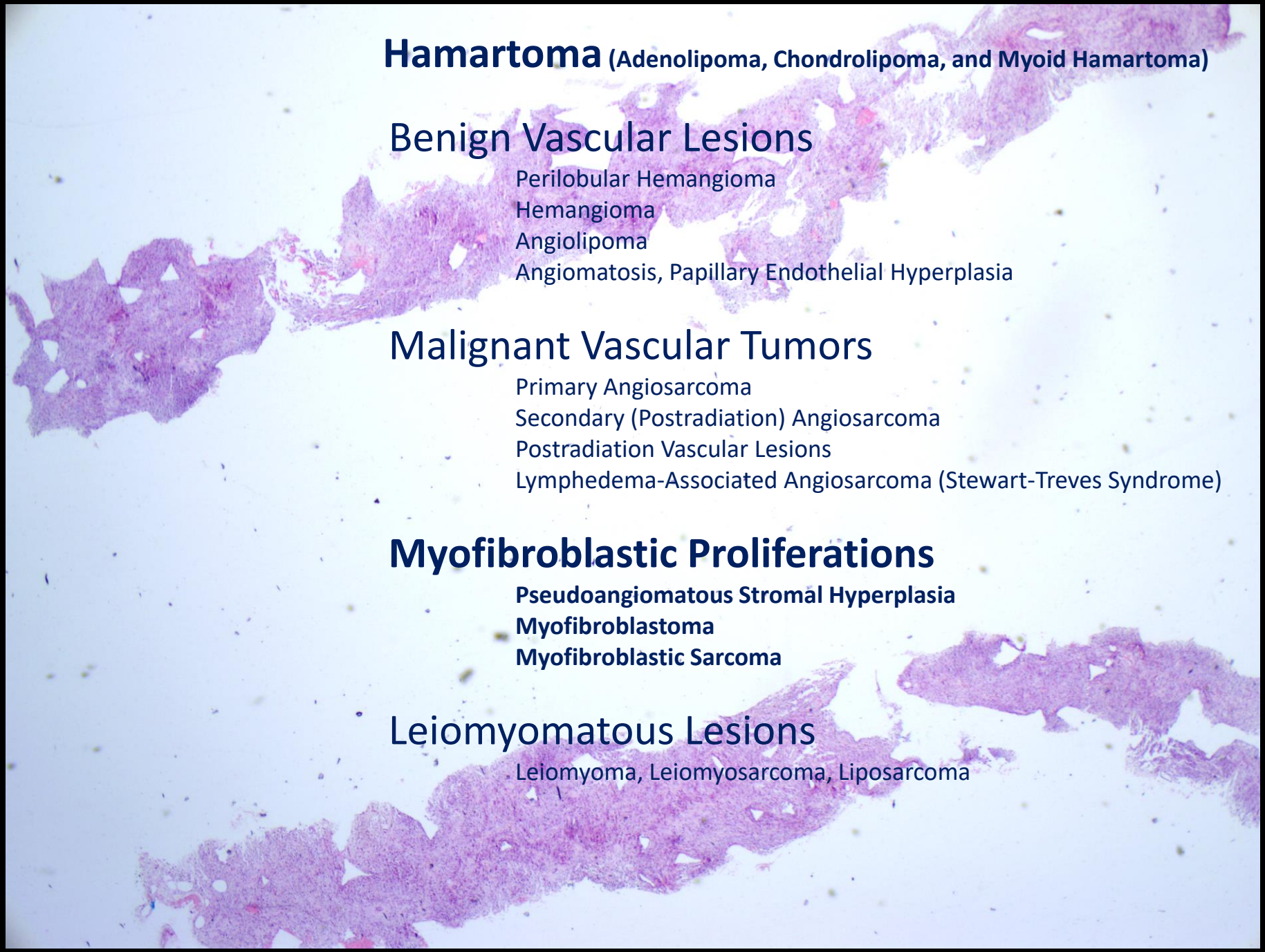
SPINDLE CELL LESIONS OF BREAST

MITUAL AMIN

OAKLAND UNIVERSITY WILLIAM BEAUMONT SCHOOL OF MEDICINE



Hamartoma **(Adenolipoma, Chondrolipoma, and Myoid Hamartoma)**

Benign Vascular Lesions

Perilobular Hemangioma
Hemangioma
Angiolipoma
Angiomatosis, Papillary Endothelial Hyperplasia

Malignant Vascular Tumors

Primary Angiosarcoma
Secondary (Postradiation) Angiosarcoma
Postradiation Vascular Lesions
Lymphedema-Associated Angiosarcoma (Stewart-Treves Syndrome)

Myofibroblastic Proliferations

Pseudoangiomatous Stromal Hyperplasia
Myofibroblastoma
Myofibroblastic Sarcoma

Leiomyomatous Lesions

Leiomyoma, Leiomyosarcoma, Liposarcoma

Approach to Spindle Cell Lesions of Breast

THE HOLY MANTRA

- Rule out spindle cell (metaplastic) carcinoma
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- Rule out spindle cell (metaplastic) carcinoma

- Rule out other spindle cell lesions

An Algorithmic Approach to Spindle Cell Lesions of the Breast

Varma, Sonal MD; Shin, Sandra J. MD

Advances In Anatomic Pathology Issue: Volume 20(2), March 2013, p 95–109

(1) Composition of the cellular proliferation;

(2) Presence of cytomorphologic atypia

(3) Growth pattern: tumor border characteristics

(4) Mitotic activity

(5) Adjacent or admixed cells and/or tissue;

(5) Clinico-radiologic features

MONOPHASIC LESIONS WITH PURE PLEOMORPHIC SPINDLE CELL ONLY

- monophasic type of metaplastic carcinoma
- sarcomas like malignant fibrous histiocytoma (MFH), angiosarcoma, and other high grade sarcomas

MONOPHASIC LESIONS WITH PURE BLAND SPINDLE CELLS ONLY

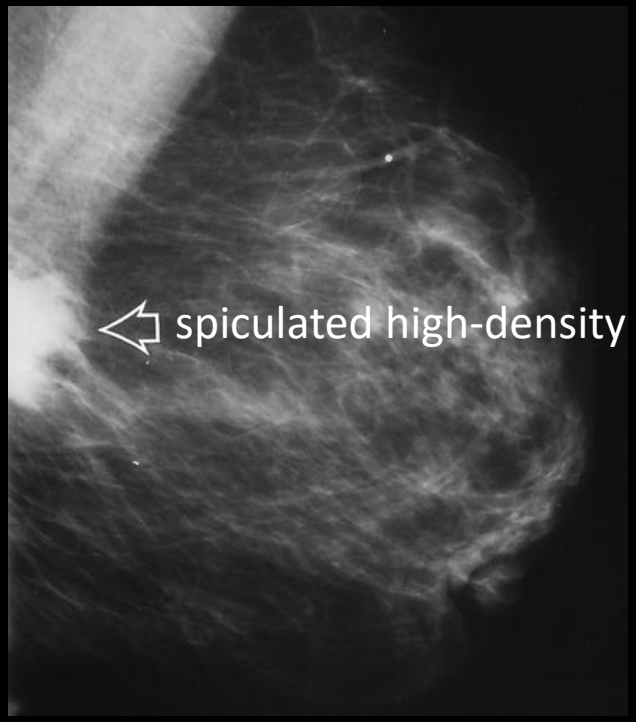
- Fibromatosis
- fibromatosis like metaplastic carcinoma
- dermatofibrosarcoma protuberance (DFSP).

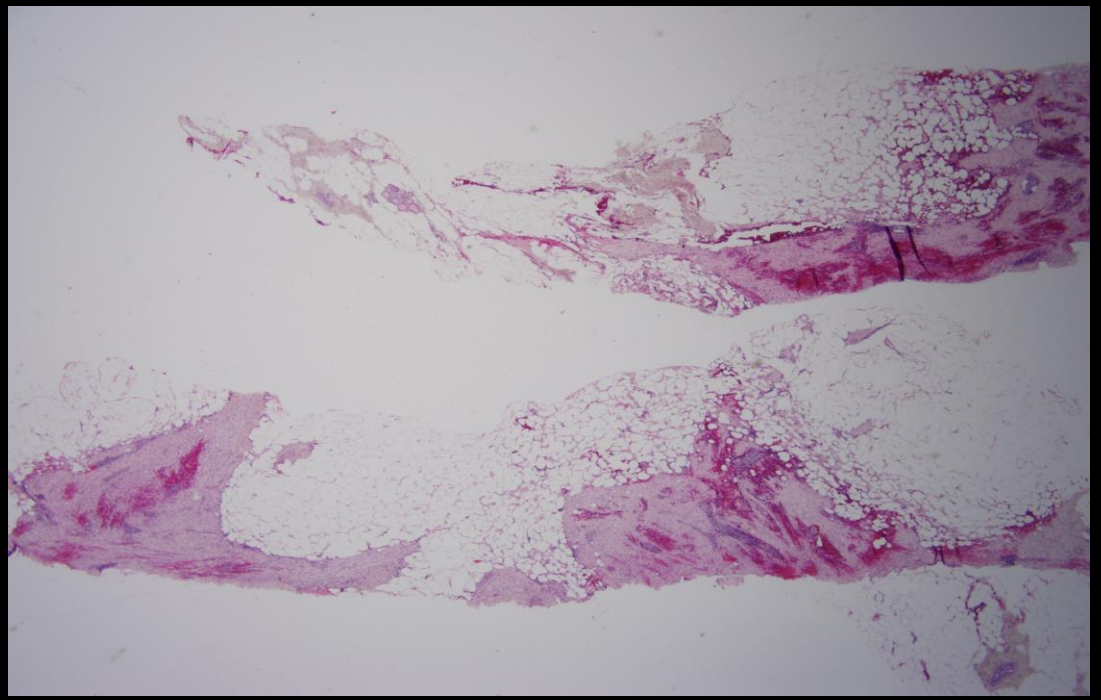
FIBROMATOSIS

- LESS THAN 0.2% OF ALL PRIMARY BREAST LESIONS
- LOCALLY AGGRESSIVE BENIGN MESENCHYMAL NEOPLASM
- YOUNG WOMEN, 45 YEARS (30-60 YEARS)
- TRAUMA, SURGERY, IMPLANTS, GARDNER SYNDROME
- **CLINICALLY AND RADIOLOGICALLY SUSPICIOUS FOR MALIGNANCY**
- POSITIVE MARGINS AND LOCAL RECURRENCE

GROSS EXAMINATION

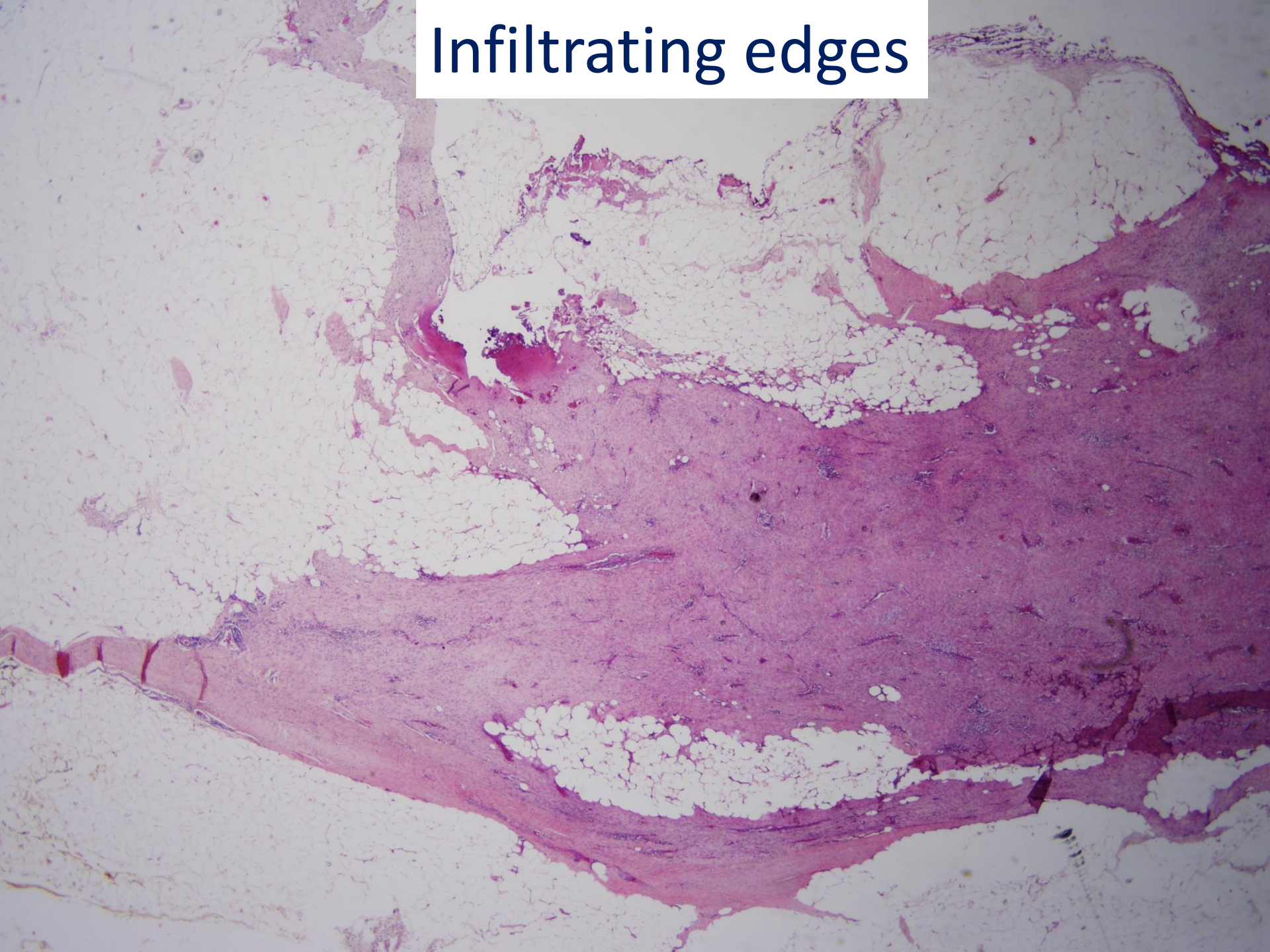
- FIRM, ILL-DEFINED, STELLATE EDGES
- 2-3 CM SIZE



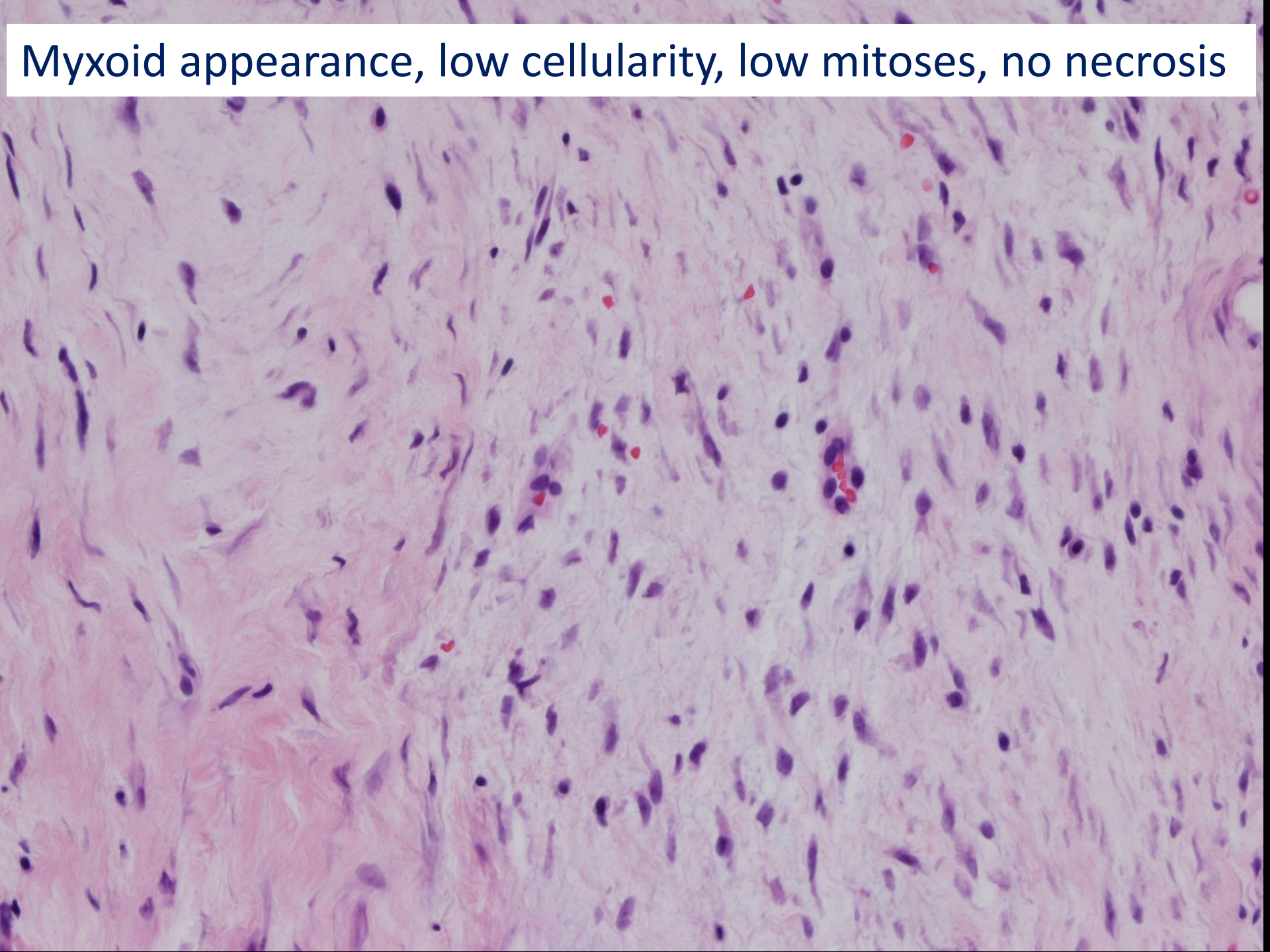


http://pubs.rsna.org/doi/full/10.1148/radiographics.19.suppl_1.g99oc07s11

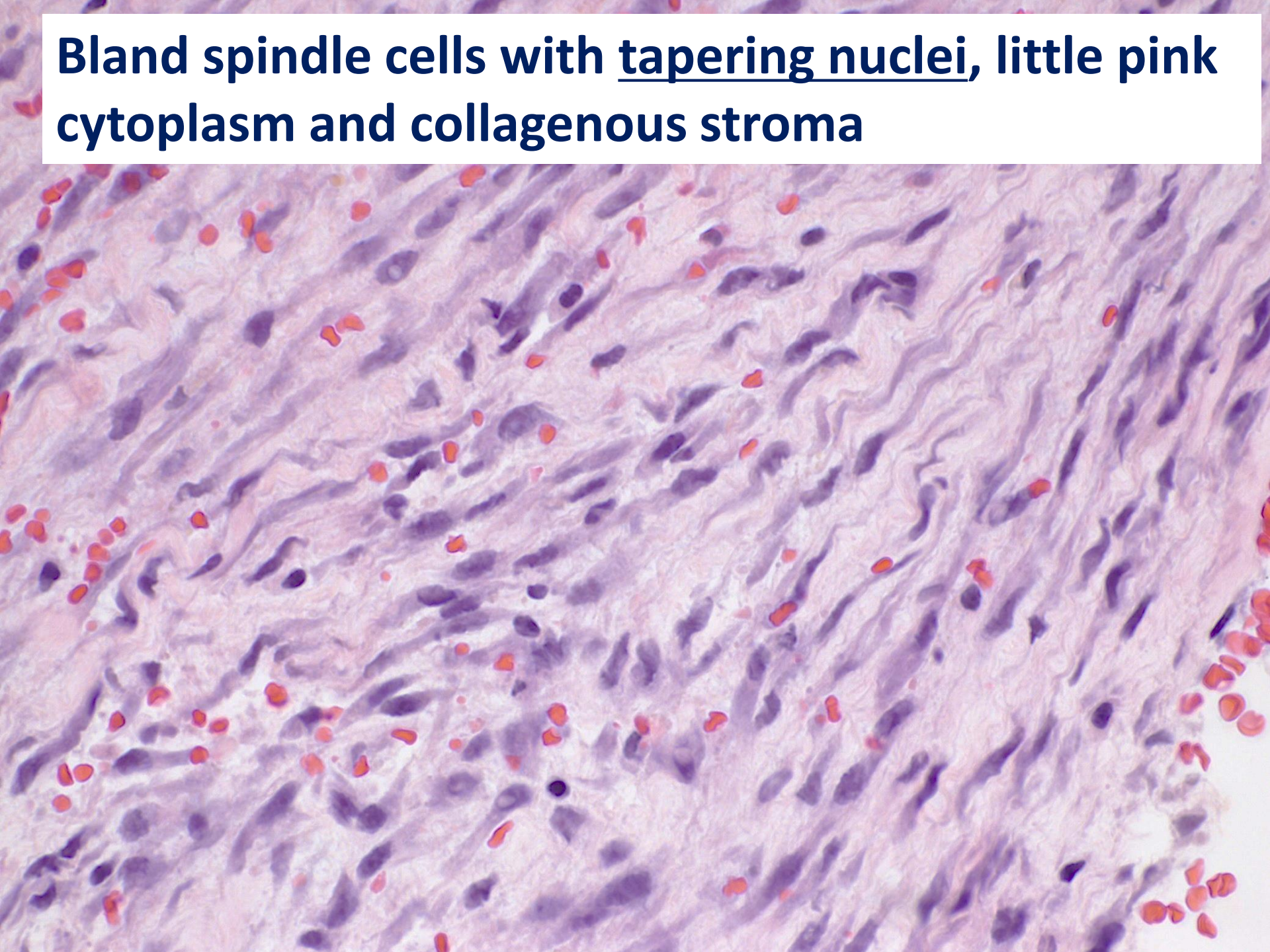
Infiltrating edges

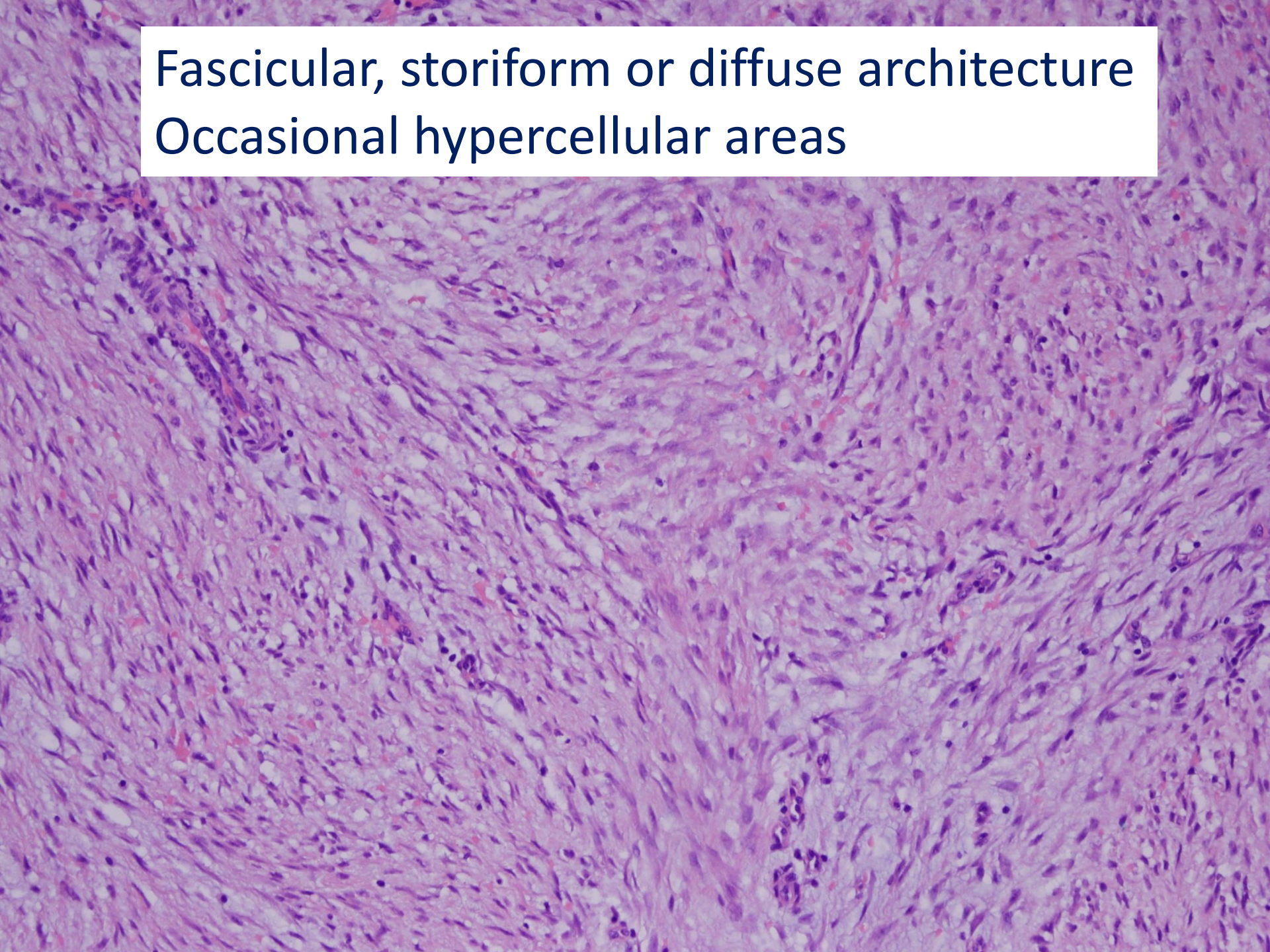


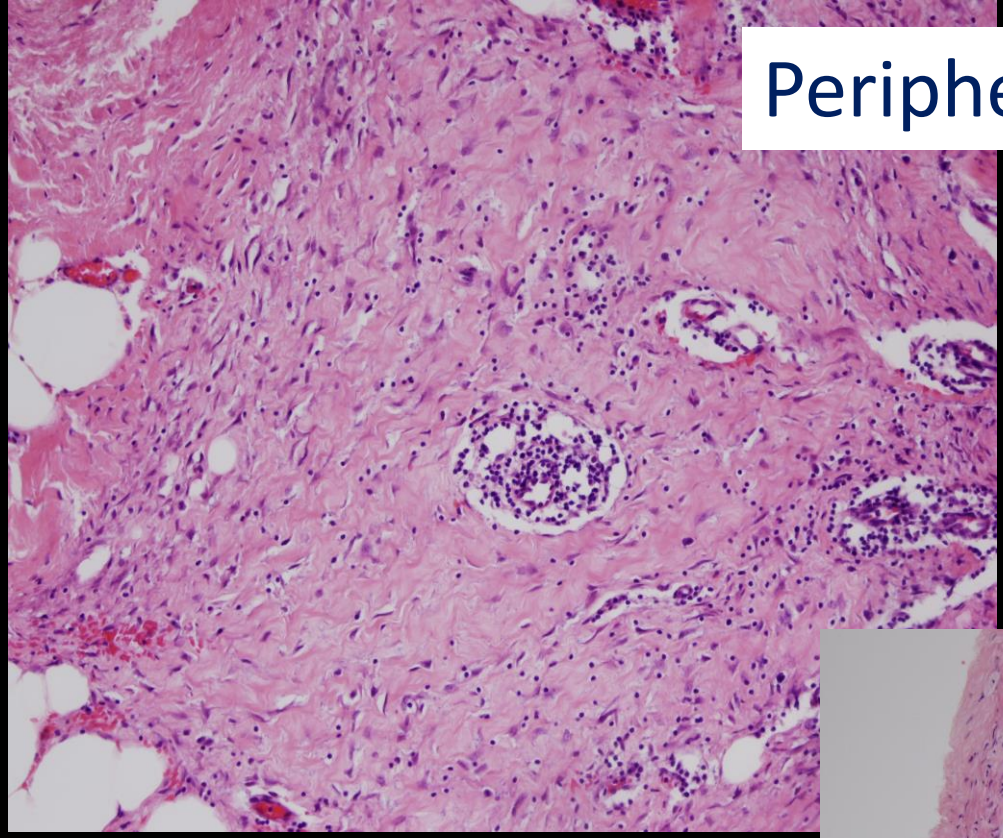
Myxoid appearance, low cellularity, low mitoses, no necrosis



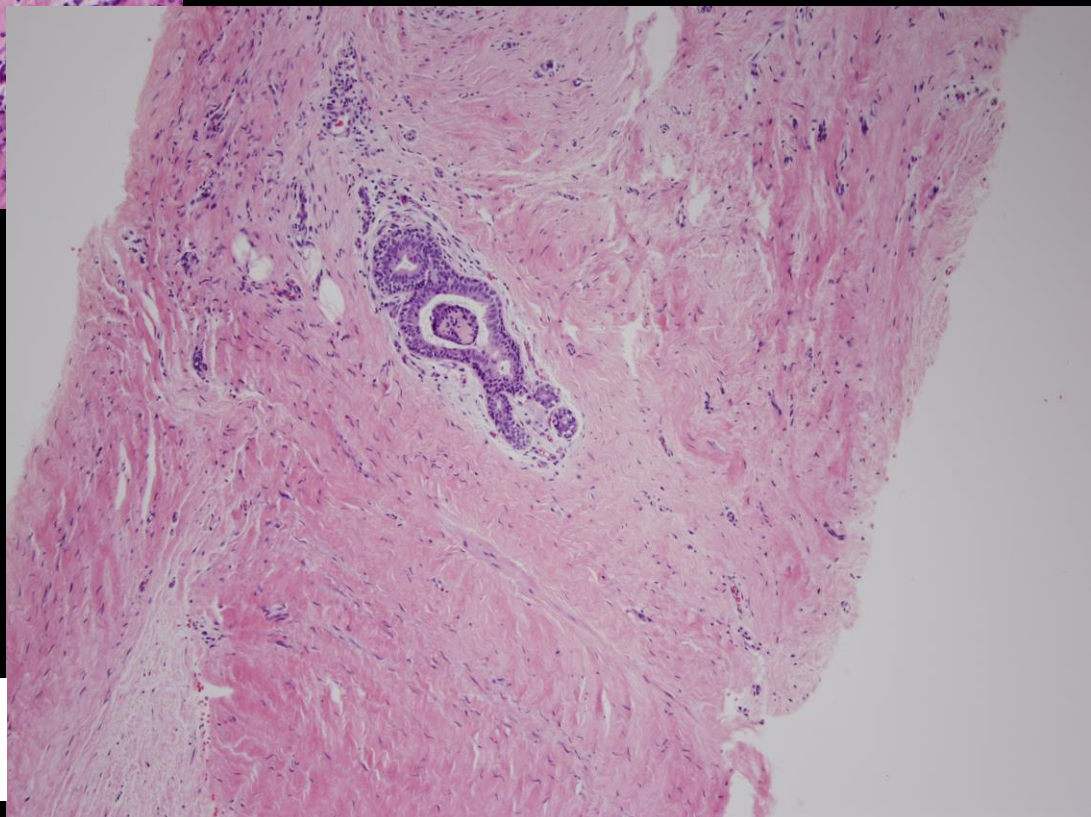
Bland spindle cells with tapering nuclei, little pink cytoplasm and collagenous stroma




Fascicular, storiform or diffuse architecture
Occasional hypercellular areas

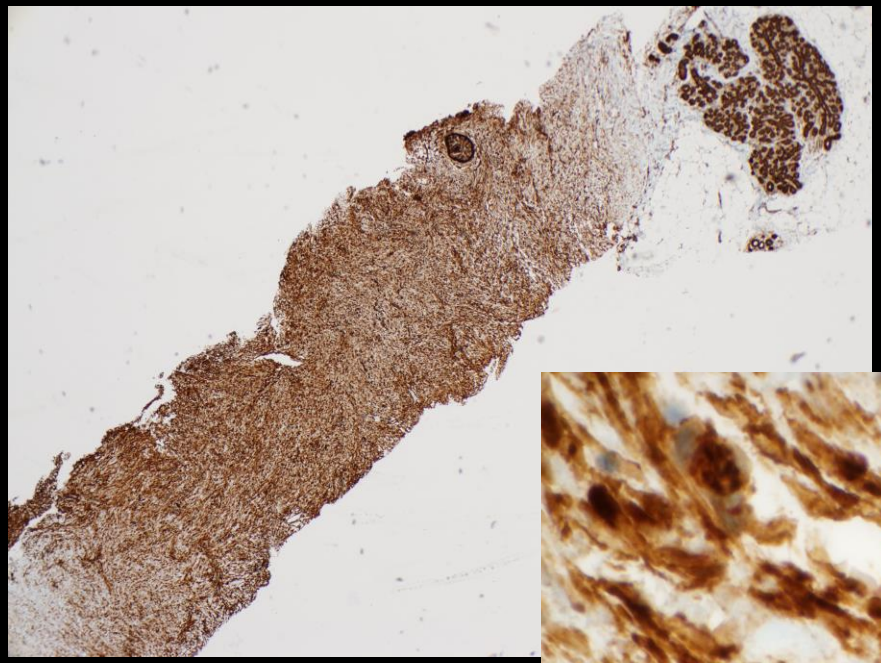


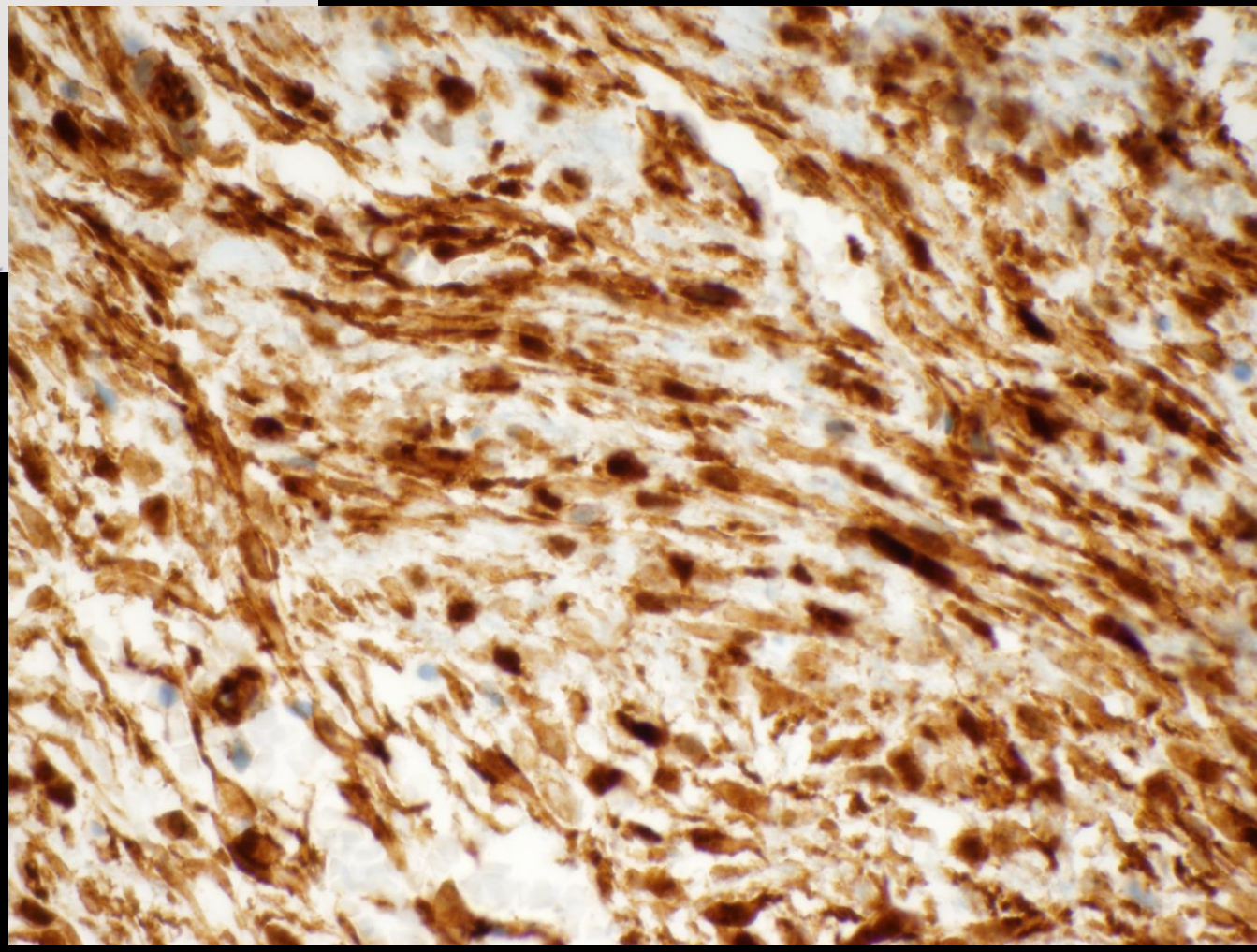
Peripheral lymphoid aggregates



Keloid-like stroma

IMMUNOHISTOCHEMISTRY





- B-CATENIN NUCLEAR STAINING
- ACTIN, DESMIN, S-100

- EXTRAMAMMARY FIBROMATOSIS ER+ IN 30% CASES, BUT MAMMARY FIBROMATOSIS IS MOSTLY ER NEGATIVE

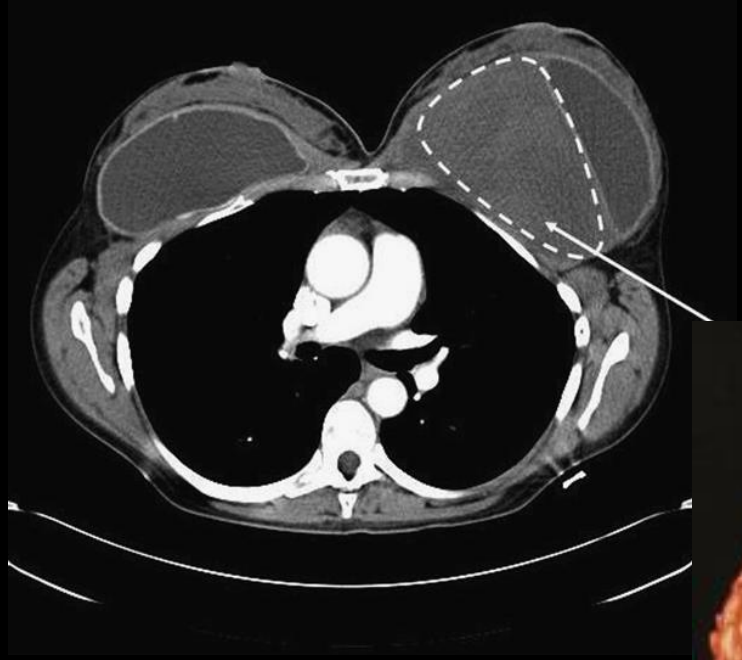
DIFFERENTIAL DIAGNOSIS

- Fibromatosis-like Metaplastic carcinoma
- Nodular fasciitis
- Scar tissue

CLINICAL COURSE

- High local recurrence rate 24-77% over 10 years
- Wide surgical excision
- Radiation in unresectable tumors
- Hormonal treatment
- Anti-inflammatory agents: NSAIDS
- Chemotherapy

Nodular Fasciitis

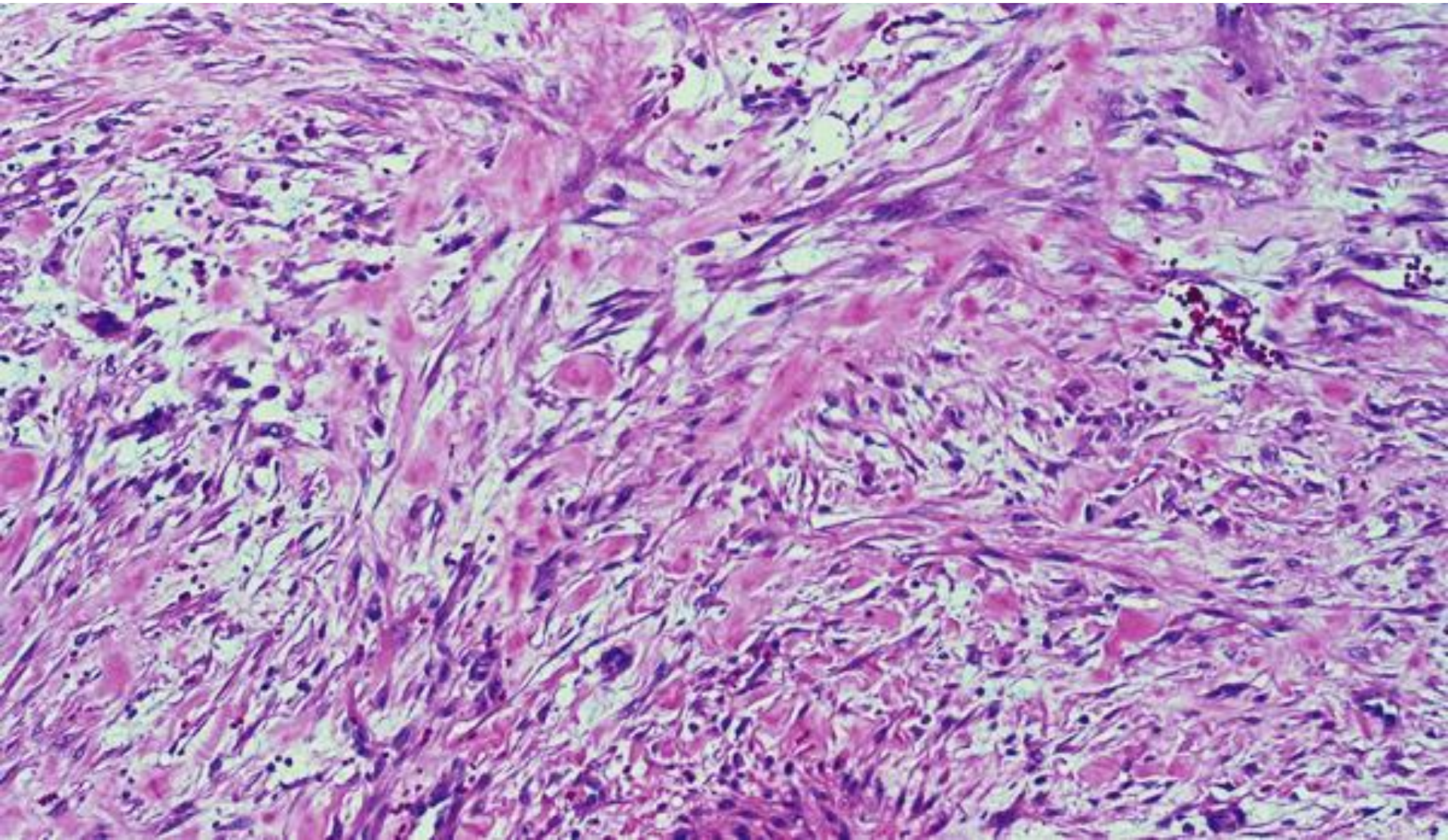


On gross examination, NF lesions typically lack a capsule but have sharp circumscription

Grobmeyer et al. The American Surgeon, July 2009, Volume 75, Number 7, 610-614

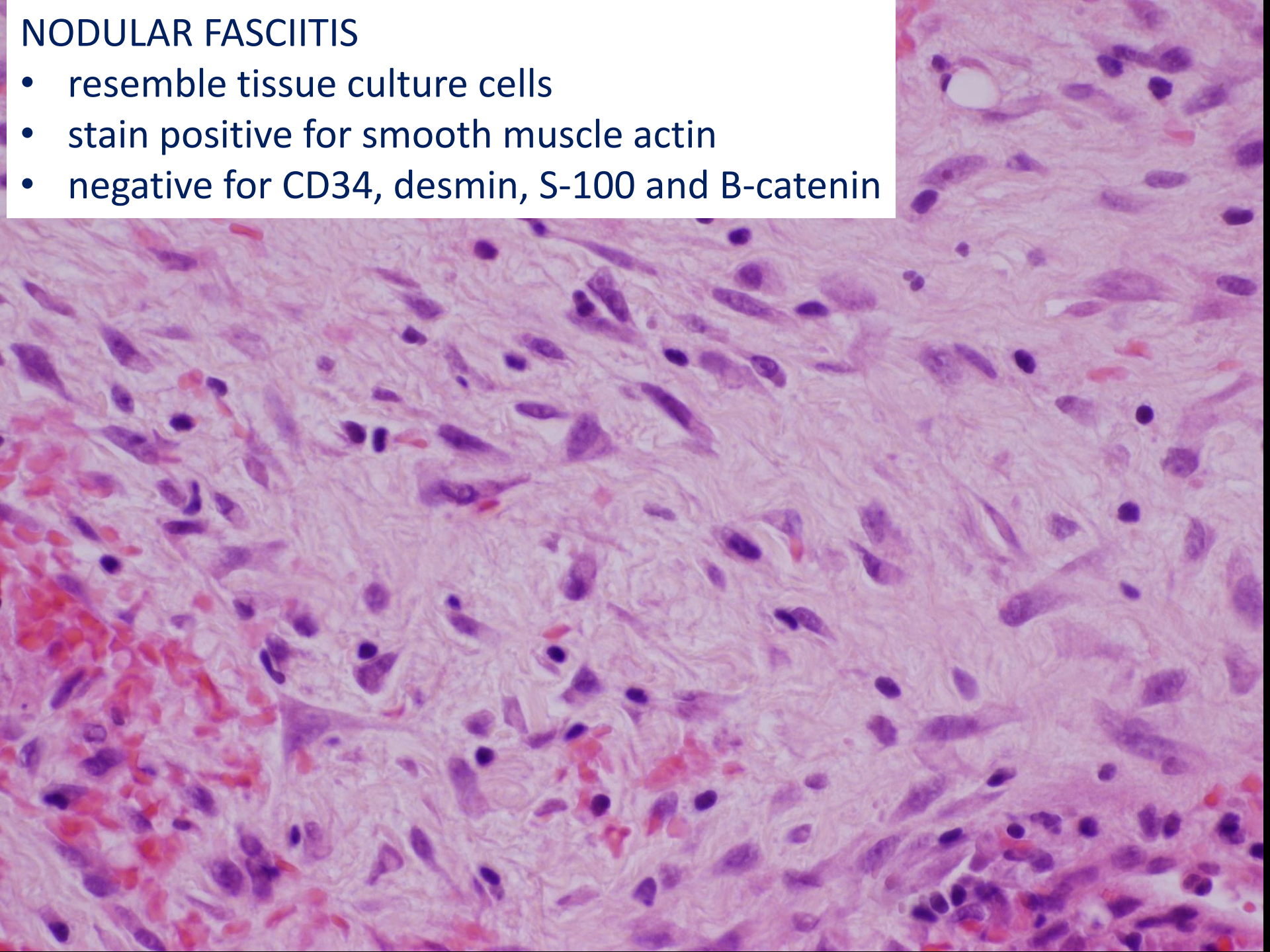
NF is very hypercellular and characterized by the presence of numerous variably shaped, immature myofibroblasts

Mitotic figures are abundant but the cells lack the cytologic atypia and lack necrosis seen with soft tissue sarcomas

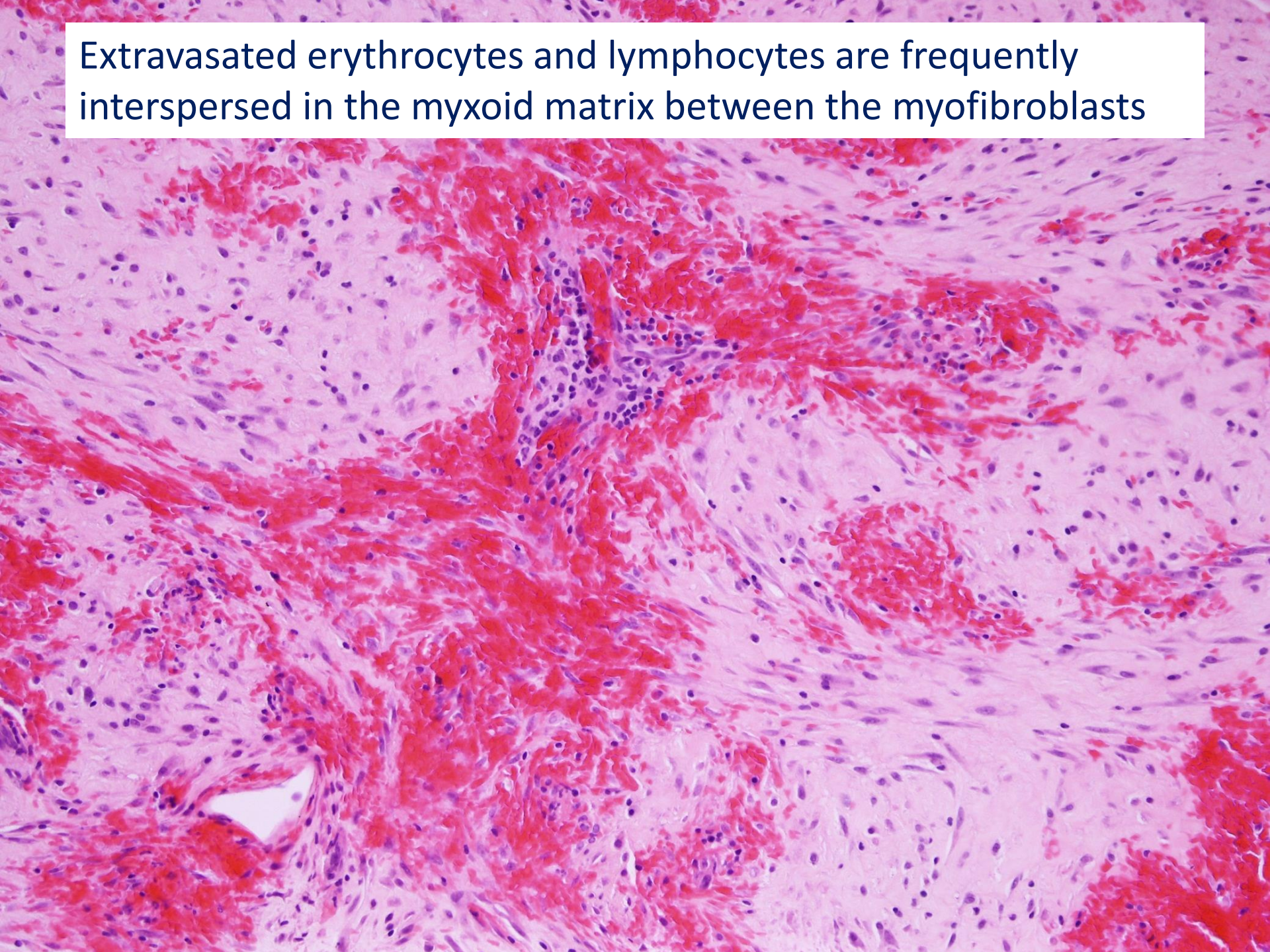


NODULAR FASCIITIS

- resemble tissue culture cells
- stain positive for smooth muscle actin
- negative for CD34, desmin, S-100 and B-catenin



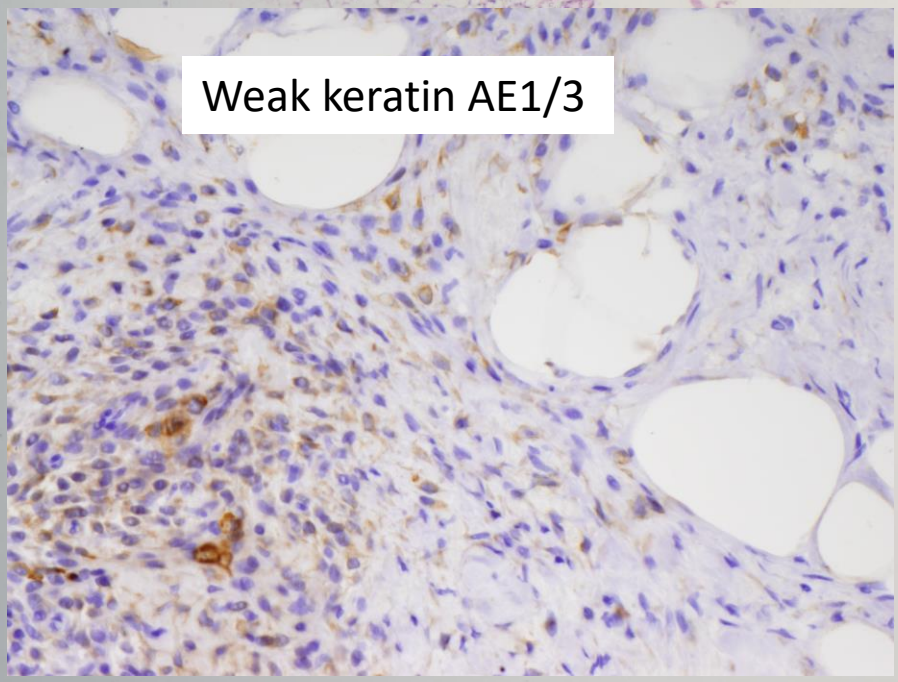
Extravasated erythrocytes and lymphocytes are frequently interspersed in the myxoid matrix between the myofibroblasts



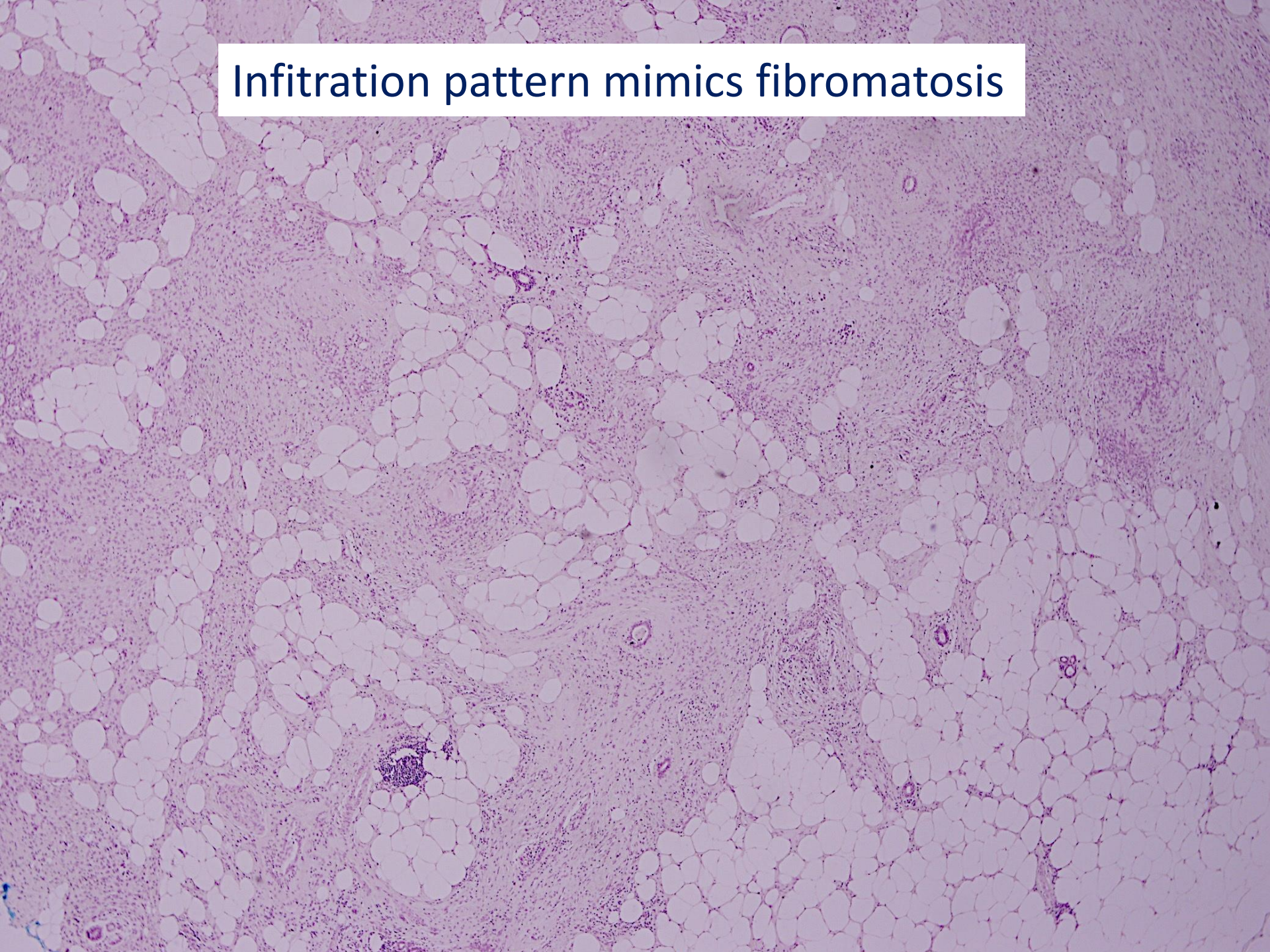
Breast - Nodular Fasciitis

- resolution of symptoms without recurrence after marginal resection
- Recurrences are rare
- No need for radical resection, wide margins or debilitating resections of adjacent structures such as nerves
- May spontaneously regress (sometimes after incomplete resection)
- Watchful waiting
- No role for radiation

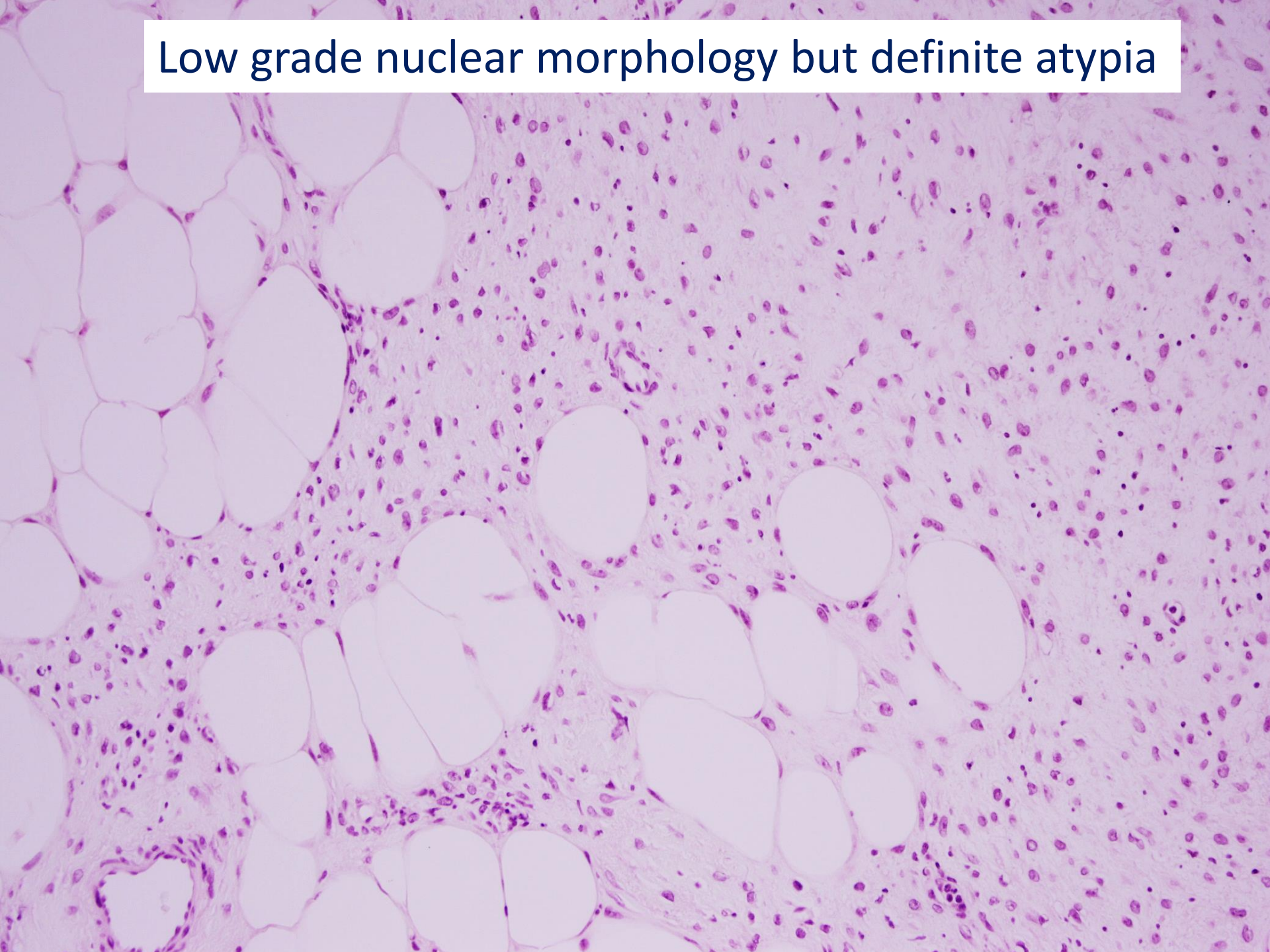
Grobmeyer et al. The American Surgeon, July 2009, Volume 75, Number 7, 610-614

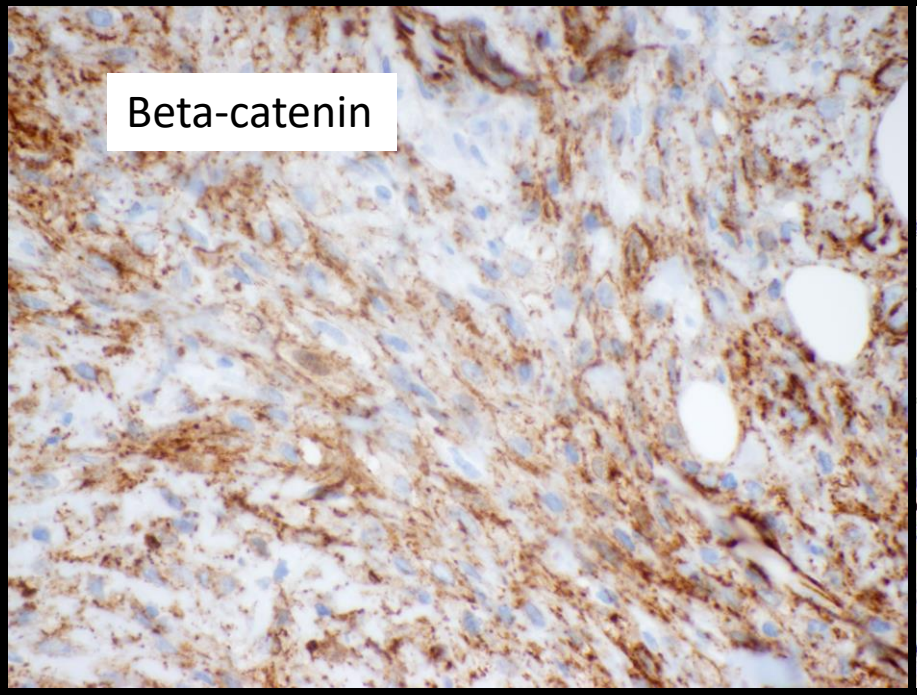


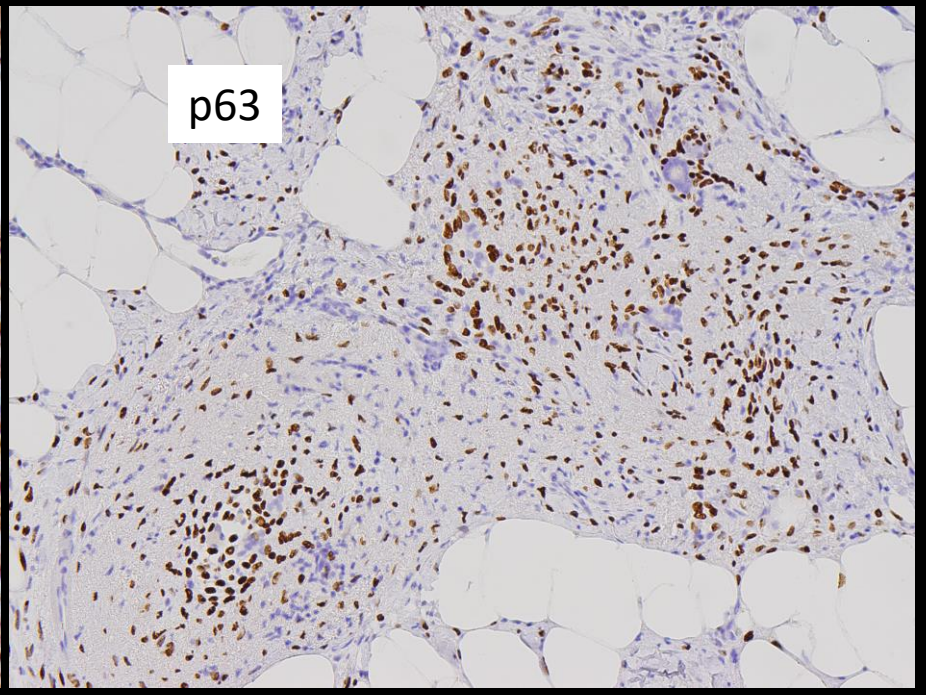
Fibromatosis-like Metaplastic carcinoma

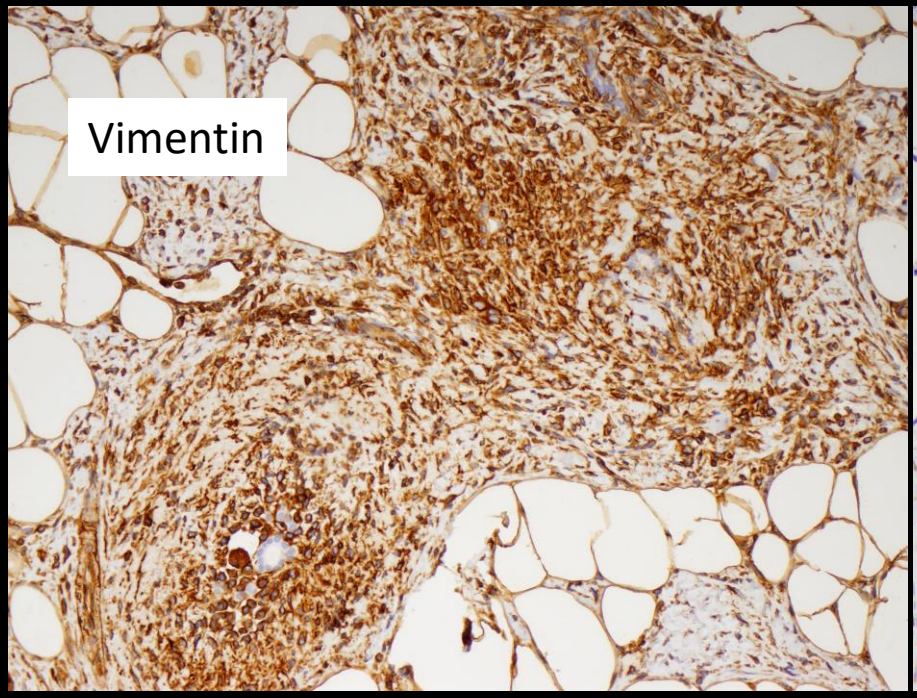

Infitration pattern mimics fibromatosis

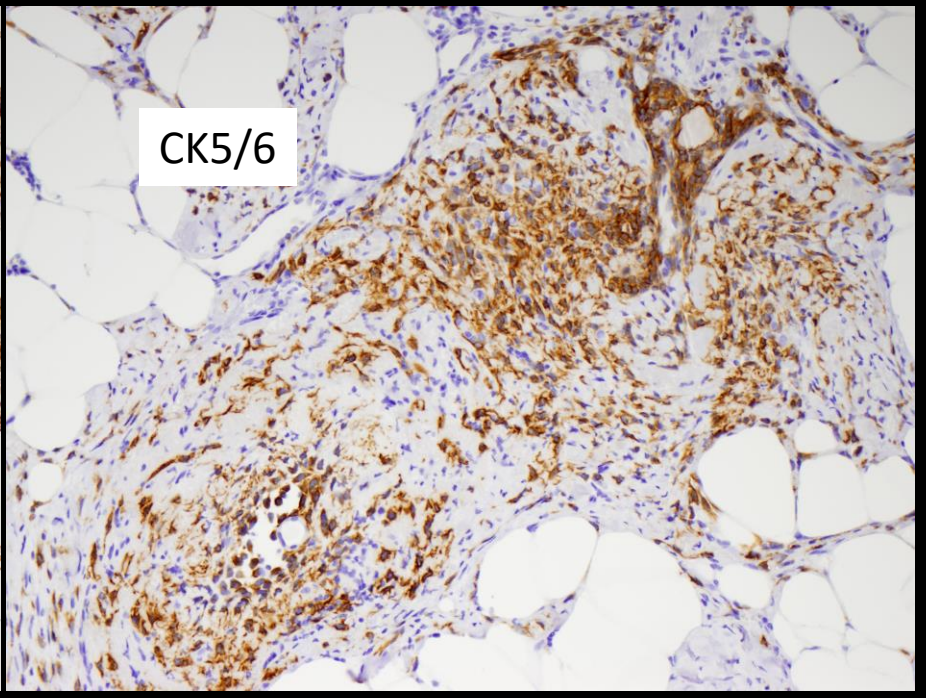
Low grade nuclear morphology but definite atypia




Beta-catenin


p63


Vimentin


CK5/6

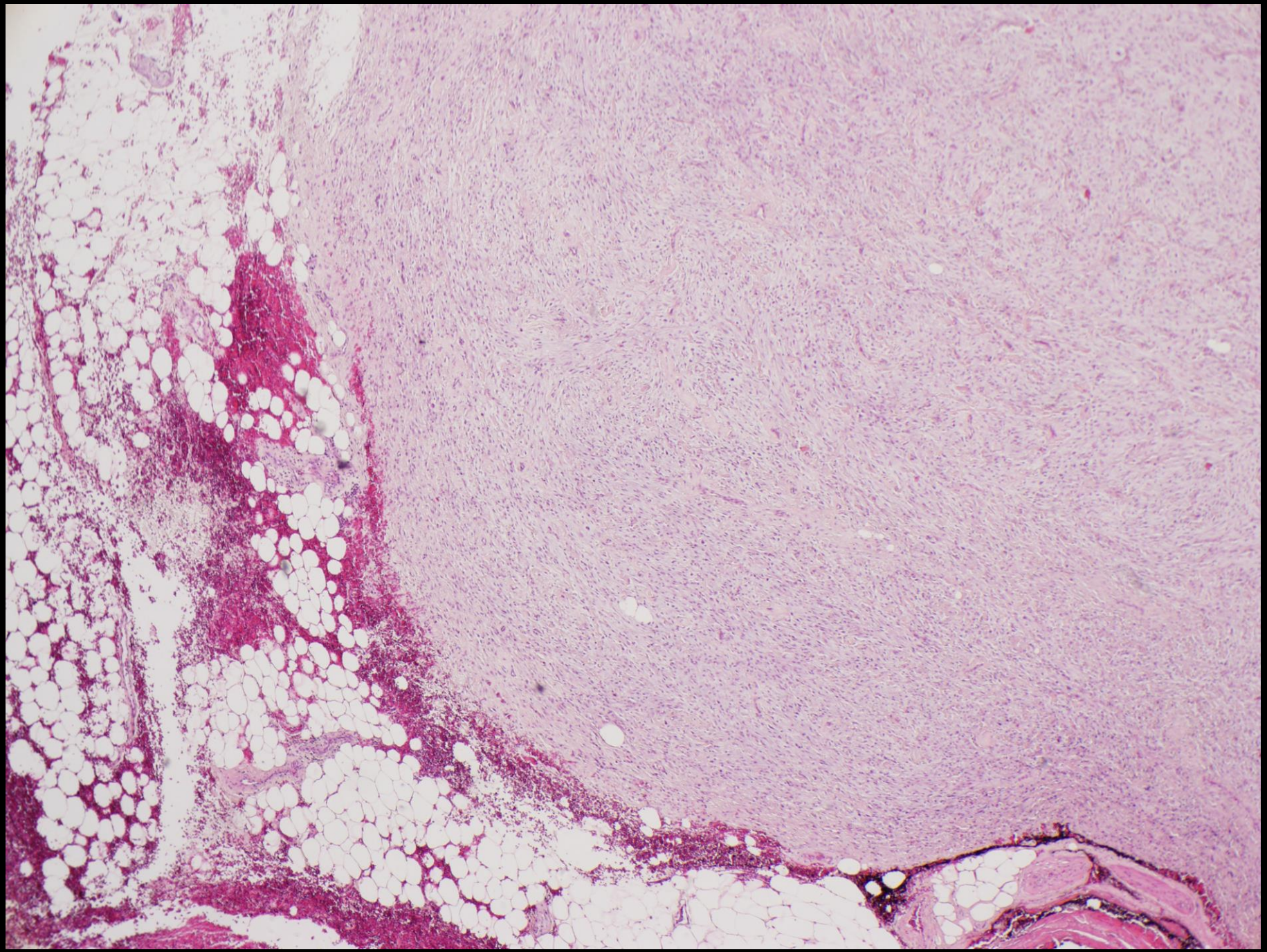
MYOFIBROBLASTOMA

Am J Surg Pathol. 1987 Jul;11(7):493-502.

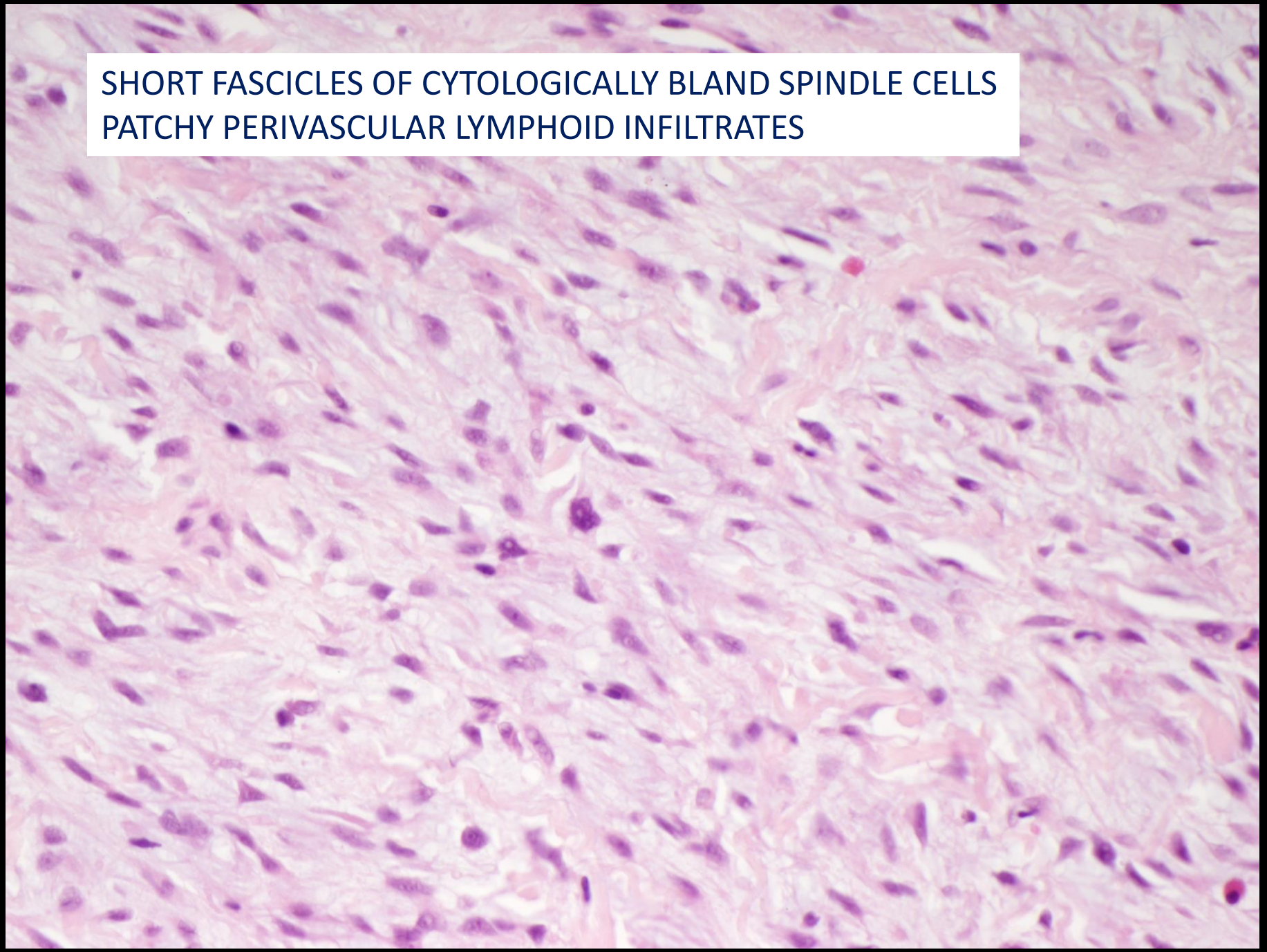
Myofibroblastoma of the breast. Sixteen cases of a distinctive benign mesenchymal tumor.

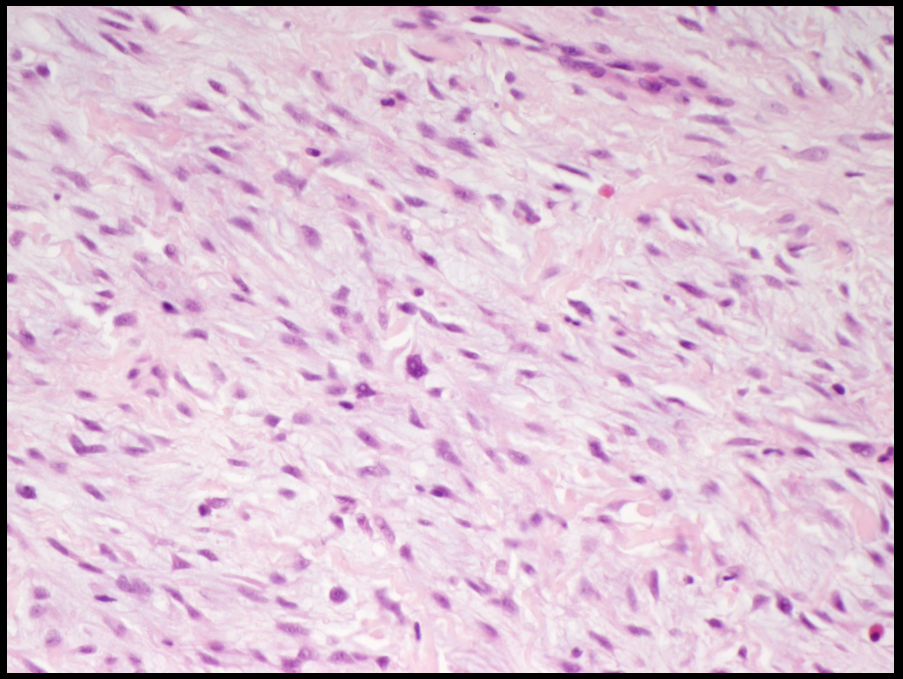
Wargotz ES, Weiss SW, Norris HJ.

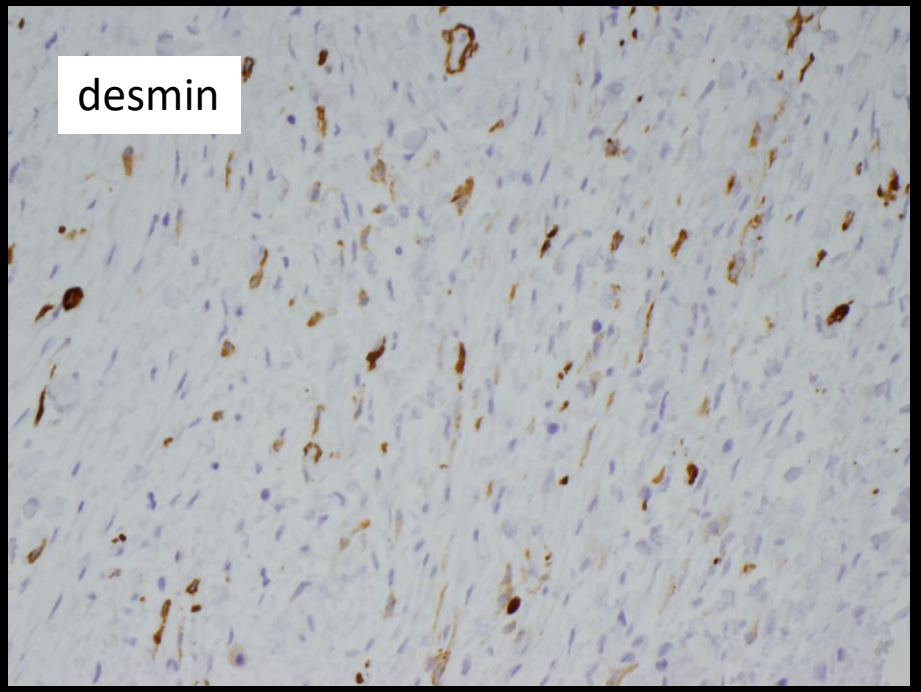
- ORIGINALLY DESCRIBED IN MALES
- AVERGAGE AGE: 63 YEARS (25-87 YEARS)
- No race predeliction
- SLOW GROWING, PALPABLE, painless NODULE
- Gynecomastia, androgen ablation therapy for prostate ca

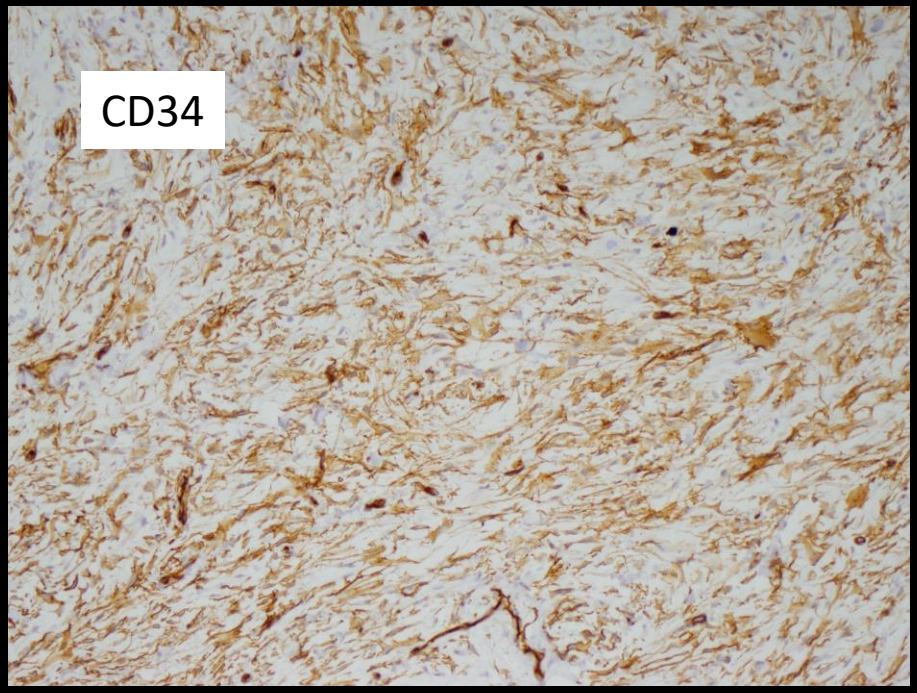


SHORT FASCICLES OF CYTOLOGICALLY BLAND SPINDLE CELLS
PATCHY PERIVASCULAR LYMPHOID INFILTRATES









IMMUNOHISTOCHEMISTRY:
CD34
DESMIN
ER/PR

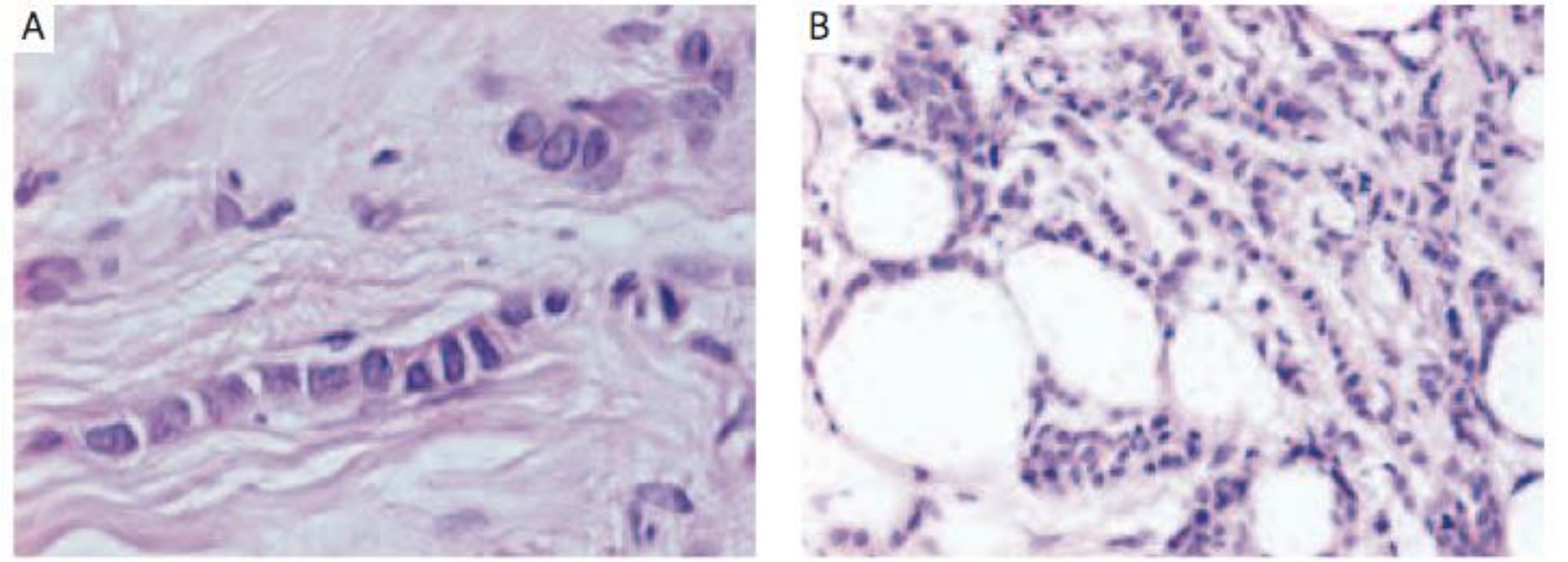
MYOFIBROBLASTOMA

- Collagenized
  - Broad bands of collagen, similar to PASH
- Epithelioid
  - > 50% is epithelioid
  - Negative for CD34 in some cases
- Cellular
  - Cellular, less collagen
- Infiltrative

Pol J Pathol 2012; 2: 131-133

Myofibroblastoma: a potential pitfall in core needle biopsy of breast lesions

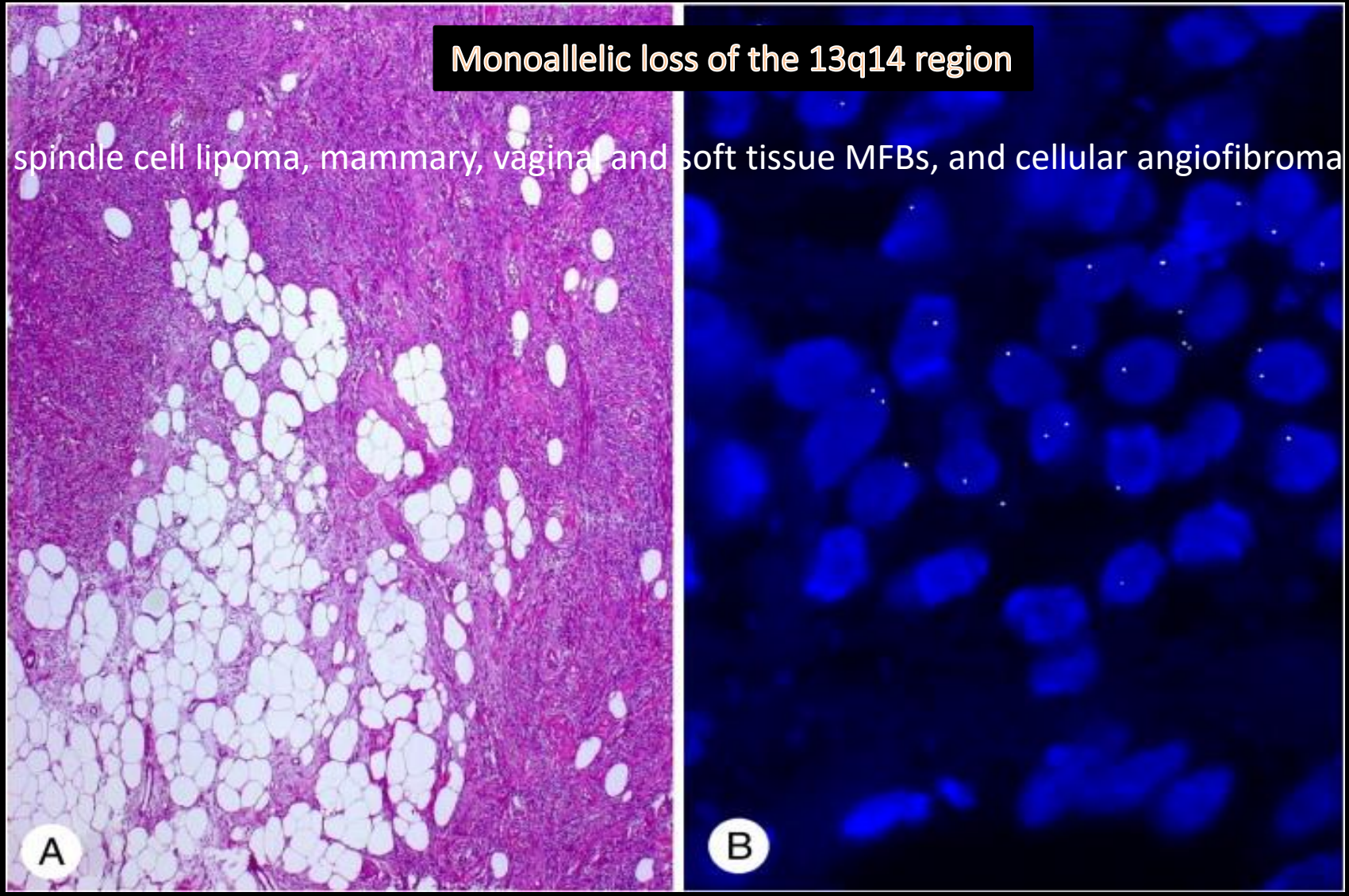
Elwira Bakuła-Zalewska[1], Piotr Piasek[1], Jarosław Wawryszuk[2], Henryk A. Domanski[3]



resulting in a false diagnosis of lobular carcinoma in the core needle biopsy (can be ER/PR positive)

Monoallelic loss of the 13q14 region

spindle cell lipoma, mammary, vaginal and soft tissue MFBs, and cellular angiofibroma



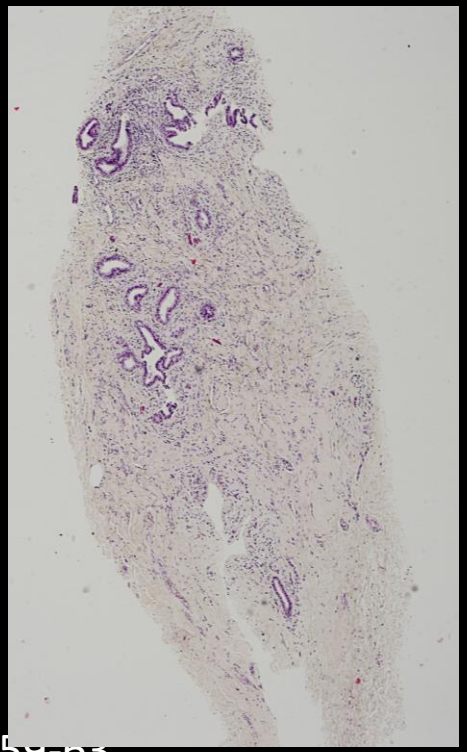
MFB, lipomatous variant: FISH analysis showing monoallelic loss of FOXO1/13q14 loci as indicated by the presence of 1 fusion red/green signal in most tumor cells

Magro et al. Hum Pathol 43, 2012; 1887-93

PASH

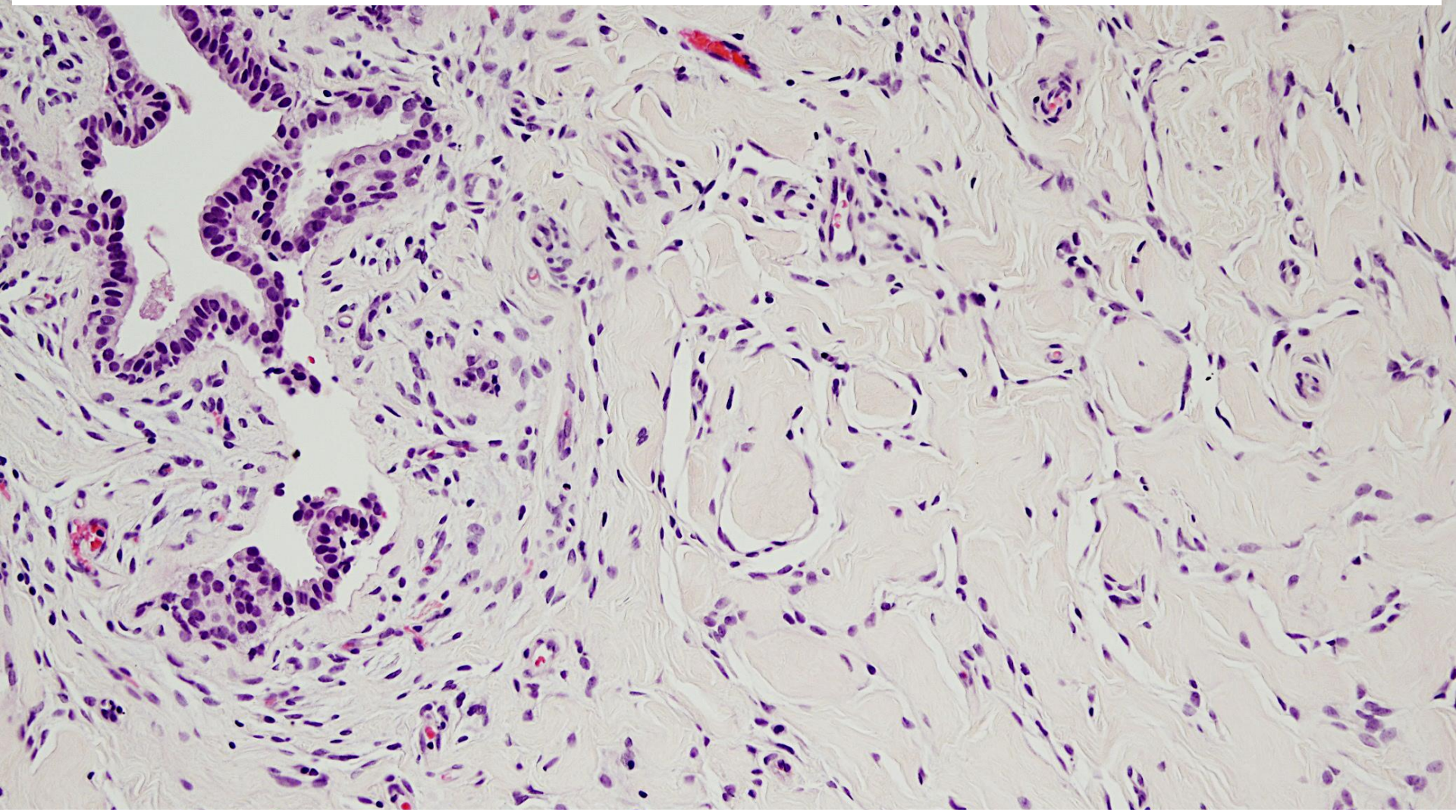
- 23% (of 200) of breast biopsies
- Usually coincident with other pathology
- Can be the dominant pathology
- Hormonal etiology possible
- LOCALIZED STROMAL OVERGROWTH WHICH SIMULATES LOW GRADE ANGIOSARCOMA
- Can grow over time
- Can recur after excision

PASH lesions on mammography and ultrasound indicated that most presented as oval or round well circumscribed masses.



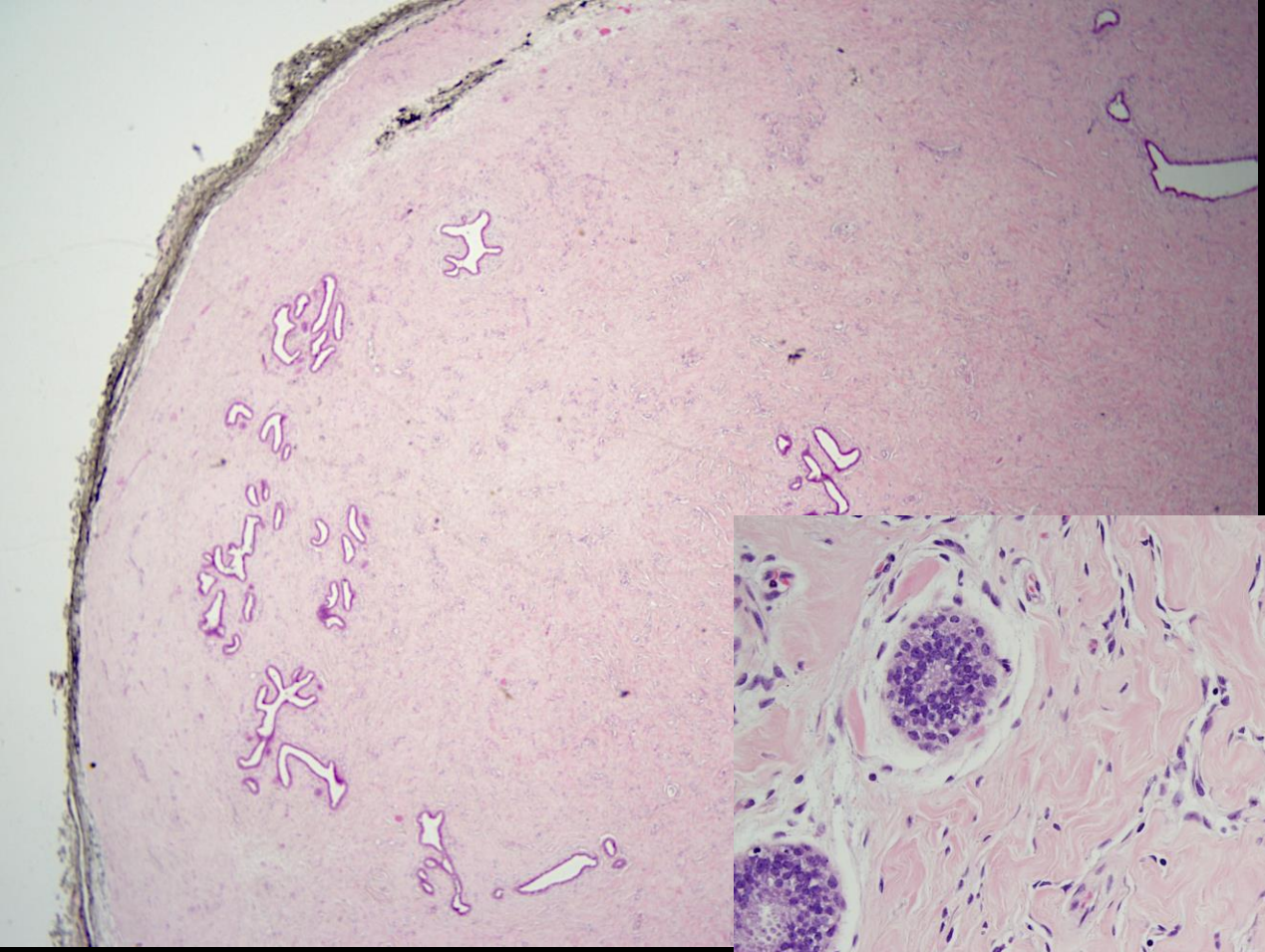
Hargaden et al. AJR Am J Roentgenol. 2008 Aug;191(2):359-63.

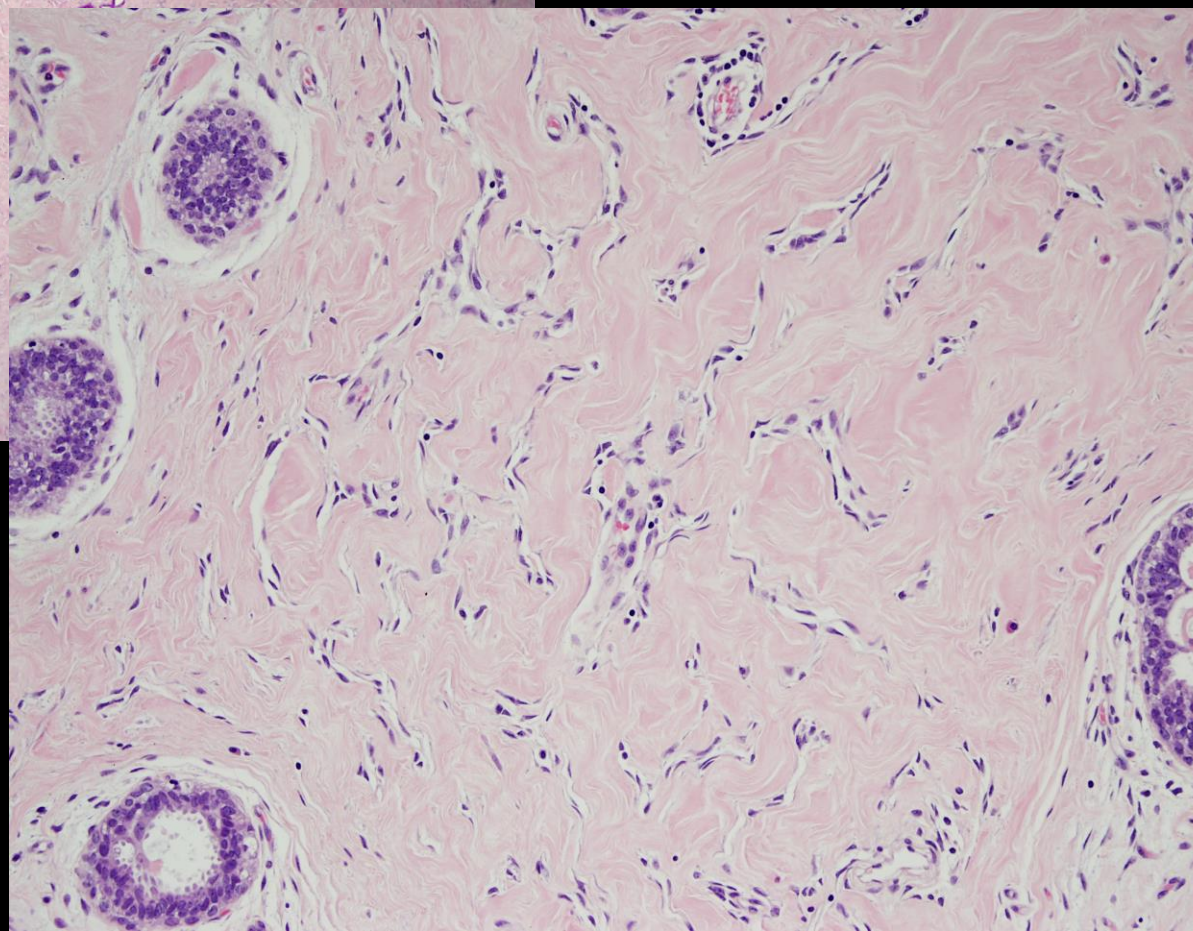
interanastomosing angulated and slit-like spaces lined by slender spindle cells and surrounded by dense collagenous stroma



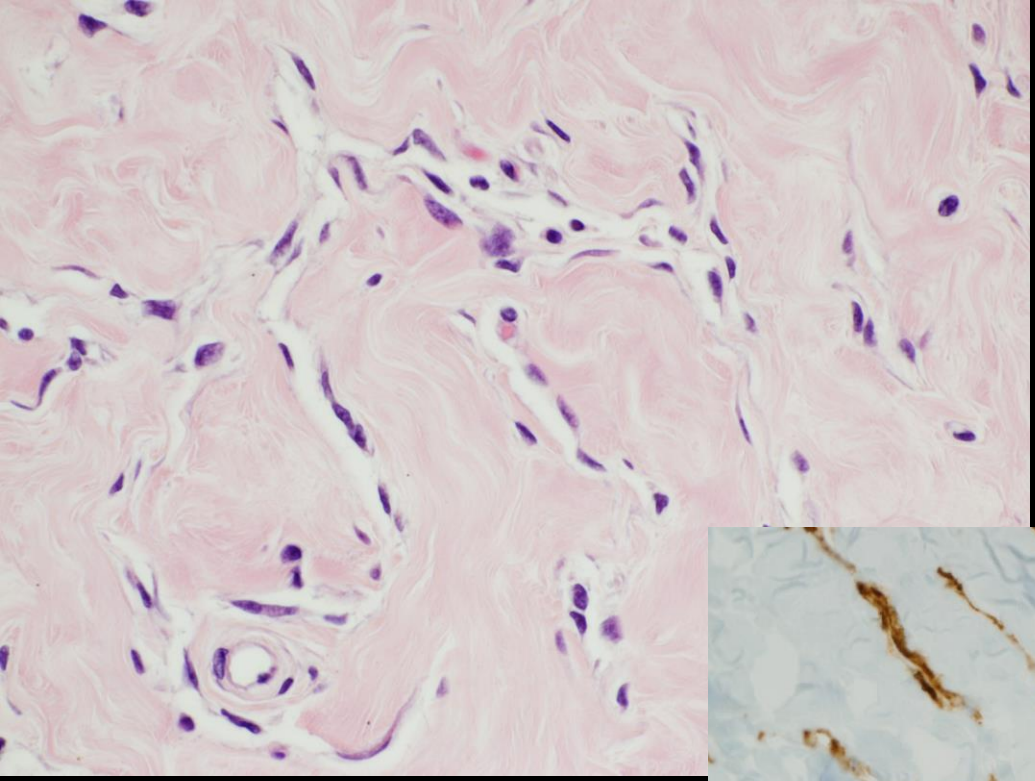
•slits lined by myofibroblastic cells are probably a fixation artifact induced by the retraction of the collagenous stroma

•potential misdiagnosis as low-grade angiosarcoma



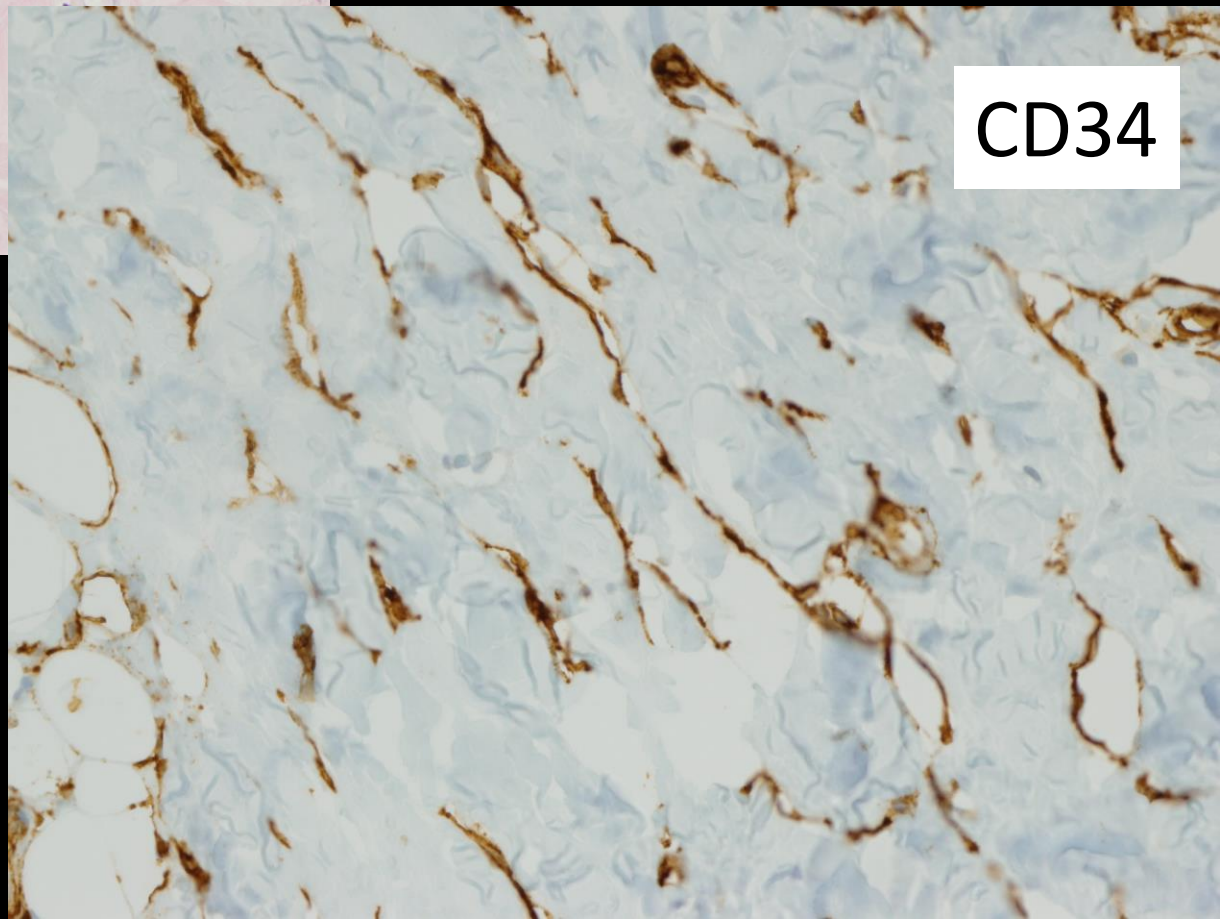


- Glandular elements separated by increased amounts of stroma
- Fibroadenoma-like features

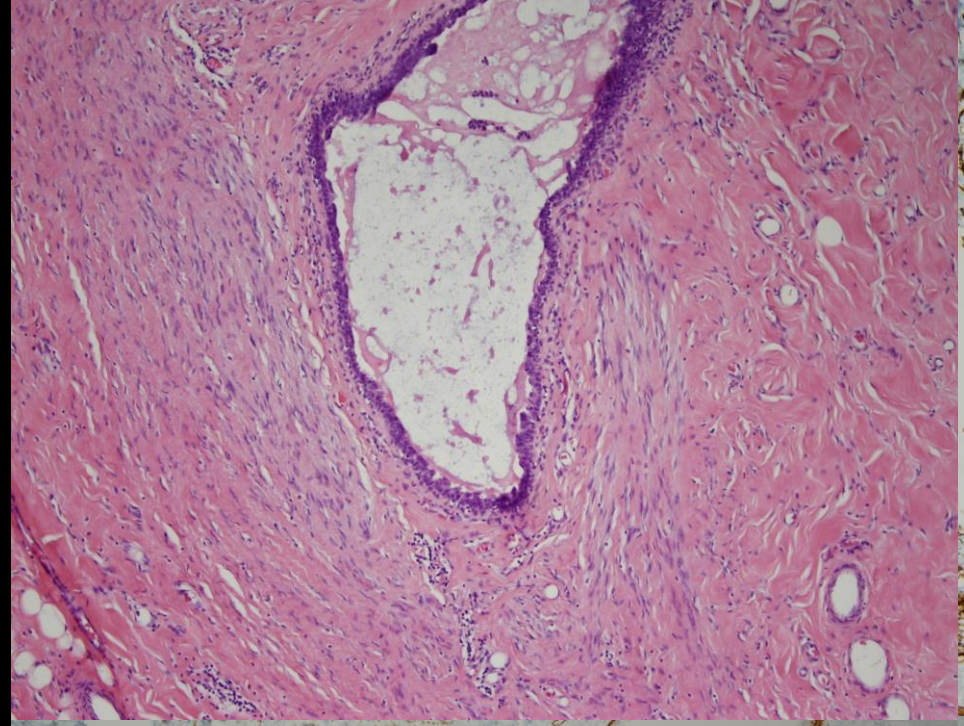


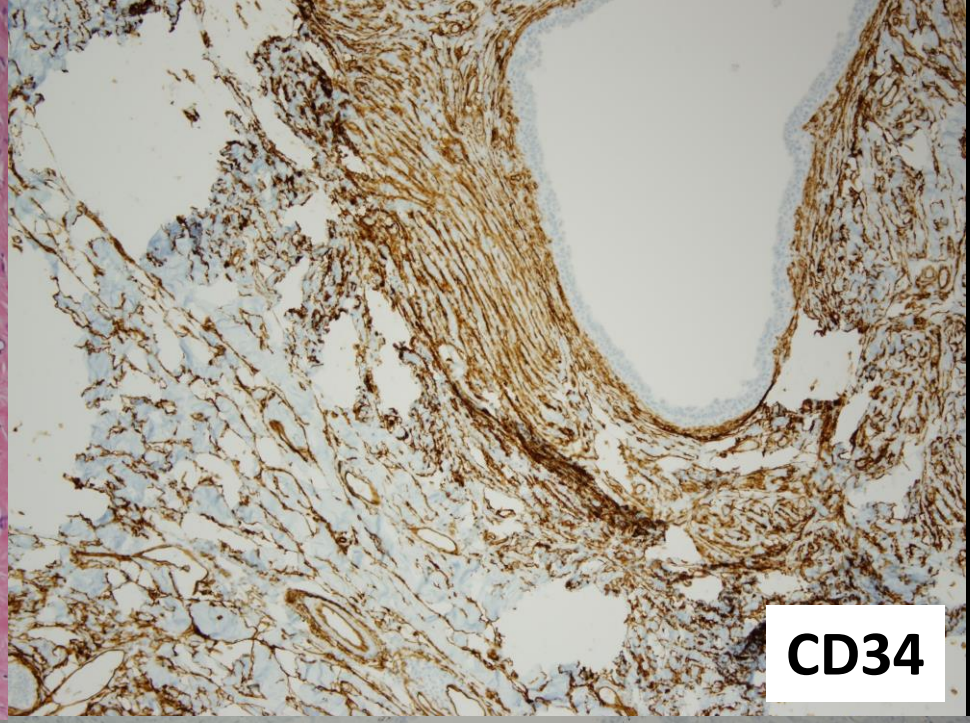
Anastomosing slit-like spaces, outlined by bland spindle cells – myofibroblasts

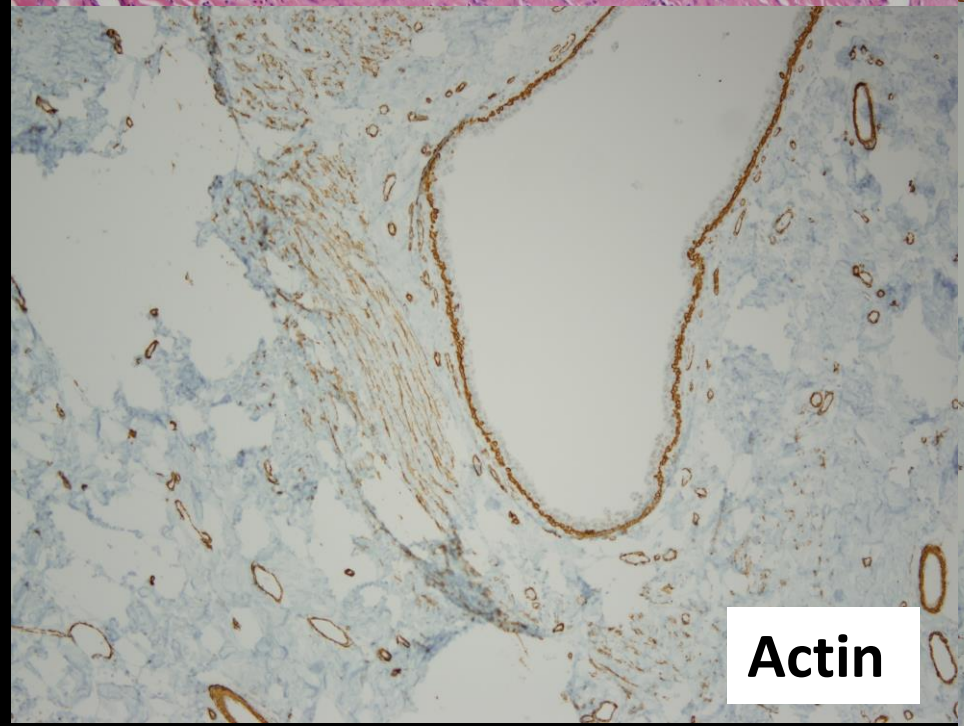
Slit-like spaces are seen on frozen sections and are not artifacts

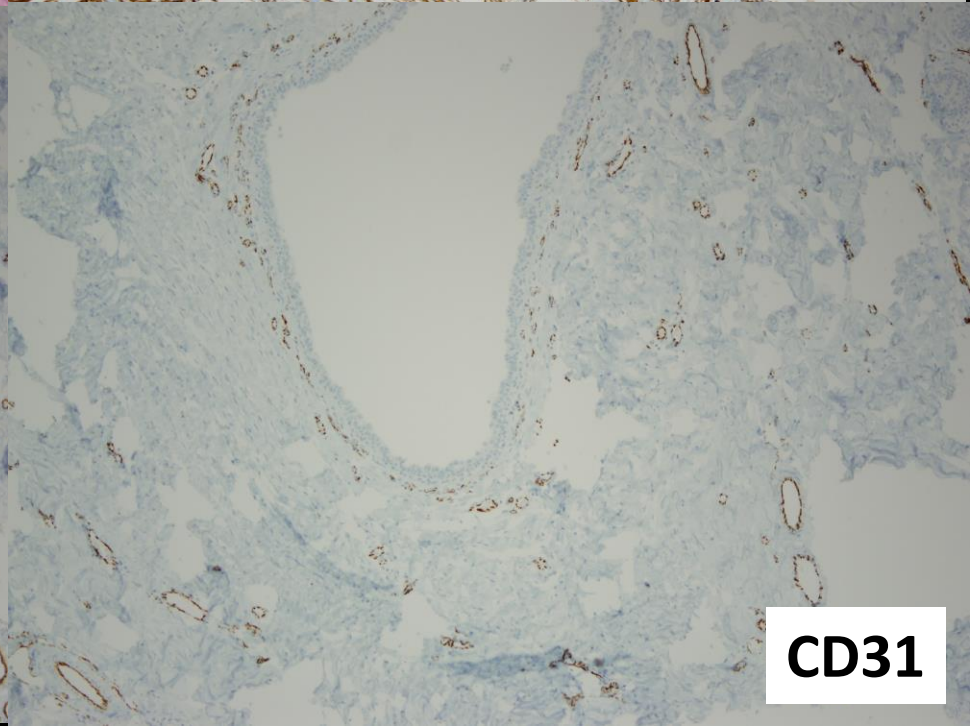


- Negative: FVIII, cytokeratin, S-100
- Positive
  - Vimentin (20/20)
  - CD34 (16/17)
  - Smooth muscle actin (16/19)
- Variable
  - ER (4/14), PR (7/14)
  - Desmin (4/19)

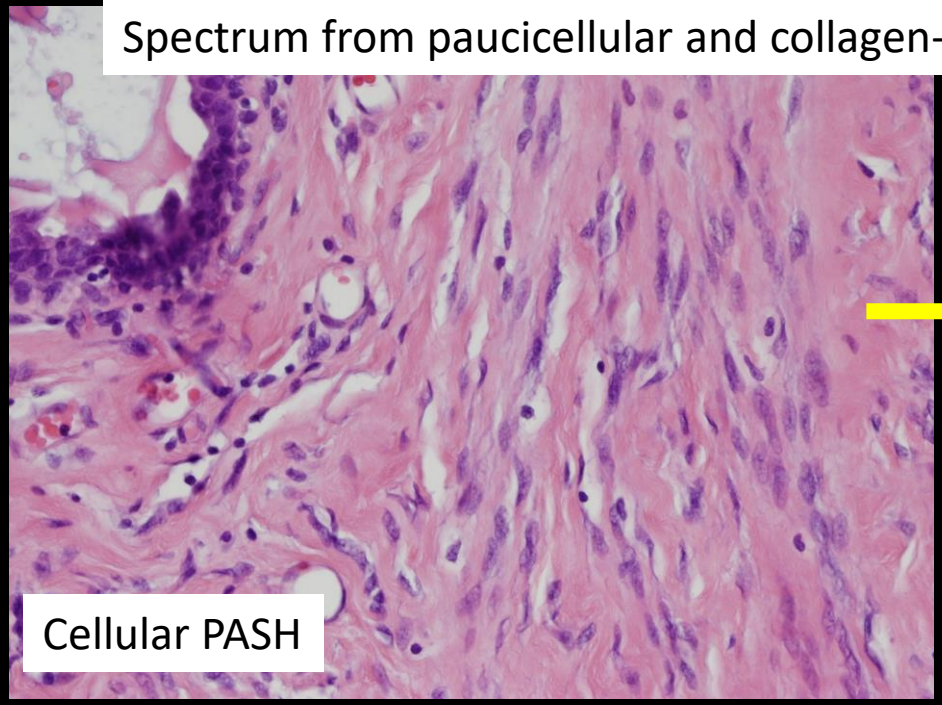


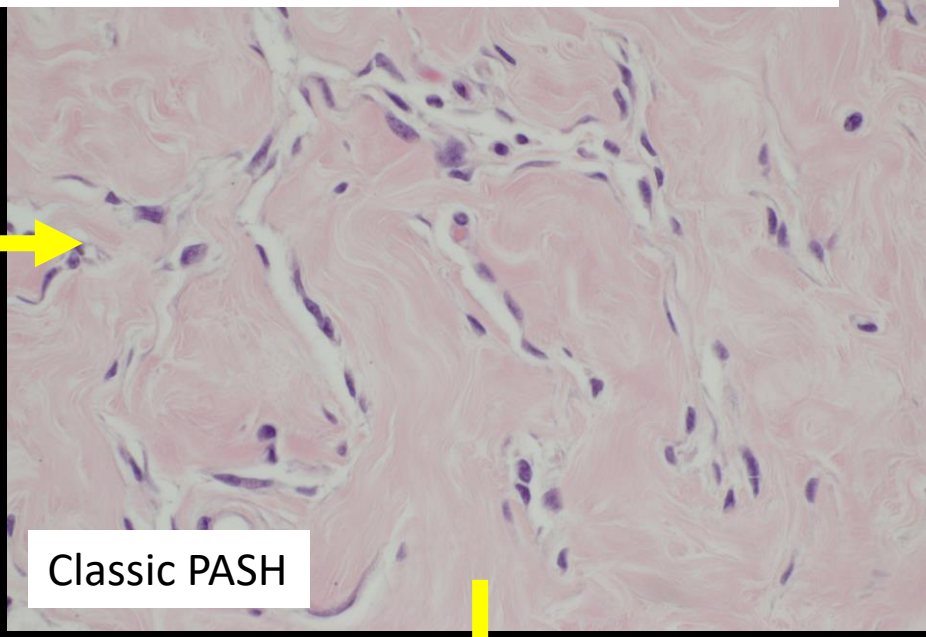

CD34

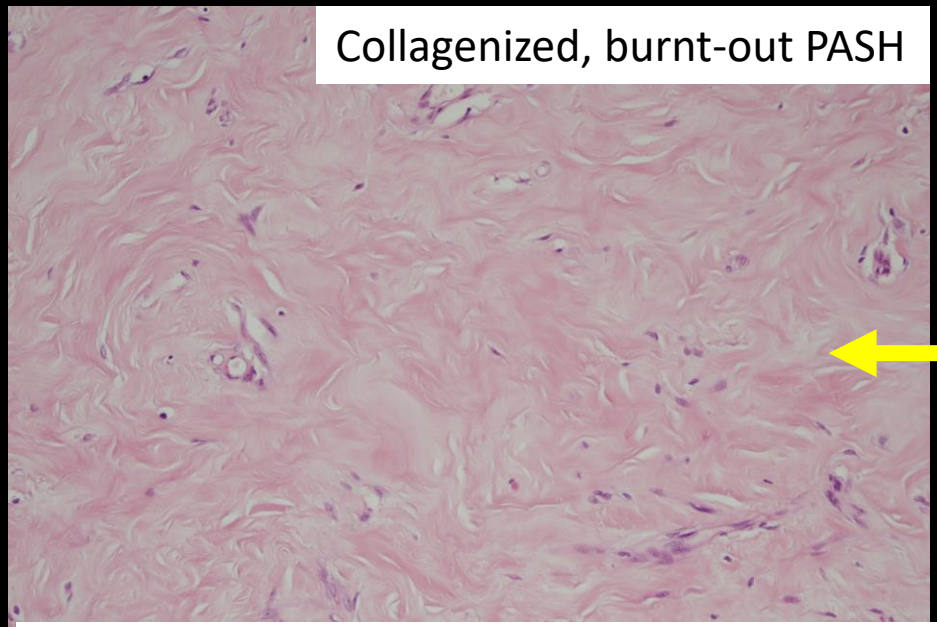

Actin

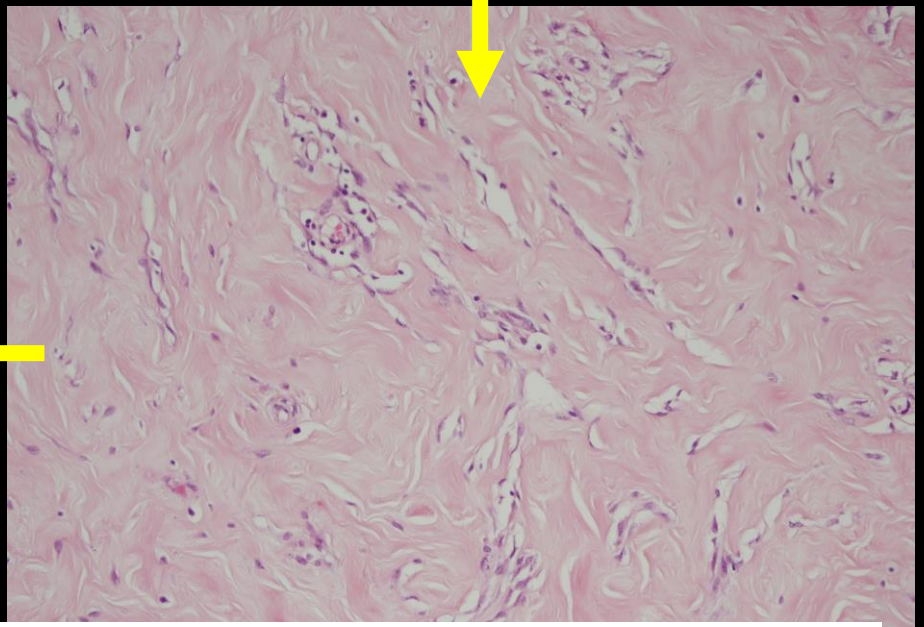

CD31

Spectrum from paucicellular and collagen-rich to classic PASH to cellular PASH

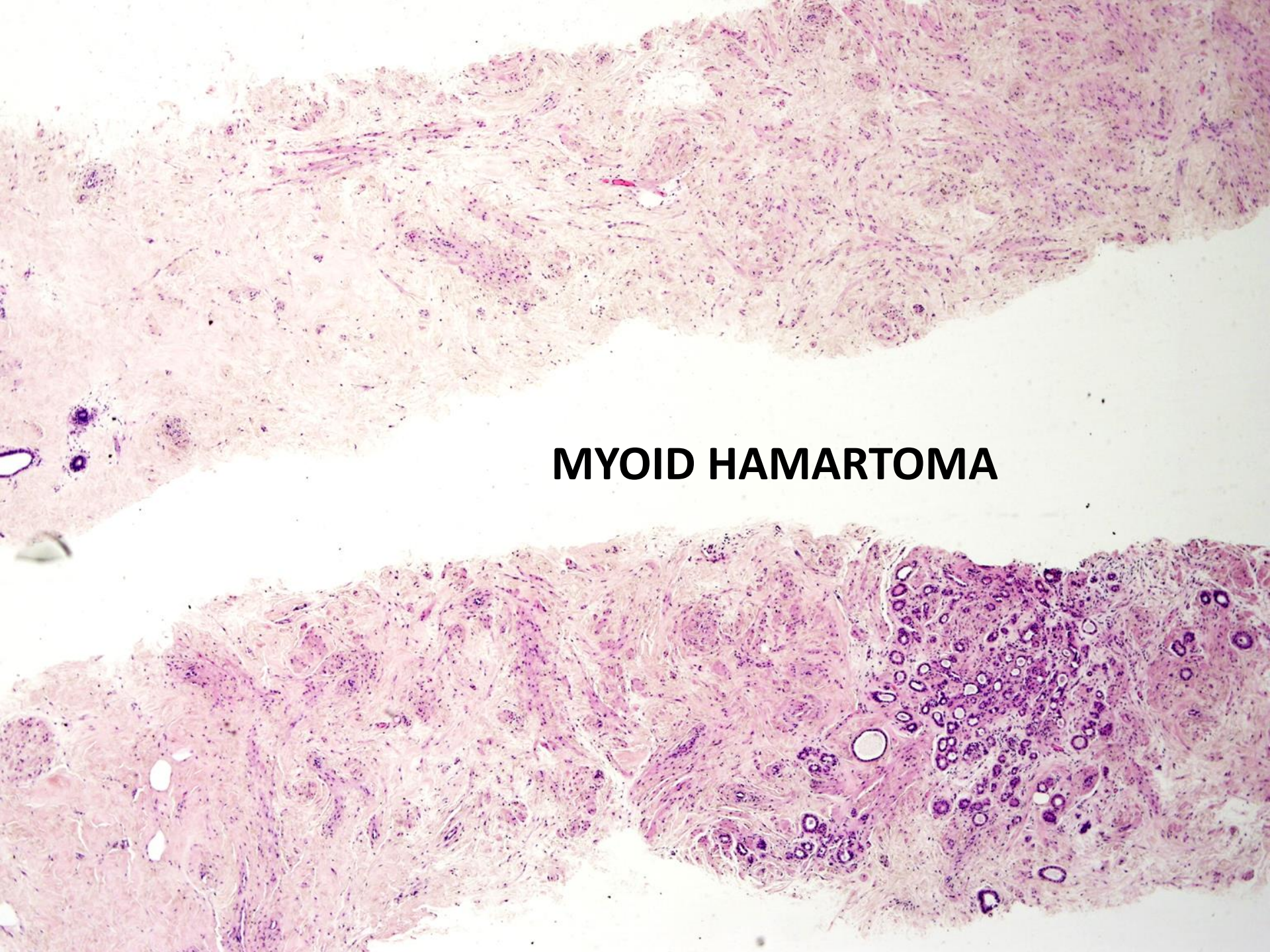


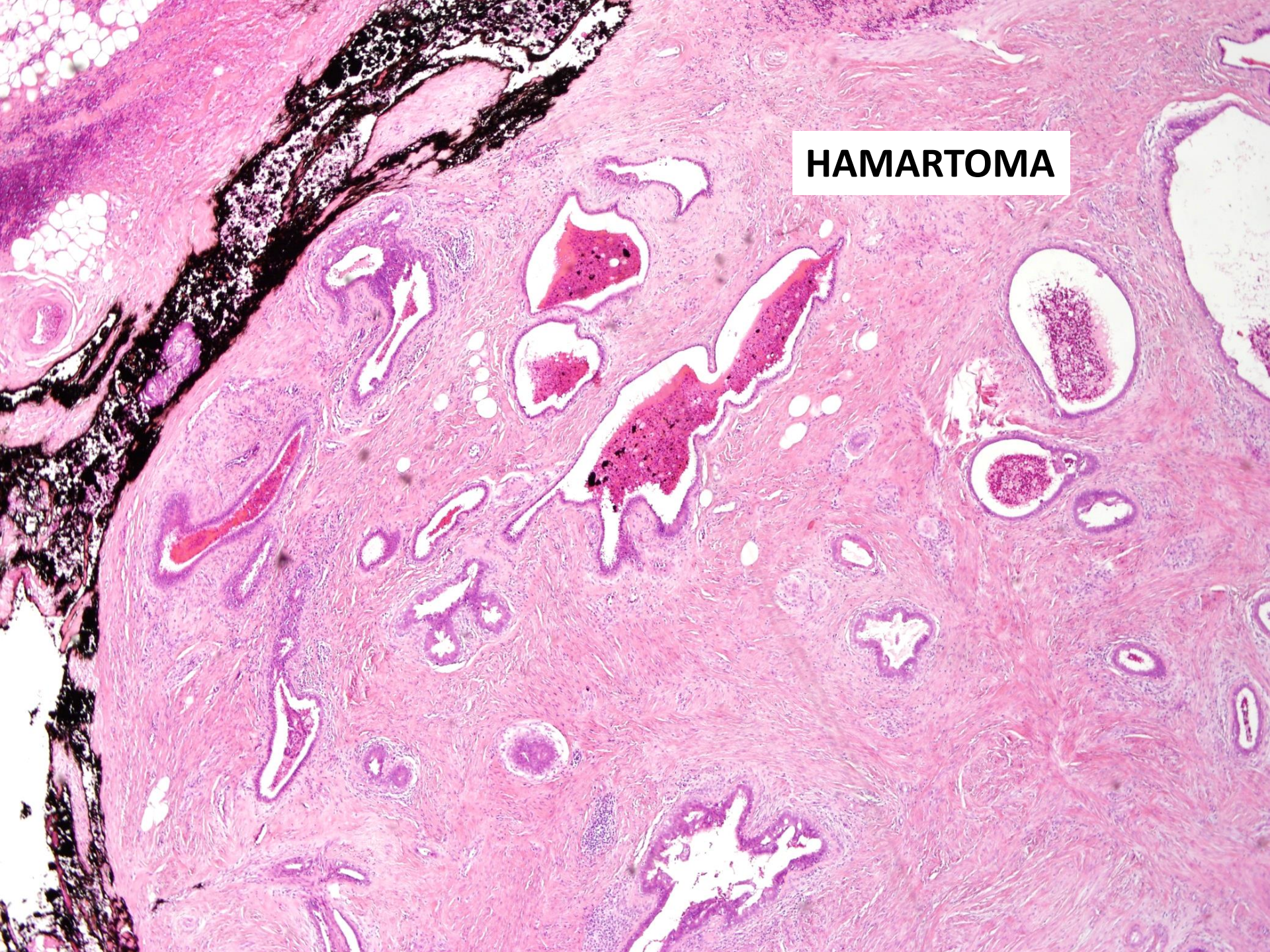




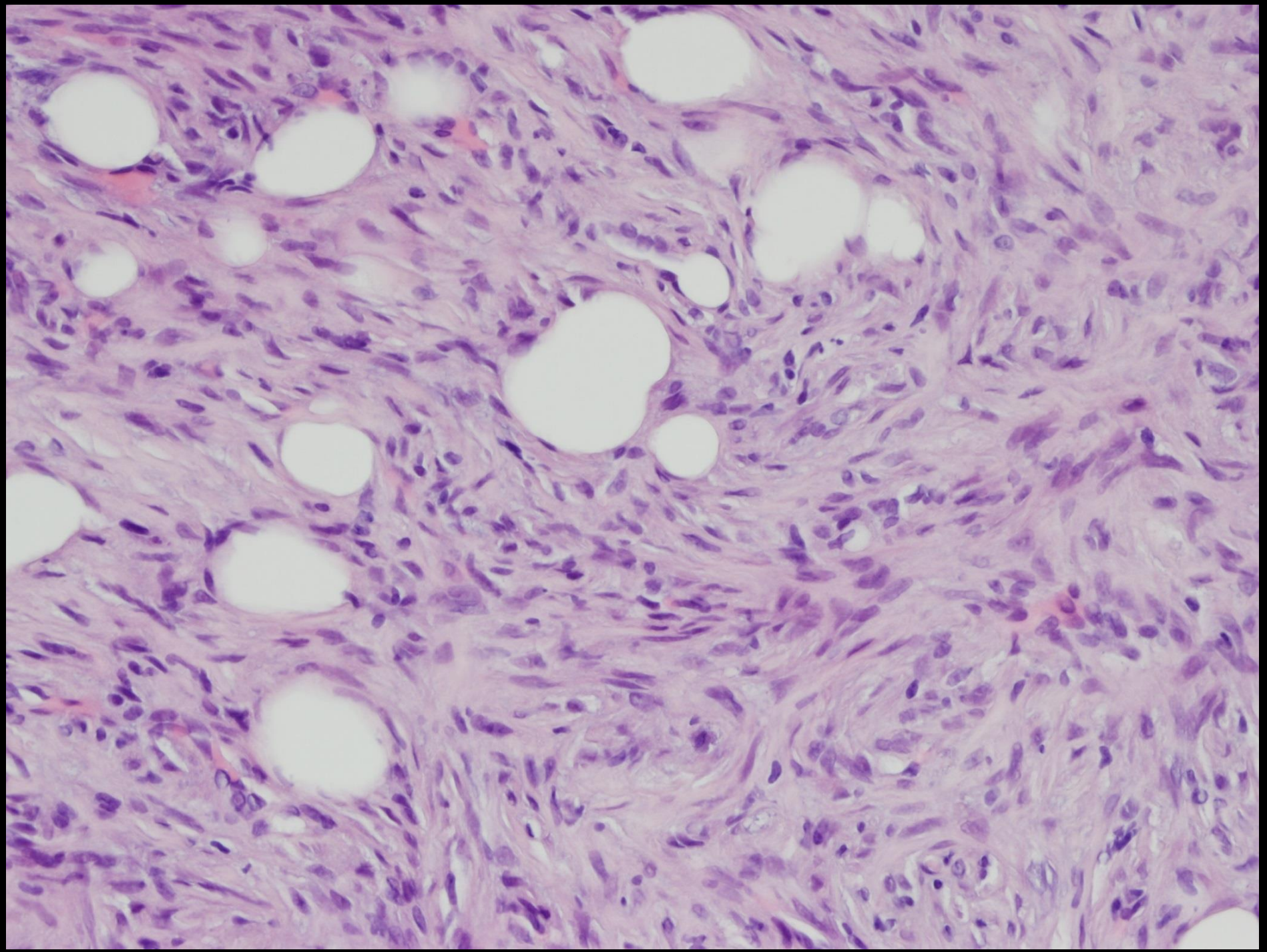


Cellular PASH resembles myofibroblastoma, maybe there is PASH-myofibroblastoma complex

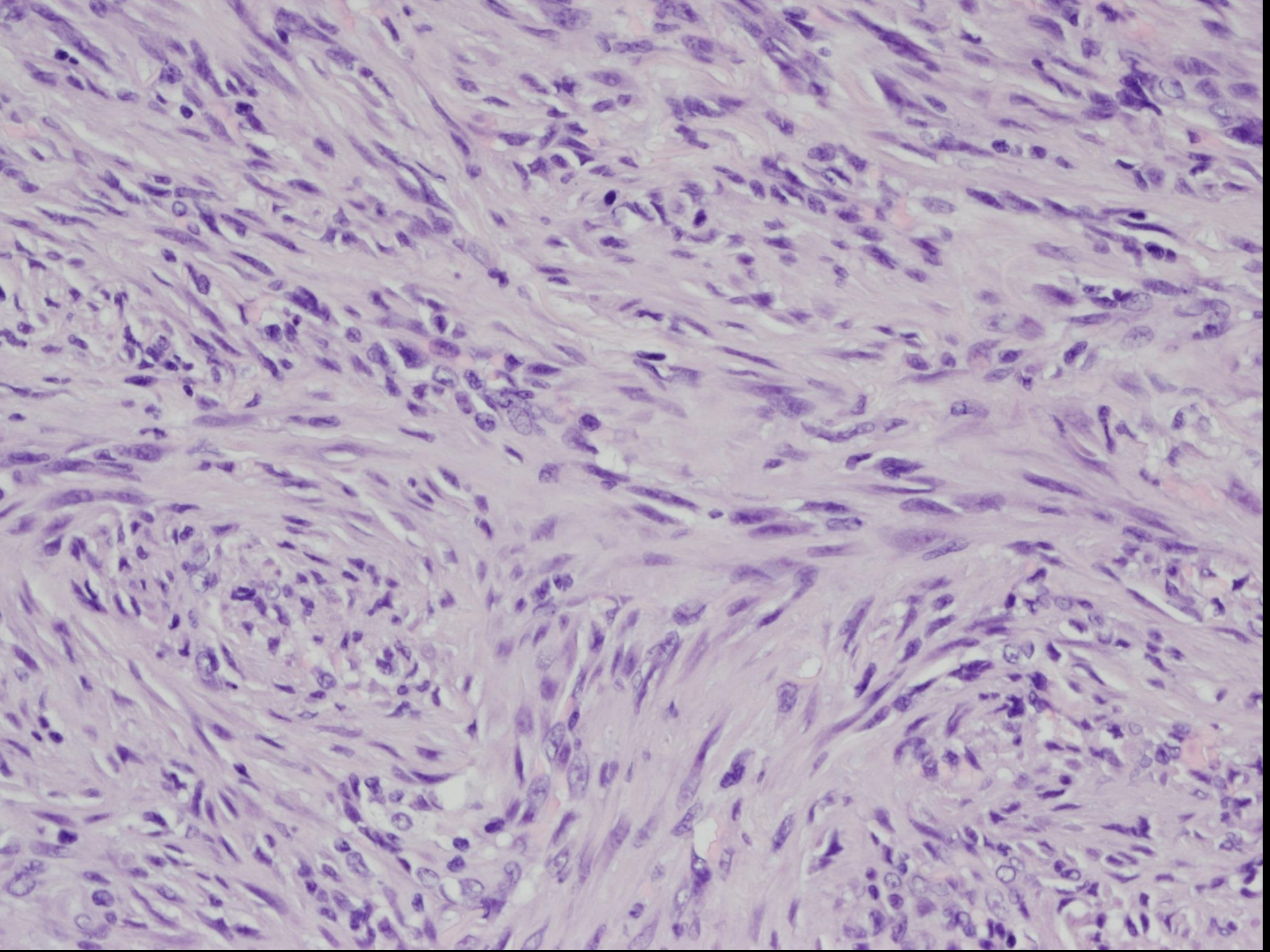

MYOID HAMARTOMA

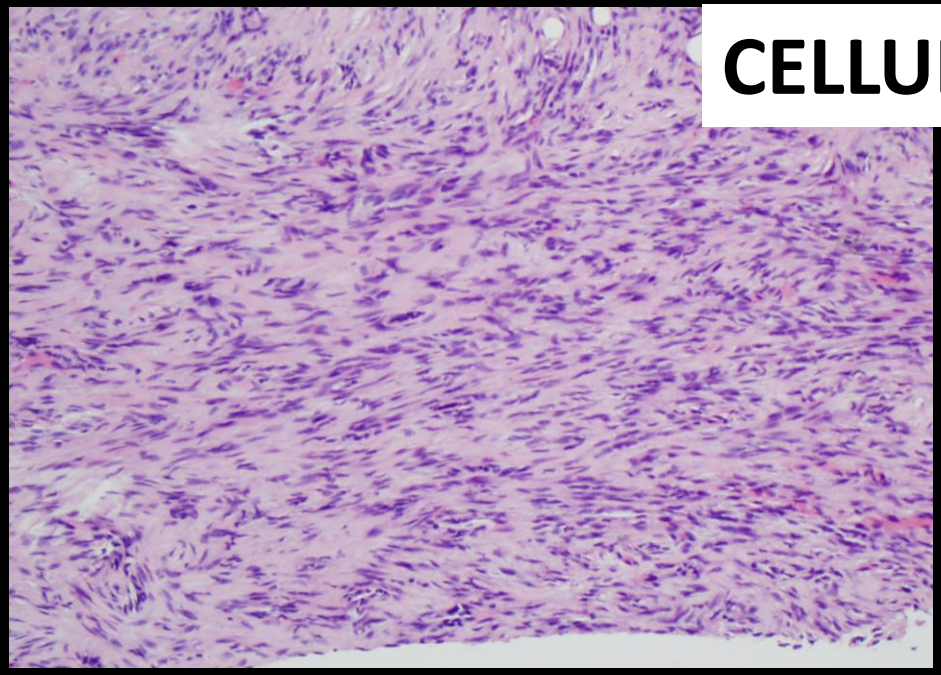

HAMARTOMA


“Breast mass”

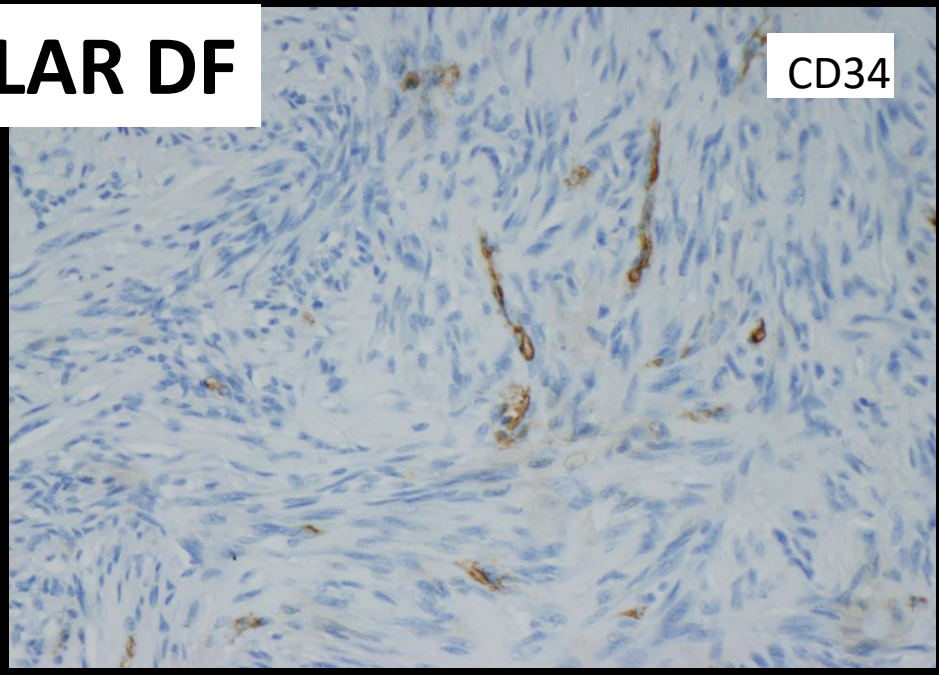


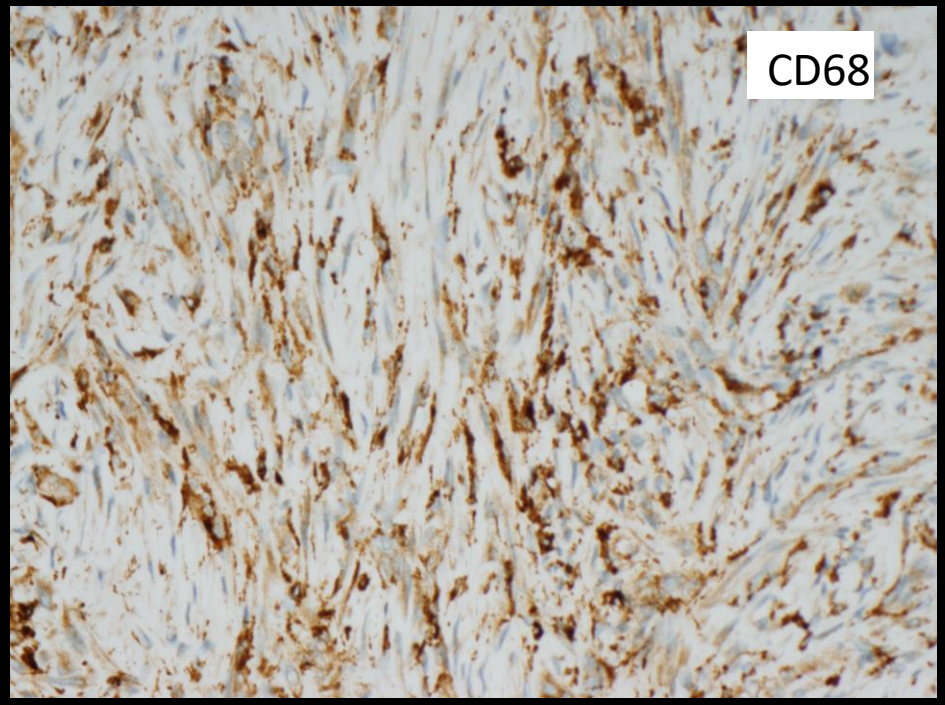

“Resection specimen”

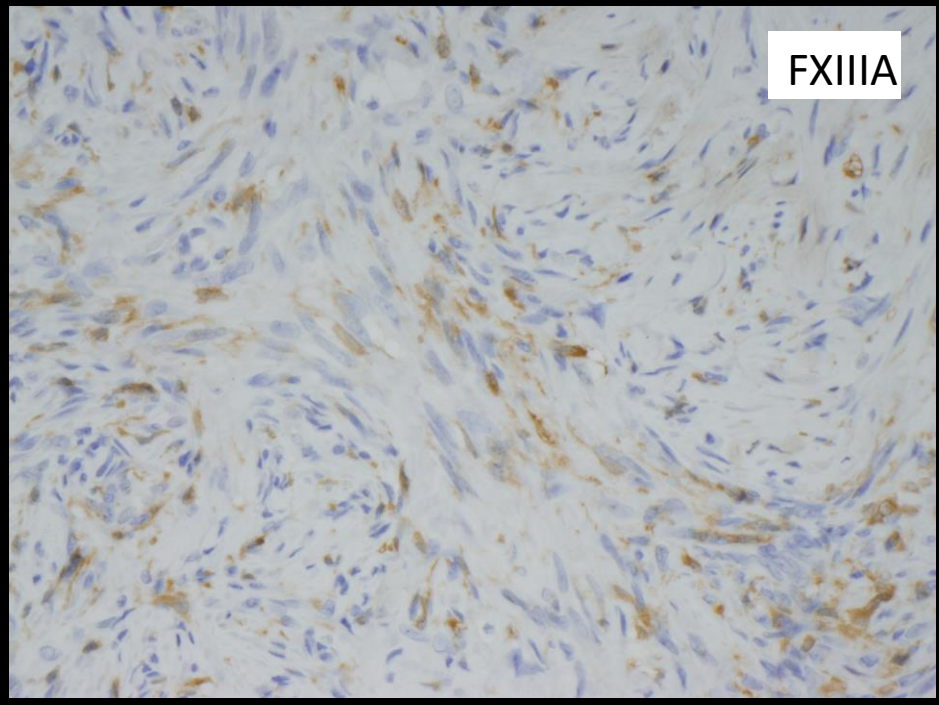




CELLULAR DF







Recent developments in the histological diagnosis of spindle cell carcinoma, fibromatosis and phyllodes tumour of the breast

A H S Lee **Histopathology VOLUME 52,** pages 45–57, January 2008

- CD34: expressed in normal stroma, phyllodes tumors, myofibroblastoma, myoid hamartoma, PASH
- but does not appear to be present in spindle cell carcinomas, fibromatoses, nodular fasciitis

Role of Cytokeratins

- AE1/AE3
- CK5 or CK5/6, CK14, 34βE12
- CAM5.2 and CK7 in a minority
- DO NOT RELY SOLELY AS EXCEPTIONS OCCUR
  - Leiomyosarcomas, phyllodes tumor stroma, inflammatory myofibroblastic tumor, metastatic melanoma
- P63 (occ. sarcomas and phyllodes show focal +)

Nuclear staining of B-catenin

- Fibromatosis: 80% cases
- Occ spindle cell carcinoma
- Phyllodes tumors

- Problem: Strong staining makes it difficult to assess whether nuclear or just cytoplasmic

Varma, Sonal; Shin, Sandra. **An Algorithmic Approach to Spindle Cell Lesions of the Breast.** Advances in Anatomic Pathology. 20(2):95-109, March 2013.

Pure spindle cell lesions with bland cytomorphology	
Spindle cell metaplastic carcinoma	Keratins (CKAE1/3, 34βE12, CK7, Cam 5.2) ±, p63 ±, β-catenin ±, CD34−, ER−, PR−, Her2−
Fibromatosis	β-catenin +; actin ±, desmin ±, bcl2−, CD34−, ER−, PR−
PASH tumor	CD34 +, PR > ER, bcl2 +, CD99 +; SMA ±, desmin ±
Myofibroblastoma	CD34 +, SMA ±, desmin ±, vimentin +, bcl2 +, CD99 +; S100−, HMB45−, β-catenin−, EMA−, keratins−, ER ±, PR ±, AR ±
Low-grade angiosarcoma	CD31 +, CD34 +, factor VIII +; FLI1 +, keratins−
Cellular angiolipoma	CD31 +, CD34 +, factor VIII +; keratins−
Biopsy site changes	CD68 ±, β-catenin ±
Inflammatory myofibroblastic tumor	ALK-1 + (50%), CD68 +, β-catenin−
Mixed spindle and epithelial/epithelioid/glandular lesions	
Spindle cell metaplastic carcinoma	See above
Phyllodes tumor (stroma)	No specific markers, CD34 +, bcl2 +, keratins ±
Low-grade adenosquamous carcinoma	Circumferential myosin ± and p63 ±; keratins ± "core" staining
Epithelial displacement in biopsy site	Myoepithelial markers (p63, SMM) ± around epithelial cells
Pure spindle cell lesions with atypical/malignant cytomorphology	
Spindle cell metaplastic ca	See above
Phyllodes tumor (stroma)	See above
Angiosarcoma	Same as low-grade angiosarcoma (see above)
Other sarcomas	As per histogenesis
Spindle cell melanoma	S100 +, A103 +, HMB45 +; keratins−

PASH indicates pseudoangiomatous stromal hyperplasia.

TABLE 4 Immunohistochemical Profiles of Subgroups of Mammary Spindle Cell Lesions

NEW KIDS ON THE BLOCK

Cellular Spindled Histiocytic Pseudotumor Complicating Mammary Fat Necrosis

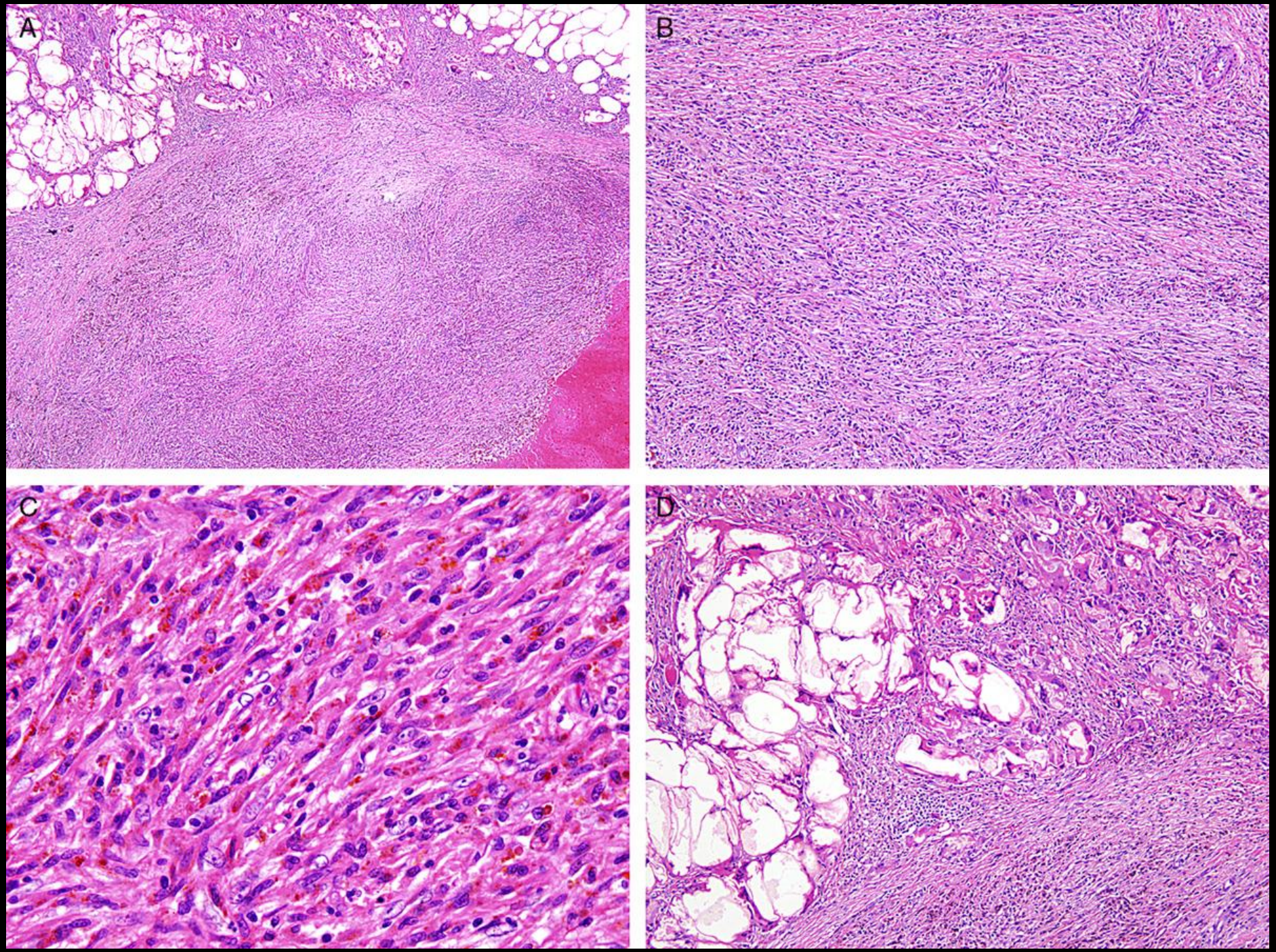
A Potential Diagnostic Pitfall

Andrew P. Sciallis, MD, Beiyun Chen, MD, PhD, and Andrew L. Folpe, MD

- Exaggerated histiocytic reaction to fat necrosis
- 20 cases, mean age 58 y; range, 24 to 70 y

- Moderately cellular, fascicular spindle cell proliferation
- Mitotically active
- Normochromatic, lightly eosinophilic Mild nuclear variability, folded or grooved nuclei, and indistinct nucleoli
- Admixed chronic inflammatory cells and multinucleated giant cells
- fat necrosis frequently at periphery
- CD163, CD11c, CD68, CD31

Am J Surg Pathol 2012;36:1571–1578


A
B
C
D

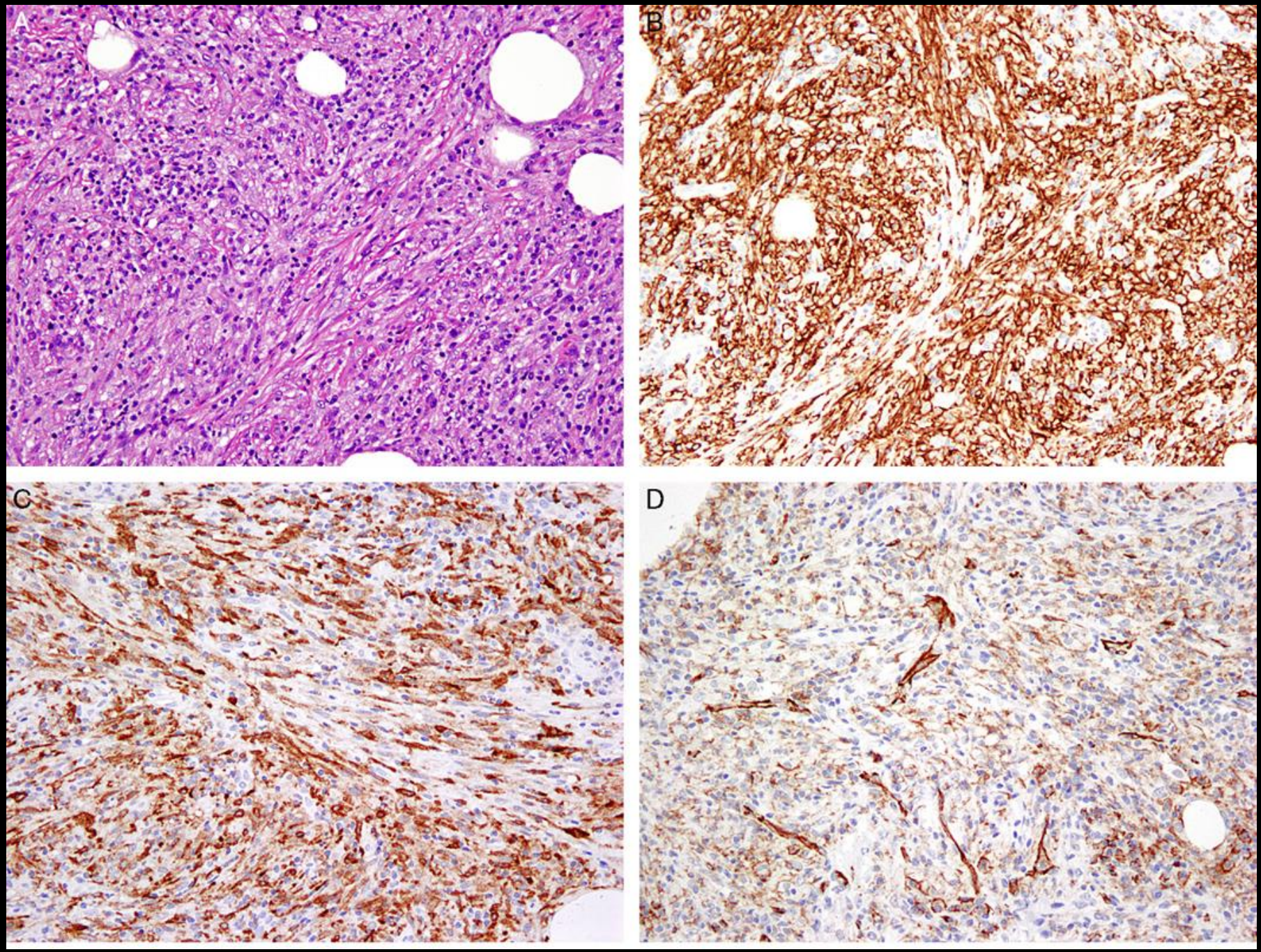


FIGURE 5 . Cellular spindled histiocytic pseudotumor (A) showing diffuse expression of CD11c (B) and CD163 (C) and weak, granular CD31 expression (D). Keratins were negative (E).


ON MAUNI AMAVASYA - DON'T BE SCARED OF 20 MILLION PEOPLE
AND
ONCE IN A BLUE MOON – DON'T E SCARED OF SPINDLE CELL LESIONS OF BREAST
THANK YOU