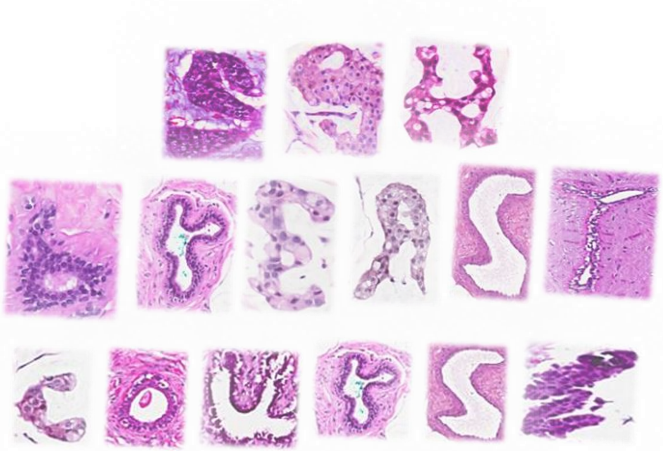
Breast Pathology Course 2020 @21

Case 1

39 year old Chinese female.
Underwent an US guided core biopsy of a right breast palpable 0300 mass.
A wide excision was subsequently performed.
The section is from the wide excision specimen.

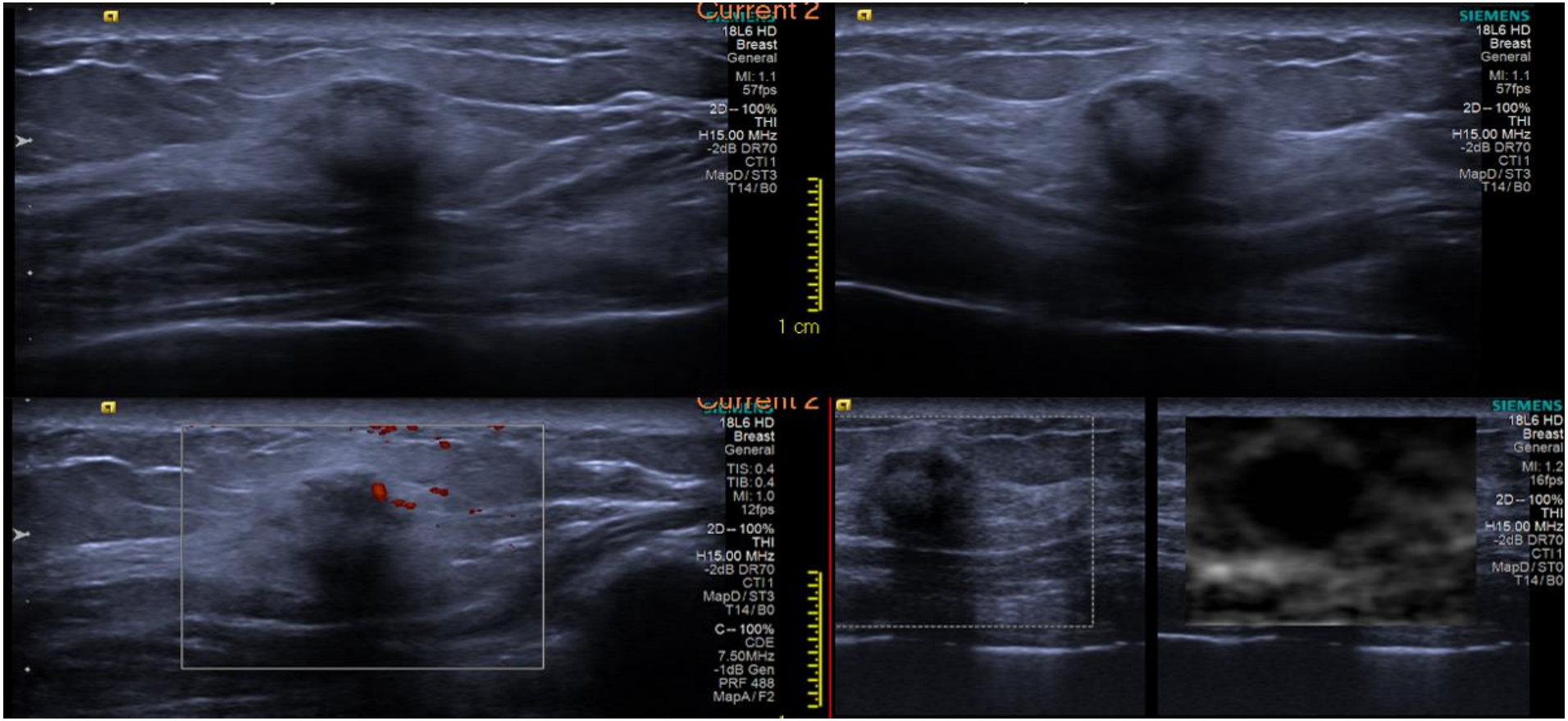


Presented by Dr Puay Hoon Tan

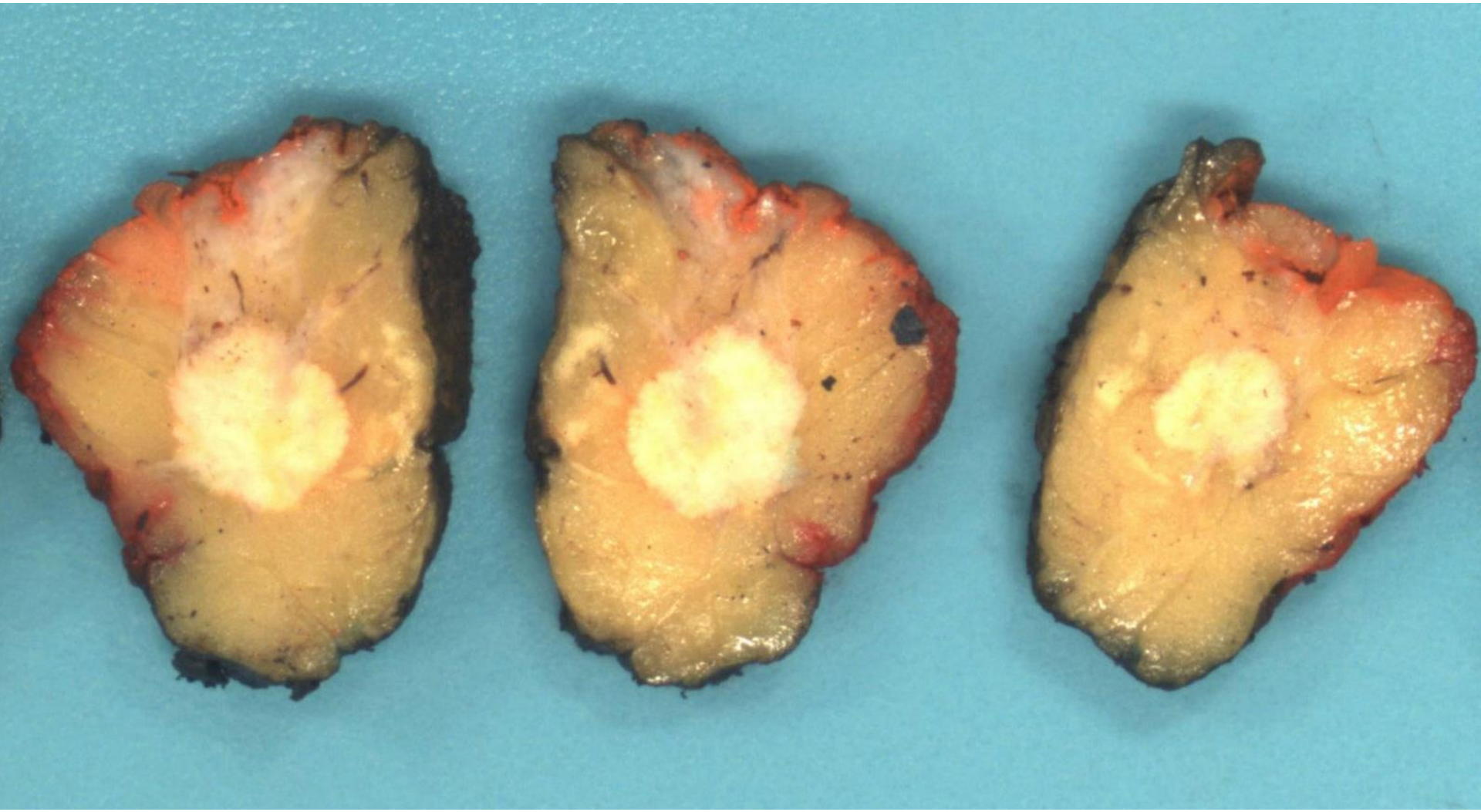
Division of Pathology
Singapore General Hospital

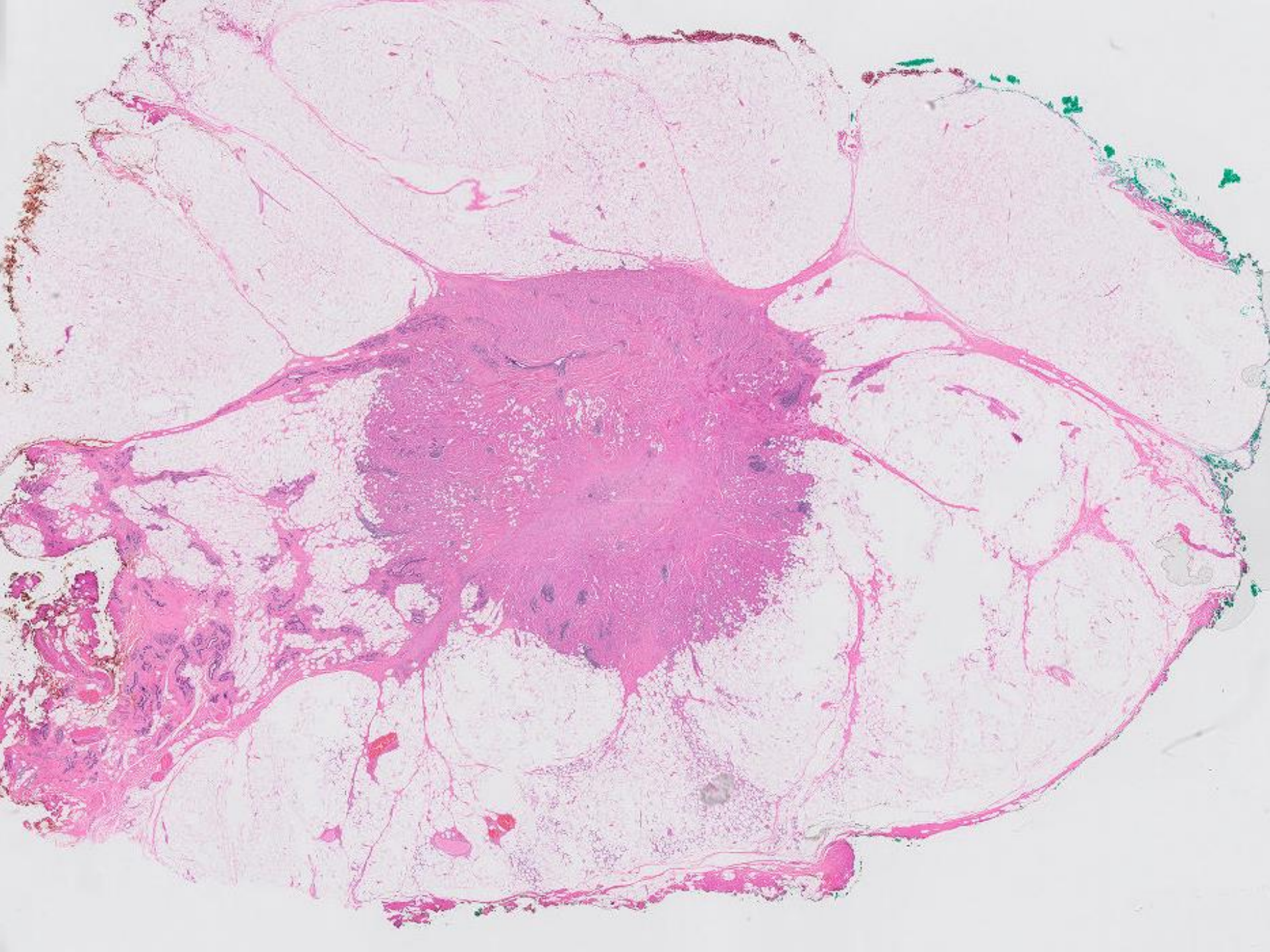
SingHealth DukeNUS
ACADEMIC MEDICAL CENTRE
PATHOLOGY

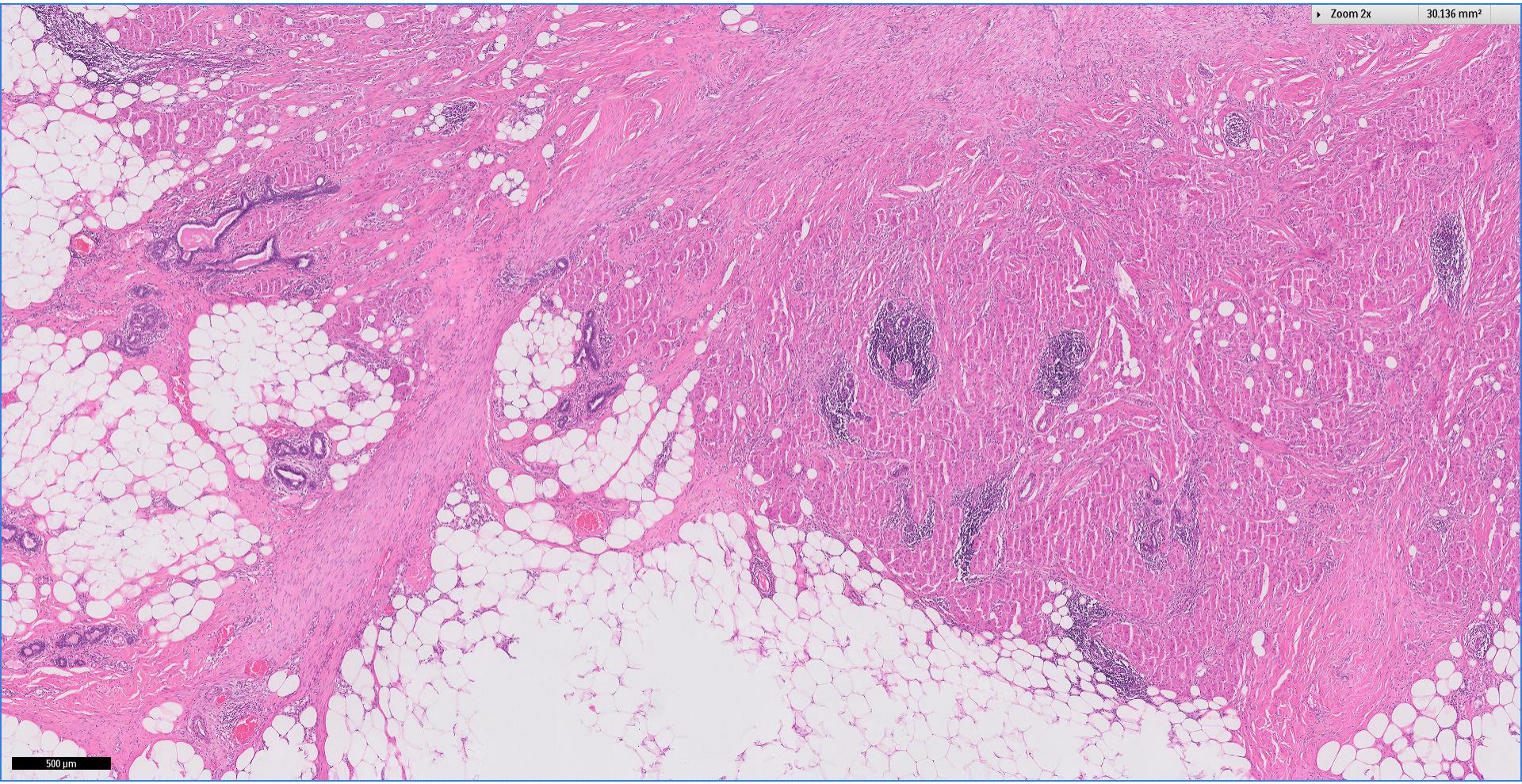
IAP
International Academy of Pathology
Singapore Division

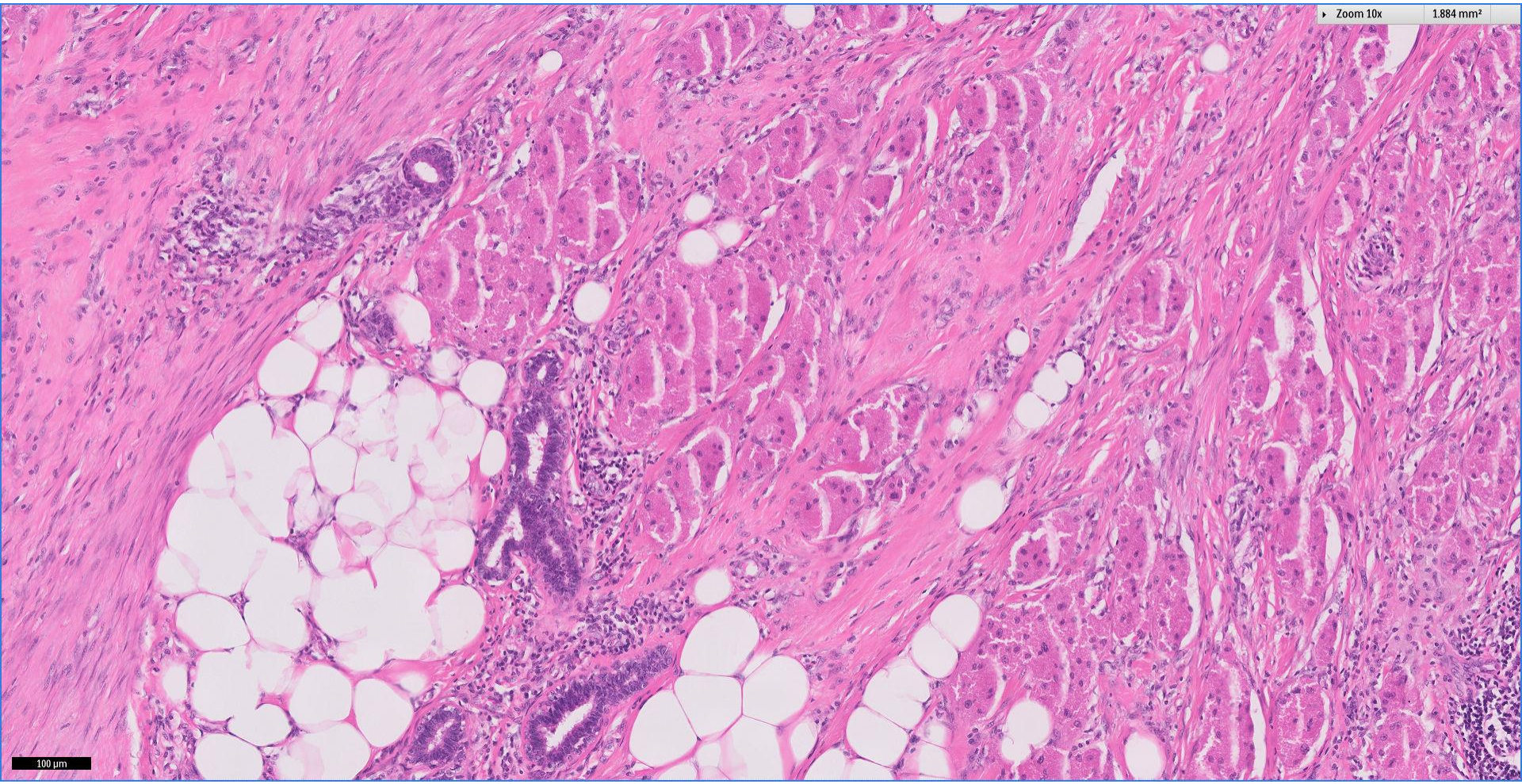


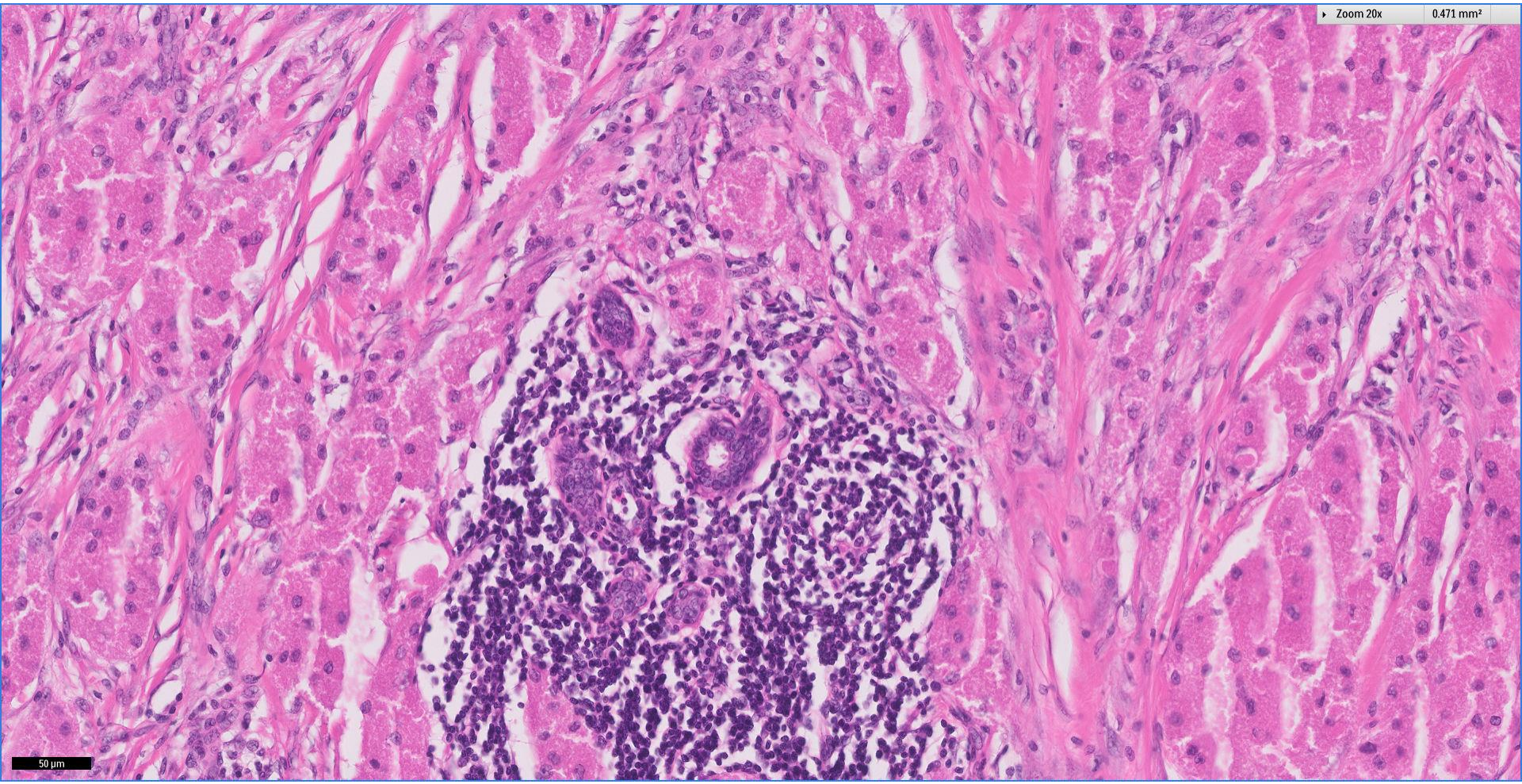
Ultrasound examination revealed a 12mm, ill-defined, rounded mass at the 3.00 position that accounted for the palpable lump, sited 34mm from the nipple at a mid-depth. The mass showed increased internal vascularity and was heterogeneous in echogenicity with mixed hyperechoic and hypoechoic areas. There was an ill-defined hyperechoic rim around the mass with an enlarged size ratio on elastographic strain imaging. No distortion was observed but there was posterior shadowing. *(Images & legend courtesy of Dr Lester Leong)*



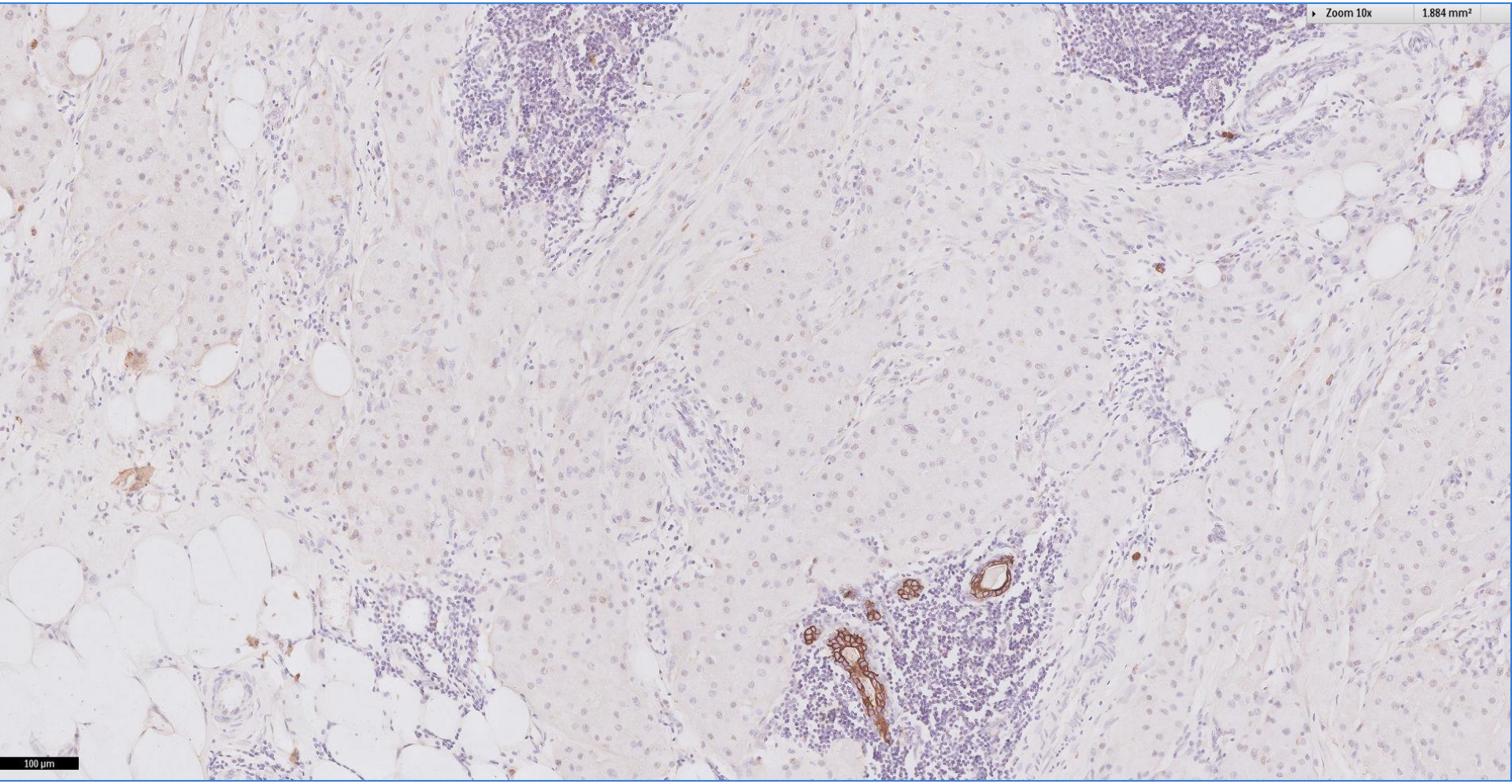



Zoom 2x
30.136 mm²
500 µm

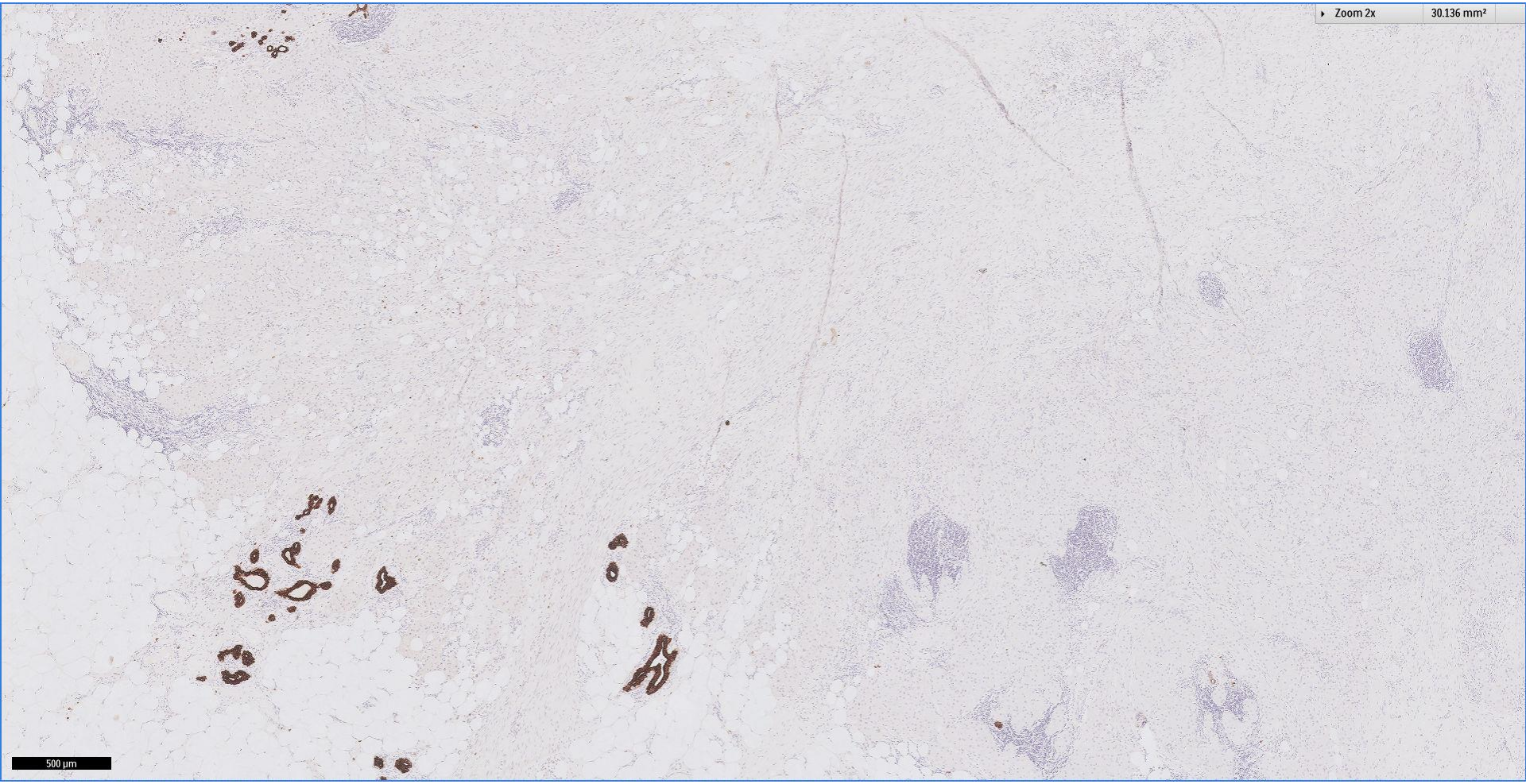

Zoom 10x
1.884 mm²
100 µm


Zoom 20x
0.471 mm²
50 µm

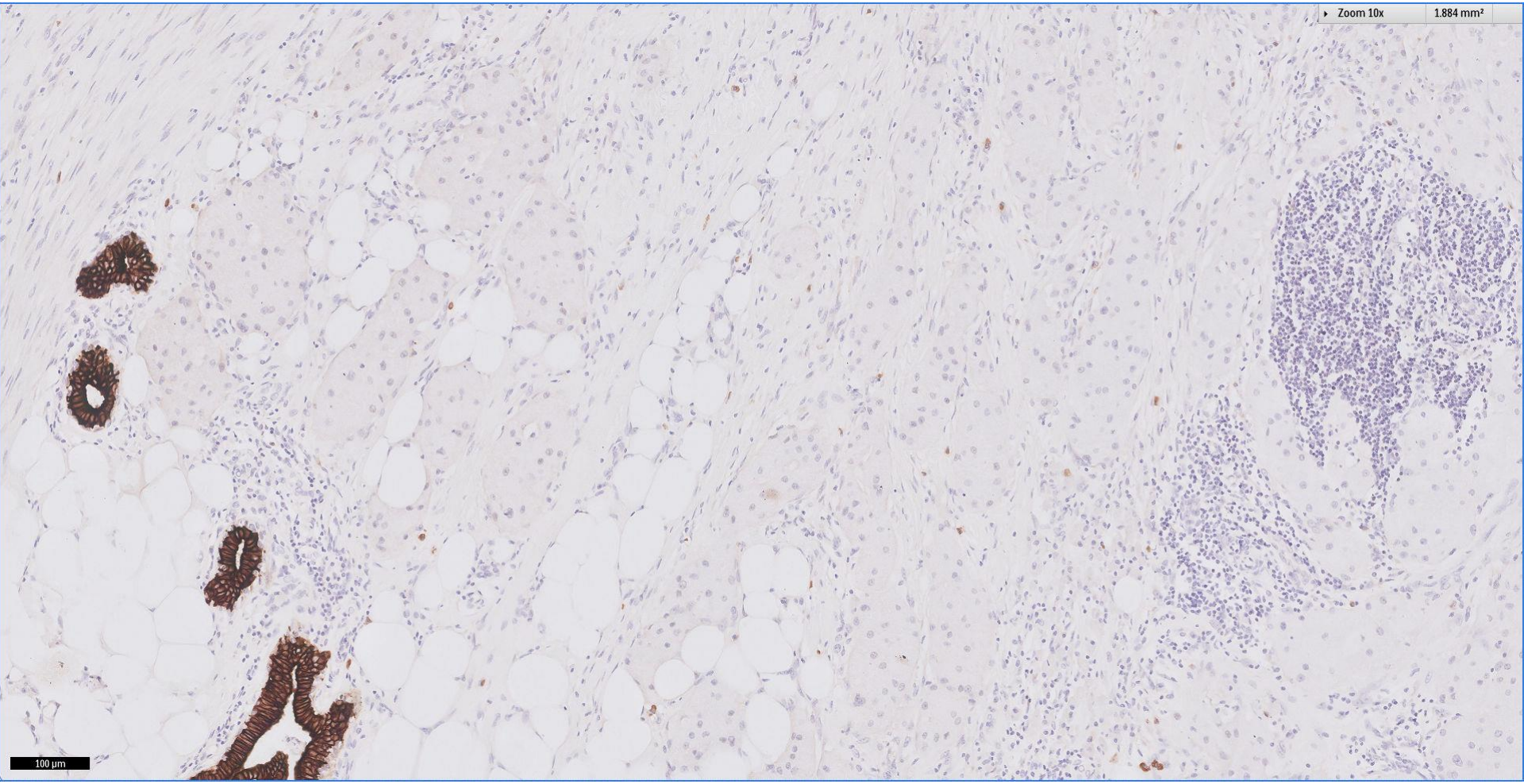
AE1/3



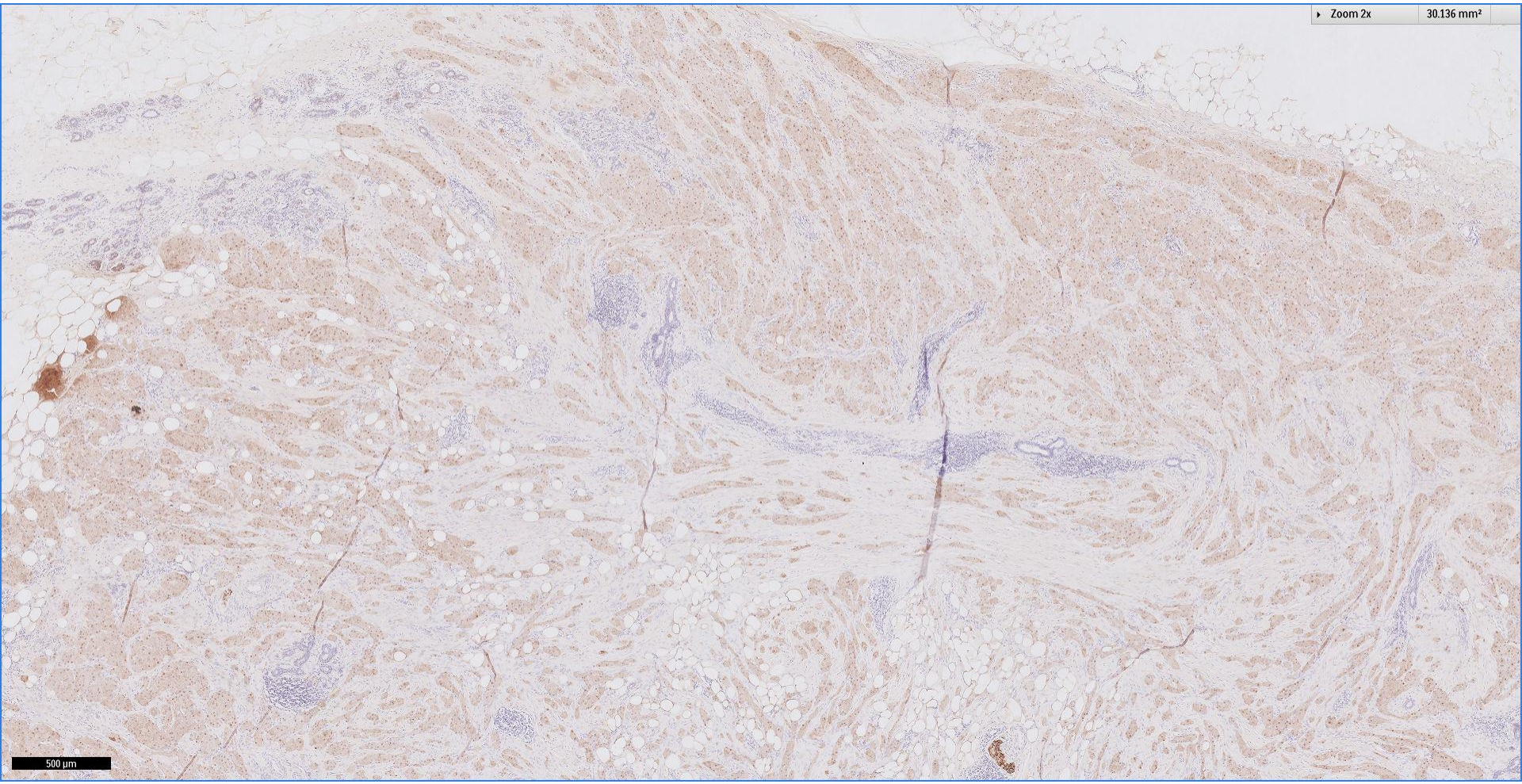
Cam5.2



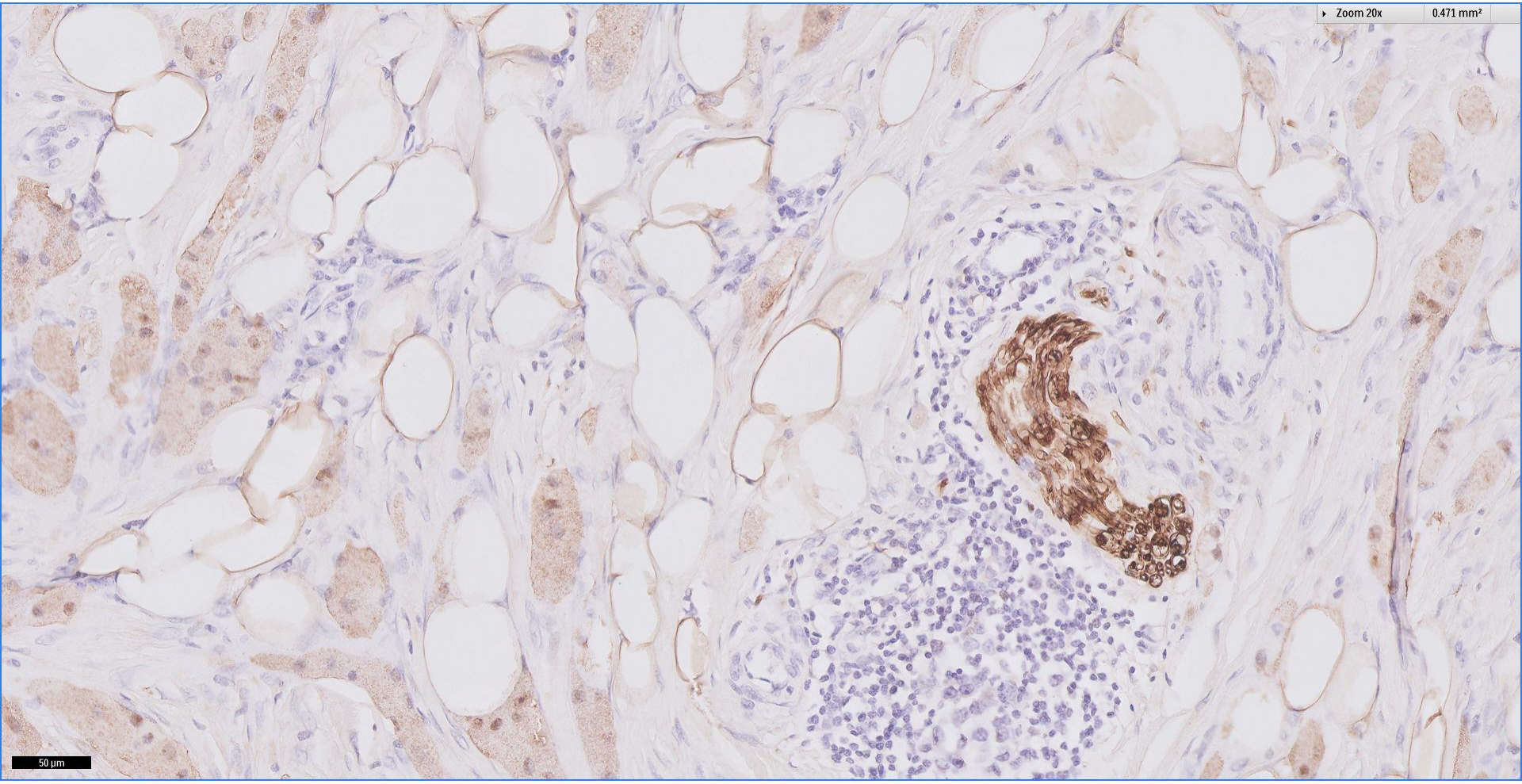
Cam5.2



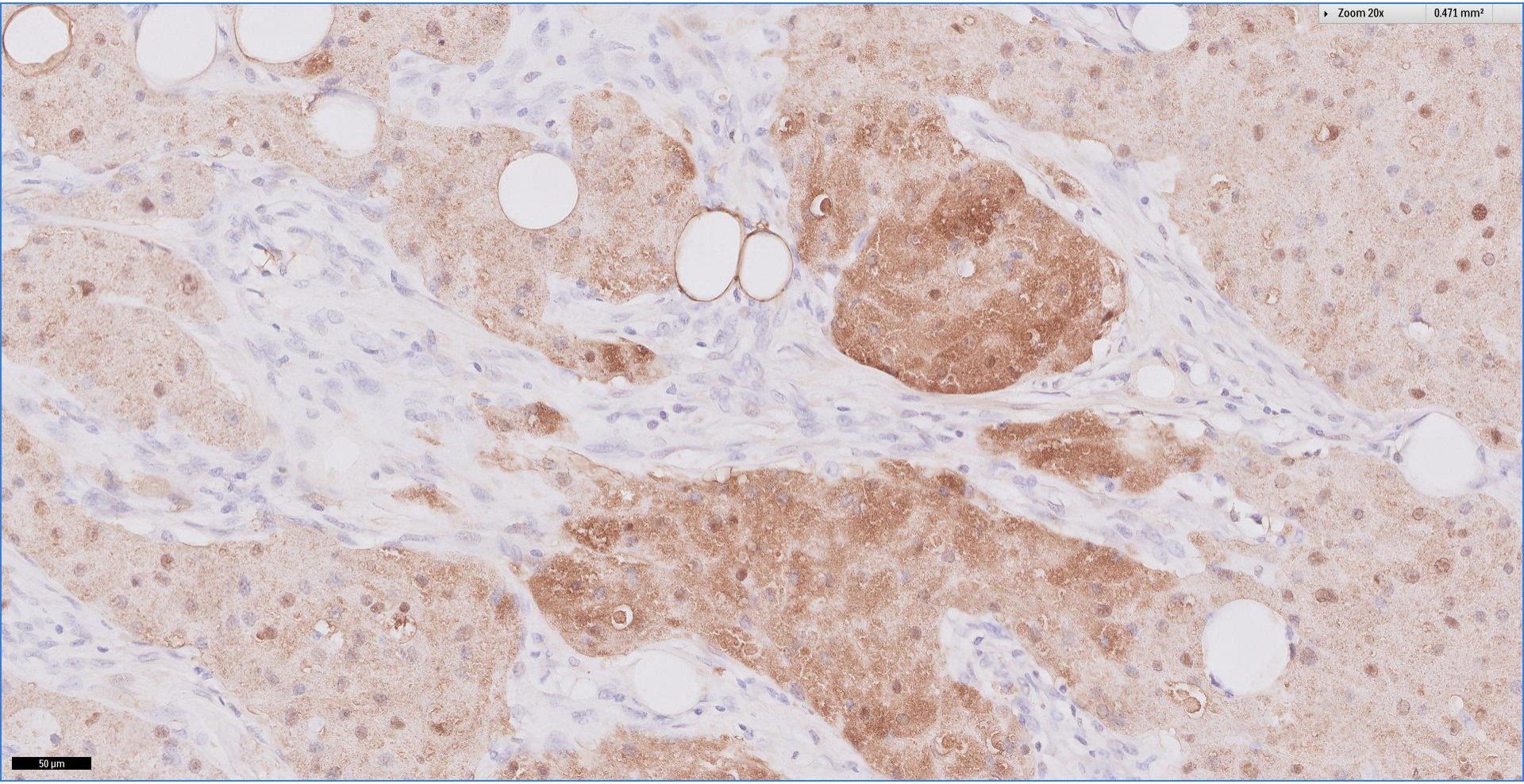
S100



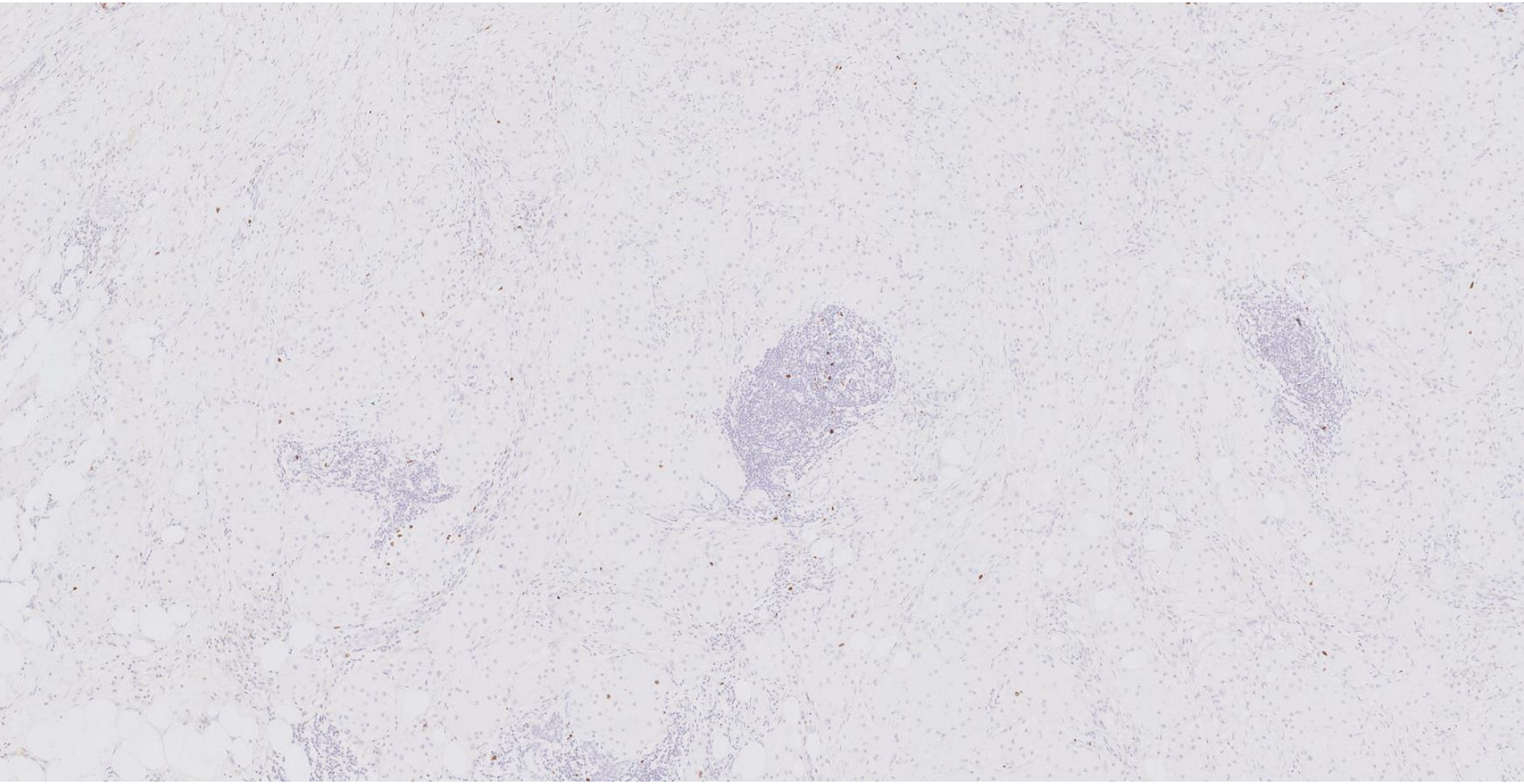
S100



S100



Ki67



Breast Pathology Course 2020 @21

Diagnosis ~
Granular cell tumour

Division of Pathology
Singapore General Hospital

SingHealth DukeNUS
ACADEMIC MEDICAL CENTRE
PATHOLOGY

IAP
International Academy of Pathology
Singapore Division

Granular cell tumour

- Benign neuroectodermal tumour derived from Schwann cells.
- Composed of epithelioid cells with abundant lysosome-rich granular eosinophilic cytoplasm.
- Up to 8% of all granular cell tumours arise in the breast.
- 0.1% of all breast tumours.
- Usually single, with multicentricity in up to 18% of cases.
- Mimics carcinoma clinicoradiologically ~ poorly defined, spiculated masses without microcalcifications.

Granular cell tumour

- Skin lesions are firm, flesh-coloured to red, with skin retraction, nipple inversion and rarely pectoral fascia involvement.
- Malignant change in 1-2% of cases.
- May occur concurrently with invasive breast carcinoma.
- Affects women with a wide age range, blacks more than whites.
- May be seen in mastectomy scars.
- Mutations in driver genes map to X chromosome.

Granular cell tumour

- Information on aetiology is limited.
- May be associated with several syndromes ~ NF1, Noonan syndrome etc.
- Peripheral nerve sheath differentiation.
- Molecular studies ~
  - Loss of function mutations in the *ATP6AP1* and *ATP6AP2* genes: role in regulating endosomal pH.
  - Other mutations in genes encoding ATPase components result in impaired vesicular acidification, altered distribution of endosomes, massive accumulation of intracytoplasmic vesicles.
  - Low mutation burden.

Granular cell tumour

- **Macroscopy**:
  - Homogeneous, white, tan colour.
  - Regular or infiltrative borders.
  - May grow to 5cm.
- **Histopathology**:
  - Infiltrative growth pattern with poorly defined borders.
  - Sheets, clusters and trabeculae of large, round to polygonal cells with abundant eosinophilic and granular cytoplasm.
  - Indistinct cell borders, may appear syncytial.
  - Central small, uniform, hyperchromatic nuclei with variably prominent nucleoli.
  - Cytoplasmic granularity results from massive accumulation of lysosomes, with larger intracytoplasmic granules surrounded by clear haloes (pustule-ovoid bodies of Milian) which are PAS positive/diastase resistant.
  - Frequent perineural and perivascular involvement.
  - Mitoses are scarce.
  - Overlying pseudoepitheliomatous hyperplasia.

Granular cell tumour

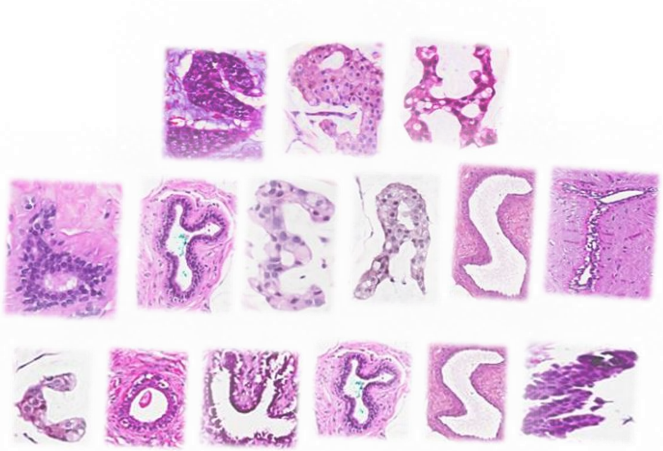
- Histopathology:
  - Malignant forms ~ larger tumour size >5cm, cellular & nuclear pleomorphism, prominent nucleoli, increased mitotic activity, tumour necrosis, local recurrence.
  - Immunohistochemistry ~
    - Strong diffuse positivity for S100.
    - Positivity for CD68, CD63, NSE.
    - Nuclear reactivity for TFE3 and MITF.
    - Negative staining for HMB45, melan-A, GFAP, keratins, NFP.
    - Ki67 proliferation index is low (<2%).

Granular cell tumour

- Differential diagnoses ~
  - Apocrine tumours
  - Naevi
  - Melanoma
  - Carcinoma
  - Alveolar soft part sarcoma
- Treatment is local excision, with minimal risk of recurrence even when margins are positive.
- Malignant forms can metastasize.

Breast Pathology Course 2020 @21

Thank you!



Division of Pathology
Singapore General Hospital

SingHealth DukeNUS ACADEMIC MEDICAL CENTRE
PATHOLOGY

IAP
International Academy of Pathology
Singapore Division