



RISK FACTORS FOR LOCAL RECURRENCE AND ONCOPLASTIC SURGERY

Alfredo Carlos S.D. Barros
Strasbourg, June 23, 2011

SCRIPT

- **Local recurrences after breast cancer treatment**

- **Frequency**
 - **Signification**
 - **Causing mechanisms**
 - **Predisposing factors**
- Clinical**
Pathological
Molecular

- **How to reduce local relapses formation**

- **Intraoperative evaluation of surgical margins**
 - **Magnetic resonance**
 - **The role of oncoplastic surgery**
- Benefits**
Hazards

LR FREQUENCY

After breast-conserving surgery and RT



5 – 15%

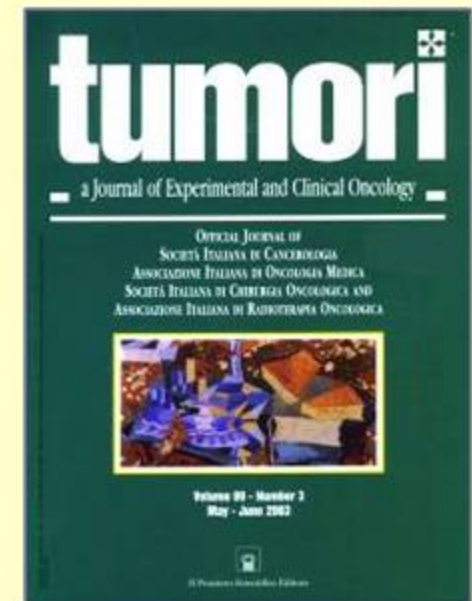
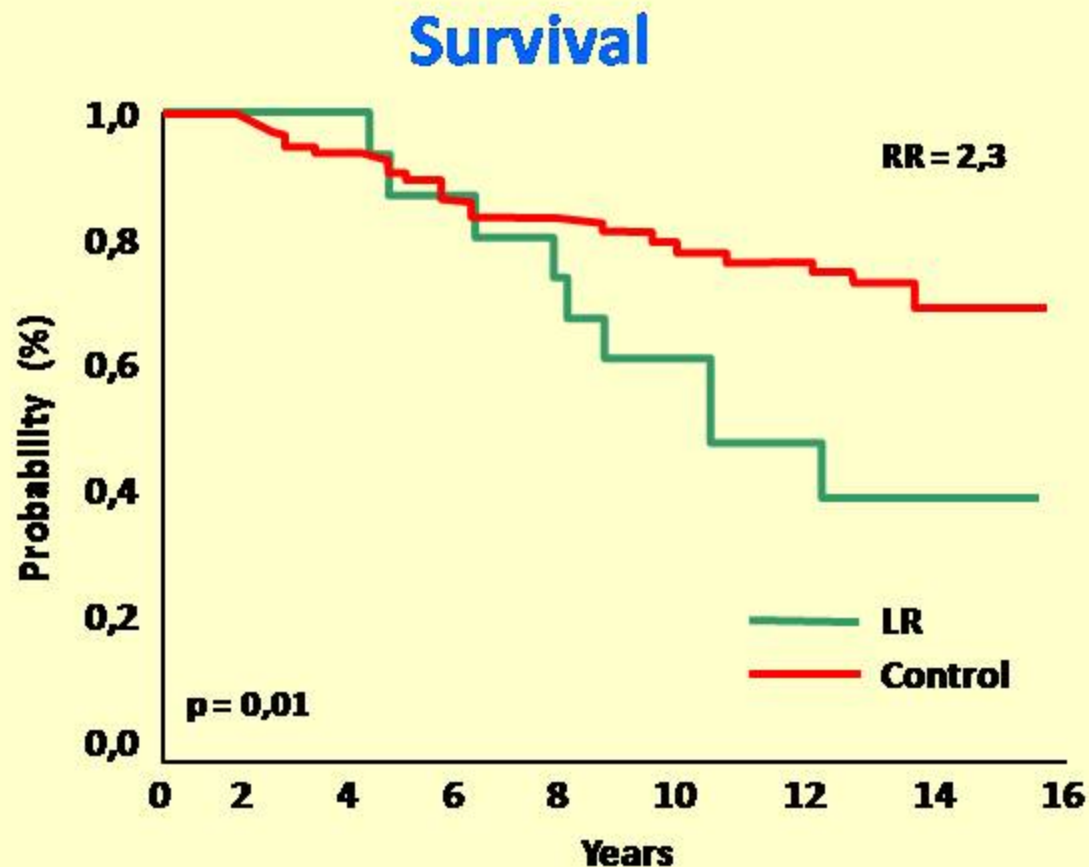
After mastectomy



2 – 8%

PROGNOSTIC EFFECT OF LR AFTER CONSERVATIVE TREATMENT

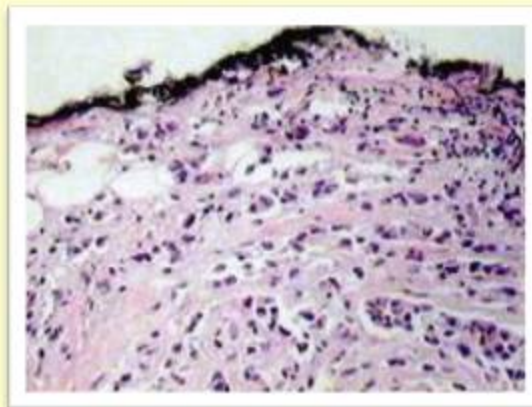
Barros ASCD, Nisida ACT, Pinotti M, Teixeira LC, Pinotti JA.
Tumori 2002; 88: 377-79.



CAUSING MECHANISMS FOR LR

True LR

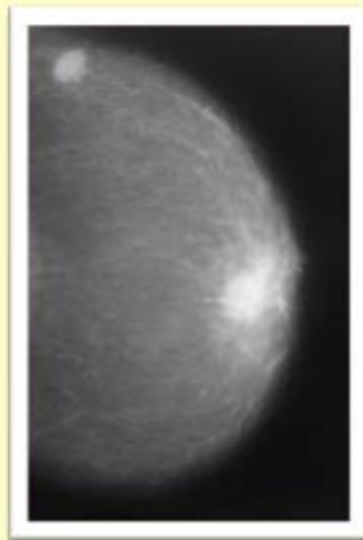
- Same quadrant
- Short interval



**Residual neoplasia
"CIC cells"**

False LR

- Other quadrant
- Long interval



**Synchronous multicentricity
New primary tumor**

STEM-CELLS AND BREAST CANCER

Al-Hajj e col.

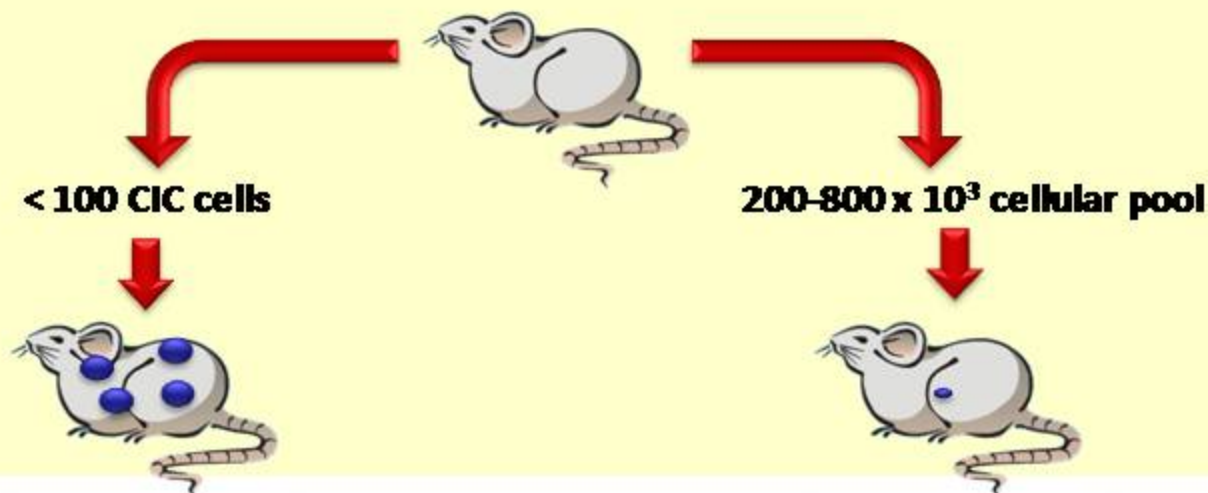
Proc Natl Acad Sci USA 2003; 100: 3983-8

Identification

- **BC cells culture**
- **Flow cytometry**
 - **Cancer initiating cells (CD44⁺, CD24⁻)**
 - **Differentiated cells**



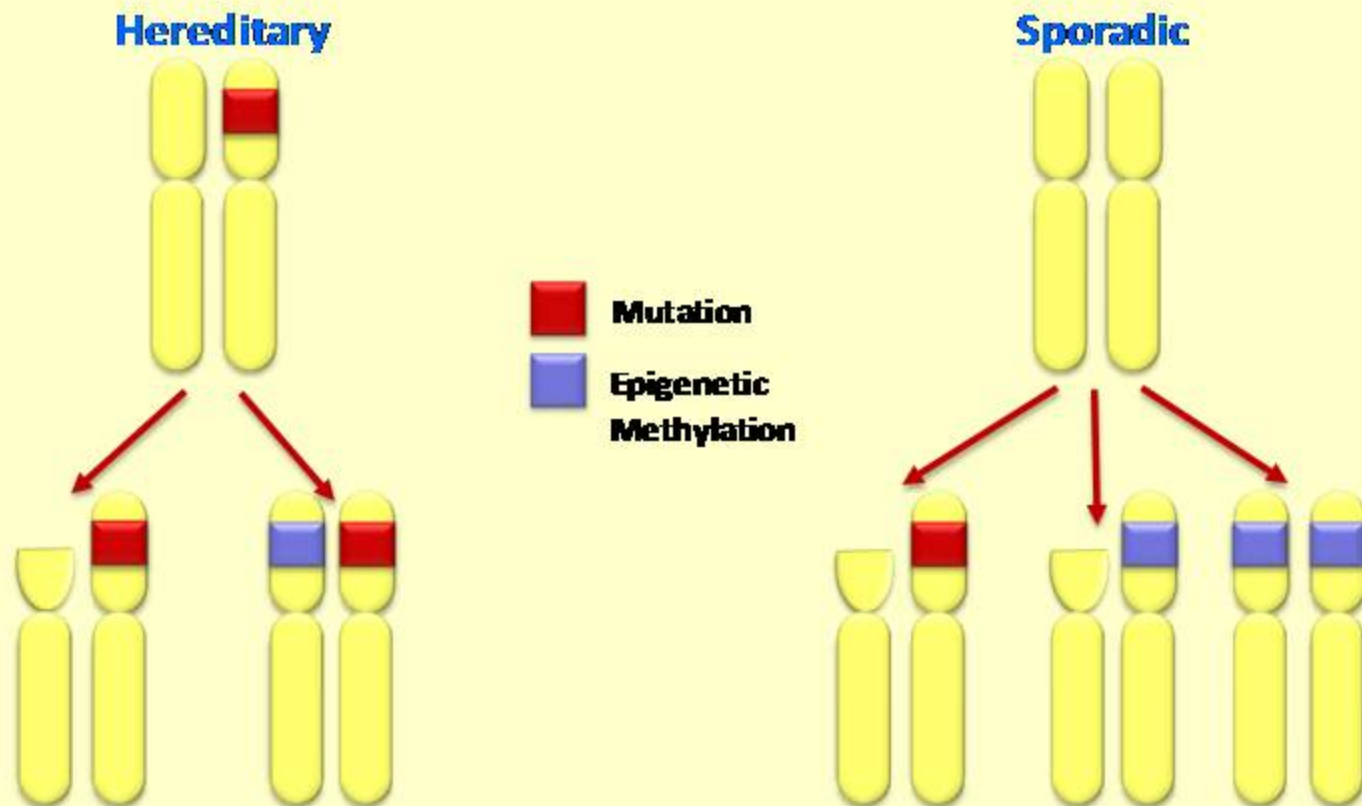
Confirmation in animal model



**IT SEEMS THAT THE MOST IMPORTANT
CAUSING FACTOR OF LOCAL RELAPSES
IS THE PERMANENCE OF RESIDUAL
CIC CELLS REFRACTORY TO THE
ADJUVANT TREATMENT.**

BREAST CANCER INITIATION

SUPPRESSOR GENES INACTIVATION (probably only in CIC cells)

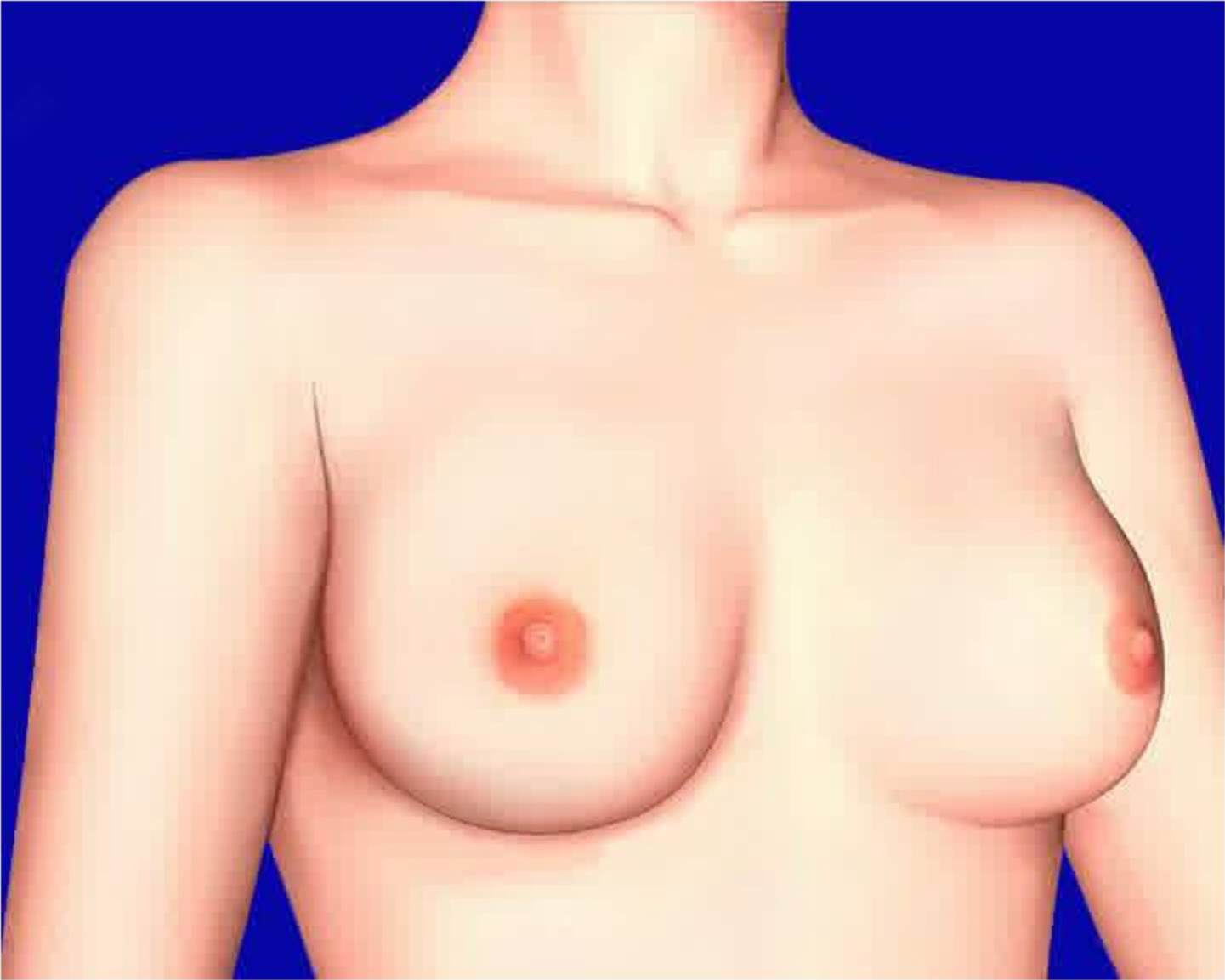


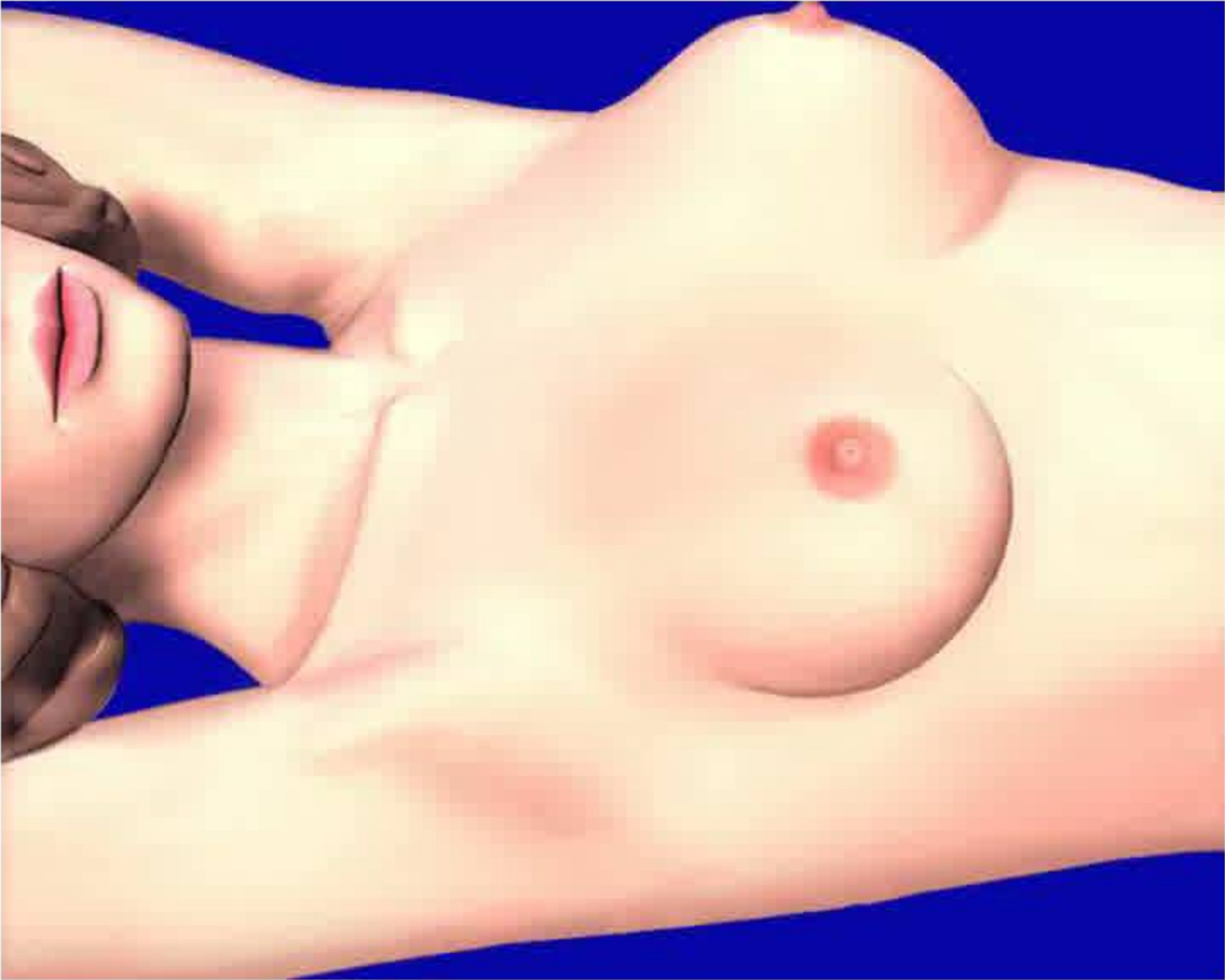
Esteller M
Epigenetics in cancer
N Engl J Med 2008; 358: 1148-59

PREDISPOSING FACTORS FOR LR

- **Clinical factors**
 - **Young age**
 - **Equivocal surgery extension**
 - **Inadequacy of radiation**

- **Pathological factors**
 - **Margin involvement**
 - **Lymph nodes status**
 - **Tumor size**
 - **Histologic grade**
 - **Multicentricity - multifocality**





MOLECULAR PREDICTORS OF LOCAL TUMOR CONTROL

- **Intrinsic molecular subtypes**
- **Genetic signatures**

BREAST CANCER INTRINSIC SUBTYPES

GENETIC CLASSIFICATION BY MICROARRAY

Analysis of 8.102 genes

Classification

1. Luminal A

RE

2. Luminal B

RE

3. Basal -like

RE , RPg , HER-2

4. HER-2 enriched

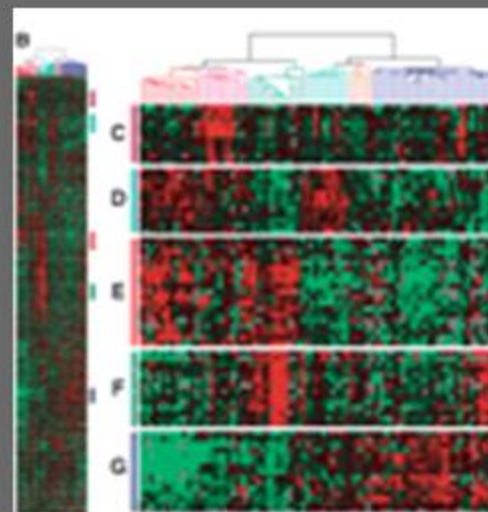
HER-2

5. Normal-like

Perou CM et al.

Molecular portrait of human breast tumours
Nature 2000; 406:747 -52.

Prognosis



Good

**Luminal A and B
normal-like**

Bad

**Basal-like
HER-2 enriched**

Sorlie et al.

Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications

PNAS 2001; 98: 10864 -74

LOCAL RELAPSE AFTER QUADRANTECTOMY AND RADIOTHERAPY

	Subtypes			
	Luminal A %	Luminal B %	HER-2 %	Basal %
Kyndi e col. (n = 489, 5 years)	2	3	13	21

LOCAL RELAPSE AFTER MASTECTOMY AND RADIOTHERAPY

	Subtypes			
	Luminal A %	Luminal B %	HER-2 %	Basal %
Nguyen e col. – 2008 (n = 793, 5 years)	0,8	1,5	8,4	7,1
Millar e col – 2009 (n = 498, 5 years)	1,0	4,3	7,7	9,8
Voduc e col. – 2010 (n = 1461, 10 years)	8	10	21	14



PATIENT REPORT

Patient:
Sex: Female
DOB: 03/11/1976
Medical Record/Patient #:
Date of Surgery: 06/25/2007
Specimen ID/Block ID: 82490-07

Requisition: R02PDR4
Date Received: 08/21/2007
Date Reported: 08/31/2007
Client: Diagnostika Labs
Treating Physician: Dr. Roberto Ibrahim

ASSAY DESCRIPTION

Oncotype DX™ Breast Cancer Assay uses RT-PCR to determine the expression of a panel of 21 genes in tumor tissue. The Recurrence Score™ is calculated from the gene expression results. The Recurrence Score range is from 0-100.

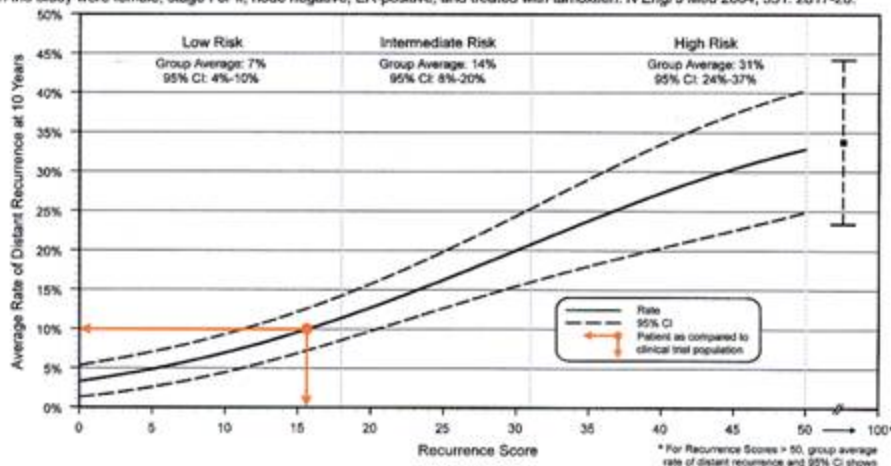
RESULTS

Recurrence Score = 16 Test results should be interpreted using the information in the Clinical Experience section below, which applies only to patients consistent with this clinical experience.

CLINICAL EXPERIENCE

Patients with a Recurrence Score of 16 in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of 10% (95% CI: 7%-13%)

The following results are from a clinical validation study with prospectively-defined endpoints involving 666 patients. The patients enrolled in the study were female, stage I or II, node negative, ER-positive, and treated with tamoxifen. *N Engl J Med* 2004; 351: 2817-26.



Laboratory Director: Patrick Joseph, MD

CLIA Number 05D1016272

This test was developed and its performance characteristics determined by Genomic Health, Inc. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. These results are adjunctive to the ordering physician's workup.

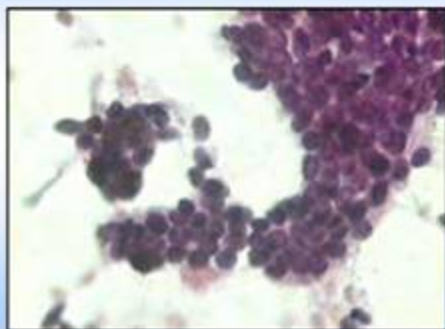
LOCAL RELAPSE AFTER QUART ACCORDING TO ONCOTYPE-DX SCORE

	Score		
	Low (%)	Intermediale (%)	High (%)
Mamounas e col. (n = 390, 10 years)	6,8	10,8	14,6

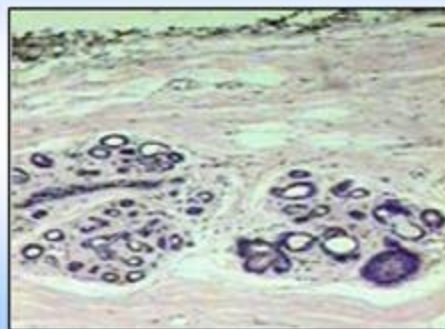
INTRAOPERATIVE SURGICAL MARGINS EVALUATION



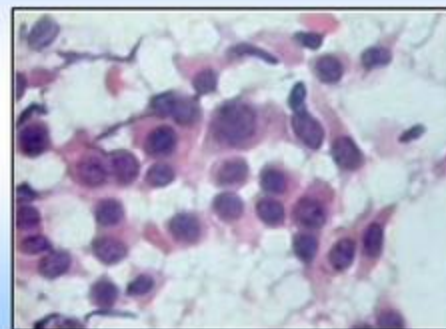
**Margem livre
Citologia**



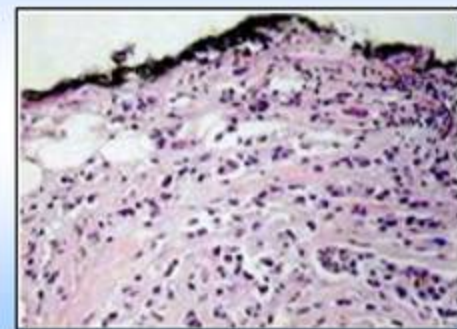
**Margem livre
Histopatologia**



**Margem comprometida
Citologia**



**Margem comprometida
Histopatologia**

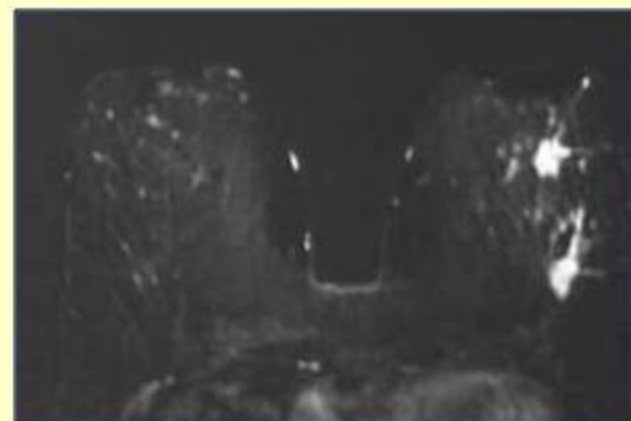


PLANEJAMENTO POR RM DO TRATAMENTO CIRÚRGICO DO CARCINOMA INFILTRATIVO INICIAL DE MAMA

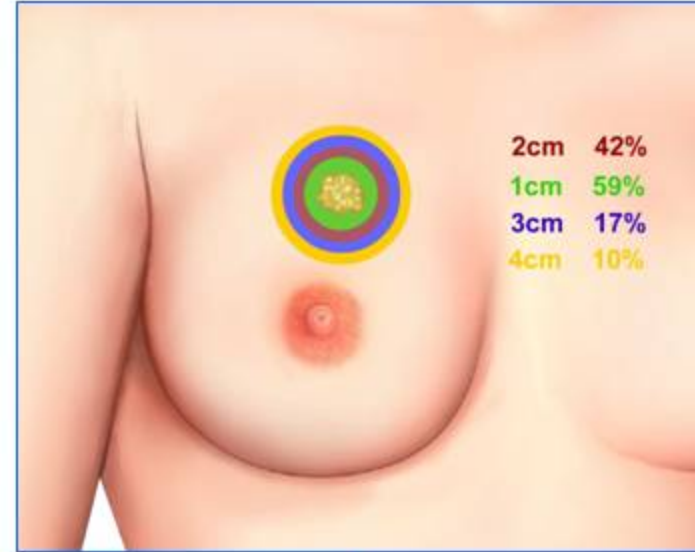
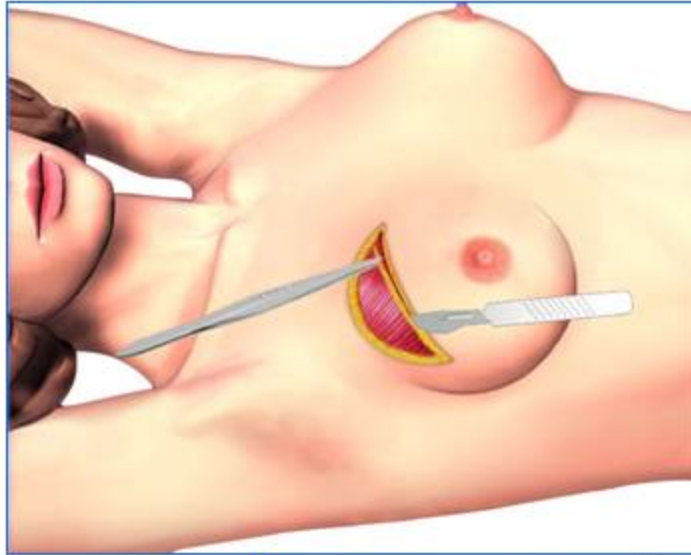
n = 117

Efeito da RM após EF-RX-US		
	n	%
Biópsias indicadas	24	20,5
Novos câncer descobertos	21	17,9
Conversão para mastectomia - adenectomia	21	17,9

Idade inferior a 50 anos
Conversão para mastectomia - adenectomia: 29%



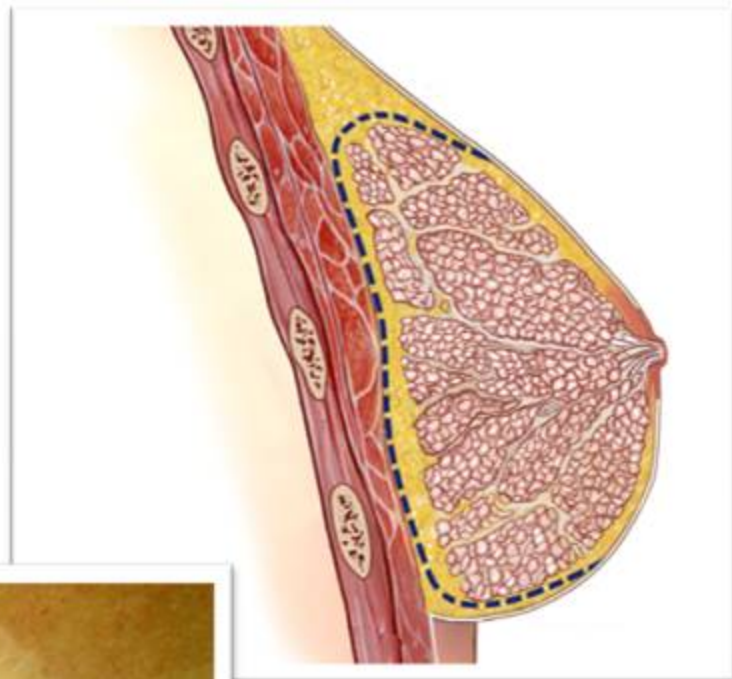
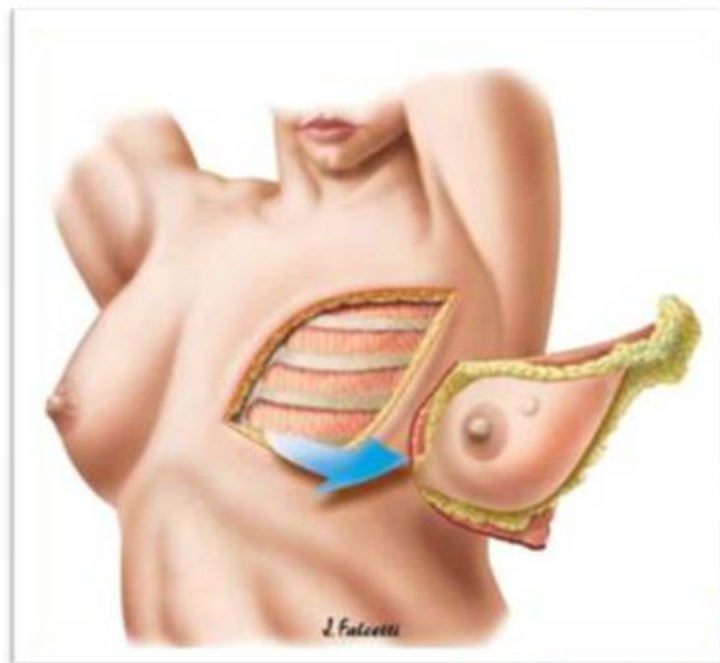
Oncoplastic surgery helps to avoid LR as it allows more adequate tissue removal.



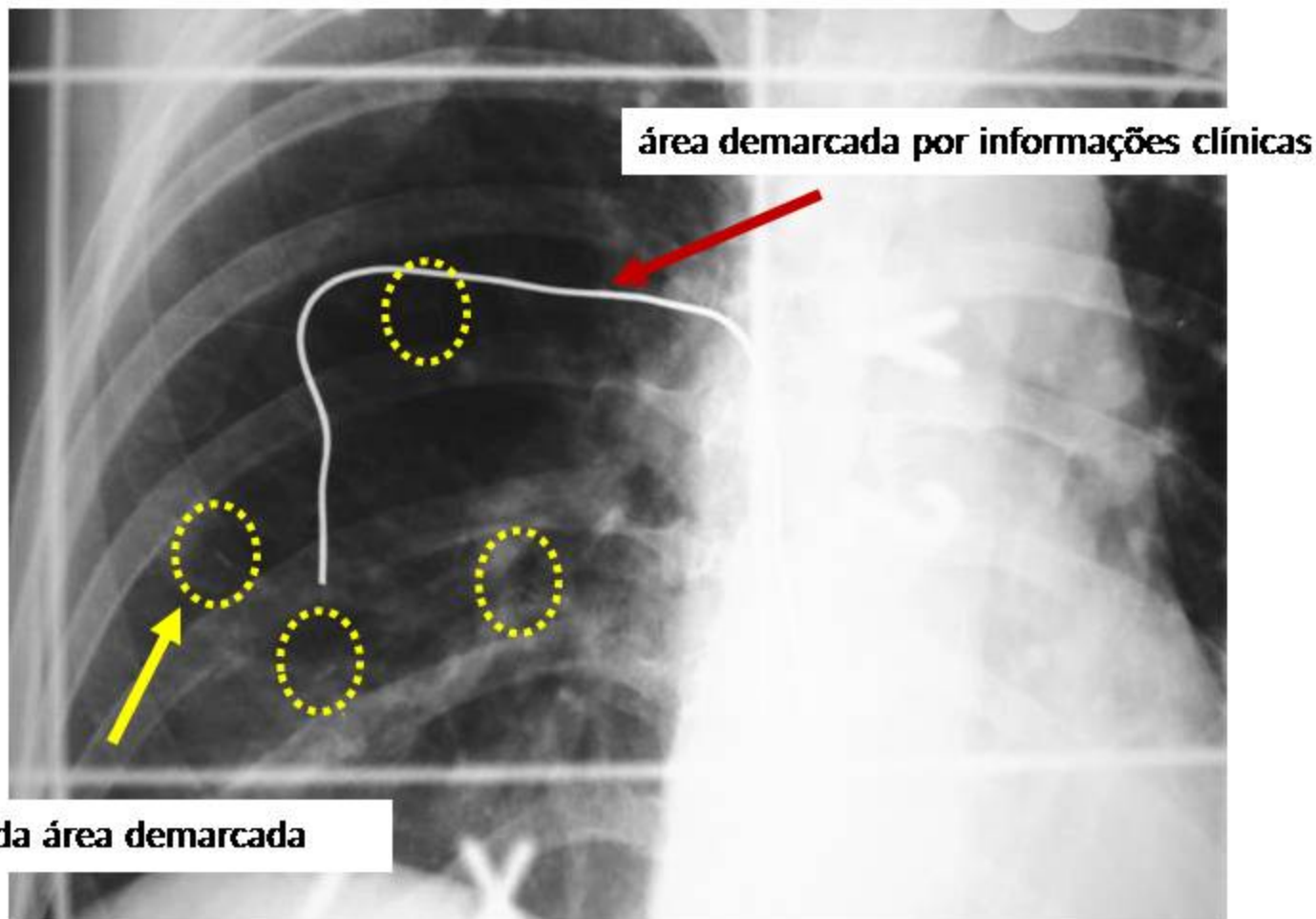




Oncoplastic surgery helps to avoid Ir as it allows more adequate tissue removal.



Caution: oncoplastic manoeuvres may interfere with radiotherapy.



Clips placement are recommended to guide the boost.

TAKE HOME MESSAGES

- **LRs have negative prognostic impact.**
- **LRs are mainly by the permanence of residual CIC cells.**
- **Clinical, morphological and molecular parameters are useful do identify patients at high-risk for LR.**
- **Besides cosmetic effects, oncoplastic surgery favors adequate resections and may reduce the chance of LR.**

Come to Brazil !

