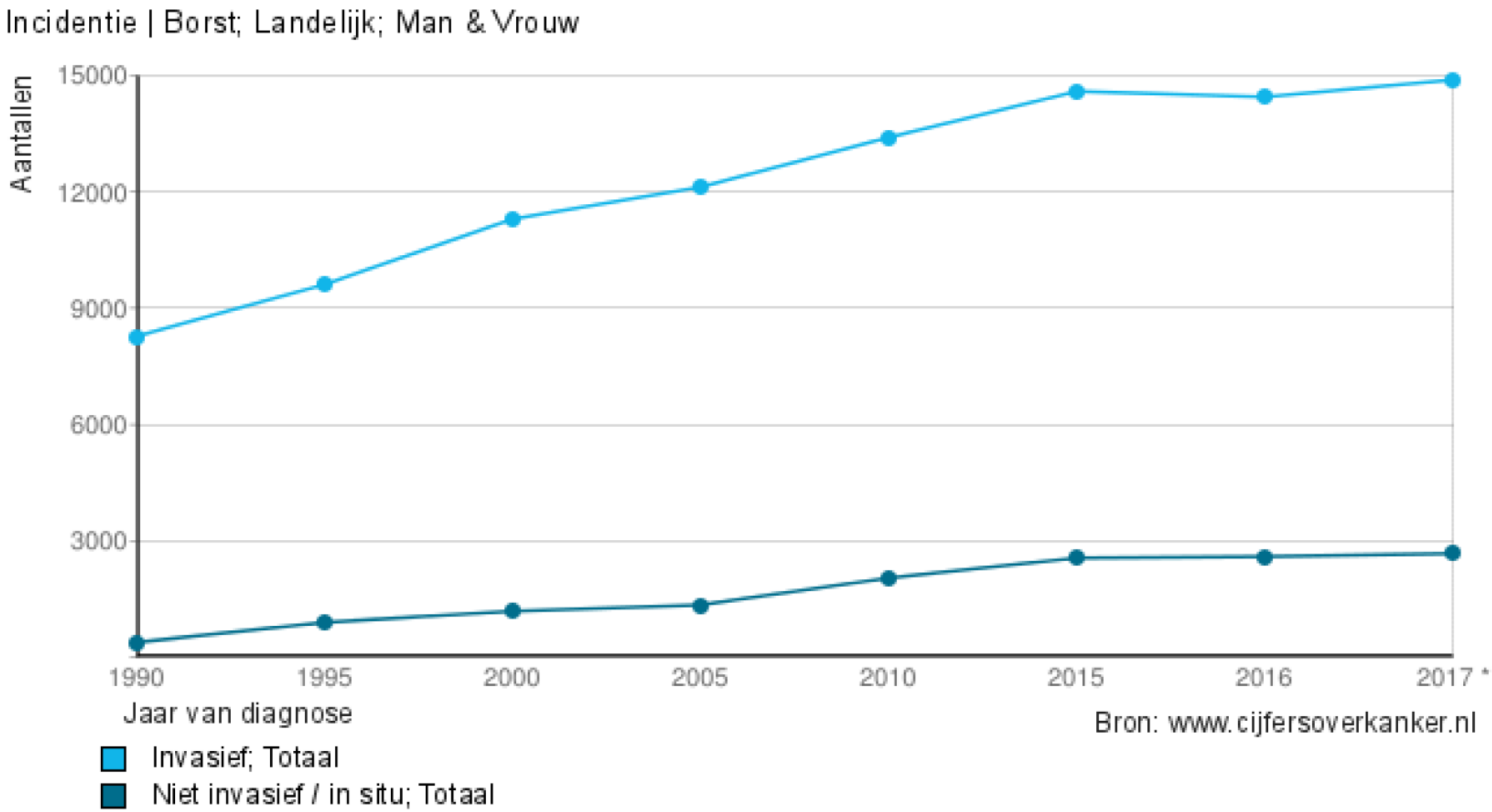
Premaligne laesies DCIS gradering & variaties

21 maart 2018

Celien Vreuls

Disclosure belangen spreker

Geen (potentiële) belangenverstrengeling

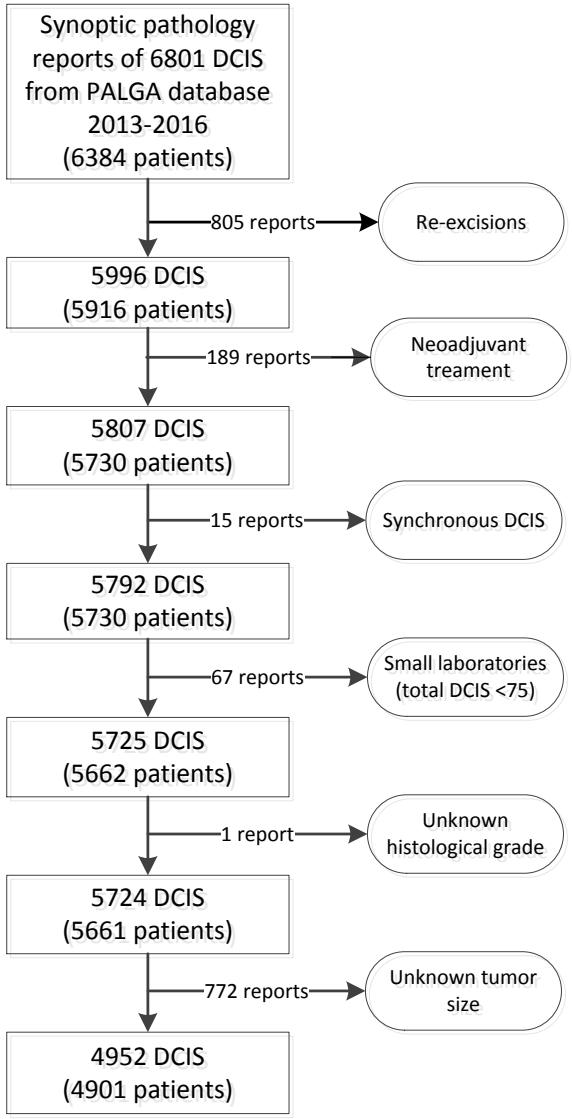

Incidentie | Borst; Landelijk; Man & Vrouw
Aantallen
15000
12000
9000
6000
3000
1990
1995
2000
2005
2010
2015
2016
2017 *
Jaar van diagnose
Bron: www.cijfersoverkanker.nl
Invasief; Totaal
Niet invasief / in situ; Totaal

Inhoud presentatie

Gradering

- Hoe doen we het nu?
- Lopende trails DCIS met betrekking behandeling
- Overzicht bekende graderingssystemen
- Gradering DCIS, in de praktijk
  - ADH/DCIS graad 1
  - DCIS graad 2
  - DCIS graad 3

  Variaties
- Speciale types DCIS



- 36 pathologie laboratoria (totaal is 46)
- Geïncludeerde DCIS
  variërend tussen de 22-324
  (median 106)

TABLE 1. Characteristics of the 4952 included ductal carcinoma in situ (DCIS)

	Total (n=4592)	Grade 1 (n=618)	Grade 2 (n=1956)	Grade 3 (n=2378)	p-value
Age (y)*	59.5 (10.1)	58.5 (10.2)	59.9 (10.1)	59.3 (10.1)	0.001
Sex, n(%)					
Female	4944 (99.8%)	616 (99.7%)	1950 (99.7%)	2378 (100.0%)	**
Male	8 (0.2%)	2 (0.3%)	6 (0.3%)	0 (0.0%)	
Tumor size (cm)*	2.4 (2.2)	1.6 (1.8)	2.1 (2.0)	2.9 (2.3)	0.000
Type of surgery, n(%)					
Mastectomy	1636 (33.0%)	130 (21.0%)	538 (27.5%)	968 (40.7%)	0.000
Breast conserving	3316 (67.0%)	488 (79.0%)	1418 (72.5%)	1410 (59.3%)	

* Mean (SD)

** Number of males too low for statistical testing

Vragenlijst DCIS

TABLE 2. Results of 78 pathologists responding to our questionnaire on histologic grading of DCIS

	n (%)		
	Total (n=79)	Breast pathologist (n=37)	General pathologist (n=42)
Laboratory			
Academic	15 (19.0%)	11 (29.7%)	4 (9.5%)
Peripheral	64 (81.0%)	26 (70.3%)	38 (90.5%)
Years of experience			
0-5	28 (35.4%)	11 (29.7%)	17 (40.5%)
6-10	15 (19.0%)	6 (16.2%)	9 (21.4%)
11-20	17 (21.5%)	9 (24.3%)	8 (19.0%)
>20	19 (24.1%)	11 (29.7%)	8 (19.0%)
Based on which guideline or reference do you grade DCIS?*			
Holland et al (1994) (22)	28 (35.4%)	14 (37.8%)	14 (33.3%)
Pinder et al (2010) (42)	16 (20.3%)	9 (24.3%)	7 (16.7%)
Intuition	16 (20.3%)	8 (21.6%)	8 (19.0%)
WHO (43)	11 (13.9%)	5 (13.5%)	6 (14.3%)
I don't know	4 (5.1%)	0 (0.0%)	4 (9.5%)
Tavassoli et al (Pathology of the Breast, 1992) (44)	3 (3.8%)	1 (2.7%)	2 (4.8%)
Van Nuys (Silverstein et al, 1995) (45)	2 (2.5%)	1 (2.7%)	1 (2.4%)
College of American Pathologists Guidelines (46)	1 (1.3%)	0 (0.0%)	1 (2.4%)
Combination (n.o.s.)	1 (1.3%)	1 (2.7%)	0 (0.0%)
How do you grade a DCIS of heterogeneous differentiation?			
Based on the highest grade	60 (76.0%)	28 (75.7%)	32 (76.2%)
I report the percentages of each grade	9 (11.4%)	4 (10.8%)	5 (11.9%)
Based on the predominant grade	7 (8.9%)	4 (10.8%)	3 (7.1%)
Not within the protocol	3 (3.8%)	1 (2.7%)	2 (4.8%)

* Multiple answers possible (n=82)
n.o.s. indicates not otherwise specified

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Lopende trails - LORD

- LORD trail

graad 1

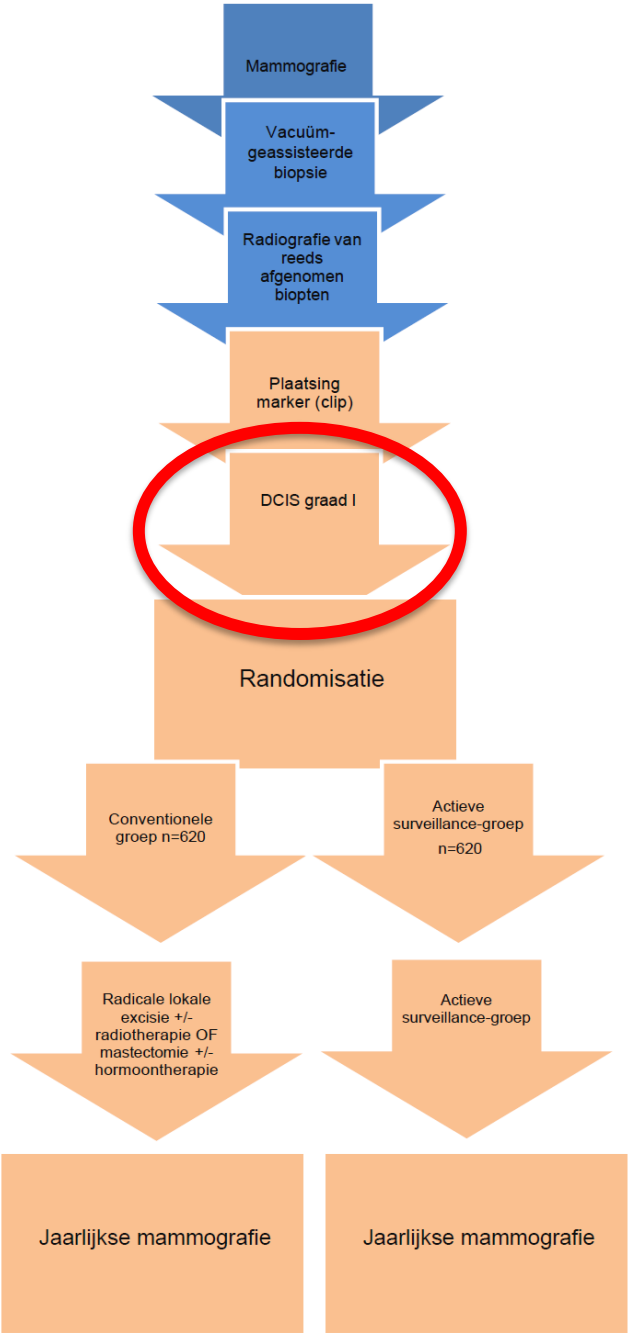
Voorkom overbehandeling van laag-gradig DCIS: doe de LORD-studie!

Prevent overtreatment of low grade DCIS: do the LORD-trial!

drs. S. Alaeikhanehshir[1], drs. L.E. Elshof[1,4], dr. K. Tryfonidis[2], C. Poncet[2], K. Aalders[2], dr. E. van Leeuwen-Stok[3], prof. dr. R.M. Pijnappel[4,5], dr. N. Bijker[6], prof. dr. E.J.T.H. Rutgers[1], mr. dr. F. van Duijnhoven[1] en dr. J. Wesseling[1]

SAMENVATTING

Sinds 1989 in Nederland het bevolkingsonderzoek naar borstkanker is geïntroduceerd, is de incidentie vrouwen met DCIS worden behandeld, is het niet goed mogelijk om uitspraken te doen over het daad-werkelijke risico dat een bepaalde DCIS-afwijking



Lopende trails - overige

- LORD = graad 1
- LORIS = graad 1 en (gedeeltelijk) graad 2
- COMET = graad 1 en 2 (alleen hormoonreceptor positieve patiënten)
- LARRIKIN = graad 1 en 2

Overzicht bekende DCIS graderingssystemen

‘There is currently no universal agreement on classification system for DCIS.’

WHO 4the edition

- Holland
- WHO
- Pinder

Gradering- volgens Holland

Ductal Carcinoma In Situ: A Proposal for a New Classification

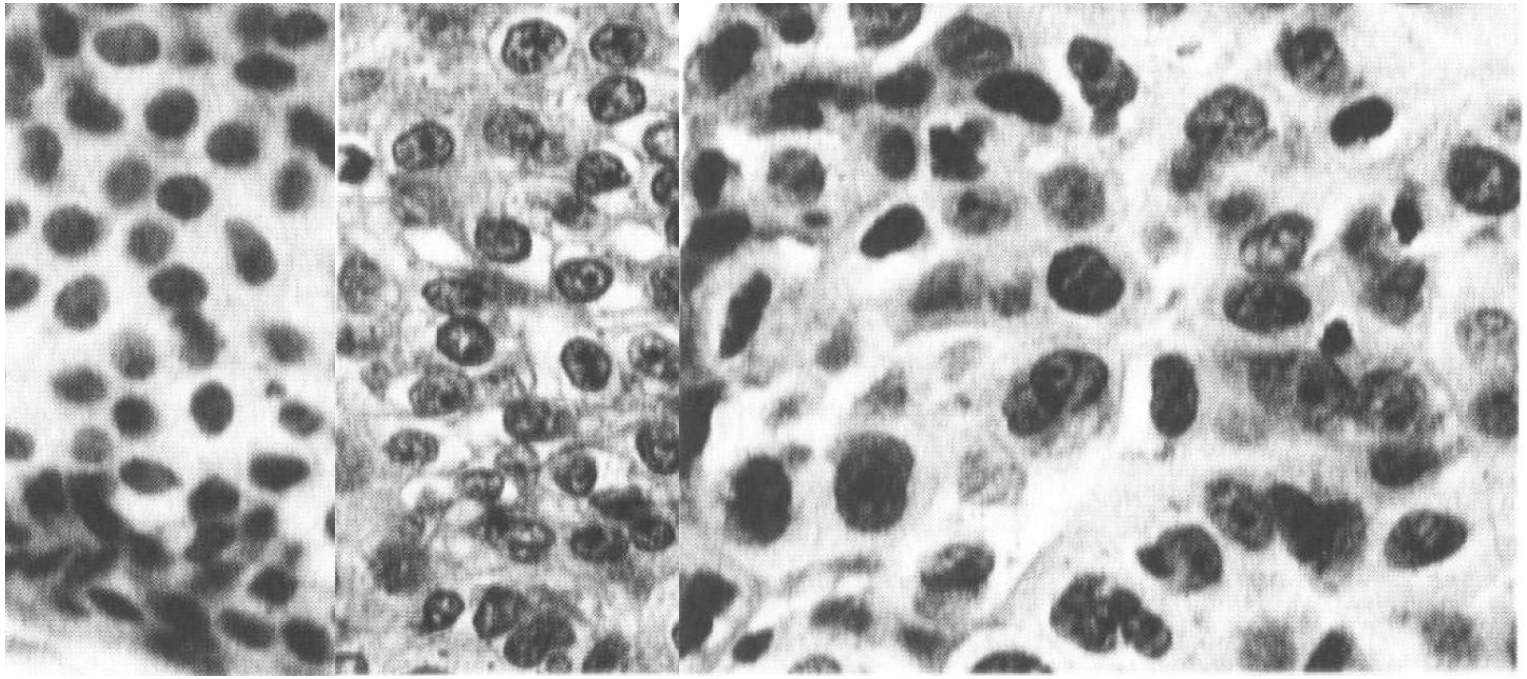
Roland Holland, MD, PHD,* Johannes L. Peterse, MD,† Rosemary R. Millis, MB, BS, FRCPath,‡
Vincenzo Eusebi, MD, FRCPath,§ Daniel Faverly, MD,* Marc J. van de Vijver, MD, PhD,‖
and Brigitte Zafrani, MD¶

● Details of a proposed new classification for ductal carcinoma in situ (DCIS) are presented. This is based, primarily, on cytonuclear differentiation and, secondarily, on architectural differentiation (cellular polarisation). Three categories are defined. First is poorly differentiated DCIS composed of cells with very pleomorphic, irregularly spaced nuclei, with coarse, clumped chromatin, prominent nucleoli, and frequent mitoses. Architectural differentiation is absent or minimal. The growth pattern is solid or pseudo-cribriform and -micropapillary (without cellular polarisation). Necrosis is usually present. Calcification, when present, is amorphous. Second, at the other end of the spectrum is well-differentiated DCIS, composed of cells with monomorphic, regularly spaced nuclei containing fine chromatin, inconspicuous nucleoli, and few mitoses. The cells show pronounced polarisation with orientation of their apical border towards intercellular spaces usually resulting in cribriform, micropapillary and clinging patterns, although a solid pattern of well-differentiated DCIS also occurs. Necrosis is uncommon. Calcifications, when present, are usually psammomatous. The third category, intermediately differentiated DCIS, is composed of cells showing some pleomorphism but not so marked as in the poorly differentiated group. There is, however, always evidence of polarization around intercellular spaces, although this is not so pronounced as in the well-differentiated group. These two criteria, cytonuclear differentiation and architectural differentiation, have been found to be more consistent throughout a DCIS lesion than previously employed criteria of architectural pattern or the presence or absence of necrosis.

Seminars in Diagnostic Pathology, VOL 11, NO 3 (AUGUST) 1994: pp 167-180

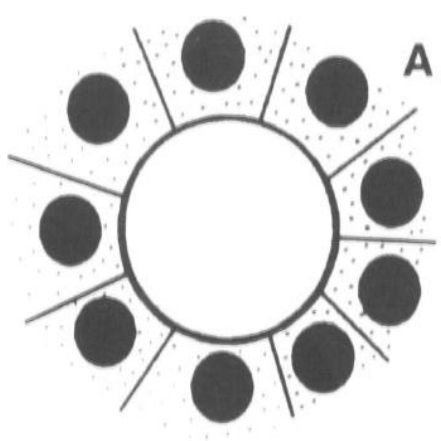
Gradering- volgens Holland

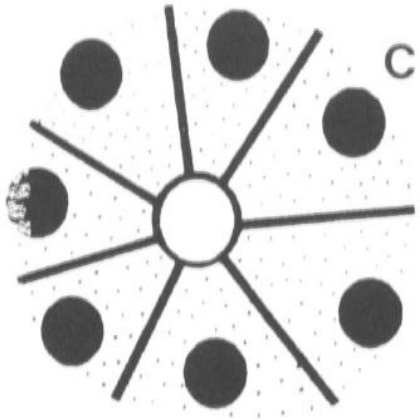
Cytonucleaire differentiatie

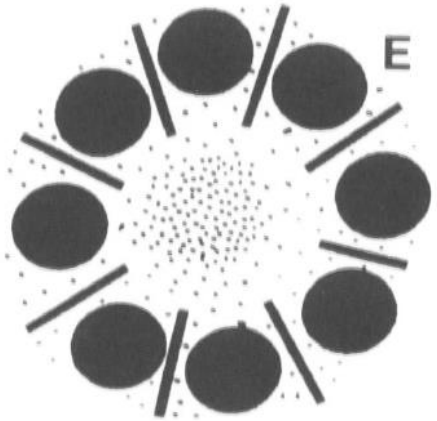


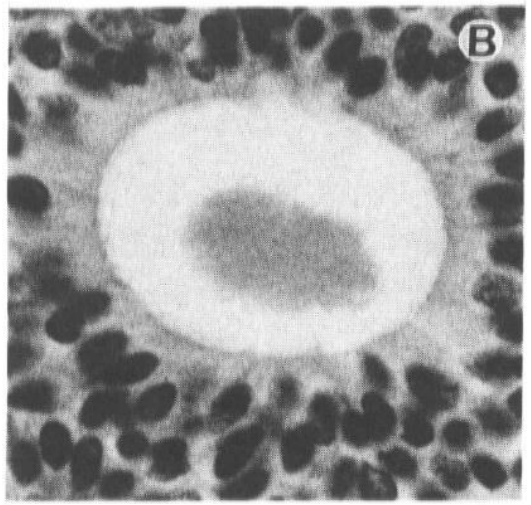
Gradering- volgens Holland

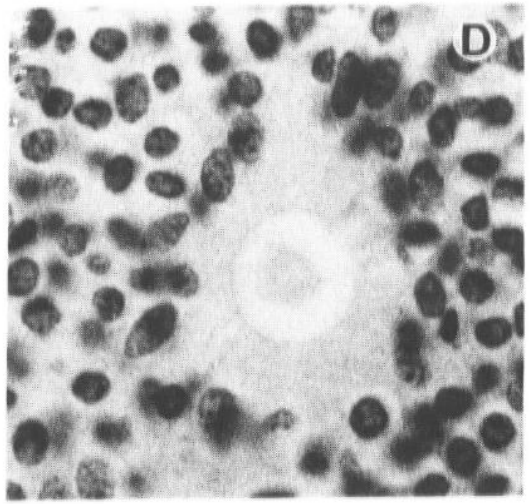
Architecturale differentiatie

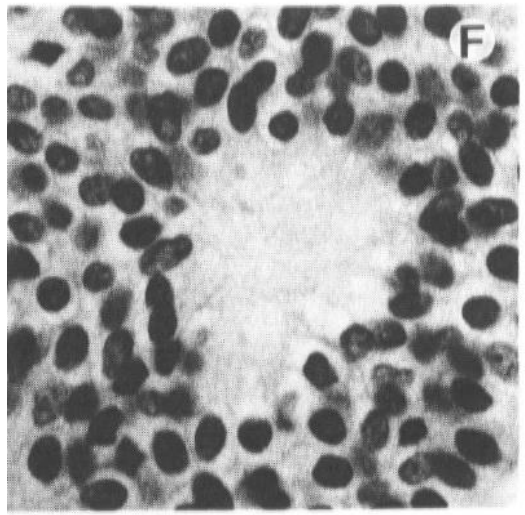






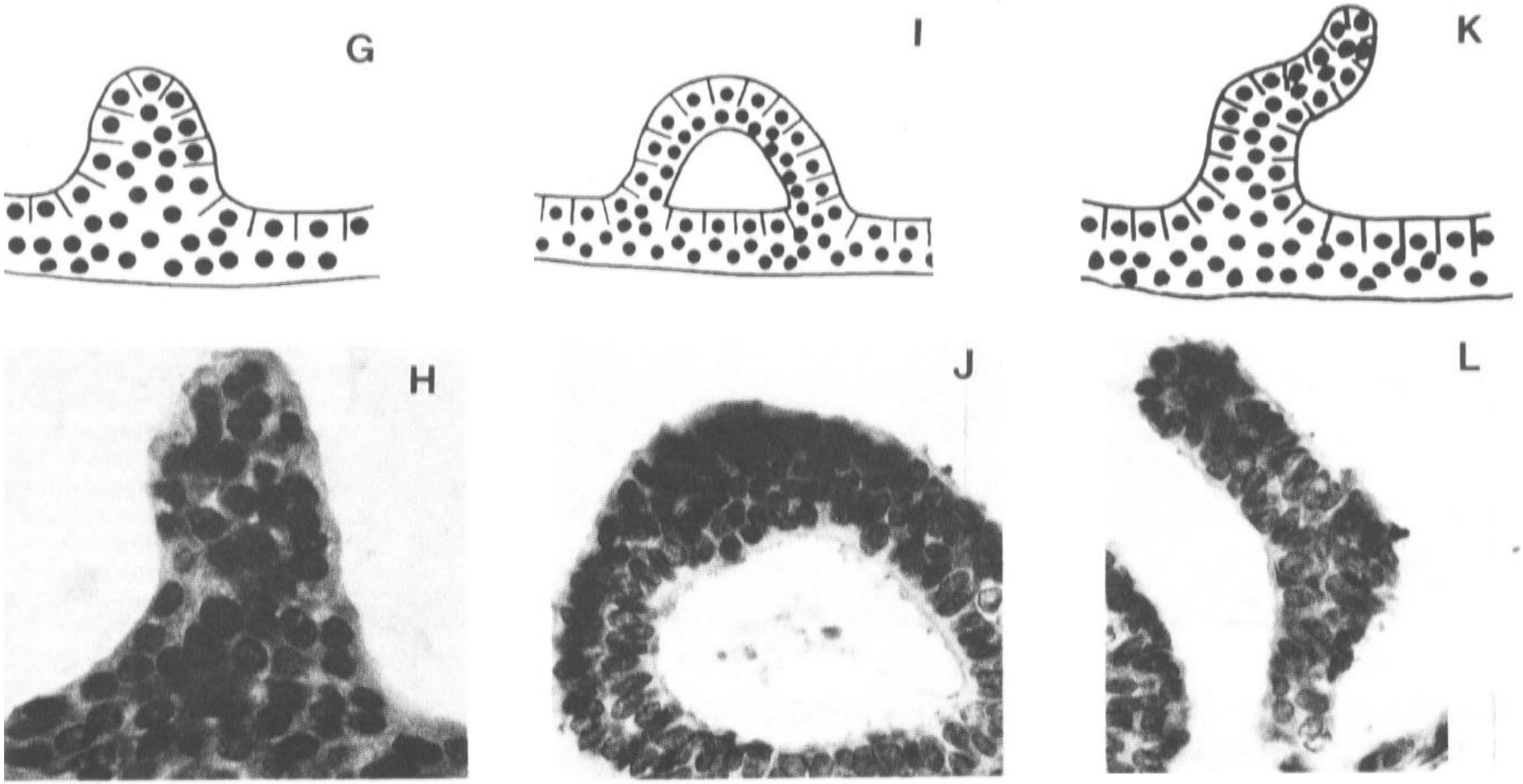






Gradering- volgens Holland

Architecturale differentiatie



Gradering- volgens Holland

Table 1. Histologic Classification of DCIS

	Poorly Differentiated	Intermediately Differentiated	Well-Differentiated
Defining Features			
Primary			
Nuclei	Pleomorphic +++ Variation in size, irregular outline and spacing	Pleomorphic + Some variation in size, outline, and spacing	Monomorphic Uniform size, regular outline and spacing
Chromatin	Coarse, clumped	Fine to coarse	Uniform, fine
Nucleoli	Prominent	Evident	Insignificant
Mitoses	Often present	Occasionally present	Rare
Secondary			
Architectural differentiation (polarisation of cells)	Absent or minimal	Present	Marked
Frequently Associated Features			
Central necrosis	Usually present, often prominent	Variable	Absent or minimal
Individual cell necrosis and autophagocytosis	Usually present	May be focally present	Absent
Growth pattern	Solid, clinging or *pseudo*-micropapillary/ cribriform	All patterns	Clinging/micropapillary/ cribriform or rarely solid
Calcification	Amorphous	Amorphous or laminated	Laminated, psammomalike or rarely amorphous

Gradering- volgens Holland

3 groepen DCIS

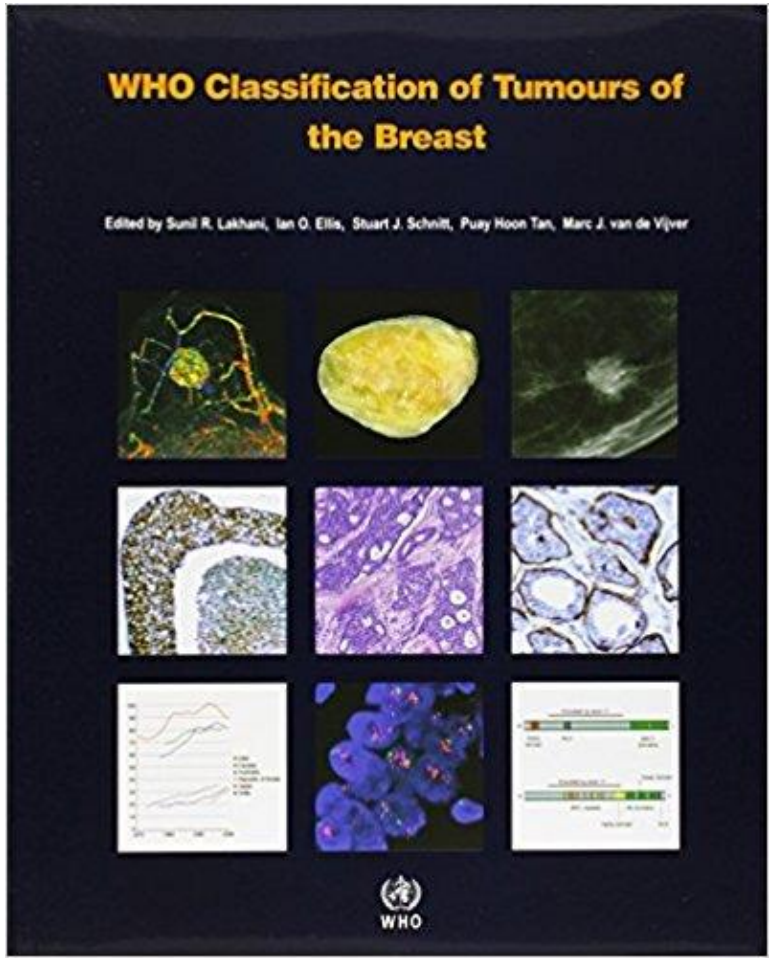
- Goed gedifferentieerd
- Matig gedifferentieerd
- Slecht gedifferentieerd

Gradering- volgens WHO

3 groepen DCIS

- Lage nucleaire graad
- Intermediaire nucleaire graad
- Hoge nucleaire graad

Heterogeniteit van DCIS kan voorkomen, advies WHO is dit ook zo in de conclusie te vermelden



Gradering- volgens Pinder

British Journal of Cancer (2010) 103, 94 – 100

www.bjcancer.com

A new pathological system for grading DCIS with improved prediction of local recurrence: results from the UKCCCR/ANZ DCIS trial

SE Pinder*[,1], C Duggan[2], IO Ellis[3], J Cuzick[4], JF Forbes[5], H Bishop[6], IS Fentiman[7] and WD George[8], on behalf of the UK Coordinating Committee on Cancer Research (UKCCCR) Ductal Carcinoma In Situ (DCIS) Working Party

[1]King's College London, Division of Cancer Studies, Research Oncology, 3rd Floor, Bermondsey Wing, Guy's Hospital, Great Maze Pond, London SE1 9RT, UK; [2]Department of Epidemiology, Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [3]Histopathology Department, Molecular Medical Sciences, Nottingham University, Nottingham City Hospital, Nottingham, UK; [4]Cancer Research UK Centre for Epidemiology, Mathematics and Statistics, Queen Mary University of London, London, UK; [5]School of Medical Practice and Population Health, University of Newcastle, NSW, Australia; [6]Department of Breast Surgery, Royal Bolton Hospital, Bolton Hospitals NHS Trust, Lancs, UK; [7]Breast Unit, Guy's Hospital, London, UK; [8]University Department of Surgery, Western Infirmary, Glasgow, UK

Gradering- volgens Pinder

confluent comedo-type necrosis. This resulted in a new four-tiered system: low (low cytonuclear grade (7.0% cases)), intermediate (intermediate cytonuclear grade (18.4% of cases), high (high cytonuclear grade, but not pure comedo (i.e. not predominantly solid architecture or <50% ducts bore necrosis) (35.1%)) and very high (high-grade DCIS of >50% solid architecture and >50% ducts bearing comedo-type necrosis (39.5% of cases)). This novel

4 groepen

- Laag (lage cytonucleaire graad)
- Intermediair (intermediaire cytonucleaire graad)
- Hoog (hoge cytonucleaire graad, geen pure comedo (i.e. geen predominante solide architectuur of <50% ducten overwegend necrose)
- Zeer hoog (hoge graad DCIS of >50% solide architectuur en >50% ducten hebben comedo-type necrose

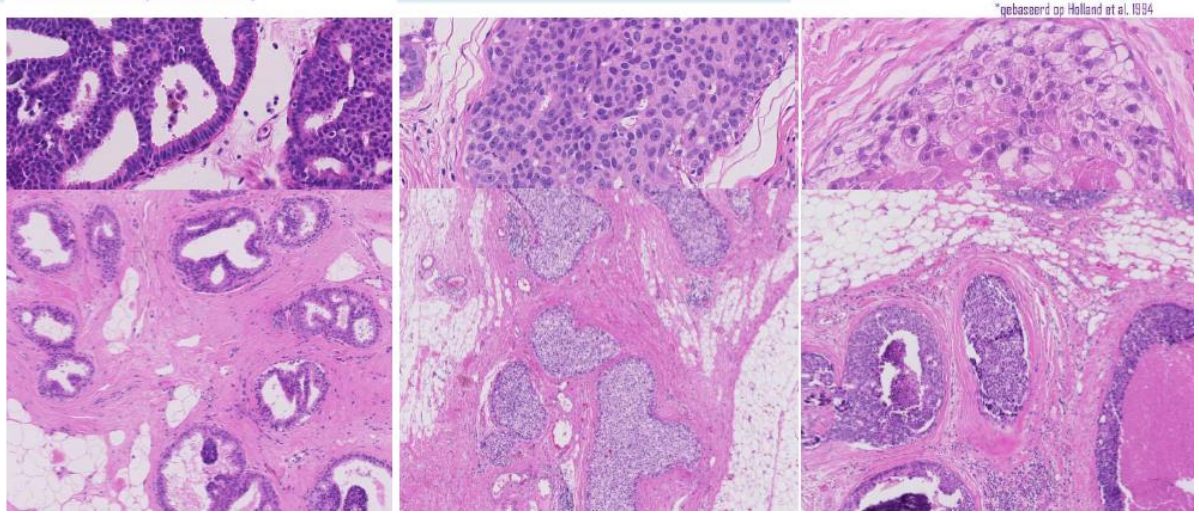
Oncoline

Zoals ook geldt voor invasieve borstkanker vormt DCIS een groep van heterogene laesies met wisselend klinisch gedrag. Bij de klassieke gradering van DCIS wordt er gekeken naar cytonucleaire differentiatie en groeipatroon. Hierbij wordt algemeen aangenomen dat een graad 1, goed gedifferentieerd DCIS bij progressie gedurende een langere tijdsperiode in bepaalde situaties aanleiding geeft tot een graad 1 invasief ductaal carcinoom (IDC), terwijl een graad 3 slecht gedifferentieerd DCIS zich sneller en vaker kan ontwikkelen tot een graad 3 IDC [Sanders 2005].

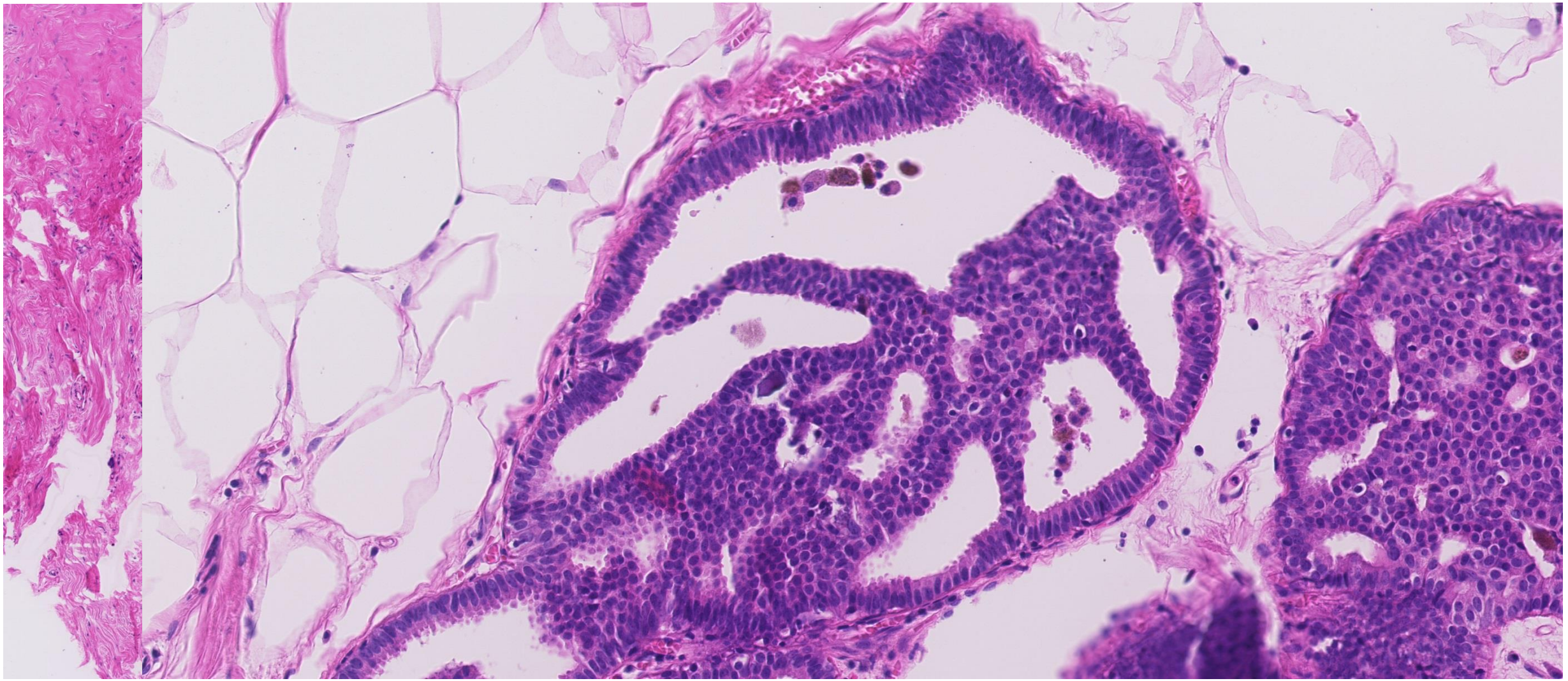
Graderen in de praktijk, enkele voorbeelden….

Bepalende kenmerken		ADH/DCIS graad 1	DCIS graad 2	DCIS graad 3
Primair	Kern	Monomorf, uniform	Pleomorf +	Pleomorf ++
	Chromatine	Fijn	Fijn-vesiculair	Vesiculair-grof
	Nucleoli	Minimaal	Evident	Prominent
	Mitosen	Zelden	Soms aanwezig	Vaak aanwezig
Secundair	Architecturale differentiatie	Uitgesproken polarisatie	Enige polarisatie	Geen of geringe polarisatie
Frequent geassocieerde kenmerken				
	Centrale necrose	Afwezig/ minimaal	Variabel	Vaak aanwezig, meestal prominent
	Apoptose	Afwezig	Eventueel focaal	Meestal aanwezig
	Groeipatroon	Micropapillair, cribriform, (zelden solide)	Alle patronen	Solide, cribriform, micropapillair
	Calcificaties	Psammoma-like (zelden amorf)	Amorf	Amorf

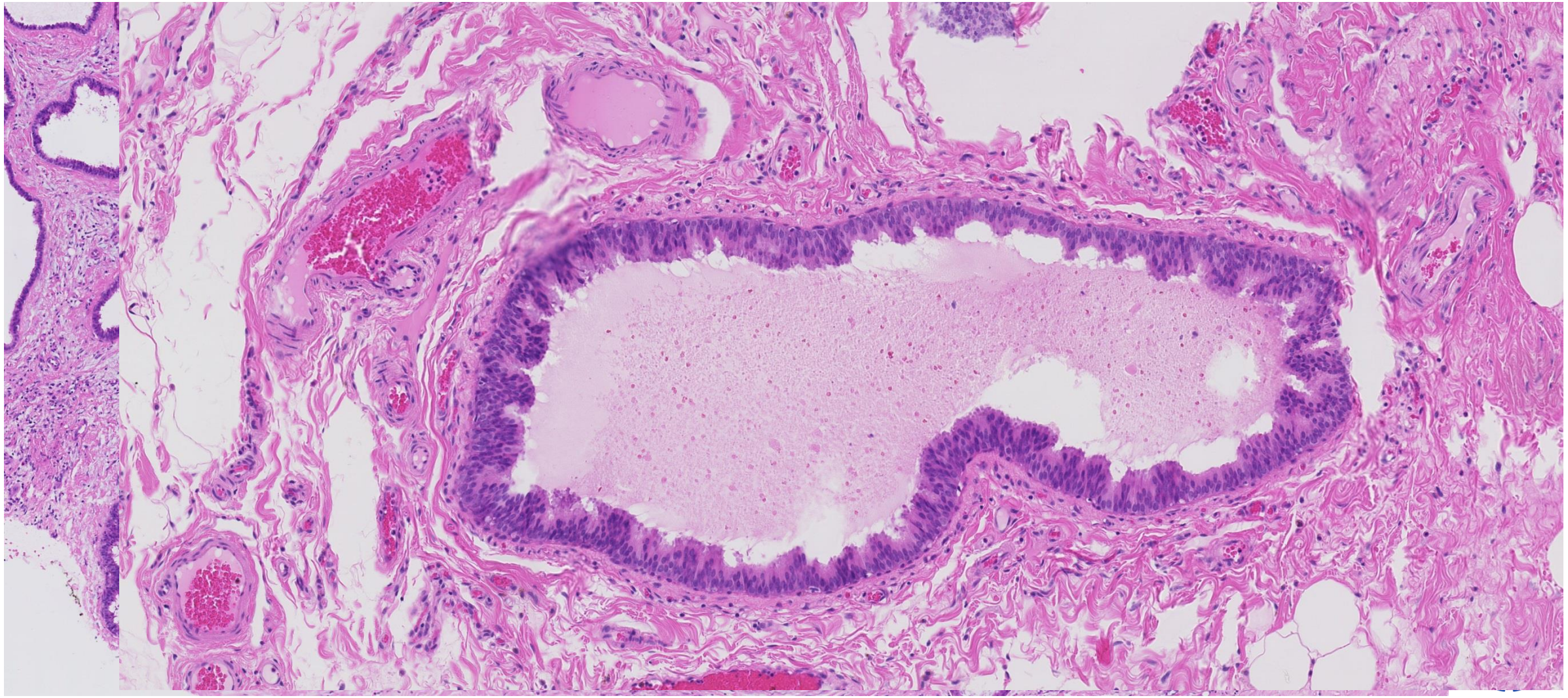
*gebaseerd op Holland et al. 1994



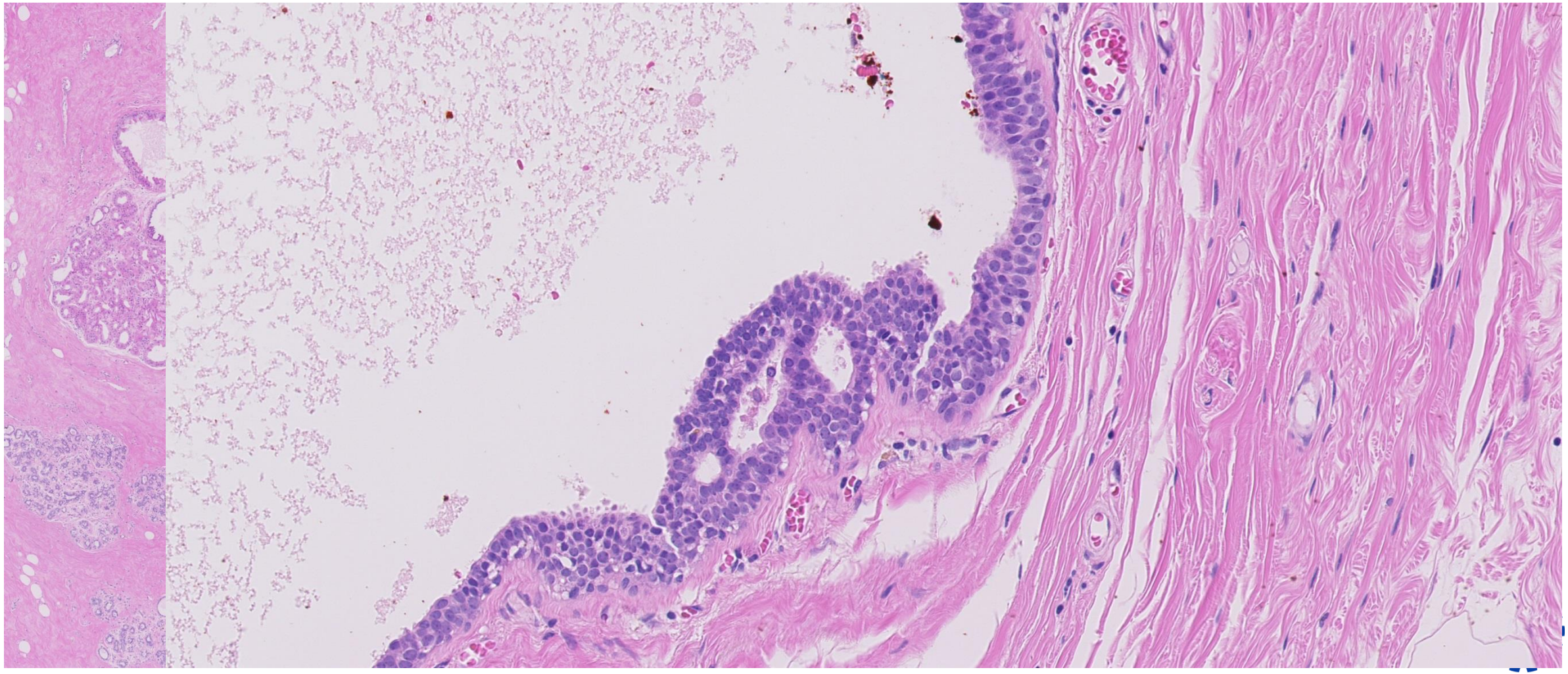
Gradering DCIS graad 1



Gradering DCIS graad 1



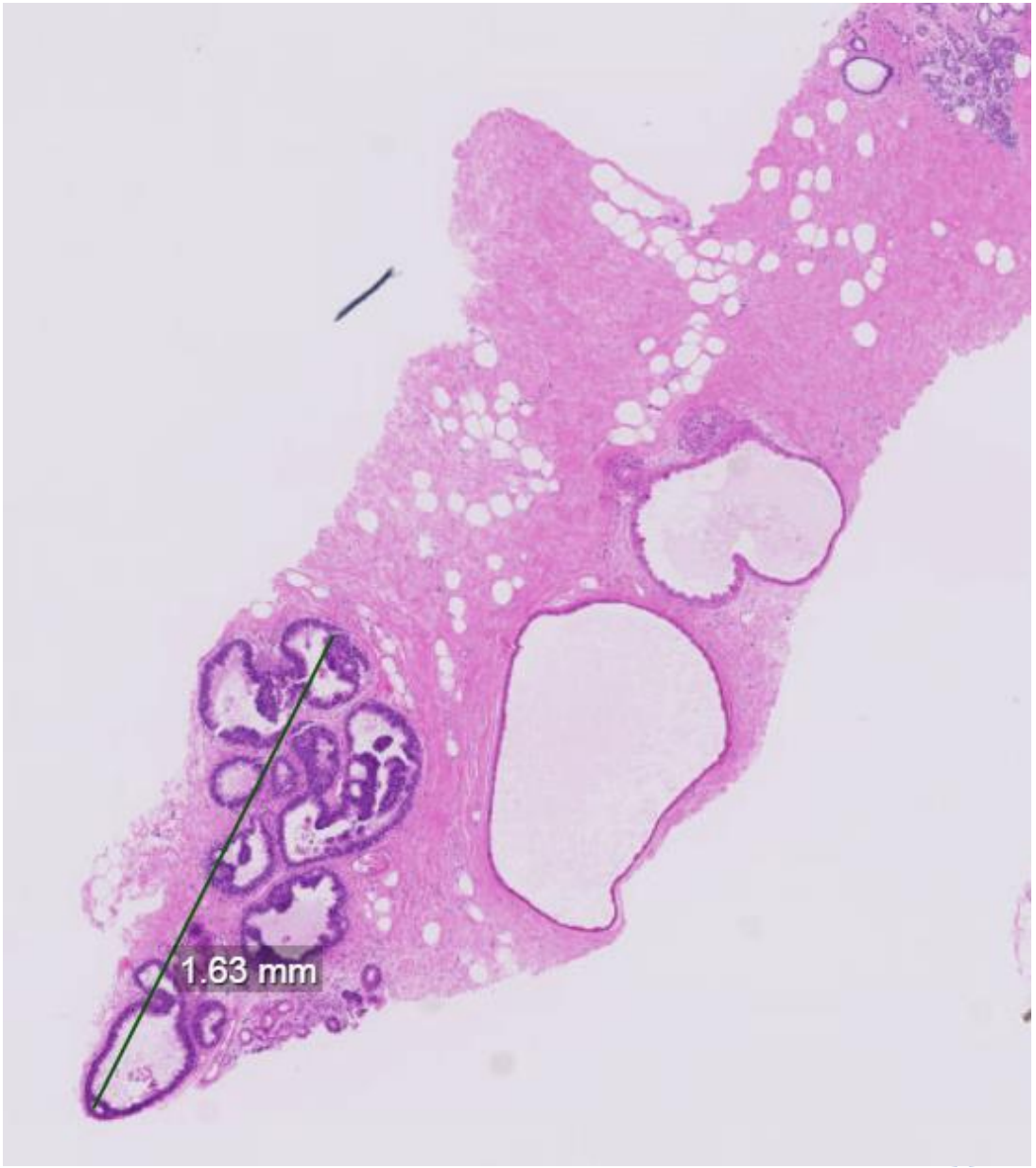
Gradering DCIS graad 1



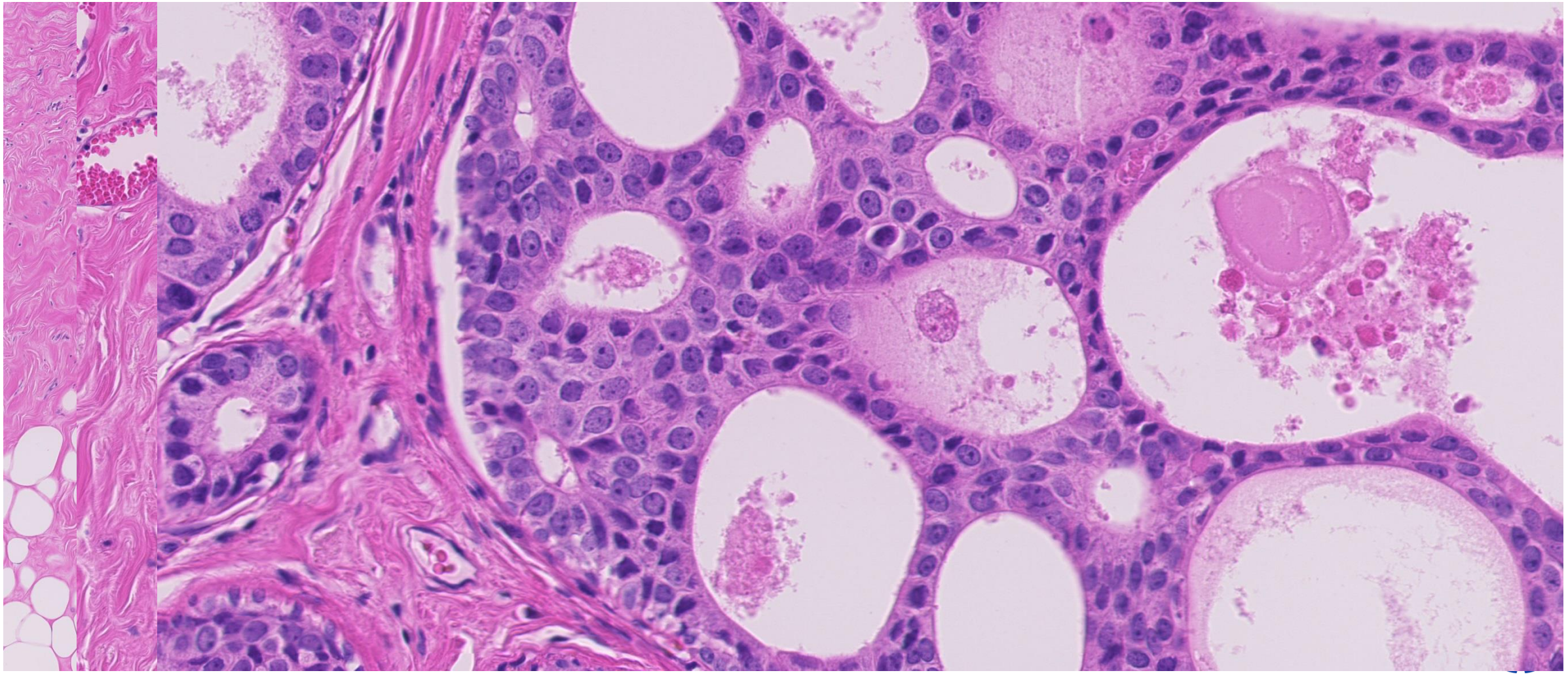
DCIS graad 1 versus ADH

Criteria WHO

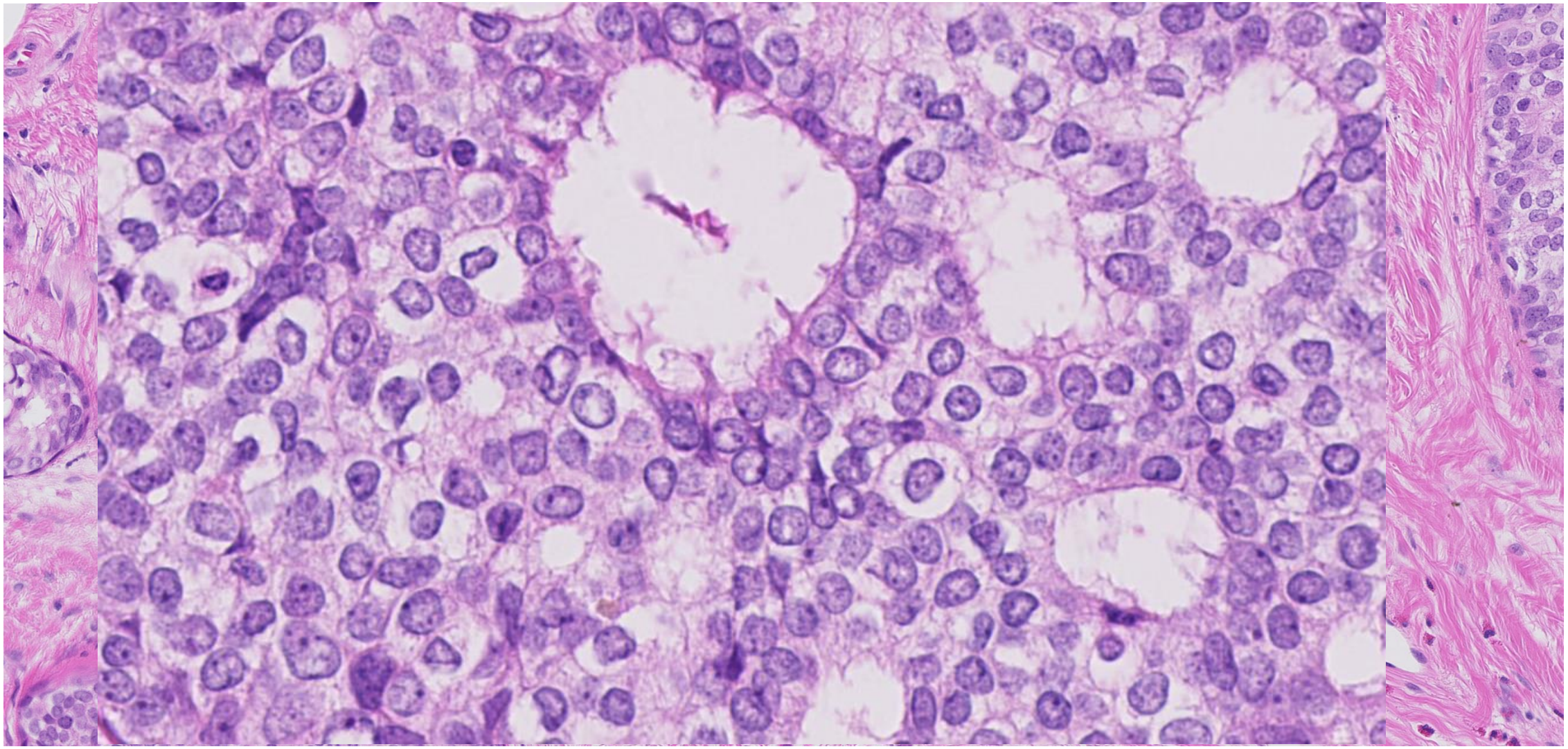
- diameter groter dan 2 mm



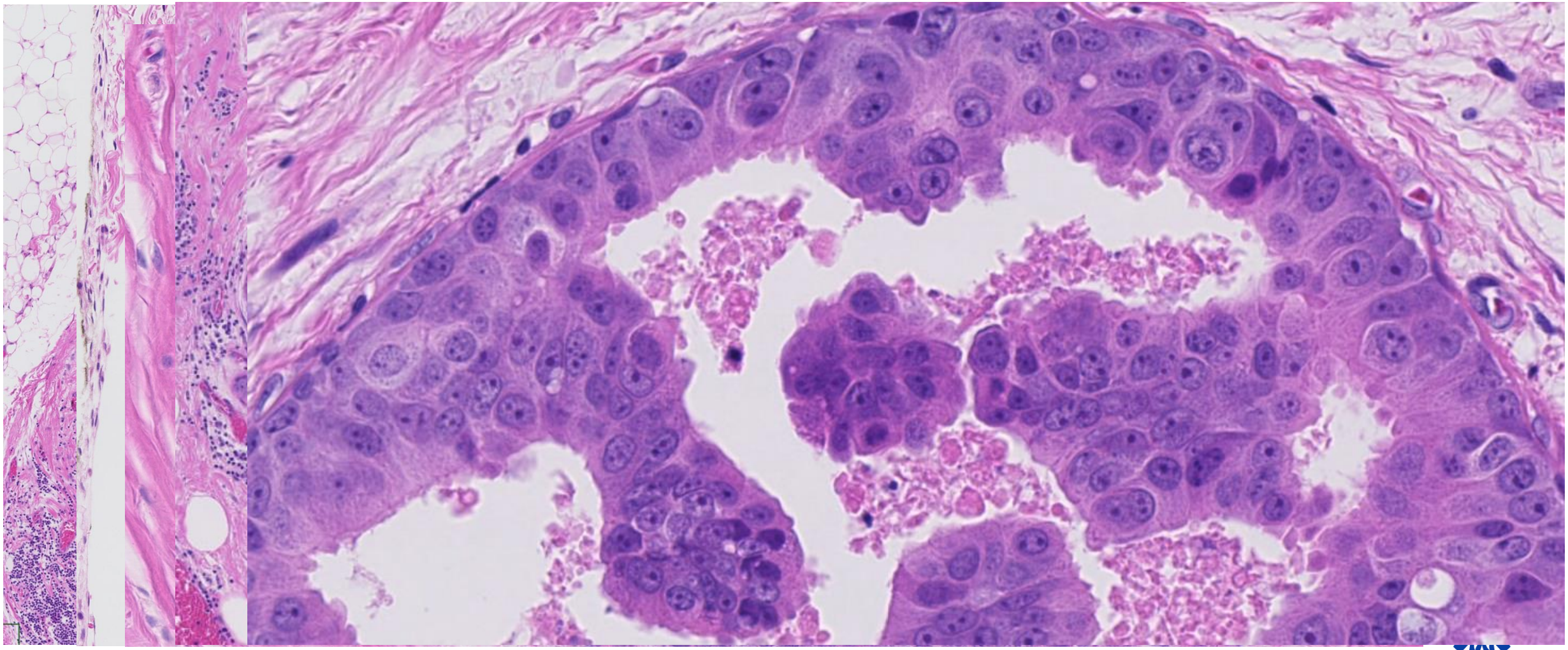
Gradering DCIS graad 2



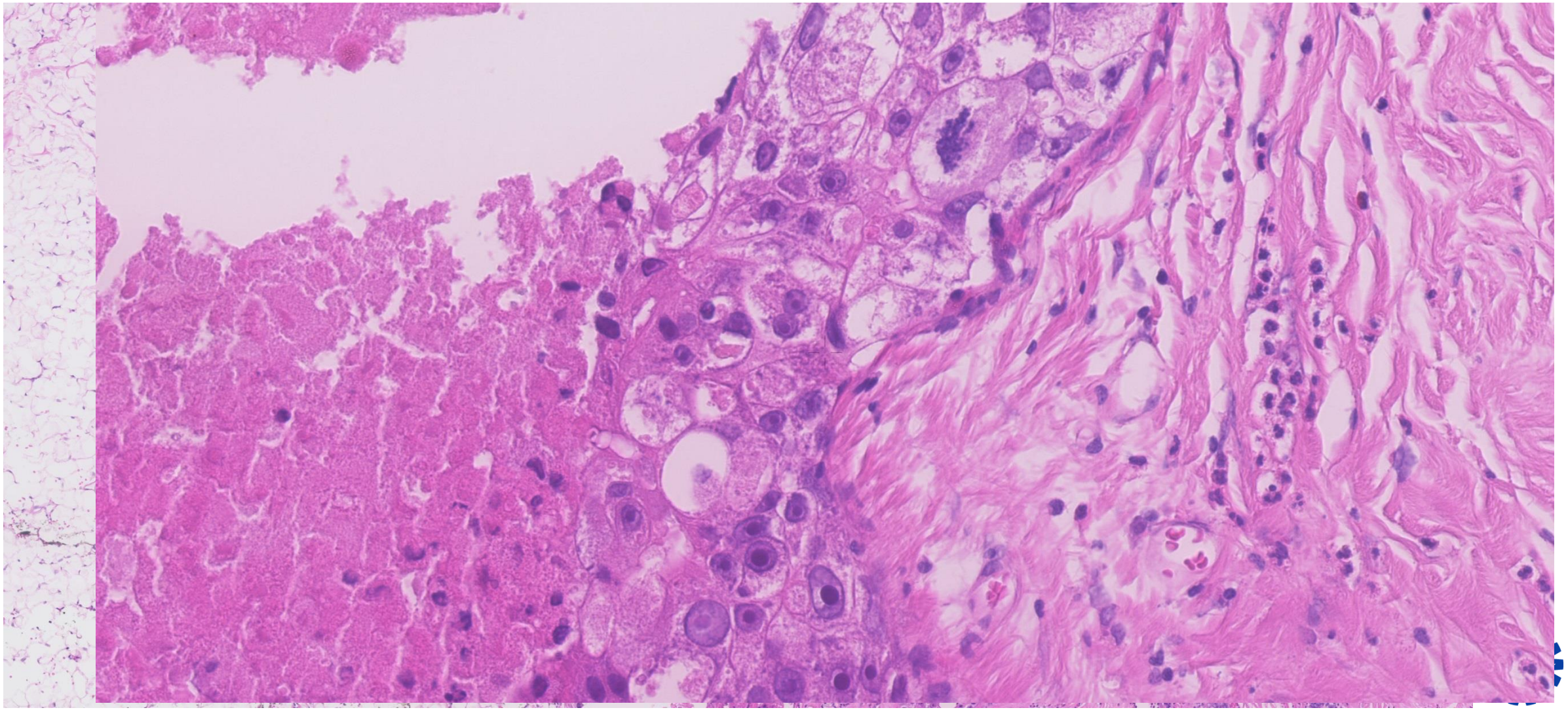
Gradering DCIS graad 2



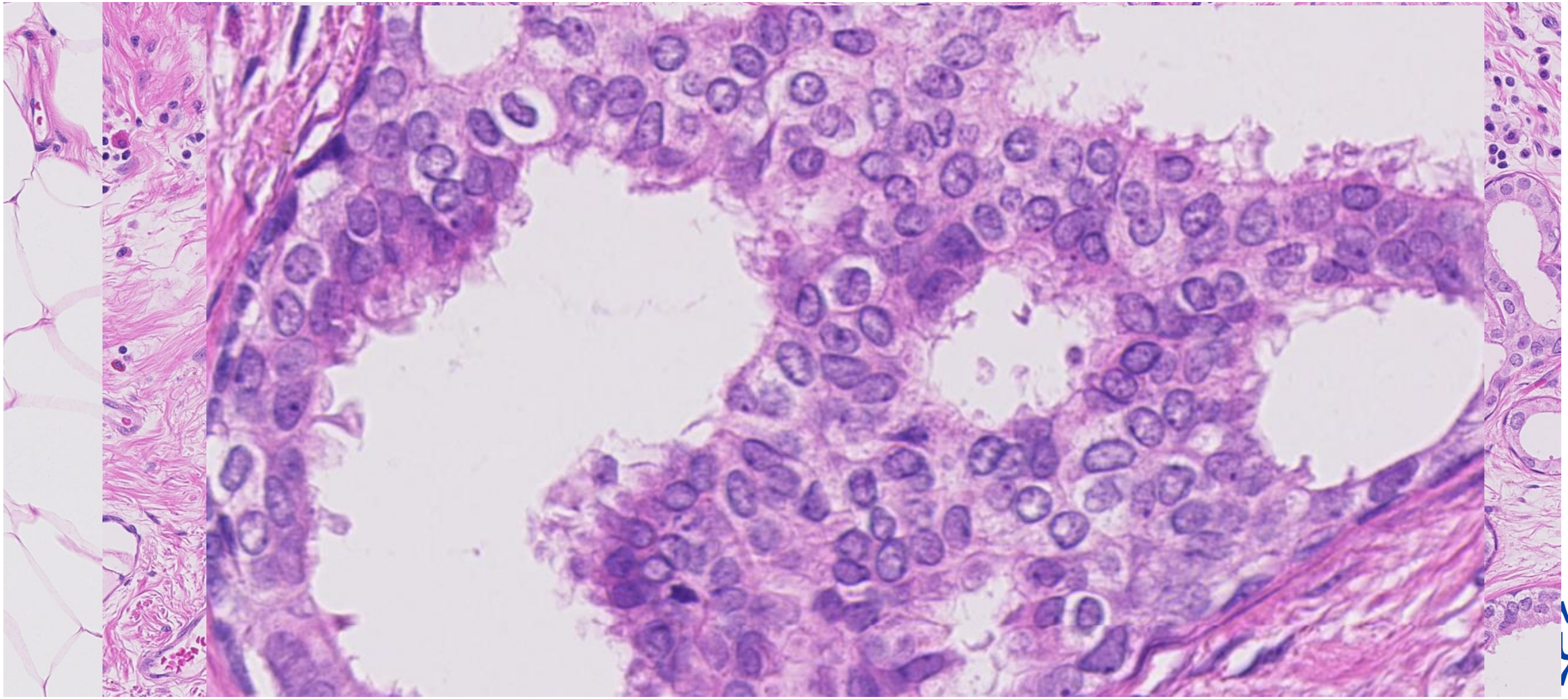
Gradering DCIS graad 3



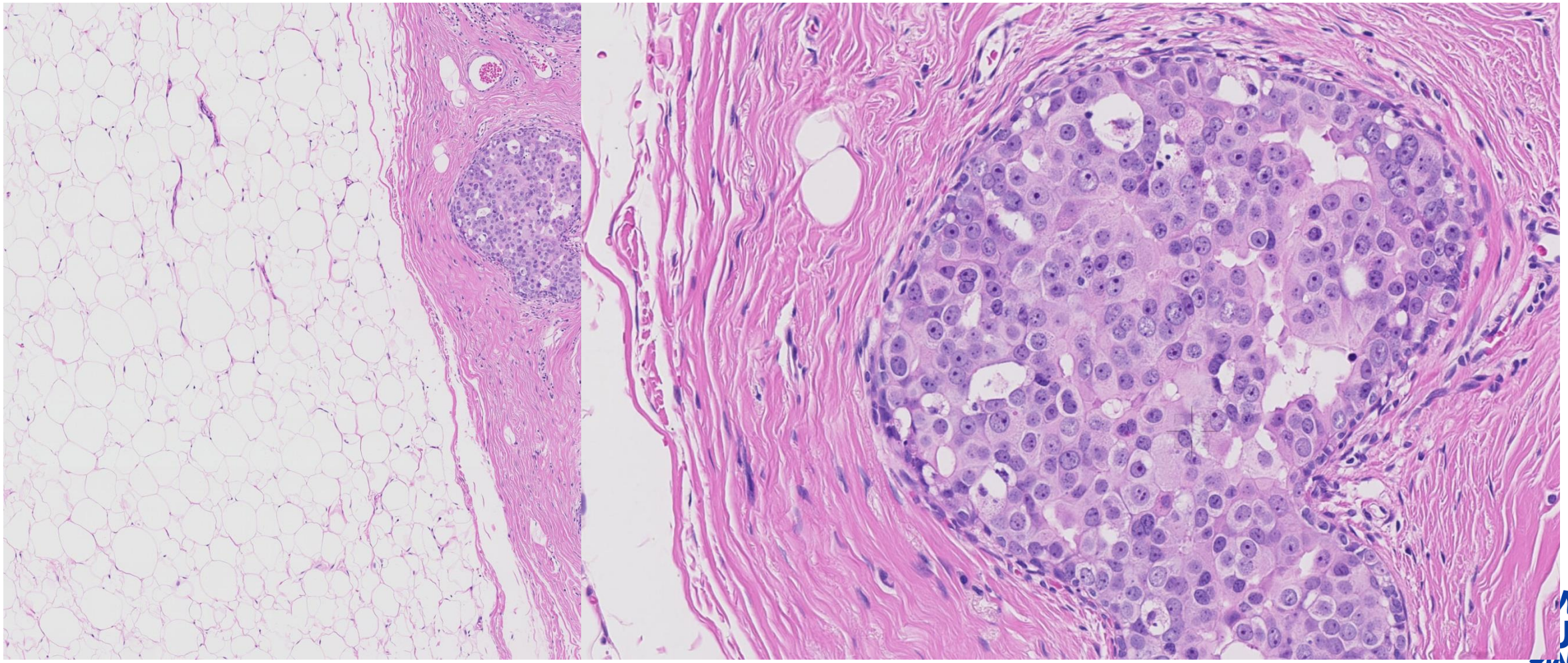
Gradering DCIS graad 3



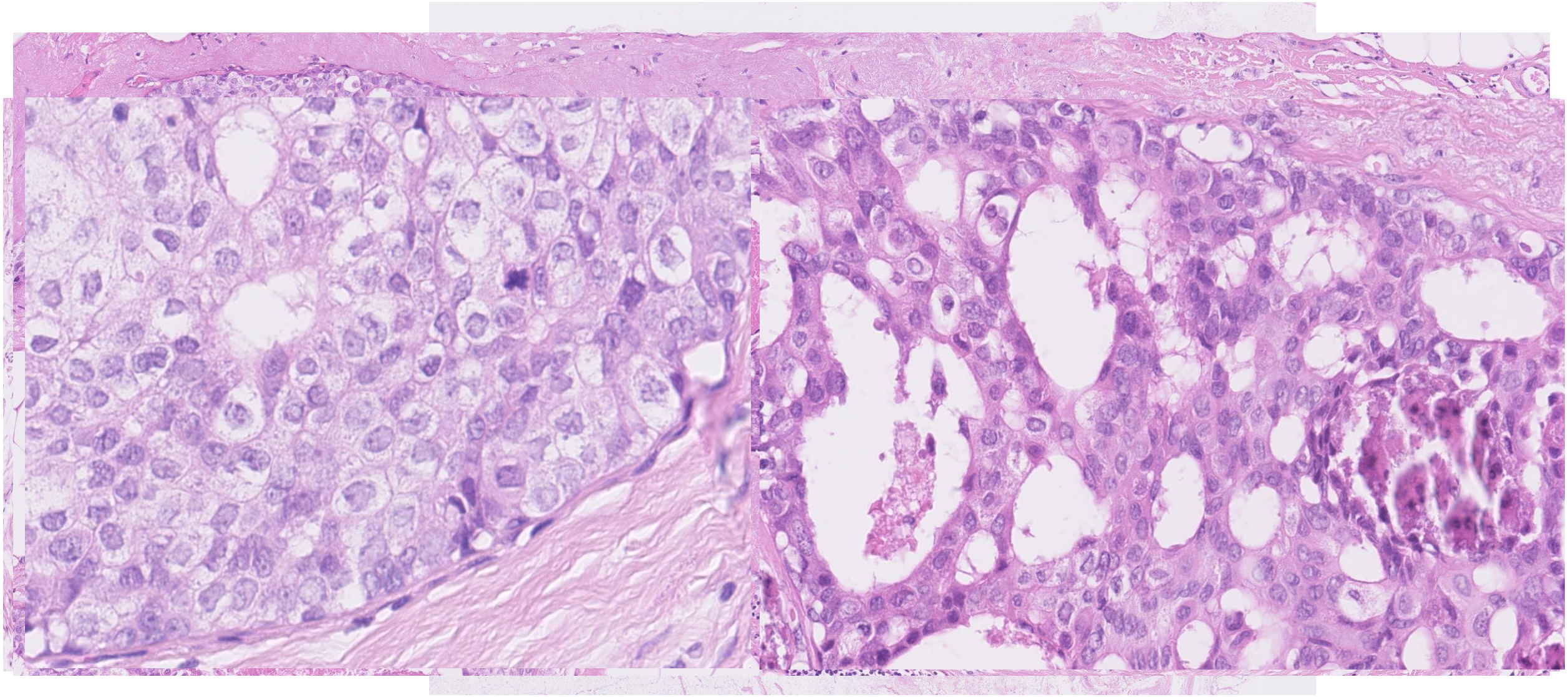
Gradering DCIS graad 1 of 2??



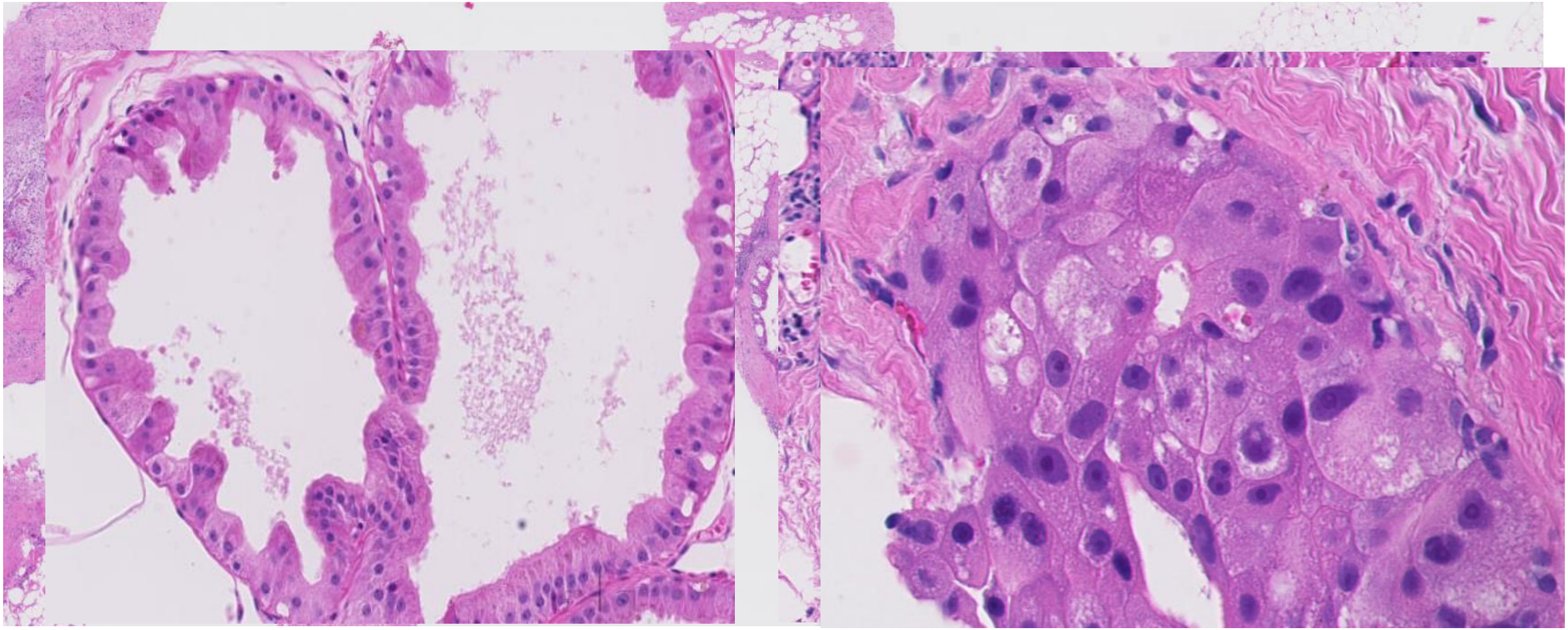
Gradering DCIS graad 2 of 3??



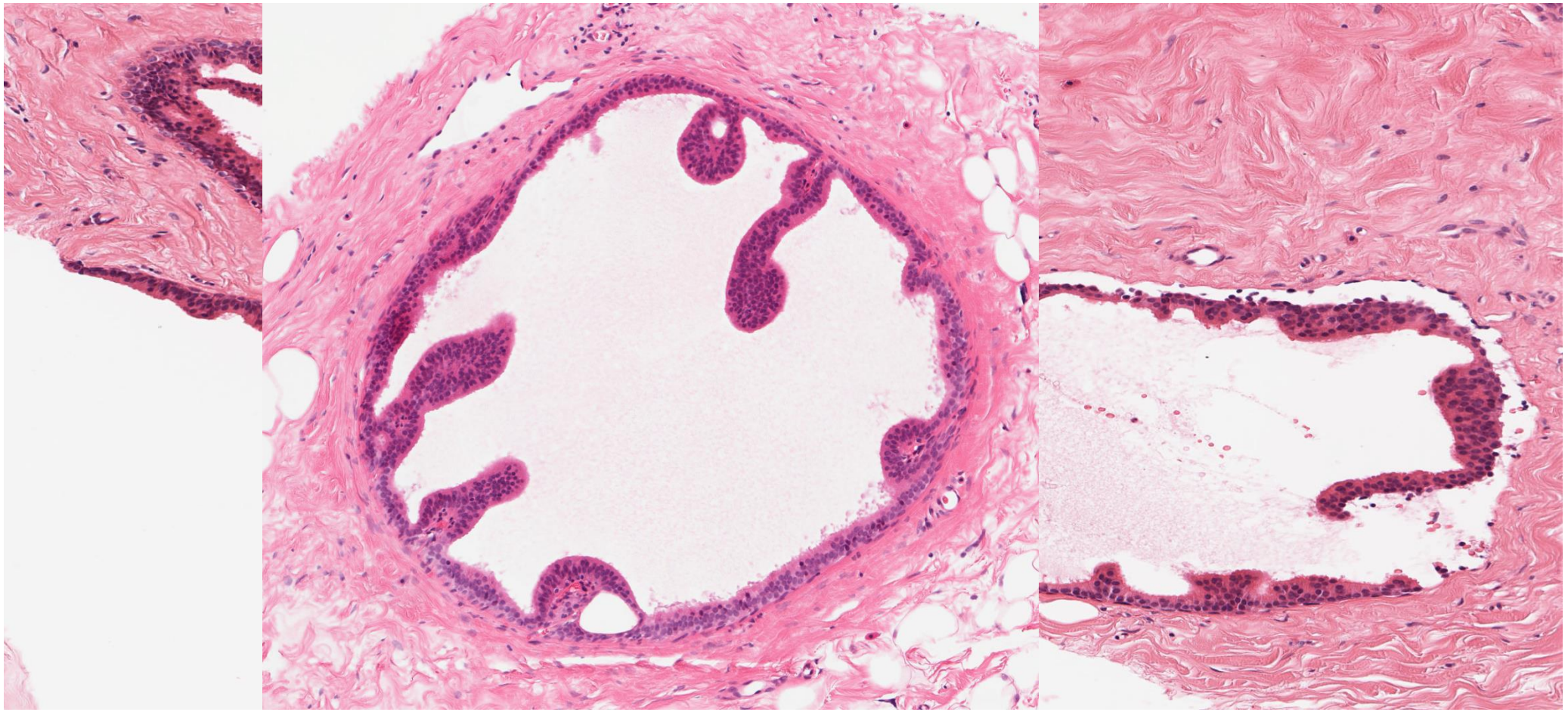
Gradering DCIS graad 2 of 3??



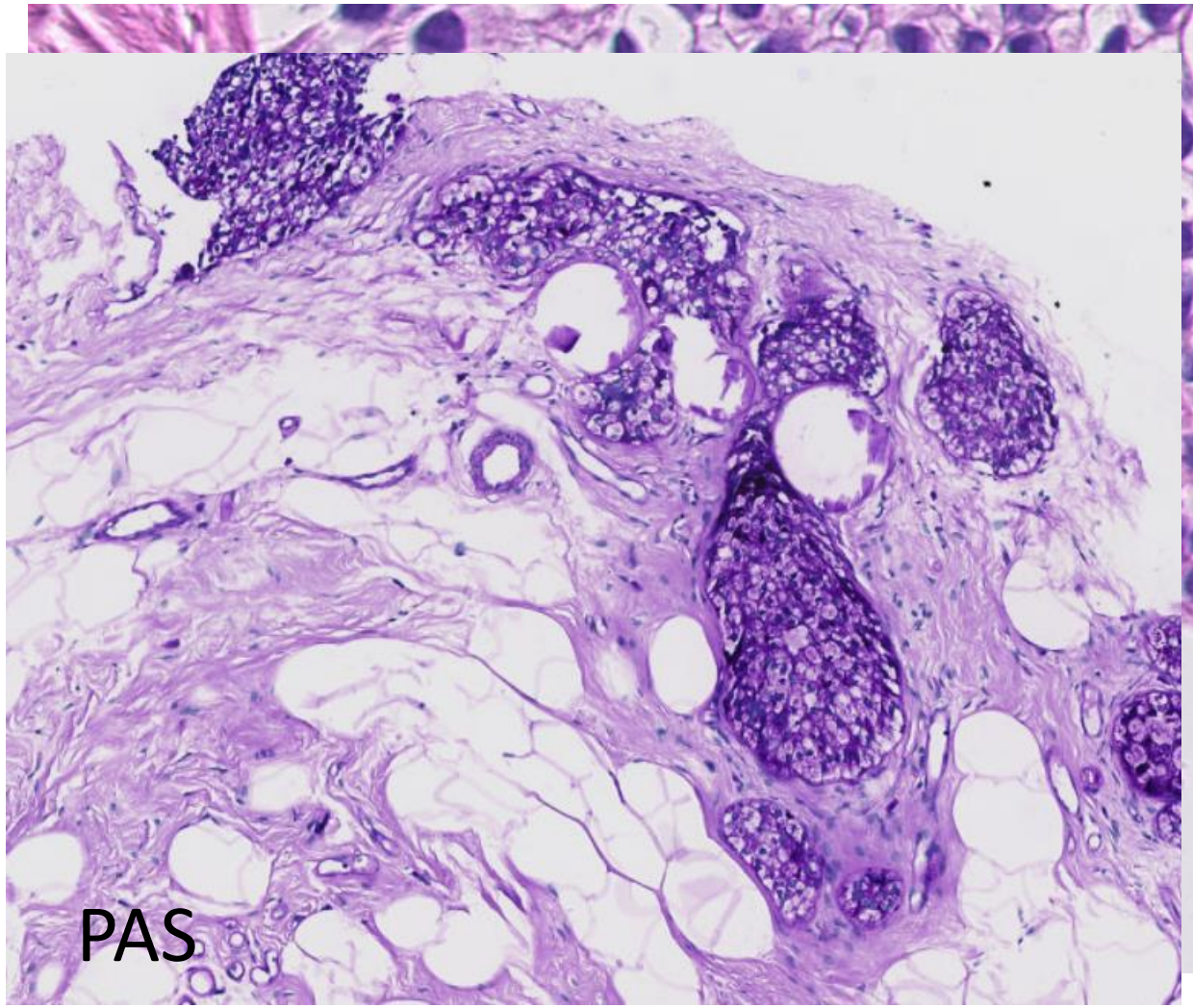
Apocriene DCIS

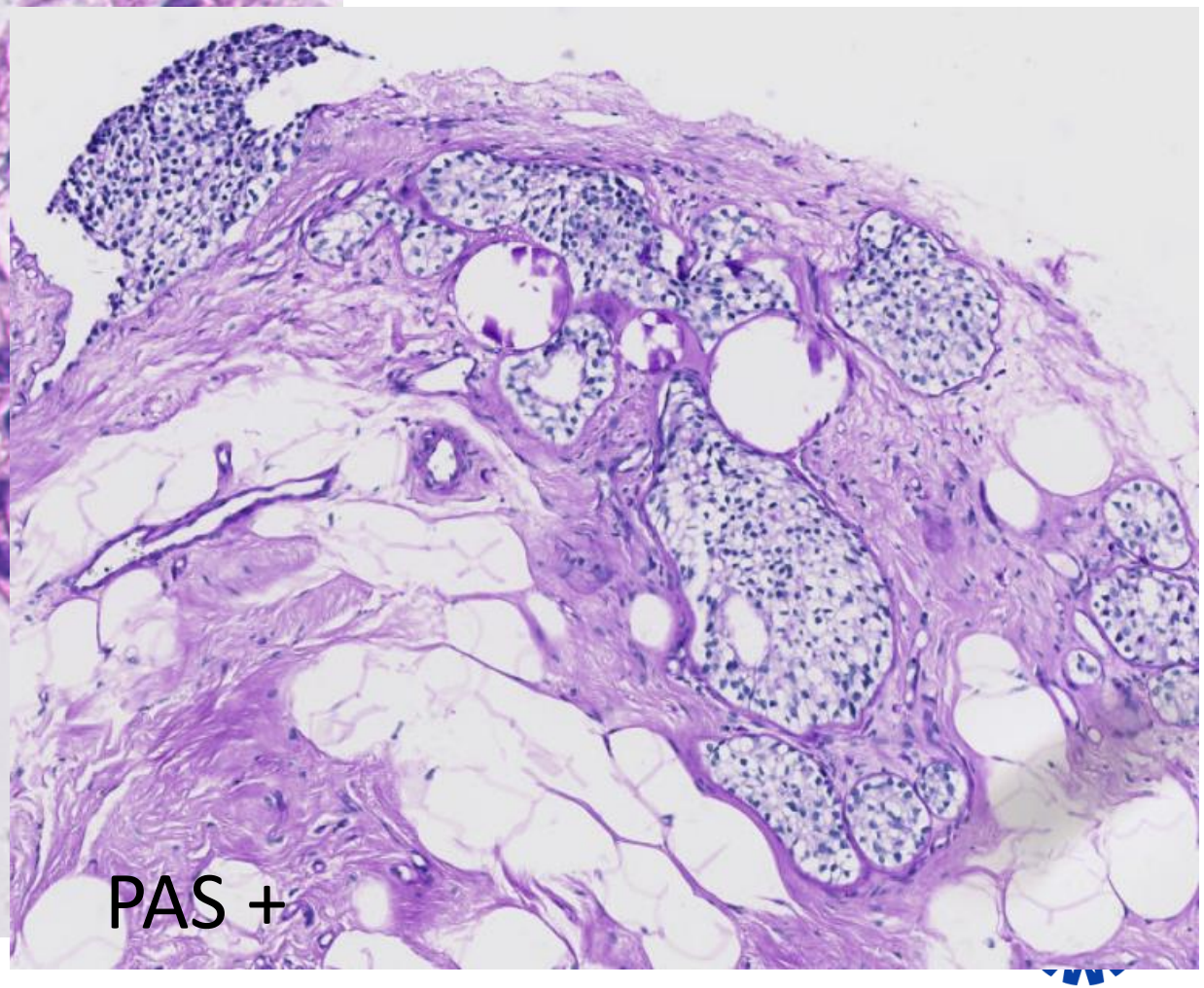


Apocriene ADH

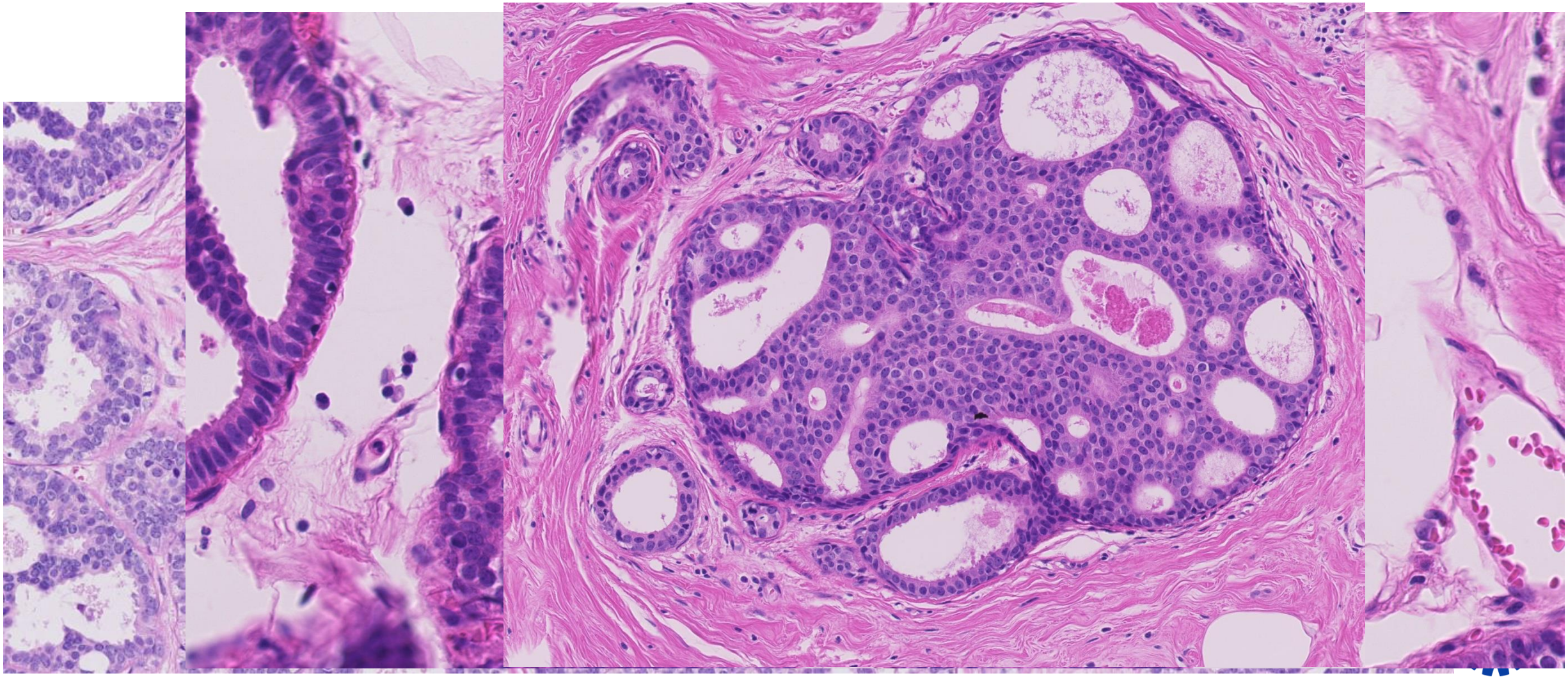


Clearcell DCIS

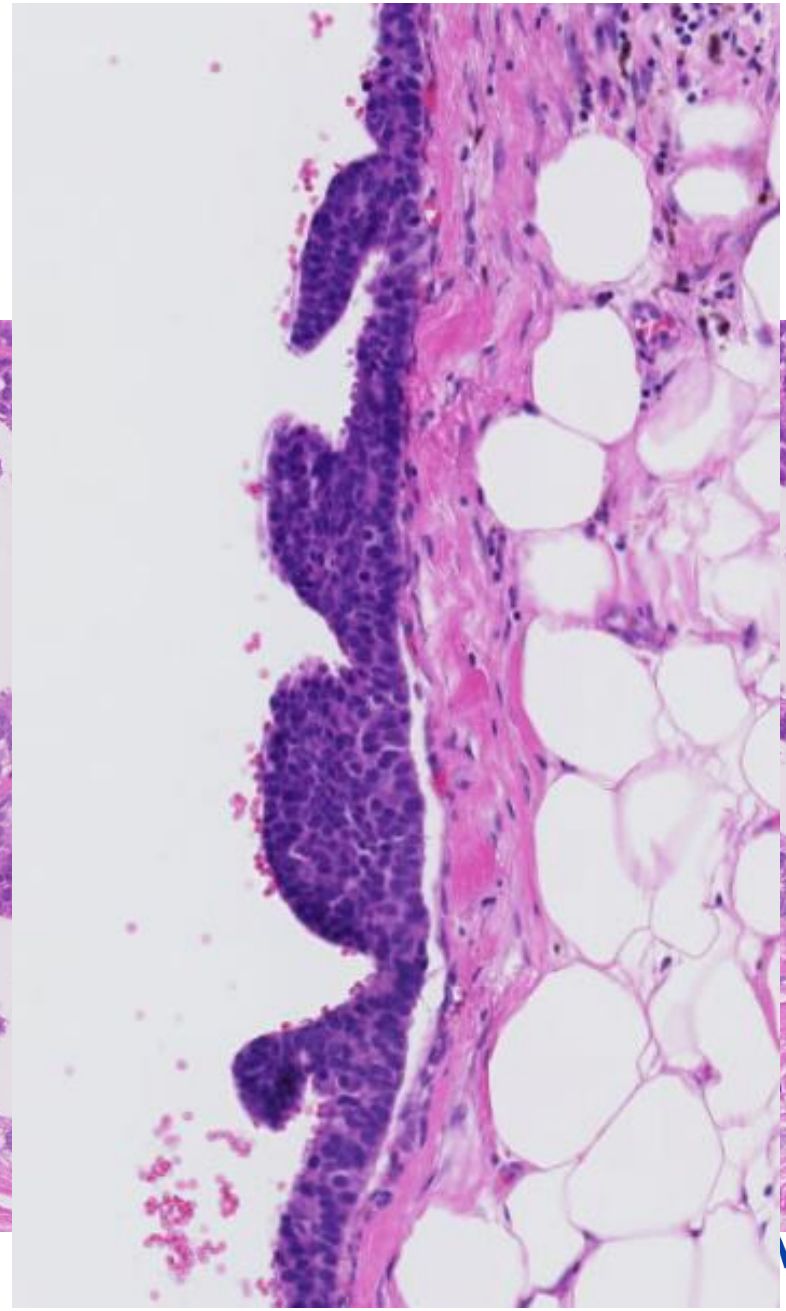




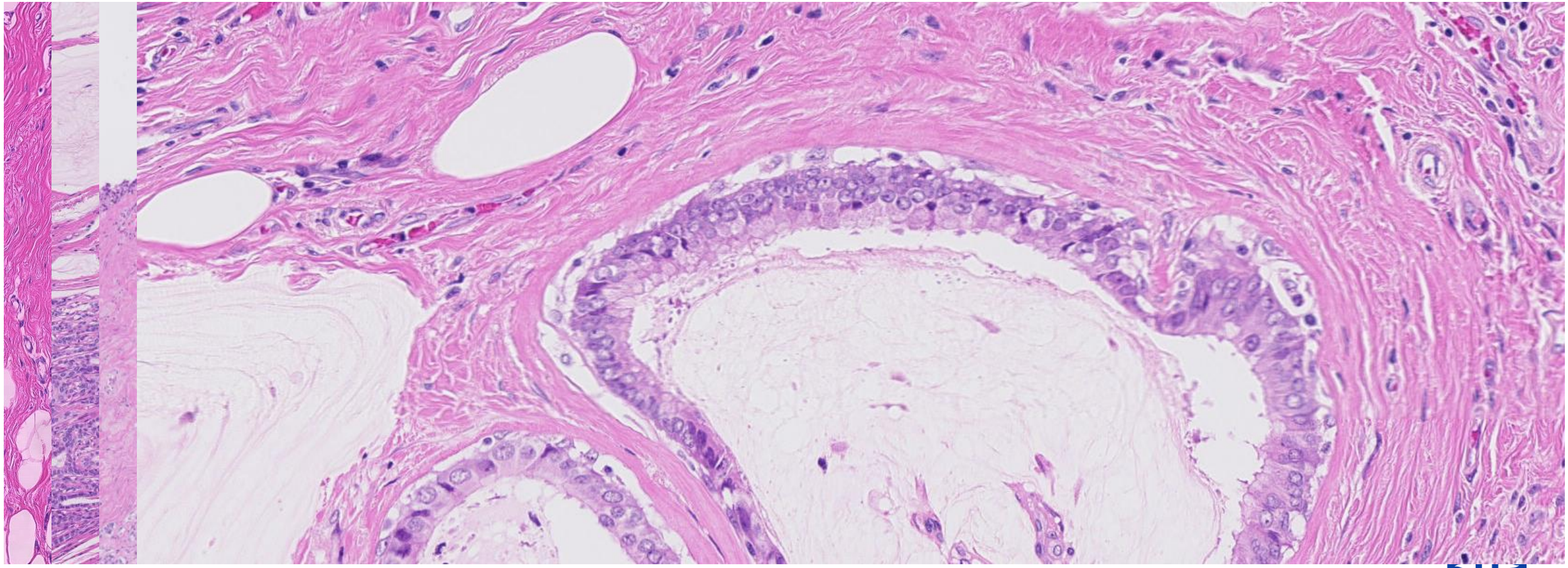
Cribriforme DCIS



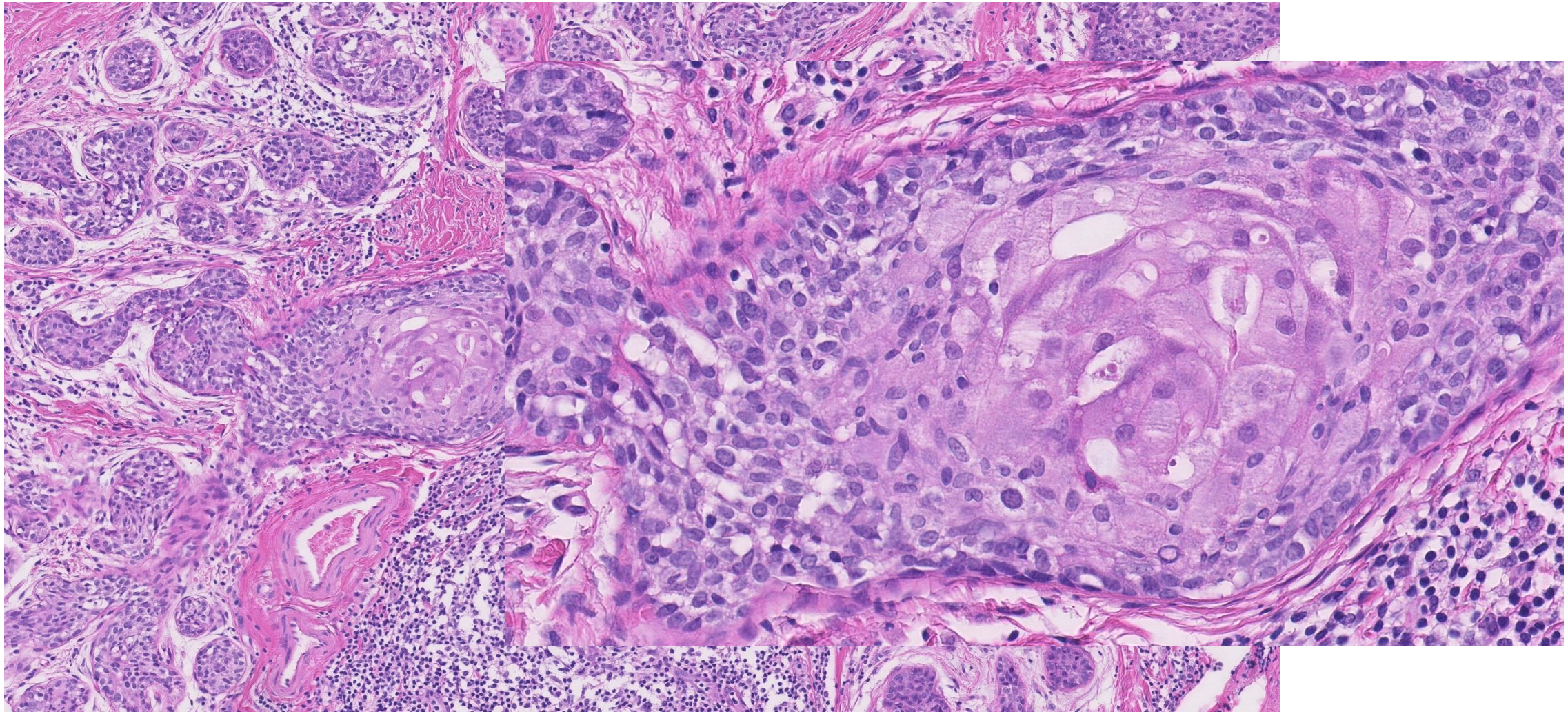
Micropapillaire DCIS



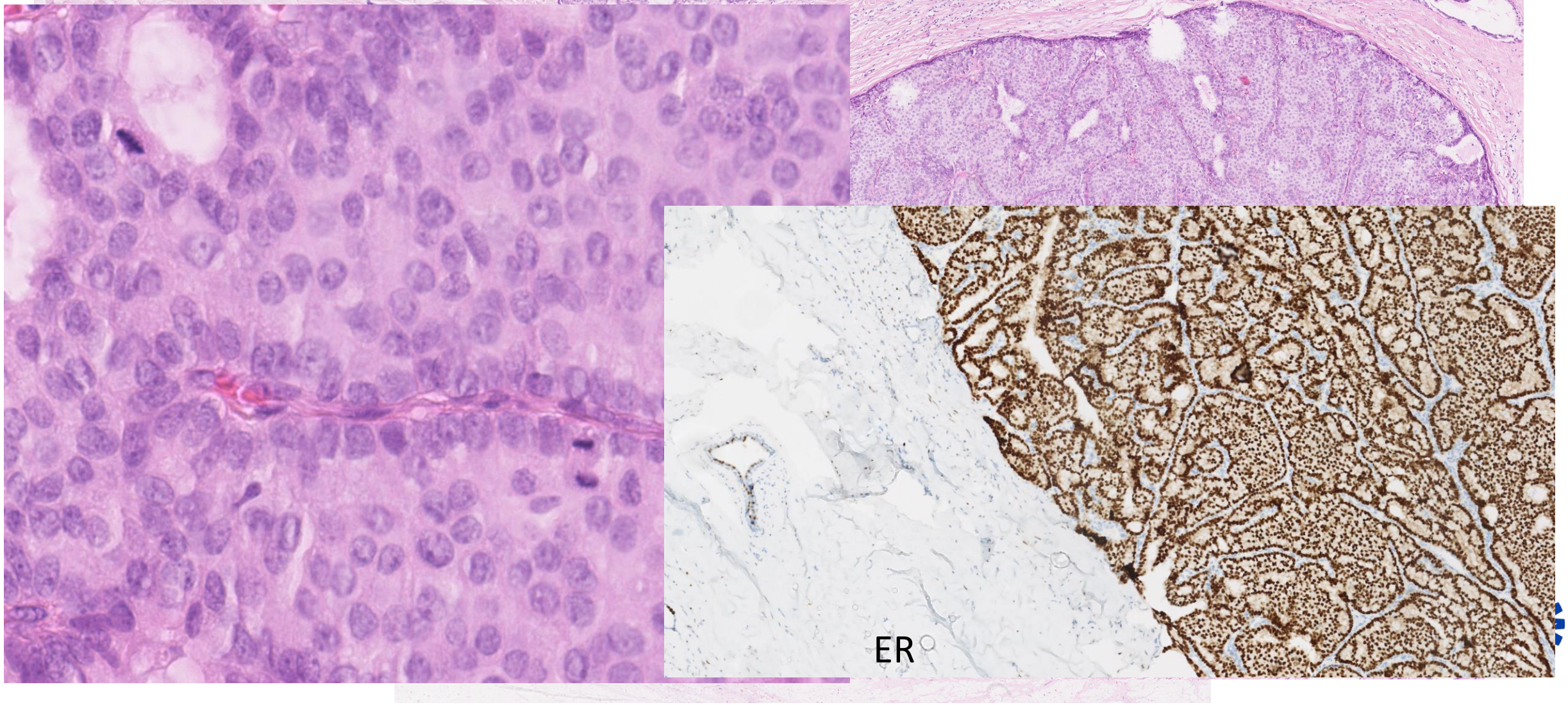
Mucineuze DCIS



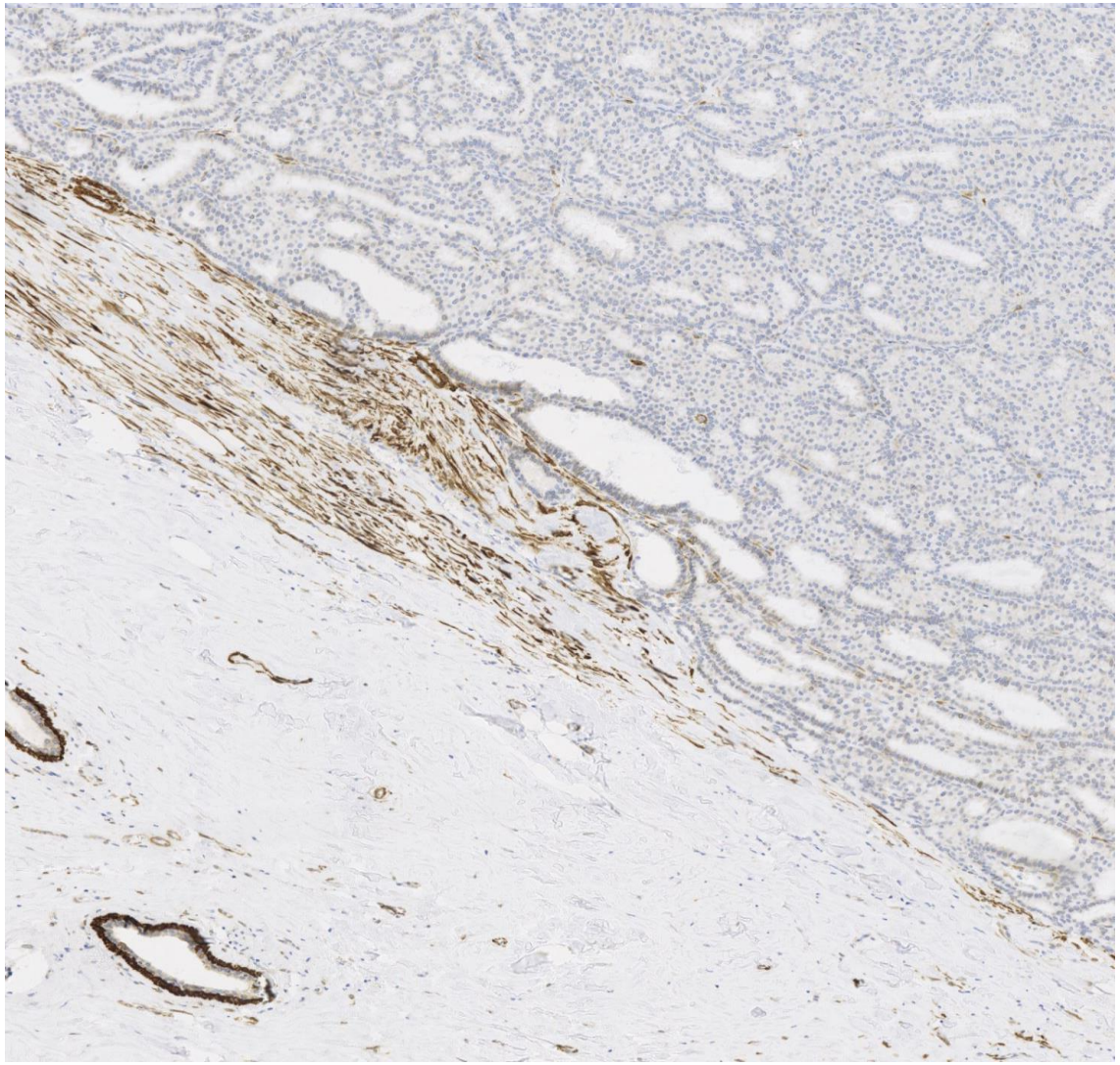
Metaplastische DCIS

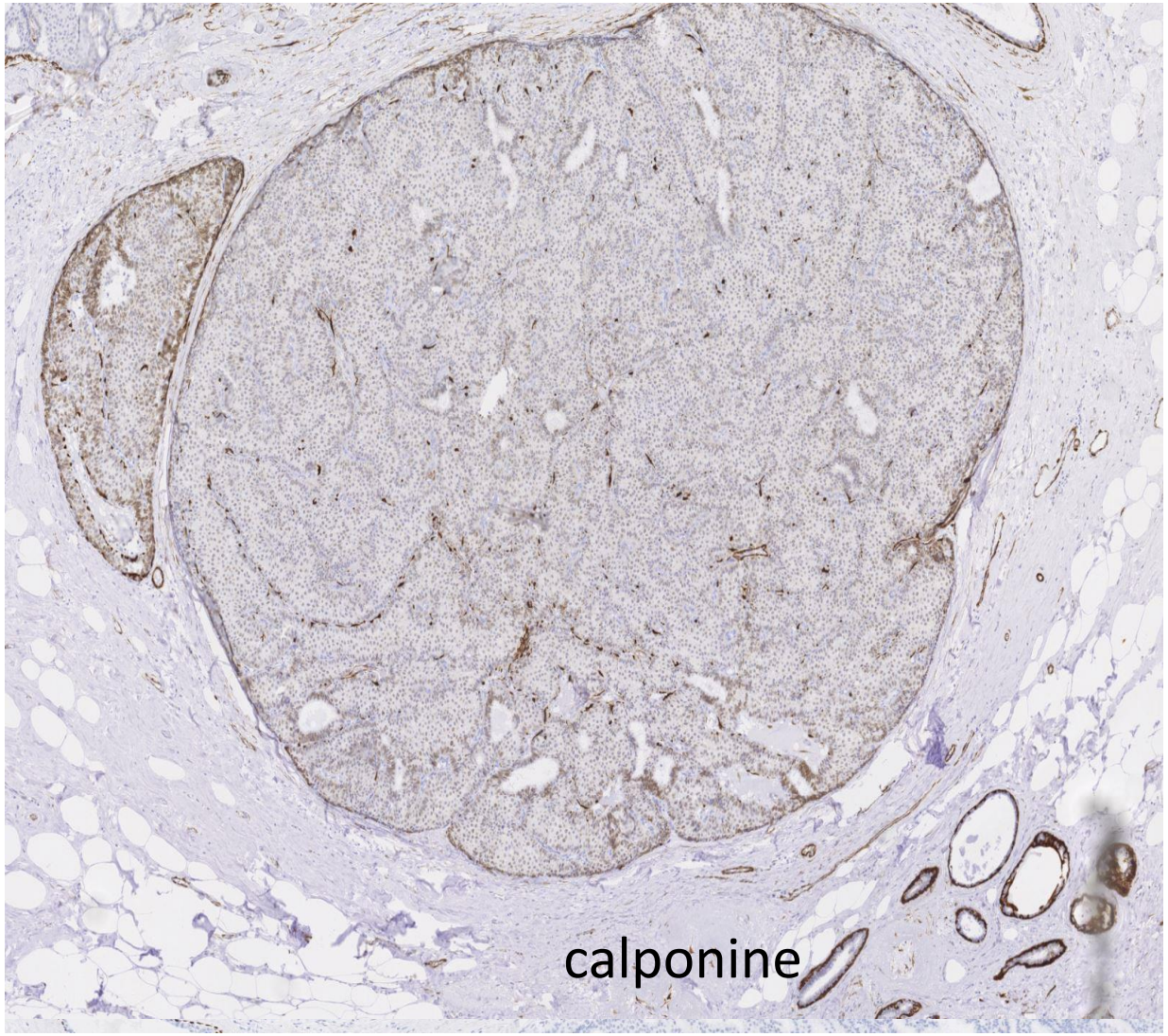


Intraductal papillary carcinoma (syn. papillary DCIS)

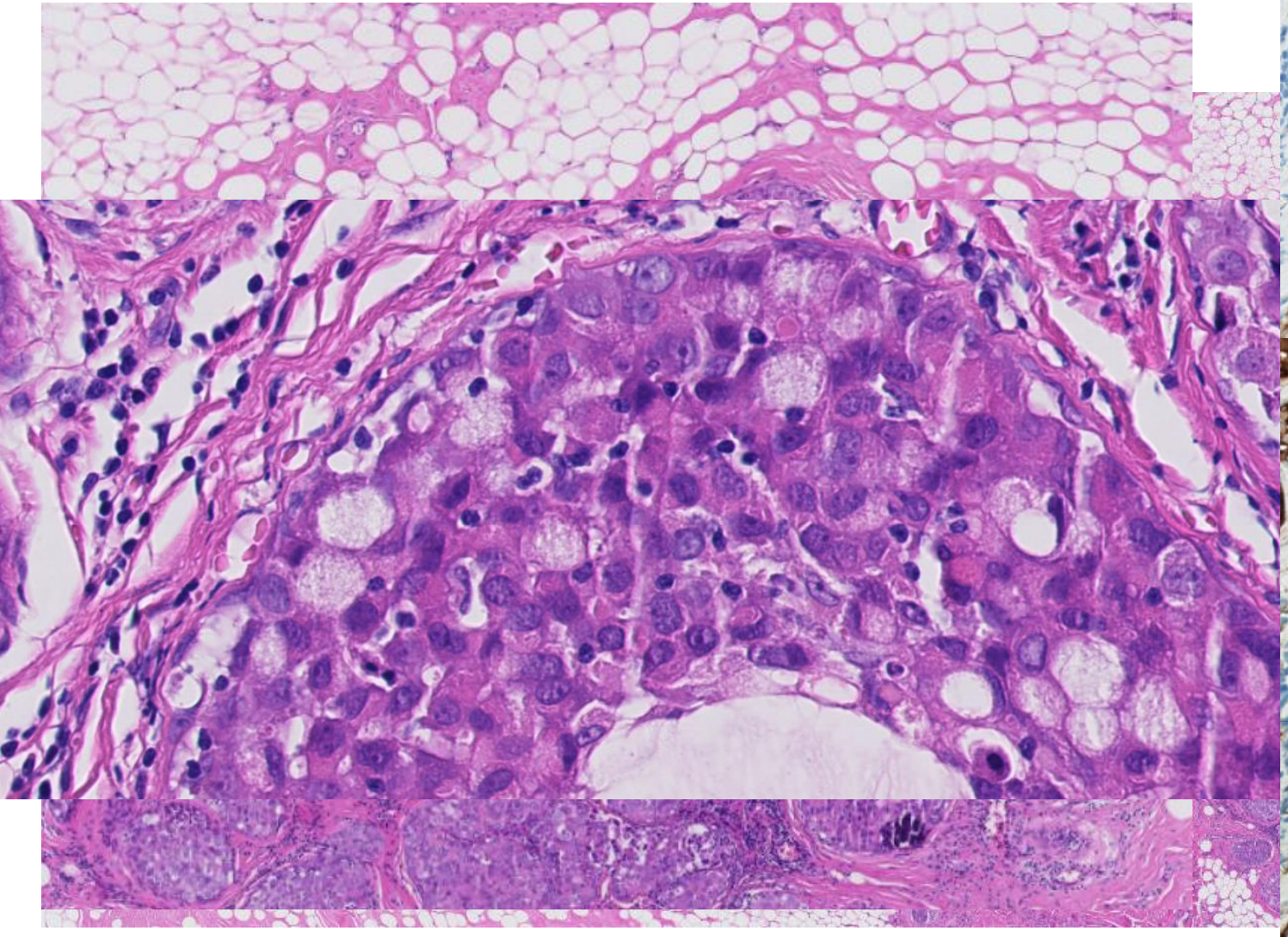


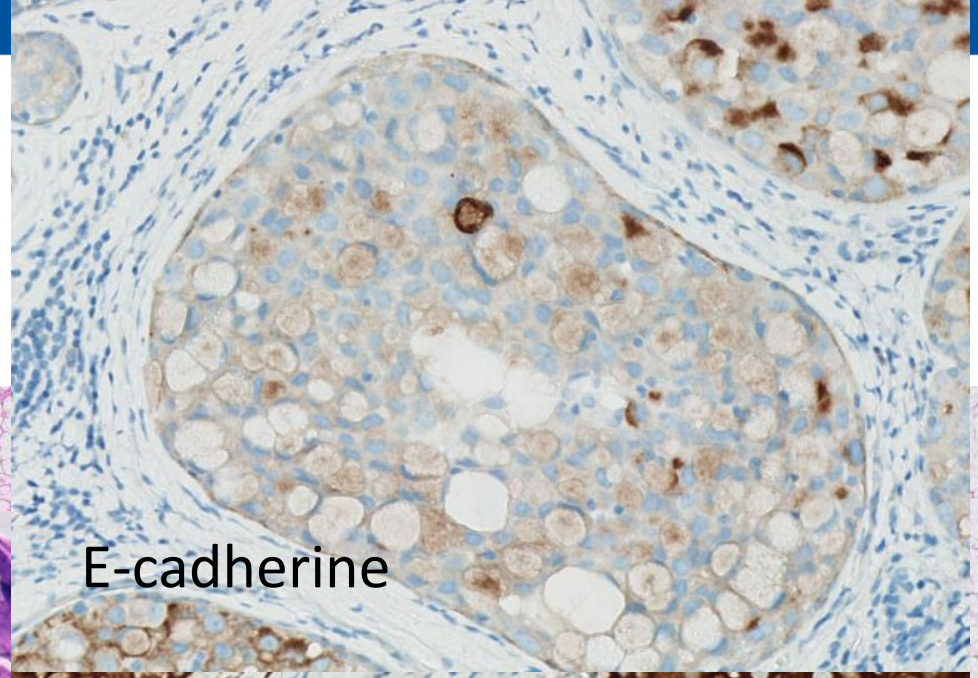
Intraductal papillary carcinoma (syn. papillary DCIS)

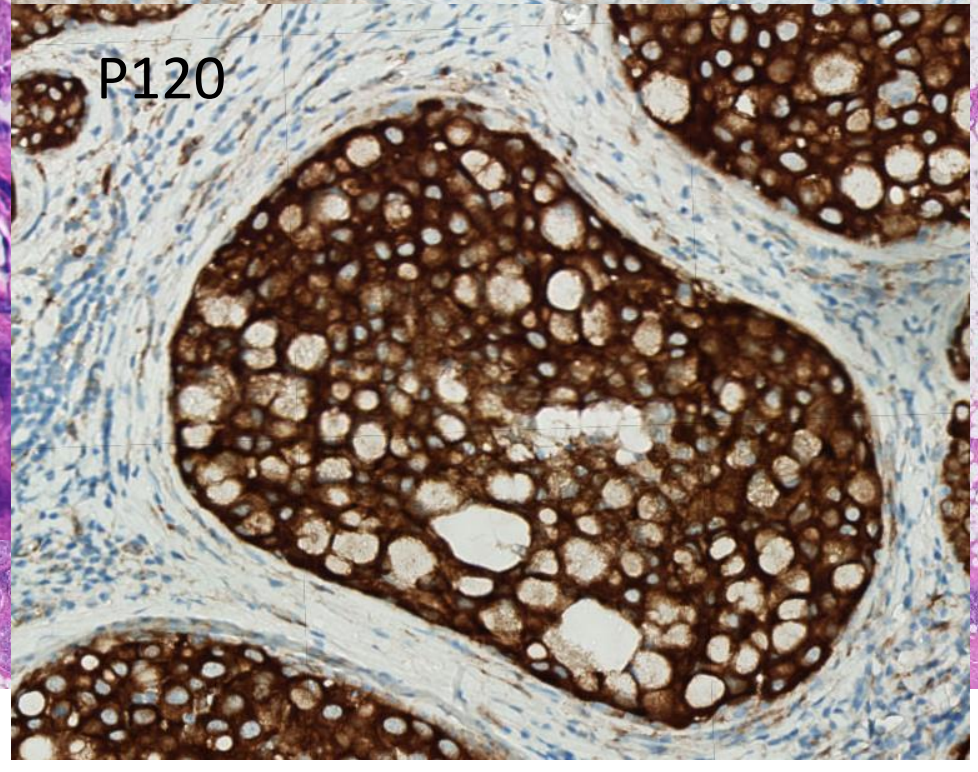




~~DCIS~~ LCIS

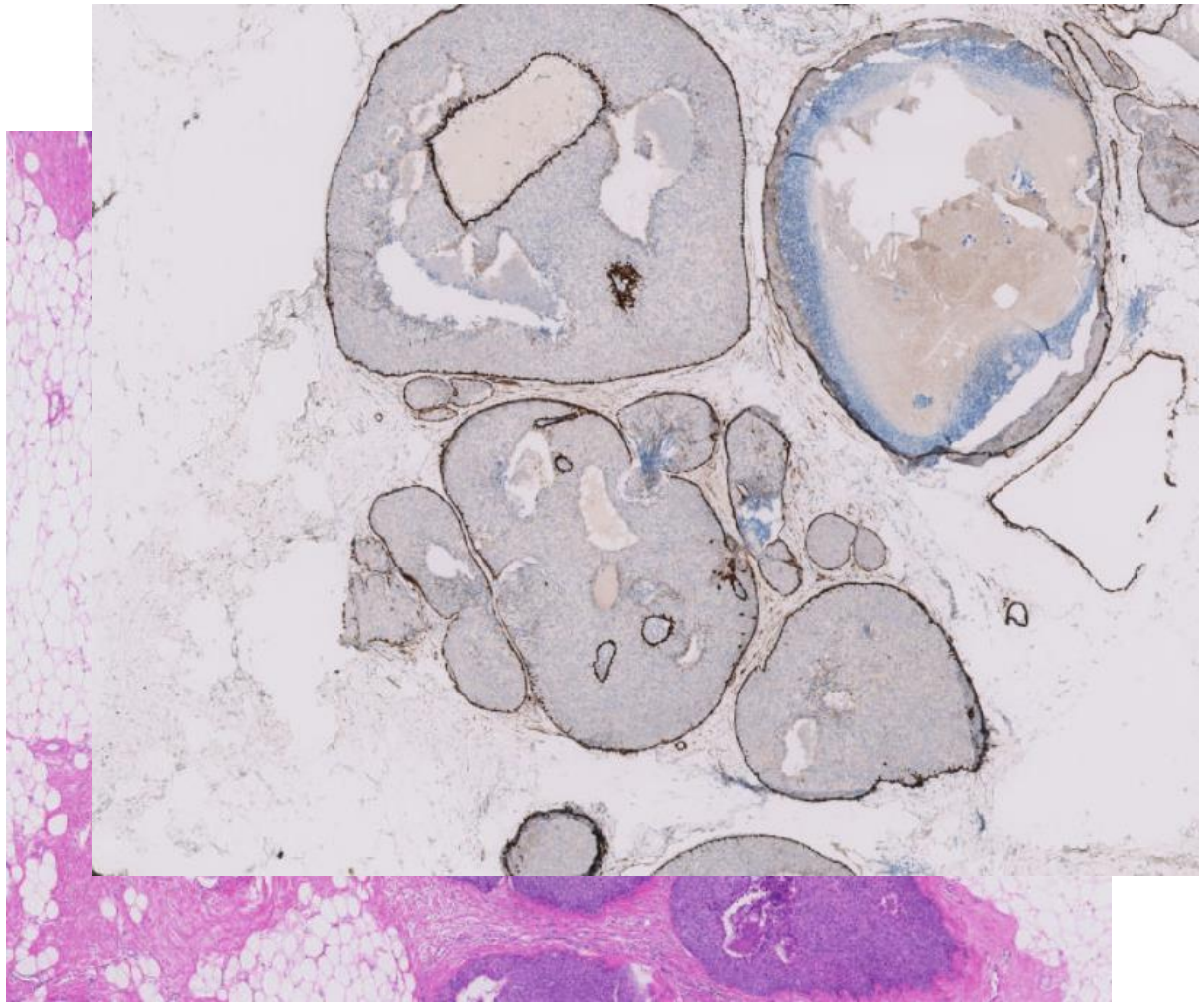


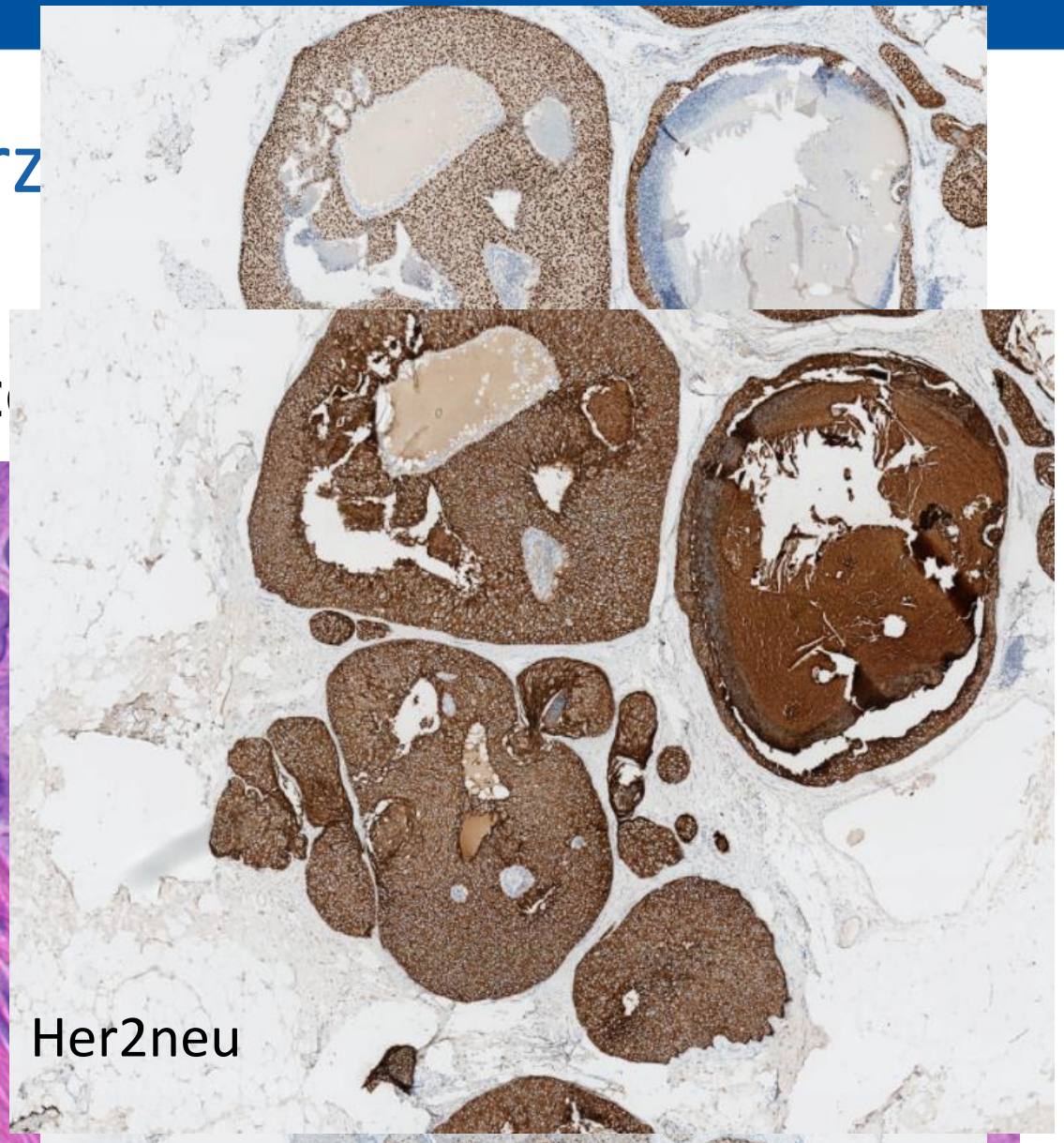




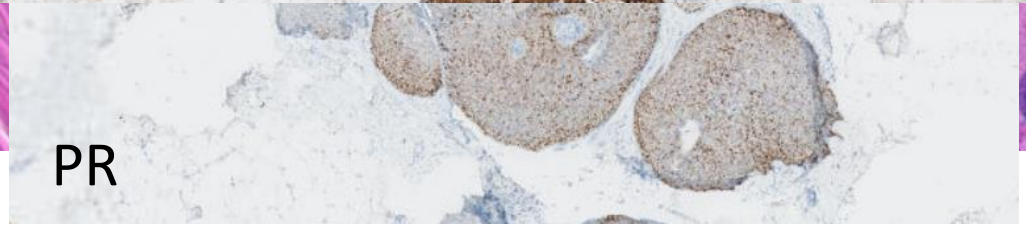
Immuunhistochemisch onderz

rec





Her2neu



PR

Immuunhistochemisch onderzoek

- Oest
- Her2
- P53
- MIB

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952 Official journal of the United States and Canadian Academy of Pathology

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Breast ductal carcinoma *in situ* carry mutational driver events representative of invasive breast cancer

Jia-Min B Pang[1,2], Peter Savas[3], Andrew P Fellowes[1], Gisela Mir Arnau[4], Tanjina Kader[5,6], Ravikiran Vedururu[1], Chelsee Hewitt[1], Elena A Takano[1], David J Byrne[1], David YH Choong[1], Ewan KA Millar[7,8,9,10], C Soon Lee[10,11,12], Sandra A O'Toole[7,11,13], Sunil R Lakhani[14,15], Margaret C Cummings[14,15], G Bruce Mann[16,17], Ian G Campbell[5,6], Alexander Dobrovic[18], Sherene Loi[3,5], Kylie L Gorringe[2,5,6,19] and Stephen B Fox[1,2,5,19]

[1]*Department of Pathology, Peter MacCallum Cancer Centre, Grattan Street, Melbourne, VIC, Australia;*
[2]*Department of Pathology, University of Melbourne, Grattan Street, Parkville, Melbourne, VIC, Australia;*
[3]*Division of Research and Cancer Medicine, Peter MacCallum Cancer Centre, Grattan Street, Melbourne, VIC,*

Immuunhistochemisch onderzoek

- Oestrogeen en progesteron receptor
- Her2neu
- P
- M

122 *Annals of Clinical & Laboratory Science, vol. 41, no. 2, 2011*

Grading Ductal Carcinoma in Situ of the Breast Using an Automated Proliferation Index

Christopher J. Stasik[1], DO, Marilyn Davis[1], BS, SCT, Bruce F Kimler[2], PhD, Fang Fan[1], MD, PhD, Ivan Damjanov[1], MD, PhD, Patricia Thomas[1], MD, Ossama W Tawfik[1], MD, PhD.
Departments of [1]Pathology and Laboratory Medicine, [2]Radiation Oncology, University of Kansas Medical Center, Kansas City, KS 66160 USA

Abstract. Tumor grade, size and margin status are the most significant factors in predicting the behavior of ductal carcinoma in-situ (DCIS). The inclusion of necrosis and nuclear grade in the grading of