CARCINOMA PAPILAR INTRAQUÍSTICO:
INTRADUCTAL o INVASOR?

Alicia Córdoba
Complejo Hospitalario de Navarra. Pamplona.

Tipos de lesión papilar de la mama

- **Benignas:**
  - Papiloma: único o múltiple.
- **Atípicas:**
  - Papiloma con atipia.
- **Malignas:**
  - Papiloma con carcinoma in situ.
  - Carcinoma in situ papilar.
  - Carcinoma encapsulado/intraquístico (Sólido-papilar).
  - Carcinoma papilar infiltrante.

Histopathology 2008, 52, 20–29. DOI: 10.1111/j.1365-2559.2007.02898.x

REVIEW

Papillary lesions of the breast: selected diagnostic and management issues

L C Collins & S J Schnitt
Department of Pathology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA

Carcinoma papilar encapsulado / intraquístico

- Descrito por: Carter D, Orr SL y Merino M. “Intraductal papillary tumors of the breast: a study of 78 cases”. Cancer 1983; 52:14-19.
- Representa entre 0,5-2% de las neoplasias.
- Crecimiento papilar limitado a un ducto dilatado.
- Se considera por ello como c.intraductal.

Concepto de carcinoma papilar: intraquístico o encapsulado

Am J Clin Pathol 2005;123:36-44

Myoepithelial Cell Staining Patterns of Papillary Breast Lesions

From Intraductal Papillomas to Invasive Papillary Carcinomas

Cheryl B. Hill, MD, and I-Tien Yeh, MD

Key Words: Papillary breast carcinoma; Myoepithelial cell; Calponin; Smooth muscle myosin heavy chain; p63

DOI: 10.1309/XG7TPQ16DMJAV8P1

Of 9 cases originally classified as intraductal papillary carcinoma, 5 showed absence of a basal MEC layer by immunohistochemical analysis. The lack of a basal MEC layer in these cases suggests a spectrum of progression from in situ to invasive disease and might help explain distant metastases from previously reported "intraductal papillary carcinoma."

- Utiliza 3 marcadores, calponina, miosina y p63.
- Mínimo 2 marcadores.
- Más específico p63, no marca miofibroblastos, ni pared vascular.

Myoepithelial Cell Staining Patterns of Papillary Breast Lesions

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- Positivo:
  - Papiloma.
  - C. intraductal papilar.
- +/-: C papilar intraquístico
- Negativo: c. papilar infiltrante.

Espectro de progresión

Intraductal	→	C.Intraquístico/encapsulado
Mioepitelio continuo		Sin mioepitelio /muy atenuado

Concepto de carcinoma papilar: encapsulado/ intraquístico

ORIGINAL ARTICLE

Intracystic Papillary Carcinomas of the Breast: A Reevaluation Using a Panel of Myoepithelial Cell Markers

Laura C. Collins, MD, Victor P. Carlo, MD,* Harry Hwang, MD,† Todd S. Barry, MD,† Allen M. Gown, MD,† and Stuart J. Schnitt, MD**

carcinomas. Given our observations, we favor the term "encapsulated papillary carcinoma" over "intracystic papillary carcinoma" for circumscribed nodules of papillary carcinoma surrounded by a fibrous capsule in which a peripheral layer of MEC is not identifiable.

TABLE 1. Antibodies to Myoepithelial Cell Markers Used in This Study

Antibody	Clone Designation	Vendor
Smooth muscle myosin heavy chain	SMMS-1	Dako (Carpinteria, CA)
Calponin	CALP	Dako (Carpinteria, CA)
p63	4A4	LabVision (Fremont, CA)
CD10	56C6	Vector Laboratories (Burlingame, CA)
CK5/6	D5/16 B4	Dako (Carpinteria, CA)

MEC mejor criterio (gold estándar)

Am J Surg Pathol • Volume 30, Number 8, August 2006

Are Encapsulated Papillary Carcinomas of the Breast In Situ or Invasive?

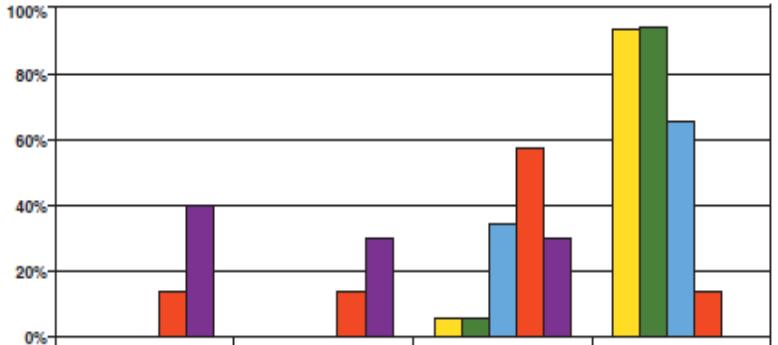
A Basement Membrane Study of 27 Cases

Nicole Nicosia Esposito, MD, David J. Dabbs, MD, and Rohit Bhargava, MD

Key Words: Papillary carcinoma; Carcinoma; Basement membrane; Collagen, type IV; Encapsulated papillary carcinoma

DOI: 10.1309/AJCP8A2UVLCYGTPU

papilloma, DCIS, and IDC. Moderate to intense collagen type IV expression was seen in all EPCs and was absent or decreased in all IDCs. All patients



	0	1+	2+	3+
Papillomas (n = 16)	0%	0%	6%	94%
DCIS (n = 28)	0%	0%	6%	94%
EPC (n = 26)	0%	0%	35%	65%
SPC (n = 7)	14%	14%	57%	14%
IDC (n = 10)	40%	30%	30%	0%

Am J Clin Pathol 2009;131:228-242

Intracystic Papillary Carcinoma of the Breast: An In Situ or Invasive Tumor? Results of Immunohistochemical Analysis and Clinical Follow-up

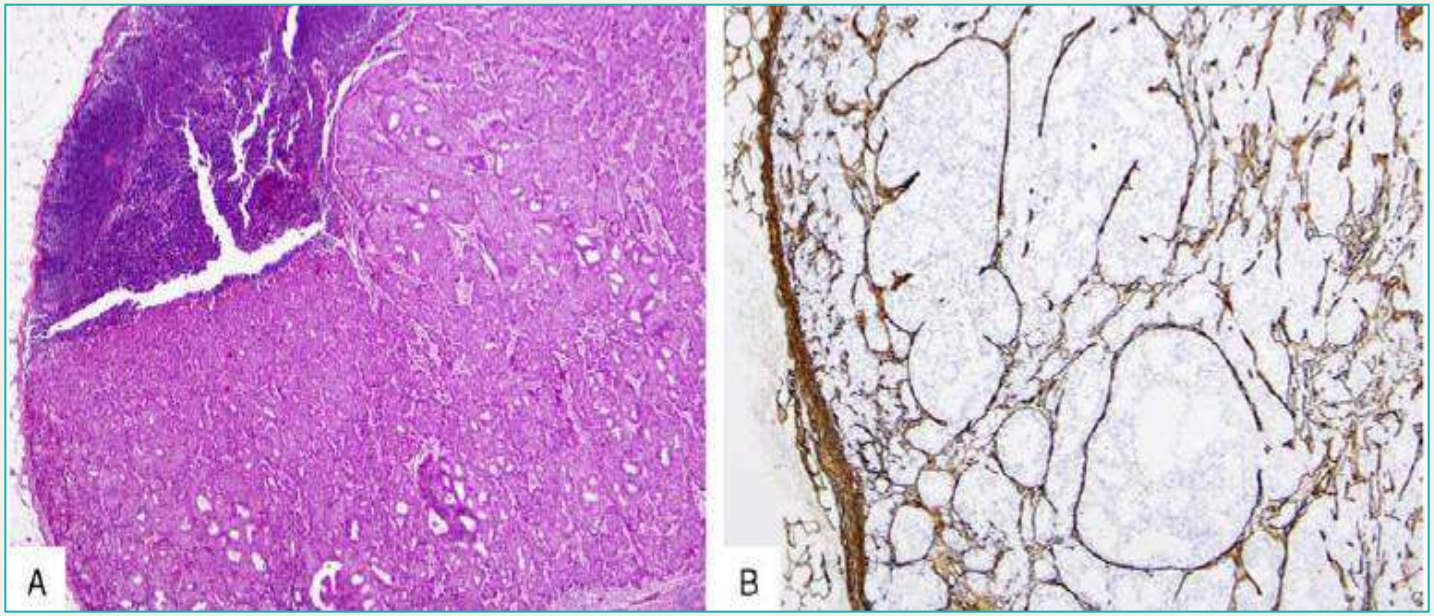
Christine A. Wynveen, MD, Tatjana Nehhozina, BSc,* Muzaffar Akram, MA, MSc,* Mohammed Hassan, BSc,* Larry Norton, MD,† Kimberly J. Van Zee, MS, MD,‡ and Edi Brogi, MD, PhD**

CONCLUSIONS

In summary, IPC is a rare carcinoma. It typically occurs in postmenopausal women, but men of the same age group can also be affected. This tumor is consistently positive for ER and negative for HER2. Complete absence or only focal presence of myoepithelium around IPC suggests that this tumor likely represents a spectrum of in situ and IC with predominance of the latter. Lymph node involvement is extremely rare in patients with pure IPC, but sentinel lymph node biopsy should be considered, in light of the debated nature of this lesion.

IPC has very indolent behavior, but long-term follow-up shows that it can recur locally after breast-conserving surgery, even if it is not associated with IC or DCIS. Consideration should be given to adjuvant radiation and to hormonal therapy for all patients with pure IPC.

- La falta de MEC alrededor de CPE representa la evidencia de crecimiento invasor.
- La presencia de colágeno IV continuo no es criterio de crecimiento intraductal porque el 19% de los CDI presentan (Visscher,1993).
- Colágeno IV positivo alrededor de las metástasis ganglionares.



Best Practices in Diagnostic Immunohistochemistry

Myoepithelial Markers in Breast Pathology

Rajan Dewar, MD, PhD; Oluwole Fadare, MD; Hannah Gilmore, MD; Allen M. Gown, MD

Cross-Reactivity Patterns in a Selection of Myoepithelial Markers[a]

Myoepithelial Marker	Cellular Localization	Myoepithelial Cells	Stromal Myofibroblasts	Vessels
Muscle-specific actin	C	3+	3+	3+
Smooth muscle actin	C	3+	3+	3+
Smooth muscle myosin heavy chains	C	3+	1+	2+
Calponin	C	3+	1+	2+
p75	C, M	3+	0–1+	2+
p63	N	3+	0	0
CD10	C	2+	1+	0
Basal-type cytokeratins	C, M	3+	0	0
Maspin	C, N	3+	0	0
P-cadherin	C	3+	0	0
S100	C, N	1+	0	0

Abbreviations: C, cytoplasmic; M, membranous; N, nuclear.

[a] Estimated composite of frequency and intensity, on a 0–3+ scale.

ORIGINAL ARTICLE

Phenotypic Alterations in Ductal Carcinoma In Situ-associated Myoepithelial Cells

Biologic and Diagnostic Implications

Justin B. Hilson, MD, Stuart J. Schnitt, MD, and Laura C. Collins, MD

grade DCIS (84.8% vs. 61.5% of cases, $P = 0.01$). We conclude that DCIS-associated MECs show immunophenotypic differences from MECs surrounding normal mammary ductal-lobular structures. The biologic significance of this remains to be determined. However, these results indicate that the sensitivity of some MEC markers is lower in DCIS-associated MECs than in normal MECs. This observation should be taken into consideration when selecting MEC markers to help distinguish in situ from invasive breast carcinomas.

(*Am J Surg Pathol* 2009;33:227–232)

- Mantenimiento de la membrana basal
- Producción de factores angiogénicos, crecimiento, invasión.
- Progresión de DCIS a c. invasor.

Diminished Number or Complete Loss of Myoepithelial Cells Associated With Metaplastic and Neoplastic Apocrine Lesions of the Breast

Trine Tramm, MD, Jee-Yeon Kim, MD,† and Fattaneh A. Tavassoli, MD‡*

and even in various papillae within papillary lesions. In summary, benign and noninvasive apocrine lesions can show reduction and occasional complete loss of ME cells. This

(*Am J Surg Pathol* 2011;35:202–211)

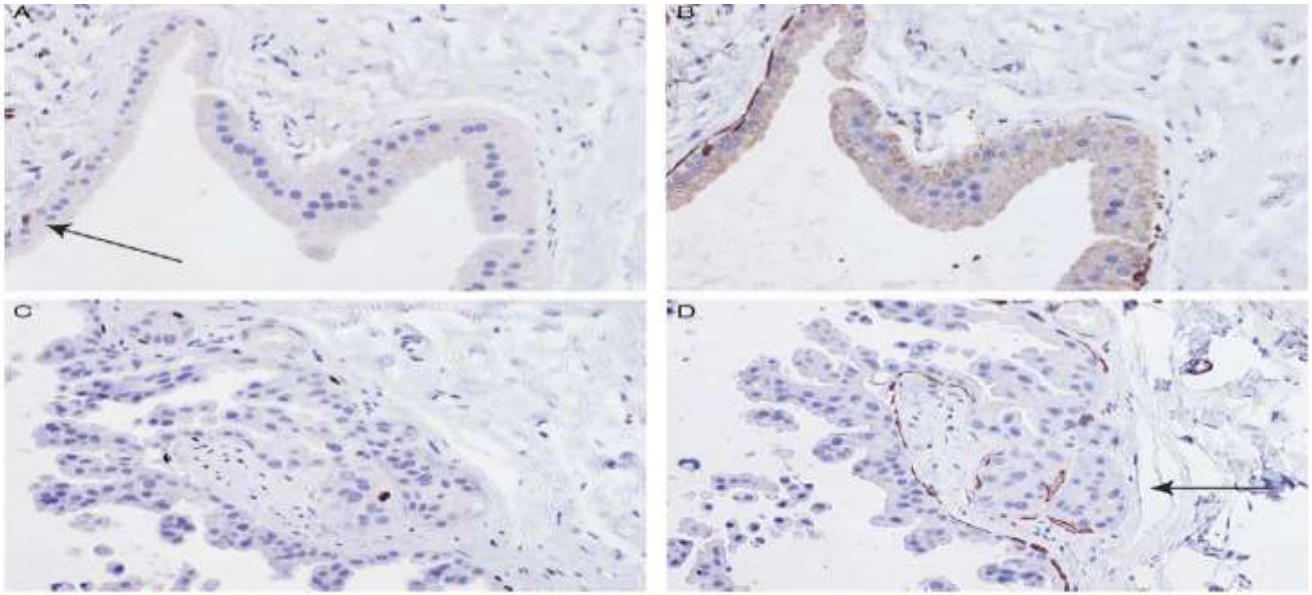


FIGURE 3. A and B, One of the cases showing patchy or lack of ME cells on both p63 (A) and Calponin (B) immunostain, in the absence of epithelial proliferation or atypia. A few p63-stained ME nuclei can be seen in the left side of the duct (A, arrow) (original magnification, × 200). C and D, Portion of a duct with apocrine DIN1 (DCIS grade 1) showing sparse ME cells on p63 (C) and prominent gaps on Calponin (D, arrow) (original magnification, × 200).

Puntos conflictivos

- Carcinoma intraductal papilar

- Carcinoma papilar encapsulado

- Carcinoma papilar encapsulado
  + carcinoma ductal infiltrante.

Puntos conflictivos

Carcinoma papilar encapsulado

Carcinoma intraductal

Carcinoma ductal infiltrante

Sistemas de estadificación/medida

DCIS

Diámetro máximo

Medida para pTNM

Sistema EWGBP

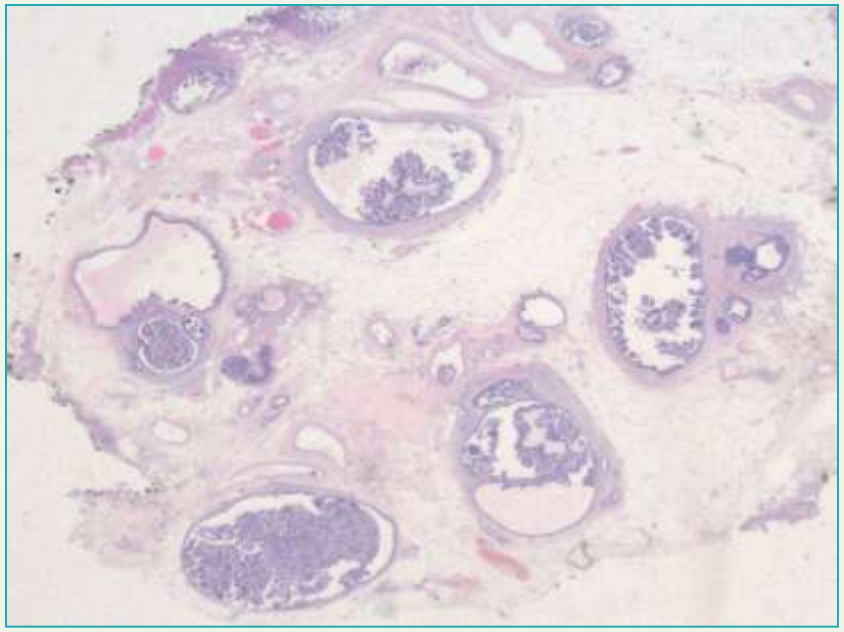
Puntos conflictivos

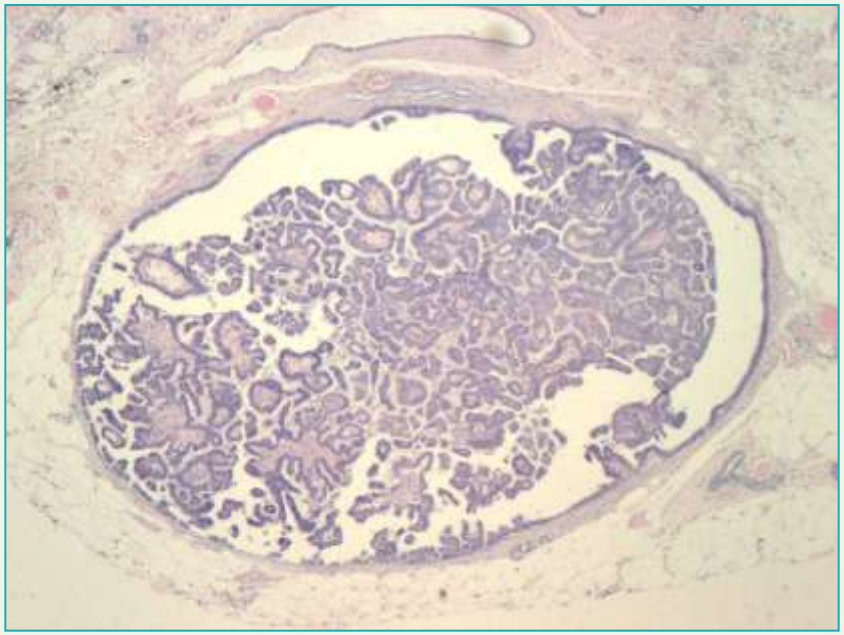
- Carcinoma intraductal papilar

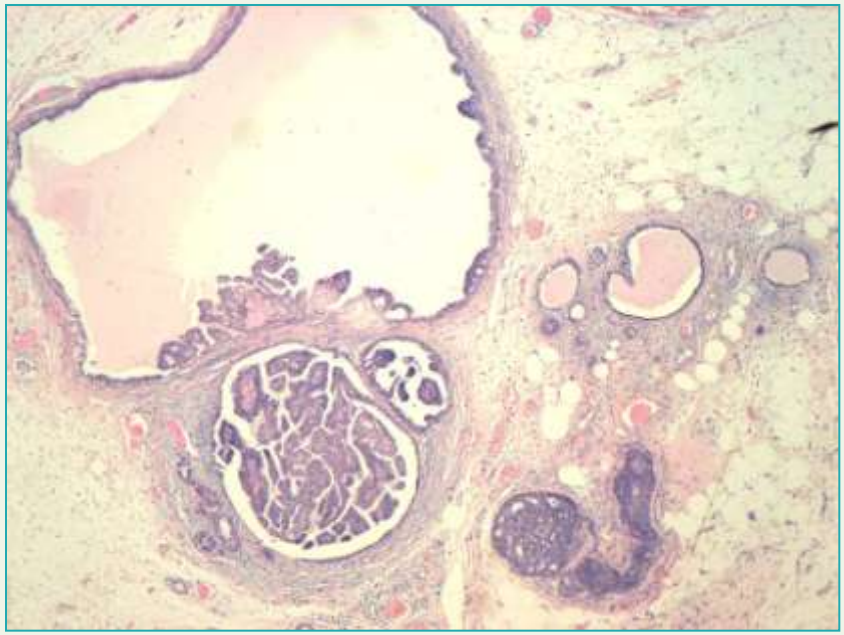
- Carcinoma papilar encapsulado

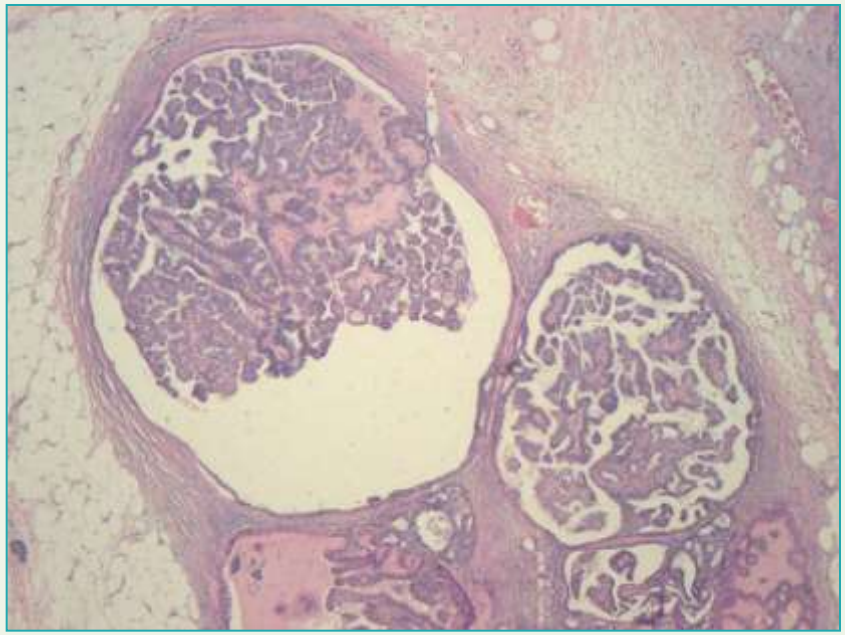
Criterios:

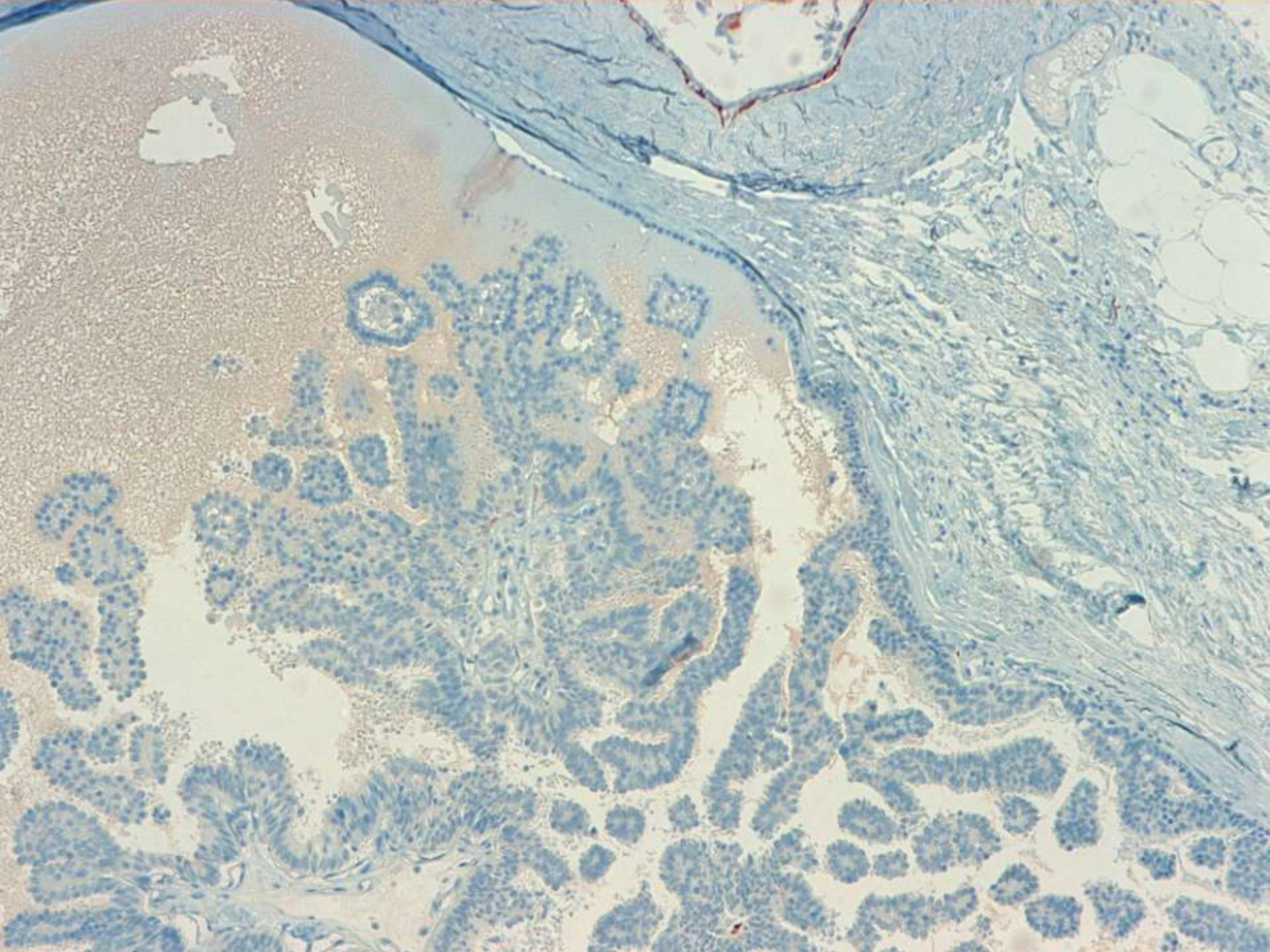
- Tamaño (????)
- Continuidad de las células mioepiteliales (???)

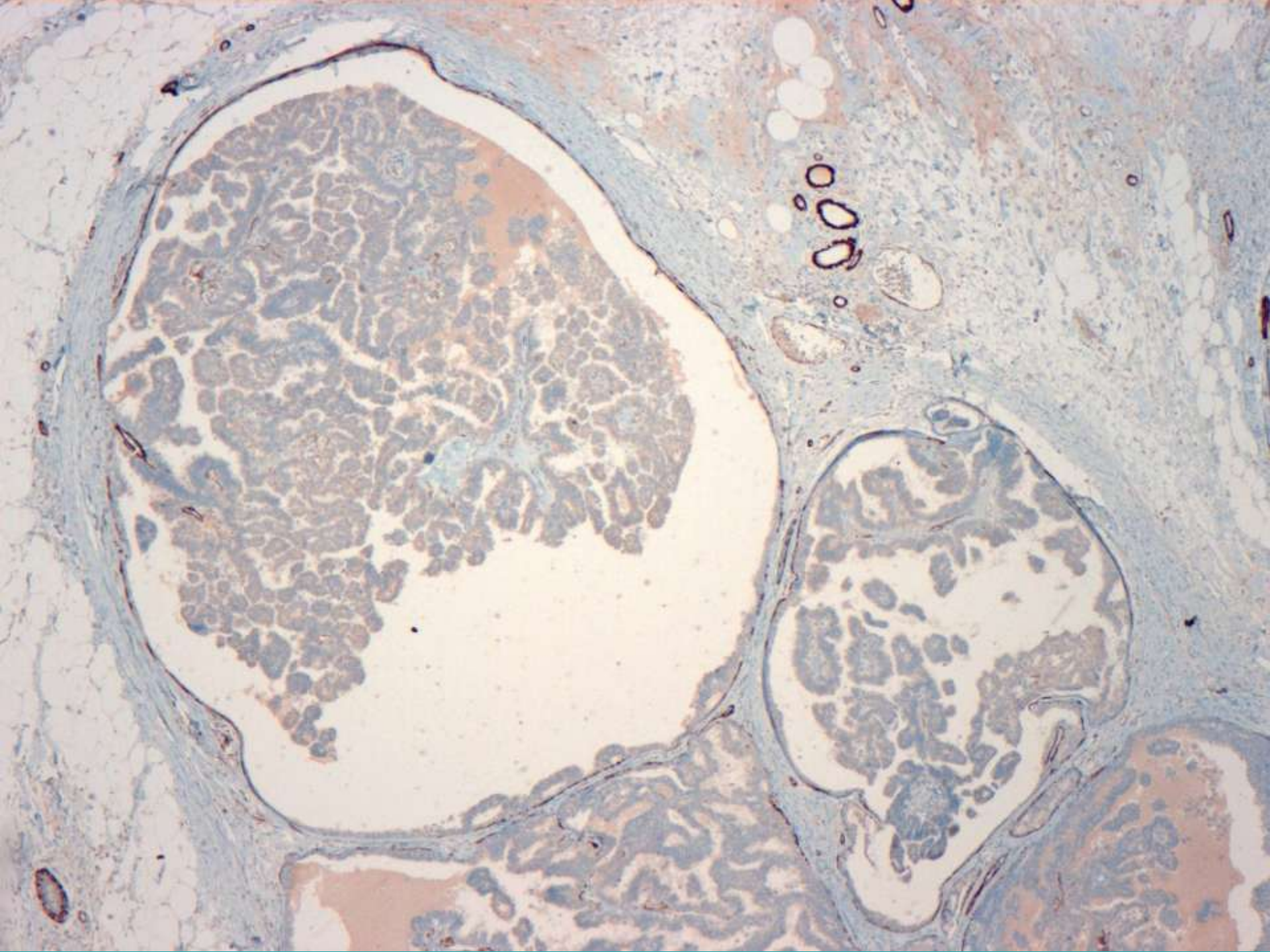


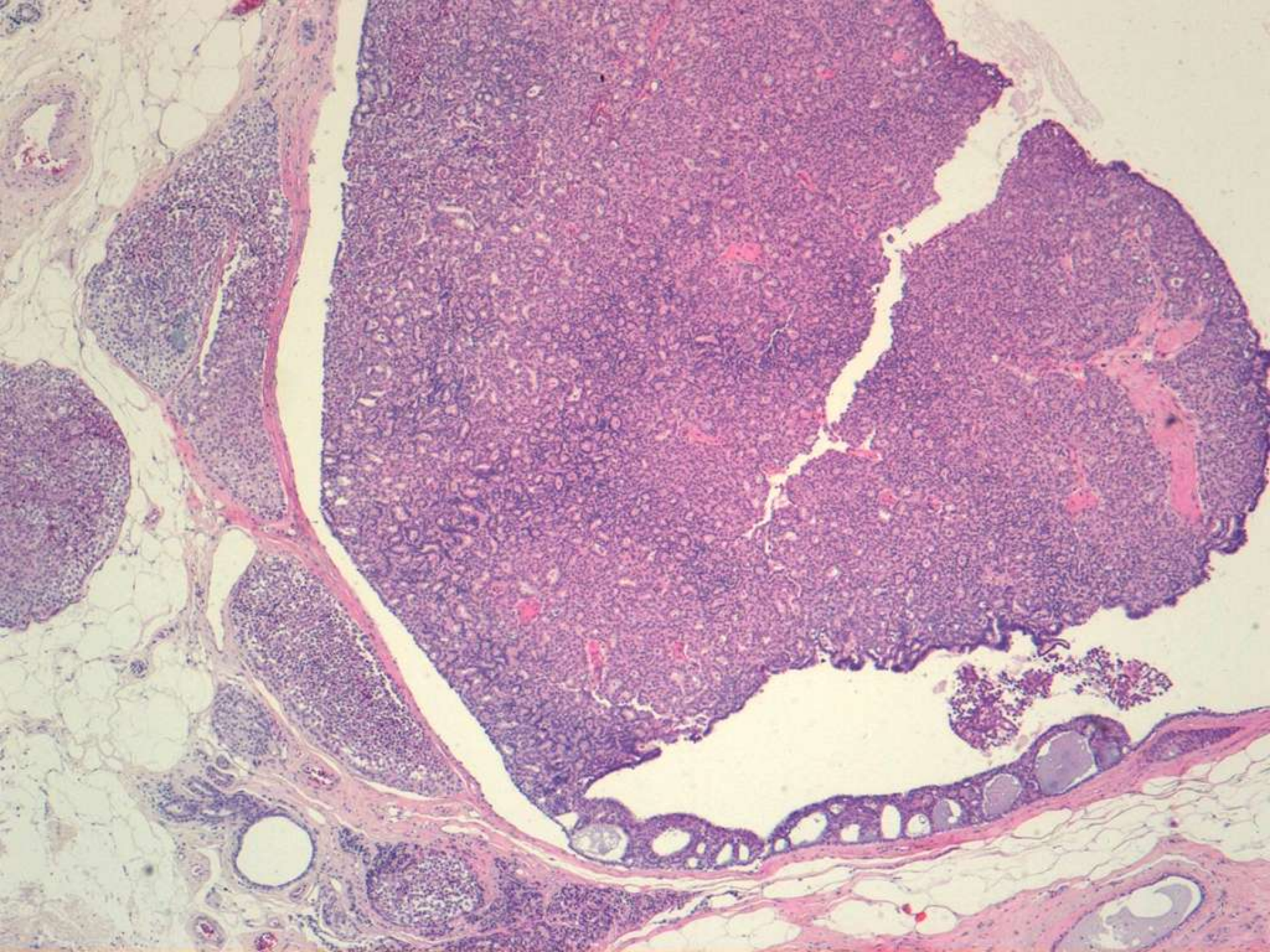


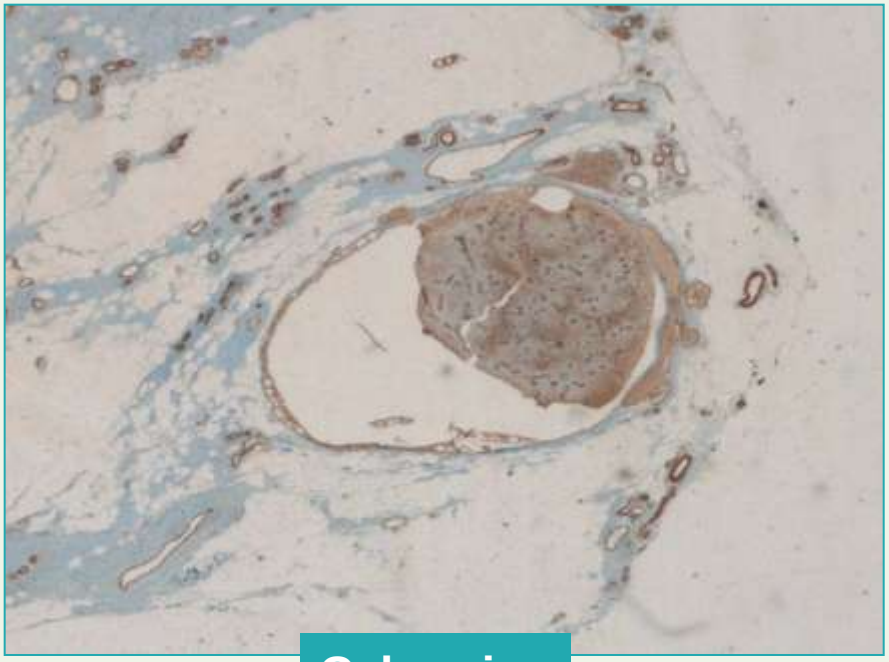


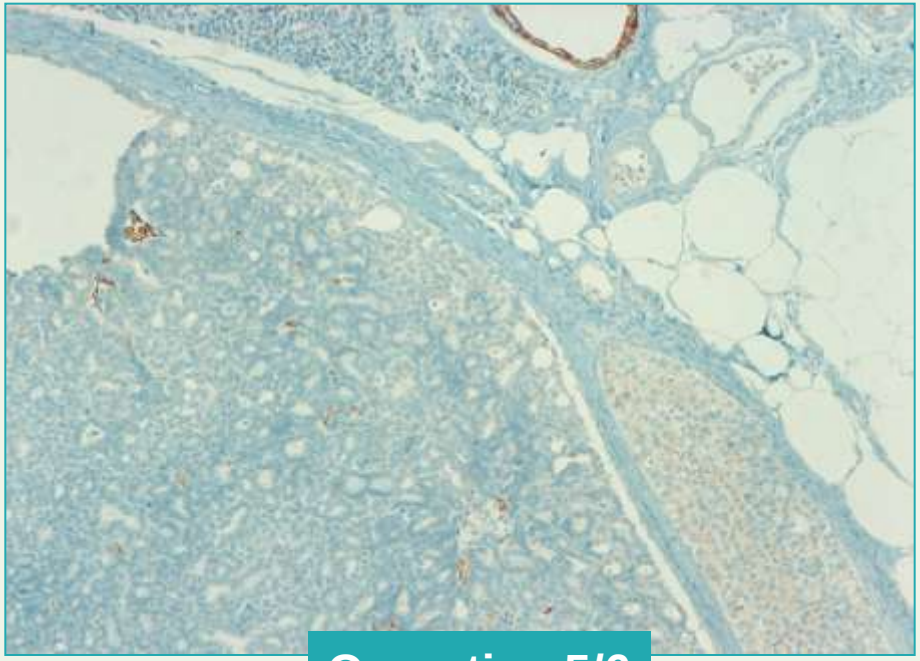




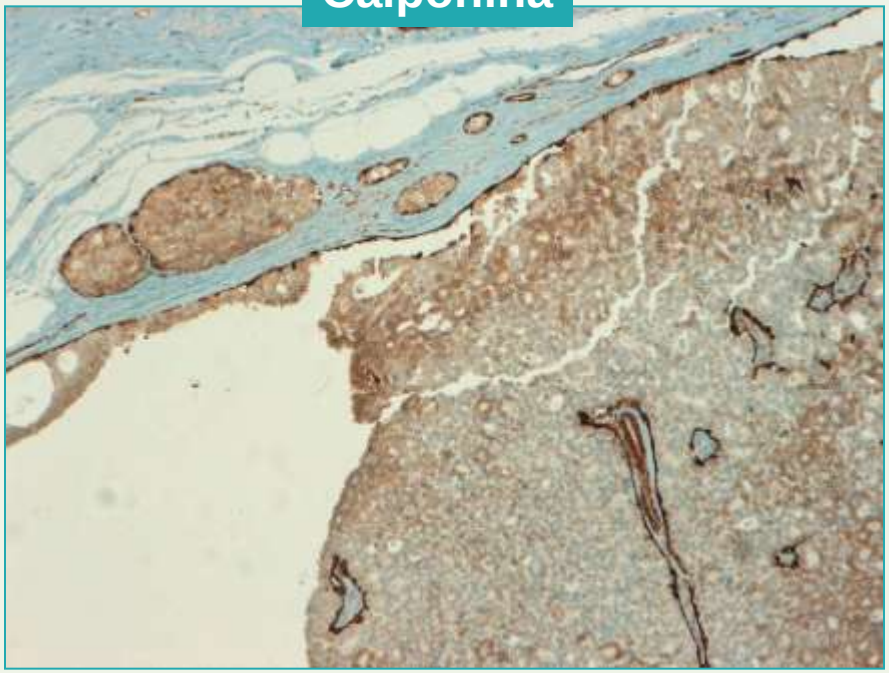








Calponina



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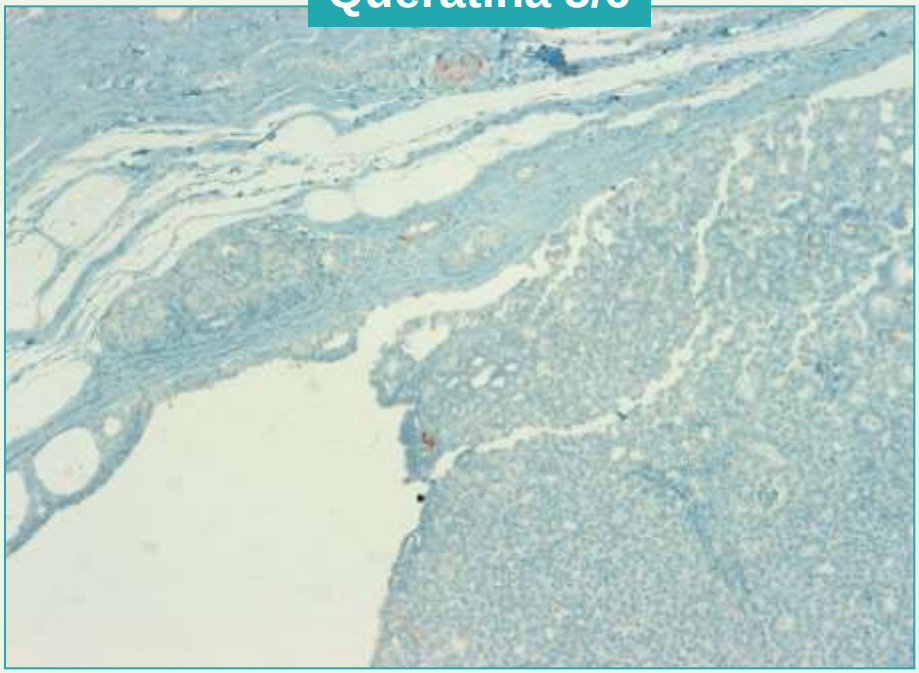
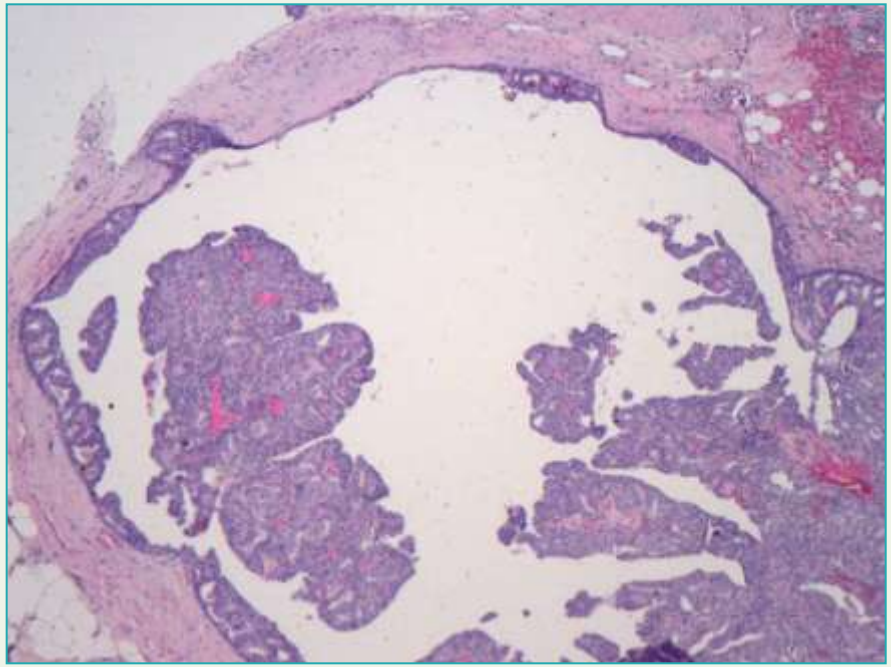
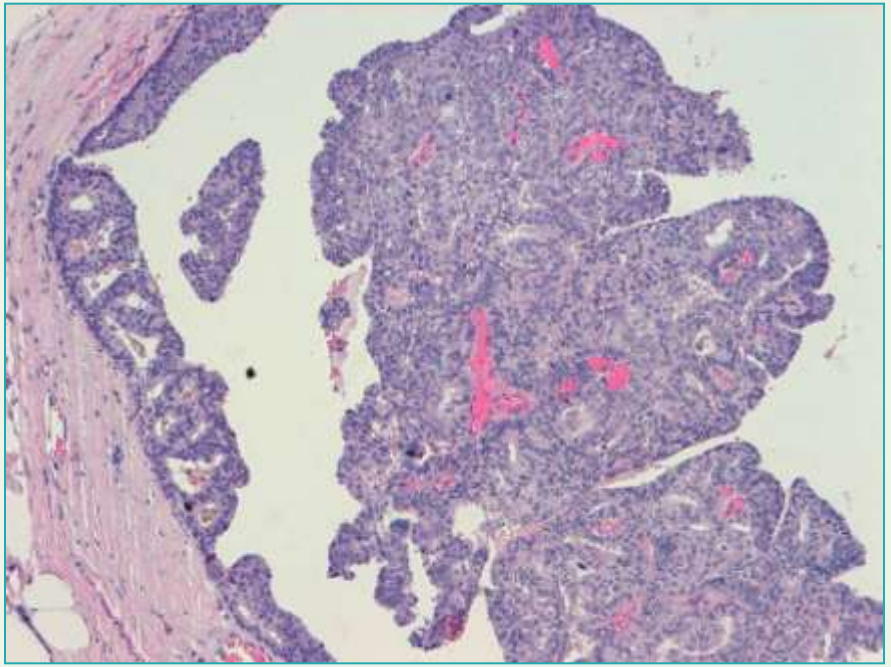
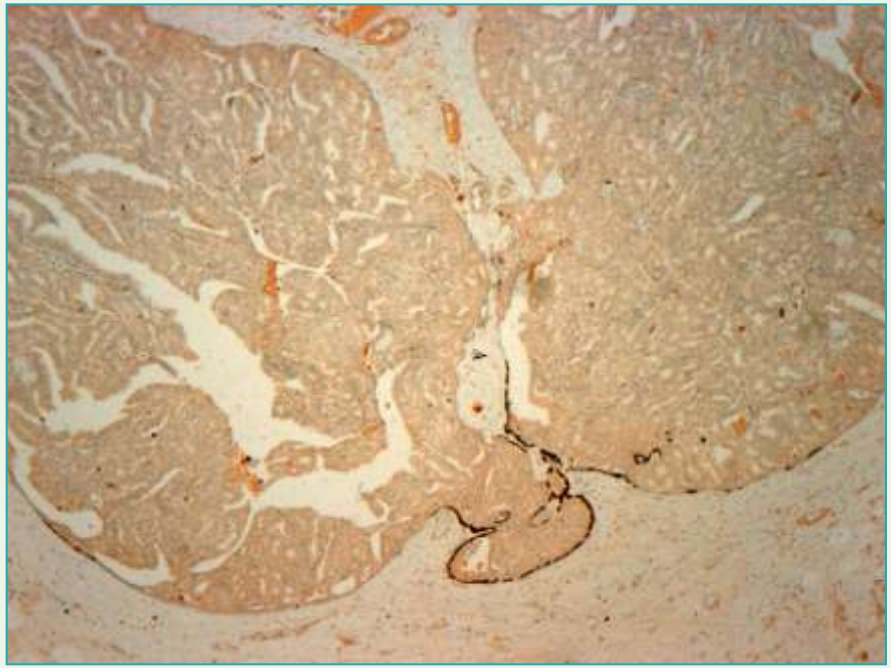
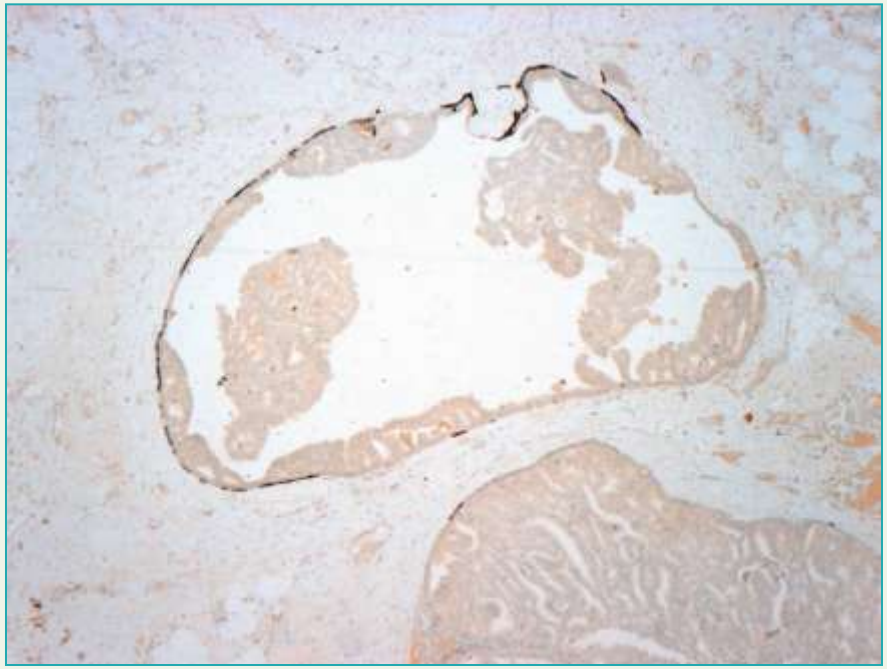
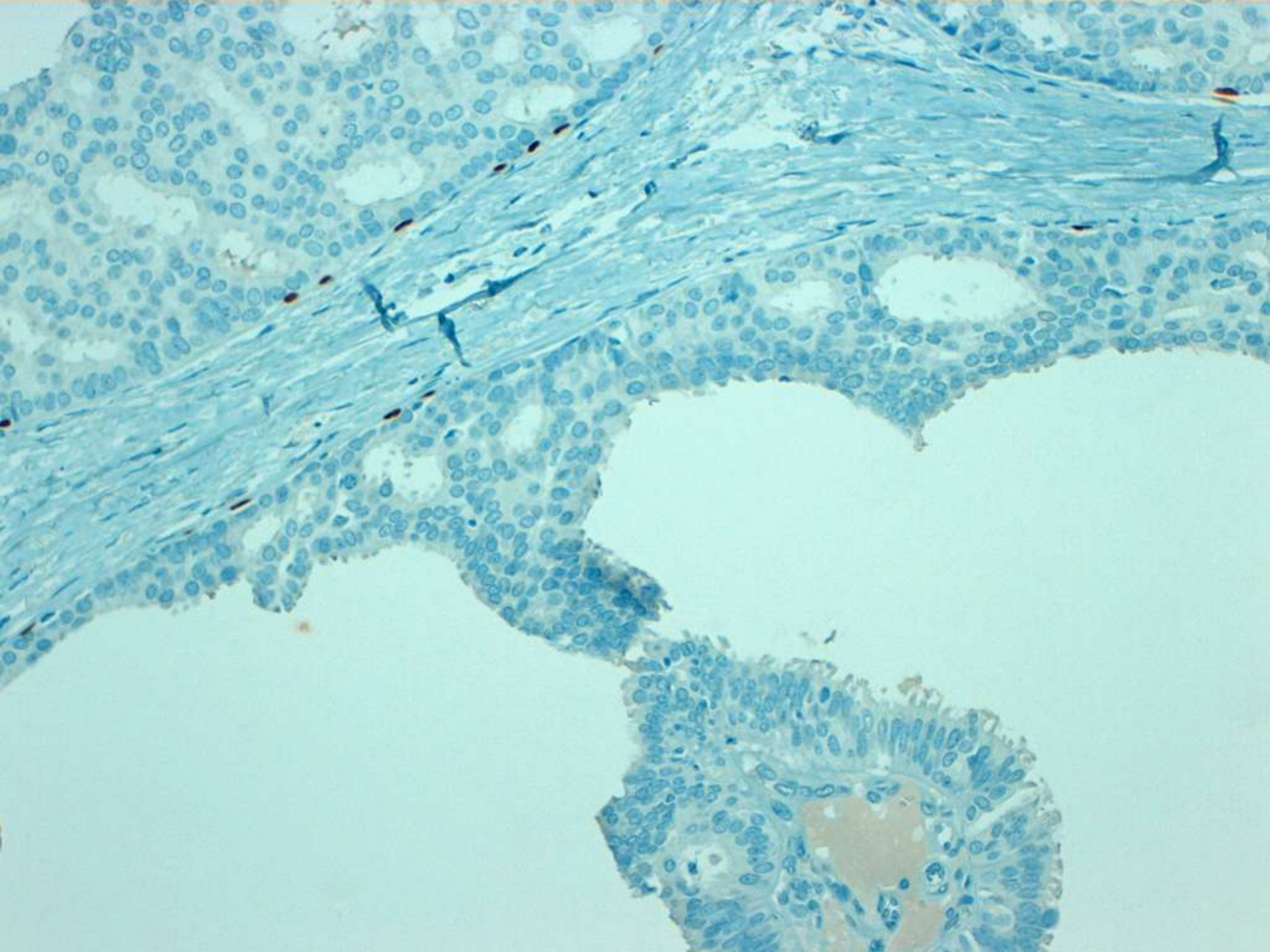












DCIS-CP encapsulado

- **Si hay capa continua:**
  - DCIS: SI ☒ NO ☐
- Si las MEC son discontinuas/focales:
  - DCIS:
    - Crecimiento difuso de distribución ductal
    - Ductos dilatados homogéneamente
  - CP intraquístico:
    - Nódulo único, formado por uno o varios quistes agrupados.

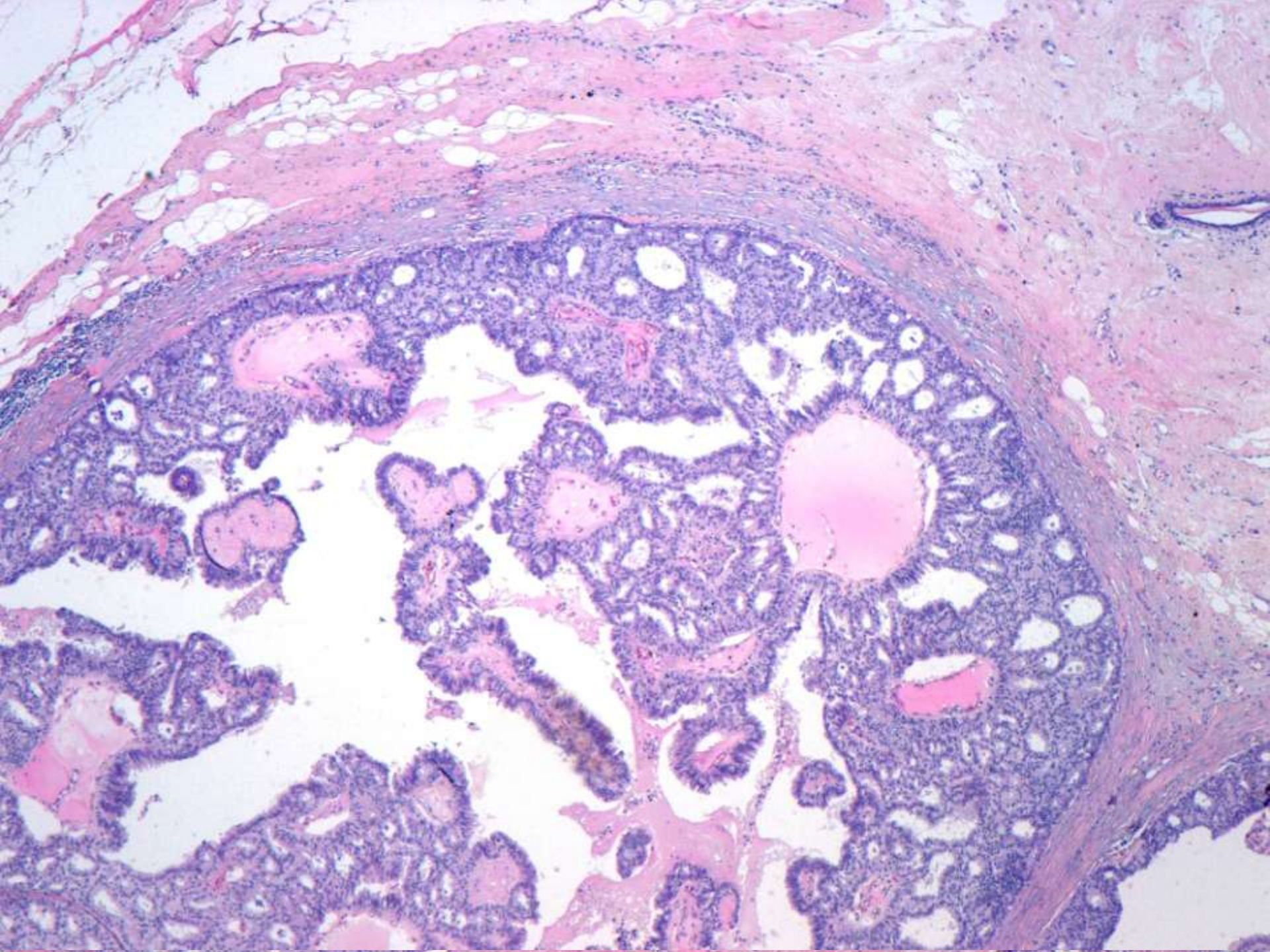
Puntos conflictivos

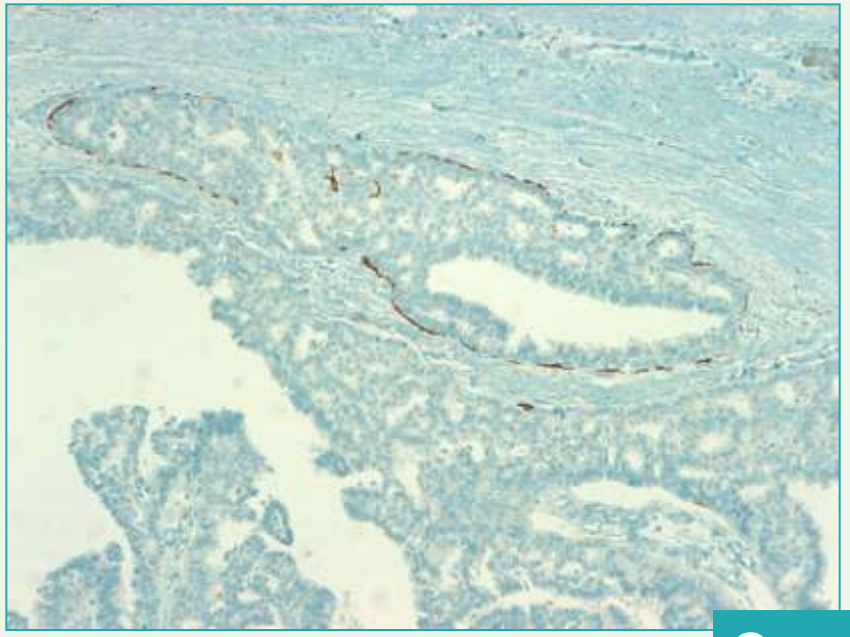
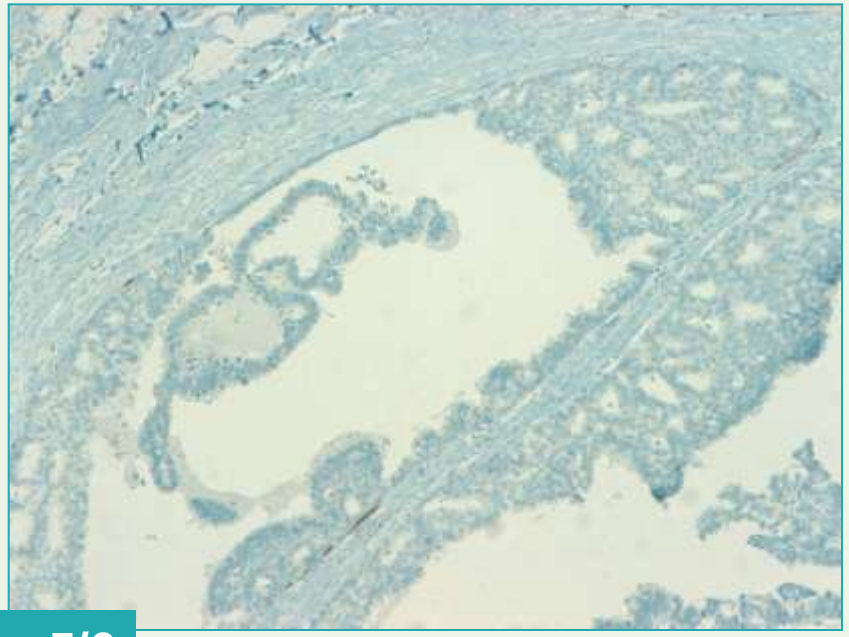
- Carcinoma papilar encapsulado:

¿Es intraductal?

¿Es infiltrante?

Sin MEC



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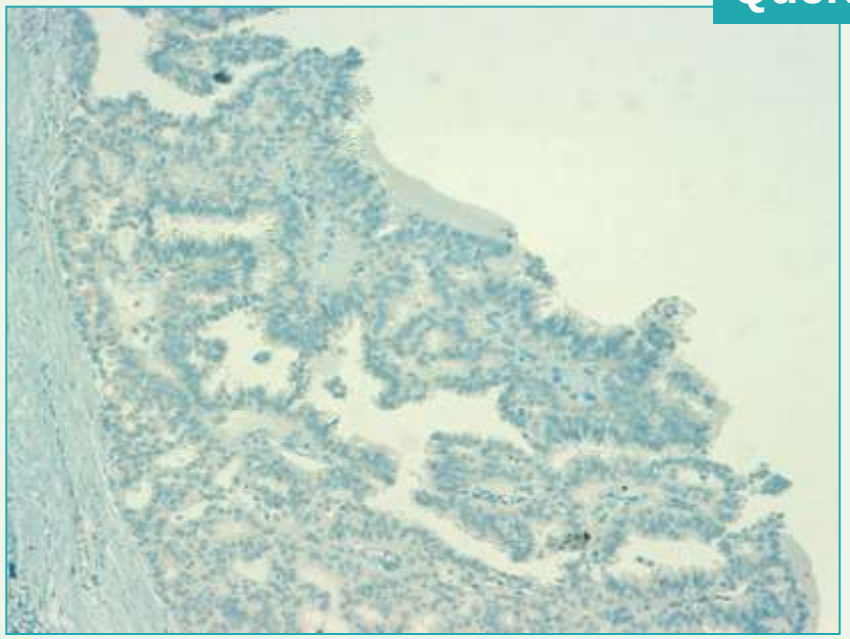
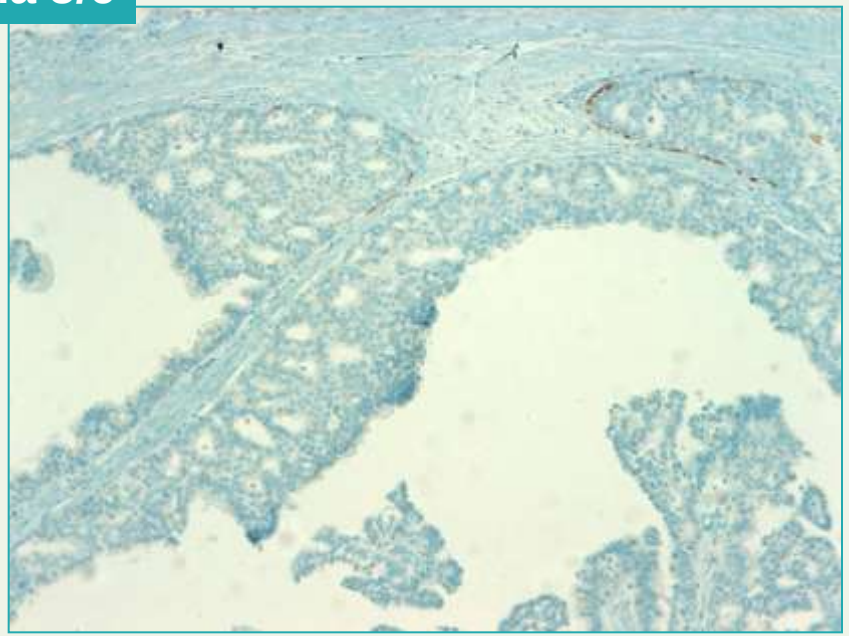
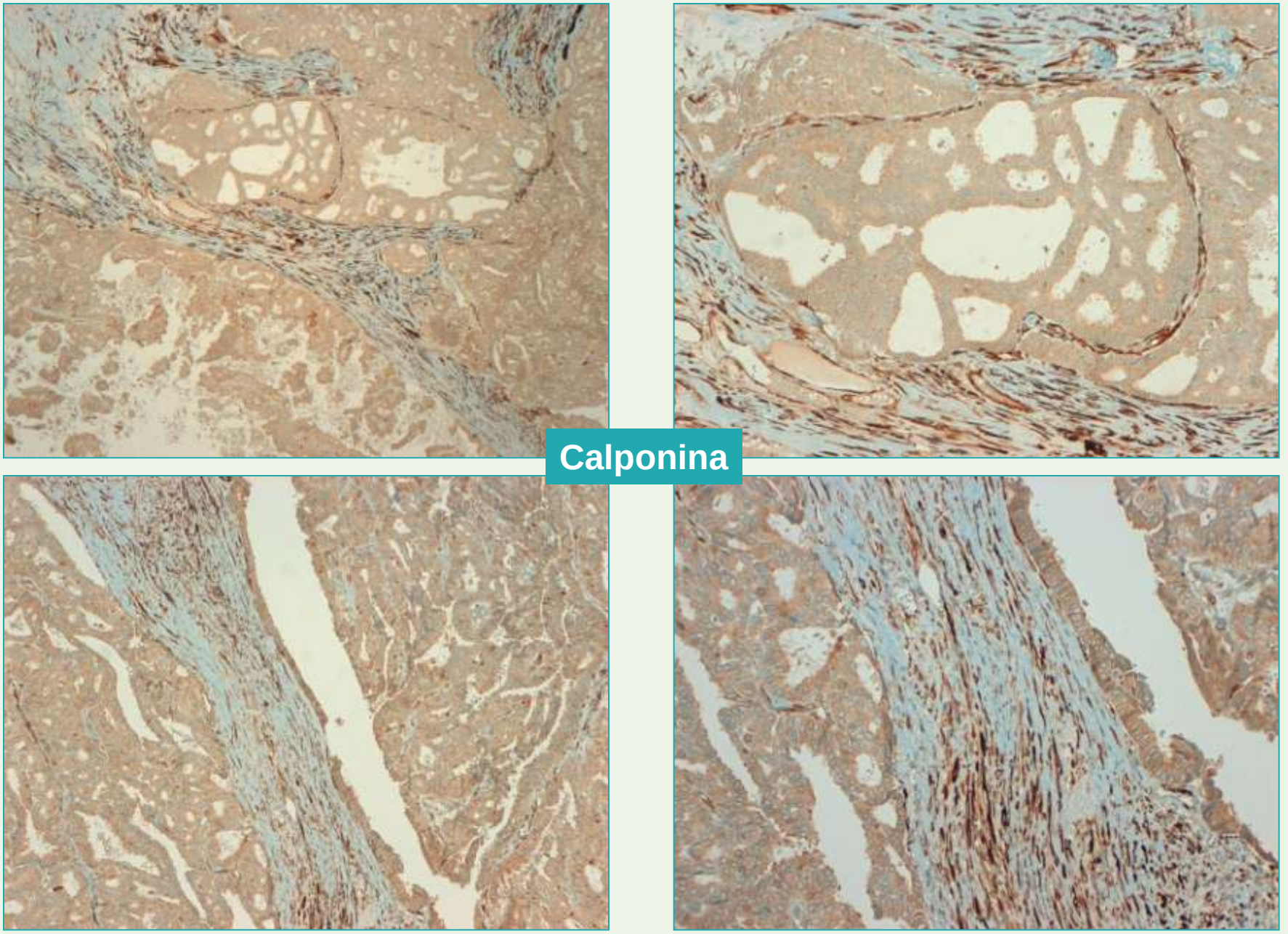
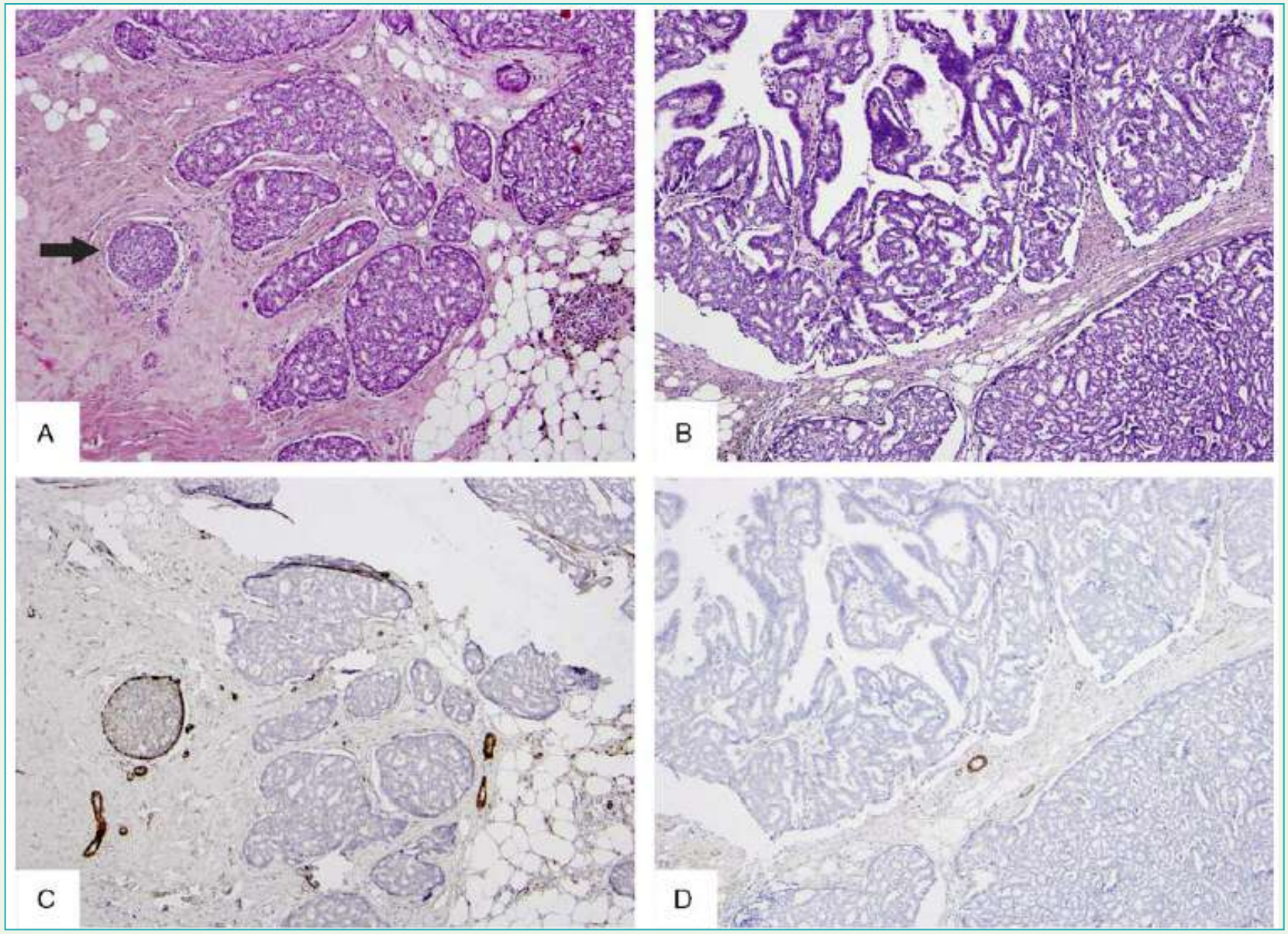




Calponina


A
B
C
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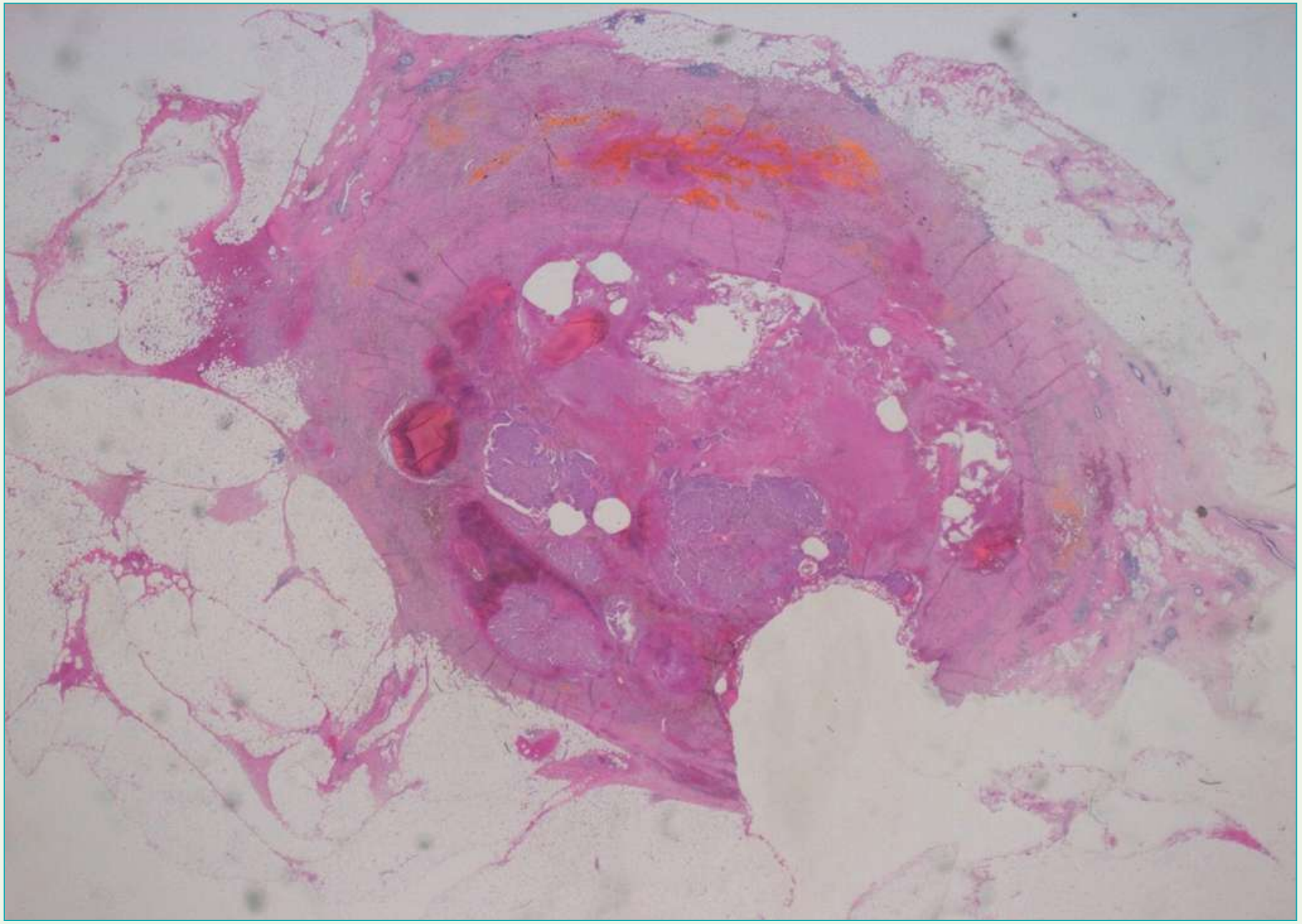
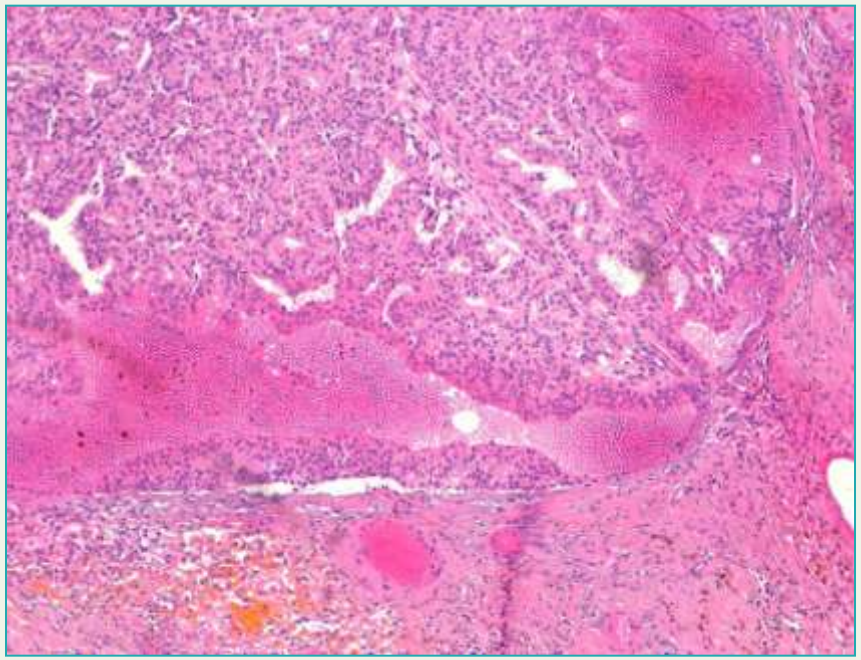
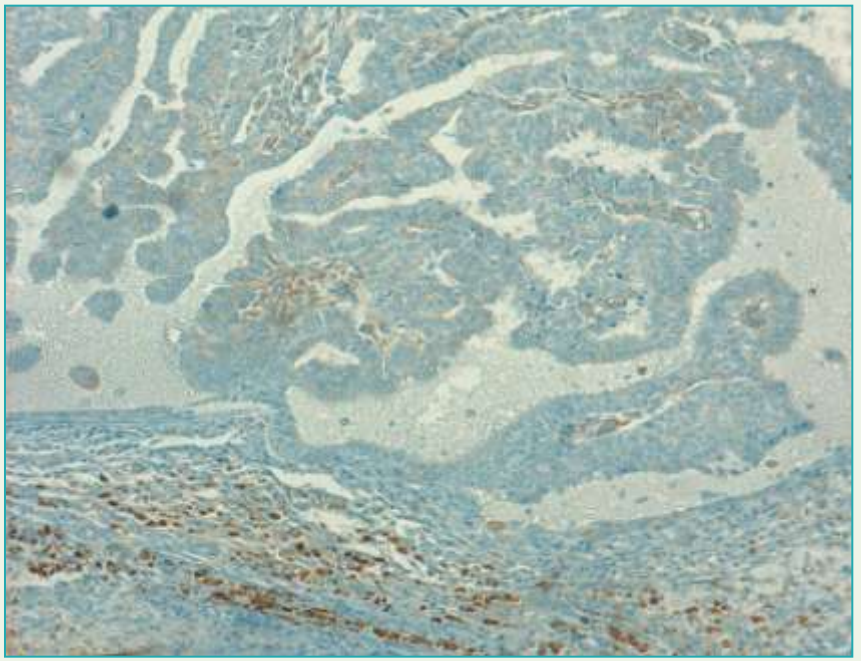
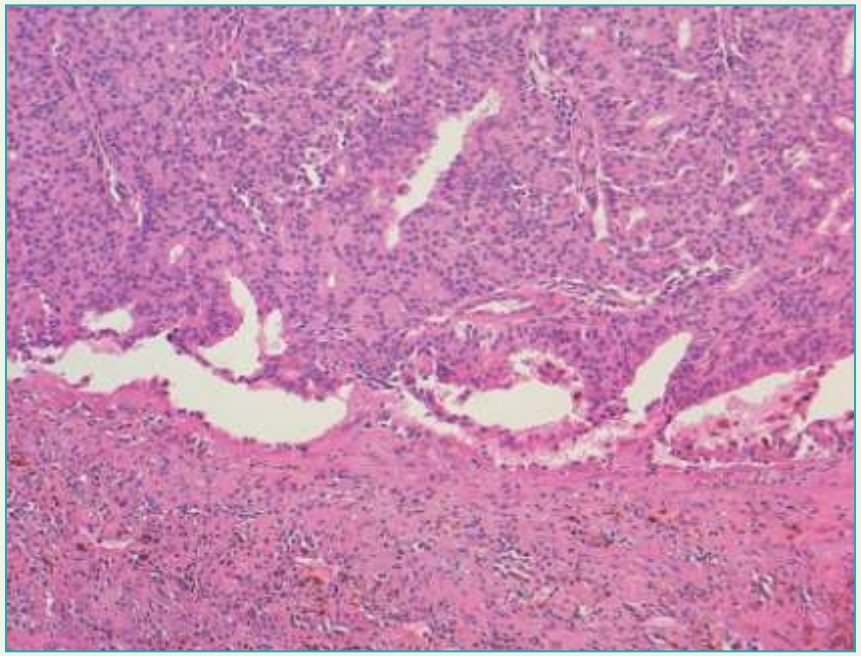
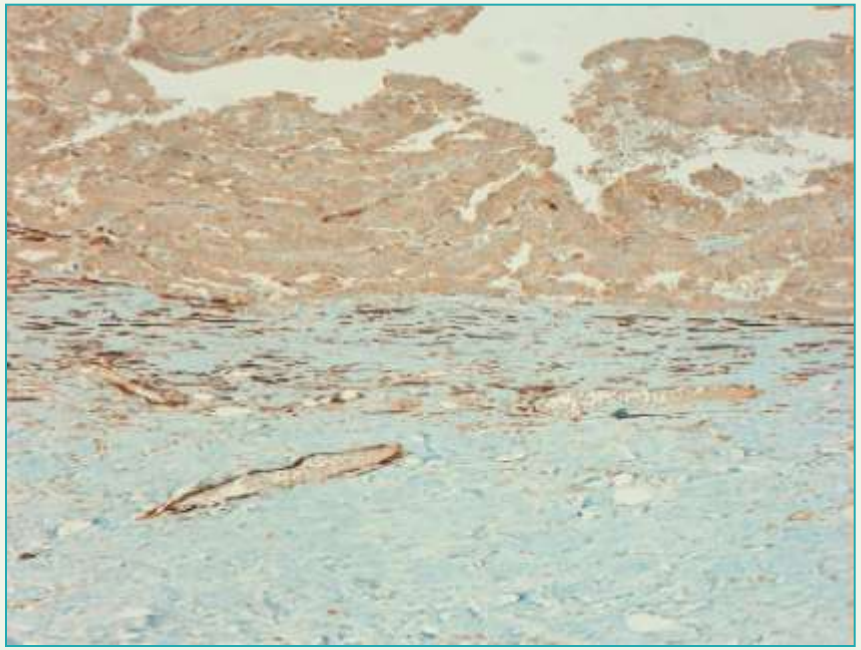






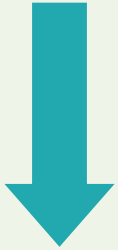




Puntos conflictivos

- Carcinoma papilar encapsulado:

Sin MEC

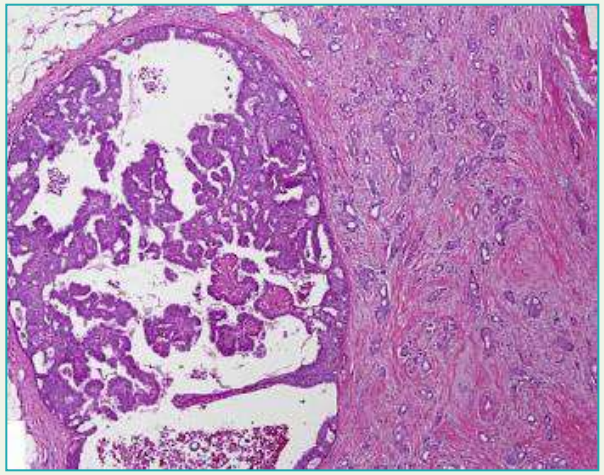


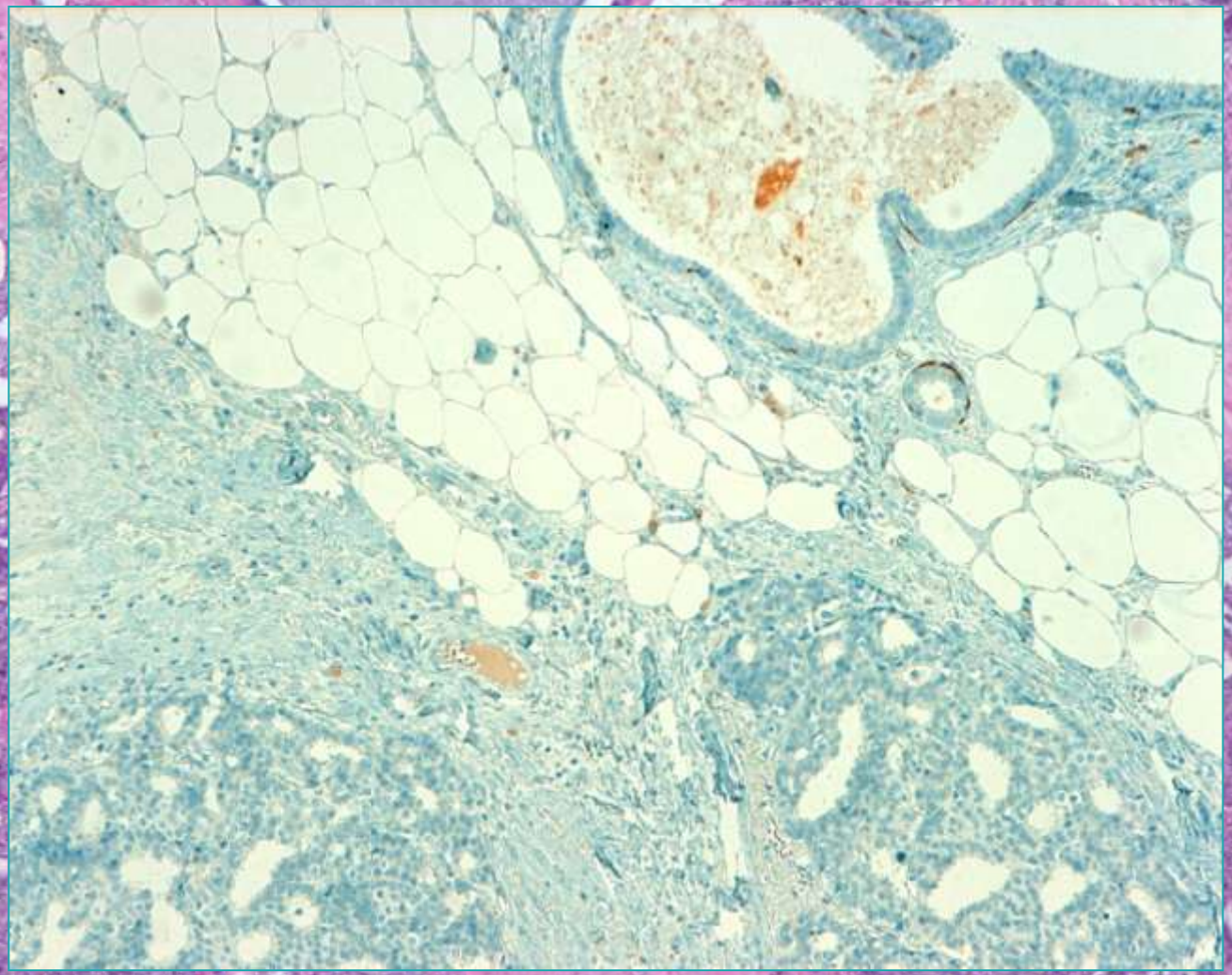
- Tiene que ser infiltrante

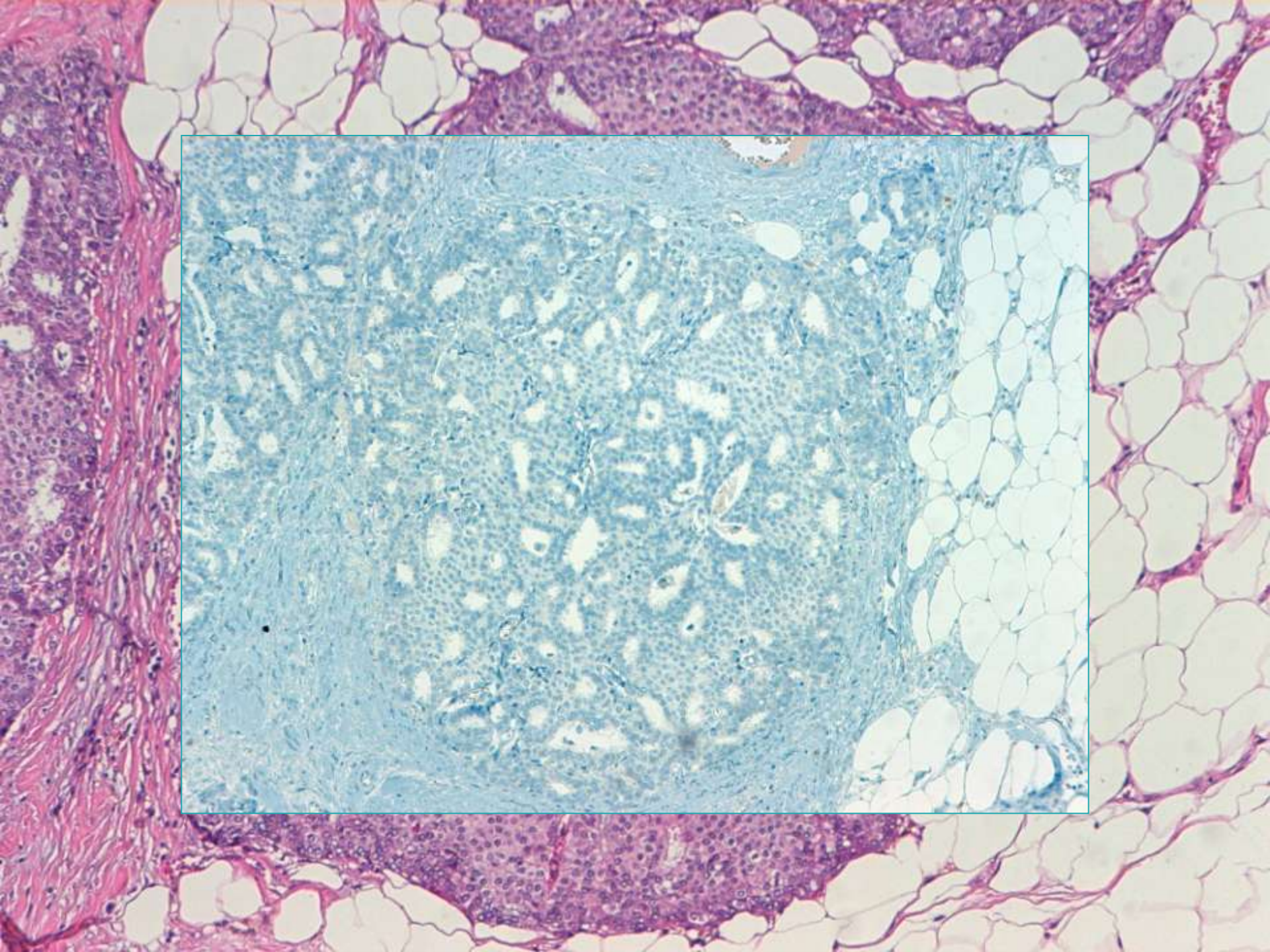
Puntos conflictivos

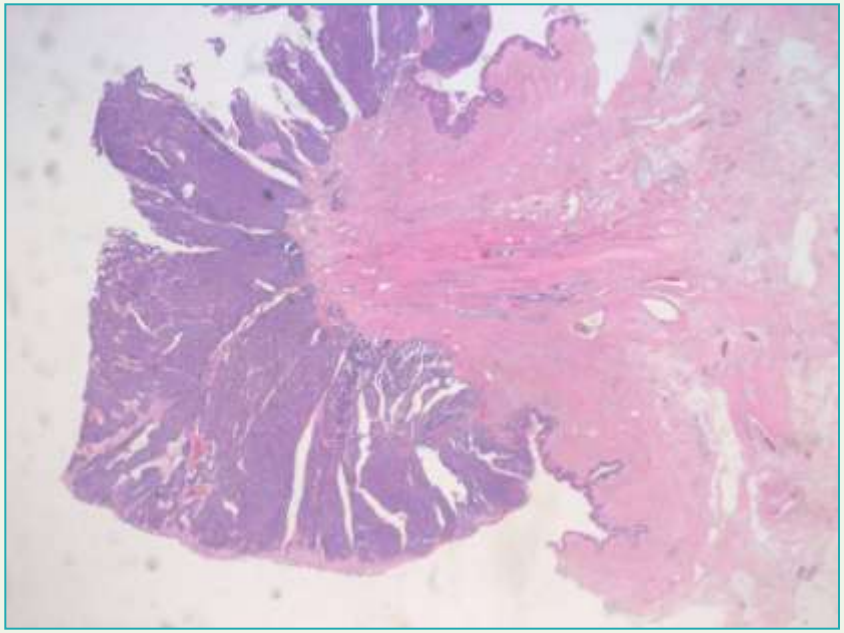
- Carcinoma papilar encapsulado:

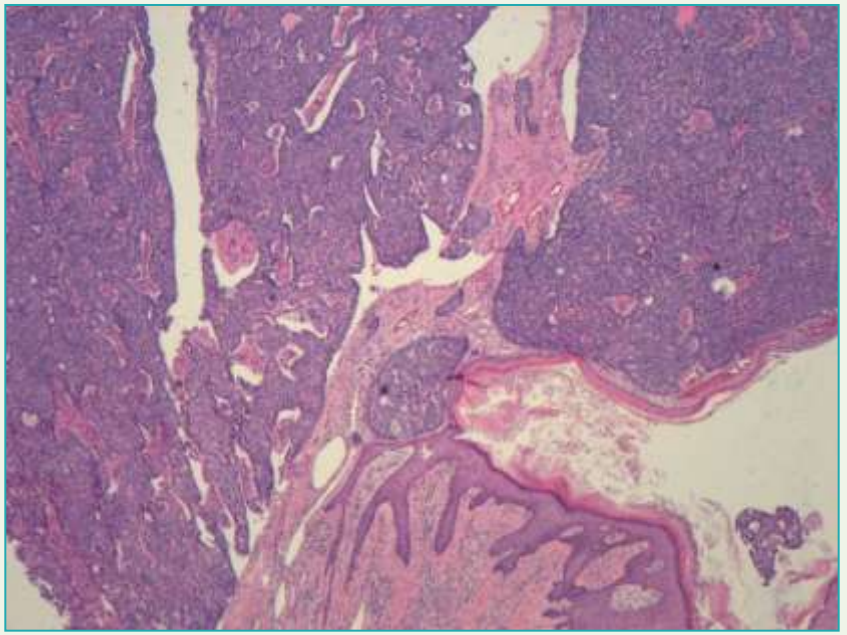
- Carcinoma papilar encapsulado
  + carcinoma ductal infiltrante

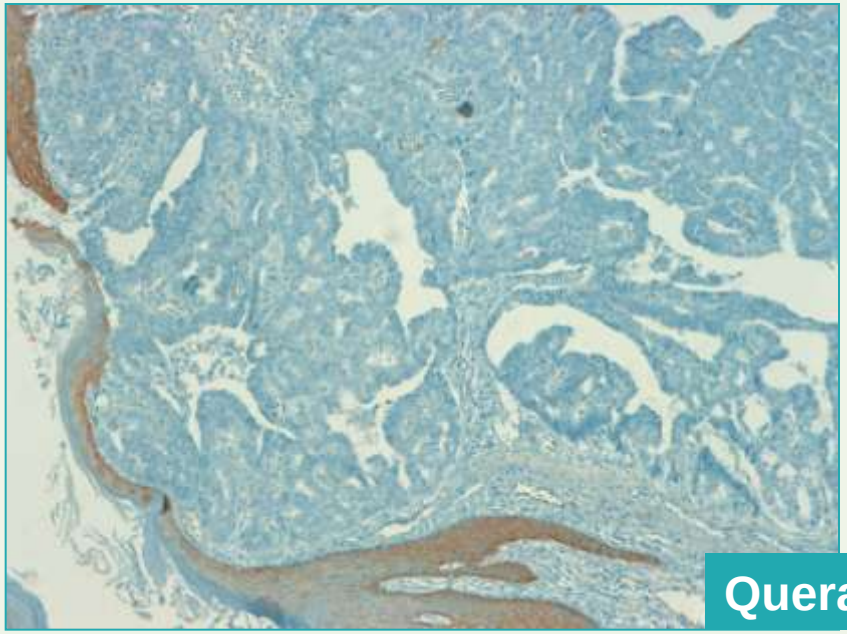


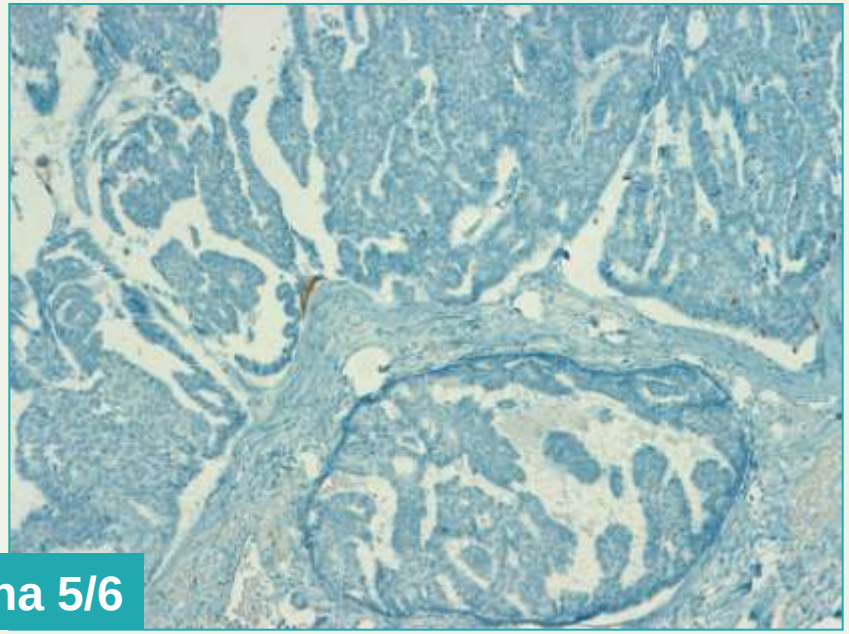






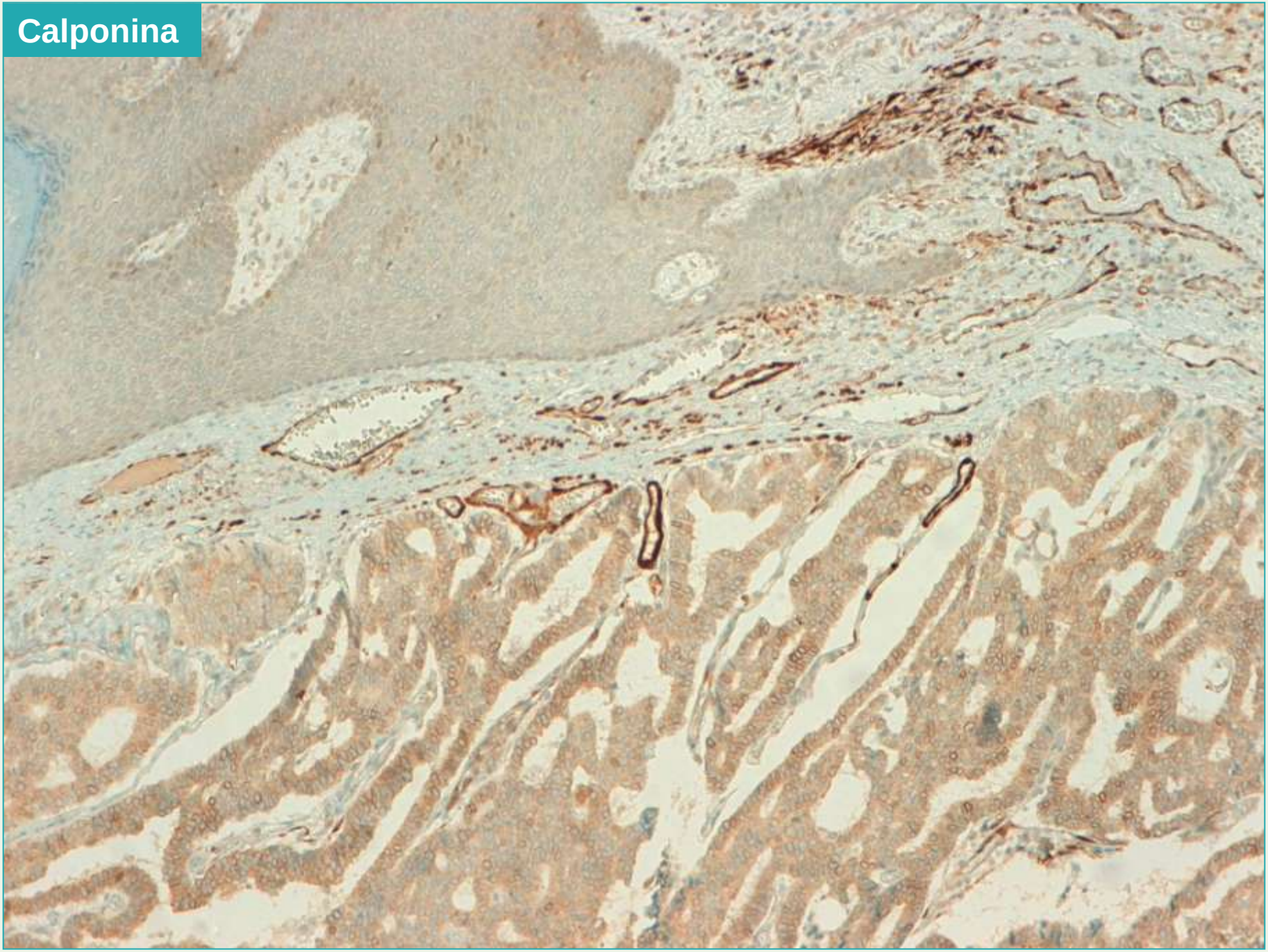






Queratina 5/6

Calponina



DCIS-CP encapsulado-C infiltrante

- Si las MEC son discontinuas/focales:
  - DCIS
  - CP intraquístico

- Si las no hay c. mioepiteliales:
  - CP encapsulado → C.infiltrante
  - CP encapsulado+ c. ductal infiltrante
  - C papilar infiltrante

¿Si es infiltrante?

- ¿Cómo medir?
  - Estudiar los MEC
  - Atender al patrón de crecimiento?
  - Focos de DCIS?
- Aplicar los criterios europeos?
- Dar la medida para pT1,2,3…?

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REVIEW

Papillary lesions of the breast: selected diagnostic and management issues

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Collins L C & Schnitt S J
(2008) *Histopathology* **52**, 20–29

Papillary lesions of the breast: selected diagnostic and management issues

The assessment and categorization of papillary lesions remains one of the most challenging areas in breast pathology. In this review, we will focus on several diagnostic and management issues related to papillary breast lesions that are frequently encountered in daily practice. These include: (i) the distinctions among papillomas with atypia (atypical papillomas), papillomas with ductal carcinoma *in situ*, and papillary ductal carcinoma *in situ*; (ii) recent developments in our understanding of encapsulated ('intracystic') papillary carcinomas and solid papillary carcinomas; and (iii) the impact of core needle biopsy on management decisions and specimen evaluation. The role of immunohistochemistry in the evaluation of these lesions, particularly the role of myoepithelial cell markers, will be emphasized.

Keywords: breast, carcinoma, ductal carcinoma *in situ*, papillary, papilloma

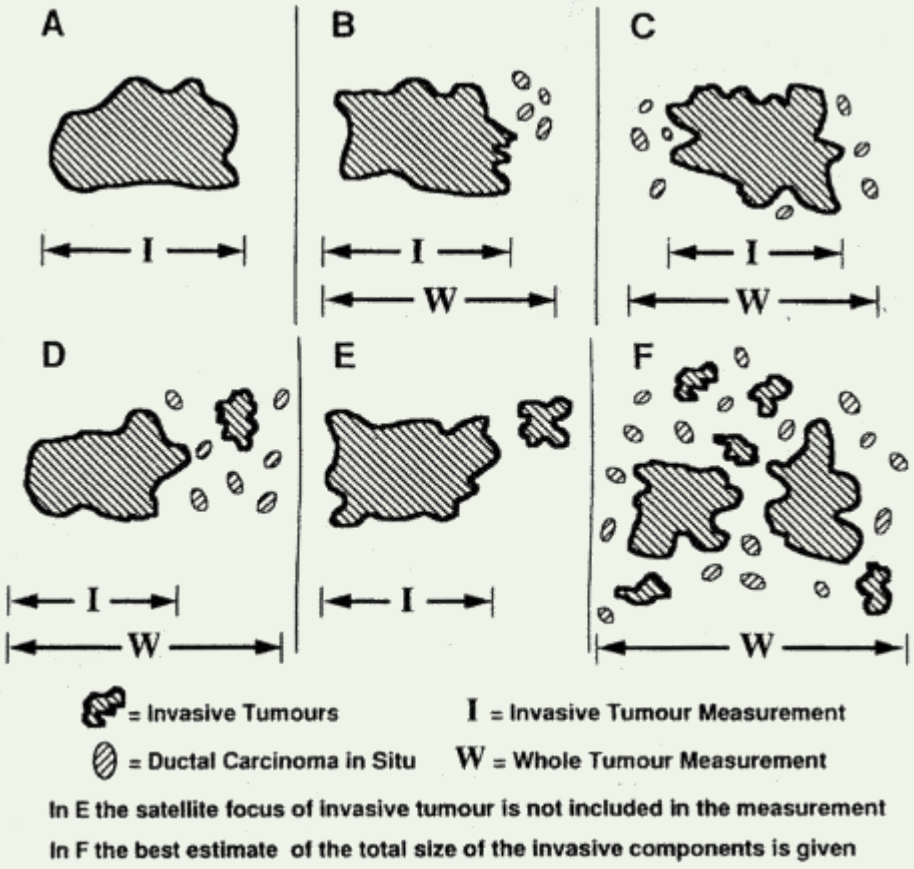
Conclusión:

"When frankly invasive carcinoma is present in association with an encapsulated papillary carcinoma, we believe it is most prudent to report only the size of the frankly invasive component as the tumour size for staging purposes in order to avoid overtreatment.

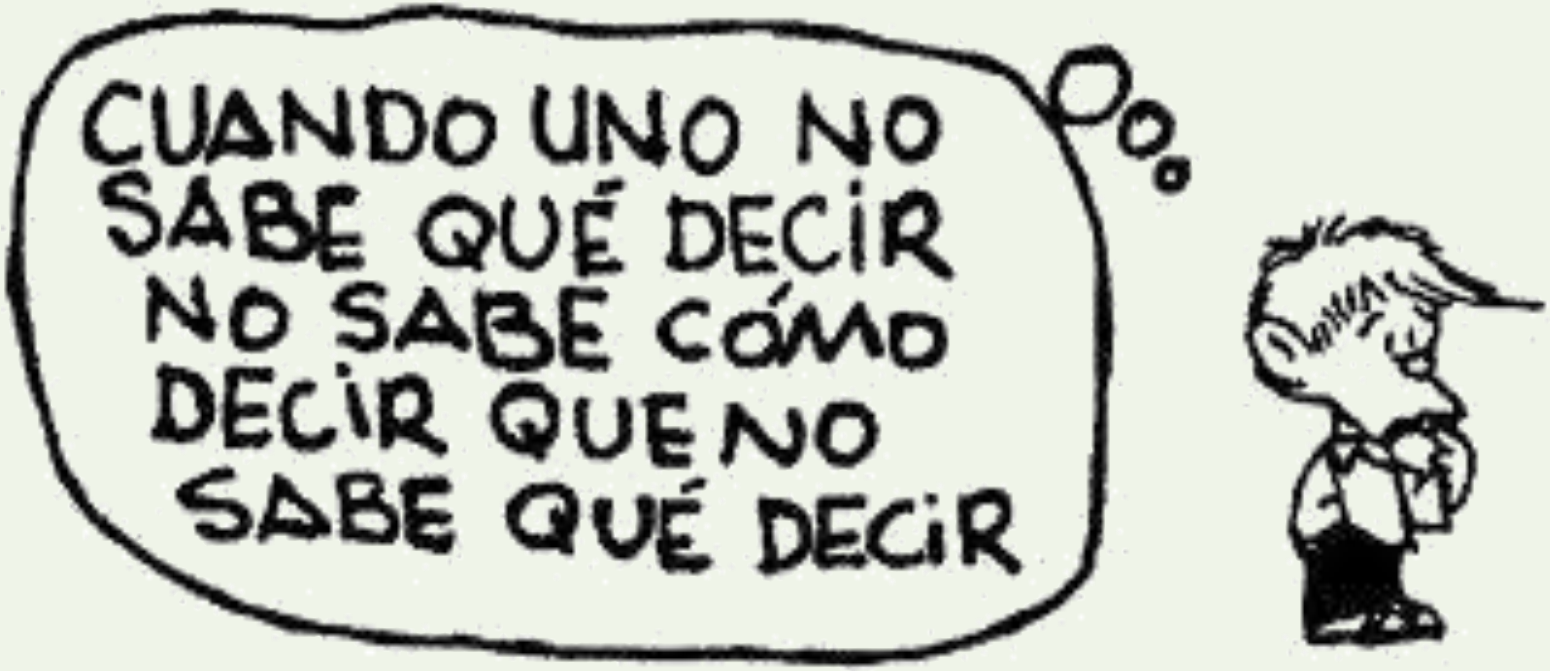
We do not take the size of the encapsulated papillary carcinoma itself into consideration in determination of the T stage.

In the absence of frankly invasive carcinoma, we render a diagnosis of ‘encapsulated papillary carcinoma’ and include an explanatory note stating that although recent studies have suggested that these may represent circumscribed nodules of low-grade invasive carcinoma rather than in situ lesions, they should be managed in a manner similar to DCIS".

QUALITY ASSURANCE GUIDELINES FOR BREAST PATHOLOGY.



Conclusión

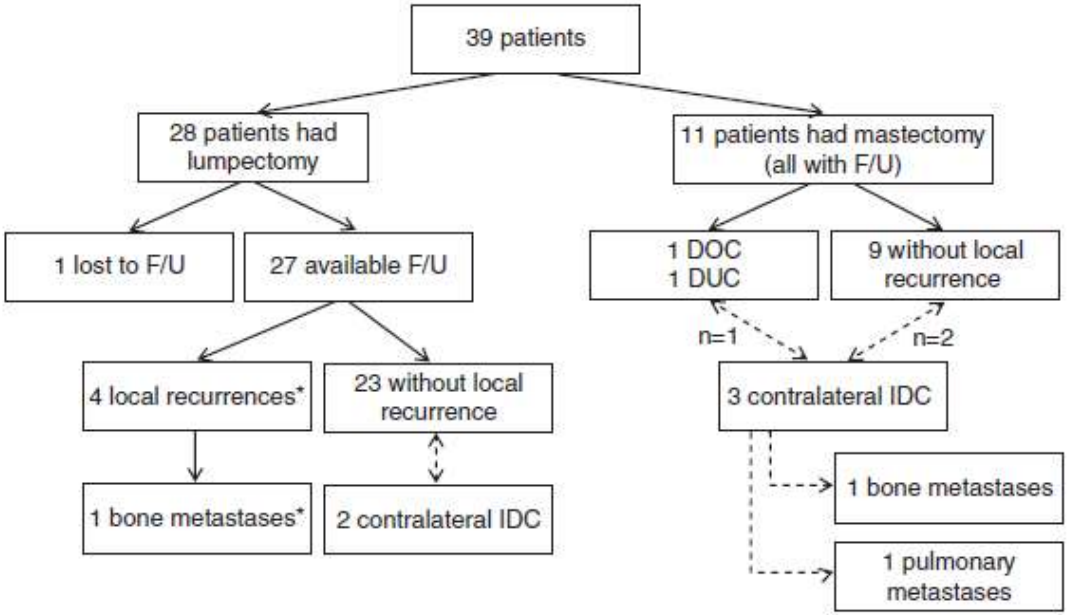

CUANDO UNO NO SABE QUÉ DECIR NO SABE CÓMO DECIR QUE NO SABE QUÉ DECIR

Conclusión

- Ausencia de MEC determina un crecimiento invasor.
- La compresión no es motivo para su atenuación ➡ papiloma tiene revestimiento continuo.
- Semejanza con el carcinoma papilar de tiroides encapsulado, no se duda de su capacidad de infiltración.
- El buen comportamiento clínico no justifica su consideración como intraductal. El c.tubular, c.cribiforme y c.adenoide quístico, son infiltrantes y presentan muy escasas metástasis.
- Las MEC tienen un papel muy activo en el paso de intraductal-infiltrante.
- Su expresión varia de ducto normal-DCIS.

Intracystic Papillary Carcinoma of the Breast: An In Situ or Invasive Tumor? Results of Immunohistochemical Analysis and Clinical Follow-up

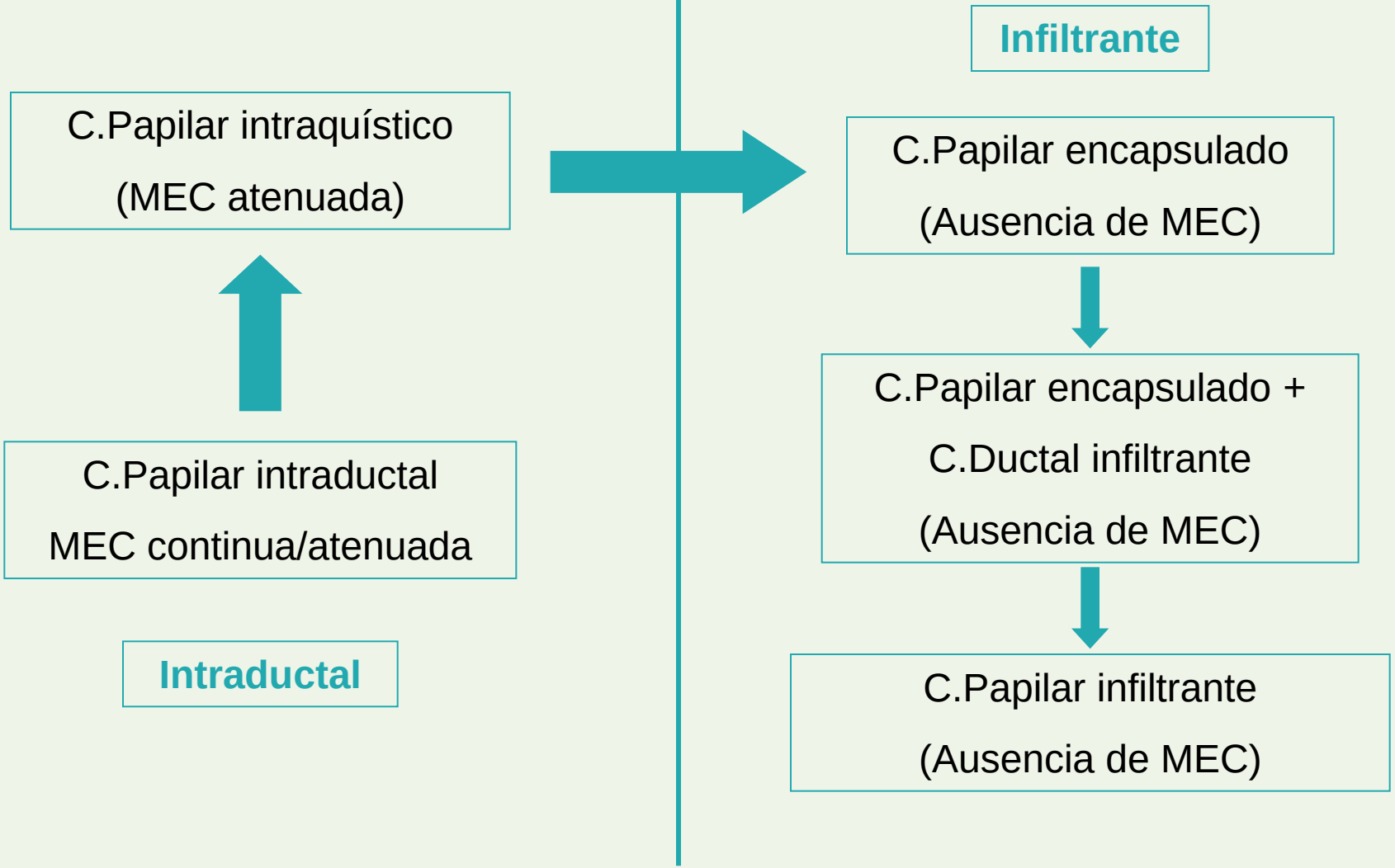
Christine A. Wynveen, MD, Tatjana Nehhozina, BSc,* Muzaffar Akram, MA, MSc,* Mohammed Hassan, BSc,* Larry Norton, MD,† Kimberly J. Van Zee, MS, MD,‡ and Edi Brogi, MD, PhD**



F/U=follow-up; DOC=died of other causes; DUC=died of unknown causes; IDC=invasive ductal carcinoma
*=1 patient received radiation therapy for the primary IPC

FIGURE 9. Patient follow-up and outcome. DOC indicates died of other causes; DUC, died of unknown causes; F/U, follow up; IDC, invasive ductal carcinoma. *One patient received radiation therapy for the primary intracystic papillary carcinoma.

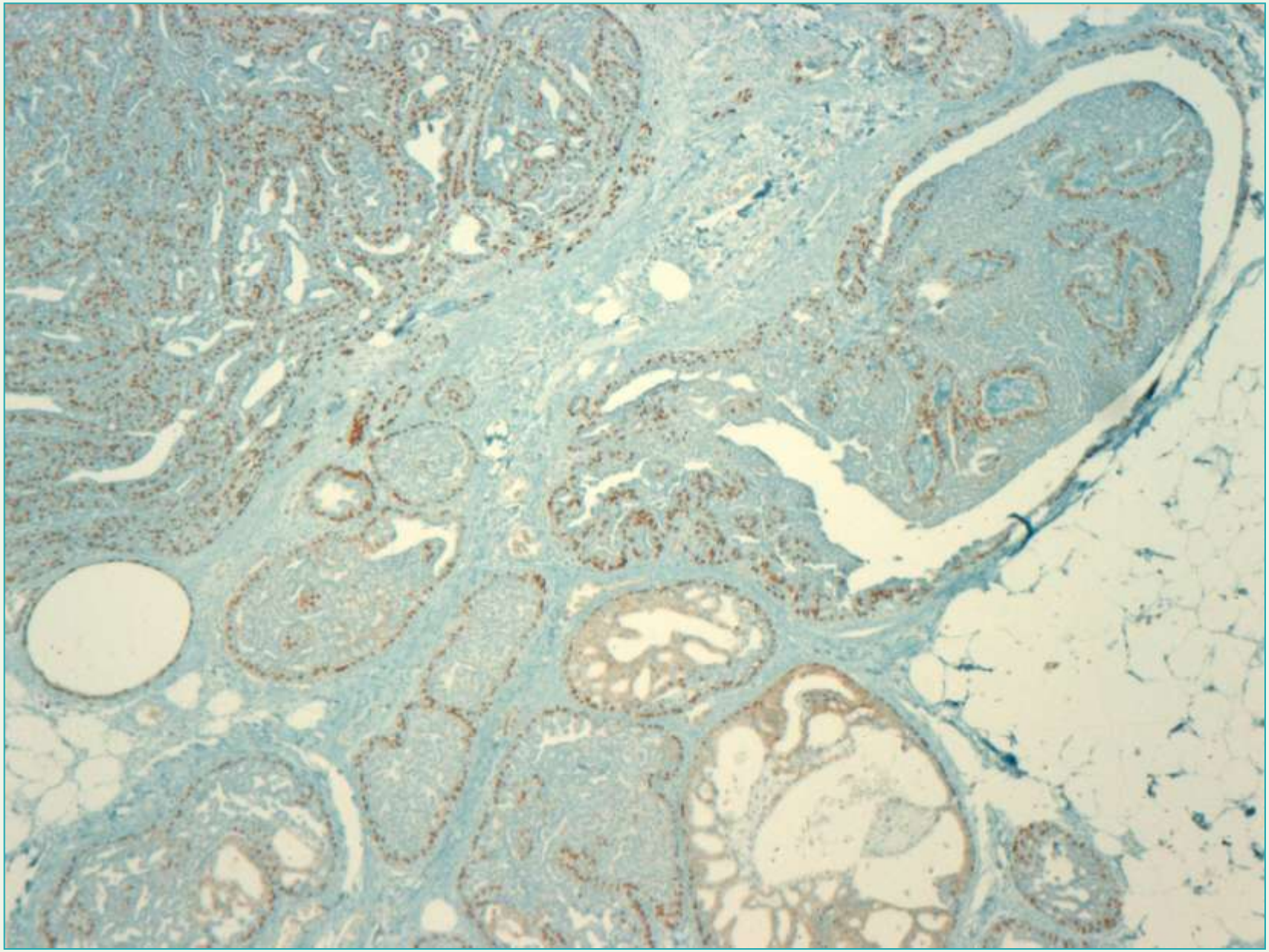
Conclusión: Espectro de progresión



Conclusión

- Es un espectro continuo.
- Si el carcinoma papilar encapsulado **no es** intraductal hay que diferenciarlo bien del carcinoma intraductal papilar y definir los criterios diferenciales.
- Si el carcinoma papilar encapsulado **no es** solo infiltrante. La forma de medida será similar al carcinoma ductal infiltrante con extenso componente intraductal.
- No debemos precisar en todos los casos donde termina uno y empieza el otro.

Muchas Gracias



DCIS-CP encapsulado

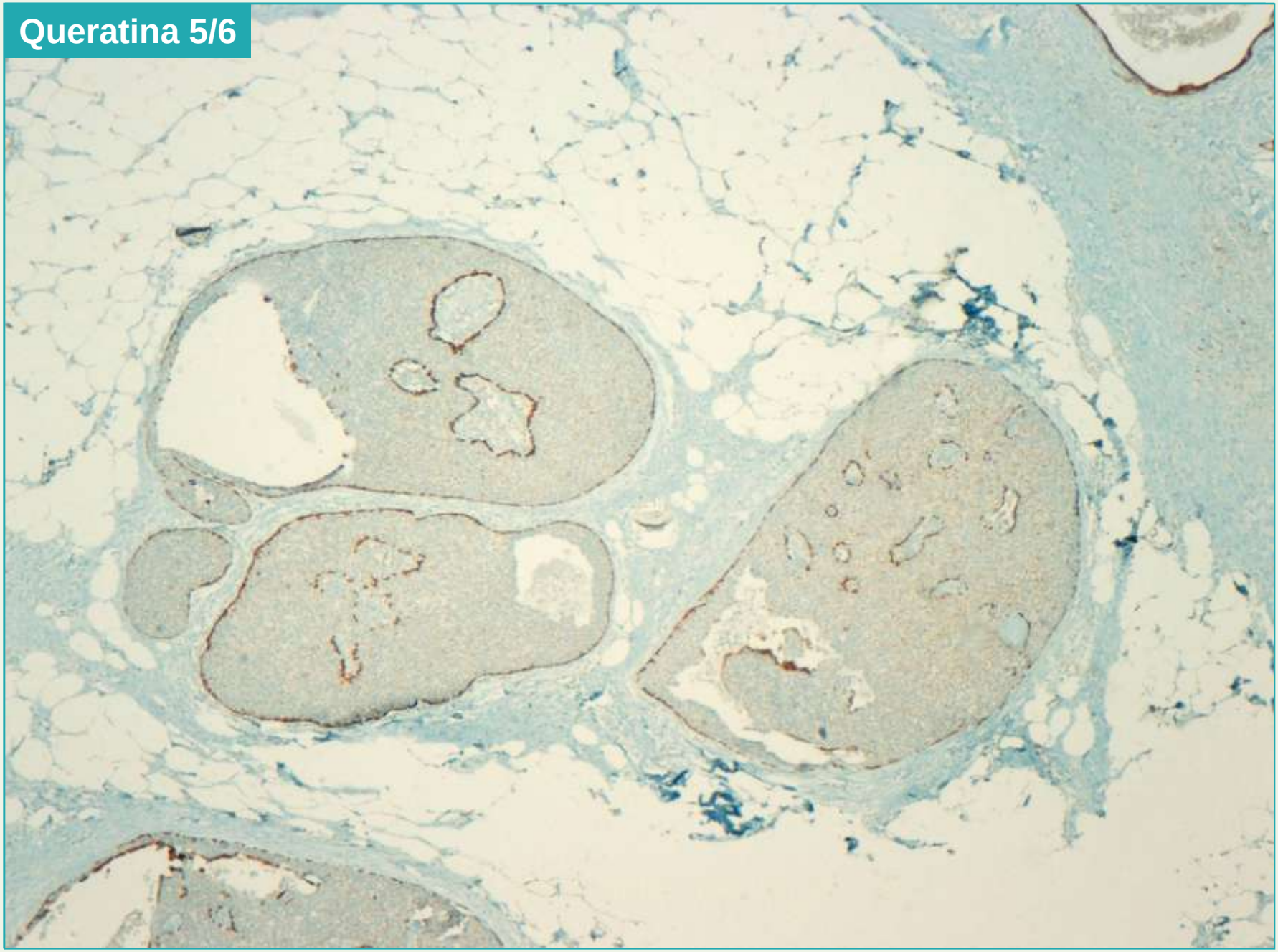
- **Si hay capa continua:**
  - DCIS: SI [X] NO [ ]
  - Si las MEC son discontinuas/focales:
    - DCIS: SI [ ] NO [X]
    - CP encapsulado: SI [X] NO [ ]
  - Si las no hay c. mioepiteliales:
    - CP encapsulado SI [X] NO [ ]
    - C papilar infiltrante SI [X] NO [ ]

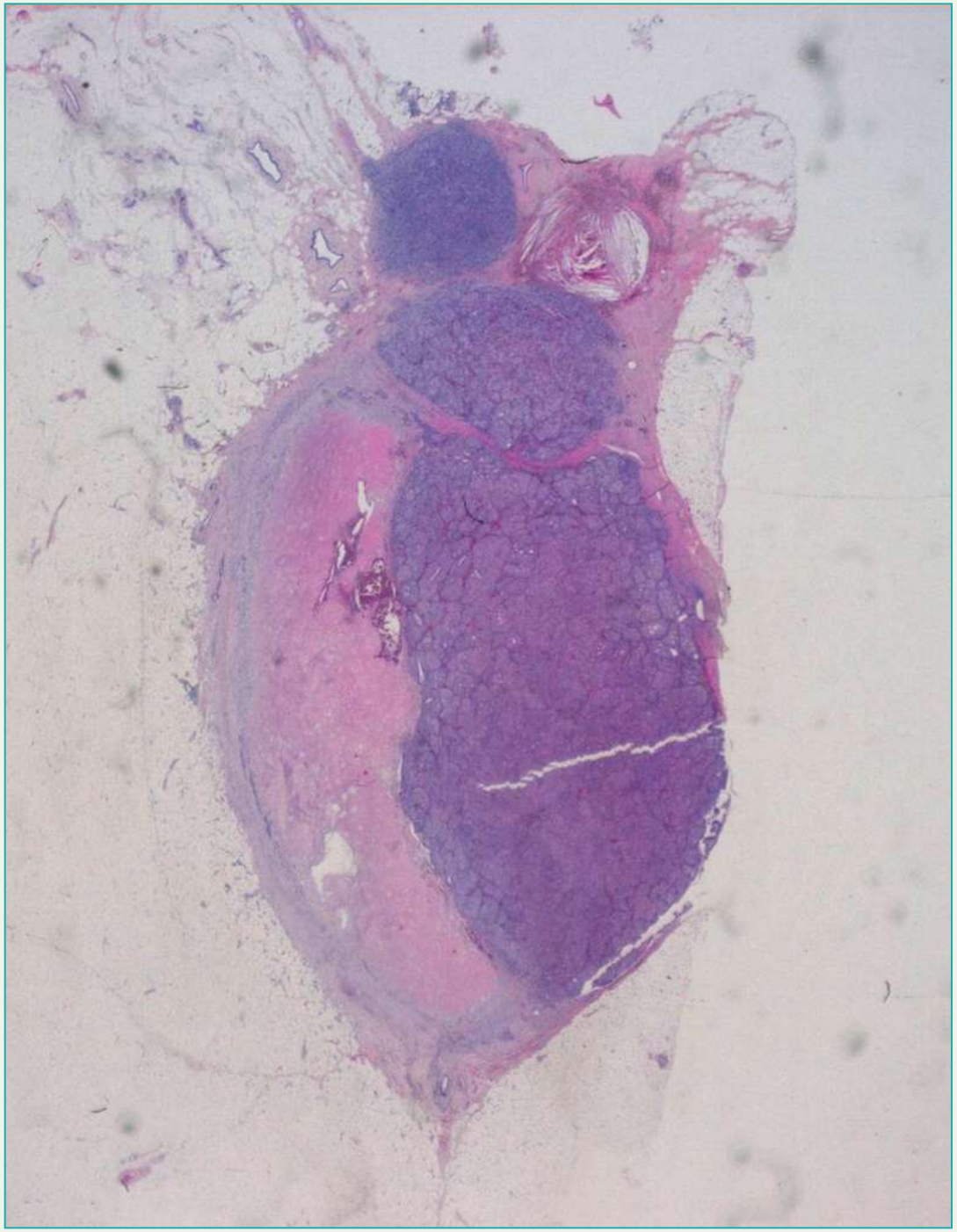
Término *papila* RAE

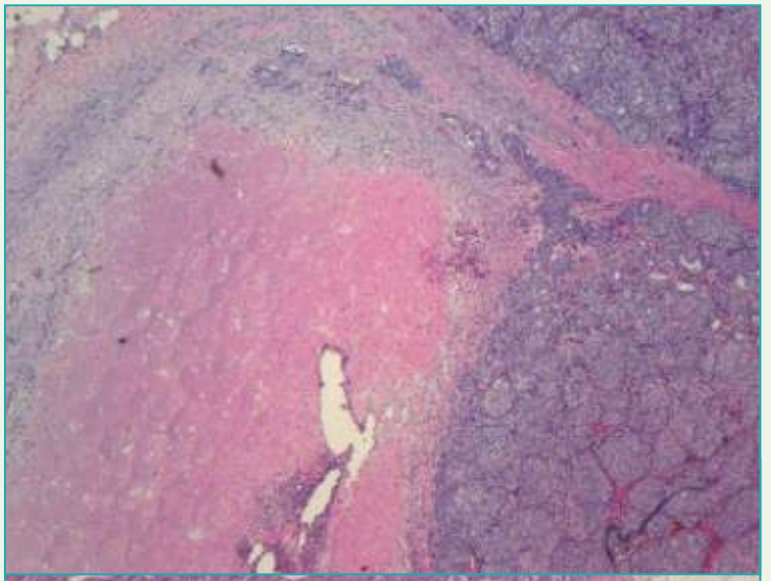
- Del lat. *papilla*

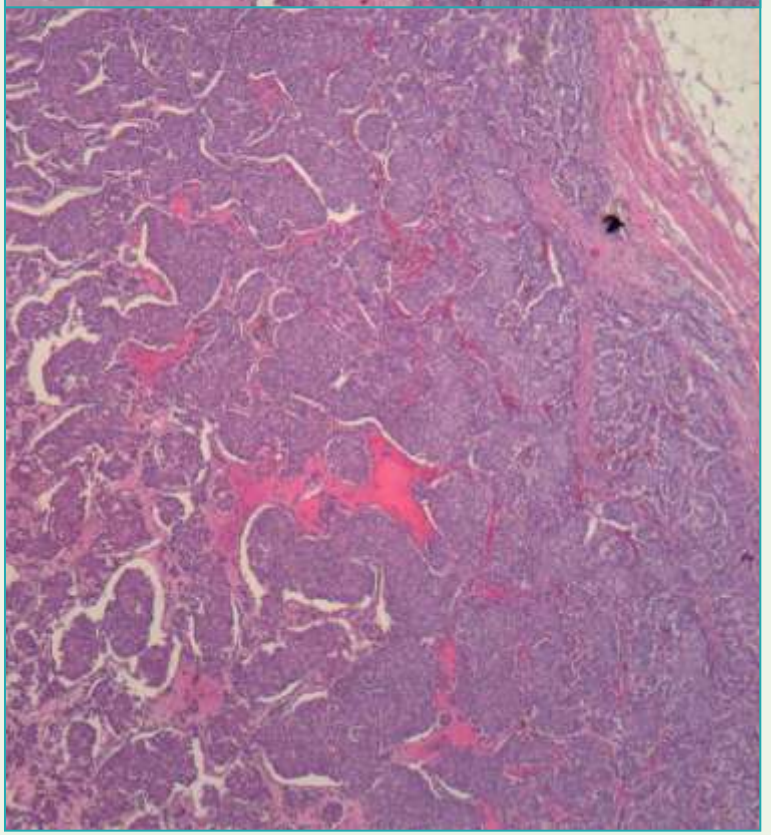
- **1.** f. *Anat.* Cada una de las pequeñas prominencias cónicas, generalmente sensoriales, formadas en la piel y en las membranas mucosas, especialmente de la lengua, por las ramificaciones de los nervios y de los vasos.

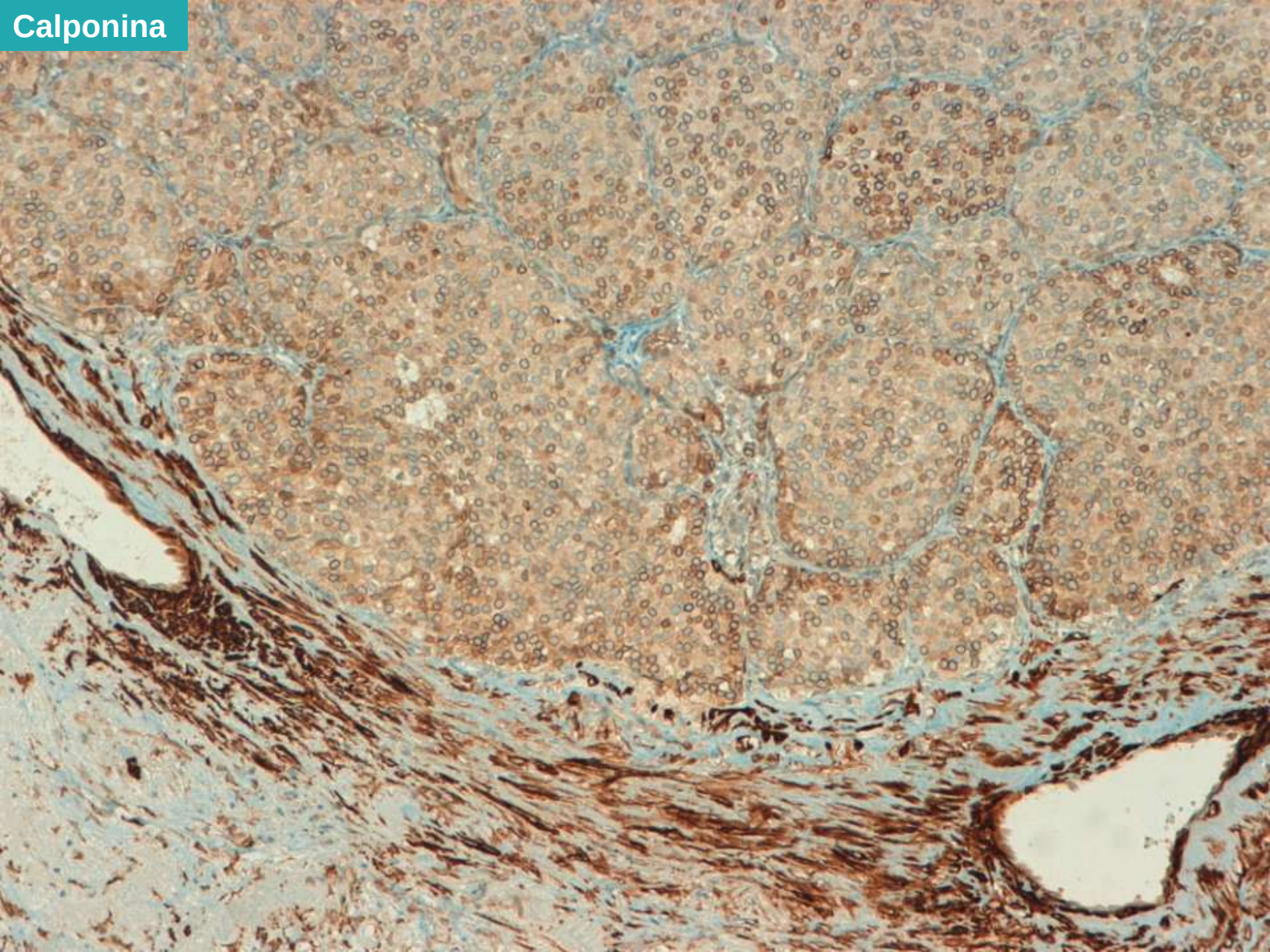
Queratina 5/6










Calponina