

# Unusual Breast Lesions Every Pathologist Needs to Know About

Stuart J. Schnitt, M.D.

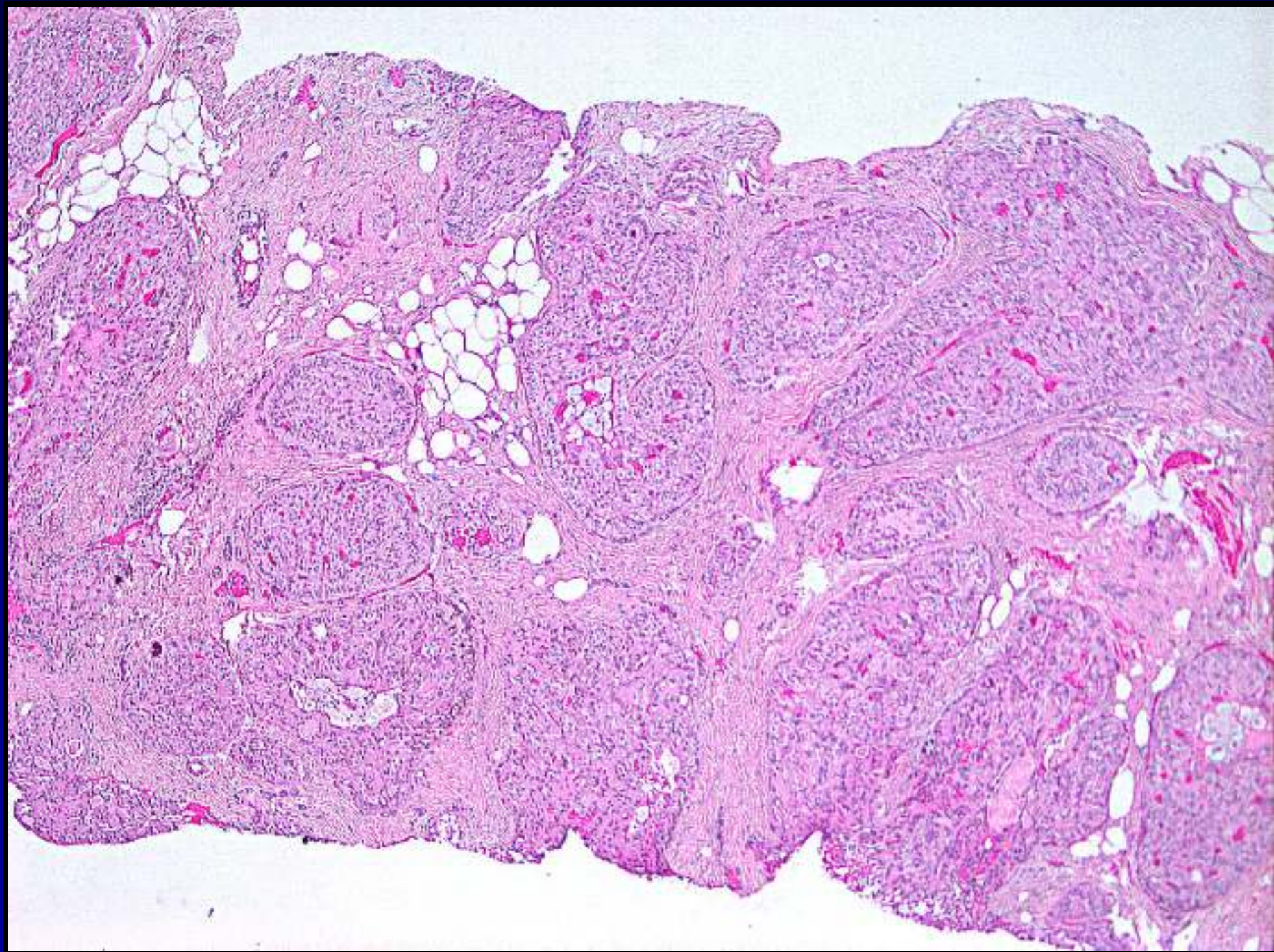
Brigham and Women's Hospital,  
Dana-Farber Cancer Institute, and  
Harvard Medical School

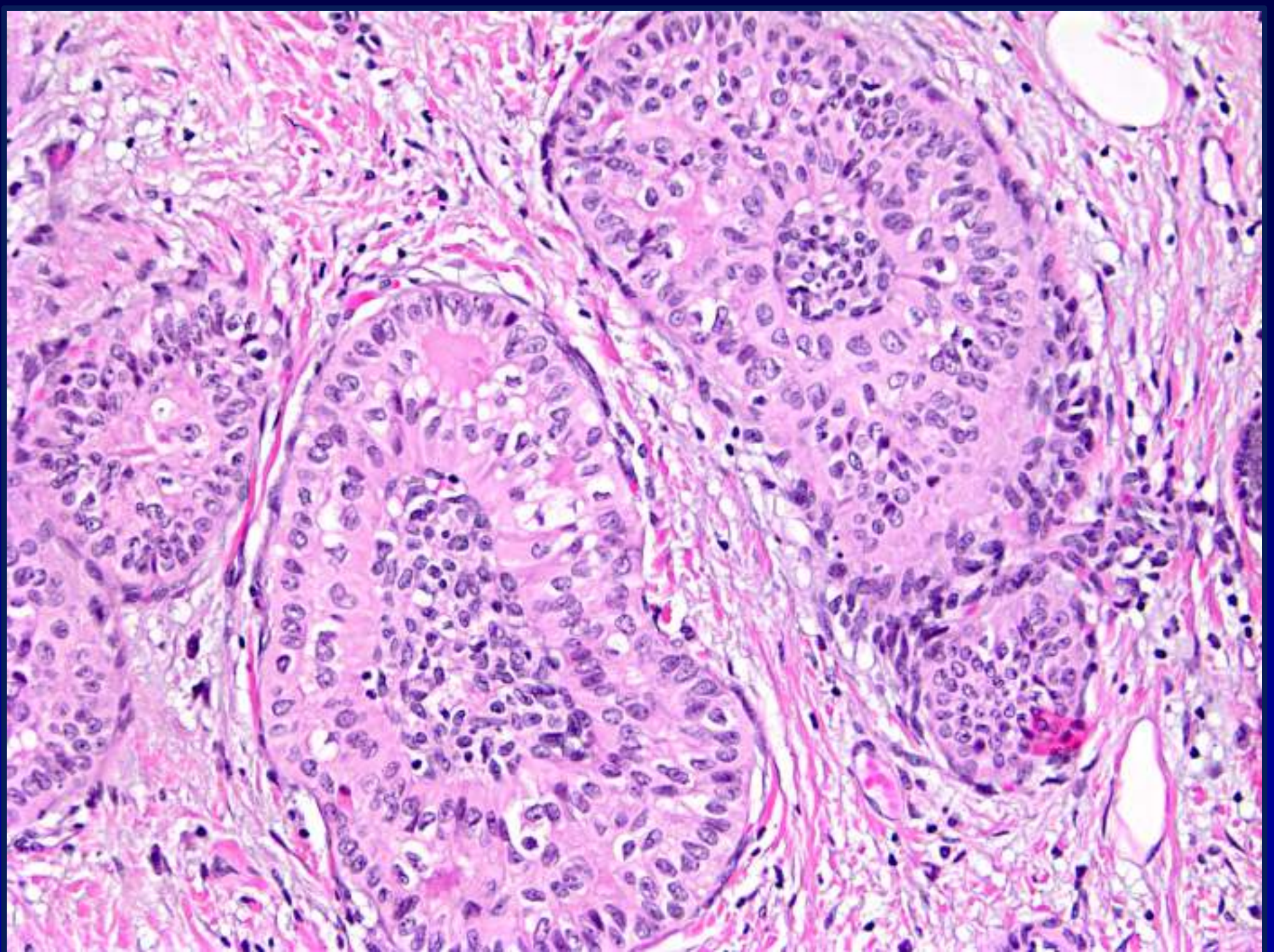
Boston, MA

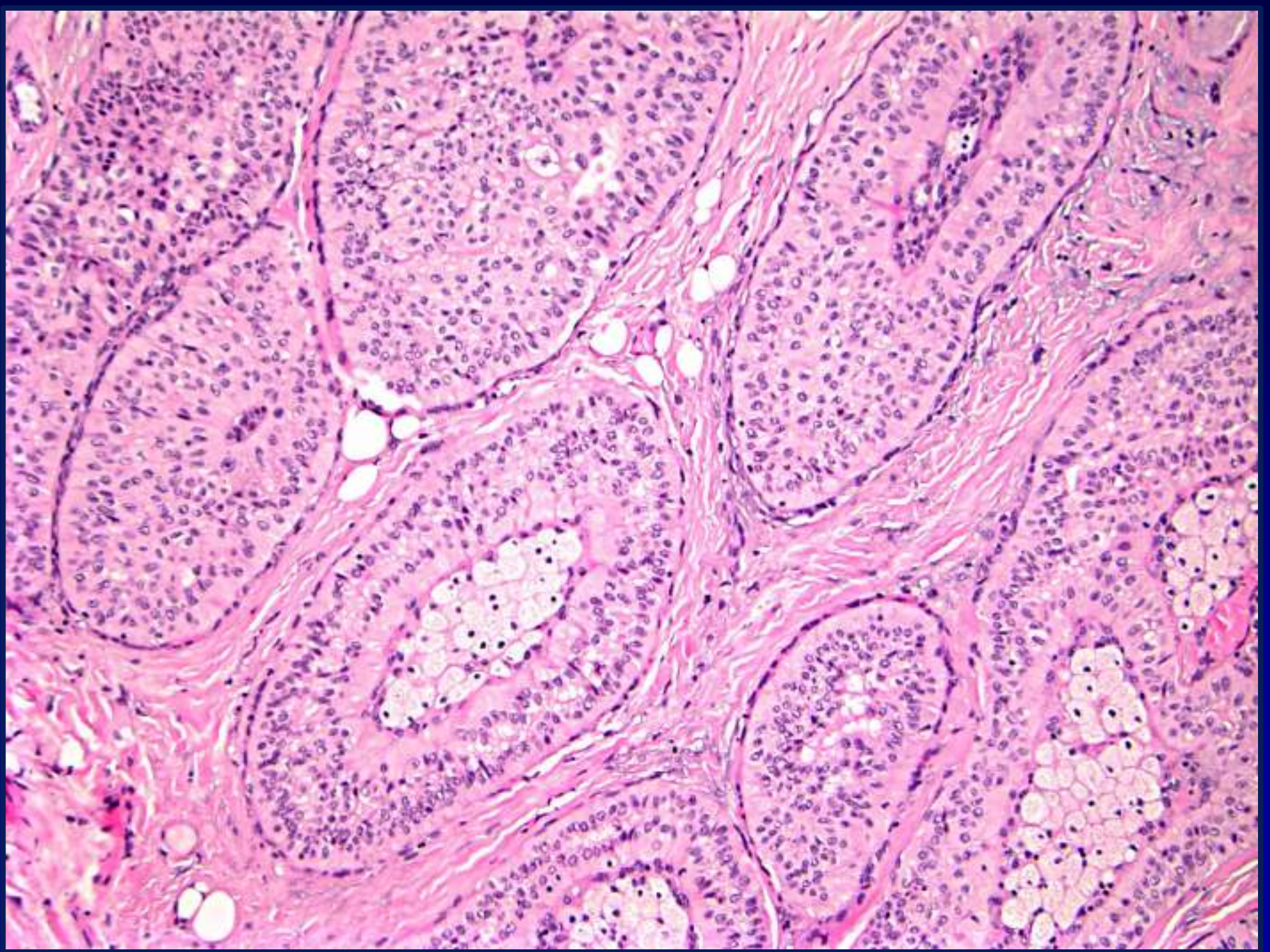


# Case 1

- A 68 year old female was found to have left breast mass in the 2:00 position on a screening mammogram.
- An ultrasound-guided core needle biopsy was performed.







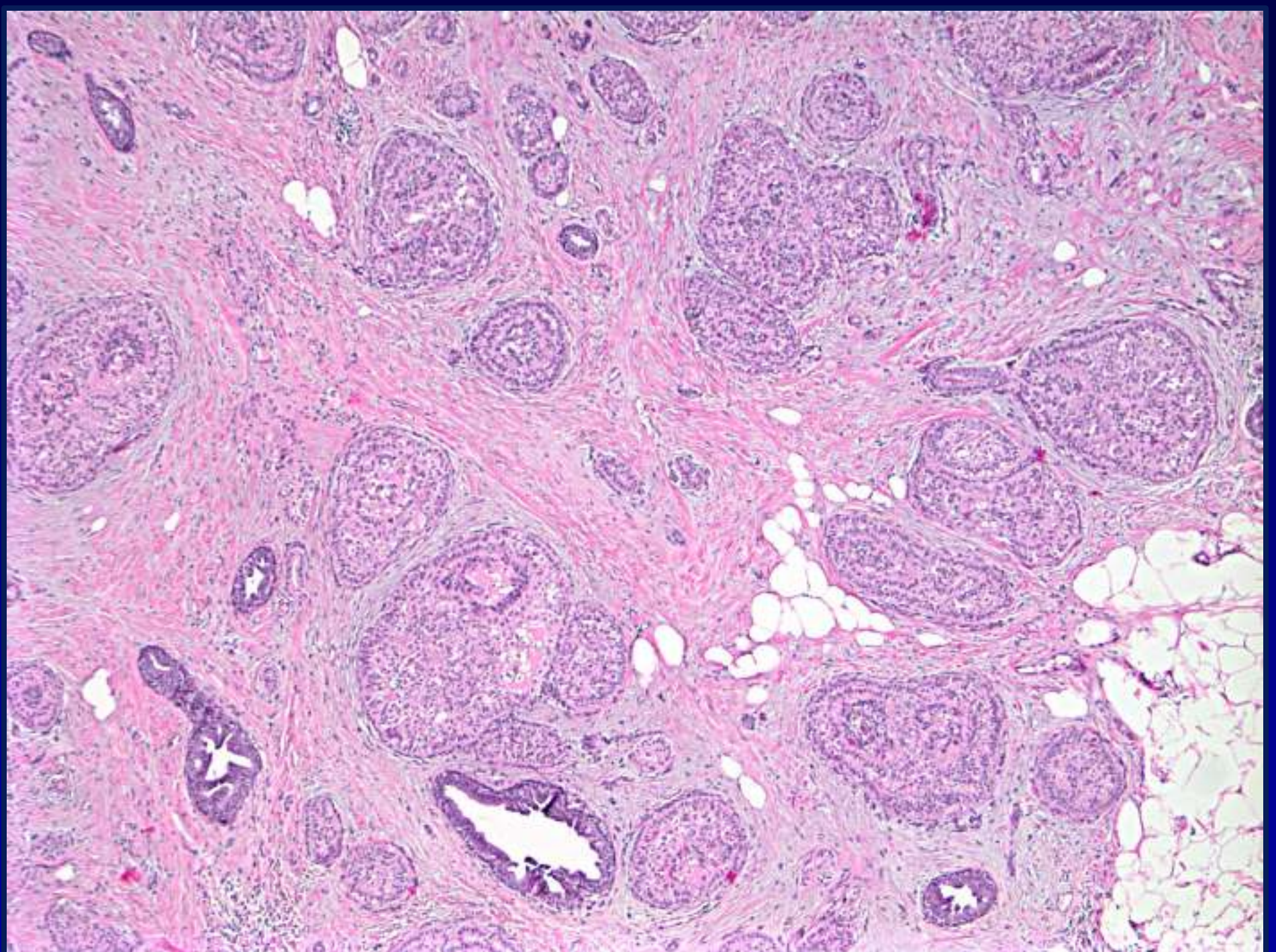
**Original Diagnosis:**

**Ductal carcinoma in situ**

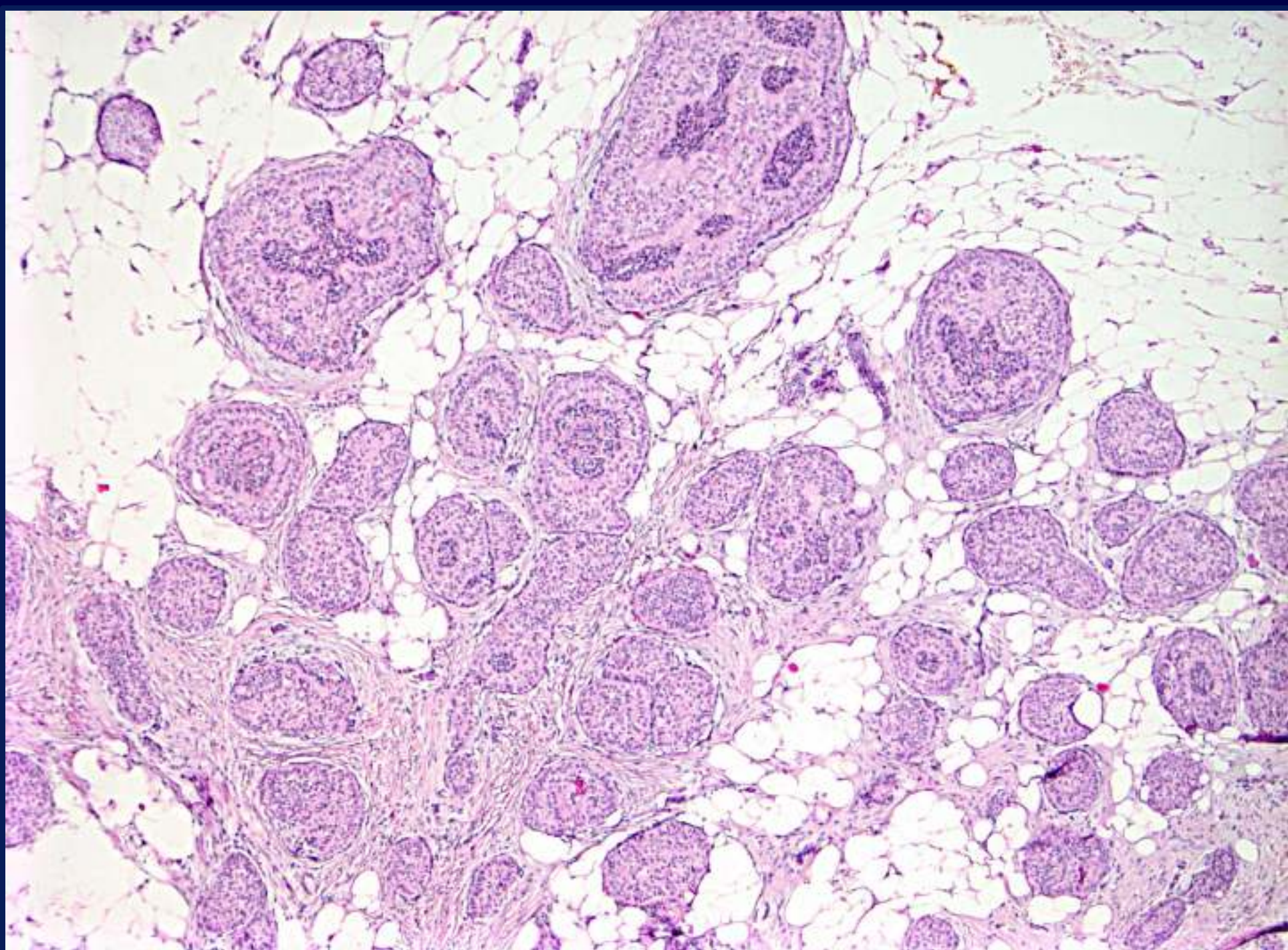
# Excision Specimen

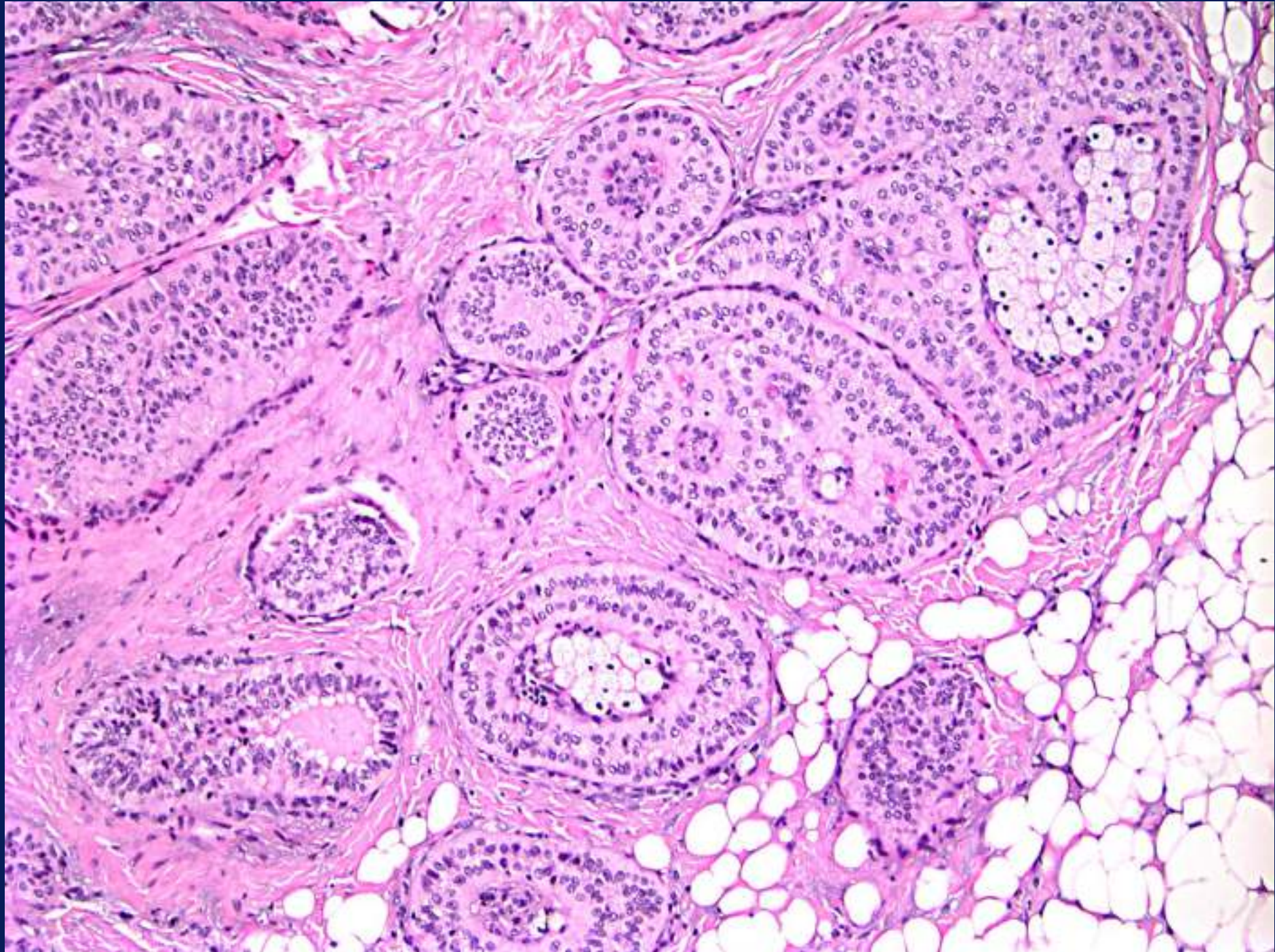
## Gross Examination

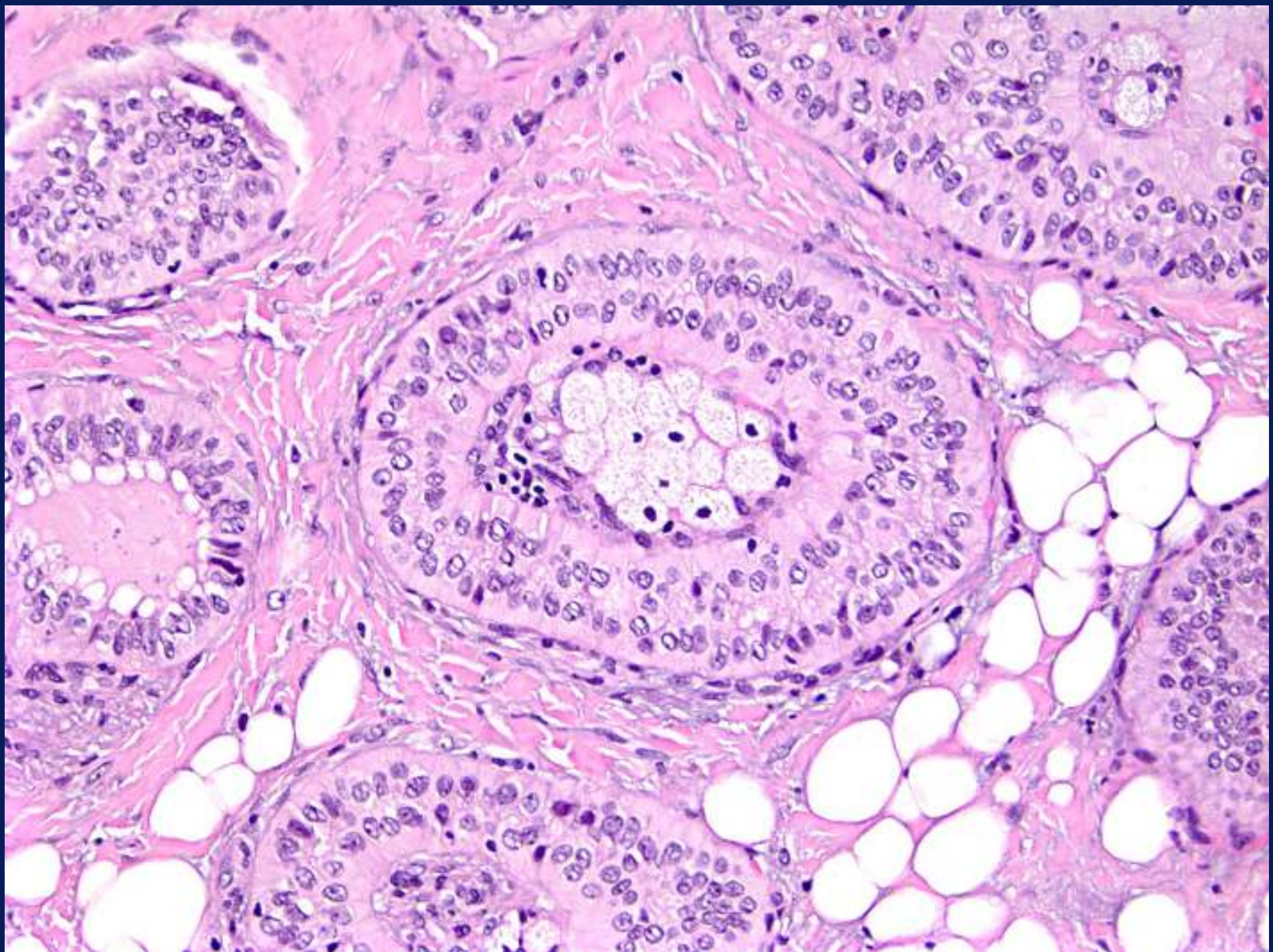
- **7 x 4.7 x 2 cm fibrofatty specimen containing a firm, relatively circumscribed mass measuring 0.9 cm**



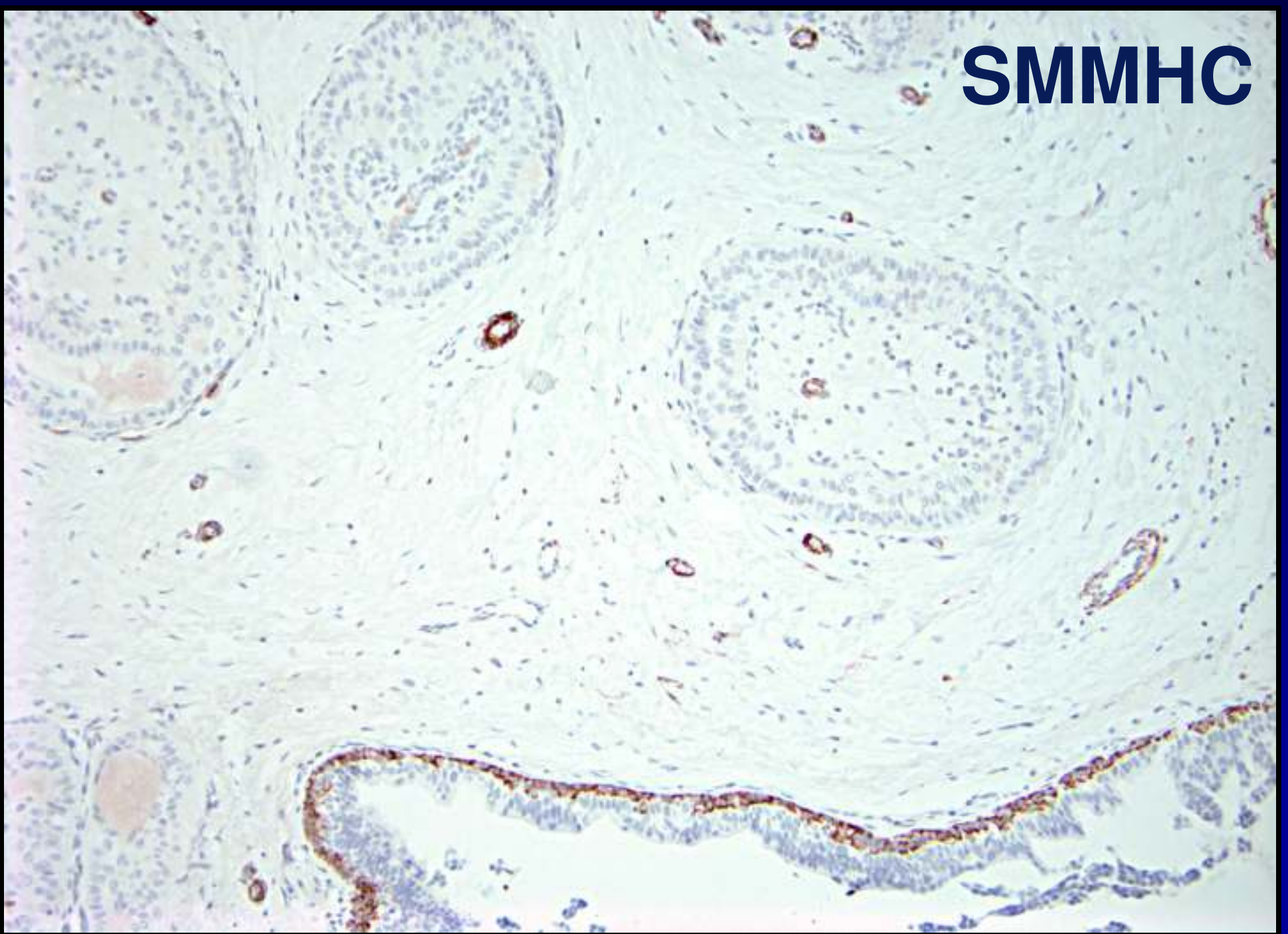




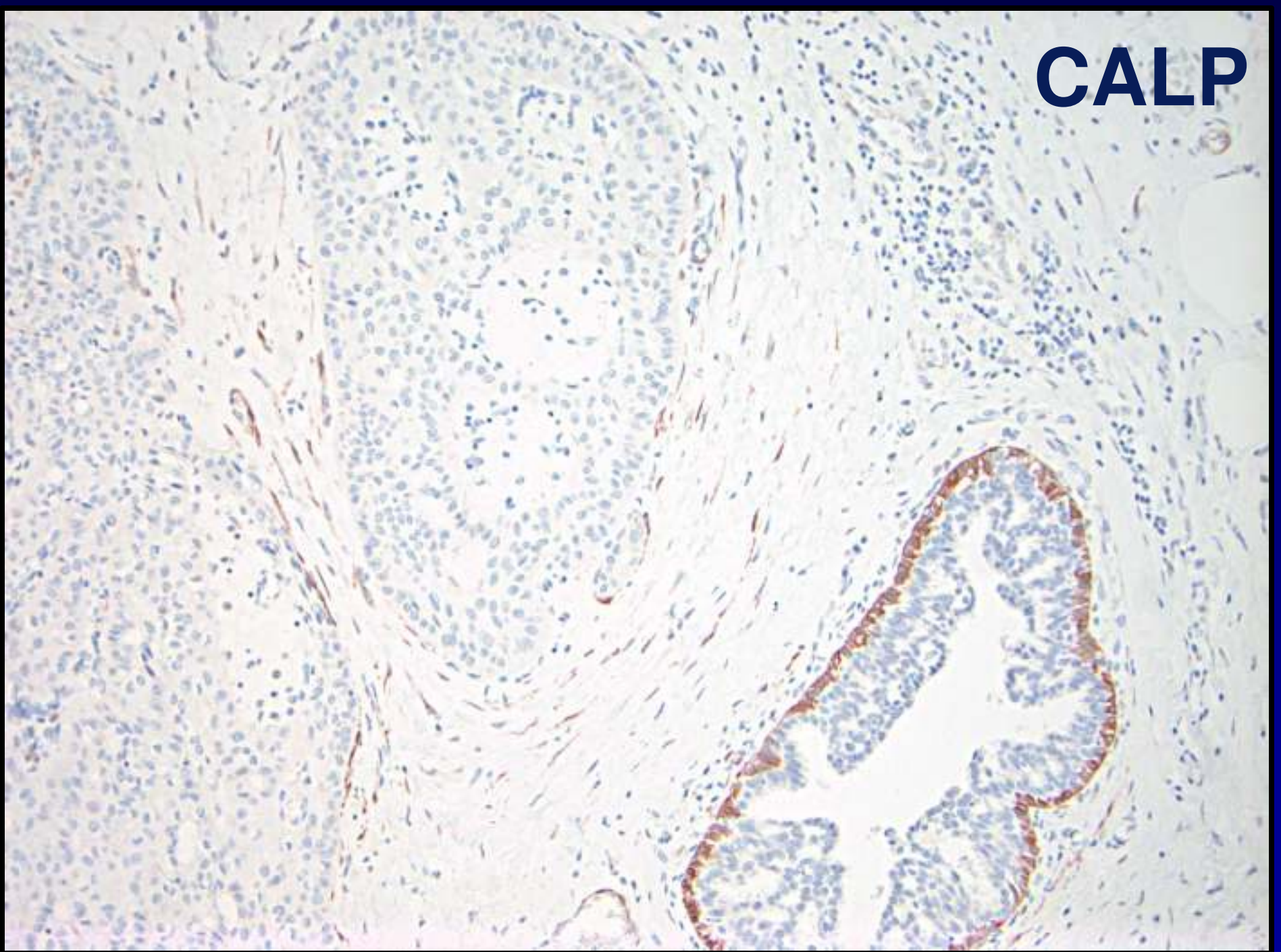




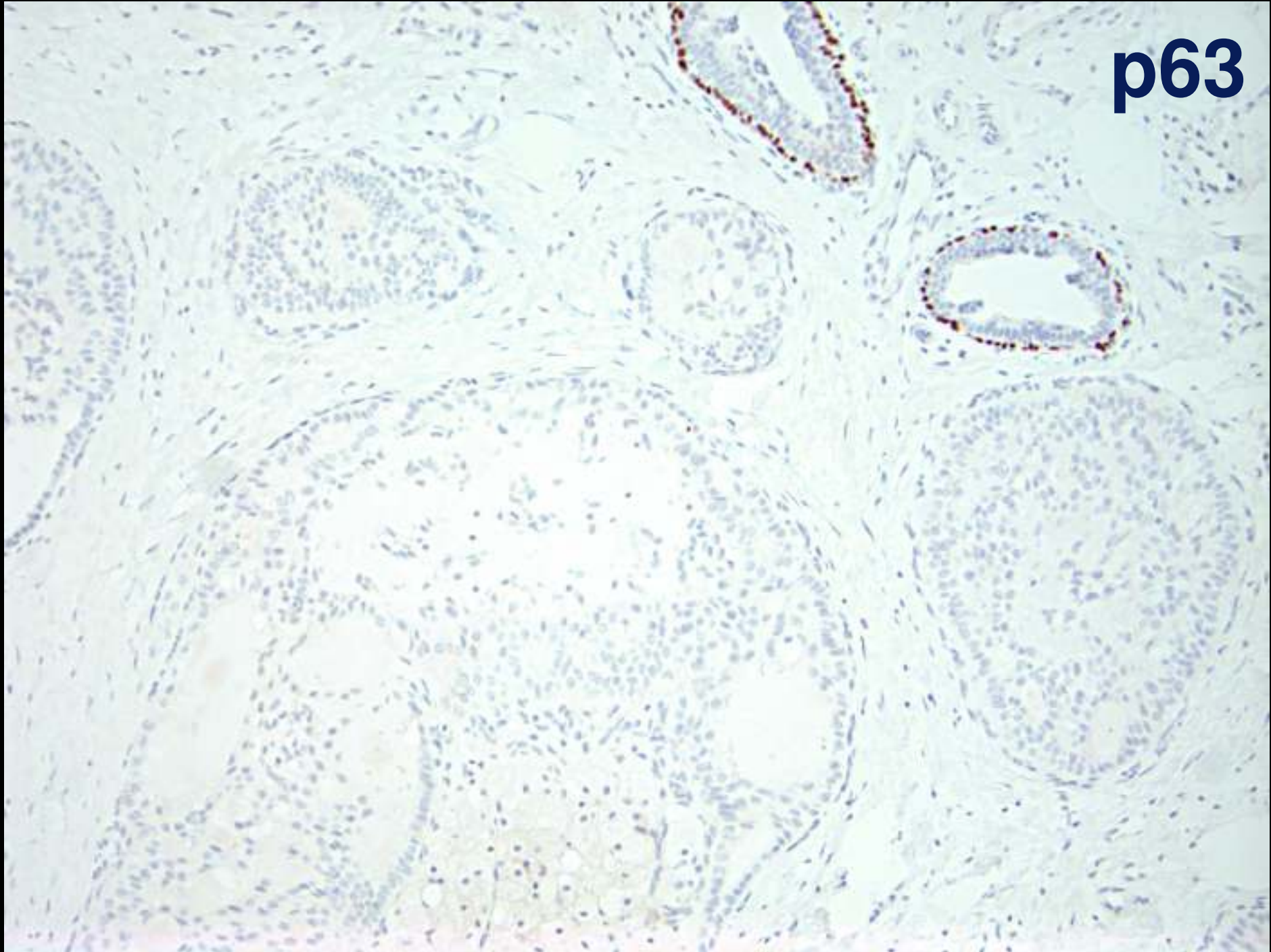
**SMMHC**



**CALP**



**p63**



**CK7**

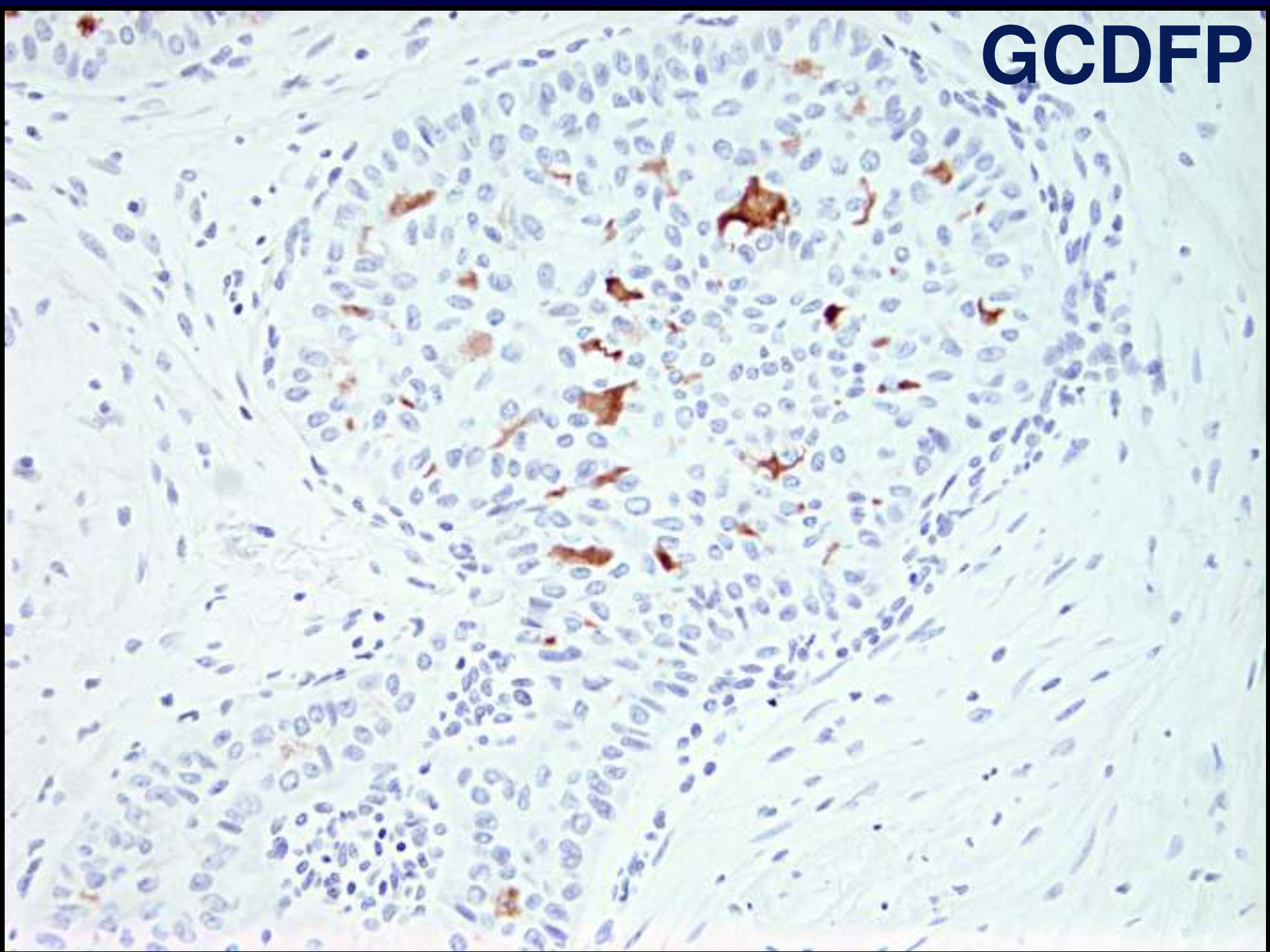


**CK5/6**

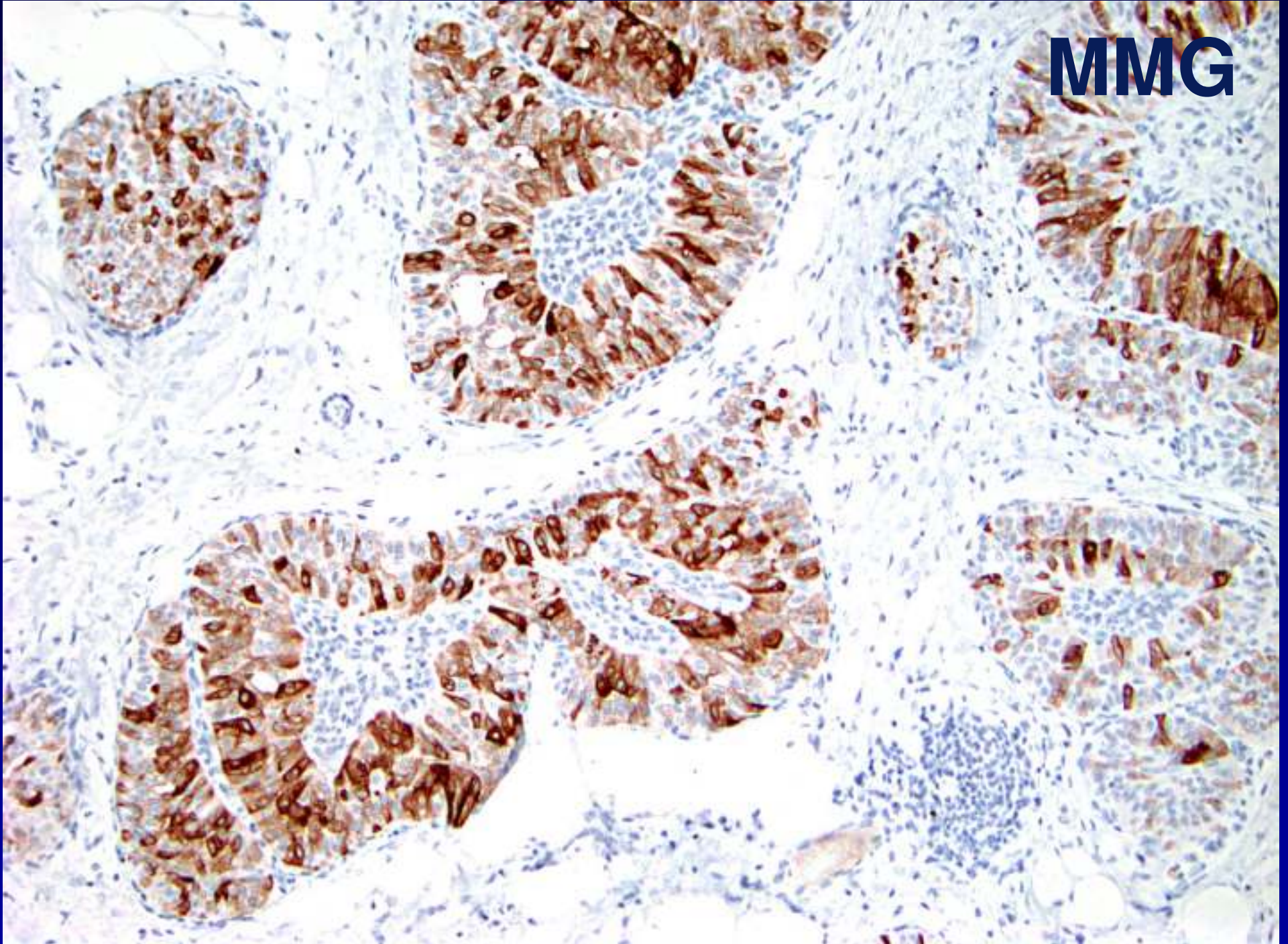




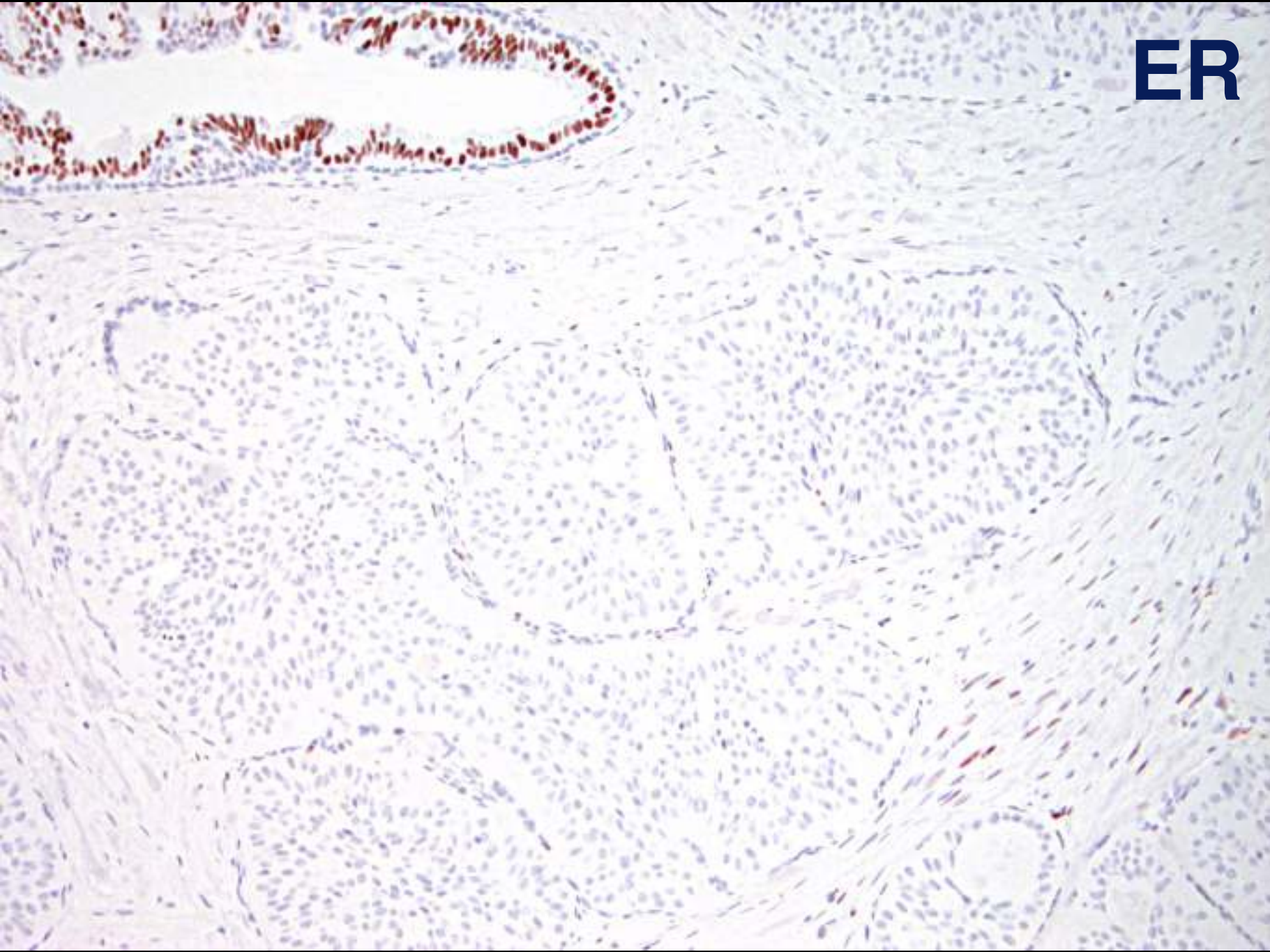
**GCDFP**



**MMG**



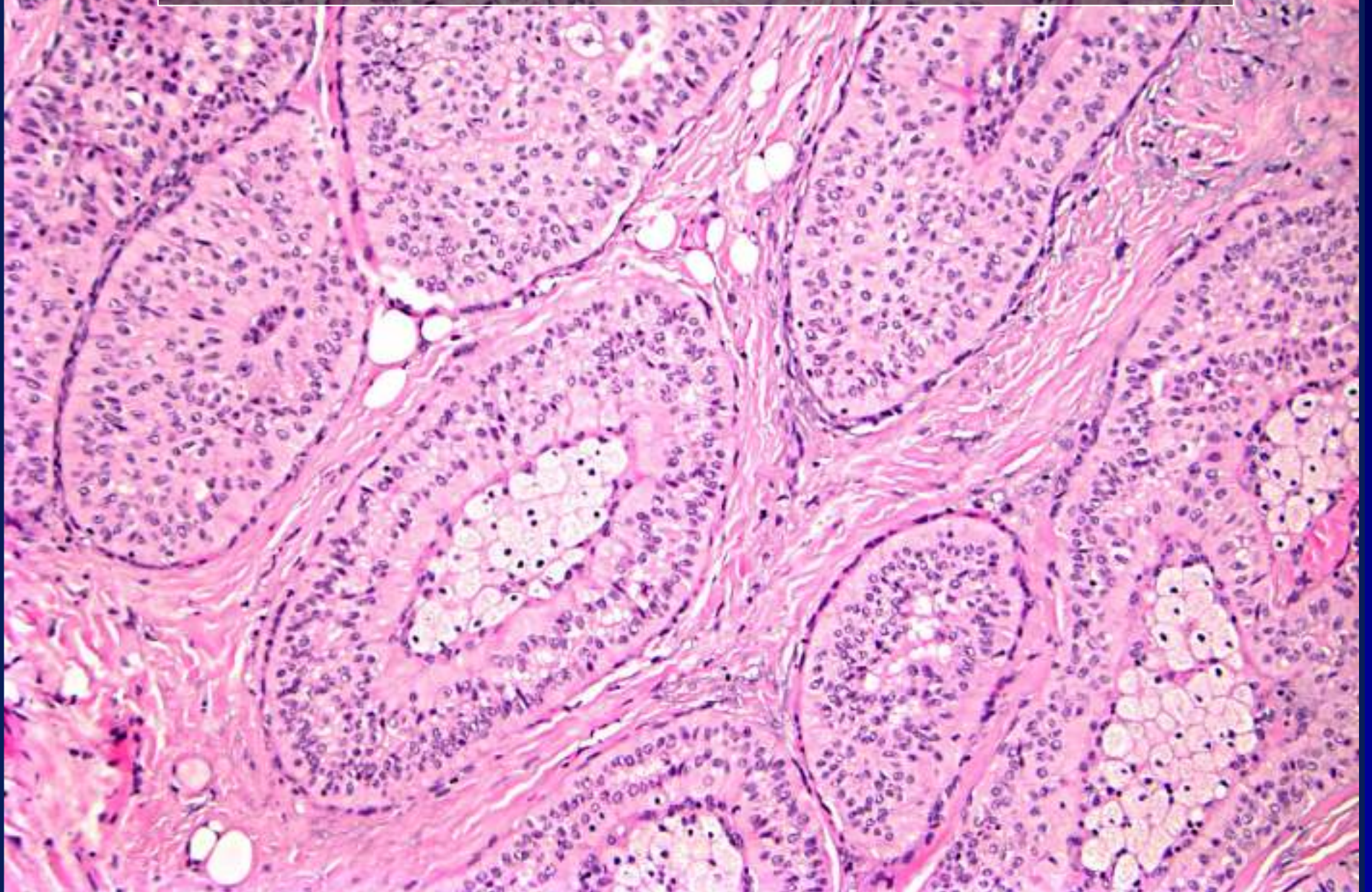
**ER**



# Other Markers

- **Also PR negative and HER2 negative (triple negative)**
- **CK20 negative**
- **TTF-1 negative**
- **Thyroglobulin negative**

**So, what's the diagnosis?**

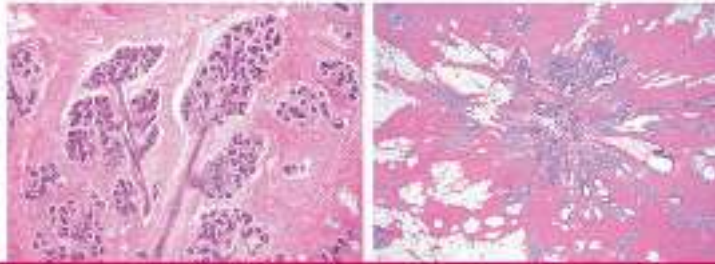




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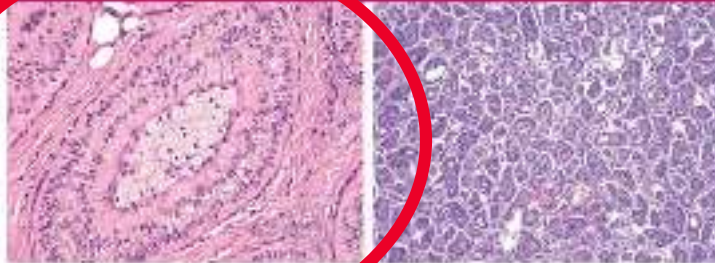
BIOPSY INTERPRETATION SERIES

Stuart J. Schnitt  
Laura C. Collins



# Biopsy Interpretation of the Breast

3rd Edition



Series Editor  
Jonathan I. Epstein

# Diagnosis

**Solid Papillary Carcinoma  
with Reverse Polarity (SPCRP)**

# **Solid Papillary Carcinoma with Reverse Polarity (SPCRP)**

- **Initially reported as “breast tumor resembling tall cell variant of papillary thyroid carcinoma” (Eusebi, 2003)**
  - **Solid papillary carcinoma resembling tall cell variant of papillary thyroid carcinoma (Foschini, 2017)**
- **Rare: 40 reported cases**

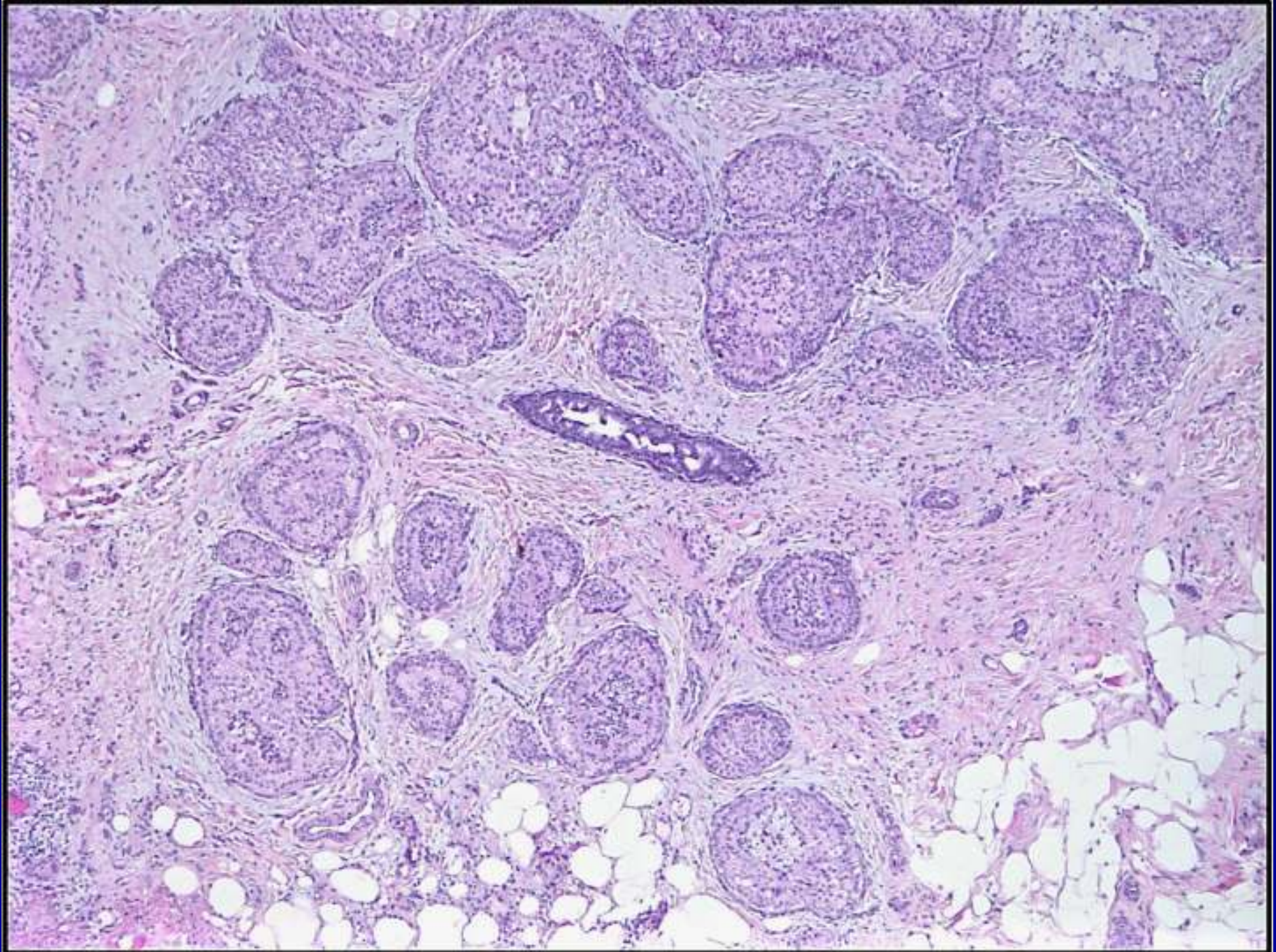


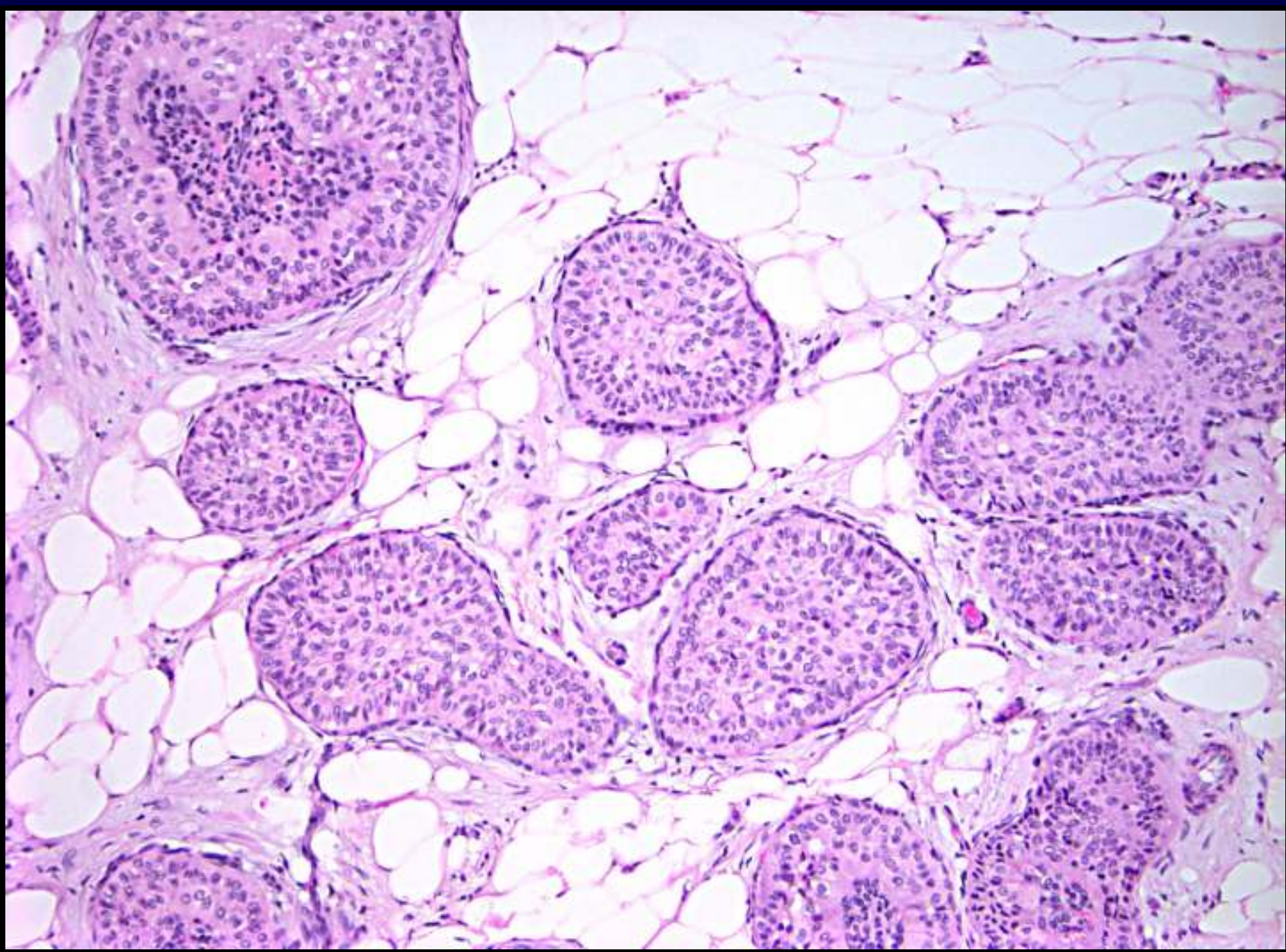
# **Solid Papillary Carcinoma with Reverse Polarity (SPCRP)**

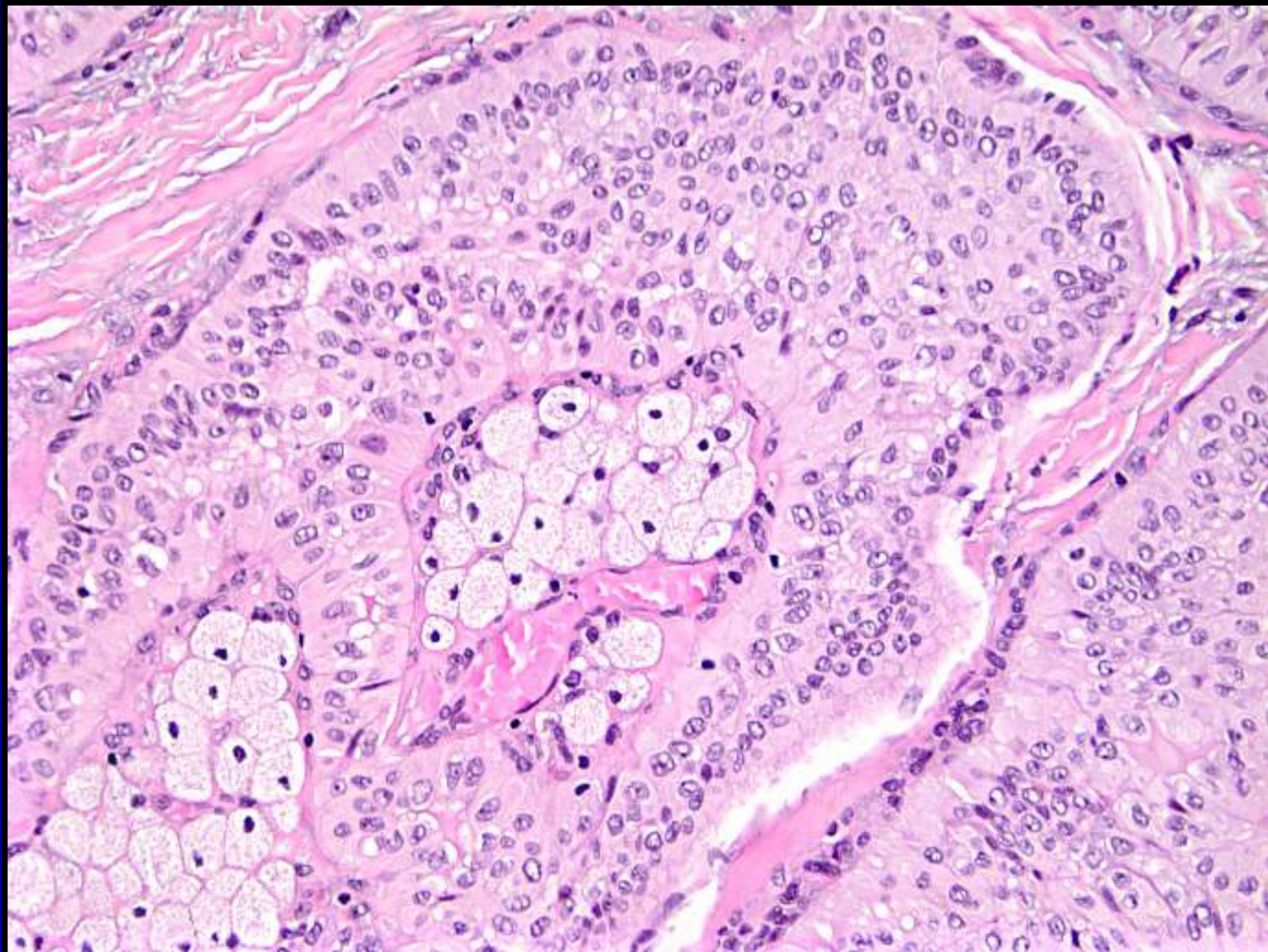
- **Primarily older women (median age, 64 yrs)**
- **Small, mostly mammographically detected (median size, 1.5 cm)**

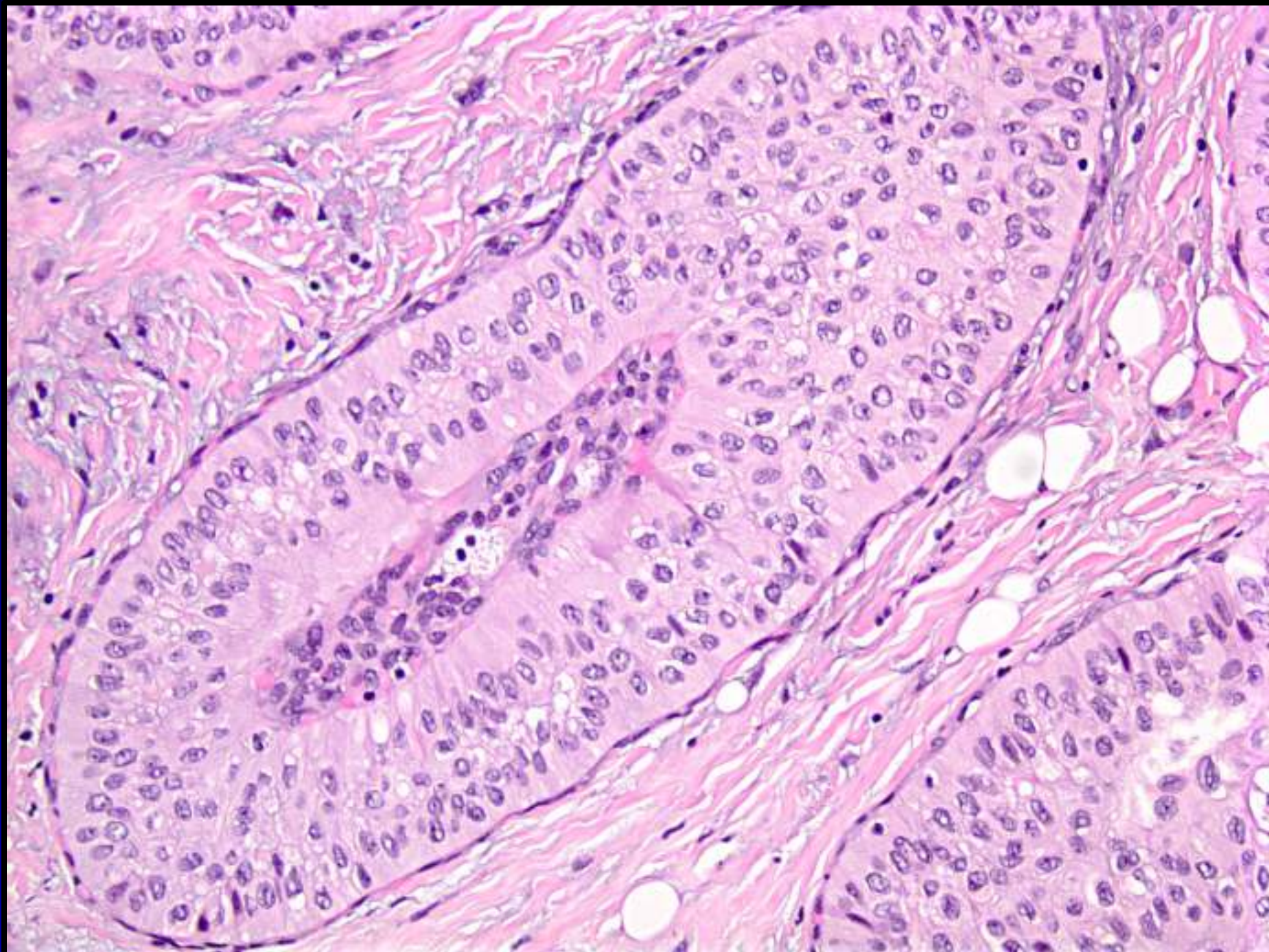
# **Solid Papillary Carcinoma with Reverse Polarity (SPCRP)**

- **Solid, circumscribed nodules of columnar epithelial cells haphazardly distributed throughout breast stroma**
- **Many nodules contain fibrovascular cores, some with foamy histiocytes**
- **Columnar epithelium often present in double layer with cells appearing back to back**
- **Nuclear grooves/inclusions may be seen**
- **Nuclei at apical rather than basal pole (reverse polarity)**





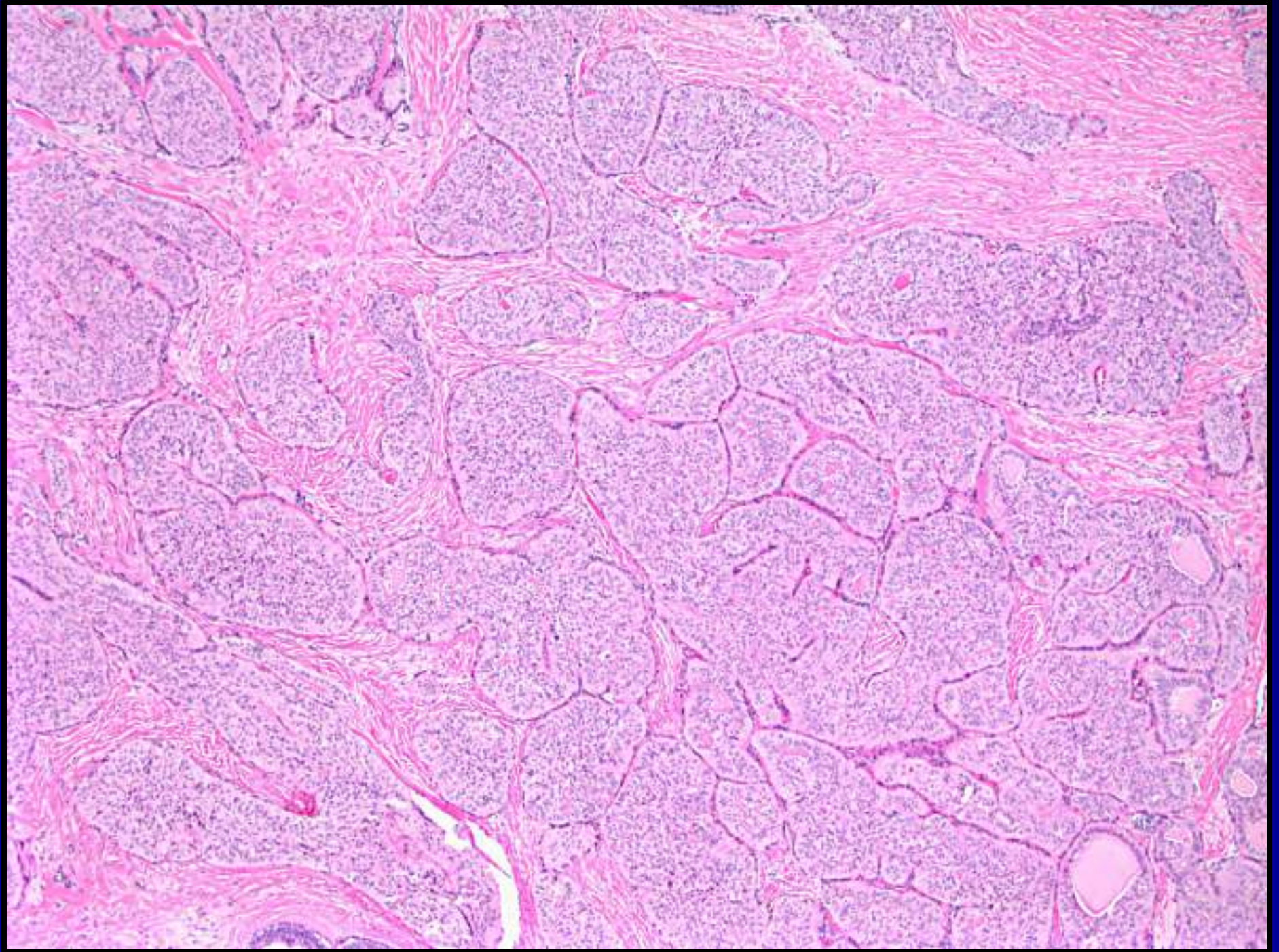




# **Solid Papillary Carcinoma with Reverse Polarity (SPCRP)**

**Less Frequent Histologic Features**

- **Jigsaw pattern of cell nests**

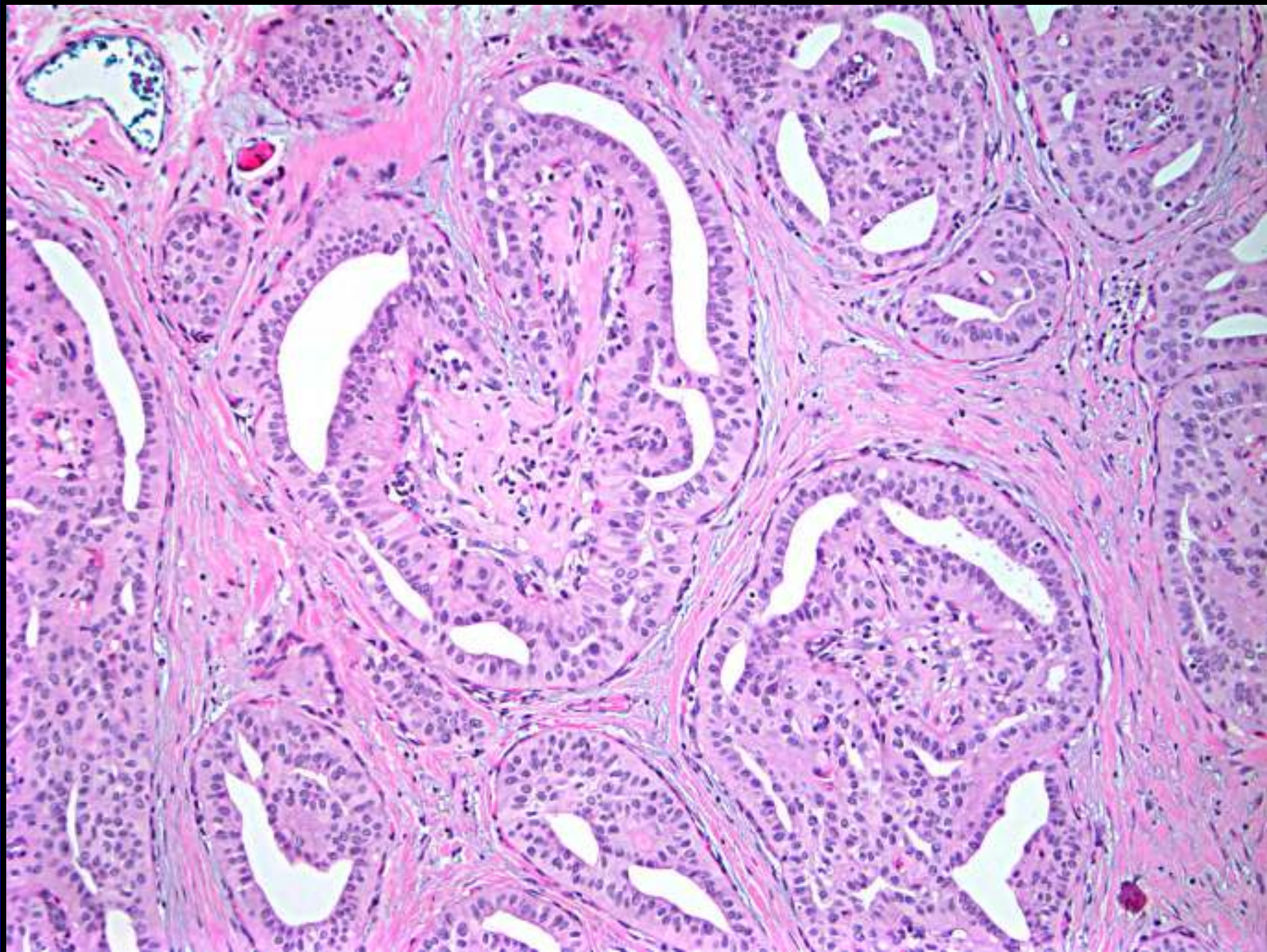


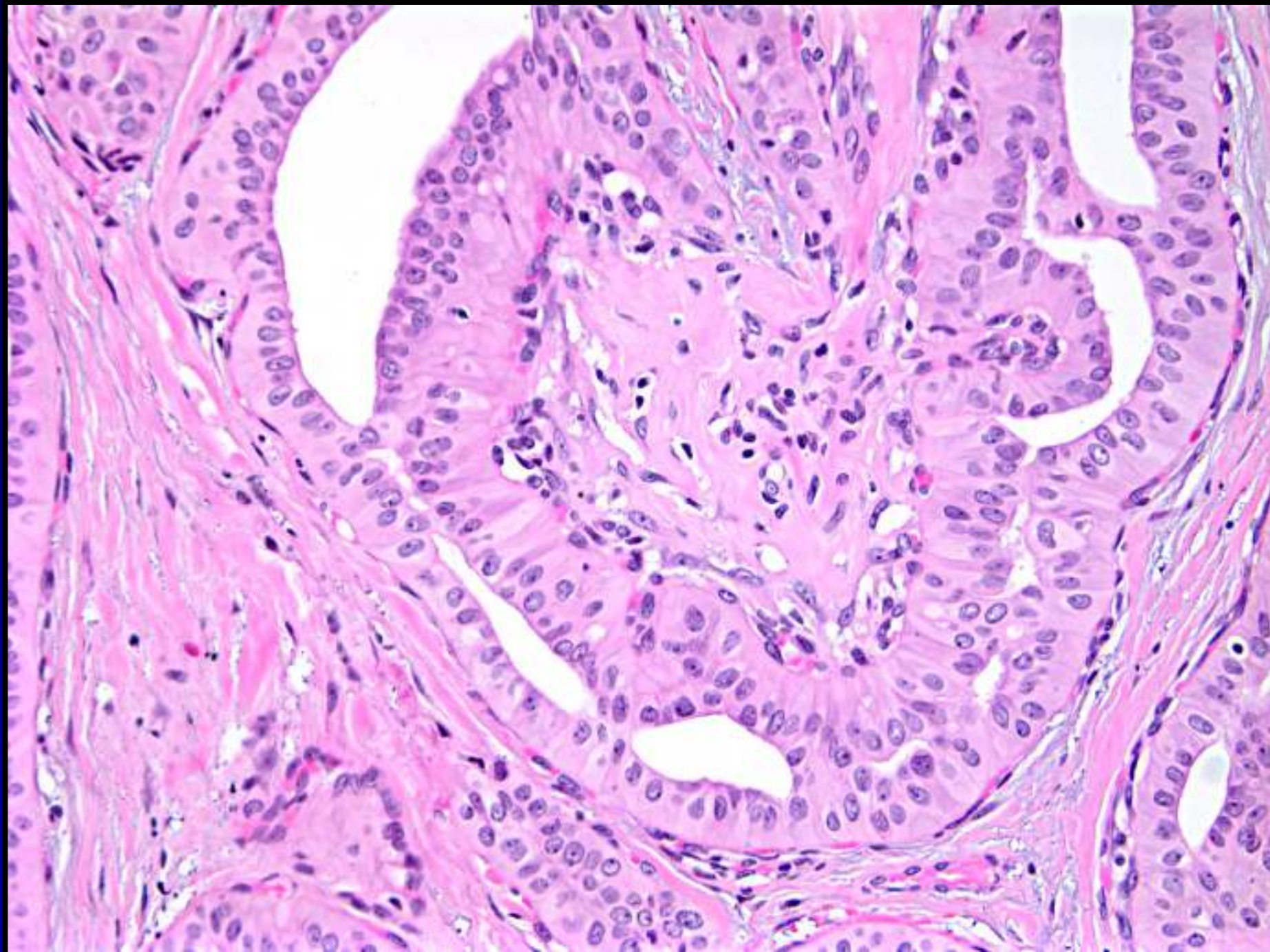


# **Solid Papillary Carcinoma with Reverse Polarity (SPCRP)**

**Less Frequent Histologic Features**

- **Jigsaw pattern of cell nests**
- **Frankly papillary areas**





# **Solid Papillary Carcinoma with Reverse Polarity (SPCRP)**

## **Immunophenotype**

- **No myoepithelial cells around tumor nodules**
- **Positive for low AND high molecular weight cytokeratins**
- **GCDFP and mammaglobin each positive in ~60%**
- **All cases negative for TTF-1 and thyroglobulin**

# **Solid Papillary Carcinoma with Reverse Polarity (SPCRP)**

## **Immunophenotype**

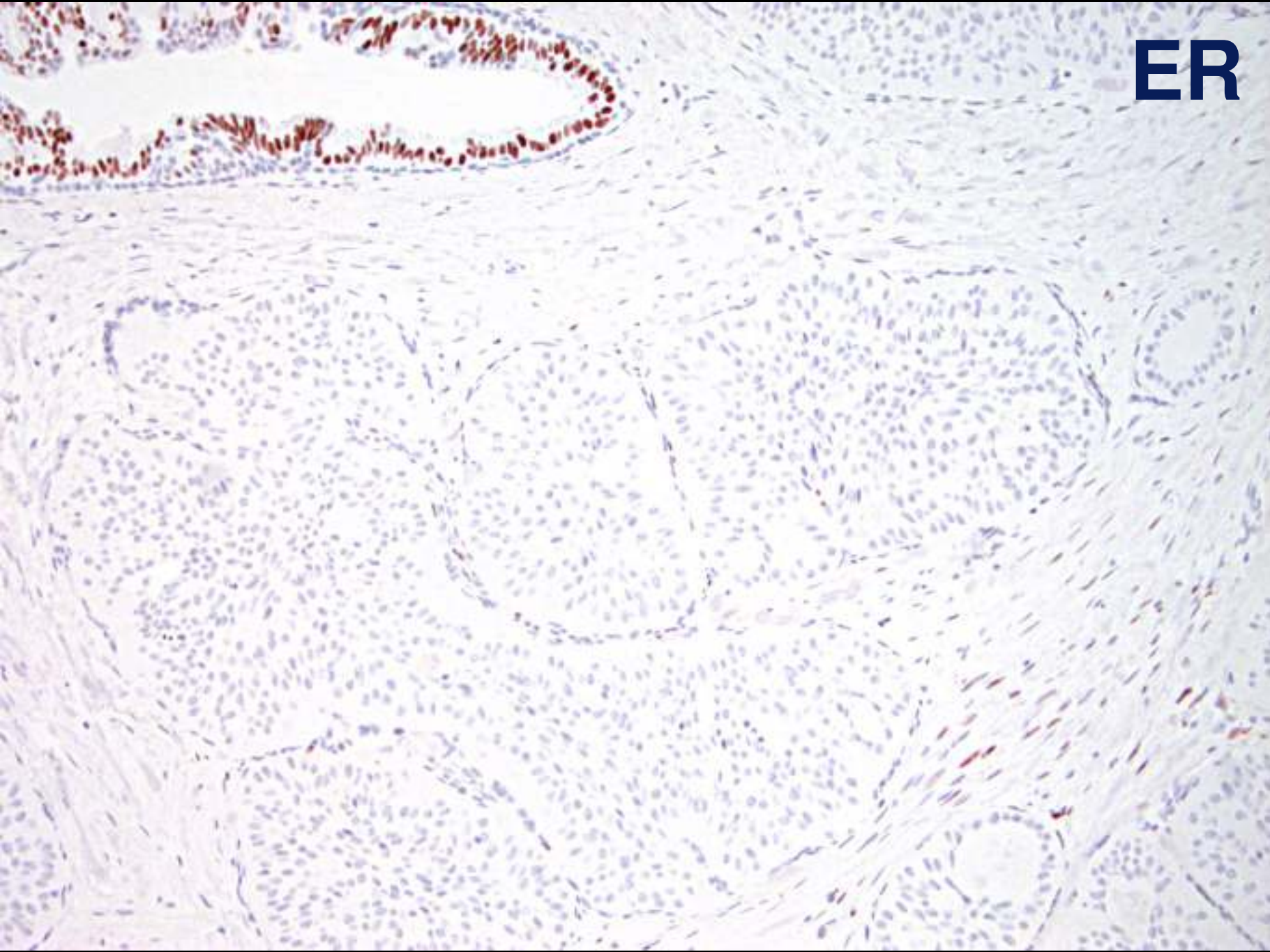
- **62% entirely ER negative; remainder low ER positive (1-10%)**
- **15% PR positive**
- **All cases HER2 negative**
- **Low proliferation rate by Ki67 (<5%)**
- **Rich vascular network around nests on CD31 and CD34 stains**

# **Solid Papillary Carcinoma with Reverse Polarity (SPCRP)**

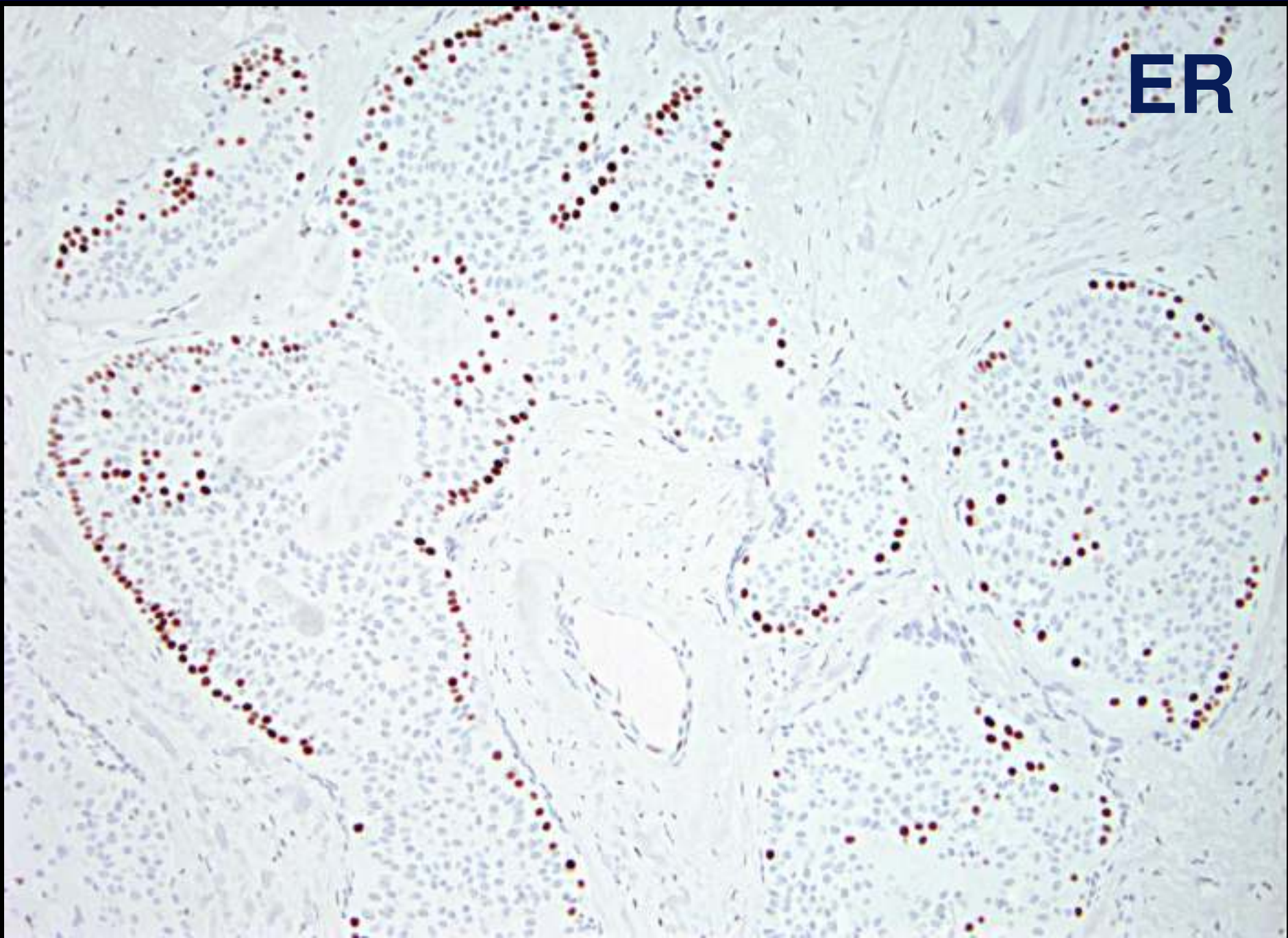
## **Immunophenotype**

- **E-cadherin: Strong lateral membrane staining**
- **MUC1: Apical membrane staining seen on ends of cells closest to nucleus (reverse polarity)**

**ER**

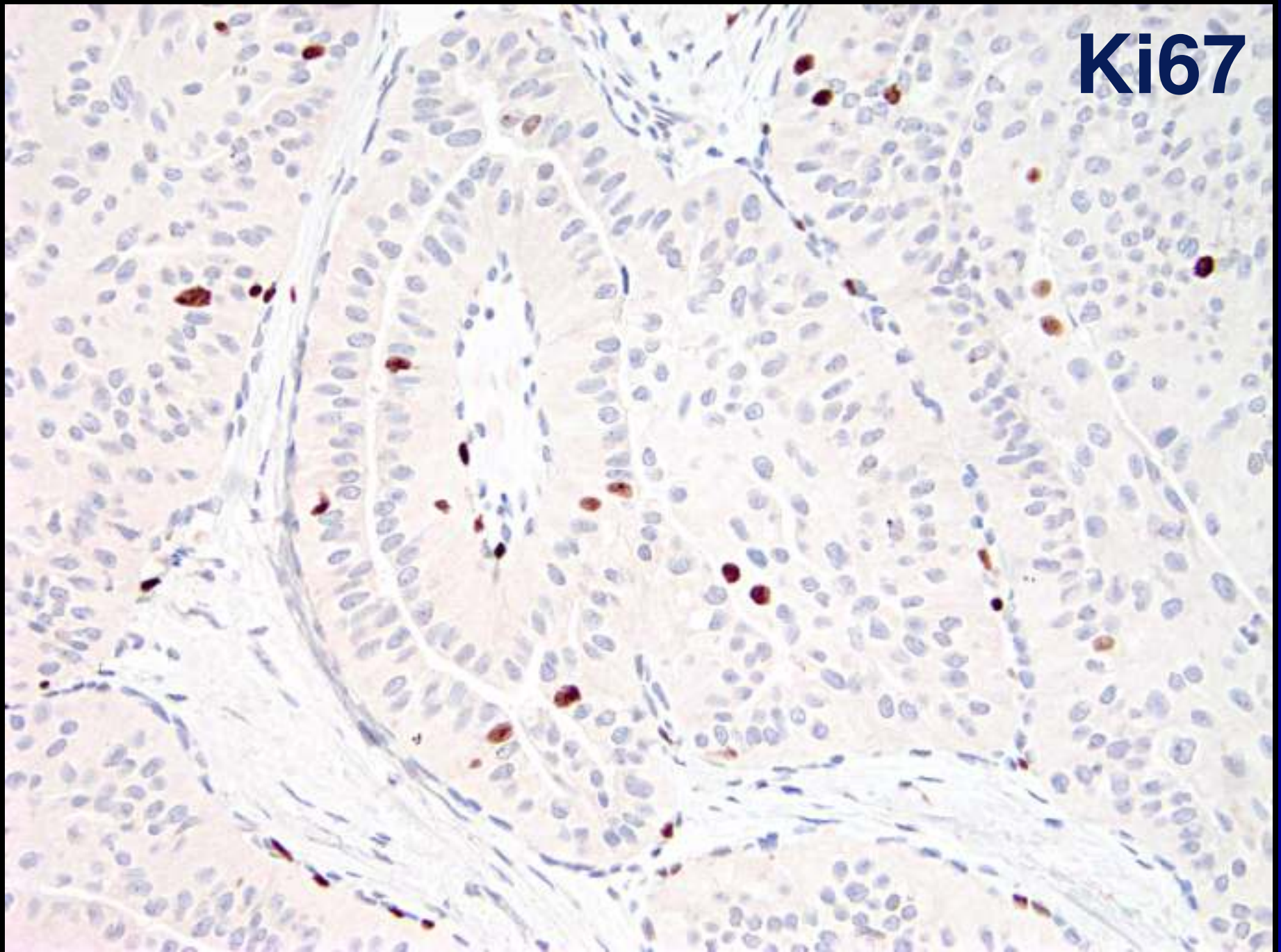


ER

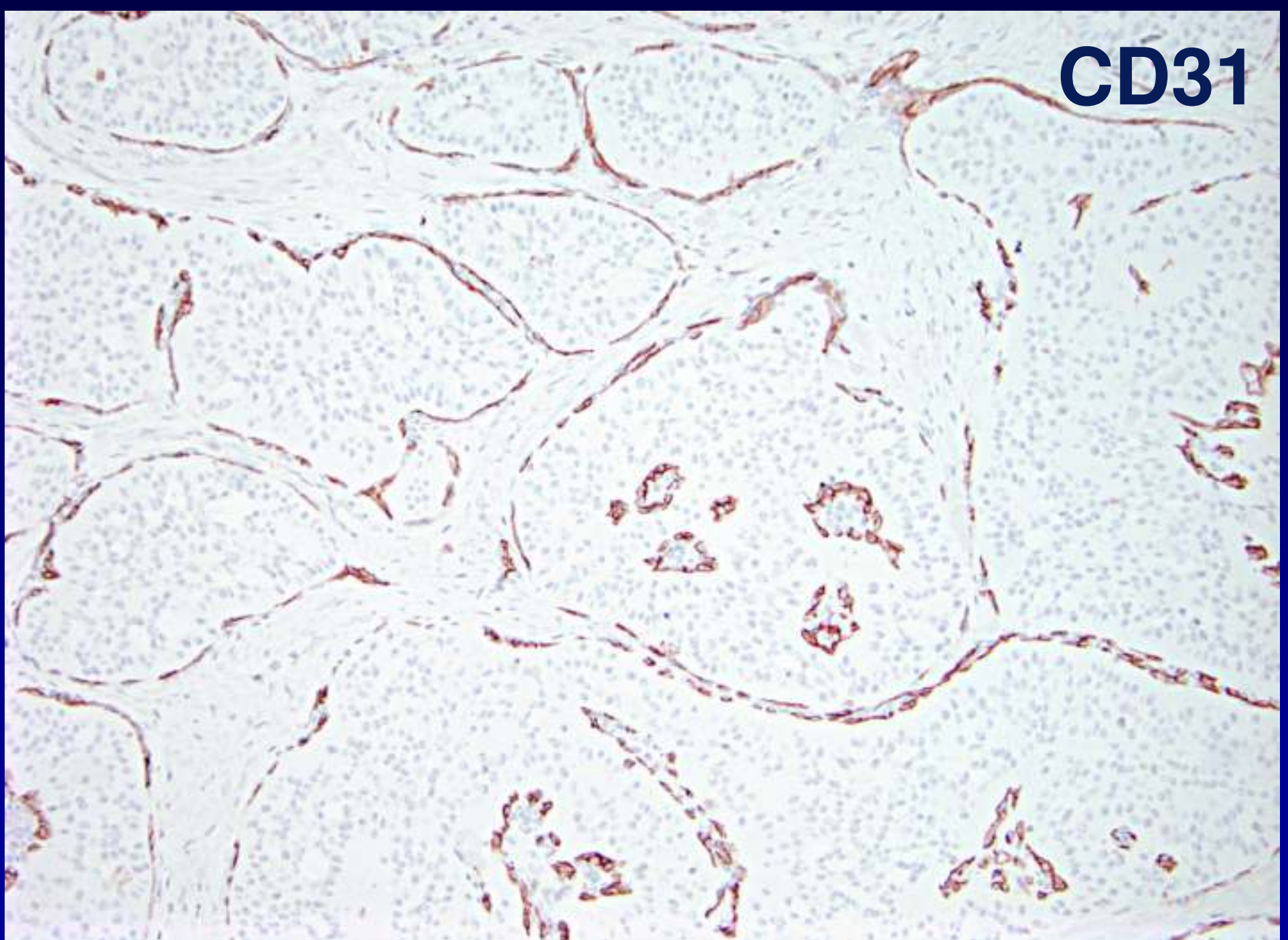




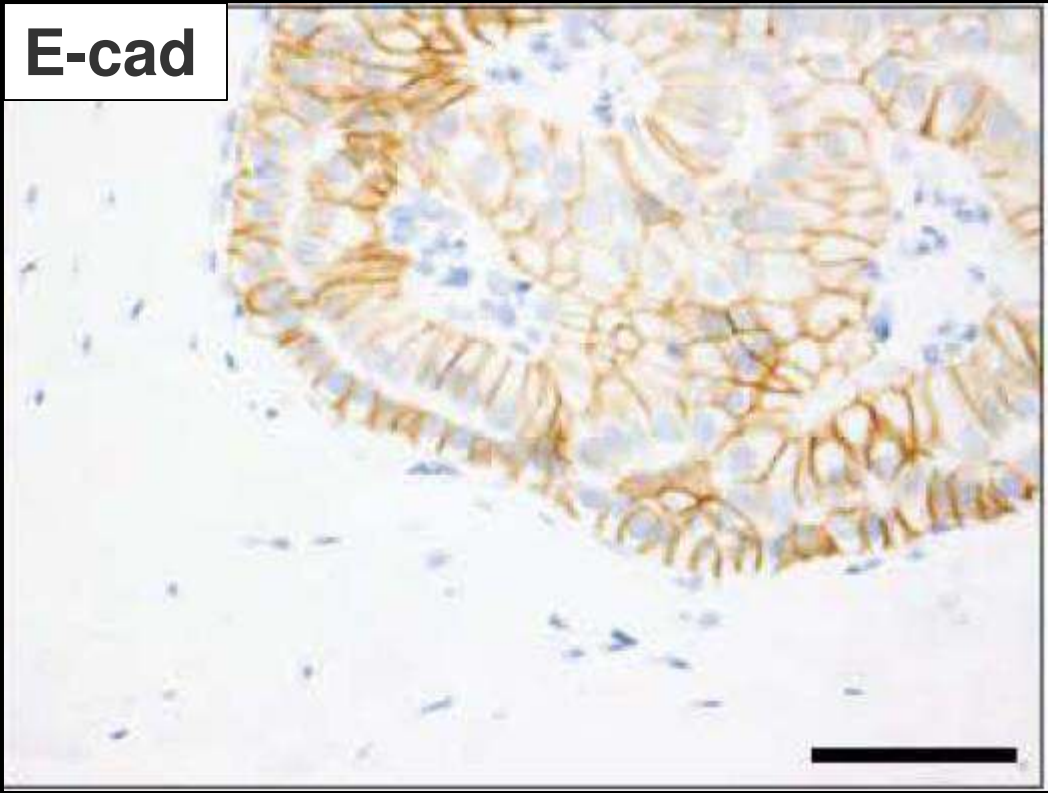
**Ki67**



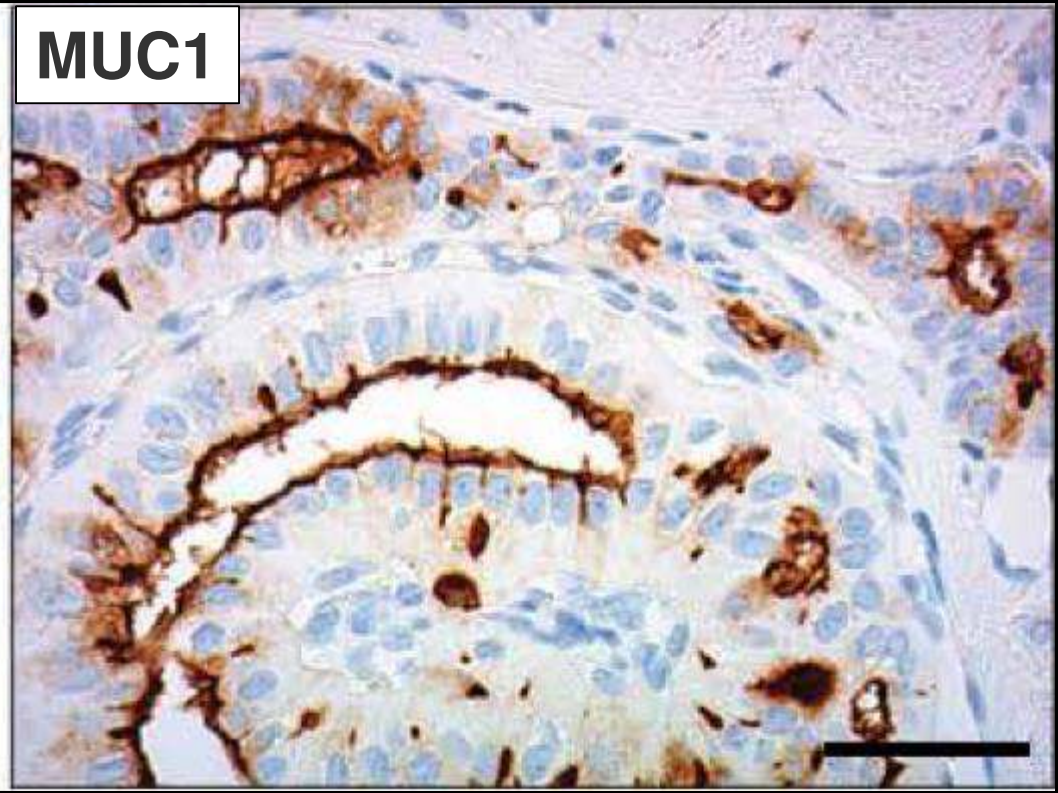
**CD31**



**E-cad**



**MUC1**



***IDH2* Mutations Define a Unique Subtype of Breast Cancer with Altered Nuclear Polarity**

2016

Sarah Chiang<sup>1</sup>, Britta Weigelt<sup>1</sup>, Huei-Chi Wen<sup>1</sup>, Fresia Pareja<sup>1</sup>, Ashwini Raghavendra<sup>1</sup>, Luciano G. Martelotto<sup>1</sup>, Kathleen A. Burke<sup>1</sup>, Thais Basili<sup>1</sup>, Anqi Li<sup>1</sup>, Felipe C. Geyer<sup>1</sup>, Salvatore Piscuoglio<sup>1</sup>, Charlotte K.Y. Ng<sup>1</sup>, Achim A. Jungbluth<sup>1</sup>, Jörg Balss<sup>2</sup>, Stefan Pusch<sup>2</sup>, Gabrielle M. Baker<sup>3</sup>, Kimberly S. Cole<sup>4</sup>, Andreas von Deimling<sup>2,5</sup>, Julie M. Batten<sup>6</sup>, Jonathan D. Marotti<sup>7</sup>, Hwei-Choo Soh<sup>8</sup>, Benjamin L. McCalip<sup>9</sup>, Jonathan Serrano<sup>10</sup>, Raymond S. Lim<sup>1</sup>, Kalliopi P. Siziopikou<sup>11</sup>, Song Lu<sup>12</sup>, Xiaolong Liu<sup>13</sup>, Tarek Hammour<sup>14</sup>, Edi Brogi<sup>1</sup>, Matija Snuderl<sup>10</sup>, A. John Iafrate<sup>6,15</sup>, Jorge S. Reis-Filho<sup>1</sup>, and Stuart J. Schnitt<sup>15,16</sup>

- ***IDH2* mutations in 10/13 cases (77%)**
  - Not previously reported in breast cancers
- **8 concurrently displayed mutations in PI3 kinase pathway (*PIK3CA* or *PIK3R1*)**
- **Functional studies**
  - *IDH2* and *PIK3CA* mutations appear to be driver alterations resulting in reverse polarization phenotype

# Breast Tumor Resembling Tall Cell Variant of Papillary Thyroid Carcinoma

A Solid Papillary Neoplasm With Characteristic Immunohistochemical Profile and Few Recurrent Mutations

Rohit Bhargava, MD,<sup>1</sup> Anca V. Florea, MD,<sup>2</sup> Manuela Pelmus, MD,<sup>2</sup> Mirosława W. Jones, MD,<sup>1</sup> Marguerite Bonaventura, MD,<sup>1</sup> Abigail Wald, PhD,<sup>3</sup> and Marina Nikiforova, MD<sup>3</sup>

AJCP, 2017

Case	Mutations
1	IDH2
2	ATM
3	IDH2, PIK3CA, ATM

# **Solid Papillary Carcinoma with Reverse Polarity**

## **Outcome**

- **Generally indolent behavior**
- **3 reported cases with axillary lymph node mets**
- **One reported case with bone mets**

# Conclusions

- **Solid papillary carcinoma with reverse polarity (SPCRP) represents a histologically low grade invasive breast carcinoma with distinctive morphologic, immunophenotypic and genotypic features**

# Conclusions

- Same lesion previously described as “breast tumor resembling the tall cell variant of papillary thyroid carcinoma”, but
  - No staining for thyroglobulin or TTF-1
  - No BRAF mutations
  - Distinct mutational profile (*IDH2* mutations)
  - Unrelated to thyroid carcinomas
  - Solid papillary carcinoma with reverse polarity (SPCRP) preferred term



# Case 1

## Diagnosis

**Solid papillary carcinoma with reverse polarity (SPCRP)**

