CALGB 40903: Phase II Single-Arm Study of Neoadjuvant letrozole for ER(+) Postmenopausal DCIS

Alliance for Clinical Trials in Oncology 2014 Group Meeting

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DukeMedicine

Clinical Research Professionals Education Meeting
Friday May 9, 2014

Disclosures

GHI: Advisory Board

Merck: Research Funding

I hate overtreating DCIS!

Objectives

- Describe the role of breast cancer screening in the detection of DCIS
- Understand what is currently known about the biology of DCIS
- Explain the current treatment recommendations for DCIS, including indications for adjuvant radiation
- Identify how CALGB 40903 addresses some of the unknown questions in DCIS


The New York Times Magazine
MYSTERIES
OF FITNESS
THE
PSYCHOLOGY
OF LYING
Our
Feel-Good
War on Breast
Cancer
Has raising awareness become more important than saving lives? BY PEGGY ORENSTEIN

The New York Times

Prone to Error: Earliest Steps to Find Cancer

By STEPHANIE SAUL
Published: July 19, 2010

In 2007, Monica Long 49 year old divorced mother of three girls went for her annual mammogram

A biopsy was performed at Cheboygan Memorial Hospital, and a diagnosis of DCIS was made.

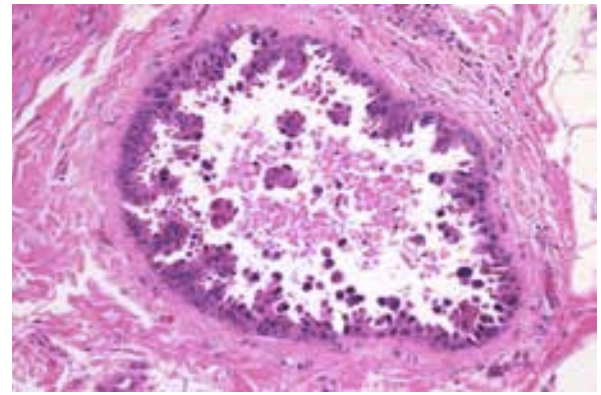
Underwent lumpectomy and radiation

Changed care providers—new pathologists disputed the original diagnosis, claiming that the patient had never had DCIS

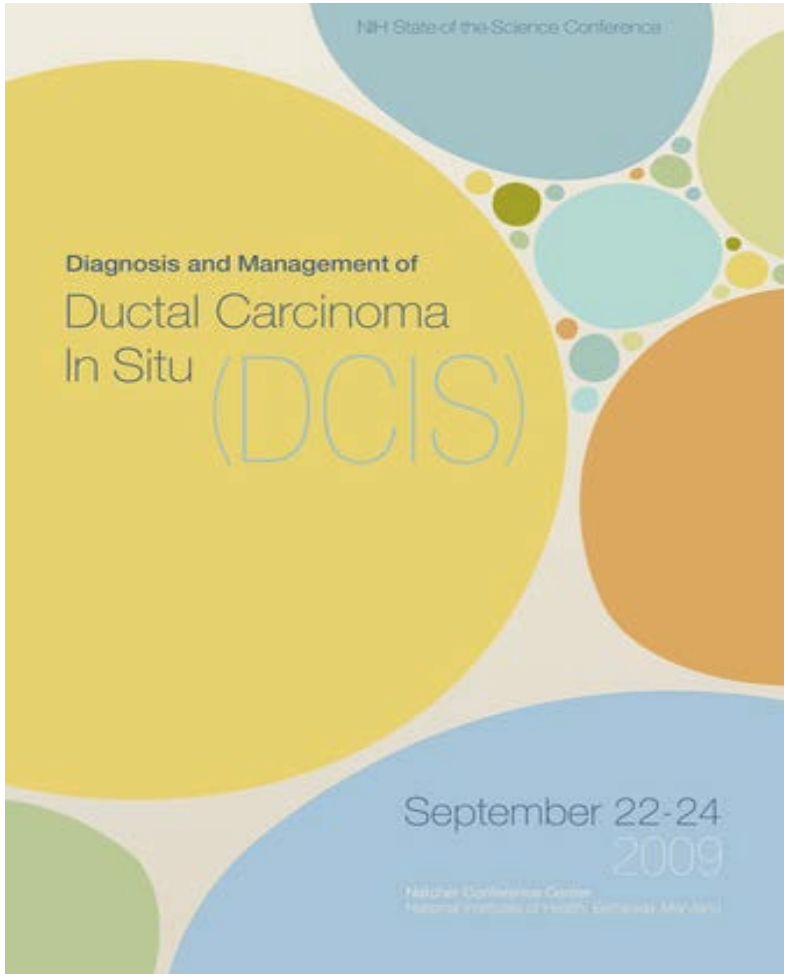
Epidemiology of DCIS

- Ductal carcinoma ***in situ, precancer, preinvasive cancer***
- Estimated incidence of DCIS: almost 50,000 new cases annually
- Usually diagnosed by calcifications on mammography in asymptomatic patient
- DCIS now comprises over 20% of all mammographically detected breast cancers

- ***Nonobligate precursor of invasive cancer; rate and likelihood of progression are unknown***



American Cancer Society. Cancer Facts and Figures 2011. Ernster VL, et al. *J Natl Cancer Inst*. 2002.

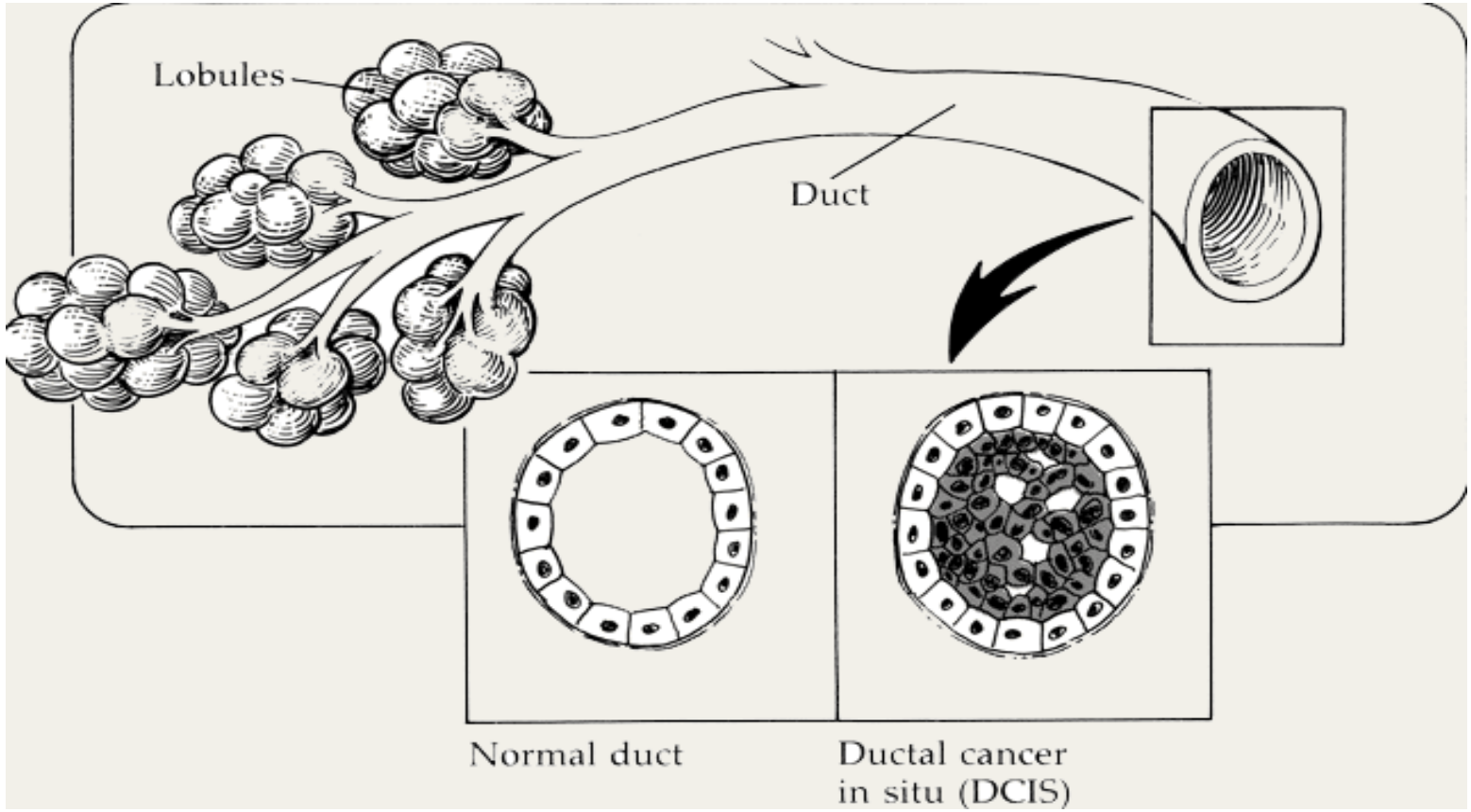


NIH State-of-the-Science Conference:
Diagnosis and Management of Ductal Carcinoma in Situ (DCIS)

September 22-24, 2009
Bethesda, Maryland

Conclusions: The diagnosis and management of DCIS is **highly complex** with **many unanswered questions**, including the fundamental natural history of untreated disease. Because of the noninvasive nature of DCIS, coupled with its favorable prognosis, **strong consideration should be given to remove the anxiety-producing term "carcinoma" from the description of DCIS**. The outcomes in women treated with available therapies are excellent. Thus, the primary question for future research must focus on the accurate identification of patient subsets diagnosed with DCIS...

DCIS is Part of a Pathologic Continuum



Burstein HJ, et al. *N Engl J Med*. 2004.

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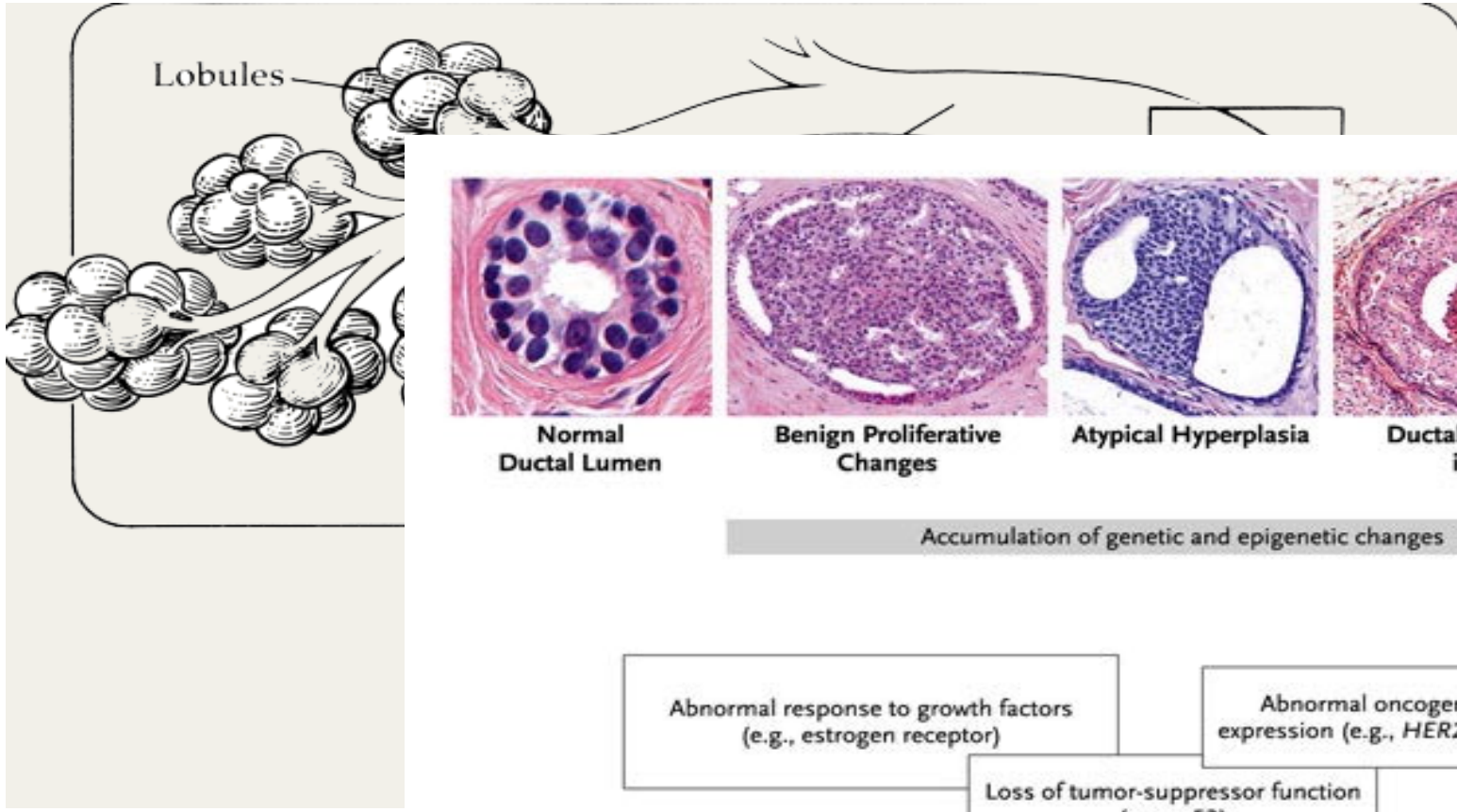

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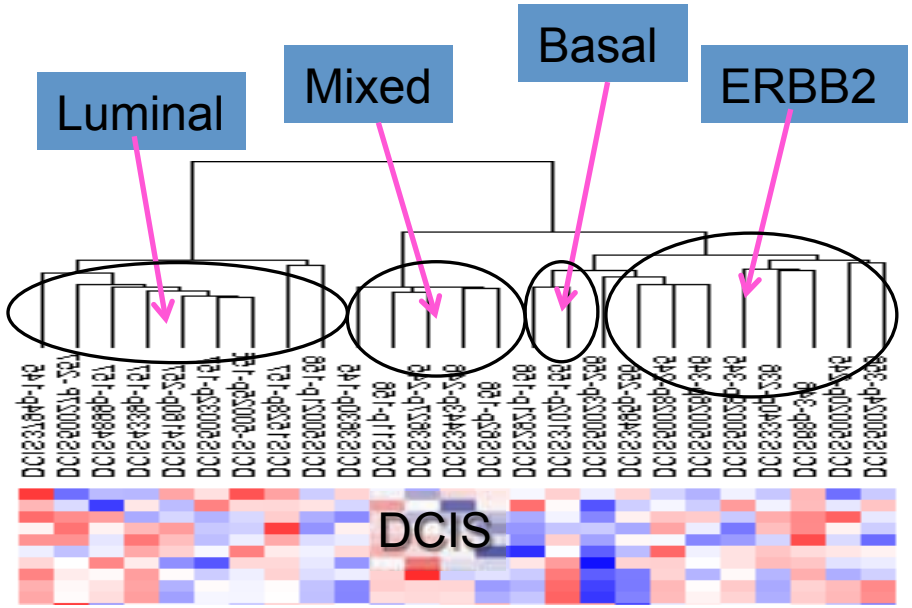
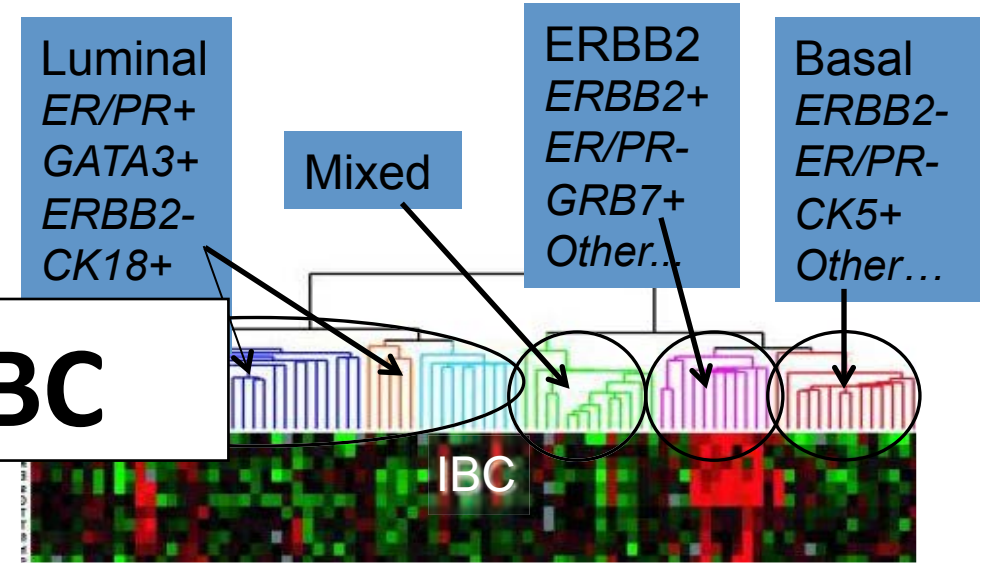
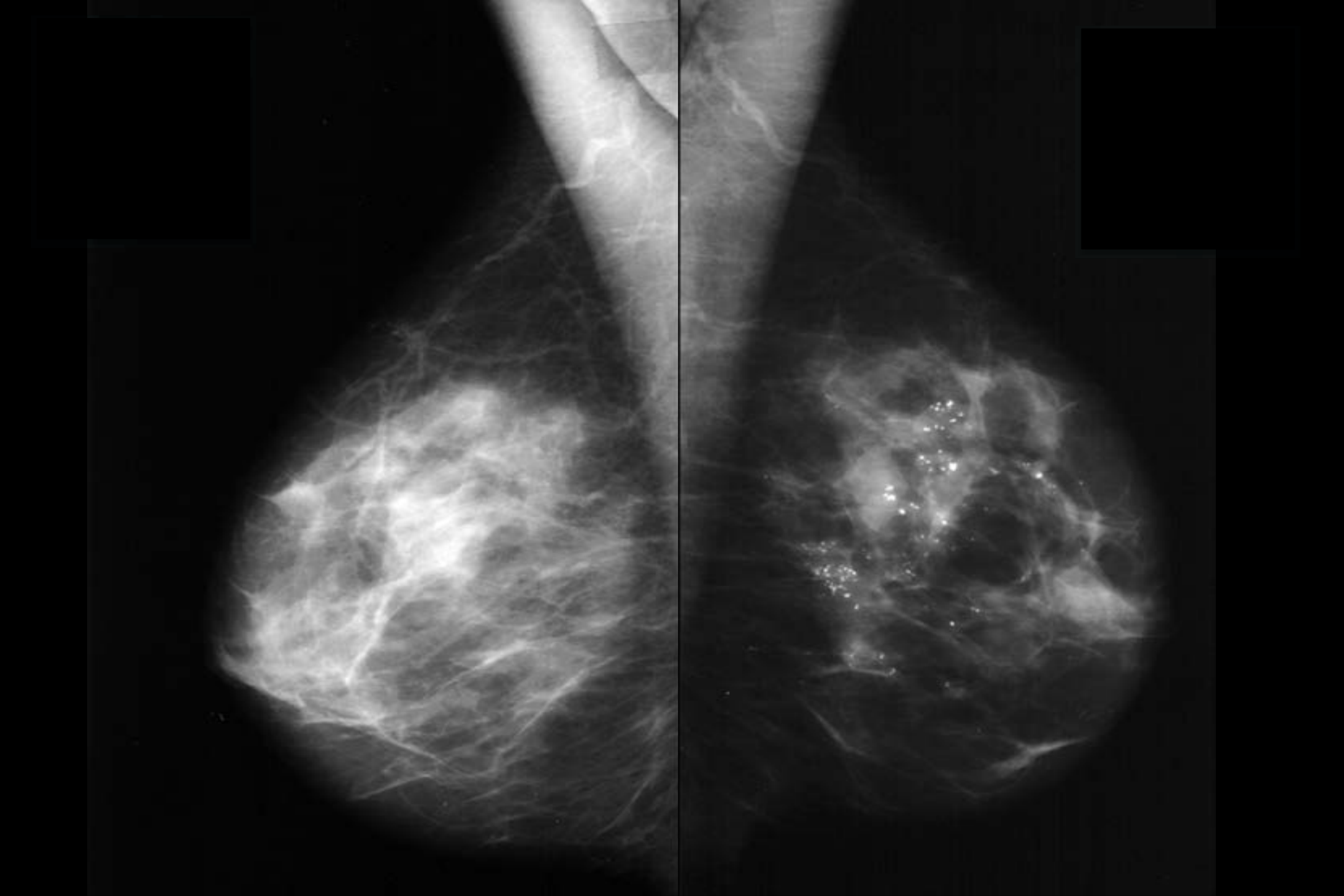
Molecular Classification of DCIS and invasive cancer

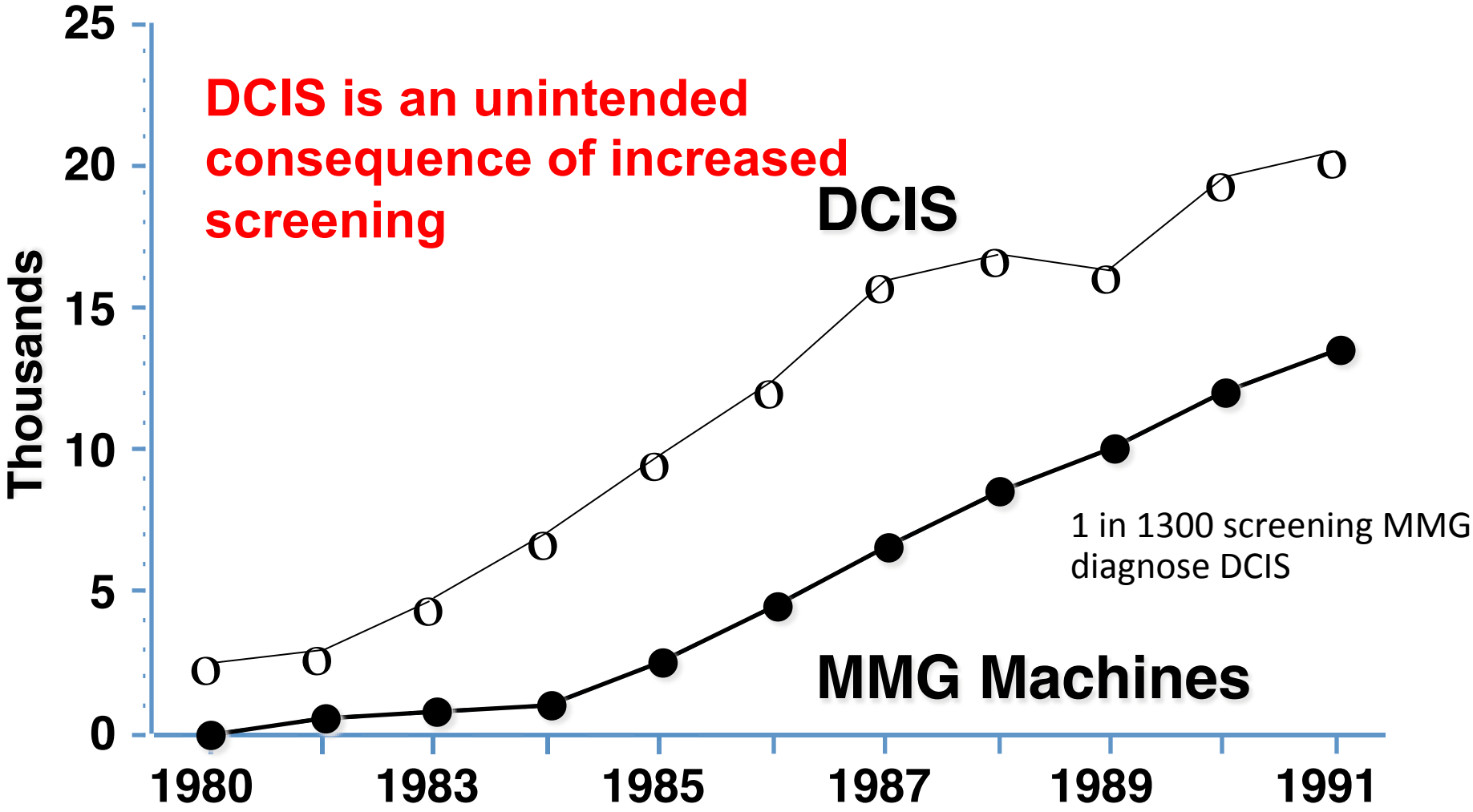


DCIS ≈ IBC

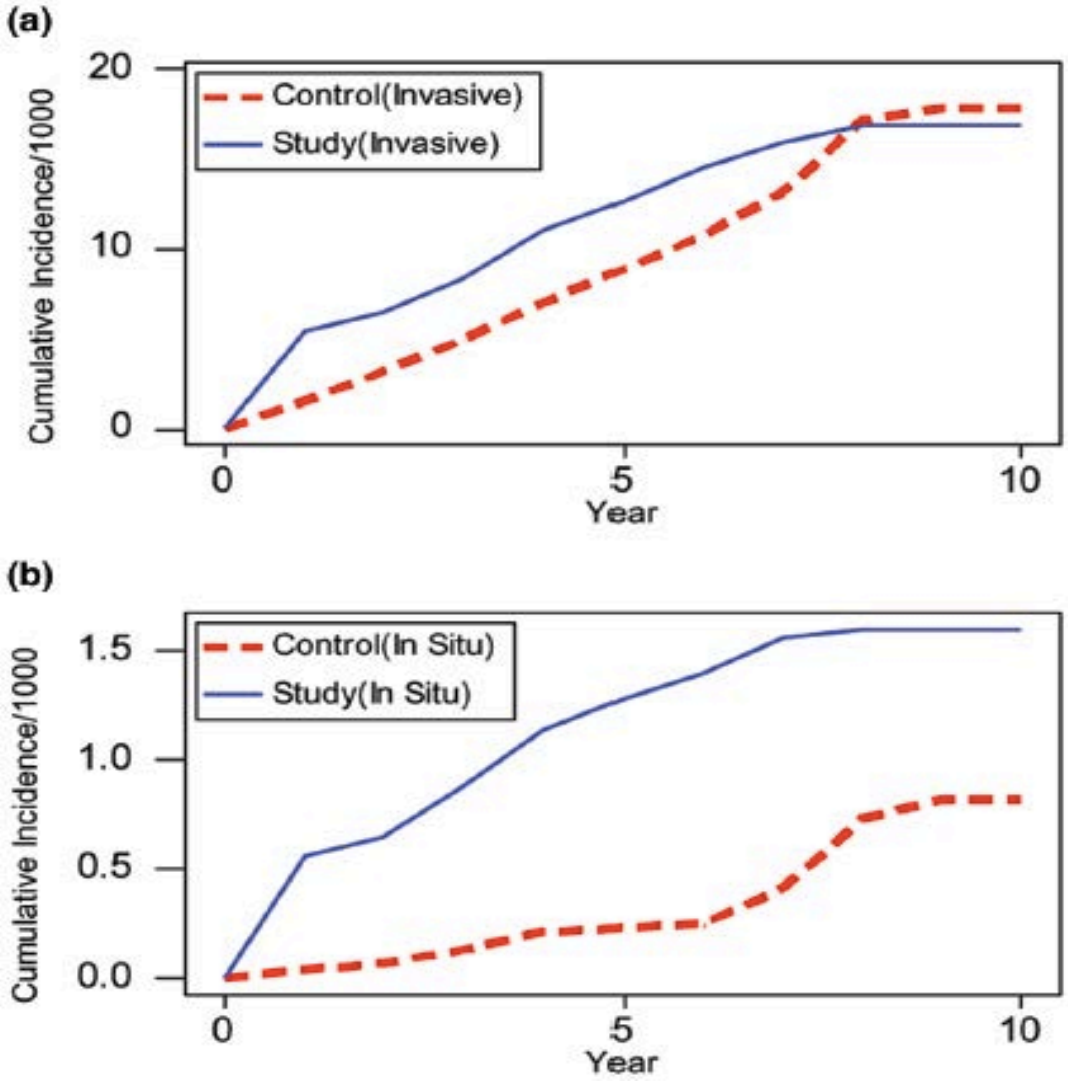




DCIS Increased as the Number of Mammography Machines Increased



Screening increases the detection of DCIS: Swedish Two-County Trial



Cumulative incidence of breast cancers in study and control groups of
the Swedish Two-county Trial.
(a) Invasive cancers. **(b)** In situ cancers.

Duffy S et al, Breast Cancer Research 2005

Weighing the benefits and harms of mammographic screening

Benefits vs. harms of screening mammography per 1,000 women			
Age	**Mortality reduction**	**No. of women with at least 1 false alarm**	**No. of women overdiagnosed**
40	0.1-1.6 lives saved	510-690	?-11
50	0.3-3.2 lives saved	490-670	3-14
60	0.5-4.9 lives saved	390-540	6-20

"Mammography has both benefits and harms — that's why it's a personal decision"

versus

"Mammograms save lives."

Welch G et al, JAMA Internal Medicine, 2014

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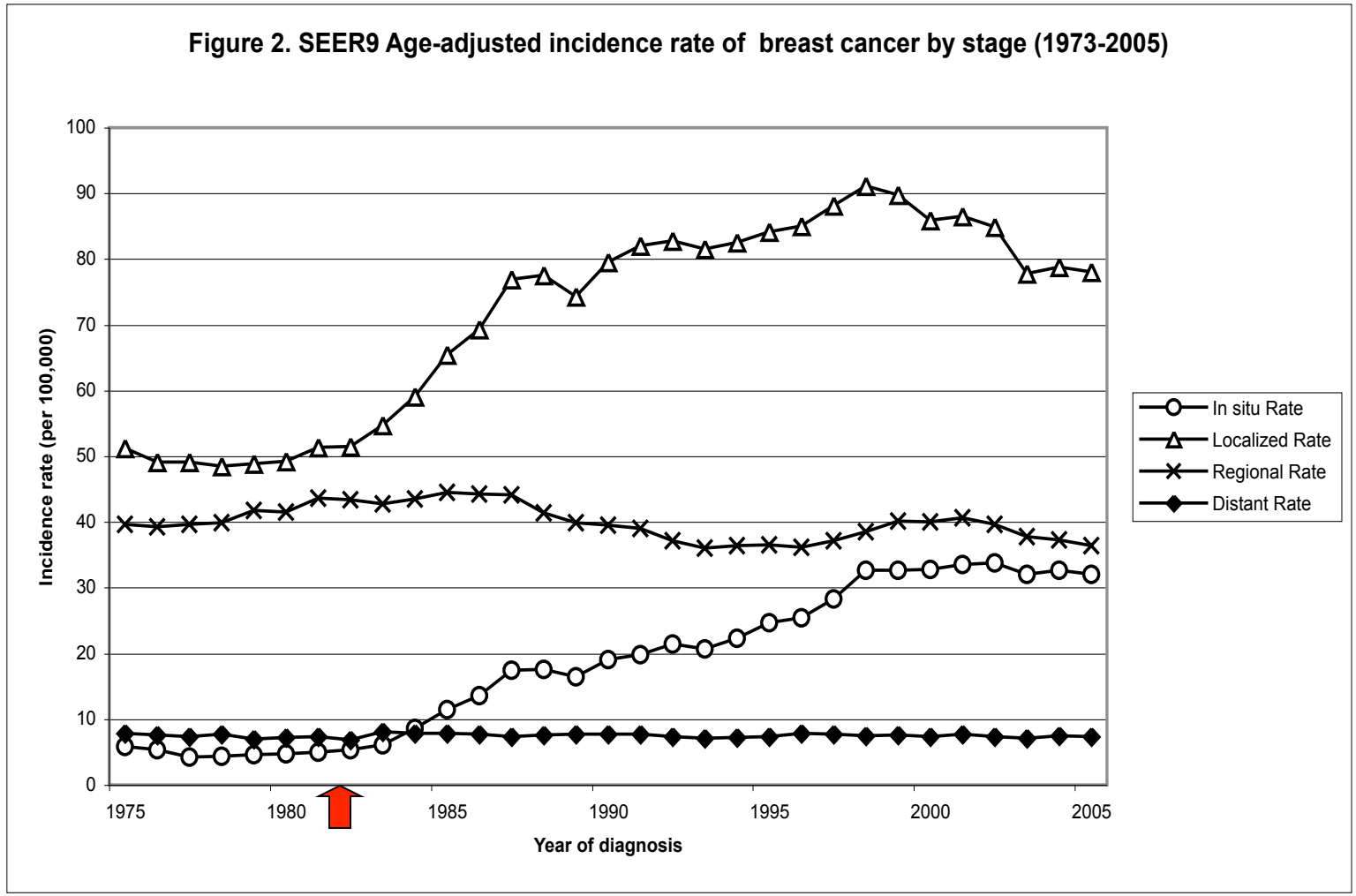
“Overdiagnosis” according to Wikipedia:

The diagnosis of "disease" that will never cause symptoms or death during a patient's lifetime. Overdiagnosis is a side effect of testing for early forms of disease which may turn people into patients unnecessarily and may lead to treatments that do no good and perhaps do harm.

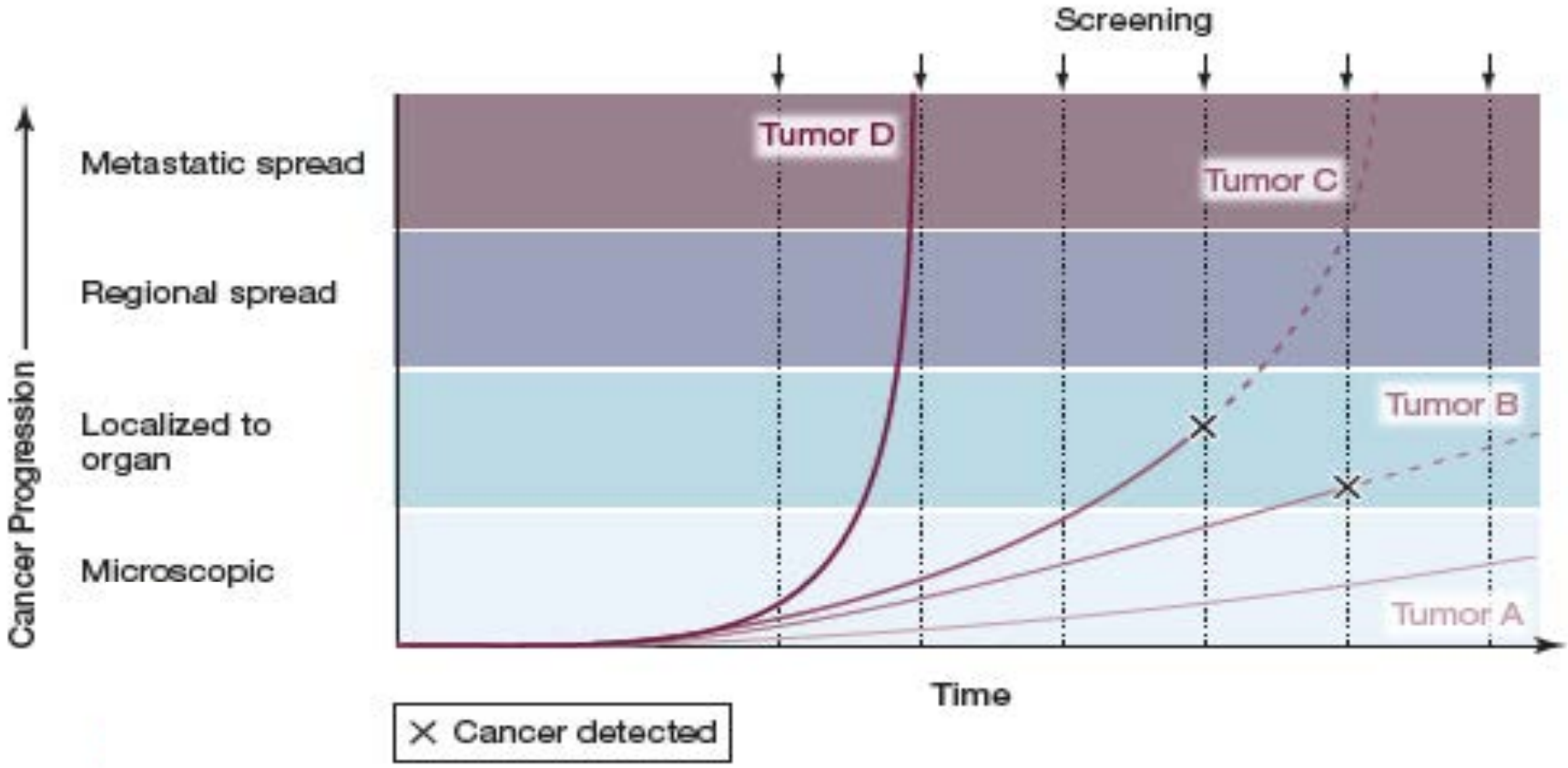
Overdiagnosis occurs when a disease is diagnosed correctly, but the diagnosis is irrelevant. A correct diagnosis may be irrelevant because **treatment for the disease is not available, not needed, or not wanted, “or does not add benefit.”**



SEER 9 age-adjusted incidence rate of ductal carcinoma in situ and invasive breast cancer for all females, 1973-2005. Mammography screening was introduced in the early 1980s

Ozanne E et al, BCRT 2011

Some patients are diagnosed with “cancer” that does not progress



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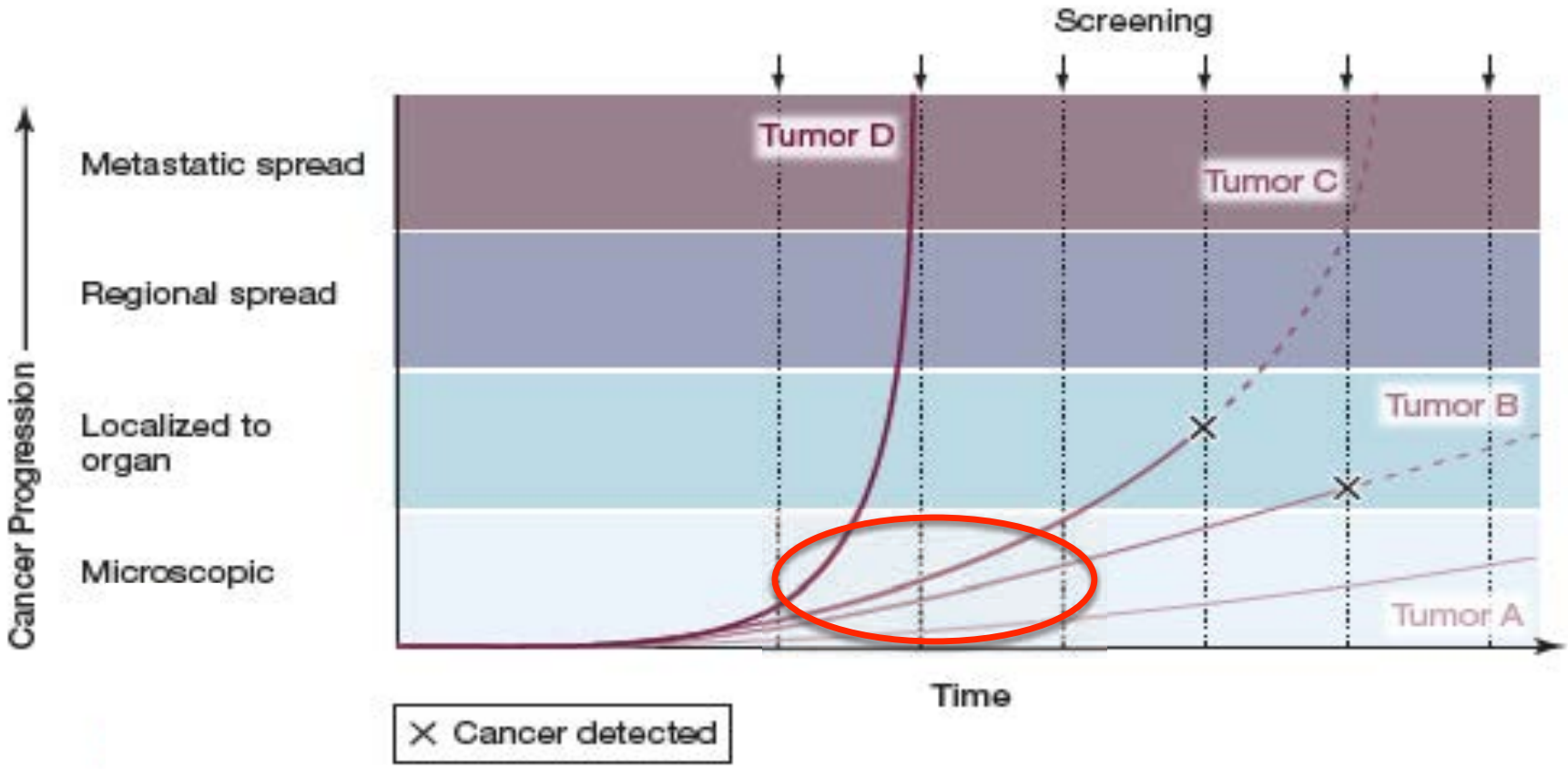
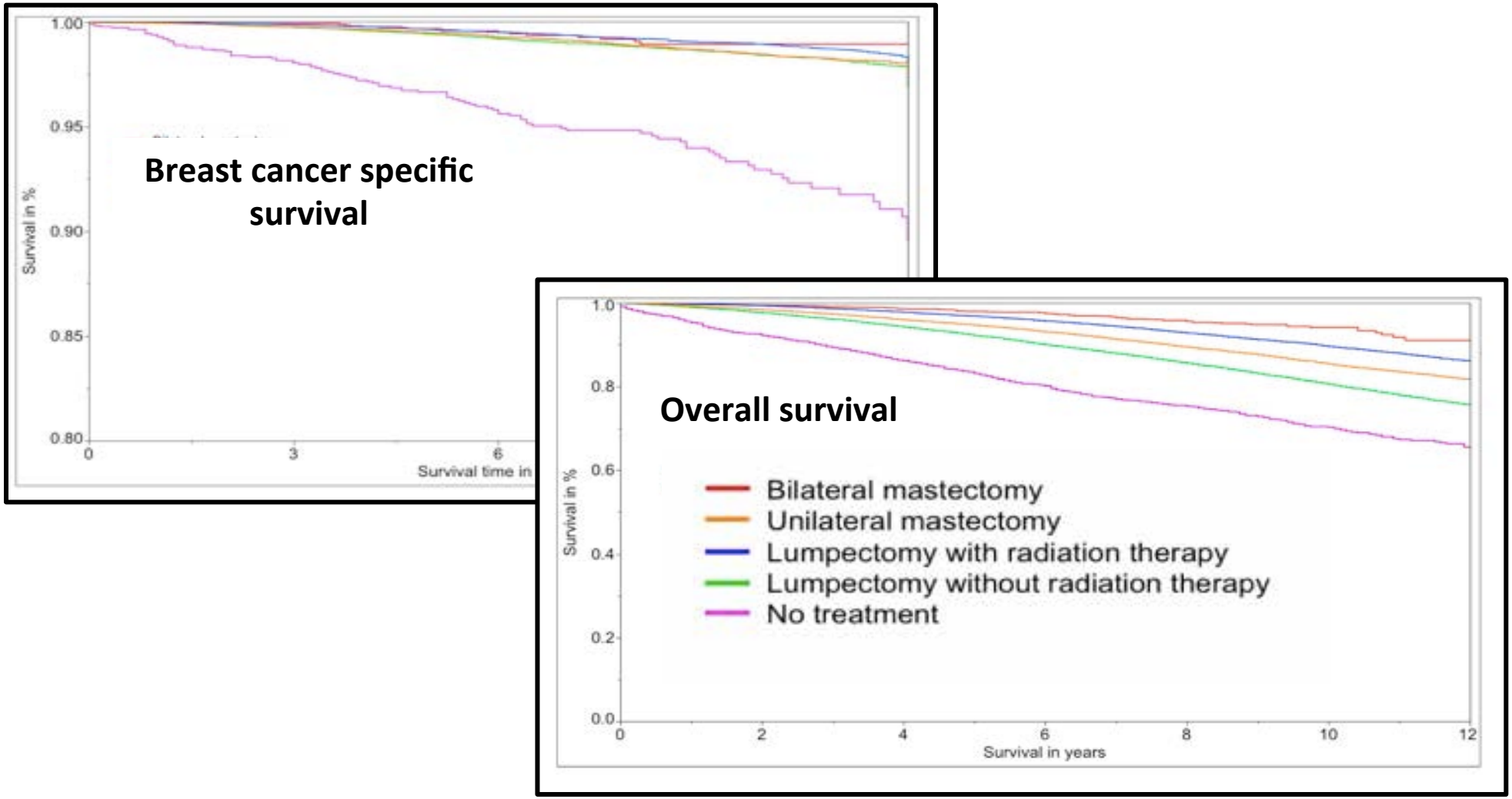
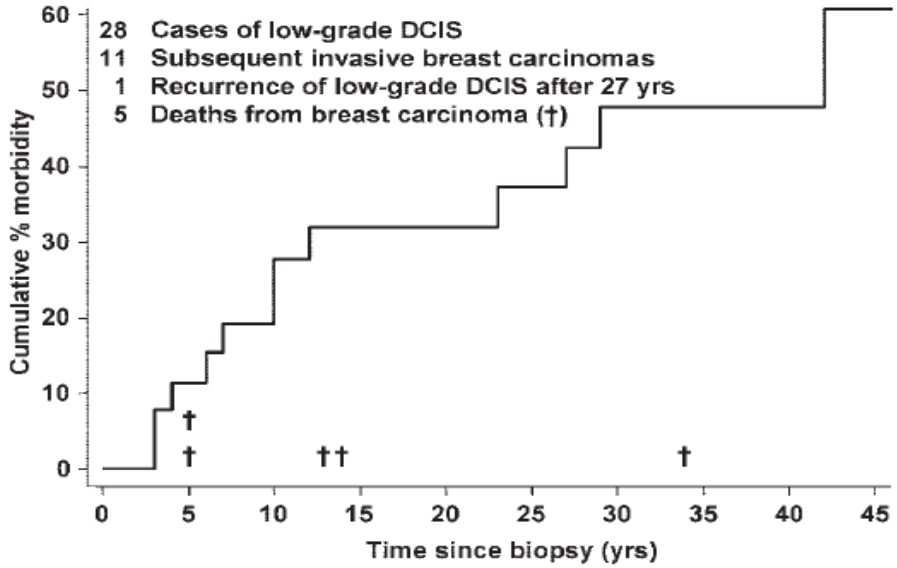


DCIS and competing causes of mortality



SEER 1991-2010; unpublished data

Natural history of DCIS



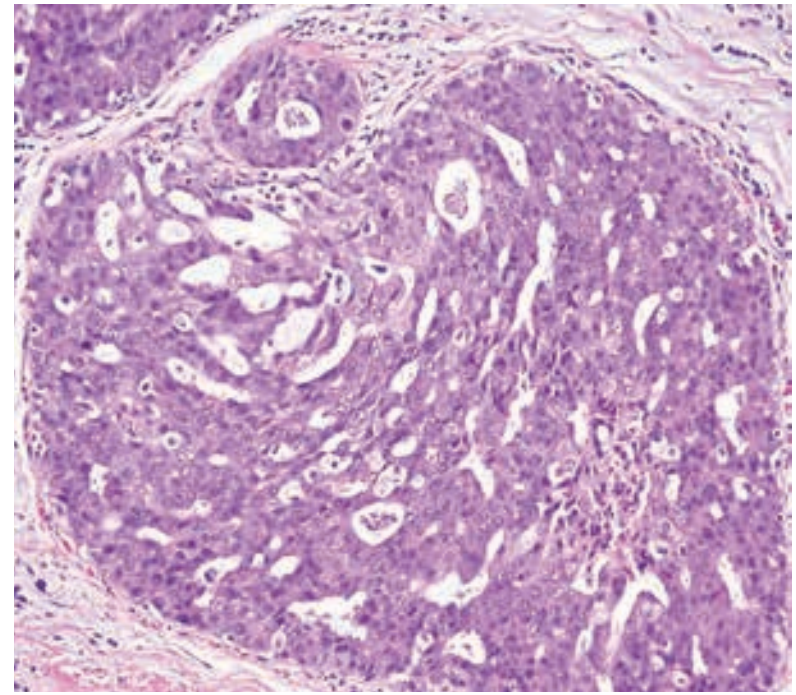
Vanderbilt Cohort
Sanders et. al. *Cancer* 2005

Nurses' Health Study
Collins et. al. *Cancer* 2005

DCIS grade	N	Subsequent DCIS	Subsequent invasive ca
Low	4	1	2
Intermediate	6	2	2
High	3	1	2
Total	**13**	**4**	**6**

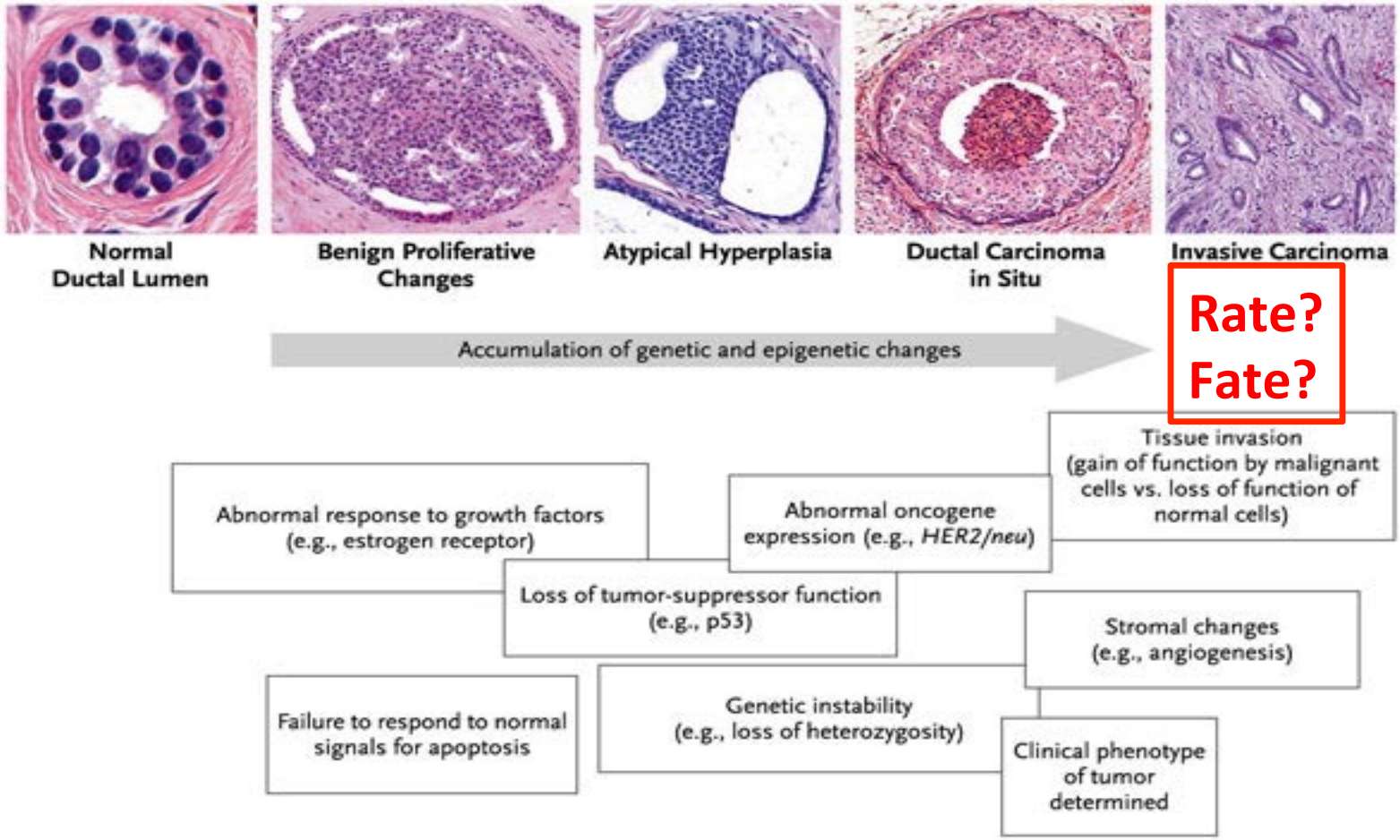
Disease reservoir of DCIS

- 7 autopsy series examined the prevalence of breast cancer in women not known to have had breast cancer in life
  - Invasive cancer 1.3% (0-1.8%)
  - DCIS 8.9% (0-14.7%)
- Series reporting a higher level of scrutiny tended to discover more cases of cancer



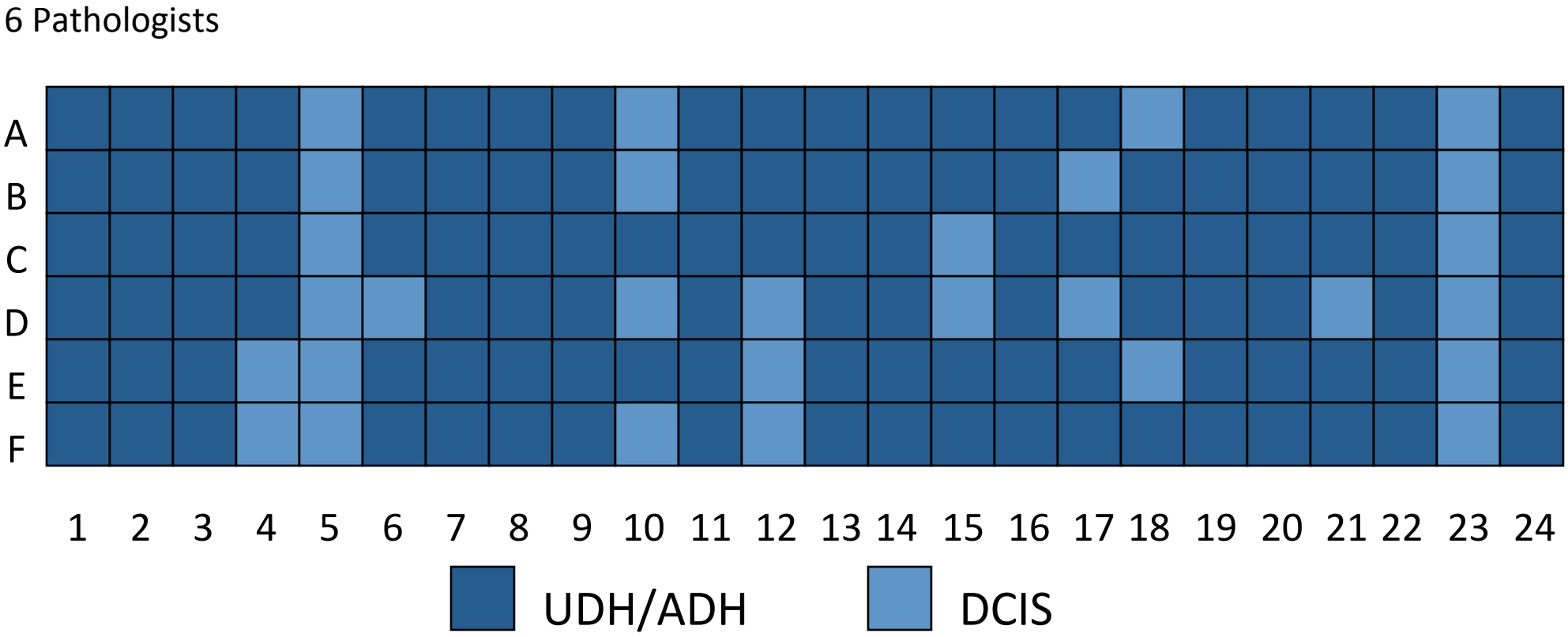
Welch HG, *Ann Intern Med*, 1997, 127:1023-8

DCIS is Part of a Continuum of Pathologic Change



Burstein HJ, et al. *N Engl J Med*. 2004.

Pathologists don’t always agree who has DCIS



24 biopsies of proliferative breast lesions

8 cases were discordant

Schnitt SJ, Am J Surg Pathol 1992;16:1133-1143

NCCN Guidelines for Treatment of DCIS

DCIS Stage 0
Tis, N0, M0

- History and physical exam
- Diagnostic bilateral MMG
- Pathology review
- Determination of tumor ER status
- Genetic counseling if patient is high risk for hereditary breast cancer

- **Total mastectomy**
- **Lumpectomy + whole breast radiation therapy**
- **Lumpectomy only**
- with or without sentinel node biopsy +/- reconstruction

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ADH/ALH

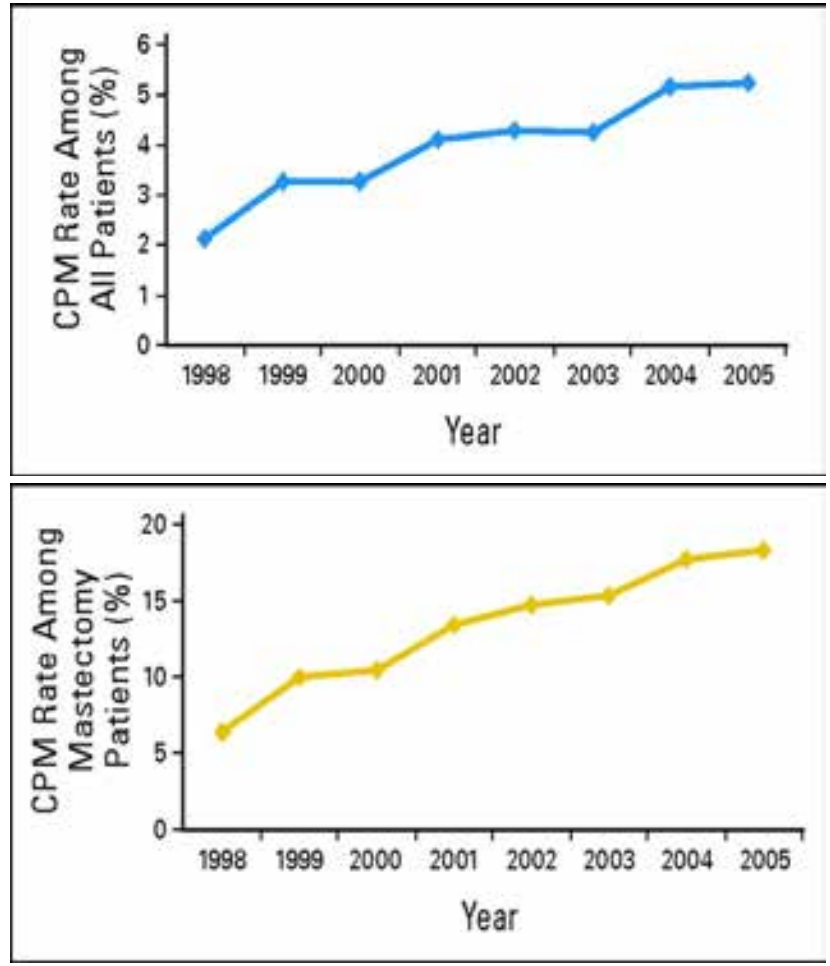
- History and physical exam
- Diagnostic bilateral MMG
- Pathology review
- Determination of tumor ER status
- Genetic counseling if patient is high risk for hereditary breast cancer

- **Consider chemoprevention**
- **Active surveillance**

Mastectomy:

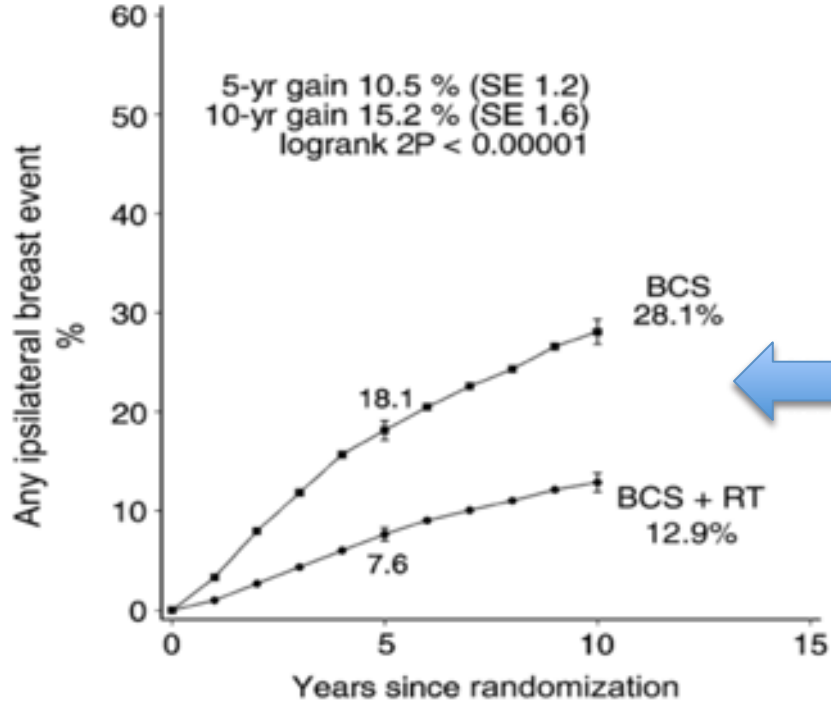
Contralateral Mastectomy for DCIS

- SEER database of 51,030 women diagnosed with unilateral DCIS between 1998 and 2005
- 2,072 women chose contralateral prophylactic mastectomy (4.1% of all patients, 13.5% of patients undergoing mastectomy)
- Between 1998 and 2005, the contralateral prophylactic mastectomy rate in women undergoing ipsilateral mastectomy for DCIS increased from **<u>6.4% to 18.4%</u>**



Tuttle JM; JCO 2009

Radiation Reduces Risk of DCIS Recurrence After Lumpectomy



Absolute reduction IBTR: 15.2%

- Overall, there is over a 50% proportional reduction in ipsilateral events with radiation following lumpectomy; the absolute magnitude of the reduction was dependent on baseline recurrence risk

EBCTCG. *J Natl Cancer Inst Monogr*. 2010.

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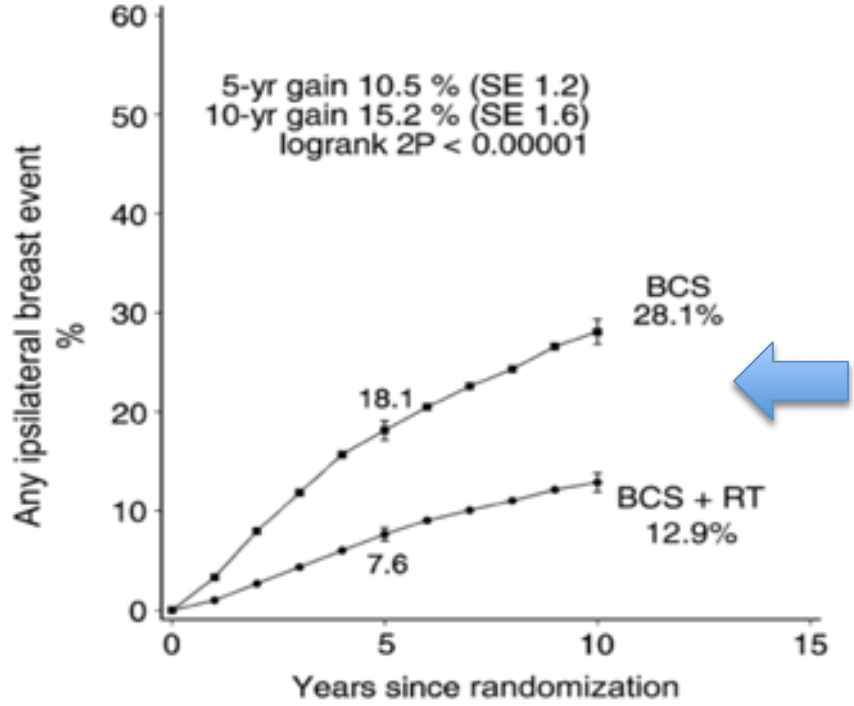


Absolute reduction IBTR: 15.2%

This benefit was independent of patient age, tumor size, margin status

EBCTCG. *J Natl Cancer Inst Monogr*. 2010.

Lumpectomy only:

To radiate or not to radiate? Defining a low risk DCIS subset

- Clinical data
  - Grade, size, ER, PR, Her2.patient characteristics
  - Van Nuys Prognostic Index
  - clinical nomogram
- Molecular tools
  - DCIS Score
  - Other emerging markers
- Decision aids

1. Macdonald HR, et al. *Am J Surg*. 2006;192:420-2.
2. Silverstein MJ,Lagios MD. *J Natl Cancer Inst*. 2010;41:193-6.
3. Rudloff U, et al. *J Clin Oncol*. 2010;28:3762-69.
4. Ringberg A, et al. *Eur J Cancer*. 2001;37:1514-22.
5. Kerlikowske K, et al. *J Natl Cancer Inst*. 2010;102:627-37.

Van Nuys Prognostic Index (VNPI)

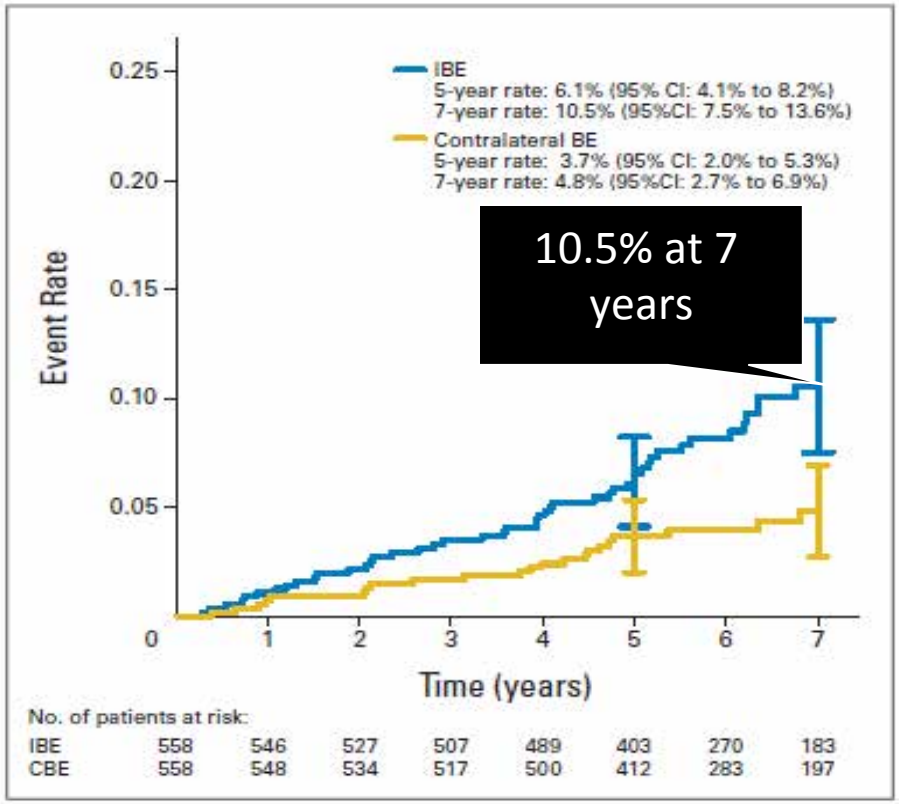
Factor	1	2	3
Size	≤15 mm	16-40 mm	>40 mm
Margin	≥ 10 mm	1-9 mm	<1 mm
Pathology	grade 1/2 no necrosis	grade 2 necrosis	grade 3
Age	>60 years	40-60 years	<40 years

Silverstein MJ, Lagios MD, *J Natl Cancer Inst Monogr*. 2010;41:193-6.

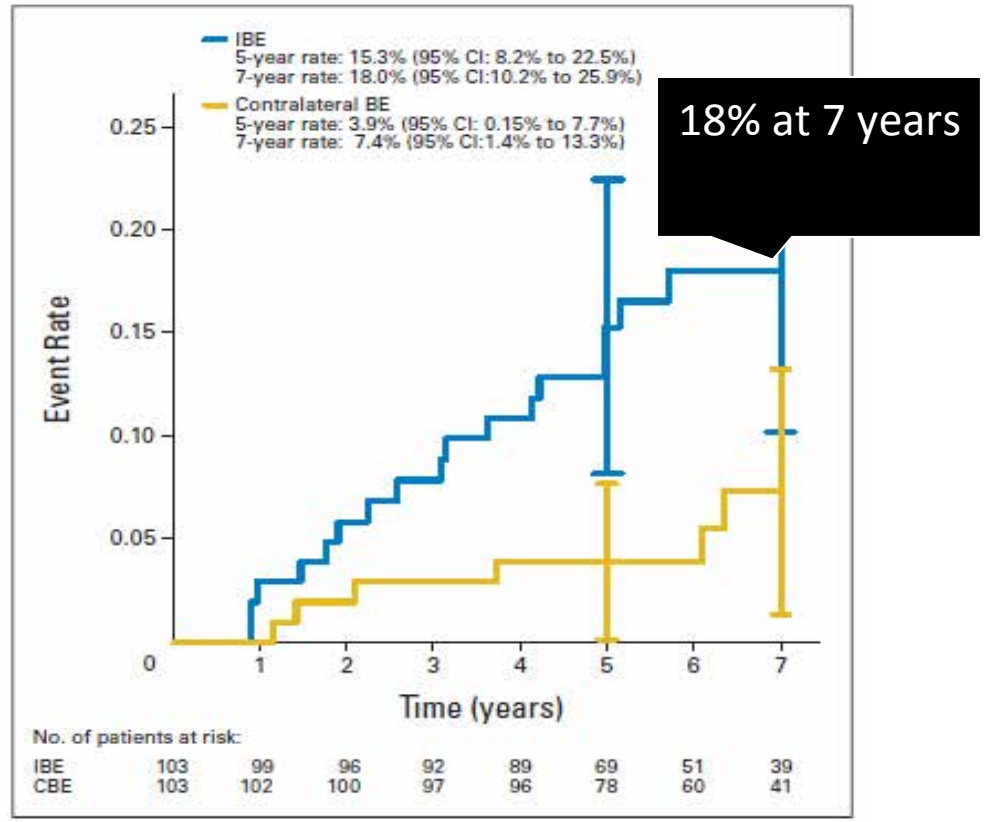
Outcomes of excision alone for DCIS

Study	n	Follow up	LRR	Grade, margin
DFCC, 1994	158	5-year	12%	1-2 1 cm
E5194, 1997	670	7-year	10.5% 18%	1-2 3 mm
	246 **45** **36**	**10-year**	**12%** **24%** **27%**	**LOW** **INTERMED** **HIGH**
RTOG 9408, 1999	298	5-year	3.2%	1-2 3 mm
NSABP B17, 1985	403	12-year	32%	All; 15% grade 3 Close/+ 17%
EORTC	503	10-year	26	All; 18% grade 3 Close/+ 16%

ECOG E5194 – Ipsilateral and Contralateral Breast Events at 7 years



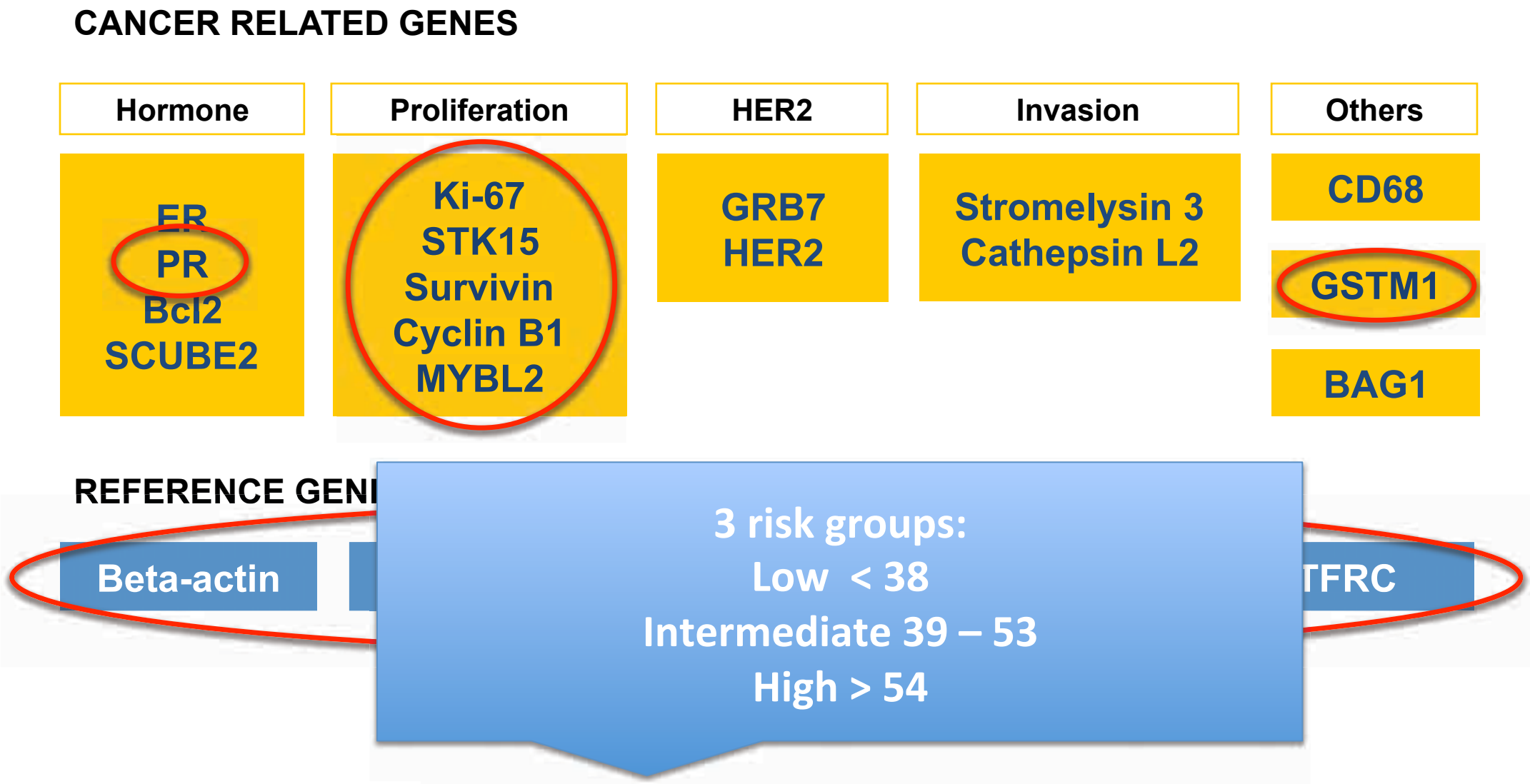
Low-Intermediate Grade



High Grade

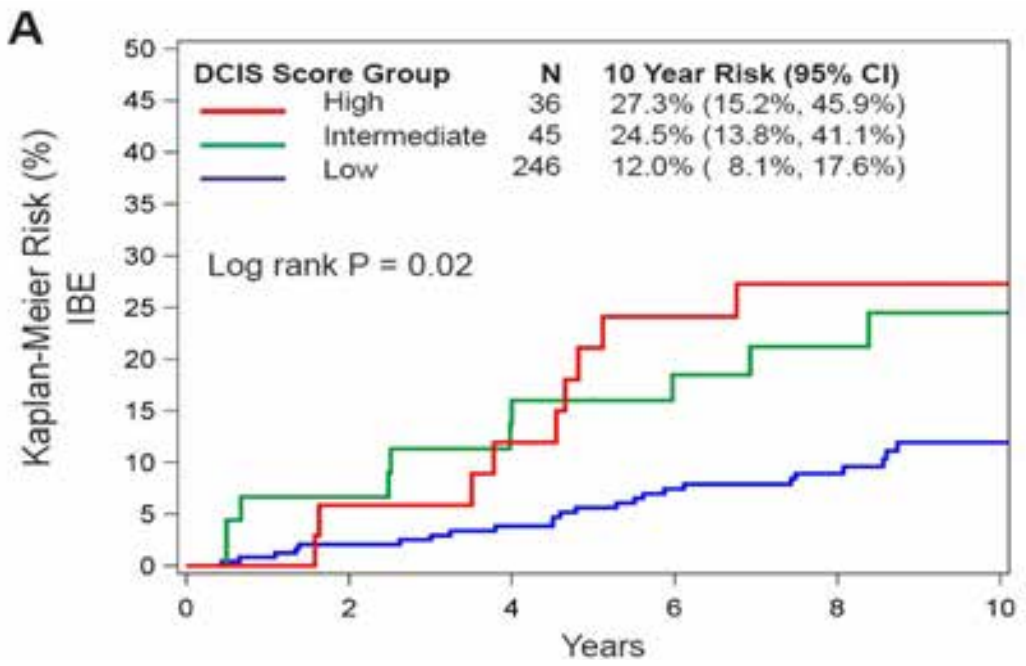
Hughes LL, et al. *J Clin Oncol*. 2009.

The "**DCIS Score**" is a subset of the **Recurrence Score**

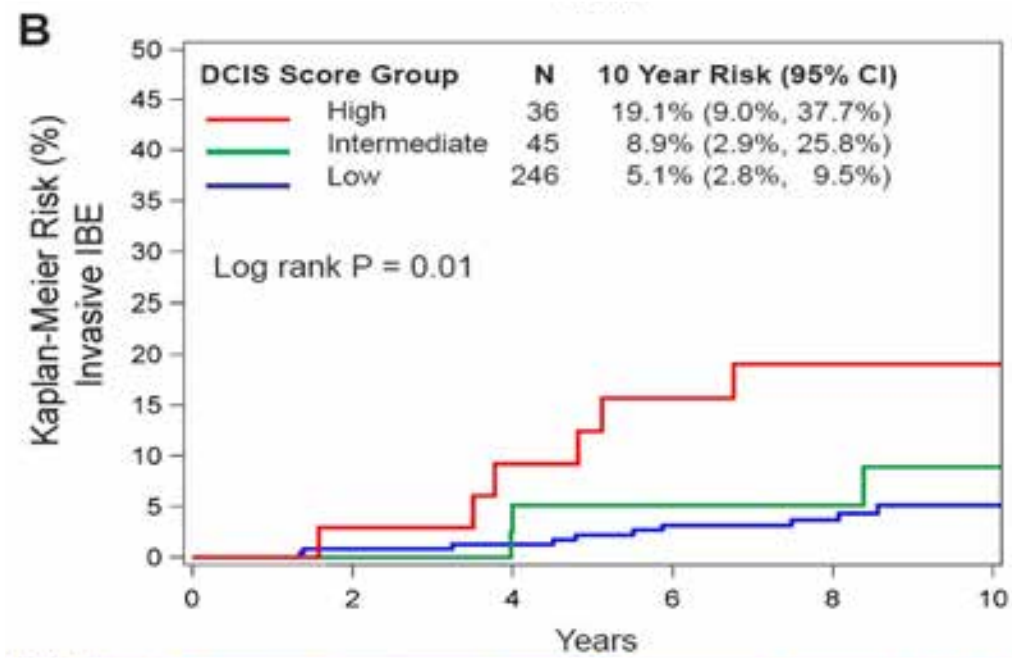


DCIS Score™: 10-Year Ipsilateral Breast Events (IBE) by Risk Group

ANY IBE



INVASIVE IBE



Solin L, et al. SABCS 2011(abstr S4-6), JNCI 2013

RESULTS

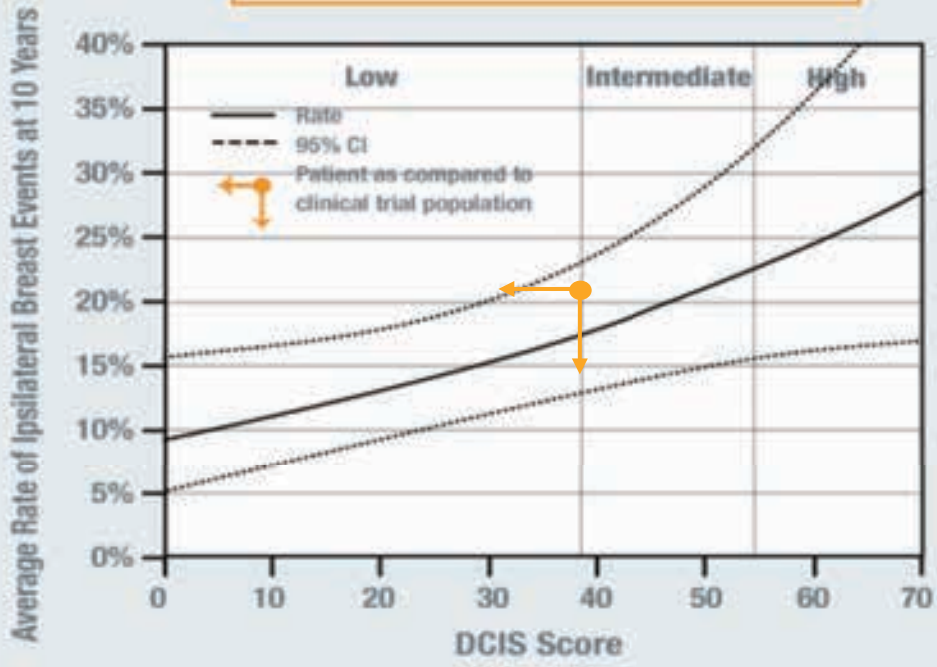
DCIS Score™ = 12

CLINICAL EXPERIENCE: PROGNOSIS FOR DCIS PATIENTS

The Clinical Validation study included female patients with **DCIS** treated with local excision without irradiation, and required clear surgical margins ≥ 3 mm and a lesion size of ≤ 2.5 cm. Approximately a third of patients were treated with tamoxifen. The average 10 year rate for ipsilateral breast events for patients who had a DCIS Score of **12** was:

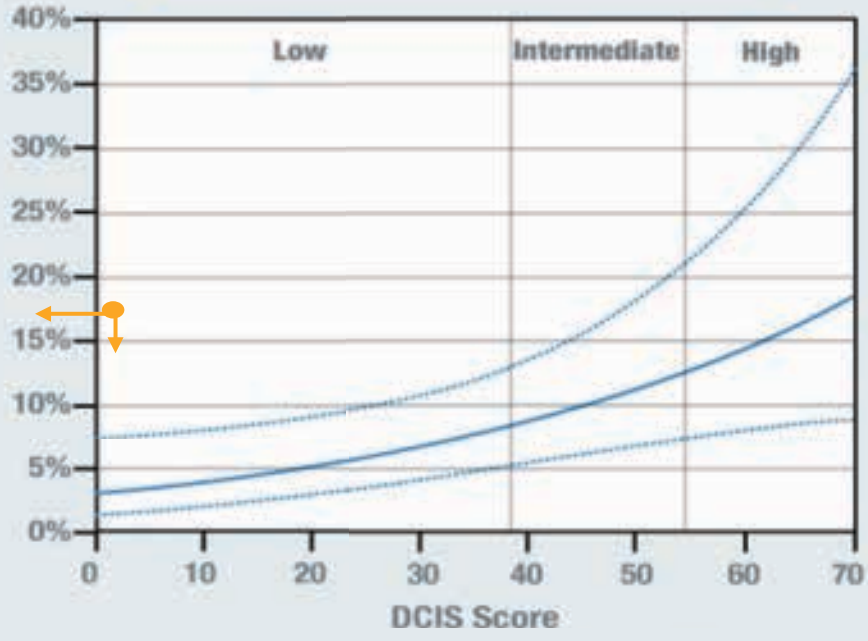
Any Local Event (DCIS or Invasive)

11% (95% CI: 8%-17%)



Invasive Local Event

4% (95% CI: 2%-8%)



Are there sufficient data on which to base treatment decisions?

- Small dataset with total of 46 recurrences; very few with high DCIS Score
- Analysis based on 10-year follow up recurrence data
- Individualized recurrence estimates could serve as a starting point for discussions regarding adjuvant RT
- Additional validation studies are needed to determine more generalized utility

Adjuvant Tamoxifen for DCIS

- 2 prospective randomized studies
  - NSABP B-24 (n=1798, 7 years f/u)
  - UKCCCR Trial (2x2 design n=2606, 4 years f/u)

	n	f/u	margins	pts<50 yo	Ipsilateral recurrence (T/P)
NSABP	1804	83 months	any	33%	7.7%/11.1% (p<0.05)
UKCCCR	1701	53 months	negative	10%	13%/15% (p=0.42)

	DVT	PE	stroke
tamoxifen	9	2	5
placebo	2	1	1

Studies in Progress and Future Directions in DCIS Treatment

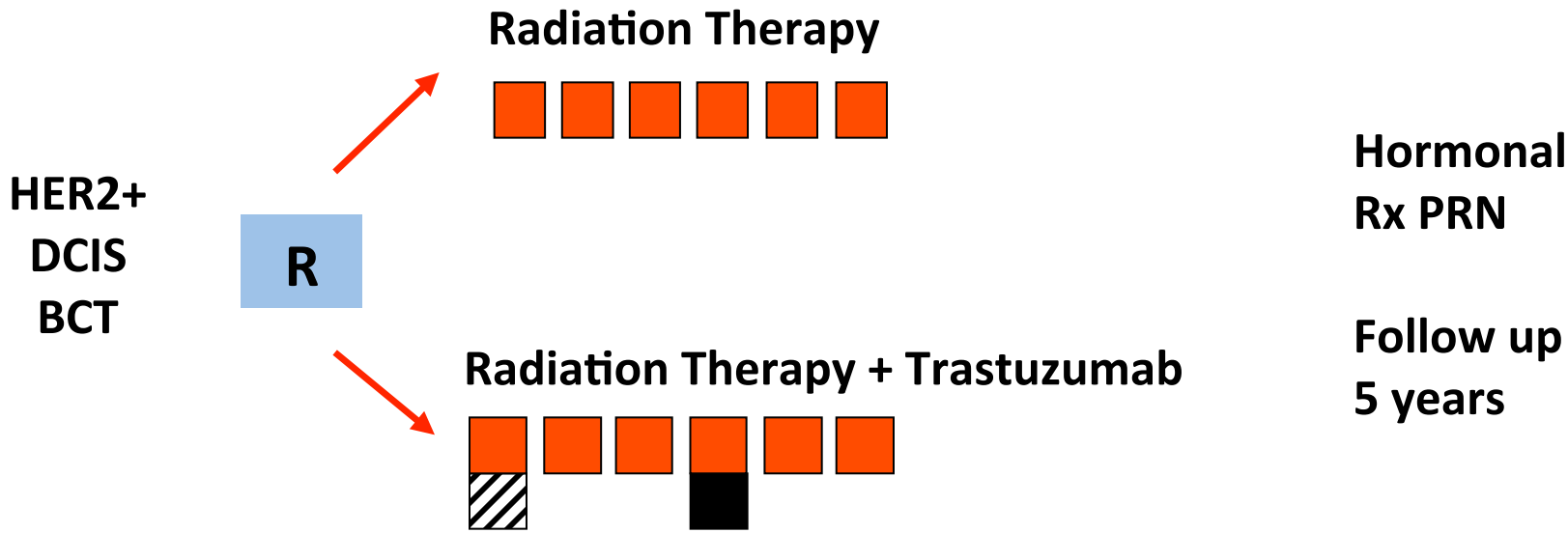
Ongoing Clinical Trials of AI for DCIS

- **NSABP B-35**
  - Opened Jan 2003
  - Target accrual: 3000 postmenopausal DCIS with lumpectomy+RT
  - Randomized to adjuvant anastrazole or tamoxifen
  - Primary endpoint: time to any breast cancer event

- **IBIS II for DCIS**
  - Opened Sept 2003
  - Cancer Research UK
  - Target Accrual: 4000 postmenopausal DCIS with lumpectomy+/- RT
  - Randomized to adjuvant anastrozole or tamoxifen
  - Primary endpoints: any new or recurrent brCA

Schema: NSABP B43

Phase III Randomized Study of Radiotherapy With Versus Without Trastuzumab (Herceptin®) in Women With HER2-Positive Ductal Carcinoma In Situ Undergoing Lumpectomy (enrollment target: 2000; activated 11/2008)

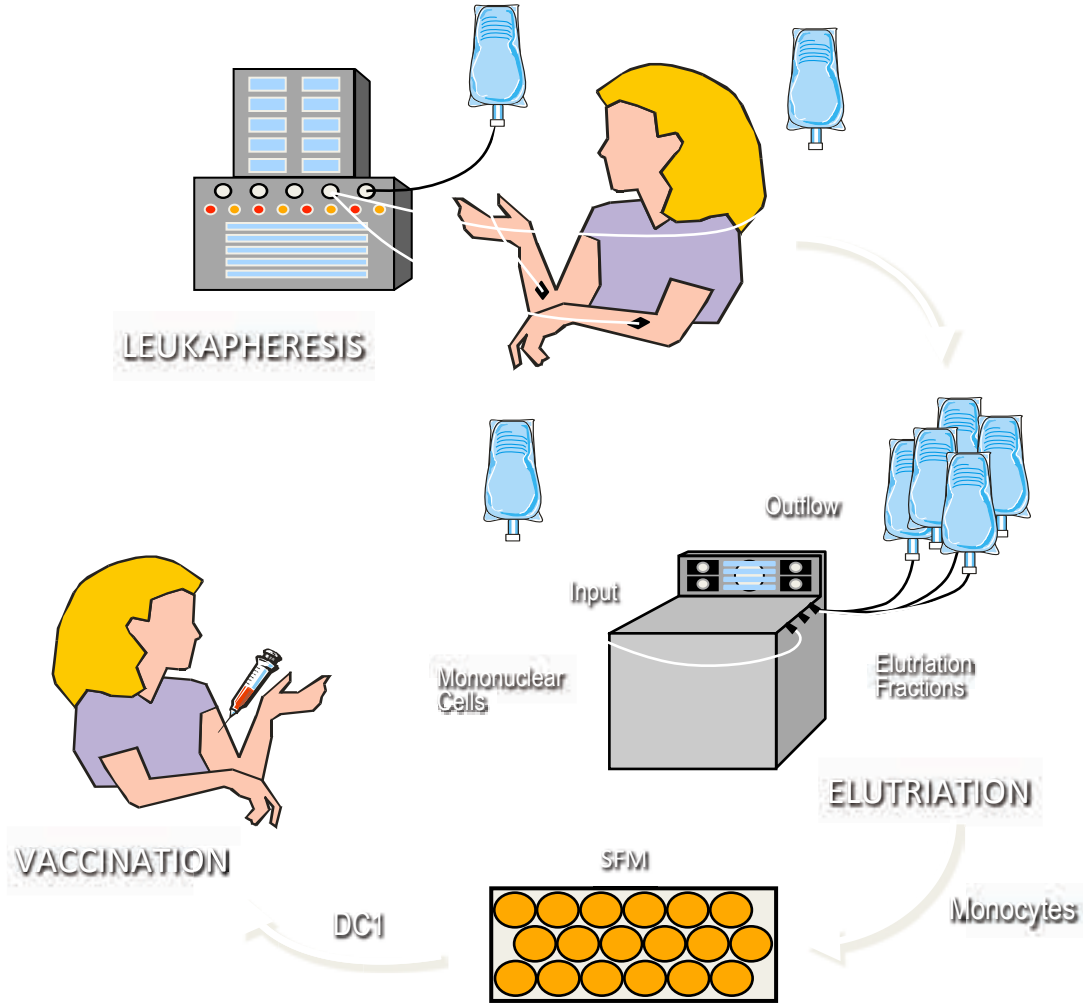


q3-week Trastuzumab cycles x 2

Trastuzumab 8 mg/kg loading dose

Trastuzumab 6 mg/kg final dose

Her2 targeted Dendritic Cell Vaccine: Protocol for DC1 Preparation (U Penn)

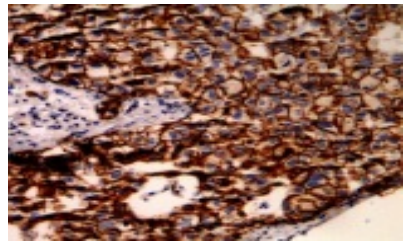


DC1 Activated with GM-CSF, IL-4, IFN-γ, LPS, pulsed with MHC class II and MHC class I HER-2/neu peptides, 40 hours total culture

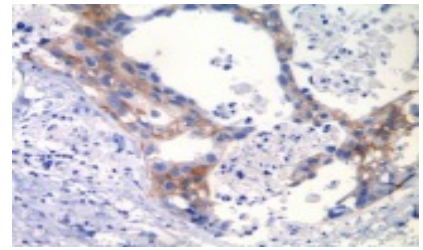
Response to Her-2 targeted dendritic cell vaccine

A

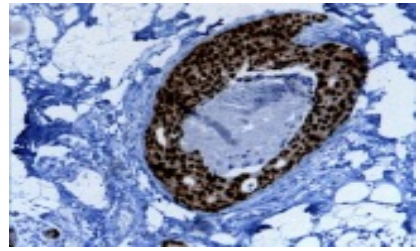
Pre Vaccine HER-2/neu



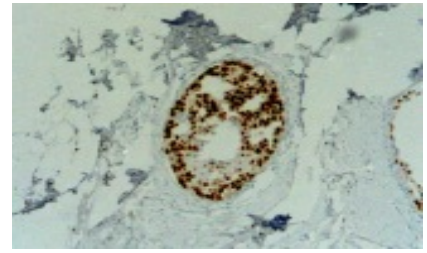
Post Vaccine HER-2/neu



Pre Vaccine ER



Post Vaccine ER



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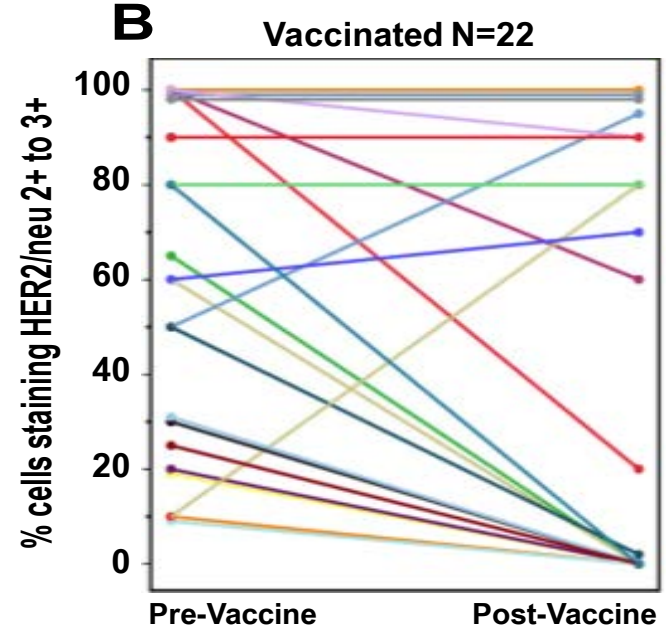


C

Percent of cells staining HER-2/neu 2+ to 3+ Pre- and Post-vaccination
Patients sorted by Phenotype and Pre-vaccination HER-2/neu expression

ER^{pos} $HER\text{-}2/neu^{pos}$					
% Pre-vaccine	% Post-vaccine	Percent Change	% Pre-vaccine	% Post-vaccine	Percent Change
10	0	-100%*	65	0	-100%*
20	0	-100%*	80	0	-100%*
20	0	-100%*	80	80	0%
25	0	-100%*	90	90	0%
30	0	-100%*	100	90	-10%
50	2	-96%*	100	>90	0%
50	95	+90%	100	100	0%
60	70	+17%	100	100	0%

ER^{neg} $HER\text{-}2/neu^{pos}$		
% Pre-vaccine	% Post-vaccine	Percent Change
10	0	-100%*
10	80	+700%
30	0	-100%*
60	0	-100%*
100	20	-80%
100	60	-40%

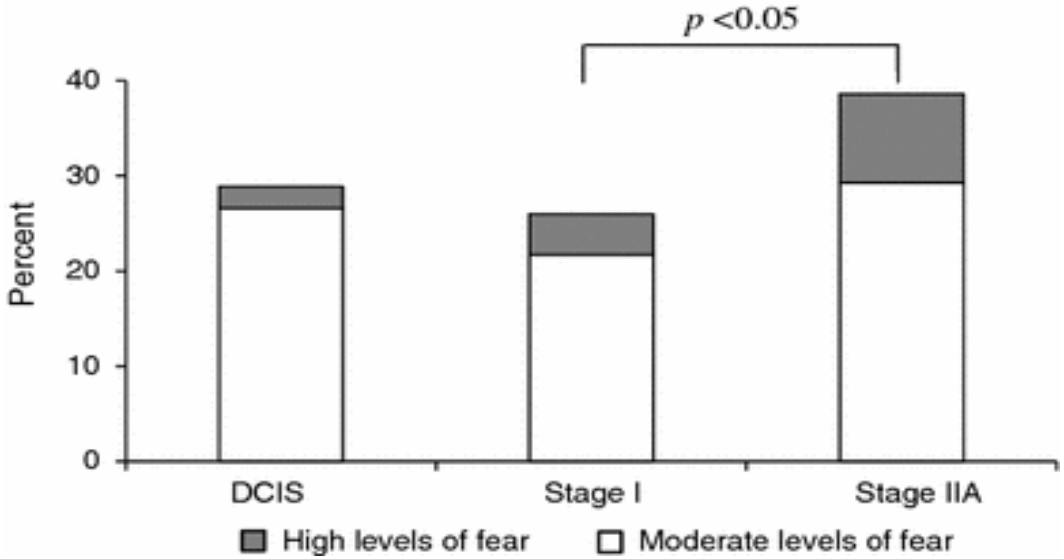
*patient scored as $HER\text{-}2/neu^{neg}$

Sharma A, Czerniecki B, Cancer 2012

But what about the patient?

The Worried Well…

Fear of cancer recurrence in 506 women with DCIS Stage I-II breast cancer



FCR scores 2 years post surgery in women who were free of recurrence

- Prospectively enrolled in a quality-of-life study
- Completed interviews at 4-6 weeks, 6 months, and 2 years post surgery.
- Mean fear of cancer recurrence (FCR scores) determined, using four items from the Concern About Recurrence Scale (CARS)

Liu Y et. al. *BCRT* 2011

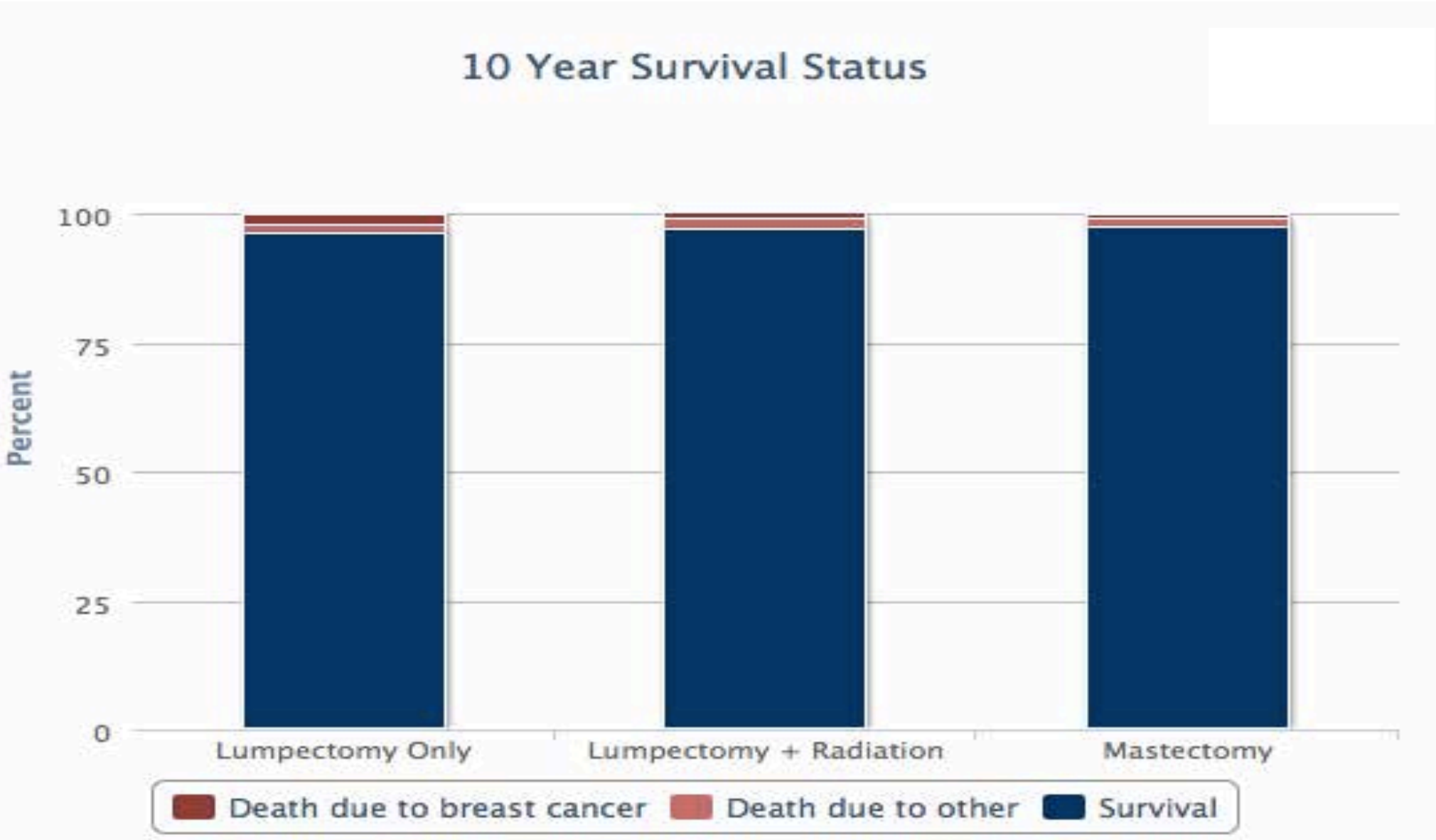
Introduction	In the following three scenarios, please imagine that you are the patient receiving each diagnosis explained. Keep in mind that in each scenario, the diagnosis is different but the treatment options and risks are the same.		
Scenario	**Scenario 1** Based on the results of your last mammogram, your doctor suggested that you get a breast biopsy. The biopsy showed an abnormality in the breast tissue. The condition is not bothering you and is not dangerous to your health right now. Your diagnosis is **non-invasive breast cancer**, also called pre-invasive breast cancer. You have the 3 treatment options described below…		
	Surgery	**Medication**	**Active Surveillance**
Main Treatment	Surgically removing part or all of the breast Mammography every 6 months for 5 years	Daily medication for 5 years Mammography every 6 months for 5 years	Mammography every 6 months for 5 years
Chance of developing invasive breast cancer* in the next 10 years:	3% (3 in 100 chance)	17% (1 in 6 chance)	30% (3 in 10 chance)
*Invasive breast cancer is the type of cancer that can spread to other parts of your body.			
Chance of dying from breast cancer* in the next 10 years:	0.30% (3 in 1000 chance)	1.70% (1 in 60 chance)	3% (3 in 100 chance)
*Women who develop invasive breast cancer have some chance of dying from the disease.			
Side Effects: Mild:	Psychological discomfort associated with the removal of part or all of the breast	Hot flashes	None
Serious but rare:	Surgical complications, Death	Blood clots, Cataracts, Endometrial cancer	None

Words Matter: patient treatment choice based on terminology used to describe clinical scenario

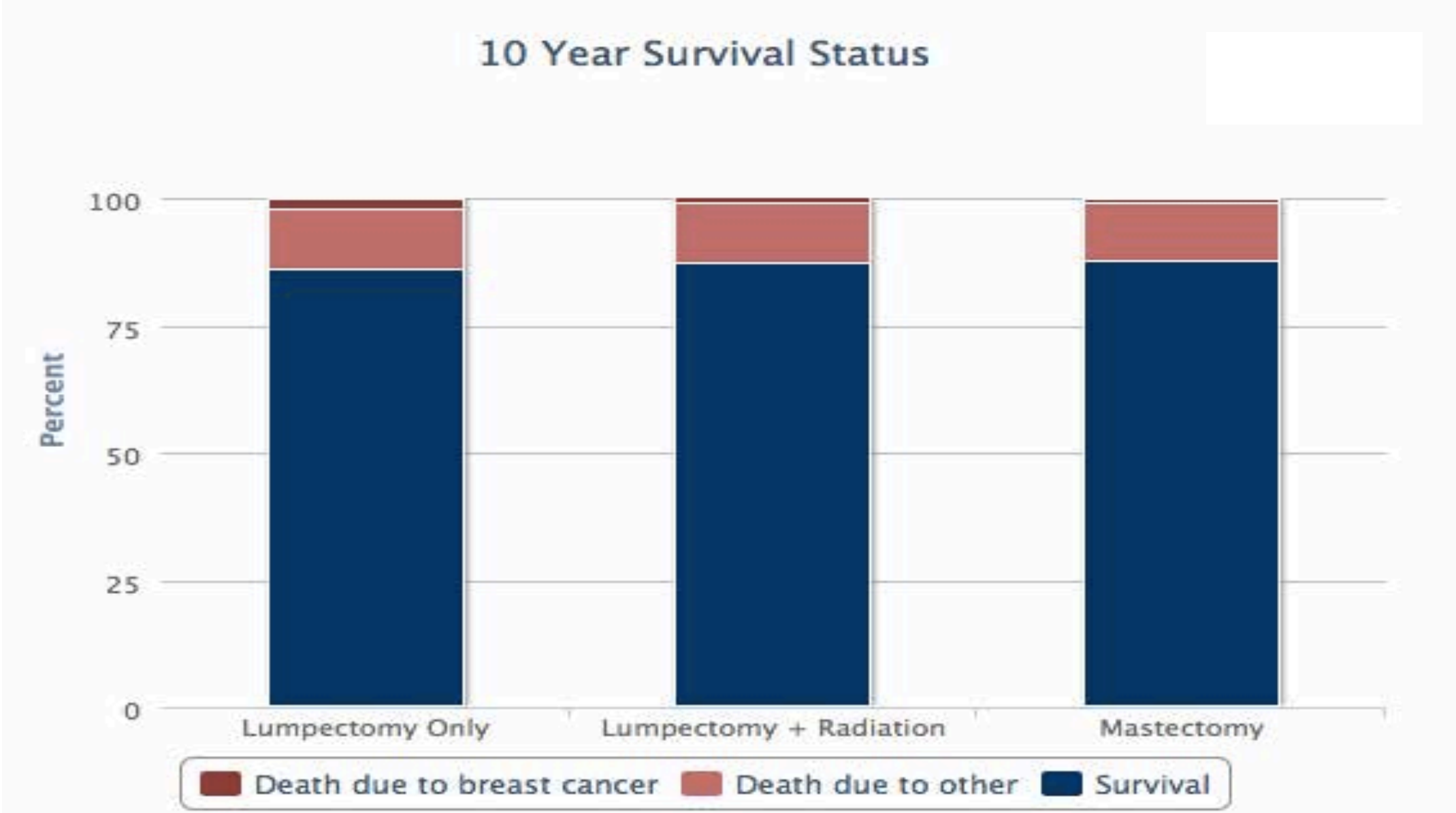
N=394		Terms used to describe DCIS		
		Cancer *n (%)*	Lesion *n (%)*	Abnormal cells *n (%)*
Treatment Options	Surgery	186 (47)	136 (34)	124 (31)
	Medication	79 (20)	70 (18)	82 (21)
	Active surveillance	129 (33)	188 (48)	188 (48)

Omer Z et al, JAMA Internal Med 2013

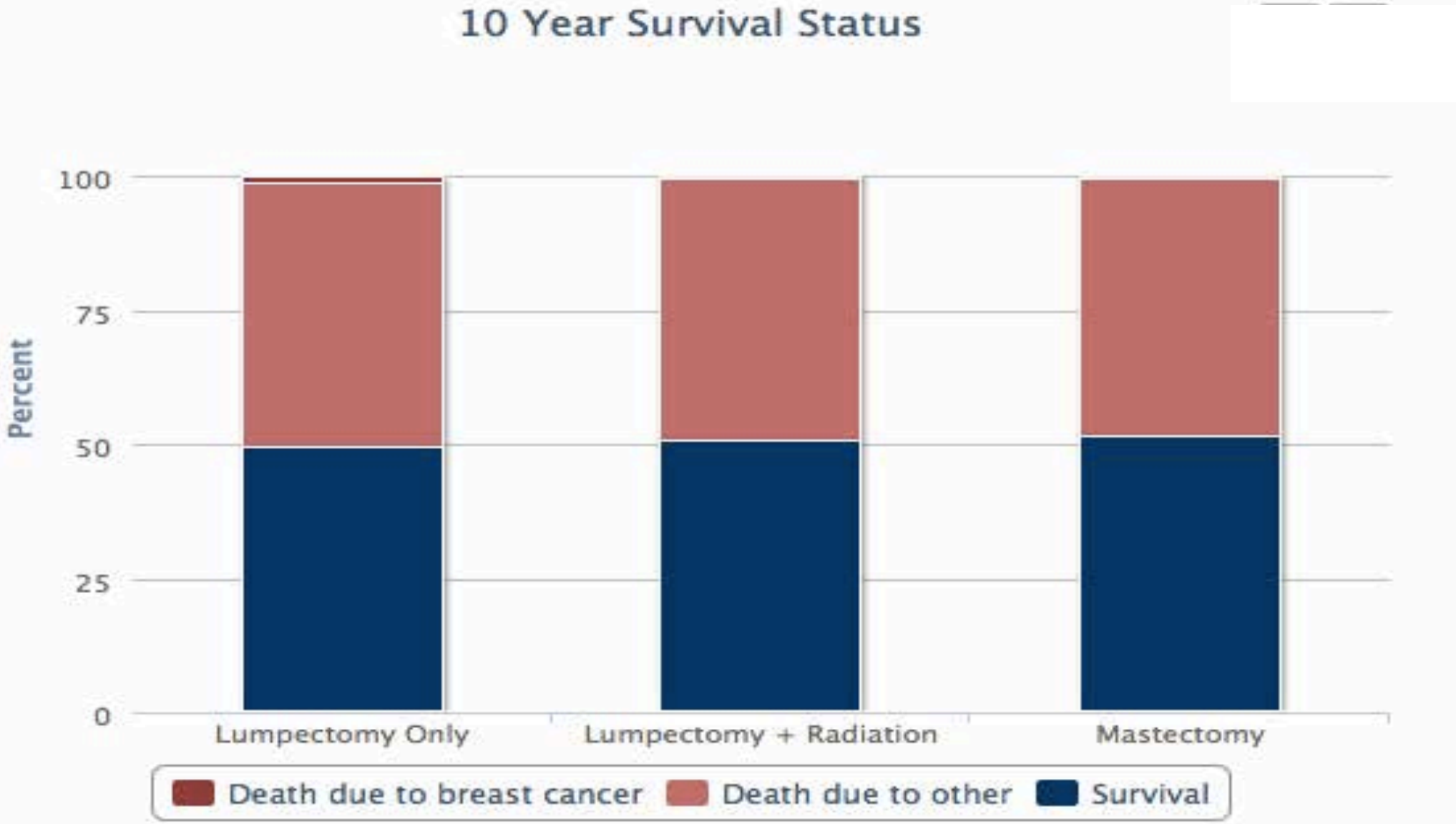
40 year old with DCIS



55 year old with DCIS

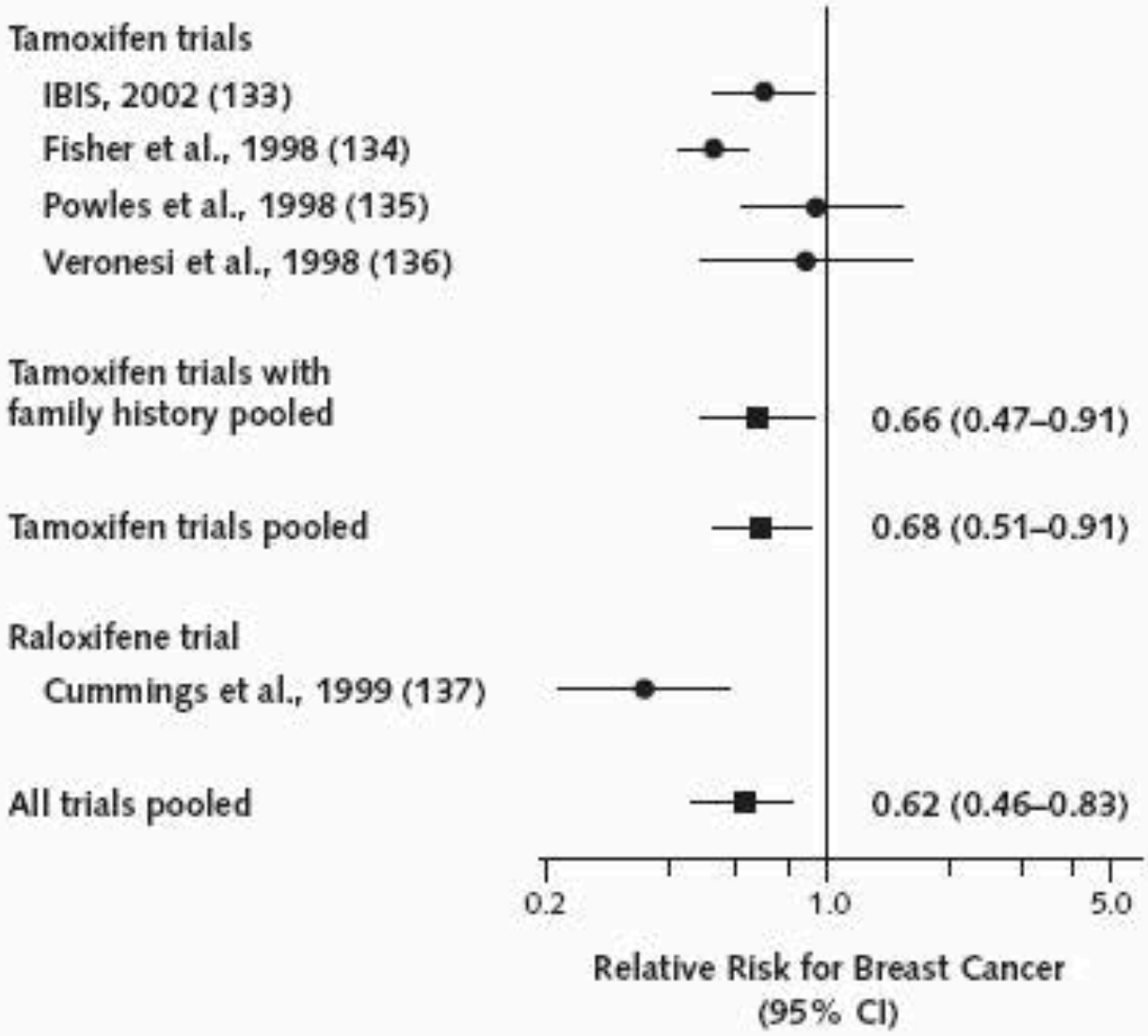


70 year old with DCIS



Last but not least…

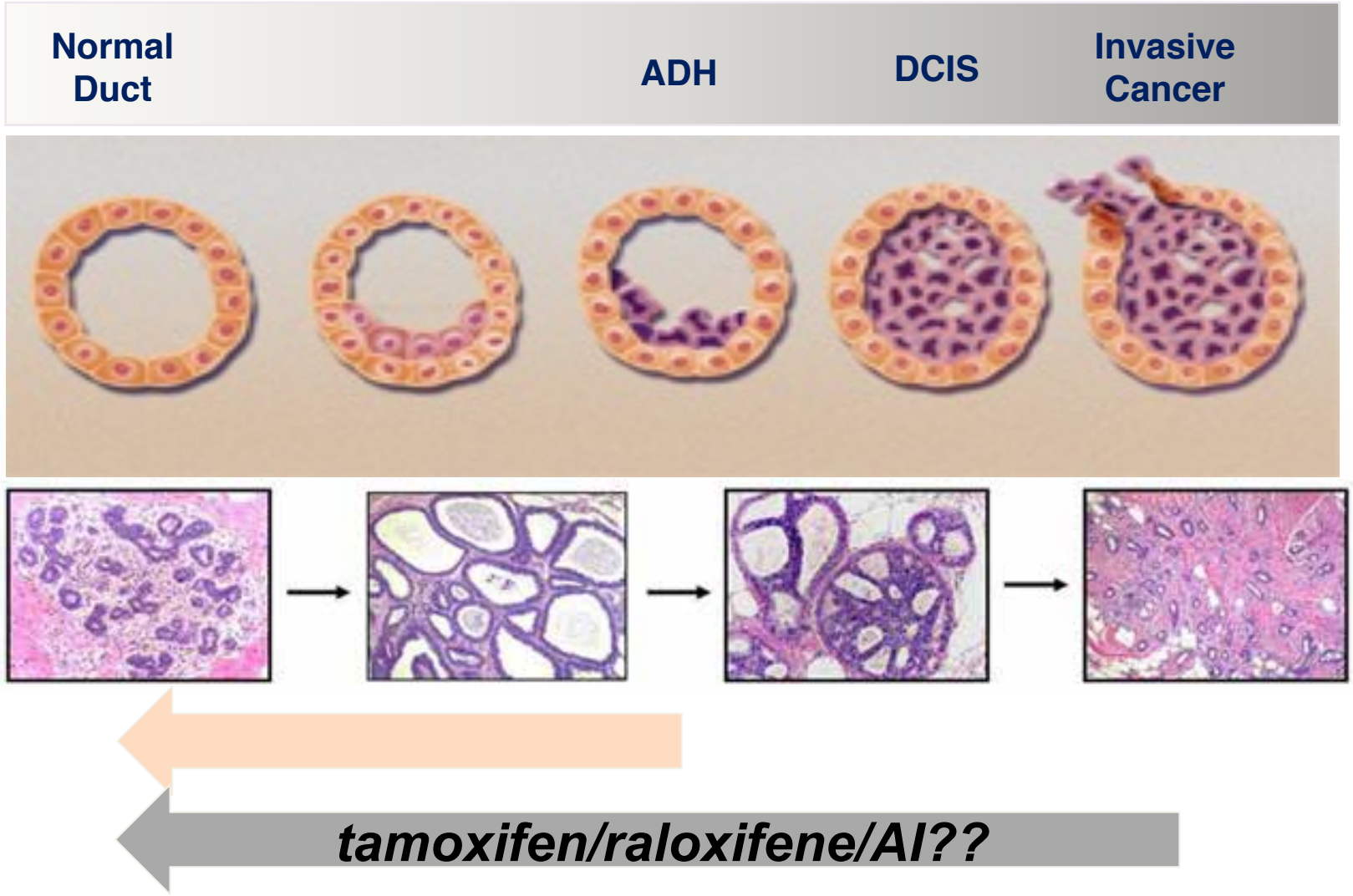
Figure 2. Relative Risks for Breast Cancer in Chemoprevention Trials



Notes: Error bars represent 95% CIs. IBIS = International Breast Cancer Intervention Study.

USPSTF, 2008

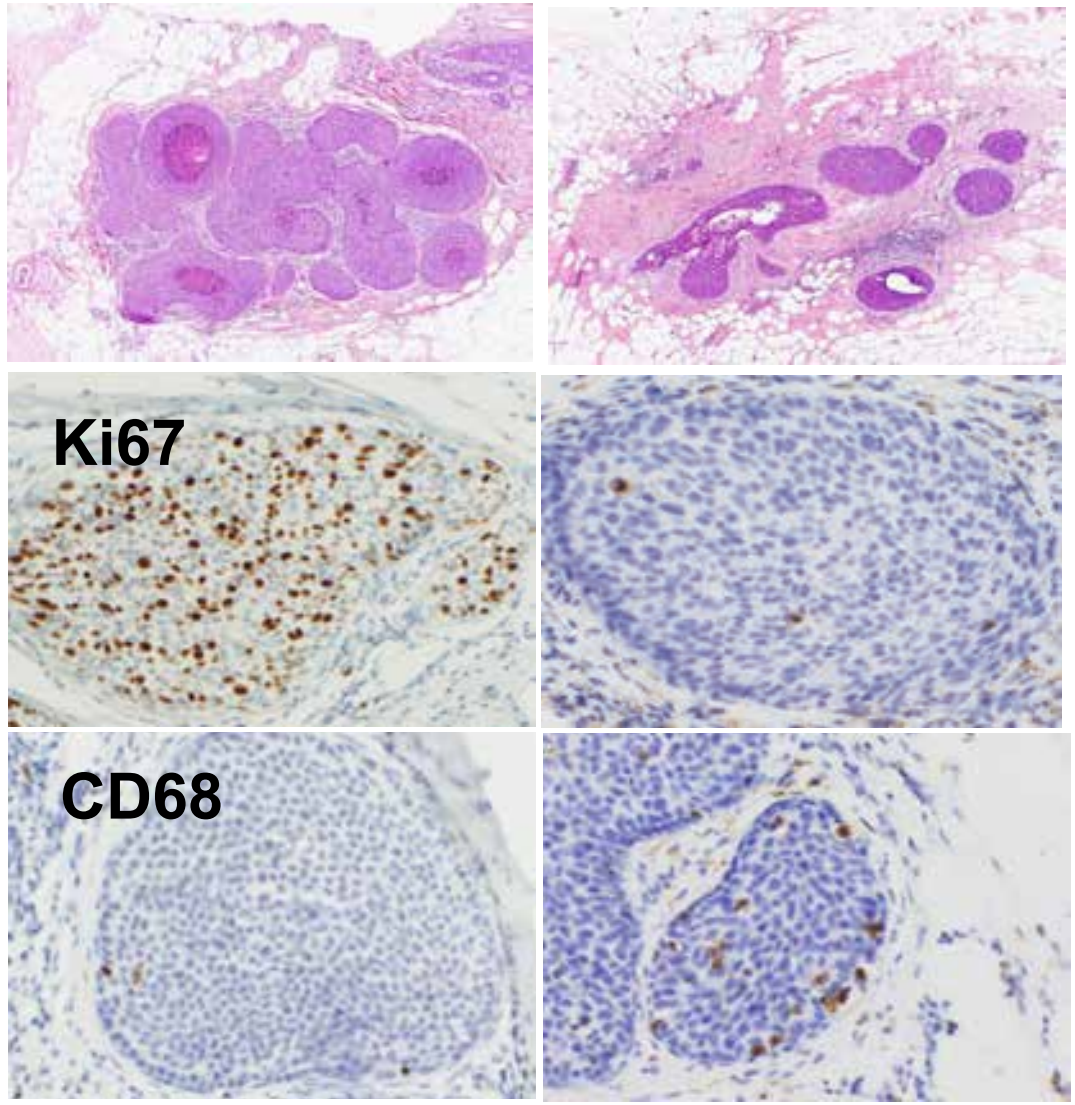
Histologic Model of Cancer Progression: Can progression be reversed?

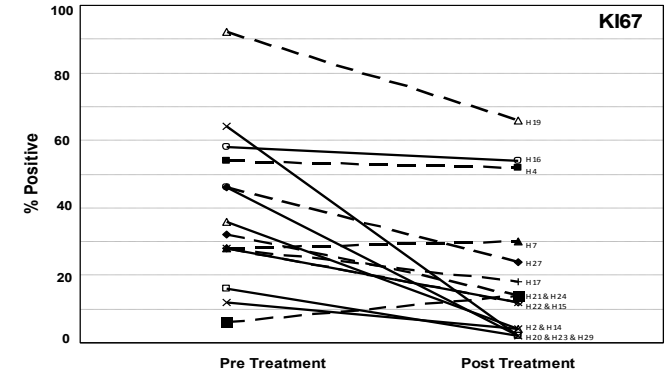


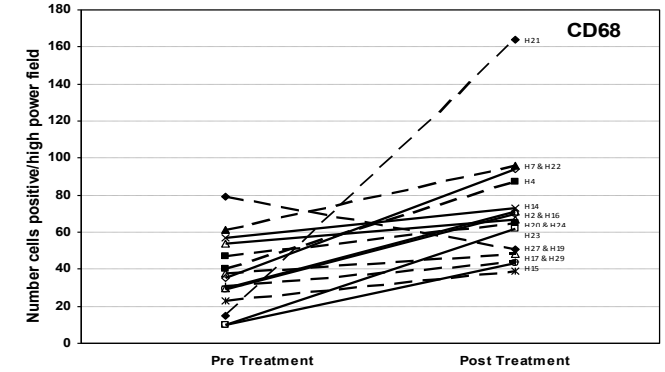
Challenges to implementation of active surveillance for DCIS

- Limited validation of biomarkers to predict magnitude and timeline of risk for invasive cancer
- Need to educate providers and patients regarding impact of DCIS on breast cancer specific survival
- Mandatory requirement for accurate imaging studies
  - MMG not effective
  - Expense of MRI may be prohibitive
  - Breast MRI as a research tool
- Pilot study of MRI imaging in patients with DCIS undergoing neoadjuvant hormonal therapy
  - No change on MMG at 3 months
  - Premenopausal patients excluded

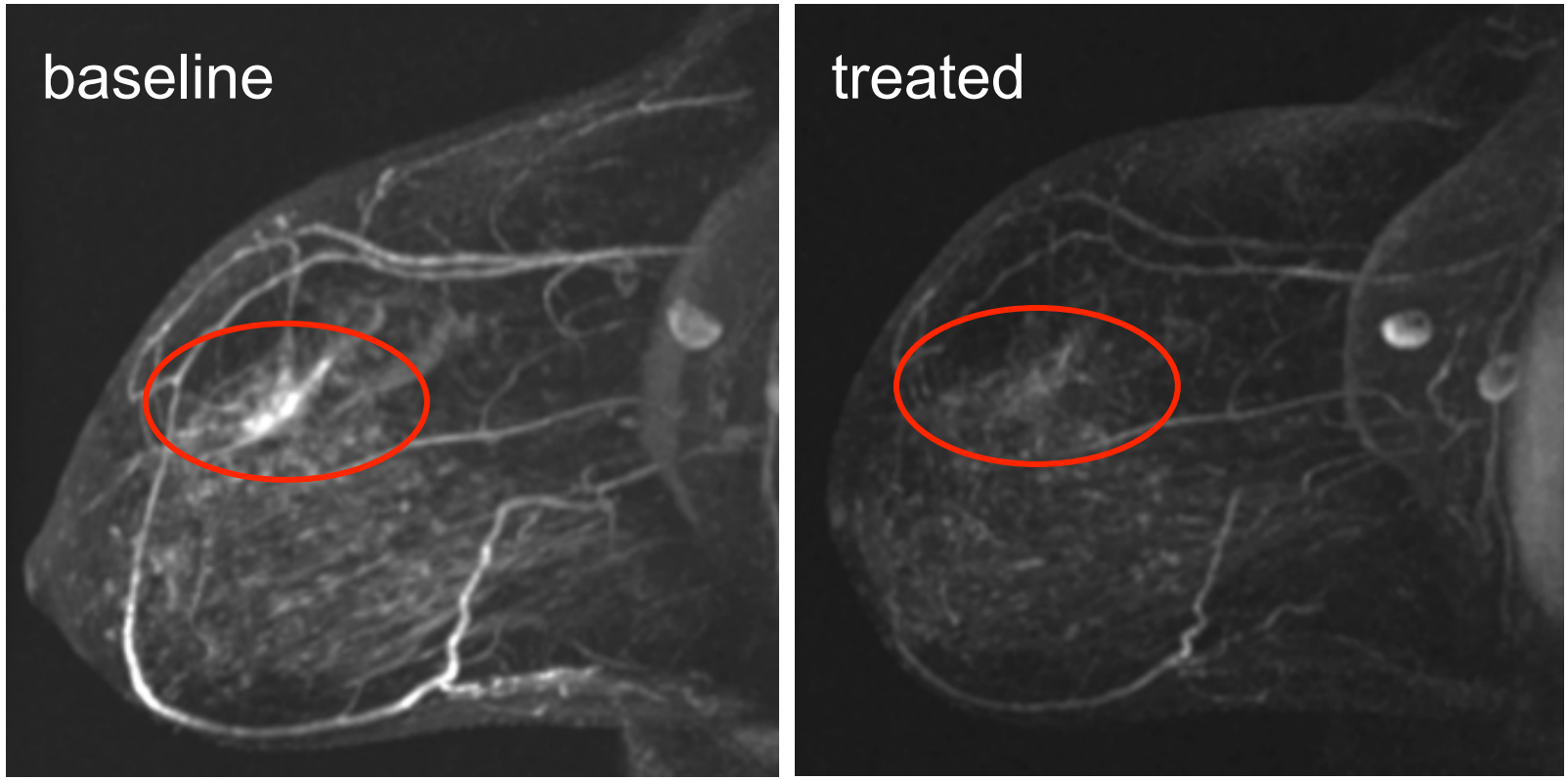
Alteration of biomarker expression is associated with endocrine treatment for DCIS







MRI assessment of letrozole response



Responder: ER-positive, postmenopausal

CALGB 40903:

Phase II Single-Arm Study of Neoadjuvant letrozole for ER(+) postmenopausal DCIS

- **Endpoints:**
  - Primary: radiographic response on MRI
    - Change in MRI maximum tumor volume
  - Secondary:
    - Mammographic extent of disease
    - Candidacy for breast conservation
    - Frequency of reexcisions
    - Frequency of complete pathologic response
    - Frequency of invasive cancer at final pathology
    - Treatment-related adverse events

CALGB 40903:

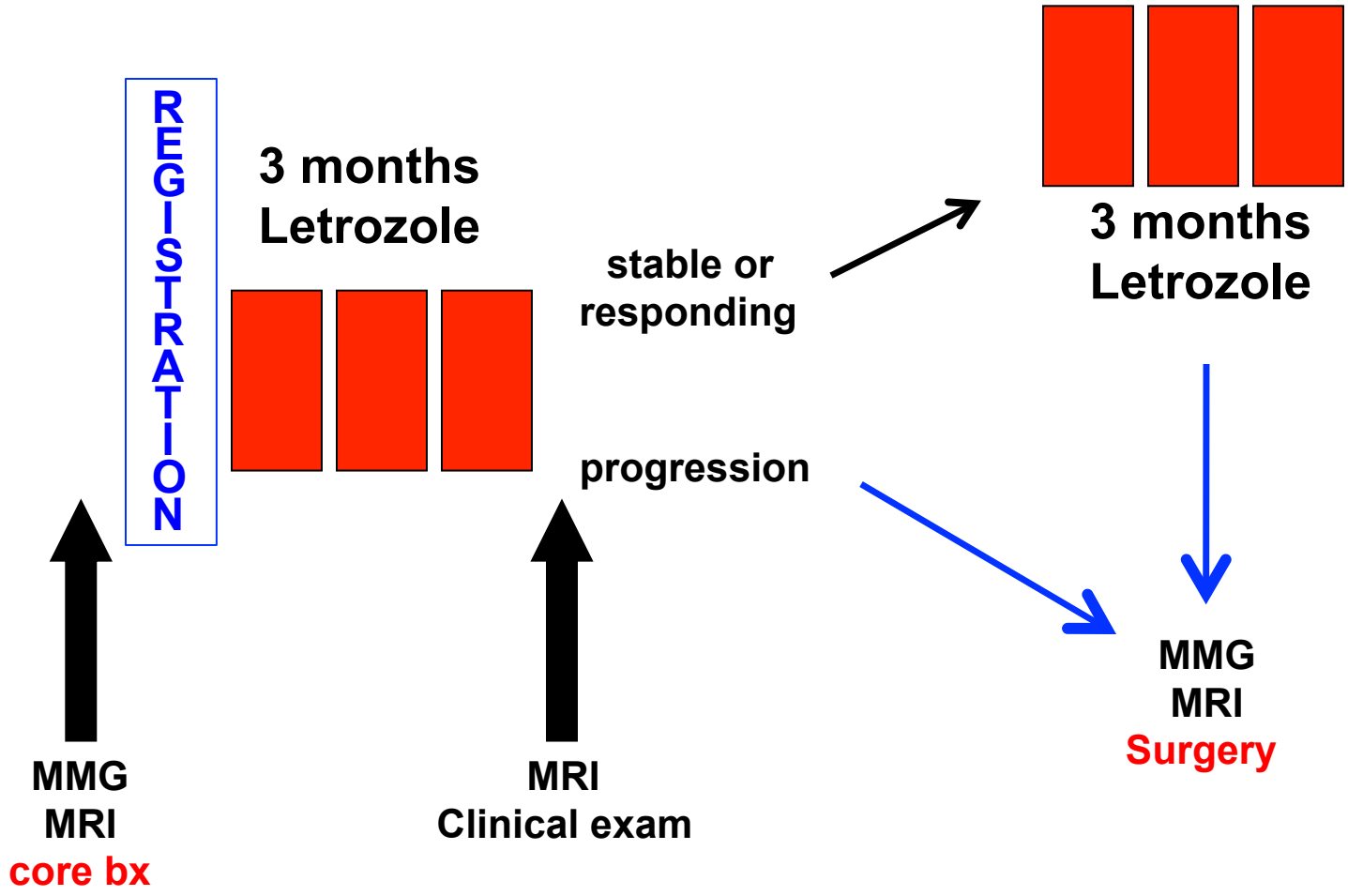
Phase II Single-Arm Study of Neoadjuvant letrozole for ER(+) postmenopausal DCIS

- **Study Design:**
  - Phase II single arm study of 6 months preoperative letrozole

- **Inclusion Criteria:**
  - DCIS without invasion on core biopsy
  - Postmenopausal
  - ER and/or PR (+)
  - Radiographically measureable disease (**1-5** cm extent of calcifications
  - Visible on MRI (will likely need 120 screened to accrue 96 women)

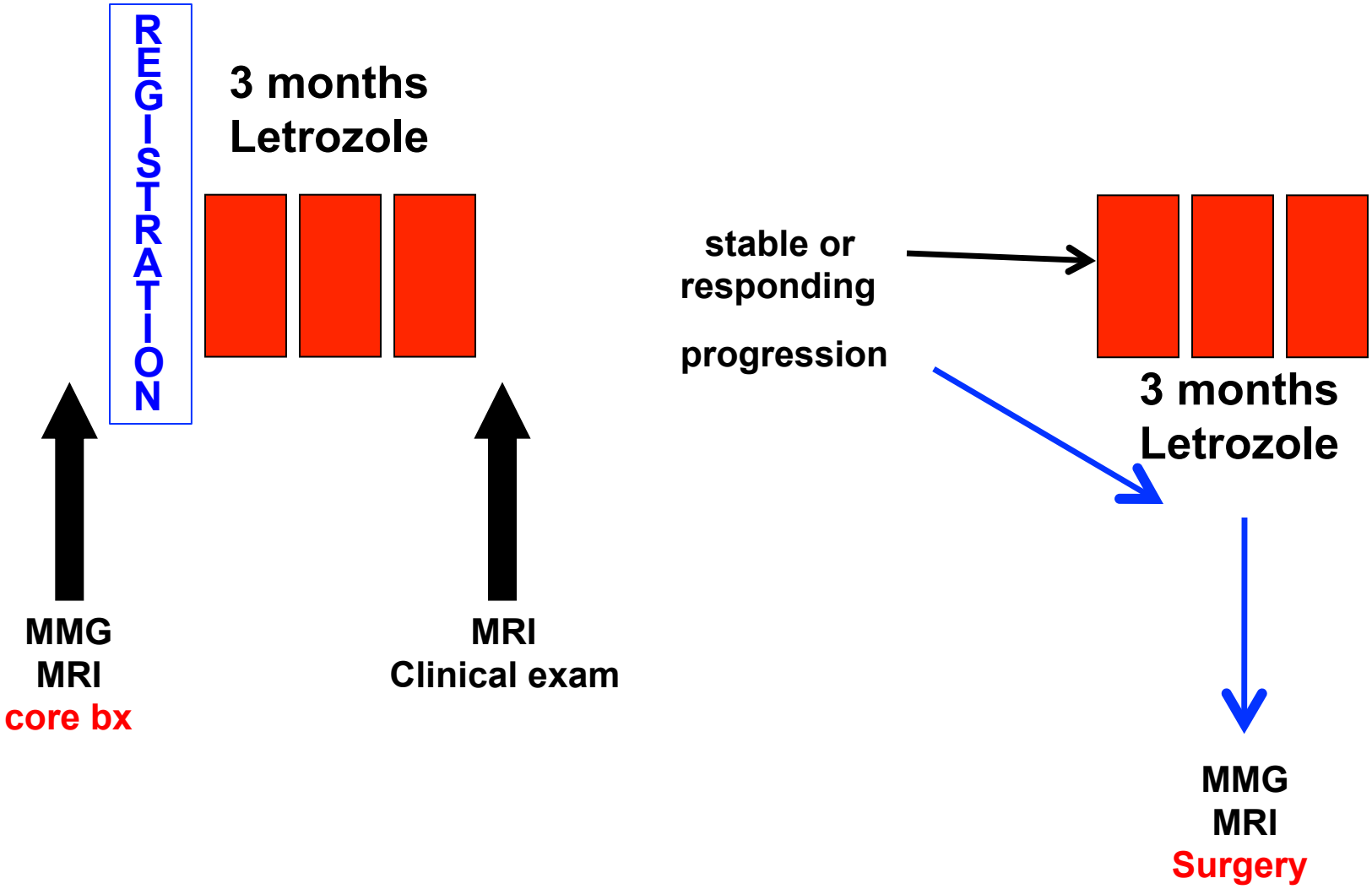
CALGB 40903:

Phase II Single-Arm Study of Neoadjuvant letrozole for ER(+) postmenopausal DCIS



CALGB 40903:

Phase II Single-Arm Study of Neoadjuvant letrozole for ER(+) postmenopausal DCIS



CALGB 40903:

Phase II Single-Arm Study of Neoadjuvant letrozole for ER(+) postmenopausal DCIS

- **Accrual Goal:**
    - 96 patients over 3 years
- **Site Qualifications:**
    - ACRIN certified site (all sites with previous MRI studies through ACRIN will qualify)
    - CCOPs encouraged to participate

CALGB 40903:

Phase II Single-Arm Study of Neoadjuvant letrozole for ER(+) postmenopausal DCIS

- **Correlative Endpoints:**
  - Primary:
    - Predictive and prognostic tissue biomarkers associated with letrozole response (good vs. poor responders)
    - Proliferative genes
    - Cell cycle genes
    - Macrophage activation assays (CSF1, CD68)
    - DCIS Score
    - PAM50
  - Secondary:
    - Pharmacogenomic predictors of AI-induced arthralgias

Companion Study to CALGB 40903—PI: Kimmick

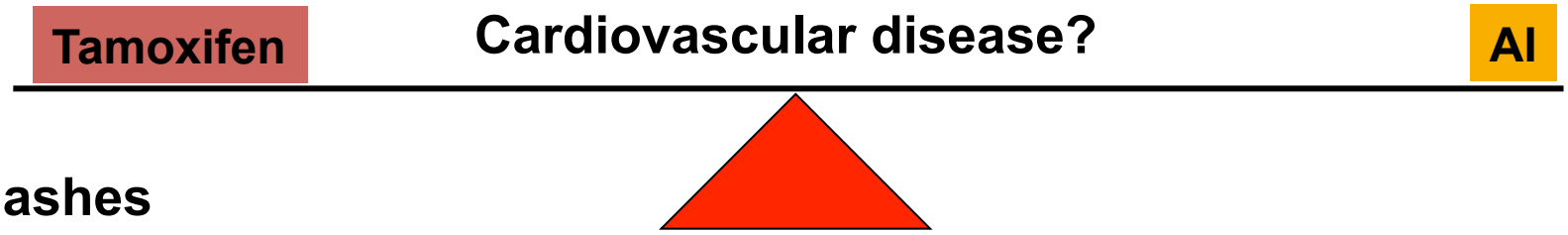
QOL and musculoskeletal symptoms associated with taking letrozole before surgery for ER+ DCIS

AIs and Tamoxifen: Potential Risks and Benefits

↓ Contralateral BC
↓ Osteoporosis risk
↓ Myalgia
↓ Hyperlipidemia

↓ Contralateral BC
↓ Deep vein thrombosis
↓ Endometrial cancer
↓ Hot flashes

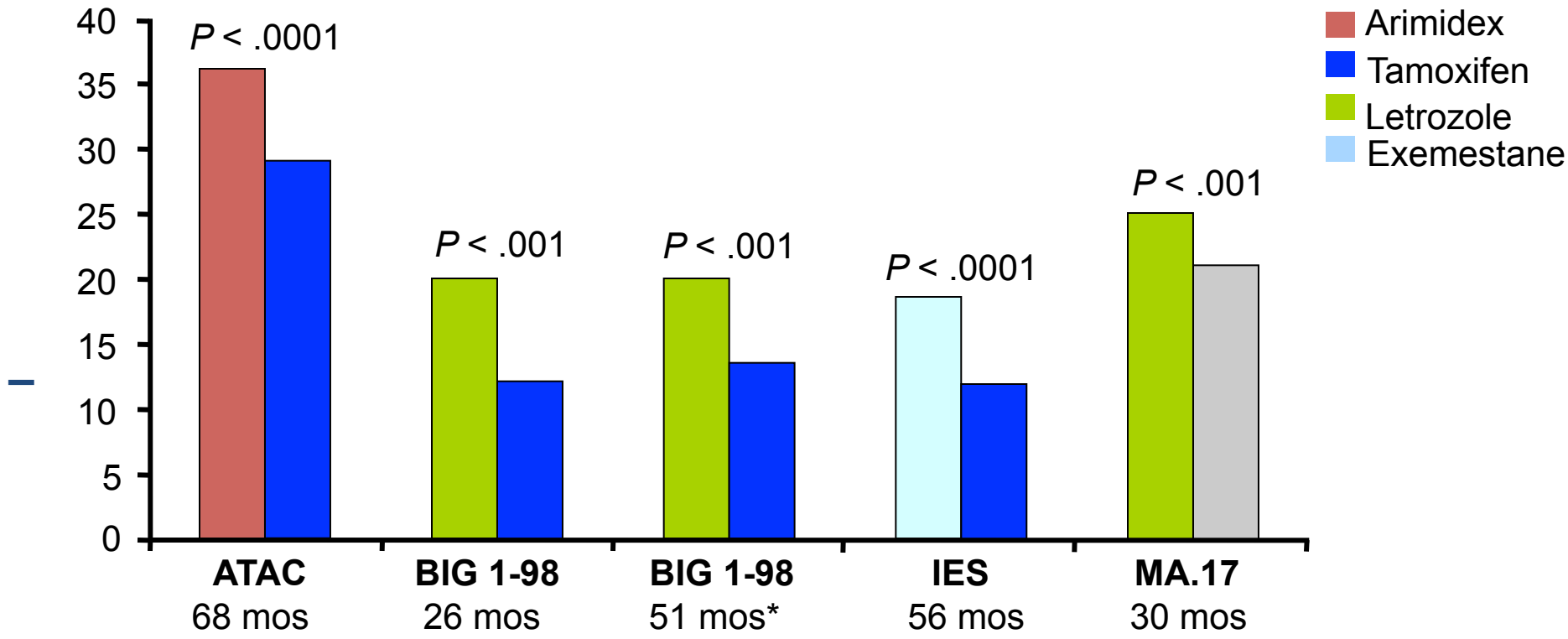
Neurocognition?
Sexual function?
Cardiovascular disease?



↑ Hot flashes
↑ Thromboemboli
↑ Endometrial cancer
↑ Genitourinary adverse effects

↑ Arthralgia/myalgia
↑ Osteoporosis risk

Arthralgia in Adjuvant AI Trials



*51-mo analysis restricted to monotherapy arms.

ATAC Trialists' Group. Lancet. 2005;365:360. Coates AS, et al. J Clin Oncol. 2007;25:486-492. Coombes RC, et al. Lancet. 2007;369:559-570. Goss PE, et al. J Natl Cancer Inst. 2005;97:1262-1271.

CALGB 40903:
Phase II Single-Arm Study of Neoadjuvant letrozole for ER(+) postmenopausal DCIS
QOL companion: Primary Aims:

- Assess side effects associated with letrozole therapy.
- Examine the association between letrozole therapy associated side effects and quality of life.
- Examine the relationship between letrozole therapy side effects and medication taking behavior.

QOL Measures

Measures to Assess Side Effects: Menopause Specific Quality of Life Questionnaire (MENQOL), Brief Pain Inventory (BPI), Pain and Stiffness (WOMAC)

Measures to Assess QOL and psychosocial functioning: Functional Assessment of Cancer Therapy – General (FACT-G), Self-Efficacy for Coping with Side Effects (modified version of a standard self-efficacy scale)

Measures to assess medication-taking behavior: Morisky Medication Adherence Scale (MMAS), Beliefs about Medicines Questionnaire (BMQ), Self-Efficacy for Taking Medications (Self-Efficacy for Appropriate Medication Use Scale - SEAMS)

CALGB 40903:

Phase II Single-Arm Study of Neoadjuvant letrozole for ER(+) postmenopausal DCIS

- **Important to keep in mind:**
  - Surgery up to patient and surgeon
  - Adjuvant treatment not predetermined
  - No follow up required
  - Patients who refuse surgery will be excluded from analysis of some, but not all endpoints

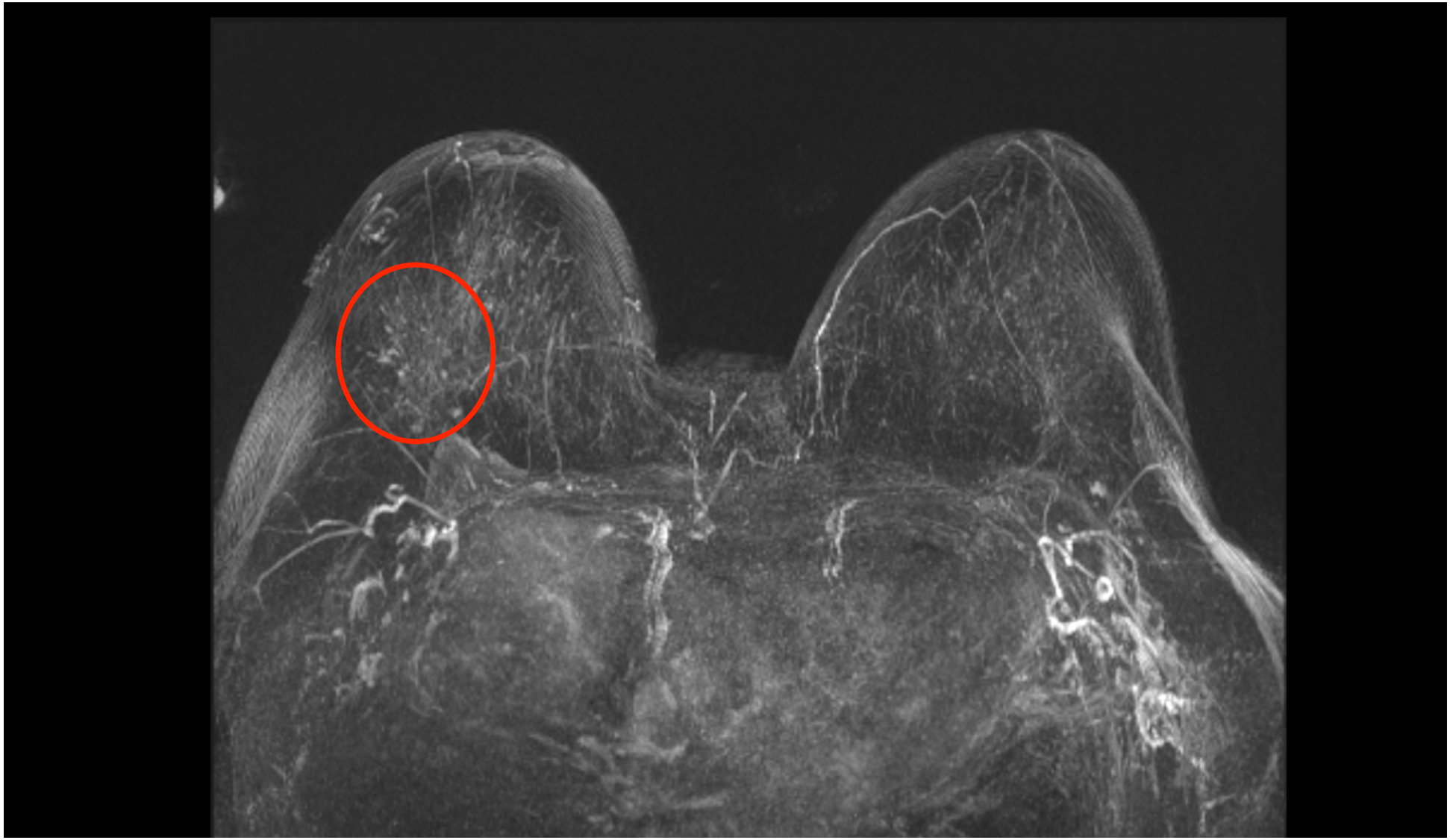
Update CALGB 40903: 4/14

- 52 sites submitted to IRB
- 20 sites open (Duke, MD Anderson, UCSF, Christiana Care, Bay Area Tumor Institute, Cedars Sinai, DFCI, Mayo, Missouri Baptist, OSU, St. Elizabeth, Pardee, Bethesda, Columbus Regional)
- 49 patients accrued (of 96)

- First modification submitted to DCP
  - Up to 7 cm of disease
  - Includes microinvasion
  - Fewer blood draws
  - More accommodating windows for trial requirements

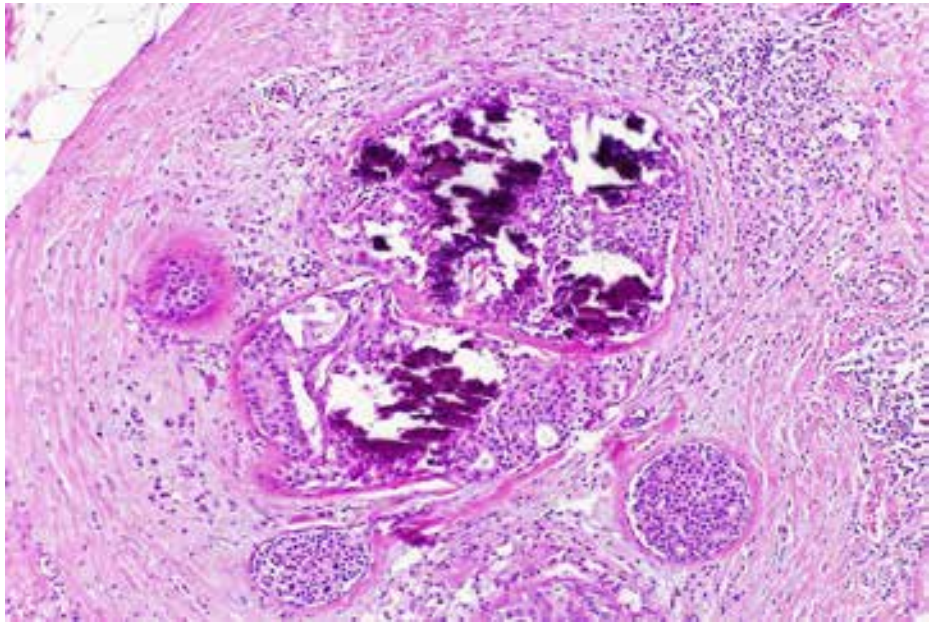
Baseline MRI

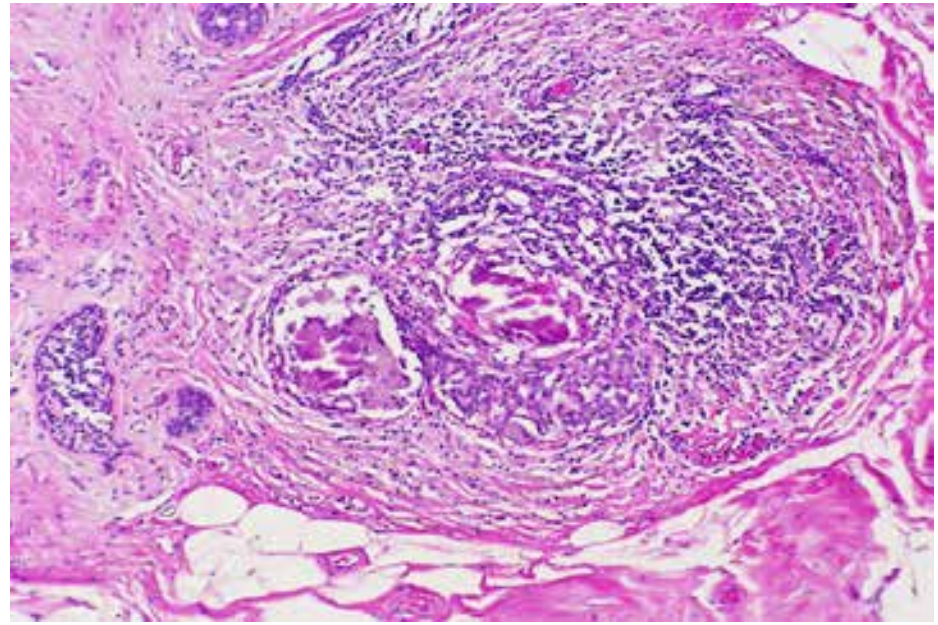
3-month MRI



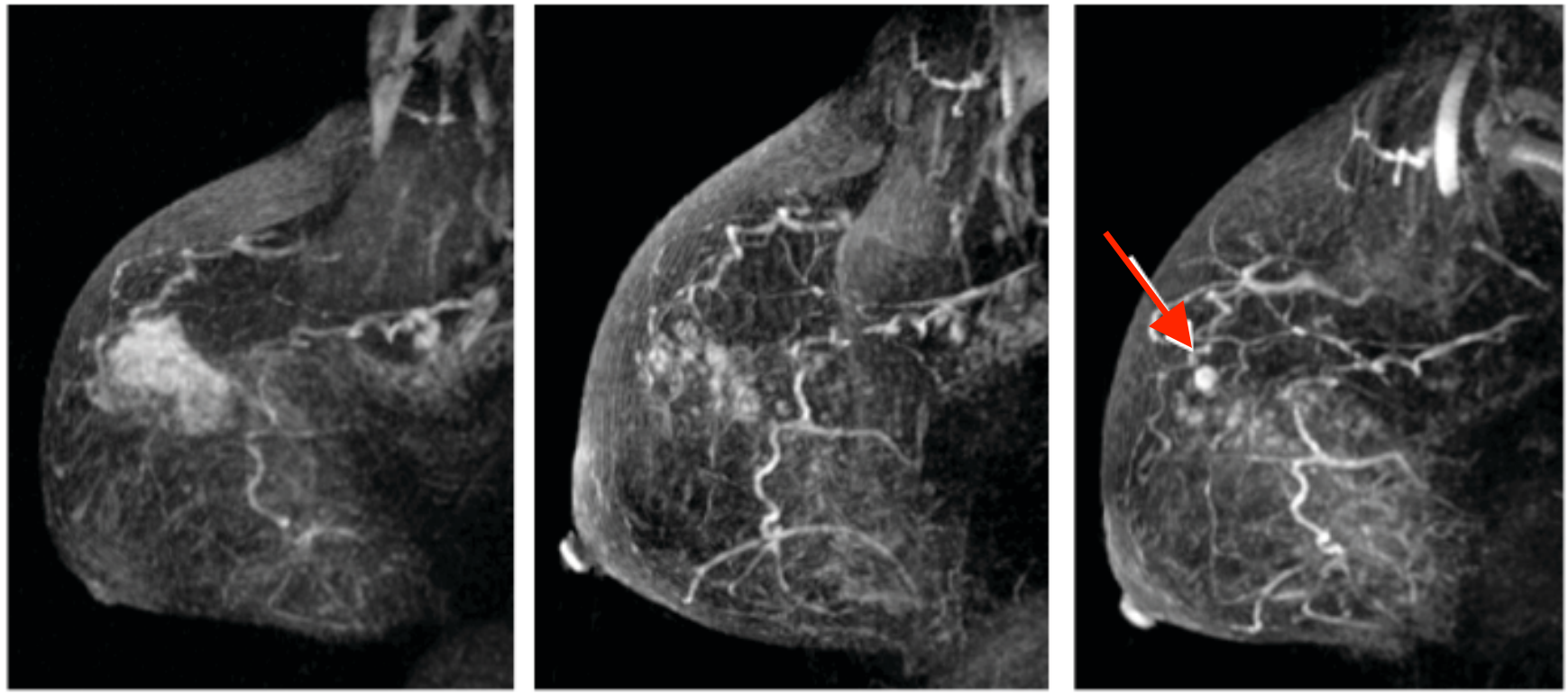
6-month MRI

DCIS following 6 months AI





“Active surveillance” with MRI monitoring

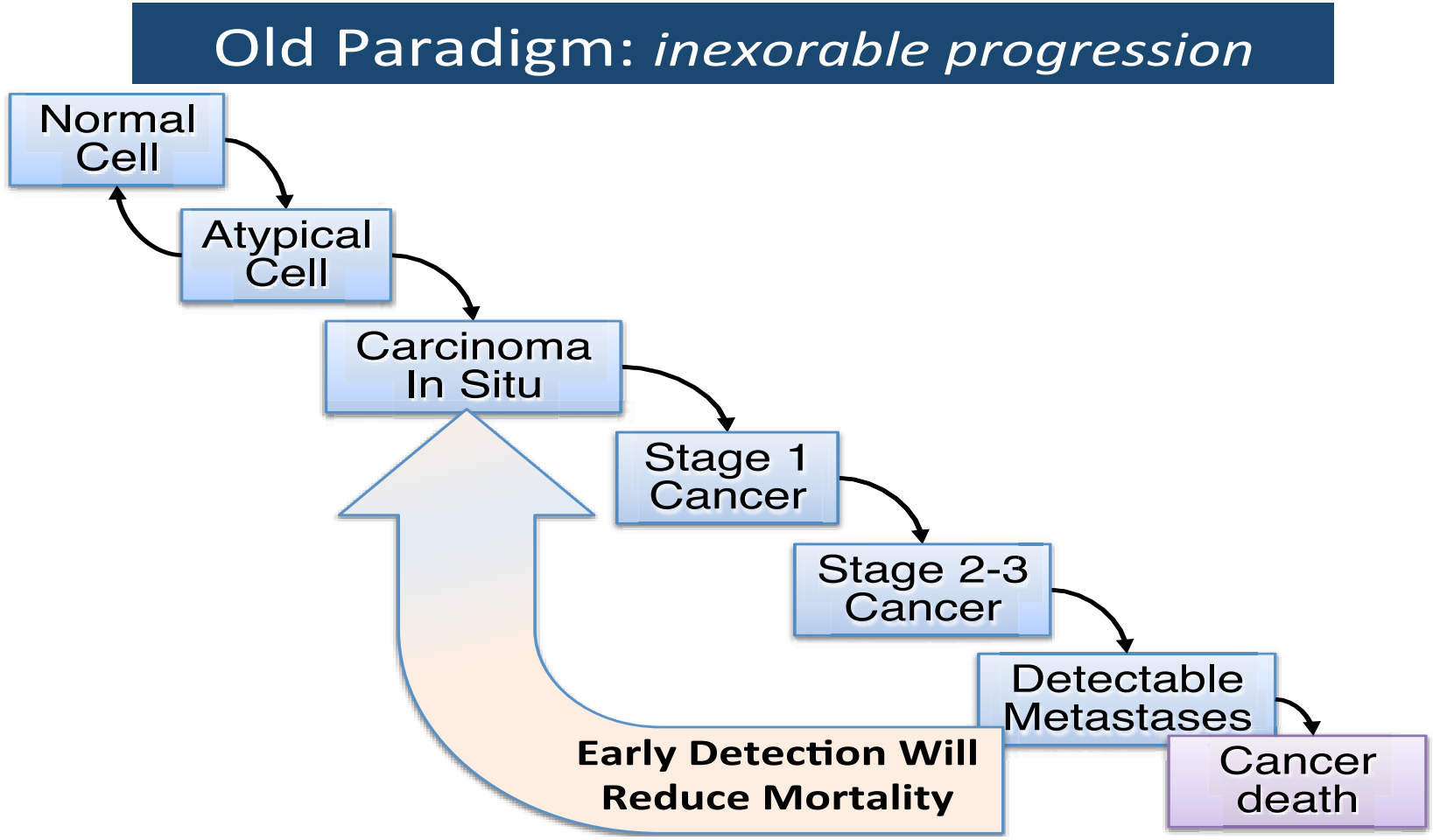


58 year old woman with high grade DCIS. (a) Baseline MRI shows extensive abnormal clumped ductal enhancement in the upper breast. (b) Breast MRI at 19.3 months since diagnosis demonstrates improved appearance of abnormal enhancement in the right breast. (c) Breast MRI at 25.5 months since diagnosis demonstrated continual improvement in clumped ductal enhancement with a new 6 mm mass enhancement (white arrow) representing 8 mm of Grade 3 ER-/PR-/Her2neu+ IDC at surgery.

Conclusion:

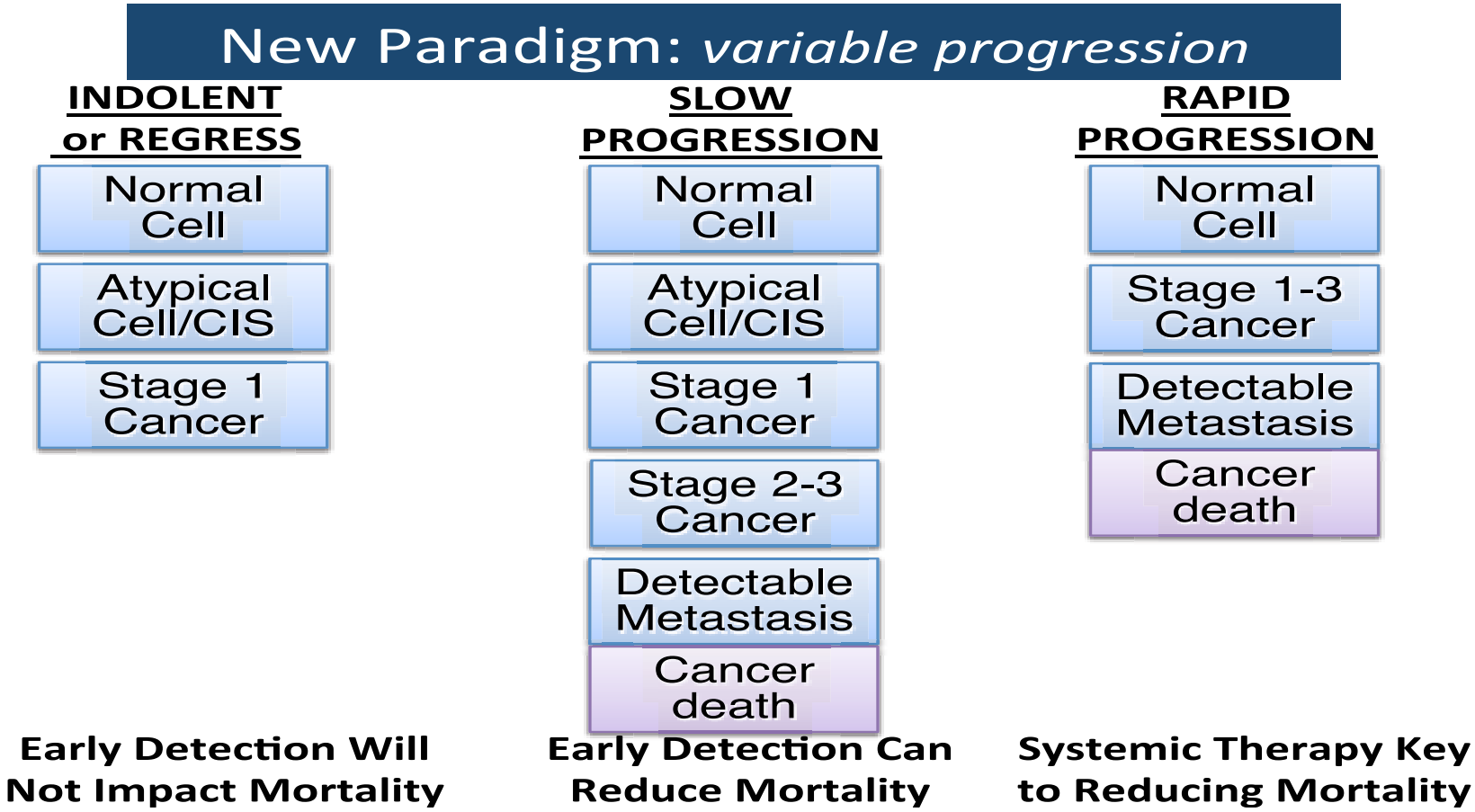
- DCIS is a precursor lesion to invasive cancer
- Excellent outcome with current treatments
- Not all DCIS will become invasive cancer but invasive recurrence impacts breast cancer specific mortality
- We currently lack reliable tools to predict invasive progression
- Patient anxiety precludes limited treatment or active surveillance

"Old school…"



Esserman LJ et al, Lancet Oncology, in press

"…new rules!"

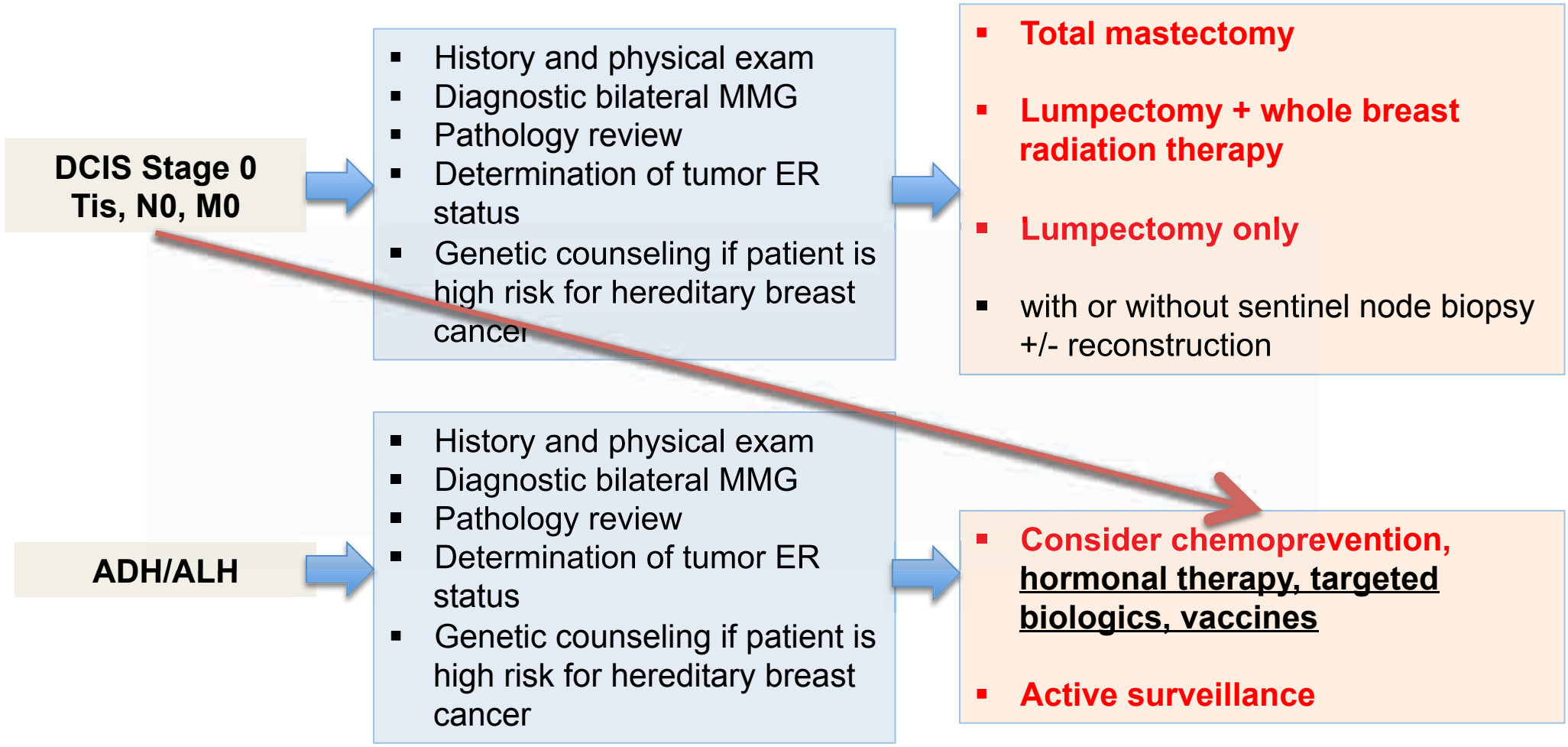


Esserman LJ et al, Lancet Oncology, in press

Table 2. Recommendations to the NCI

1. Recognize that over-diagnosis occurs and is common.
2. Embrace the development of new terminology to replace the word "cancer" where appropriate, when data and/or companion diagnostics support the classification of low risk lesions as IDLE conditions.
3. Create observational registries for IDLE conditions and conditions with low or uncertain risk of progression to cancer.
4. Mitigate over diagnosis by testing strategies that lower the chance of detecting unimportant lesions.
5. Embrace new concepts for how to approach cancer progression and prevention.

NCCN Guidelines for Treatment of DCIS



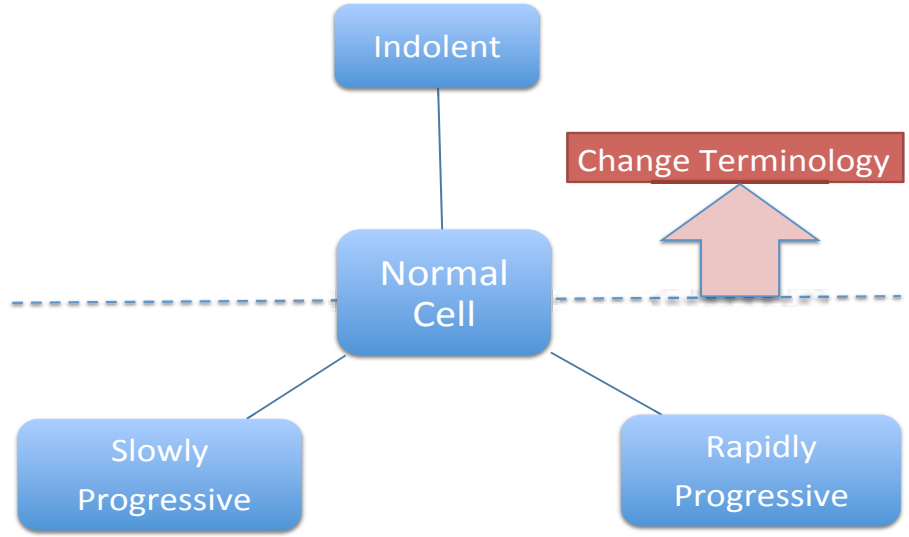
Thank you!

Thank You!

Questions?

shelley.hwang@duke.edu

Biology Determines The Impact of Screening/Treatment



Lumpectomy and radiation:

EBCTCG Overview: RT reduces recurrence in DCIS

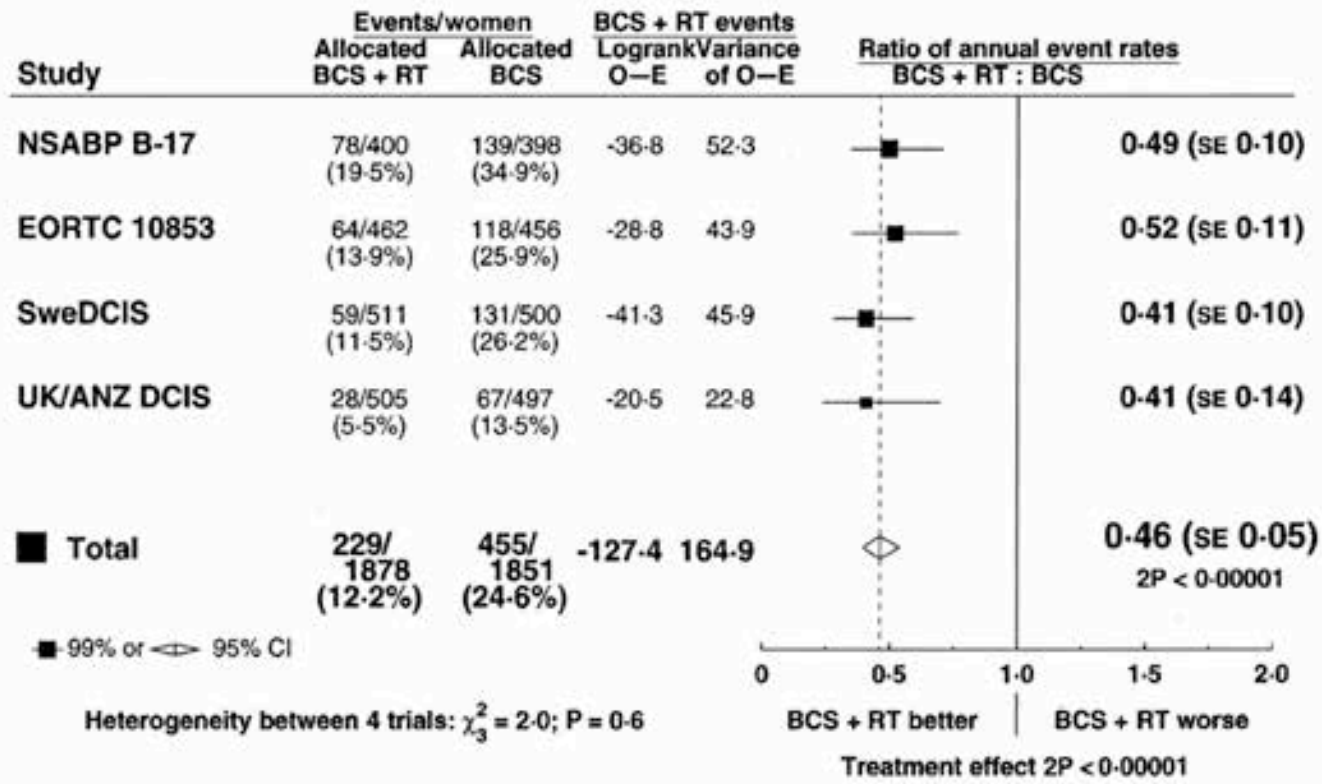


Figure 2. Effect of radiotherapy (RT) after breast-conserving surgery (BCS): ratio of annual event rates of any ipsilateral breast event by trial. SE = standard error; CI = confidence interval.

Journal of the National Cancer Institute Monographs, No. 41, 2010