

CASE 2

49 year old Chinese lady participated in the National Breast Screening Program (BreastScreen Singapore). She was found on mammography to have a '2.4 cm heterogeneous area' in the right breast, and a '1 cm nodule' in the left breast.

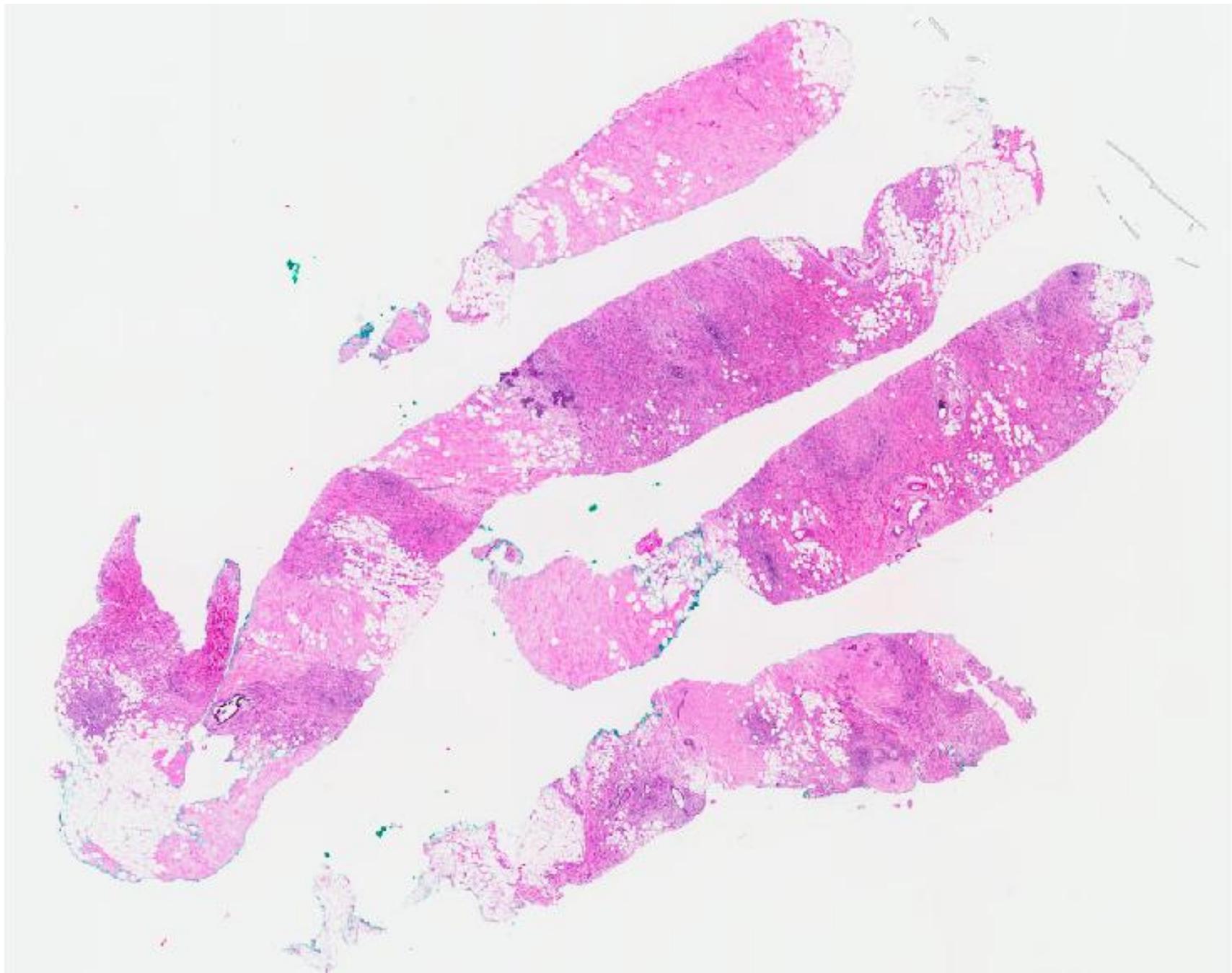
Radiological impression was:

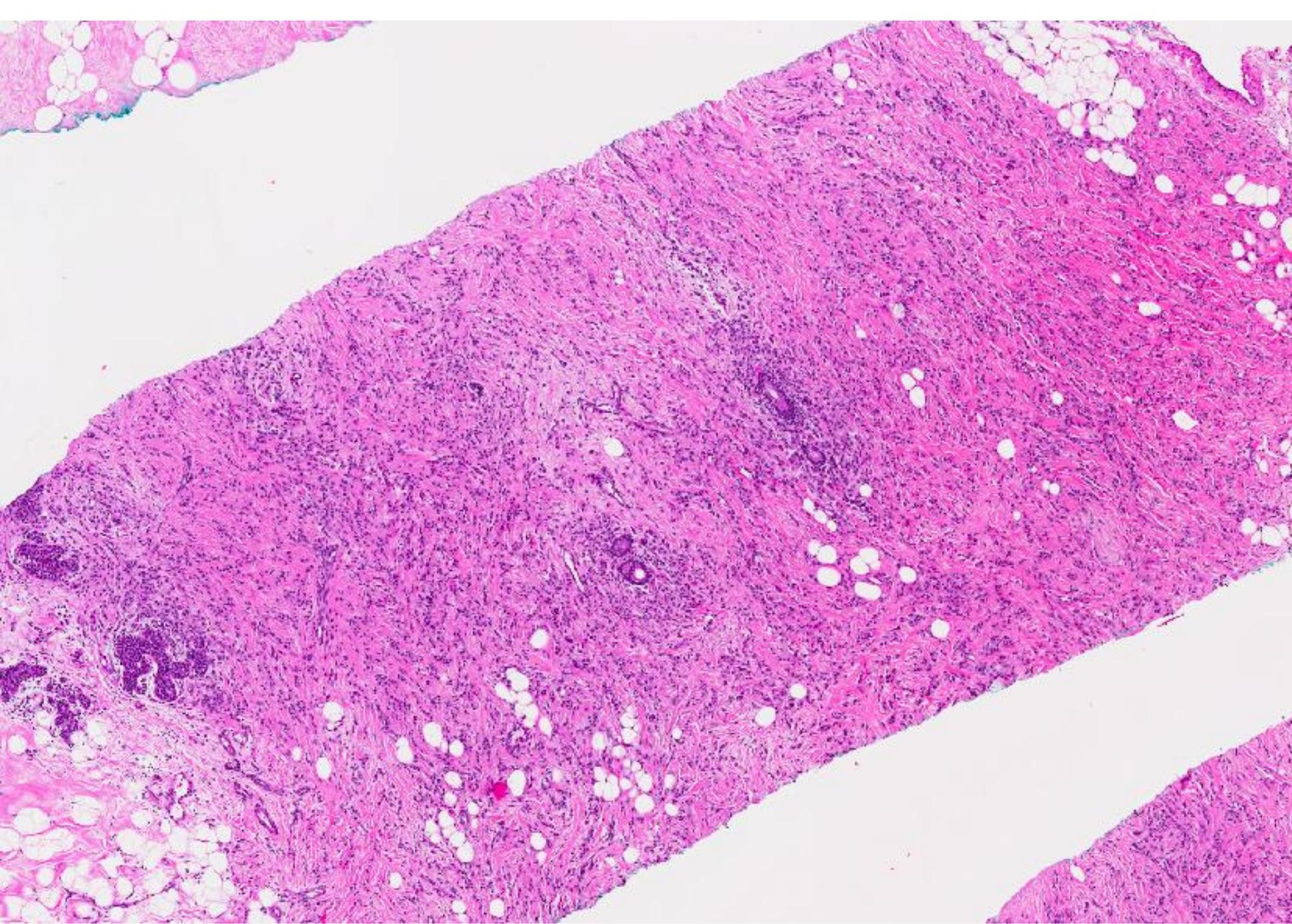
Right breast- ?fibrocystic change, ?cancer

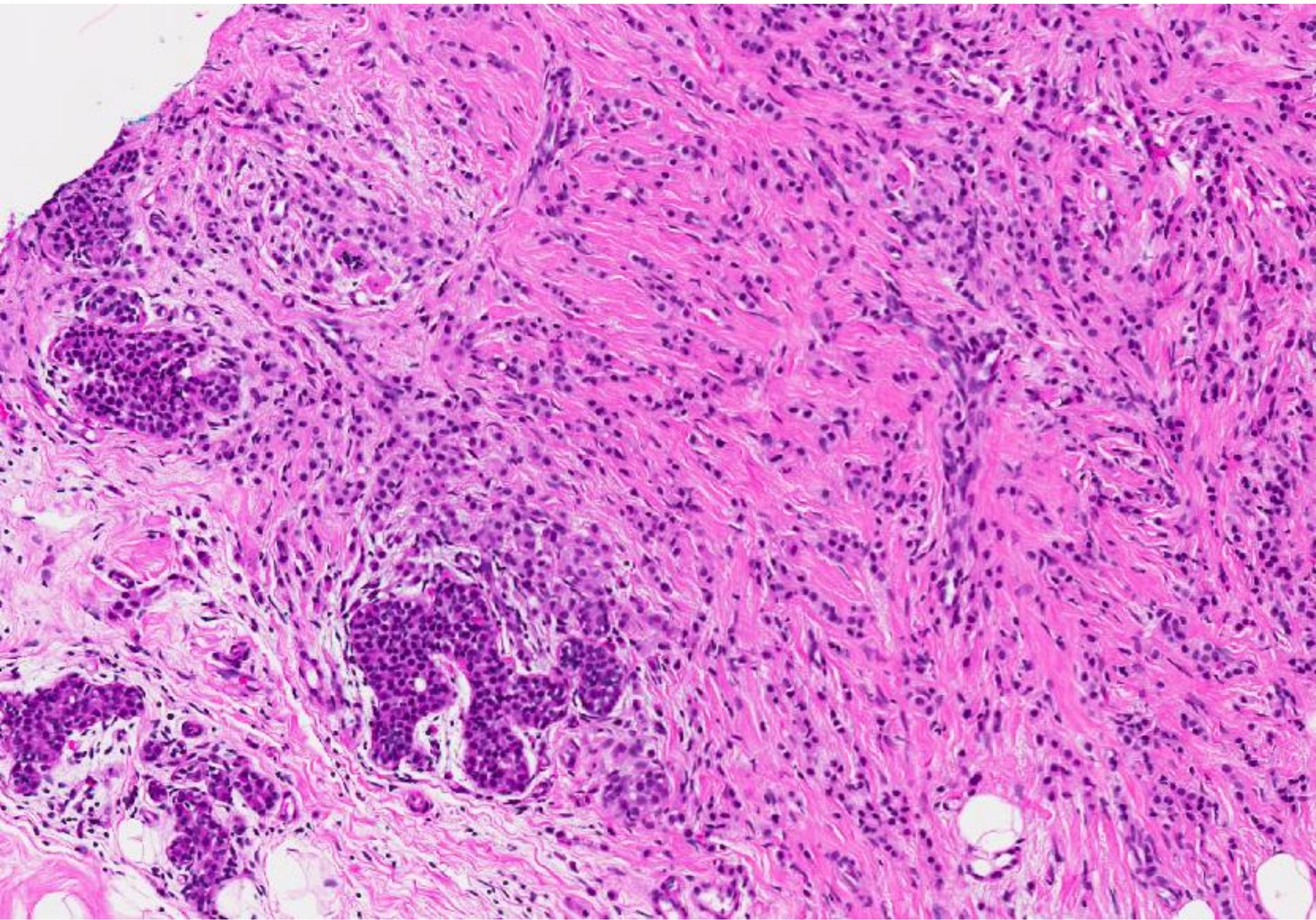
Left breast- ?fibroadenoma

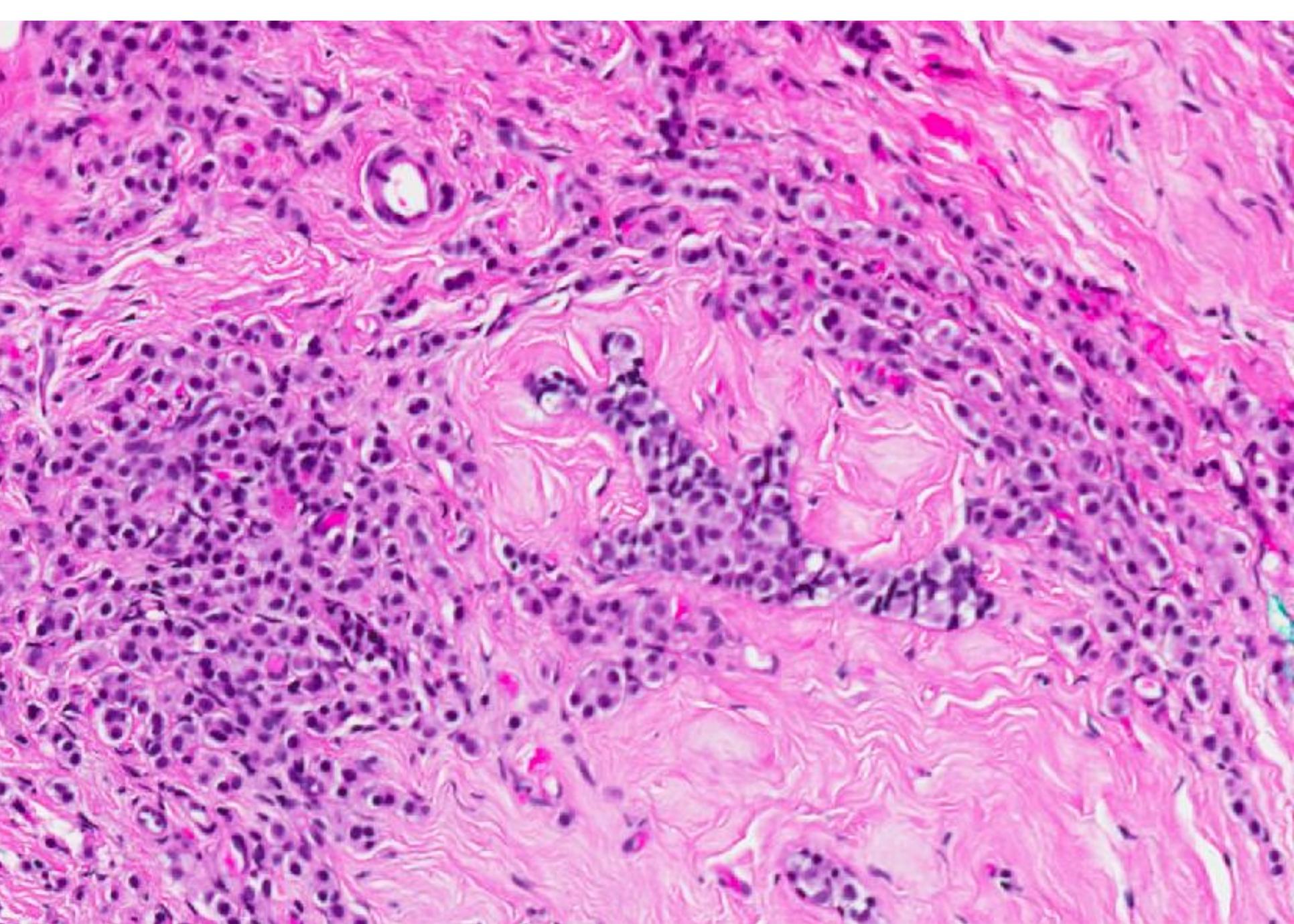
Ultrasound guided trucut biopsies were performed for the right breast (A) and left breast (B).

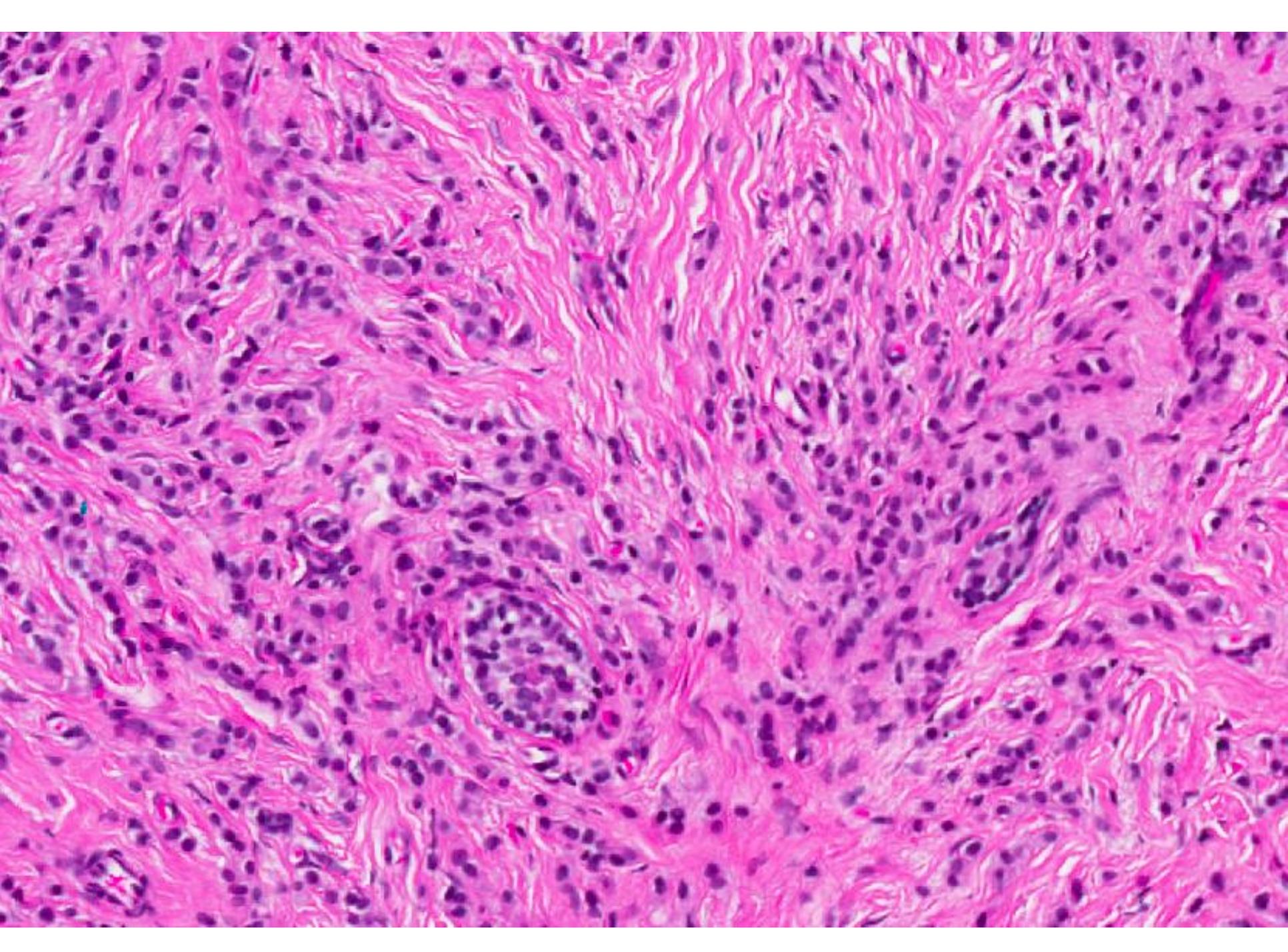
Right breast



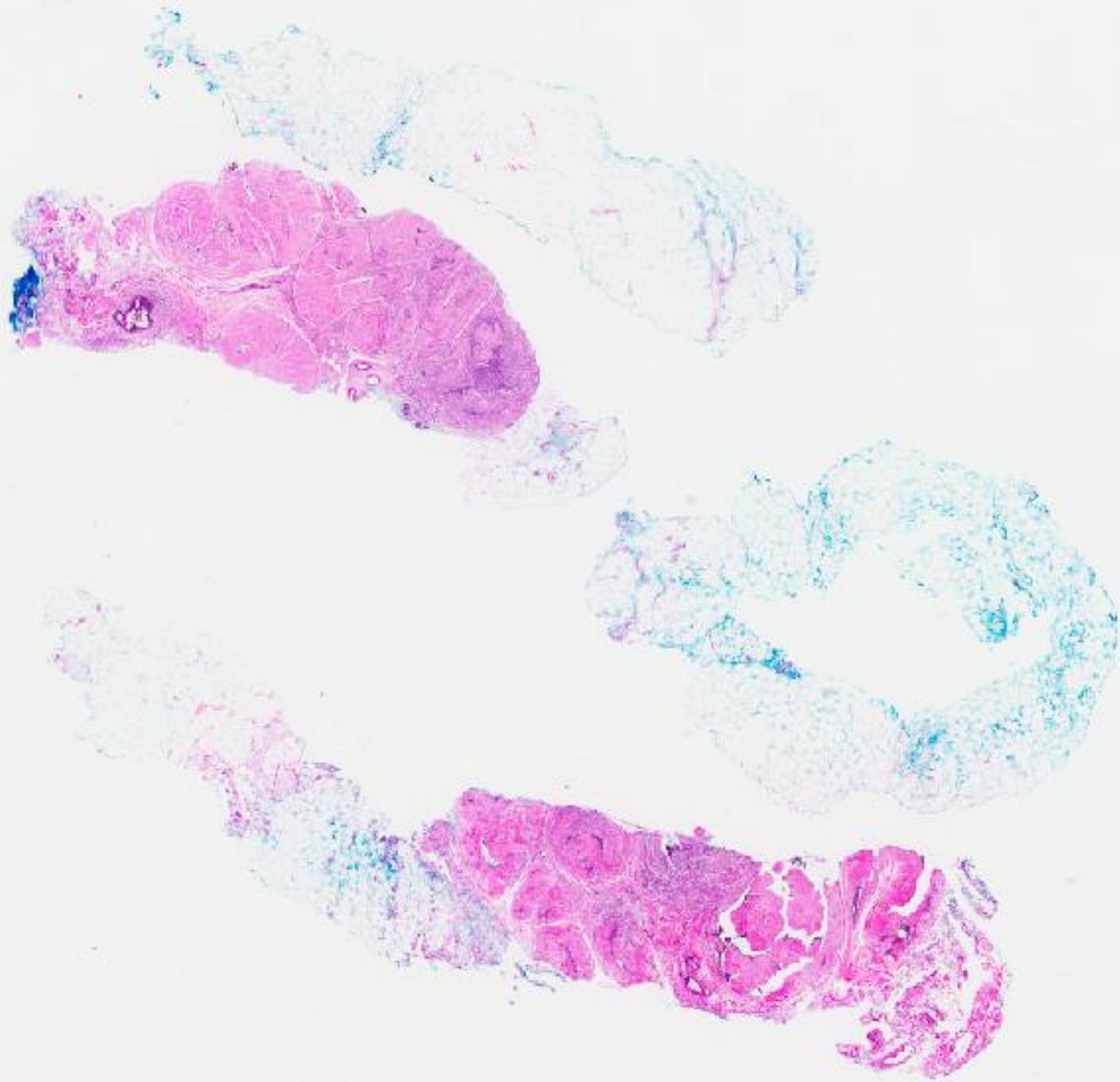


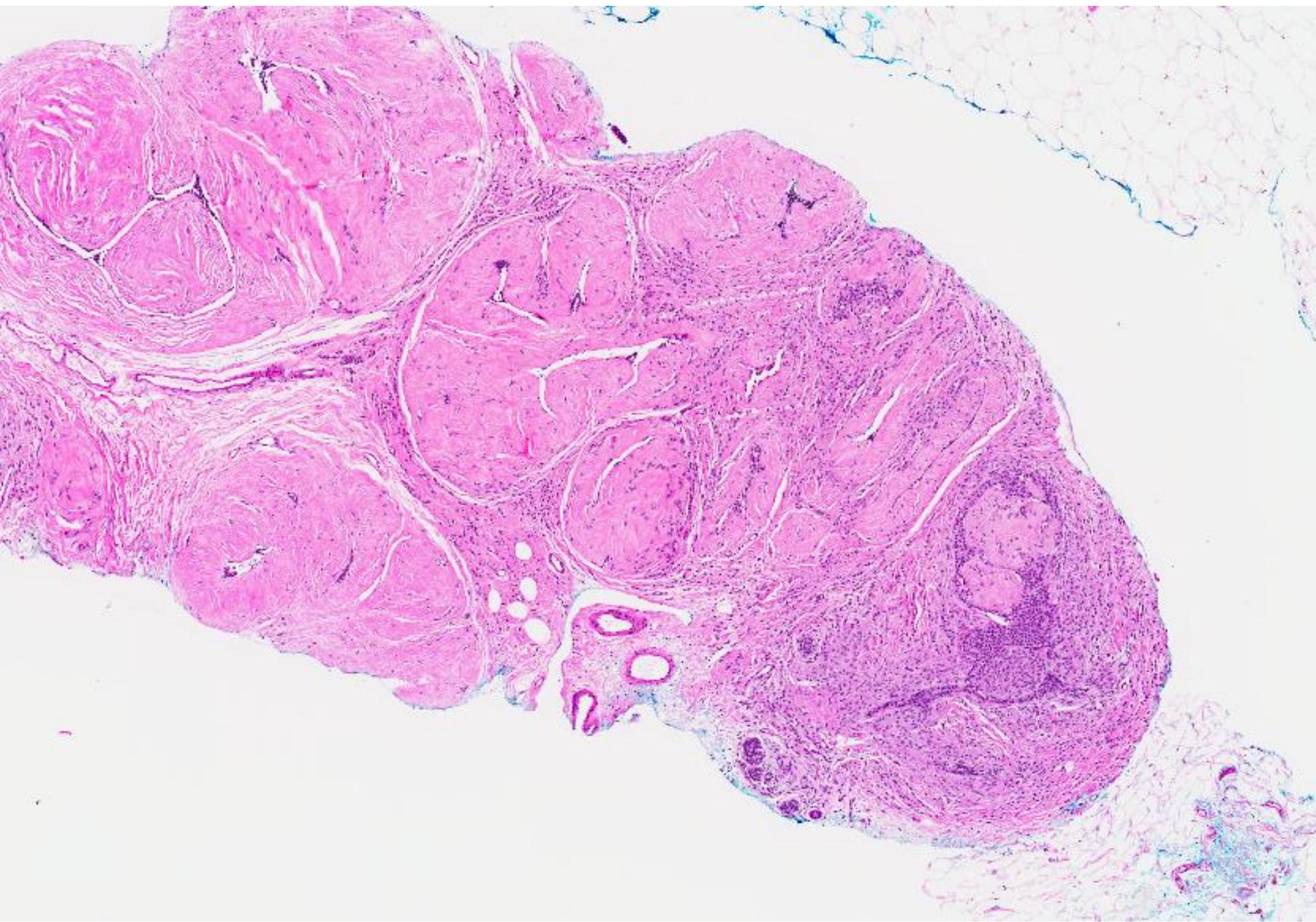


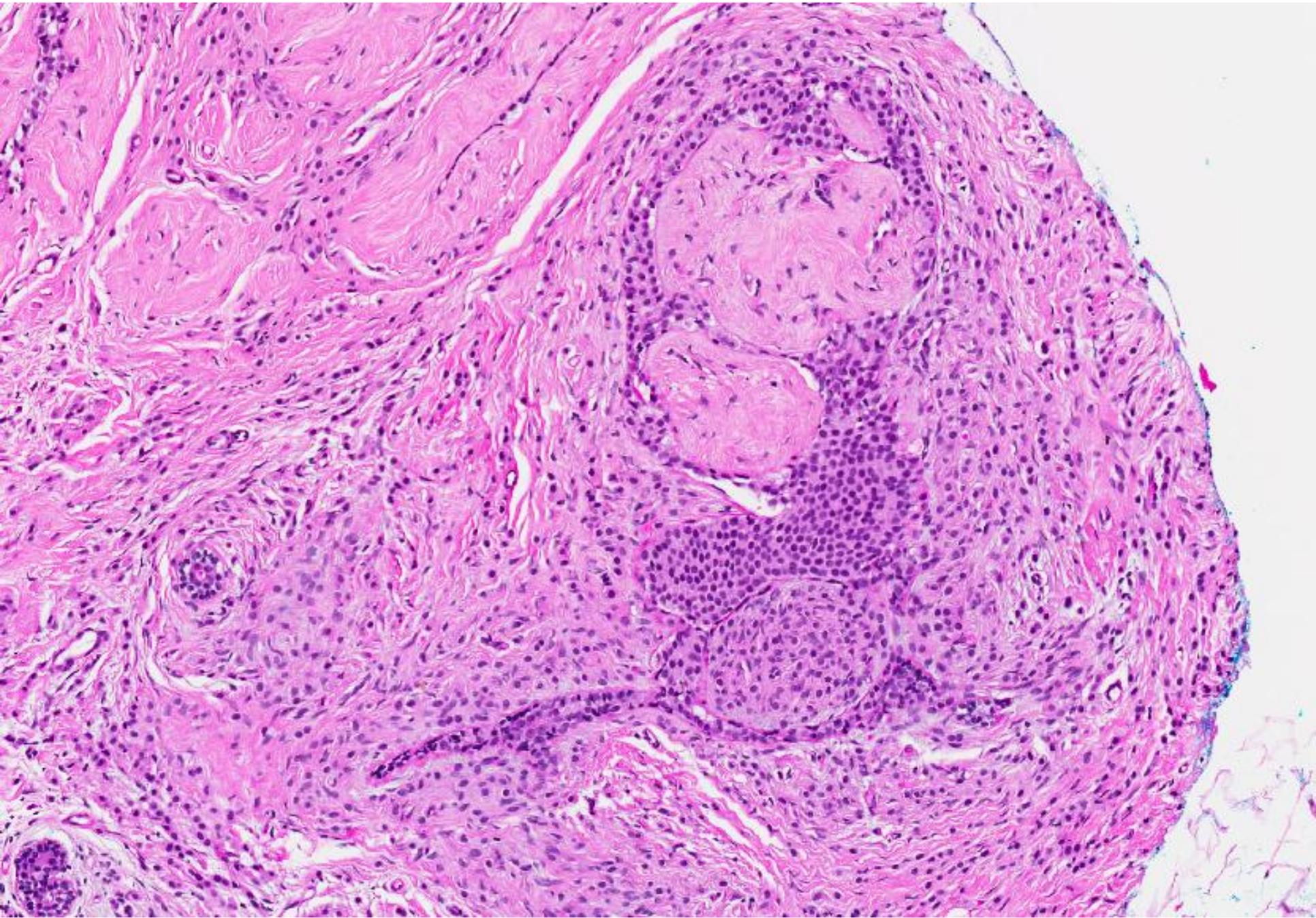


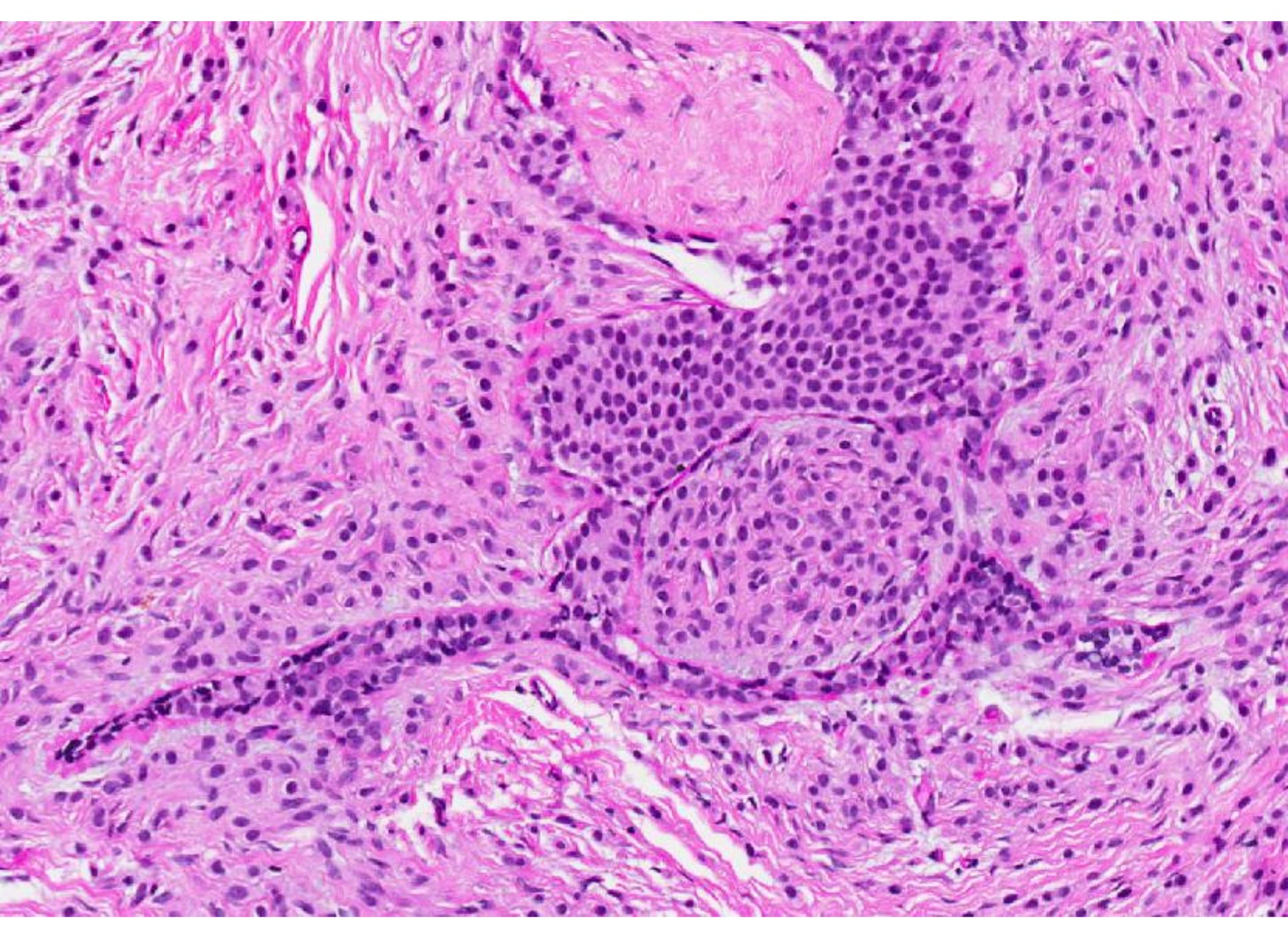


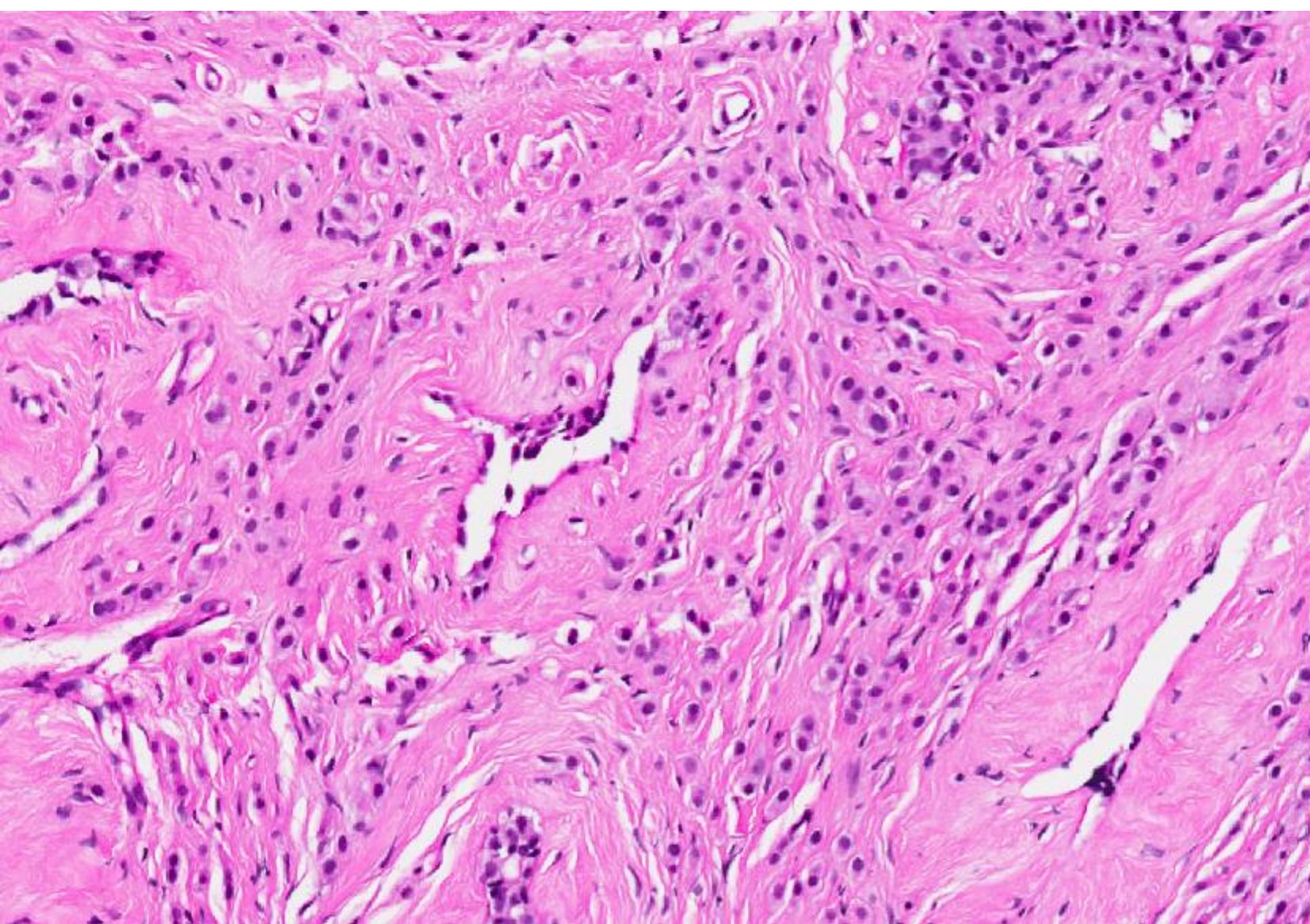
Left breast











Diagnosis

- Bilateral invasive lobular carcinoma (ILC), classic type.
- Left breast ILC involves a fibroadenoma.

Invasive lobular carcinoma

- 1st described with lobular carcinoma in situ in 1941 by Foote and Stewart.
 - Desmoplastic stromal reaction.
 - Linear arrangement of tumour cells.
 - Targetoid growth pattern.
- Accounts for < 5% to 14% of invasive breast cancer.
- Incidence increases since 1980s, attributable to increased use of hormone replacement therapy.
- Median age at diagnosis between 57 to 65 years.
- Contralateral tumours, including synchronous tumours, in 5% to 19% of cases.

Invasive lobular carcinoma:

Clinical features

- Ill-defined mass.
- Vague thickening.
- Fine diffuse nodularity.

Invasive lobular carcinoma: Imaging

- Mass:
 - Heterogeneous hypoechoic mass with angular or ill-defined margins, posterior acoustic shadowing.
 - Lobulated and well-circumscribed mass.
 - Asymmetric density.
 - Spiculated mass.
- Calcifications are uncommon.
- Mammographically and ultrasonographically silent.
- Mammographic size tends to be less than macroscopic measured size.
- MRI correlates more closely with pathologic tumour size than ultrasound.

Invasive lobular carcinoma:

Pathology

- **Macroscopy:**
 - Occult and grossly inapparent.
 - Diffuse breast involvement.
 - Firm hard tumour with irregular borders.
 - Gray white with scirrhous or fibrous appearance.
 - Haemorrhage, necrosis, cysts, calcifications are uncommon.
- **Microscopy:**
 - Thread-like strands of tumour cells.
 - Cytoplasmic globules.

Invasive lobular carcinoma: **Pathology**

- Microscopic subtypes:
 - Classical
 - Variant:
 - Trabecular
 - Alveolar
 - Solid
 - Tubulolobular
 - Pleomorphic, histiocytoid, myoid

Invasive lobular carcinoma: **Immunoprofile**

- 80% -95% ER positivity.
- 60% -70% PR positivity.
- Rate of ER positivity highest (100%) in alveolar and lowest (10%) in pleomorphic ILC.
- HER2 amplification and overexpression is rare, though evident in some pleomorphic ILCs.
- Proliferation rate, measured by MIB1/Ki67 labelling, is generally low in ILC, although higher in the variants.
- E-cadherin loss, but 15% of ILC can express E-cadherin, often in an aberrant manner.

Invasive lobular carcinoma: **Genetics**

- Diploid in about 50% of cases on flow cytometry.
- Alterations in DNA copy number:
 - Loss of chromosomal arm 16q.
 - Gain of material on 1q and 16p.
- Pleomorphic ILCs exhibit similar alterations, but in addition contain amplifications at loci such as 8q24, 17q12 and 20q13, which are characteristic of high-grade ductal carcinomas.
- Inactivation of E-cadherin is the most commonly identified genetic alteration in ILC, occurring as an early event in oncogenesis.
- Most frequently classified as luminal A-type molecular tumours, but they can also be classified as luminal B, HER2, normal-like or basal-like.

Invasive lobular carcinoma: **Prognosis**

- Several studies have reported a more favourable outcome for ILC than IDC, whereas others found no significant differences or a worse prognosis for ILC.
- Patients with ILC have a better or similar outcome to those with IDC in the first 10 years following diagnosis; but long-term prognosis for ILC is worse than IDC.
- Favourable outcome for classical type than for variants, such as pleomorphic and solid.
- Higher frequency of metastases to bone, gastrointestinal tract, uterus, meninges, ovary and serosa.

Learning points

- Histological appearances of ILC, classical pattern, and potential of underdiagnosis on core biopsy when tumour cells are sparse.
- Protean radiological appearances.
- Difficulties in size assessment.
- Use of MRI for accurate radiological sizing after a core biopsy diagnosis of ILC is made.