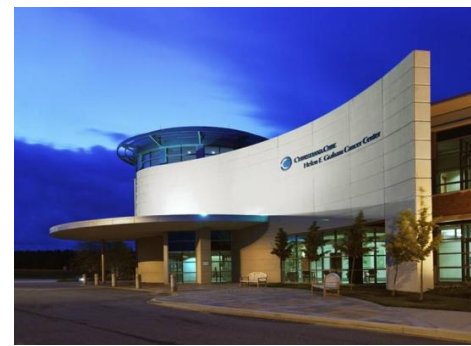


Axillary Nodal Staging in Breast Cancer: Should Results of Z0011 Change Clinical Practice ?

Diana Dickson-Witmer, MD, FACS
Associate medical director
Christiana Care Breast Center
Helen F Graham Cancer Center
Newark, Delaware



Summary



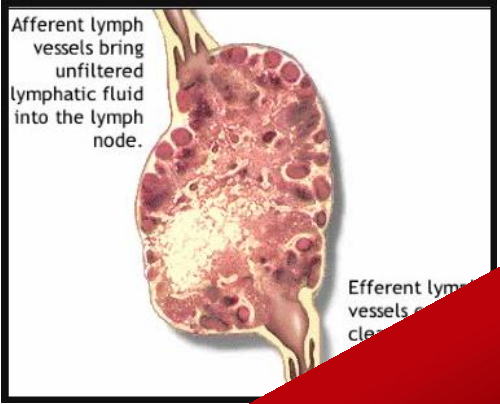
- **Yes**, clinical practice should change.
- Completion axillary node dissection may safely be omitted in breast conservation patients if:

T1 and T2 (tumor 5cm or less), clinically node negative

Must have whole breast radiation

Must have appropriate systemic therapy



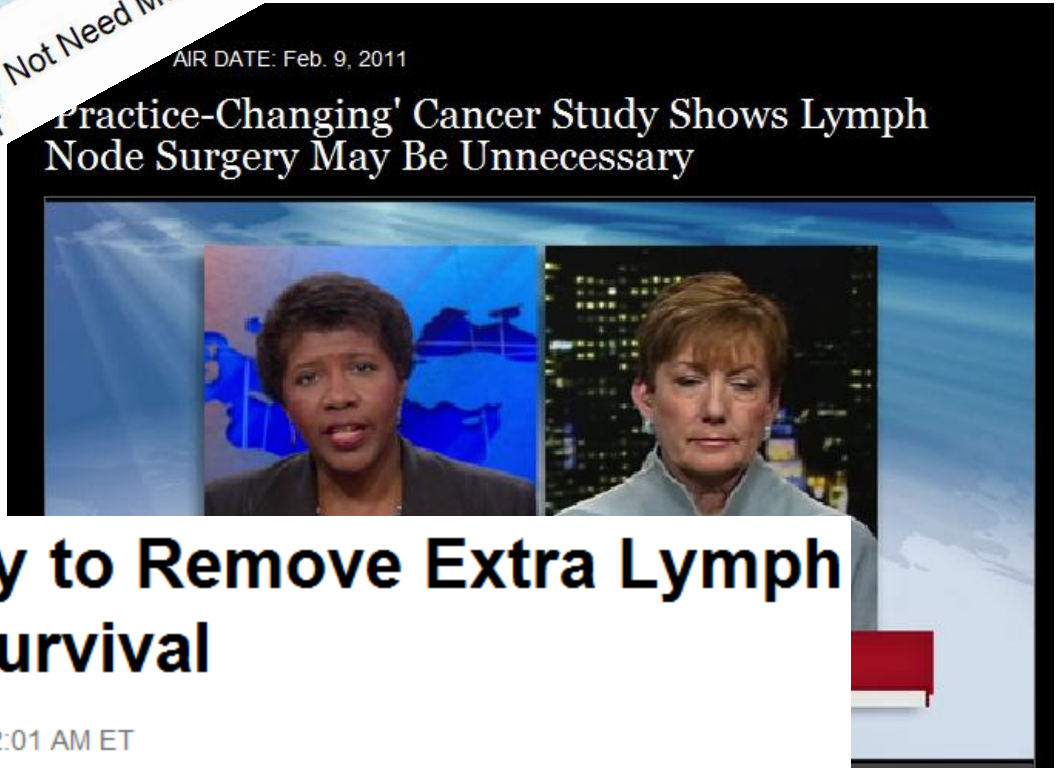


Breast cancer treatment may change

Lymph node removal may not be needed in some cases

Updated: Wednesday, 09 Feb 2011, 6:08 PM EST
Published : Wednesday, 09 Feb 2011, 6:08 PM EST

Featured Article
Some Women May Not Need More Extensive Lymph Node Surgery for Breast Cancer



AIR DATE: Feb. 9, 2011

'Practice-Changing' Cancer Study Shows Lymph Node Surgery May Be Unnecessary

Issue Home
NEWS
Featured Article: Some Women May Not Need More Extensive Lymph Node Surgery for Breast Cancer
... May Slow the ...-Stage Prostate

Lym
By DF
Put

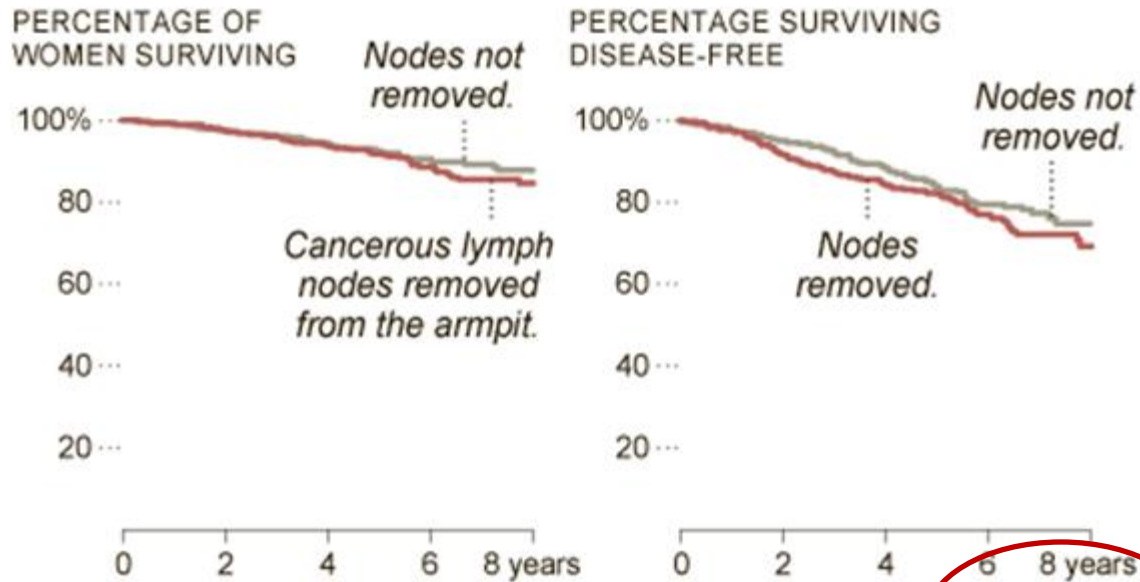
Bloomberg

Breast Cancer Surgery to Remove Extra Lymph Nodes Doesn't Help Survival

By Rob Waters and Michelle Fay Cortez - Feb 9, 2011 12:01 AM ET

Reassessing a Type of Surgery

A study of women with early-stage breast cancer found that the standard and longstanding practice of removing cancerous lymph nodes from the armpit did not improve survival or make the cancer less likely to occur.



Source: JAMA

THE NEW YORK TIMES

Theme for the past 30 years:

Impact a patient's body and life less, while achieving the same good chance for cure.

But this has not always been the theme.

Sequential Theories of Breast Cancer Biology

Systemic

Halstedian

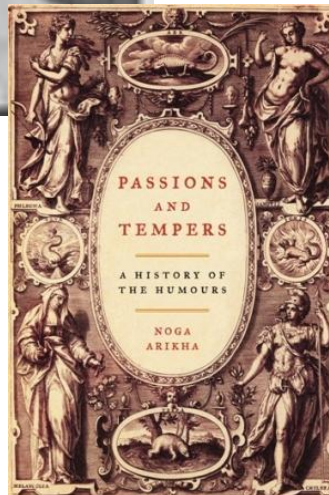
Spectrum

Systemic theory

The island
of Kos

Hippocrates

460 BC



- Hippocrates postulated a “humoral” theory of disease.
- The essence of life was “inner heat”, and energy produced by the heart, from food people eat.

Hippocrates 460 BC



- The body has four “humors”: **blood**, phlegm, **yellow bile** and **black bile**.
- An imbalance among these 4 humors made people sick.

Since breast cancer was believed to result from an excess of Black Bile, mastectomy was thought to be of no use.

Halsted's Radical Mastectomy

1882



Halsted took advantage of anesthesia and antiseptics to subordinate speed of operation to thoroughness and safety.



Halstedian theory



Halsted

- He performed a meticulous, almost bloodless operation.

Billroth (1829-1894)

Radical mastectomy

Operative mortality: 18.5%

3 yr survival: 4.7%

Halsted (1852-1922)

Radical mastectomy

Operative mortality: 2%

3yr disease free survival: 42.4%

Halsted



- Halsted demonstrated that local control was possible, and that it was , therefore, reasonable to undertake surgical measures to that end.
- Owen Wangensteen 1957: Super-radical mastectomy removed axillary nodes, supraclav, IM and mediastinal nodes.

(return to)
Systemic theory



Dr. Bernard Fisher

NSABP B-04

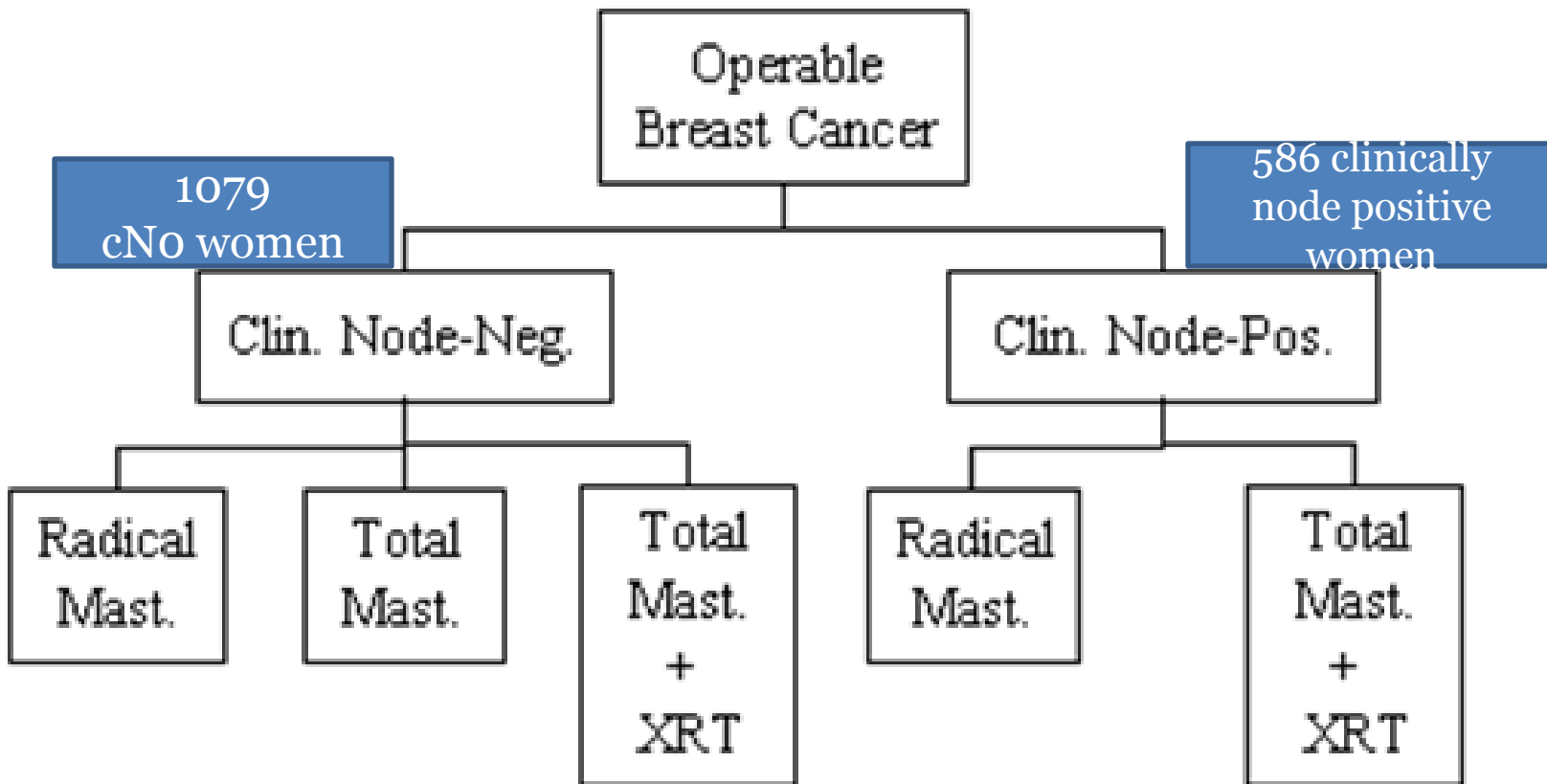
1971

A Protocol for the Evaluation of Radical
Mastectomy and Total Mastectomy With and
Without Radiation in the Primary Treatment
of Cancer of the Female Breast

Systemic theory

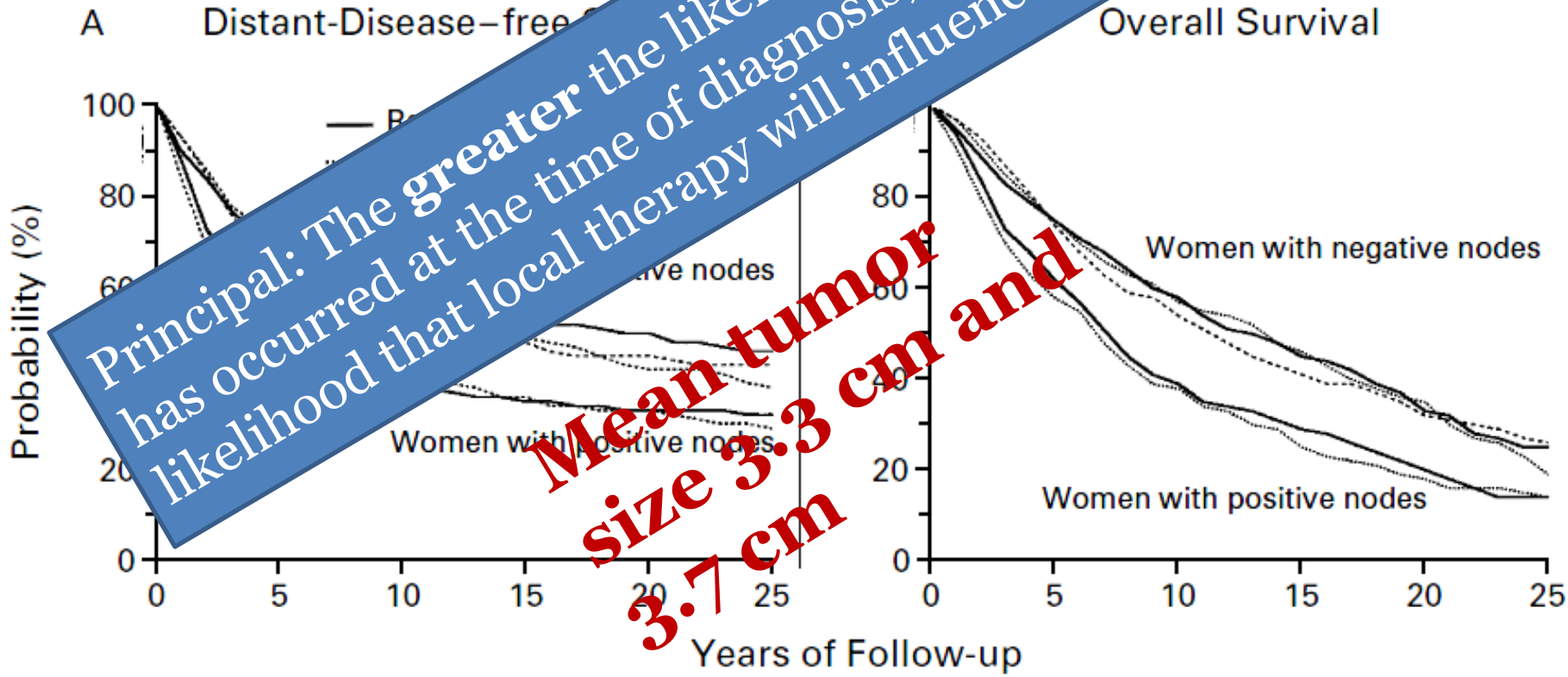
NSABP B-04

First report in
1977



Systemic therapy

NSABP B-04



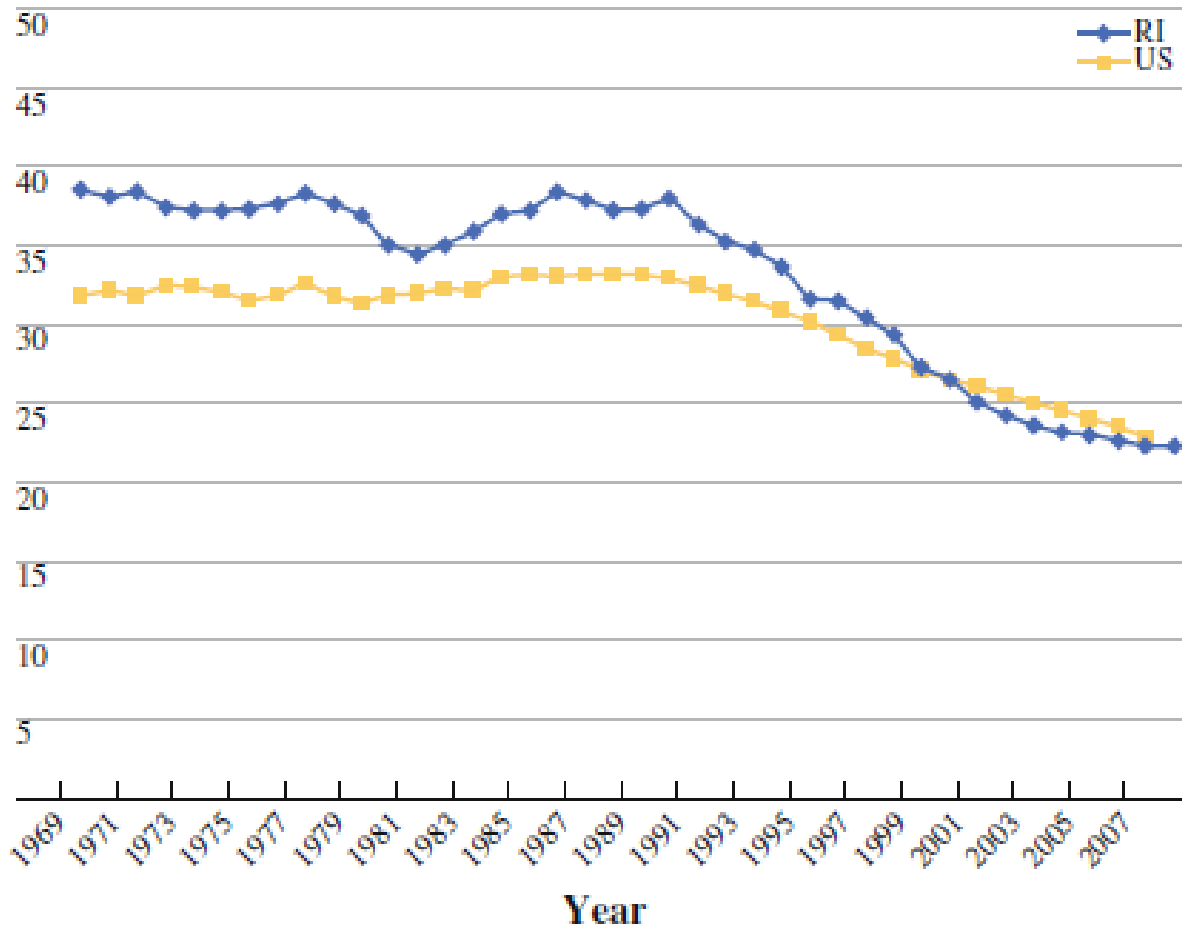
a retreat from radical surgery for breast cancer

- **1972**: 48% of patients had radical mastectomy
- **1977**: first report of B-04 results
- **1981**: 3.4% of patients had radical mastectomy
- **1985**: 10 yr results of B-06 published (breast conservation)

a retreat from radical surgery for breast cancer

- From 1977 on, surgery for breast cancer was becoming less and less aggressive.
and yet;
- Between 1990 and 2003 the rate of death from breast cancer fell 24%.
- Half of this is attributed to systemic therapy and local control; half is attributed to increased screening

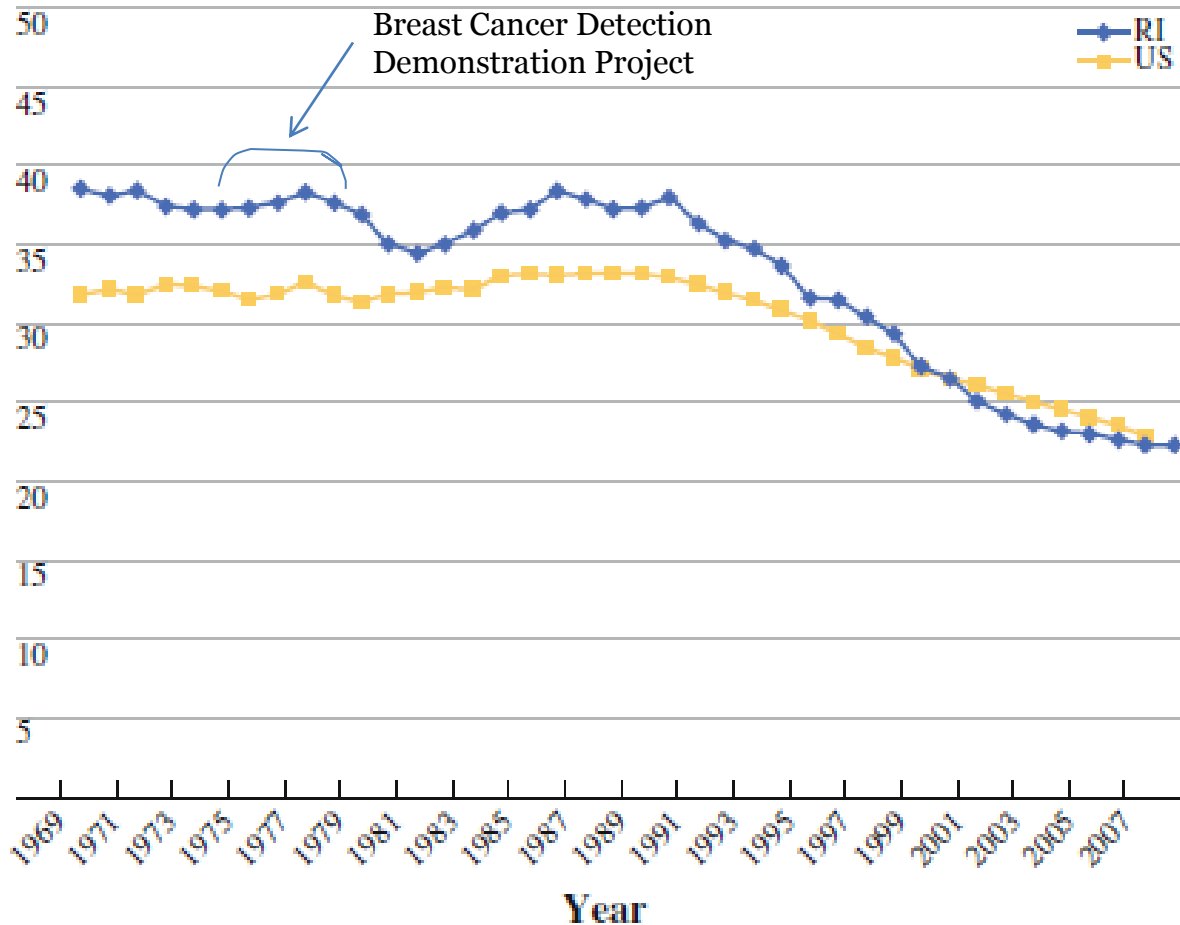
Breast Cancer mortality per 100,000



Impact of screening mammography programs on breast cancer mortality. Age-standardized female breast cancer mortality

Cady B, Annals of Surg Oncol, April 2011, 18(4): 903-906

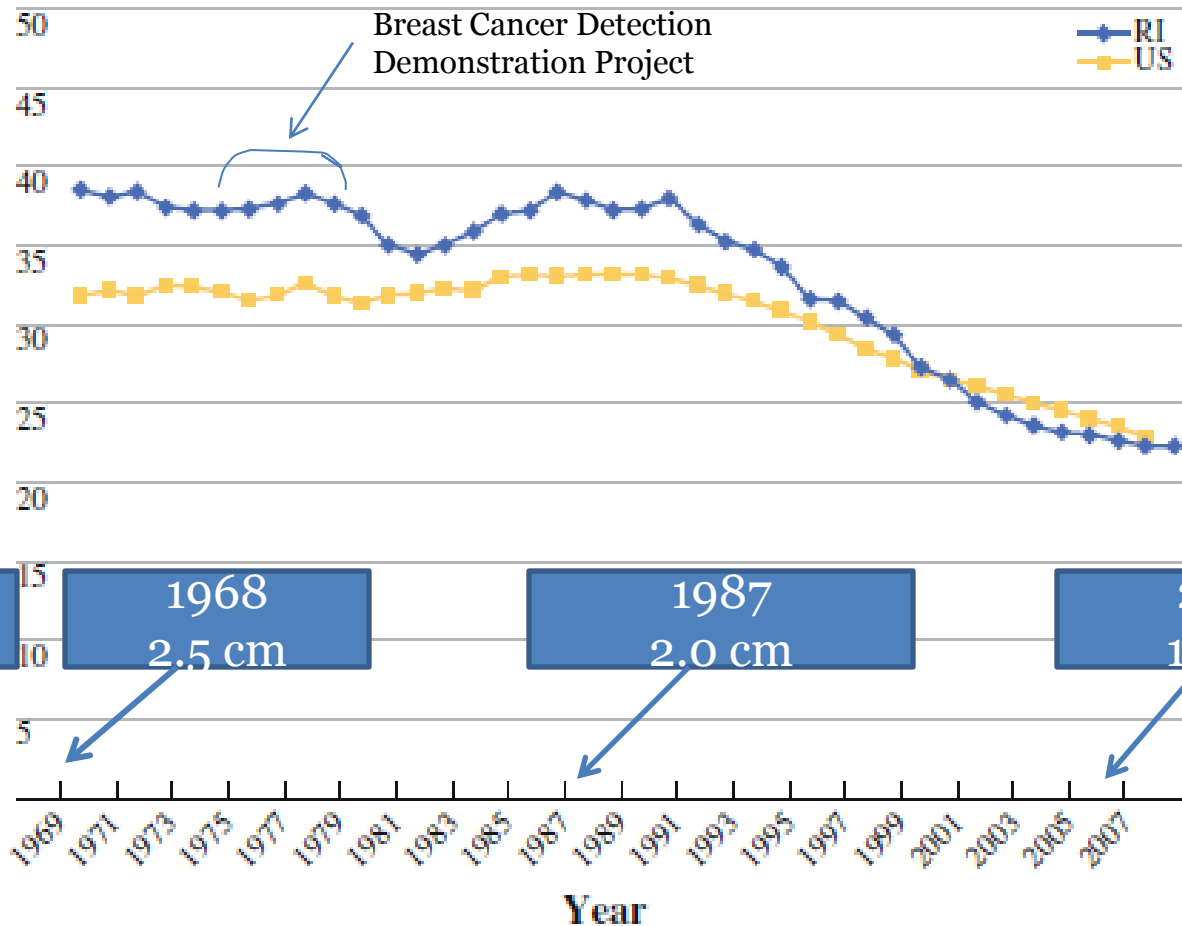
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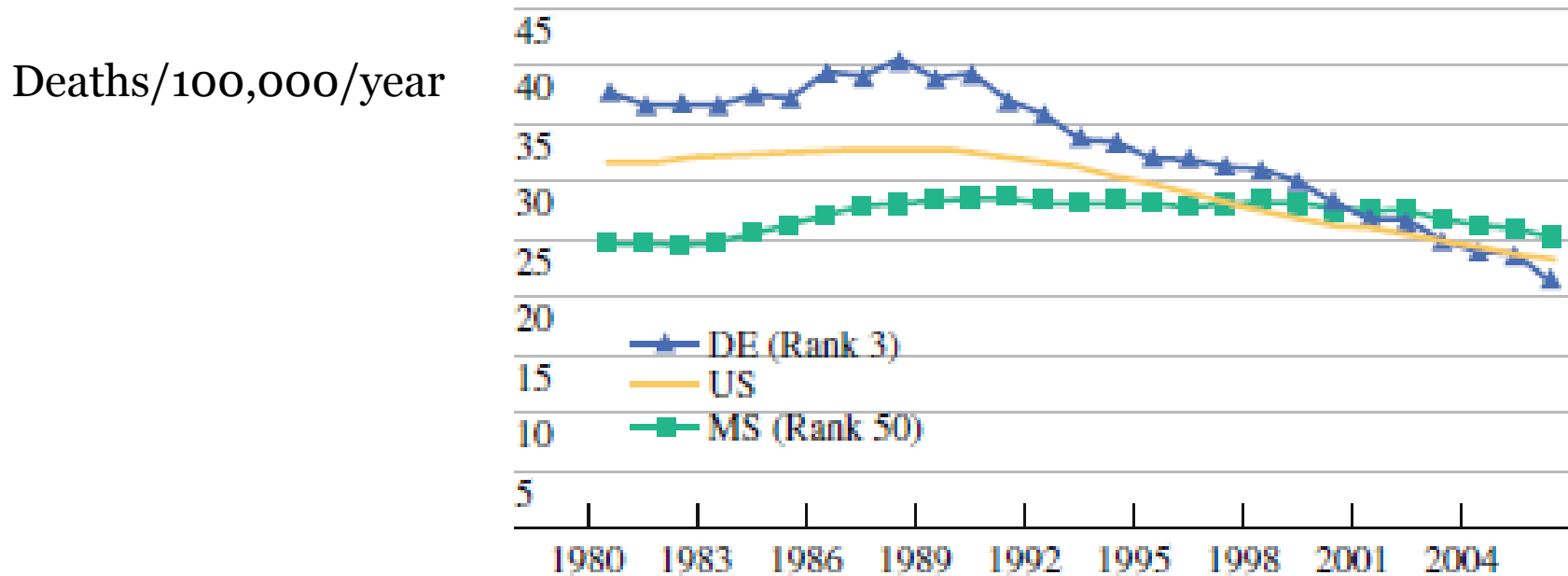
Breast Cancer mortality per 100,000



Impact of screening mammography programs on breast cancer mortality. Age-standardized female breast cancer mortality

Cady B, Annals of Surg Oncol, April 2011, 18(4): 903-906

Comparison of breast cancer mortality in states with high and low rates of mammographic screening.



Principal:

the **less** the likelihood that systemic spread has occurred at the time of diagnosis, the **greater** the likelihood that local therapy will influence survival.

42,000 women, 78 randomized trials

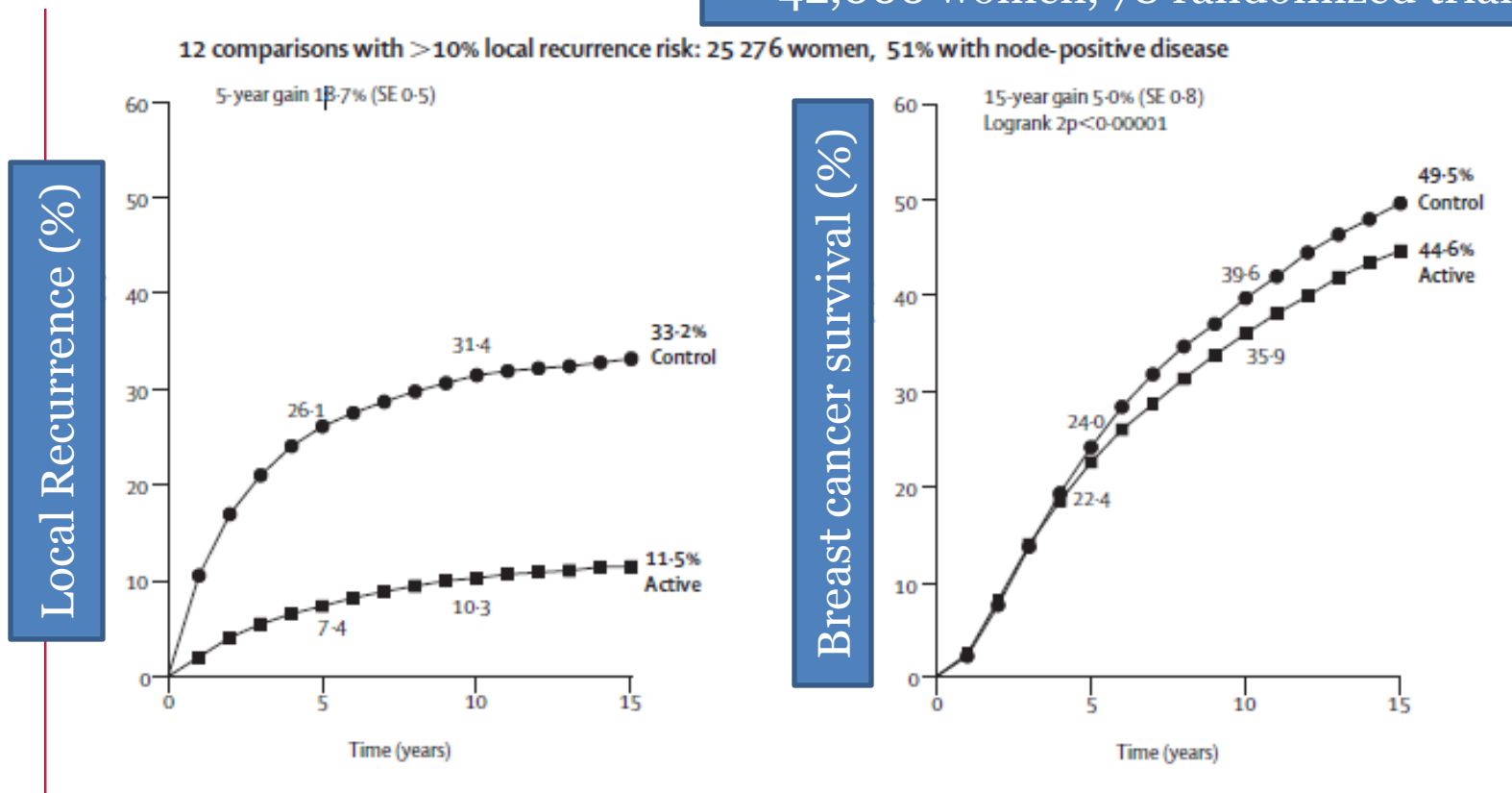


Figure 5: Local recurrence and breast cancer mortality for treatment comparisons that produce a less than 10% (upper panels) or more than 10% (lower panels) absolute reduction in 5-year local recurrence risk—15-year probabilities

If local recurrences effect survival, why were there no differences in survival between groups in B-04 ?

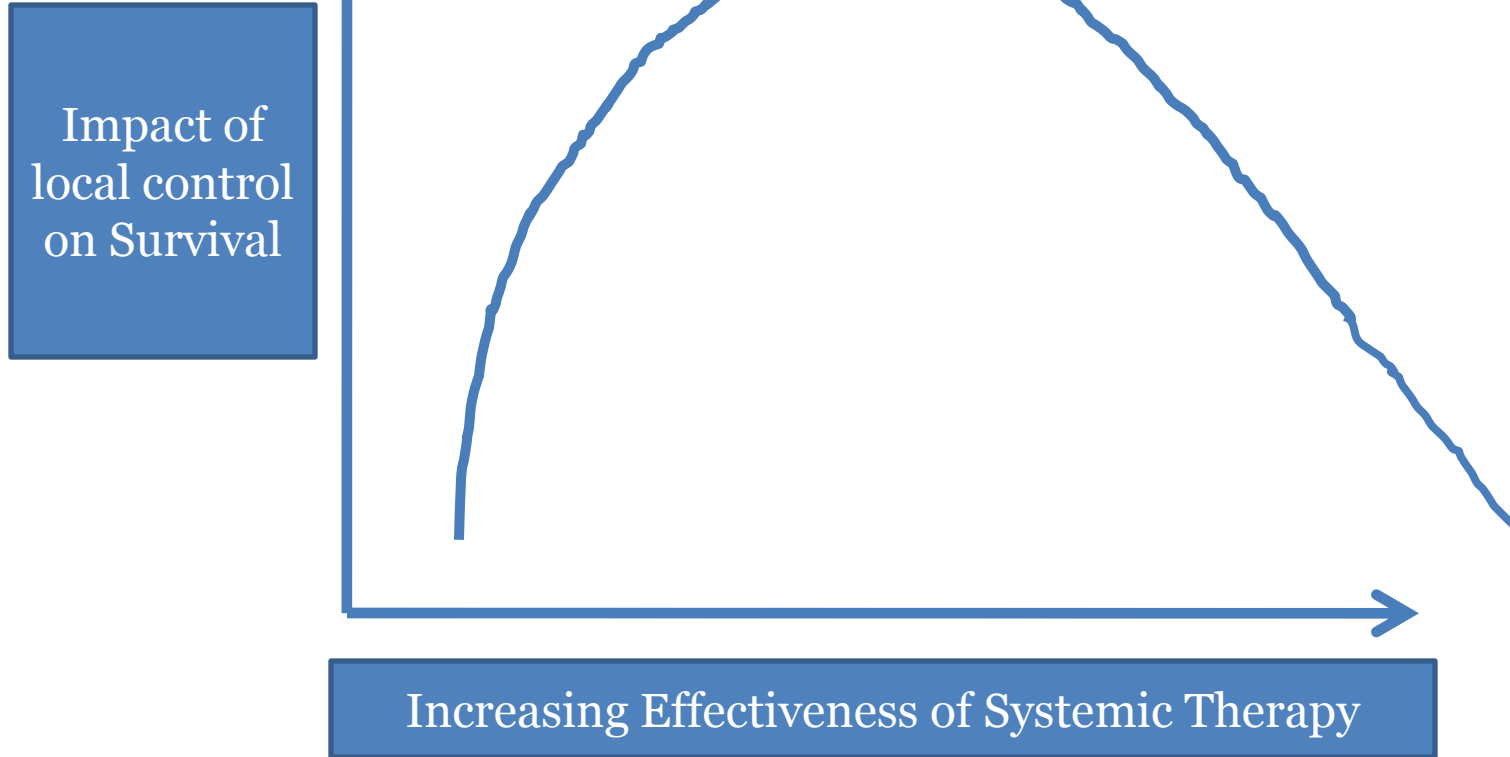
- B-04 regional recurrence:

Principal: The **greater** the likelihood that systemic spread has occurred at the time of diagnosis, the **lower** the likelihood that local therapy will influence survival.

- Mean diameter of tumors: 3.3 cm to 3.7 cm
- Probability of systemic metastasis high

EarlyBreastCancerTrialists'CollaborativeGroup; Lancet 2005;365:1687-717

Hypothetical Benefit of Local Tumor Control on Survival with Increasing Effectiveness of Systemic Therapy

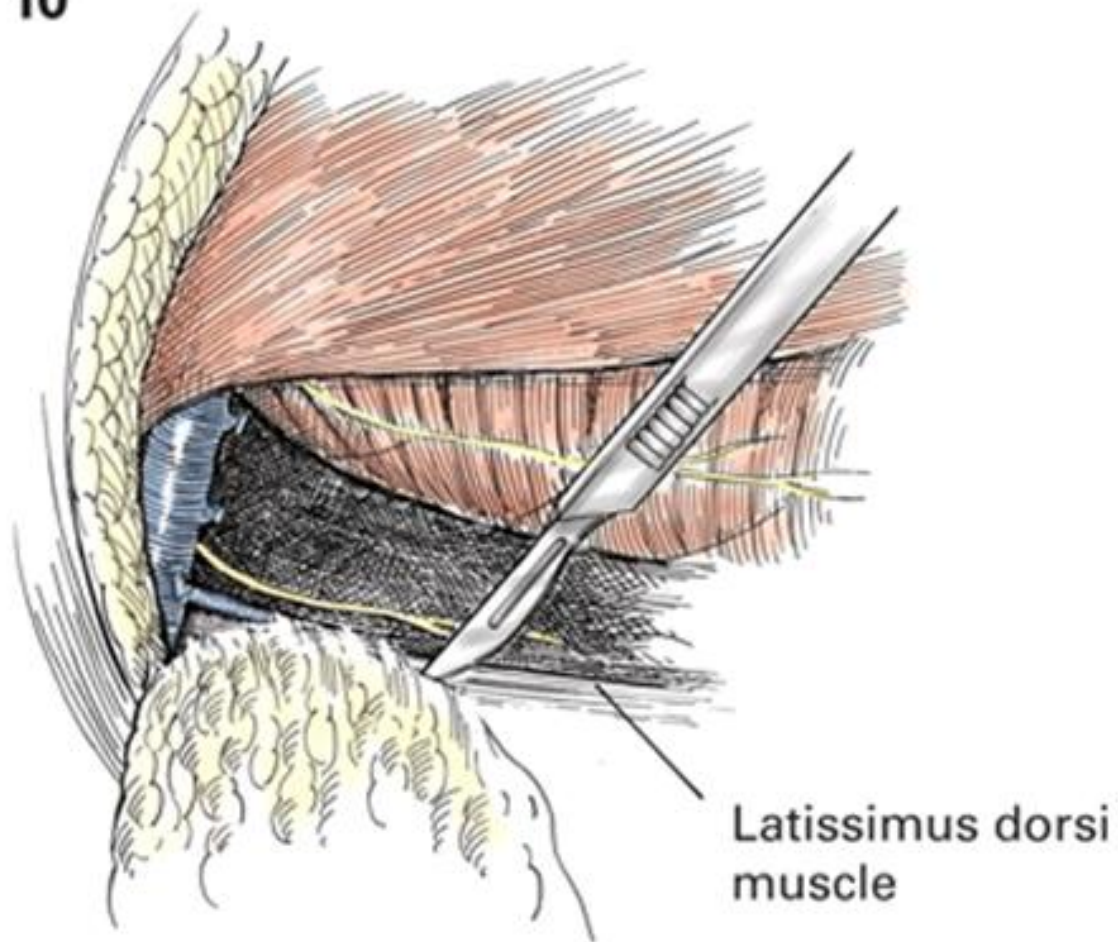


The benefit of local therapy on survival increases with increasingly effective systemic therapy, but only to a certain threshold of effectiveness.

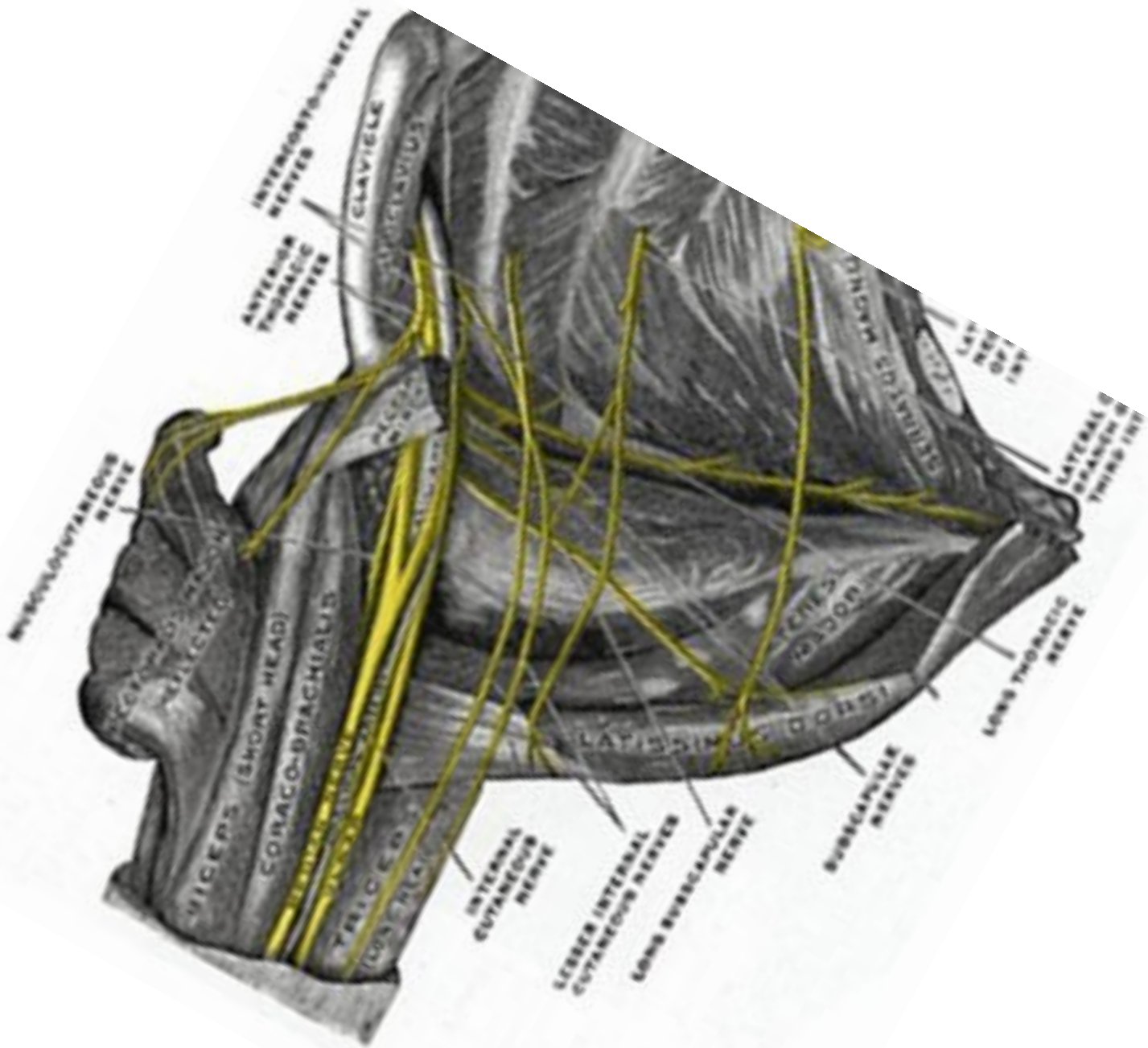
Punglia RS, Morrow M, Local therapy and Survival in Breast Cancer. NEJM June 7, 2007;356:2399-2405

Figure 10

10



Source: Zollinger RM, Ellison EC: *Zollinger's Atlas of Surgical Operations, 9th Edition*:
<http://www.accesssurgery.com>

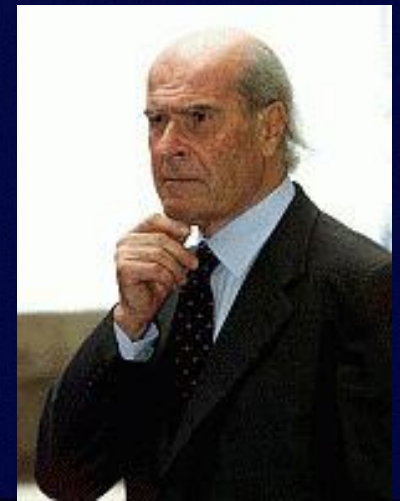


Veronesi: Breast Cancer Advocate

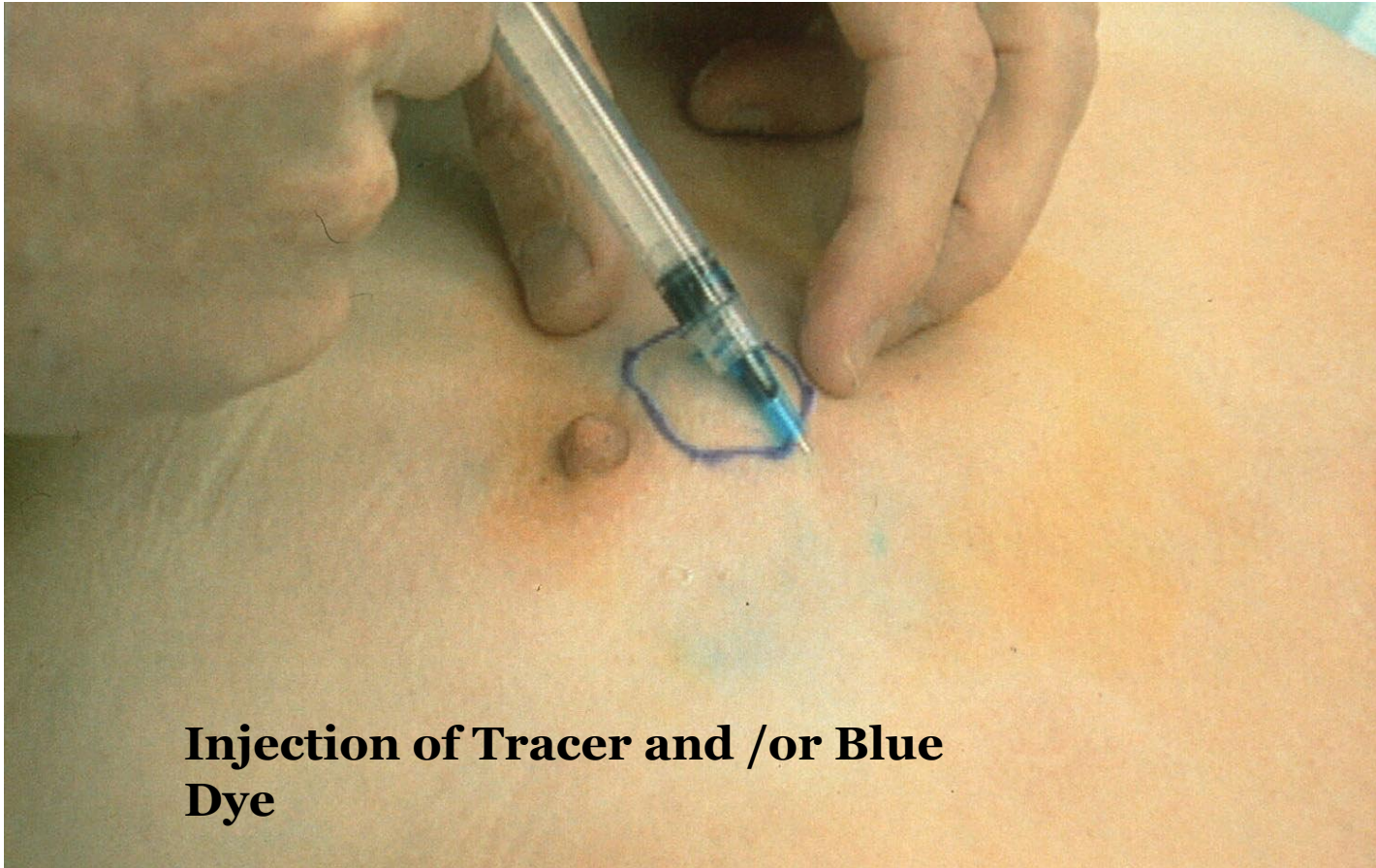
Sentinel Node Biopsy

- The sentinel node is an accurate predictor of the status of the rest of the nodal basin
- Veronesi, Lancet 349:1864-1867, 1997
- 70%-80% of axillary node dissections might be avoided!

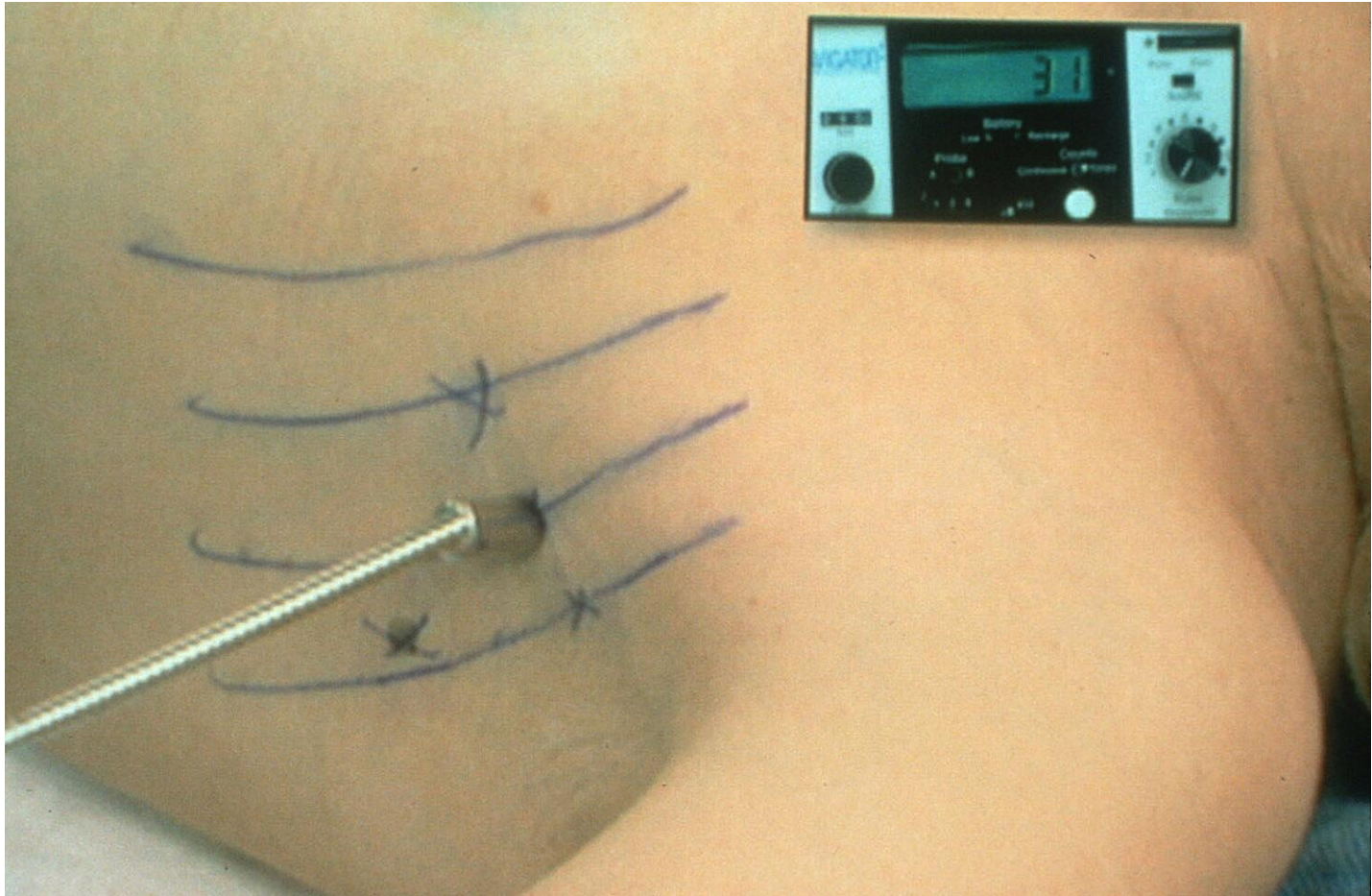
**Umberto
Veronesi**

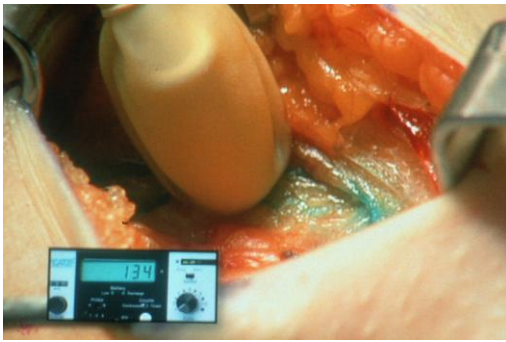


Sentinel Lymph Node Biopsy



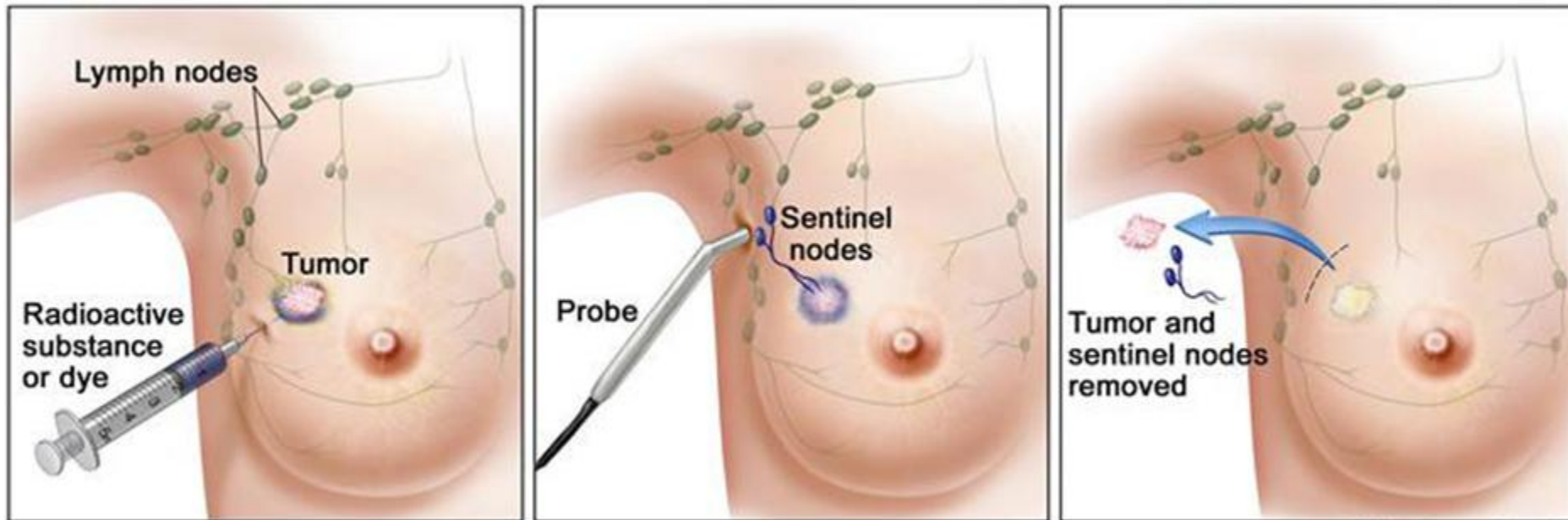
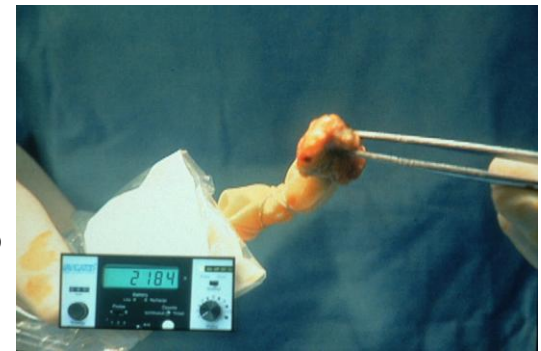
Sentinel Lymph Node Biopsy





Risk of lymphedema:

Axillary node dissection: 20%
SLN biopsy: 7%



NSABP B-32 and ACOSOG Z0010: Axillary node dissection is **not beneficial** if sentinel nodes are negative.

What about the 20% - 30% of patients with positive sentinel nodes ?

Back to what you asked me to discuss:

Lymph Node Study Shakes Pillar of Breast Cancer Care

By DENISE GRADY

Published: February 8, 2011

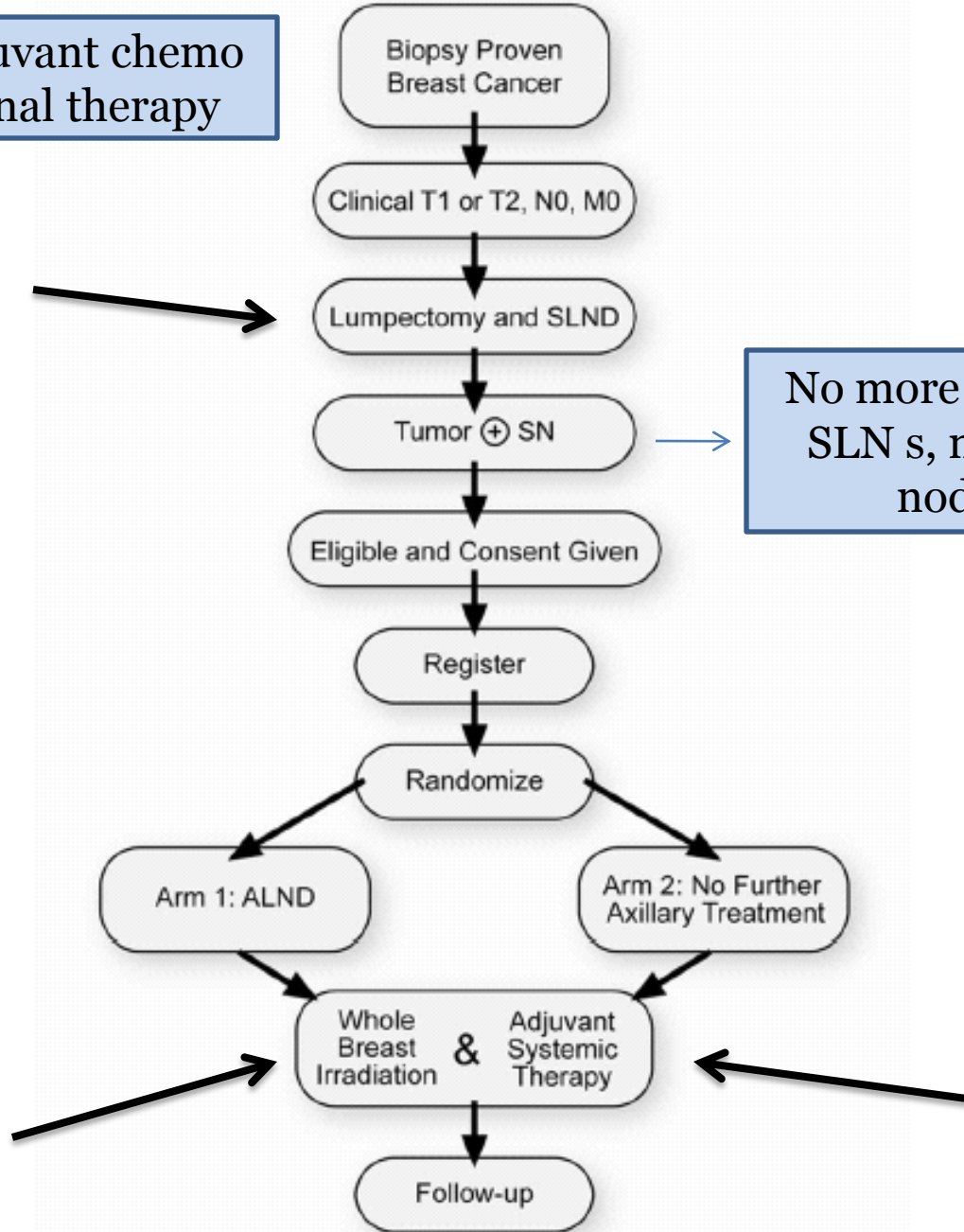
American College of Surgeons Oncology Group
Z0011

American College of Surgeons Oncology Group Z0011

- Prospective randomized trial to determine the effects of complete axillary node dissection on survival of patients with sentinel lymph node metastasis of breast cancer.
- 891 clinically node negative patients, T1No and T2No, with 1 or 2 H&E positive SLN's
- Randomized to ALND or SLN alone

Z0011 Study Design Schema

No neoadjuvant chemo
or hormonal therapy



No more than 2 positive
SLN s, no gross extra-
nodal tumor

Eligible and Consent Given

Register

Randomize

Arm 1: ALND

Arm 2: No Further
Axillary Treatment

Whole Breast Irradiation & Adjuvant Systemic Therapy

Follow-up

Were the two arms of the SLN positive group equivalent in other characteristics?

Characteristic	No. (%)	
	ALND (n = 420)	SLND Alone (n = 436)

Age, median (range)y	56(24-92)	54(25-90)
Missing	7	10
Clinical T stage		
T1	284(67.9)	303(70.6)
T2	134(32.1)	126(29.4)
Missing	2	7
Tumor size, median (range), cm	1.7(0.4-7.0)	1.6(0.0-5.0)

Were the two arms of the SLN positive group equivalent in other characteristics?

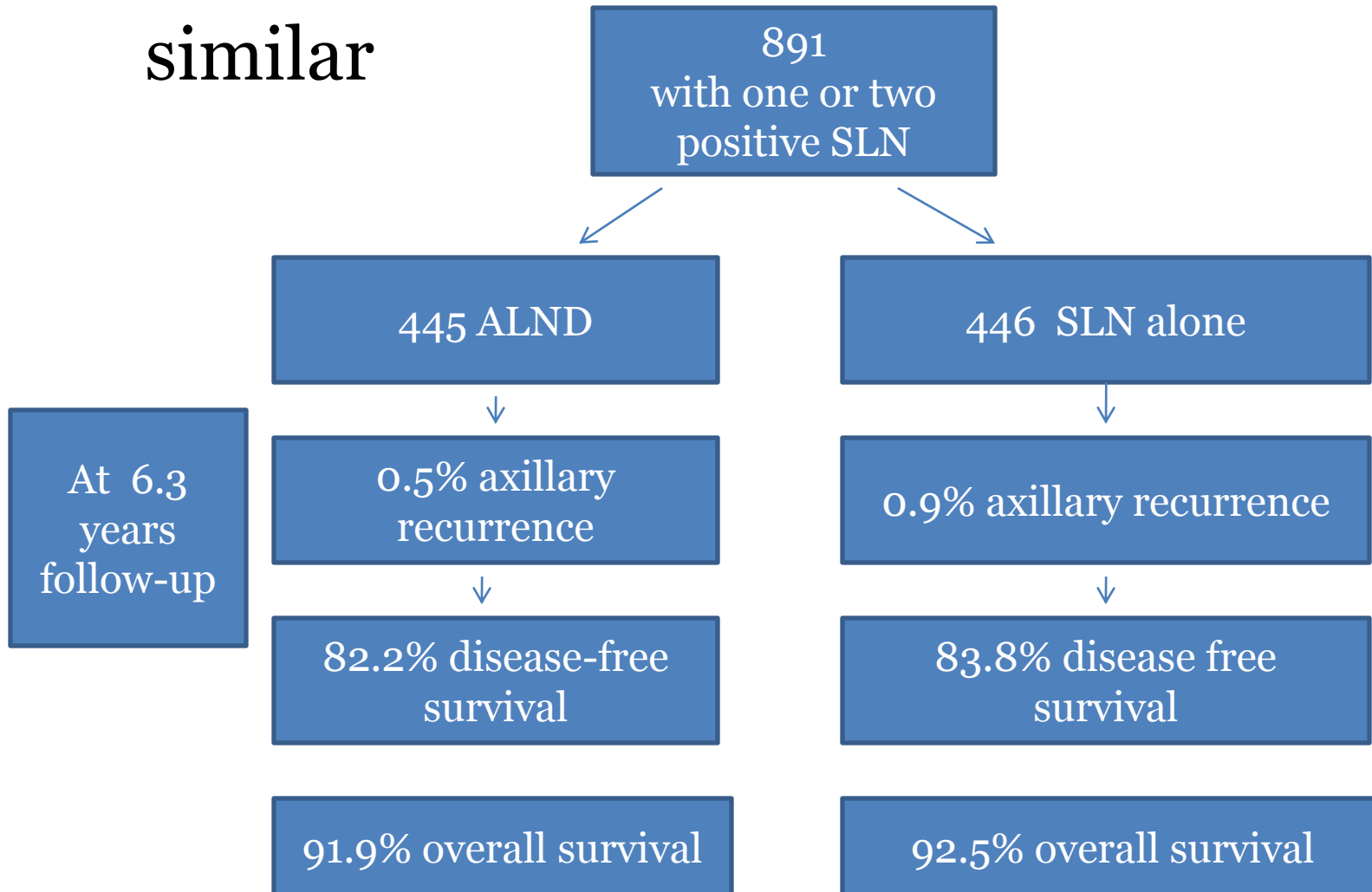
Characteristic	No. (%)	
	ALND (n = 420)	SLND Alone (n = 436)
Receptor status		
ER+/PR+	256 (66.8)	270 (68.9)
ER+/PR-	61 (15.9)	54 (13.8)
ER-/PR+	3 (0.8)	4 (1.0)
ER-/PR-	63 (16.5)	64 (16.3)
Missing	37	44
LVI		
Yes	129 (40.6)	113 (35.2)
No	189 (59.4)	208 (64.8)
Missing	102	115

Were the two arms of the SLN positive group equivalent in other characteristics?

Characteristic	No. (%)	
	ALND (n = 420)	SLND Alone (n = 436)
Modified Bloom-Richardson score		
1	71 (22.0)	81 (25.6)
2	158 (48.9)	148 (46.8)
3	94 (29.1)	87 (27.5)
Missing	97	120
Tumor type		
Infiltrating ductal	344 (82.7)	356 (84.0)
Infiltrating lobular	27 (6.5)	36 (8.5)
Other	45 (10.8)	32 (7.5)
Missing	4	12

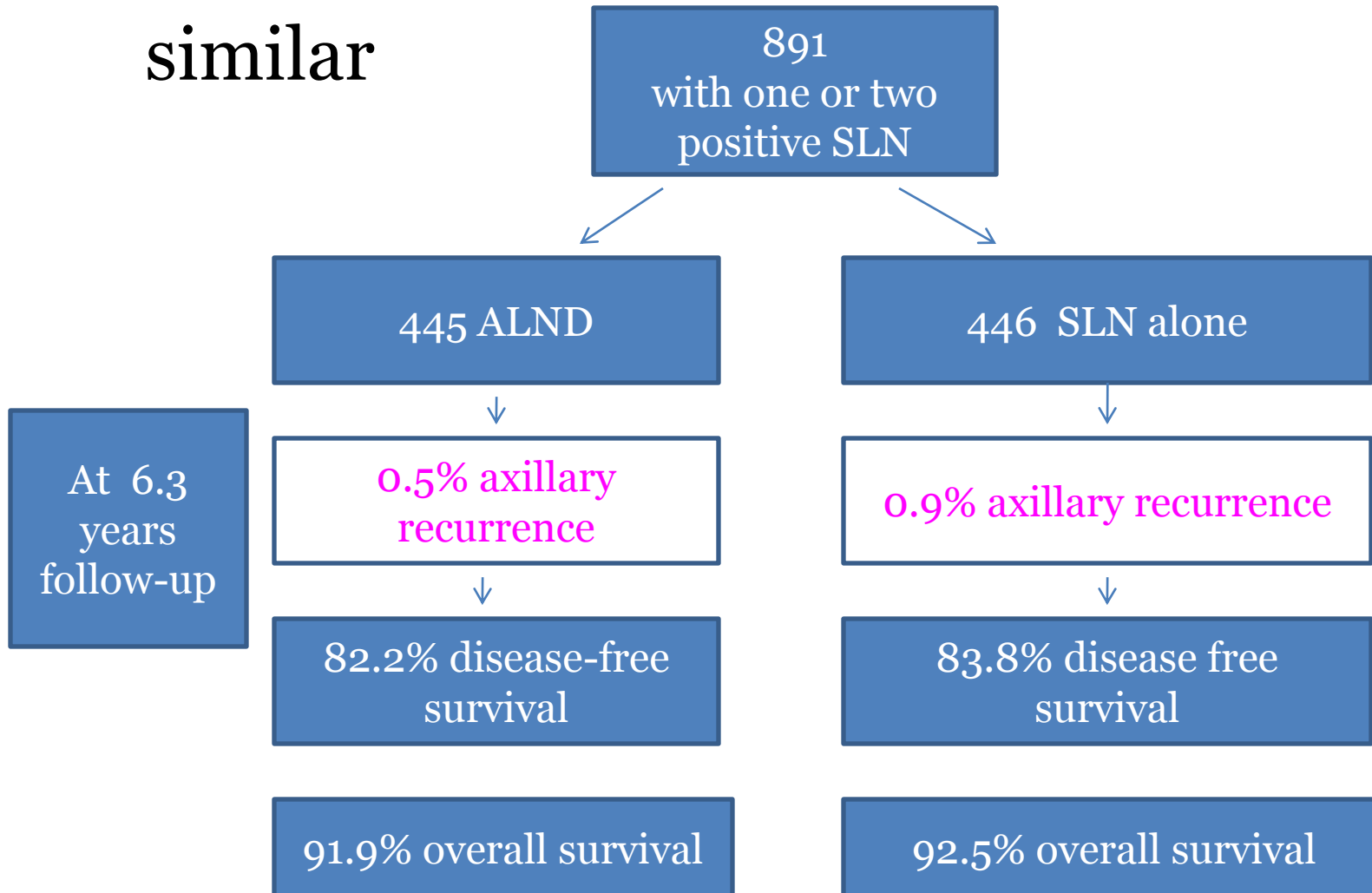
ACOSOG Z0011

- Clinical and tumor characteristics were similar



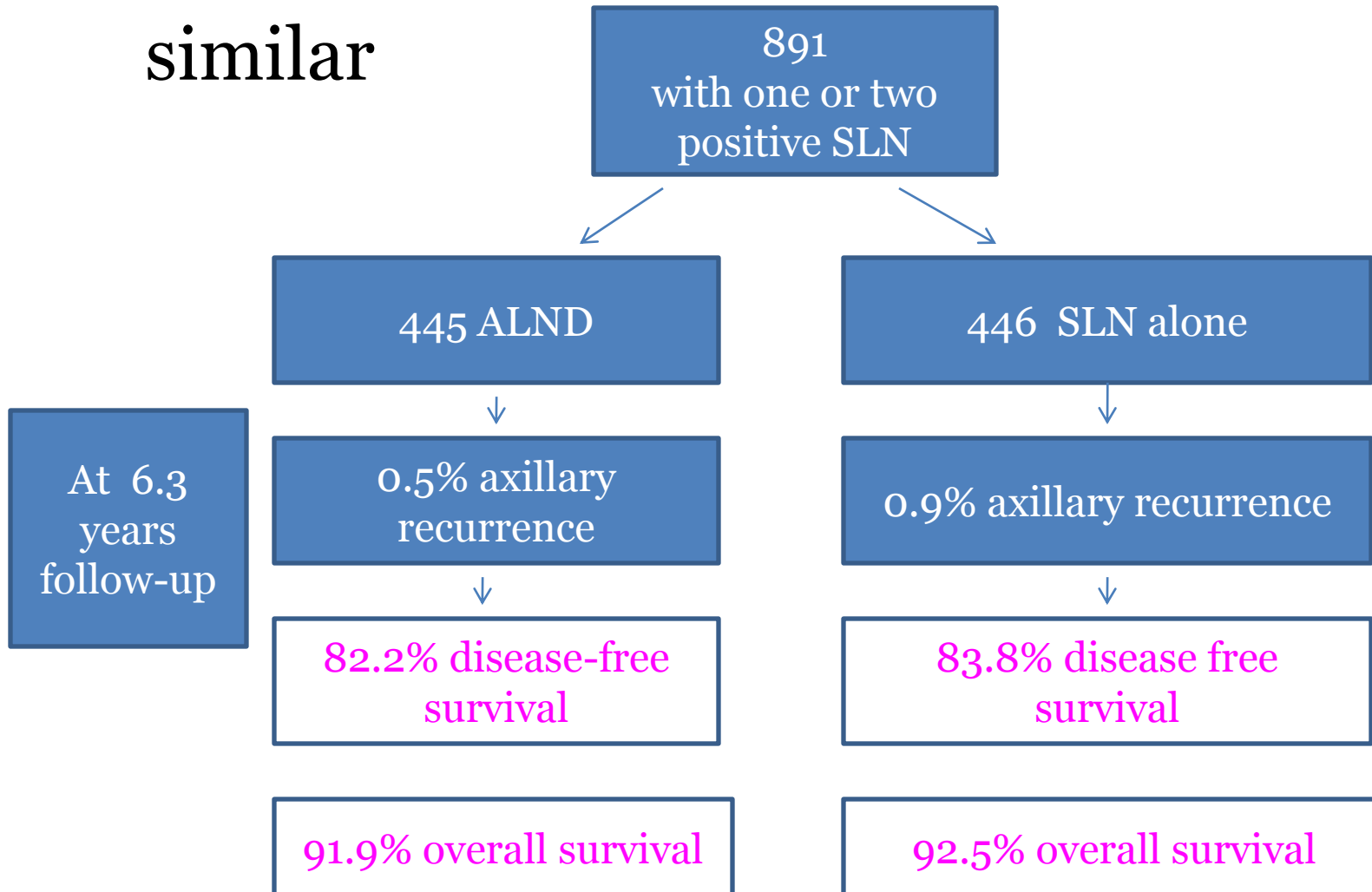
ACOSOG Z0011

- Clinical and tumor characteristics were similar



ACOSOG Z0011

- Clinical and tumor characteristics were similar



Is it just too early to see the axillary recurrences in Z0011?

- Axillary recurrence is usually an early event; at a median of 14.8 months in B-04
- In B-04, only 7 of 68 axillary recurrences occurred after 5 years
- Greco et al: median time to axillary recurrence was 30.6 months among 401 patients with breast cancer and radiation, but no axillary surgery.

ACOSOG Z0011

- All had:

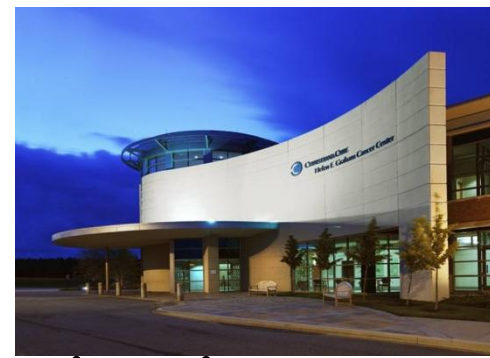
whole breast irradiation

appropriate adjuvant systemic therapy

no neoadjuvant systemic therapy

breast conserving surgery

Summary



- **Yes**, clinical practice should change in view of the Z0011 trial results.

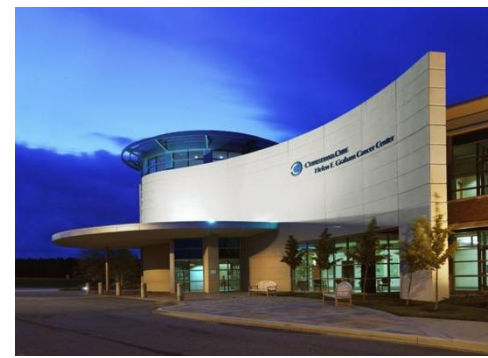
- Completion axillary node dissection may safely be omitted in breast conservation if:

T1 and T2, clinically node negative patients

Must have whole breast radiation

Must have appropriate systemic therapy





Thank you for your attention !

Diana Dickson-Witmer, MD, FACS
Helen F Graham Cancer Center
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