



Nova classificació de l'Adenocarcinoma de Pulmó

José Ramirez. Anatomia Patològica. Hospital Clínic. Barcelona

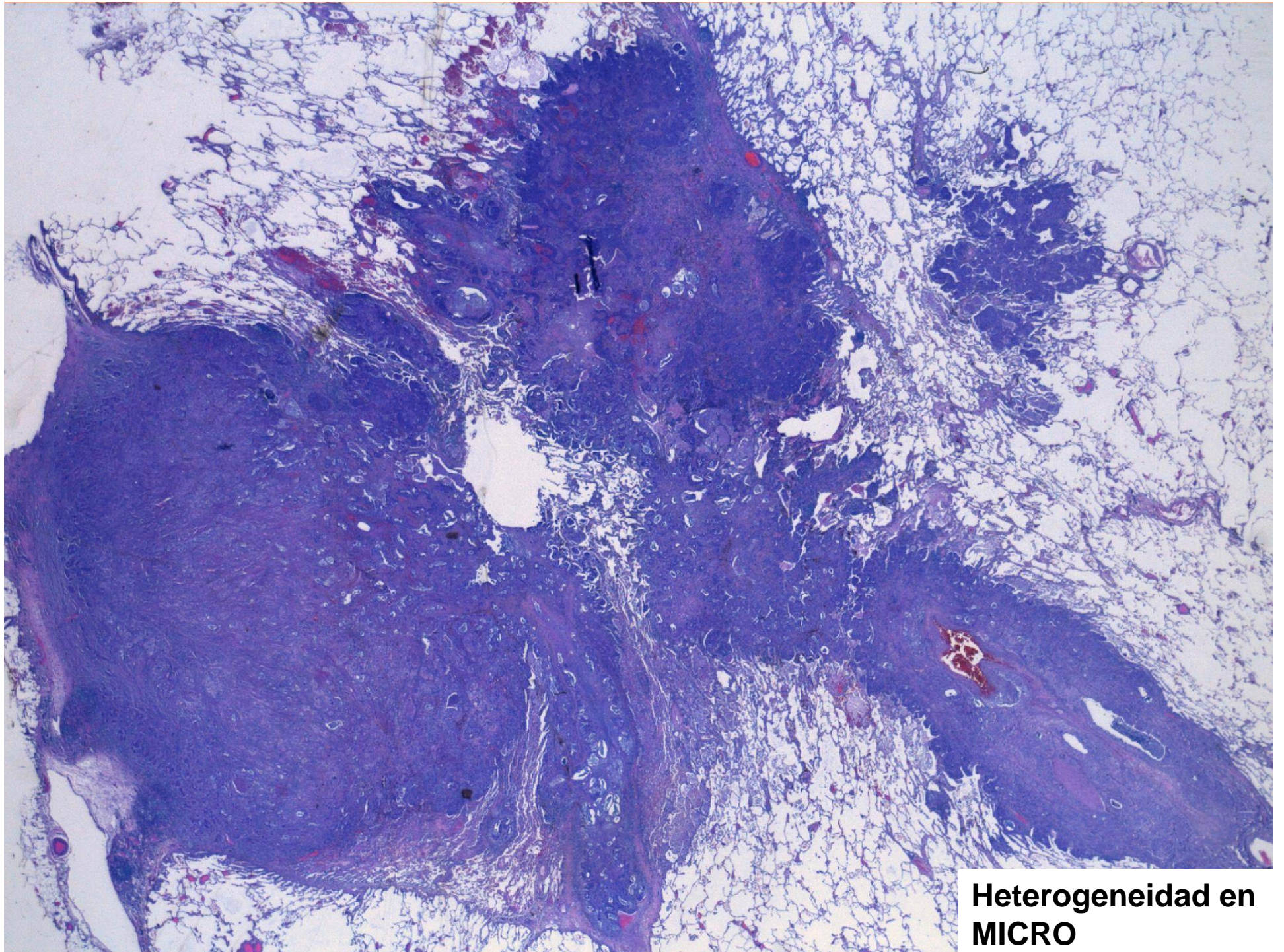


Adenocarcinoma pulmonar

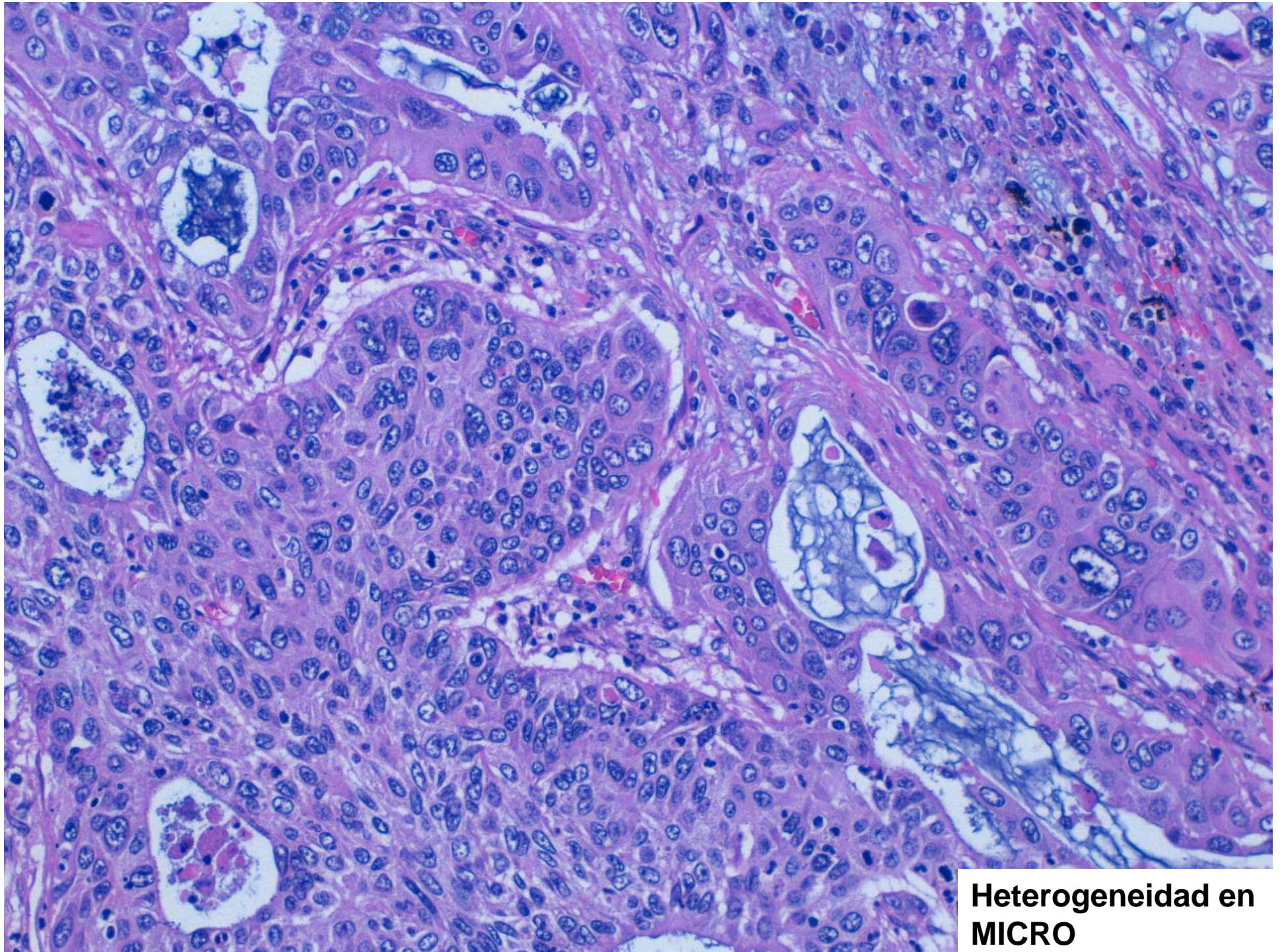
- 1981. OMS
- 1995. Clasificación radiológica. Noguchi.
- 1999/2004. Clasificación de la OMS
- 2009. Dianas terapéuticas (TKI)
- 2011. Propuesta de nueva clasificación de Adenocarcinoma JTO 2011;6:244-285
- 2012. Discusiones e intentos de pautas para patólogos: tipo histológico y dianas terapéuticas



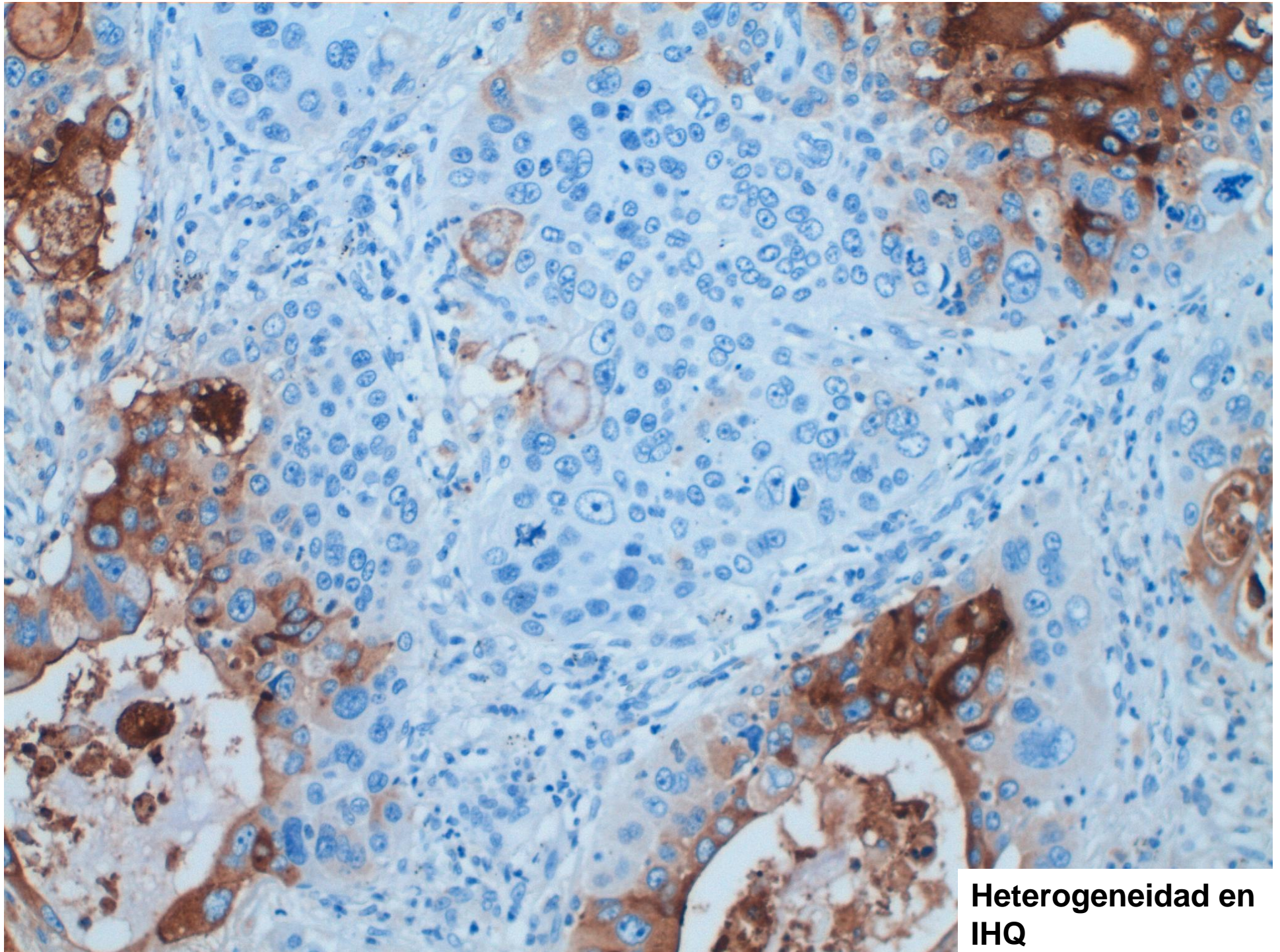
**Heterogeneidad en
MACRO**



**Heterogeneidad en
MICRO**



**Heterogeneidad en
MICRO**



**Heterogeneidad en
IHQ**



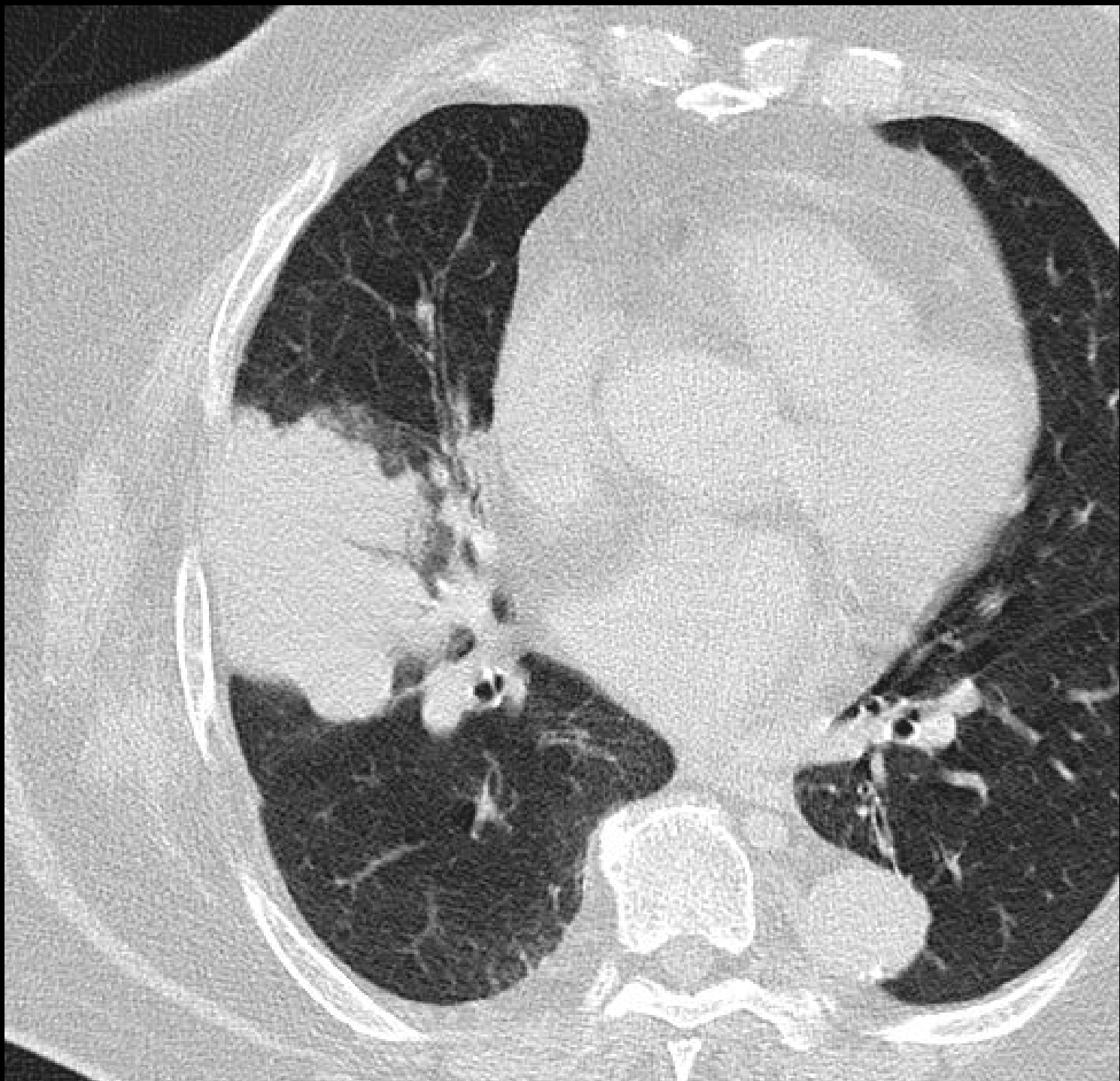
Clasificación OMS 2004

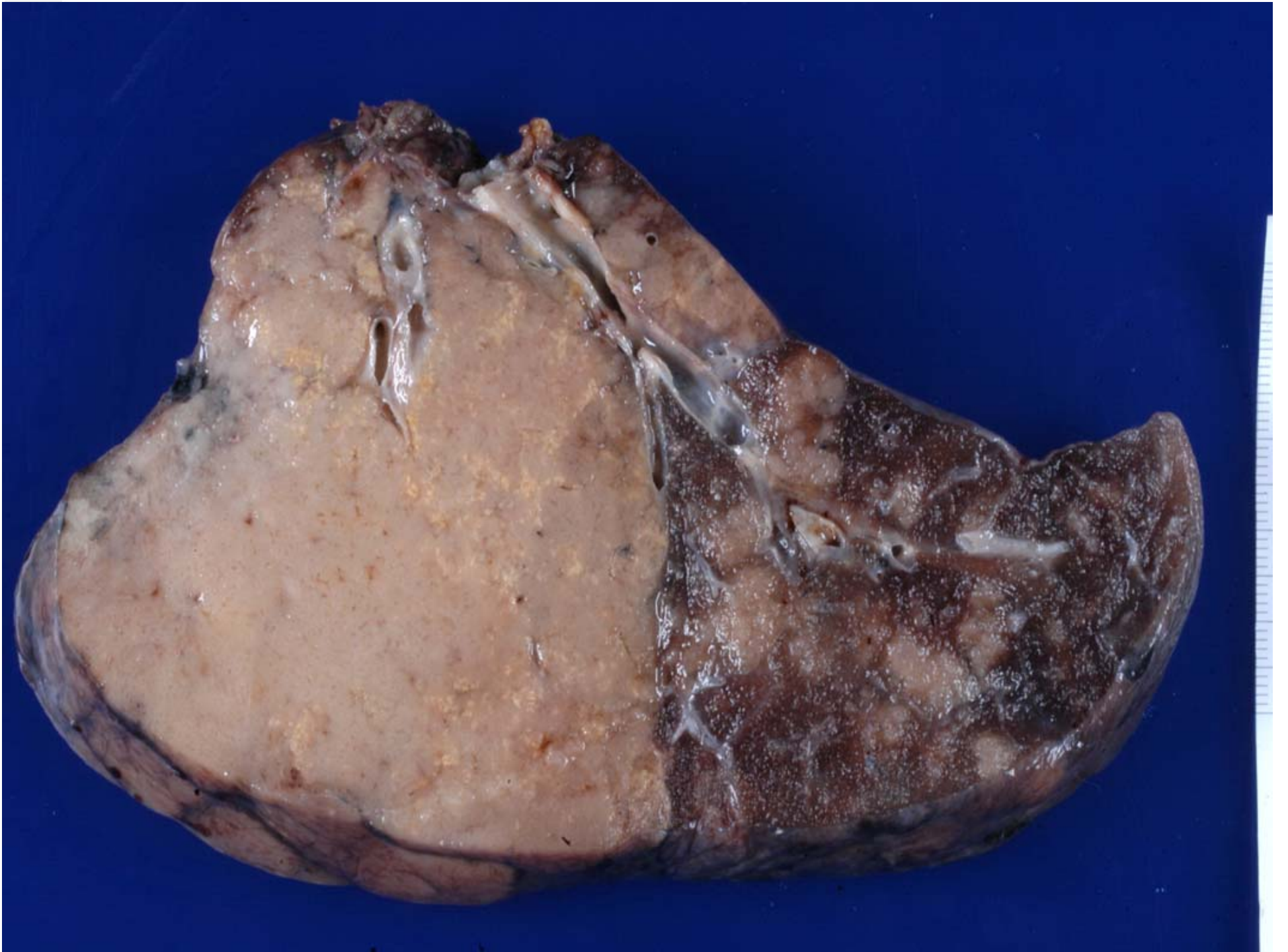
- Carcinoma escamoso
- Carcinoma células pequeñas (microcítico)
- Adenocarcinoma
- Carcinoma de células grandes
- Carcinoma adenoescamoso
- Carcinoma sarcomatoide
- Tumor carcinoide
- Carcinoma tipo glándula salival

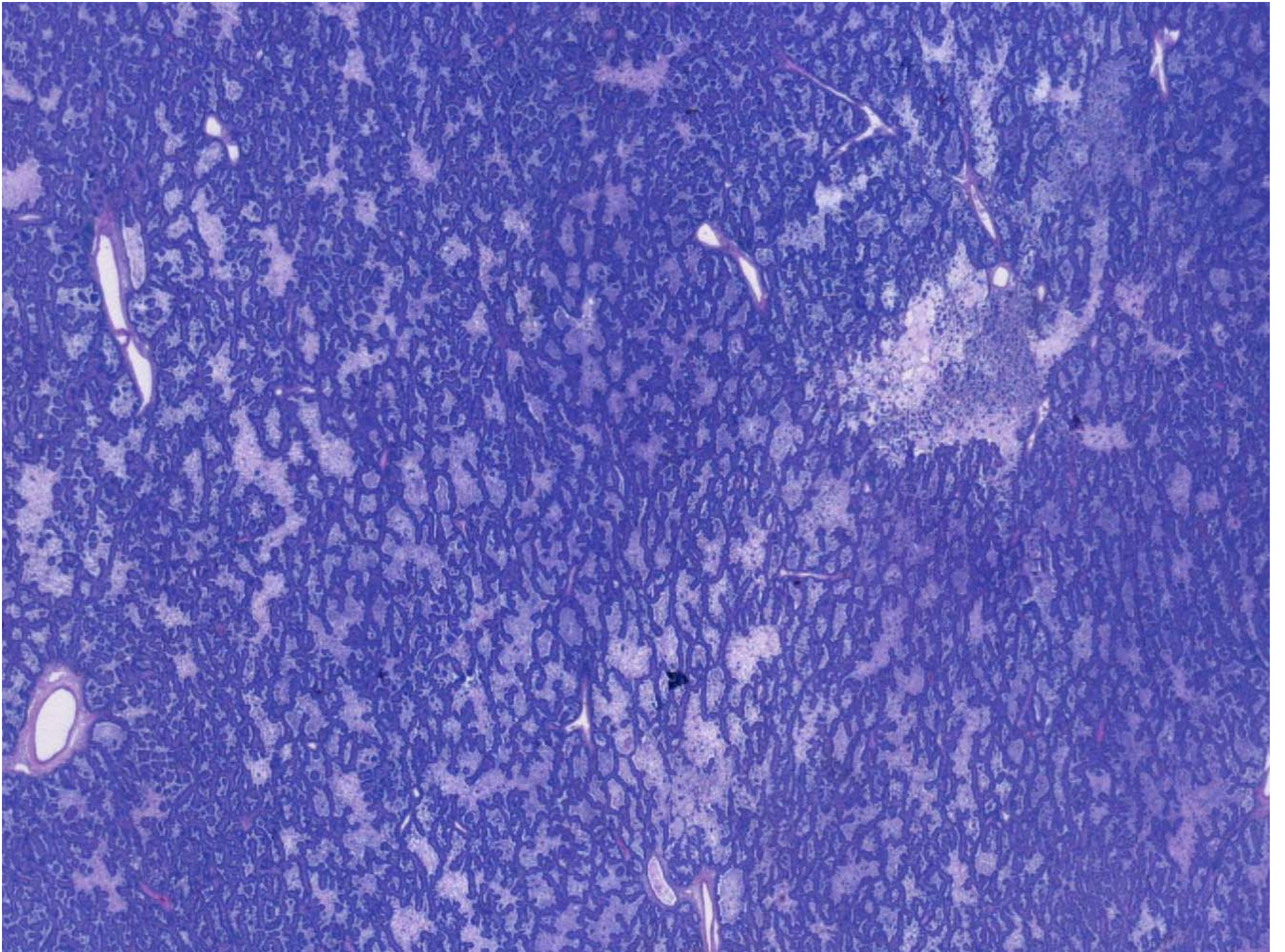


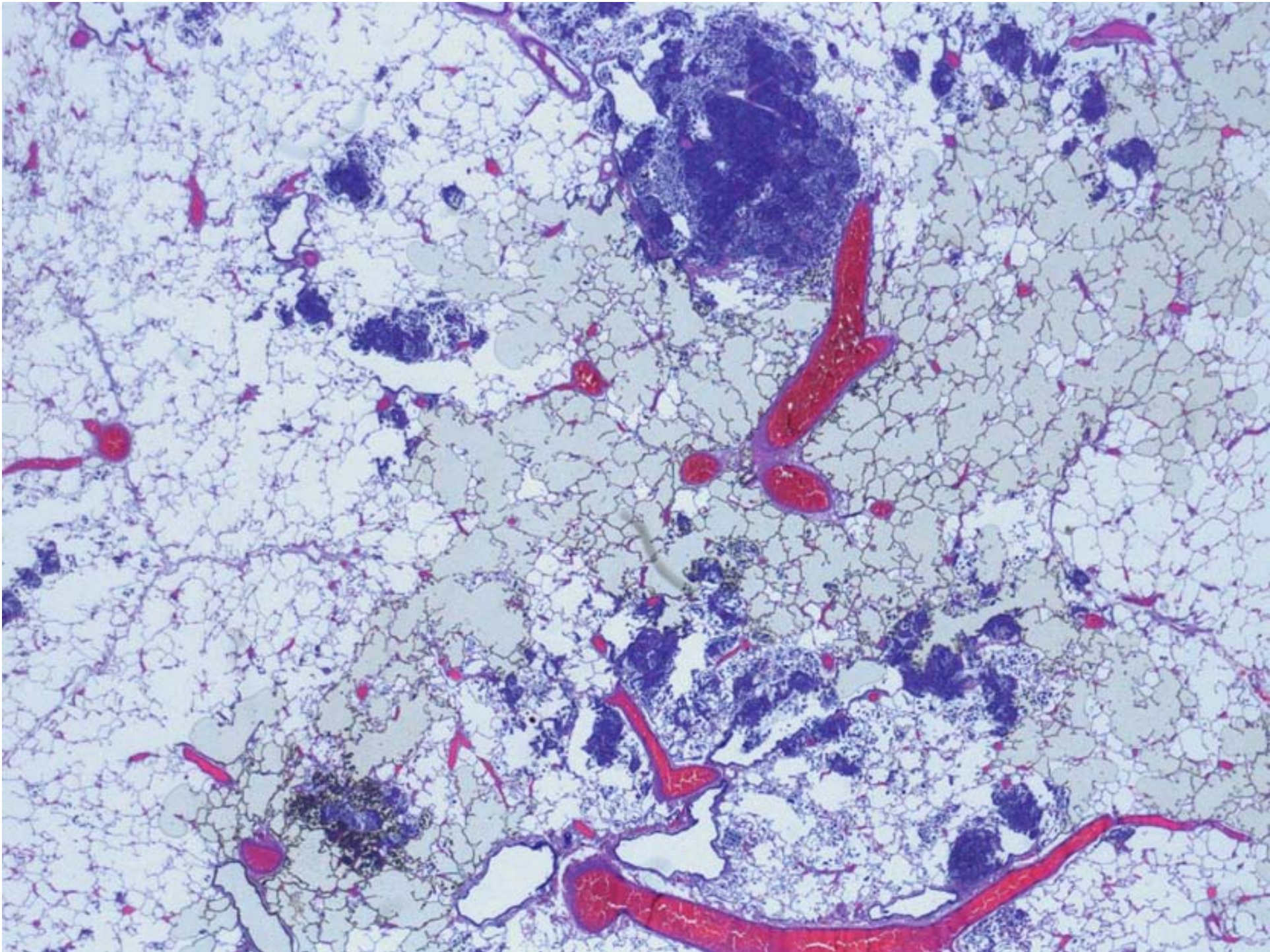
Clasificación OMS 2004

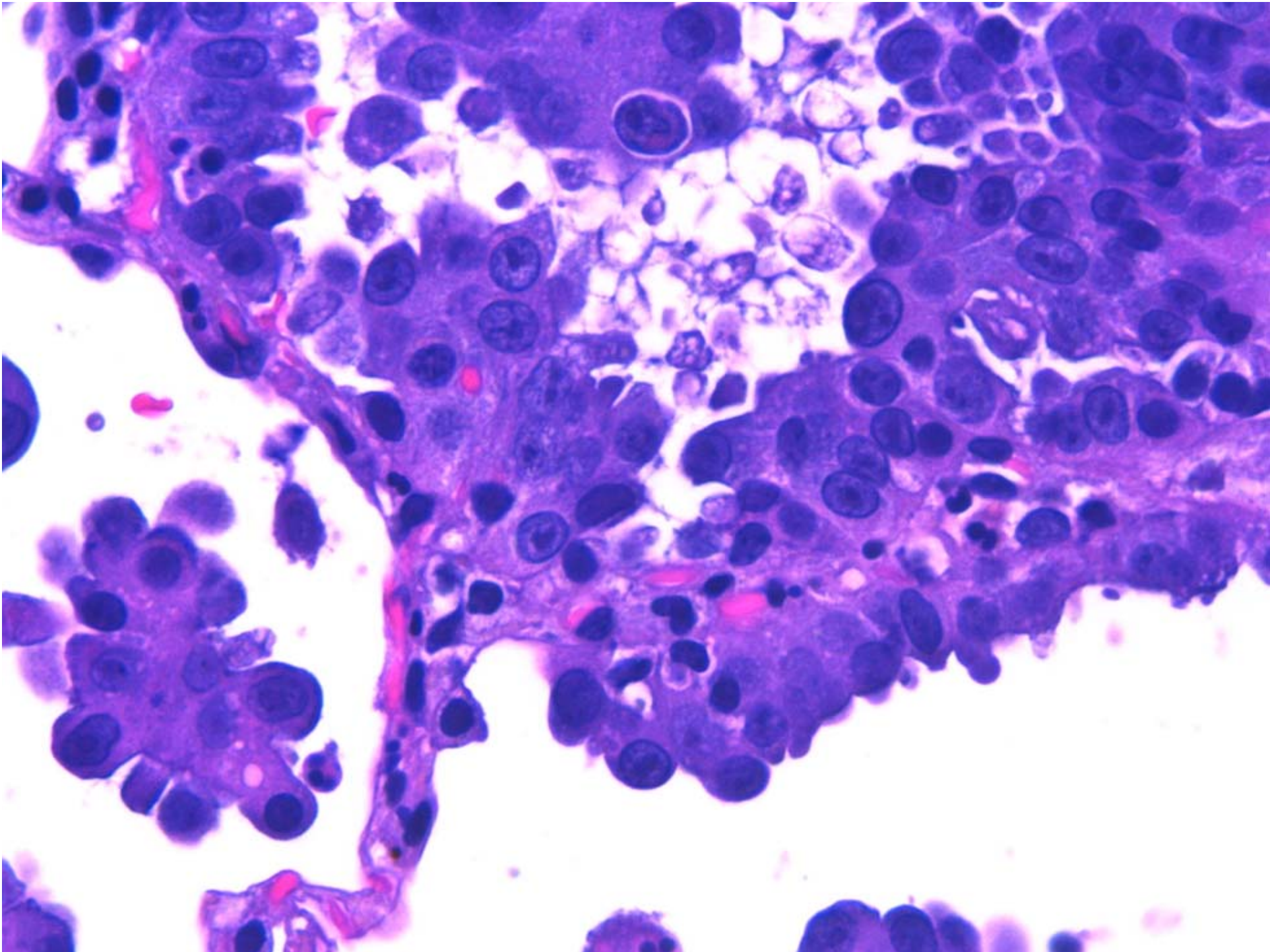
- Carcinoma escamoso
- Carcinoma células pequeñas (microcítico)
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OMS 2004. Adenocarcinoma

- Adenocarcinoma Mixto
- Adenocarcinoma Acinar
- Adenocarcinoma Papilar
- **Carcinoma Bronquioloalveolar (No infiltra)**
- Adenocarcinoma Solido con producción de moco



BAC: Adenocarcinoma no infiltrante

- Adenocarcinoma in situ (100% LE en 5a)
- Minimamente invasivo (criterios de Kerr)
- Multifocal = pronóstico malo
- Micropapilar = peor pronóstico
- *La mayor parte de las publicaciones de BAC desde 2004 son adenocarcinomas mixtos.*



¿Hay alguna cara que se corresponda con mejor pronóstico?

International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society International Multidisciplinary Classification of Lung Adenocarcinoma

William D. Travis, MD, Elisabeth Brambilla, MD, Masayuki Noguchi, MD, Andrew G. Nicholson, MD, Kim R. Geisinger, MD, Yasushi Yatabe, MD, David G. Beer, PhD, Charles A. Powell, MD, Gregory J. Riely, MD, Paul E. Van Schil, MD, Kavita Garg, MD, John H. M. Austin, MD, Hisao Asamura, MD, Valerie W. Rusch, MD, Fred R. Hirsch, MD, Giorgio Scagliotti, MD, Tetsuya Mitsudomi, MD, Rudolf M. Huber, MD, Yuichi Ishikawa, MD, James Jett, MD, Montserrat Sanchez-Cespedes, PhD, Jean-Paul Sculier, MD, Takashi Takahashi, MD, Masahiro Tsuboi, MD, Johan Vansteenkiste, MD, Ignacio Wistuba, MD, Pan-Chyr Yang, MD, Denise Aberle, MD, Christian Brambilla, MD, Douglas Flieder, MD, Wilbur Franklin, MD, Adi Gazdar, MD, Michael Gould, MD, MS, Philip Hasleton, MD, Douglas Henderson, MD, Bruce Johnson, MD, David Johnson, MD, Keith Kerr, MD, Keiko Kuriyama, MD, Jin Soo Lee, MD, Vincent A. Miller, MD, Iver Petersen, MD, PhD, Victor Roggli, MD, Rafael Rosell, MD, Nagahiro Saijo, MD, Erik Thunnissen, MD, Ming Tsao, MD, and David Yankelewitz, MD





Nuevos conceptos (J Thorac Oncol 2011;6:244-285)

- Lesiones preinvasivas
- Adenocarcinoma mínimamente invasivo
- Adenocarcinoma infiltrante, variantes.

- **RECOMENDACIÓN:**
- **Dejar de utilizar el término Bronquioloalveolar.**



Lesiones preinvasivas

- Hiperplasia adenomatosa atípica: <math><0.5\text{ cm}</math>.
- Adenocarcinoma in situ: de 0.5 a 3 cm.
 - **Mucinoso**
 - **No mucinoso**
 - **Mixto mucinoso/no mucinoso**



Adenocarcinoma mínimamente invasivo

- Tamaño entre 0.5 y 3 cm.
- Infiltración ≤ 0.5 cm.
- Variantes:
 - **No mucinoso: habitual**
 - **Mucinoso: raro**
 - **Mixto: No-mucinoso / mucinoso: rare**

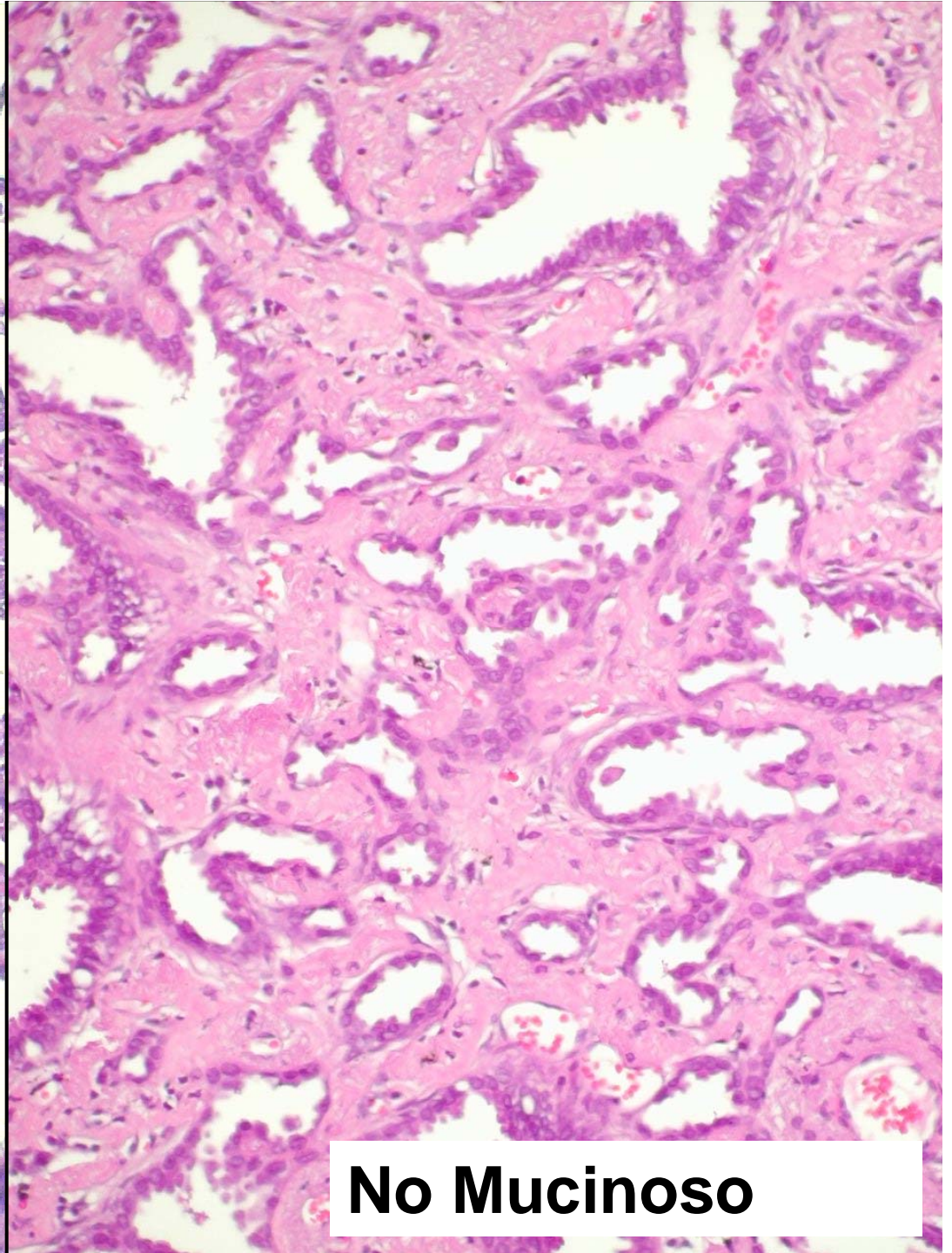
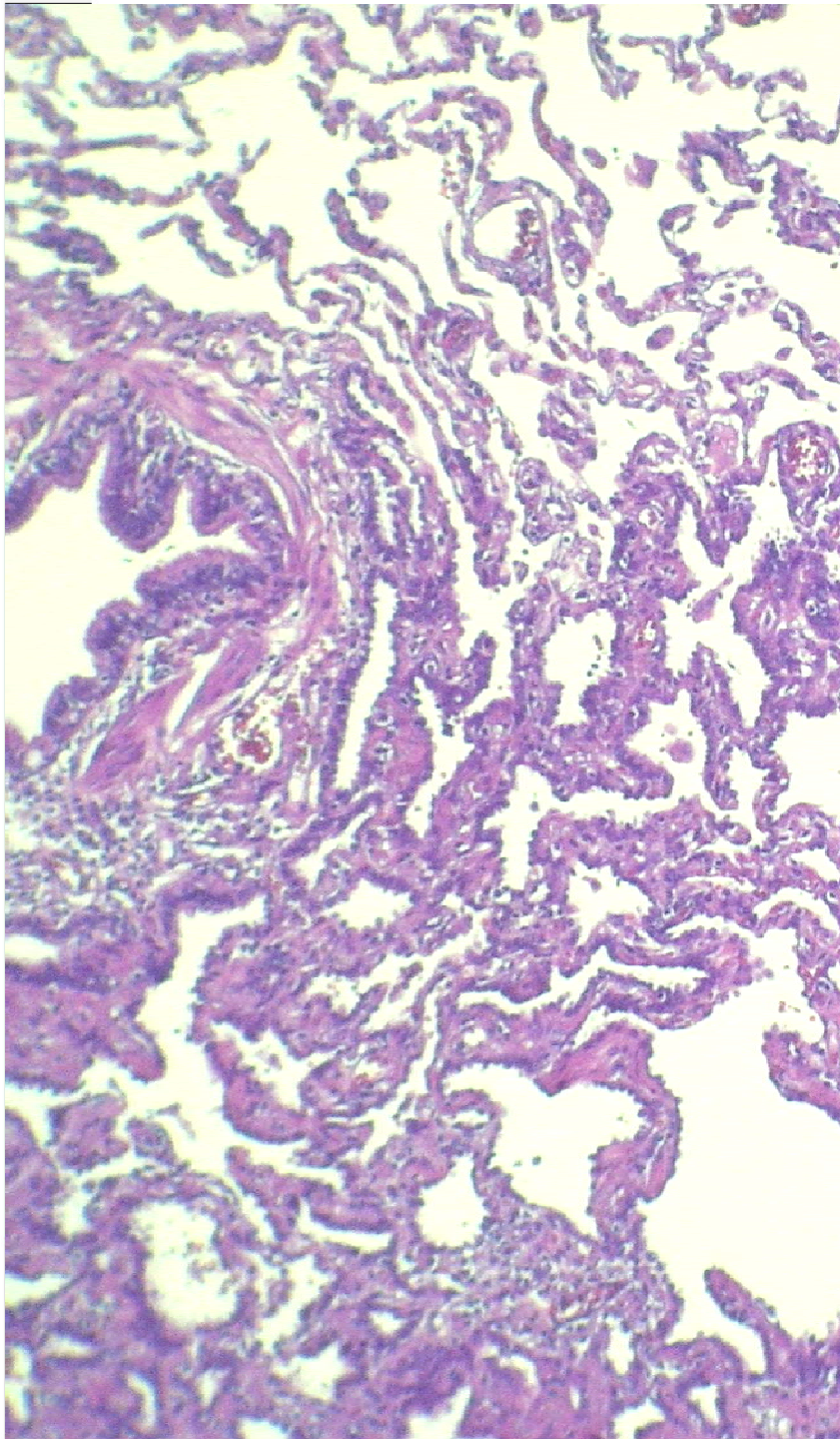


Adenocarcinoma infiltrante

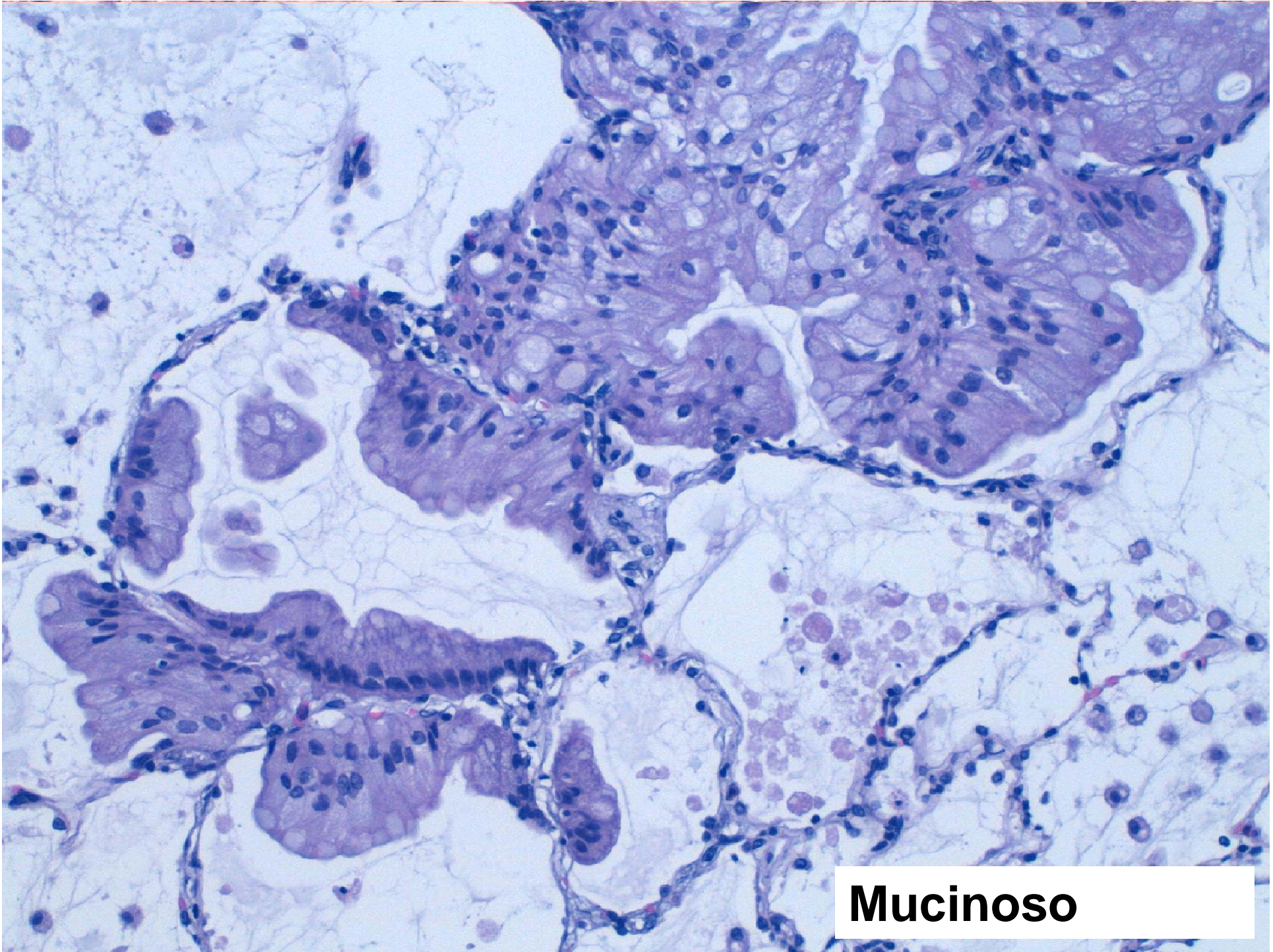
- **Predominio lepidico: patrón no mucinoso cubriendo los septos alveolares,**



so Invasivo



No Mucinoso



Mucinoso



Adenocarcinoma mucinoso/no mucinoso

	Invasive Mucinous Adenocarcinoma (Formerly Mucinous BAC)	Nonmucinous AIS/MIA/LPA (Formerly Nonmucinous BAC)
Female	49/84 (58%) ^{52,120-123}	101/140 (72%) ^{52,120-123}
Smoker	39/87 (45%) ^{52,120-122,124}	75/164 (46%) ^{52,120-122,124}
Radiographic appearance	Majority consolidation; air bronchogram ¹²⁵ Frequent multifocal and multilobar presentation ^{56,125-128}	Majority ground-glass attenuation ^{21,56,58,103,129-134}
Cell type	Mucin-filled, columnar, and/or goblet ^{50-52,125,135}	Type II pneumocyte and/or Clara cell ^{50-52,125,135}
Phenotype		
CK7	Mostly positive (~88%) ^{a54,55,136-139}	Positive (~98%) ^{a54,55,136-139}
CK20	Positive (~54%) ^{a54,55,136-139}	Negative (~5%) ^{a54,55,136-139}
TTF-1	Mostly negative (~17%) ^{1a54,55,120,137-139}	Positive (~67%) ^{a54,55,120,137-139}
Genotype		
<i>KRAS</i> mutation	Frequent (~76%) ^{a55,94,121,127,140-144}	Some (~13%) ^{a55,121,127,140-144}
<i>EGFR</i> mutation	Almost none (~3%) ^{a55,121,127,140-142}	Frequent (~45%) ^{a55,121,127,140-142}

Table 4 Survival according to IASLC/ATS/ERS adenocarcinoma histological subtypes

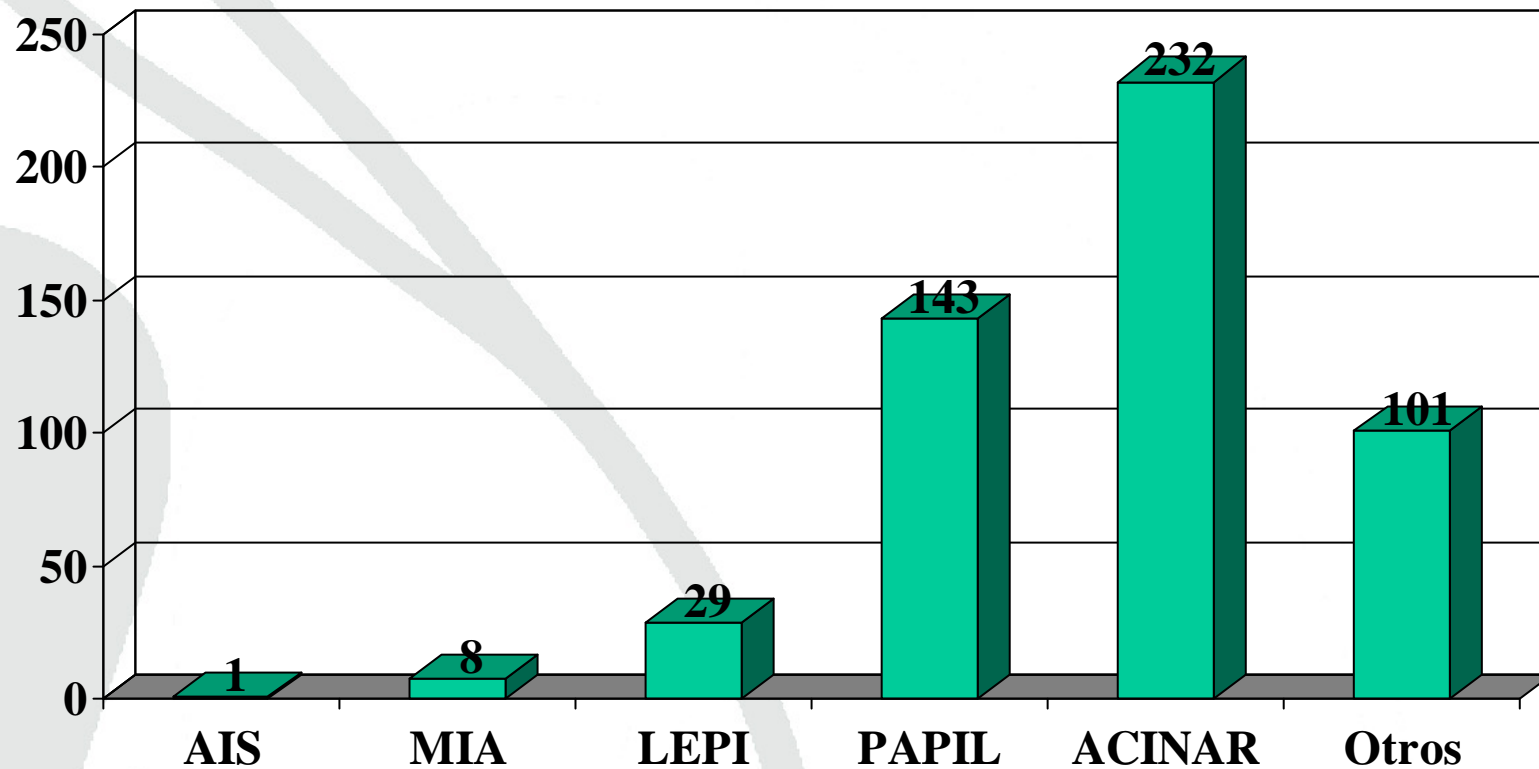
<i>IASLC/ATS/ERS classification subtypes</i>	<i>Number (%)</i>	<i>Disease-free survival at 5 years</i>
<i>Low grade</i>		
Adenocarcinoma <i>in situ</i>	1 (0.2%)	100%
Minimally invasive adenocarcinoma, non-mucinous	7 (1%)	100%
Minimally invasive adenocarcinoma, mixed mucinous and non-mucinous	1 (0.2%)	100%
<i>Intermediate grade</i>		
Lepidic predominant	29 (6%)	90%
Acinar predominant	232 (45%)	84%
Papillary predominant	143 (28%)	83%
<i>High grade</i>		
Micropapillary predominant	12 (2%)	67%
Solid predominant	67 (13%)	70%
Colloid predominant	9 (2%)	71%
Invasive mucinous adenocarcinoma, mixed mucinous/non-mucinous	13 (3%)	76%

PRONÓSTICO EXCELENTE

MAL PRONÓSTICO



514 Adenocarcinoma Estadio - I





Problemas de la nueva clasificación

- Solo aplica a piezas de resección
- Obliga a un estudio completo en los tumores de menos de 3 cm.
- Requiere medir focos de invasión
- Asegurar la infiltración puede ser difícil / subjetivo
- **No se define claramente la actitud quirúrgica**
- **Abre la problemática de biopsias intra/peroperatorias**



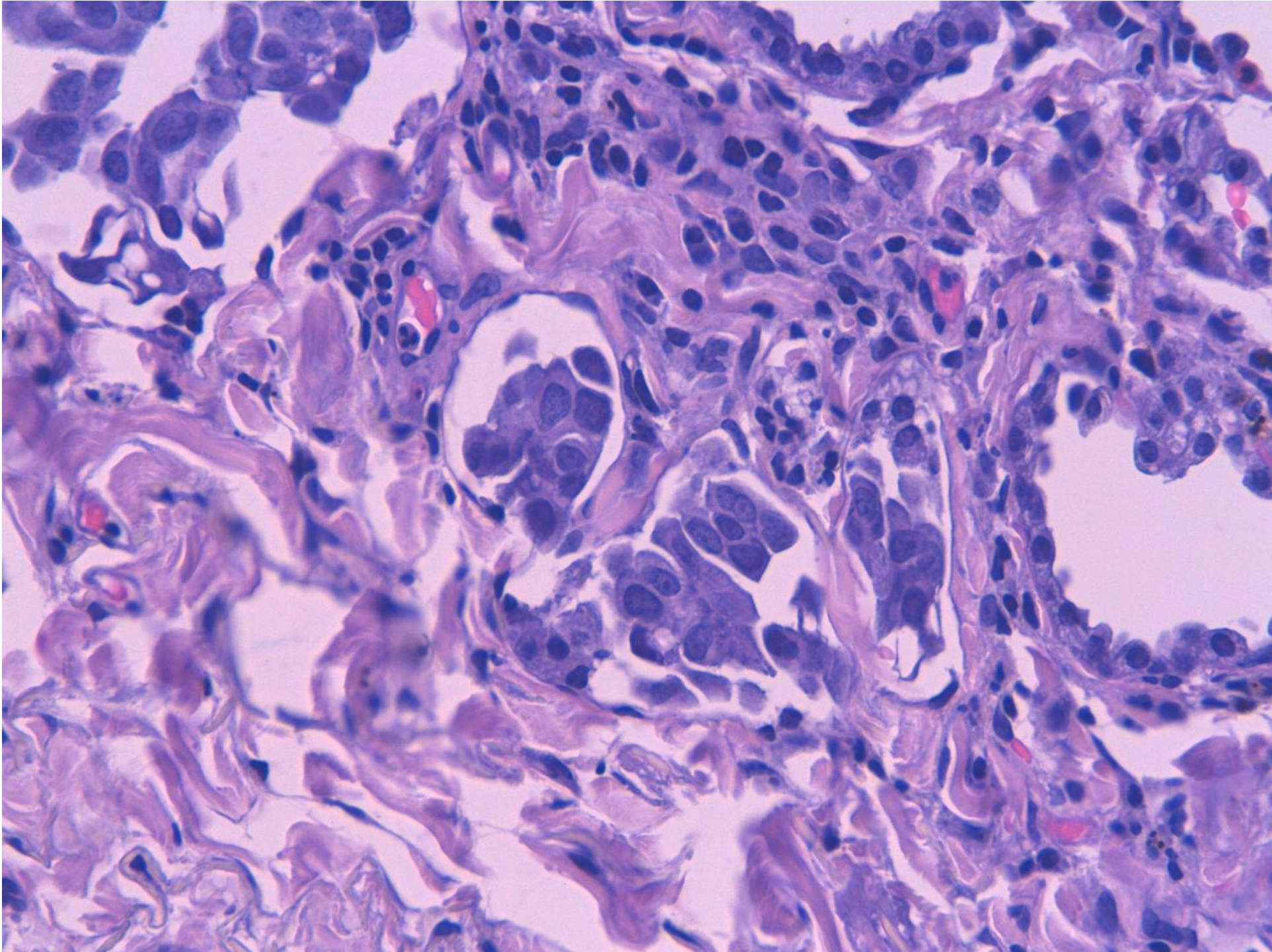
Criterios de infiltración en casos dudosos

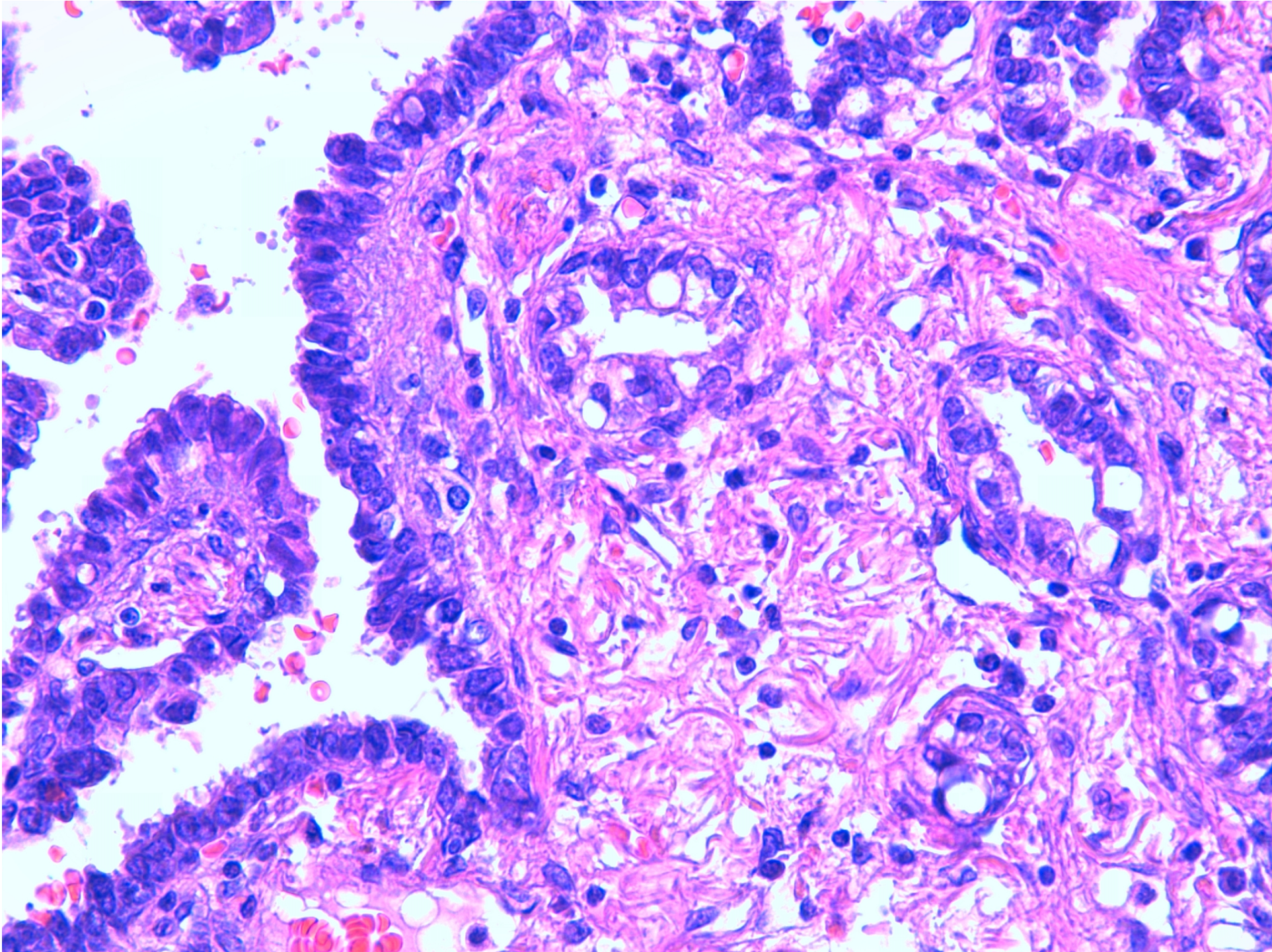
1. Kerr:

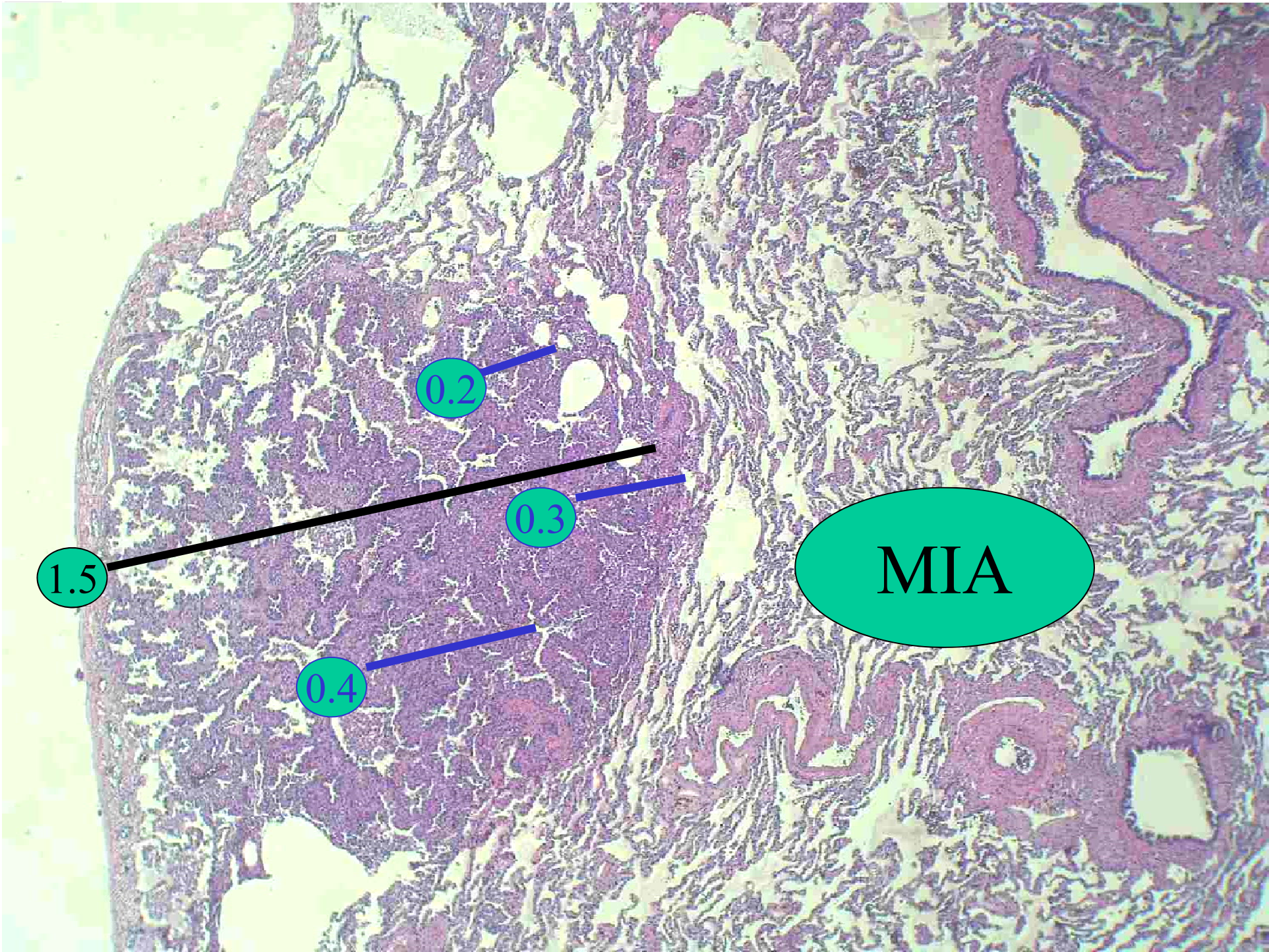
1. Cicatrización
2. Neofibroplasia
3. Destrucción trama elástica
4. Otros patrones de adenocarcinoma

2. Borkzuch

1. Forma de las glándulas, de bordes agudos









Good practice in Pathology

J Thorac Oncol 2011;6:244-285

1. When a diagnosis is made in a small biopsy or cytology specimen in conjunction with special studies, it should be clarified whether the diagnosis was established based on light microscopy alone or whether special stains were required.
2. Tissue specimens should be managed not only for diagnosis but also to maximize the amount of tissue available for molecular studies.
3. To guide therapy for patients with advanced lung adenocarcinoma, each institution should develop a multidisciplinary team that coordinates the optimal approach to obtaining and processing biopsy/cytology specimens to provide expeditious diagnostic and molecular results.



Good practice in Pathology

J Thorac Oncol 2011;6:244-285

4. The terms AIS or MIA should not be used in small biopsies or cytology specimens. If a noninvasive pattern is present in a small biopsy, it should be referred to as lepidic growth.
5. The term large cell carcinoma should not be used for diagnosis in small biopsy or cytology specimens and should be restricted to resection specimens where the tumor is thoroughly sampled to exclude a differentiated component.



Bloques de parafina





Bloques de parafina

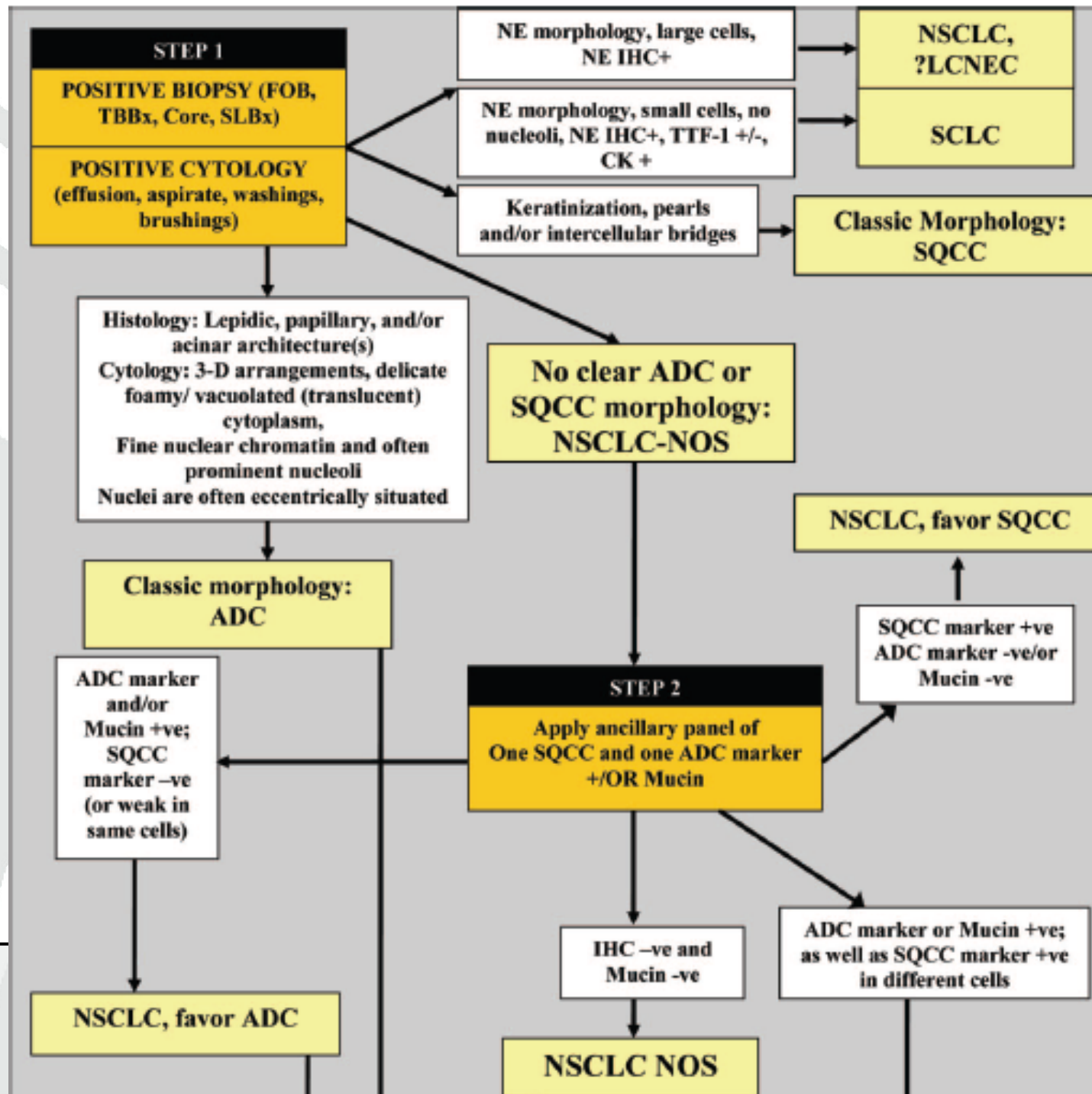
La muestra es muy importante para el paciente

Es necesario tener protocolos adecuados



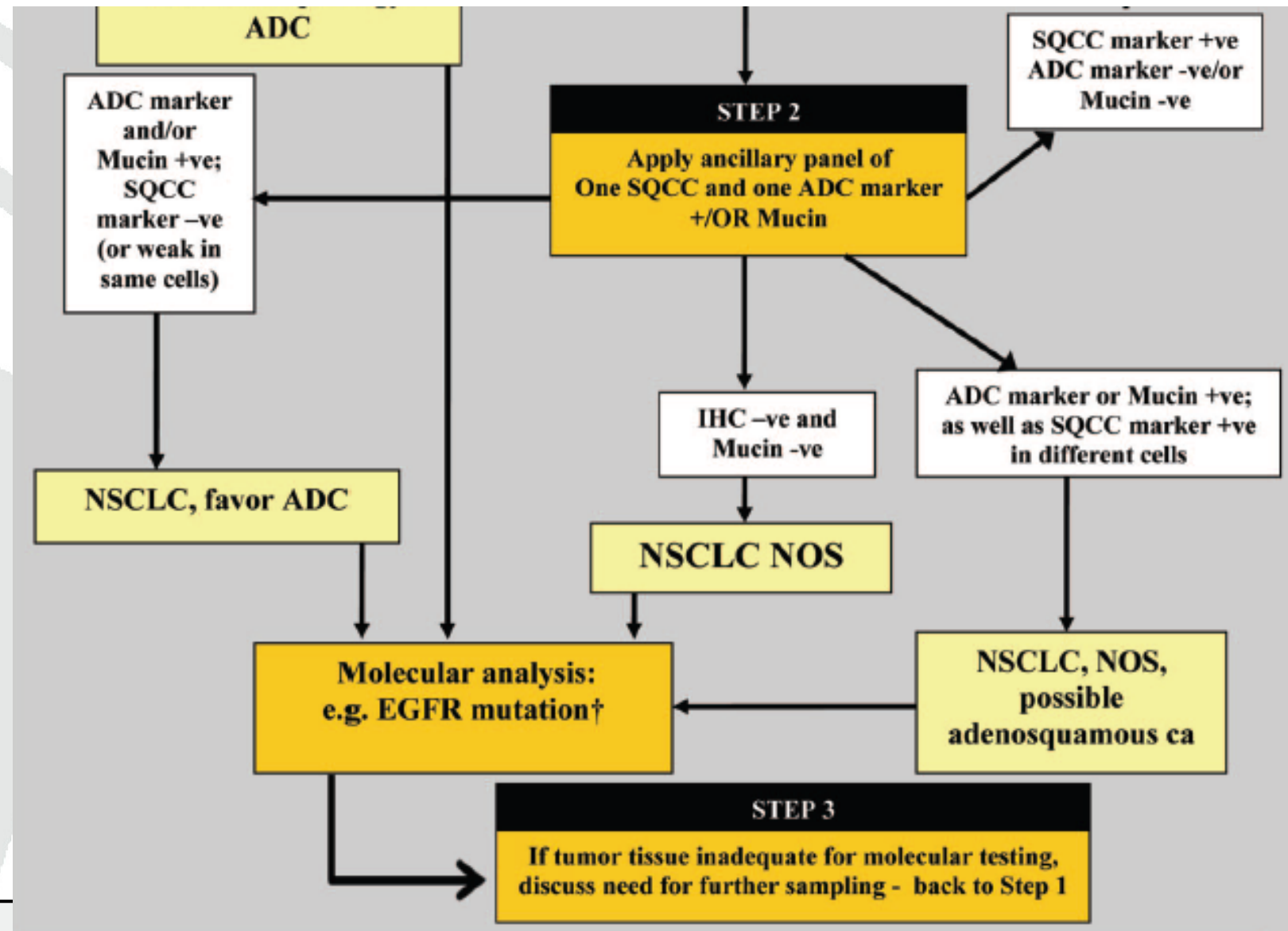
ALGORITMO DIAGNÓSTICO

J Thorac Oncol 2011;6:244-285



ALGORITMO DIAGNÓSTICO

J Thorac Oncol 2011;6:244-285





Pautas para patólogos

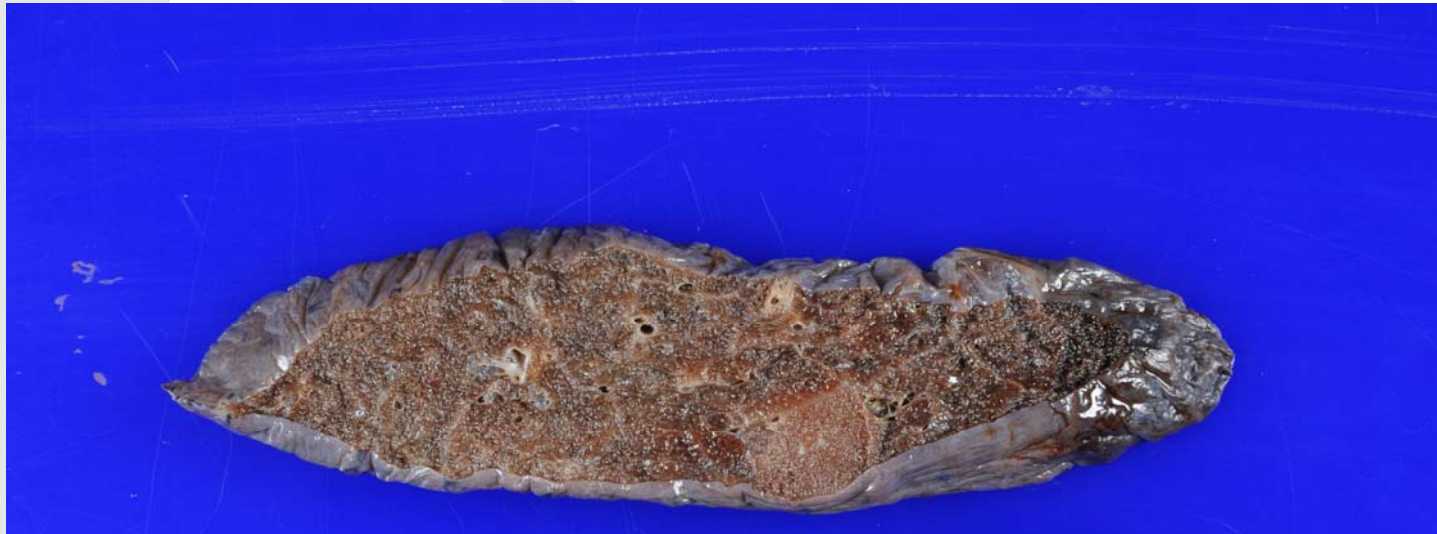
- Tipo histológico exacto
- Diagnóstico completo para aplicar TNM
- Aplicar la nueva clasificación
- 2011: Mutaciones de EGFR en no escamosos
- 2013: traslocación EML4/ALK por FISH
- Participar en ensayos: Kras / Braf / microRNA,

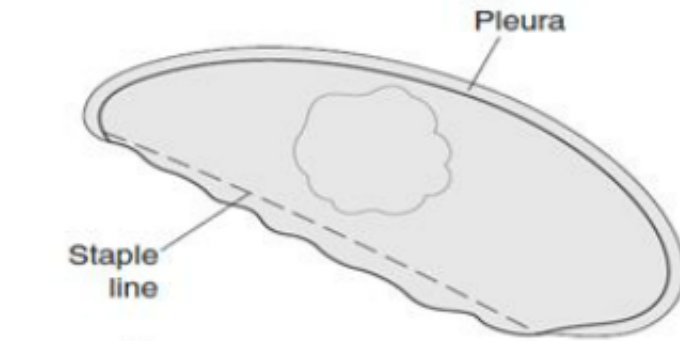


Implicaciones quirúrgicas



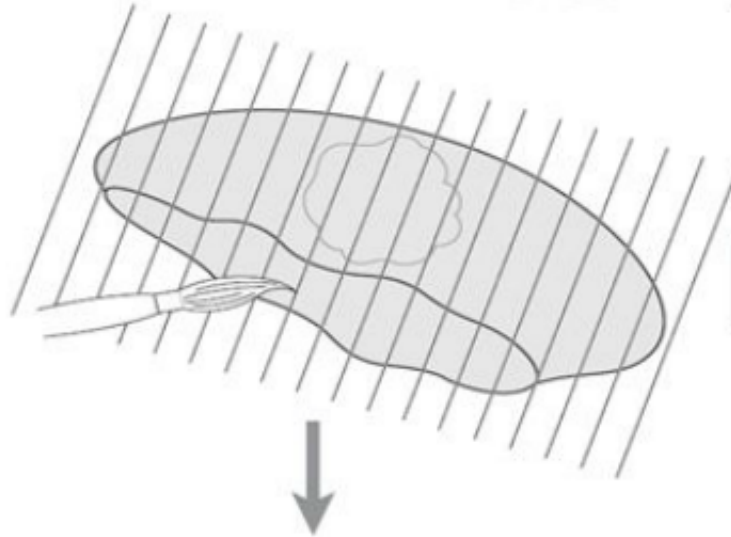
Eur Respir J 2012; 39: 478–486



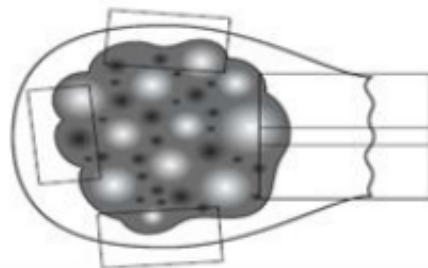


1. Locate the lesion and paint the overlying pleura

2. Cut off the stapled margin



3. Paint the cut parenchymal margin and serially slice perpendicular to it



4. Block tumour in relation to lung, pleura and parenchymal margin

Localizar la lesión y pintar

Cortar el margen grapado

Pintar el margen y cortar.

Descripción de la lesión y del resto del pulmón.

Recogemos secciones de cualquier lesión, pleura y parénquima no afectado.







Wedge resection specimen factors

Pleural surface–based margin distance (mm)	12.4
Gross cut-surface margin distance (mm)	3.9
Microscopic margin distance (mm)	1.2

Wedge Resection Specimens

No Adenocarcinoma

No. (%) of specimens	17 (55)
Mean microscopic margin distance (mm)	2.4
Mean gross cut-surface margin distance (mm)	4.4
Mean pleural surface–based margin distance (mm)	13.6
Mean adenocarcinoma maximum dimension (mm)	19.4

parenchymal stretching and pulling induced by staples. A substantial component of the marginal tissue had been artificially pulled into place and held under tension by the staples.



Survival After Segmentectomy and Wedge Resection in Stage I Non–Small-Cell Lung Cancer

Cardinale B. Smith, MD, MSCR,† Scott J. Swanson, MD,‡ Grace Mhango, MPH,§
and Juan P. Wisnivesky, MD, DrPH§ |*

In summary, these results suggest that segmentectomy compared with wedge resection may lead to improved survival among patients with stage IA NSCLC.

(J Thorac Oncol. 2012;00:00-00)

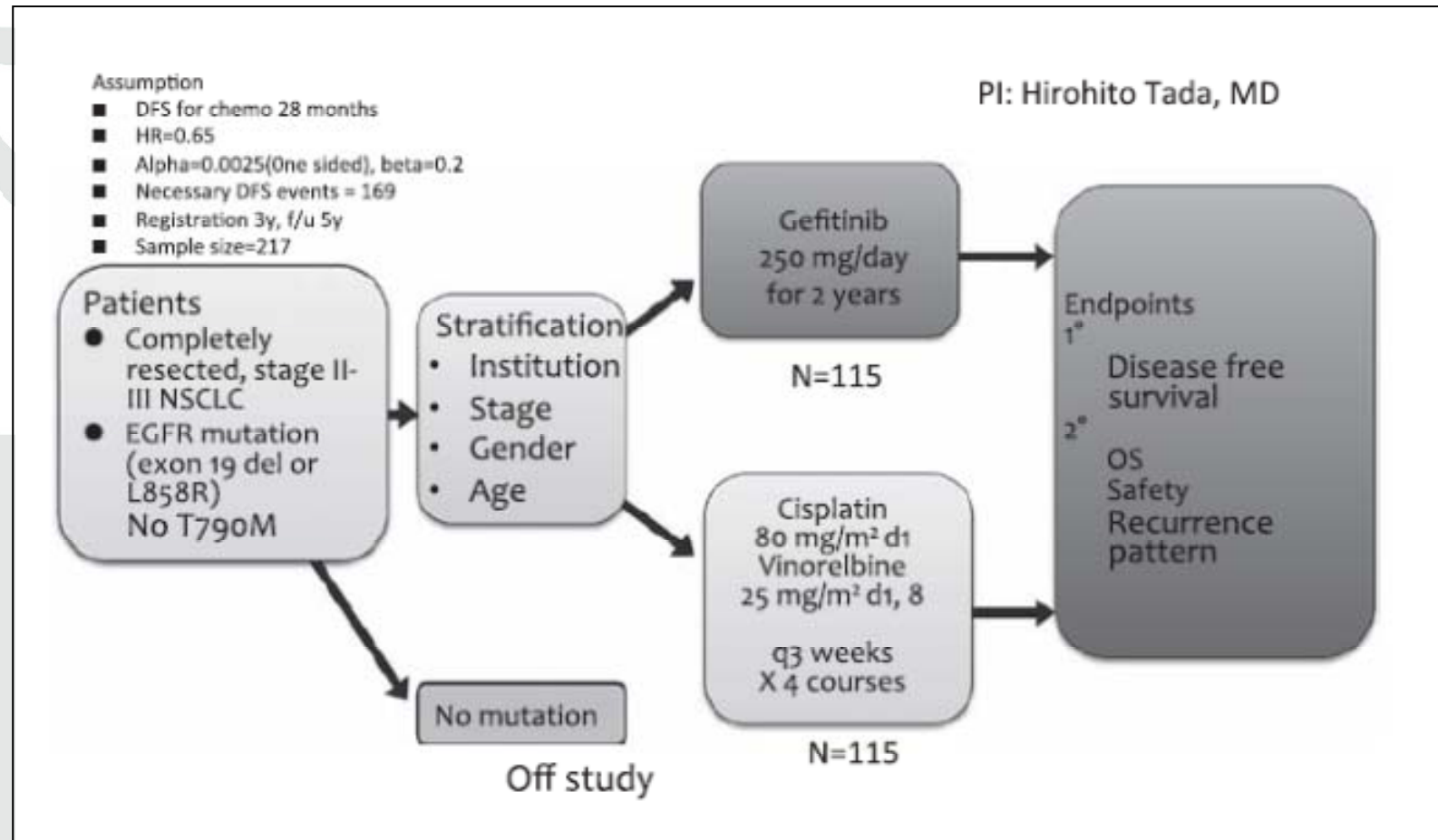


FIGURE 1. Schema of ongoing randomized phase III trial of adjuvant gefitinib versus cisplatin and vinorelbine in completely resected (stages II–III) NSCLC patients with mutated *EGFR* (WJOG6410L, IMPACT study). NSCLC, non–small-cell lung cancer.



Lesiones ex-Bronquioloalveolar

- **Hiperplasia adenomatosa atípica**
 - $< 0,5$ cm
- **Adenocarcinoma in situ**
 - $> 0,5$ cm. ≤ 3 cm.
 - No evidencia de invasión
- **Adenocarcinoma mínimamente invasivo**
 - Tamaño: $> 0,5$ cm. ≤ 3 cm.
 - Infiltración: ≤ 0.5 cm.
- **Lepidic predominant adenocarcinoma (non-mucinous)**
 - Infiltration $> 0,5$ cm. o tamaño > 3 cm.
- **Adenocarcinoma mucinoso infiltrante**



jramirez@clinic.ub.es