1er CONGRESO ESTATAL DE CANCER DE LA MUJER

CLASIFICACION HISTOLOGICA, INMUNOLOGICA Y MOLECULAR DEL CANCER DE MAMA

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WHO Classification of Tumours of the Breast

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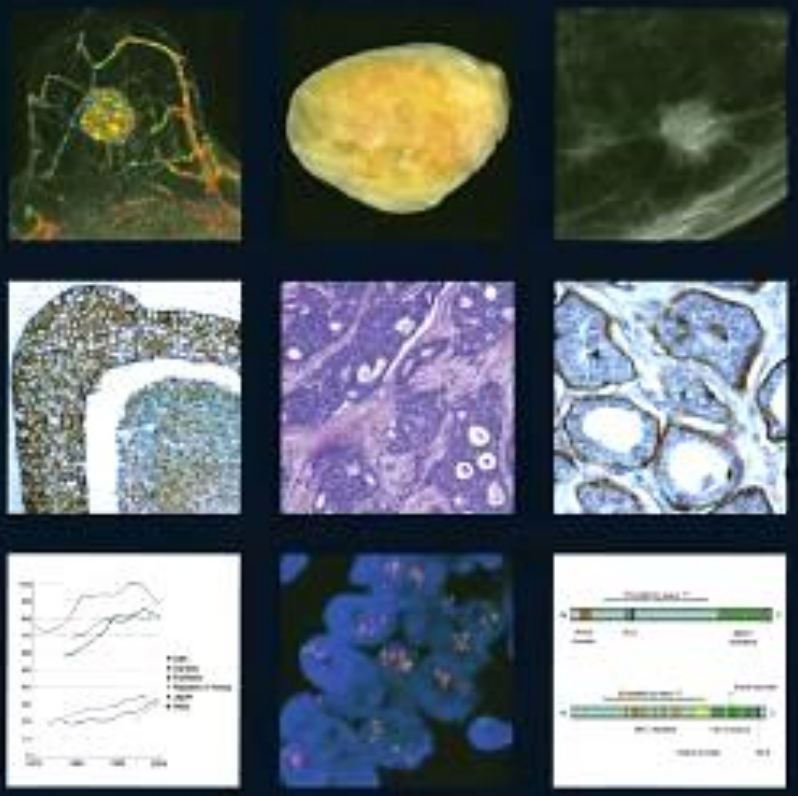


WHO

WHO classification of tumours of the breast

EPITHELIAL TUMOURS

Microinvasive carcinoma

Invasive breast carcinoma

Invasive carcinoma of no special type (NST)	8500/3
Pleomorphic carcinoma	8022/3
Carcinoma with osteoclast-like stromal giant cells	8035/3
Carcinoma with choriocarcinomatous features	
Carcinoma with melanotic features	
Invasive lobular carcinoma	8520/3
Classic lobular carcinoma	
Solid lobular carcinoma	
Alveolar lobular carcinoma	
Pleomorphic lobular carcinoma	
Tubulolobular carcinoma	
Mixed lobular carcinoma	
Tubular carcinoma	8211/3
Cribriform carcinoma	8201/3
Mucinous carcinoma	8480/3
Carcinoma with medullary features	
Medullary carcinoma	8510/3
Atypical medullary carcinoma	8513/3
Invasive carcinoma NST with medullary features	8500/3
Carcinoma with apocrine differentiation	
Carcinoma with signet-ring-cell differentiation	
Invasive micropapillary carcinoma	8507/3*
Metaplastic carcinoma of no special type	8575/3
Low-grade adenosquamous carcinoma	8570/3
Fibromatosis-like metaplastic carcinoma	8572/3
Squamous cell carcinoma	8070/3
Spindle cell carcinoma	8032/3
Metaplastic carcinoma with mesenchymal differentiation	
Chondroid differentiation	8571/3
Osseous differentiation	8571/3
Other types of mesenchymal differentiation	8575/3
Mixed metaplastic carcinoma	8575/3
Myoepithelial carcinoma	8982/3

Rare types

Carcinoma with neuroendocrine features	
Neuroendocrine tumour, well-differentiated	8246/3
Neuroendocrine carcinoma, poorly differentiated (small cell carcinoma)	8041/3
Carcinoma with neuroendocrine differentiation	8574/3
Secretory carcinoma	8502/3
Invasive papillary carcinoma	8503/3
Acinic cell carcinoma	8550/3
Mucoepidermoid carcinoma	8430/3
Polymorphous carcinoma	8525/3
Oncocytic carcinoma	8290/3
Lipid-rich carcinoma	8314/3
Glycogen-rich clear cell carcinoma	8315/3
Sebaceous carcinoma	8410/3
Salivary gland/skin adnexal type tumours	
Cylindroma	8200/0
Clear cell hidradenoma	8402/0*

Epithelial–myoepithelial tumours

Pleomorphic adenoma	8940/0
Adenomyoepithelioma	8983/0
Adenomyoepithelioma with carcinoma	8983/3*
Adenoid cystic carcinoma	8200/3

Precursor lesions

Ductal carcinoma in situ	8500/2
Lobular neoplasia	
Lobular carcinoma in situ	
Classic lobular carcinoma in situ	8520/2
Pleomorphic lobular carcinoma in situ	8519/2*
Atypical lobular hyperplasia	

Intraductal proliferative lesions

Usual ductal hyperplasia
Columnar cell lesions including flat epithelial atypia
Atypical ductal hyperplasia

Papillary lesions

Intraductal papilloma	8503/0
Intraductal papilloma with atypical hyperplasia	8503/0
Intraductal papilloma with ductal carcinoma in situ	8503/2*
Intraductal papilloma with lobular carcinoma in situ	8520/2
Intraductal papillary carcinoma	8503/2
Encapsulated papillary carcinoma	8504/2
Encapsulated papillary carcinoma with invasion	8504/3
Solid papillary carcinoma	
In situ	8509/2
Invasive	8509/3

Benign epithelial proliferations

Sclerosing adenosis
Apocrine adenosis
Microglandular adenosis

Radial scar/complex sclerosing lesion	
Adenomas	
Tubular adenoma	8211/0
Lactating adenoma	8204/0
Apocrine adenoma	8401/0
Ductal adenoma	8503/0

MESENCHYMAL TUMOURS

Nodular fasciitis	8828/0*
Myofibroblastoma	8825/0
Desmoid-type fibromatosis	8821/1
Inflammatory myofibroblastic tumour	8825/1
Benign vascular lesions	
Haemangioma	9120/0
Angiomatosis	
Atypical vascular lesions	
Pseudoangiomatous stromal hyperplasia	
Granular cell tumour	9580/0
Benign peripheral nerve-sheath tumours	
Neurofibroma	9540/0
Schwannoma	9560/0
Lipoma	8850/0
Angiolipoma	8861/0
Liposarcoma	8850/3
Angiosarcoma	9120/3
Rhabdomyosarcoma	8900/3
Osteosarcoma	9180/3
Leiomyoma	8890/0
Leiomyosarcoma	8890/3

FIBROEPITHELIAL TUMOURS

Fibroadenoma	9010/0
Phyllodes tumour	9020/1
Benign	9020/0
Borderline	9020/1
Malignant	9020/3
Periductal stromal tumour, low grade	9020/3
Hamartoma	

TUMOURS OF THE NIPPLE

Nipple adenoma	8506/0
Syringomatous tumour	8407/0
Paget disease of the nipple	8540/3

MALIGNANT LYMPHOMA

Diffuse large B-cell lymphoma	9680/3
Burkitt lymphoma	9687/3
T-cell lymphoma	
Anaplastic large cell lymphoma, ALK-negative	9702/3
Extranodal marginal-zone B-cell lymphoma of MALT type	9699/3
Follicular lymphoma	9690/3

METASTATIC TUMOURS

TUMOURS OF THE MALE BREAST

Gynaecomastia	
Carcinoma	
Invasive carcinoma	8500/3
In situ carcinoma	8500/2

CLINICAL PATTERNS

Inflammatory carcinoma	8530/3
Bilateral breast carcinoma	

TNM classification of carcinomas of the breast

TNM Clinical Classification[a]

T – Primary Tumour

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
Tis (DCIS)	Ductal carcinoma in situ
Tis (LCIS)	Lobular carcinoma in situ
Tis (Paget)	Paget disease of the nipple with no tumour

Note: Paget disease associated with a tumour is classified according to the size of the tumour.

T1	Tumour 2 cm or less in greatest dimension
T1mic	Microinvasion 0.1 cm or less in greatest dimension*
T1a	More than 0.1 cm but not more than 0.5 cm in greatest dimension
T1b	More than 0.5 cm but not more than 1 cm in greatest dimension
T1c	More than 1 cm but not more than 2 cm in greatest dimension
T2	Tumour more than 2 cm but not more than 5 cm in greatest dimension
T3	Tumour more than 5 cm in greatest dimension
T4	Tumour of any size with direct extension to chest wall or skin only as described in T4a to T4d

Note:Chest wall includes ribs, intercostal muscles, and serratus anterior muscle but not pectoral muscle.

T4a	Extension to chest wall
T4b	Oedema (including peau d'orange), or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast
T4c	Both 4a and 4b, above
T4d	Inflammatory carcinoma[b]

Notes: * Microinvasion is the extension of cancer cells beyond the basement membrane into the adjacent tissues with no focus more than 0.1cm in greatest dimension. When there are multiple foci of microinvasion, the size of only the largest focus is used to classify the microinvasion (Do not use the sum of all individual foci). The presence of multiple foci of microinvasion should be noted, as it is with multiple larger invasive carcinomas.

[b] Inflammatory carcinoma of the breast is characterized by diffuse, brawny induration of the skin with an erysipeloid edge, usually with no underlying mass. If the skin biopsy is negative and there is no localized measurable primary cancer, the T category is pTX when pathologically staging a clinical inflammatory carcinoma (T4d). Dimpling of the skin, nipple retraction, or other skin changes, except those in T4b and T4d, may occur in T1, T2, or T3 without affecting the classification.

N – Regional Lymph Nodes[a]

NX	Regional lymph nodes cannot be assessed (e.g. previously removed)
N0	No regional lymph node metastasis
N1	Metastasis in movable ipsilateral axillary lymph node(s)
N2	Metastasis in fixed ipsilateral axillary lymph node(s) or in clinically apparent* ipsilateral internal mammary lymph node(s) in the absence of clinically evident axillary lymph node metastasis
N2a	Metastasis in axillary lymph node(s) fixed to one another or to other structures
N2b	Metastasis only in clinically apparent* internal mammary lymph node(s) and in the absence of clinically evident axillary lymph node metastasis
N3	Metastasis in ipsilateral infraclavicular lymph node(s) with or without axillary lymph node involvement; or in clinically apparent* ipsilateral internal mammary lymph node(s) in the presence of clinically evident axillary lymph node metastasis; or metastasis in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
N3a	Metastasis in infraclavicular lymph node(s)
N3b	Metastasis in internal mammary and axillary lymph nodes
N3c	Metastasis in supraclavicular lymph node(s)

Note: * clinically apparent = detected by clinical examination or by imaging studies (excluding lymphoscintigraphy)

M – Distant Metastasis

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

pTNM Pathological Classification

pT – Primary Tumour

The pathological classification requires the examination of the primary carcinoma with no gross tumour at the margins of resection. A case can be classified pT if there is only microscopic tumour in a margin.
The pT categories correspond to the T categories.

Note: When classifying pT the tumour size is a measurement of the invasive component. If there is a large in situ component (e.g. 4 cm) and a small invasive component (e.g. 0.5 cm), the tumour is coded pT1a.

pN – Regional Lymph Nodes[a]

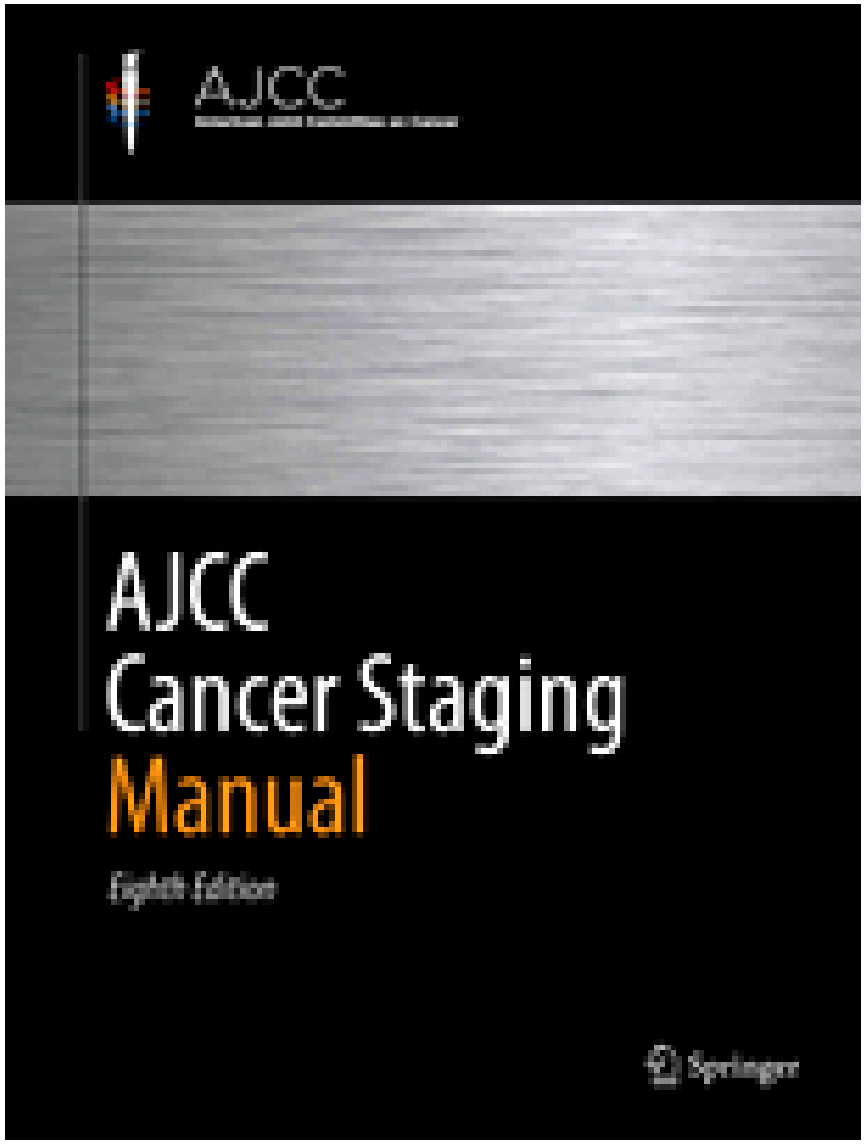
pNX	Regional lymph nodes cannot be assessed (not removed for study or previously removed)
pN0	No regional lymph node metastasis*
pN1mi	Micrometastasis (larger than 0.2 mm, but none larger than 2 mm in greatest dimension)
pN1	Metastasis in 1 - 3 ipsilateral axillary lymph node(s), and/or in internal mammary nodes with microscopic metastasis detected by sentinel lymph node dissection but not clinically apparent**
pN1a	Metastasis in 1-3 axillary lymph node(s), including at least one larger than 2 mm in greatest dimension
pN1b	Internal mammary lymph nodes with microscopic metastasis detected by sentinel lymph node dissection but not clinically apparent
pN1c	Metastasis in 1 - 3 axillary lymph nodes and internal mammary lymph nodes with microscopic metastasis detected by sentinel lymph node dissection but not clinically apparent
pN2	Metastasis in 4 - 9 ipsilateral axillary lymph nodes, or in clinically apparent*** ipsilateral internal mammary lymph node(s) in the absence of axillary lymph node metastasis
pN2a	Metastasis in 4-9 axillary lymph nodes, including at least one that is larger than 2 mm
pN2b	Metastasis in clinically apparent internal mammary lymph node(s), in the absence of axillary lymph node metastasis
pN3	Metastasis in 10 or more ipsilateral axillary lymph nodes; or in infraclavicular lymph nodes; or in clinically apparent ipsilateral internal mammary lymph nodes in the presence of one or more positive axillary lymph nodes; or in more than 3 axillary lymph nodes with clinically negative, microscopic metastasis in internal mammary lymph nodes; or in ipsilateral supraclavicular lymph nodes
pN3a	Metastasis in 10 or more axillary lymph nodes (at least one larger than 2 mm) or metastasis in infraclavicular lymph nodes
pN3b	Metastasis in clinically apparent internal mammary lymph node(s) in the presence of one or more positive axillary lymph node(s); or metastasis in more than 3 axillary lymph nodes and in internal mammary lymph nodes with microscopic metastasis detected by sentinel lymph node dissection but not clinically apparent
pN3c	Metastasis in supraclavicular lymph node(s)

Note: * Cases with only isolated tumour cells (ITC) in regional lymph nodes are classified as pN0. ITC are single tumour cells or small clusters of cells, not more than 0.2 mm in greatest dimension, that are usually detected by immunohistochemistry or molecular methods but which may be verified on H&E stains. ITCs do not typically show evidence of metastatic activity (e.g., proliferation or stromal reaction).
** not clinically apparent = not detected by clinical examination or by imaging studies (excluding lymphoscintigraphy).
*** clinically apparent = detected by clinical examination or by imaging studies (excluding lymphoscintigraphy) or grossly visible pathologically.

pM – Distant Metastasis

The pM categories correspond to the M categories.

TNM 2018



Consenso Mexicano sobre diagnóstico y tratamiento del cáncer mamario

Séptima revisión
Colima **2017**

ELSEVIER

IMSS · ISSTE · SALUD · Secretaría de Salud · CMO · Consenso mexicano sobre diagnóstico y tratamiento del cáncer mamario · SMeO · Asociación Mexicana de Mastología A.C. · Hospital General de México · FUCAM A.C.

http://consensocancermamario.com

LESIONES PRECURSORAS

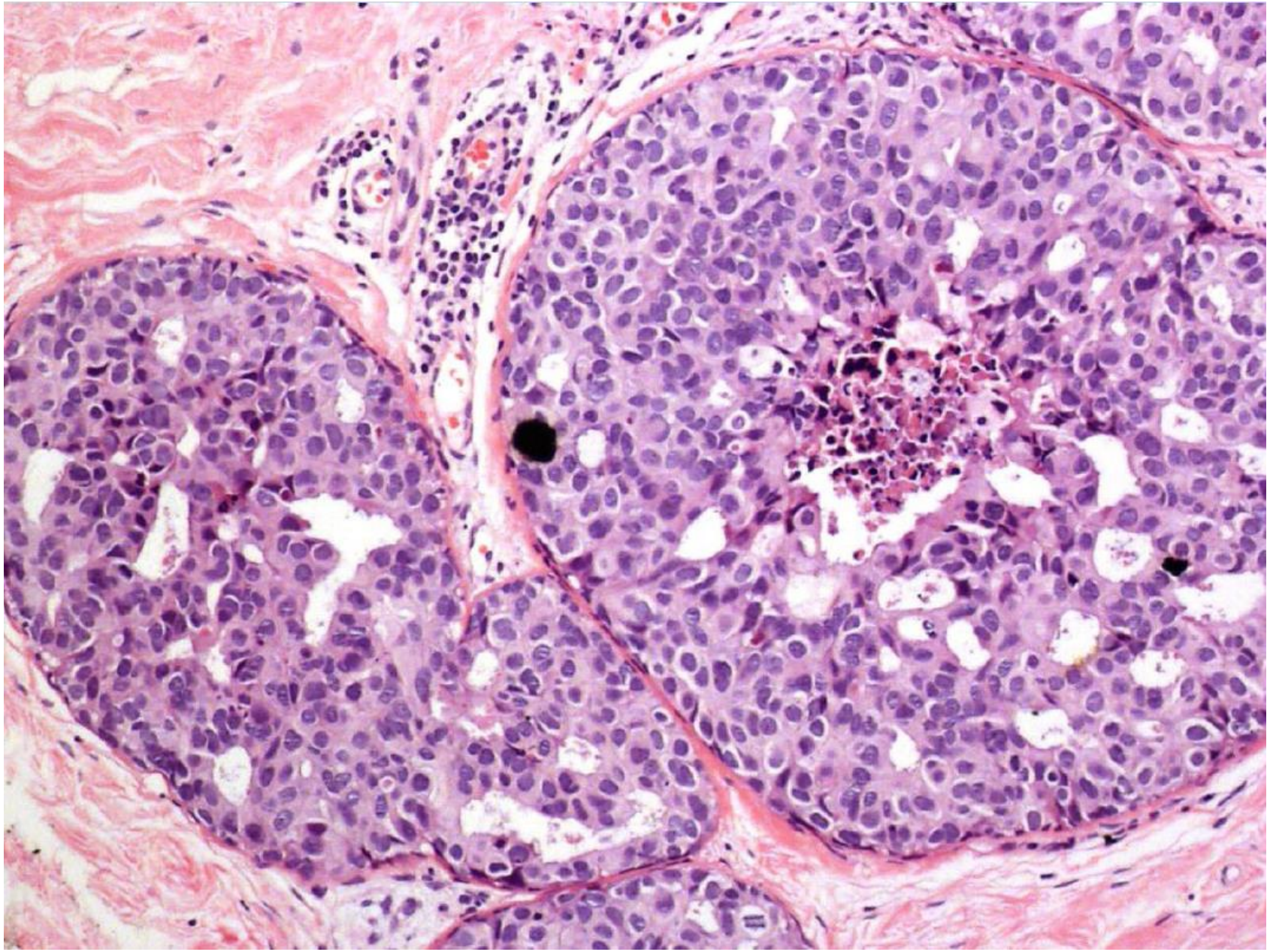
- Grupo de lesiones con proliferación celular de características citológicas y arquitectural diversa
- Origen en la unidad terminal ducto-lobular
- Confinadas en sistema mamario ducto-lobular
- Asociadas con incremento en riesgo de desarrollar carcinoma invasor

Sunil R. Lakhani, et. al.
WHO Classification of Tumor of the Breast.
4ª ed, 2012

CARCINOMA DUCTAL IN SITU

- Proliferación neoplásica de células epiteliales con atipia
- Confinada al sistema mamario ducto-lobular
- Diagnóstico de 20-25% con métodos actuales de pesquisa

Sunil R. Lakhani, et. al.
WHO Classification of Tumor of the Breast.
4ª ed, 2012



CARCINOMA DUCTAL IN SITU

- Clasificación y grado
  - Bajo grado nuclear
  - Intermedio grado nuclear
  - Alto grado nuclear
- Se recomienda incluir hallazgo de necrosis, patrón arquitectural, polarización celular, tamaño/extensión, localización de calcificaciones, estado de márgenes quirúrgicos

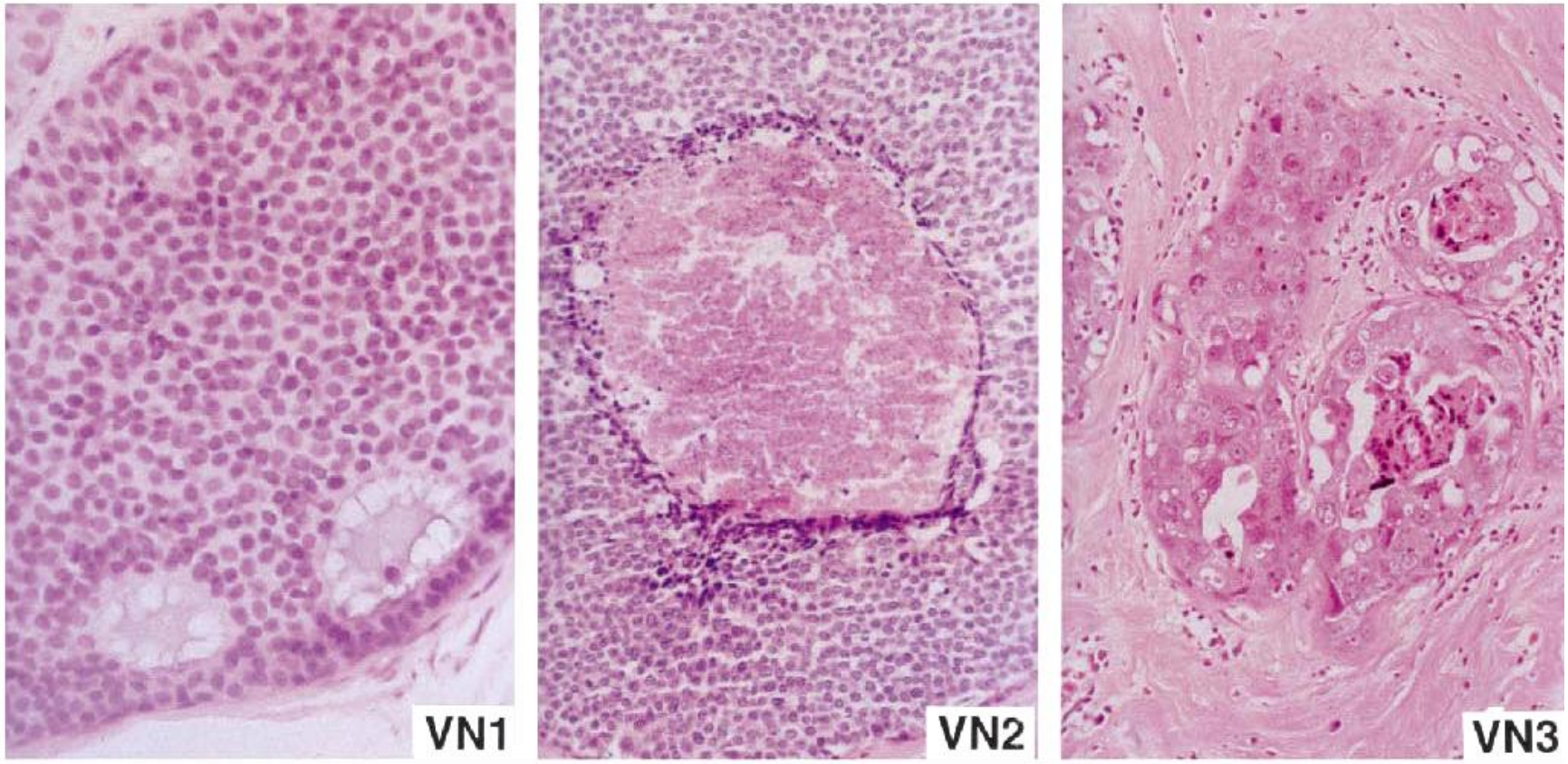
Sunil R. Lakhani, et. al.
WHO Classification of Tumor of the Breast.
4ª ed, 2012

CARCINOMA DUCTAL IN SITU

- Derterminar las características histológicas del CDIS es importante porque:
  - Determina el manejo clínico-quirúrgico
  - Se correlaciona con recurrencia local
  - Se correlaciona con enfermedad residual

Arch Pathol Lab Med. 2009;133:31–37

INDICE PRONOSTICO DE VAN NUYS



VAN NUYS

Van Nuys Prognostic Index			
Predictor	Score		
	1	2	3
Size of tumour (mm)	≤ 15	16–40	>40
Margin width (mm)	>10	1–10	<1
Grade	Non high grade, no comedo necrosis	Non high grade with comedo necrosis	High grade with or without comedo necrosis

World Journal of Surgical Oncology 2008, 6:61

Tabla 5. Vías oncogénicas en carcinoma ductal *in situ*.

Grado	Alteraciones citogenéticas	Datos histo-patológicos	Evolución	
Bajo grado	Patrón simple de alteraciones genómicas Pérdida 16q Ganancia 1q	Núcleos pequeños grado I Ausencia de necrosis Receptores hormonales positivos	Periodo largo de tiempo 10 a 20 años	Carcinoma invasor bien diferenciado
Alto grado	Patrón complejo de alteraciones genómicas Pérdidas 16q, 11q,14q, 8p, 13q y 18q Ganancias 1q, 17q, 8q, 20q y 5p Amplificaciones 17q12, 17q22-24, 6q22, 8q22,11q13 y 20q13	Grado nuclear alto Presencia de comedo-necrosis Receptores hormonales negativos, HER-2 neu positivo	→ Periodo corto de tiempo 2 a 5 años →	Carcinoma invasor poco diferenciado

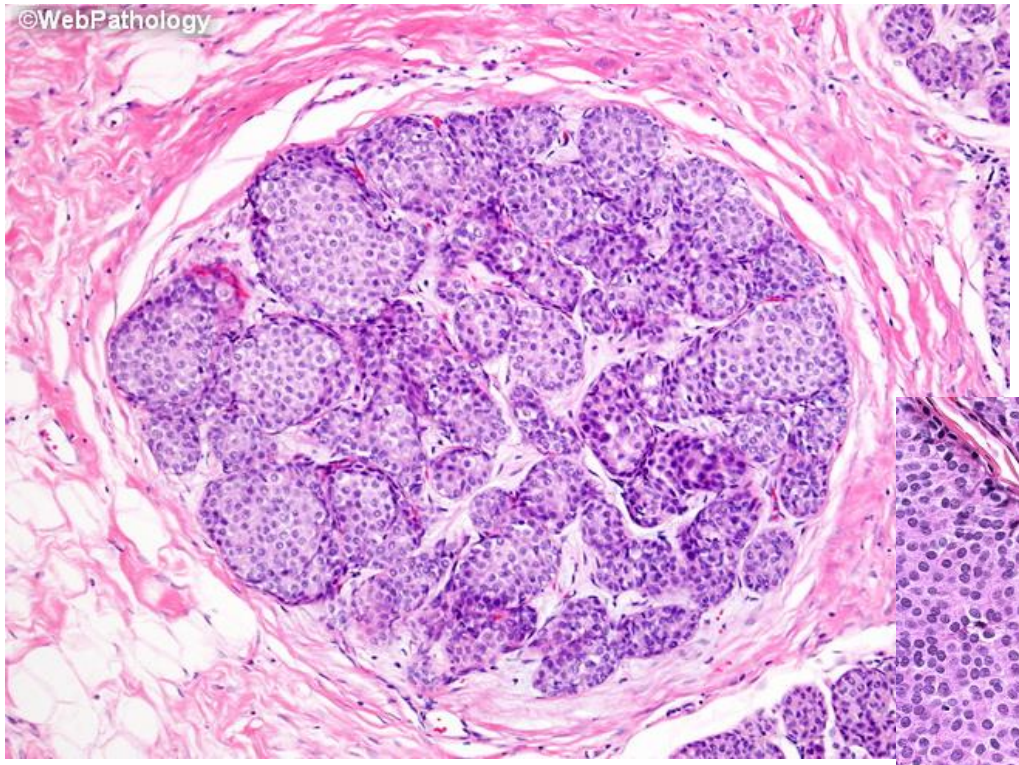
Consenso 2017

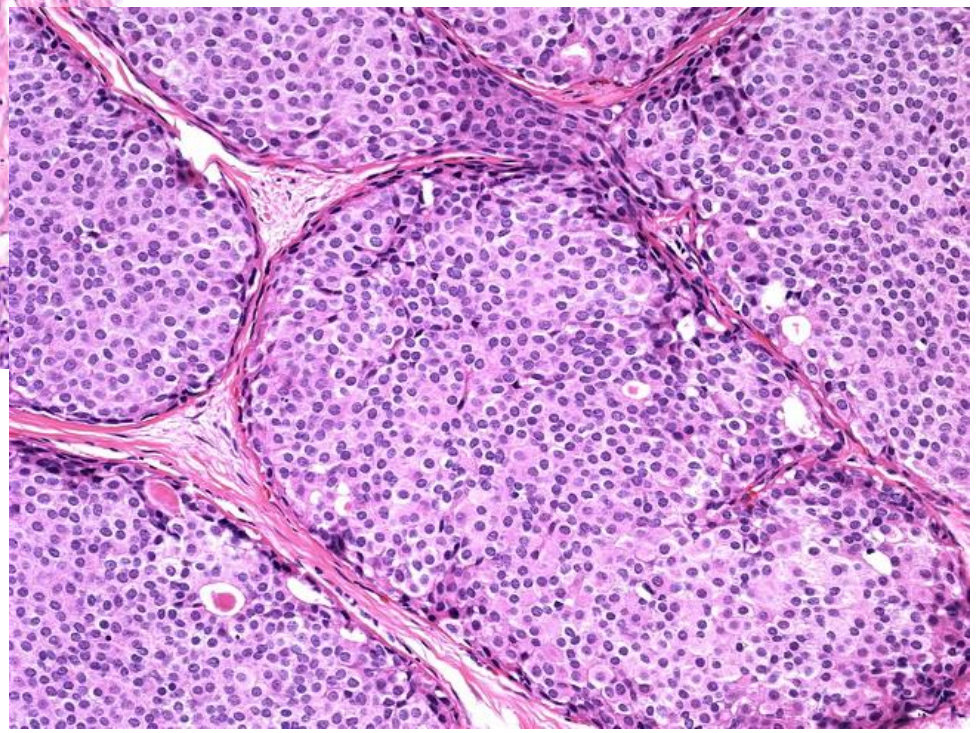
CARCINOMA LOBULAR IN SITU

- Lesión epitelial atipica confinada en la unidad terminal ducto-lobular y caracterizada por proliferación de células pequeñas no cohesivas, con/sin invasión pagetoide del ducto terminal
- Hallazgo de 0.5-4% en biopsia
- Series con resultados diversos: 22%-25% lesión de mayor grado en la escisión vs 93% sin lesión

Cancer 2008;112:2152-58

CARCINOMA LOBULAR IN SITU





CARCINOMA LOBULAR IN SITU

- Criterios histológicos:
  - Más de la mitad del acino de una unidad lobular esta distendido y distorsionado
  - Células pequeñas, no cohesivas
  - Núcleo uniforme
  - Variante pleomorfico
  - Ausencia de expresión de E-Caderina

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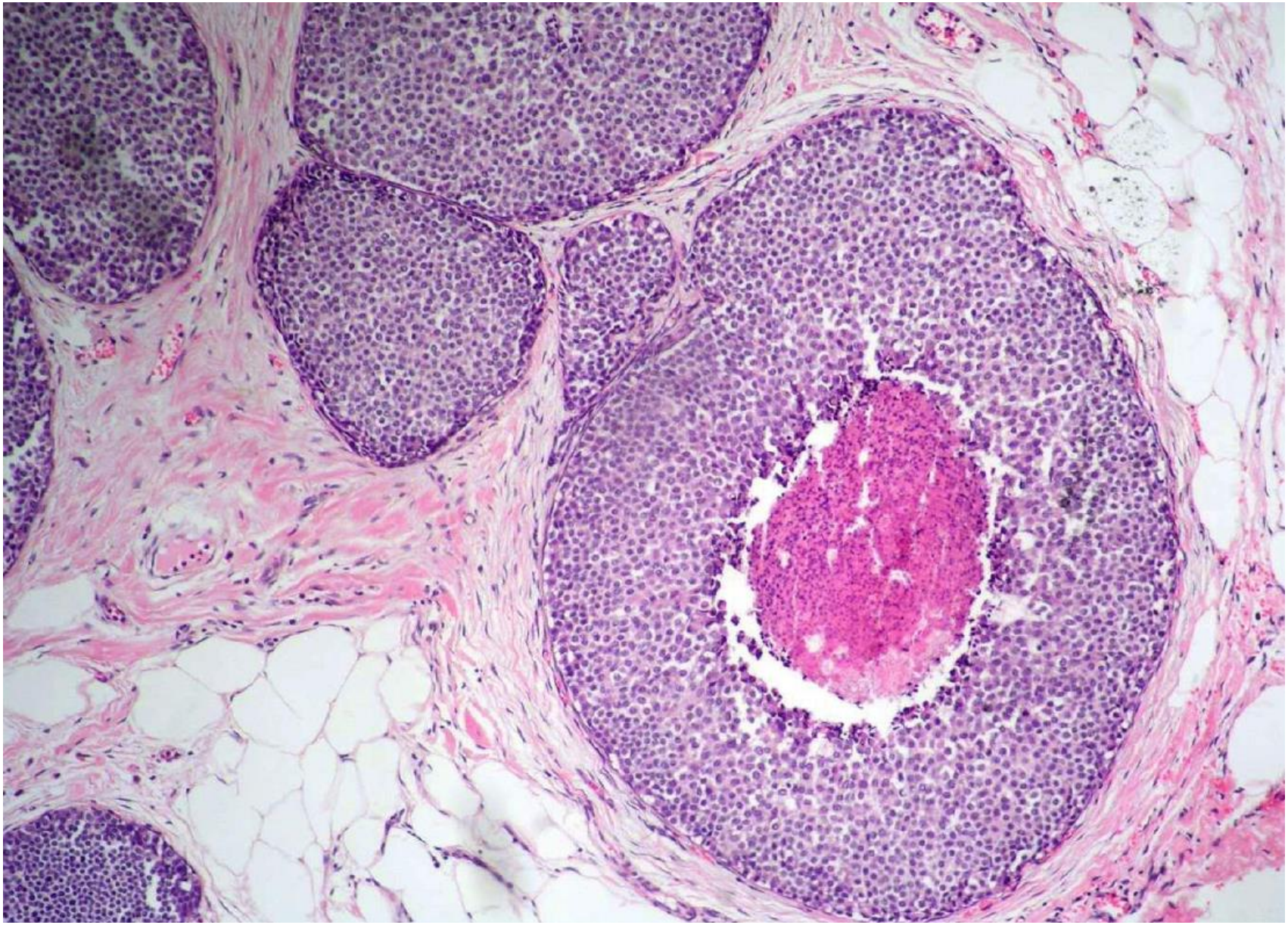
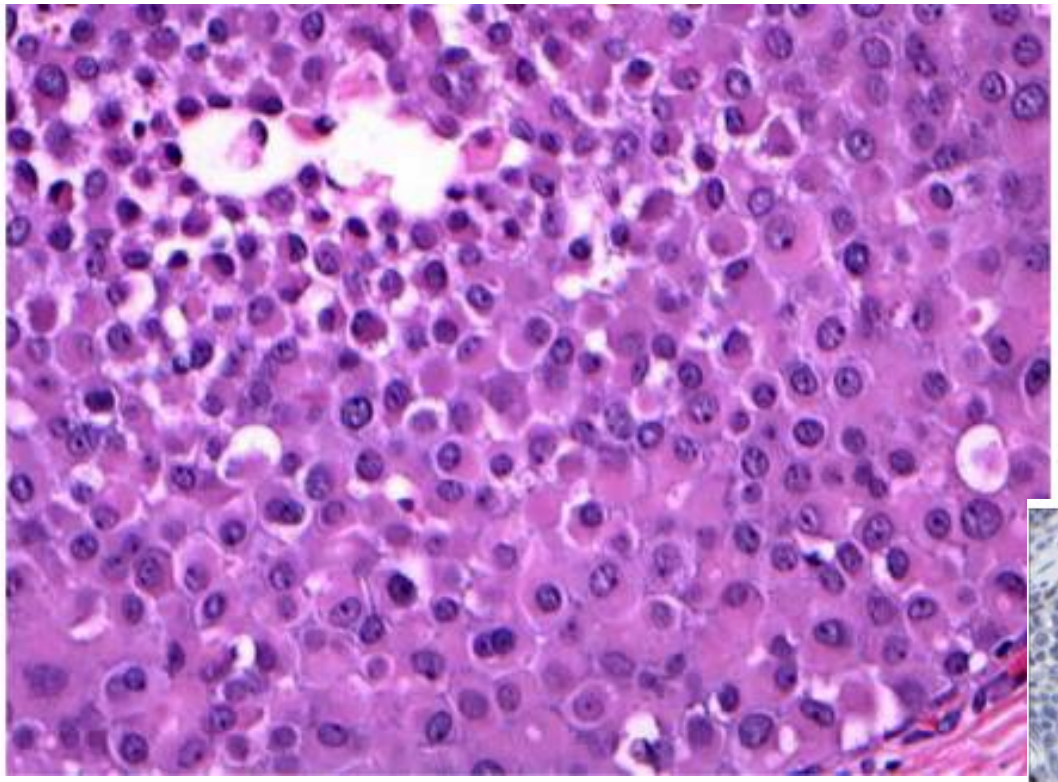
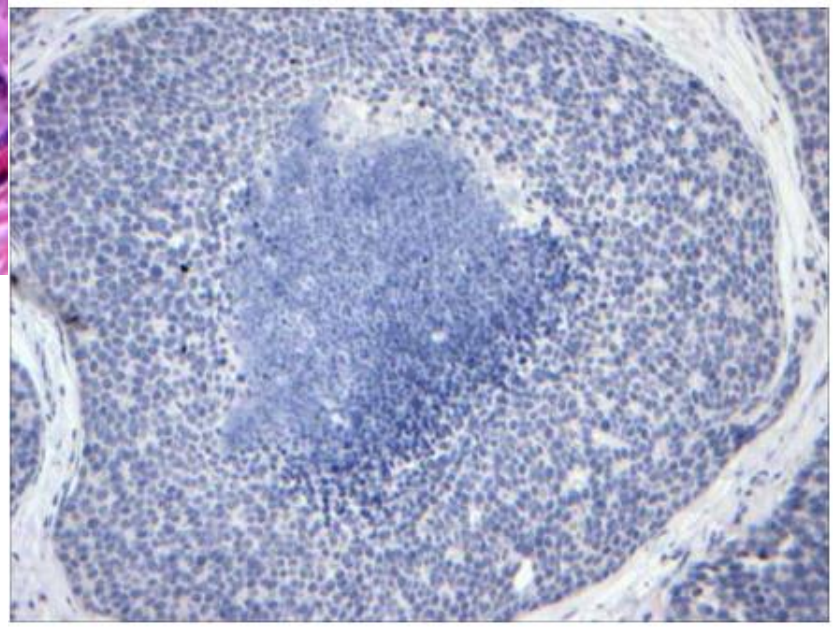
4ª ed, 2012



CARCINOMA LOBULAR IN SITU



Variante Pleomórfica



E-caderina

CARCINOMA INVASOR DE TIPO NO ESPECIAL

- Neoplasia que rompe la unidad lobular e infiltra el estroma
- Sinónimos:
  - Carcinoma ductal infiltrante
  - Carcinoma invasor NOS
  - Carcinoma invasor de tipo no especifico
- 40- 70 %

Sunil R. Lakhani, et. al.
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CARCINOMA INVASOR DE TIPO NO ESPECIAL

- Criterios histológicos:
  - Arquitectura variable: cordones, grupos ó nódulos, trabéculas, sólido ó sincicios, glándulas o estructuras tubulares
  - Citología variable
  - Núcleos con grado variable
  - Actividad mitosica ausente ó extensa
  - Variantes: pleomórfico, osteoclasto-like, coriocarcinomatoso, melanotico

GRADO HISTOLOGICO

Scarff-Bloom-Richardson
Elston&Ellis
Nottingham

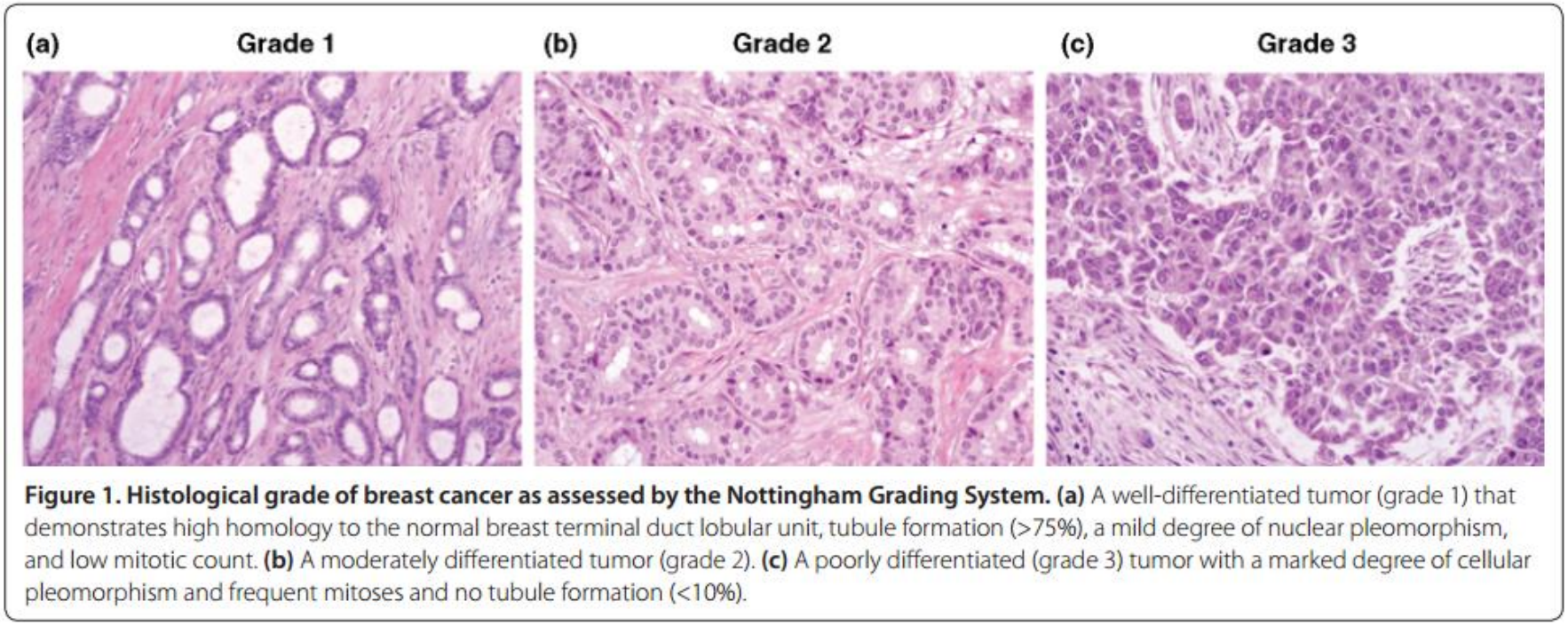

Figure 1. Histological grade of breast cancer as assessed by the Nottingham Grading System. (a) A well-differentiated tumor (grade 1) that demonstrates high homology to the normal breast terminal duct lobular unit, tubule formation (>75%), a mild degree of nuclear pleomorphism, and low mitotic count. **(b)** A moderately differentiated tumor (grade 2). **(c)** A poorly differentiated (grade 3) tumor with a marked degree of cellular pleomorphism and frequent mitoses and no tubule formation (<10%).

Breast Cancer Research 2010, 12:207

GRADO HISTOLOGICO

	Score
TUBULOS Y GLANDULAS	
≥75%	1
10-75%	2
≤10%	3
PLEOMORFISMO NUCLEAR	
Pequeño, regular y uniforme	1
Incremento en tamaño y variabilidad	2
Marcada variación	3
MITOSIS (diámetro de campo)	
<5 / 10 cap	1
5-10 / 10 cap	2
>10 / 10 cap	3
GRADO	**TOTAL**
Grado 1	3-5
Grado 2	6-7
Grado 3	8-9

CARCINOMA INVASOR SUBTIPO ESPECIAL

- Carcinoma lobular invasor
- Carcinoma tubular
- Carcinoma cribiforme
- Carcinoma con características medulares
- Carcinoma metaplasico
- Carcinoma con diferenciación apocrina
- Tumores tipo glándula salival/anexos cutáneos
- Carcinoma adenoideo quistico
- Carcinoma mucoepidermoide
- Carcinoma polimorfo
- Carcinoma mucinoso
- Carcinoma con diferenciación de células en anillo de sello
- Carcinoma con características neuroendocrinas
- Carcinoma papilar invasor
- Carcinoma micropapilar
- Carcinoma inflamatorio
- Carcinoma bilateral y no sincrónico
- Tipos y variantes raros

CARCINOMA LOBULAR INVASOR

- Neoplasia compuesta de células no cohesivas dispersas ó en patrón linear, en un estroma fibroso
- 5-15%
- Subtipos histológicos:
  - Sólido
  - Alveolar
  - Pleomorfico
  - Tubulolobular

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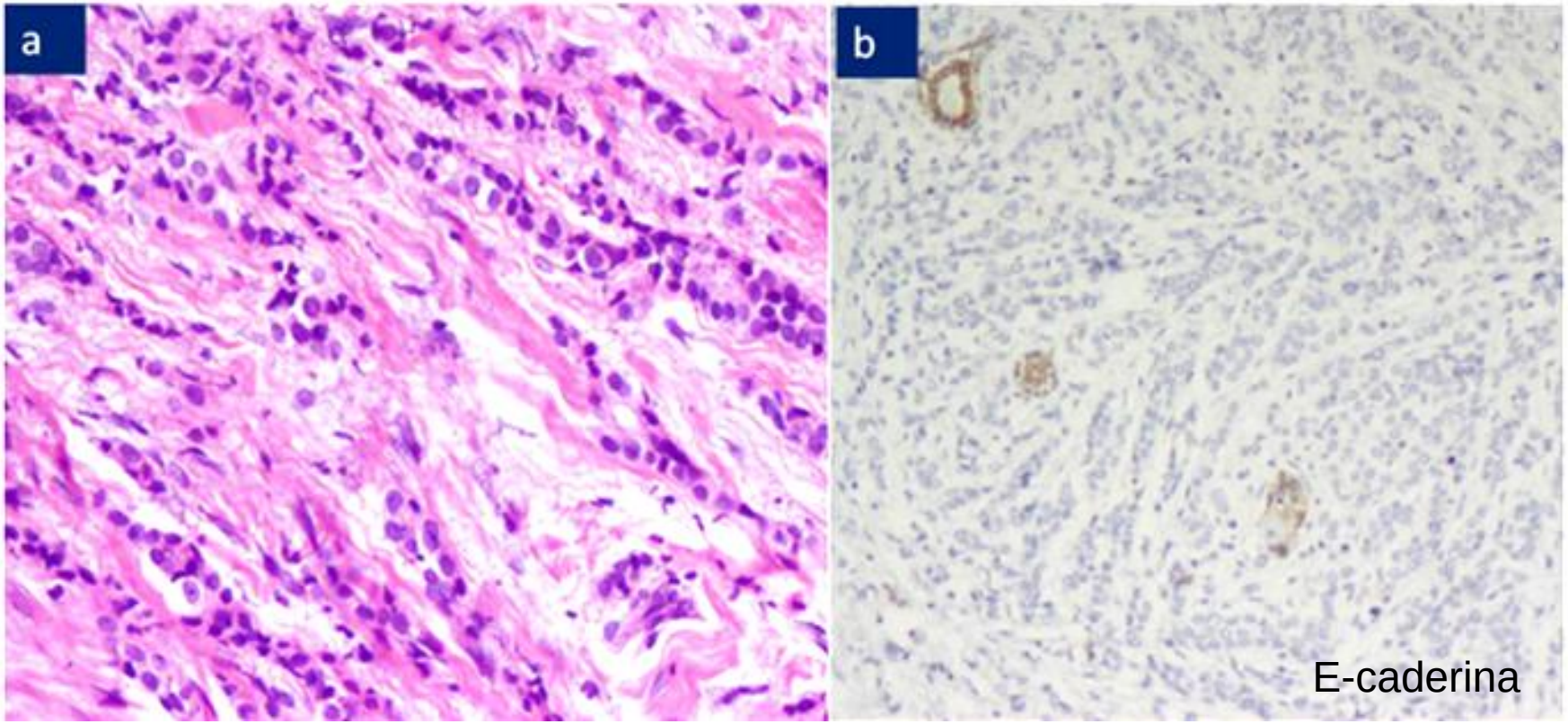
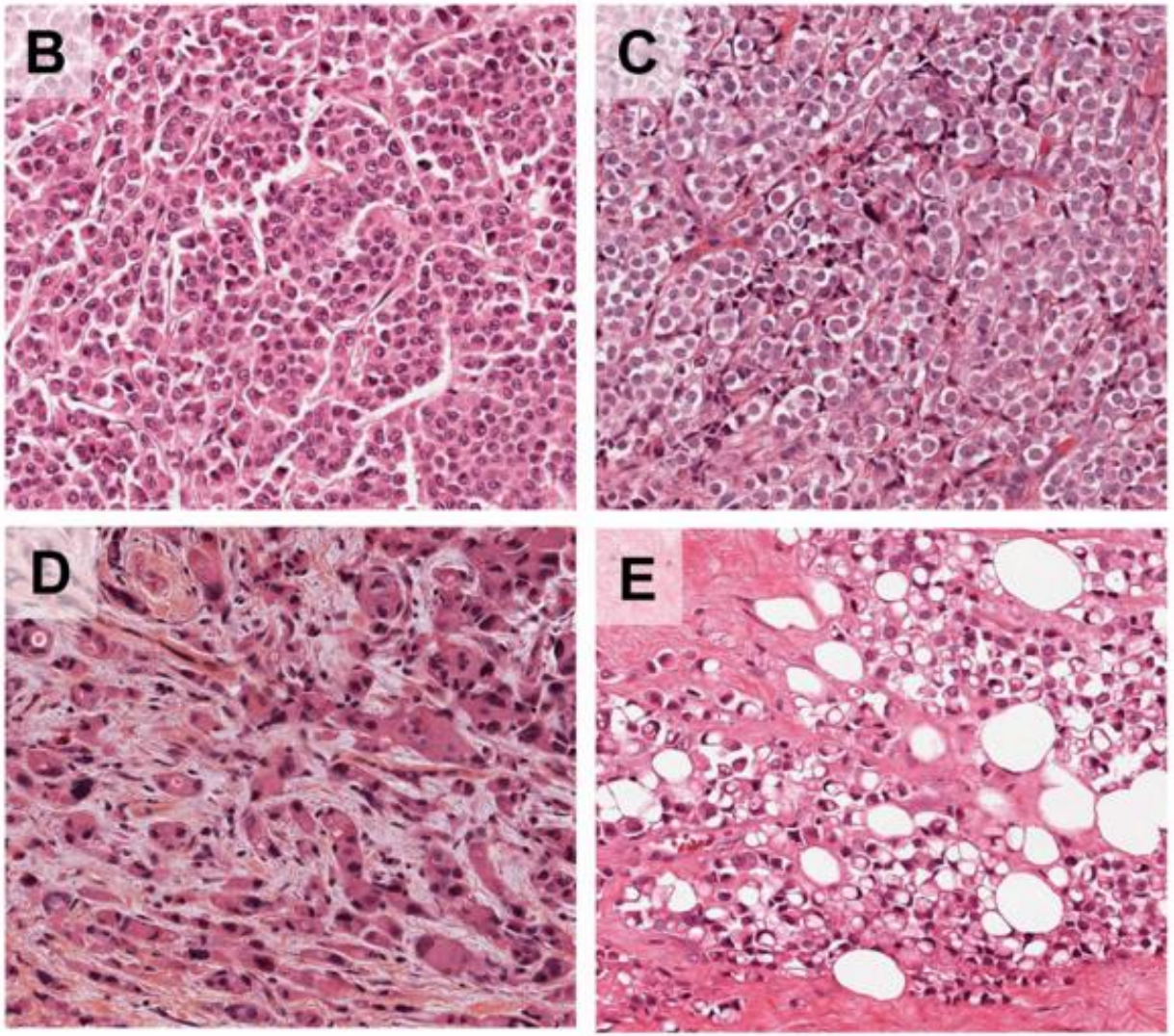
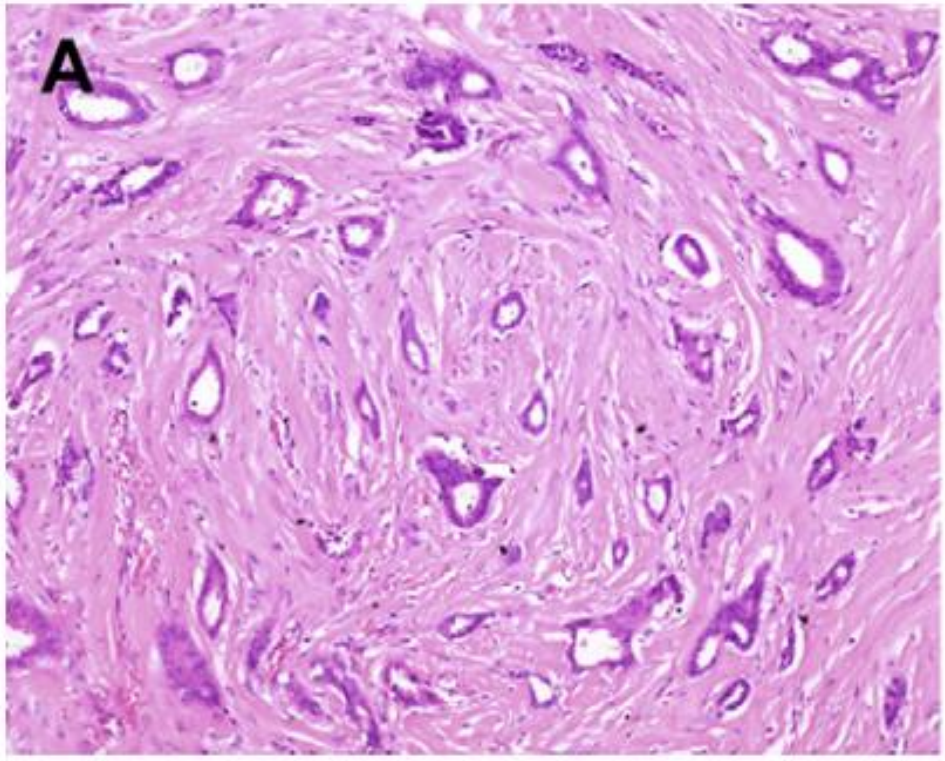
CARCINOMA LOBULAR INVASOR



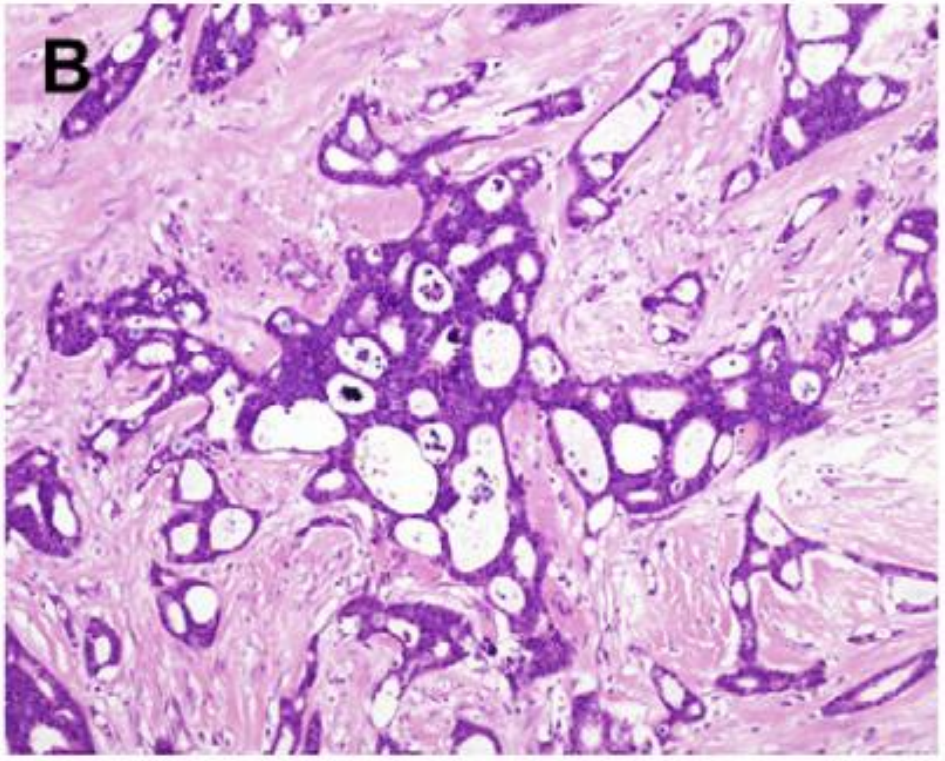
CARCINOMA LOBULAR INVASOR SUBTIPOS



CARCINOMA
SUBTIPO ESPECIAL

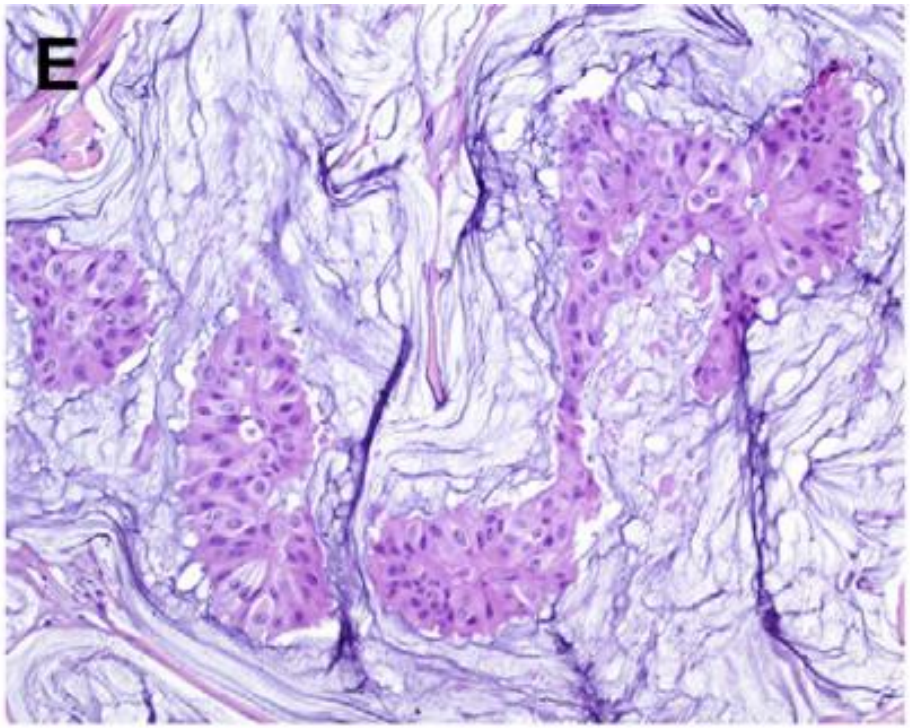


TUBULAR

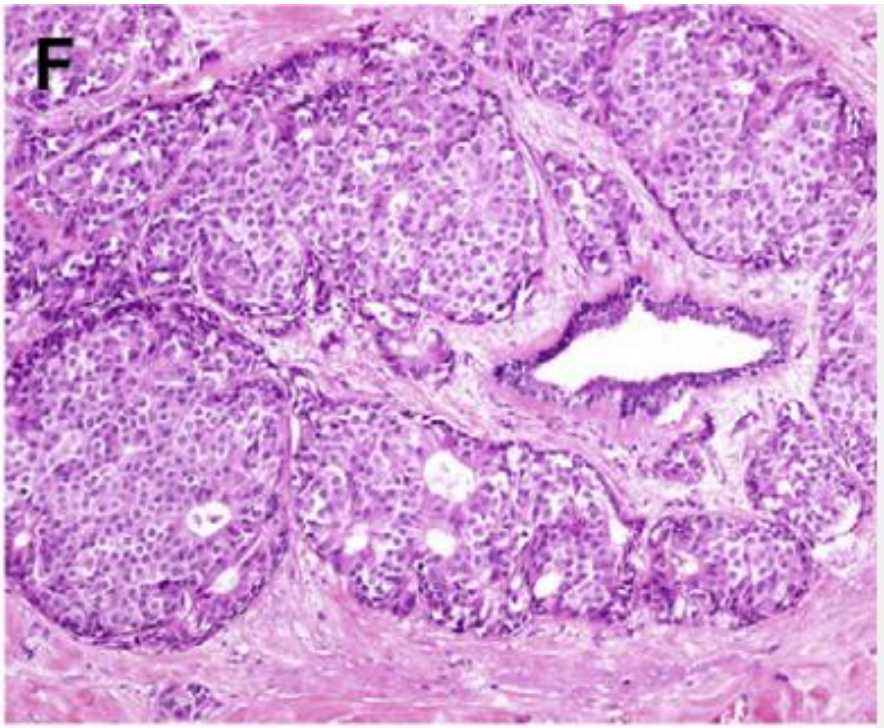


CRIBIFORME

CARCINOMA
SUBTIPO ESPECIAL

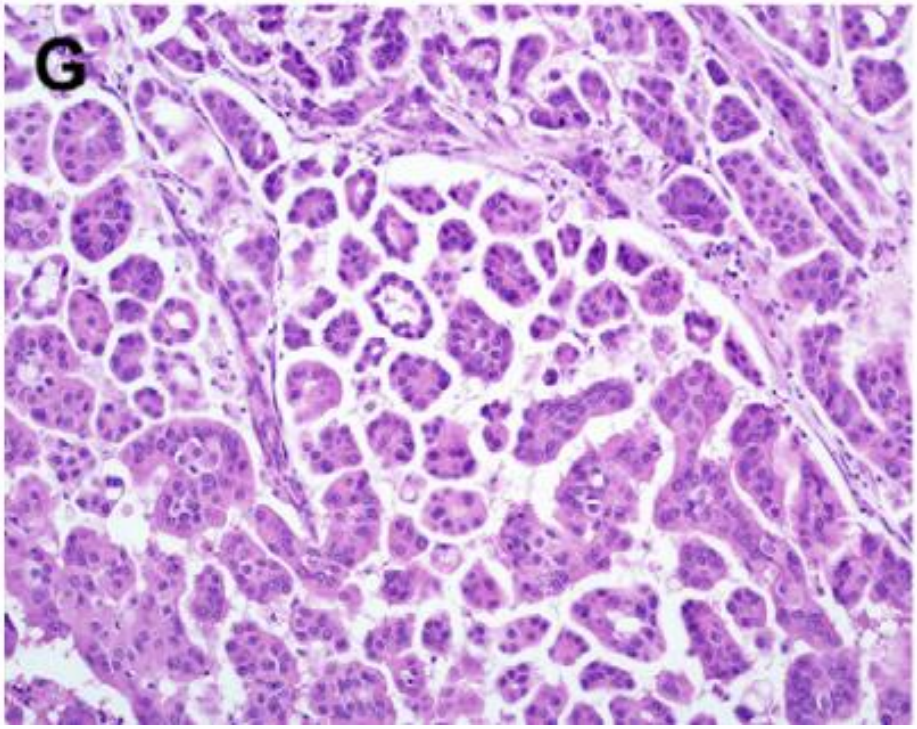


MUCINOSO

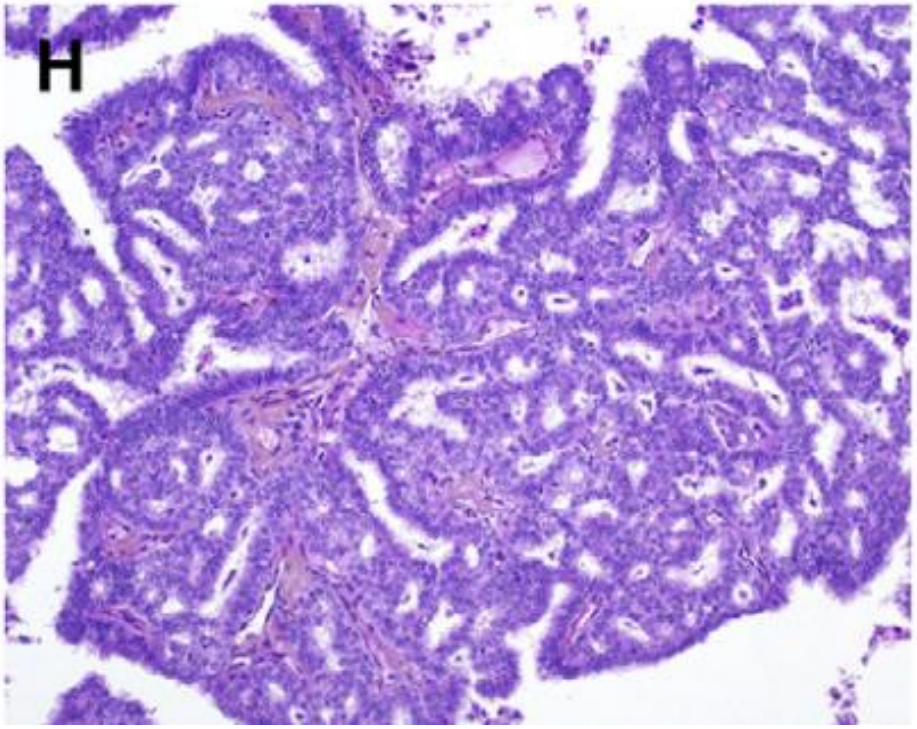


NEUROENDOCRINO

CARCINOMA
SUBTIPO ESPECIAL

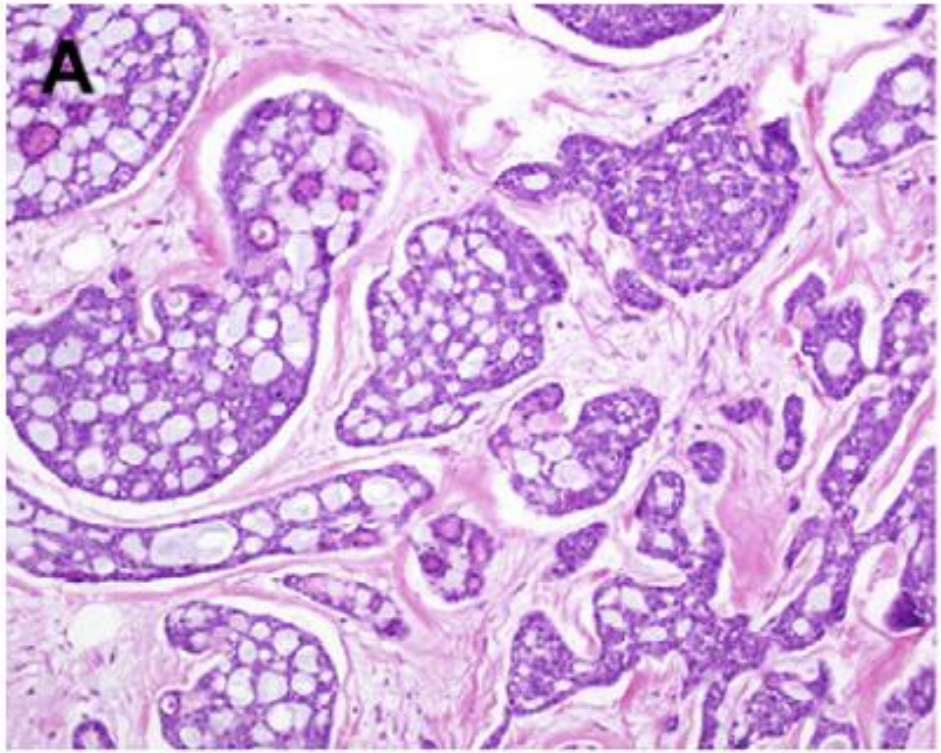


MICROPAPILAR

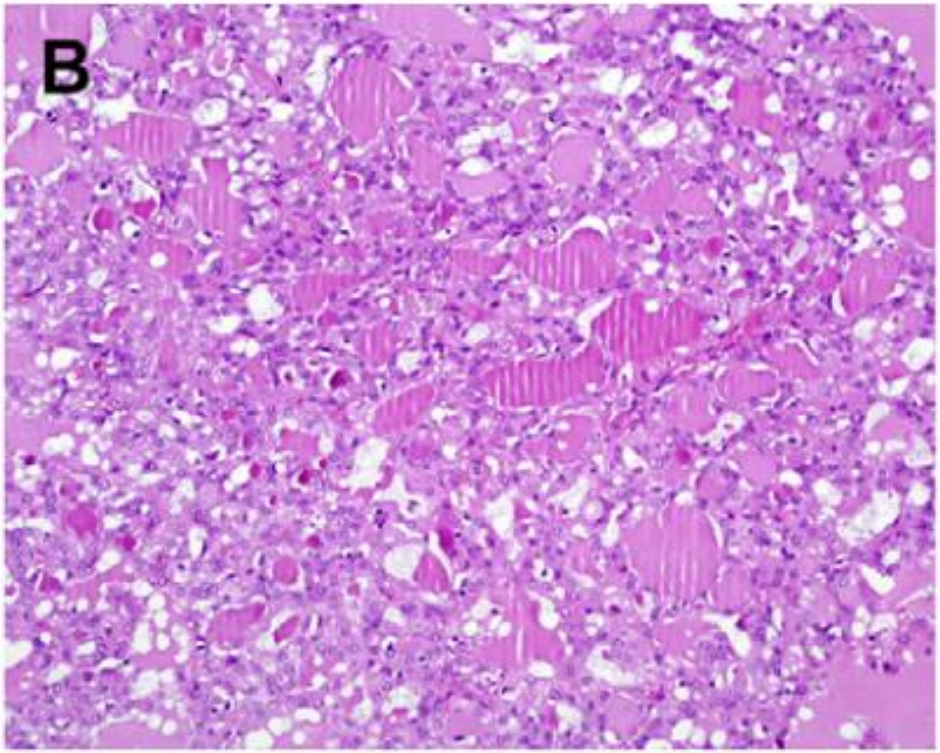


PAPILAR INVASOR

CARCINOMA
SUBTIPO ESPECIAL

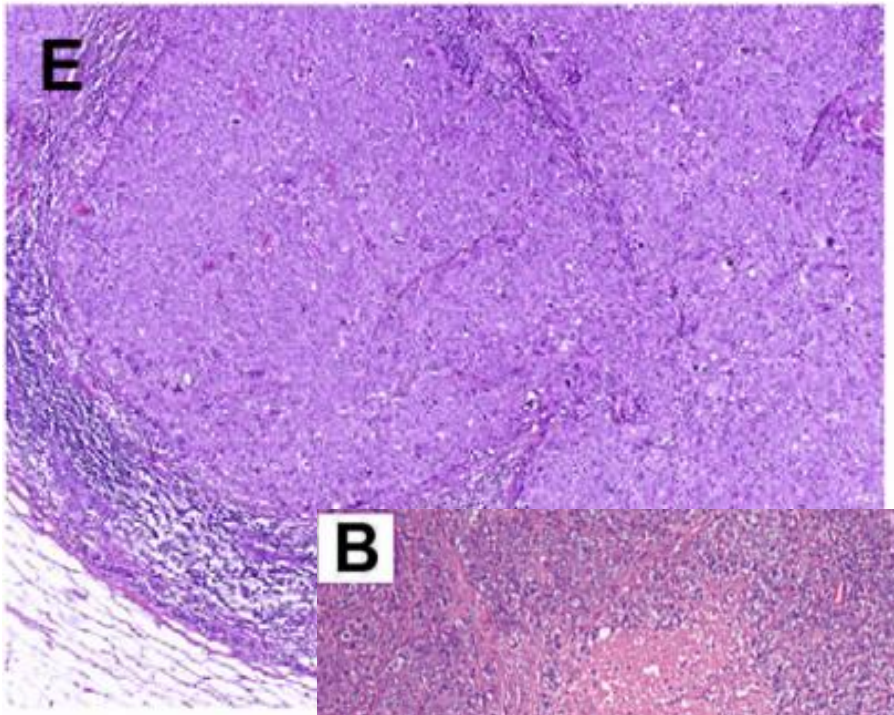


ADENOIDEO
QUISTICO

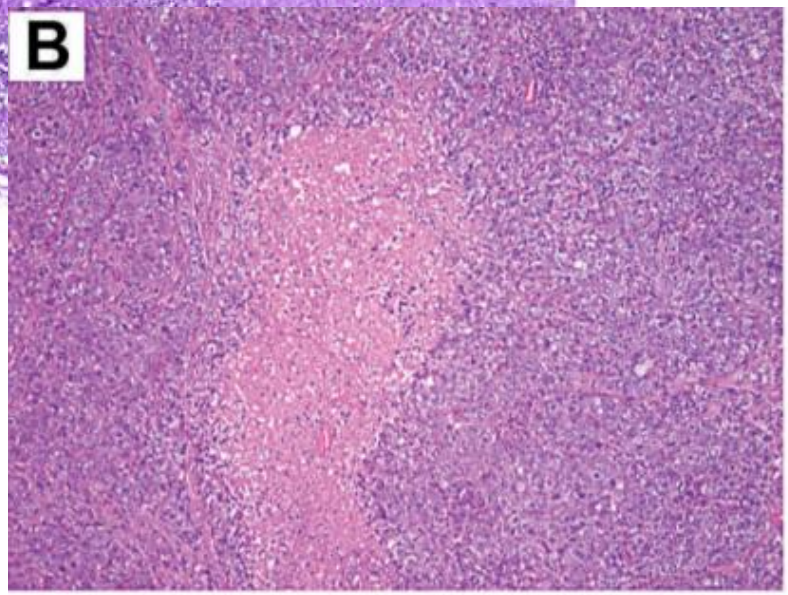


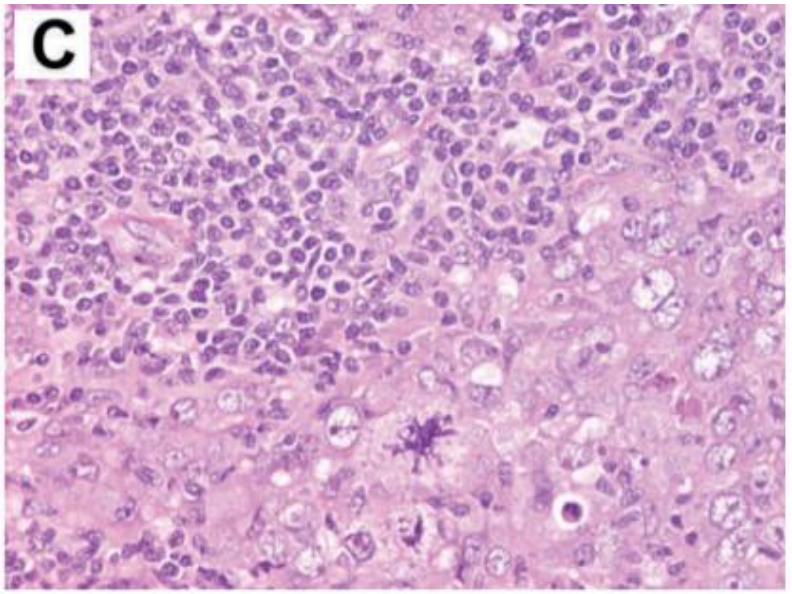
SECRETOR

CARCINOMA
SUBTIPO ESPECIAL



CARCINOMA CON CARACTERISTICAS MEDULARES





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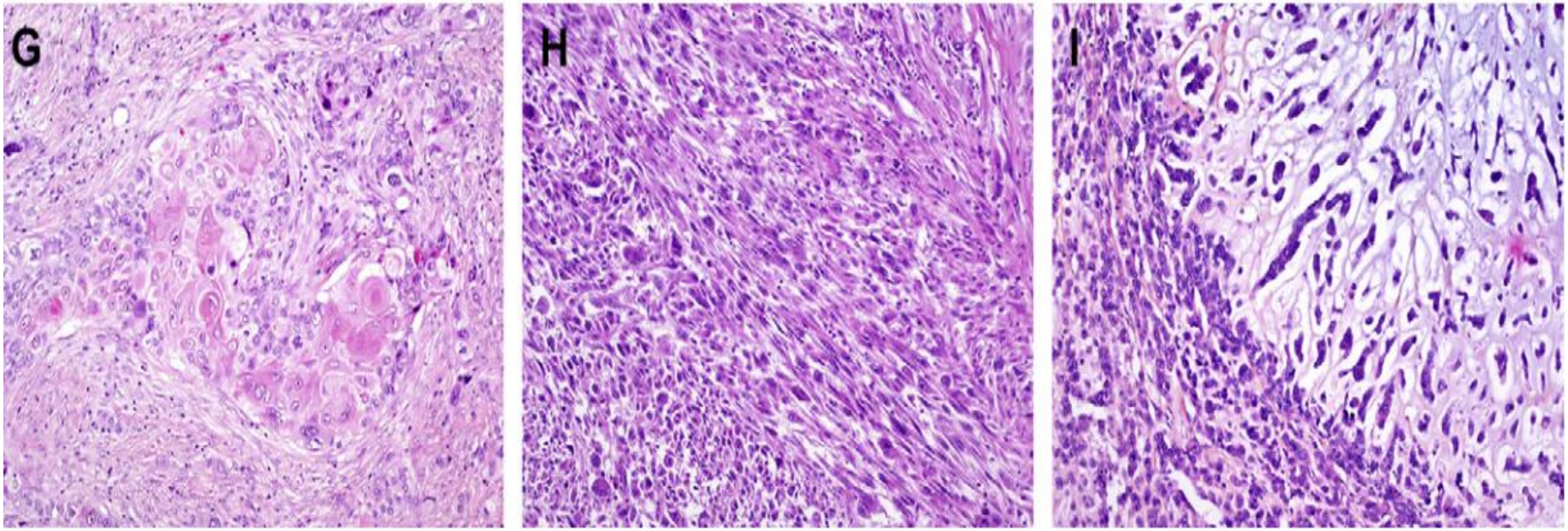
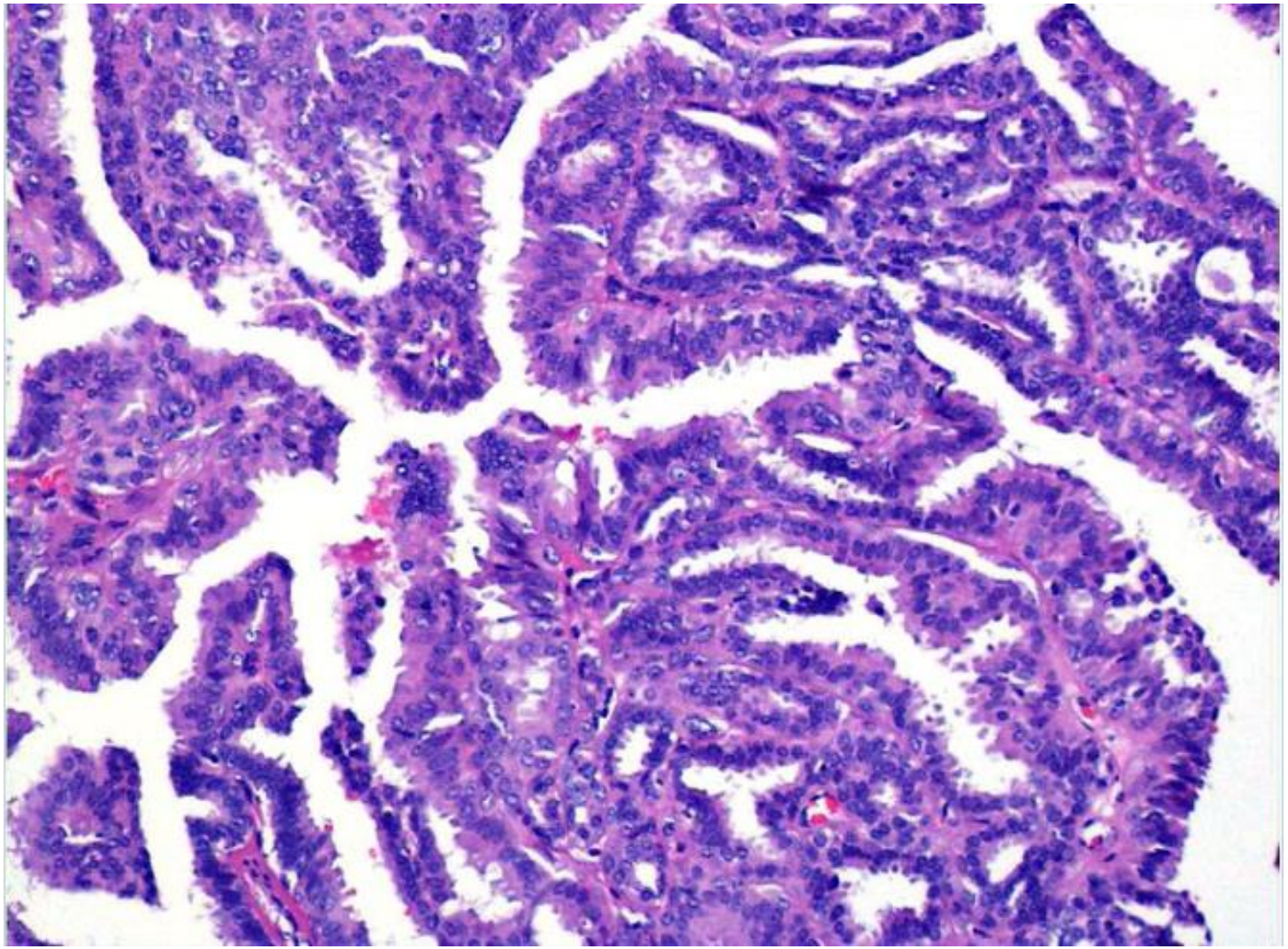


CARCINOMA METAPLASICO

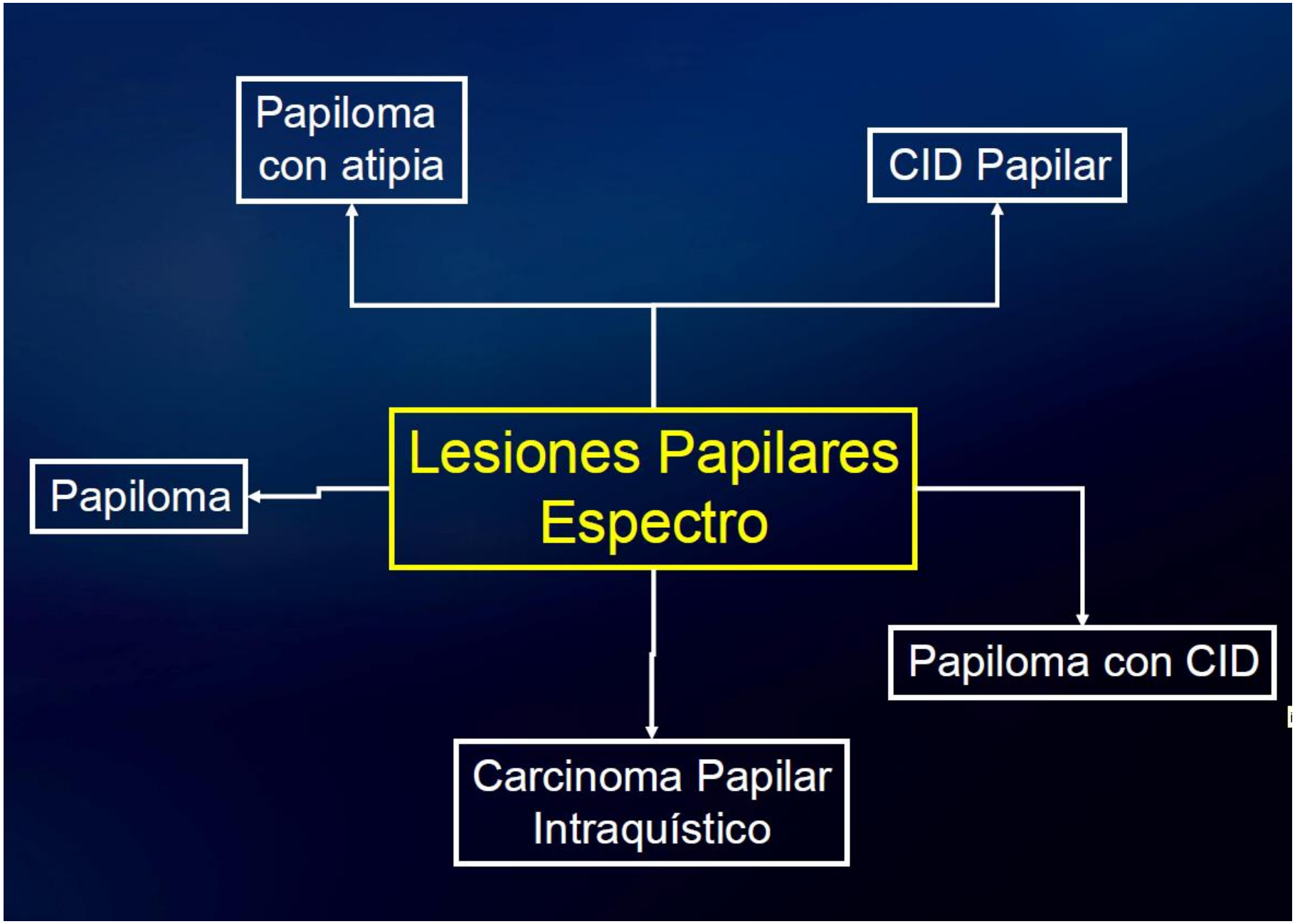
NEOPLASIA PAPILAR



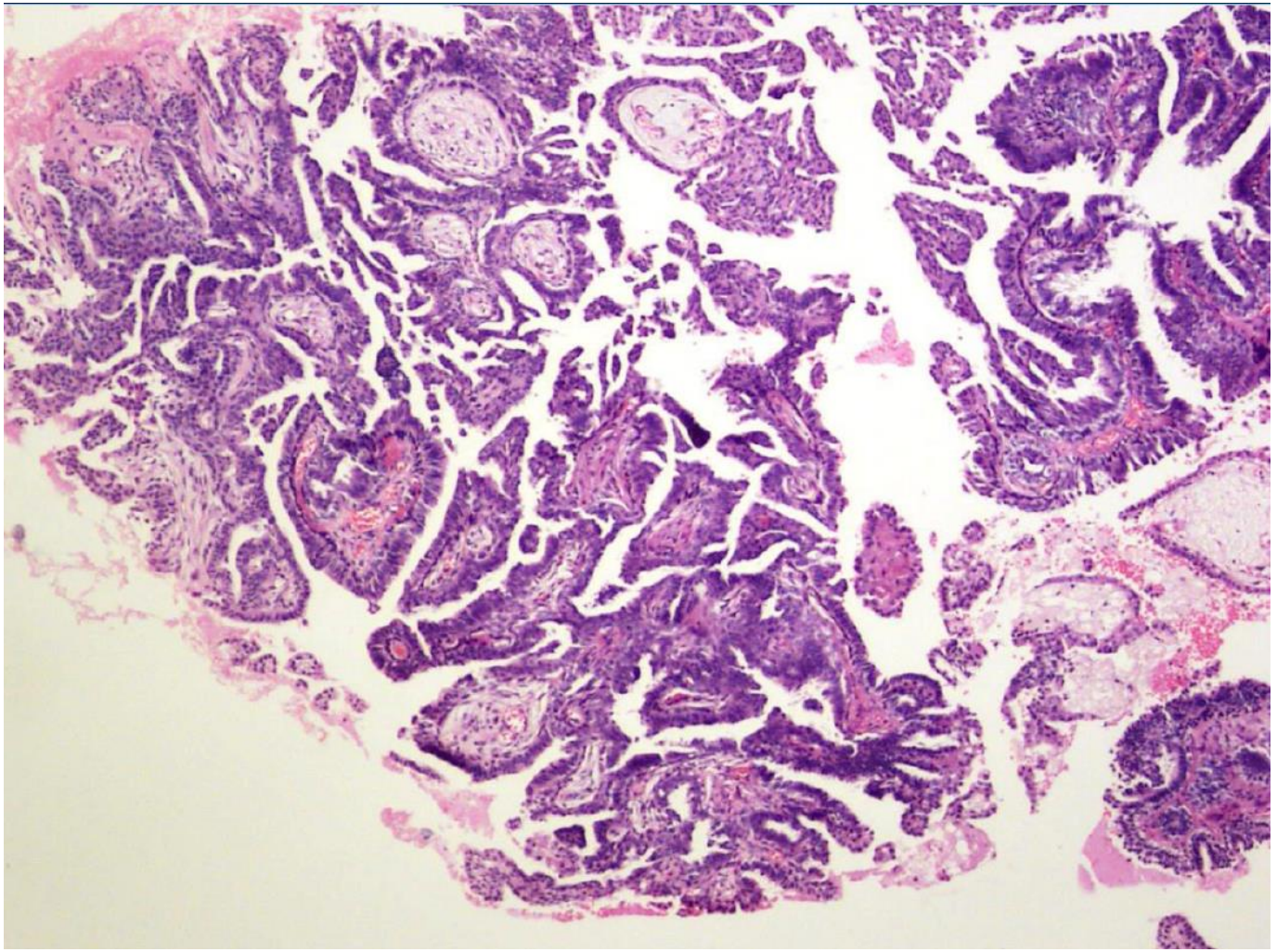
NEOPLASIA PAPILAR

- Varias designaciones para esta lesión y varios tipos
- Naturaleza focal de la atipia
- Multifragmentación secundaria al procedimiento
- Diagnóstico preciso es difícil por el tejido fragmentado y la poca probabilidad de que la porción periférica de la lesión se incluya en el proceso
- Toda lesión papilar con atipia requiere escisión para diagnóstico definitivo

Arch Pathol Lab Med Vol 140, July 2016


Papiloma con atipia
CID Papilar
Lesiones Papilares Espectro
Papiloma
Papiloma con CID
Carcinoma Papilar Intraquístico

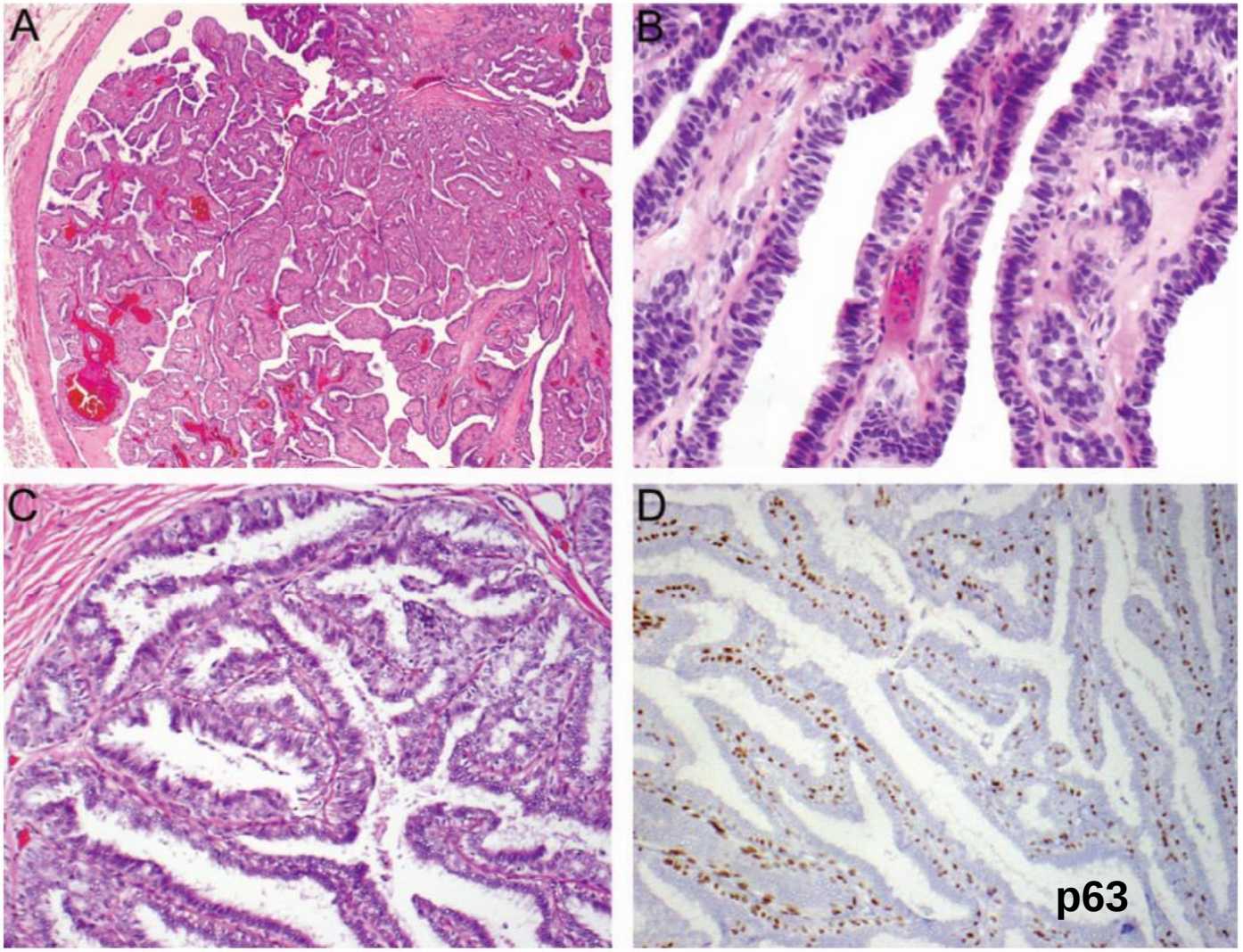
NEOPLASIA PAPILAR



NEOPLASIA PAPILAR

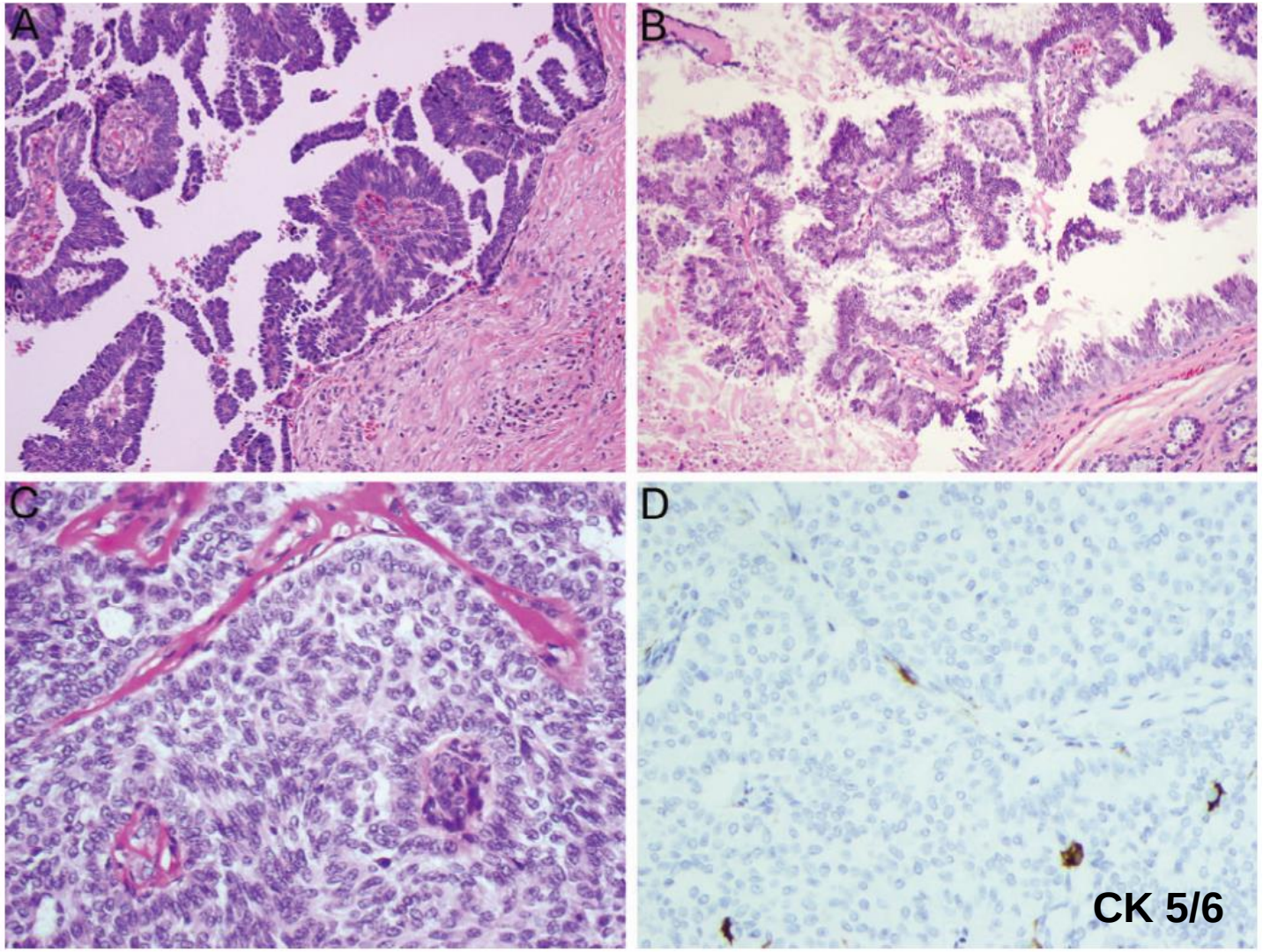
- Frondas papilares-estroma
- Capa de células:
  - Epiteliales (cúbicas/columnares)
  - Mioepiteliales
- Aspecto complejo: sobrecrecimiento de estos elementos
- Valoración asertiva de capsula o pared de ducto
- Marcadores para células mioepiteliales: p63, AML, CK 5/6, CD10

PAPILOMA INTRADUCTAL



Arch Pathol Lab Med Vol 140, July 2016

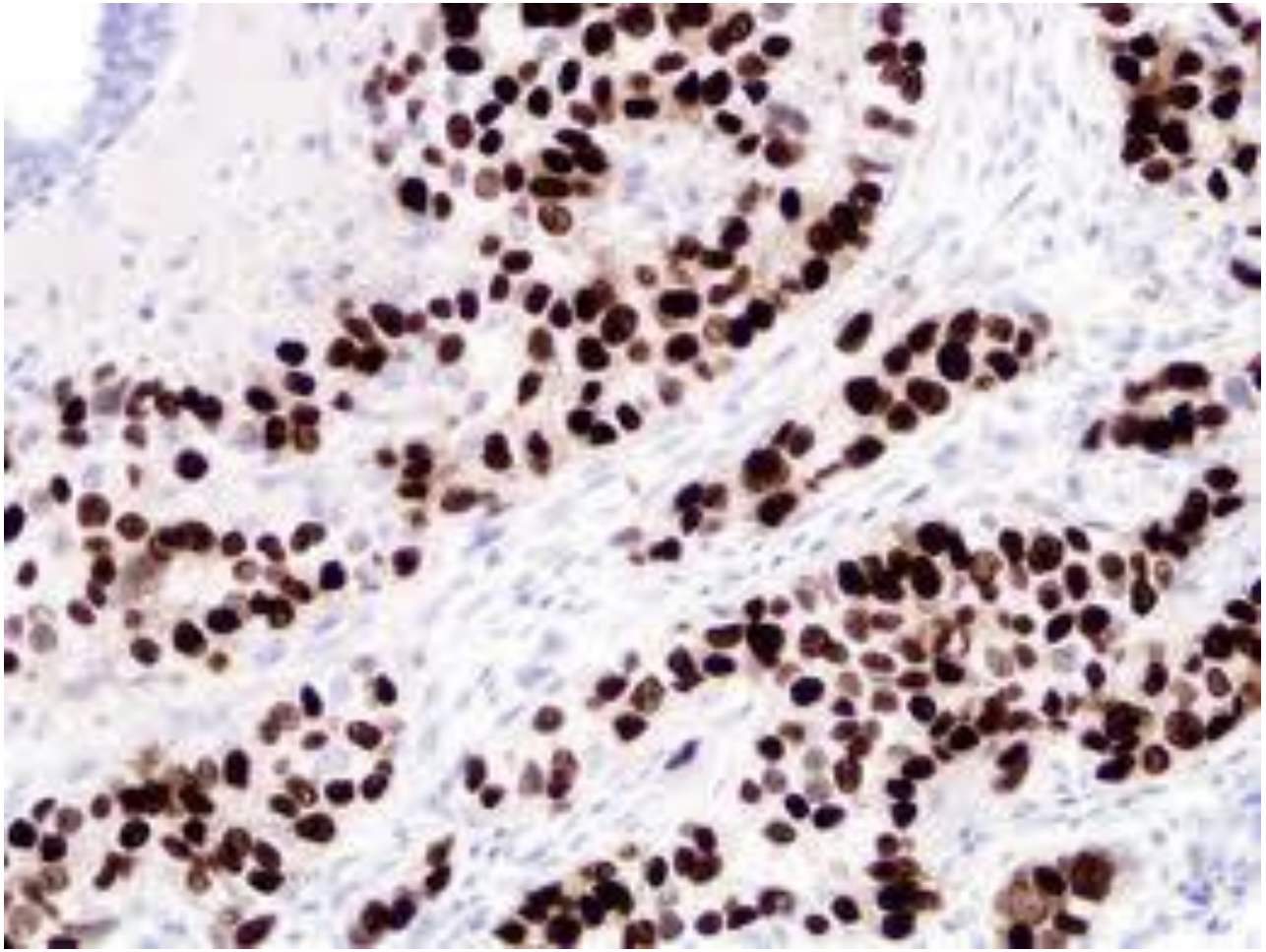
Carcinoma Papilar Intraductal



INMUNOHISTOQUIMICA

- Biomarcadores moleculares
- Receptores hormonales
  - Receptores de estrógeno
  - Receptores de progesterona
- HER-2 (ERBB2)
  - Gen Her-2
  - Receptor del factor de crecimiento de membrana celular
- Factores pronóstico-predictivos

RECEPTORES HORMONALES



RECEPTORES HORMONALES

Special Article

American Society of Clinical Oncology/College of American Pathologists Guideline Recommendations for Immunohistochemical Testing of Estrogen and Progesterone Receptors in Breast Cancer (Unabridged Version)

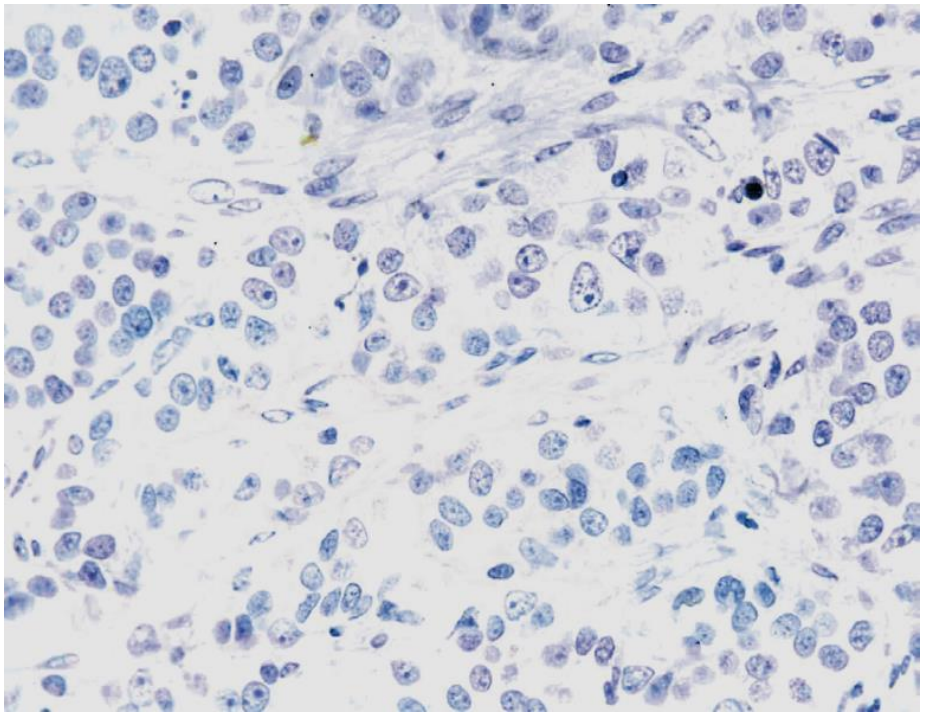
M. Elizabeth H. Hammond; Daniel F. Hayes; Mitch Dowsett; D. Craig Allred; Karen L. Hagerty; Sunil Badve; Patrick L. Fitzgibbons; Glenn Francis; Neil S. Goldstein; Malcolm Hayes; David G. Hicks; Susan Lester; Richard Love; Pamela B. Mangu; Lisa McShane; Keith Miller; C. Kent Osborne; Soonmyung Paik; Jane Perlmutter; Anthony Rhodes; Hironobu Sasano; Jared N. Schwartz; Fred C. G. Sweep; Sheila Taube; Emina Emilia Torlakovic; Paul Valenstein; Giuseppe Viale; Daniel Visscher; Thomas Wheeler; R. Bruce Williams; James L. Wittliff; Antonio C. Wolff

Arch Pathol Lab Med Vol 134, July 2010

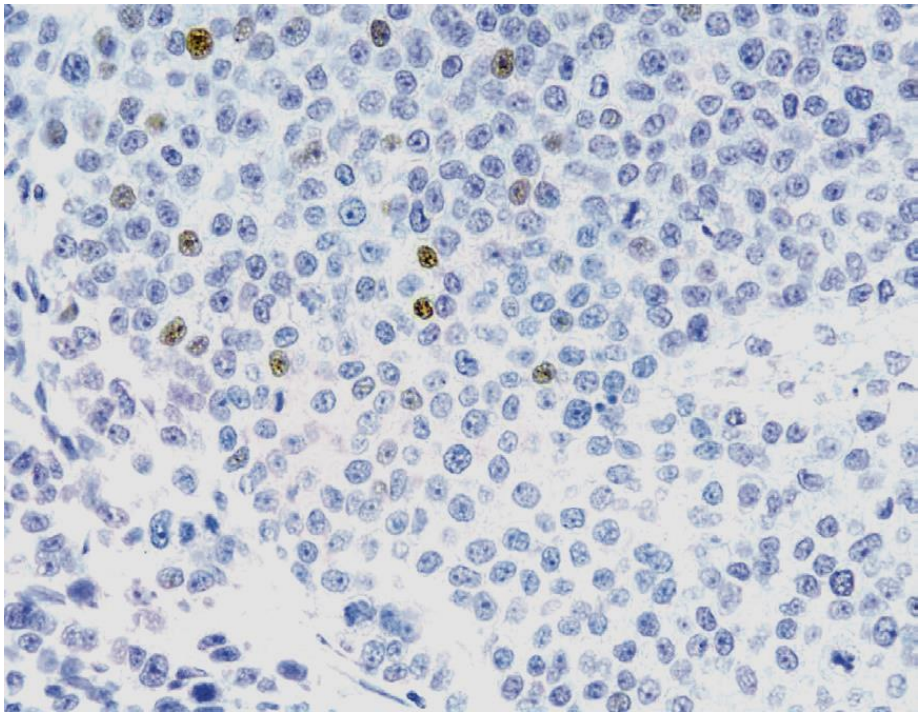
ASCO-CAP score

Porcentaje

Intensidad



Negative



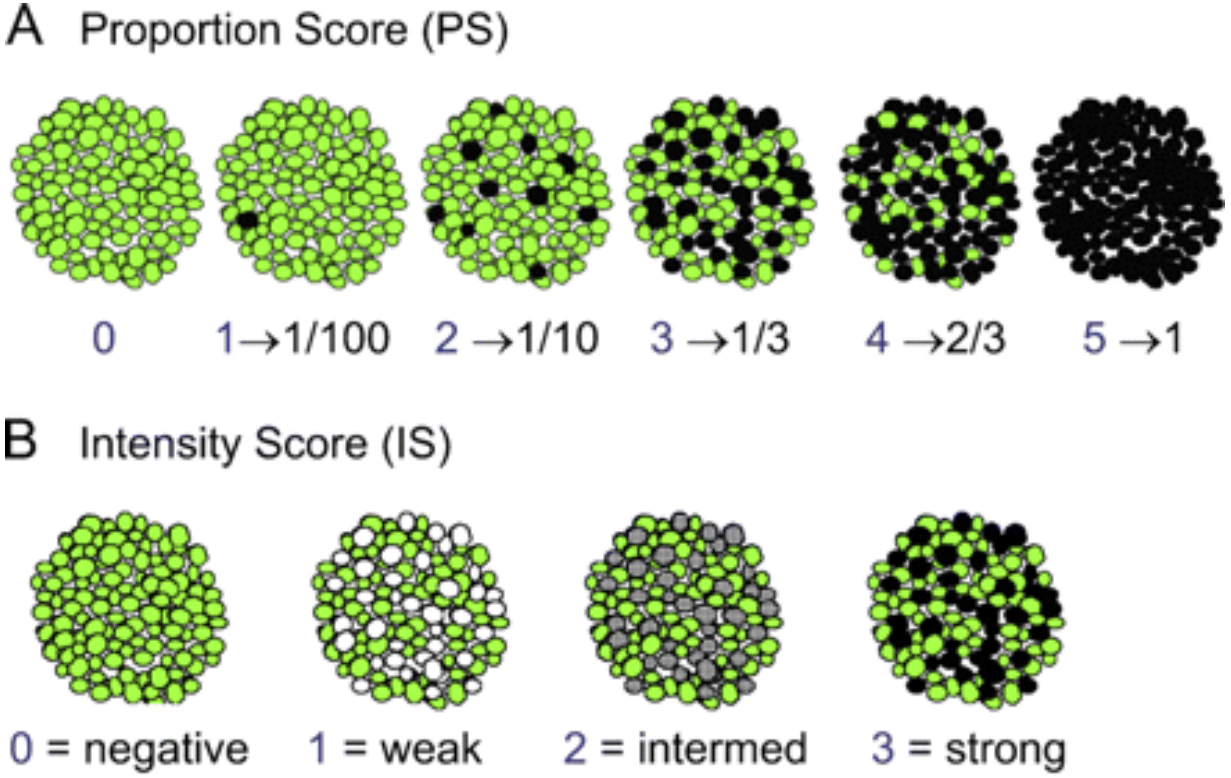
Positivo

ASCO-CAP score

Table 7. Summary of Guideline Recommendations for ER and PgR Testing by IHC in Breast Cancer Patients

	Recommendation	Comments
Optimal algorithm for ER/PgR testing	Positive for ER or PgR if finding of ≥ 1% of tumor cell nuclei are immunoreactive. Negative for ER or PgR if finding of < 1% of tumor cell nuclei are immunoreactive in the presence of evidence that the sample can express ER or PgR (positive intrinsic controls are seen). Uninterpretable for ER or PgR if finding that no tumor nuclei are immunoreactive and that internal epithelial elements present in the sample or separately submitted from the same sample lack any nuclear staining.	These definitions depend on laboratory documentation of the following: 1. Proof of initial validation in which positive ER or PgR categories are 90% concordant and negative ER or PgR categories are 95% concordant with a clinically validated ER or PgR assay.[3] 2. Ongoing internal QA procedures, including use of external controls of variable ER and PgR activity with each run of assay, regular assay reassessment, and competency assessment of technicians and pathologists. 3. Participation in external proficiency testing according to the proficiency testing program guidelines. 4. Biennial accreditation by valid accrediting agency.

ALLRED SCORE



Allred Score = PS + IS (range 0-8)

J Histochem Cytochem 2010; 58 (2): 95-10

HER2

Special Article

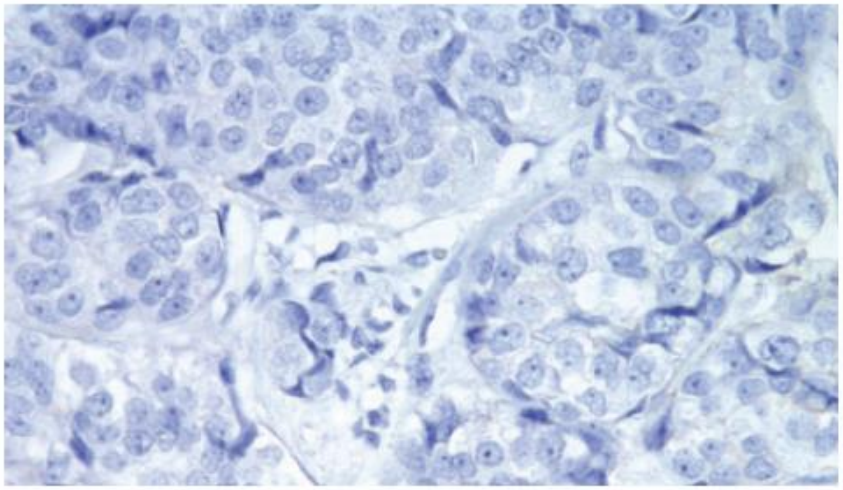
Recommendations for Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer

American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Update

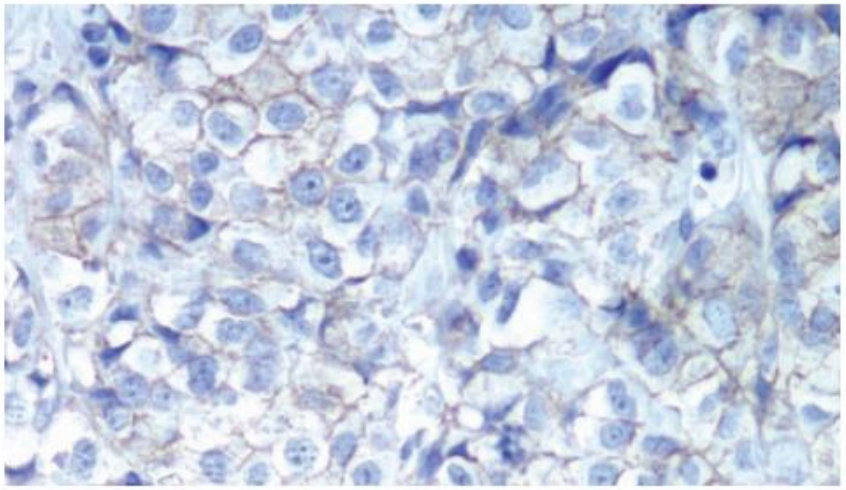
Antonio C. Wolff, M. Elizabeth H. Hammond*, David G. Hicks*, Mitch Dowsett*, Lisa M. McShane*, Kimberly H. Allison, Donald C. Allred, John M.S. Bartlett, Michael Bilous, Patrick Fitzgibbons, Wedad Hanna, Robert B. Jenkins, Pamela B. Mangu, Soonmyung Paik, Edith A. Perez, Michael F. Press, Patricia A. Spears, Gail H. Vance, Giuseppe Viale, and Daniel F. Hayes**

Arch Pathol Lab Med. doi: 10.5858/arpa.2013-0953-SA

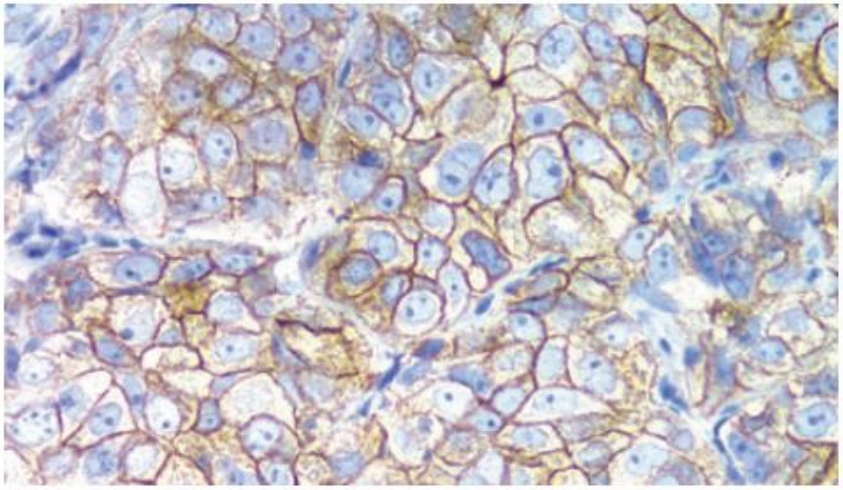
Her-2 SCORE



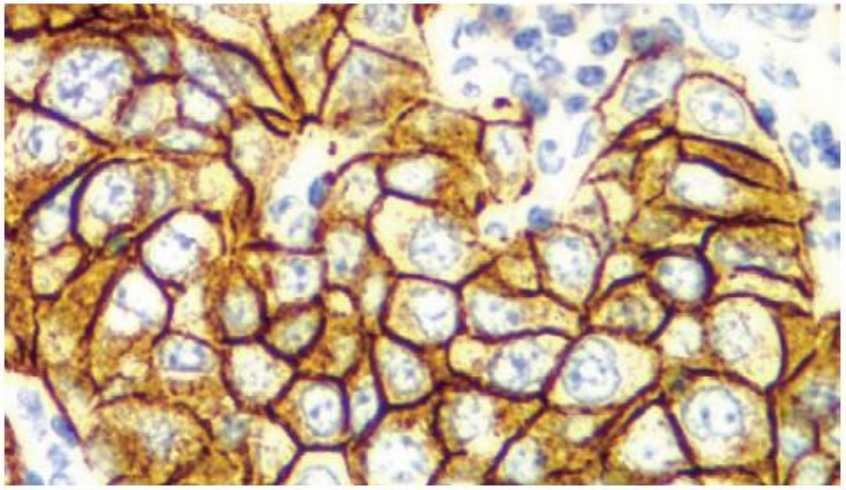
Score: **0** (40x)



Score: **1+** (40x)

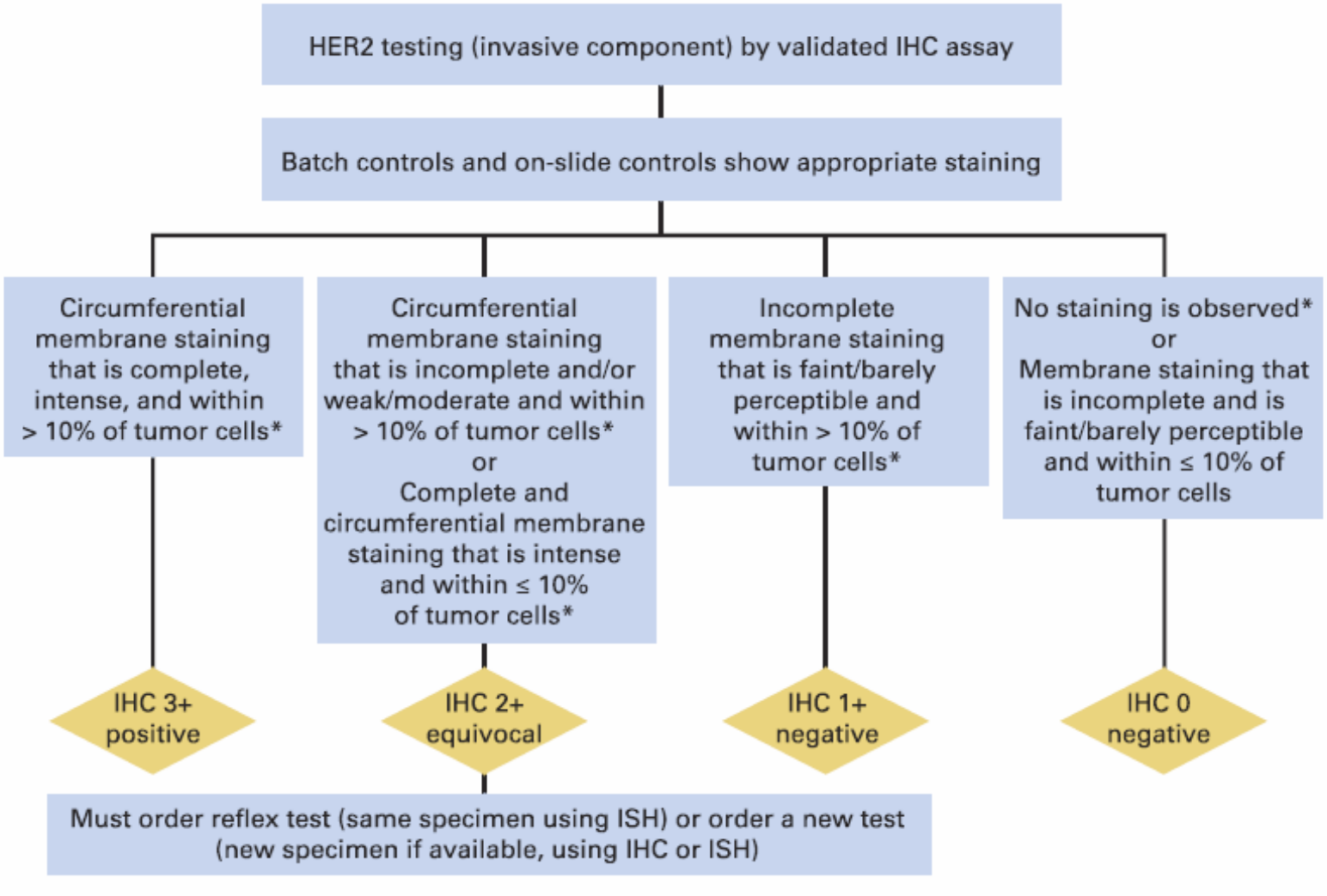


Score: **2+** (40x)



Score: **3+** (40x)

HERCEP-test



ASCO/CAP HER2 Testing Guideline

HIBRIDACION IN SITU HER2

CAP Laboratory Improvement Programs

Template for Reporting Results of Biomarker Testing of Specimens From Patients With Carcinoma of the Breast

Patrick L. Fitzgibbons, MD; Deborah A. Dillon, MD; Randa Alsabeh, MD; Michael A. Berman, MD; Daniel F. Hayes, MD; David G. Hicks, MD; Kevin S. Hughes, MD; Sharon Nofech-Mozes, MD; for the Members of the Cancer Biomarker Reporting Committee, College of American Pathologists

Arch Pathol Lab Med Vol 138, May 2014

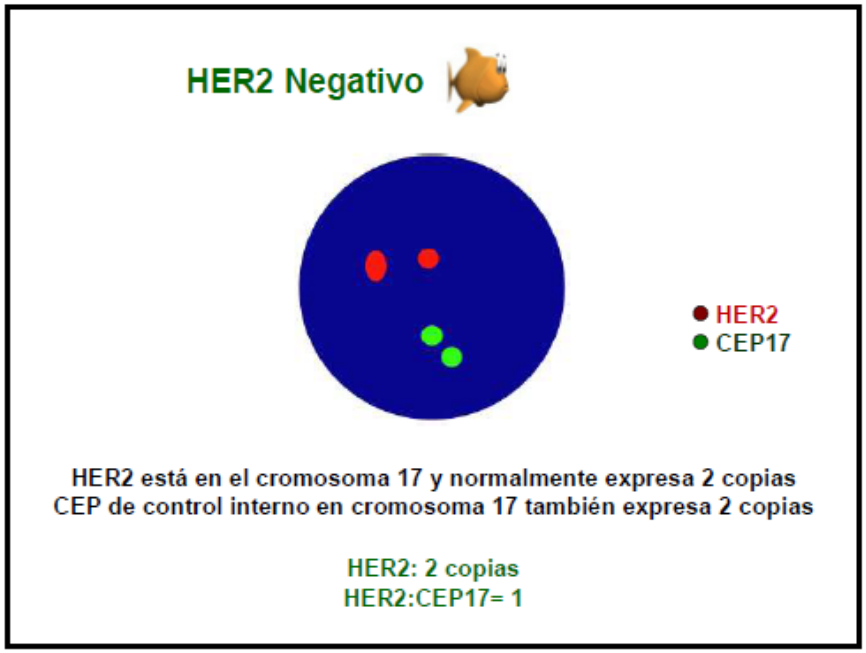
HIBRIDACION IN SITU HER2

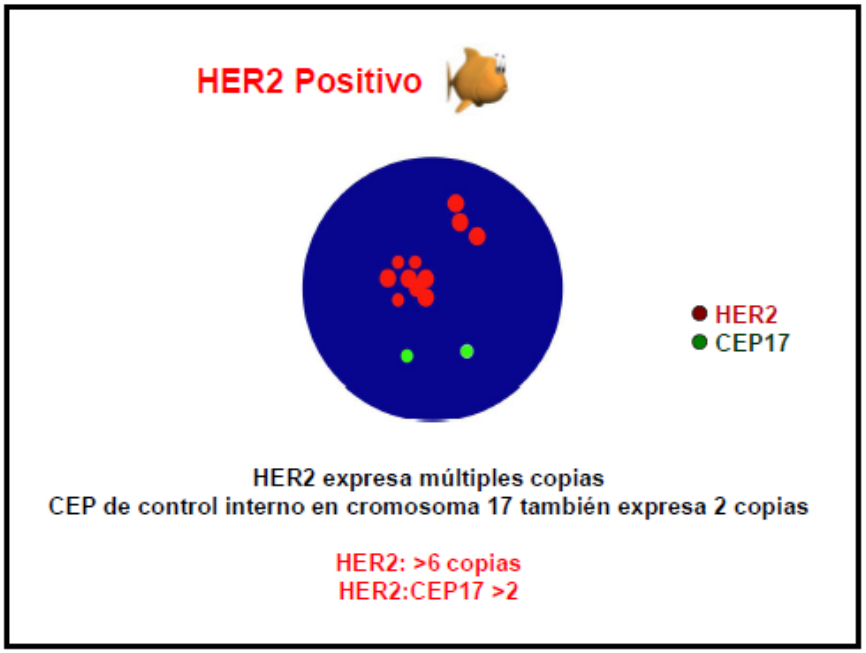
METODOS

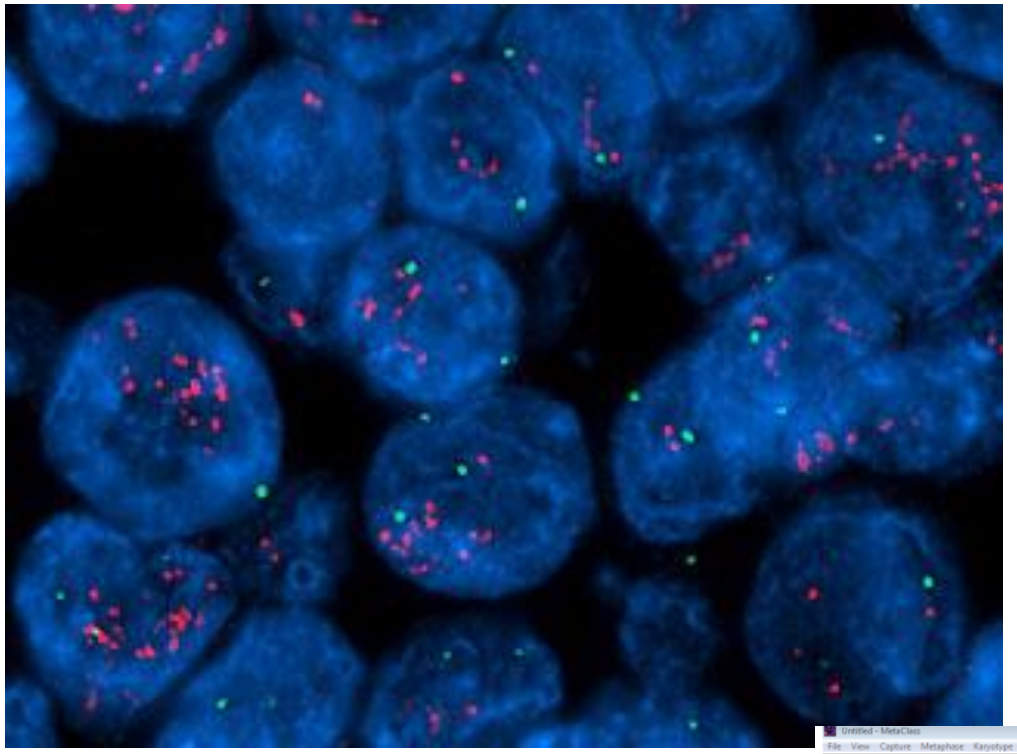
- Hibridación in situ fluorescente (FISH)
- Hibridación in situ cromogénica (CISH)
- Hibridación in situ silver-enhanced (SISH)

Arch Pathol Lab Med Vol 138, May 2014

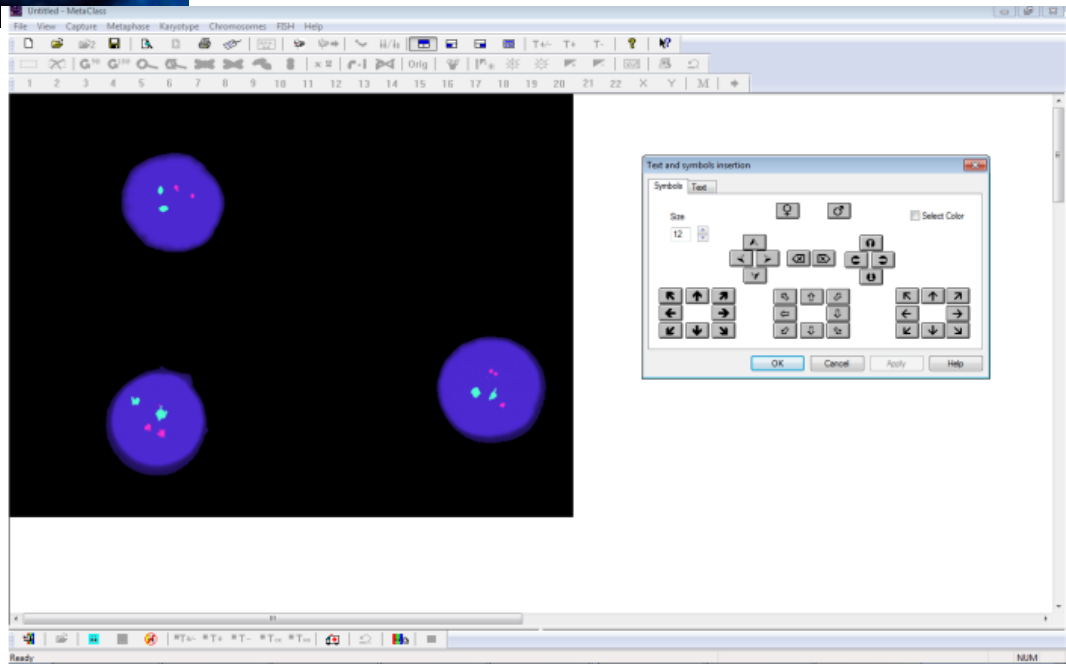
FISH HER-2


HER2 Negativo
HER2
CEP17
HER2 está en el cromosoma 17 y normalmente expresa 2 copias
CEP de control interno en cromosoma 17 también expresa 2 copias
HER2: 2 copias
HER2:CEP17= 1


HER2 Positivo
HER2
CEP17
HER2 expresa múltiples copias
CEP de control interno en cromosoma 17 también expresa 2 copias
HER2: >6 copias
HER2:CEP17 >2



FISH


Untitled - MetaClass
File View Capture Metaphase Karyotype Chromosomes FISH Help
Text and symbols insertion
Symbols Text
Size
12
Select Color
OK
Cancel
Apply
Help
Ready
NUM

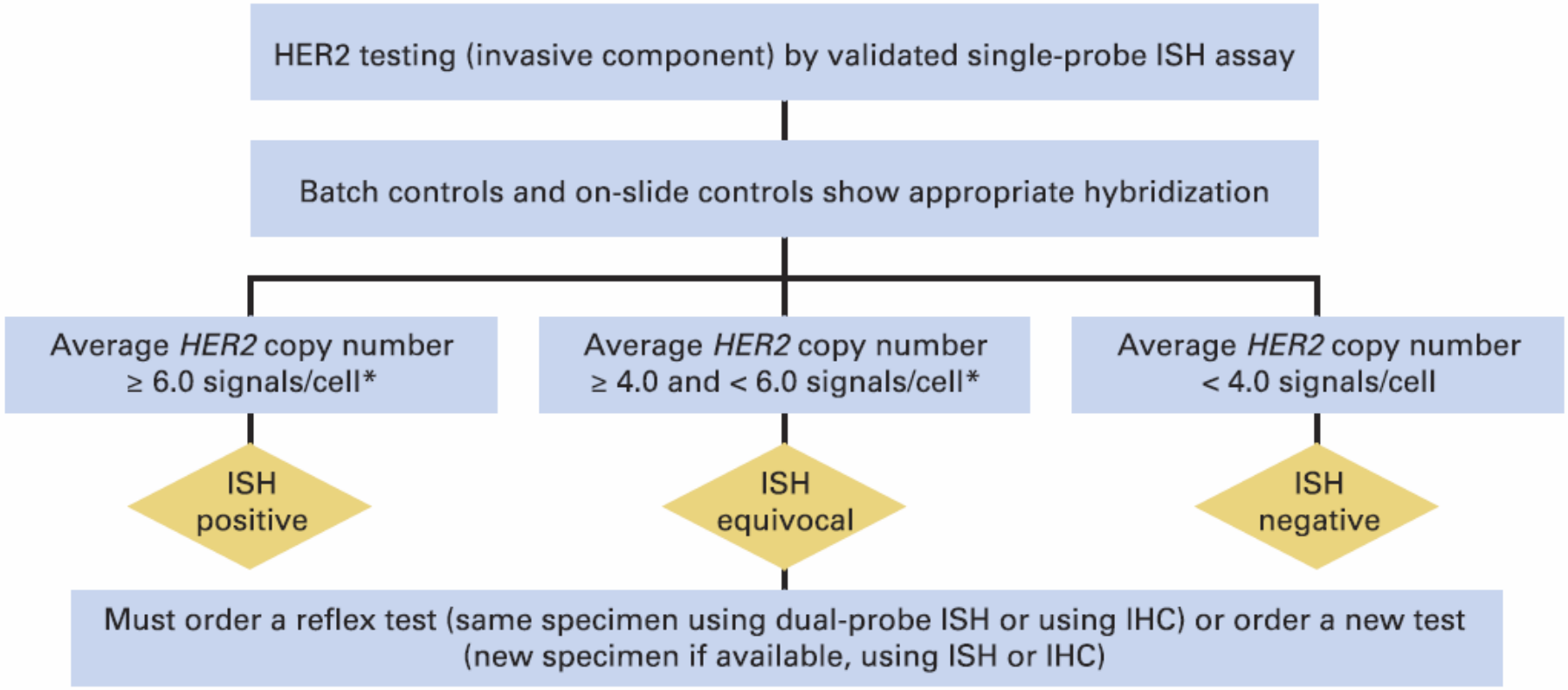
FISH Dual HER-2/CEP 17

Ratio of *HER2*/CEN-17 signals	*HER2* Gene Status	Result
< 2	Non-Amplified	Negative
≥ 2	Amplified	Positive

Results at or near the cut-off (1.8 – 2.2) should be interpreted with caution. In those cases, count an additional 20 nuclei and recalculate the ratio.

Arch Pathol Lab Med Vol 138, May 2014

FISH Simple HER-2



CLASIFICACION POR INMUNOHISTOQUIMICA

- Aproximación a subtipos moleculares
- Predicción más acertada del comportamiento de la neoplasia
- Mejorar las estrategias de tratamiento

CLASIFICACION POR INMUNOHISTOQUIMICA

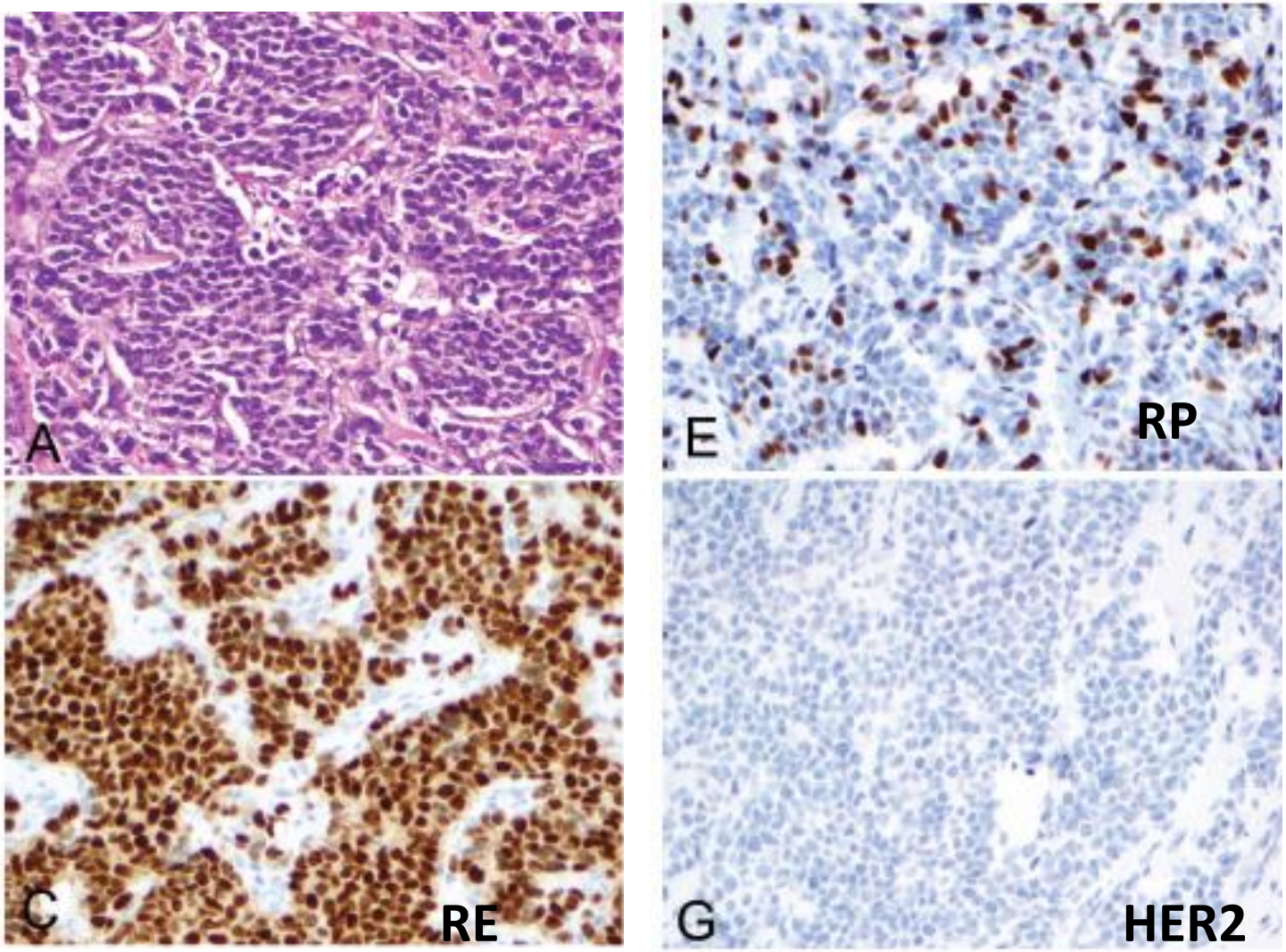
Table 2: Molecular typing of breast cancer based on common immunohistochemical markers (Abd El-Rehim et al., 2005; Goldhirsch et al., 2011)

Molecular intrinsic subtype	Clinico-pathological definition	ER	PR	HER2	Ki67	Basal markers*
Luminal A	Luminal A	+	+ or –	–	Low	-
Luminal B	Luminal B (HER2 negative)	+	+ or –	–	High	-
Luminal B	Luminal B (HER2 positive)	+	+ or –	Overexpressed	Low or high	-
HER2	HER2 positive (non-luminal)	–	–	Overexpressed	Usually high	+/-
Basal	Triple negative (ductal)	–	–	–	Usually high	+

* CK5/6 or CK14

Surgical Patholoy 2012;5:701-717

LUMINAL A



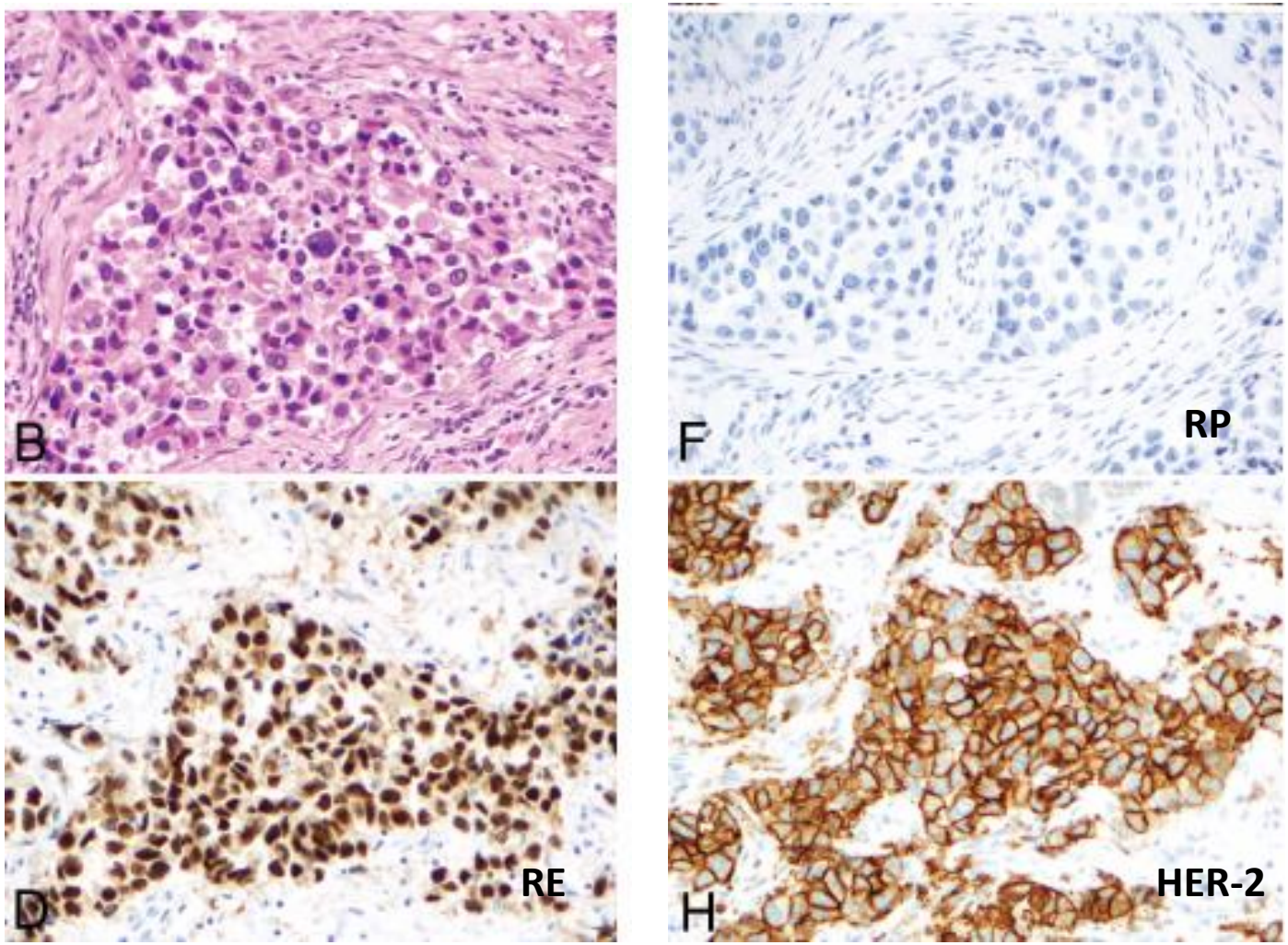
Arch Pathol Lab Med. 2011;135:544–557

LUMINAL A

- 50-60%
- Neoplasia de bajo grado histológico
- Tipos histológicos especiales
- Bajos niveles de expresión en genes de proliferación
- Buen pronoóstico
- Respuesta a tratamiento con tamoxifen

World J Clin Oncol 2014 August 10; 5(3): 412-424

LUMINAL B



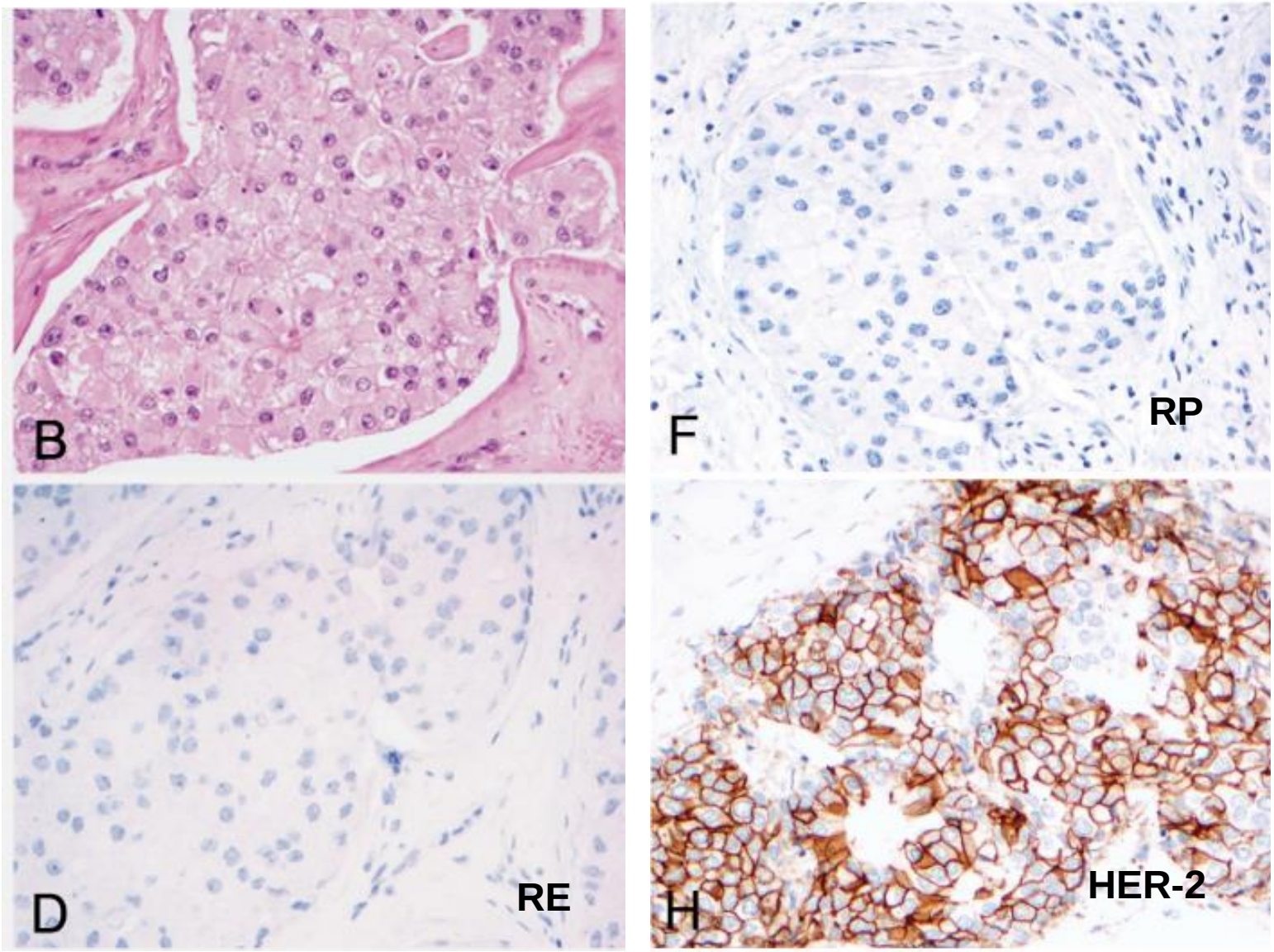
Arch Pathol Lab Med. 2011;135:544–557

Luminal B

- 15-20%
- Alto grado histológico
- Altos niveles de expresión en genes de proliferación
- Mal pronostico
- Alto indice de recurrencia y baja sobrevida

World J Clin Oncol 2014 August 10; 5(3): 412-424

HER-2

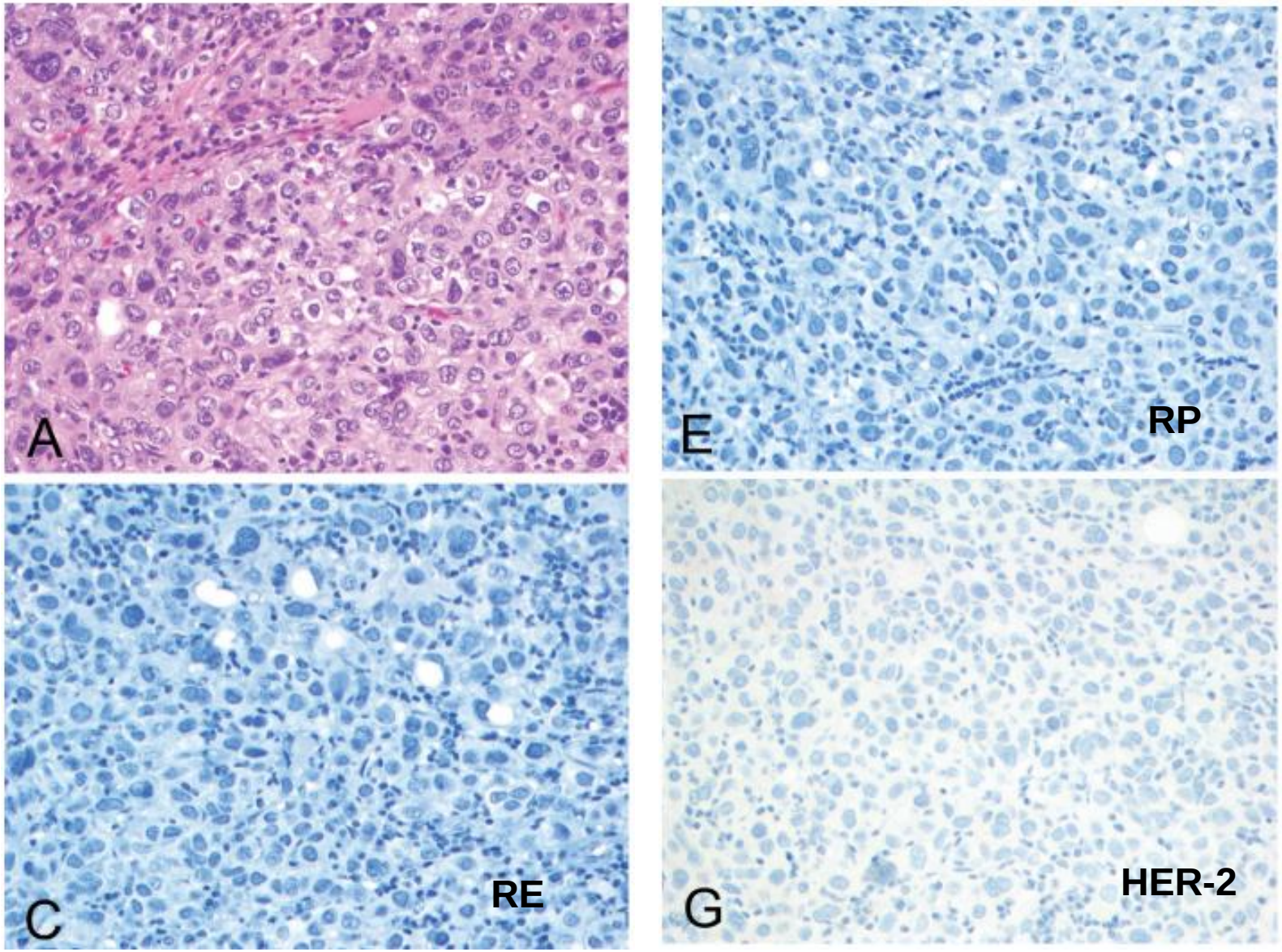


HER-2

- 15-20%
- Comportamiento clínico y biológico agresivo
- Alto grado histológico
- Altos índices de proliferación
- Tratamiento con trastuzumab

World J Clin Oncol 2014 August 10; 5(3): 412-424

TRIPLE NEGATIVO



TRIPLE NEGATIVO

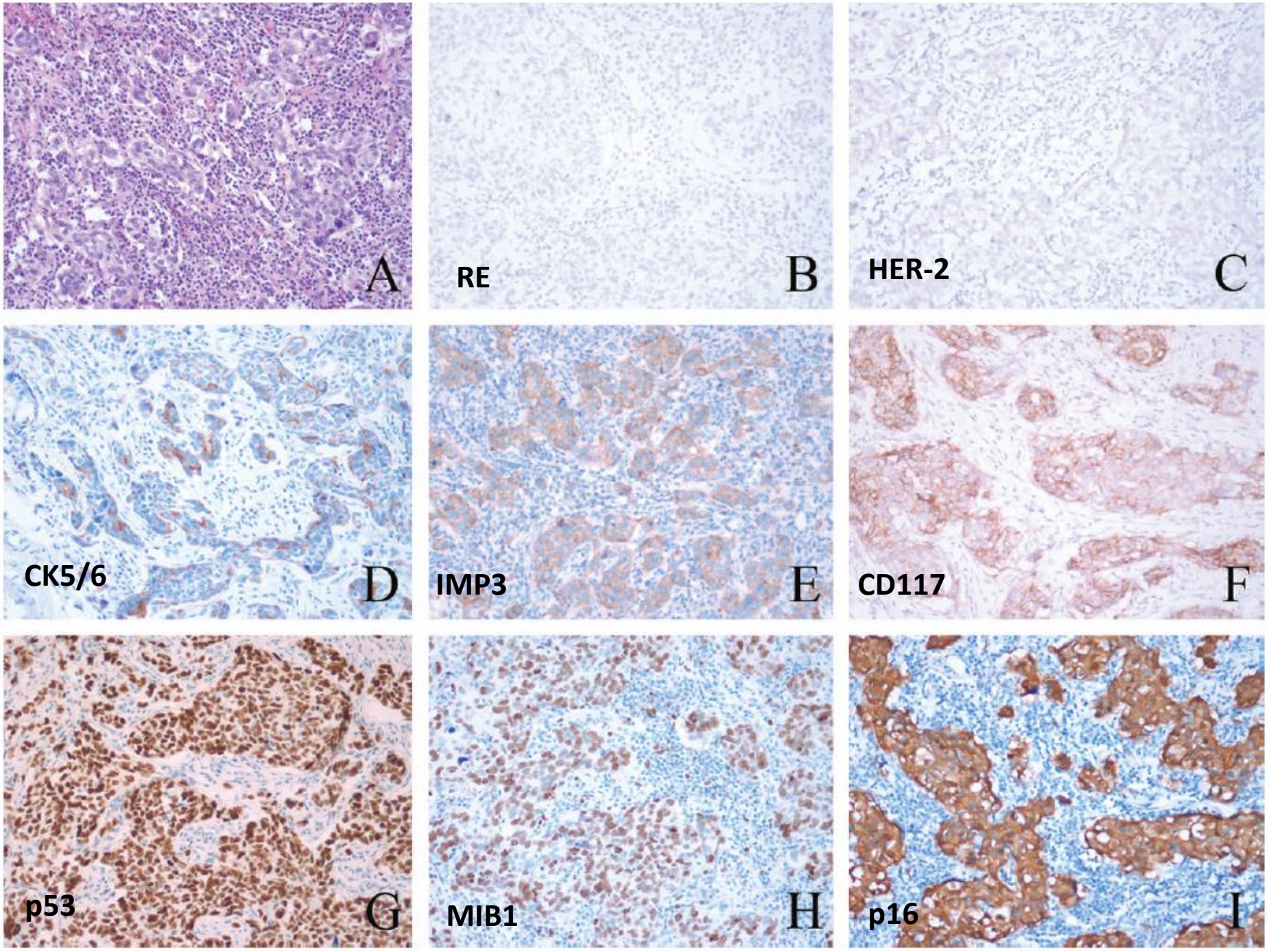
- 12-17 %
- Predominio en mujeres jóvenes
- En tumores de alto grado histológico
- Asociación con alto riesgo de recurrencia y muerte de 3 a 5 años al diagnóstico
- No existe terapia blanco
- Muestra genética heterogénea

Arch Pathol Lab Med. 2016;140:806–814

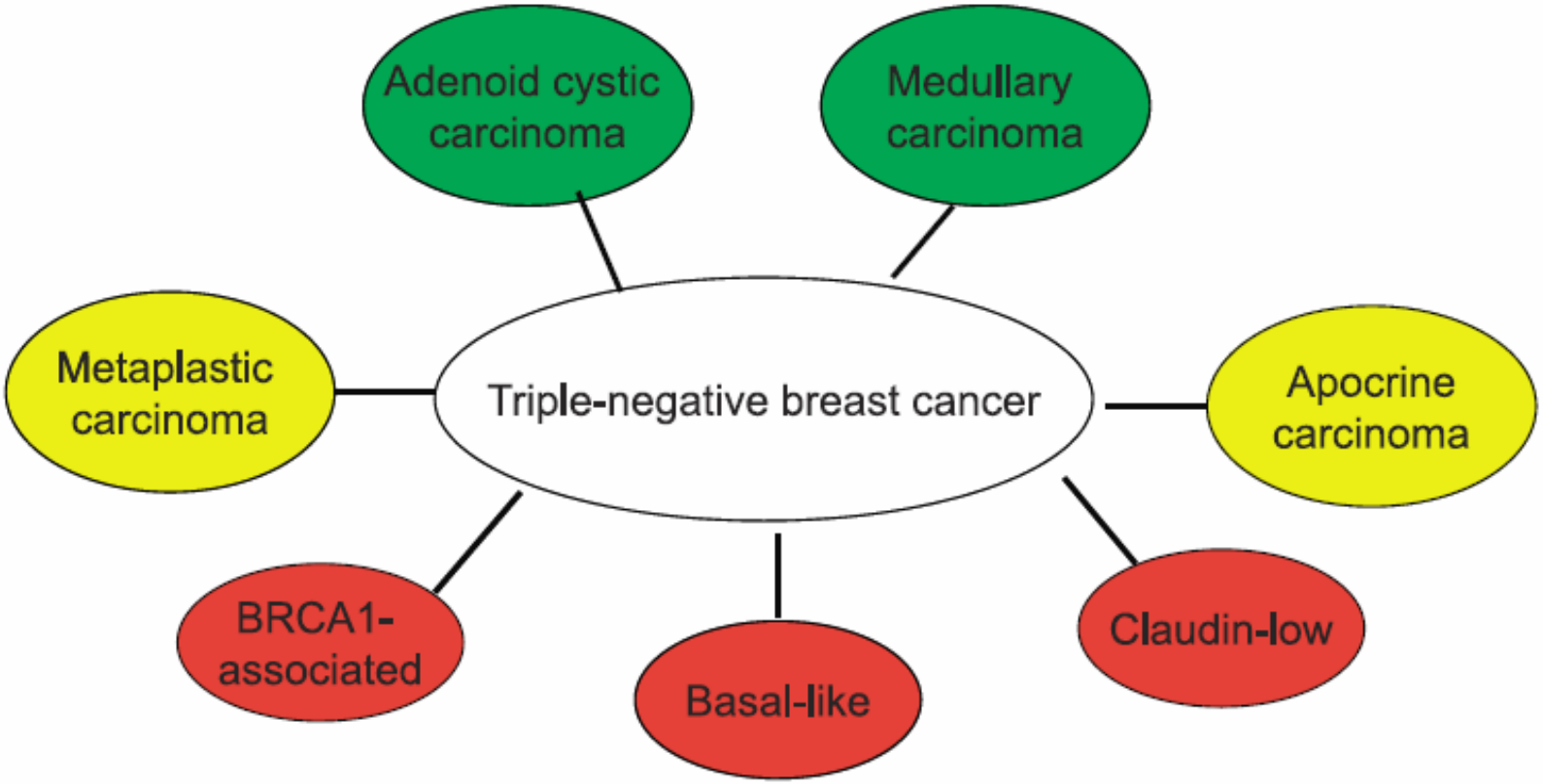
TRIPLE NEGATIVO SUBTIPOS

- Basal-like 1
- Basal-like 2
- Inmunomodulador
- Mesenquimal
- Mesenquimal-like de celulas madre
- Luminal asociado a andrógenos (LAR)

Breast Cancer (2016) 2, 16036


A
RE
B
HER-2
C
CK5/6
D
IMP3
E
CD117
F
p53
G
MIB1
H
p16
I

CANCER CON FENOTIPO TRIPLE NEGATIVO



Arch Pathol Lab Med. 2014;138:37–43

CLASIFICACIÓN TRIPLE NEGATIVOS

BAJO GRADO

a) Glándula salival-Like
   - Adenoideo
   - Secretor
   - Polimorfo
   - Mucoepidermoide

b) Familia de neoplasias TN de bajo grado (proliferación hiperplasica

c) Bajo claudina/ basal-like intrinseco
   - Metaplasico cel. fusiformes

d) Basal-like
   - Metaplasico escamoso
   - Metaplasico condroide

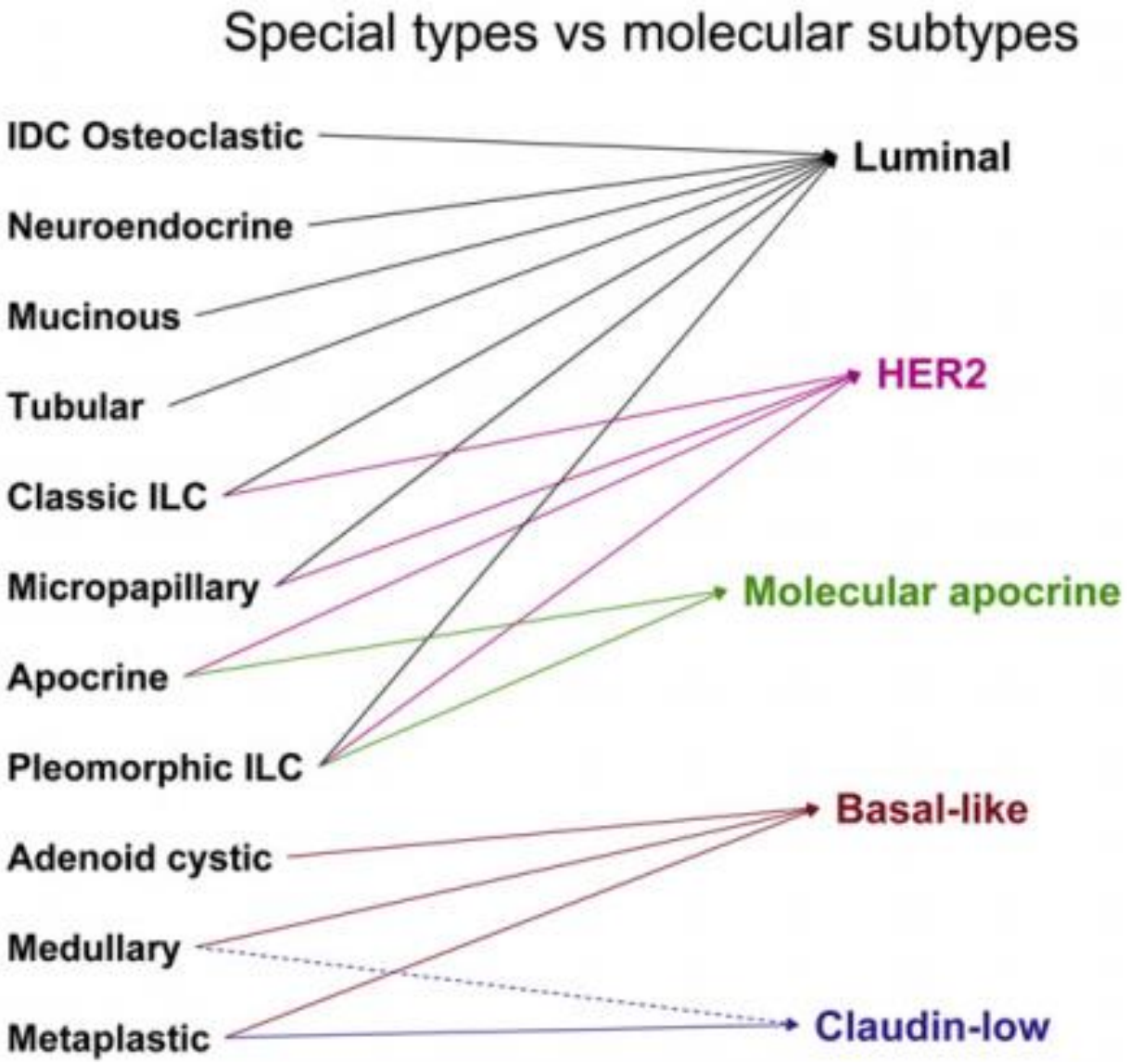
GRADO INTERMEDIO

- Carcinoma medular

ALTO GRADO

- Metaplasico
- Neuroendocrino
- Ca ductal de alto grado

J Breast Cancer (2016) 2, 16036



Molecular Oncology 4 (2010) 192 E208

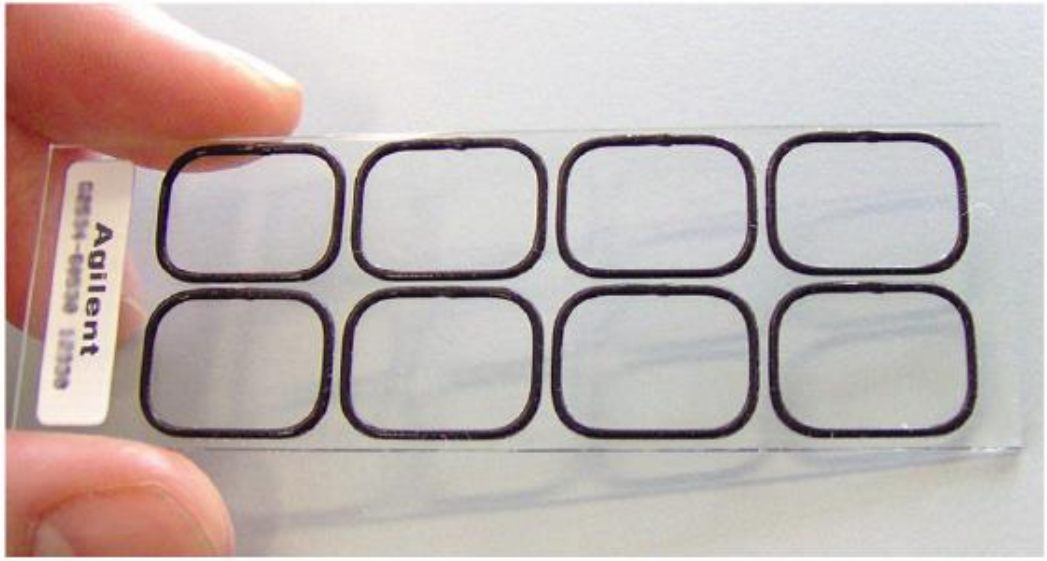
Tabla 4. Características de los subtipos moleculares y asignación de los tipos histológicos especiales de cáncer de mama.

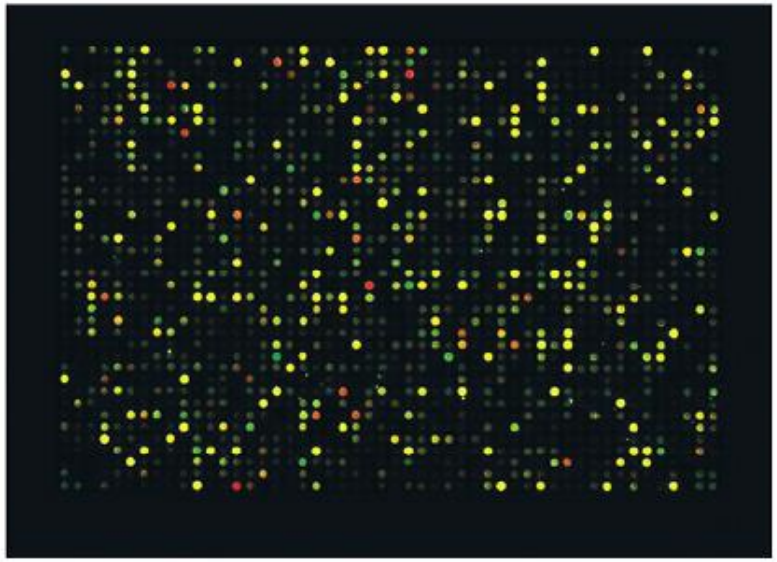
Subtipo molecular	ER, PR, HER2	Marcador adicional	Micro arreglos de proliferación	Tipo histológico especial
BASAL-LIKE	ER – PR – HER-2 –	CK5/6 + EGFR +	Alto	Adenoideo quístico Células acinares Medular Metaplásico Lobular pleomorfo Secretor
HER/ER-	ER – PR – HER-2 +	CK5/6 +/– EGFR +/–	Alto	Apocrino Lobulillar Micropapilar Lobulillar pleomórfico
NORMAL BREAST-LIKE	ER –/+ PR desconocido HER –	CK5/6 EGFR +	Bajo	Medular Metaplásico
LUMINAL	ER + (–) PR +/– HER – (+)		Bajo/alto	Apocrino Carcinoma ductal osteoclástico Lobulillar Micropapilar Mucinoso Neuroendocrino Lobulillar pleomorfo Tubular
MOLECULAR APOCRINO	ER – PR – HER0 +/–	AR + CK5/6 +/– EGFR +/–	Alto	Apocrino Lobulillar pleomorfo
BAJO CLAUDINA	ER – PR – HER-2 –	CLDN bajo/– CDH1 bajo/– CK5/6 +/– EGFR +/–	Alto	Metaplásico Medular (?)
RELACIONADO-INTERFERÓN	ER –/+ PR desconocido HER-2–	STAT1	Alto	Medular (?)

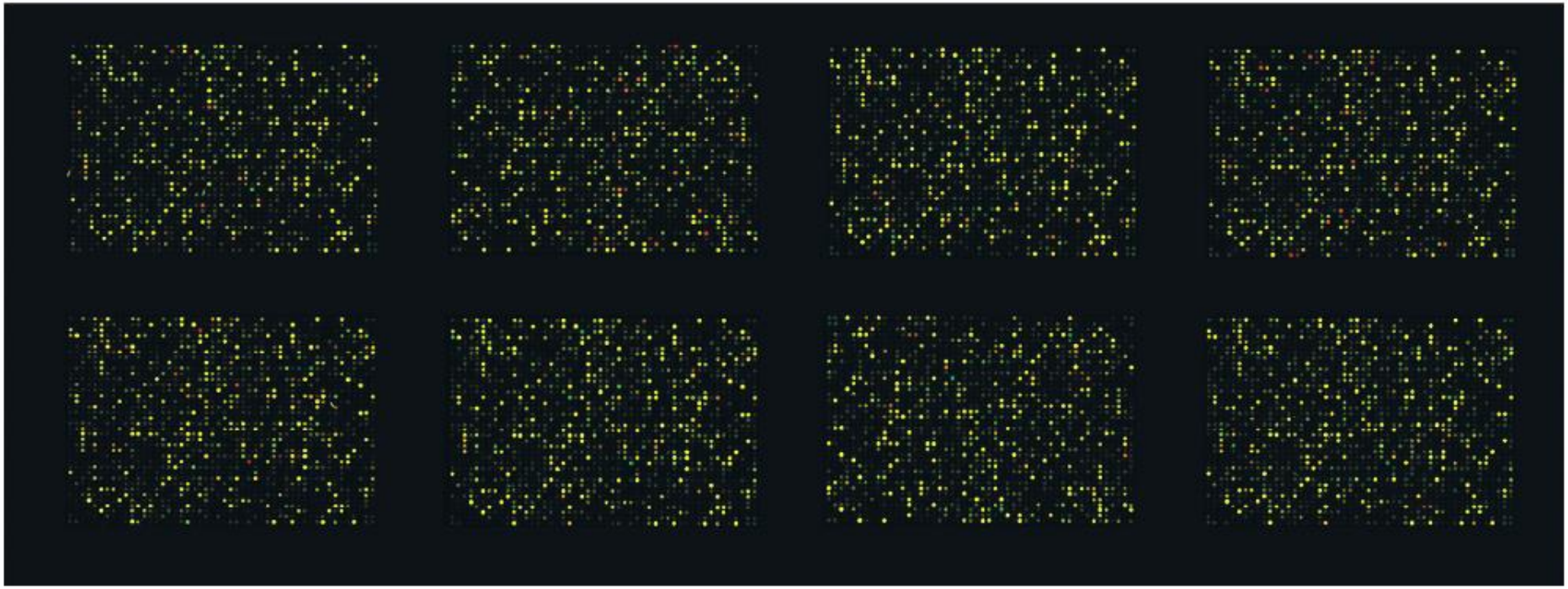
CONSENSO 2017

EXPRESION GENETICA

- Era de la oncología de precisión...
- tratamiento se guía por la identificación del blanco molecular en particular o vía que está deteriorada
- Correlacionar los resultados con la morfología

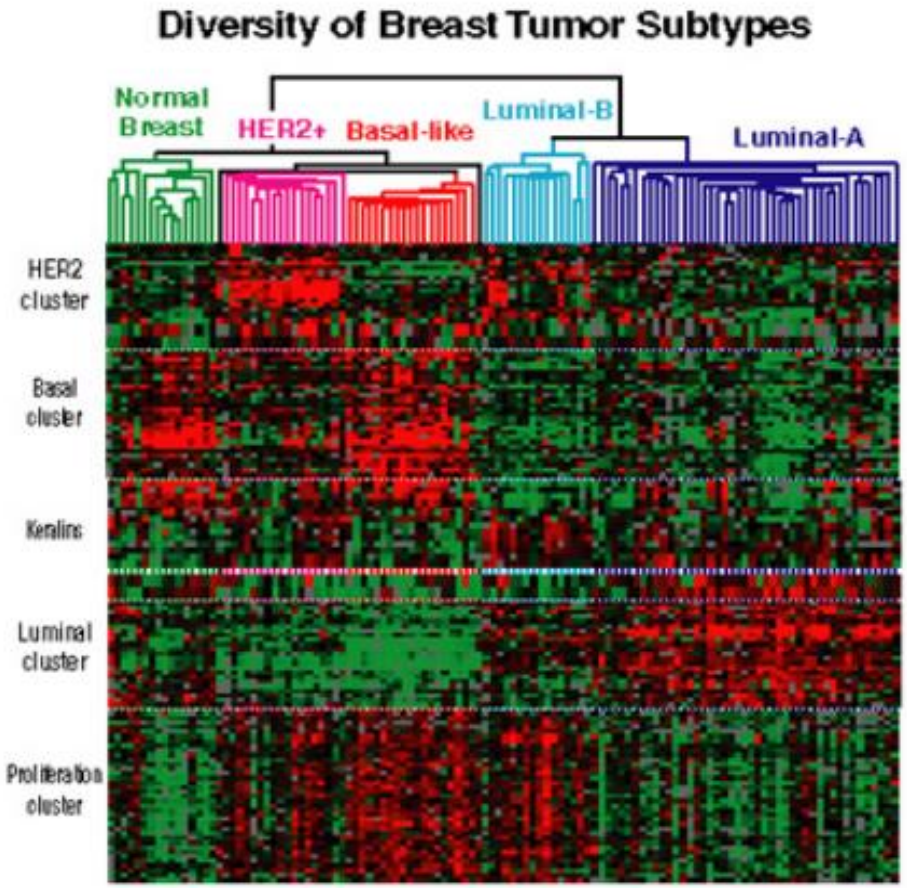

Agilent





CLASIFICACION DE PEROU

ARRAY/PCR



Clin Cancer Res 2005;11:5678-5685.

PERFILES DE EXPRESION GENETICA APROBADOS POR OMS

- Perfil de 70-genes (MammaPrint)
- Indice grado genómico (GGI)
- Subtipos intrínsecos (Prosigna/PAM 50)
- Indice de recurrencia 21-genes (OncotypeDX)

Sunil R. Lakhani, et. al.
WHO Classification of Tumor of the Breast.
4ª ed, 2012

Table 2 First generation gene expression signatures

Gene signature	MammaPrint	OncotypeDX	MapQuantDX	Breast cancer index	PAM 50 assay
Starting material	FF or stabilized RNA, FFPE	FFPE	FFPE, FF	FFPE	FFPE
Analytical platform	Microarray, RT-PCR	qRT-PCR	Microarray, qRT-PCR	qRT-PCR	nCounter
Number of genes	70	21	97/9	7	50
Indications	Stage Ⅰ / Ⅱ, 5 cm, ER (+), Node (-)/[1-3 Node (+)]	ER(+), Node (-)	ER (+), G2	ER (+)	All, Node (-) untreated
Application	Clinical outcome	Clinical outcome, benefit from chemotherapy	Molecular grading prediction of response to TMX	Clinical outcome, prediction of response to TMX	Subtype definition, risk of relapse without treatment
FDA approved	Yes	No	No	No	No
ASCO and NCCN recommendation	No	Yes	No	No	No

FF: Fresh frozen; FFPE: Formalin fixed paraffin embedded; G: Grade; TMX: Tamoxifen.

World J Clin Oncol 2014 August 10; 5(3): 412-424

mammaprint®

decoding breast cancer.

MAMMAPRINT

- MammaPrint es un test de pérfil genético desarrollado por Agendia
- Método expresión del ARN (ácido ribonucleico), usando un microarray en el que se encuentran fijadas secuencias de 70 genes seleccionados
- Predictor de riesgo de metástasis a 10 años
- Grupos
  - ALTO RIESGO 50%
  - BAJO RIEGO 10-15%

J Clin Oncol 25:5287-5312.

MAMMAPRINT

- Pacientes menores de 53 años
- Estadios I y II, sin involucro de ganglios
- Requiere tejido fresco congelado
- Representativo de neoplasia mínimo 30%
- Recepción de tejido máximo en 5 dias


oncotype DX®
Breast Cancer Assay

ONCOTYPE

- Prueba genética que permite analizar la expresión de 21 genes pronósticos y predictivos
- Técnica de transcripción inversa de la cadena de polimerasa en tiempo real (RT-PCR)
- Prueba pronóstica y predictiva de metástasis (10 años) y de respuesta al tratamiento (tamoxifeno vs tamoxifeno más quimioterapia)

J Clin Oncol 25:5287-5312.

ONCOTYPE

- Subgrupo clínico bien definido
  - Estadios I y II de la enfermedad
  - Receptores estrogénicos positivos
  - Sin involucro ganglionar
- Tejido fijado con formalina e incluido en parafina

ONCOTYPE

- GRUPOS
  - Índice de recurrencia < 18: grupo de pacientes de bajo riesgo y buen pronóstico.
  - Índice de recurrencia 18-30: grupo de pacientes de riesgo intermedio.
  - Índice de recurrencia >31: grupo de pacientes de alto riesgo y pronóstico desfavorable.

genomic health | oncotype DX Breast Cancer Assay

Genomic Health, Inc.
301 Penobscot Drive
Redwood City, CA 94063
Tel (866) ONCOTYPE (866-662-6897)
www.oncotypeDX.com

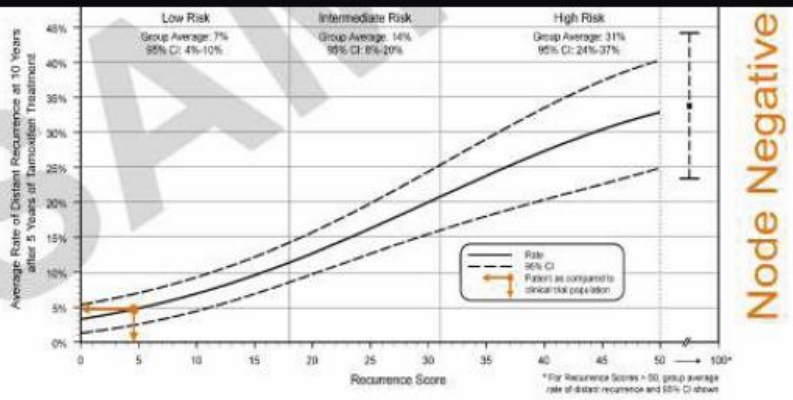
PATIENT REPORT

Patient: Doe, Jane
Sex: Female
DOB: 01/01/1950
Medical Record/Patient #: 556677771
Date of Surgery: 1/25/2008
Specimen ID/Block ID: SURG-0001

Requisition: R00003G
Order Received: 2/01/2008
Date Reported: 2/13/2008
Client: Community Medical Center
Treating Physician: Dr. Harry D Smith
Submitting Pathologist: Dr. John P Williams
Additional Recipient: Dr. Sally M Jones

ASSAY DESCRIPTION

Directrices de la ASCO-CAP no recomiendan las pruebas basadas en el ARNm



Laboratory Director: Patrick Joseph, MD

CLIA Number 05D1018272

VISION MOLECULAR EN CANCER DE MAMA

- El cáncer de mama es una enfermedad heterogénea con múltiples subtipos
- Utilidad cuando permite predecir el comportamiento clínico
- Recordar que las pruebas moleculares no son pruebas de diagnóstico