

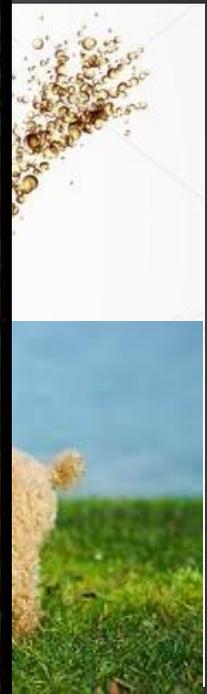
TIPOS E SUBTIPOS do CÂNCER de MAMA

Estado da Arte em Ginecologia e Obstetrícia



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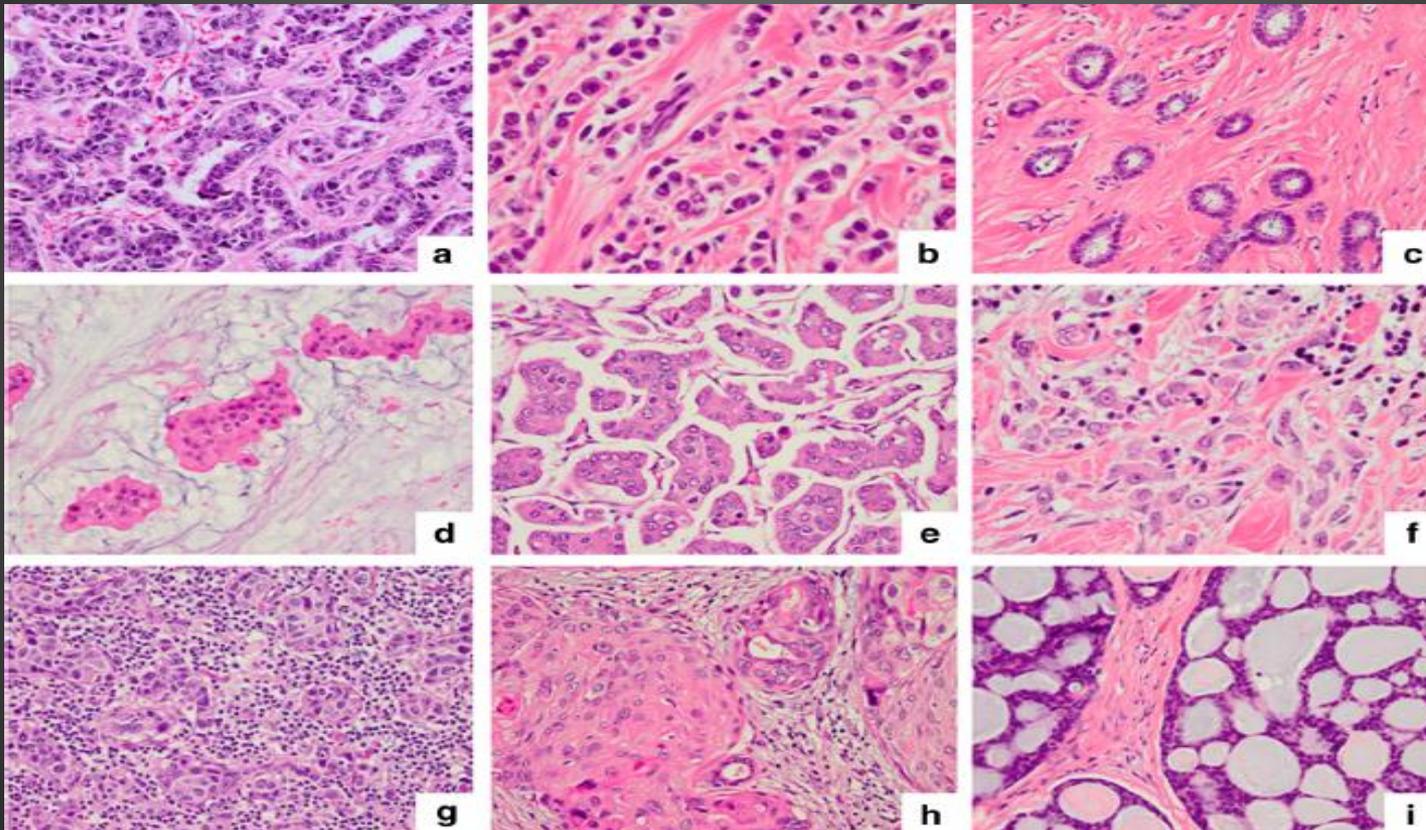
Rodrigo Gregório Brandão
Mastologista pela EPM - UNIFESP
Mestre pela EPM - UNIFESP
Doutorando pela EPM - UNIFESP



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TIPOS HISTOLÓGICOS



GRAU 1

Bem diferenciado

Similar ao tecido normal, porém há mais células, que estão um pouco diferentes do normal, dividindo-se pouco

GRAU 2

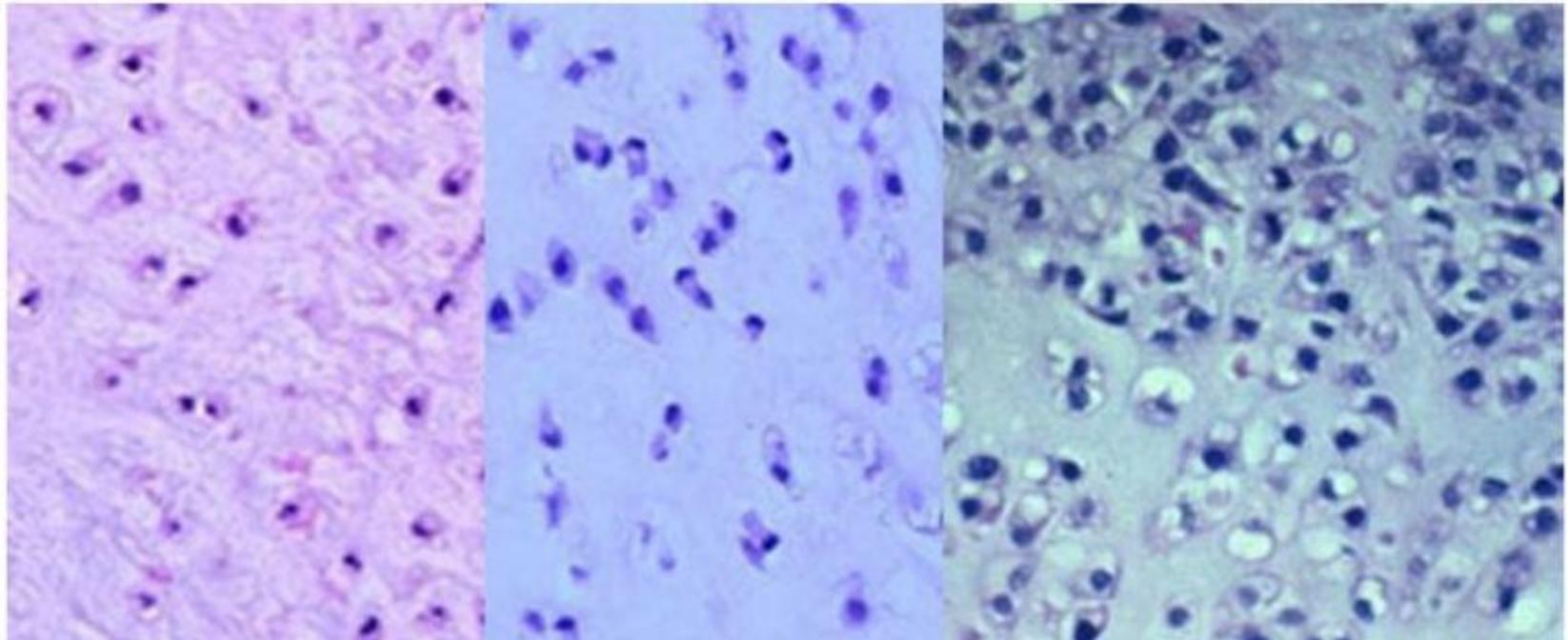
Moderadamente diferenciado

Há mais células do que no grau 1, que também estão ainda mais diferentes

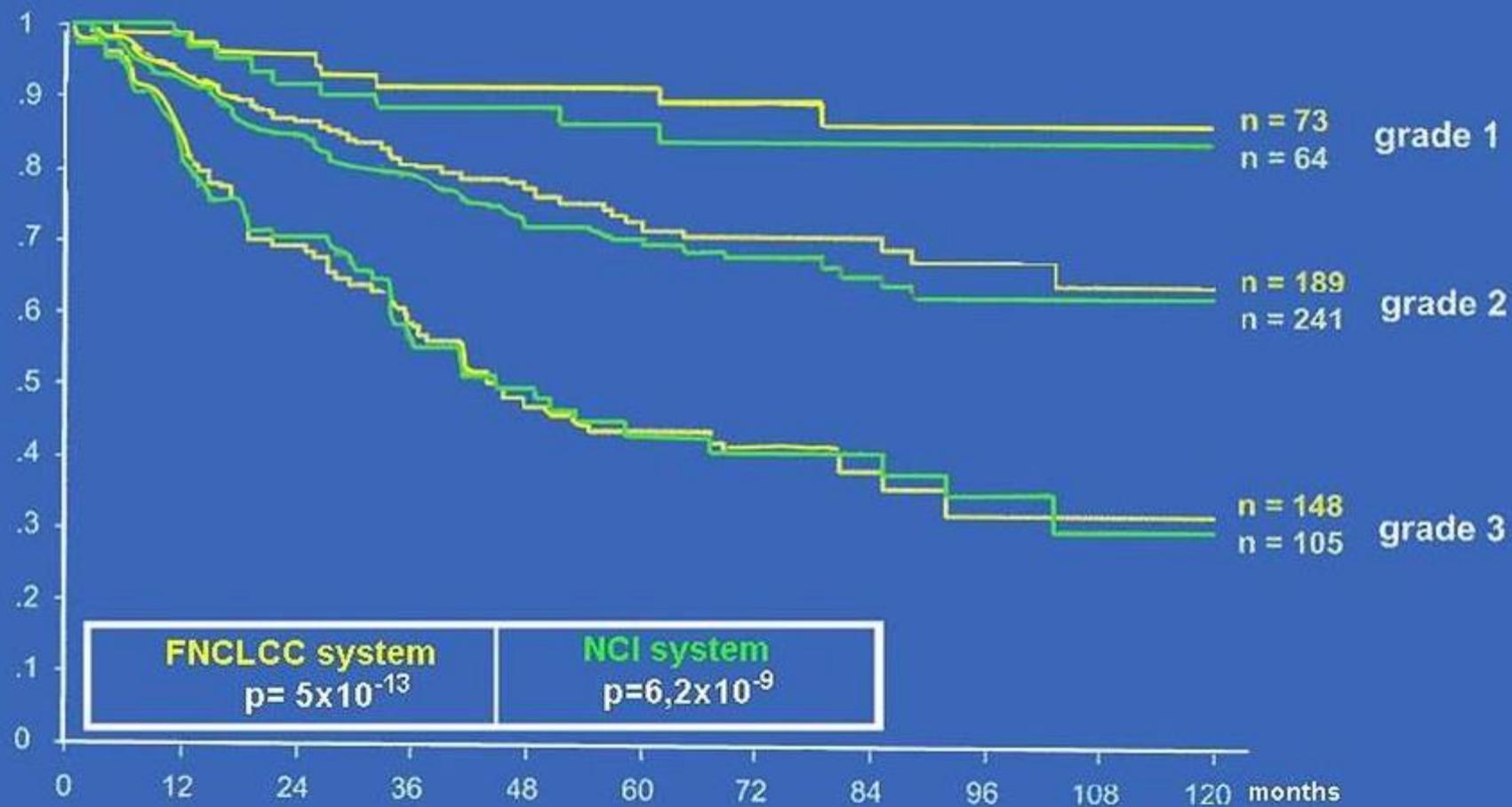
GRAU 3

Pouco diferenciado

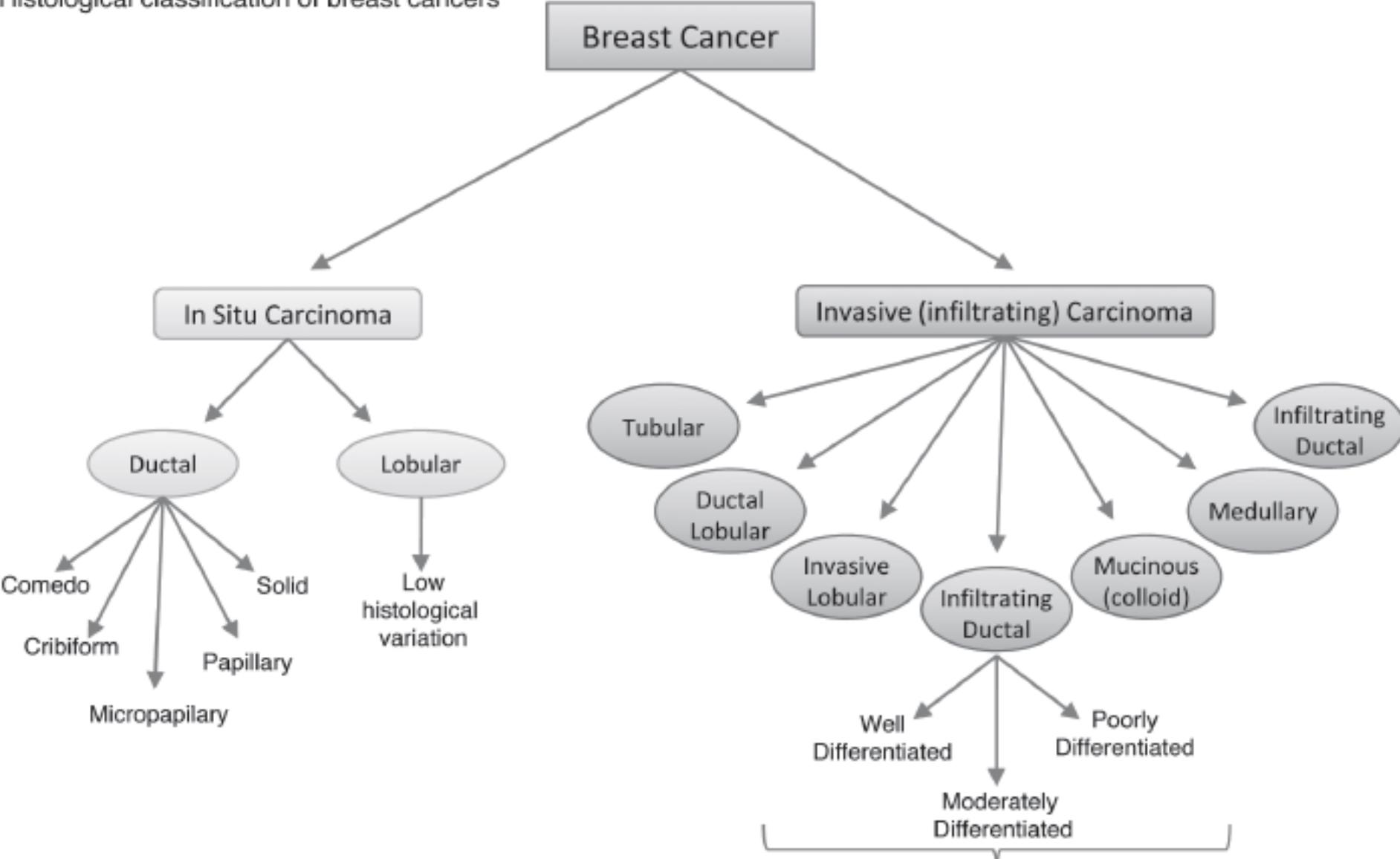
Alta quantidade de células, que estão muito diferentes do normal, dividindo-se frequentemente



----- AGRESSIVIDADE + + + + + + + + +



Histological classification of breast cancers



This classification is based on
1. Nuclear Pleomorphism
2. Glandular/Tubule Formation
3. Mitotic Rate (per 10 HPF)

CARCINOMA DUCTAL IN SITU

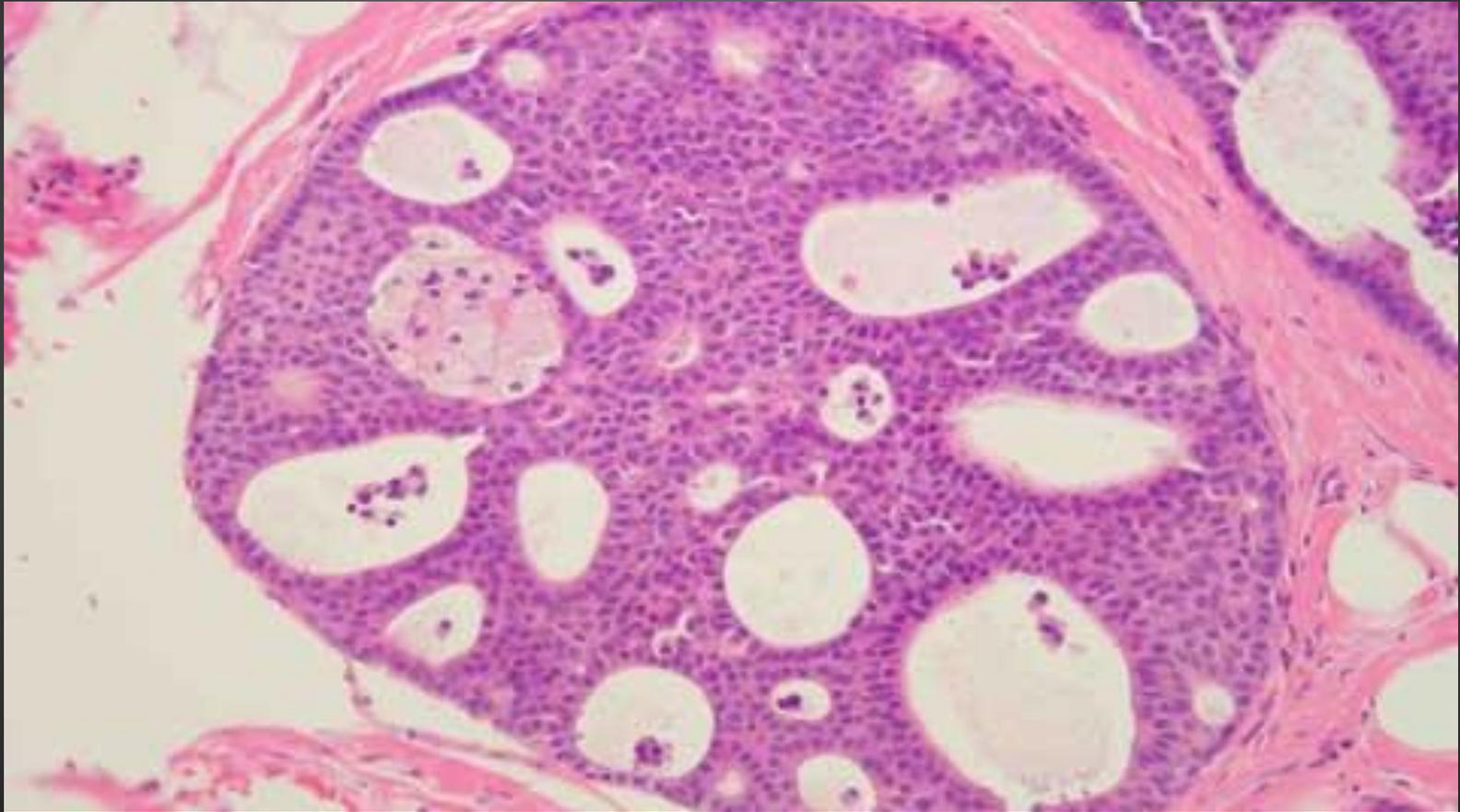
- CDIS
- Proliferação + atipias
- Camada mioepitelial preservada
- Lesão precursora
- Grau do CDIS

Sólido
Cribriforme
Papilífero
Micropapilífero
Comedo

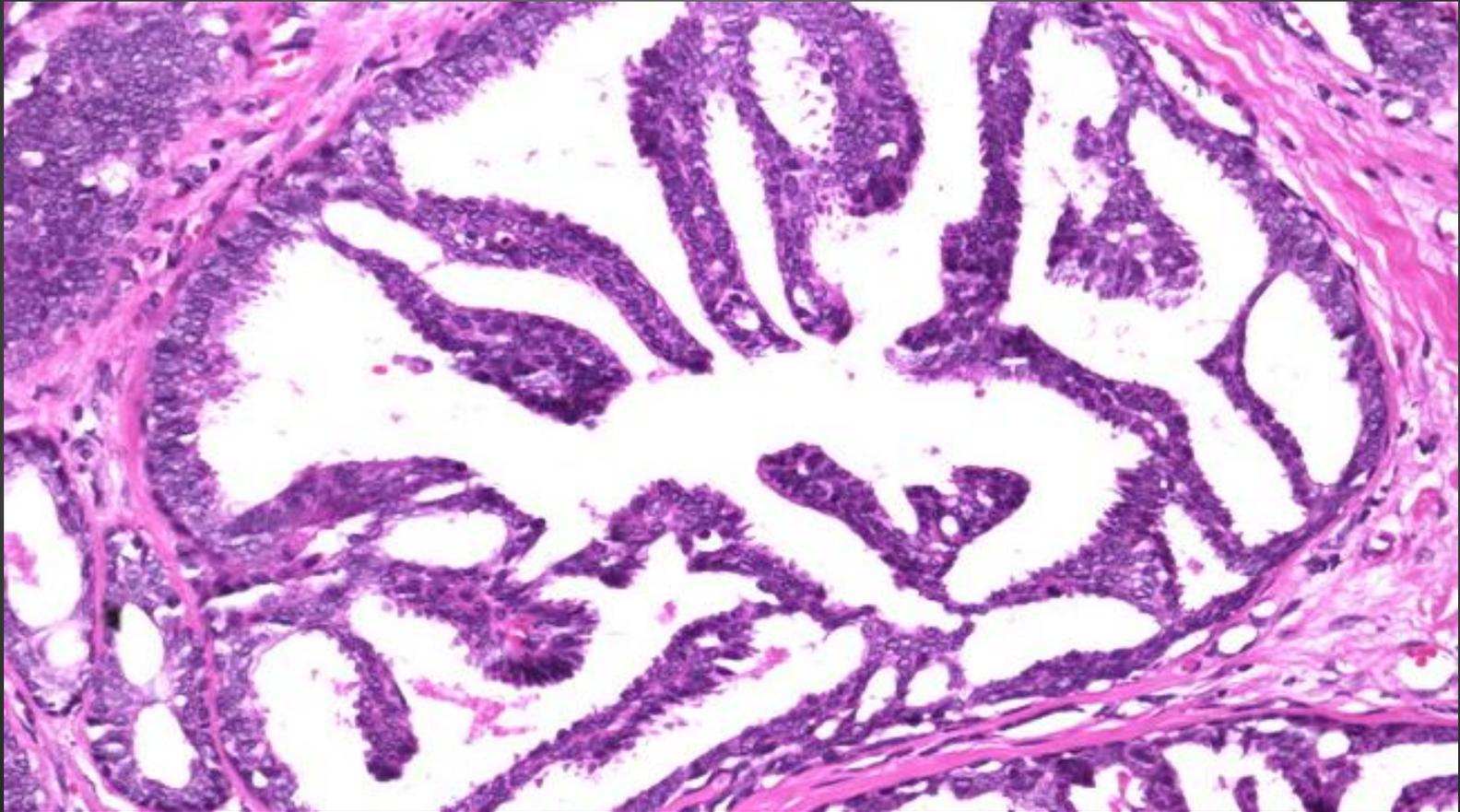
Grau 1
Grau 2
Grau 3



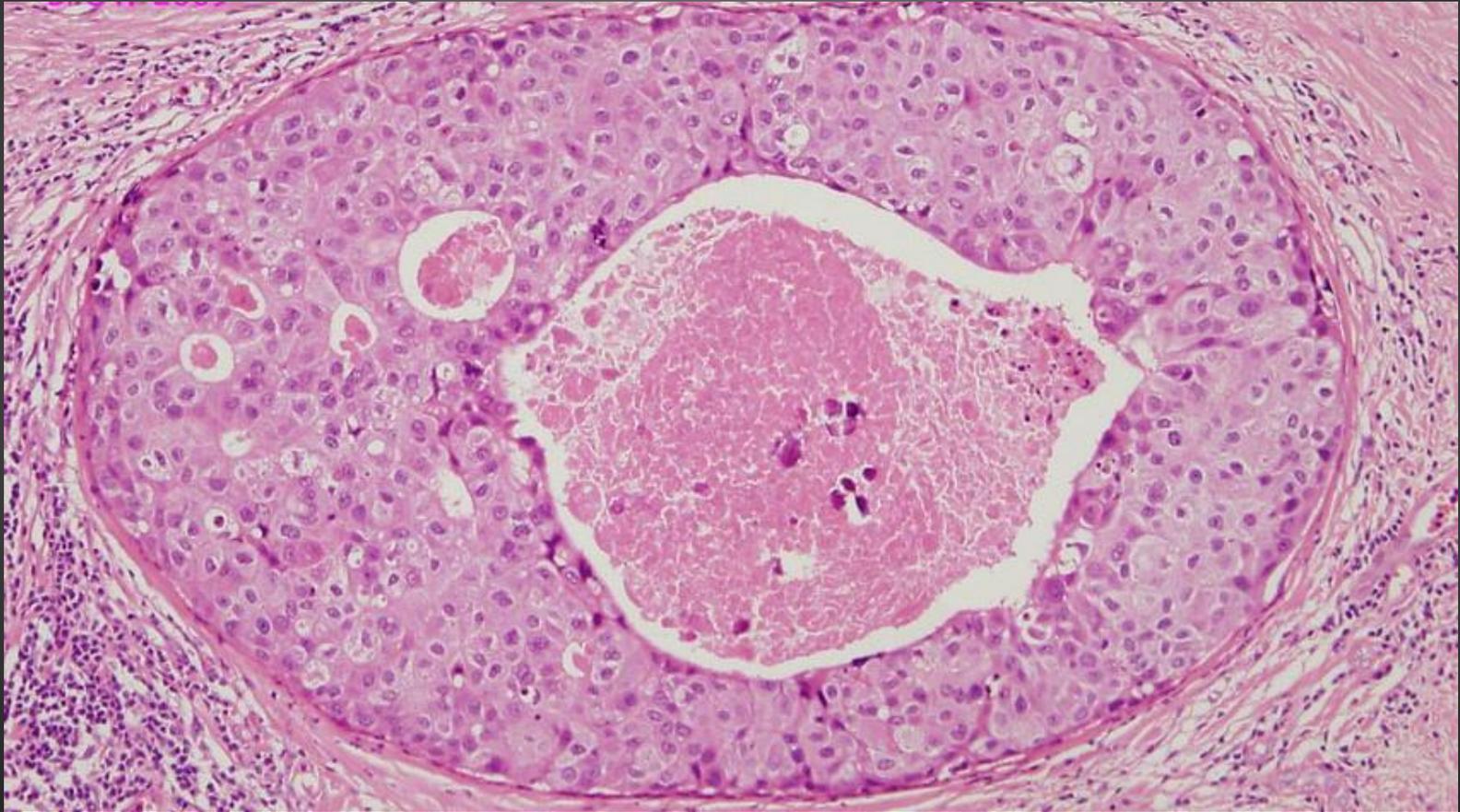
TIPOS HISTOLÓGICOS



TIPOS HISTOLÓGICOS



TIPOS HISTOLÓGICOS



CARCINOMA LOBULAR IN SITU

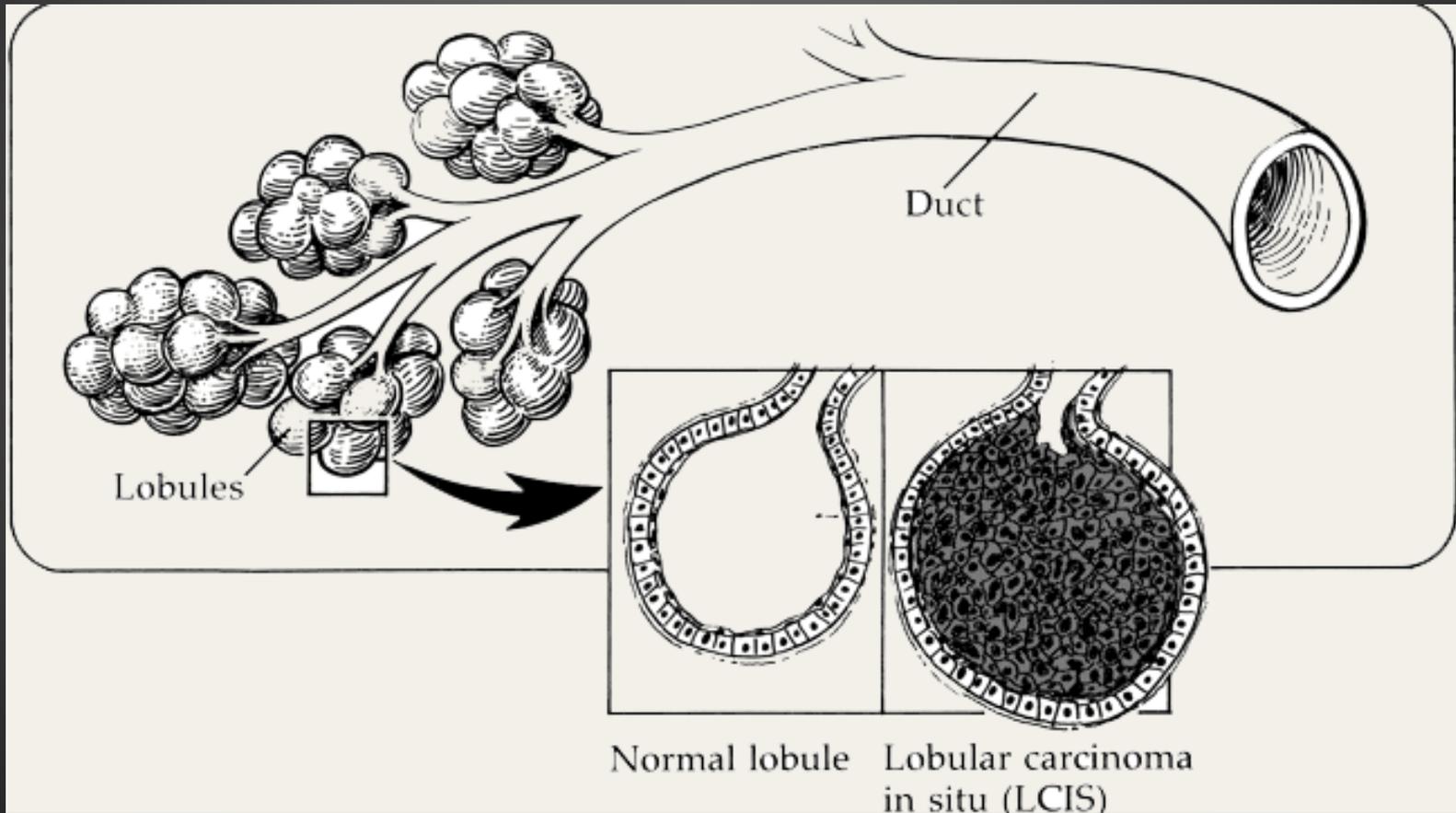
- CLIS
- Proliferação de células pequenas, uniformes e pouco coesas
- Fator de risco (não obrigatório/te precursor)
- Achado acidental
- Multicêntricos e bilaterais

Perda E-caderina
Perda Beta-Catenina
Citoqueratinas de alto peso molec
(CK 8/18)

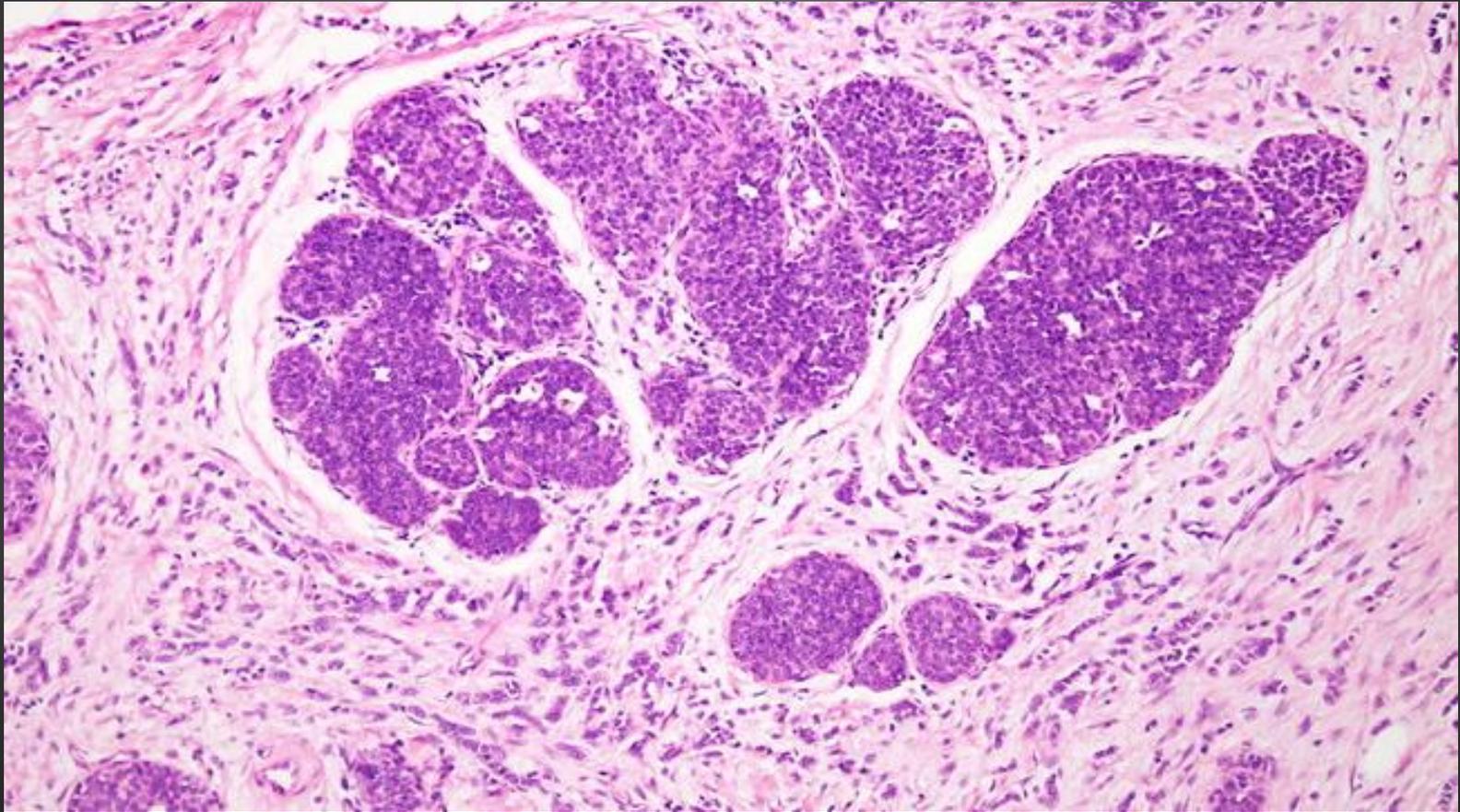
RR 7-12
Carcinomas lobulares ou ductais



TIPOS HISTOLÓGICOS



TIPOS HISTOLÓGICOS



CARCINOMA LOBULAR INVASIVO

- 2º subtipo + frequente - 5-15%
- Faixa etária + avançada
- Células pequenas, uniformes e não coesivas
- Invasão estromal em fileira única (fila indiana)
- Inativação da E-caderina
- TH
- Apresentação clínico-radiológica

FORMA CLÁSSICA

PLEOMÓRFICO

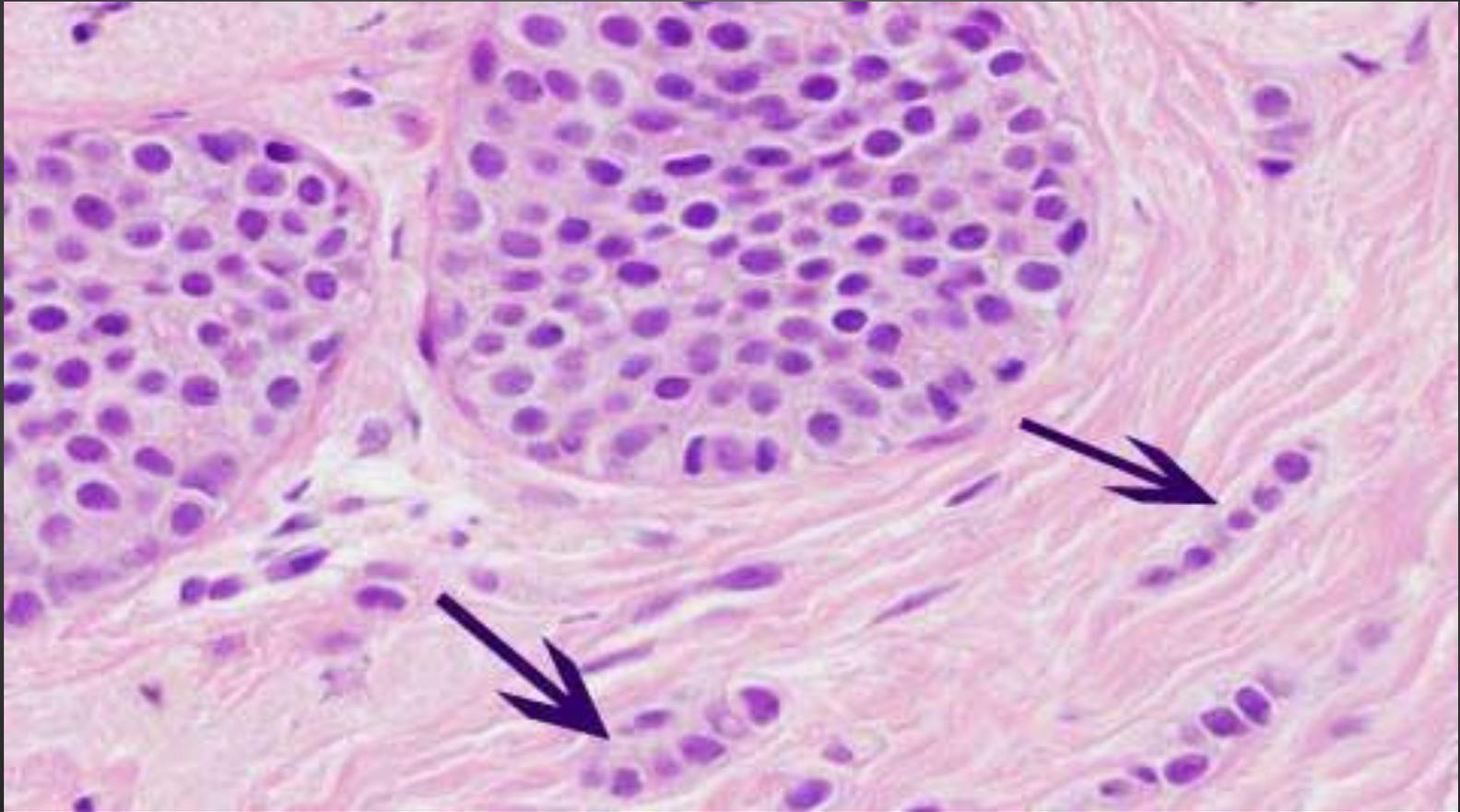


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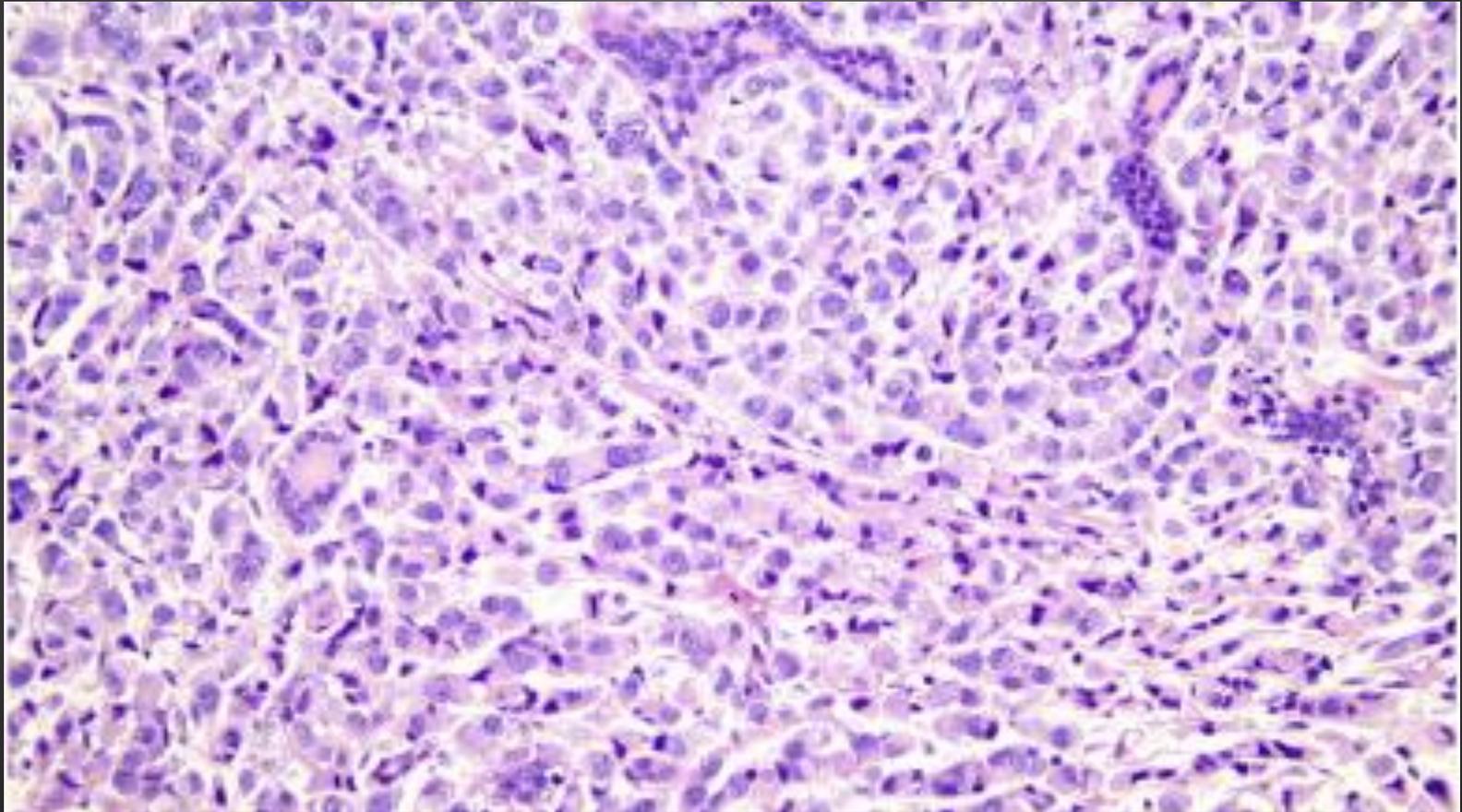
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TIPOS HISTOLÓGICOS



TIPOS HISTOLÓGICOS



CARCINOMA DUCTAL INVASIVO

- Carcinoma invasivo SOE (WHO)
- + Comum 75%
- Proliferação ao longo dos ductos com invasão estromal (coesas)
- Heterogêneos - morfologia e comportamento
- Necrose e calcificações: até 60% casos (MMG)

Tipo
Celular

IH

Secreção

Arquitetura



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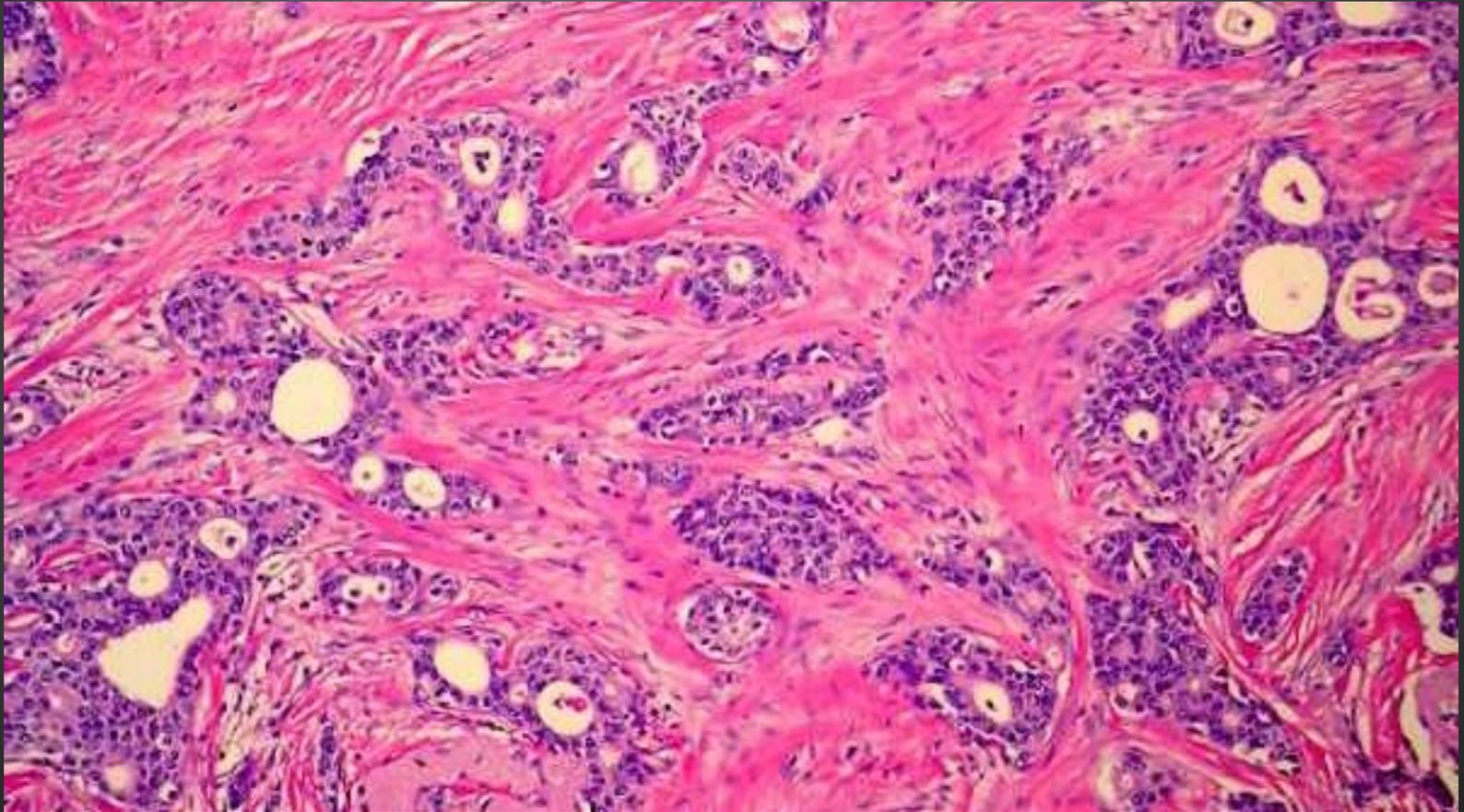
TIPOS HISTOLÓGICOS



TIPOS HISTOLÓGICOS



TIPOS HISTOLÓGICOS





SUBTIPOS ESPECIAIS

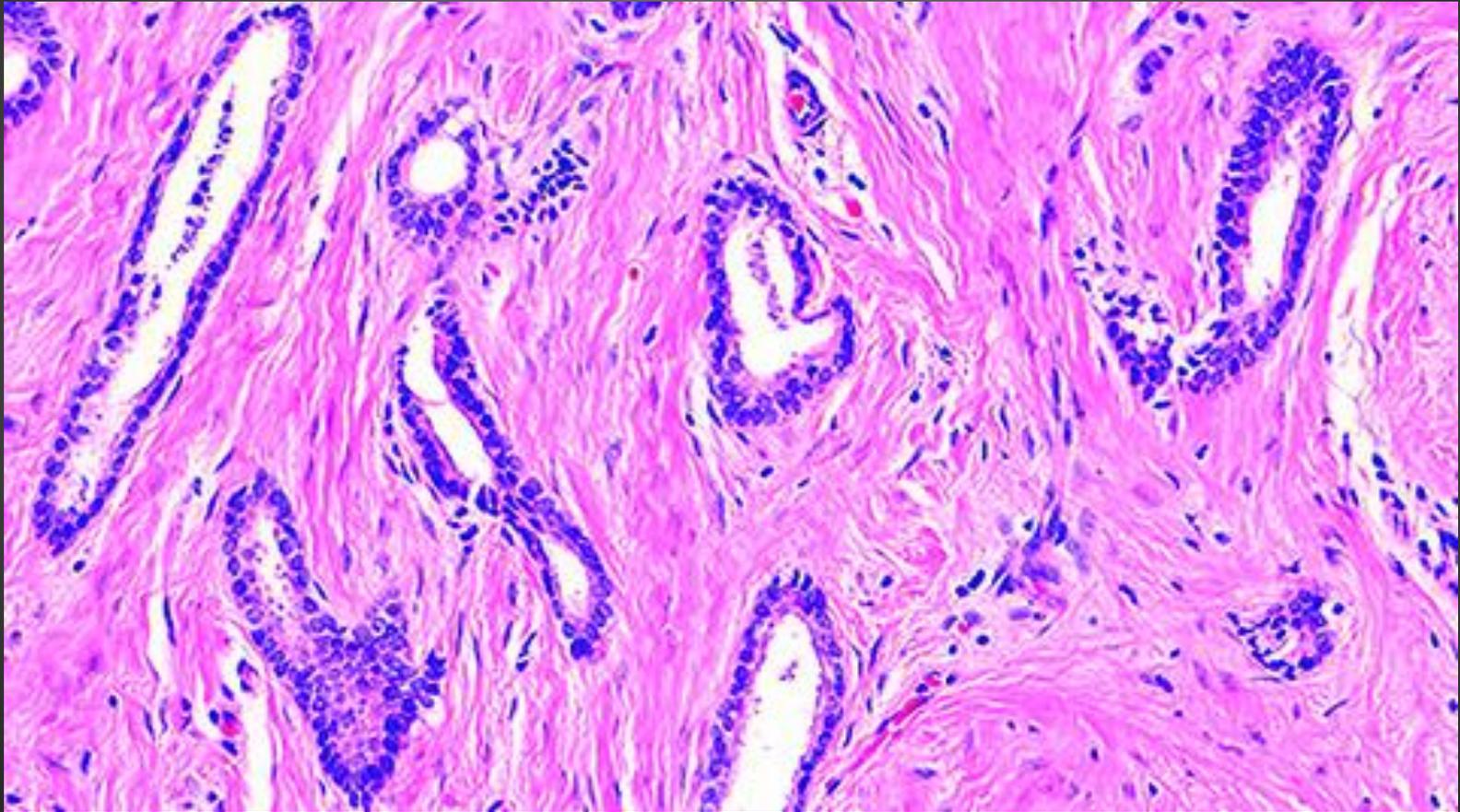


CARCINOMA TUBULAR

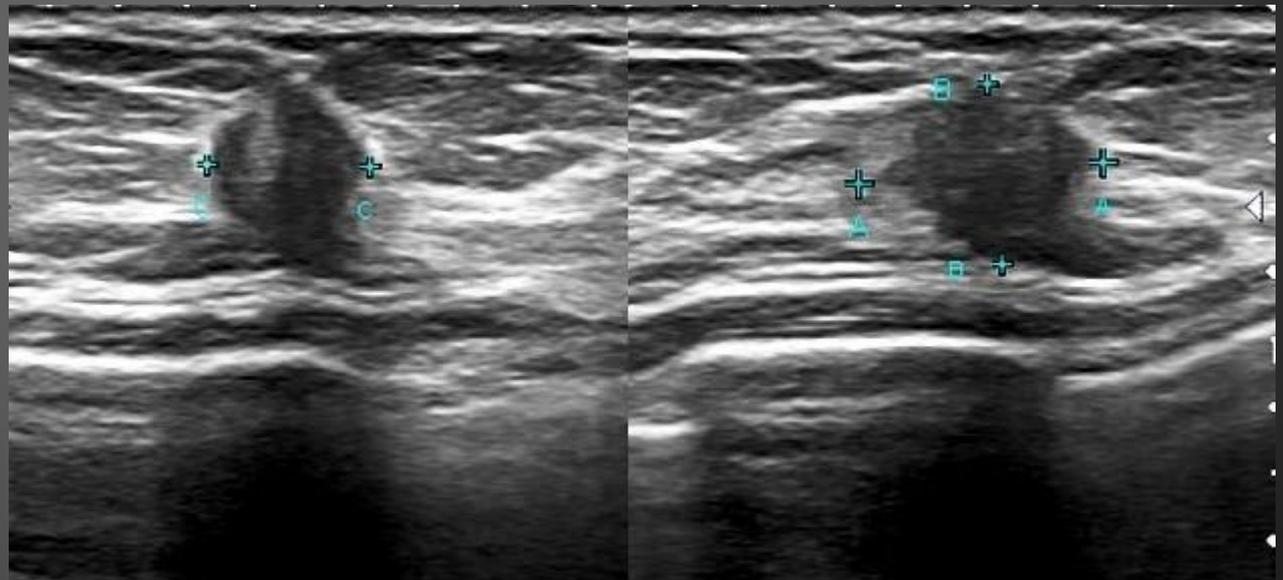
- 2% dos carcinomas mamários
- Bem diferenciado
- Idosas
- Ótimo prognóstico
- Coexiste com lesões precursoras
- Puro x Misto



TIPOS HISTOLÓGICOS



TIPOS HISTOLÓGICOS

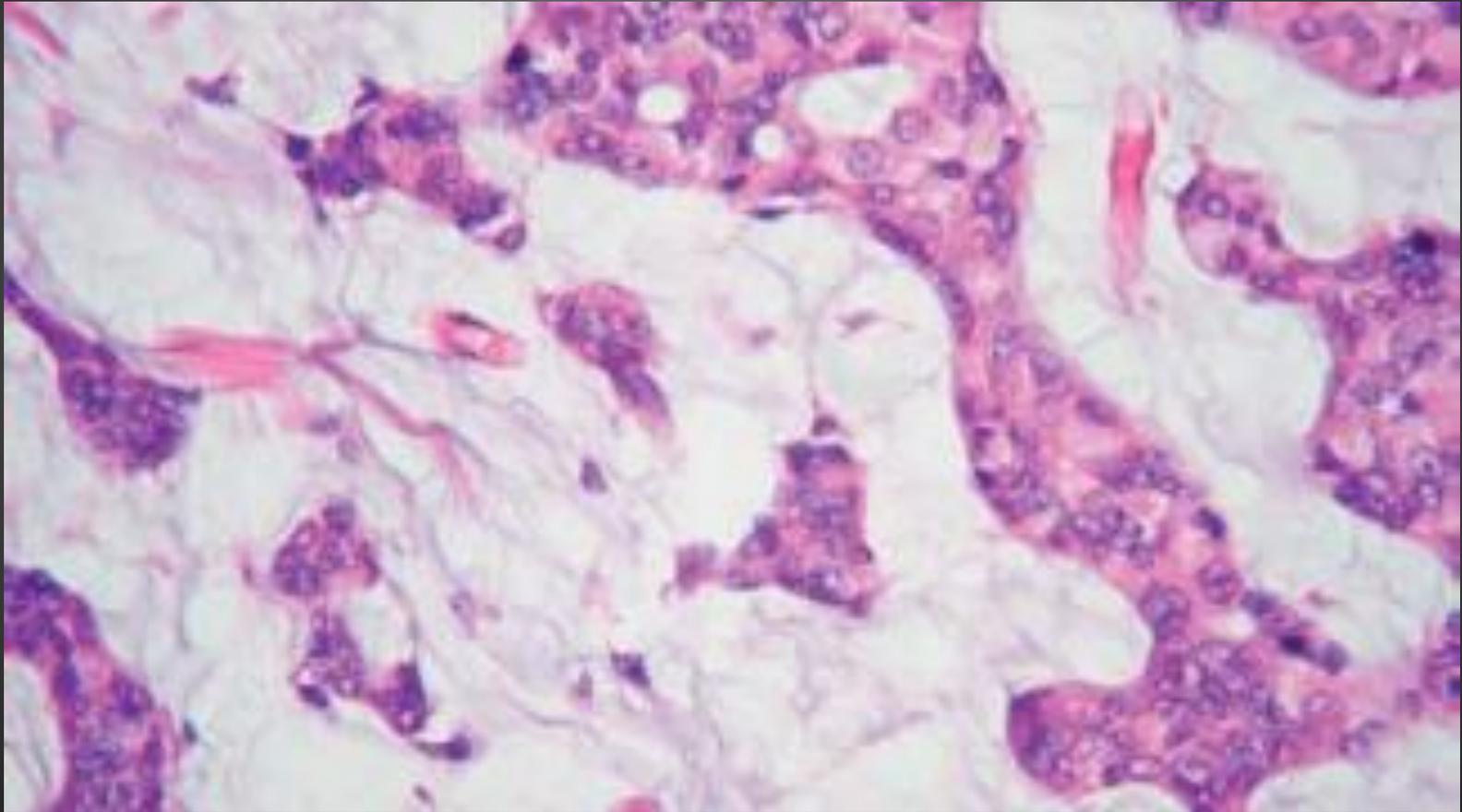


CARCINOMA MUCINOSO

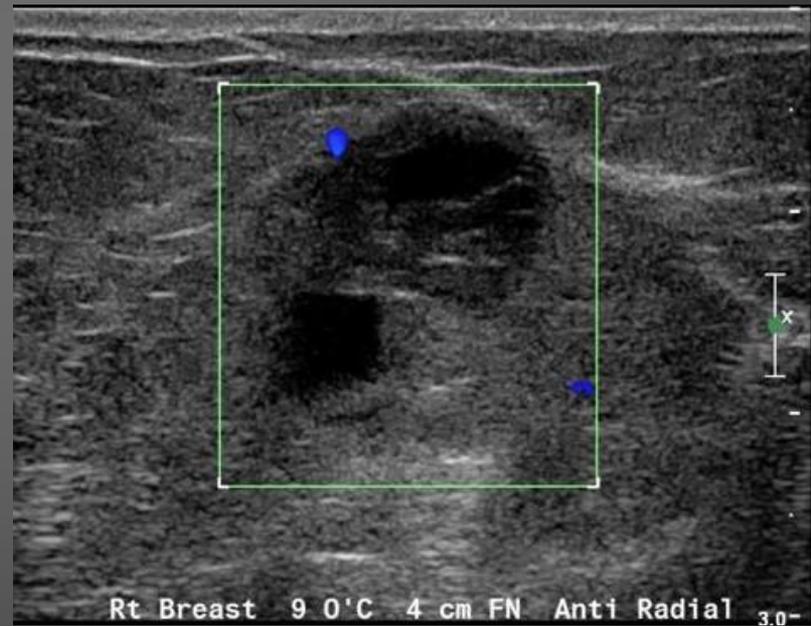
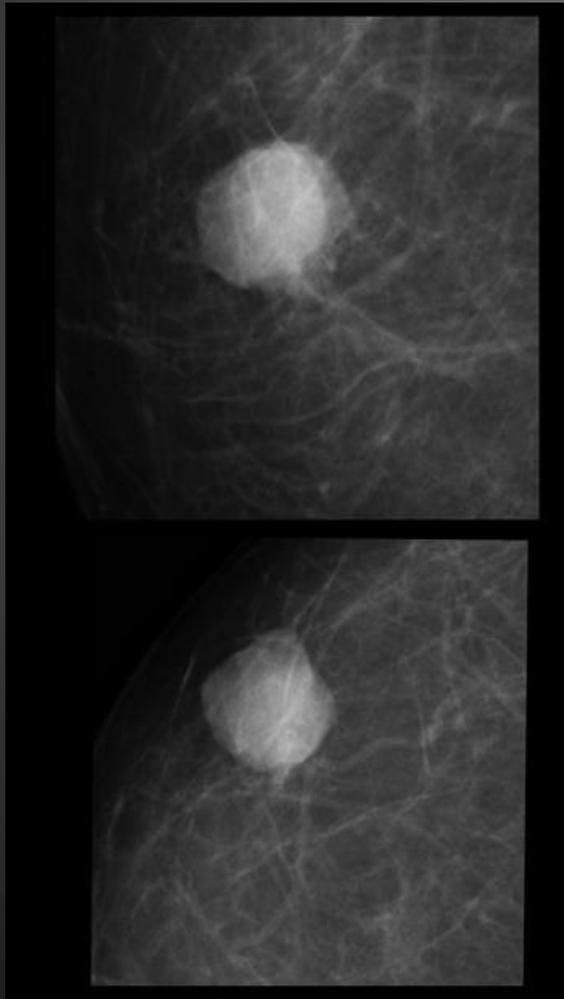
- Raro
- Bem diferenciado
- Idosas
- Ótimo prognóstico
- Infiltração mucinosa (90%) + mucina extracelular (33%)
- Puro x Misto
- Carcinomas em “anel de sinete”



TIPOS HISTOLÓGICOS



TIPOS HISTOLÓGICOS

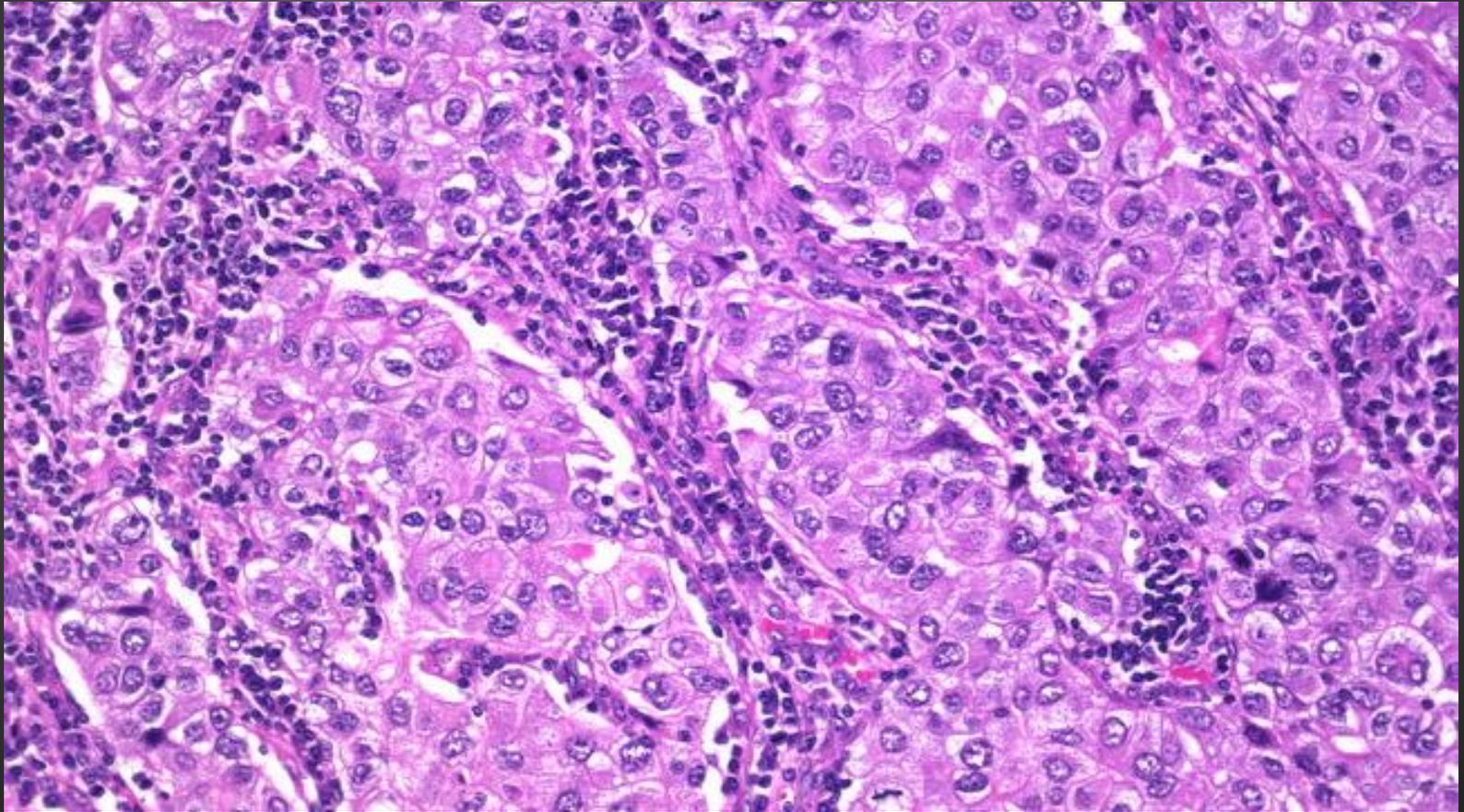


CARCINOMA MEDULAR

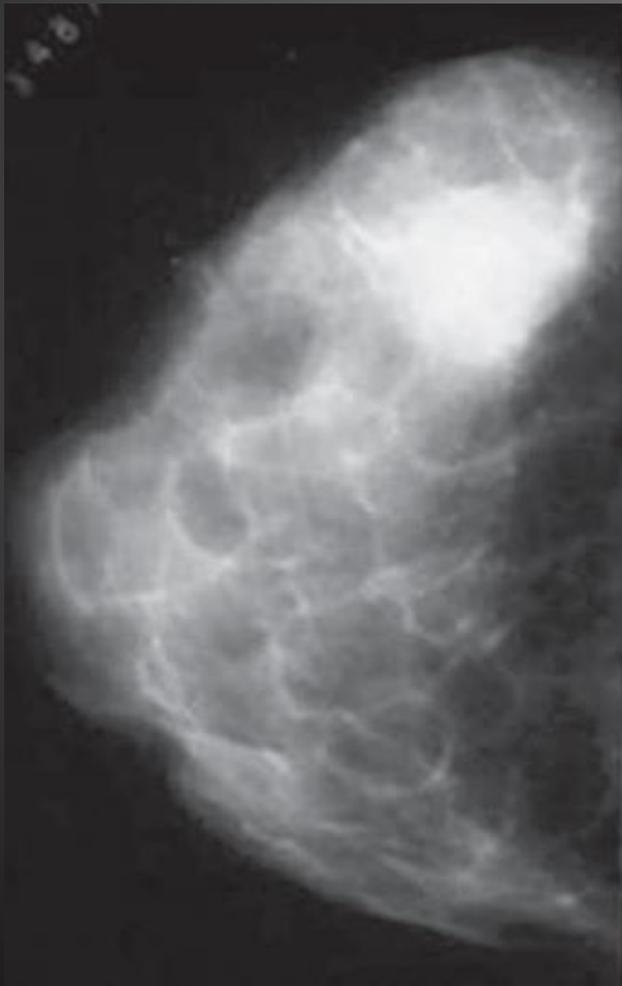
- Raro (0,5%)
- Bem diferenciado
- Morfologia anaplásica, alto grau nuclear e baixa fibrose
- Infiltrado linfocitoplasmático
- Faixa etária mais jovem (26% x 6,6% abaixo 35 anos)
- BRCA 1
- TN
- Prognóstico mais favorável em rel aos não especiais



TIPOS HISTOLÓGICOS



TIPOS HISTOLÓGICOS

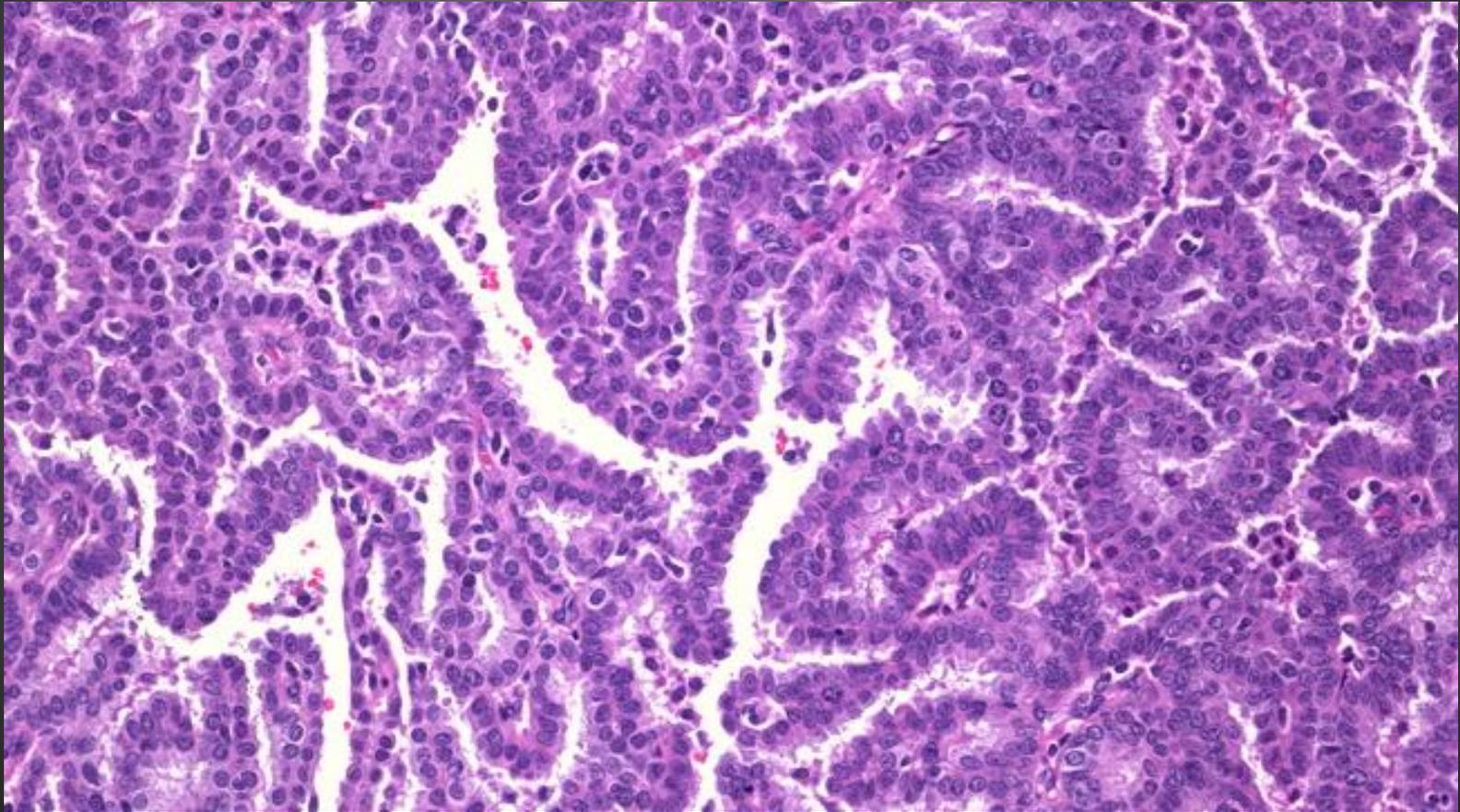


CARCINOMA PAPILÍFERO

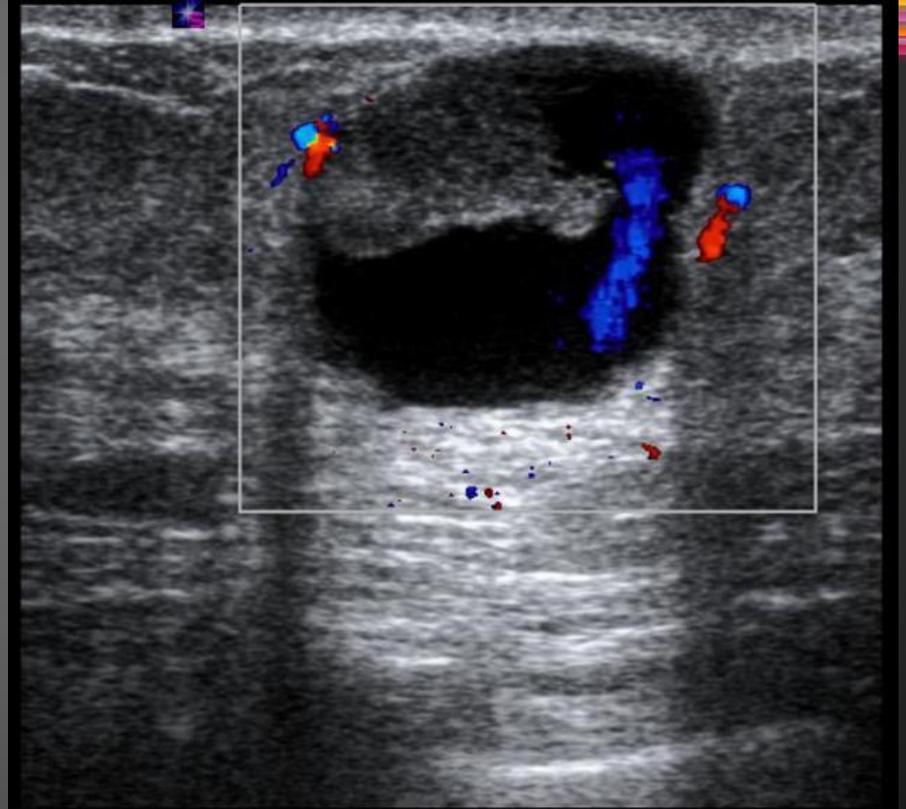
- 1-2%
- Bem diferenciado
- Morfologia papilífera (90%)
- Infiltrado linfocitoplasmático
- Pós-menopausa e brancas
- **Carcinoma invasivo micropapilífero**

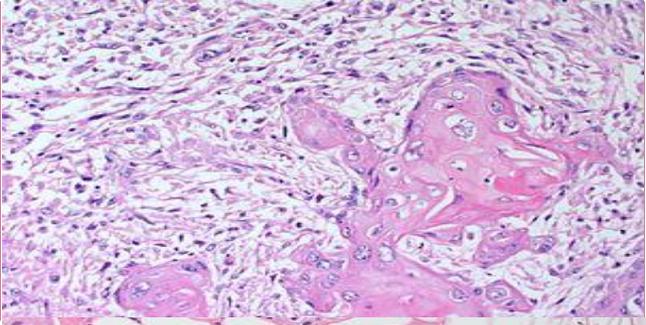
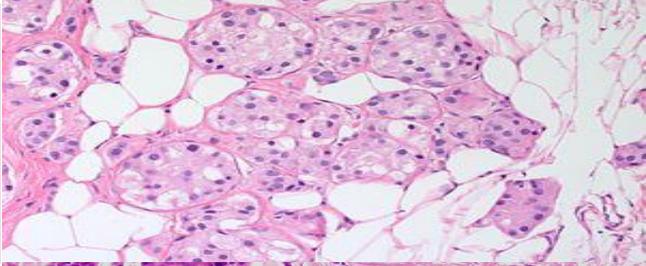
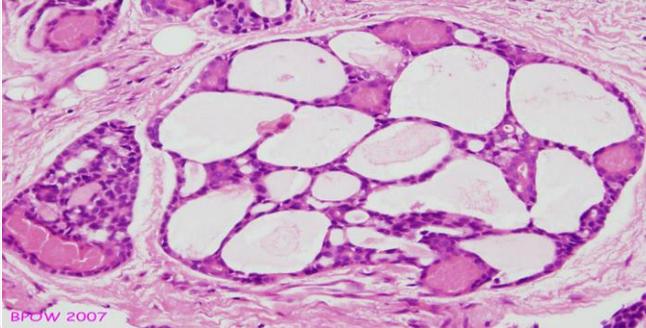
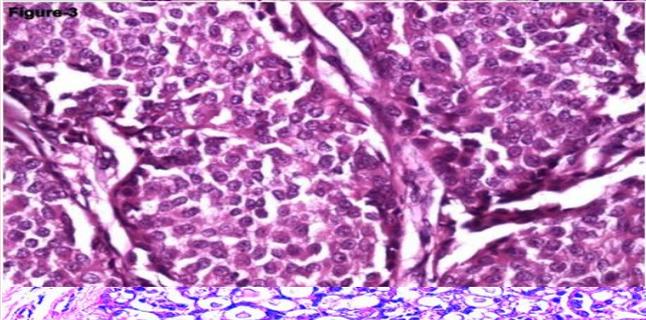
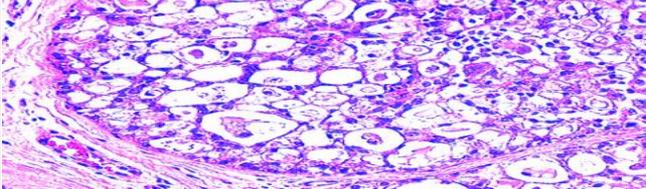


TIPOS HISTOLÓGICOS



TIPOS HISTOLÓGICOS



Carcinoma Metaplásico	<ul style="list-style-type: none"> - Agressivo - Diferenciação (escamosa, fusiforme, mesenquimal) - Pós-menopausa - Diagnóstico microscópico incerto 	
Carcinoma Apócrino	<ul style="list-style-type: none"> - Secreção apócrina - Puros - muito raros - Citoplasma amplo, eosinófilo e granuloso - Comportamento = CINE 	
Carcinoma Adenoide-cístico	<ul style="list-style-type: none"> - 0,1% - Glândula salivar - Células epiteliais, glandulares e escamosas - Ótimo prognóstico - TN 	
Carcinoma Neuroendócrino	<ul style="list-style-type: none"> - Marcadores neuroendócrinos (50%) - Grau diferenciação 	
Carcinoma Secretor	<ul style="list-style-type: none"> - Juvenil - 0,01% - Ótimo prognóstico - TN 	

BPOW 2007

Figure 3

CLASSIFICAÇÃO MOLECULAR



SUBTIPOS MOLECULARES

	Luminal A	Luminal B	Her2 positive	Triple negative (85% basal-like)
Percentage at diagnosis	40%	20%	10-15%	15-20%
Receptor expression	Estrogens and progesterone	Her2		
Treatment strategies	Chemotherapy			
		Her2 targeted therapies		
	Hormonal manipulation			
	Novel targeted therapies			

SUBTIPOS MOLECULARES

SUBÓTIMA



Clinical implications of the intrinsic molecular subtypes of breast cancer

Aleix Prat ^{a, b, c, *}, Estela Pineda ^{a, b}, Barbara Adamo ^{a, b}, Patricia Galván ^{a, c}, Aranzazu Fernández ^{a, b}, Lydia Gaba ^{a, b}, Marc Díez ^{a, b}, Margarita Viladot ^{a, b}, Ana Arance ^{a, b}, Montserrat Muñoz ^{a, b}

The Breast 24 (2015) S26–S35

Table 1

Distribution of the PAM50 intrinsic subtypes within the pathology-based groups.^a

IHC-based group	References	N	PAM50 intrinsic subtype distribution			
			Luminal A	Luminal B	HER2-enriched	Basal-like
HR+/HER2–	[10,14,16–22]	4295	60.3%	31.9%	6.6%	1.2%
Luminal A	[10,14,17,21]	637	62.2%	27.0%	10.2%	0.6%
Luminal B	[10,14,17,21]	317	34.1%	51.1%	11.0%	3.8%
HER2+	[6,23–26]	831	17.6%	26.8%	44.6%	11.0%
HER2+/HR+	[25,26]	182	33.0%	46.2%	18.7%	2.2%
HER2+/HR–	[25,26]	168	19.0%	4.2%	66.1%	10.7%
TNBC	[12–15]	868	1.6%	3.2%	9.1%	86.1%

^a The data has been obtained from the different publications. Several studies have performed a standardized version of the PAM50 assay (RT-qPCR-based or nCounter-based) from formalin-fixed paraffin-embedded tumour tissues [10,14,17,19–22], while others have performed the microarray-based version of the PAM50 assay [6,16,18,23–26].



SUBTIPOS MOLECULARES

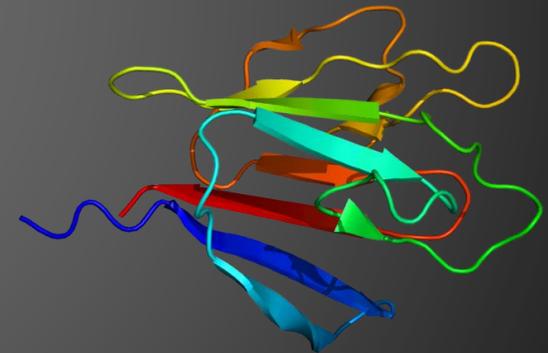
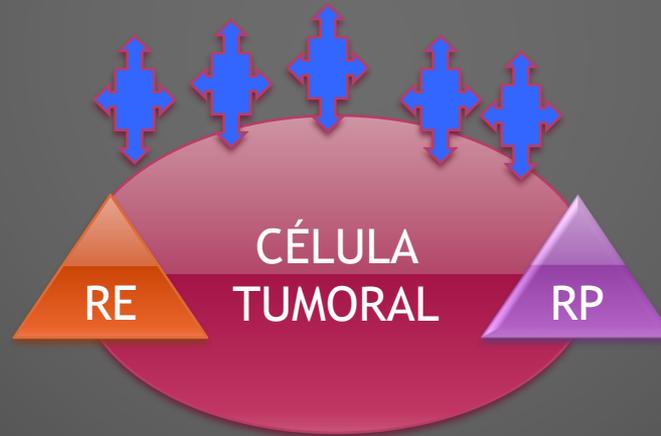
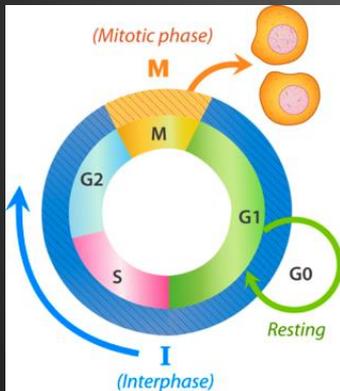
- Biomarcadores tradicionais

Produtos protéicos de genes medidos e avaliados como indicadores de processos biológicos normais, patogênicos ou respostas farmacológicas a uma intervenção terapêutica



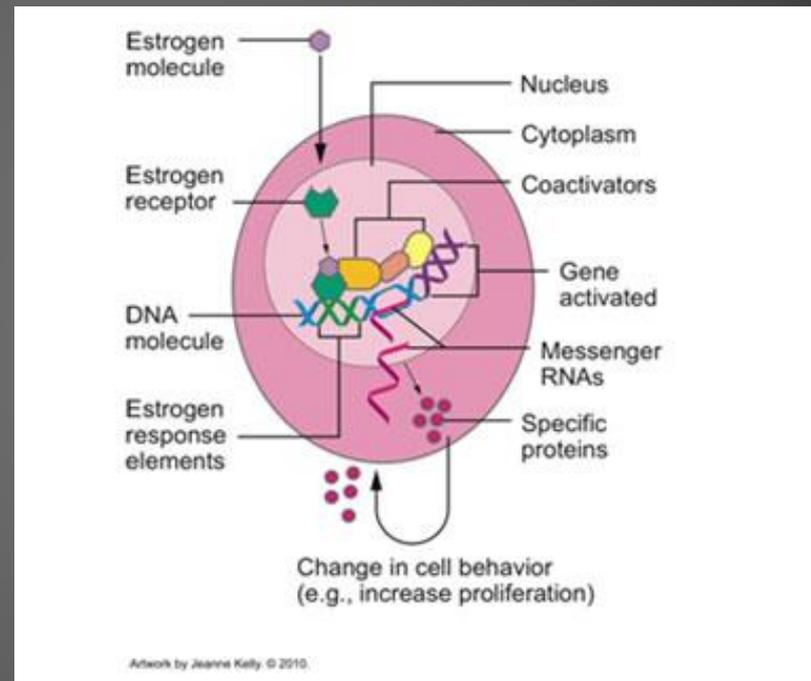
SUBTIPOS MOLECULARES

- Biomarcadores tradicionais
- RE, RP, HER 2 **Ki67**



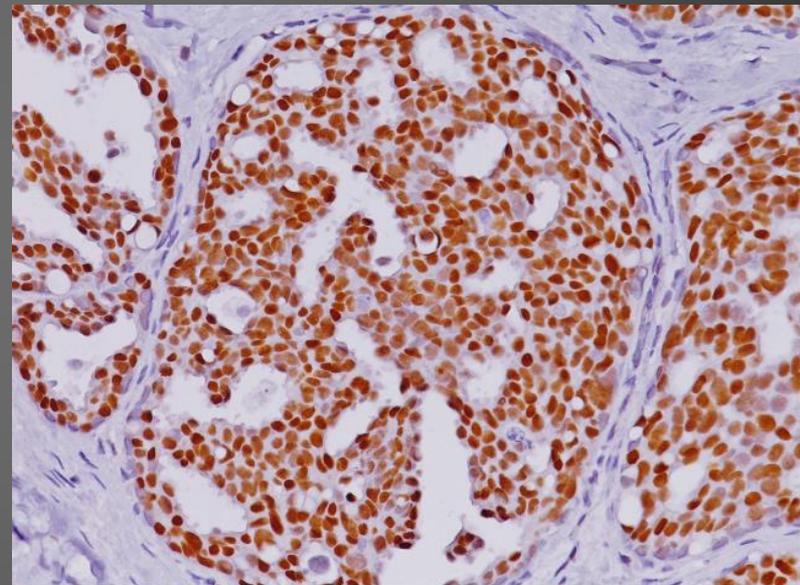
SUBTIPOS MOLECULARES

- RE, RP
- 1950 (bioq)
- Impacto prognóstico e preditivo
- RE alfa e beta (fatores antogônicos)



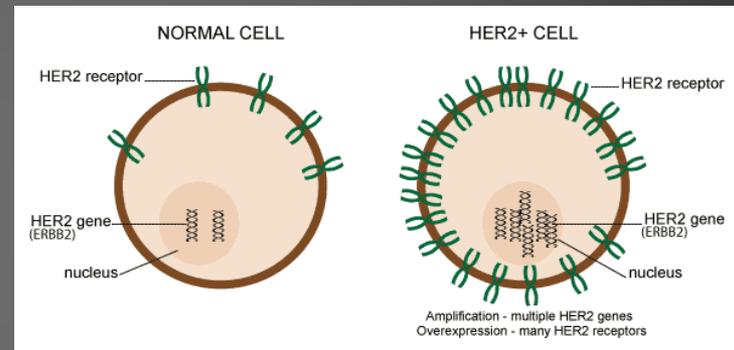
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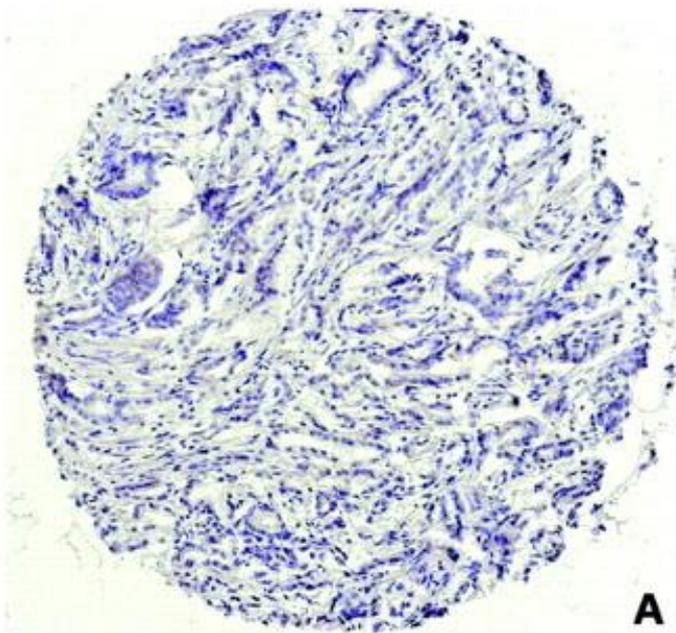
- RE, RP
- RE+ RP- aberrância
- RE- RP+ incerto
- Graduação Allred



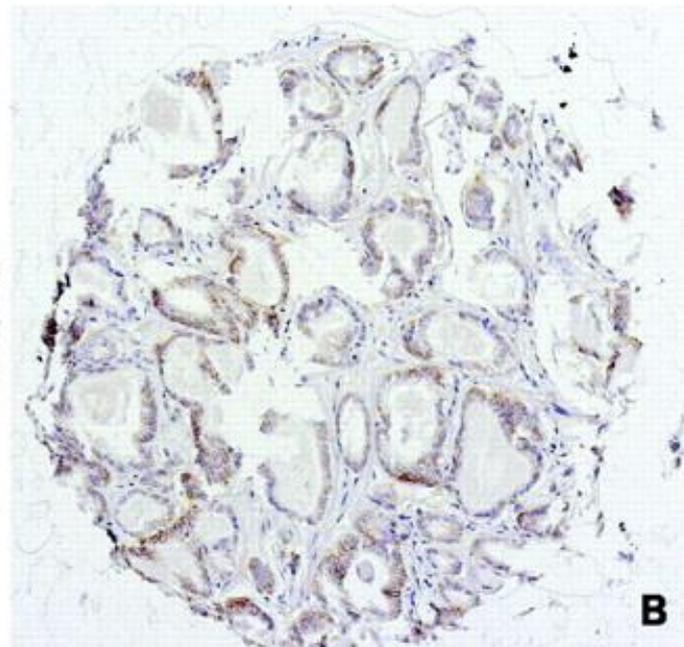
SUBTIPOS MOLECULARES

- HER 2 (gene e proteína)
- Preditivo e prognóstico
- Antracíclicos/Trastuzumab
- 13-20% CA de Mama
- 1/2 casos RH+

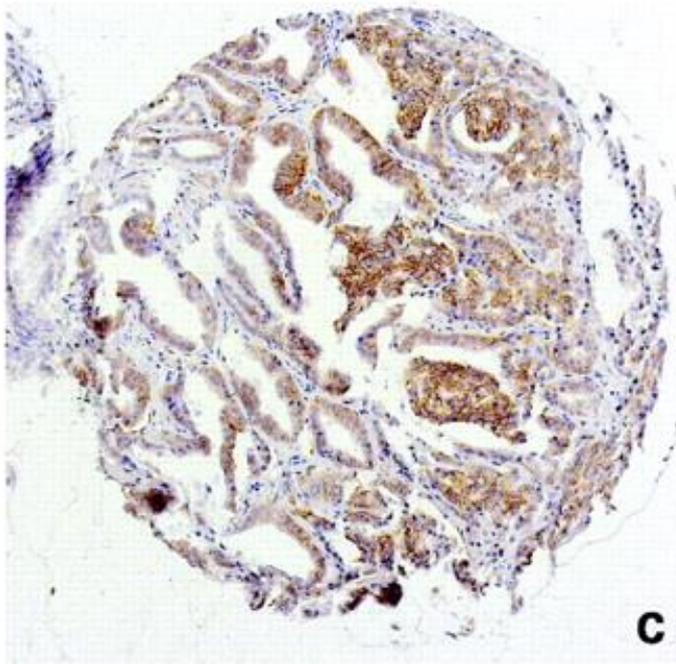




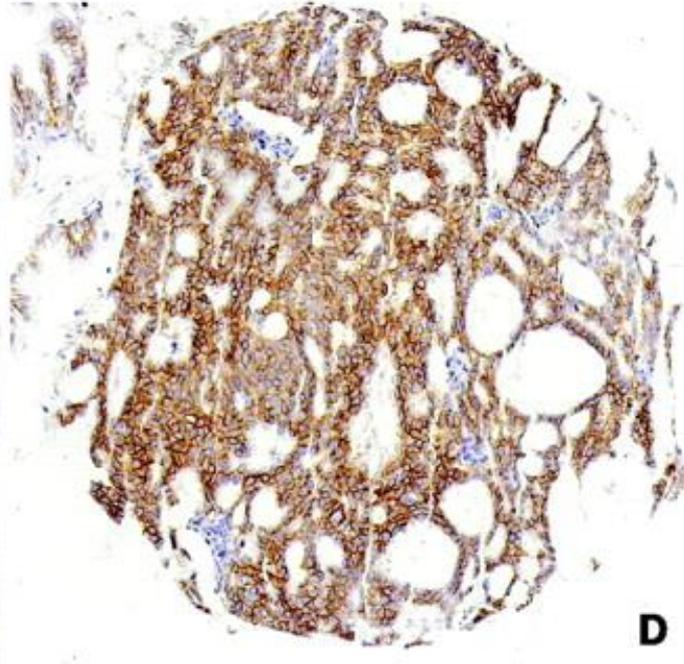
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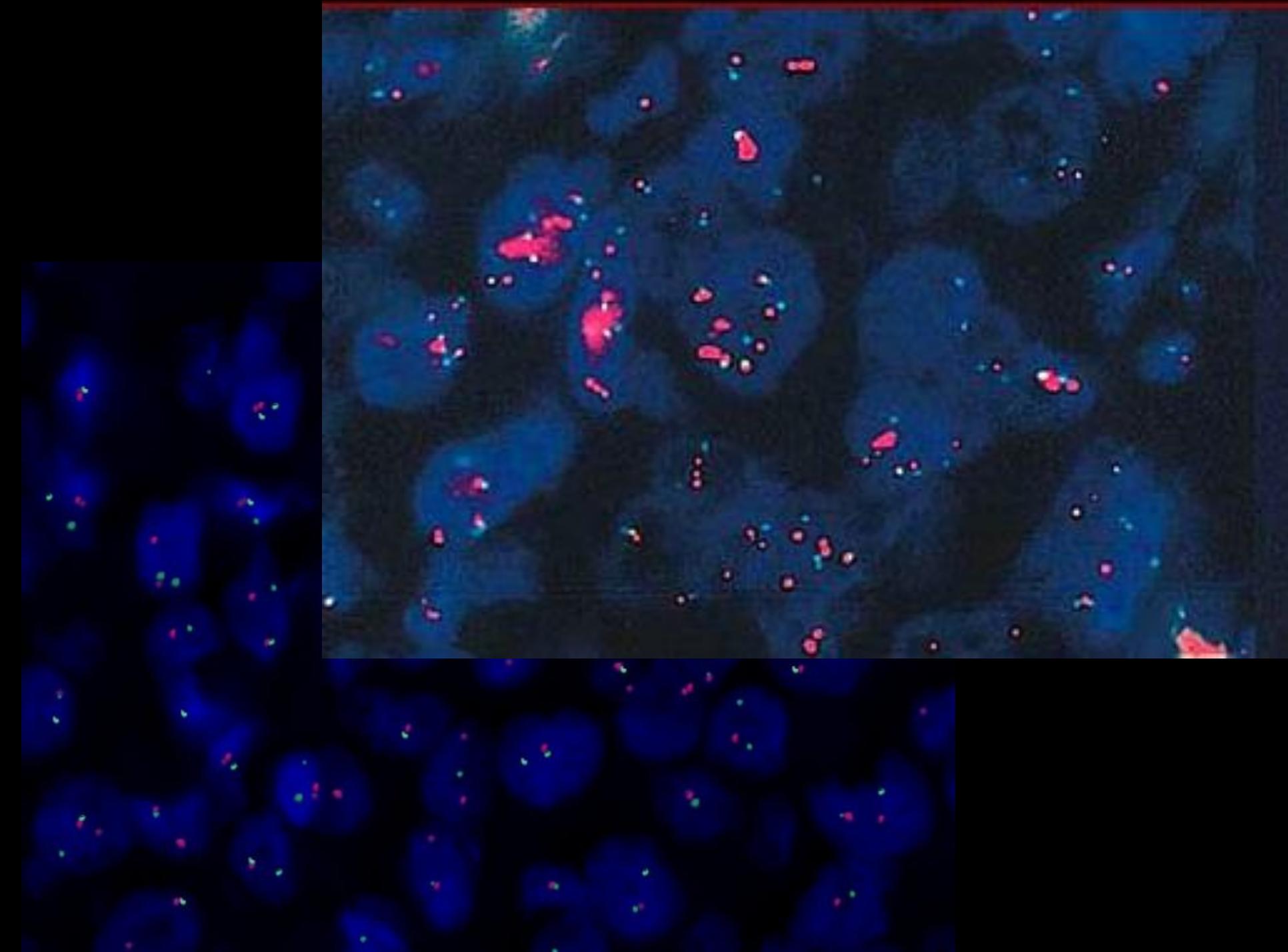
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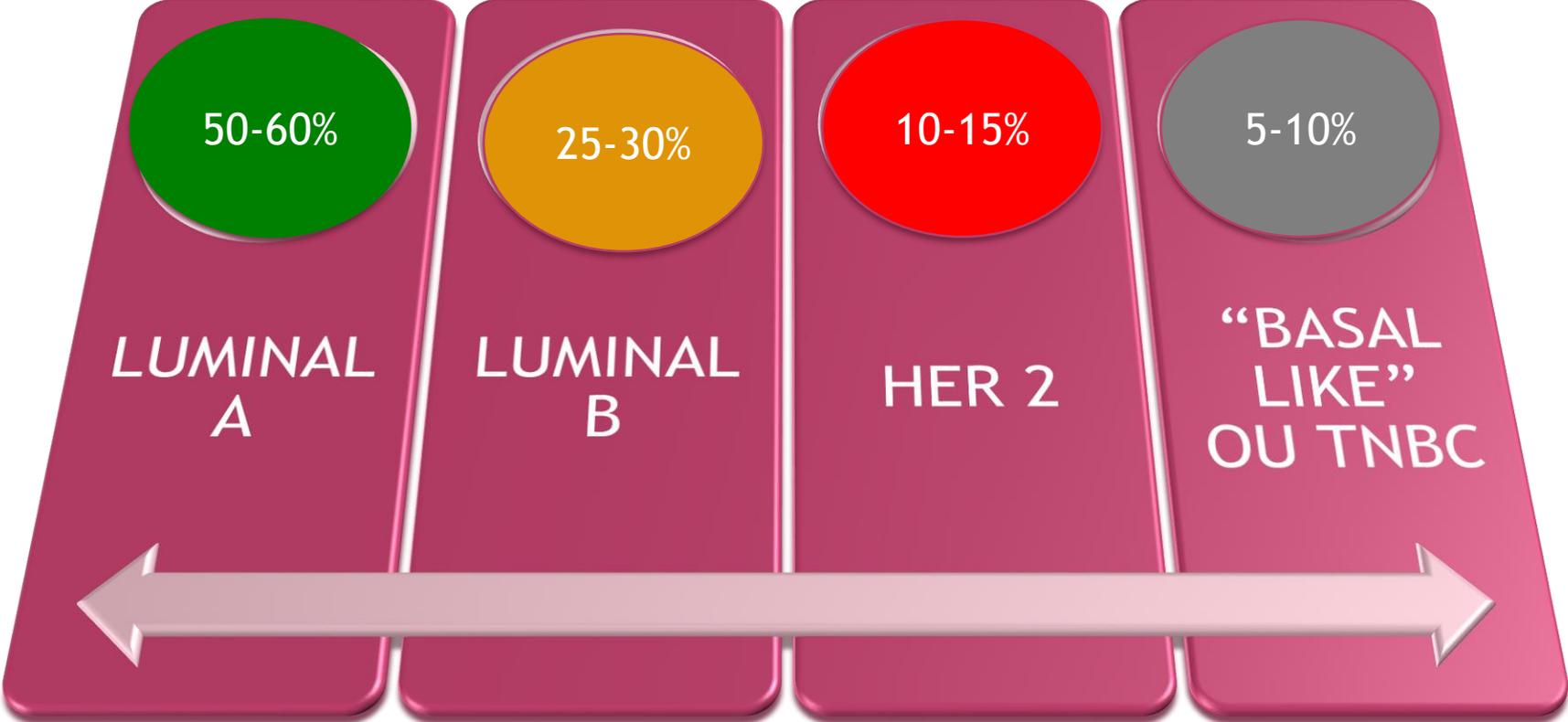


C



D





Molecular classification of breast cancer

Darina Vuong · Peter T. Simpson · Benjamin Green ·
 Margaret C. Cummings · Sunil R. Lakhani

Virchows Arch (2014) 465:1–14

7

Table 1 Molecular subtypes of breast cancer

Intrinsic subtypes by gene expression profiling	Histological types	Histological grade	ER status by IHC	HER2 status by IHC/ISH	Ki67 by IHC	Key molecular features [62]	Predominant integratal cluster association [65]
Luminal A	IC-NST, classic lobular, tubular, cribriform, mucinous, neuroendocrine	1–2	ER+	HER2–	Low	<i>PIK3CA</i> mutations, <i>MAP3K1</i> mutations, <i>ESR1</i> high expression, <i>XBP1</i> high expression, <i>GATA3</i> mutations, <i>FOXA1</i> mutations, quiet genomes; gain of 1q, 8q, loss of 8p, 16q	Int cluster 2, Int cluster 3, Int cluster 4, Int cluster 7, Int cluster 8
Luminal B	IC-NST, micropapillary	2–3	ER+/-	HER2 +/-	High	<i>TP53</i> mutations, <i>PIK3CA</i> mutations, <i>Cyclin D1</i> amplification, <i>MDM2</i> amplification, <i>ATM</i> loss, enhanced genomic instability, focal amplifications (e.g. 8p12, 11q13)	Int cluster 1, Int cluster 2, Int cluster 6, Int cluster 9
HER2	IC-NST, apocrine, pleomorphic lobular	2–3	ER+/-	HER2+	High	<i>HER2</i> amplification, <i>TP53</i> mutations, <i>PIK3CA</i> mutations, <i>FGFR4</i> high expression, <i>EGFR</i> high expression, APOBEC mutations, <i>Cyclin D1</i> amplification, high genomic instability	Int cluster 5
Basal-like	IC-NST, medullary, metaplastic, adenoid cystic, secretory	3	ER–	HER2–	High	<i>TP53</i> mutations, <i>RB1</i> loss, <i>BRCAl</i> loss, high expression of DNA repair proteins, <i>FOXM1</i> activation, high genomic instability, focal amplifications (e.g., 8q24)	Int cluster 4, Int cluster 10

+ positive, – negative, +/- mostly positive, -/+ mostly negative, *ER* oestrogen receptor, *HER2* human epidermal growth factor receptor 2, *IC-NST* invasive carcinoma no special type, *IHC* immunohistochemistry, *ISH* in situ hybridisation

SUBTIPOS MOLECULARES IMPLICAÇÕES PROGNÓSTICAS

LUMINAL A/B

- Maior SLD
- Menor RPC à QT neo (não é fator preditivo)
- Menor/Sem impacto SG com QT
- Agentes específicos - Paclitaxel semanal
- Melhor resp HT (5 x 10 anos)
- Luminal B SLD em 5 x 10 anos
- “T” e “N” devem ser usados em conjunto



SUBTIPOS MOLECULARES IMPLICAÇÕES PROGNÓSTICAS

HER 2+

- RH- taxa de RPC 18 para 48%
- Trastuzumab melhor RH- do que RH+
- Her 2+ e DUPLO BLOQUEIO



SUBTIPOS MOLECULARES IMPLICAÇÕES PROGNÓSTICAS

“BASAL LIKE”

- Tendência a piores resultados
- PoliQT
- Assinatura “proliferação” e “luminal” (RPC)
- Antraciclinas e taxanos neoadjuvantes
- Manutenção da capecitabina



Obrigado

