

# Spécificités Biopathologiques

## **Cancers du sein des femmes jeunes**



# Entité anatomo pathologique , femme jeune ?

- **7%** des cancers du sein sont observés <40 ans
- **Séries sont limitées statistiquement**
- **Les différences biopathologiques ne sont observées que pour les patientes < 40 ans**
- **Entre 40-50ans les profils = >50 ans**

# CIC et femmes jeunes

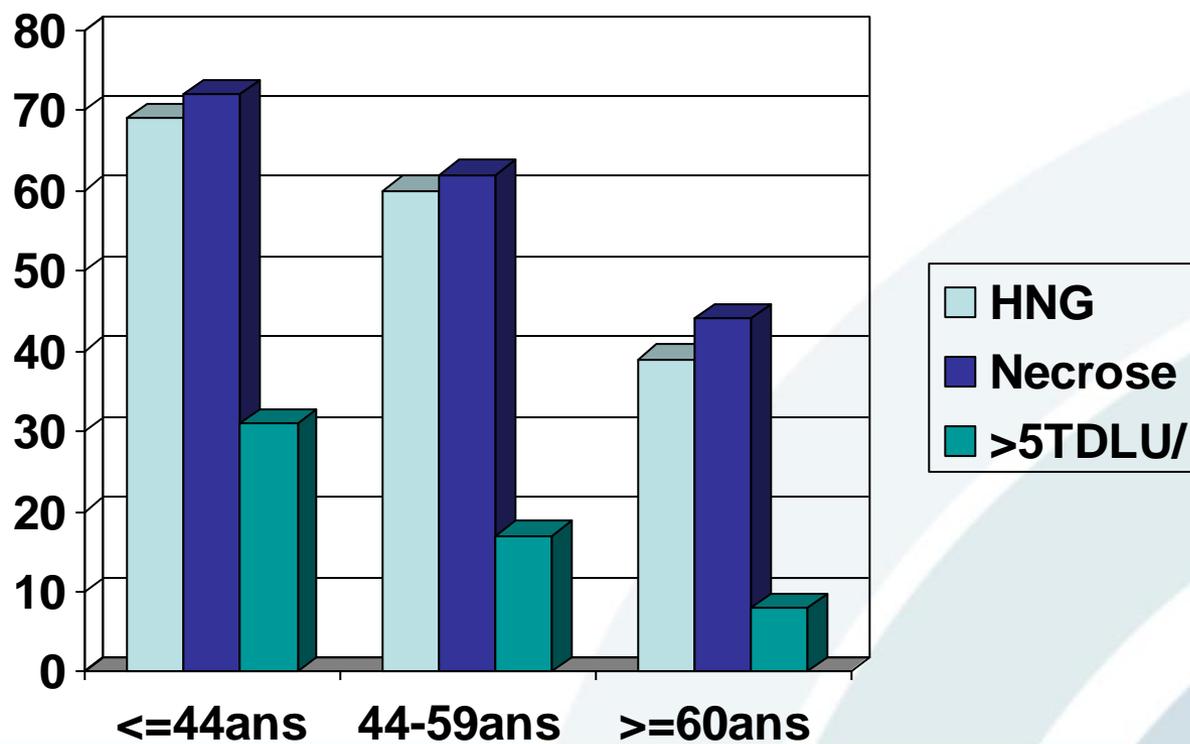
## Profil des CIC des patientes de < 40ans

- ✓ CIC < 40ans 6-13% / > 50ans 13- 32%
- ✓ Facteur de récurrence locale X 2.4
- ✓ Taille moyenne 
- ✓ Grade 3 et nécrose 
- ✓ Marges non saines 24% /13%

# Age at Diagnosis and Outcome for Women With Ductal Carcinoma-In-Situ of the Breast: A Critical Review of the Literature

*J Clin Oncol 20:2736-2744. © 2002 by American Society of Clinical Oncology.*

By Frank A. Vicini and Abram Recht

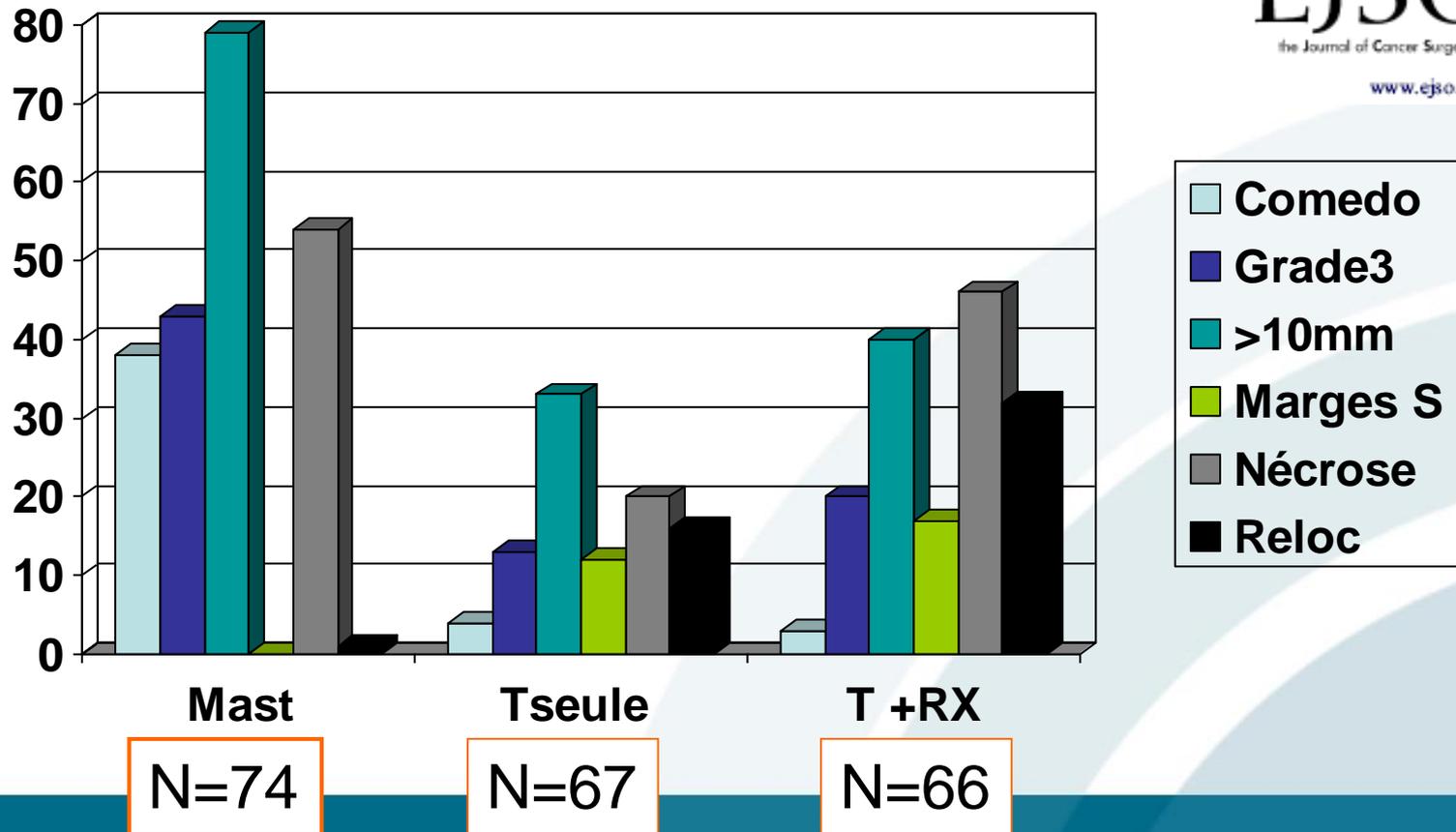


# Ductal carcinoma in situ of the breast in younger women: A subgroup of patients at high risk

C. Tunon-de-Lara <sup>a,\*</sup>, C. Lemanski <sup>b</sup>, C. Cohen-Solal-Le-Nir <sup>c</sup>, B. de Lafontan <sup>d</sup>,  
 C. Charra-Brunaud <sup>e</sup>, L. Gonzague-Casabianca <sup>f</sup>, H. Mignotte <sup>g</sup>, E. Fondrinier <sup>h</sup>, S. Giard <sup>i</sup>,  
 P. Quetin <sup>j</sup>, H. Auvray <sup>k</sup>, B. Cutuli <sup>l</sup>

207 cas de CIC <40ans

**EJSO**  
 the Journal of Cancer Surgery  
[www.ejsso.com](http://www.ejsso.com)



## Ductal carcinoma in situ of the breast in younger women: A subgroup of patients at high risk

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### Facteurs Prédicatifs de Récidive Locale

**EJSO**  
the Journal of Cancer Surgery  
[www.ejsso.com](http://www.ejsso.com)

<b>Paramètre</b>	<b>P</b>
<b>Type comédo</b>	<b>0.004</b>
<b>Taille &gt;10mm</b>	<b>0.011</b>
<b>Nécrose</b>	<b>0.02</b>
<b>Marges positives</b>	<b>0.019</b>

# The University of Southern California/Van Nuys prognostic index for ductal carcinoma in situ of the breast

Melvin J. Silverstein, M.D.\*

Aide au choix thérapeutique pour les CIC des patientes de moins de < 40ans

<b>Score</b>	<b>1</b>	<b>2</b>	<b>3</b>
<b>Taille mm</b>	<b>&lt;=15</b>	<b>16-40</b>	<b>&gt;=41</b>
<b>Marges</b>	<b>&gt;=10</b>	<b>1-9</b>	<b>&lt;1</b>
<b>Necrose et Grade</b>	<b>Absente Grade 1-2</b>	<b>Nécrose Grade1-2</b>	<b>Nécrose +/- Grade 3</b>
<b>AGE</b>	<b>&gt;60</b>	<b>40-60</b>	<b>&lt;40</b>

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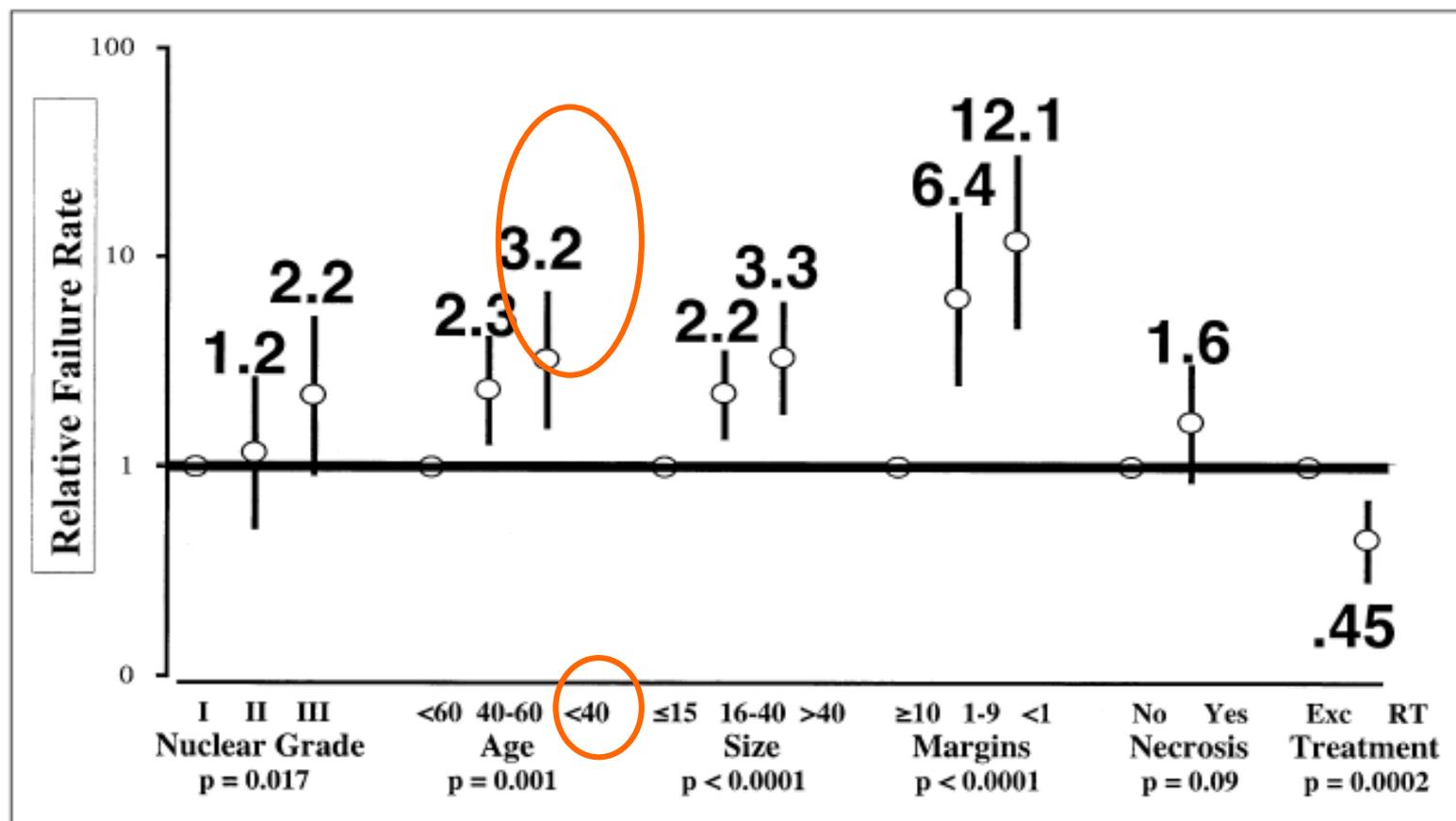


Fig. 1. Cox multivariate analysis of factors affecting ductal carcinoma in situ recurrence-free survival (conservatively treated patients only).

# Biopathologie et risque de récurrence locale

## Effect of breast-duct anatomy and wound-healing responses on local tumour recurrence after primary surgery for early breast cancer

Mariella Mannino, John Yarnold

Les patientes de moins de 35ans ayant une chirurgie conservatrice présentent **9 fois** plus de risque de récurrence locale

Cependant ce risque pourrait être lié aux modalités de la chirurgie conservatrice

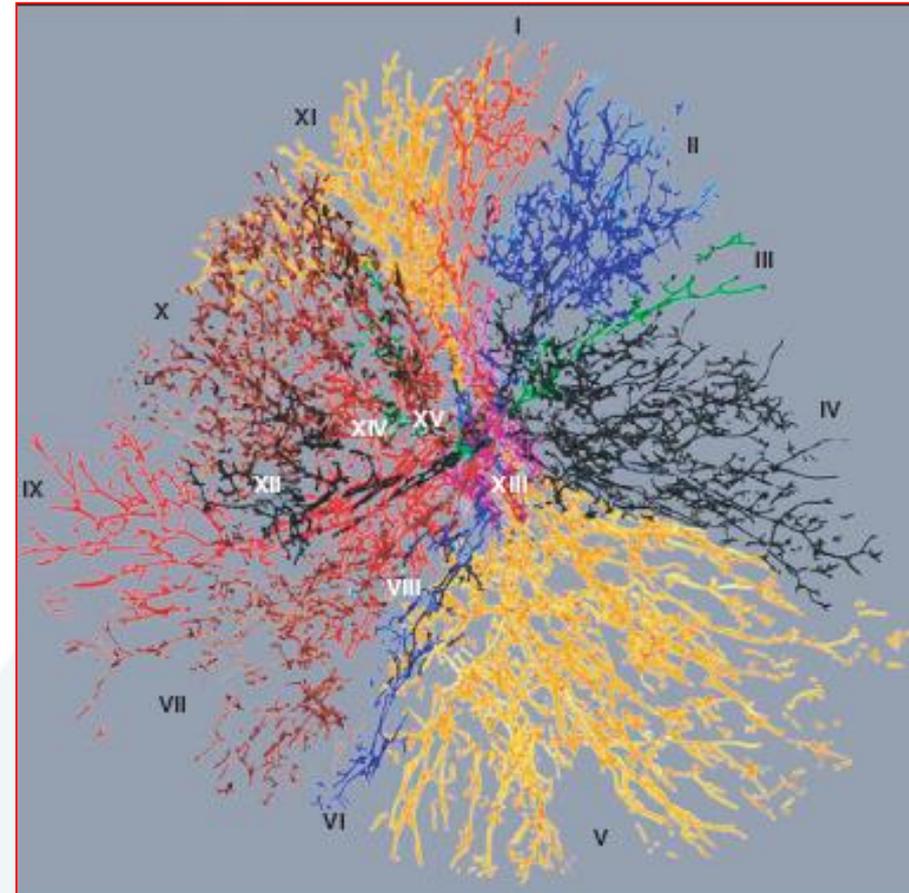
La révision histologique de 1724 cas ( EORTC),

**Seule la composante intra canalaire apparait discriminante**

# Effect of breast-duct anatomy and wound-healing responses on local tumour recurrence after primary surgery for early breast cancer

« Breast Ductoscopy »  
reconstruction en 3D  
Chaque système coloré  
est indépendant .

L'extension du CIC se fait à  
l'intérieur d'une seule unité  
l'involution canalaire qui débute  
à 30 ans explique les  
variations d'extension canalaire

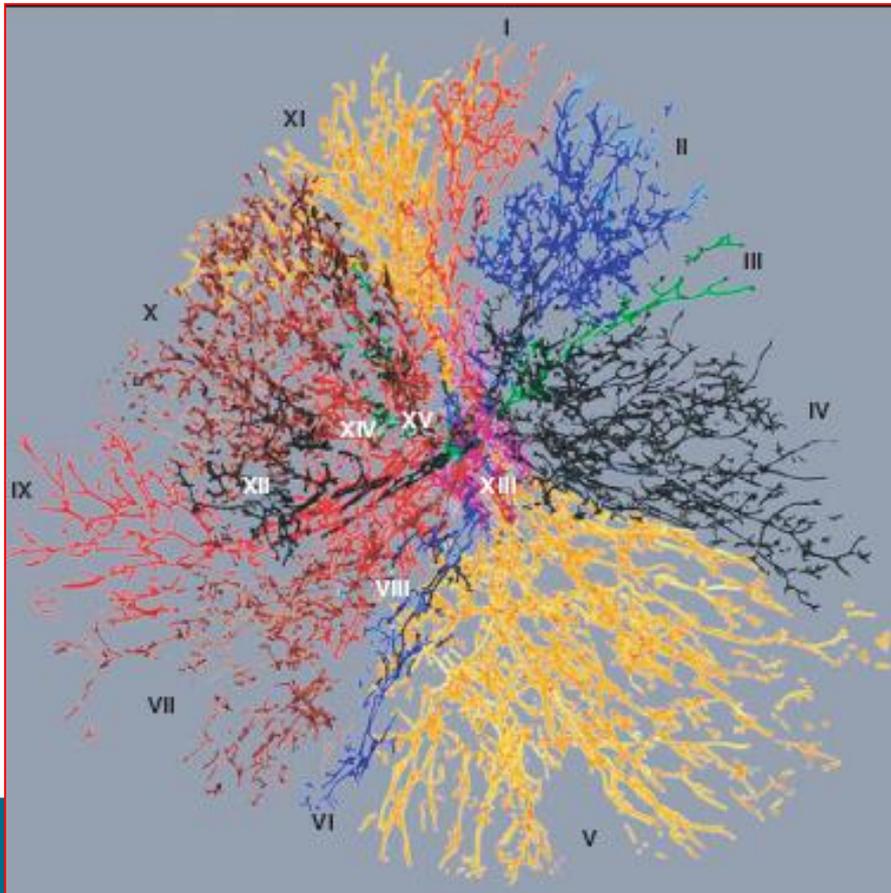


Mariella Mannino, John Yarnold

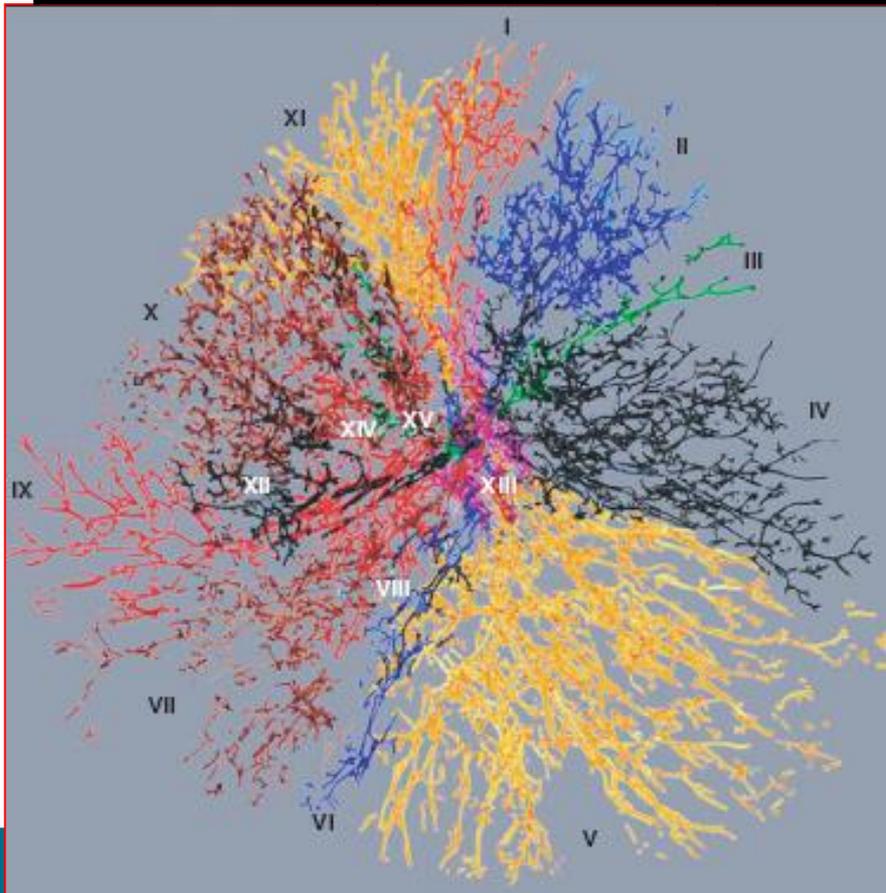
Lancet Oncol 2009; 10: 425-29

L'analyse en coupes s eries de 2mm ( 47 niveaux de coupes)  
de chirurgie conservatrice , les distances d'extension  
endocanalaire sont inversement proportionnelles   l' ge

<40 ans



	<b>&lt;40 ans</b>	<b>40-49 ans</b>	<b>&gt;50 ans</b>	
<b>Extension CIC mm</b>	<b>22.7mm</b>	<b>14.3mm</b>	<b>7mm</b>	
<b>Exérèse incomplète</b>	<b>35%</b>	<b>21%</b>	<b>14%</b>	<b>P=0.008</b>



## Two Distinct Local Relapse Subtypes in Invasive Breast Cancer: Effect on their Prognostic Impact

Patrizia Casalini,<sup>1</sup> Maria Luisa Carcangiu,<sup>2</sup> Raija Tammi,<sup>6</sup> Päivi Auvinen,<sup>7</sup> Veli-Matti Kosma,<sup>7,8</sup> Pinuccia Valagussa,<sup>3</sup> Marco Greco,<sup>4</sup> Andrea Balsari,<sup>5</sup> Sylvie Ménard,<sup>1</sup> and Elda Tagliabue<sup>1</sup>

Characteristic	Age ≤50 y		Age >50 y	
	HR (95% CI)	P*	HR (95% CI)	P*
Lymph nodes (positive vs. negative)	1.44 (0.70-2.94)	0.3222	<b>3.34</b> (1.31-8.51)	<b>0.0113</b>
Tumor size (>1 vs. ≤1 cm)	1.63 (0.67-3.96)	0.2813	1.56 (0.52-4.72)	0.4270
DCIS (presence vs. absence)	1.18 (0.53-2.63)	0.6834	1.73 (0.66-4.56)	0.2563
Grade (G3 vs. G1 and G2)	0.76 (0.27-2.19)	0.6182	0.96 (0.32-2.90)	0.9435
MIB1 (positive vs. negative)	1.94 (0.92-4.09)	0.0833	1.19 (0.39-3.59)	0.7560
Desmoplasia (presence vs. absence)	1.35 (0.68-2.71)	0.3932	0.97 (0.37-3.55)	0.9494
Inflammation (presence vs. absence)	0.67 (0.32-1.38)	0.2743	0.94 (0.36-2.49)	0.9069
HER2 (positive vs. negative)	1.16 (0.45-3.01)	0.7617	2.29 (0.75-6.97)	0.1442
P53 (positive vs. negative)	1.07 (0.44-2.60)	0.8829	0.82 (0.24-2.82)	0.7568
ER (positive vs. negative)	0.89 (0.42-1.85)	0.7485	<b>0.39</b> (0.16-0.97)	<b>0.0424</b>
BCL2 (positive vs. negative)	0.66 (0.33-1.35)	0.2550	0.61 (0.25-1.50)	0.2839
Hyaluronan in tumor cells (positive vs. negative)	<b>2.48</b> (0.61-3.87)	<b>0.0364</b>	0.75 (0.27-2.11)	0.5849
Hyaluronan in stroma (strong vs. moderate and weak)	1.54 (0.61-3.87)	0.3621	0.60 (0.22-1.65)	0.3181

La présence de Hyaluronan est prédictif de RL chez < 50 ans

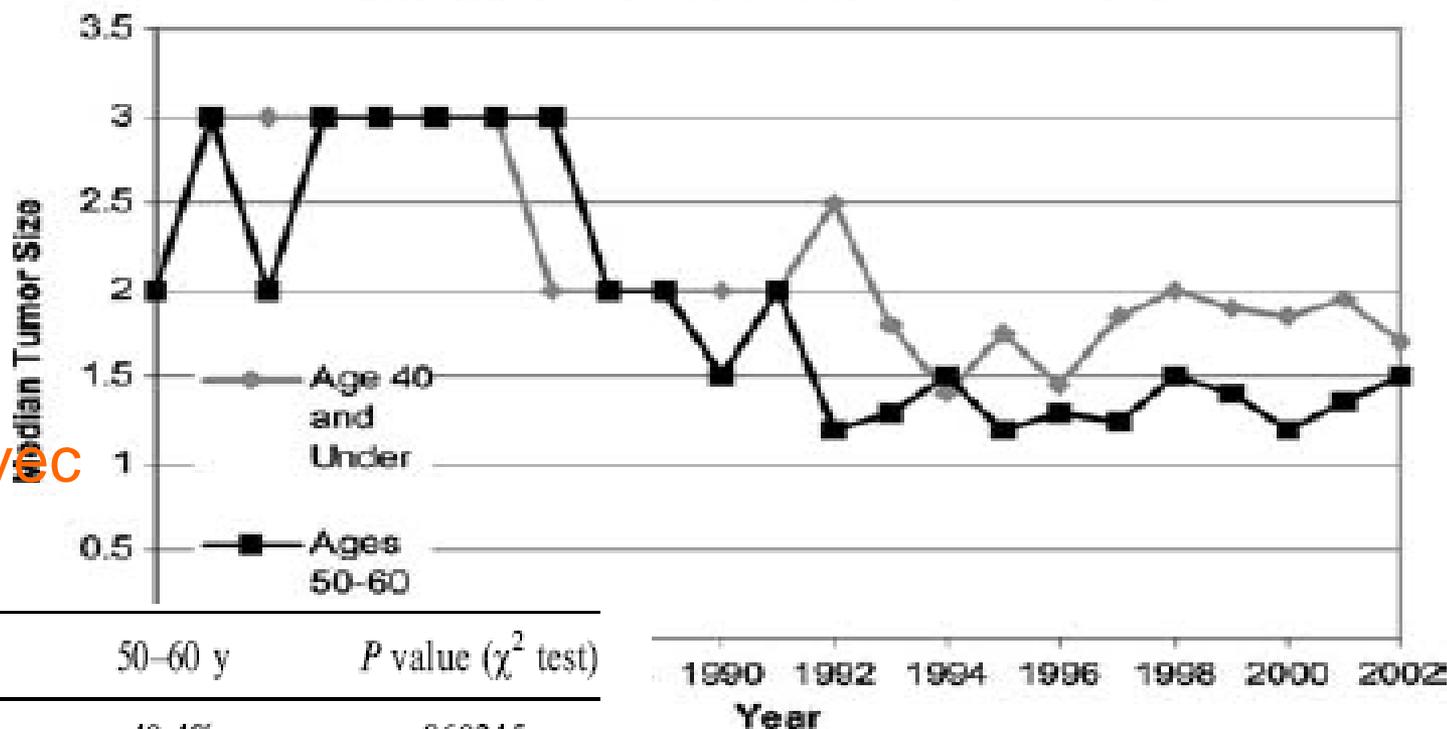
# Biopathologie et risque métastatique

# Breast Cancer Diagnosis in Women $\leq 40$ versus 50 to 60 Years: Increasing Size and Stage Disparity Compared With Older Women Over Time

*Annals of Surgical Oncology* 13(8): 1072-1077

Katherina Zabicki,

**Median Tumor Size by Year of Diagnosis**

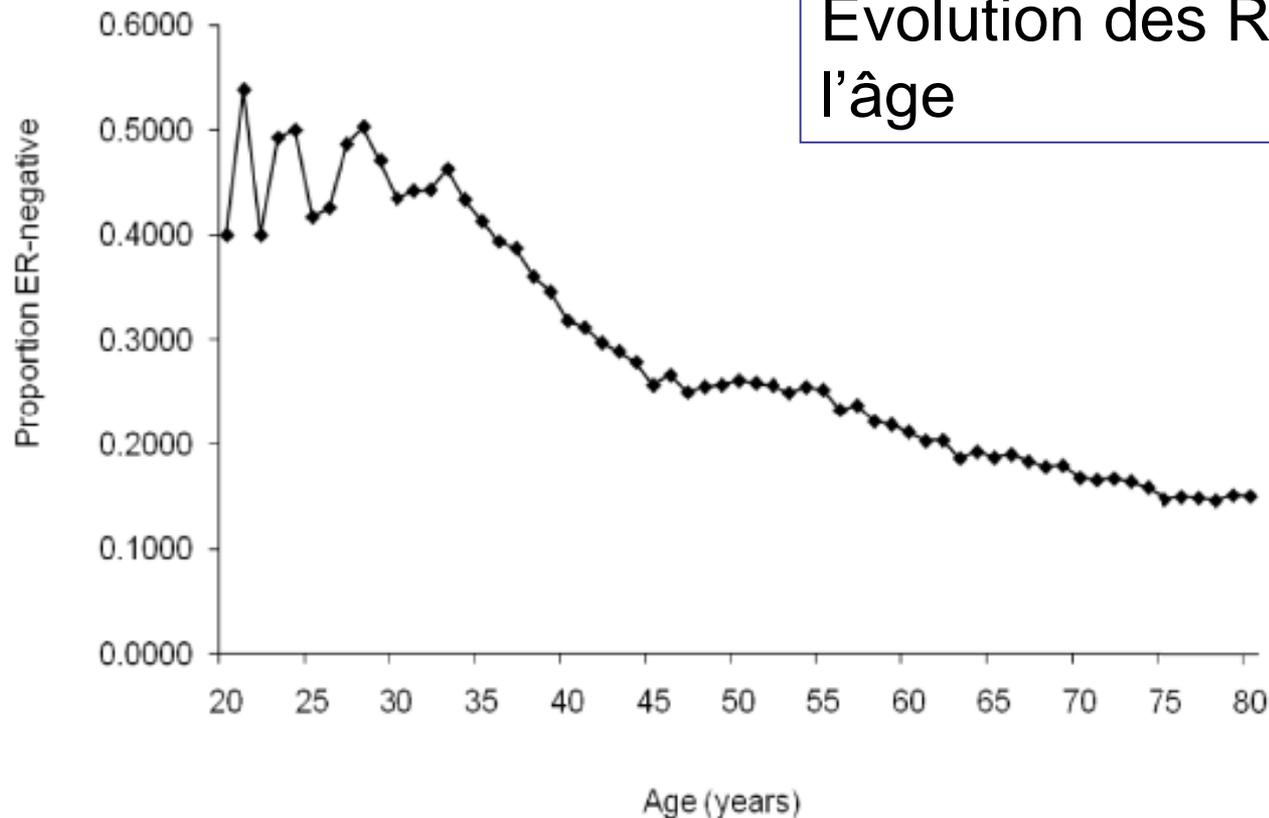


N+ baissent avec le dépistage

Period	$\leq 40$ y	50-60 y	P value ( $\chi^2$ test)
1983-1987	41.3%	40.4%	.860245
1988-1992	27.3%	26.8%	.929774
1993-1997	31.9%	26.1%	.111663
1998-2002	35.2%	23.9%	.0000921

# Incorporating tumour pathology information into breast cancer risk prediction algorithms

Nasim Mavaddat<sup>\*1</sup>, Timothy R Rebbeck<sup>2</sup>, Sunil R Lakhani<sup>3</sup>, Douglas F Easton<sup>1</sup> and Antonis C Antoniou<sup>1</sup>



# Tumor Biology of Breast Cancer in Young Women

Nancy Klauber-DeMore\*

Comparison of Biomarkers Reported in Studies of Breast Cancer in Young Women

Author	Age	N	ER-Negative	HER-2/neu Positive	Grade 3	Ki-67
Gajdos [2]	<36	101	52%	NA	80%	NA
	>36	631	31% $p < 0.001$	NA	44% $p < 0.001$	NA
Colleoni [8]	<35	185	39%	40%	62%	62%
	35–50	1242	21% $p < 0.001$	37% NS	37% $p < 0.001$	53% $p < 0.001$
Bertheau [9]	<35	50	NA	26%	NA	NA
	36–50	62	NA	34% NS	NA	NA
Maru [10]	23–30	44	55%	44%	68%	NA
Choi [11]	25–45	103	58%	28%	NA	39%
Jimor [13]	<35	133	80%	NA	73%	NA

ER neg 21/80%

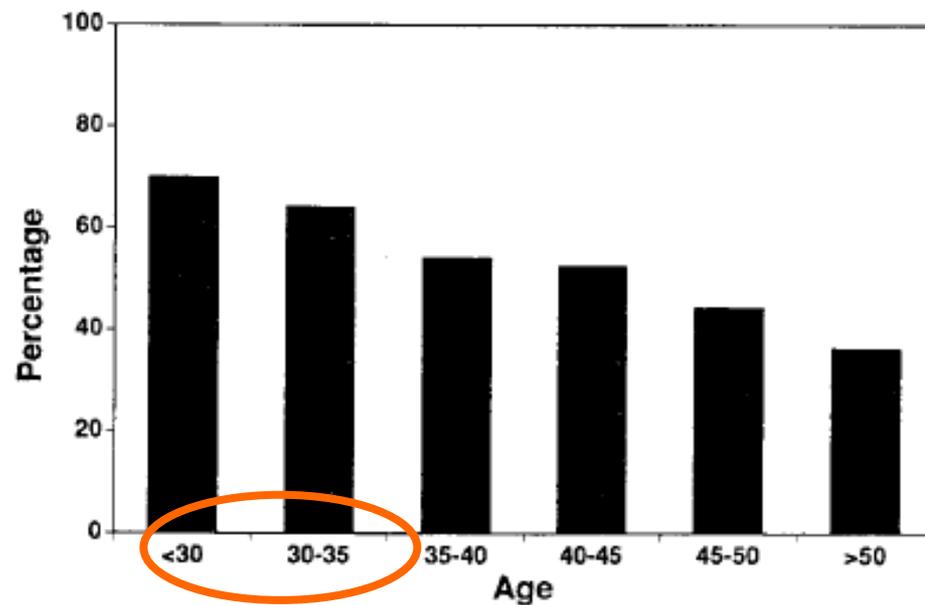
HER2 pos 28/44%

Grade 3 37 /80 %

Ki67 39/62%

# Breast Cancer Outcome and Predictors of Outcome: Are There Age Differentials?

*Kathy S. Albain, D. Craig Allred, Gary M. Clark\**

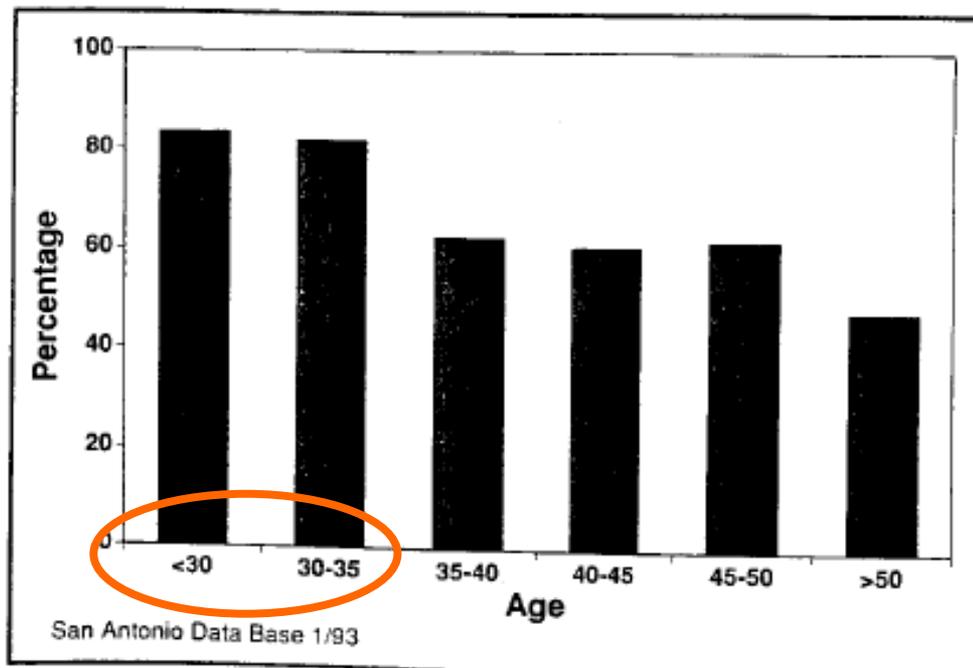


San Antonio Data Base 1/93

Corrélation inverse de la phase S avec l'âge  $p < 0.001$

# Breast Cancer Outcome and Predictors of Outcome: Are There Age Differentials?

*Kathy S. Albain, D. Craig Allred, Gary M. Clark\**



Corrélation inverse  
de la P53  
avec l'âge  $p < 0.001$

# Descriptive Analysis of Estrogen Receptor (ER)-Negative, Progesterone Receptor (PR)-Negative, and HER2-Negative Invasive Breast Cancer, the So-called Triple-Negative Phenotype

*A Population-Based Study From the California Cancer Registry* *Cancer* 2007;109:1721-8.

Katrina R. Bauer, MS CTR<sup>1</sup>  
Monica Brown, PhD<sup>2</sup>  
Rosemary D. Cress, DrPH<sup>1,3</sup>  
Carol A. Parise, PhD<sup>4</sup>  
Vincent Caggiano, MD<sup>4,5</sup>

<b>&lt;40 ans</b>	<b>23.4%</b>	<b>P&lt;0.001</b>
<b>40-49 ans</b>	<b>15.6%</b>	<b>13224 cas &lt;49 ans</b>

Pathol Oncol Res. 2010 Sep 17.  
**Breast Cancer under 40 Years of Age: Increasing  
Number and Worse Prognosis.**

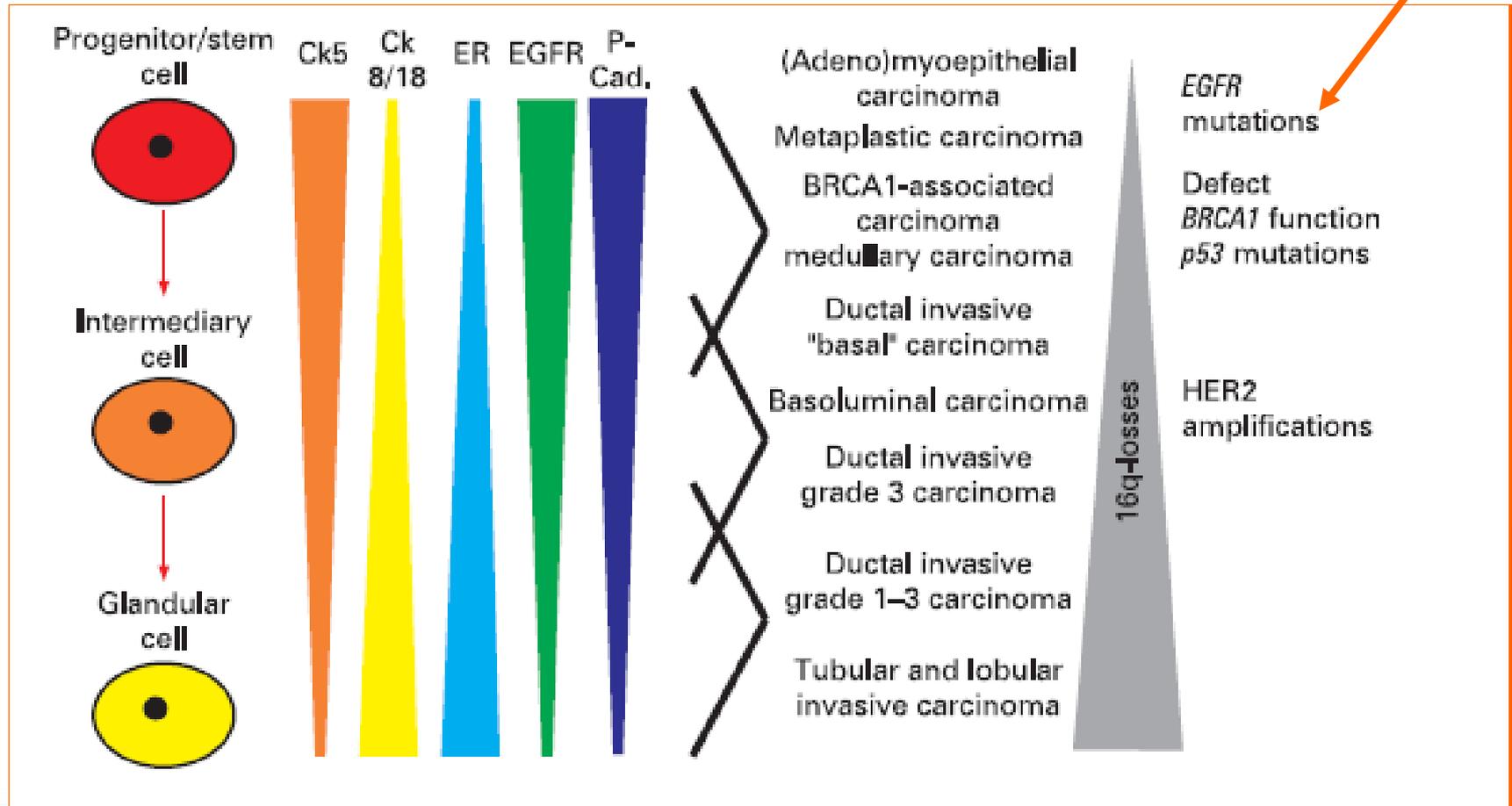
Dobi A, Kelemen G, Kaizer L, Weiczner R, Thurzó L,  
Kahán Z.

<b>Etude cas contrôle</b>	<b>&lt;40ans 141cas</b>	<b>&gt;40ans 300cas</b>
<b>Triple Neg</b>	<b>25%</b>	<b>13%</b> <b>P=0.026</b>

## Synthèse revue bibliographique ST Paul 2009

<b>Facteurs</b>	<b>&lt;35/40 ans</b>	<b>40-50 ans pré-ménopause</b>
<b>Taille Plus importante</b>	<b>Oui (4)</b>	<b>+/- (1) baisse avec le dépistage</b>
<b>Grade 3</b>	<b>Oui (4)</b>	<b>Moins évident (1)</b>
<b>Type histologique Spécifique</b>	<b>Médullaire</b>	<b>Non</b>
<b>Ganglions positifs</b>	<b>Oui (2)</b>	<b>NE</b>
<b>EVPT positif</b>	<b>Oui (3)</b>	<b>NE</b>
<b>EIC positif</b>	<b>Oui</b>	<b>Oui obtenu en intégrant &lt;50 ans</b>
<b>RE négatif</b>	<b>Oui</b>	<b>Oui</b>
<b>Prolifération élevée</b>	<b>Oui</b>	<b>Non</b>
<b>P53 muté</b>	<b>Oui</b>	<b>Non</b>
<b>BRCA1 muté</b>	<b>Plus fréquent</b>	<b>Non</b>
<b>HER2 positif</b>	<b>OUI</b>	<b>NE</b>

# Caractéristique Femmes jeunes



# Biopathologie et risque mutation

# Cancers Medullaire et Mutation BRCA1

## BRCA1 / Medullaire

Eisinger : 19%  
Lakhani : 13%  
Verhoog : 8.7%  
Johanson : 0%  
Robson : 0%

## Medullaire / BRCA1

Eisinger : 11%  
Mutation somatique  
Iau (2004) : 14.2%  
Mutations germinale

**Major improvement in the efficacy of  
BRCA1 mutation  
R. Lidereau et al., 2000**

**Analyse multivariée**

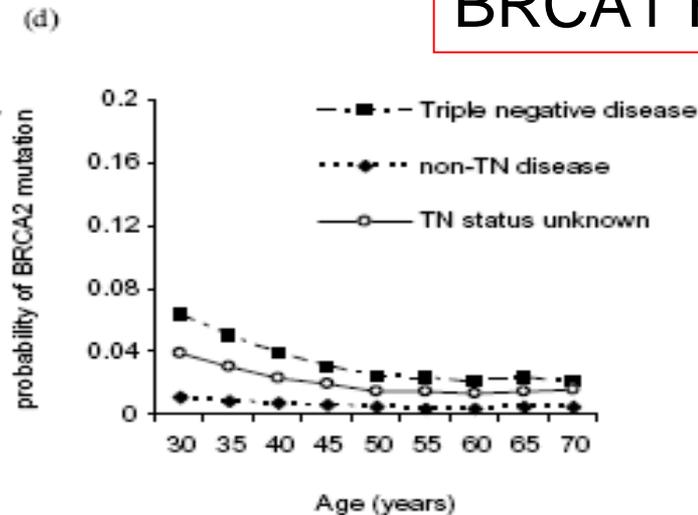
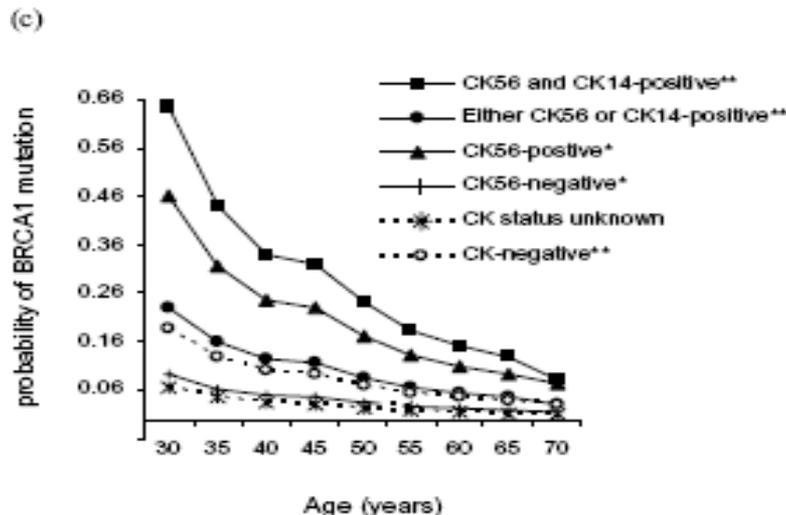
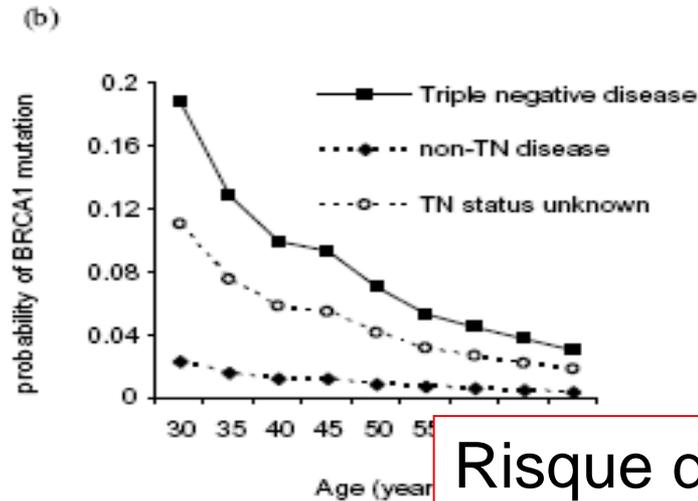
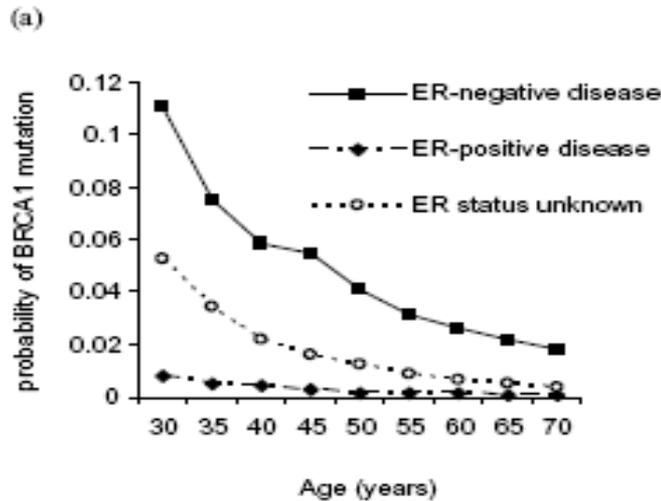
**Age <35y + ER- + TD 3 = 28.6%**

**Age <35y = 8.6%**

**autre profil = 3.6%**

# Incorporating tumour pathology information into breast cancer risk prediction algorithms

Nasim Mavaddat<sup>1</sup>, Timothy R Rebbeck<sup>2</sup>, Sunil R Lakhani<sup>3</sup>, Douglas F Easton<sup>1</sup> and Antonis C Antoniou<sup>1</sup>



Risque de mutation BRCA1 RE et age

# Incorporating tumour pathology information into breast cancer risk prediction algorithms

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Risque de mutation  
BRCA1/ RE et age <50ans



<b>RE neg</b>	<b>5%</b>
<b>Triple Neg</b>	<b>7%</b>
<b>Triple Neg et Ck5/6 ou CK14</b>	<b>24%</b>

## Commentaires

- **Difficultés pour distinguer les caractéristiques biopathologiques du facteur age**
- **La structure canalaire des femmes jeunes / Récidive locale**
- **Tailles tumorales / hors dépistage**
- **La plus grande fréquence des carcinomes basaux triple neg ,mais également HER2 ?**
- **Recherche de mutations BRCA1**
- **Chimiothérapie plus adaptée**

Centre régional de lutte contre le cancer Provence-Alpes-Côte d'Azur



INSTITUT PAOLI-CALMETTES