

Malpighi's portrait. Engraving from a painting of Carlo Cignani (1628-1724).



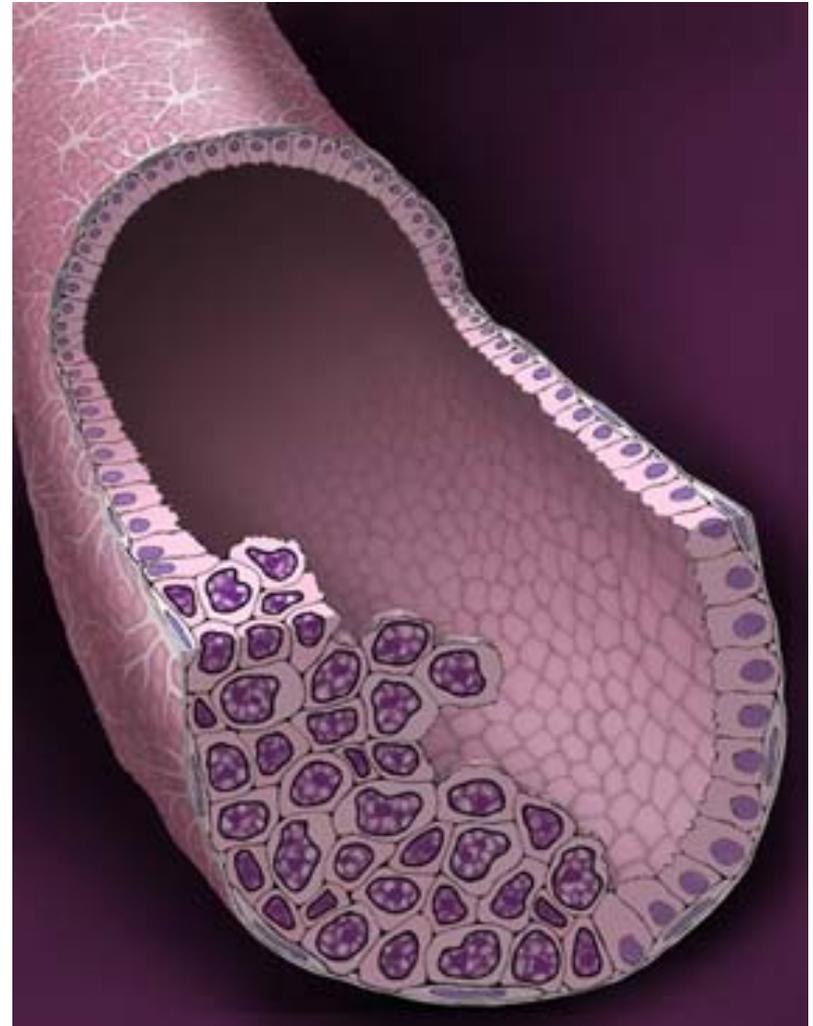
*Università di Bologna*

# **CARCINOMA IN SITU DELLA MAMMELLA**

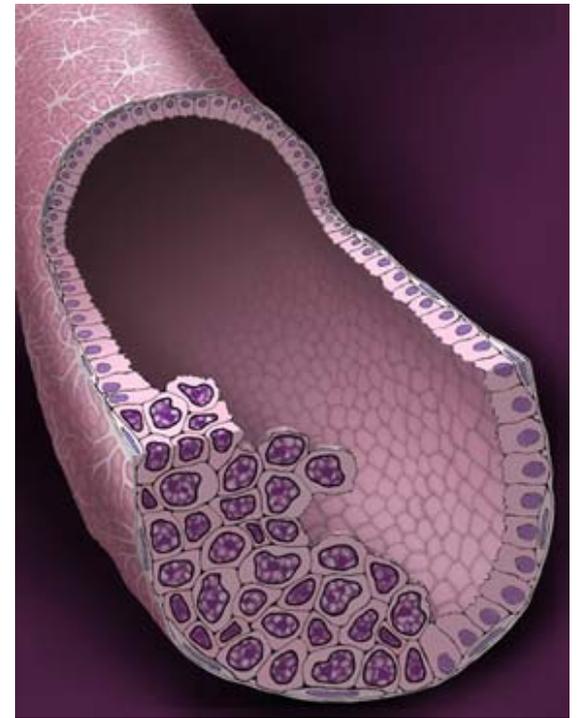
**Maria Pia Foschini**  
**Sezione di Anatomia, Istologia**  
**e Citologia Patologica**  
**Università di Bologna**  
**Ospedale Bellaria**

# Carcinoma in situ

- **Proliferazione neoplastica confinata all'interno del dotto o acino**



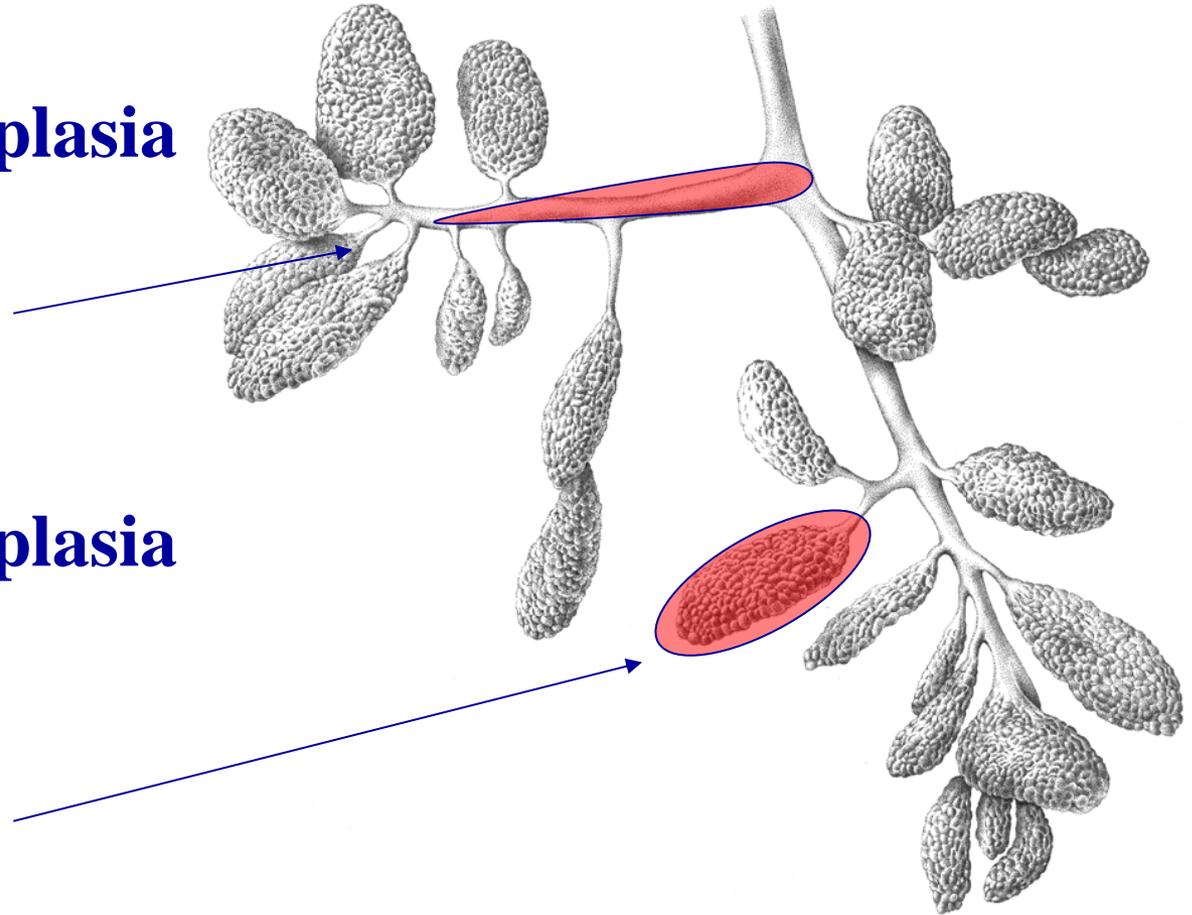
# Carcinoma in situ



- *NON potenziale metastatico*
- **Tavassoli: Terminologia alternativa**
  - “Neoplasia duttale intraepiteliale” **DIN**
  - “Neoplasia lobulare” **LN**

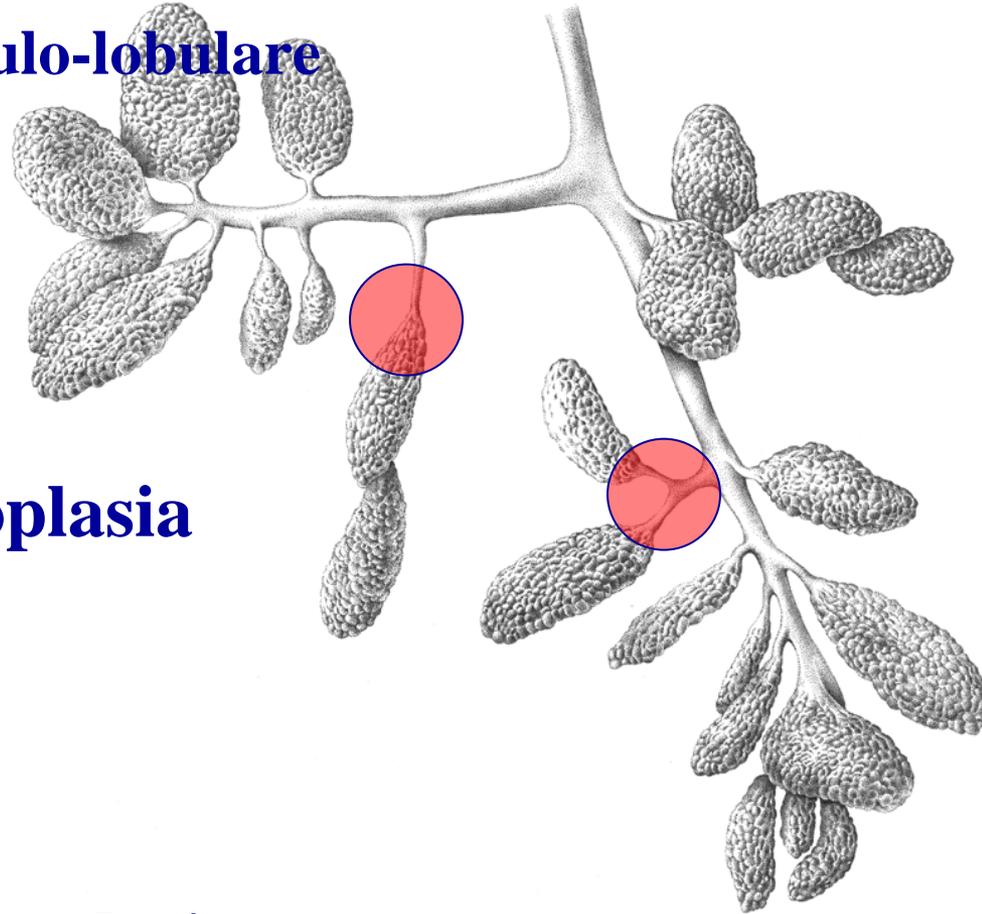
# Carcinoma in situ

- Carcinoma\ neoplasia  
duttale in situ
- CDIS\ DIN
- Carcinoma\ neoplasia  
lobulare in situ
- CLIS\ LN



**Origine dalla TDLU**

**Unità terminale duttulo-lobulare**



**•Carcinoma\ neoplasia  
duttale in situ  
CDIS\DN**

**•Carcinoma\ neoplasia  
lobulare in situ CLIS\LN**

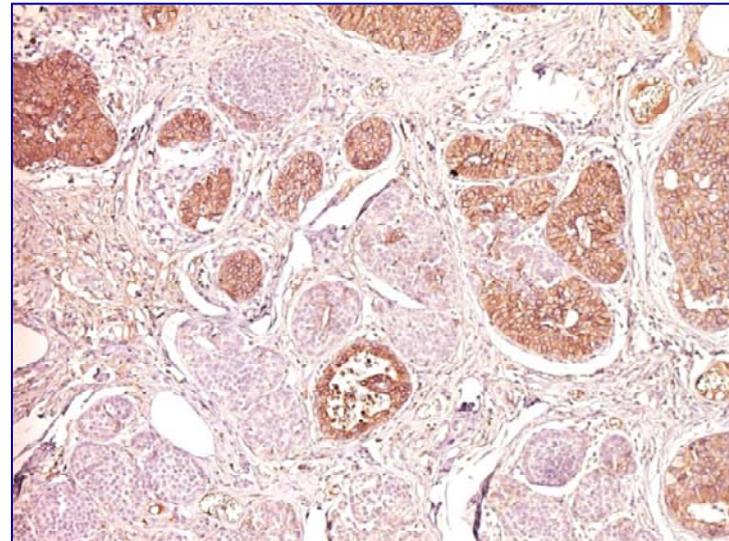
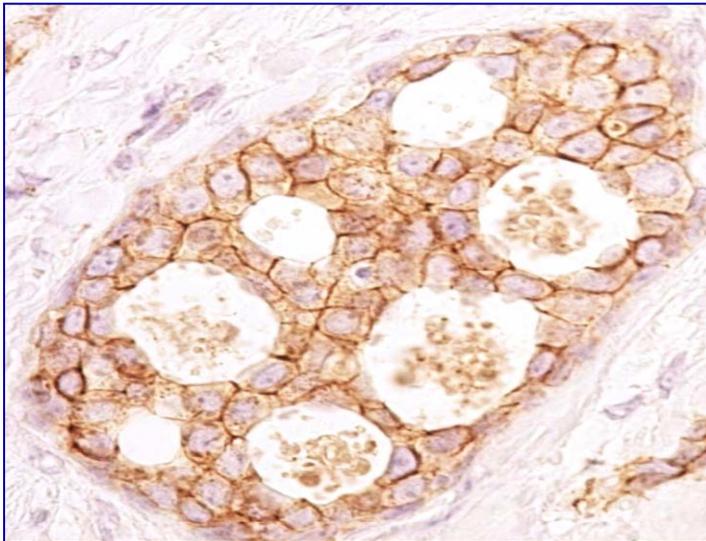
**CDIS\DN**

**CLIS\LN**

**DIVERSO ASPETTO MORFOLOGICO**

**DIVERSA ESPRESSIONE DI CADHERINA E**

**DIVERSO TIPO DI CRESCITA ED  
ESTENSIONE NELLA GHIANDOLA  
MAMMARIA**



# CIDS \DIN

- Vari sistemi di grading

*Grading CDIS secondo*

*Holland R, Peterse JL, Millis RR, Eusebi V,  
Faverly D, van de Vijver MJ, Zafrani B.*

*Ductal carcinoma in situ: a proposal for a new  
classification.*

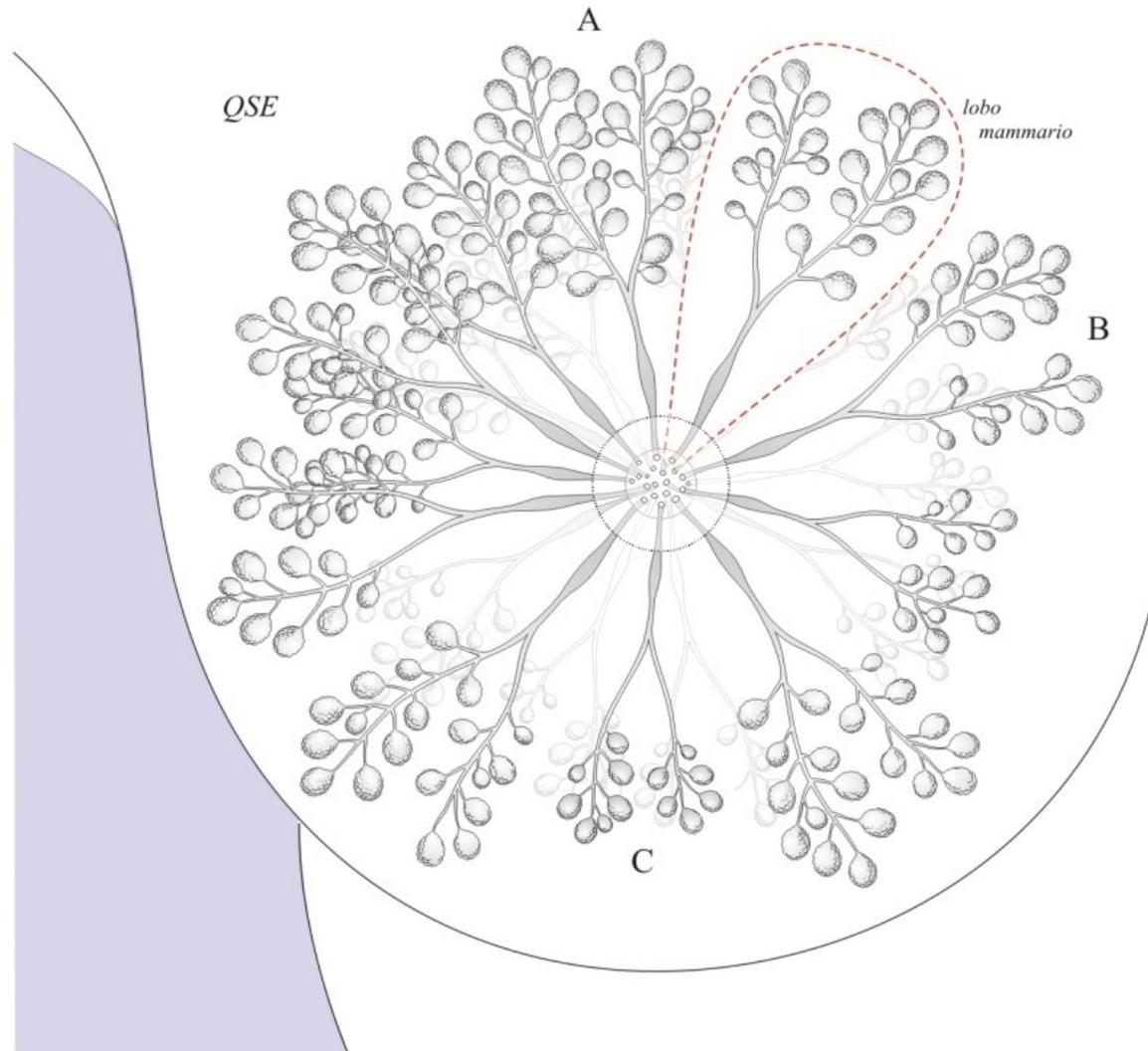
*Semin Diagn Pathol 1994;11:167-80.*

**Basata sull'aspetto citologico**

**Buona correlazione con aspetto mammografico ed estensione  
nella ghiandola mammaria**

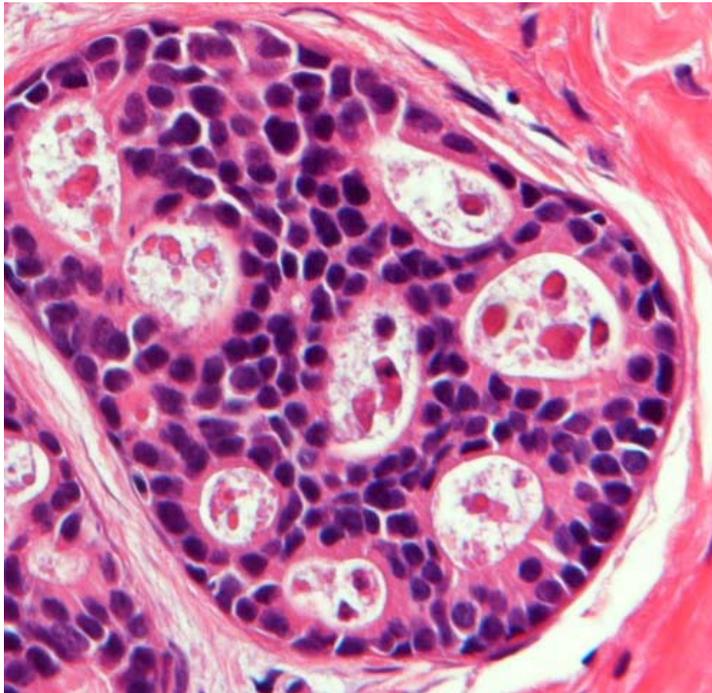
# Tot T. The theory of the sick breast lobe and the possible consequences

Int J Surg Pathol. 2007 Oct; 15(4):369-75

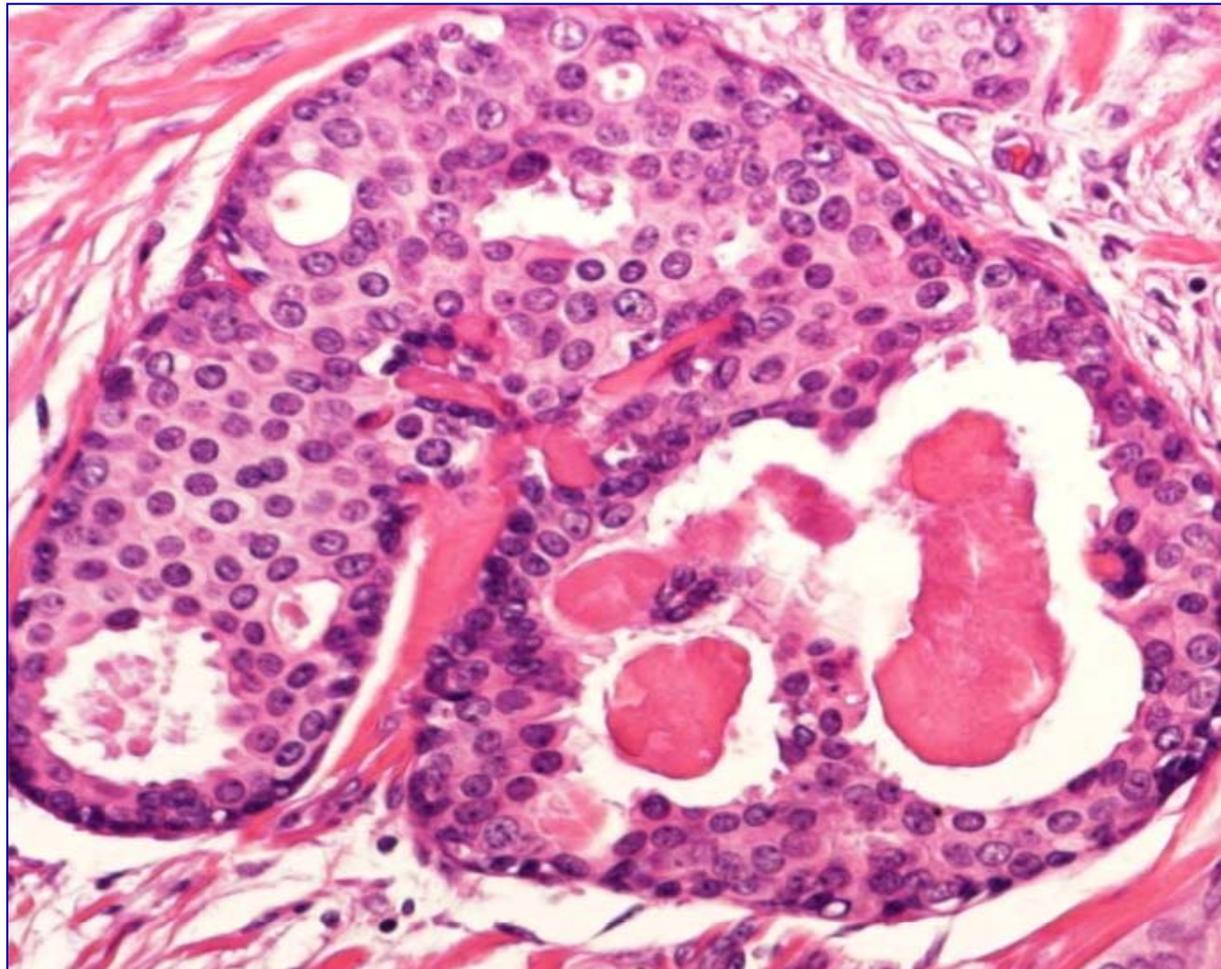


# Carcinoma duttale in situ

- Ben differenziato
- Grado 1
- Buona prognosi
- Poco differenziato
- Grado 2 - 3
- Aggressivo

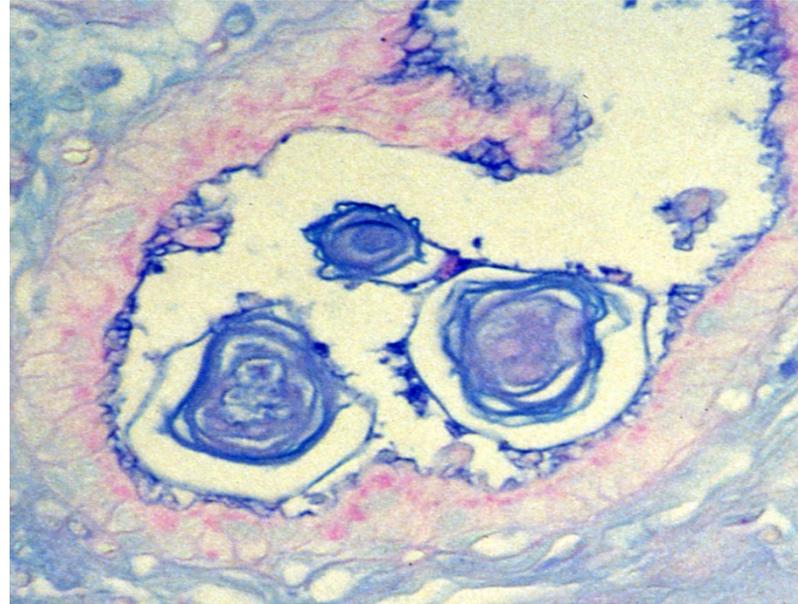


# CDIS\DIN grado 1



# CDIS: **Microcalcificazioni**

- Ben differenziato
- **Microcalcificazioni lamellari (psammomatose)**
- **Deposito di Sali di calcio su mucine**



## **Microcalcifications in Ductal Carcinoma In Situ of the Breast:**

### **Histochemical and Immunohistochemical Study**

MARIA P. FOSCHINI, MD, ADELE FORNELLI, MD,  
JOHANNES L. PETERSE, MD, STEFANO MIGNANI, MD,  
AND VINCENZO EUSEBI, MD, FRCPATH

Thirty cases of ductal carcinoma in situ (DCIS) of the breast, showing histological microcalcifications, were studied to clarify their mechanism of formation. Undecalcified sections revealed three types of calcium precipitates: type I and II granular calcifications (GCs) and laminar calcifications (LCs). In type I GCs the core on which the calcium had deposited was constituted mainly by nuclear debris. Type II GCs were predominantly composed by mucosubstances. LCs were the result of calcium deposits on mucoid or proteinaceous material, arranged in concentric lamellae. LCs and type II GCs were mainly

present in well and intermediately differentiated DCIS. Type I GCs were observed in only DCIS with necrosis, frequently being present in intermediately and poorly differentiated DCIS. HUM PATHOL 27:178-183. Copyright © 1996 by W.B. Saunders Company

*Key words:* microcalcification, psammoma body, breast, ductal carcinoma in situ.

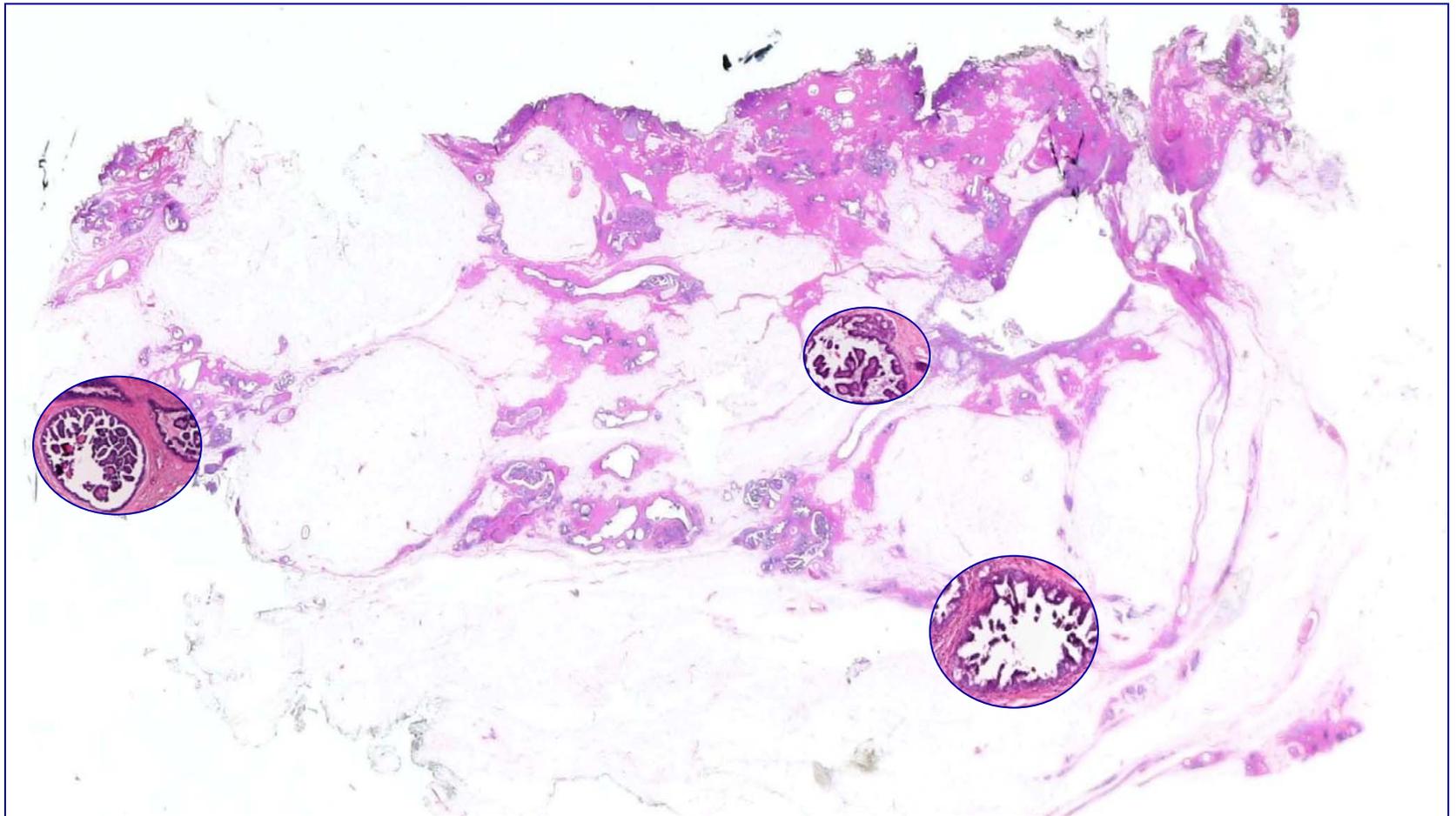
*Abbreviations:* DCIS, ductal carcinoma in situ; GC, granular calcification; LC, laminar calcification; HE, hematoxylin-eosin; AB, Alcian blue; PAS, periodic acid-Schiff; EMA, epithelial membrane antigen.

# CDIS Ben differenziato

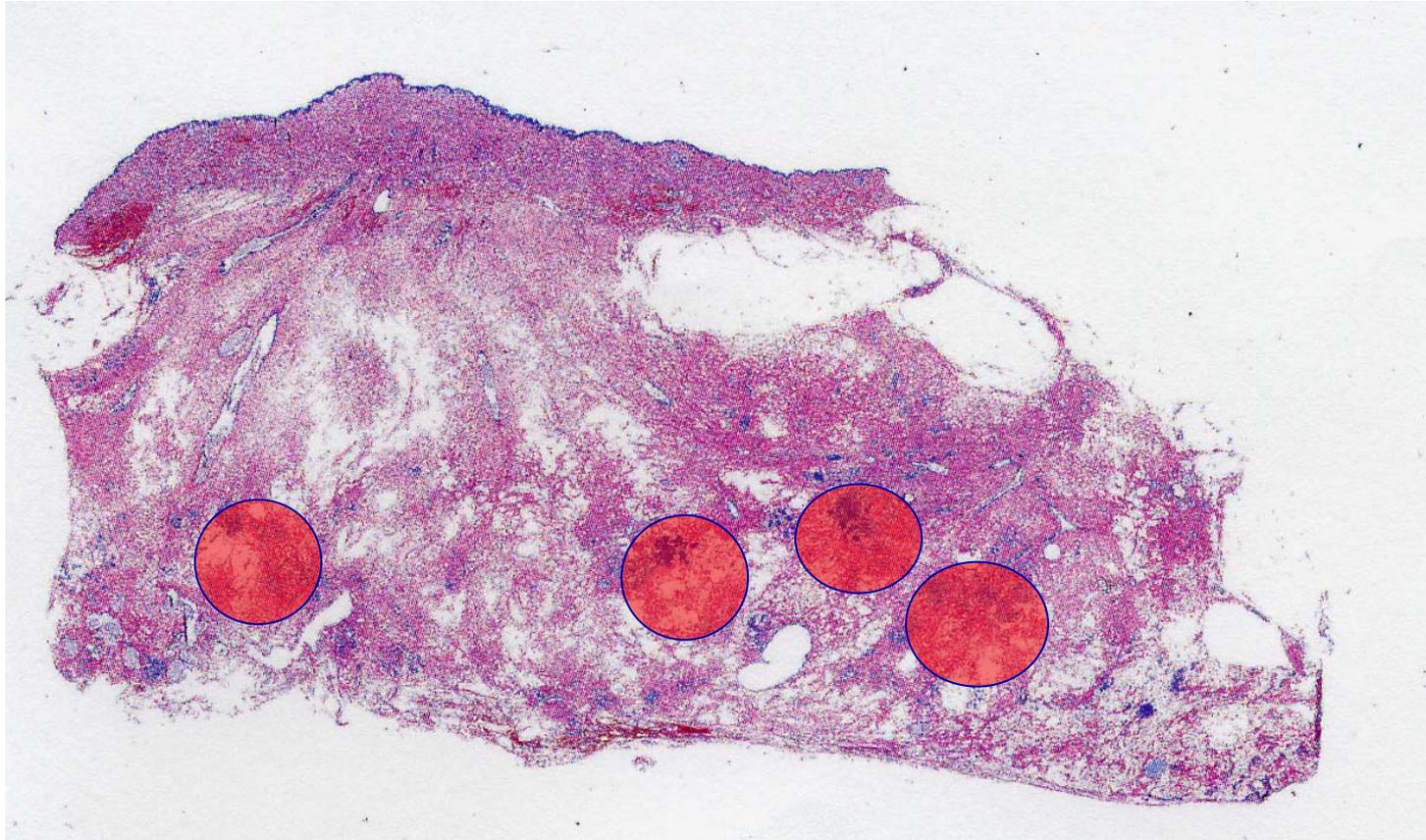
•Le cellule neoplastiche proliferano lungo uno stesso sistema duttale, ma in maniera discontinua



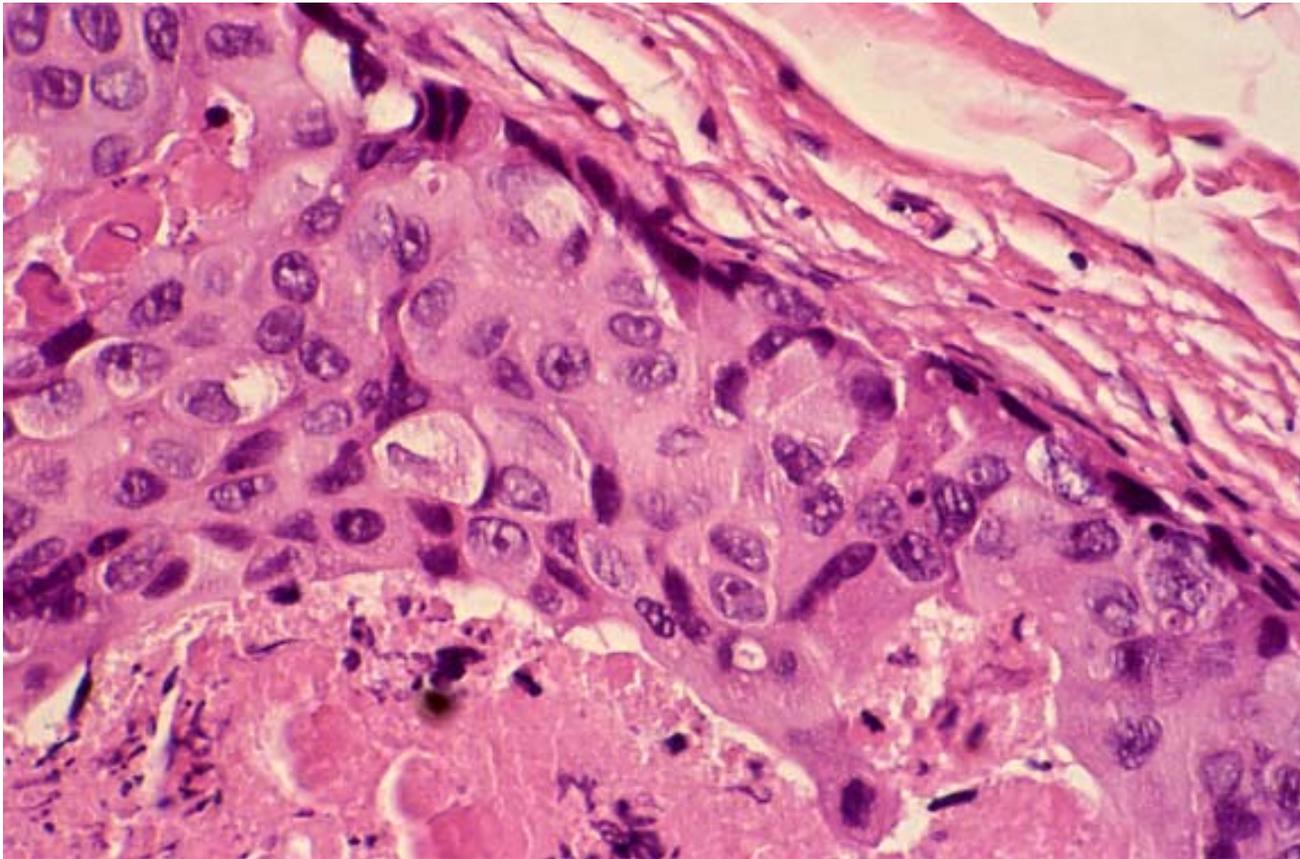
# CDIS GRADO 1



# CDIS Ben differenziato



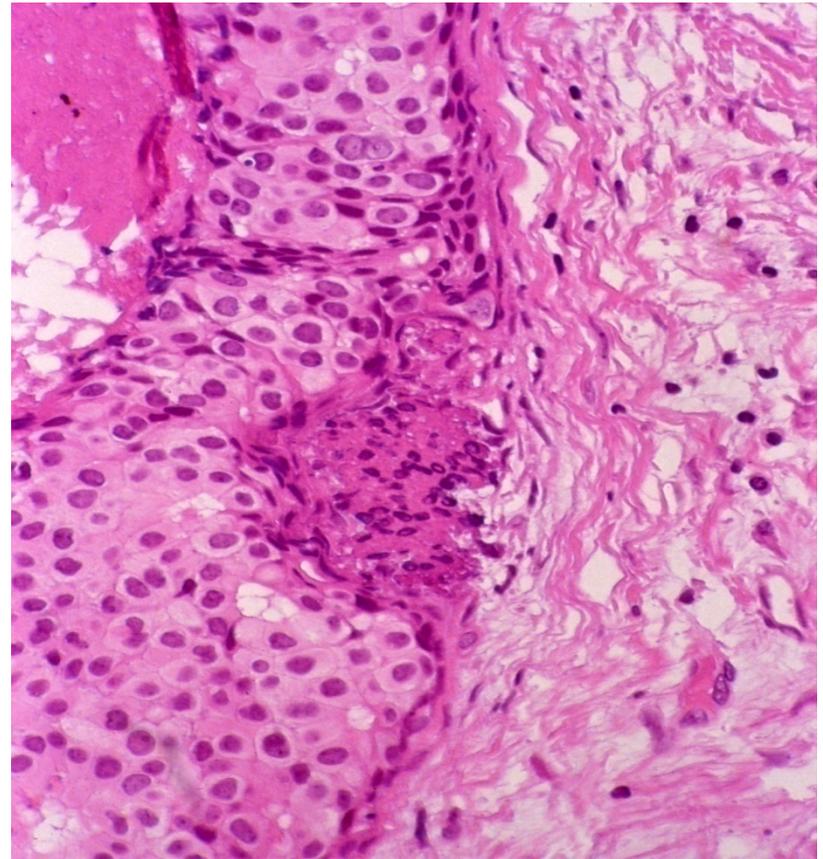
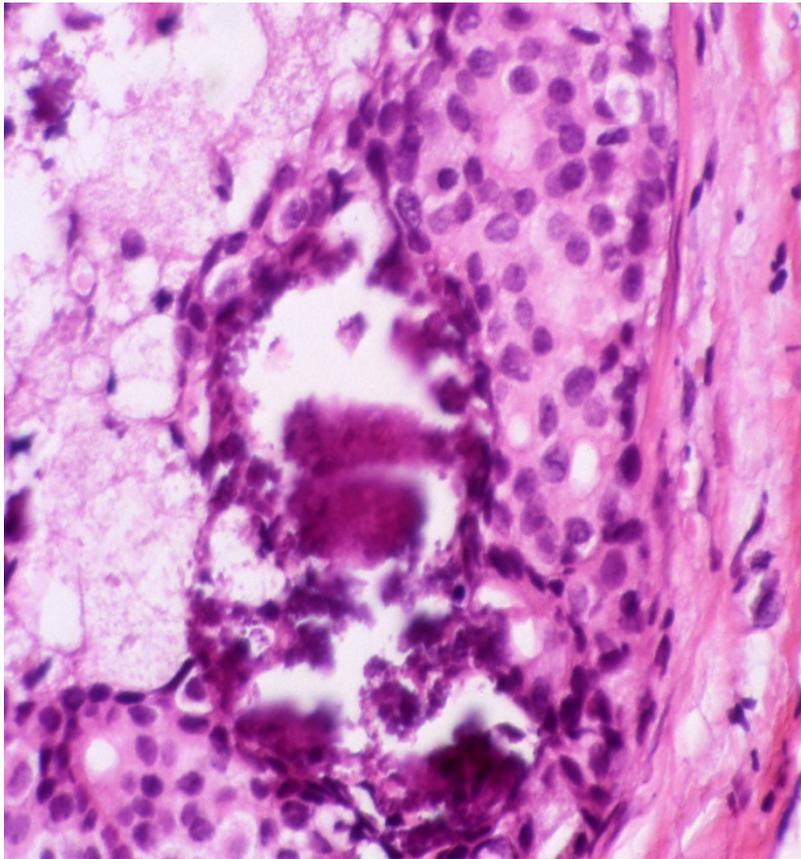
# CDIS Poco differenziato



# **CDIS Poco differenziato**

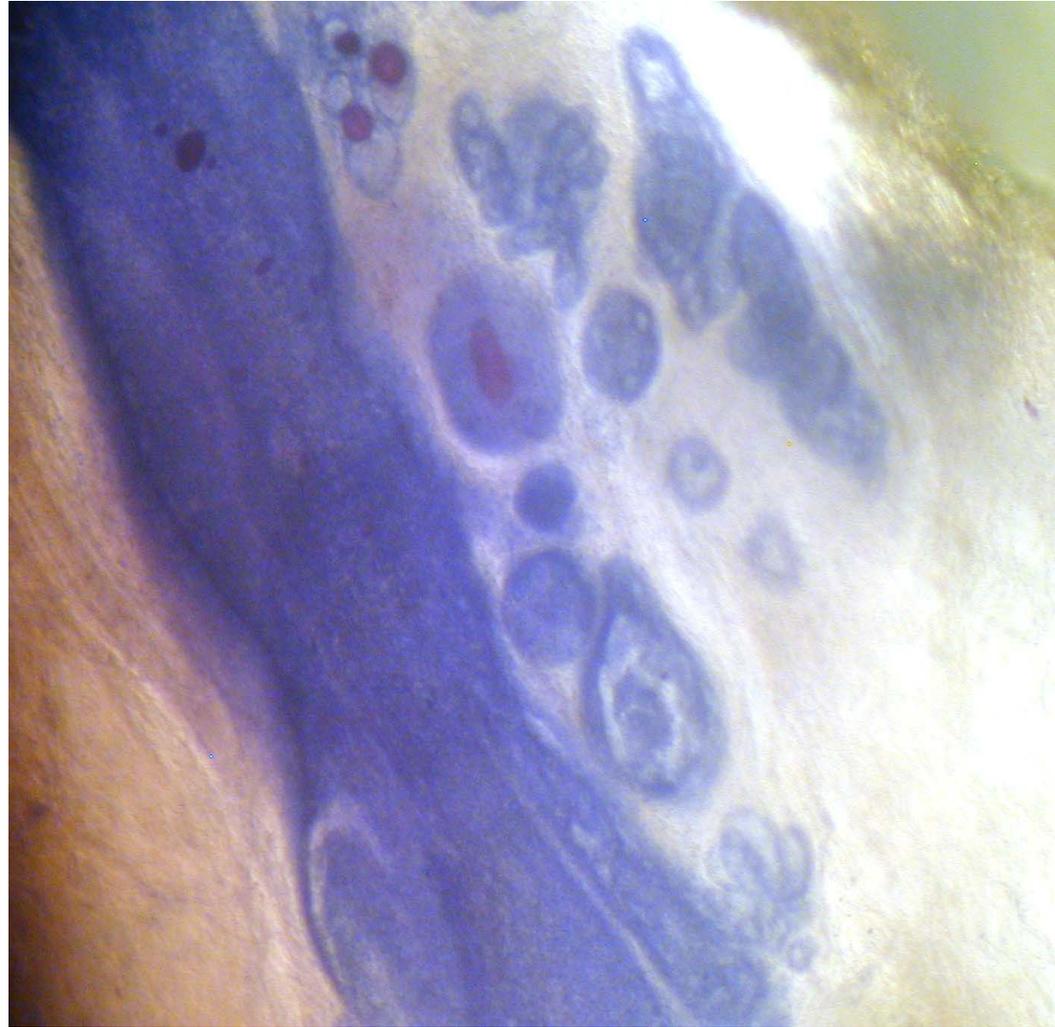
**Microcalcificazioni granulari**

**• Deposito di Sali di calcio su detriti di cellule necrotiche**



# CDIS Poco differenziato

- Ricostruzione 3D
- Cresce in maniera continua, senza interruzioni lungo lo stesso sistema duttale (nel 90% dei casi)

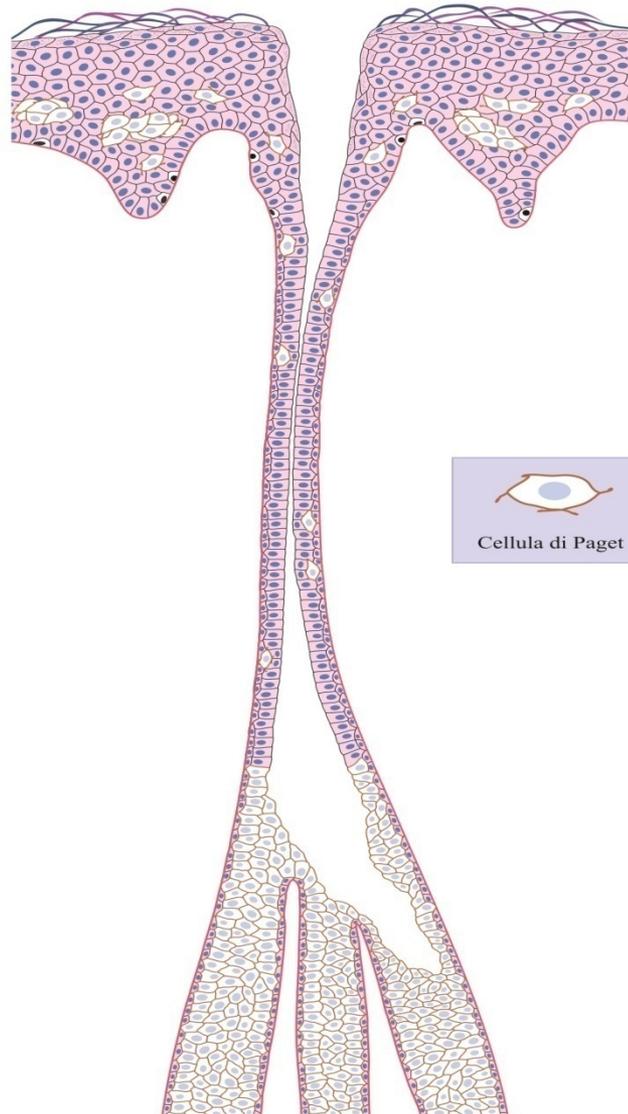


[Faverly DRG, et al. *Semin Diagn Pathol* 1994;11:193-8.

Estensione verso i

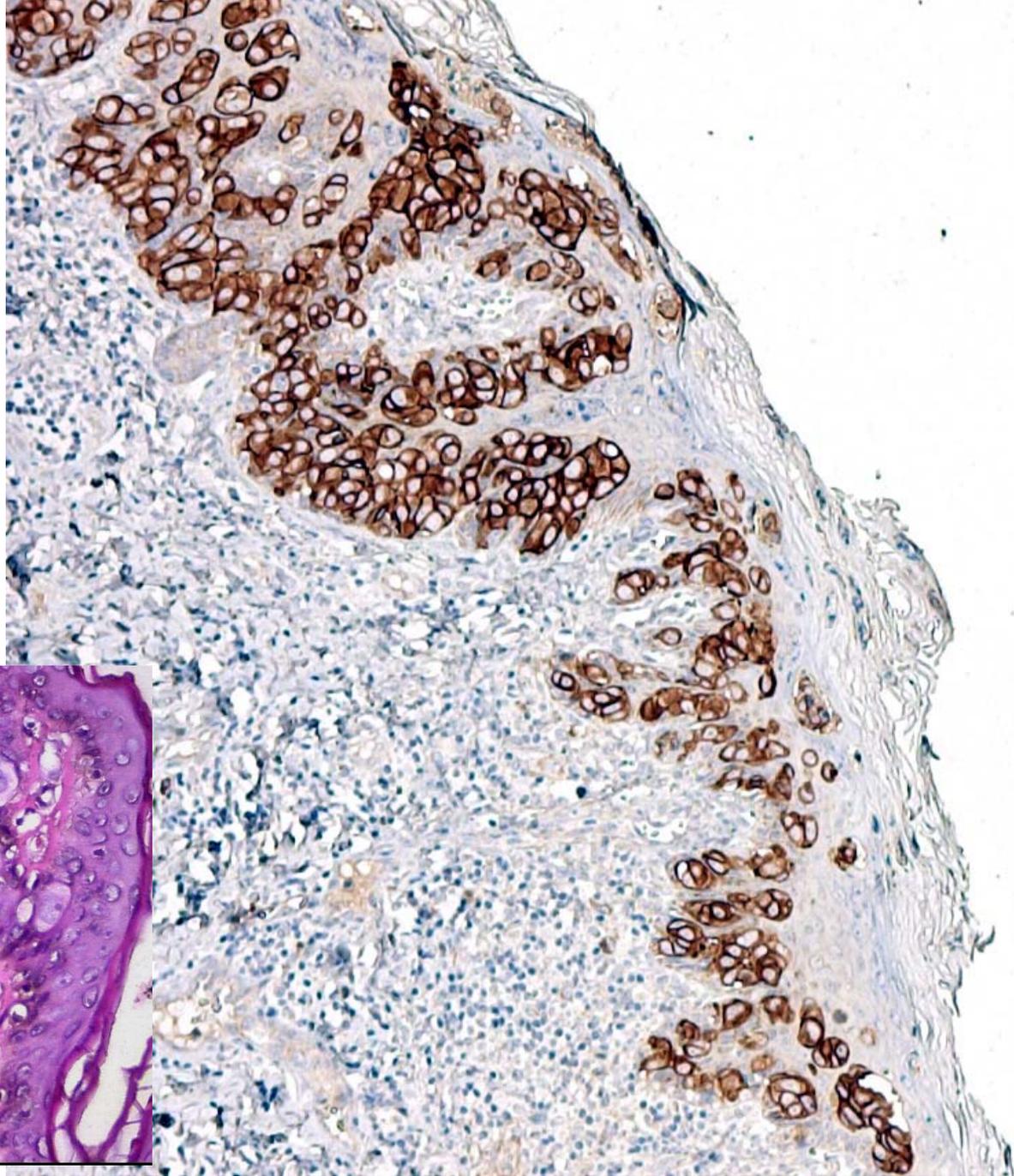
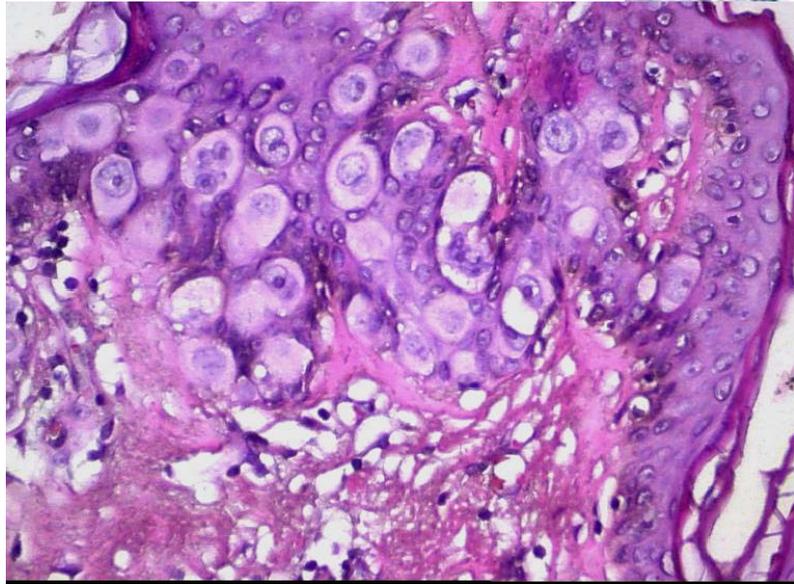
Dotti galattofori

E la cute del  
capezzolo

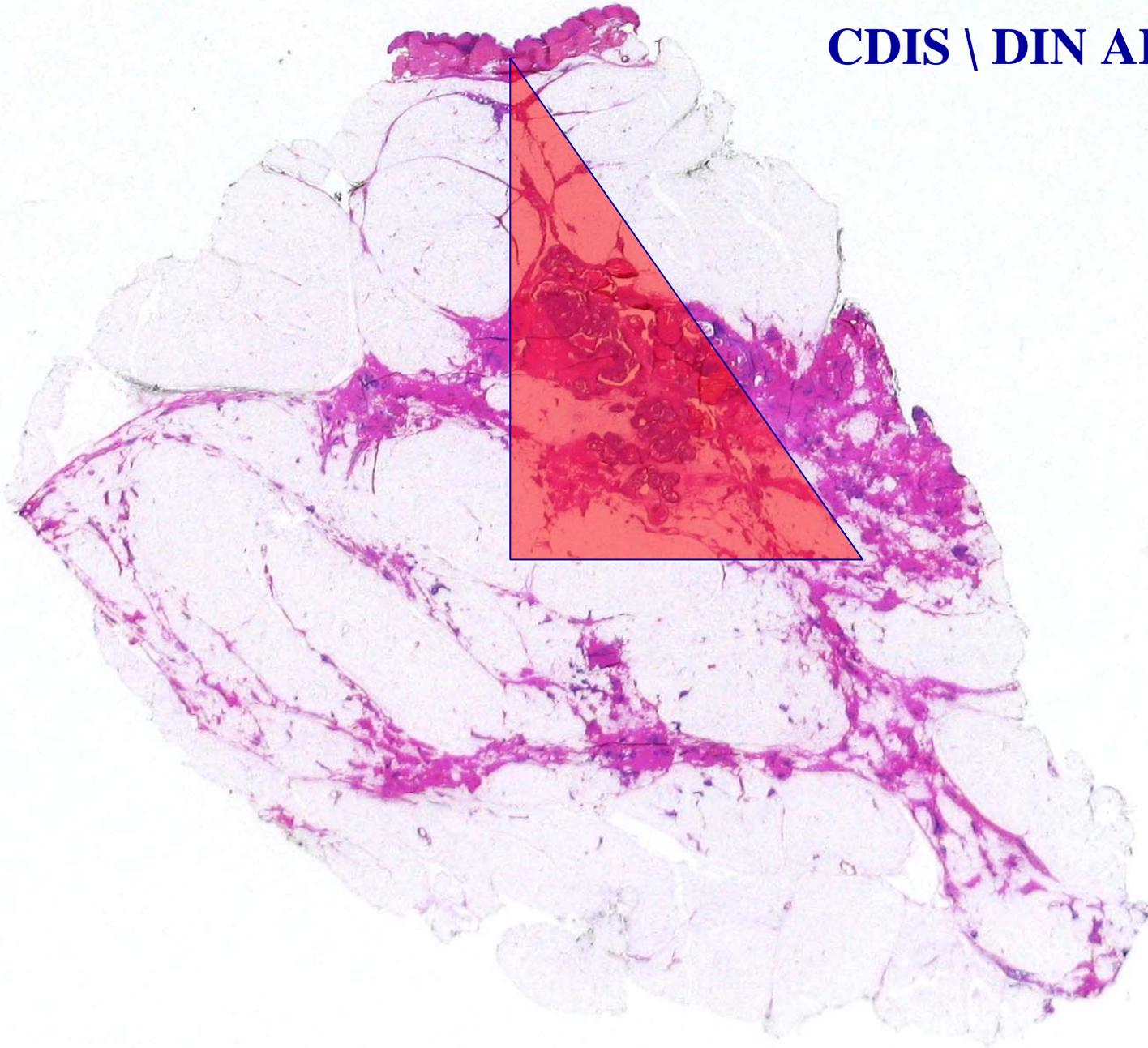


  
Cellula di Paget

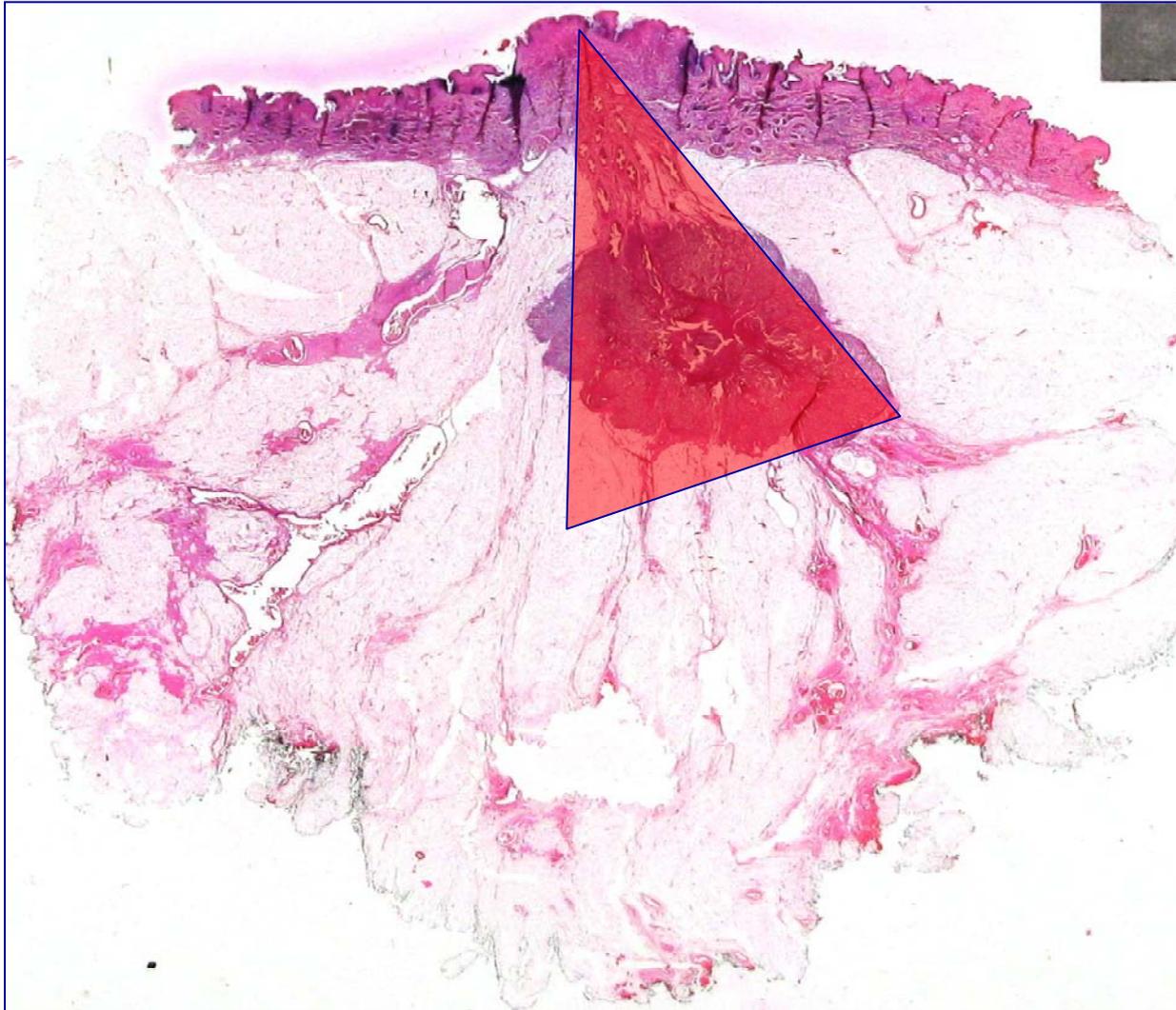
# Carcinoma di Paget



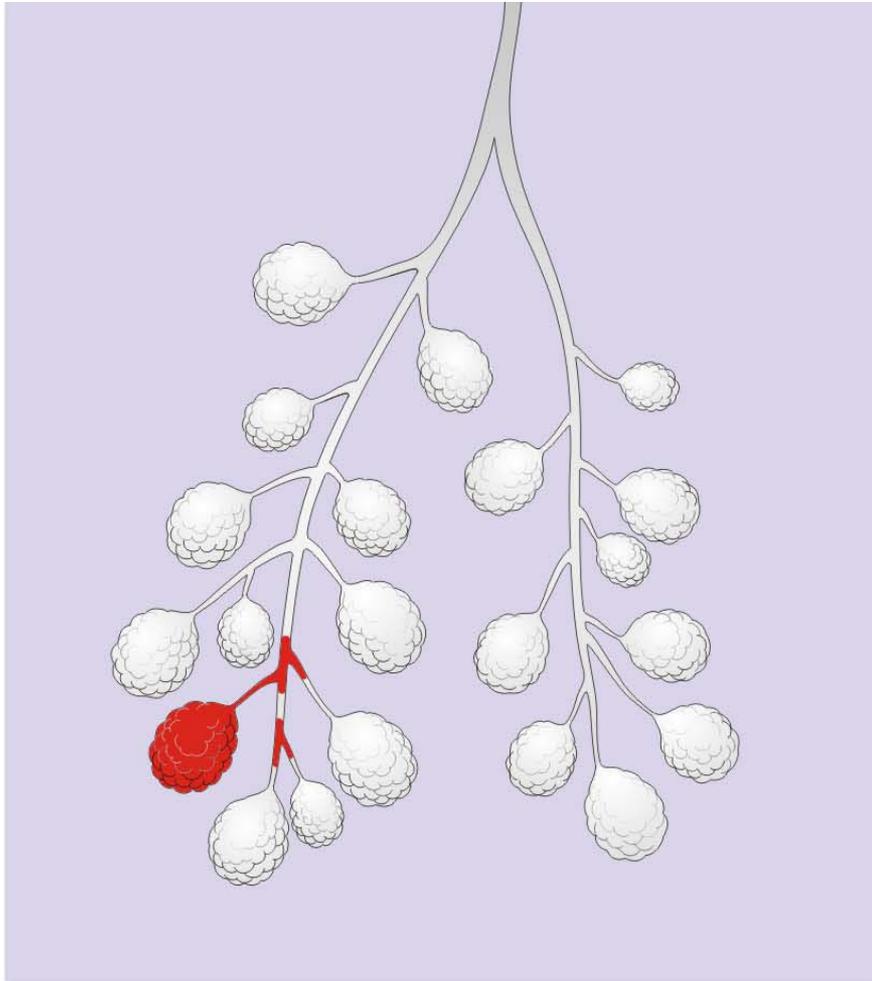
**CDIS \ DIN ALTO GRADO**



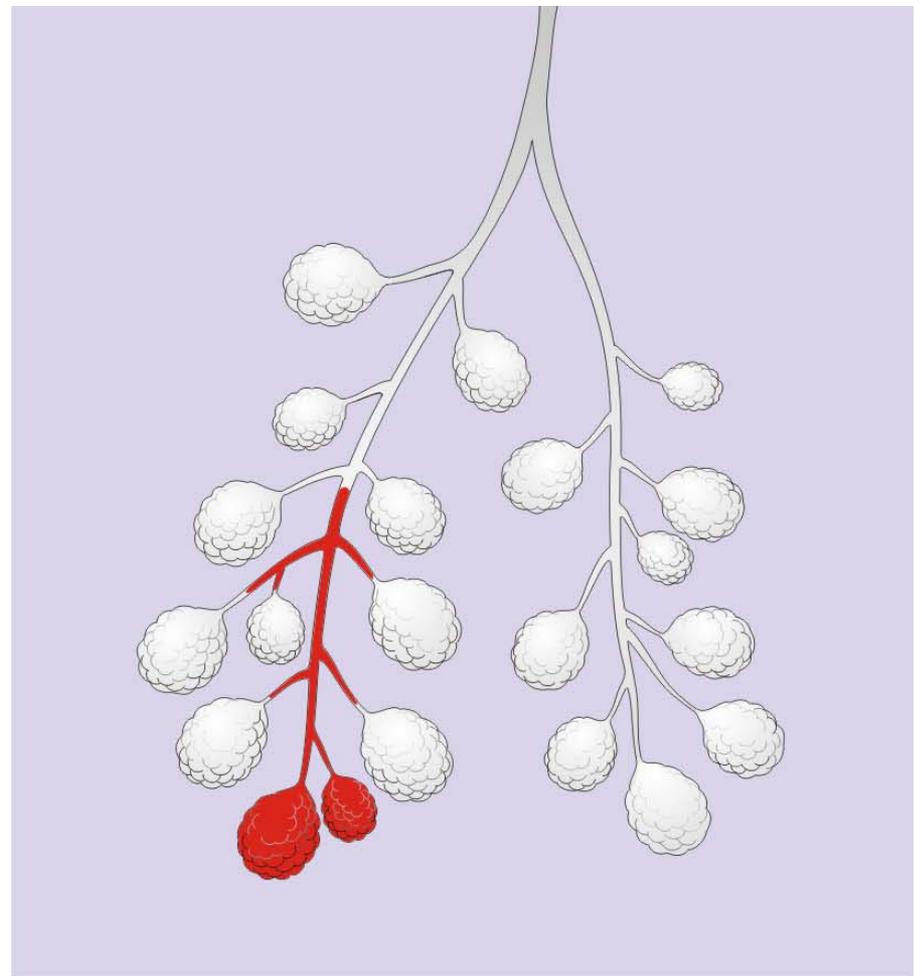
# CDIS/DIN ALTO GRADO



**CDIS \ DIN BEN  
DIFFERENZIATO**



**CDIS \ DIN POCO  
DIFFERENZIATO**

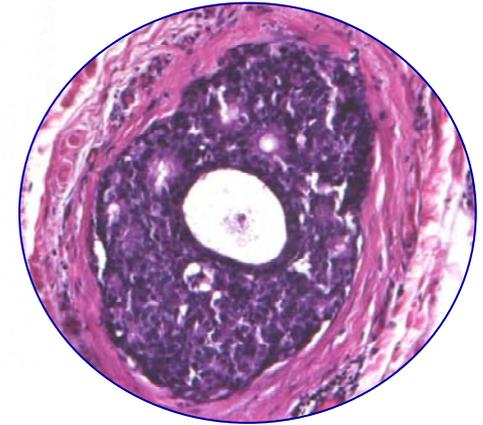




Original contribution

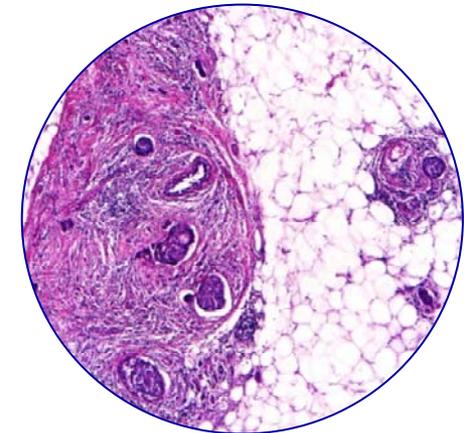
## The impact of large sections on the study of in situ and invasive duct carcinoma of the breast<sup>☆</sup>

Maria P. Foschini MD<sup>a,\*</sup>, Federica Flamminio MD<sup>a</sup>, Rossella Miglio PhD<sup>d</sup>,  
Daniela G. Calò PhD<sup>d</sup>, Maria C. Cucchi MD<sup>b</sup>, Riccardo Masetti MD<sup>c</sup>,  
Vincenzo Eusebi MD, FRCPath<sup>a</sup>



### •45 MACROSEZIONI SU MASTECTOMIE

38 CDIS & CDI; 7 Solo CDIS

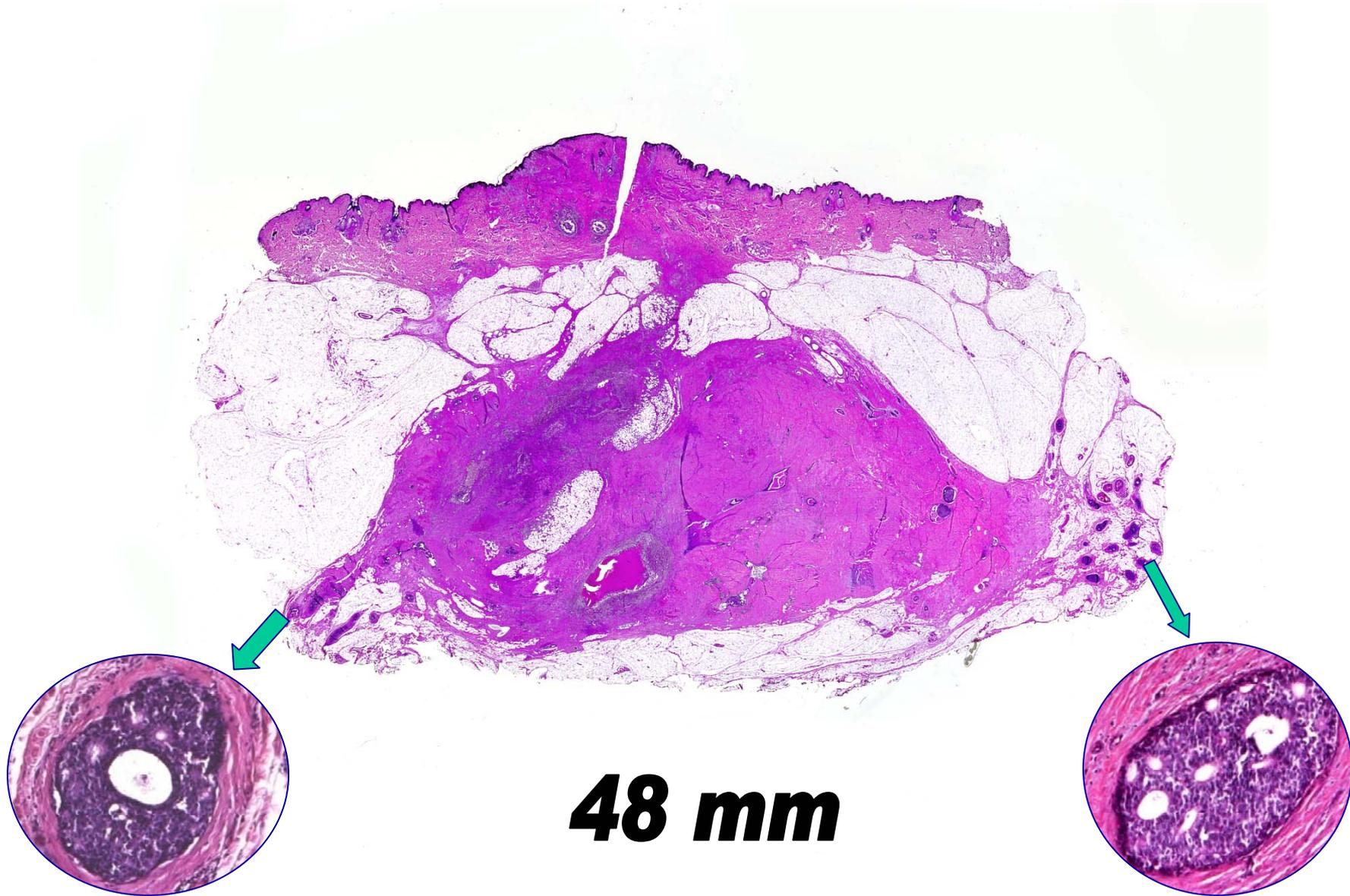


*Grading CDIS secondo Holland et al. 1994*

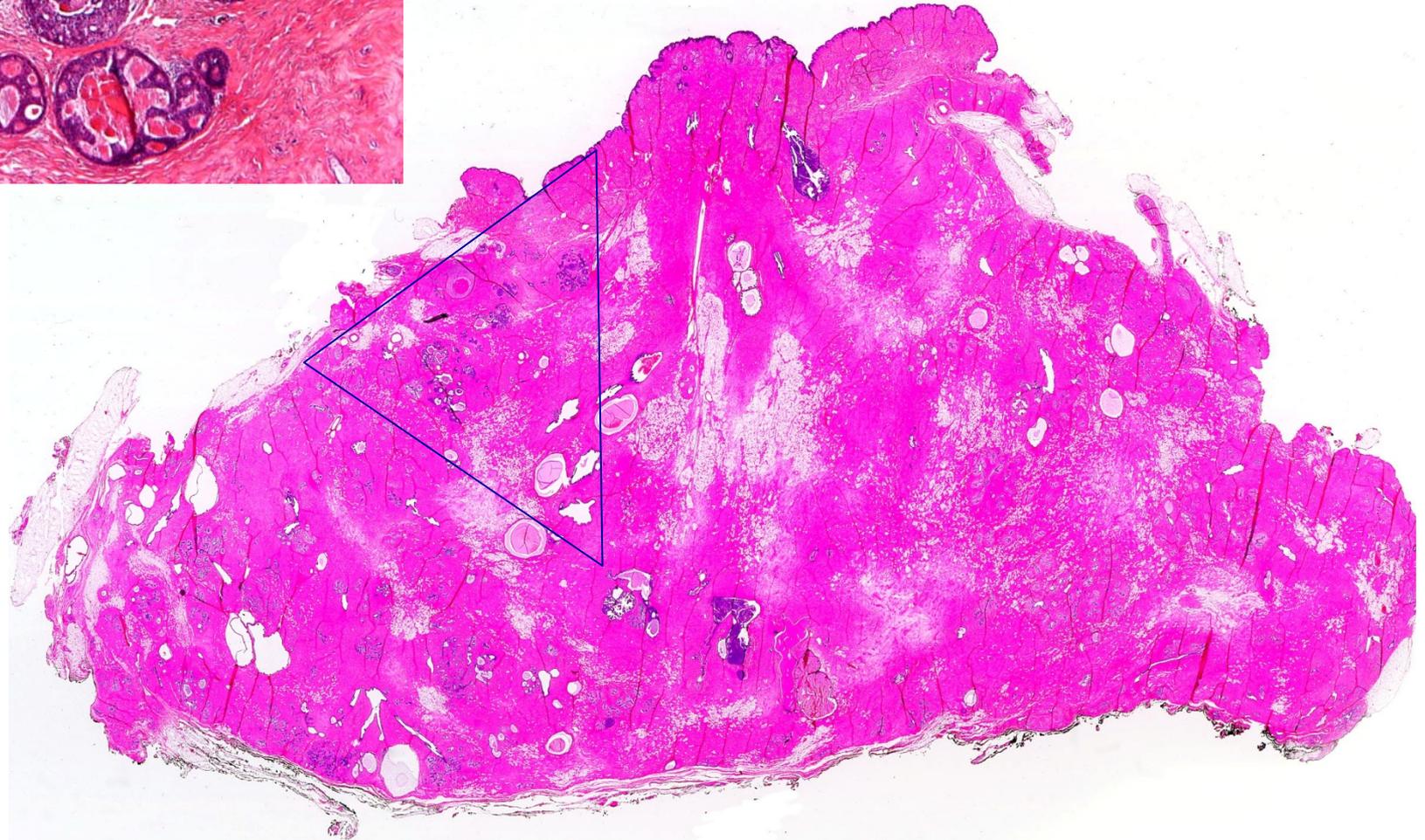
*Grading CDI secondo Elston & Ellis, 1991*

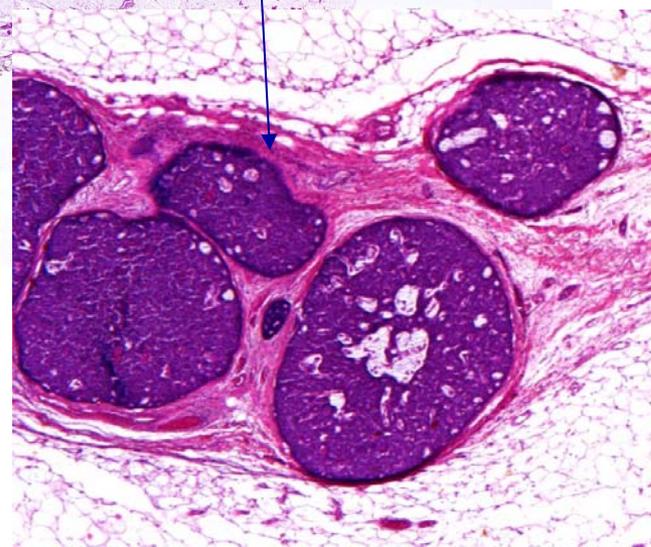
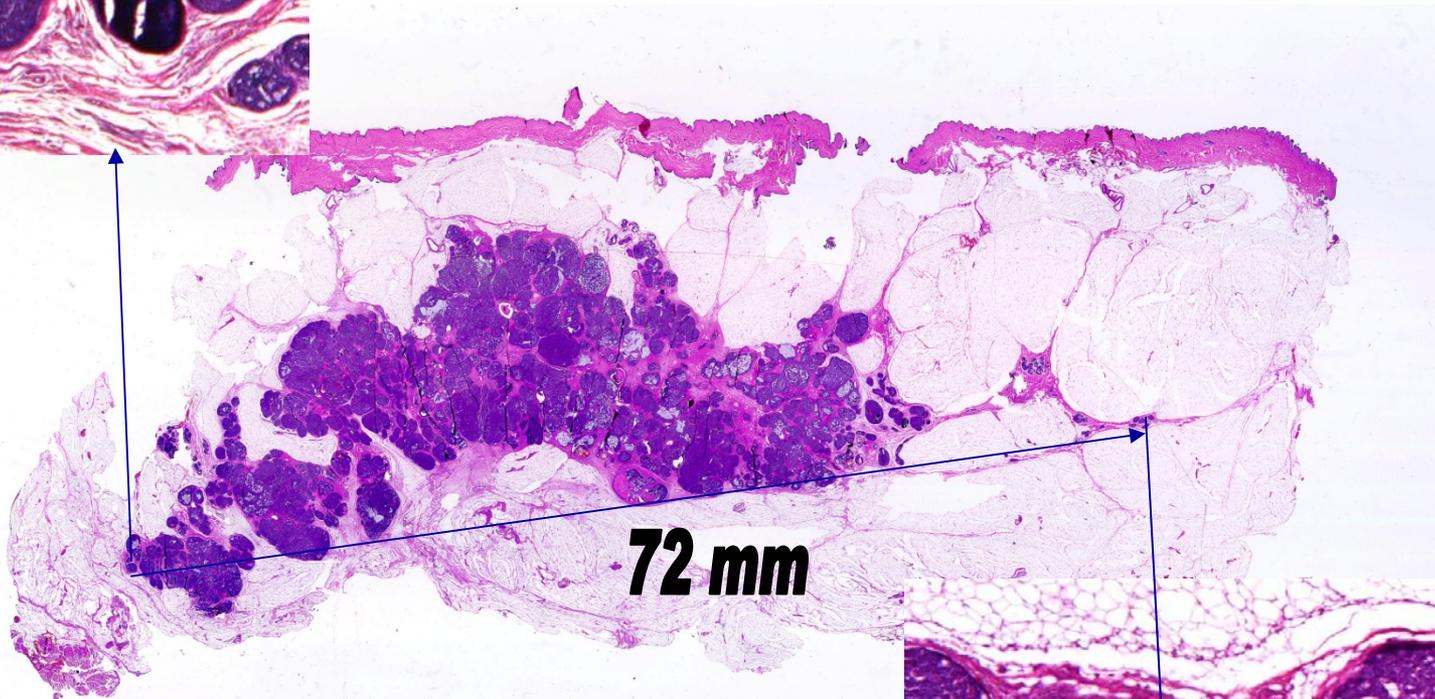
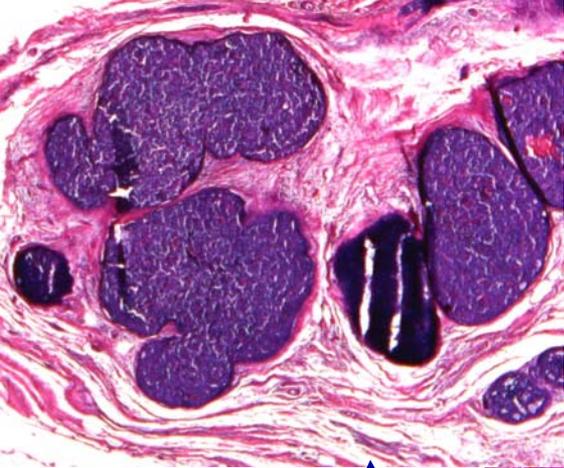
# Estensione CDIS / CLIS

Type	N. Foci Range (Mean)	>20 Foci	MD mm Range (Mean)	MD > 20mm
<b>LN - LCIS</b>	<b>2 - 77 (27.12)</b>	<b>6 (46%)</b>	<b>5 - 112 (37.9)</b>	<b>9 (69.23%)</b>
<b>DCIS gr1</b>	<b>1 &gt; 100 (35)</b>	<b>8 (61.5%)</b>	<b>12-55 (35.41)</b>	<b>10 (76.9%)</b>
<b>DCIS gr2</b>	<b>1 &gt; 100 (15.36)</b>	<b>5 (25%)</b>	<b>1-72 (15.36)</b>	<b>5 (26.3%)</b>
<b>DCIS gr3</b>	<b>1 &gt; 100 (21.28)</b>	<b>4 (33.3%)</b>	<b>1-51 (21.81)</b>	<b>5 (41.6%)</b>



**48 mm**





**CDIS\|DIN**

**Multicentrico**

**o**

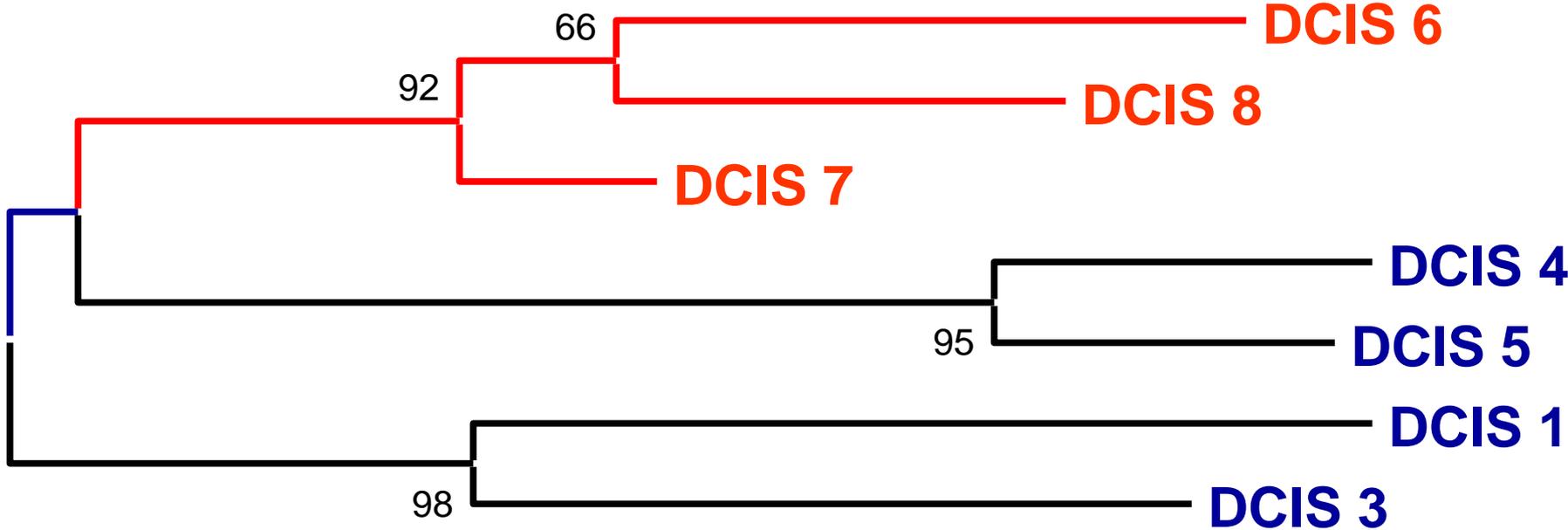
**Multifocale**

# CASE 1 G1 mtDNA

DCIS  
1,3,  
4,5,



DCIS  
6,7,8

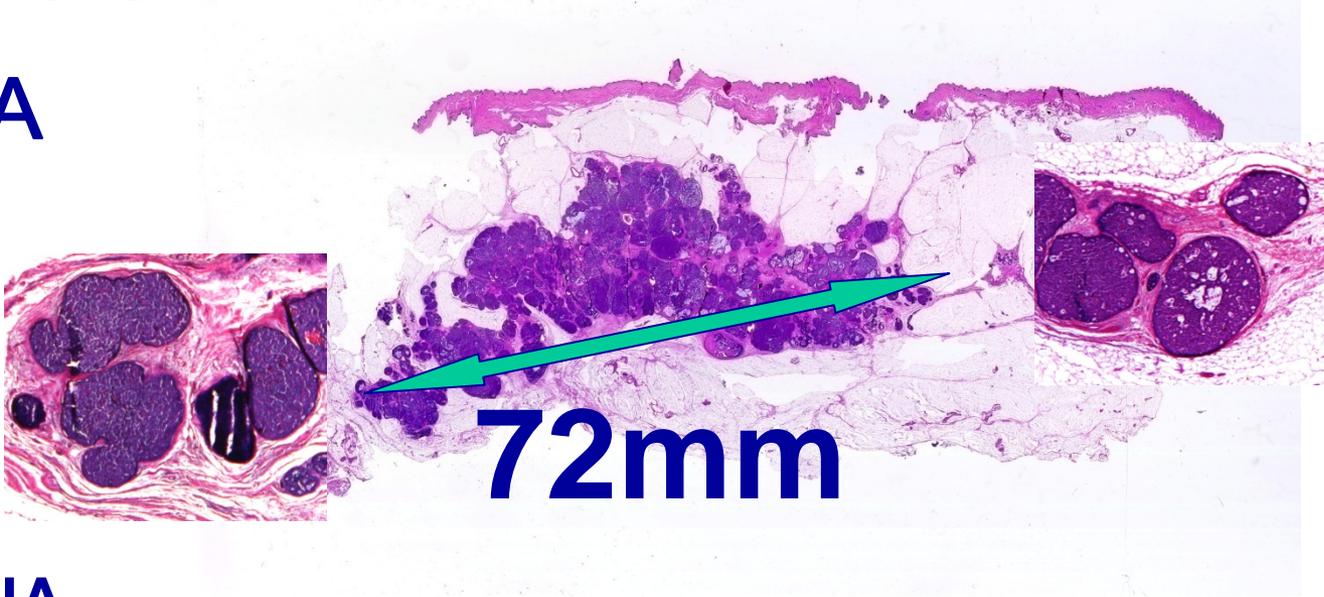


0.001

# CASE 6 G2

mtDNA

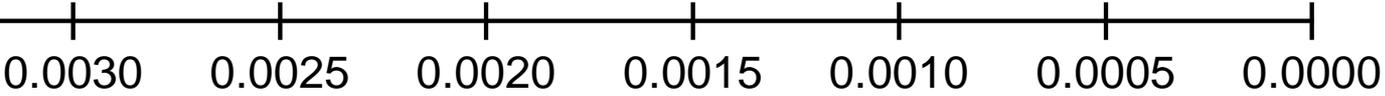
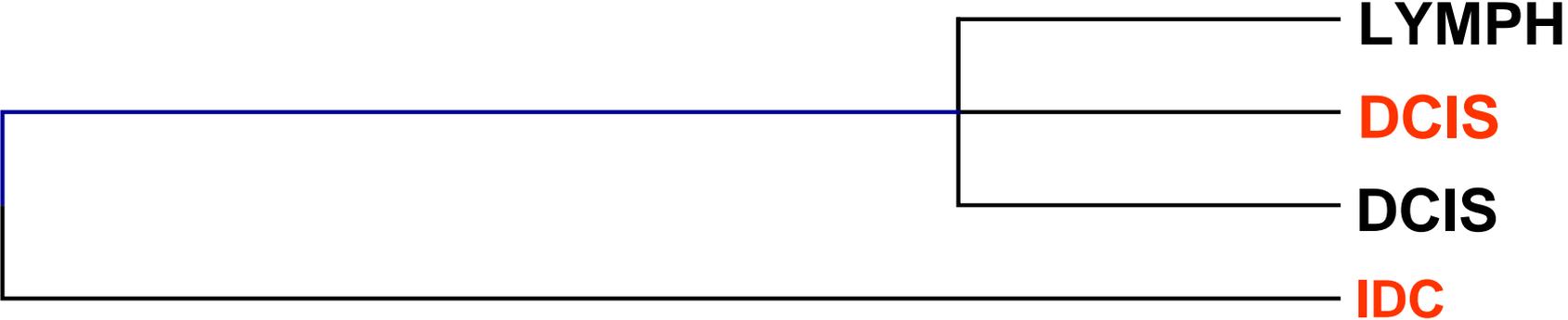
DCIS  
IDC



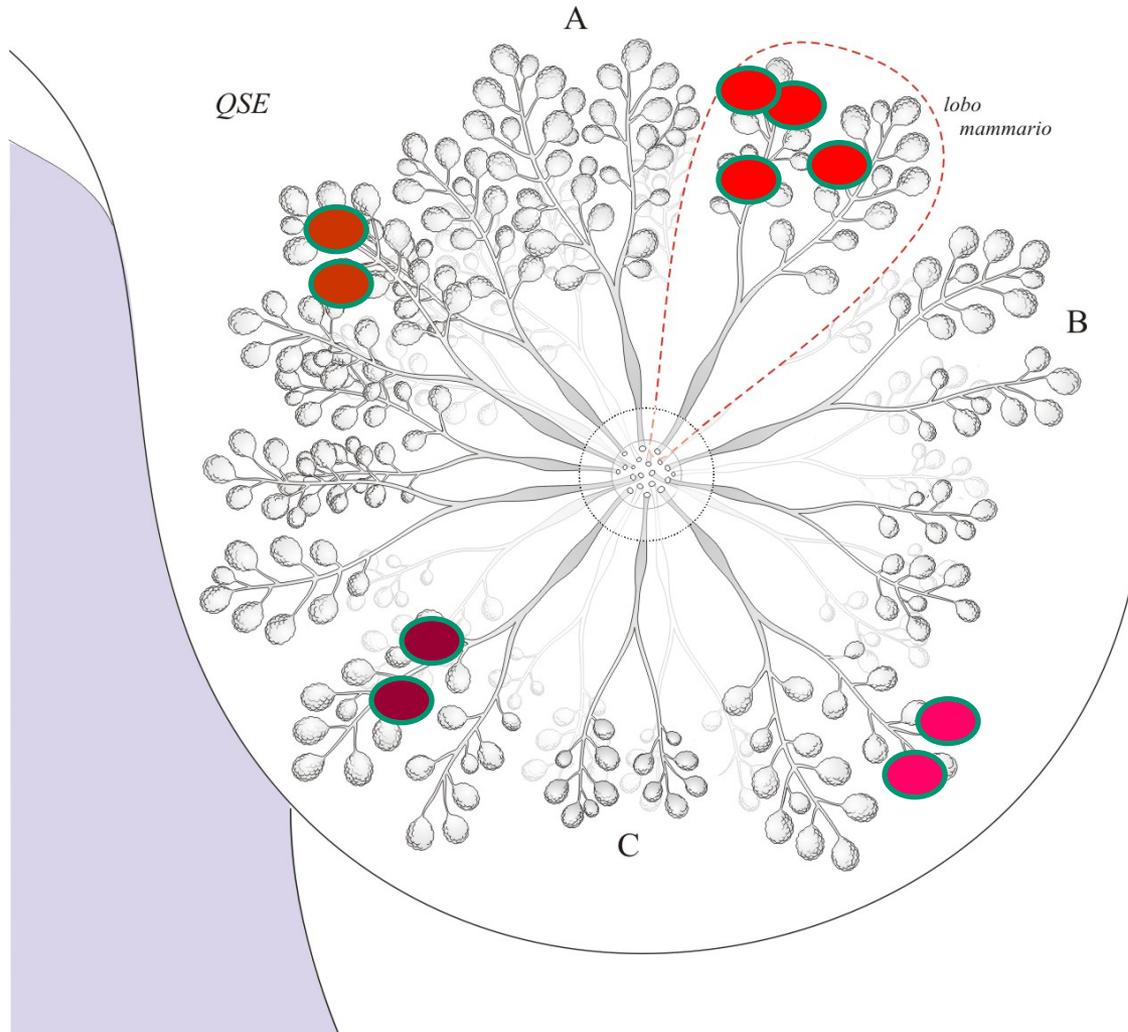
DCIS

72mm

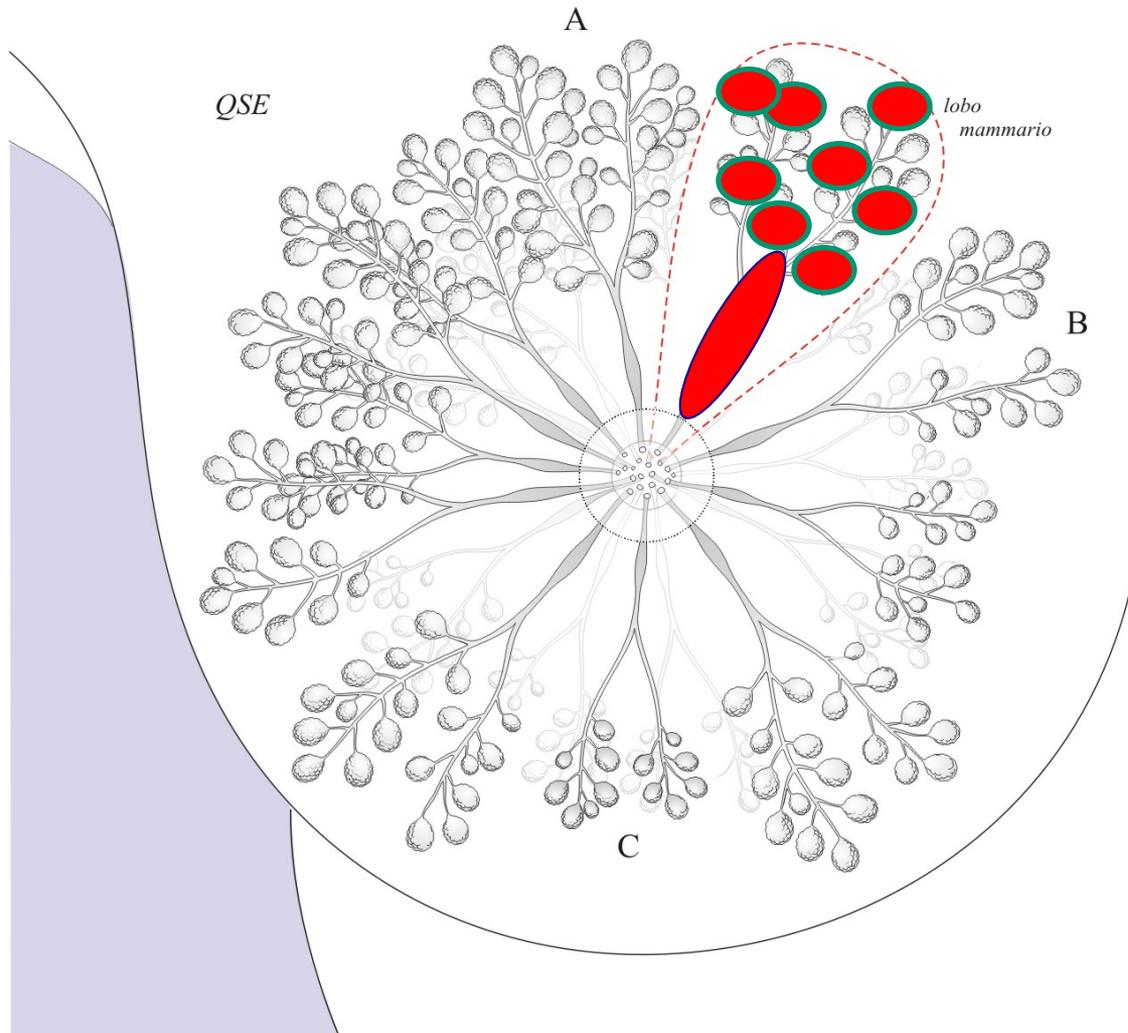
mtDNA



# CARCINOMA DUTTALE IN SITU BEN DIFFERENZIATO



# CARCINOMA DUTTALE IN SITU POCO DIFFERENZIATO



**Estensione CDIS\|DIN**

**RELAZIONE CON  
MARGINI DI RESEZIONE**

# CDIS / DIN

## valutazione margini di resezione

*Margine > 3cm 22% residui neoplastici*

*Margine > 2cm: 39% residui neoplastici*

*Margine > 1 cm: 47% residui neoplastici*

*Faverly DR, Hendrics JHCL, Holland R, breast carcinomas of limited extent. Cancer 2001;91:647-659*

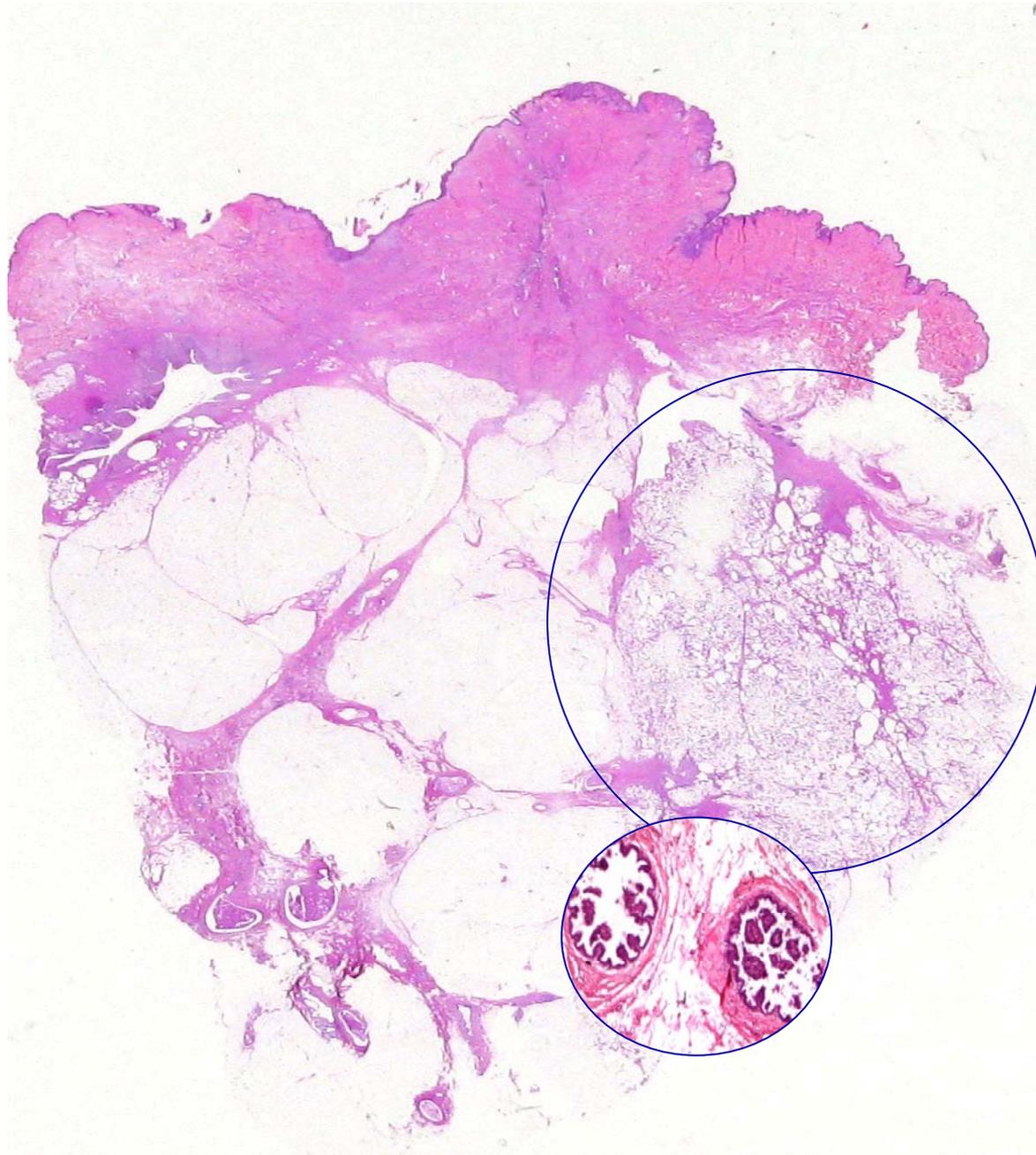
# CDIS / DIN

## valutazione margini di resezione

residui neoplastici:

In genere CDIS di basso grado

*Faverly DR, Hendrics JHCL, Holland R, breast carcinomas of limited extent. Cancer 2001;91:647-659*



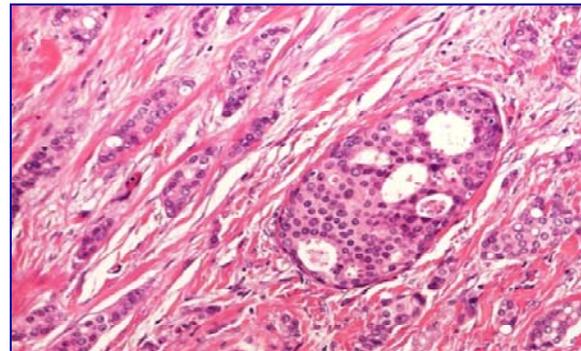
**CDIS \ DIN**

**RELAZIONE CON  
CARCINOMA INFILTRANTE**

# CDIS\CDI

## relazione “spaziale”

- N. FOCI CDIS G1  
IN CDI: • 112\229 (48.9%)
- N. FOCI CDIS G2  
IN CDI: • 184/398 (46.2%)
- N. FOCI CDIS G3  
IN CDI: • 73/185 (39.45%)



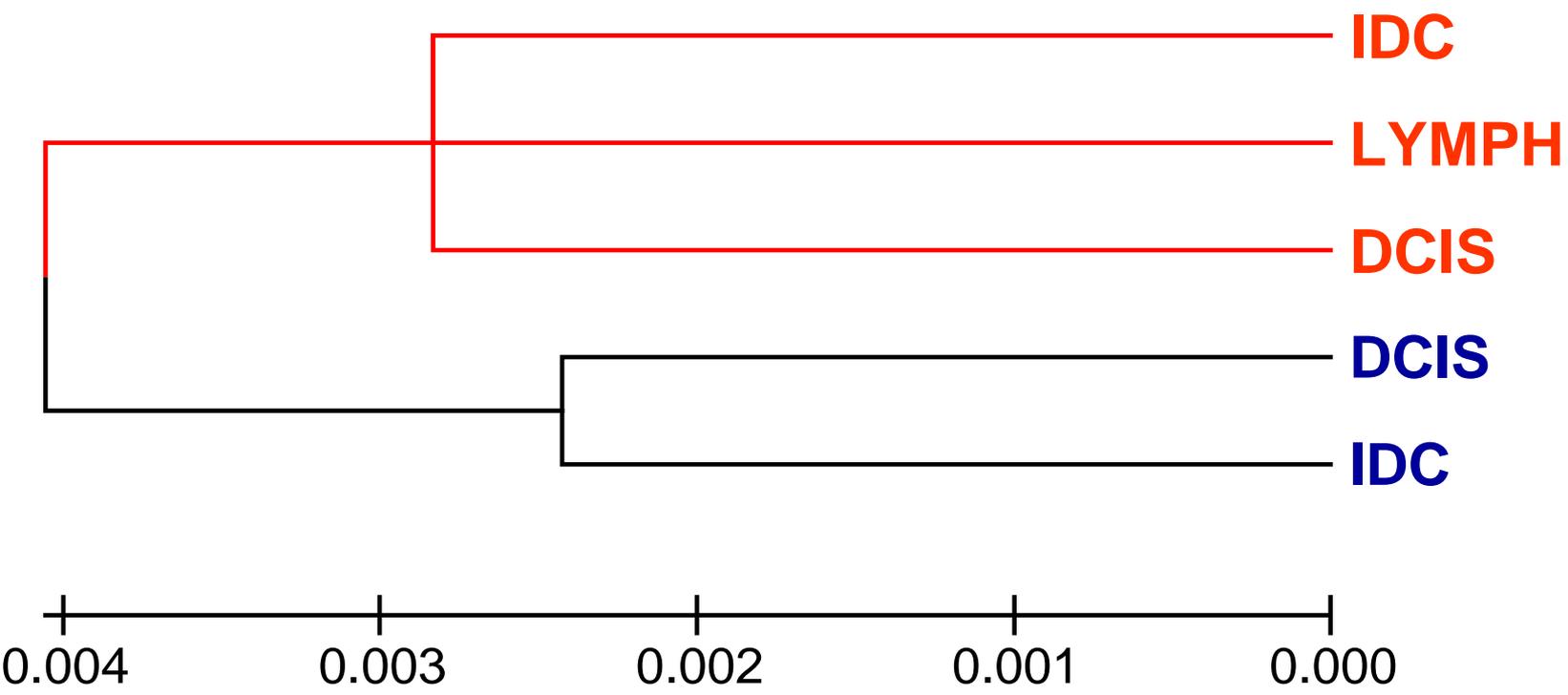
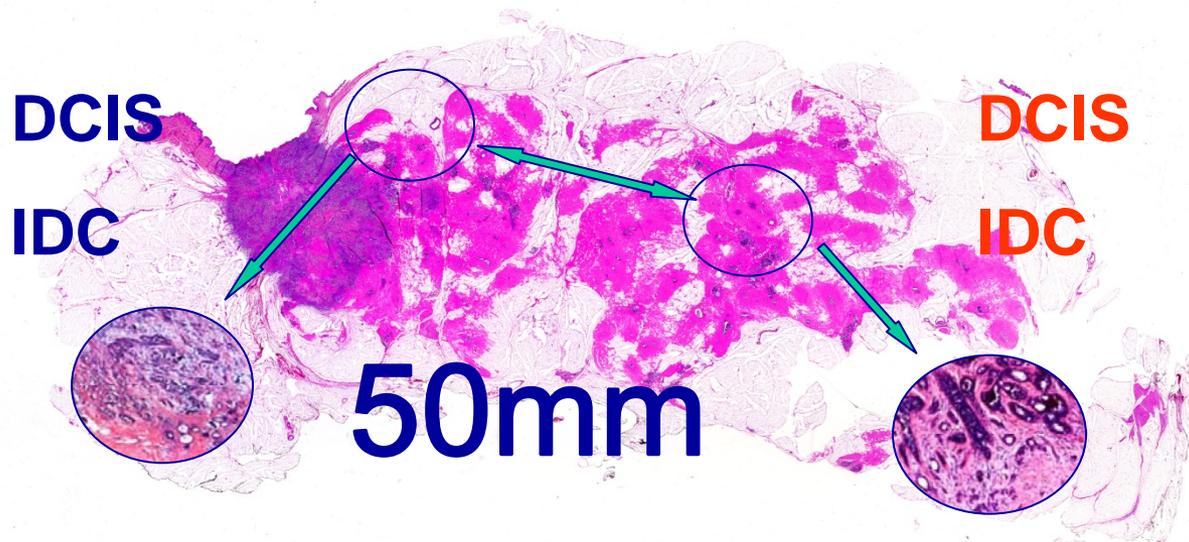
# CDIS / DIN relazione invasivo

**Dimostrata una relazione clonale tra CDIS /  
DIN e relativo carcinoma invasivo**

*Aubele et al. Extensive ductal carcinoma in situ with  
small foci of invasive ductal carcinoma: evidence of  
genetic resemblance by CGH. In J Cancer 2000;85:82-  
86*

# CASE 2 G1

mtDNA



# **CDIS / DIN**

## **relazione invasivo**

- **CDIS / DIN di basso grado**
- **Alterazioni su 1q e LOH 16q**
- **Simili al carcinoma invasivo di tipo tubulare, tubulo-lobulare, lobulare e duttale invasivo G1**

*Reis-Filho JS, Lakhani SR: Genetic alterations in pre-invasive breast lesions. Breast Cancer Research 2003;5:313-319.*

# **CDIS / DIN**

## **relazione invasivo**

- **DCIS / DIN di alto grado**
- **Alterazioni su p53, amplificazione c-ERB-B2**
- **Simili a carcinoma duttale invasivo di grado 3**

*Reis-Filho JS, Lakhani SR: Genetic alterations in pre-invasive breast lesions. Breast Cancer Research 2003;5:313-319.*

**DCIS / DIN**

**Rischio di trasformazione in  
carcinoma infiltrante**

# Long-Term Follow-Up of In Situ Carcinoma of the Breast

Vincenzo Eusebi, MD, FRCPath,\* Elisa Feudale, MD,‡ Maria P. Foschini, MD,\* Andrea Micheli, DS,||  
Alberto Conti, MD,§ Cristina Riva, MD,† Silvana Di Palma, MD,‡ and Franco Rilke, MD, FRCPath‡

● Eighty cases of duct carcinoma in situ (DCIS) of the breast have been investigated by a cohort-retrospective study. These consisted of 8.5 per 1,000 of 9,446 breast biopsies originally diagnosed as benign, between 1964 and 1976, with a mean follow-up of 17.5 years. There were forty-one cases (51%) of DCIS of clinging type (CC); 30 cases (37.%) of CC associated with other types of DCIS; nine cases of DCIS other than CC two of which were DCIS of comedo-type. Invasive duct carcinoma (IDC) subsequently developed in 11 patients (14%), whereas DCIS recurred in 5 (6%). The recurrence was ipsilateral in 12 of these 16 patients. IDC appeared more frequently, with high statistical significance, when the lesion present in the original biopsy showed pleomorphic (P) nuclei (ie, poorly differentiated cyto-nuclear morphology). The Standardized Morbidity Ratio (SMR) was 8.0 (95% CI; 2.9-17.5) with the general population as reference. IDC that developed following a lesion displaying P nuclei also showed a statistically significantly more aggressive behavior. It is suggested that when cases of DCIS are followed-up for a considerable length of time, a two-wave pattern of aggressiveness becomes apparent. IDC that develops after a poorly differentiated DCIS leads to death more precociously than that appearing after other types of DCIS, especially those showing more bland nuclear cytology.

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# INCIDENCE OF IDC IN DCIS WITH MONOMORPHIC AND PLEOMORPHIC NUCLEI

TYPE OF NUCLEUS	CASES OBSERVED	CASES EXPECTED	SMR (95% CI)
M	5	4.405	1.1 (0.4-2.6)
P	6	0.647	9.3 (3.4-20.2)
TOTAL	11	5.054	2.2 (1.1-3.9)

*Carcinoma in situ of the female breast. 10 year follow-up results of a prospective nationwide study.*

*Ottesen GL, et al. Breast Cancer Res Treat 2000, 62:197-210*

**Recidive prevalentemente nelle forme poco differenziate**

## Dopo quanto tempo ?

	<b>N. CASES</b>	<b>IDC</b>	<b>DOD</b>	<b>NED</b>	<b>INTER V YEARS</b>
<b>DCIS P</b>	<b>14</b>	<b>6</b>	<b>6</b>	<b>0</b>	<b>1-12 MEAN 8.6</b>
<b>DCIS M</b>	<b>66</b>	<b>5</b>	<b>1</b>	<b>4</b>	<b>12-20 MEAN 15.4</b>

*Carcinoma in situ of the female breast. 10 year follow-up results of a prospective nationwide study.*

*Ottesen GL, et al. Breast Cancer Res Treat 2000, 62:197-210*

CDIS basso grado “small nuclear size”

6% dopo 5 anni

16% dopo 16 anni

# Risk Factors for Recurrence and Metastasis After Breast-Conserving Therapy for Ductal Carcinoma-In-Situ: Analysis of European Organization for Research and Treatment of Cancer Trial 10853

By Nina Bijker, Johannes L. Peterse, Luc Duchateau, Jean-Pierre Julien, Ian S. Fentiman, Christian Duval, Silvana Di Palma, Joëlle Simony-Lafontaine, Isabelle de Mascarel, and Marc J. van de Vijver

**JCO 19:2263-2271, 2001**

**5 YR FU**

# **BIJKER ET AL**

## **WELL DIFFERENTIATED DCIS**

- **59 CLINGING CARCINOMA**

**0 EVENTS**

- **98 MICROPAPILLARY CARCINOMA**

**7% EVENTS**

- **115 CRIBRIFORM CARCINOMA**

**18 % EVENTS**

# Conclusioni

- **Macrosezioni utili per valutare crescita ed estensione del carcinoma mammario**
- **CDIS \DIN: distinzione tra forme di basso ed alto grado**
- **Diverse per tipo di crescita ed estensione**
- **Relazione con carcinoma infiltrante**