

Neoplasias Pulmonares

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Internista - Oncólogo Clínico

Definición

- ✦ Opacidad intrapulmonar, circular, bien definida, rodeada por pulmón ventilado, que mide $< 3\text{cm}$.
- ✦ Masas si $> 3\text{cm}$.
- ✦ Micronodulo si $< 3\text{ mm}$
- ✦ Hallazgo incidental:
 - ✦ Rx de tórax: 0,09 - 0,2%
 - ✦ TC de tórax: 8-51%



Pseudonodulos

- ✦ Fractura costal (Consolidación)
- ✦ Lesión cutánea
- ✦ Dispositivos intra o extratorácicos
- ✦ Variantes anatómicas
- ✦ Areas compuestas que incrementan la opacidad



Etiología NPS (No tumoral)

- ✦ Congénita
 - ✦ Quiste broncogénico
 - ✦ MAV
 - ✦ Atresia bronquial
- ✦ Traumática
 - ✦ Hematoma
- ✦ Miscelánea
 - ✦ Wegener
 - ✦ AR
 - ✦ Amiloidosis
 - ✦ Atelectasia redonda
 - ✦ Infecciosa

56%

Etiologia NPS - Neoplasica

- ✦ Tamizacion en fumadores:
 - ✦ 13% NPS > 5 mm
 - ✦ Carcinoma broncogenico
 - ✦ NET
 - ✦ Hamartoma
 - ✦ Metástasis
 - ✦ Linfoma

44%

Evaluación

- ✦ Radiografía simple (PA, lat)
- ✦ TC
 - ✦ Simple
 - ✦ Contraste IV
- ✦ ACAF/biopsia
- ✦ RM con GD-DTPA
- ✦ PET con FDG-F18

Consideraciones

- ✦ Experiencia
- ✦ Alto kV
- ✦ Radiografía digital
- ✦ Historia clínica
- ✦ Comparar con estudios radiológicos previos

Caracterización

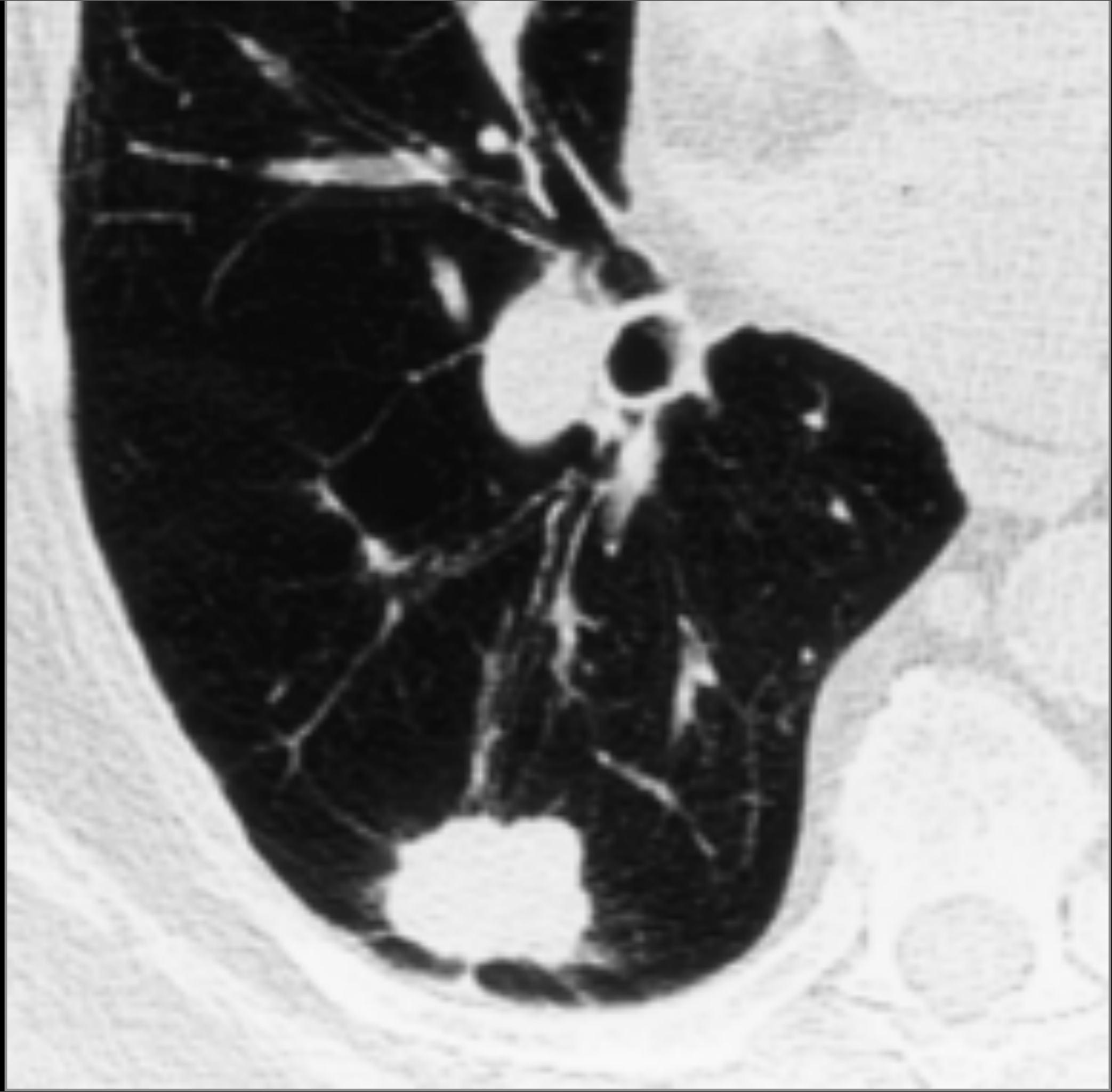
- ✦ Localización
- ✦ Tamaño
- ✦ Márgenes
- ✦ Calcificación
- ✦ Patrón de crecimiento
- ✦ Lesiones satélites

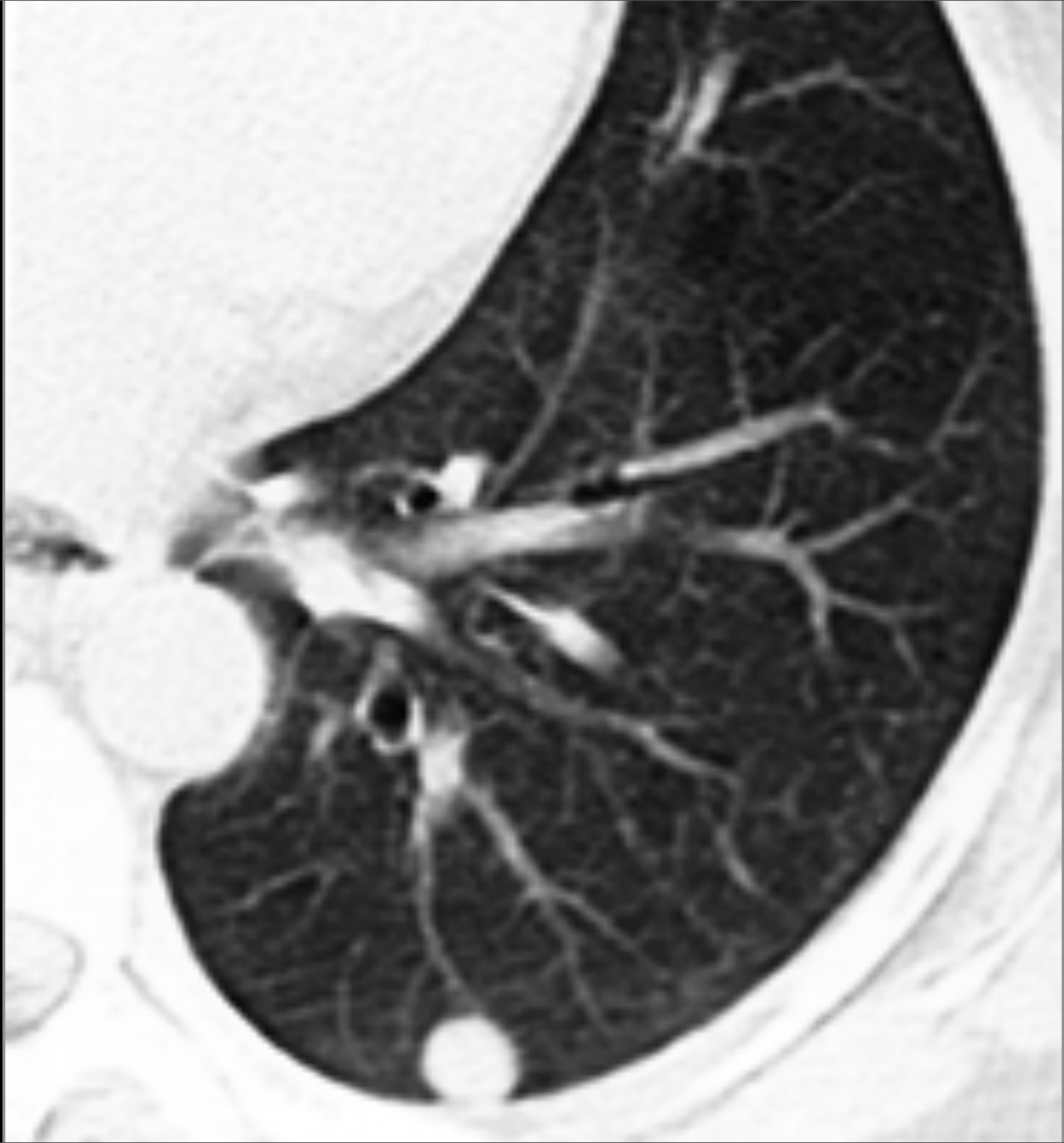
Tamaño

- ✦ 95% de las lesiones mayores de 3 cm son malignas
- ✦ 42% de las lesiones menores de 2 cm
- ✦ 15% de las lesiones menores de 1 cm

Márgenes

- ✦ Lobulaciones y espiculaciones sugieren agresividad
 - ✦ Neoplasia
 - ✦ Infección
- ✦ Bordos nítidos no la descartan





Calcificación

- ✦ Sugiere etiología benigna
- ✦ Excepciones
 - ✦ Periférica
 - ✦ Irregular
 - ✦ Heterogénea

Patrones benignos

- ✦ Difuso



- ✦ Lamelar

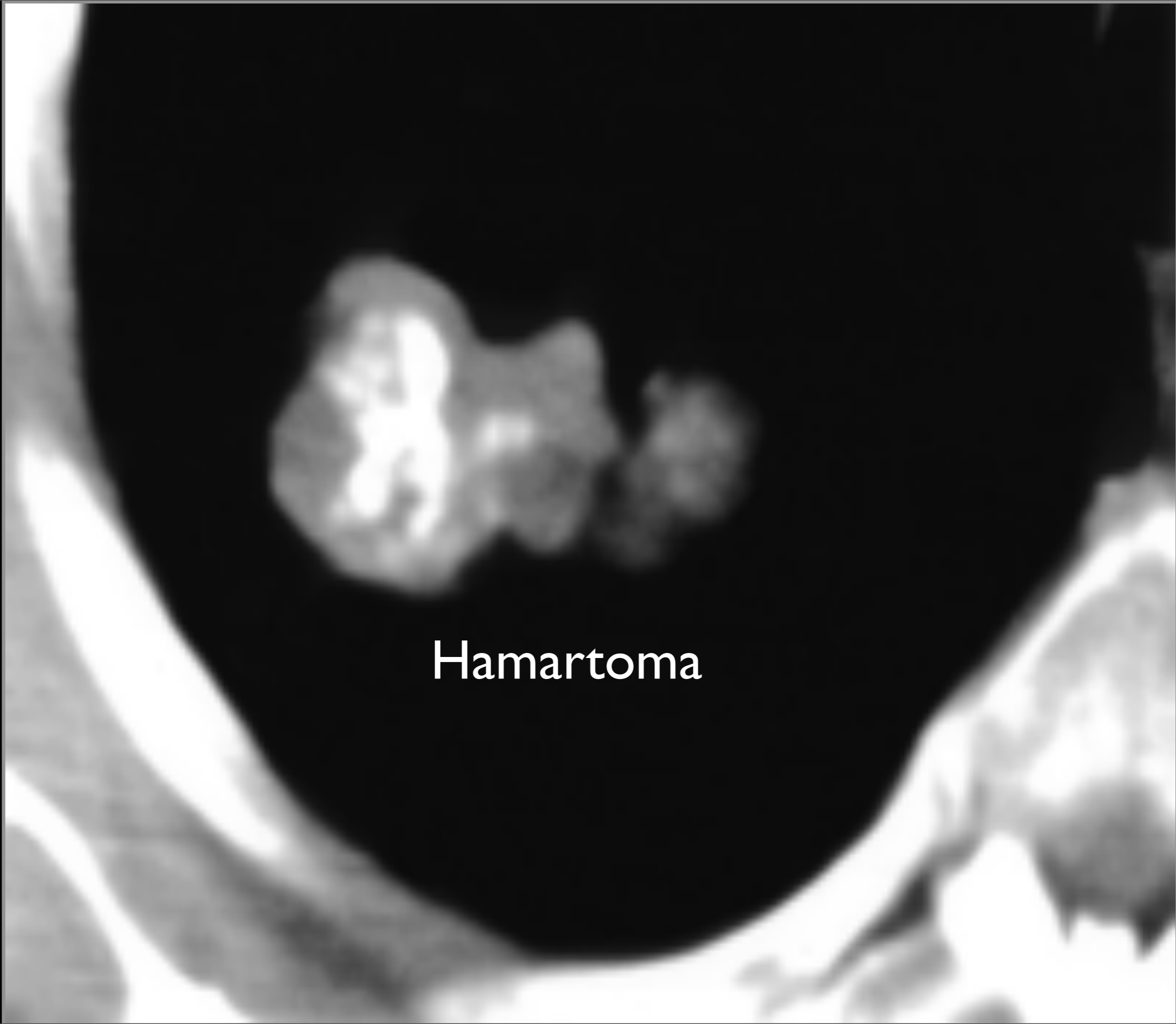


- ✦ Palomita de Maíz

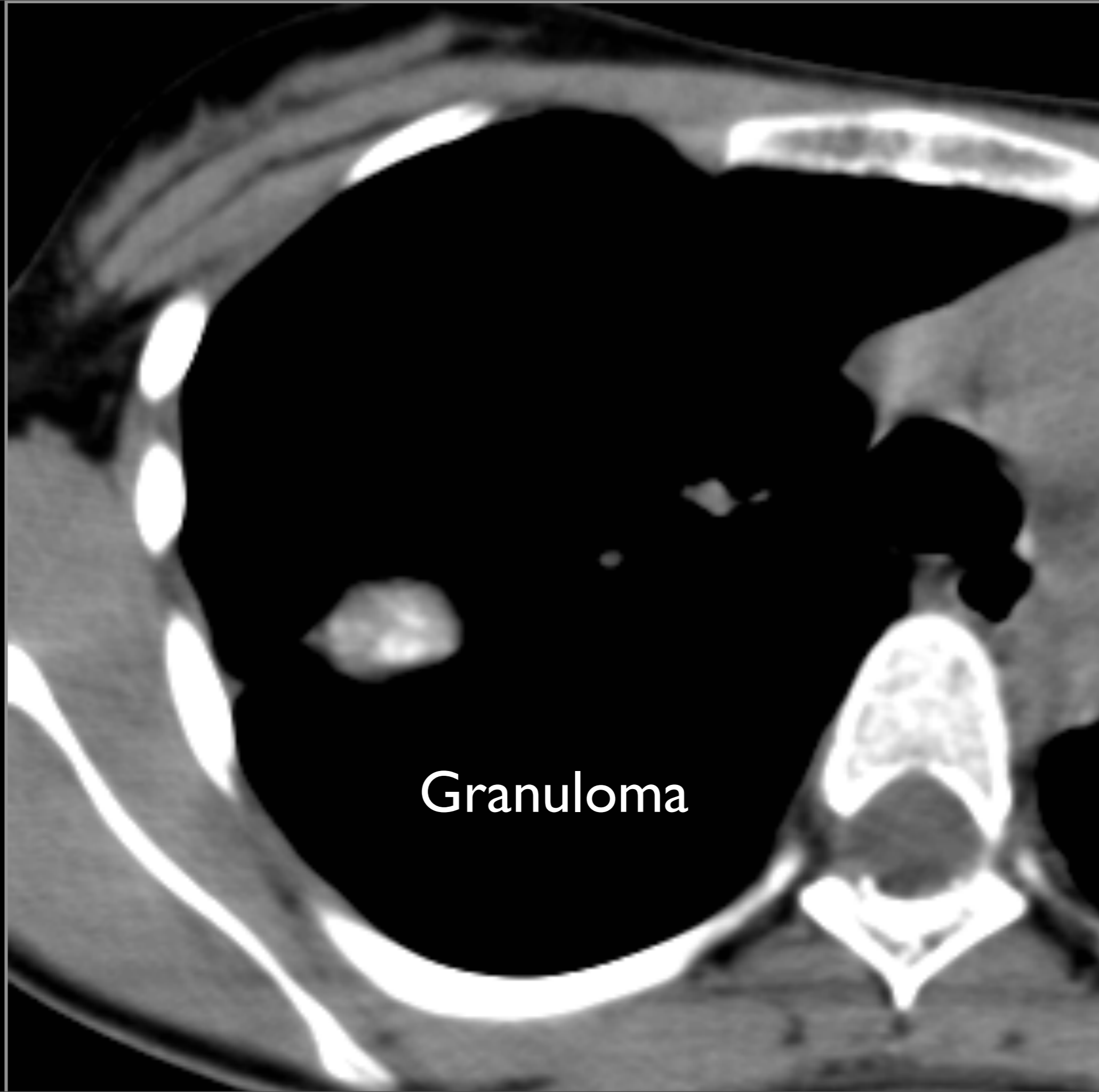


- ✦ Central

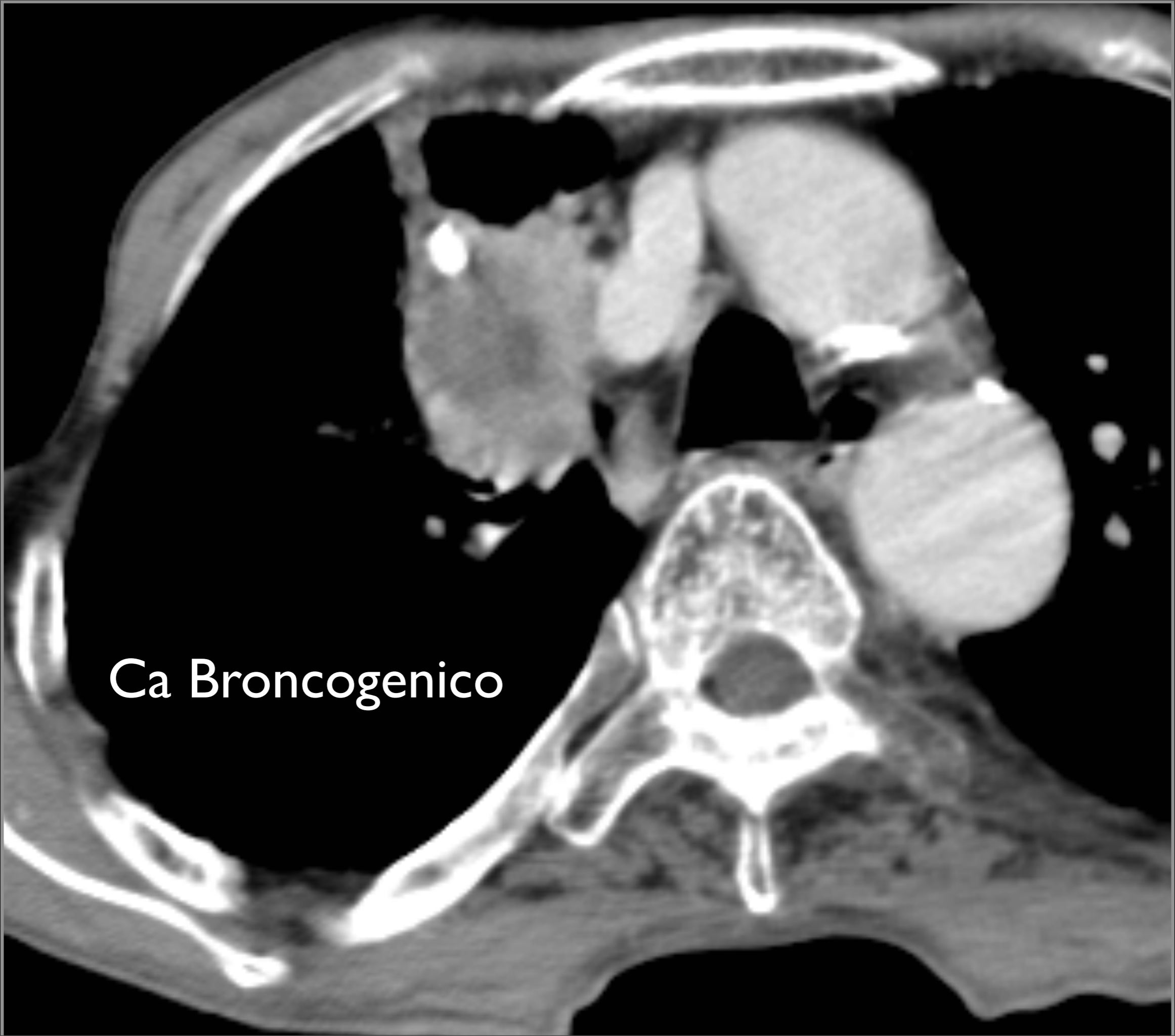




Hamartoma



Granuloma

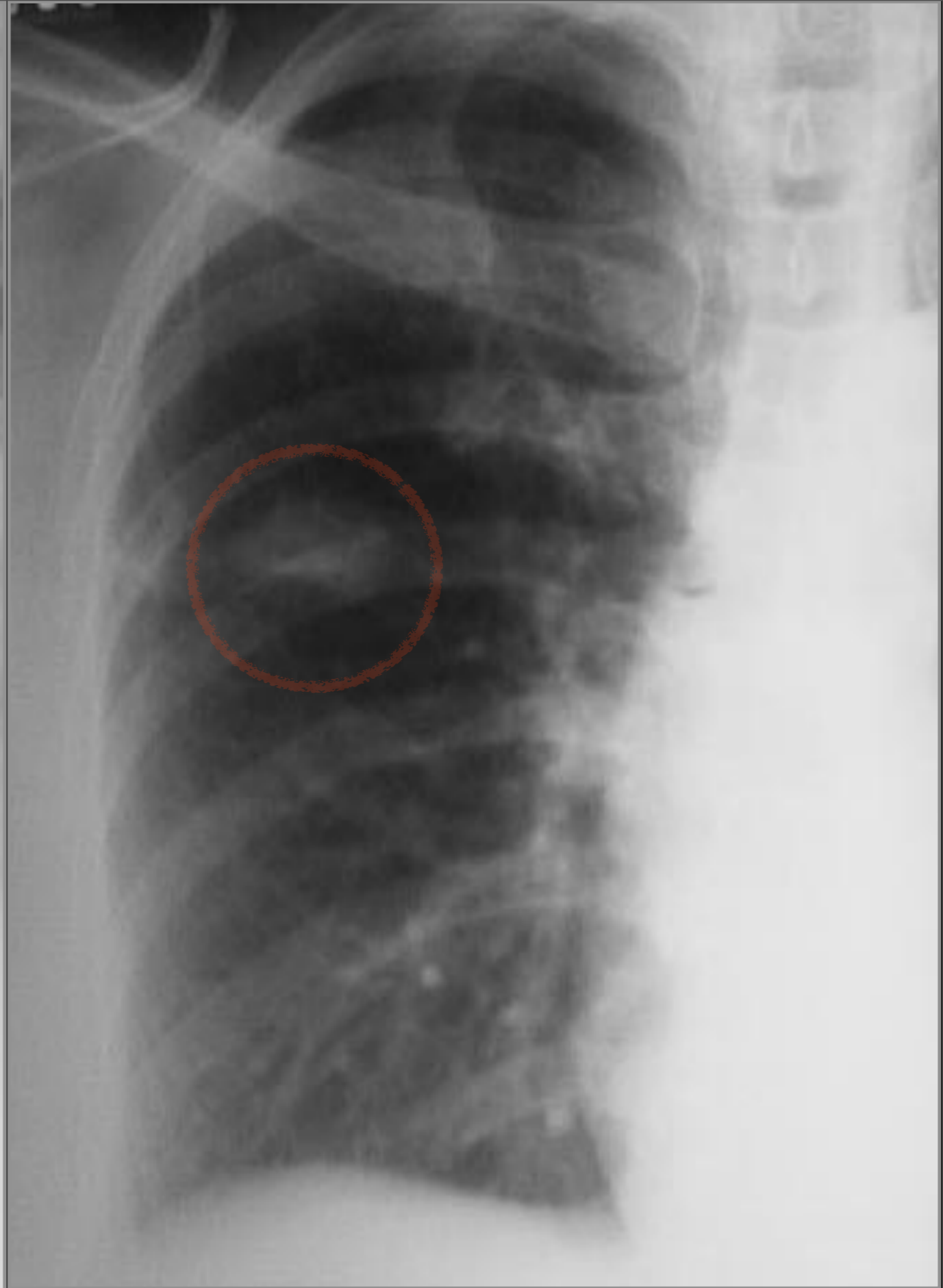
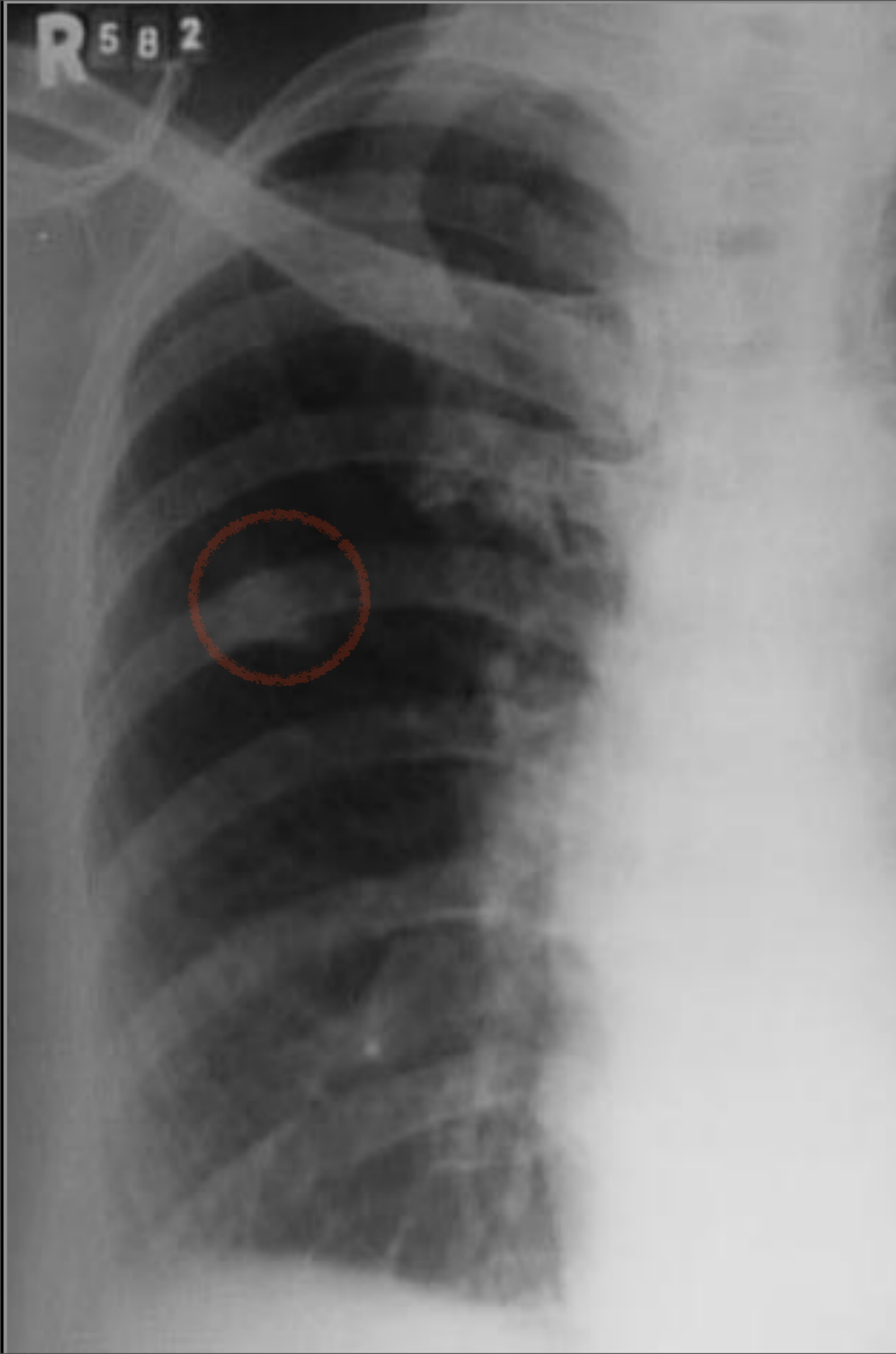


Ca Broncogenico

Patrón de crecimiento

- ✦ Tiempo de duplicación
 - ✦ Benigno
 - ✦ < 30 días
 - ✦ > 465 días
 - ✦ Incremento en volumen en 1.25 en dos dimensiones

R 5 8 2



60 días



Lesiones satélite

- ✦ Sugiere benignidad
- ✦ No se refiere a otras lesiones nodulares
- ✦ También observables en:
 - ✦ Neoplasia sobre lecho de lesión previa
 - ✦ “Scar” Ca

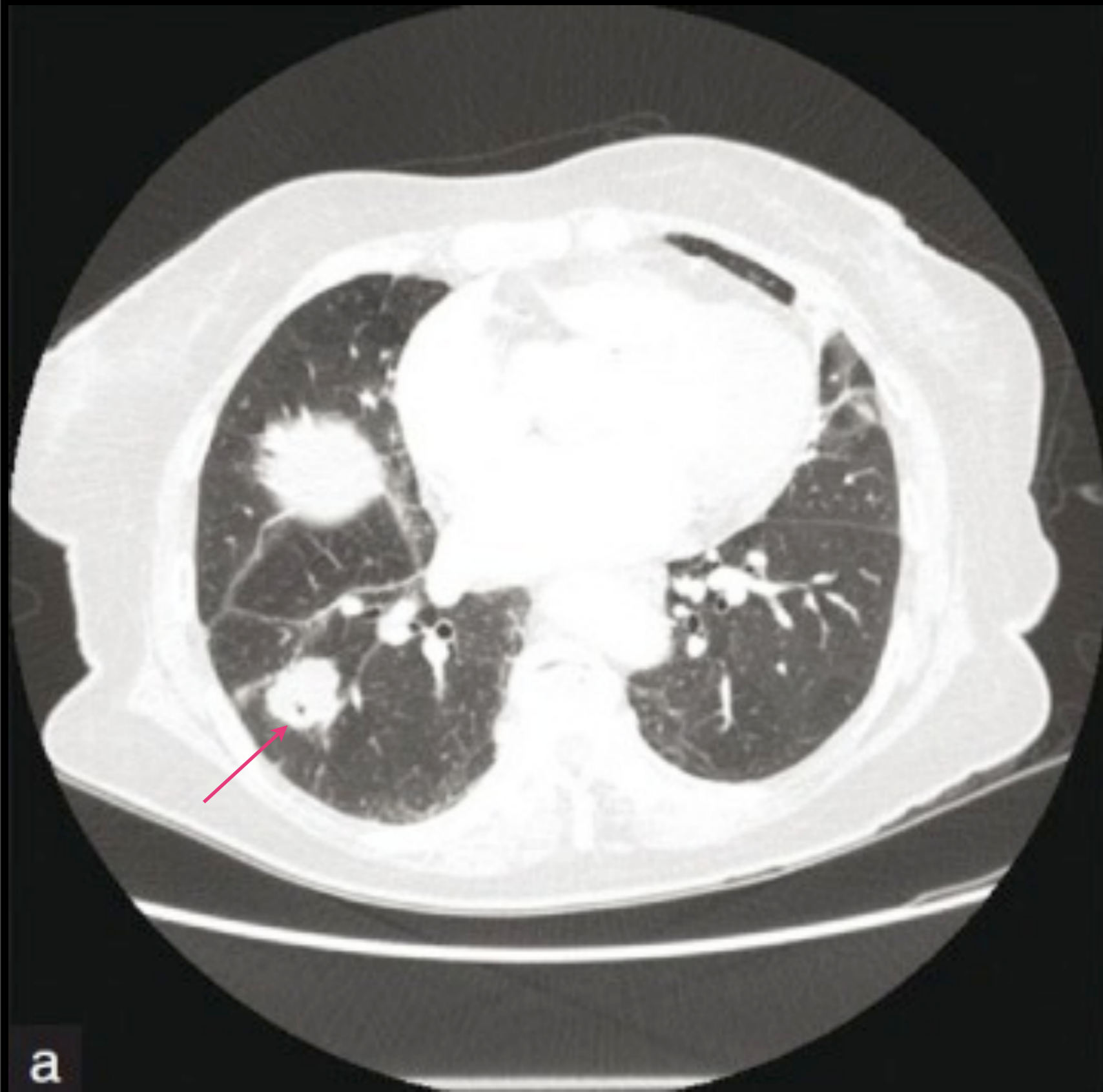
Localización

- ✦ Lóbulo superior derecho: Maligno primario
- ✦ Lóbulos inferiores: Lesiones metastasicas
- ✦ Sin valor en lesiones subpleurales

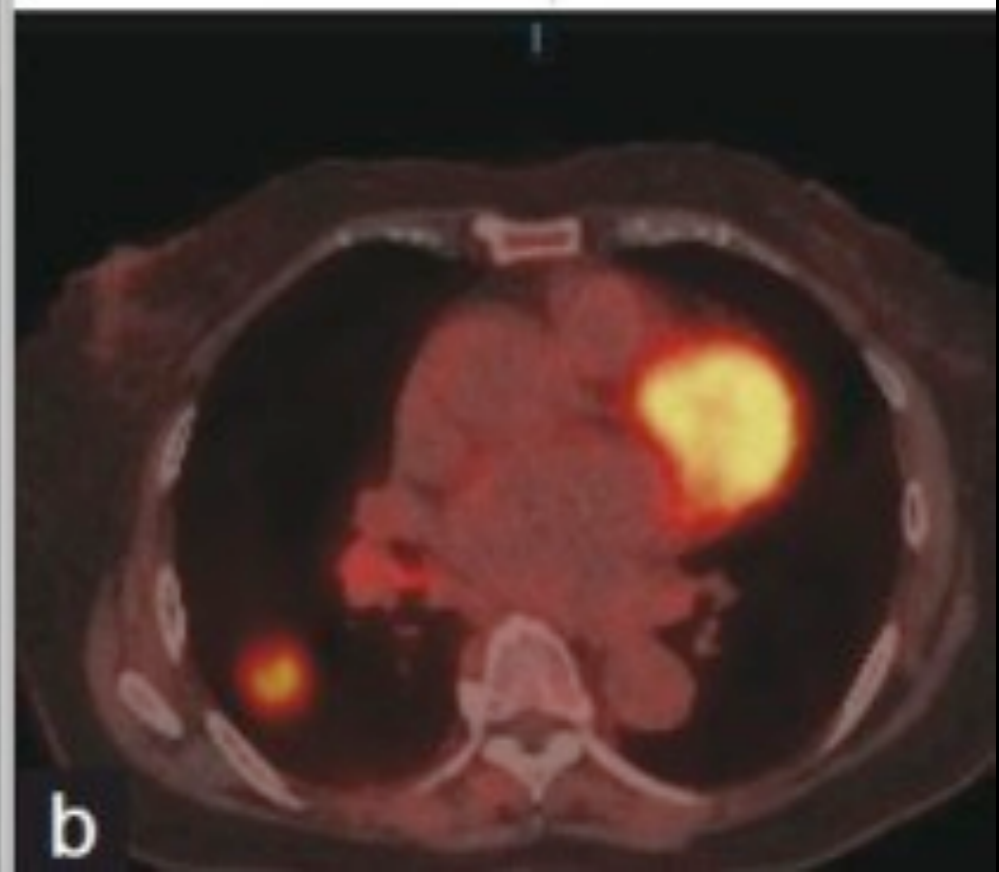
Cavilación

- ✦ Mas frecuente en lesiones malignas
 - ✦ 80% escamocelulares
- ✦ Pertinencia del grosor de la pared
 - ✦ 1 mm: 100% benigno
 - ✦ 5 - 15 mm: 51% benigno
 - ✦ > 15 mm: 95% malignos





a



b

Realce

- ✦ > 160 UH sugiere lesión benigna
 - ✦ Componente calcificado
- ✦ Ausencia de realce en fases dinámicas
- ✦ Realce > 20 UH (VPP 94,12% - VPN 84,31%)
 - ✦ Infección
 - ✦ Neoplasia

This is an axial CT scan of the chest at the level of the main bronchi. The lung fields are mostly clear, with some normal vascular markings. The mediastinum and chest wall structures are visible. The word "Simple" is overlaid in white text in the center of the image.

Simple

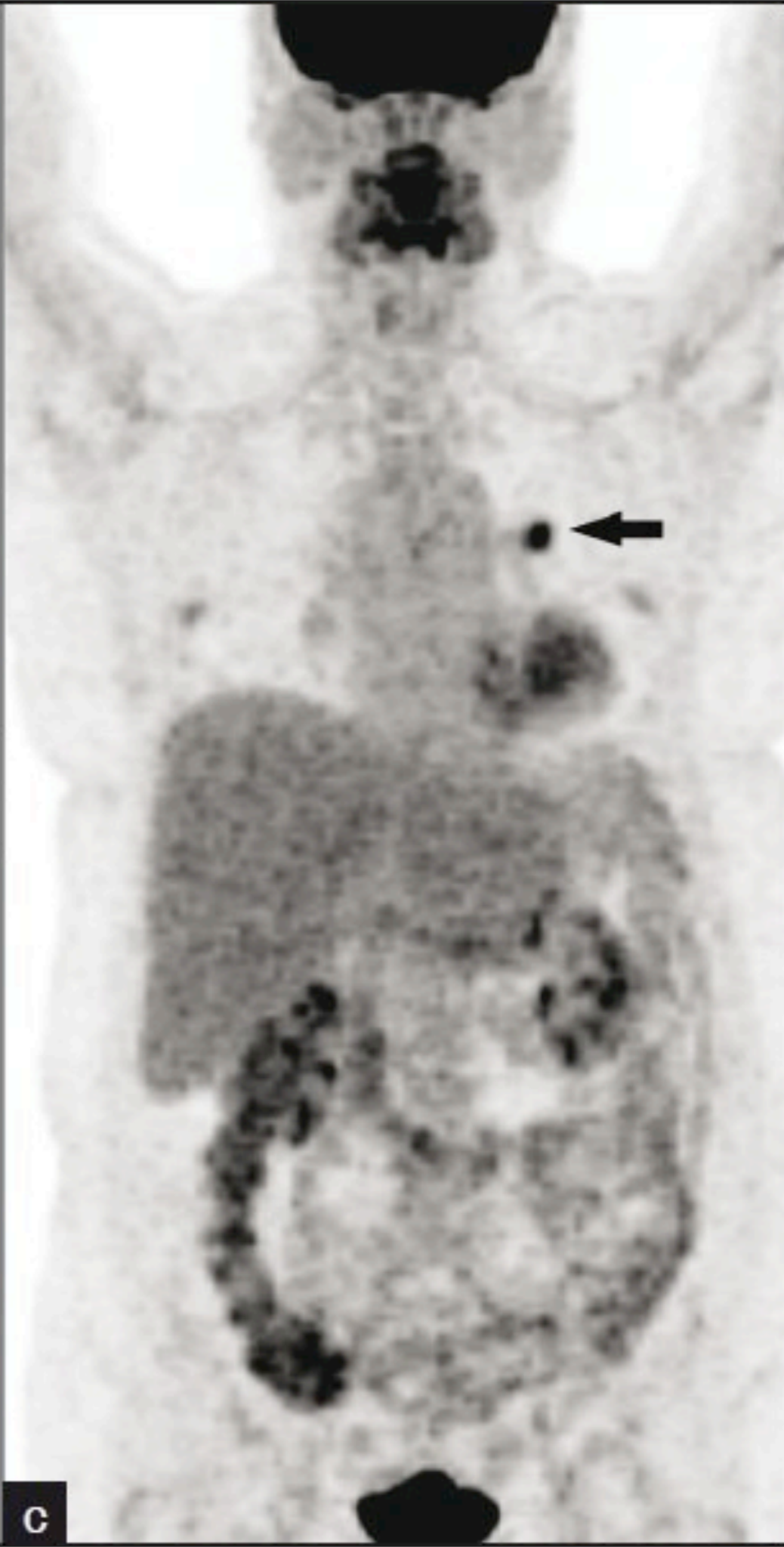
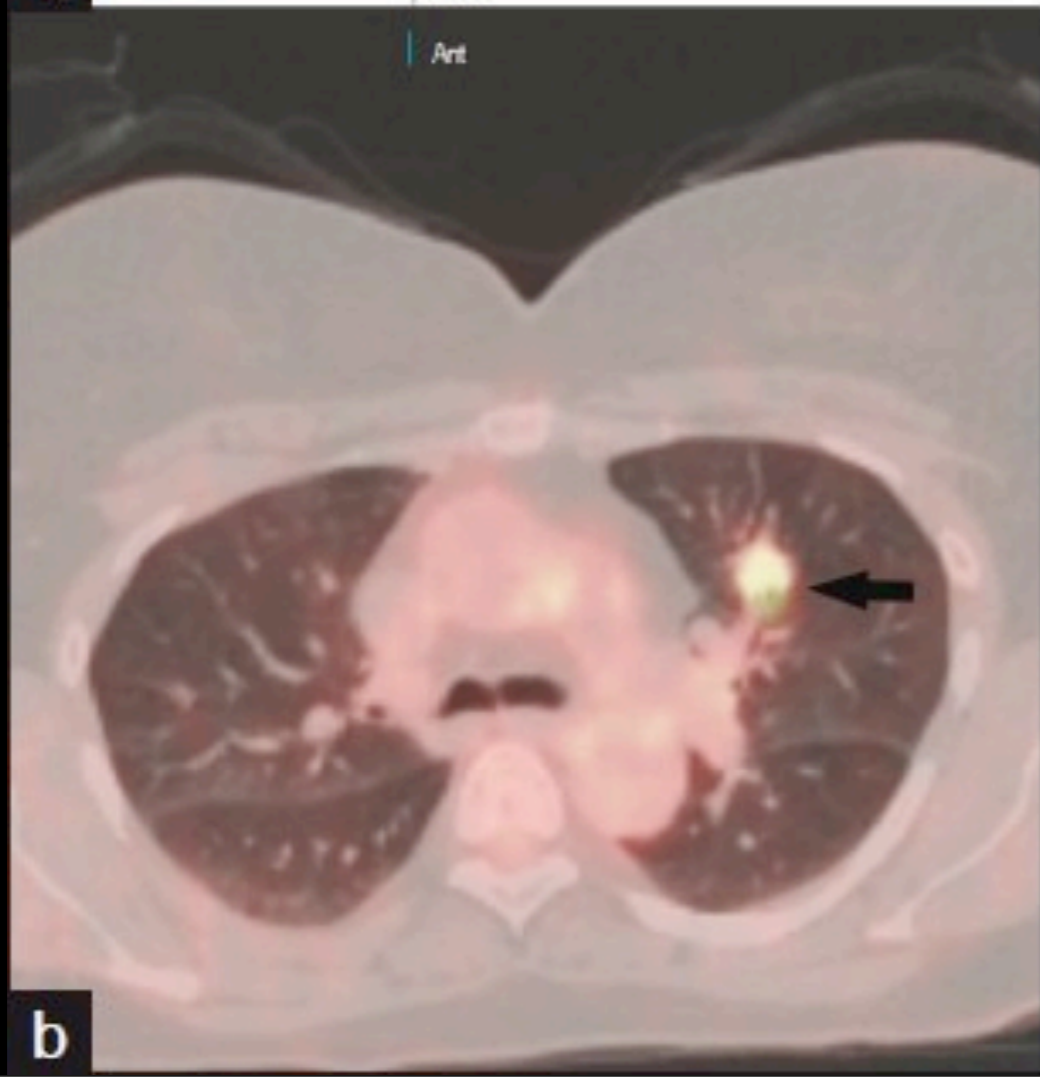
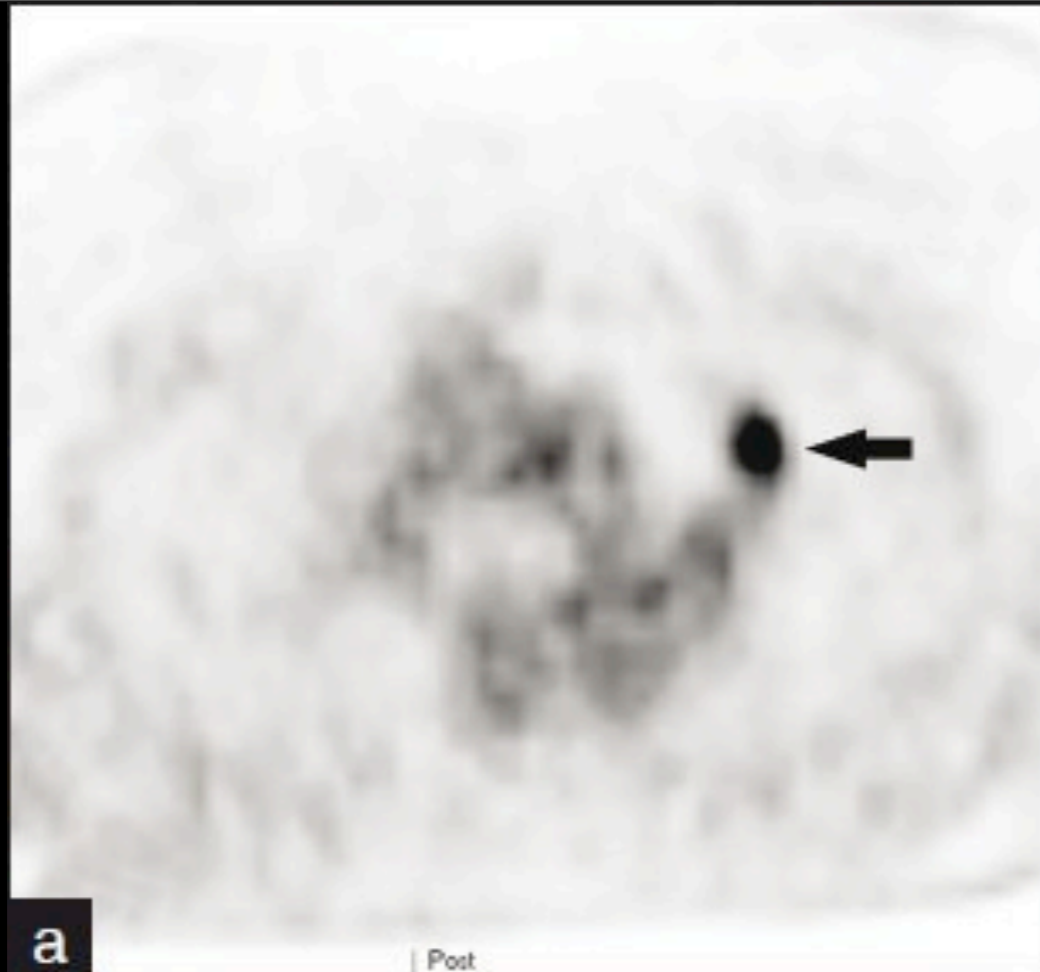
This is a contrast-enhanced axial CT scan of the chest at the same level as the simple scan. The contrast agent highlights the pulmonary vasculature and the mediastinal structures, including the heart and major vessels. The word "Contrastado" is overlaid in white text in the center of the image.

Contrastado



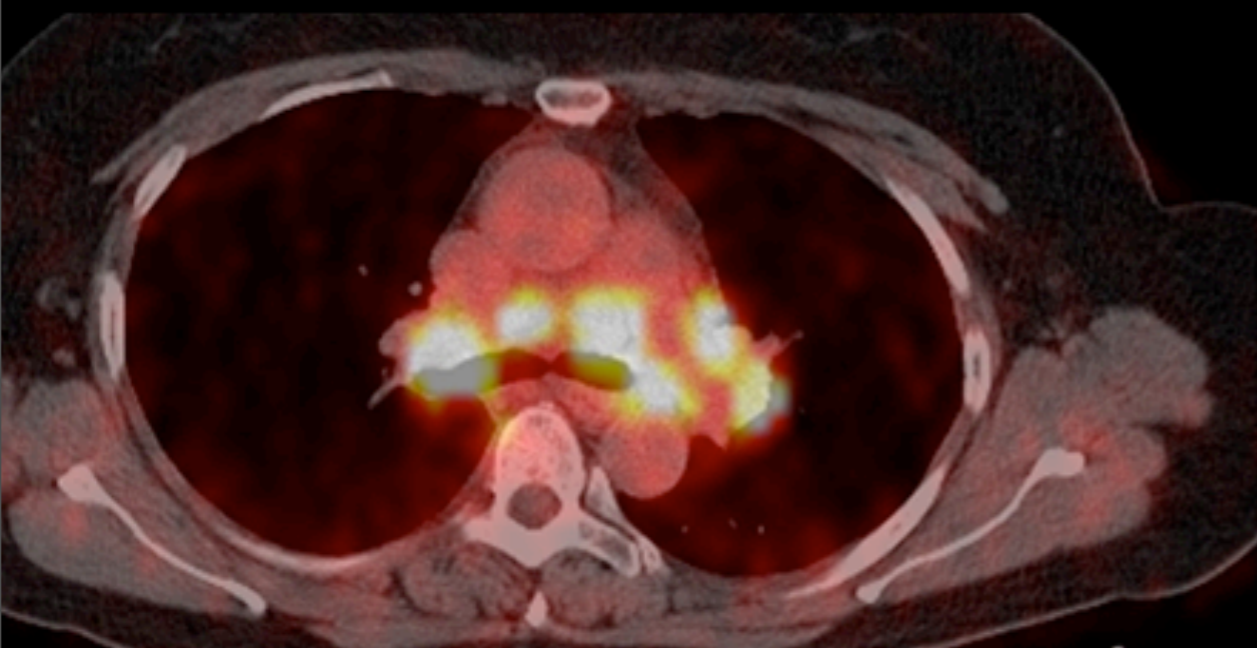
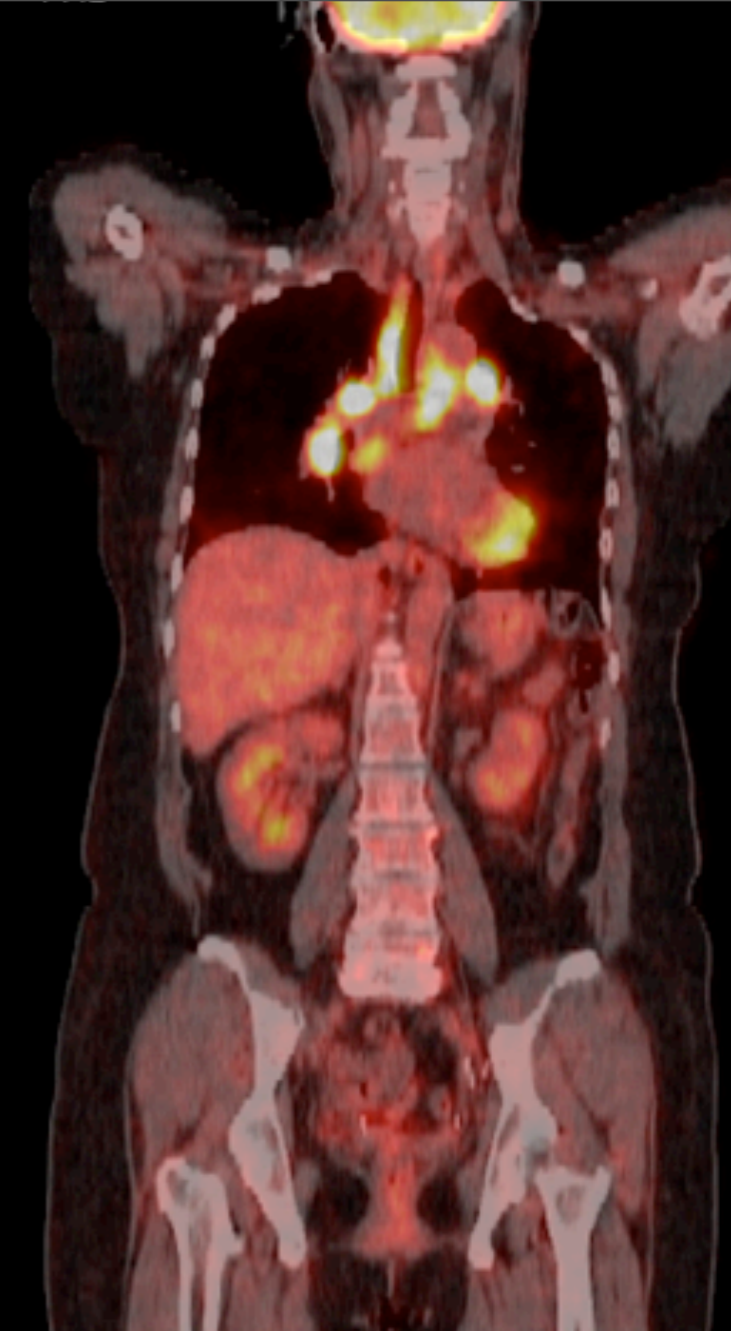
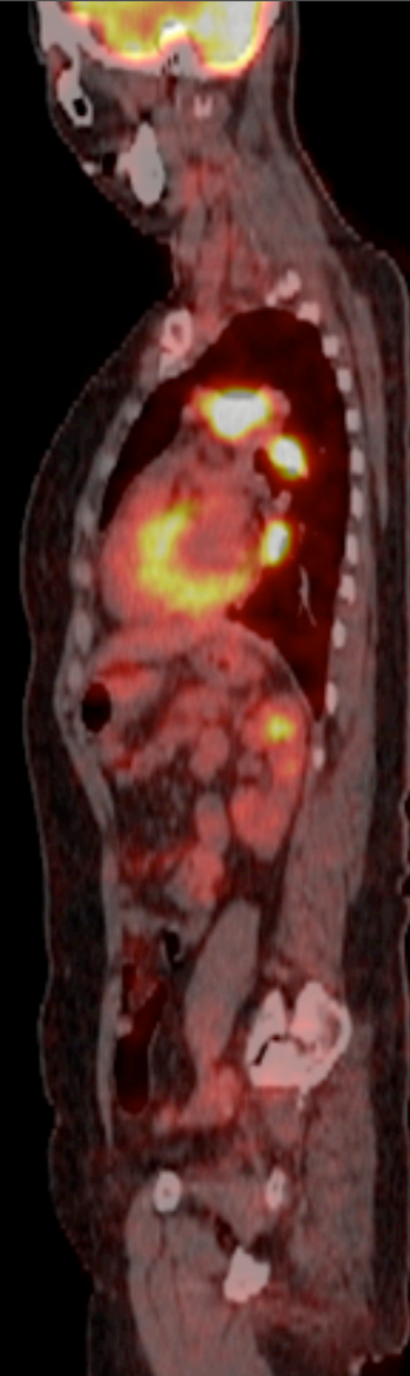
PET/CT

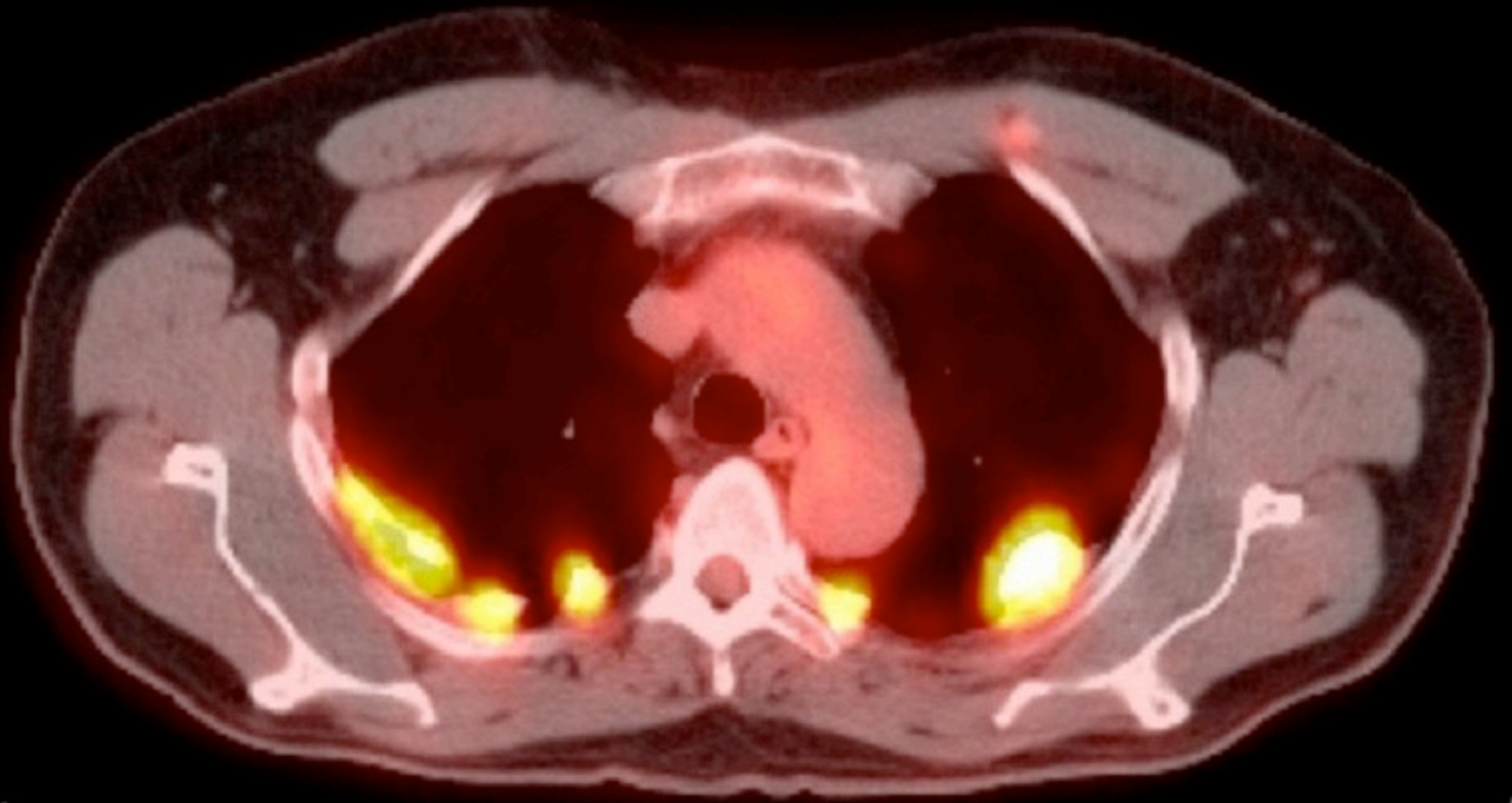
- ✦ Determinación de actividad metabólica
 - ✦ FDG-18
 - ✦ Principio de alta tasa en Neoplasias
 - ✦ Sensibilidad: 96%
 - ✦ Especificidad: 78%
 - ✦ Precisión: 92%



Falsos positivos

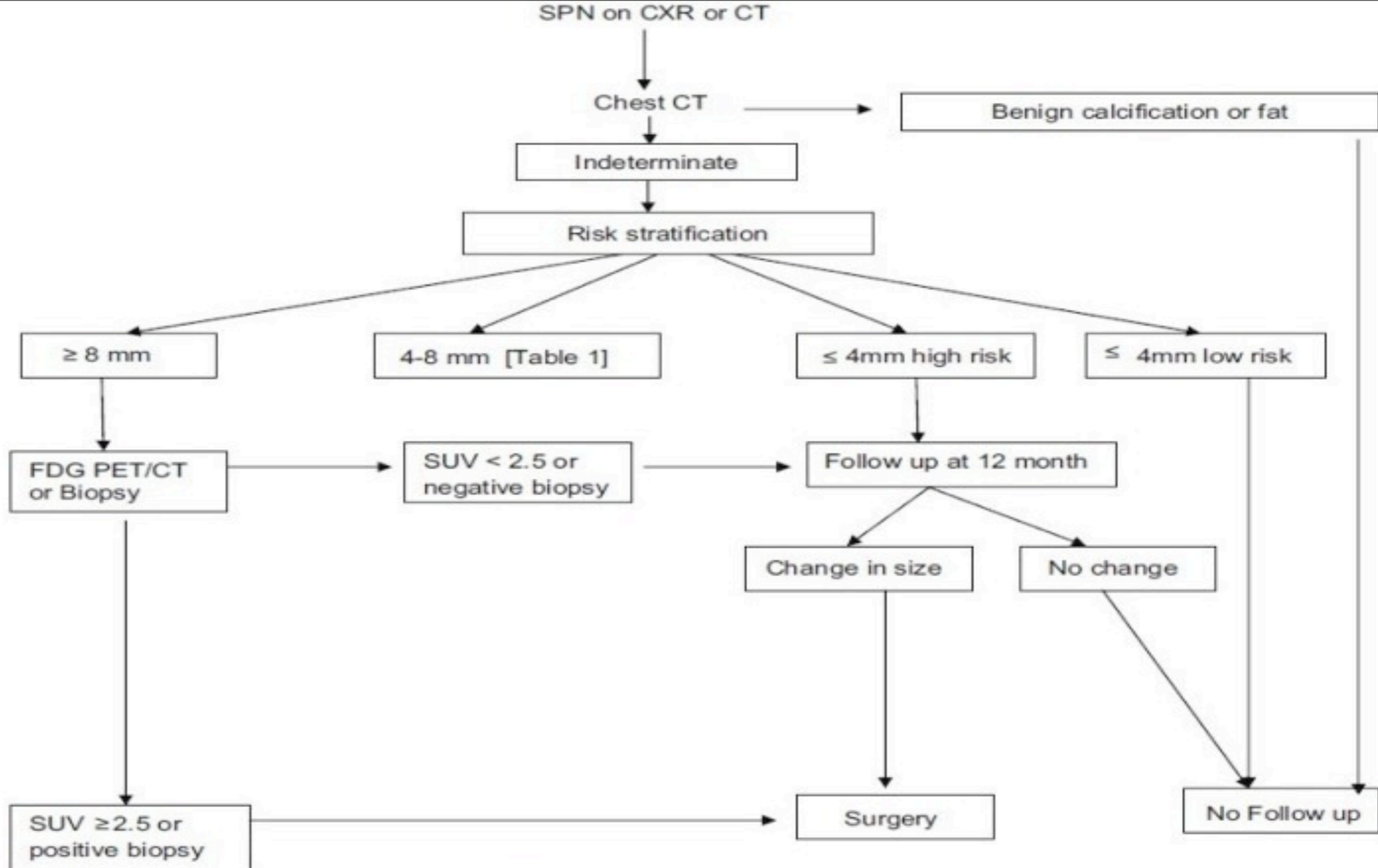
- ✦ Actividad inflamatoria
 - ✦ Sarcoidosis
 - ✦ Infecciones pulmonares
 - ✦ Pleurodesis por talco
 - ✦ Neumonitis post-irradiación
 - ✦ Post-quirúrgico





Falsos Negativos

- ✦ Carcinoma lepidico
- ✦ Adenocarcinoma cavitado
- ✦ NET bajo grado
- ✦ Lesiones adyacentes a Diafragma o pericardio
- ✦ Lesiones menores de 0,8 cm




Nodule size	Low risk patients (minimal or no smoking history or other risk factors)	High risk (history of smoking & other risk factors e.g. asbestos exposure)	Remarks
≤4 mm	No follow-up	CT at 12 months, if unchanged no further follow-up	Ground glass nodules and part solid nodules may require longer follow-up
>4–6 mm	Follow-up CT 12 months if unchanged no further follow-up	Initial follow-up CT 6-12 months, then 18-24 months follow-up CT if no change	Ground glass nodules and part solid nodules may require longer follow-up
>6–8 mm	Initial follow-up CT 6-12 months then 18-24 months if no change	Initial follow-up CT 3-6 months, then 9-12 months & 24 months if no change	
>8 mm	Follow-up CT at 3, 9 & 24 months, dynamic contrast enhanced CT, consider FDG PET± BIOPSY	Similar protocol as for low-risk patients	

Determinar probabilidad

- $X = (0.0391 * \text{Edad}) + (0.7917 * \text{Fumador}) + (1.3388 * \text{Cáncer}) + (0.1274 * \text{Diámetro}) + (1.0407 * \text{Espiculacion}) + (0.7838 * \text{Lóbulo superior}) - 6.8272$
- Probabilidad Malignidad = $100 * e^{(X)} / (1 + e^{(X)})$
 - $e \sim 2,71828\ 18284\ 59045\ 23536\ 02874\ 71352\ 66249\ 77572\ 47093\ 69995\dots$

Solitary Pulmonary Nodule Malignancy Risk (Mayo Clinic model)

 Share

Input:

Age

Smoker Current or former (1)
 Never smoker (0)

Cancer Extrathoracic cancer more than 5 years prior (1)
 None (0)

Nodule Diameter

Spiculation Yes (1)
 No (0)

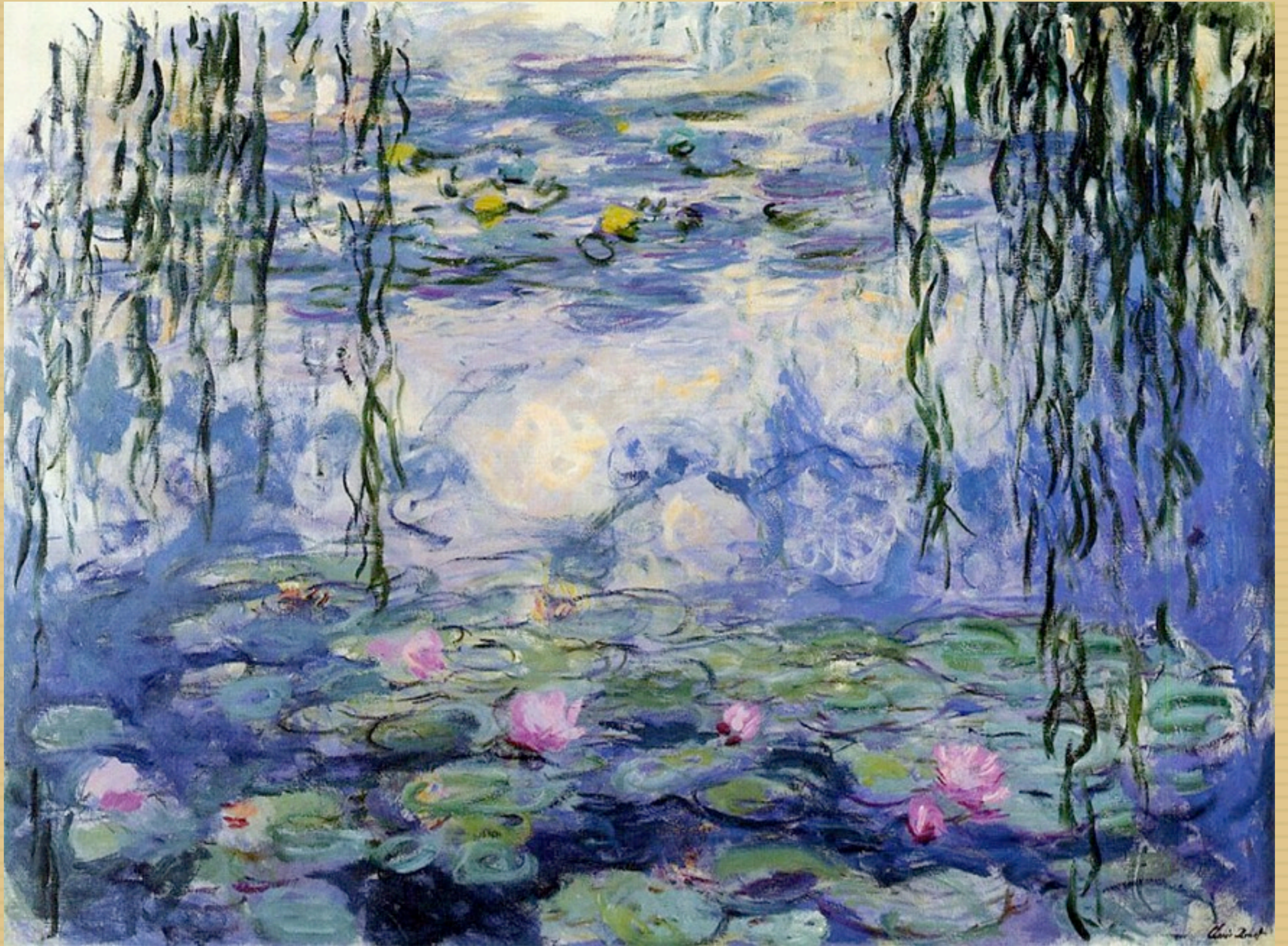
Upper Lobe Yes (1)
 No (0)

Results:

X

Malign Probability %

Decimal Precision:



Water Lilies - Claude Monet 1840 - 1926

Cáncer de Pulmón

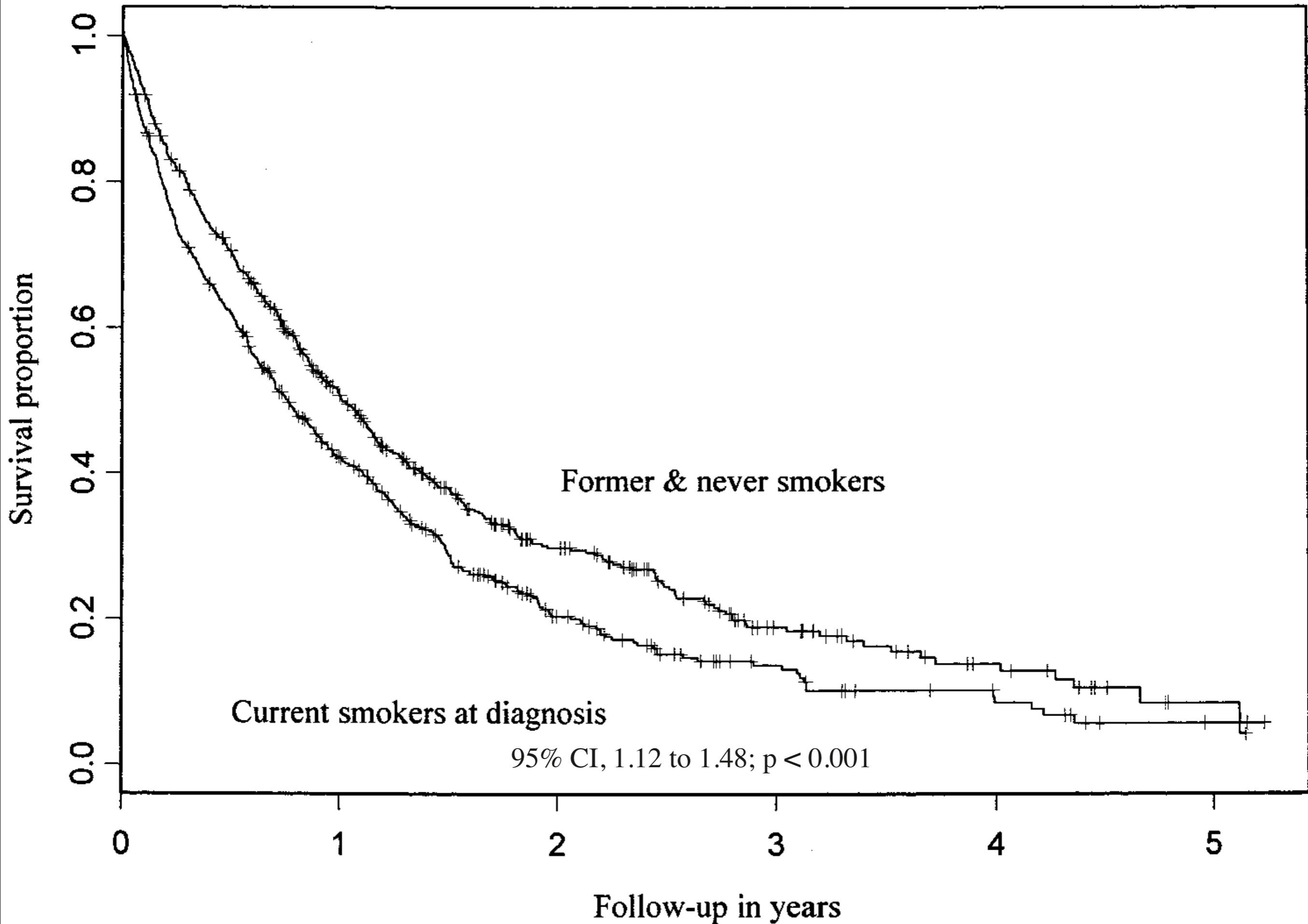
Factores de riesgo

- ✦ Cigarrillo: 80 - 90%
 - ✦ Riesgo 20 veces superior a no expuesto en fumadores activos - 9 veces con habito suspendido
 - ✦ Fumadores pasivos incremento del riesgo 20 - 30%
 - ✦ Inducción 1 mutación genética por cada 15 cigarrillos
- ✦ Exposición ocupacional

Smoking and Lung Cancer Survival*

The Role of Comorbidity and Treatment

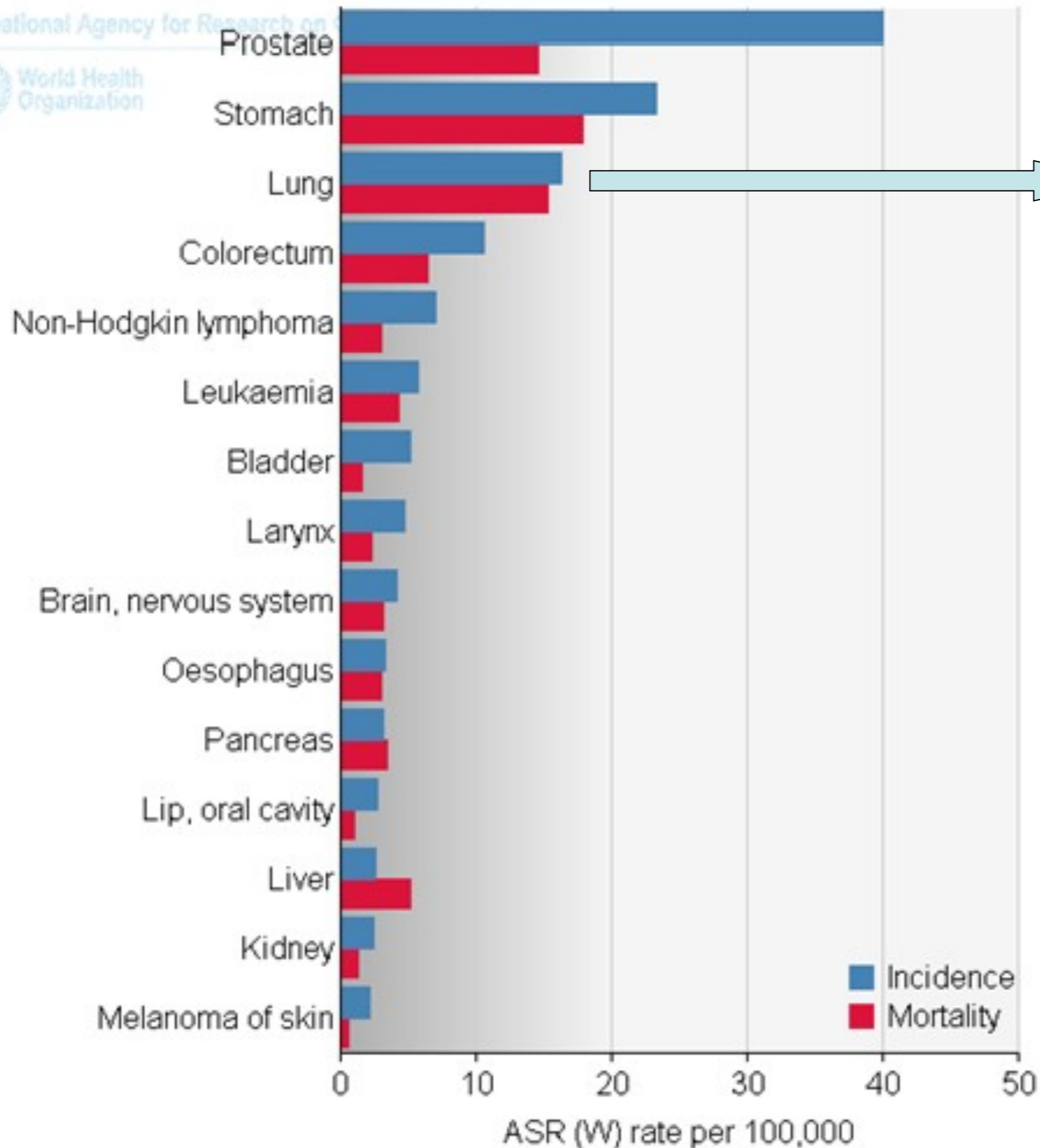
- Experiencia de un centro
- 1155 pacientes diagnosticados
- Evaluación del impacto del habito de fumar
- Ajuste por comorbilidades y edad
- Mayor probabilidades de recibir tratamiento en fumadores



Exposición ocupacional

- ✦ Asbesto
- ✦ Arsénico
- ✦ Bisclorometil eter
- ✦ Cromo hexavalente
- ✦ Gas mostaza
- ✦ Hidrocarburos policíclicos aromáticos

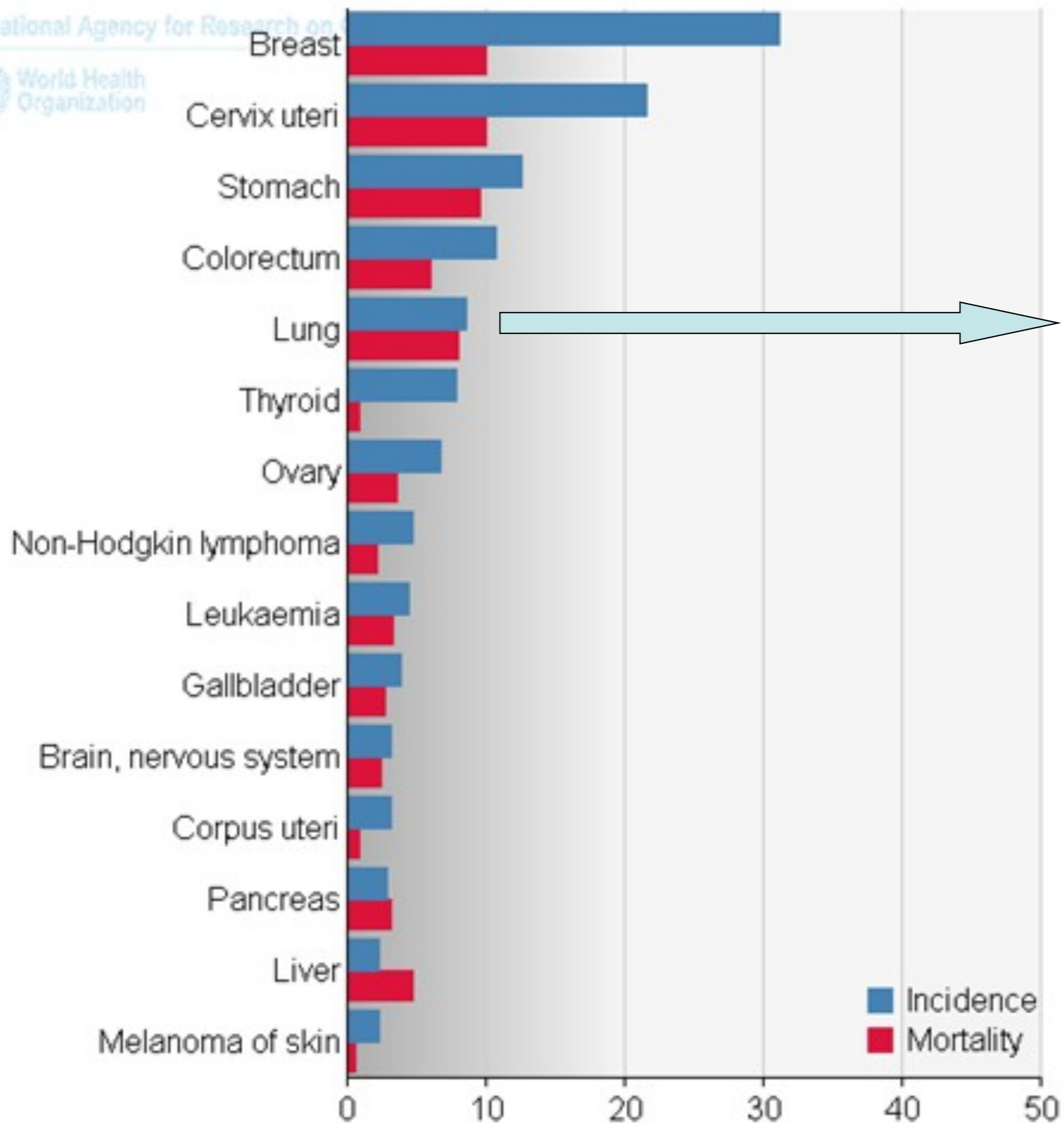
Estimated age-standardised incidence and mortality rates: men



2697 casos (9,8%)
2524 muertes
(15.1%)

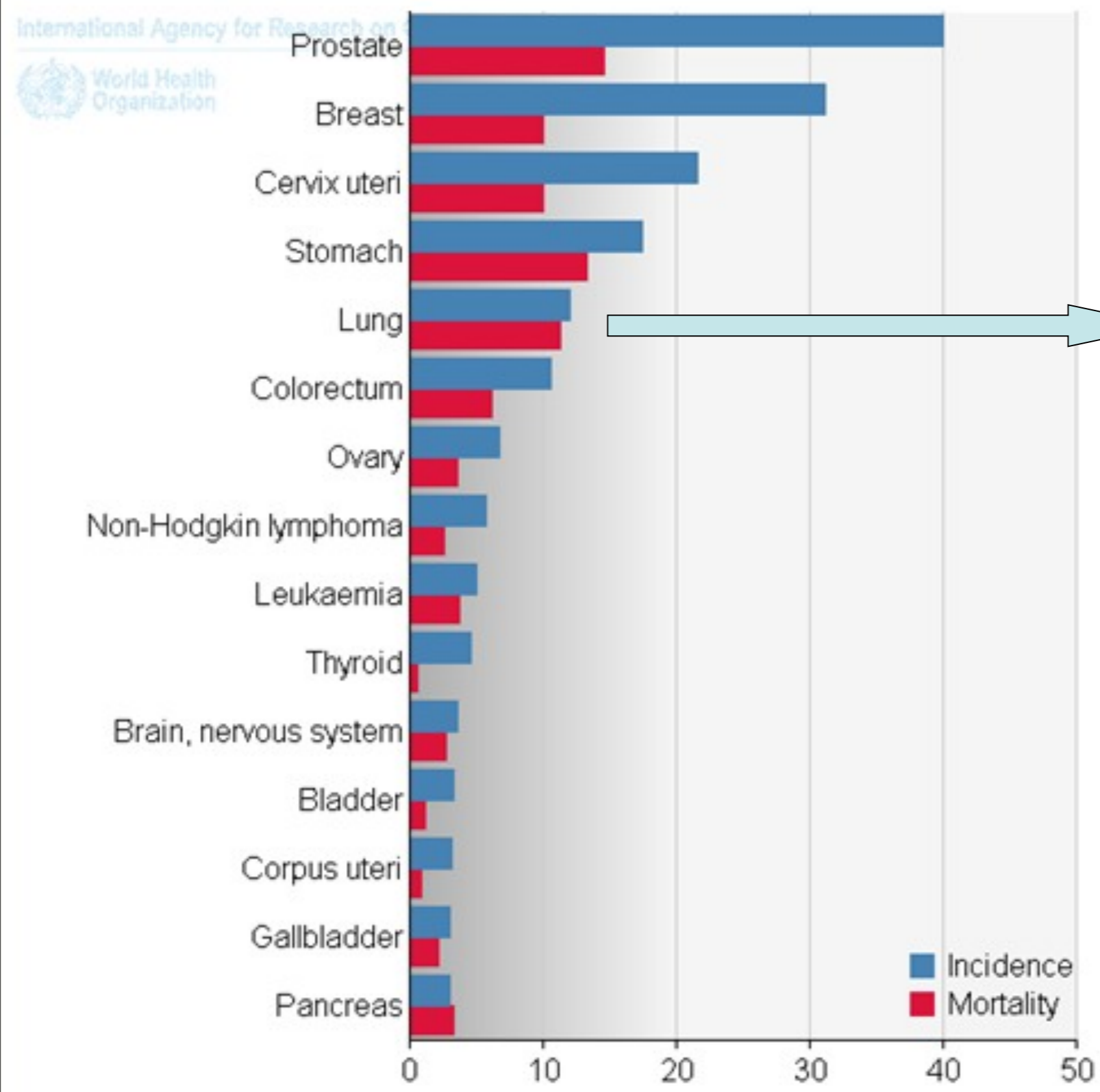
Estimated age-standardised incidence and mortality rates: women

International Agency for Research on
Cancer
World Health
Organization



1172 casos (5.7%)
1656 muertes (9.6%)

Estimated age-standardised incidence and mortality rates: both sexes



4469 casos (7.6%)
4180 muertes (12.3%)

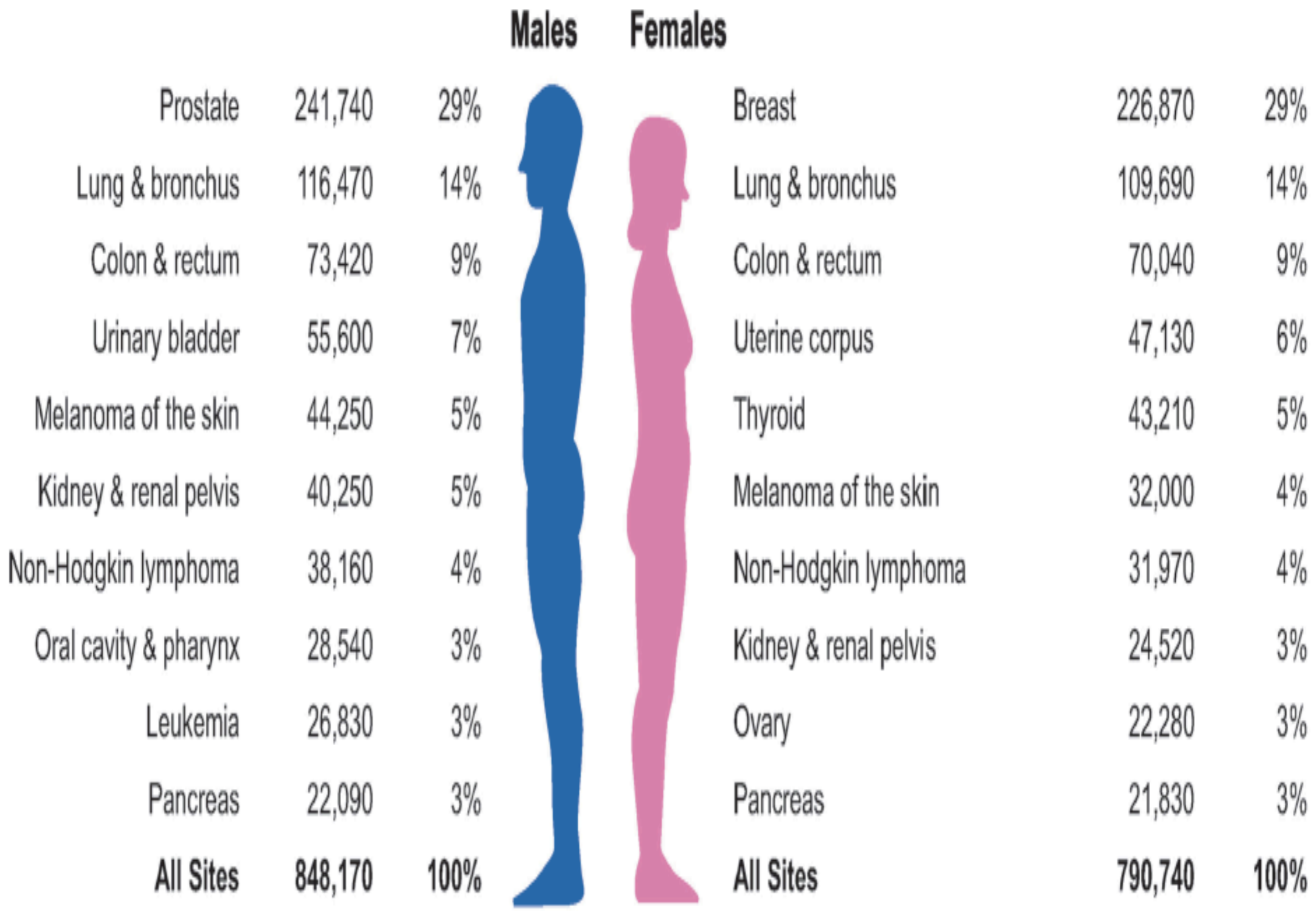
TABLE 1. Estimated New Cancer Cases and Deaths by Sex, United States, 2012*

	ESTIMATED NEW CASES			ESTIMATED DEATHS		
	BOTH SEXES	MALE	FEMALE	BOTH SEXES	MALE	FEMALE
All Sites	1,638,910	848,170	790,740	577,190	301,820	275,370
Oral cavity & pharynx	40,250	28,540	11,710	7,850	5,440	2,410
Tongue	12,770	9,040	3,730	2,050	1,360	690
Mouth	11,620	7,030	4,590	1,790	1,070	720
Pharynx	13,510	10,790	2,720	2,330	1,730	600
Other oral cavity	2,350	1,680	670	1,680	1,280	400
Digestive system	284,680	156,760	127,920	142,510	80,560	61,950
Esophagus	17,460	13,950	3,510	15,070	12,040	3,030
Stomach	21,320	13,020	8,300	10,540	6,190	4,350
Small intestine	8,070	4,380	3,690	1,150	610	540
Colont	103,170	49,920	53,250	51,690	26,470	25,220
Rectum	40,290	23,500	16,790			
Anus, anal canal, & anorectum	6,230	2,250	3,980	780	300	480
Liver & intrahepatic bile duct	28,720	21,370	7,350	20,550	13,980	6,570
Gallbladder & other biliary	9,810	4,480	5,330	3,200	1,240	1,960
Pancreas	43,920	22,090	21,830	37,390	18,850	18,540
Other digestive organs	5,690	1,800	3,890	2,140	880	1,260
Respiratory system	244,180	130,270	113,910	164,770	91,110	73,660
Larynx	12,360	9,840	2,520	3,650	2,880	770
Lung & bronchus	226,160	116,470	109,690	160,340	87,750	72,590
Other respiratory organs	5,660	3,960	1,700	780	480	300
Bones & joints	2,890	1,600	1,290	1,410	790	620
Soft tissue (including heart)	11,280	6,110	5,170	3,900	2,050	1,850
Skin (excluding basal & squamous)	81,240	46,890	34,350	12,190	8,210	3,980
Melanoma-skin	76,250	44,250	32,000	9,180	6,060	3,120
Other nonepithelial skin	4,990	2,640	2,350	3,010	2,150	860
Breast	229,060	2,190	226,870	39,920	410	39,510
Genital system	340,650	251,900	88,750	58,360	28,840	29,520
Uterine cervix	12,170		12,170	4,220		4,220
Uterine corpus	47,130		47,130	8,010		8,010
Ovary	22,280		22,280	15,500		15,500
Vulva	4,490		4,490	950		950
Vagina & other genital, female	2,680		2,680	840		840
Prostate	241,740	241,740		28,170	28,170	
Testis	8,590	8,590		360	360	
Penis & other genital, male	1,570	1,570		310	310	
Urinary system	141,140	97,610	43,530	29,330	19,670	9,660
Urinary bladder	73,510	55,600	17,910	14,880	10,510	4,370
Kidney & renal pelvis	64,770	40,250	24,520	13,570	8,650	4,920
Ureter & other urinary organs	2,860	1,760	1,100	880	510	370
Eye & orbit	2,610	1,310	1,300	270	120	150
Brain & other nervous system	22,910	12,630	10,280	13,700	7,720	5,980
Endocrine system	58,980	14,600	44,380	2,700	1,240	1,460
Thyroid	56,460	13,250	43,210	1,780	780	1,000
Other endocrine	2,520	1,350	1,170	920	460	460
Lymphoma	79,190	43,120	36,070	20,130	10,990	9,140
Hodgkin lymphoma	9,060	4,960	4,100	1,190	670	520
Non-Hodgkin lymphoma	70,130	38,160	31,970	18,940	10,320	8,620
Myeloma	21,700	12,190	9,510	10,710	6,020	4,690
Leukemia	47,150	26,830	20,320	23,540	13,500	10,040
Acute lymphocytic leukemia	6,050	3,450	2,600	1,440	820	620
Chronic lymphocytic leukemia	16,060	9,490	6,570	4,580	2,730	1,850
Acute myeloid leukemia	13,780	7,350	6,430	10,200	5,790	4,410
Chronic myeloid leukemia	5,430	3,210	2,220	610	370	240
Other leukemia†	5,830	3,330	2,500	6,710	3,790	2,920
Other & unspecified primary sites‡	31,000	15,620	15,380	45,900	25,150	20,750

TABLE 1. Estimated New Cancer Cases and Deaths by Sex, United States, 2012*

	ESTIMATED NEW CASES			ESTIMATED DEATHS		
	BOTH SEXES	MALE	FEMALE	BOTH SEXES	MALE	FEMALE
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Tongue	12,770	9,040	3,730	2,050	1,360	690
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Pharynx	13,510	10,790	2,720	2,330	1,730	600
Other oral cavity	2,350	1,680	670	1,680	1,280	400
Digestive system	284,680	156,760	127,920	142,510	80,560	61,950
Esophagus	17,460	13,950	3,510	15,070	12,040	3,030
Stomach	21,320	13,020	8,300	10,540	6,190	4,350
Small intestine	8,070	4,380	3,690	1,150	610	540
Colont	103,170	49,920	53,250	51,690	26,470	25,220
Rectum	40,290	23,500	16,790			
Anus, anal canal, & anorectum	6,230	2,250	3,980	780	300	480
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Pancreas	43,920	22,090	21,830	37,390	18,850	18,540
Other digestive organs	5,690	1,800	3,890	2,140	880	1,260
Respiratory system	244,180	130,270	113,910	164,770	91,110	73,660
Larynx					2,880	770
Lung & bronchus					87,750	72,590
Other respiratory organs					480	300
Prostate	241,740	241,740		28,170	28,170	
Testis	8,590	8,590		360	360	
Penis & other genital, male	1,570	1,570		310	310	
Urinary system	141,140	97,610	43,530	29,330	19,670	9,660
Urinary bladder	73,510	55,600	17,910	14,880	10,510	4,370
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Lymphoma	79,190	43,120	36,070	20,130	10,990	9,140
Hodgkin lymphoma	9,060	4,960	4,100	1,190	670	520
Non-Hodgkin lymphoma	70,130	38,160	31,970	18,940	10,320	8,620
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Estimated New Cases*

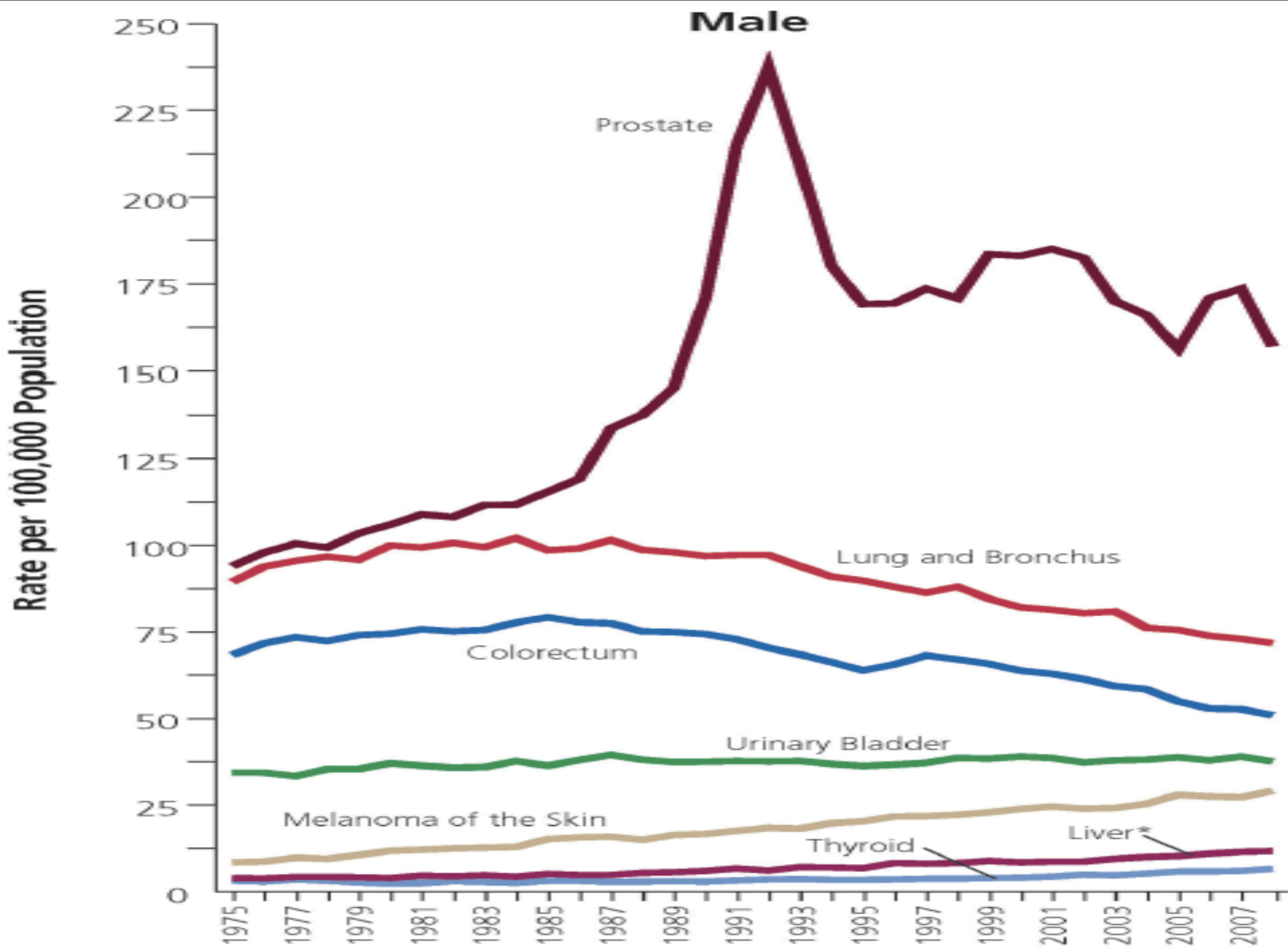


Estimated Deaths

Males **Females**



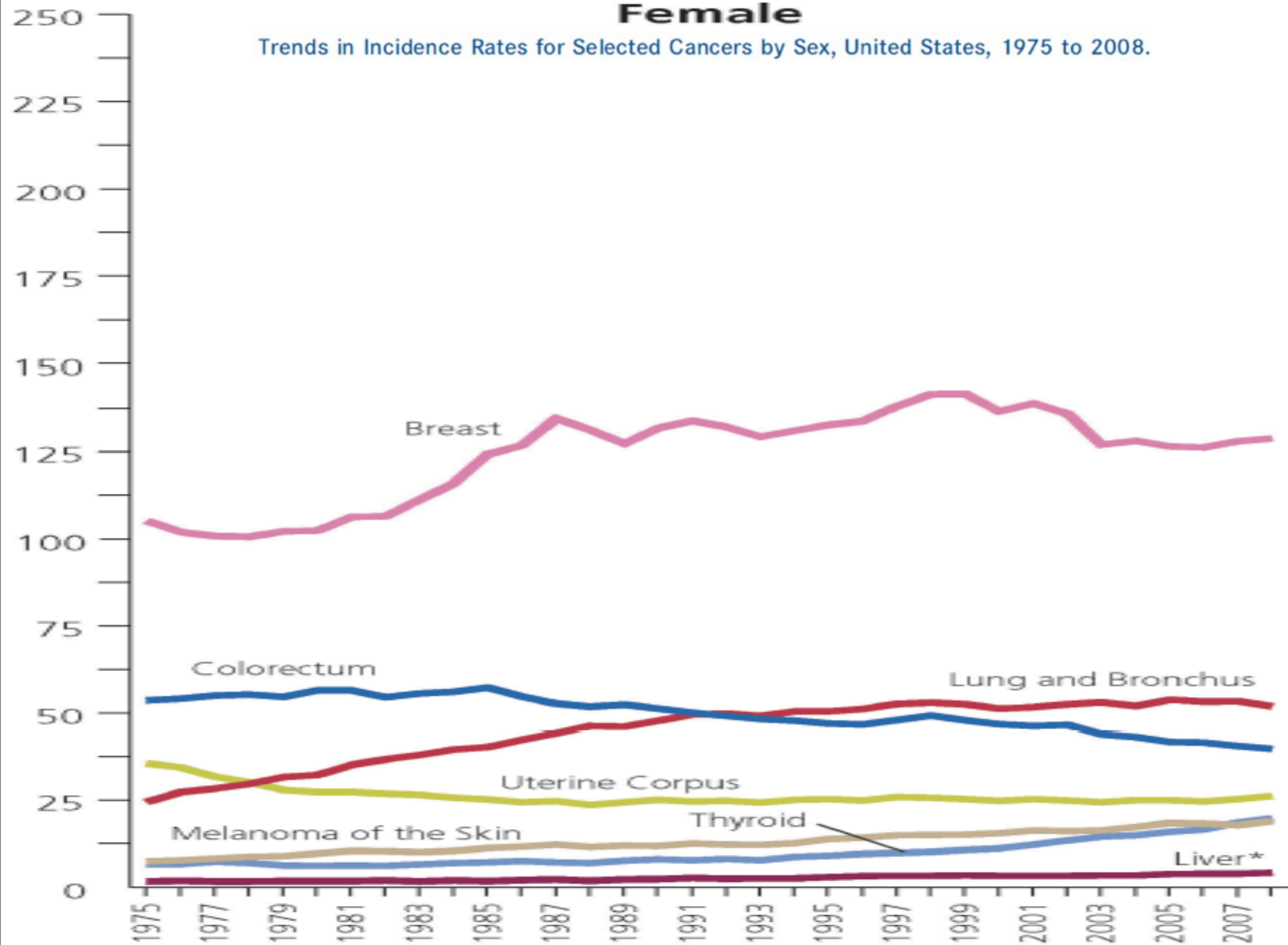
Lung & bronchus	87,750	29%		Lung & bronchus	72,590	26%
Prostate	28,170	9%		Breast	39,510	14%
Colon & rectum	26,470	9%		Colon & rectum	25,220	9%
Pancreas	18,850	6%		Pancreas	18,540	7%
Liver & intrahepatic bile duct	13,980	5%		Ovary	15,500	6%
Leukemia	13,500	4%		Leukemia	10,040	4%
Esophagus	12,040	4%		Non-Hodgkin lymphoma	8,620	3%
Urinary bladder	10,510	3%		Uterine Corpus	8,010	3%
Non-Hodgkin lymphoma	10,320	3%		Liver & intrahepatic bile duct	6,570	2%
Kidney & renal pelvis	8,650	3%		Brain & other nervous system	5,980	2%
All Sites	301,820	100%		All Sites	275,370	100%



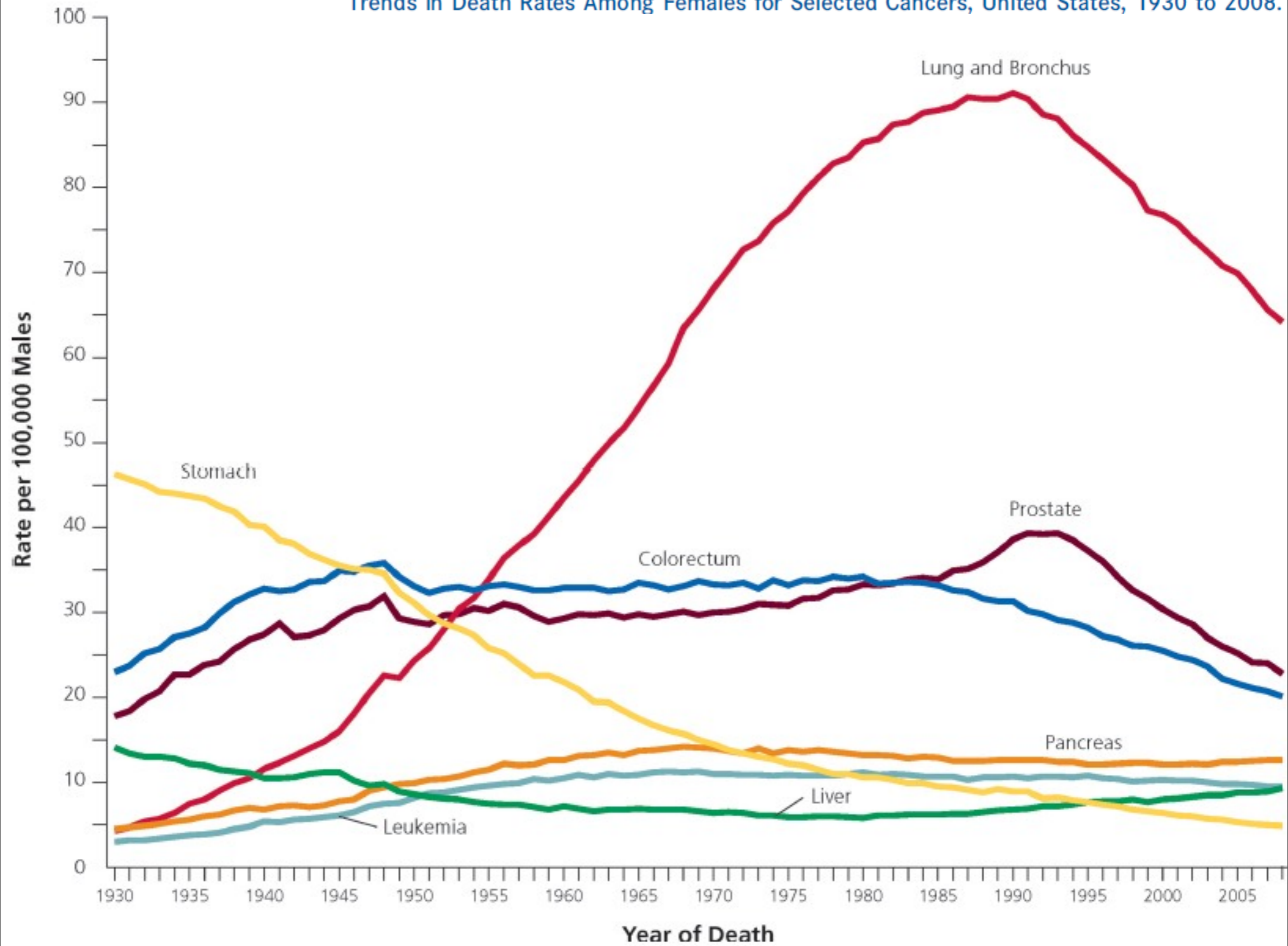
Trends in Incidence Rates for Selected Cancers by Sex, United States, 1975 to 2008.

Female

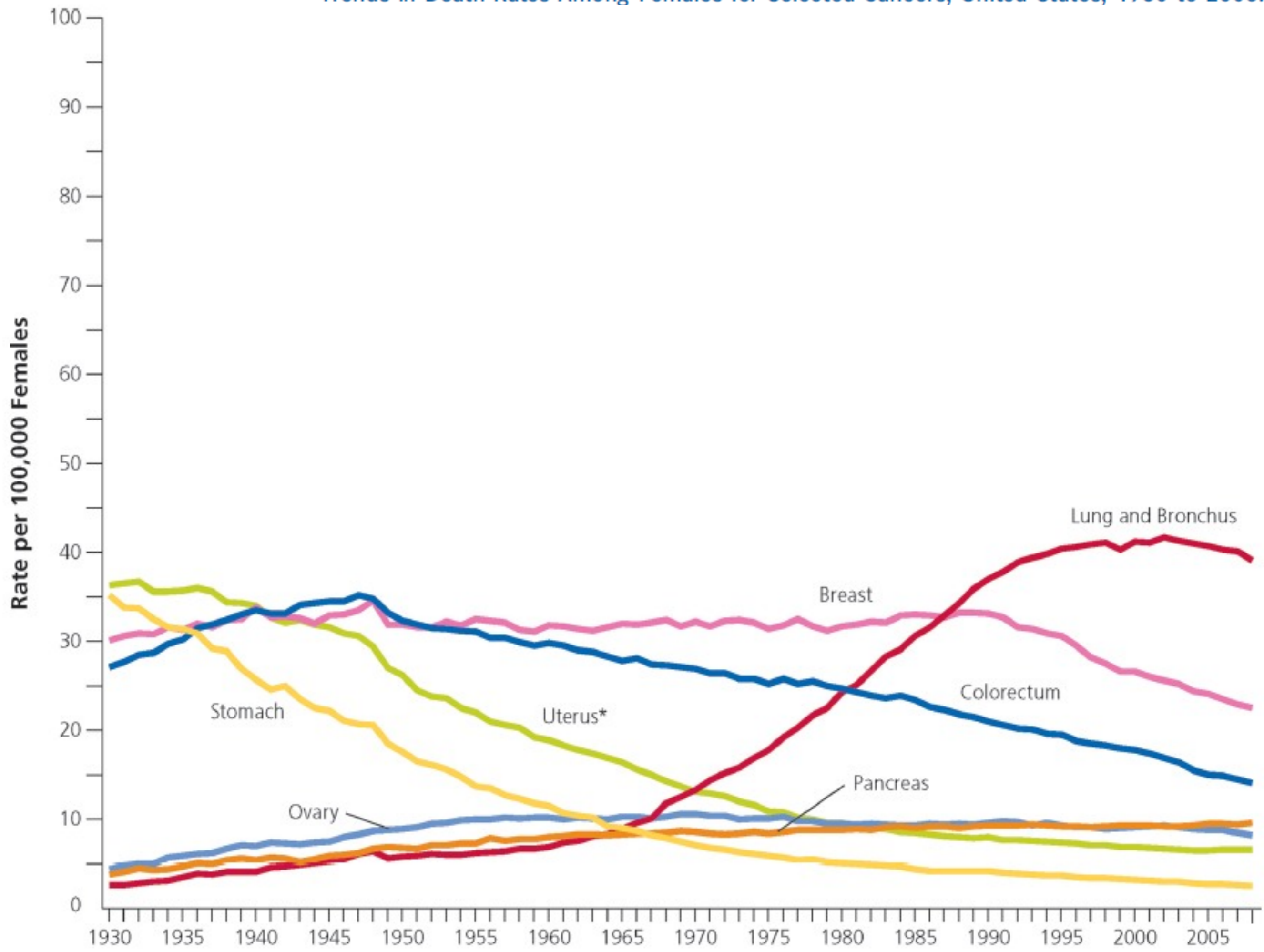
Trends in Incidence Rates for Selected Cancers by Sex, United States, 1975 to 2008.



Trends in Death Rates Among Females for Selected Cancers, United States, 1930 to 2008.



Trends in Death Rates Among Females for Selected Cancers, United States, 1930 to 2008.



Manifestaciones clínicas

- **Derivadas de Tumor**

- Tos
- Disnea
- Hemoptisis
- Neumonía postobstructiva
- Dolor torácico
- Compromiso del ápex
 - Dolor en hombro
 - Plexopatía braquial
 - Síndrome de Horner

Síndromes paraneoplásicos

- Osteoartropatía pulmonar hipertrófica
- Hipercalcemia (Escamocelular)
- Síndrome de secreción inapropiada de hormona antidiurética
- Síndrome de Cushing
- Sistema nervioso

Paraneoplásicos SNC

- Encefalomiелitis
- Neuropatía sensoria subaguda
- Opsoclonus
- Mioclonus
- Neuropatía sensorial
- Encefalopatía límbica
- Síndrome de Eaton-Lambert

Estadificacion

“Lung cancer is usually diagnosed at an advanced stage and consequently the overall 5-year survival for patients is approximately 15%. However, patients diagnosed when the primary tumor is resectable experience 5-year survivals ranging from 20 to 80%. Clinical and pathologic staging is critical to selecting patients appropriately for surgery and multimodality therapy.”

Resumen de cambios

- Clasificación recomendada para célula pequeña, no pequeña y carcinoides
- Redefinición de clasificación de T
 - T1: T1a < 2 cm, T1b 2 - 3cm
 - T2: T2a: > 3 - 5 cm, T2b: 5 - 7 cm
 - T3: > 7 cm, Múltiples nódulos tumorales en el mismo lóbulo
 - T4: Múltiples nódulos tumorales en el mismo pulmón pero diferente lóbulo

Resumen de cambios

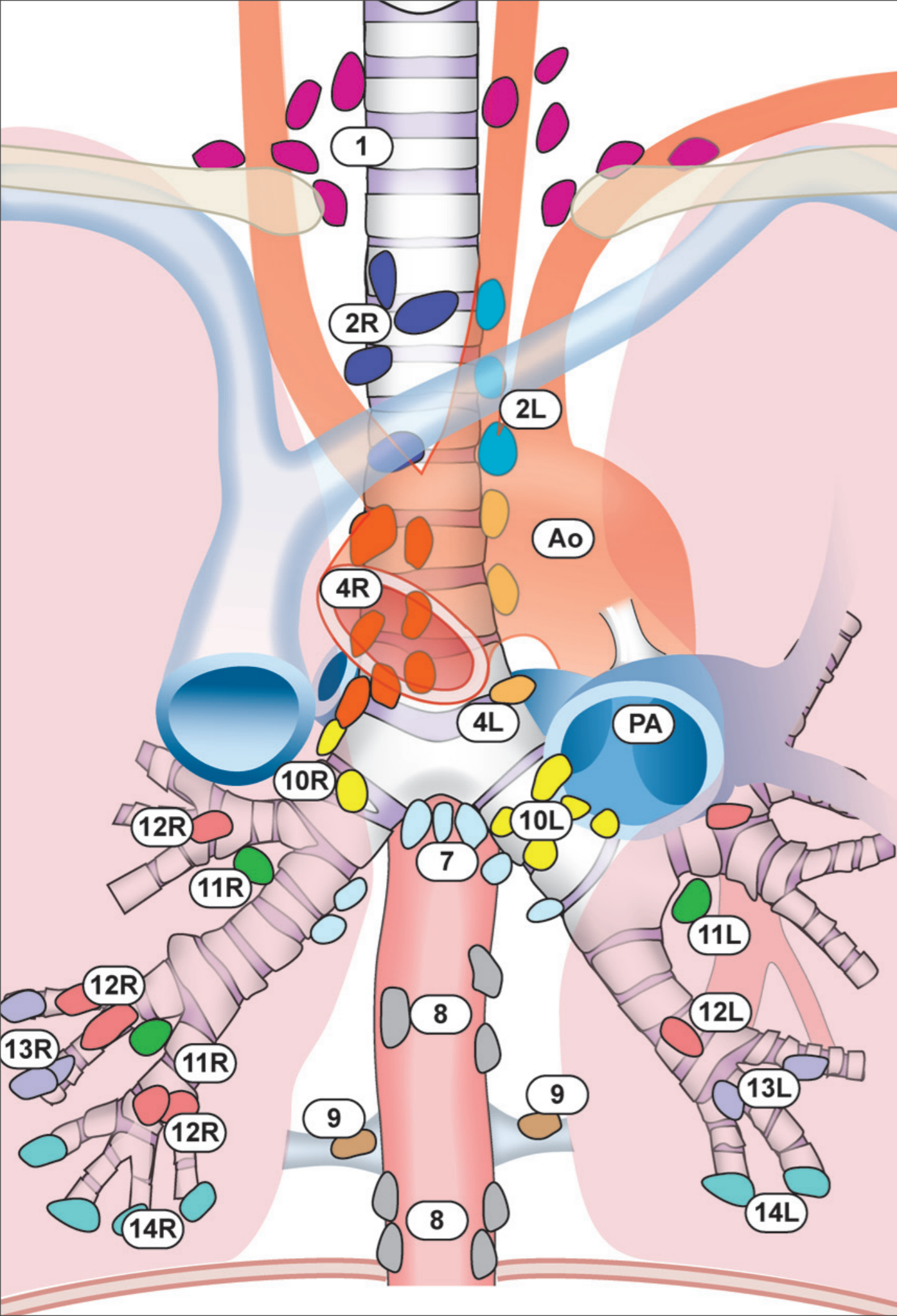
- ✦ Redefinición en clasificación de metástasis
 - ✦ M1a: Derrame pleural o pericardico maligno
Nódulos en pulmón contralateral
 - ✦ M1b: Metástasis a distancia

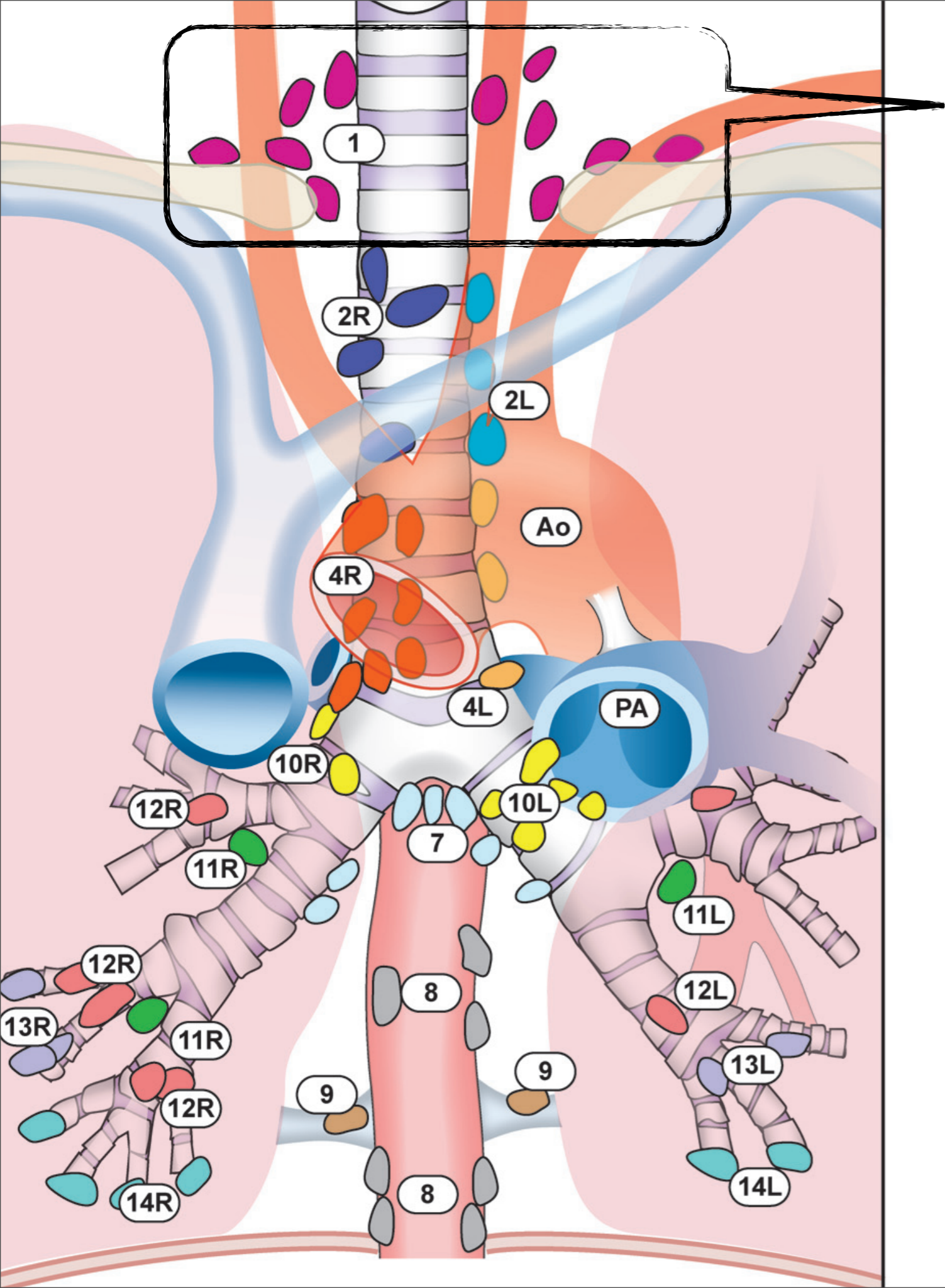
Clasificación de T

- TX Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
- T0 No evidence of primary tumor
- Tis Carcinoma in situ
- T1 Tumor 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (for example, not in the main bronchus)
 - T1a Tumor 2 cm or less in greatest dimension
 - T1b Tumor more than 2 cm but 3 cm or less in greatest dimension
- T2 Tumor more than 3 cm but 7 cm or less or tumor with any of the following features (T2 tumors with these features are classified T2a if 5 cm or less): involves main bronchus, 2 cm or more distal to the carina; invades visceral pleura (PL1 or PL2); associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung
 - T2a Tumor more than 3 cm but 5 cm or less in greatest dimension
 - T2b Tumor more than 5 cm but 7 cm or less in greatest dimension
- T3 Tumor more than 7 cm or one that directly invades any of the following: parietal pleural (PL3), chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium; or tumor in the main bronchus less than 2 cm distal to the carina, but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung or separate tumor nodule(s) in the same lobe
- T4 Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, separate tumor nodule(s) in a different ipsilateral lobe

Clasificación de N

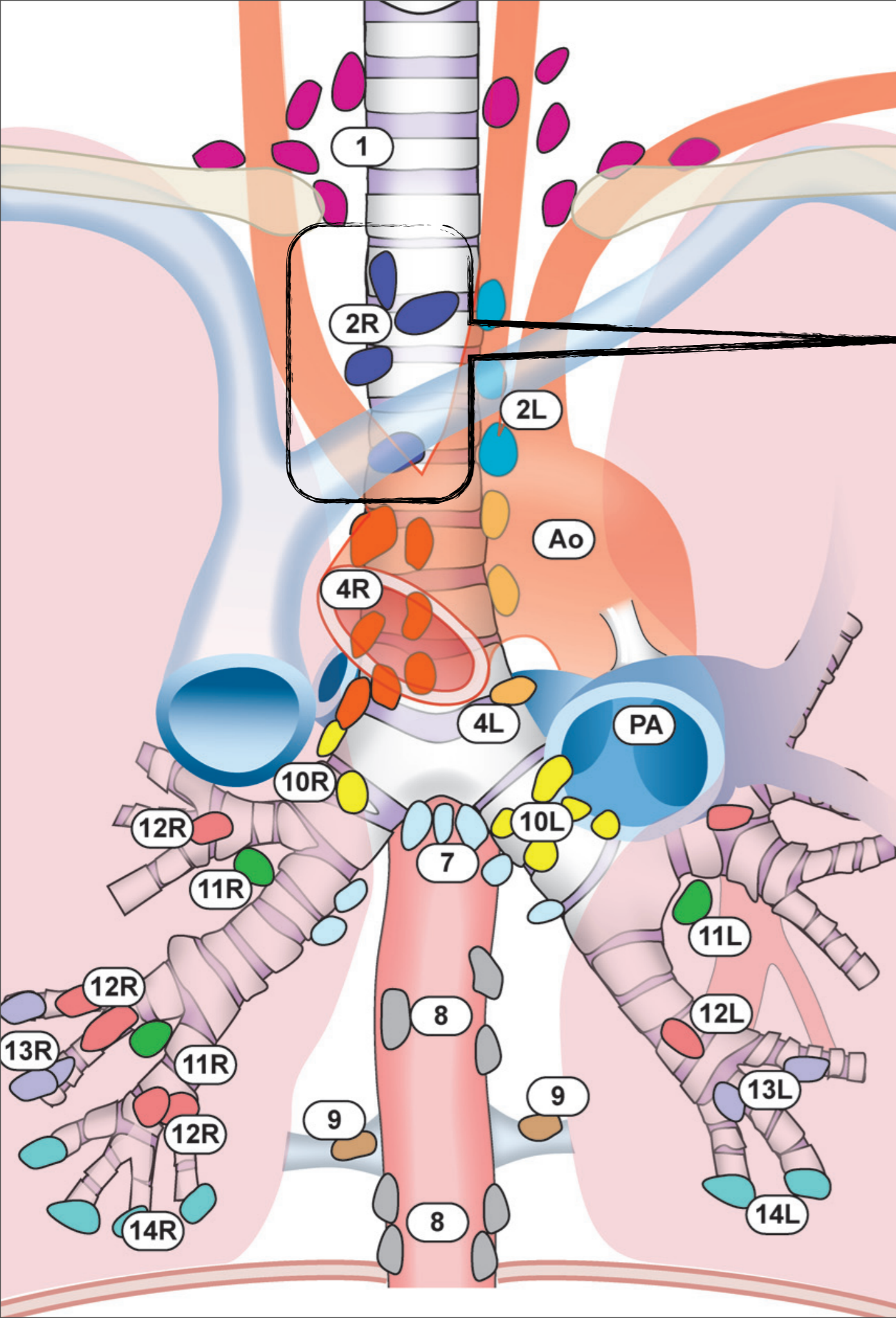
- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastases
- N1 Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
- N2 Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
- N3 Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)





Supraclavicular zone

● **1** Low cervical, supraclavicular, and sternal notch nodes



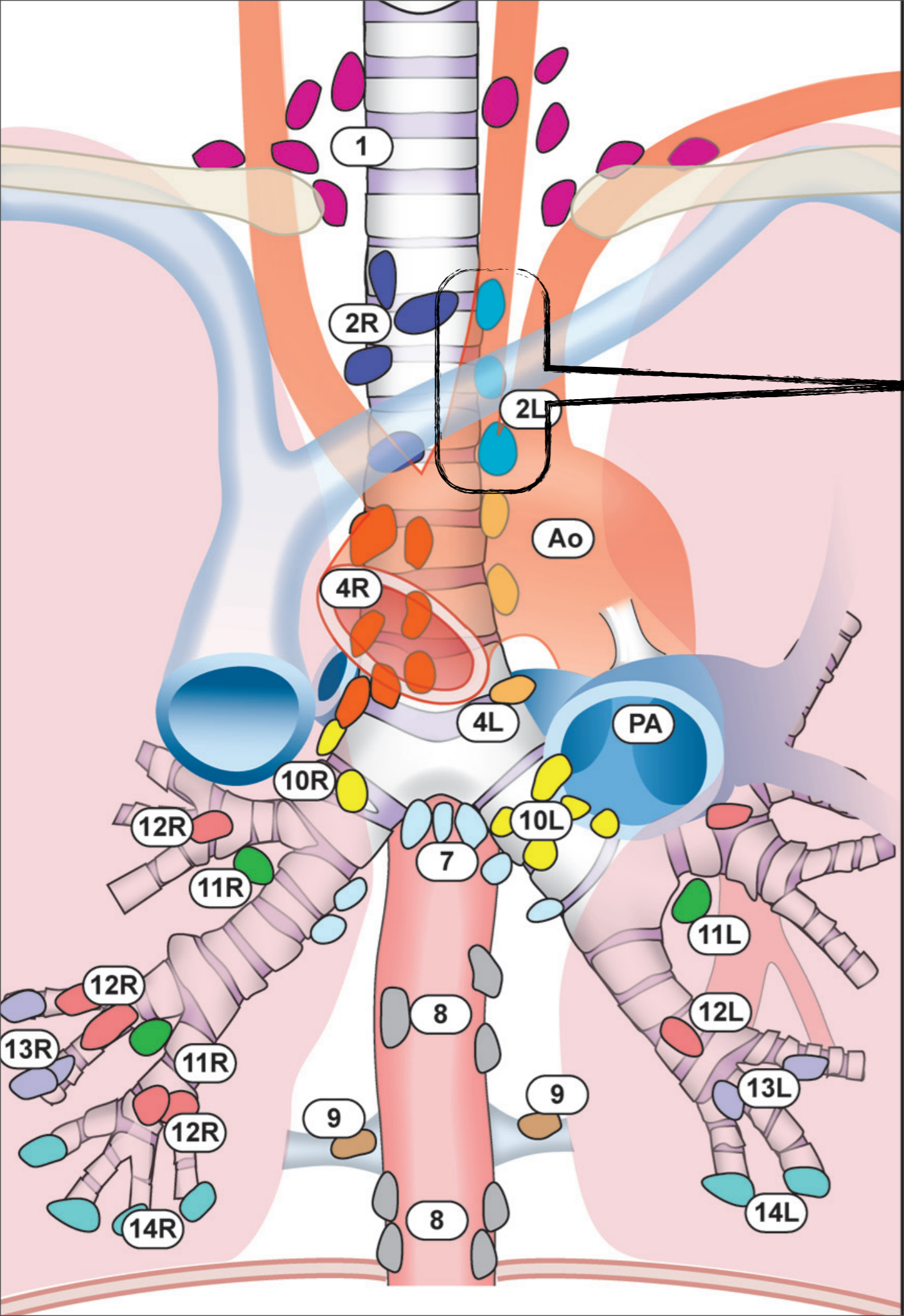
Supraclavicular zone

- 1 Low cervical, supraclavicular, and sternal notch nodes

Superior Mediastinal Nodes

Upper zone

- 2R Upper Paratracheal (right)
- 2L Upper Paratracheal (left)
- 3a Pre-vascular
- 3p Retrotracheal
- 4R Lower Paratracheal (right)
- 4L Lower Paratracheal (left)



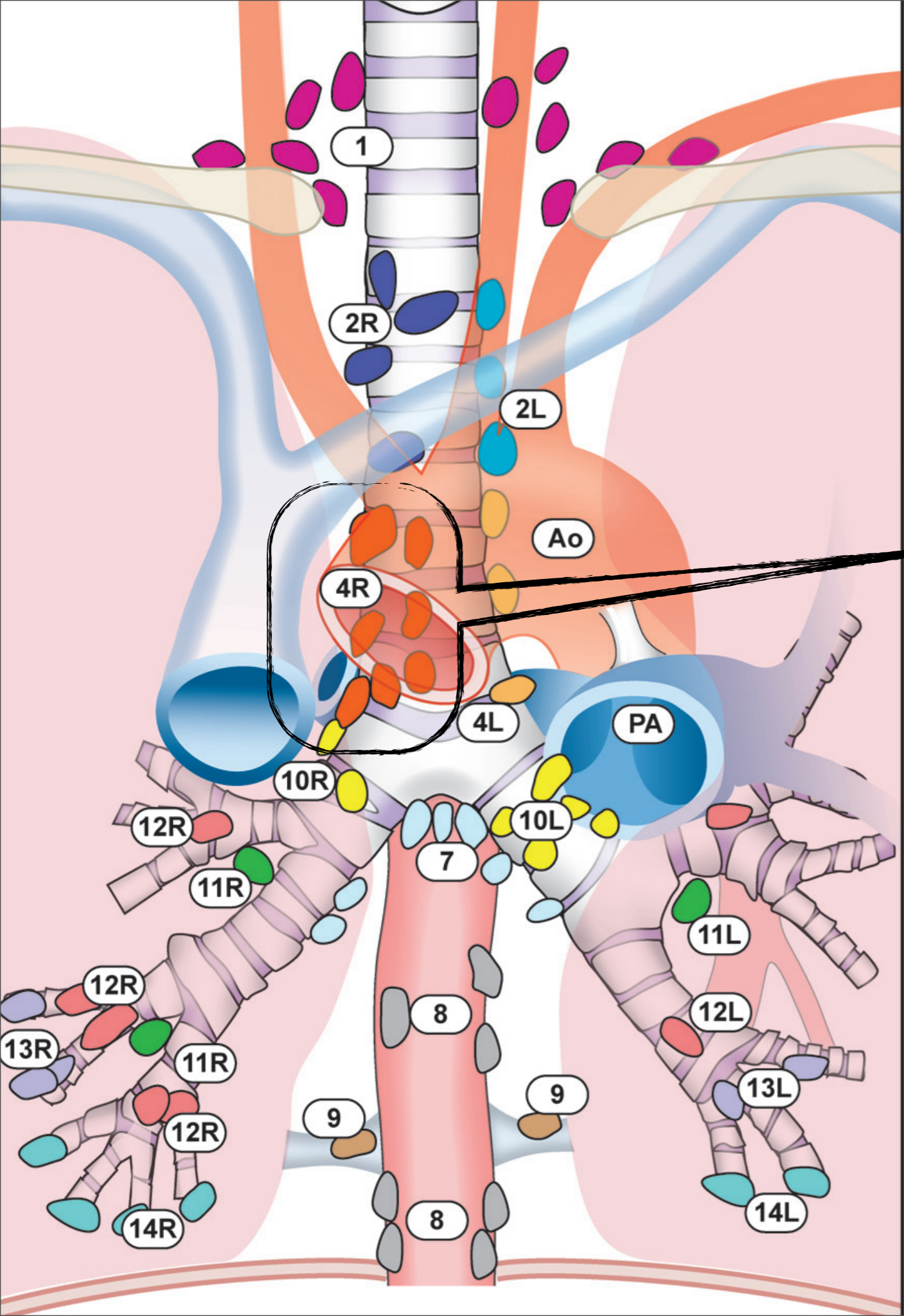
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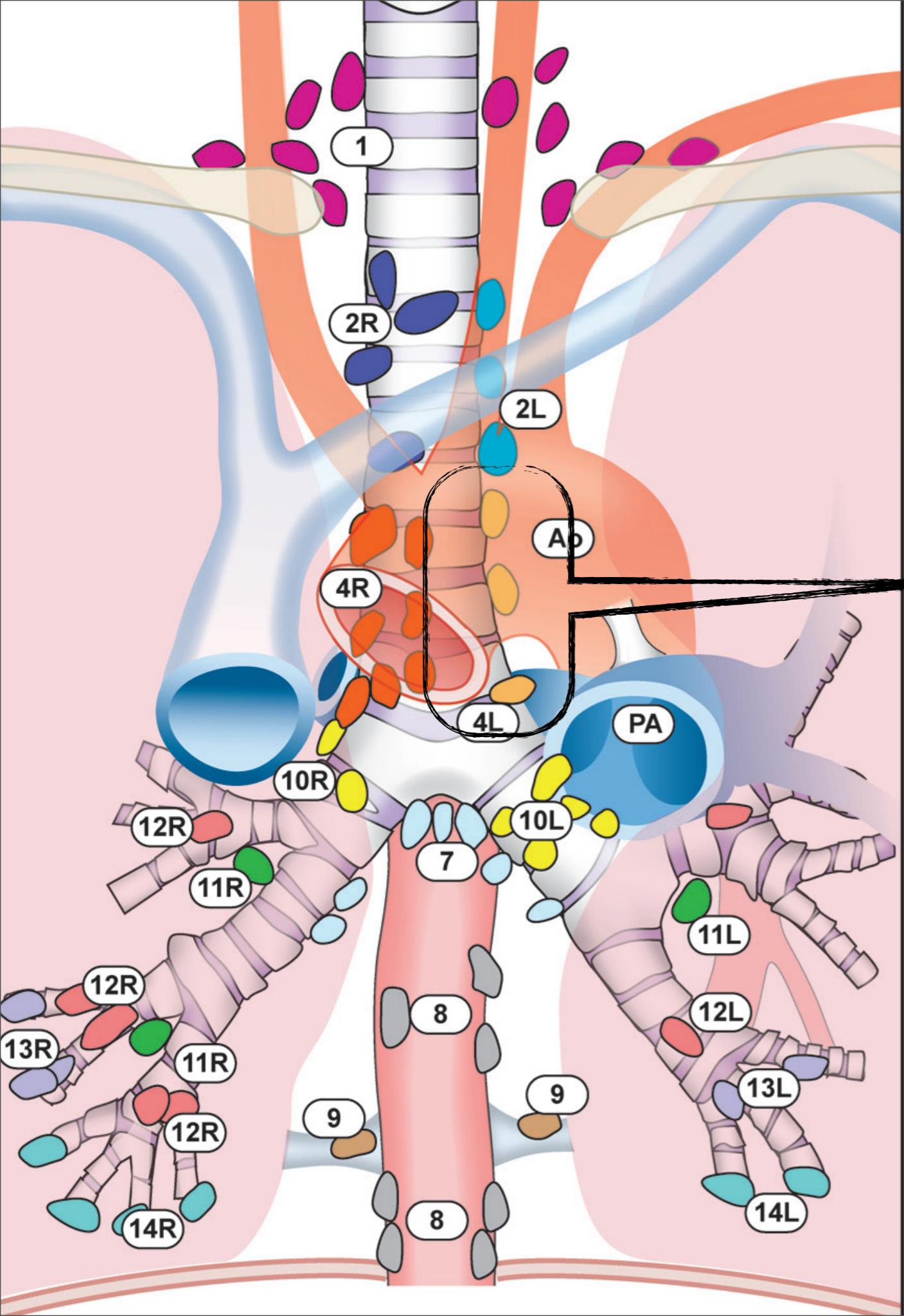
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- **4L** Lower Paratracheal (left)



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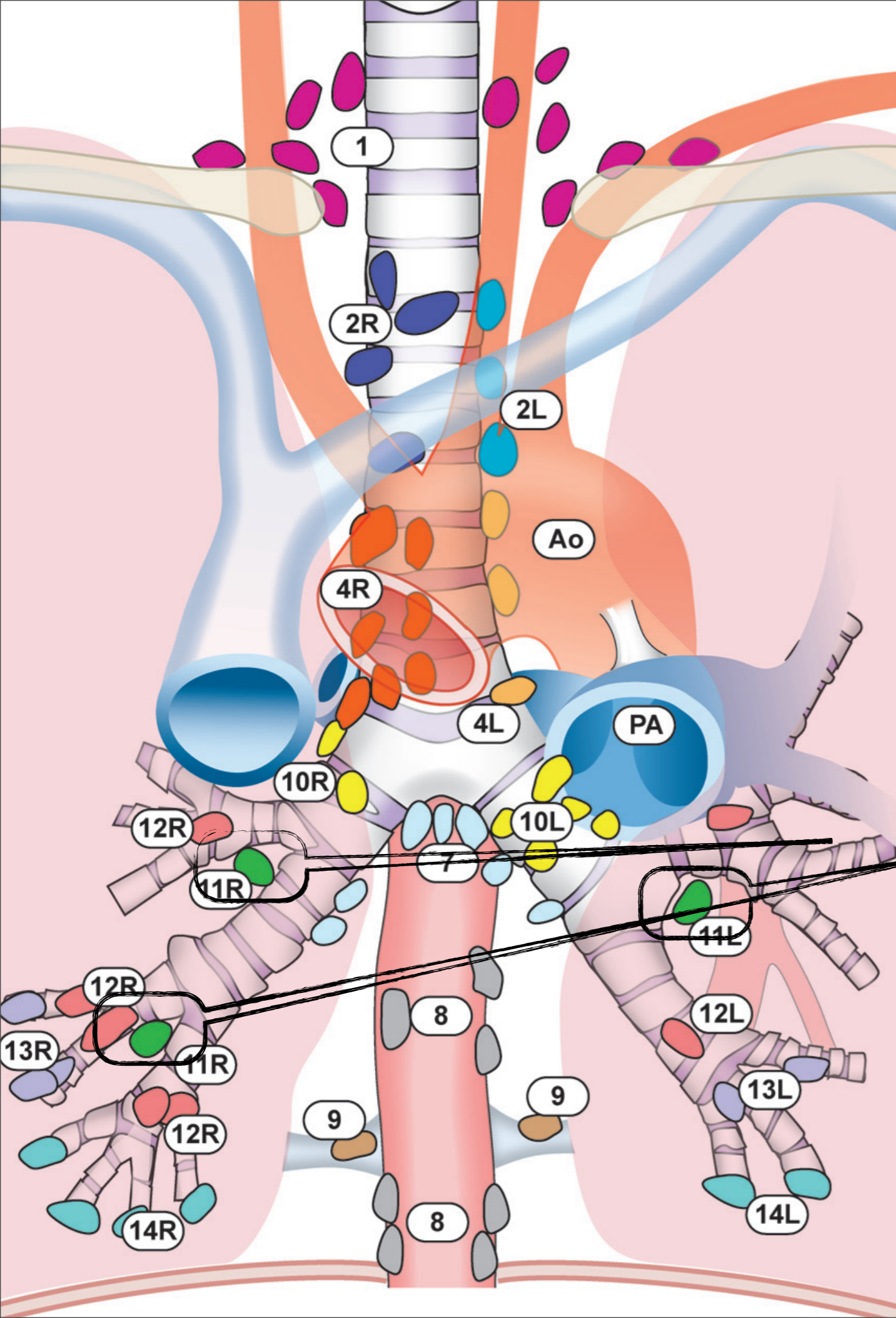
● 2L Upper Paratracheal (left)

● 3a Pre-vascular

● 3p Retrotracheal

● 4R Lower Paratracheal (right)

● 4L Lower Paratracheal (left)



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Superior Mediastinal Nodes

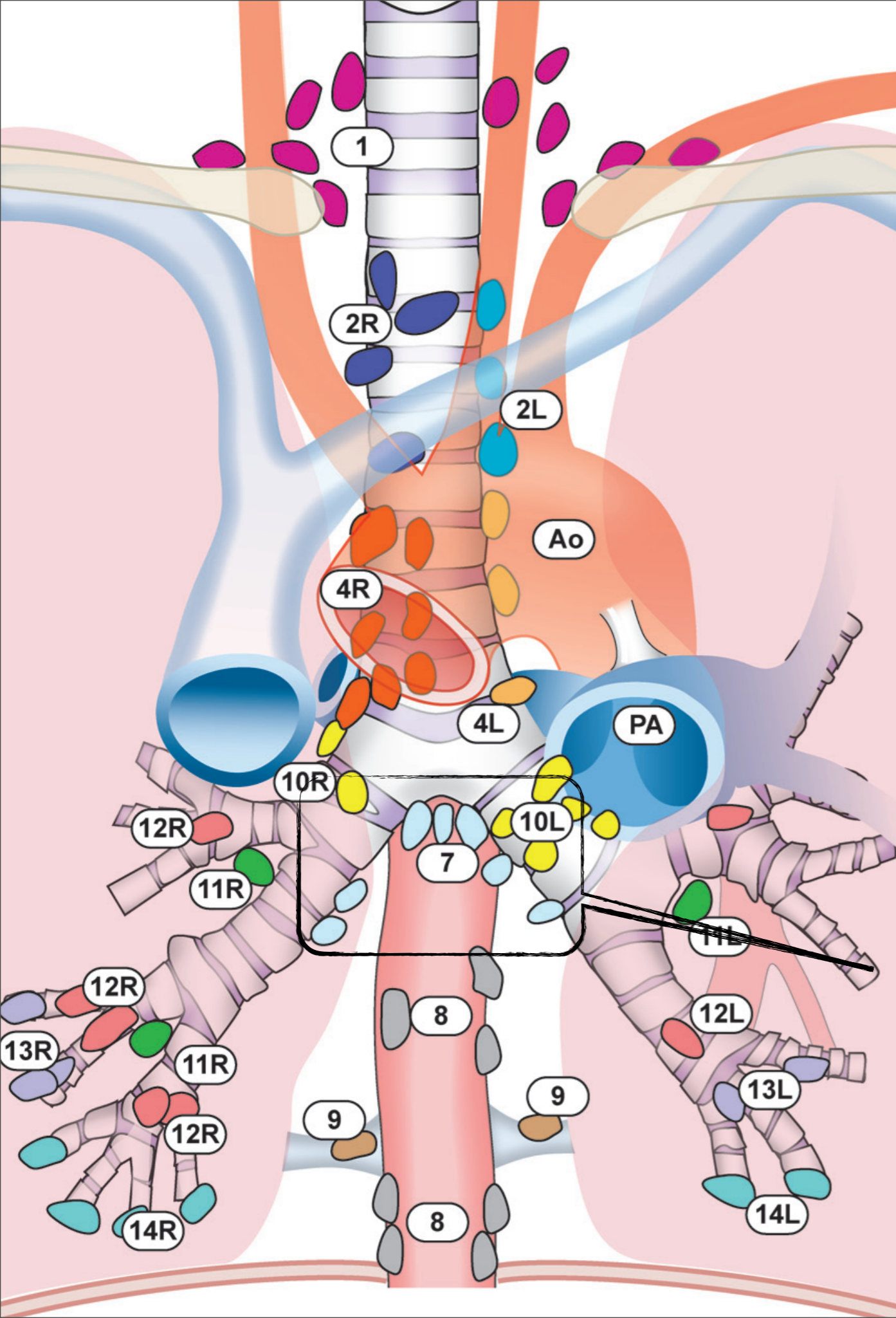
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- 4L Lower Paratracheal (left)

Aortic Nodes

AP zone

- 5 Subaortic
- 6 Para-aortic (ascending aorta or phrenic)



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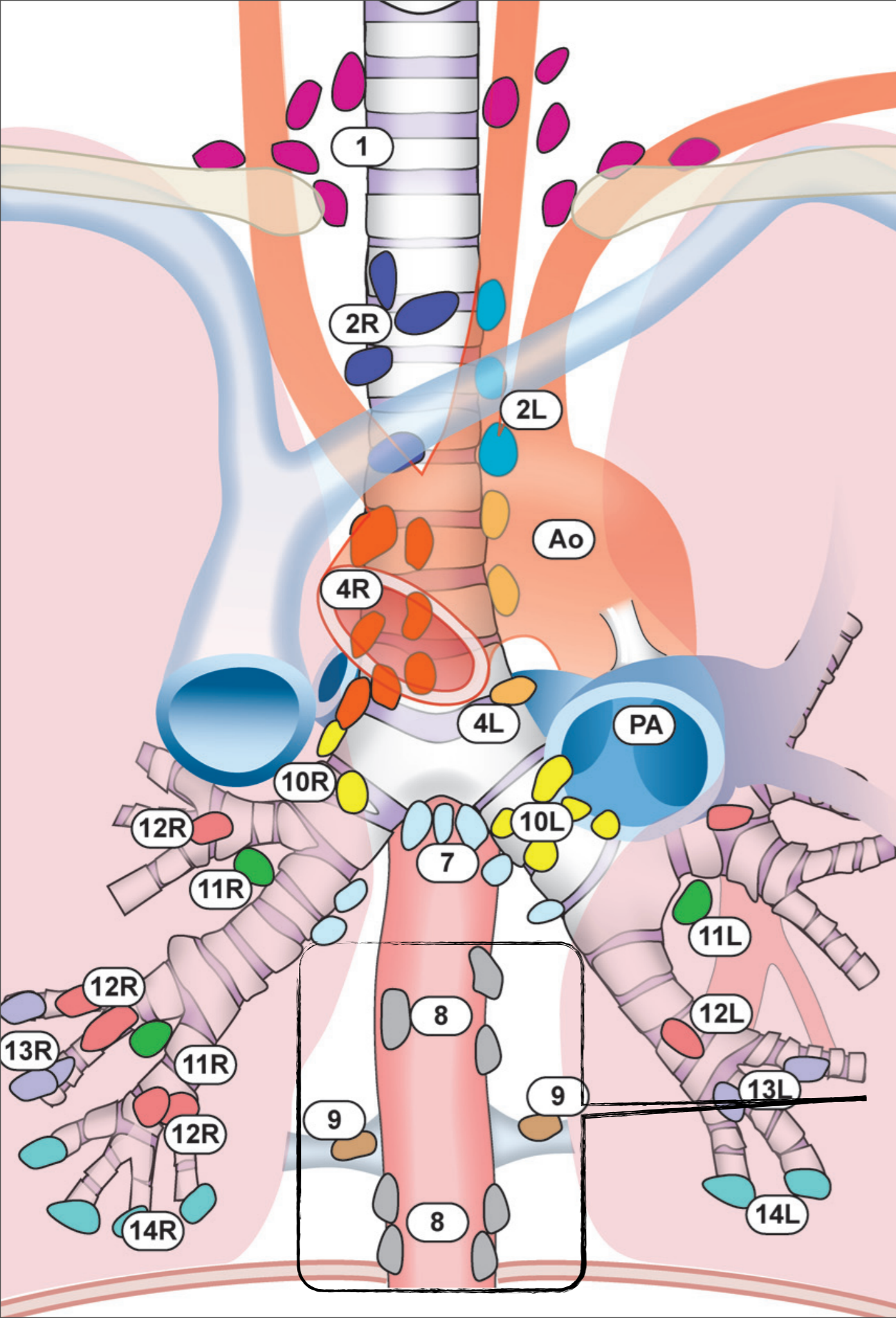
Inferior Mediastinal Nodes

Subcarinal zone

- **7** Subcarinal

Lower zone

- **8** Paraesophageal (below carina)
- **9** Pulmonary ligament



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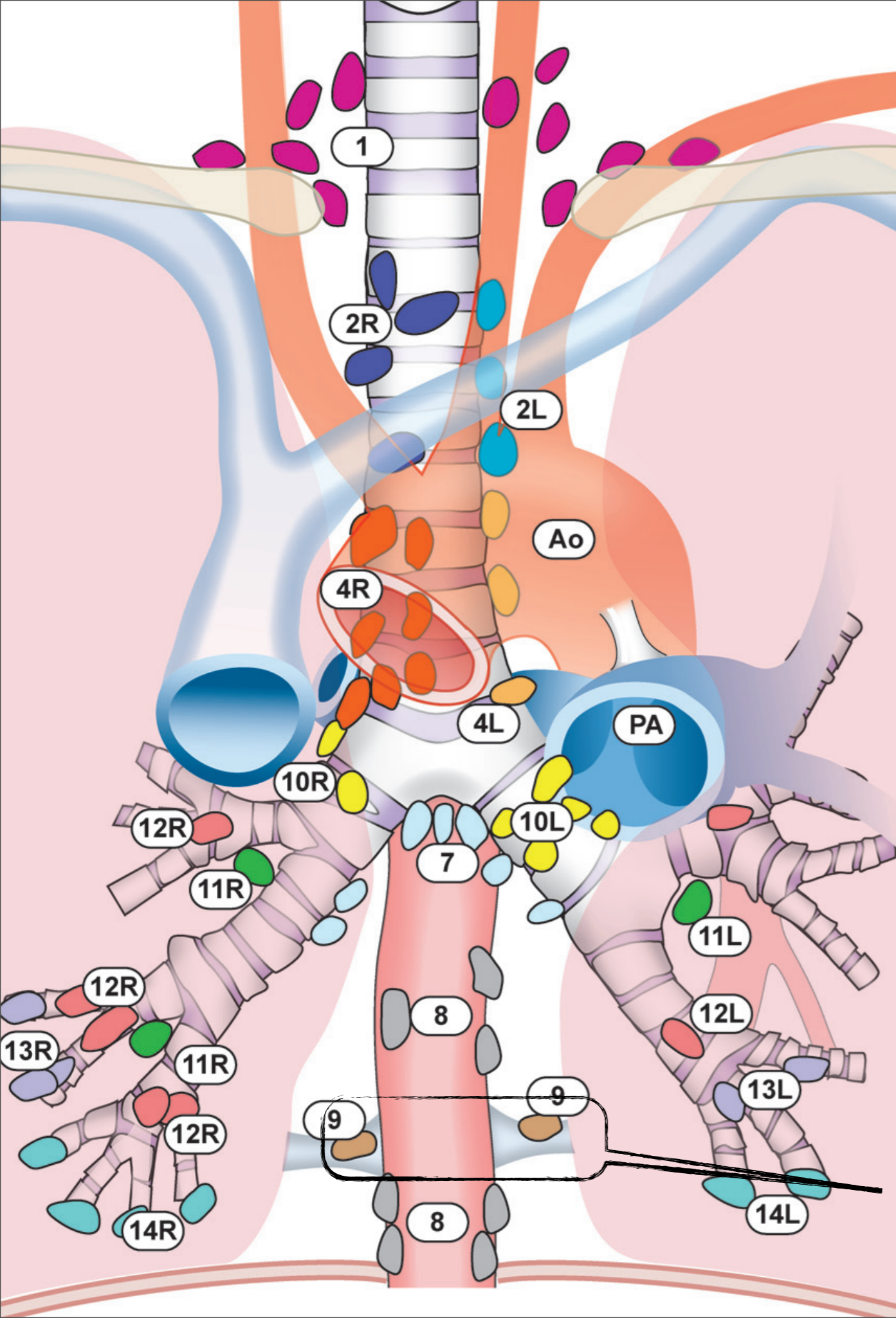
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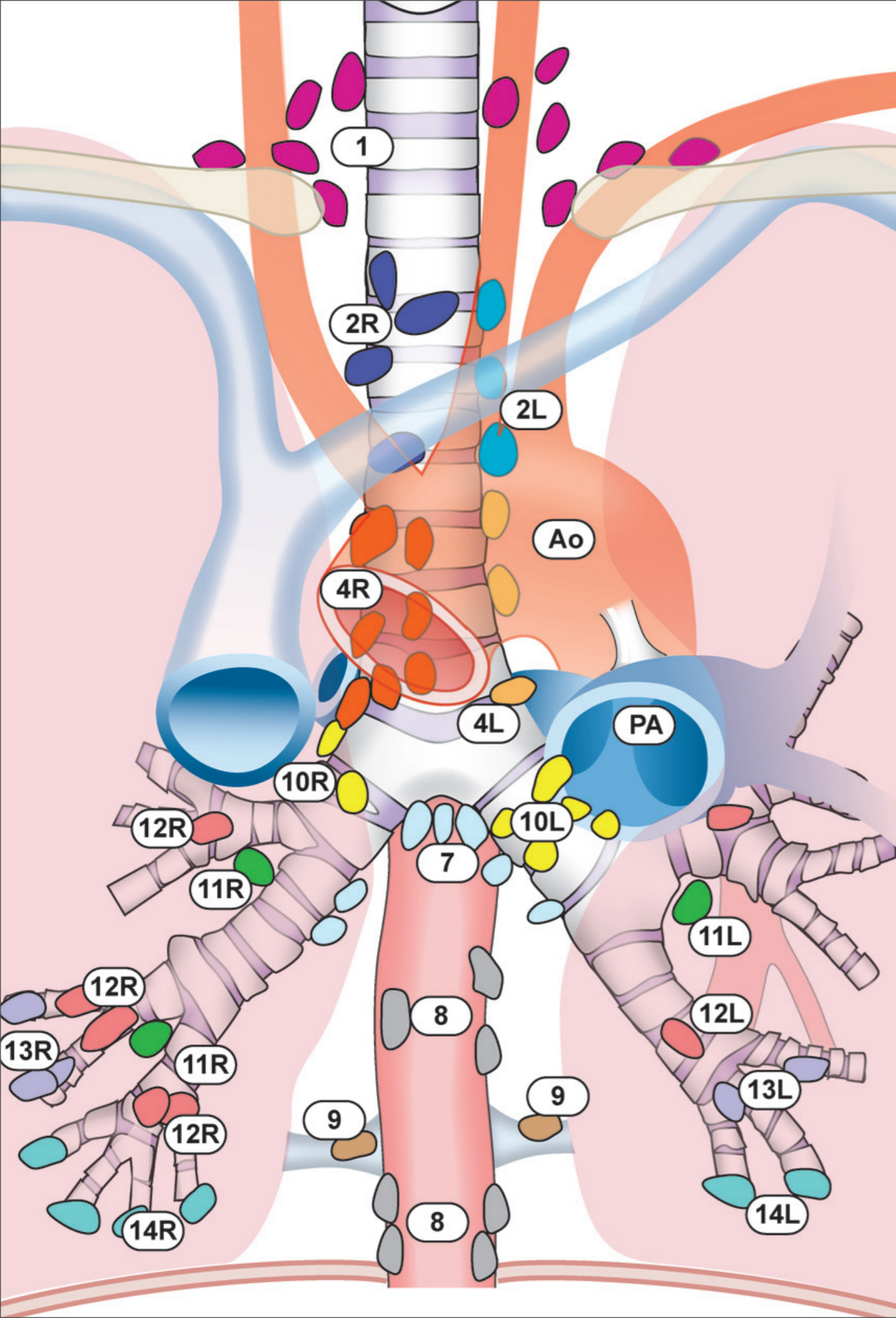
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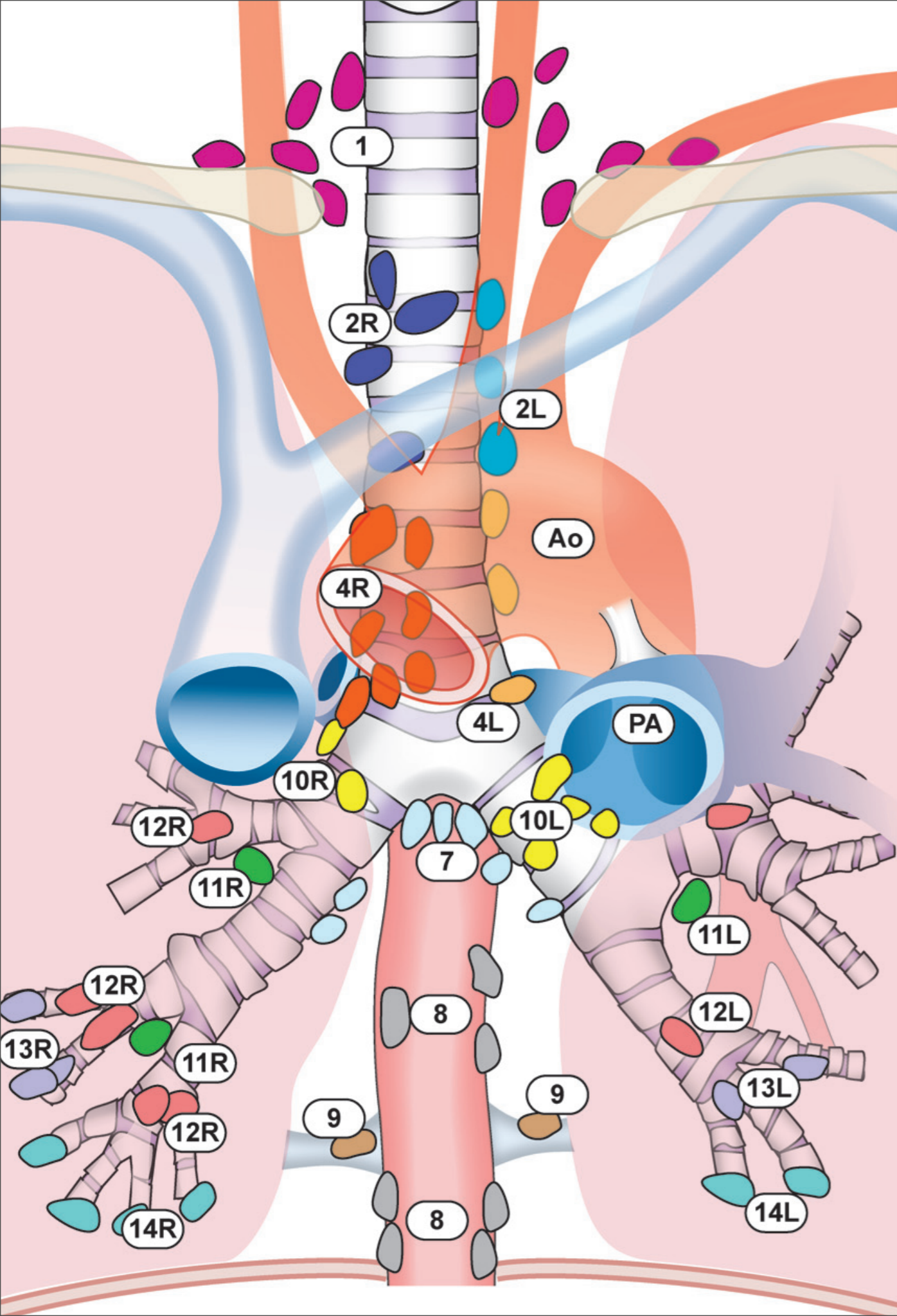
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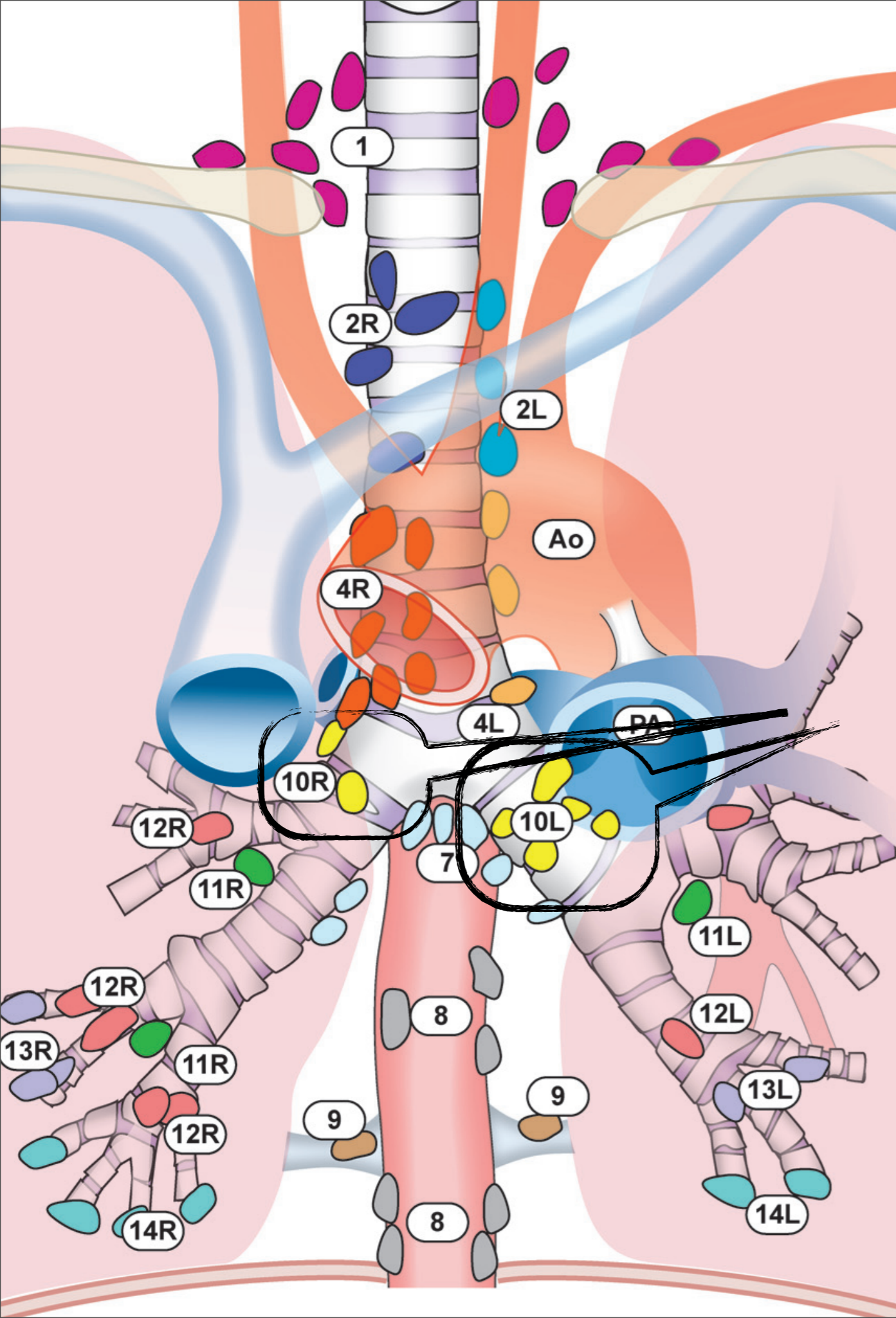
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Lower zone

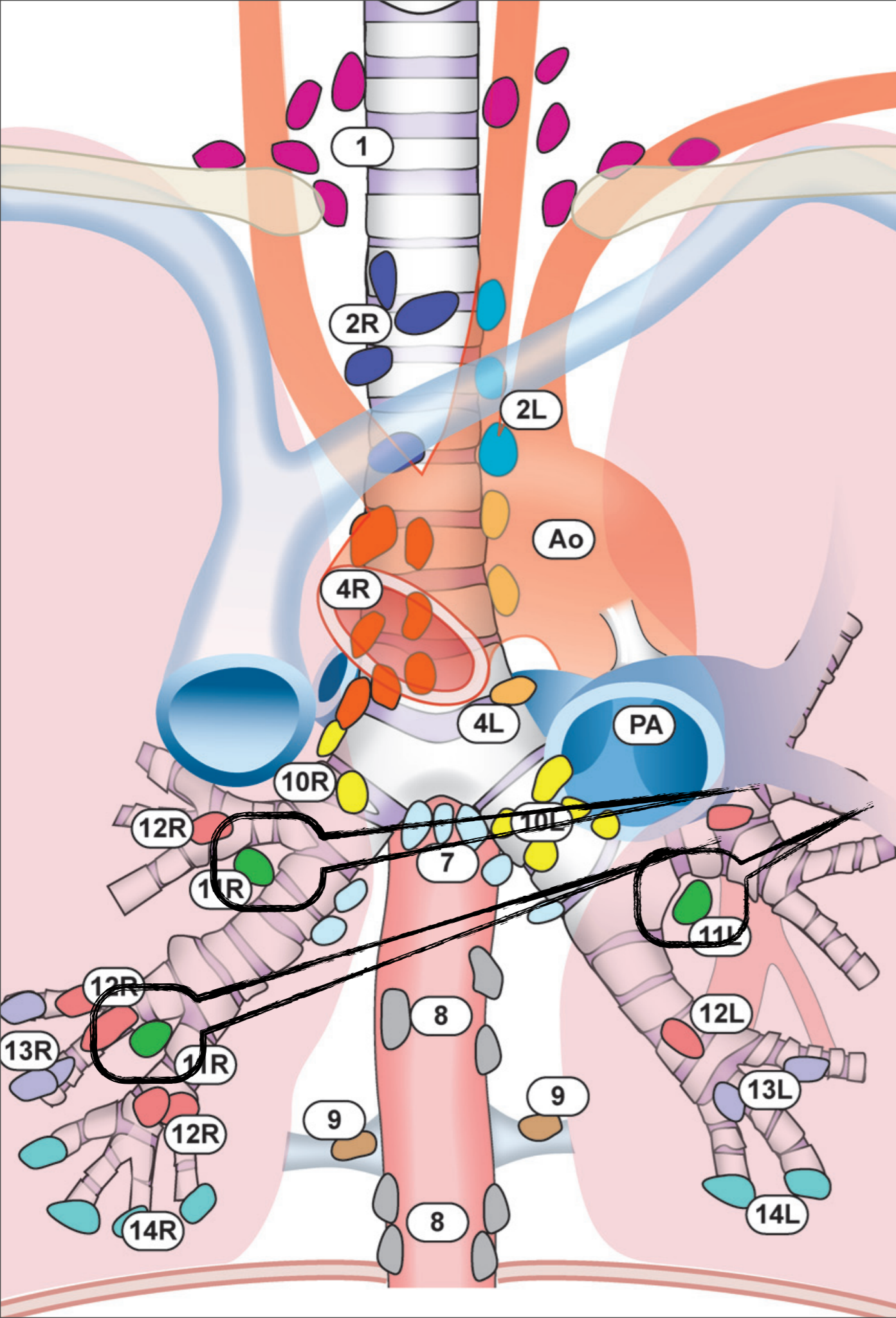
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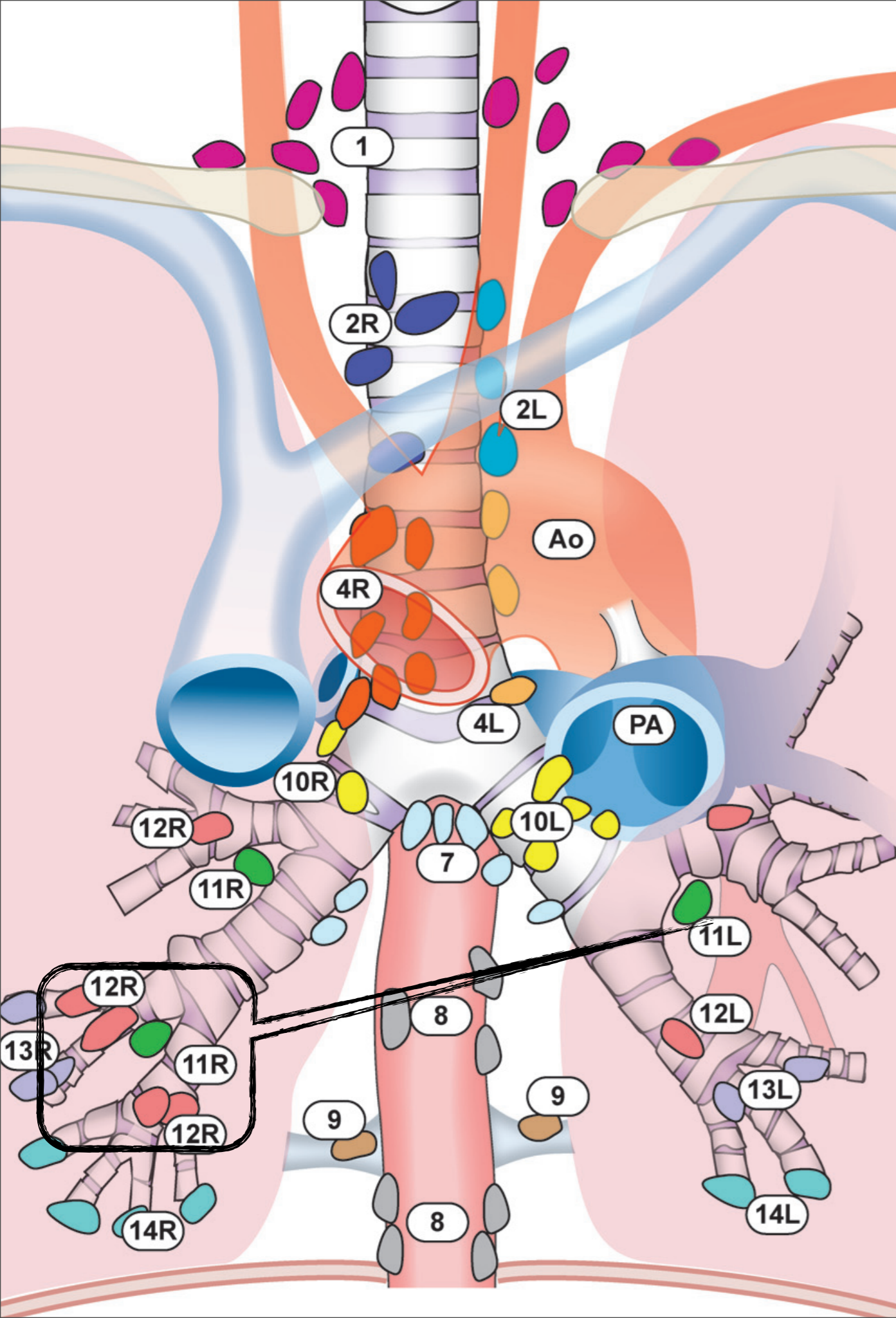
N₁ Nodes

<i>Hilar/Interlobar zone</i>	
● 10 Hilar	
● 11 Interlobar	
<i>Peripheral zone</i>	
● 12 Lobar	
● 13 Segmental	
● 14 Subsegmental	



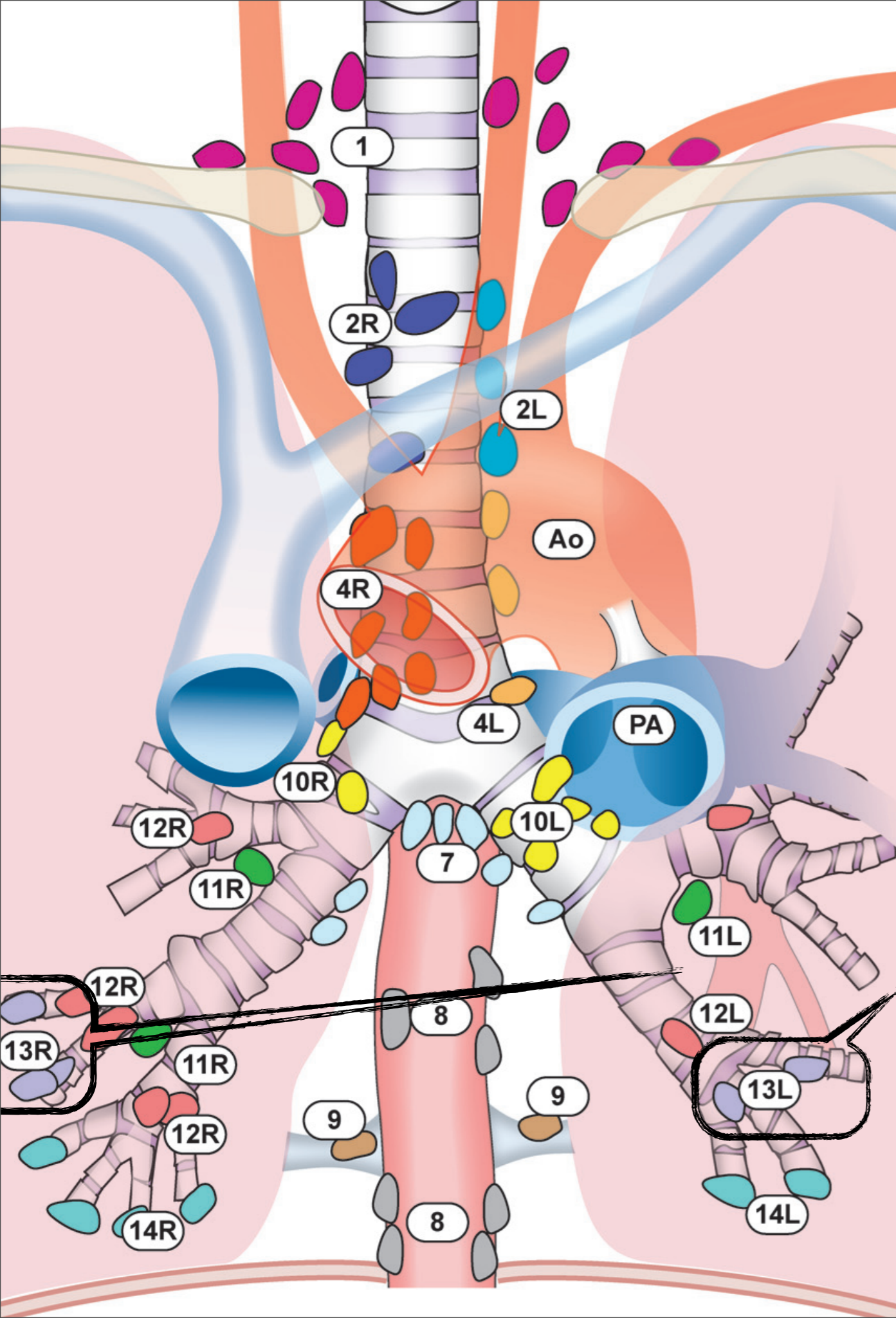
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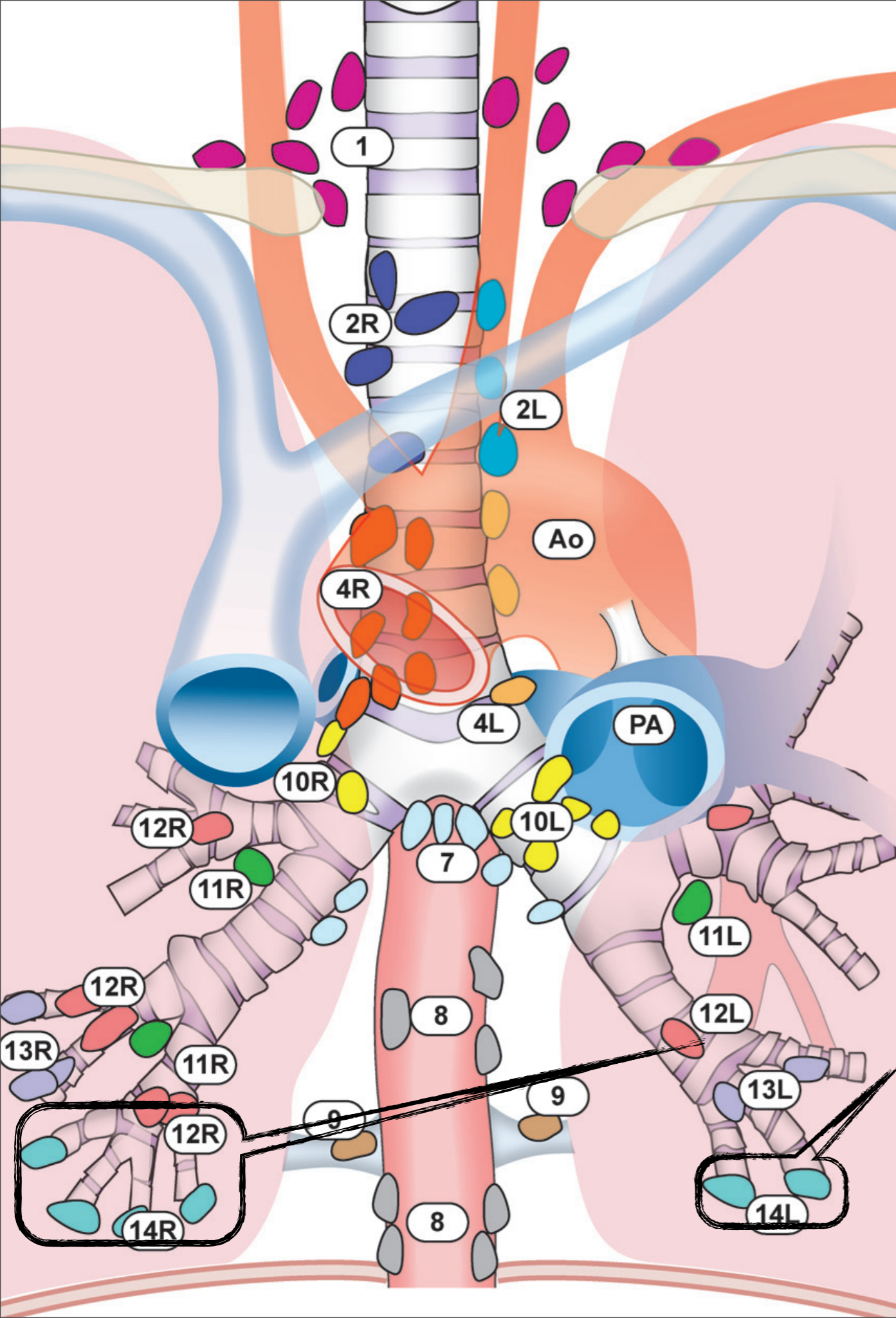
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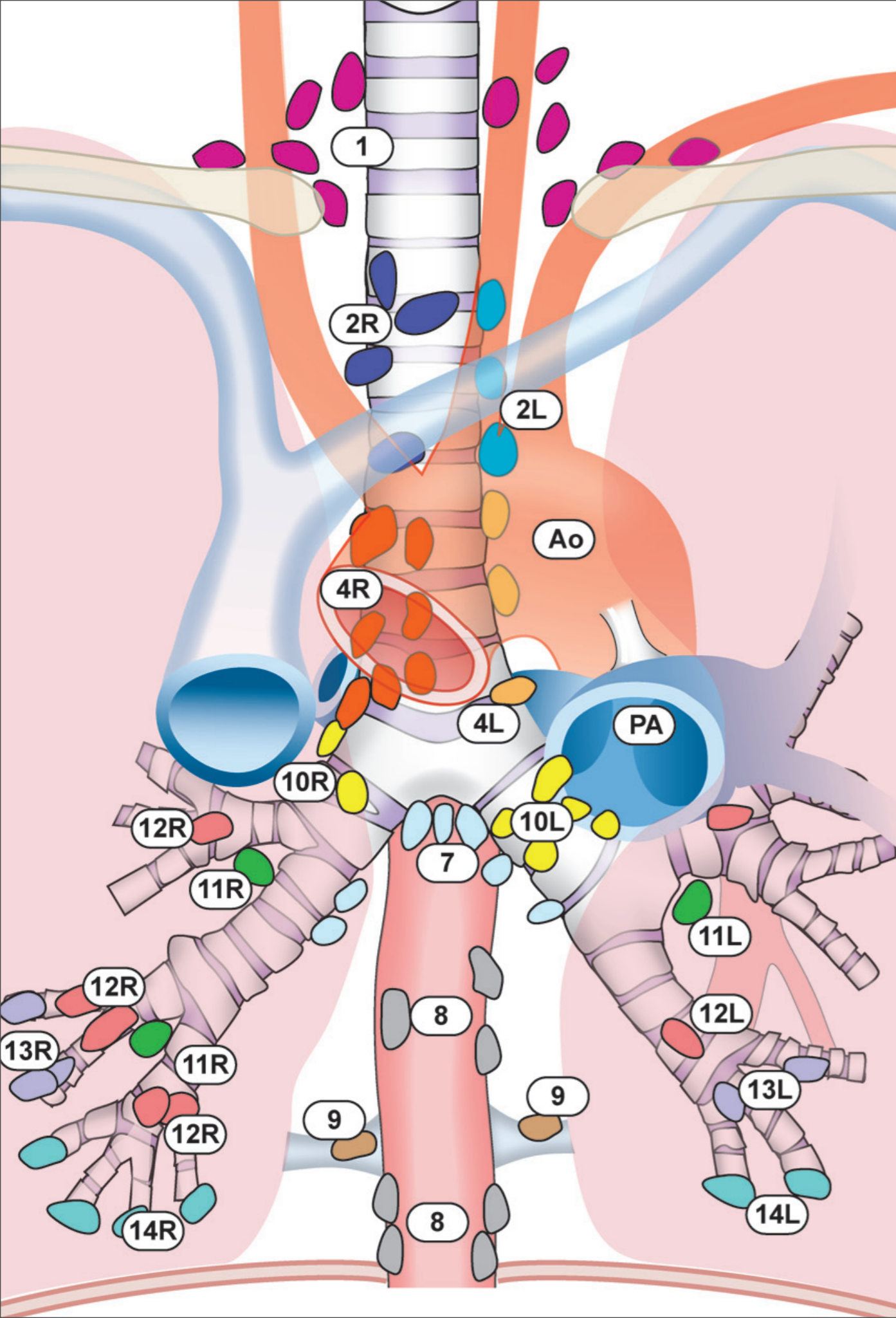
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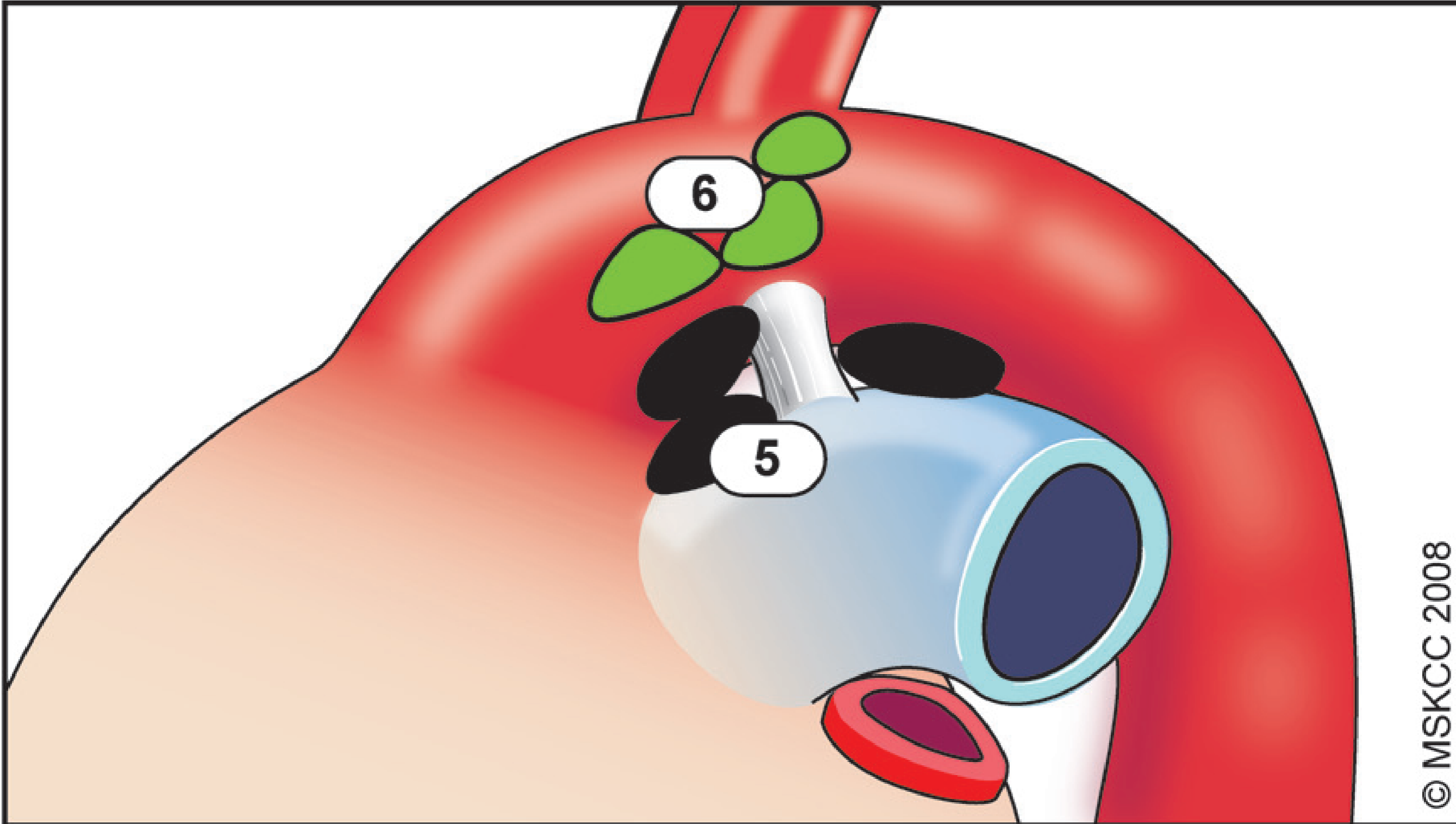
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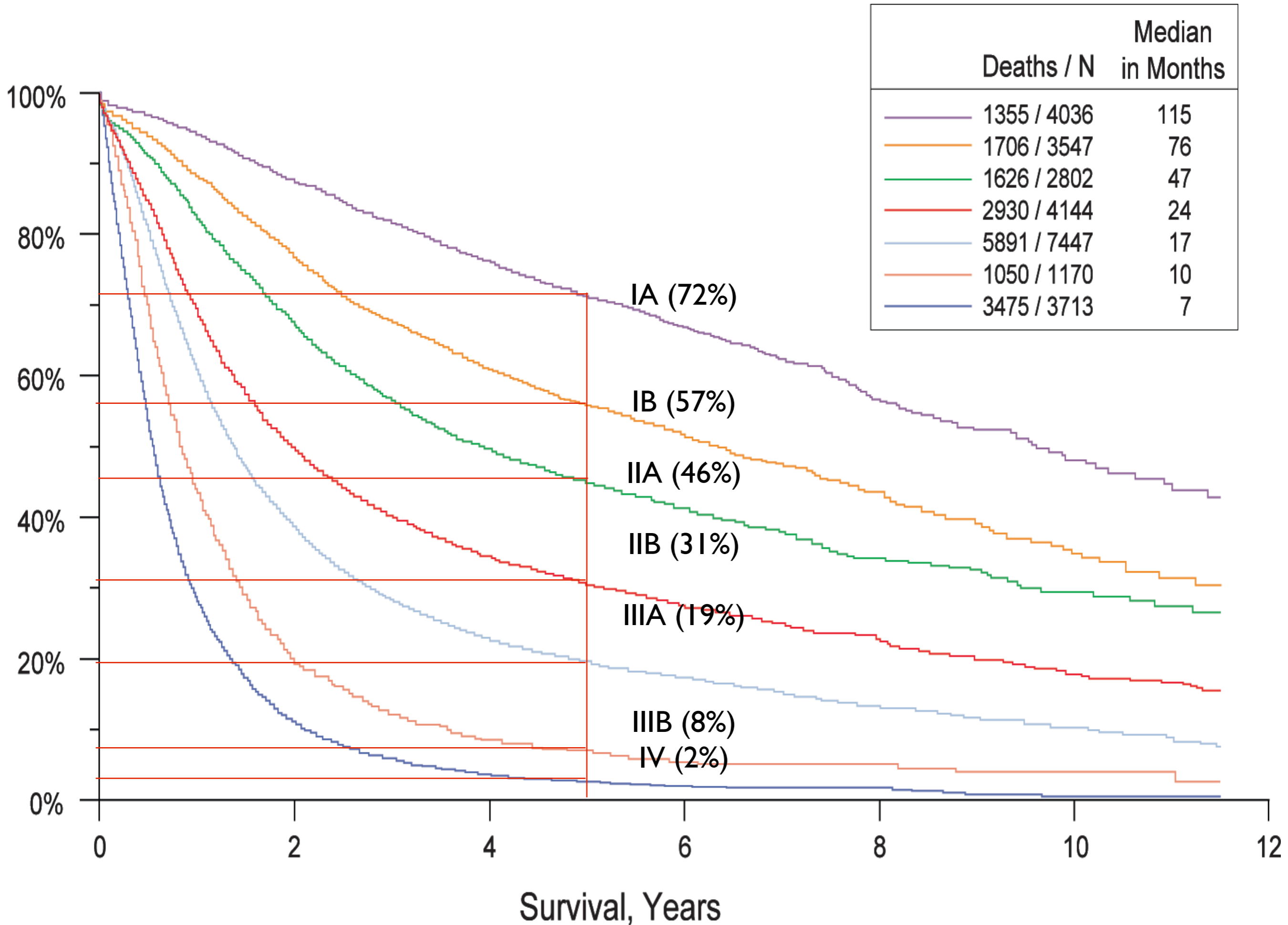
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AP zone

ANATOMIC STAGE/PROGNOSTIC GROUPS

Occult carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
	T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T1a	N1	M0
	T1b	N1	M0
	T2a	N1	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a	N2	M0
	T1b	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T3	N2	M0
	T4	N0	M0
	T4	N1	M0
Stage IIIB	T1a	N3	M0
	T1b	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N3	M0
	T4	N2	M0
	T4	N3	M0
Stage IV	Any T	Any N	M1a
	Any T	Any N	M1b



SCLC

- 1950 - Clasificación de *Veterans Administration Lung Study Group*
- Depende extensión y posibilidad de campo de RT
 - Enfermedad limitada: Compromiso de un hemitorax, aun en compromiso local o supraclavicular ipsilateral
 - IASLC - 1989: Tumores limitados a un hemitorax, con compromiso nodal regional, incluidos los ganglios hiliares, mediastinales ipsi y contralaterales y supraclaviculares bilaterales
 - Incluye derrame pleural ipsilateral independiente de citología

Clasificación Histologica

Especímenes de Resección

TABLE 1. IASLC/ATS/ERS Classification of Lung Adenocarcinoma in Resection Specimens

Preinvasive lesions

Atypical adenomatous hyperplasia

Adenocarcinoma in situ (≤ 3 cm formerly BAC) ←

Nonmucinous

Mucinous

Mixed mucinous/nonmucinous

Minimally invasive adenocarcinoma (≤ 3 cm lepidic predominant tumor with ≤ 5 mm invasion) ←

Nonmucinous

Mucinous

Mixed mucinous/nonmucinous

Invasive adenocarcinoma

Lepidic predominant (formerly nonmucinous BAC pattern, with >5 mm invasion) ←

Acinar predominant

Papillary predominant

Micropapillary predominant

Solid predominant with mucin production

Variants of invasive adenocarcinoma

Invasive mucinous adenocarcinoma (formerly mucinous BAC) ←

Colloid

Fetal (low and high grade)

Enteric

Requiere
diferenciación de
Metástasis
colorectal

Lesiones preinvasivas

- Presente 5 – 23% tejido adyacente a adenocarcinoma
- Comparte:
 - Clonalidad
 - Mutación y polimorfismo de KRAS
 - Mutaciones EGFR
 - Expresión de p53
 - Pérdida de heterocigocidad y metilación
 - Alteraciones epigenéticas en *Wnt1*
 - Expresión de FHIT

Consideraciones

- ✦ Hiperplasia alveolar atípica
 - ✦ Continuum hacia Adenocarcinoma in situ
 - ✦ Difícil de distinguir de progresión
- ✦ Adenocarcinoma in situ
 - ✦ Limitada a estructuras alveolares preexistentes
 - ✦ 100% supervivencia libre de enfermedad a 3 años

Adenocarcinoma microinvasivo

- Subtipo histológico diferente a Lepidico
- Células tumorales con infiltración al estroma miofibroblástico
- No considerable si:
 - Invade linfáticos, vasos o pleura
 - Contiene necrosis tumoral
 - Tamaño??
 - < 5 mm
- Supervivencia 100% con resección

Acercas del TTF-1..

- División anatómica de acuerdo a origen embriológico
 - Sistema de conducción aérea
 - Expresión ubicua de TTF-1 en células epiteliales
 - Regulación en desarrollo de vías aéreas pequeñas y alveolos
 - Expresión por células Claras y neumocitos de tipo II
 - Parenquima Pulmonar periférico.
 - Expresión negativa para TTF-1
 - Tumores no relacionados a unidades de transporte aéreo
 - Expresión de MUC 2-5-6 originado en células *Globet*

SCLC

- Disminución constante de la incidencia a partir de 1986 (25 → 12.5%)
- Cambios en la clasificación histológica en 4 ocasiones en las últimas tres décadas
- Introducción del carcinoma neuroendocrino de célula grande en NSCLC en 1999
- Dificultades en la distinción de este último con SCLC

Table 1. Summary of Diagnostic Criteria and Grading of Lung Neuroendocrine Tumors Based on the 2004 World Health Organization Classification

	Typical Carcinoid	Atypical Carcinoid	Large Cell Neuroendocrine Carcinoma	Small Cell Lung Carcinoma
Grade	Low	Intermediate	High	High
Morphology	Well-differentiated NET	Well-differentiated NET	Poorly differentiated NET	Poorly differentiated NET
Mitoses per 10 HPFs ^a	<2	2-10	>10 (median, 70)	>10 (median, 80)
Necrosis	None	Present (focal punctate)	Present (extensive)	Present (extensive)

Para destacar ...

- ✦ Pulmón:
 - ✦ Origen de 95% de Carcinoma de célula pequeña
 - ✦ Origen de 30% de Tumores neuroendocrinos bien diferenciados
 - ✦ Ligado casi exclusivamente al habito de fumar (SCLC)
 - ✦ Carcinoides pulmonares: 5% MEN1

Indicaciones quirúrgicas

- ✦ Ausencia de compromiso mediastinal
- ✦ Ausencia de compromiso metastásico
- ✦ Disección de ganglios linfáticos mediastinales
 - ✦ Evaluación de al menos 6 ganglios
 - ✦ 3 mediastinales
 - ✦ 3 N1 de existir
 - ✦ Incluir ganglios de estación 9 para tumores de LI
 - ✦ Mejores desenlaces con la disección mediastinal completa que con el muestreo ganglionar

Limitaciones para intervención

- Síndrome de vena cava superior
- Parálisis de cuerda vocal o N. Frenico
- Derrame pleural maligno
- Tumor a < 2 cm de la carina
- Metastasis en ganglios contralaterales
- Compromiso de la A. Pulmonar principal
- HTP moderada - FEV1 < 1 l - CVF $< 40\%$

Opciones de tratamiento

Estadio 0	Cirugía Terapia endobronquial	
Estadio IA y IB	Cirugía Radioterapia**	** Pacientes Inoperables 60 Gy, T < 4 cm Resultados similares a resección
Estadio IIA y IIB	Cirugía QT neoadyuvante ** Quimioterapia adyuvante Radioterapia ***	** Sin beneficio claro en supervivencia global *** Pacientes inoperables 60 Gy, 10% OS a 5 años

Noordijk EM, Radiother Oncol 13 (2): 83-9, 1988

Gilligan D, Lancet 369 (9577): 1929-37, 2007

Dosoretz DE, Int J Radiat Oncol Biol Phys 24 (1): 3-9, 1992

Opciones de tratamiento

IIIA	Resecada	Cirugía Neoadyuvancia ** Adyuvancia	** HR, 0.88; 95% CI, 0.76–1.01; <i>P</i> = .07 Beneficio Absoluto 5%
	Irreseccable	Radioterapia Quimioradioterapia	* Reducción 10% en mortalidad con CRT * Combinación de CDDP/ VP16
	Tumores de sulcus superior	Radioterapia Quimioradioterapia Radioterapia y Cx	** Solo hay 64% de posibilidad de resección de T3 y 39% de T4
	Tumores que invaden la pared torácica	Cirugía Cirugía y RT ** RT sola CRT seguida de CX	** Indicada si hay márgenes poco claros

Gilligan D, Lancet 369 (9577): 1929-37, 2007

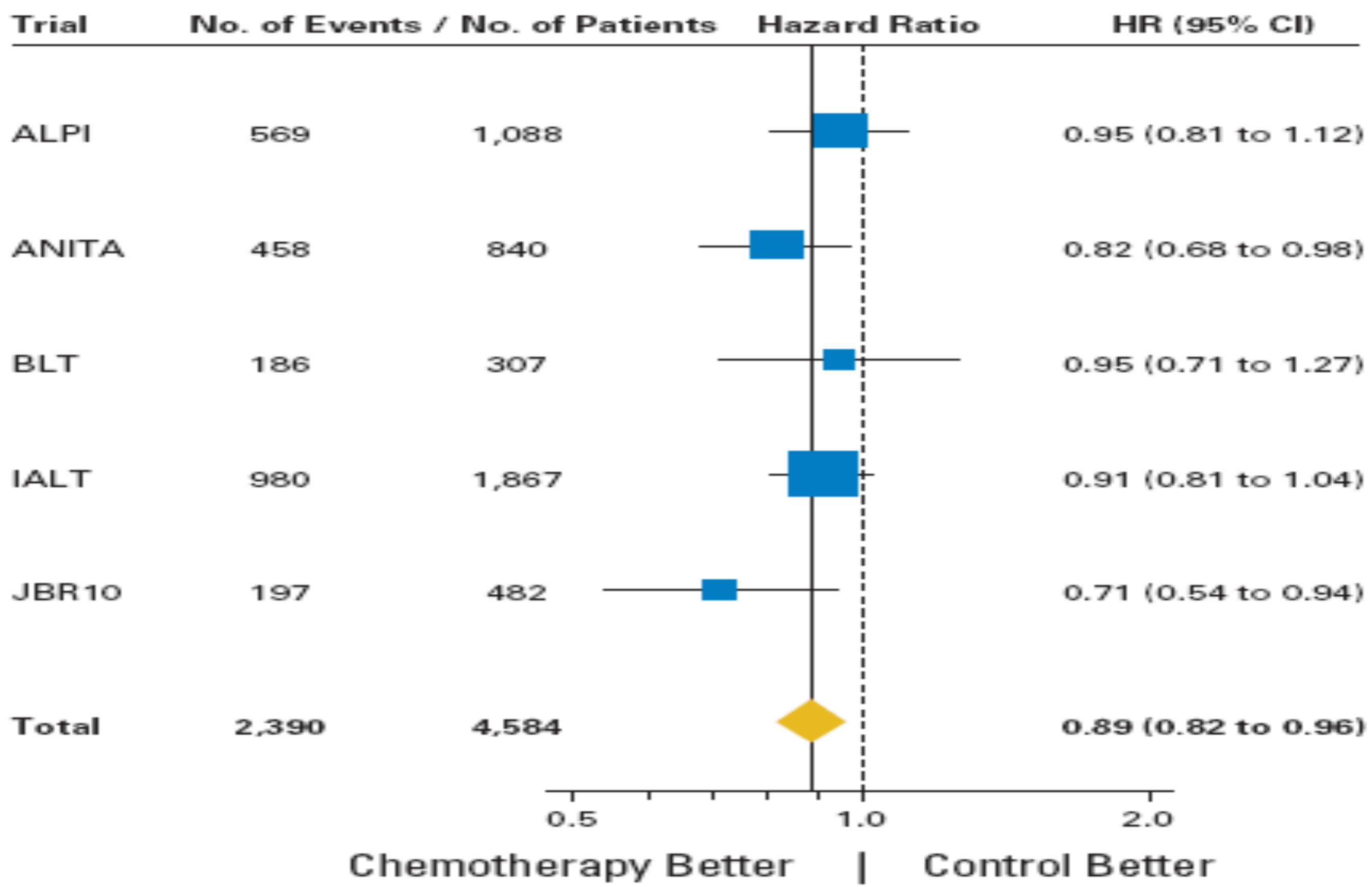
Rowell NP, Cochrane Database Syst Rev (4): CD002140, 2004

Rusch VW, J Thorac Cardiovasc Surg 119 (6): 1147-53, 2000

Lung Adjuvant Cisplatin Evaluation: A Pooled Analysis by the LACE Collaborative Group

- Identificar opciones de tratamiento efectivas para pacientes en postoperatorio
- 5 estudios incluidos
 - 4584 pacientes
 - Quimioterapia basada en CDDP
 - Tumores completamente resecados
 - Seguimiento promedio 5.2 años

Overall Survival

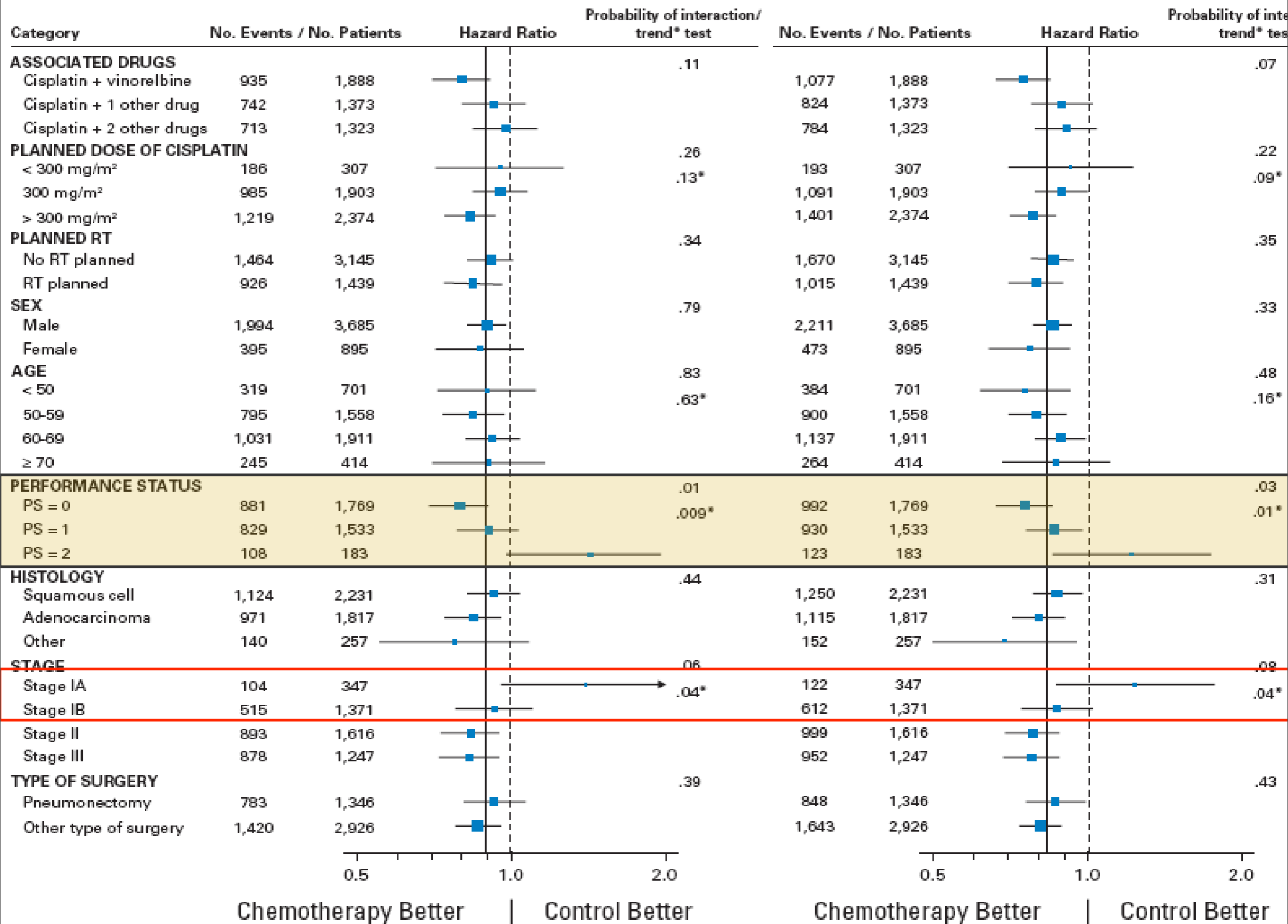


Chemotherapy effect: Logrank statistic = 8.5, $P = .005$

Test for heterogeneity: $\chi^2_4 = 4.25, P = .37, I^2 = 6\%$

Overall Survival

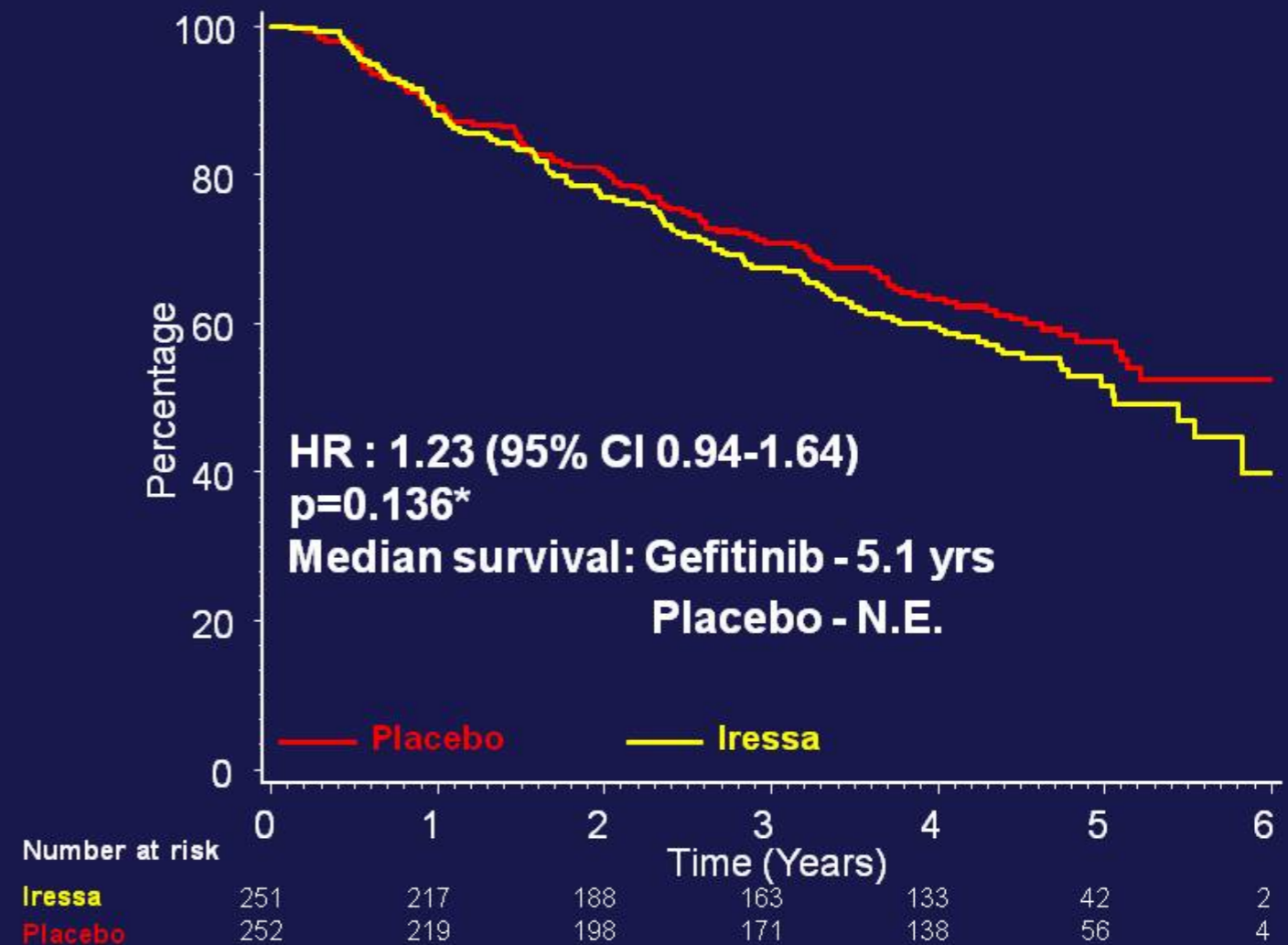
Disease-Free Survival



Terapia dirigida

- No hay datos que apoyen el uso de ITK en el escenario adyuvante
- Estudio BR-19

BR.19 - Overall Survival



*Stratified Log Rank

Opciones de tratamiento

Estadio IIB	Quimioradioterapia Radioterapia sola Quimioterapia paliativa	
Estadio IV	QT combinada Adición de Bev o Cet Inhibidores de ITK ** Inhibidores de EML4/ALK QT de mantenimiento ** Paliacion	** ITK solo para pacientes con mutación de EGFR ** En pacientes con respuesta global a régimen inicial
Enfermedad recurrente	Radioterapia QT o ITK ** Inhibidores de EML4/ALK Paliacion	** Uso de ITK independiente de mutación - Si se conoce Mut -, preferir QT

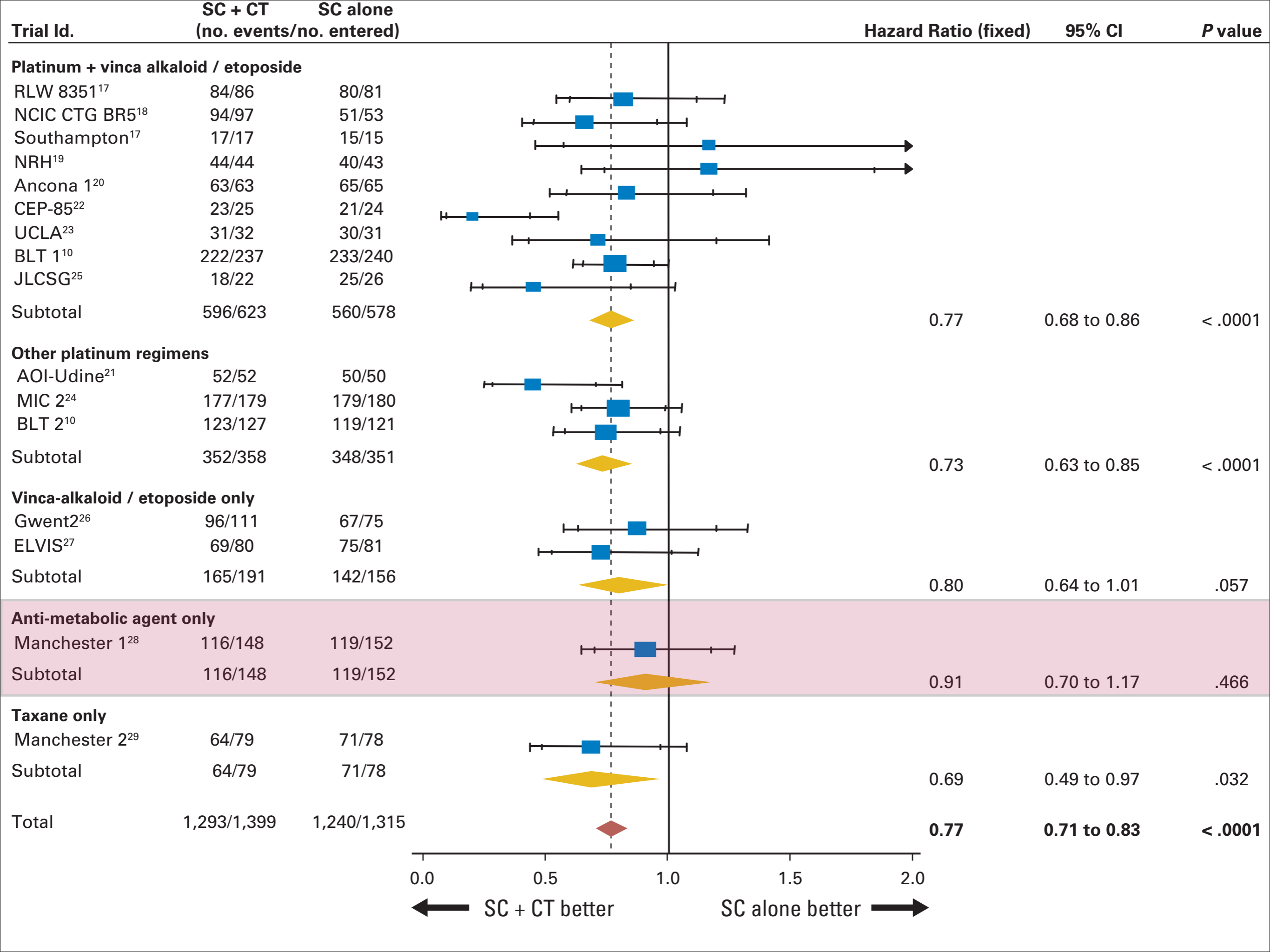
Tratamiento enfermedad metastasica

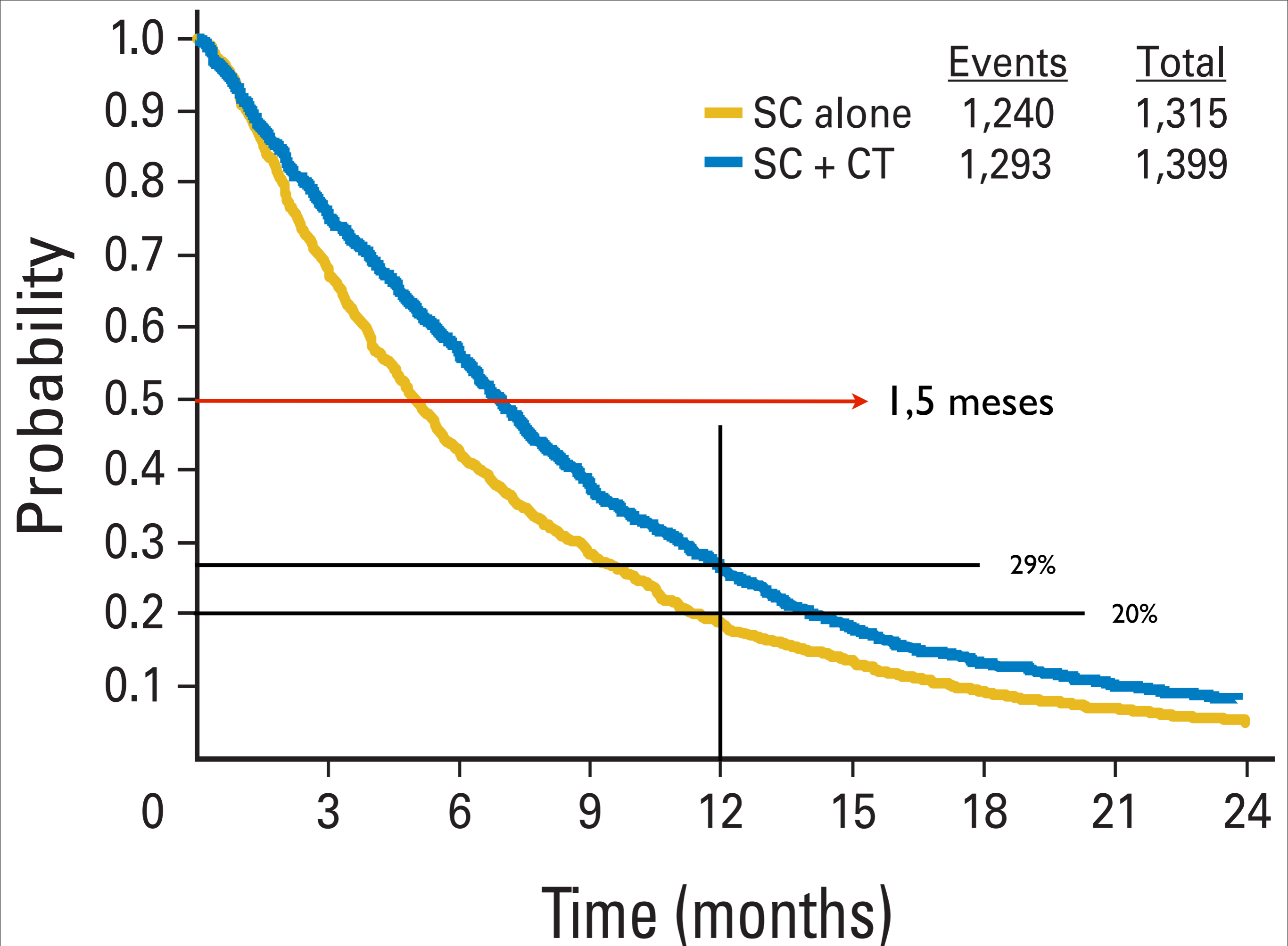
- La intervención es superior a la observación
- Terapia con monoagente
 - Pacientes ancianos o debilitados
- Beneficio en supervivencia con regímenes combinados
 - Considerar la adición de Bevacizumab o Cetuximab
 - Sin deterioro importante en la calidad de vida
 - Estudios iniciales para pacientes jóvenes con buen estado funcional

Chemotherapy in Addition to Supportive Care Improves Survival in Advanced Non–Small-Cell Lung Cancer: A Systematic Review and Meta-Analysis of Individual Patient Data From 16 Randomized Controlled Trials

NSCLC Meta-Analyses Collaborative Group

- 16 estudios clínicos
- 90% de pacientes en EC IIIB y IV
- 2714 pacientes
 - 1399 pacientes en BSC
 - 1315 asignados a QT
- Sin efecto en resultados por tipo de medicamento utilizado



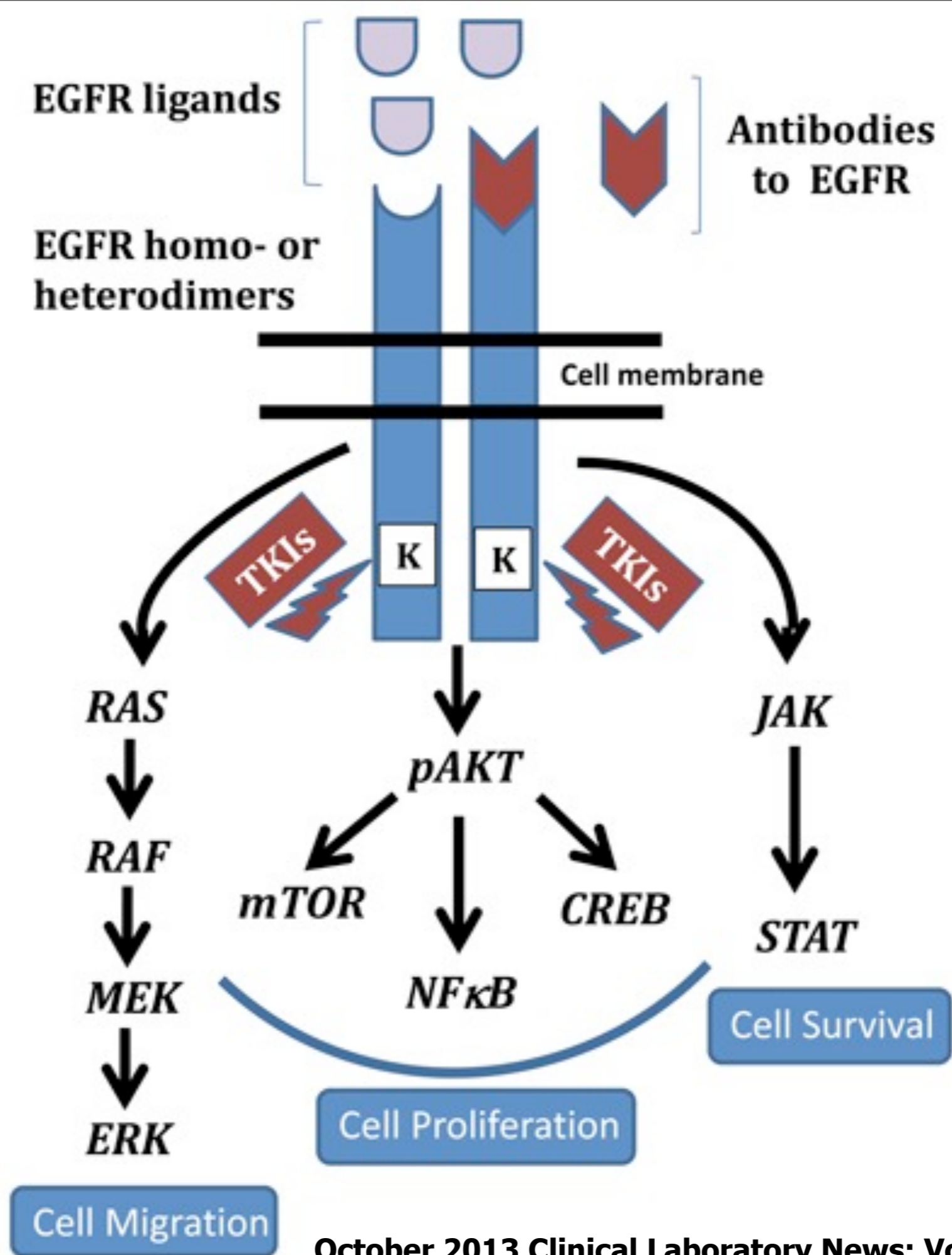


Combinaciones

- Cisplatino/Paclitaxel
- Cisplatino/Gemcitabina
- Cisplatino/Docetaxel
- Cisplatino/Pemetrexed
- Carboplatino/Paclitaxel
- Carboplatino/Pemetrexed

Terapia dirigida

- Mutaciones de EGFR (10% USA - 35% Asia)
 - Delección exon 19
 - 48% NSCLC Mut +
 - Mutación exon 21: L858R
 - 43% NSCLC Mut + - L861Q (2%)
 - Inserción Exon 20 (T790M)
 - 4-9.2% de EGFR +
 - 50% formas resistentes



Evidencia

- Erlotinib

- EURTAC (9,7 vs 5,2 meses)
- OPTIMAL (13,7 vs 4,6 meses)

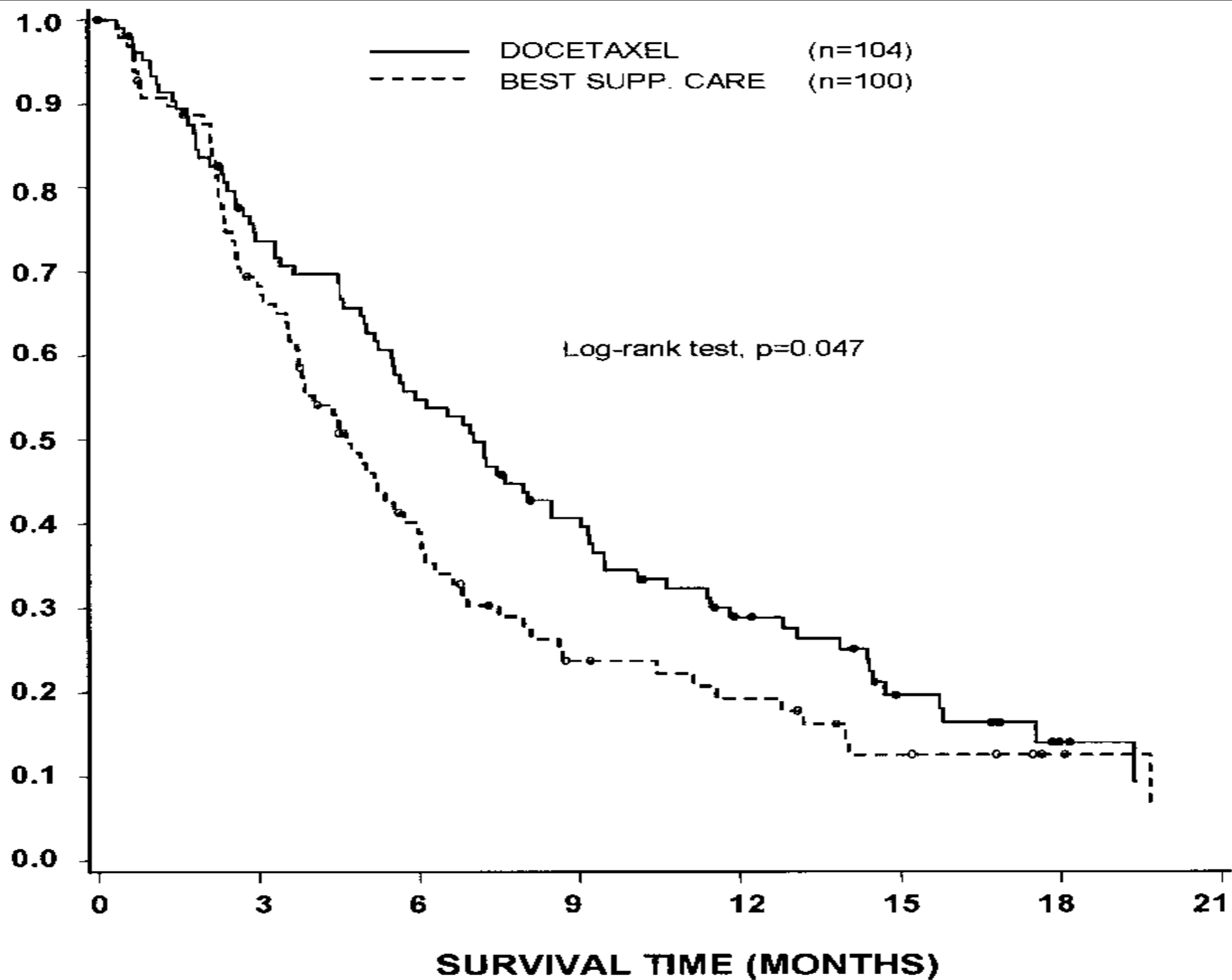
- Gefitinib

- IPASS (9,5 vs 6,3 meses)
- WJTOG 3405 (9,6 vs 6,6 meses)
- NEJ002 (10,8 vs 5,4 meses)

Terapia de segunda linea

- ✦ Consideración de tratamientos previos
- ✦ Estado orgánico y funcional
- ✦ Extension de la enfermedad
- ✦ Consideración de terapia sistematica VS Radiación
 - ✦ Manejo sistematico Vs Paliacion local

CUMULATIVE PROBABILITY





Francisco Hernandez 1932 - 2012