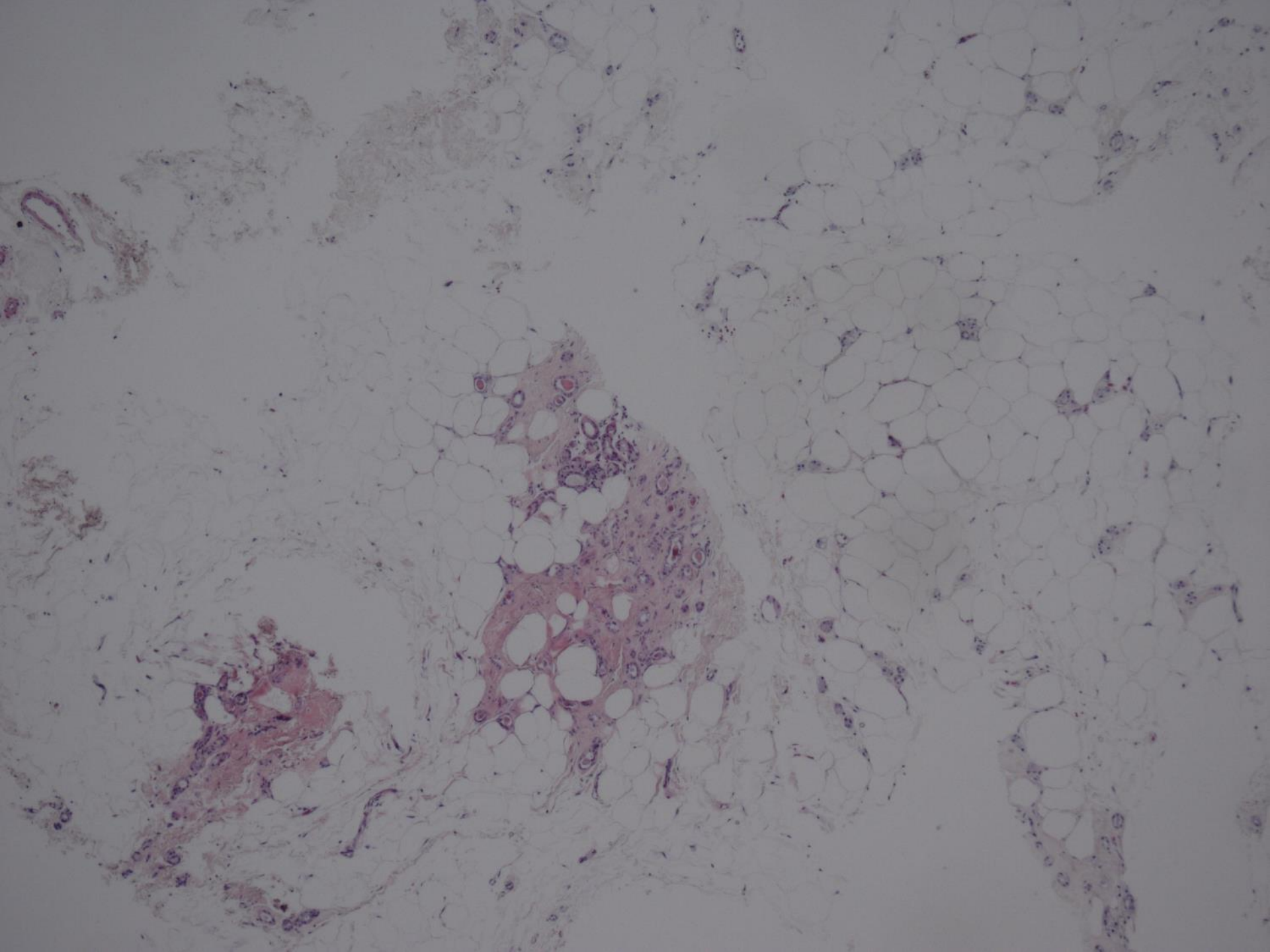
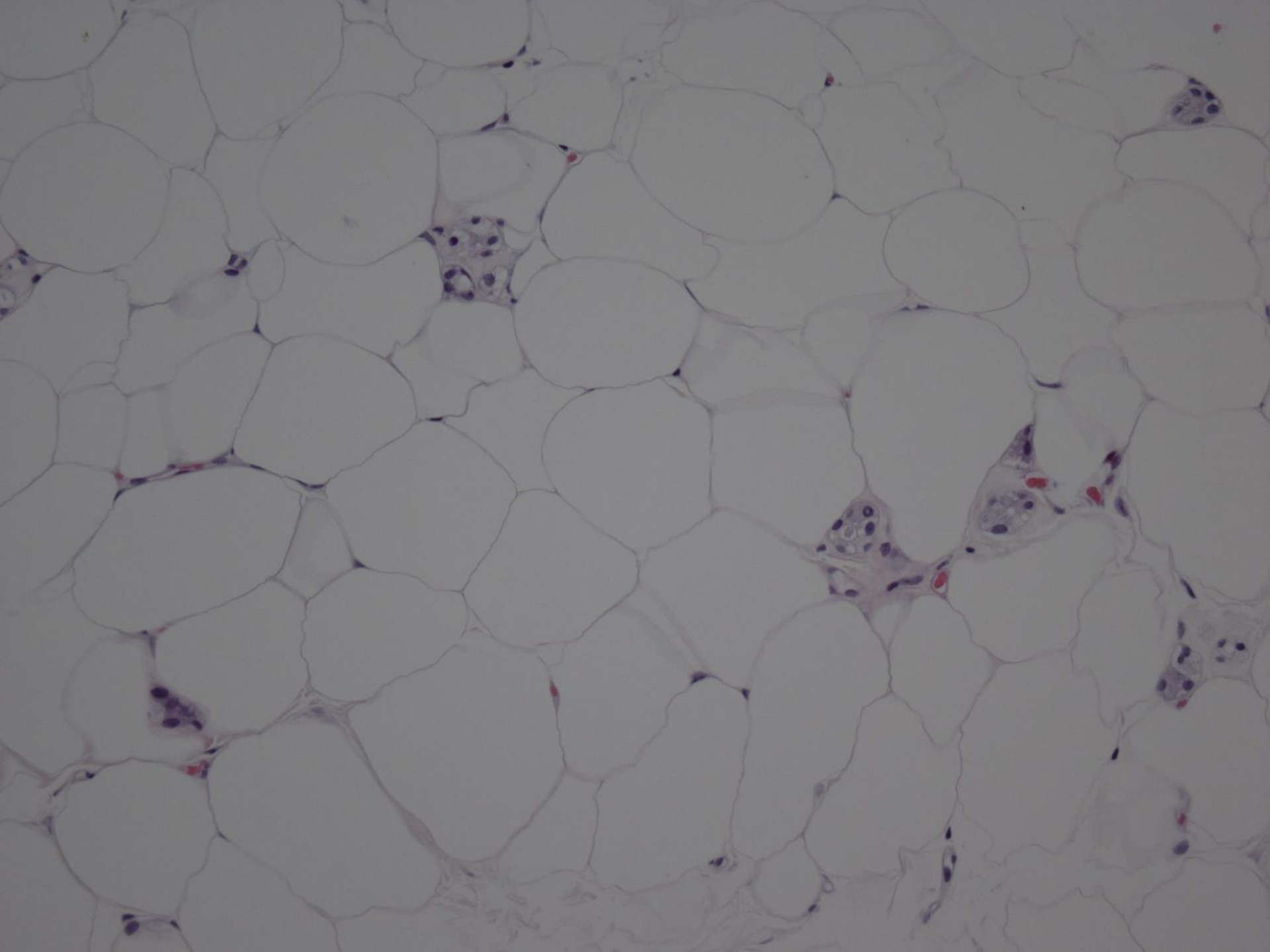
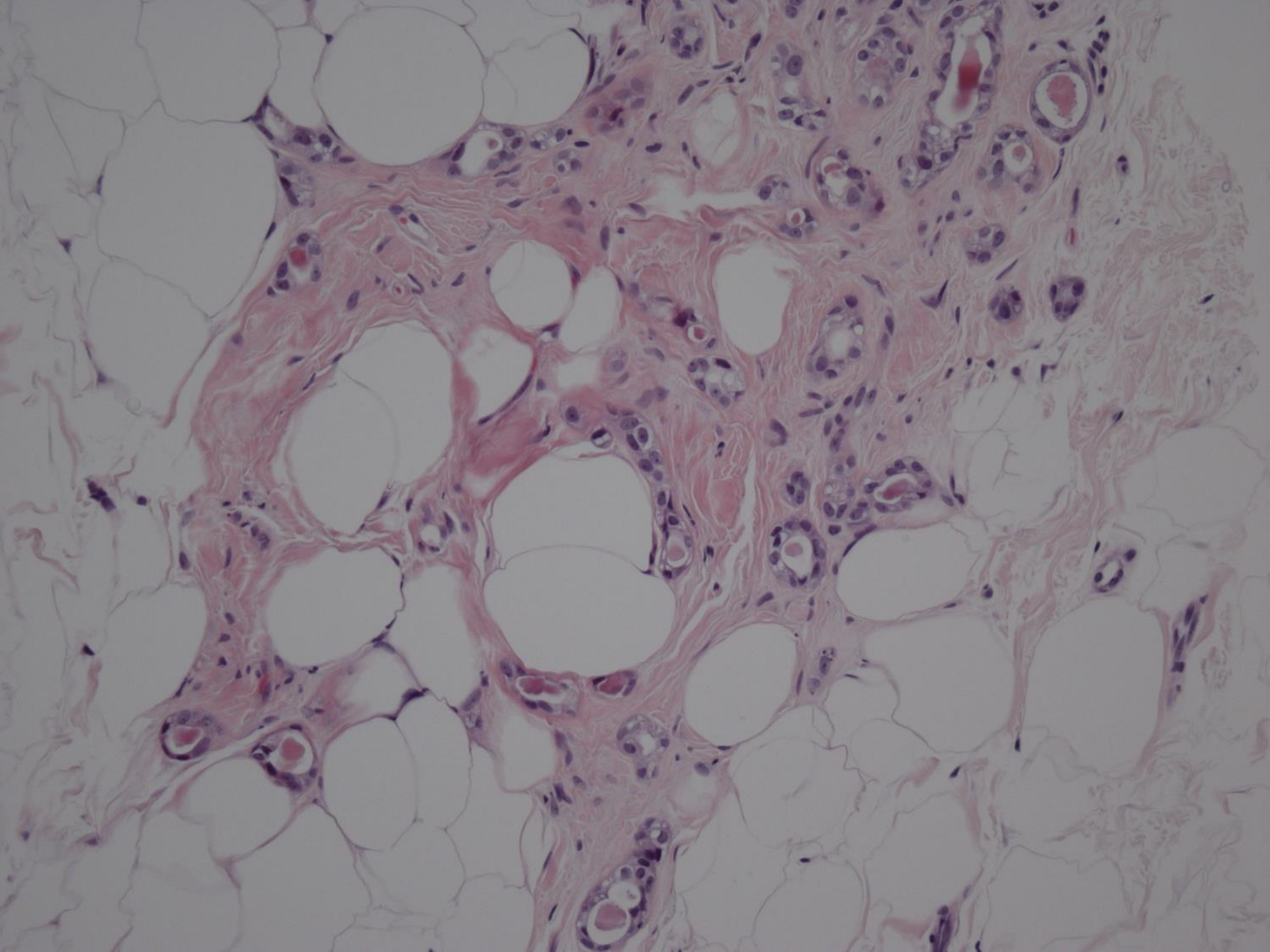
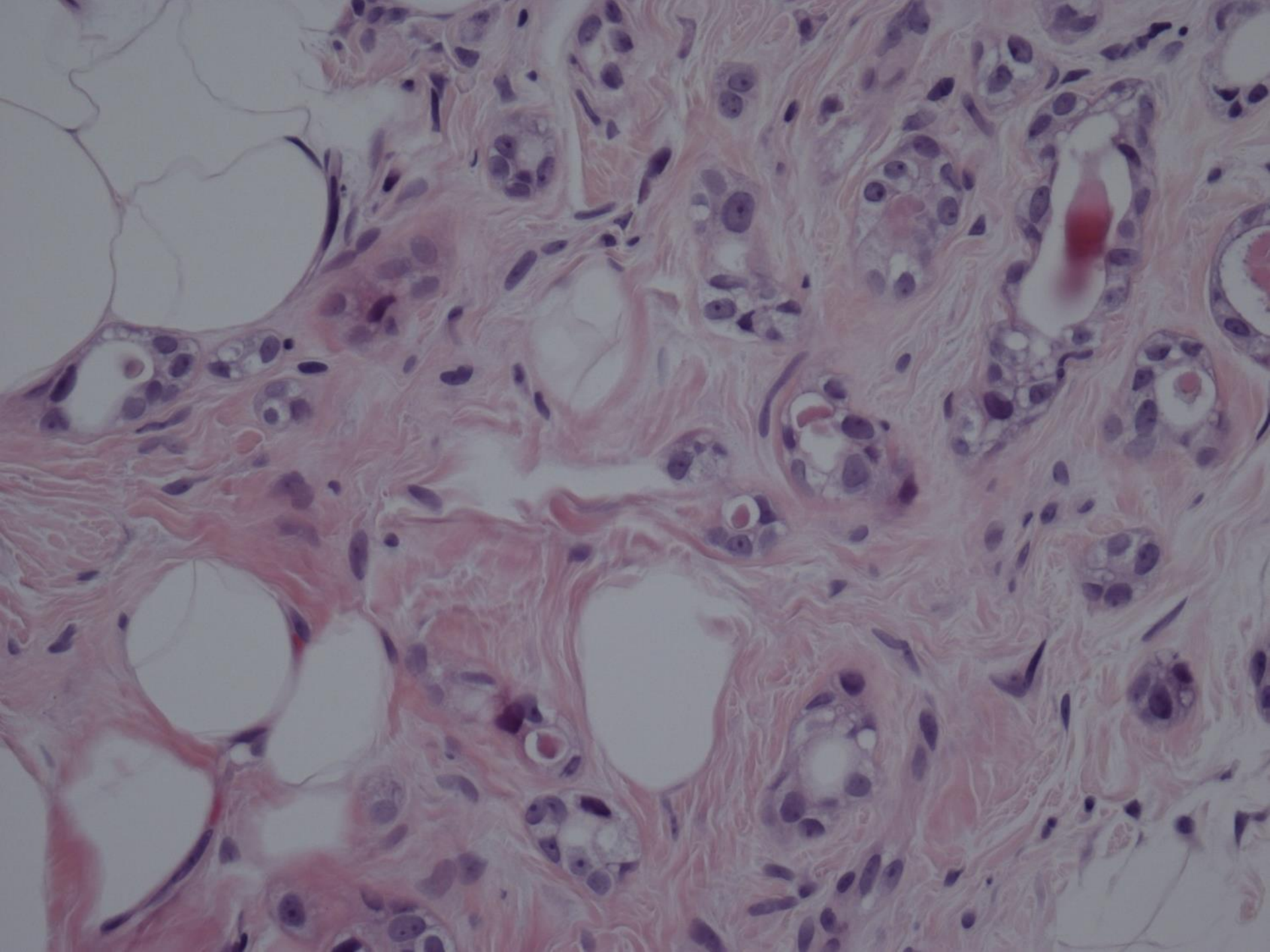
Case 5 History

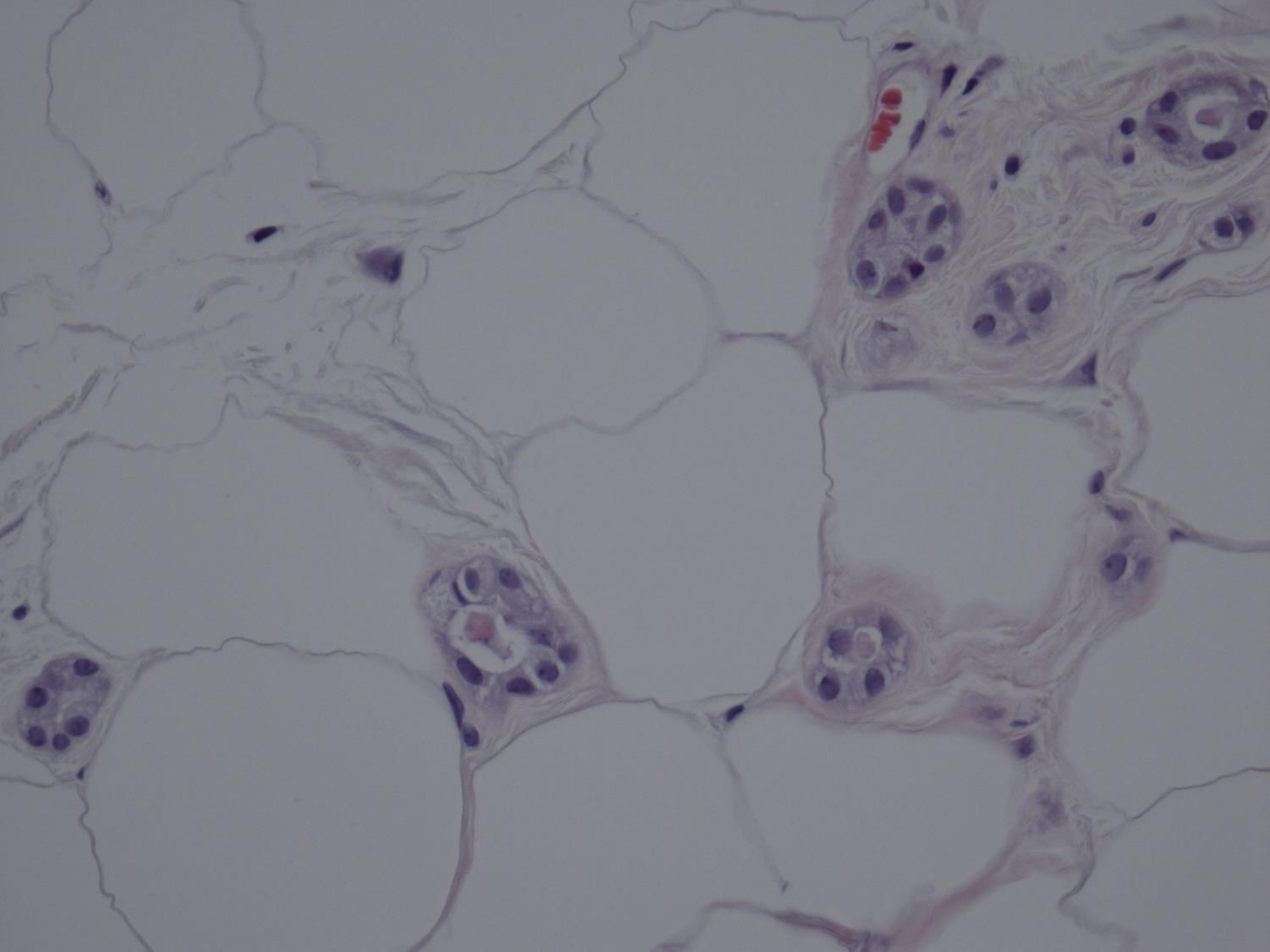
- 63 year old woman
- Indeterminate breast lesion
- Upper inner/outer quadrant
- Ultrasound core biopsy

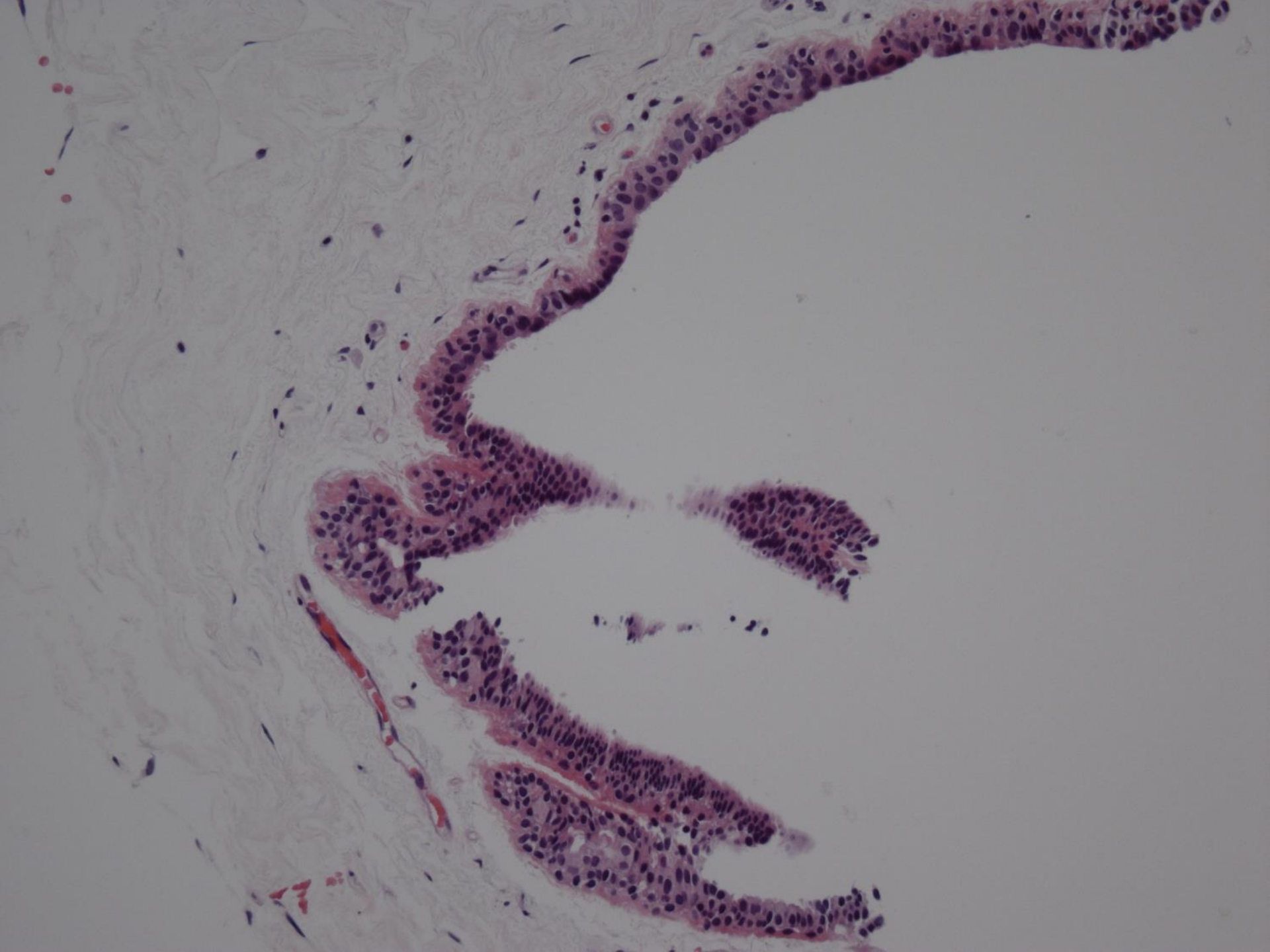










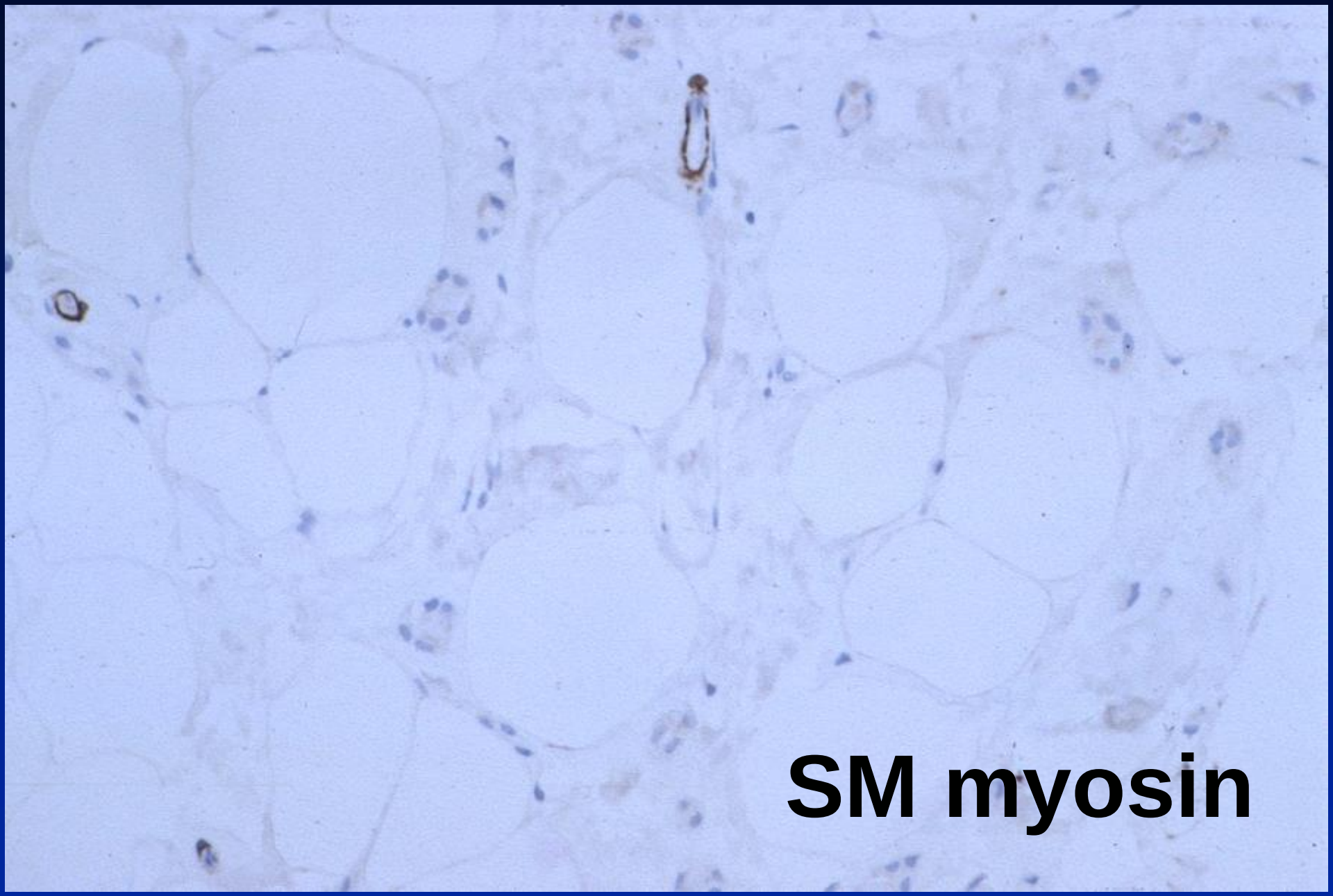


Histological features

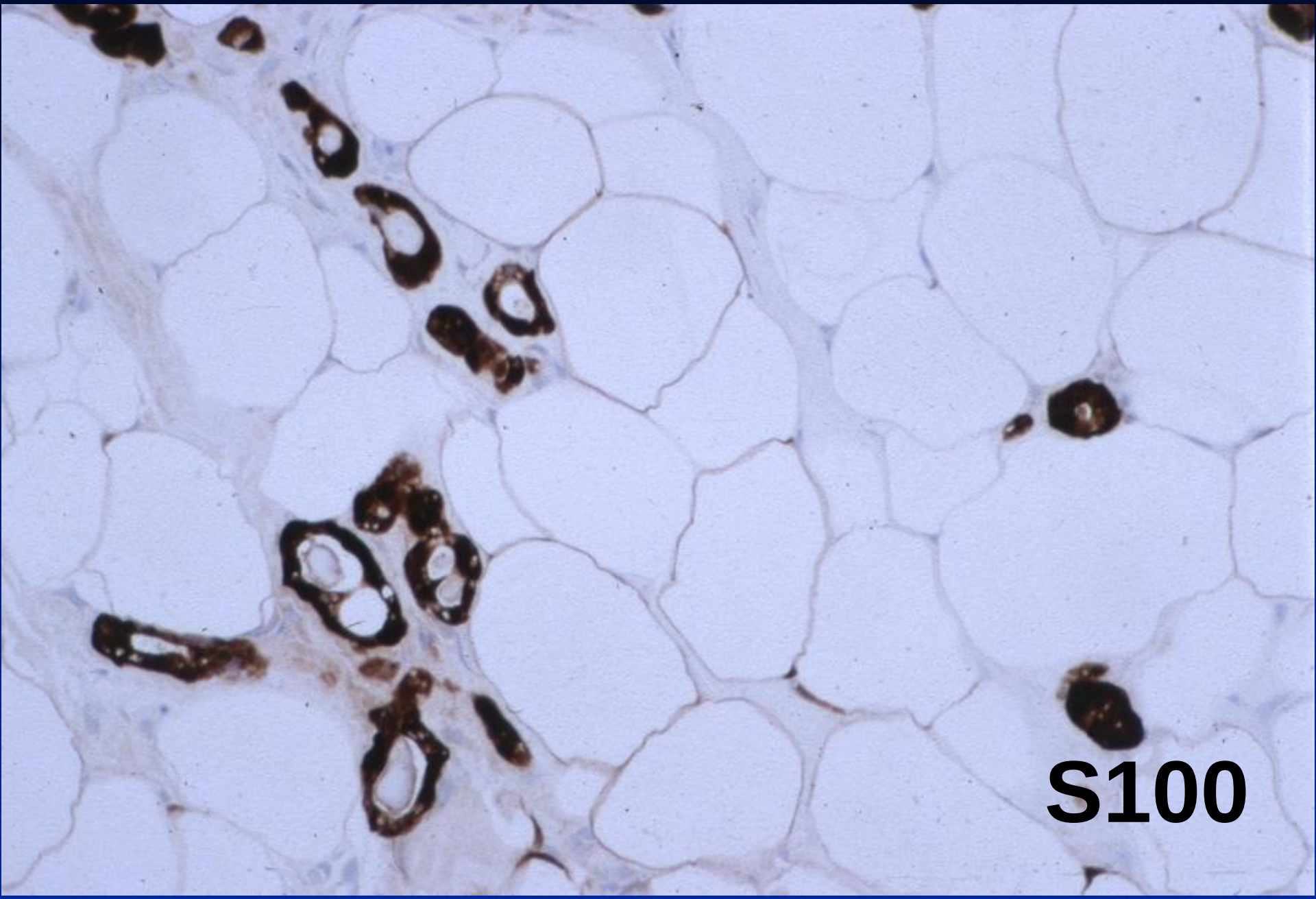
- Tubules
- Not a lobular architecture
- Extending into adipose tissue
- No tissue reaction
- Bland cytology

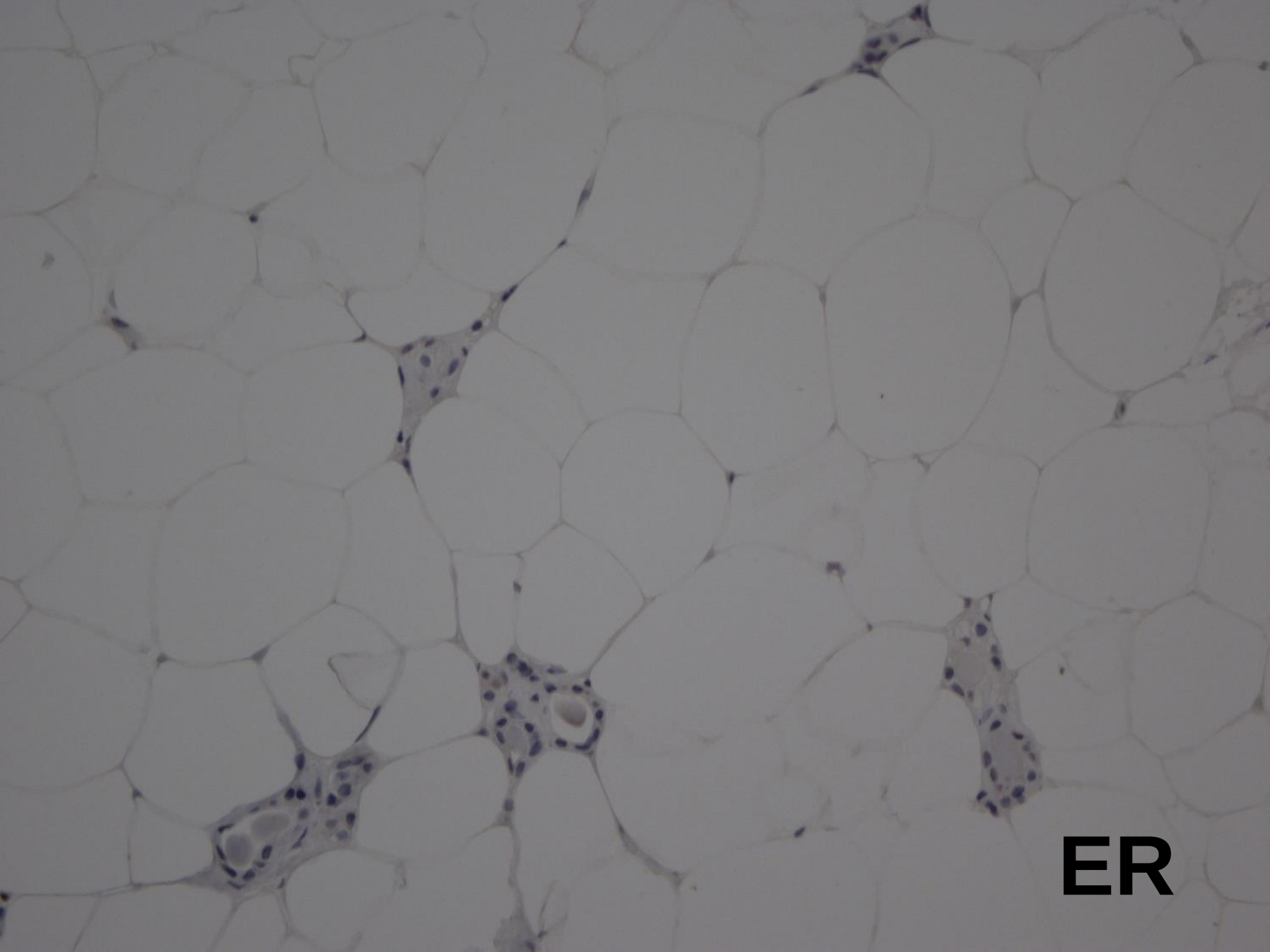
Responses

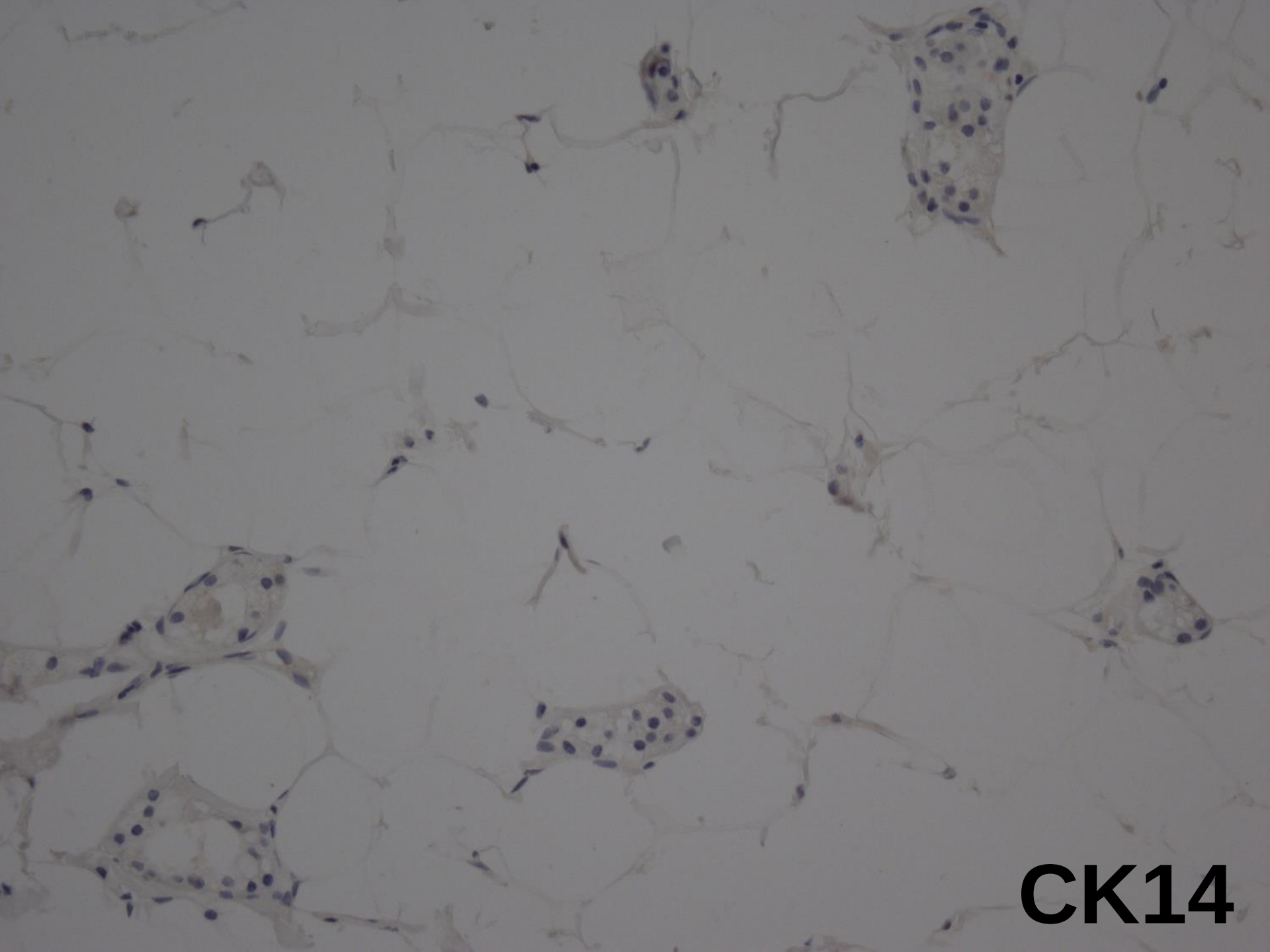
Microglandular adenosis	15
Atypical microglandular adenosis	2
Invasive carcinoma	4
Invasive NST carcinoma	4
Tubular carcinoma	1
Adenoid cystic carcinoma	1
MGA v adenocarcinoma	3
Sclerosing/tubular adenosis v invasive	2
Carcinoma in MGA	2
Involution v adenocarcinoma	1
Sclerosing adenosis + FEA	1
Unclear	3

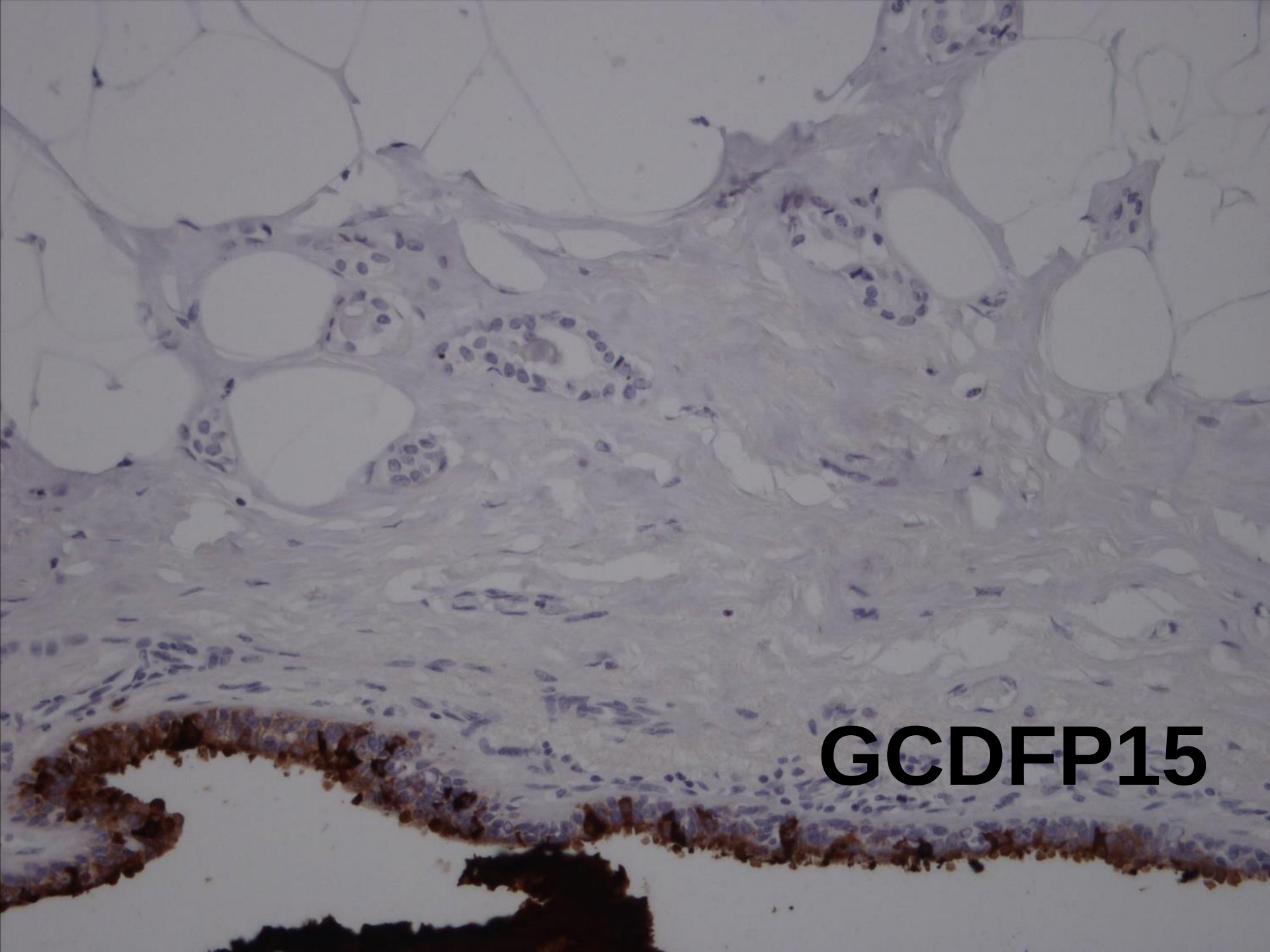

SM myosin

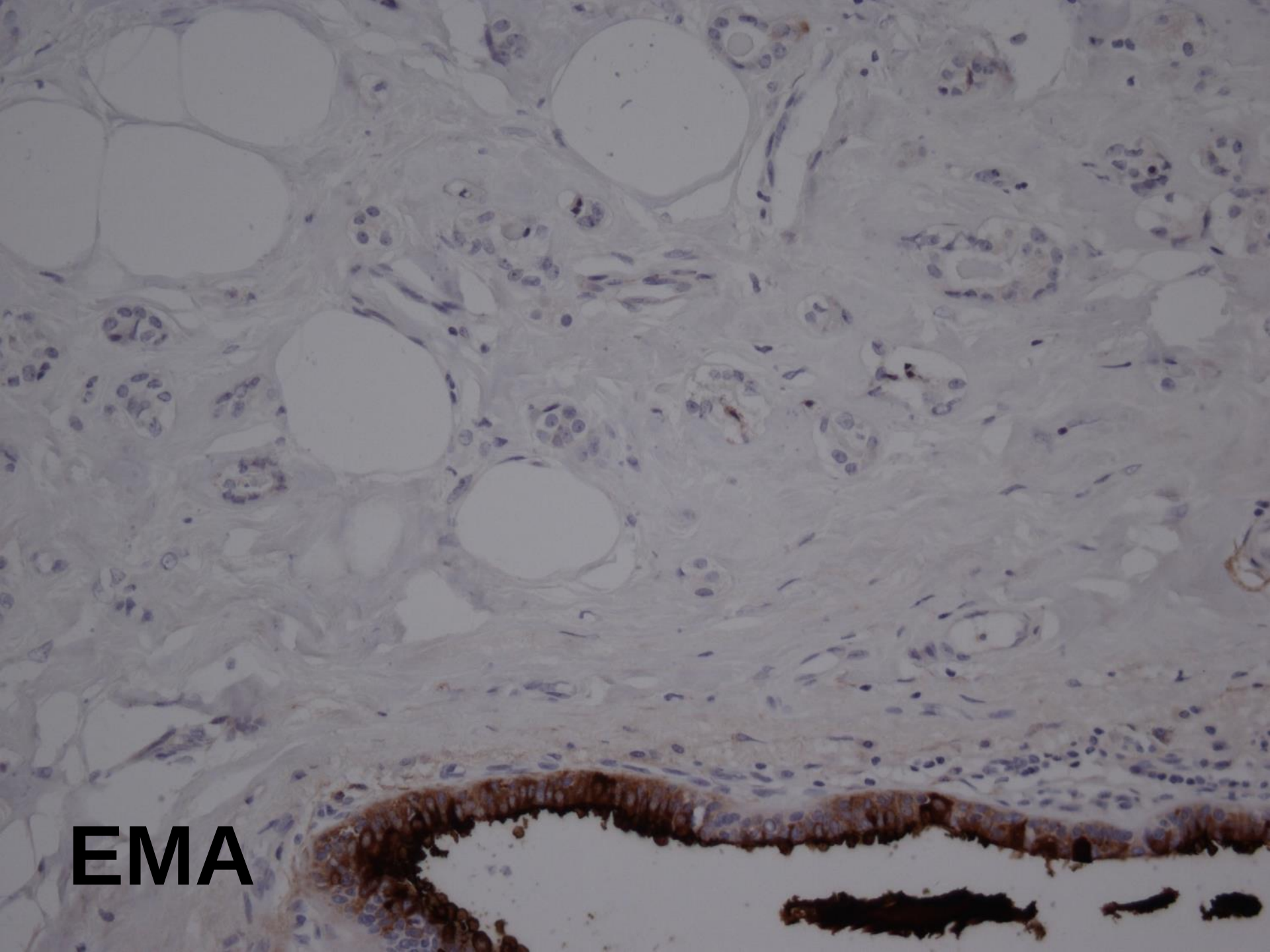

Collagen IV


S100


ER


CK14


GCDFP15

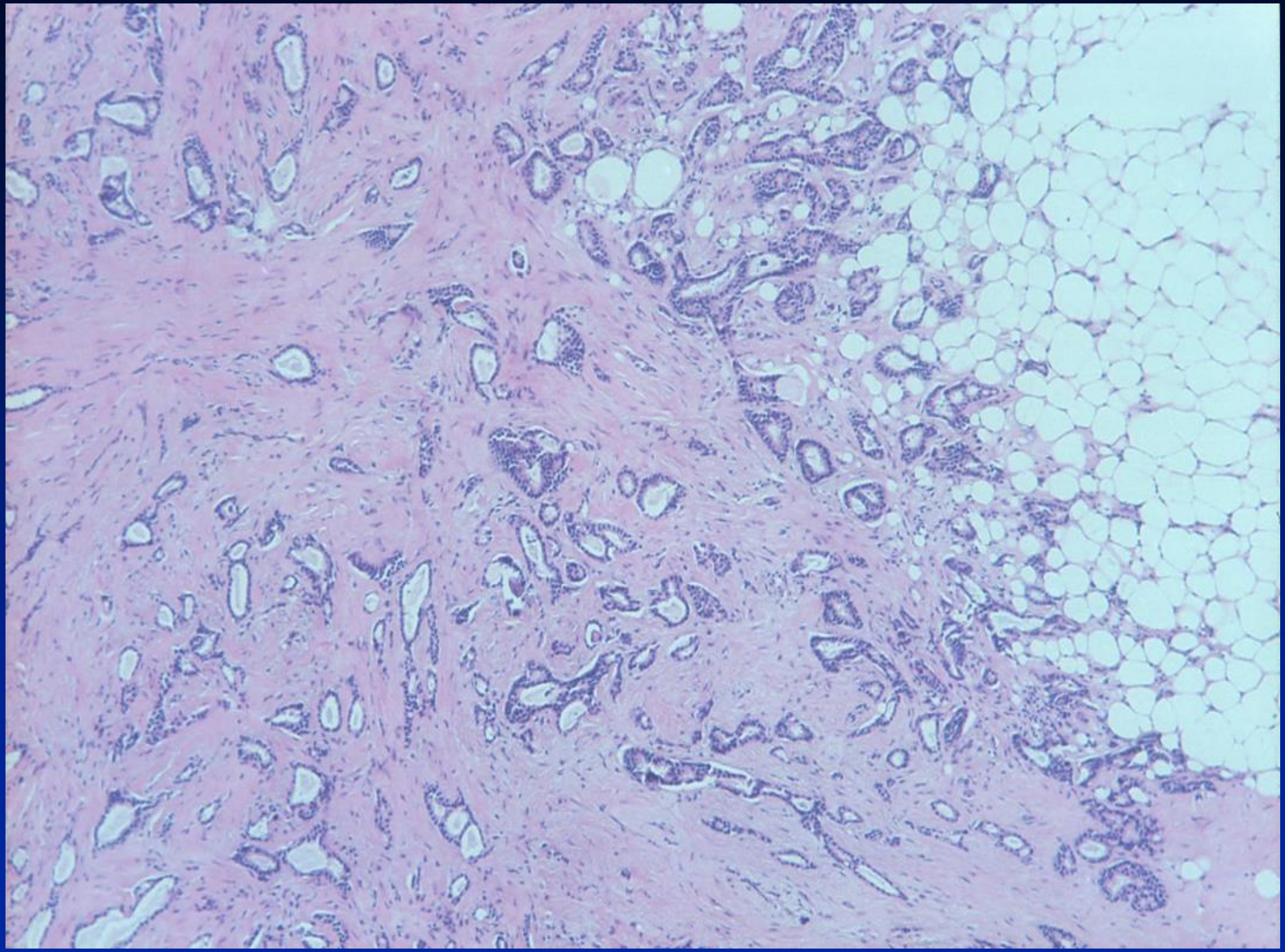

EMA

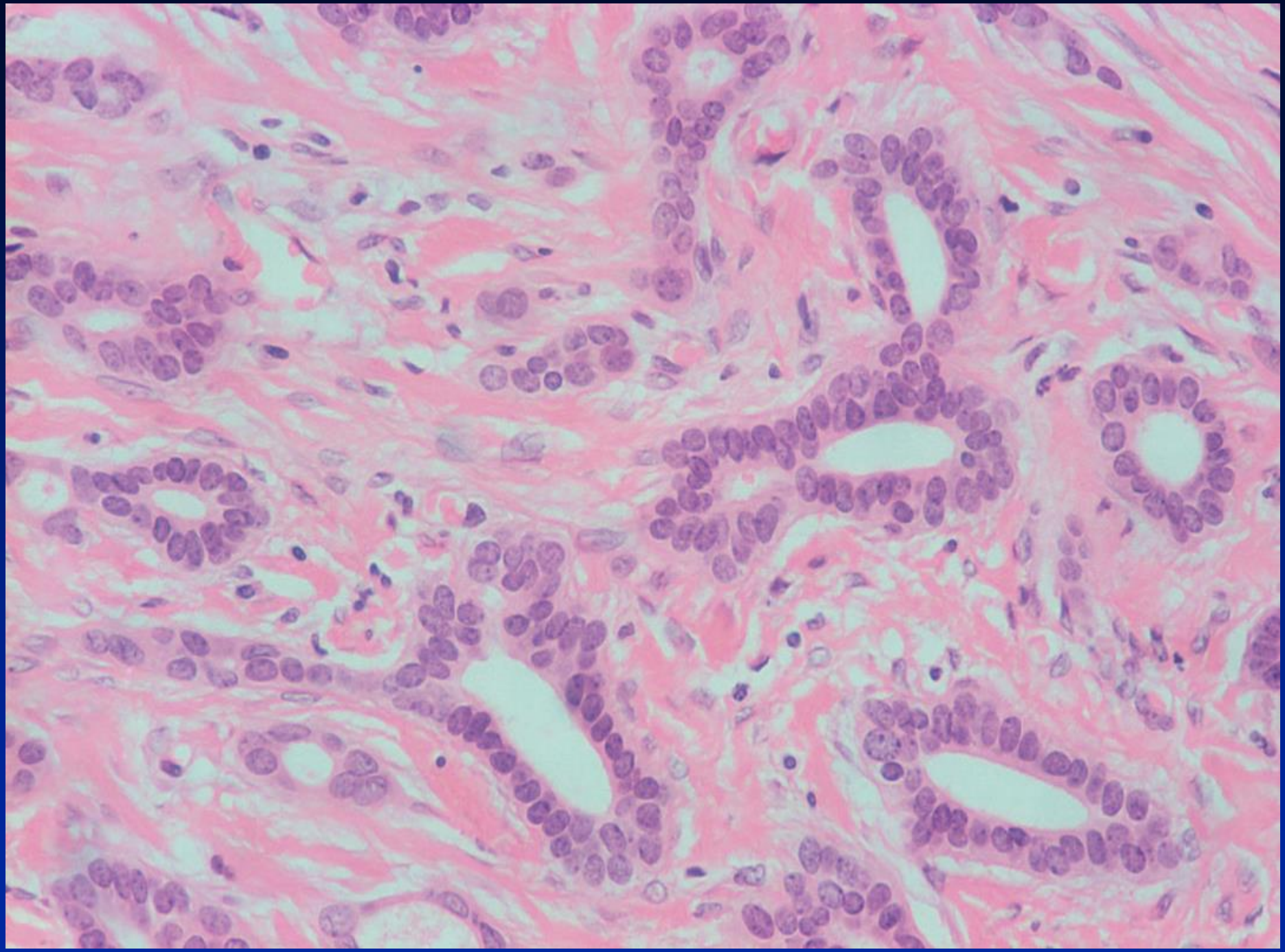
Microglandular adenosis

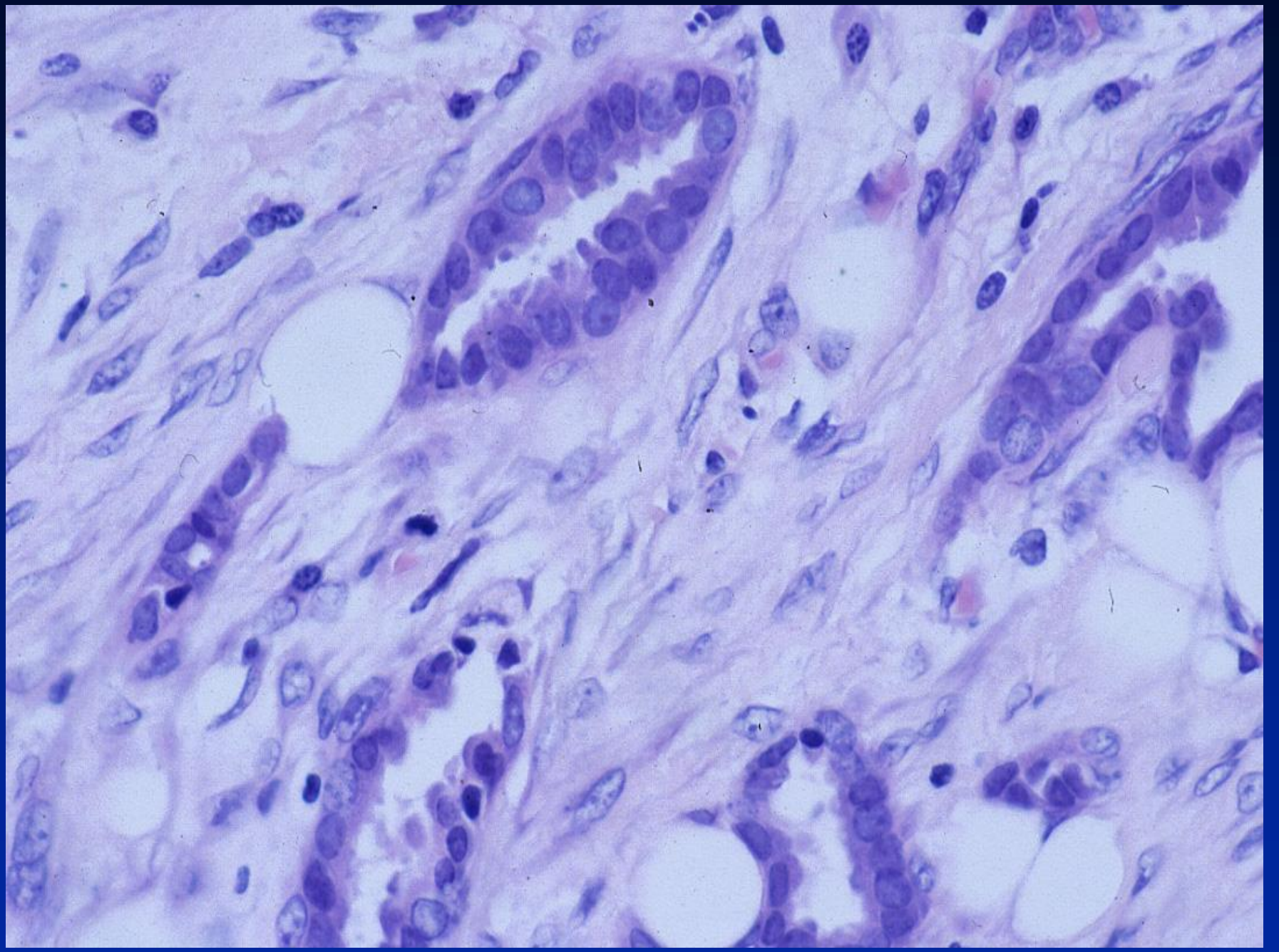
- Clue is low power – not lobular architecture
- Small tubules
- Single layer, cuboidal/flat
- Eosinophilic PAS+ luminal secretion
- Occasionally solid islands
- No stromal reaction
- Bland cytology
- Absent myoepithelial layer
- Basement membrane present
- S100 positive
- EMA, ER, PR and HER2 negative

Microglandular adenosis

- First described in AFIP fascicle 1968
- Clement PB, Azzopardi JG. Microglandular adenosis of the breast – a lesion simulating tubular carcinoma. Histopathology 1983;7:169-80.







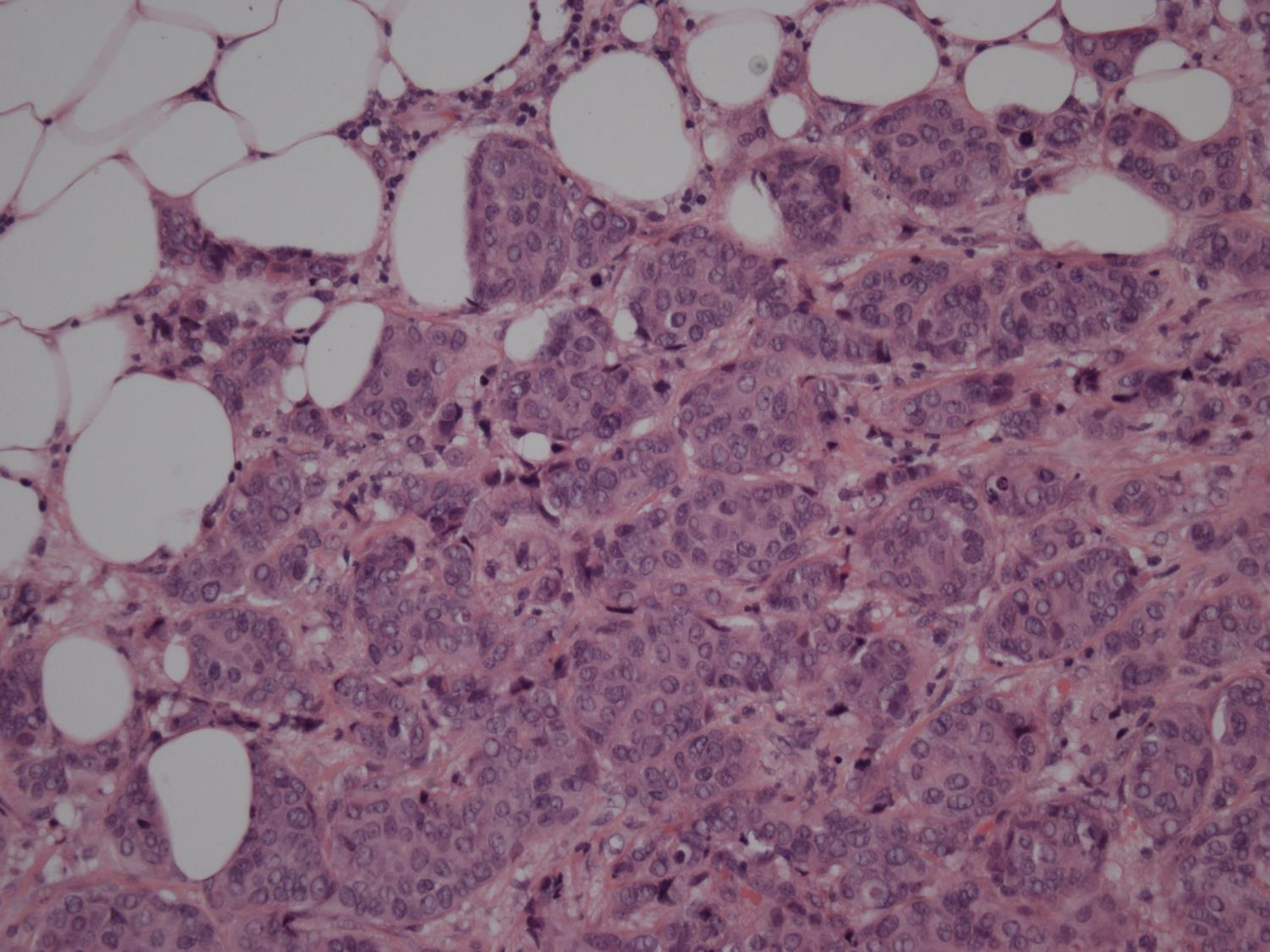
Differential diagnosis

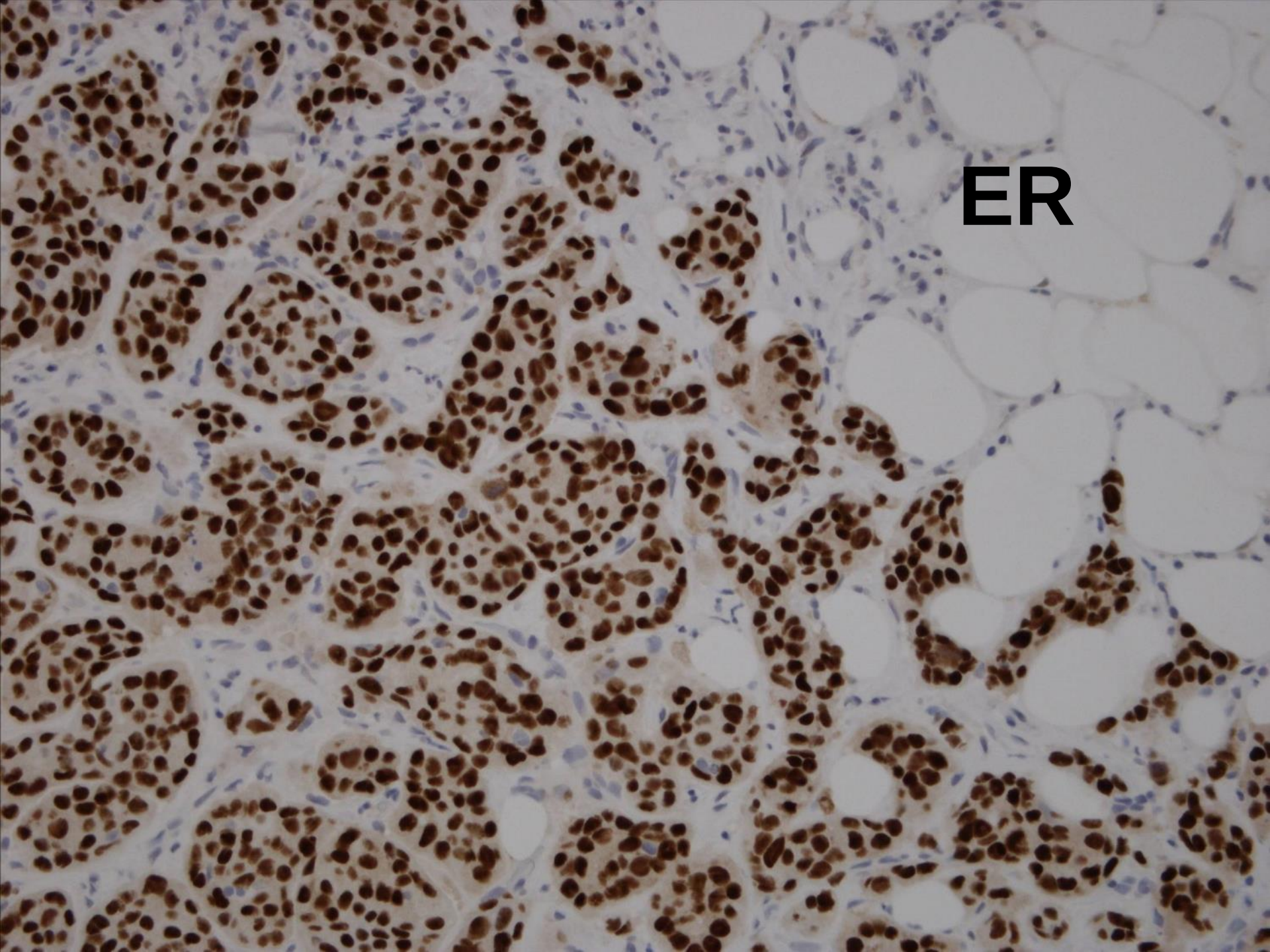
Tubular carcinoma

- Tear drop shaped tubules
- Columnar morphology
- Apocrine snouts
- Fibroelastotic stroma
- Oestrogen receptor positive

Follow up

- Underwent wide local excision and re-excision with clear margins
- 4 years later
- Upper inner/lower inner quadrant mass in the same breast

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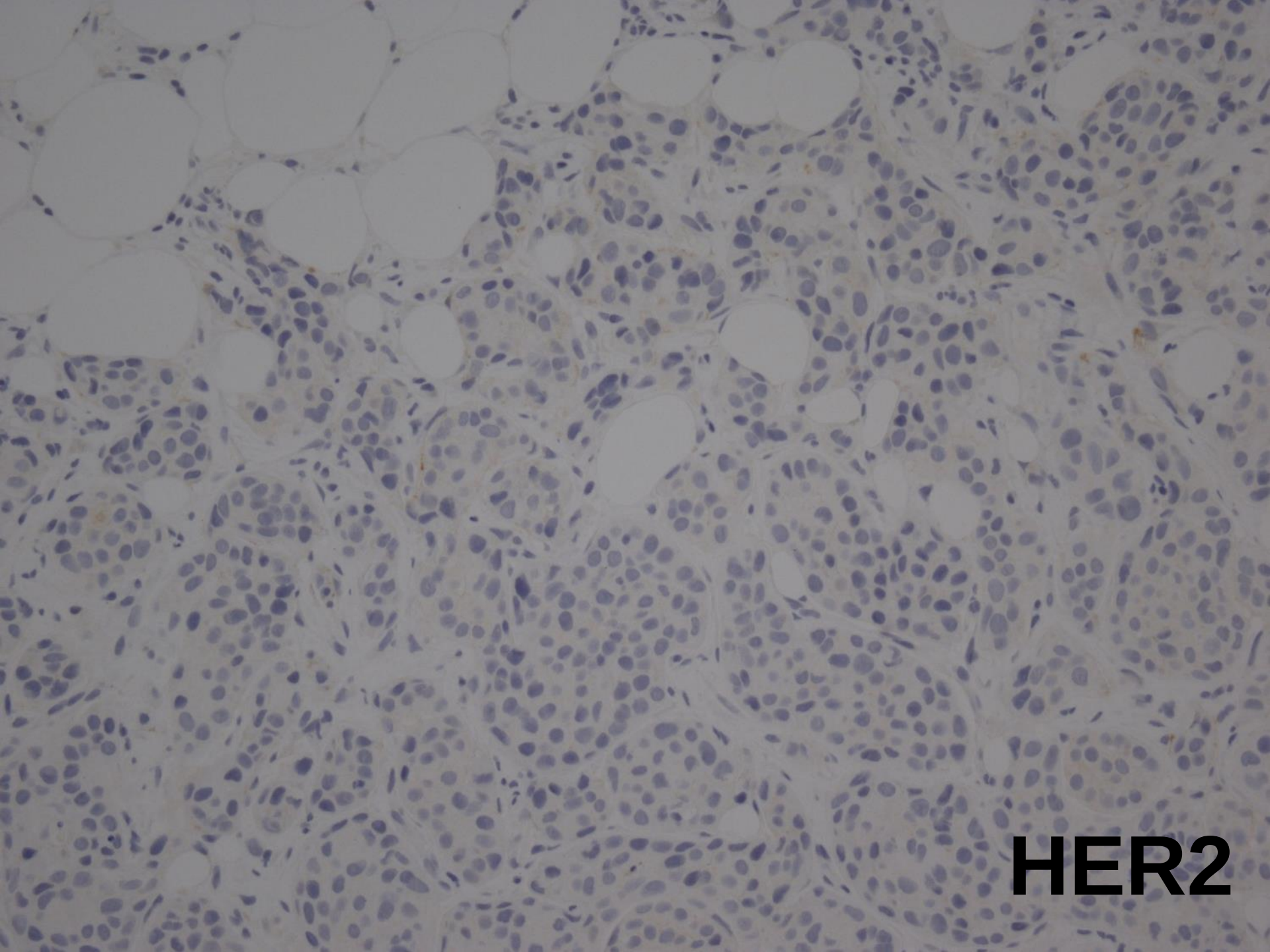

HER2

Invasive carcinoma NST

Grade 2 (T3, P2, M1)

17mm

ER positive

HER2 negative

Node negative

No residual microglandular adenosis

Microglandular adenosis

- Previously considered as benign
- But sometimes merges with carcinoma
- Often triple negative
- NST
- Adenoid cystic
- Spindle cell carcinoma
- Matrix-producing carcinoma
- Atypical microglandular adenosis

Shin SJ, al. Molecular evidence for progression of microglandular adenosis (MGA) to invasive carcinoma. Am J Surg Pathol 2009; 33; 496–504.

- Comparative genomic hybridization
- 5 MGA and 3 AMGA – no alterations
- 7 MGA and 9 AMGA – copy number changes (some widespread)
- Frequent concordance in genomic profiles between MGA and carcinoma arising in MGA
- 3 pure MGA – 2 no copy number changes and 1 with numerous gains and losses

Geyer et al. Molecular evidence in support of the neoplastic and precursor nature of microglandular adenosis. Histopathology 2012, 60, E115–E130

- 10 carcinomas associated with MGA
- NST, matrix producing, acinic cell-like, adenoid cystic
- All triple negative
- All S100+, CK8/18+
- Focal HMWCK or EGFR

Geyer et al Histopathology 2012

- Microarray comparative genomic hybridization
- MGA genetically heterogeneous
- Some had complex alterations
- Some had no copy number changes
- Similar changes in MGA and adjacent carcinoma

Guerini-Rocco et al. J Pathol 2016

236 genes analysed

MGA and AMGA with associated carcinoma

Non-synonymous somatic mutations

MGA (n = 7) median 5 (range 3-14)

AMGA (n = 3) median 3 (range 1-10)

TP53 mutations

MGA 6/7

AMGA 1/3

Identical mutation in adjacent carcinoma

Also mutations in PI3K pathway

Guerini-Rocco et al. J Pathol 2016

MGA without associated carcinoma (n = 2)

No mutations of TP53 or PI3K pathway

- **TNBCs associated with MGA /AMGA have molecular characteristics consistent with those of unselected TNBCs**
- **MGA likely constitutes a non-obligate precursor of TNBC**

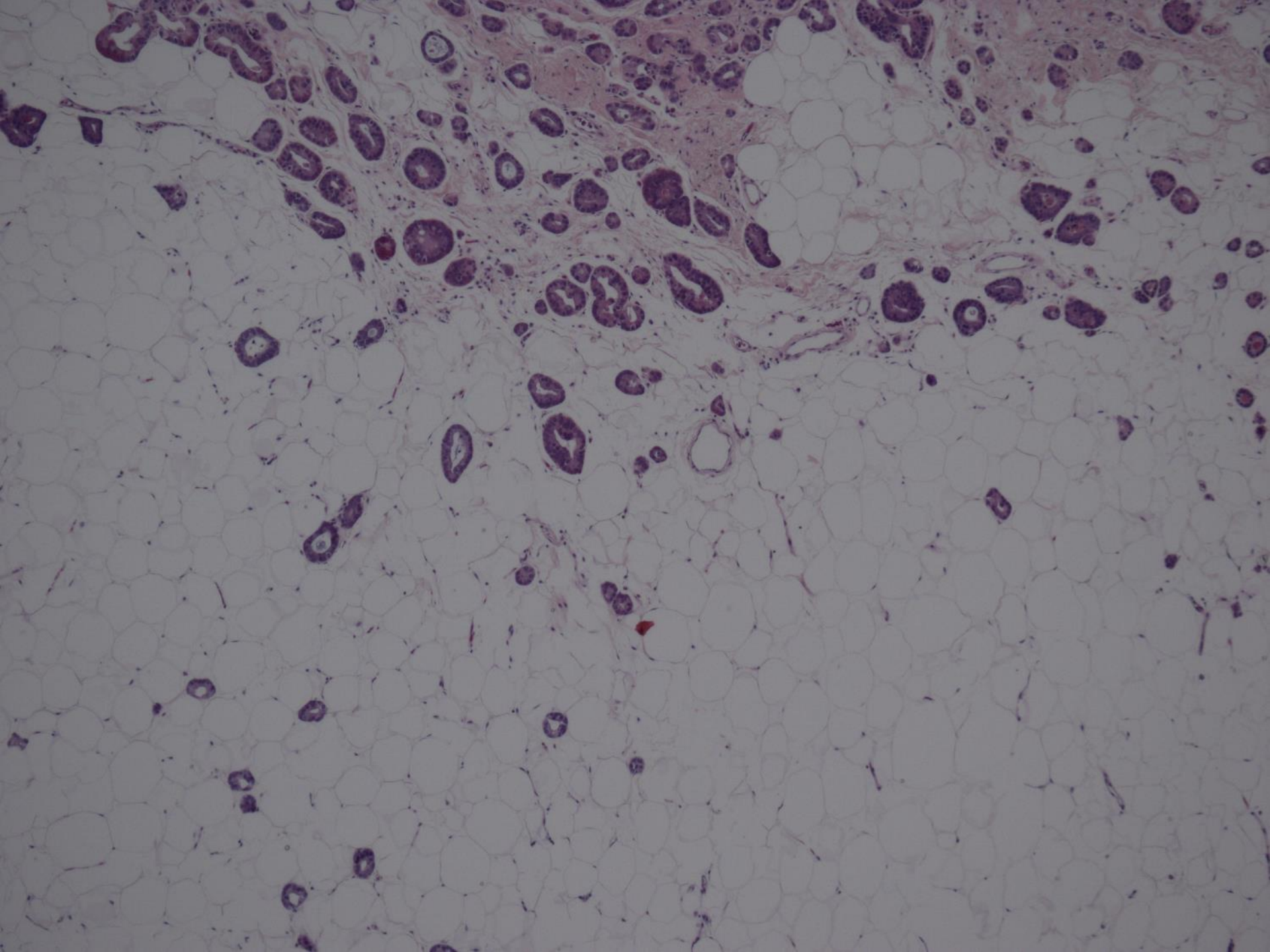
Guerini-Rocco et al. J Pathol 2016

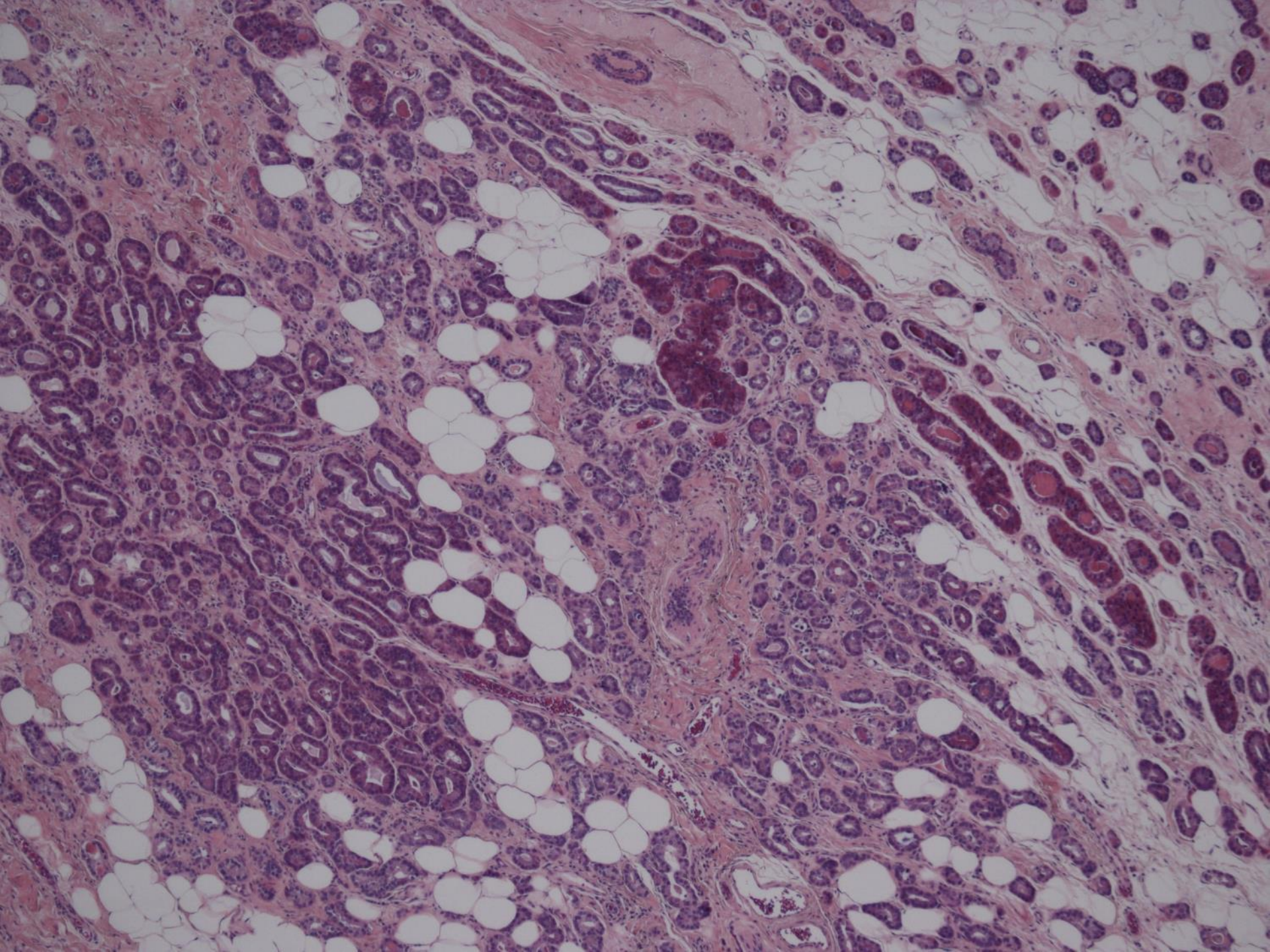
MGA with DCIS and invasive carcinoma

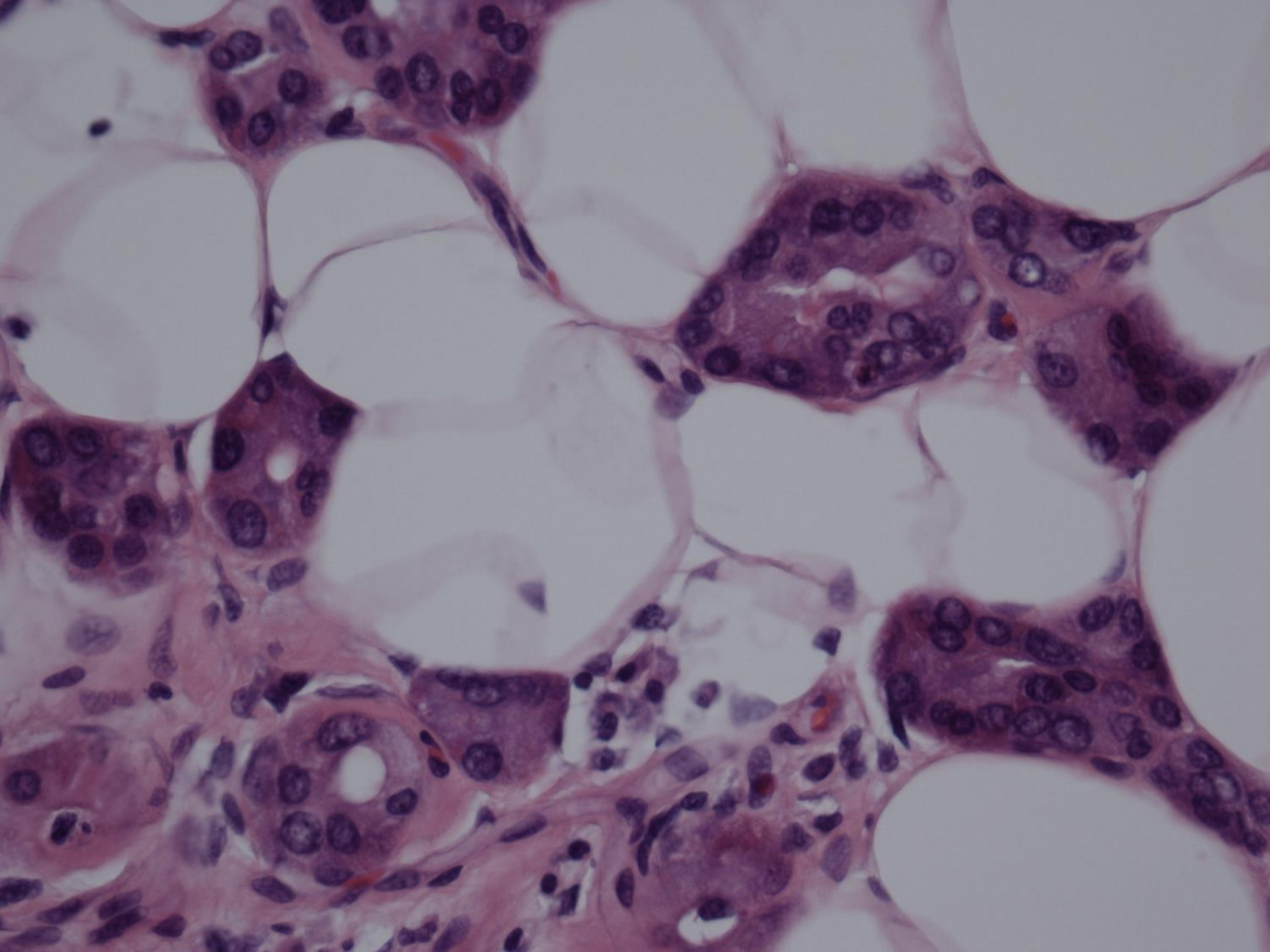
- MGA and TNBC clonally related
- DCIS not clonally related to TNBC or MGA

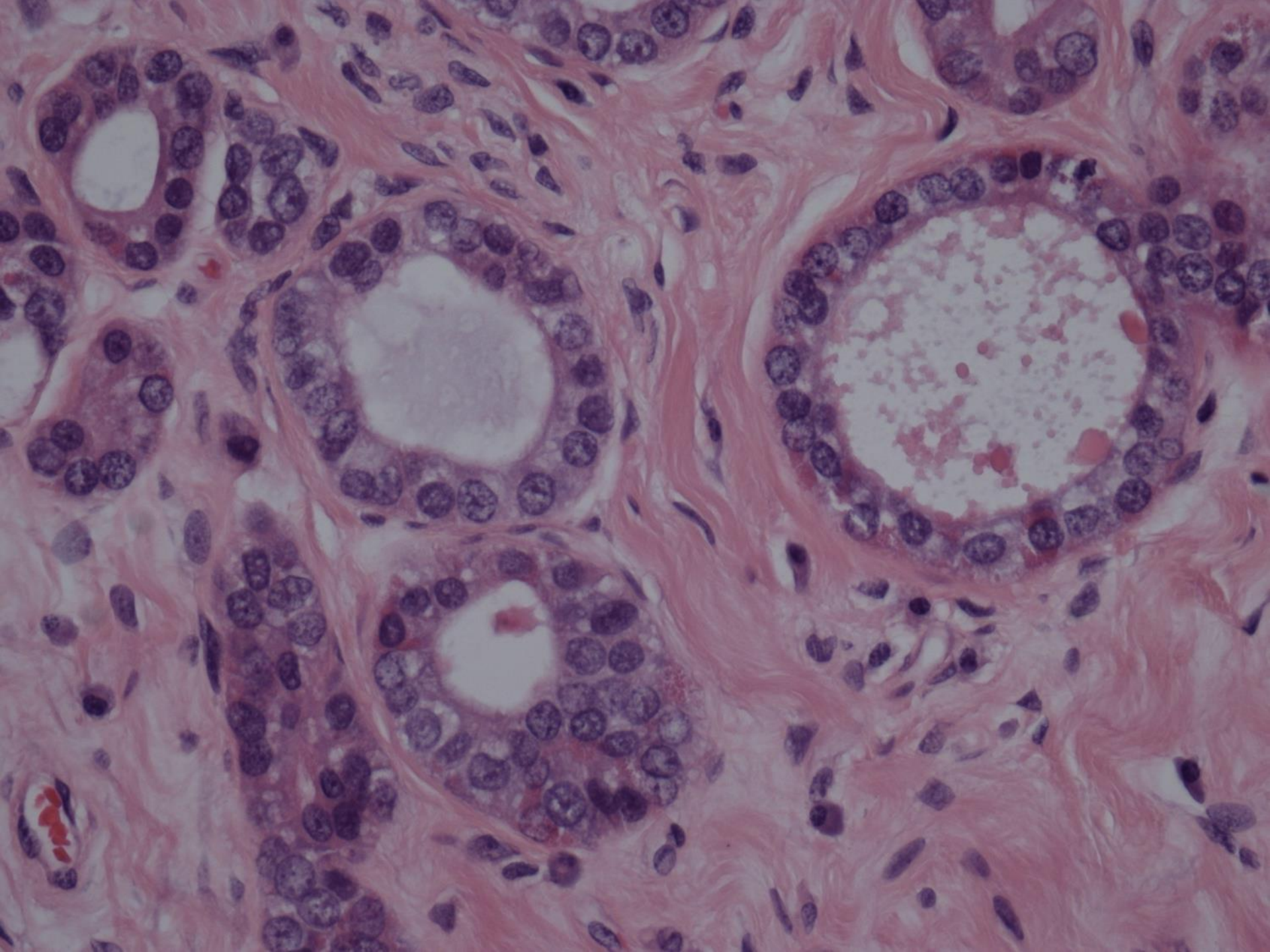
AMGA with DCIS

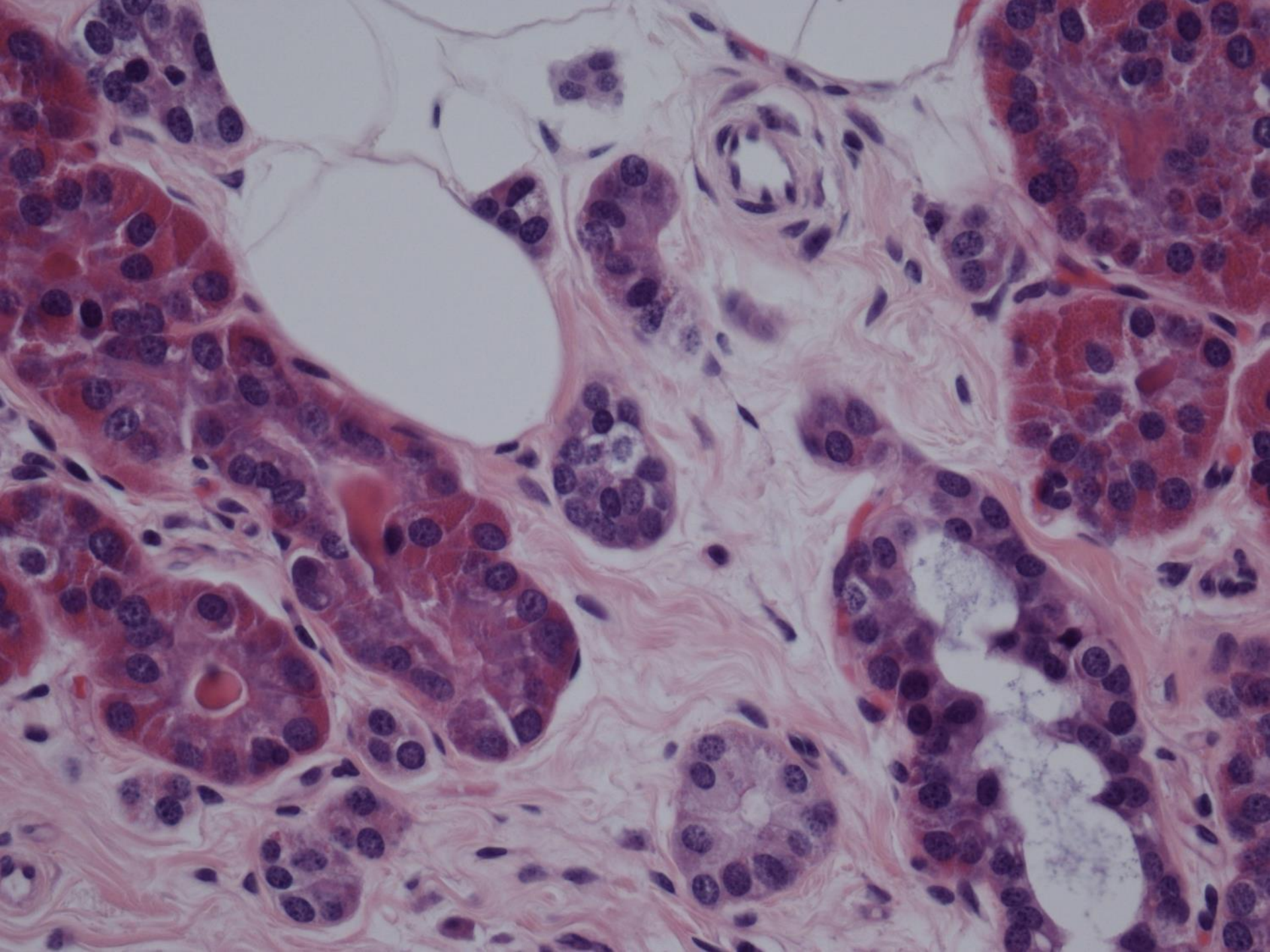
- AMGA and DCIS did not share mutations
- But did share some chromosomal gains and losses
- May have had a clonal origin, but diverged in tumour progression

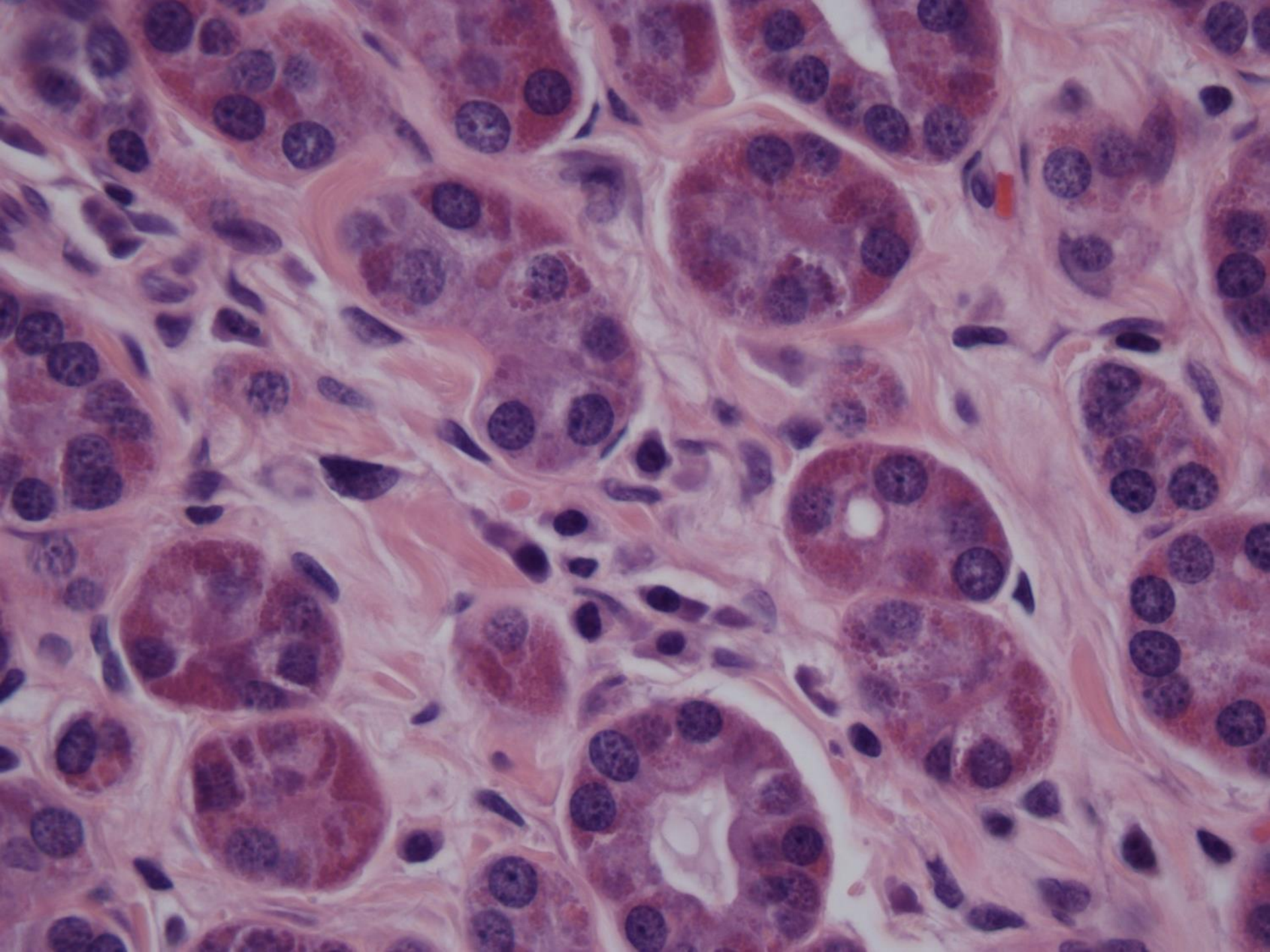


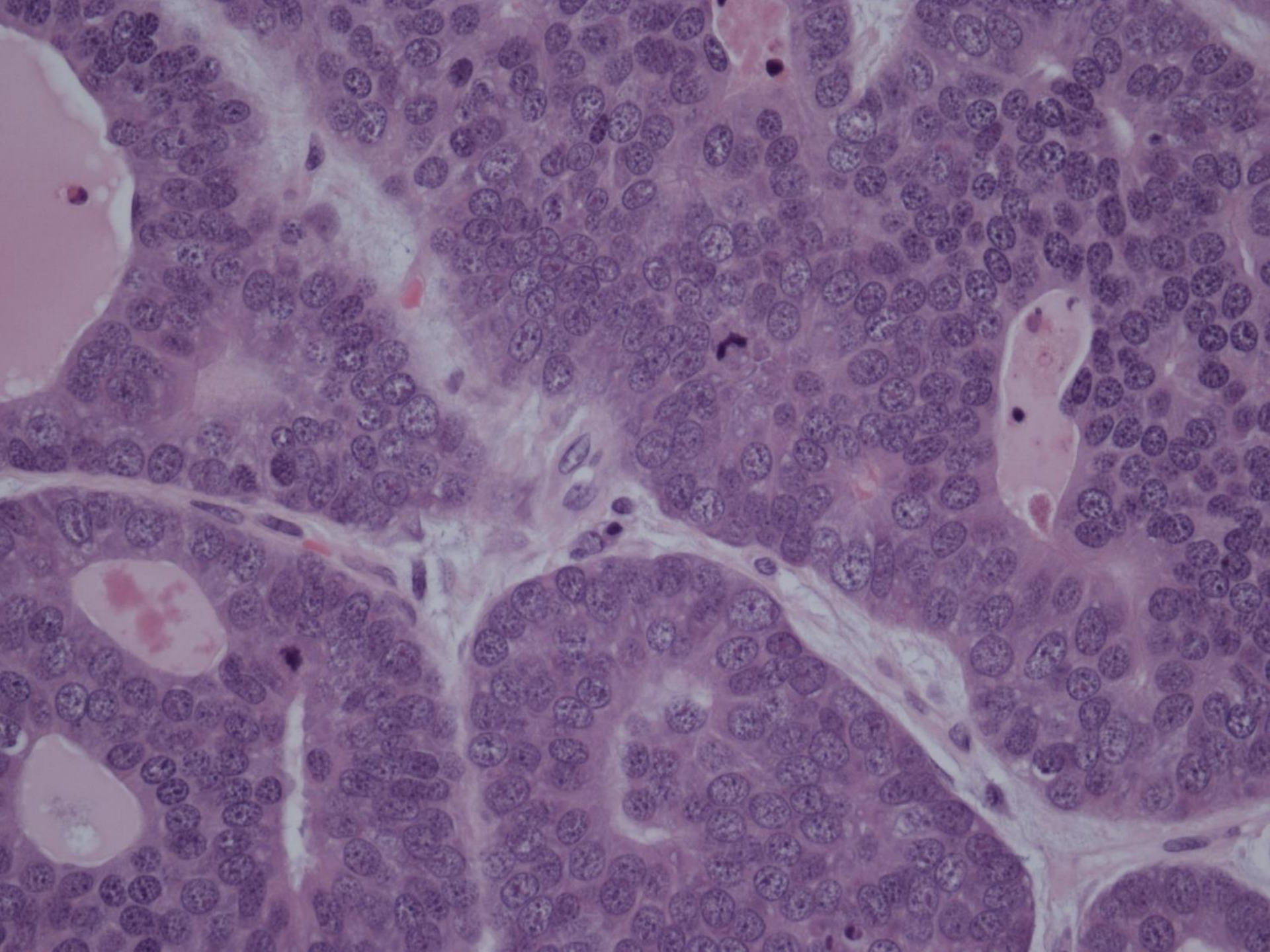


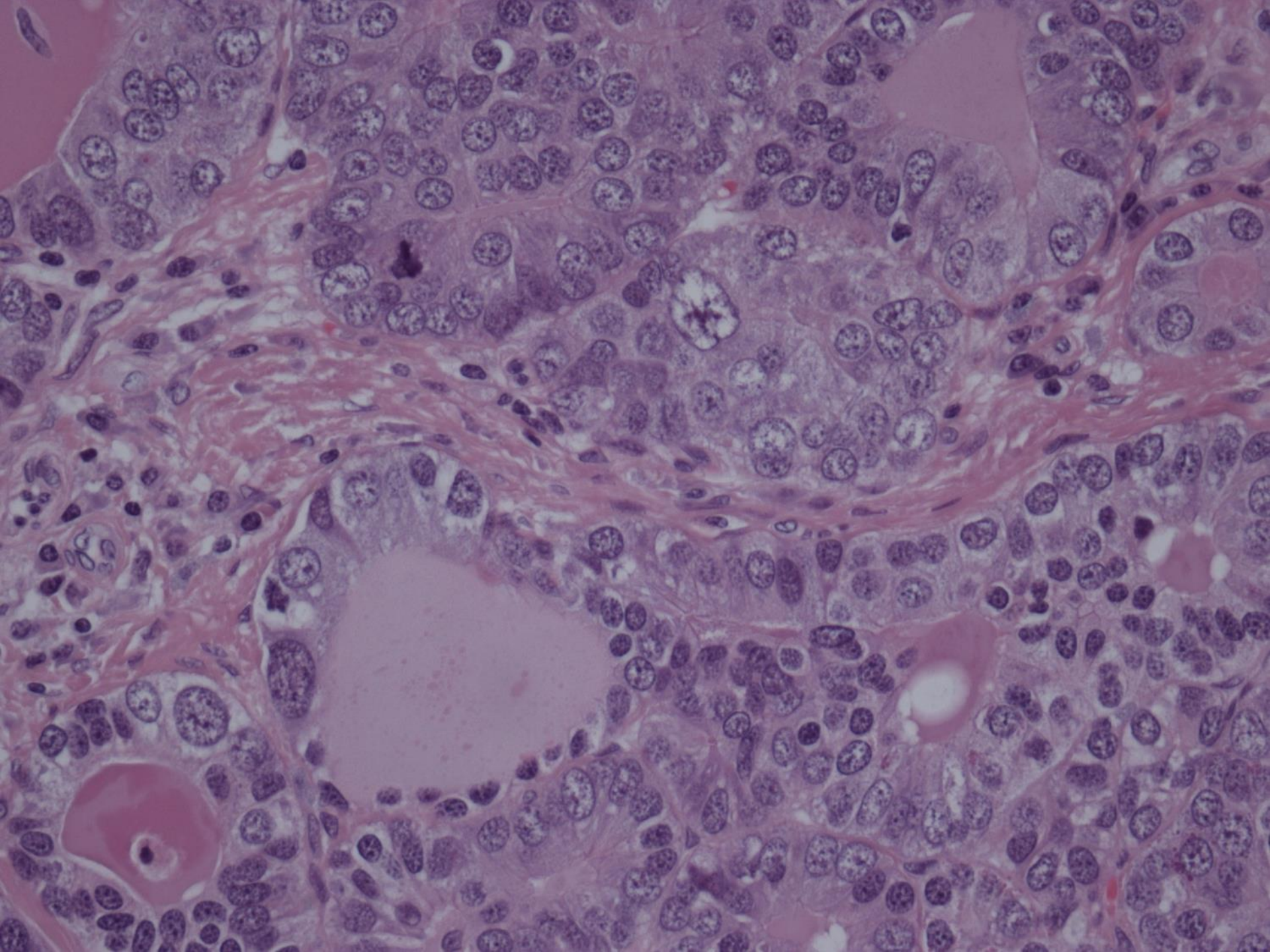












Management of microglandular adenosis

- Core biopsy: categorise as B3 with epithelial atypia
- Complete surgical excision
- Not VAB excision
- May be associated triple negative carcinoma