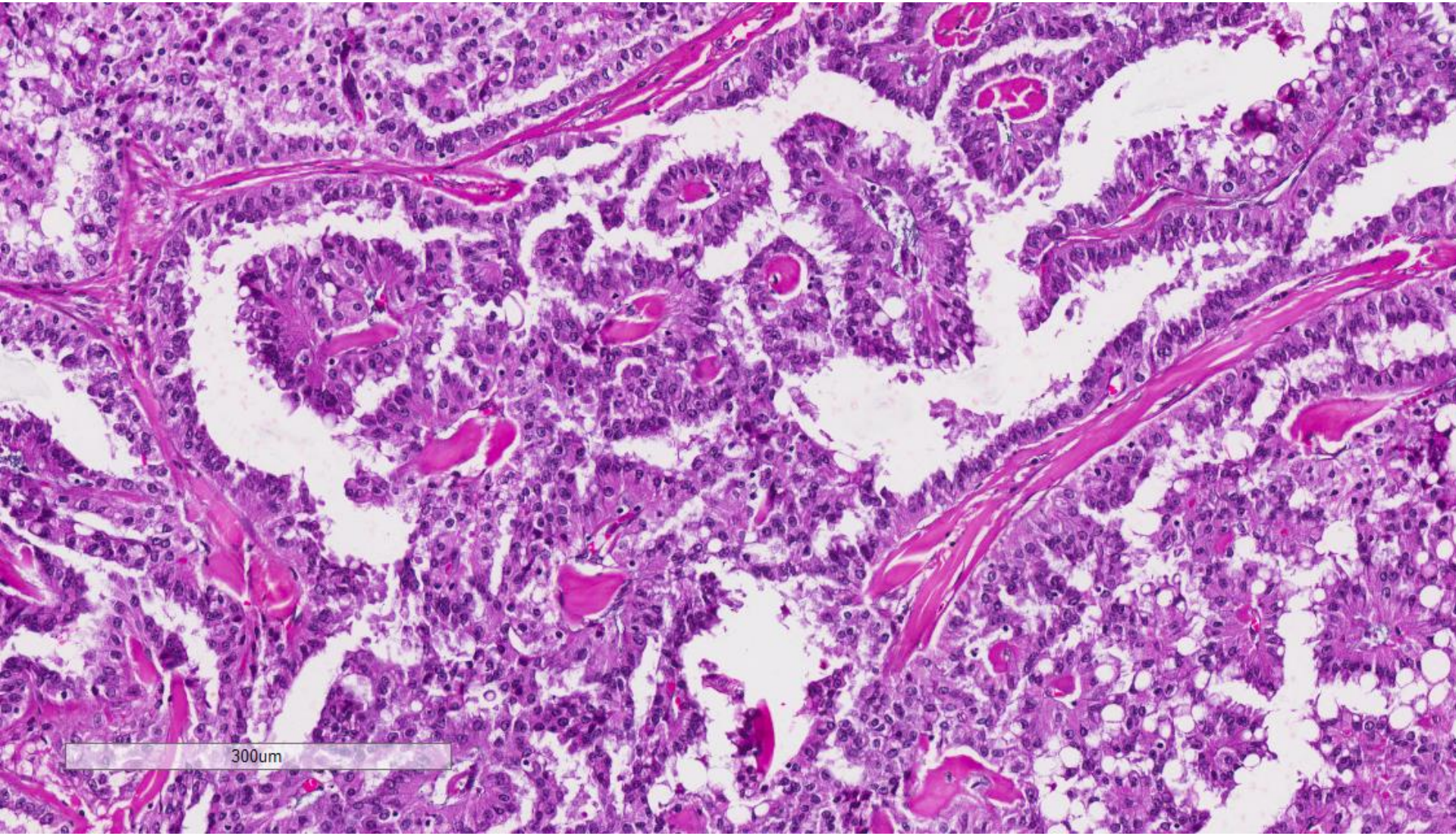
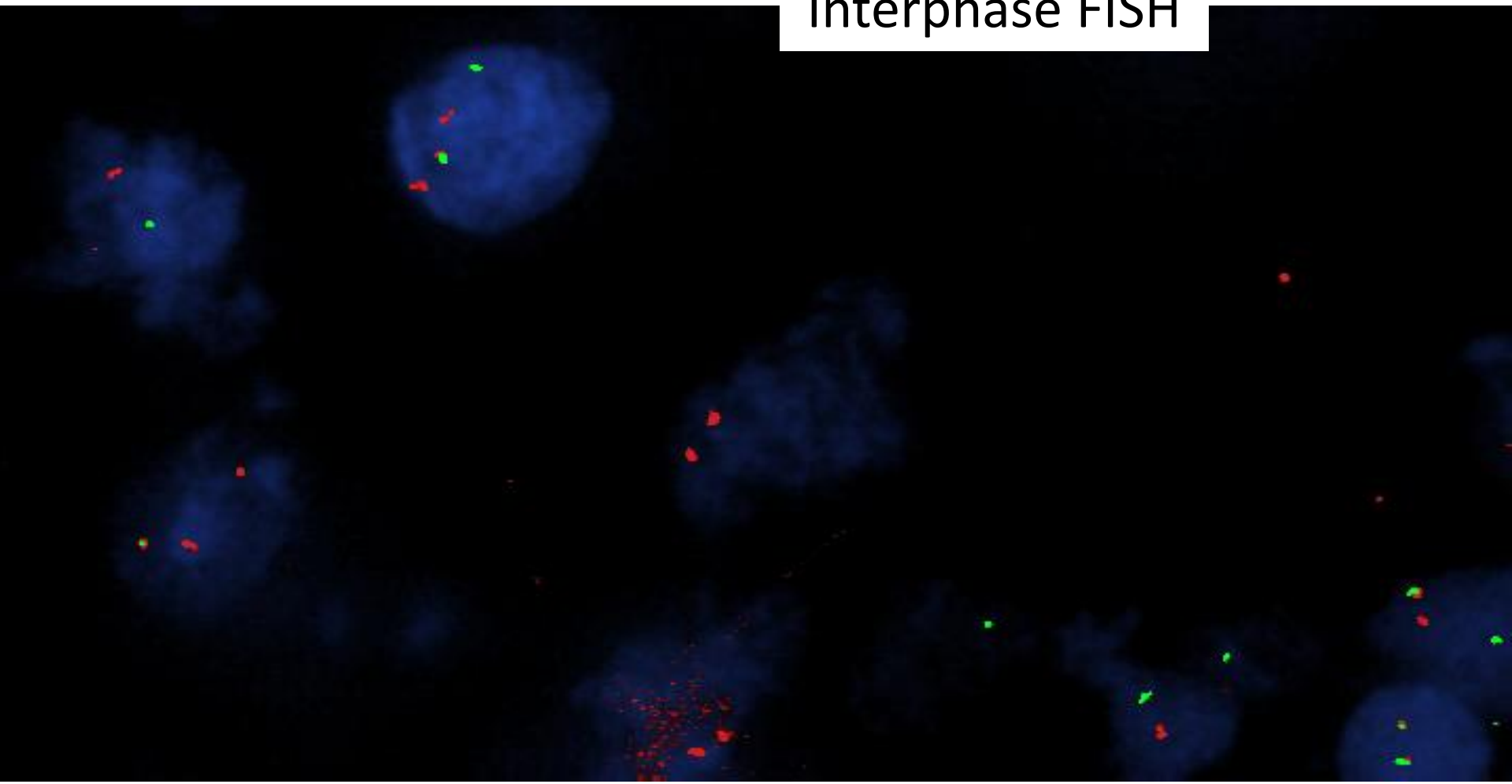

300um

Interphase FISH



The fusion (yellow) signal or a red with closely-associated green signal is the normal ETV6 gene (a normal cell will show two fusion signals, i.e. 2 yellow signals). The separated red and green signals indicate a disrupted ETV6 gene. The additional red signal shows there is an extra copy of the 5’ ETV6 gene.

Secretory carcinoma, 25 mm

ER negative, PR negative, cerbB2 negative

Secretory carcinoma

- A rare, low-grade, translocation-associated invasive carcinoma.
  - Solid, microcystic and tubular architecture.
  - Tumour cells produce intra- and extracellular secretory material.
- Classified as an ‘exceptionally rare’ type of breast cancer.
- Synonym: Juvenile breast carcinoma.
- Accounts for < 0.15% of all breast cancers.
- Both males and females are affected.
- Median age of presentation is 25 years (range, 3–87 years).

Secretory carcinoma

- Clinically well-circumscribed & mobile masses located near the areola, especially in men and children.
- Size averages 3 cm (range, 0.5–12 cm).
- Cut surface varies from grey-white to yellow-tan in colour.

Secretory carcinoma

- Histological findings:
  - Pushing borders, areas of frank invasion are frequent.
  - 3 patterns are seen in various combinations: microcystic, solid and tubular.
  - Microcystic ~ small cysts mimicking thyroid follicles that can merge into solid islands.
  - Tubular ~ lumina containing secretions.
- Most tumours contain all three patterns.
- Sclerotic tissue in the centre of the lesion may be observed.
- Cells are polygonal with granular eosinophilic to foamy cytoplasm.
- Nuclei are regular with inconspicuous nucleoli.
- Mitotic activity is minimal.
- Intracellular and extracellular secretory material is positive on staining with periodic acid-Schiff (PAS) or Alcian blue is a consistent finding.

Secretory carcinoma

- In situ carcinoma, when present, displays similar secretory features, occasionally with necrosis, or can be of low-grade type.
- Immunohistochemistry:
  - Epithelial membrane antigen (EMA), alpha lactoalbumin and S100 protein are frequently expressed.
  - Triple negativity (ER, PR, HER negative).
  - E-cadherin, keratins 8/18, CD117, and alpha-smooth-muscle actin can be expressed
- Characteristic balanced translocation, t(12;15), that creates a *ETV6-NTRK3* gene fusion.

Secretory carcinoma

- Differential diagnosis ~ acinic carcinoma (absence of *ETV6-NTRK3* translocation).
- Low-grade clinical course with a favourable prognosis, especially in children and young adults aged <20 years.
- In older patients, a more aggressive course is manifested with late recurrences arising after up to 20 years.
- Axillary lymph-node metastases rarely involve more than three lymph nodes.
- Distant metastases are extremely rare.