Controversies about Surgical Treatment of Breast Cancer

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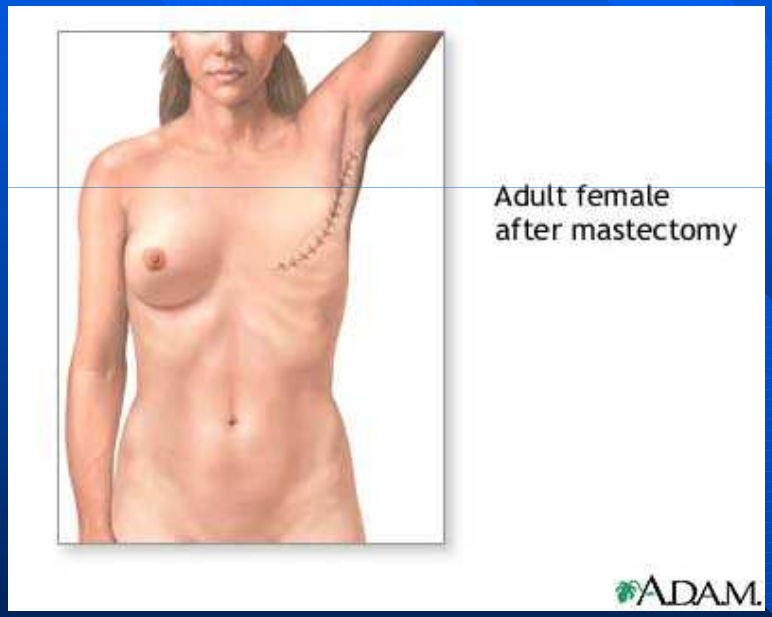
The Beginning – radical mastectomy

- Radical Mastectomy



A surgeon is not a barber anymore…

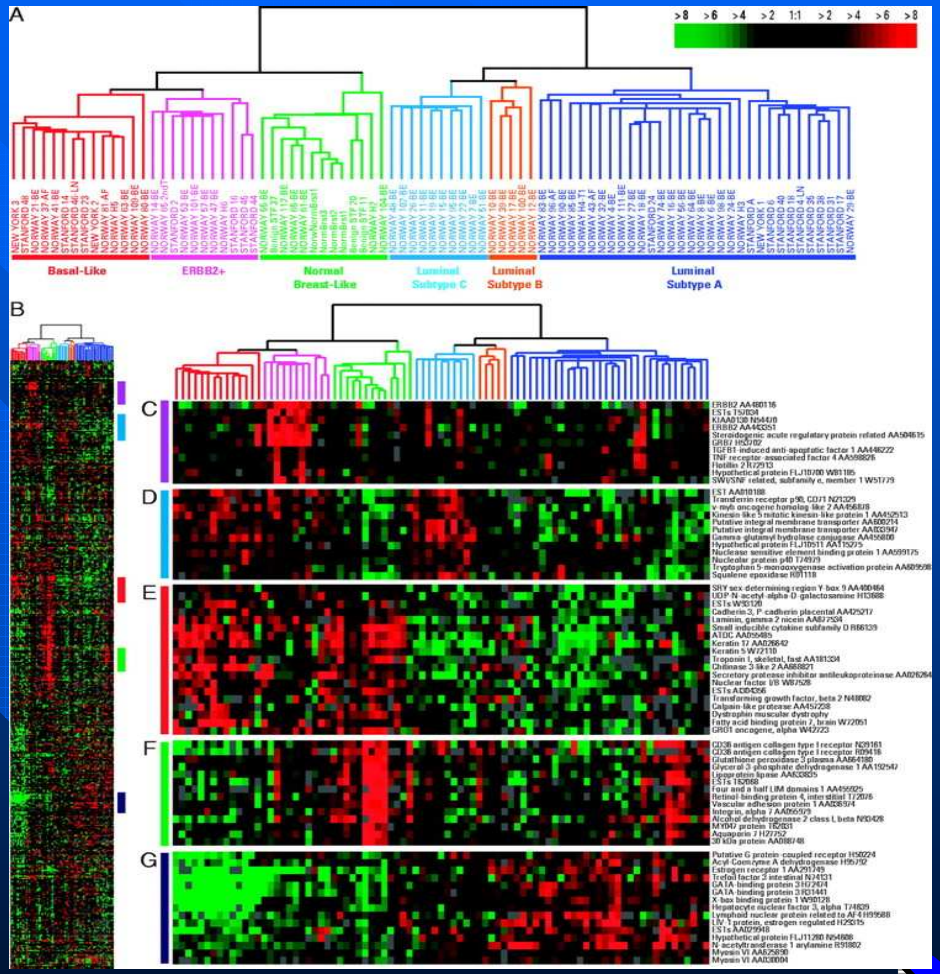
- Previously: Radical Mastectomy
- Today:
  - Modified radical Mastectomy
  - Quadrantectomy and Axillary lymph node dissection
  - Lumpectomy and Axillary lymph node dissection
  - Lumpectomy and sentinel lymph node dissection

A surgeon has become a taylor - Personalized treatment

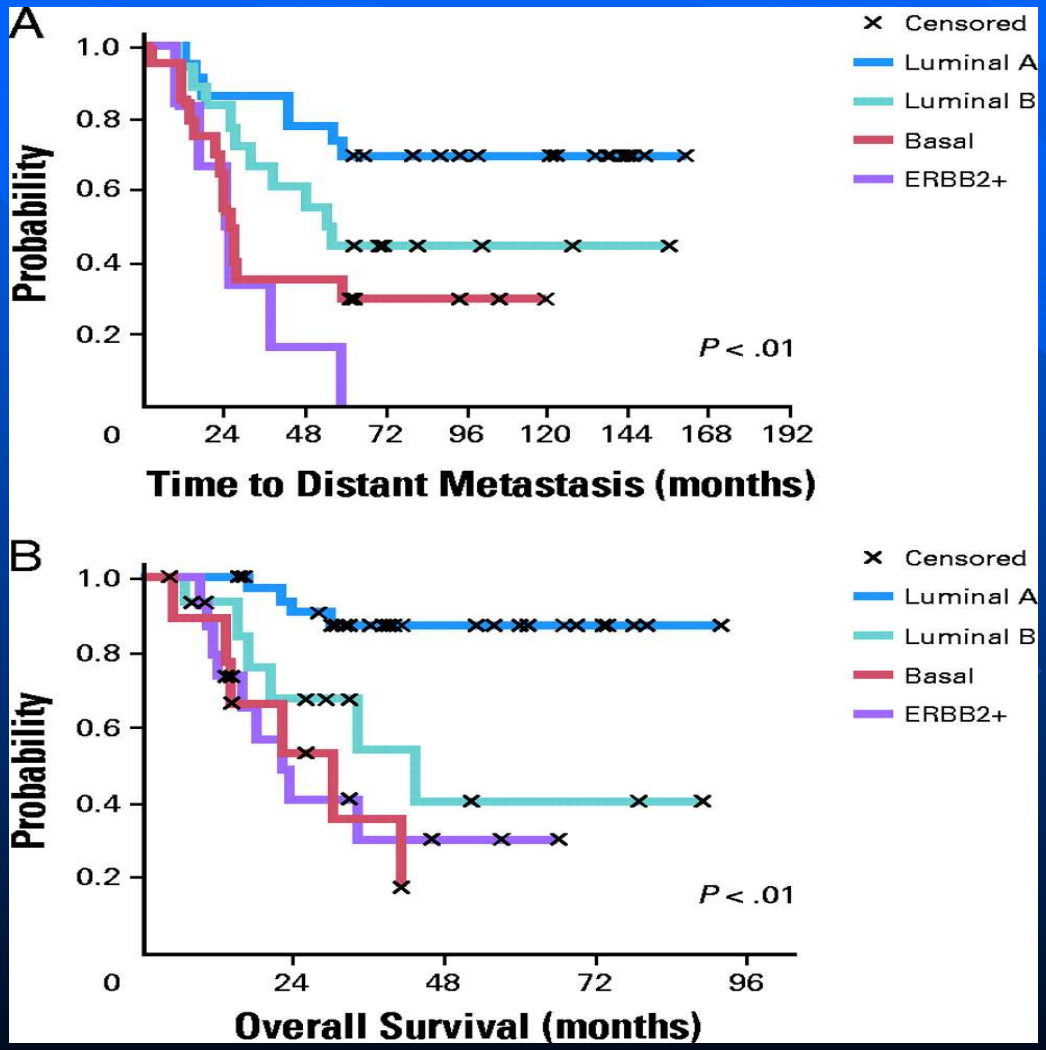
- Wide local incision with the intention of a 1 cm free margin including reconstruction of the breast where dead space should be kept to a minimum. Any oncoplastic technique should always be applied.
- Skin sparing mastectomy and immediate reconstruction.
- Sentinel node biopsy (if preoperative assessment is negative).
- Axillary lymph node dissection if pre lymph node assessment or SN is positive (> isolated tumor cells).
- Mastectomy with or without ALND.

Breast Cancer Tumor Genetic Subtypes

- **Luminal A**
  - (ER+, PR+, HER2-)
- **Luminal B**
  - (ER+, PR+, HER2+)
- **HER2**
  - (ER-, PR-, HER2+)
- **Basal**
  - (ER-, PR-, HER2-)



Breast Cancer Tumor Genetic Subtypes



Controversies about Surgical Treatment of Breast Cancer

- **Breast**
  - Bilumpectomy
  - Nipple Sparing Mastectomy
- **Axilary lymph node dissection**
  - Completion Axillary Dissection
  - DCIS

Controversies about Surgical Treatment of Breast Cancer

Breast

- Bilumpectomy - No Data
- Nipple Sparing Mastectomy
  - No Data (only descriptive reports of feasibility)
  - In a risk reducing mastectomy study the only two recurrences were in patients who underwent nipple sparing mastectomy
  - Old data of subcutaneous mastectomy had bad results

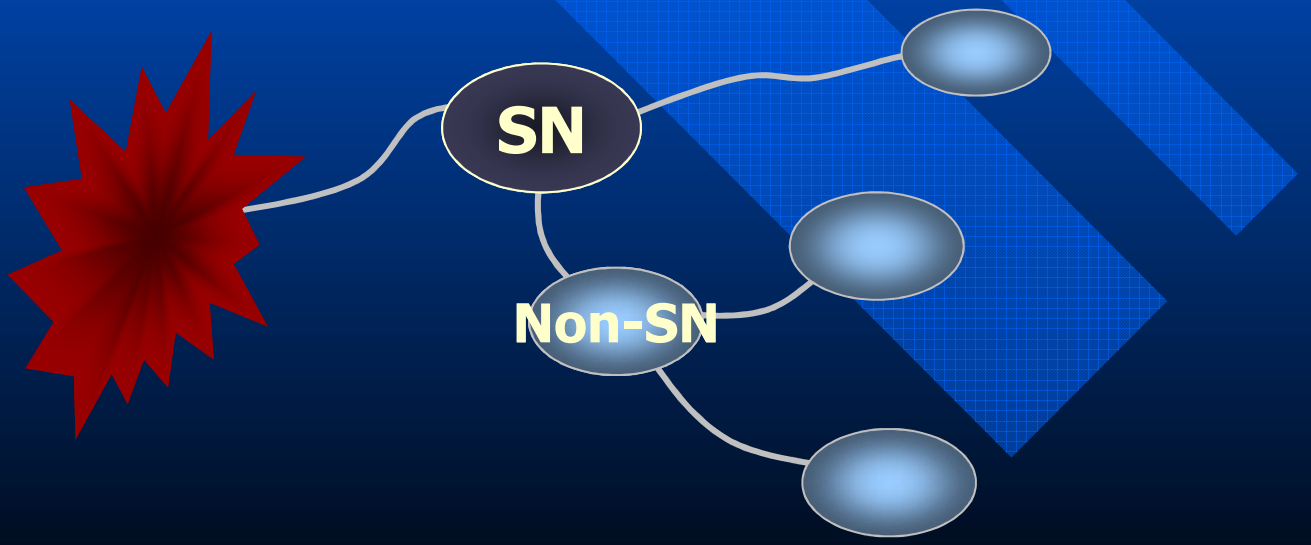
Controversies about Surgical Treatment of Breast Cancer

Axillary Lymph node Dissection

- Important component in breast cancer treatment
- Curative element in the Halstedian Concept
- Important prognostic source of information
- Regional control

SENTINEL NODE CONCEPT

- The lymph node nearest to the primary tumor site on the direct drainage pathway is the most likely site of early metastasis



NSABP B-32 randomized phase 3 trial

Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial

David N Krag, Stewart J Anderson, Thomas B Julian, Ann M Brown, Seth P Harlow, Joseph P Costantino, Takamaru Ashikaga, Donald L Weaver, Eleftherios P Mamounas, Lynne M Jalovec, Thomas G Frazier, R Dirk Noyes, Robidoux, Hugh M C Scarth, Norman Wolmark 'Andr

NSABP B-32 randomized phase 3 trial

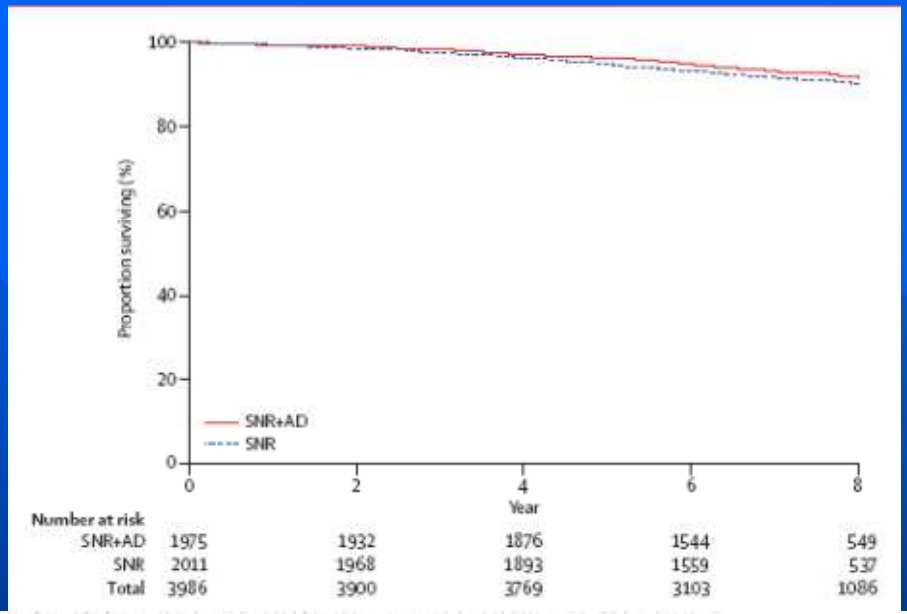
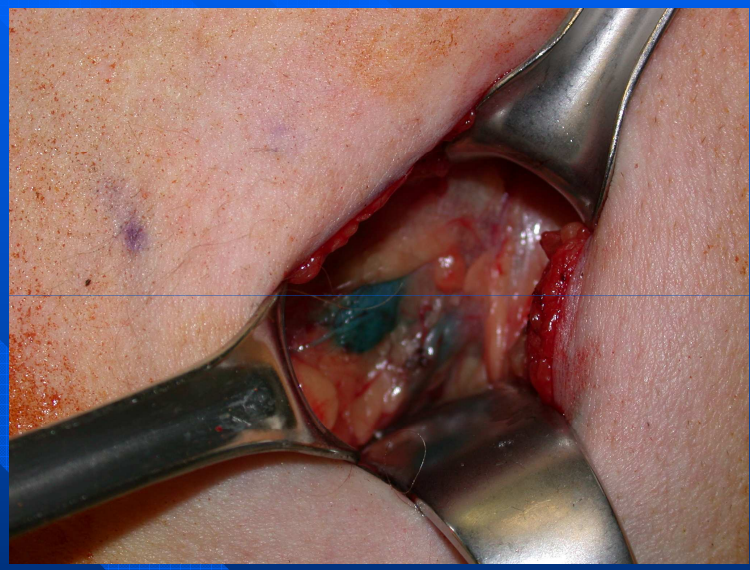


Figure 2: Overall survival for sentinel-node (SLN)-negative patients
Data as of Dec 31, 2009. For sentinal node resection (SNR) plus axillary dissection (AD), N=1975, 140 deaths. For SNR, N=2011, 169 deaths. Hazard ratio 1·20, 95% CI 0·96–1·50; p=0·12.

Conclusion: There is no significant difference in survival between SLN followed by ALND and SLN surgery alone in patients with negative SLNs.

Sentinel Node Biopsy-2012

- Standard of care
  - Better staging
  - Less morbidity
- Today Dilemma
  - Is completion ALND necessary ?
  - Is Sentinel node biopsy justified for DCIS?



Completion Axillary Dissection Following Positive Sentinel Node Biopsy

Several Retrospective Studies:

Usually associated with only one axillary L.N. are:

- Tumor size < 1 cm
- Micrometastasis
- No extranodal extension

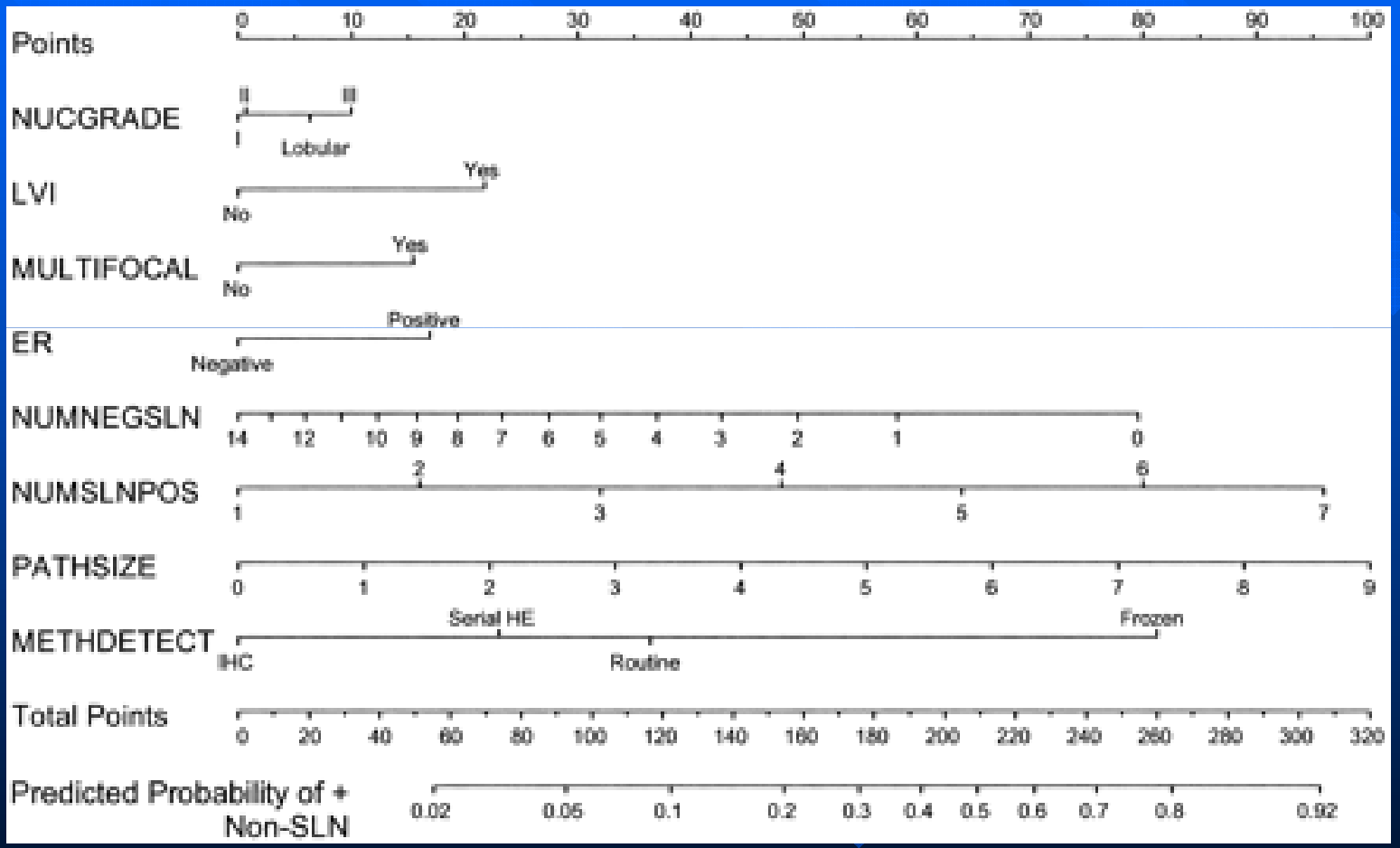
No subgroup could be identified in which axillary dissection may be omitted

Prediction of Non-SLN Metastasis With MSKCC Nomogram

- Tumor type and nuclear grade
- Lymphovascular invasion
- Multifocality of primary tumor
- Estrogen receptor status
- Number of negative SLNs
- Number of positive SLNs
- Pathologic size in centimeters
- Methods of detection of SLN metastasis

Van Zee KZ et al. Ann Surg Oncol. 2003

Prediction of Non-SLN Metastasis With MSKCC Nomogram



Van Zee KZ et al. Ann Surg Oncol. 2003

Prediction of Non-SLN Metastasis With MSKCC Nomogram

- Nomogram was examined by Receiver Operating Curve (ROC)
  - The inherent capacity of a test to discriminate a diseased from a nondiseased subject across all possible levels of positivity
  - Area under the ROC:
    - » 0.5 flipping a coin 1.0 perfect test
- 702 patients who underwent complete ALND
  - Area under ROC curve 0.76
- 373 patients prospective group
  - Area under ROC curve 0.77

Van Zee KZ et al. Ann Surg Oncol. 2003

Prediction of Non-SLN Metastasis With MSKCC Nomogram

Conclusion

Given the institutional variation in SLN technique and pathological processing we recommend that the Nomogram be validated at each institution before its use for patient counseling.

Lampert LA et al. Ann Surg Oncol. 2006

A surgeon has become a taylor - Personalized treatment

- Axillary lymph node dissection if pre lymph node assessment or SN is positive (> isolated tumor cells).
- Axillary lymph node dissection if pre lymph node assessment or SN is positive (>micrometastasis).
- Axillary lymph node dissection if pre lymph node assessment or SN is positive (> 2 lymph nodes involved).

Characteristics of Positive Sentinel Lymph Node in Breast Cancer Patients as Predictor of Non Sentinel Lymph Node Metastasis

Baruch E, Yaal-Hahoshen N, Stadler Y, Kahn P, Gat A, Sperber F, Even-Sapir E, Skornick Y, Inbar M, Schneebaum S

Breast Health Center, Department of Surgery "A", Department of Oncology, Pathology, Nuclear Medicine, and Mammography Unit of Radiology
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14th Congress of the European Society of Surgical Oncology

10-12 September, 2008 – The Netherlands - Hague

Testing the nomogram on our population: Patients

- From November 1994 through July 2007, 568 breast cancer patients underwent SLN biopsy at the Tel Aviv-Sourasky Medical Center.
- 103 (18%) had a positive SLN biopsy.
- 80 of them had consecutive CALND.
  - 13 of them had Neo-adjuvant therapy prior to the SLN biopsy.

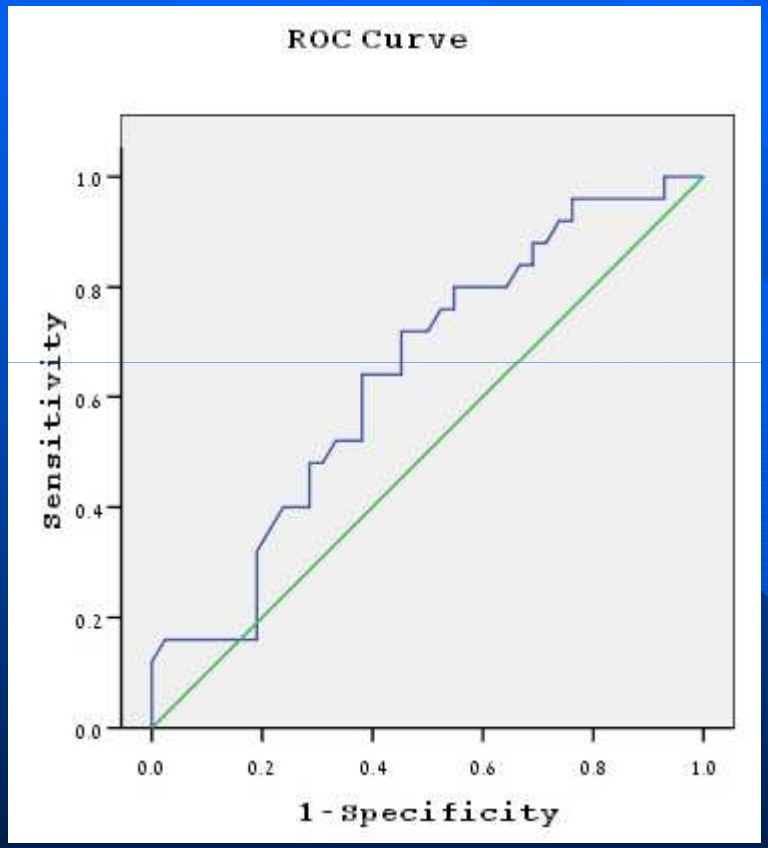
Testing the nomogram on our population: Methods

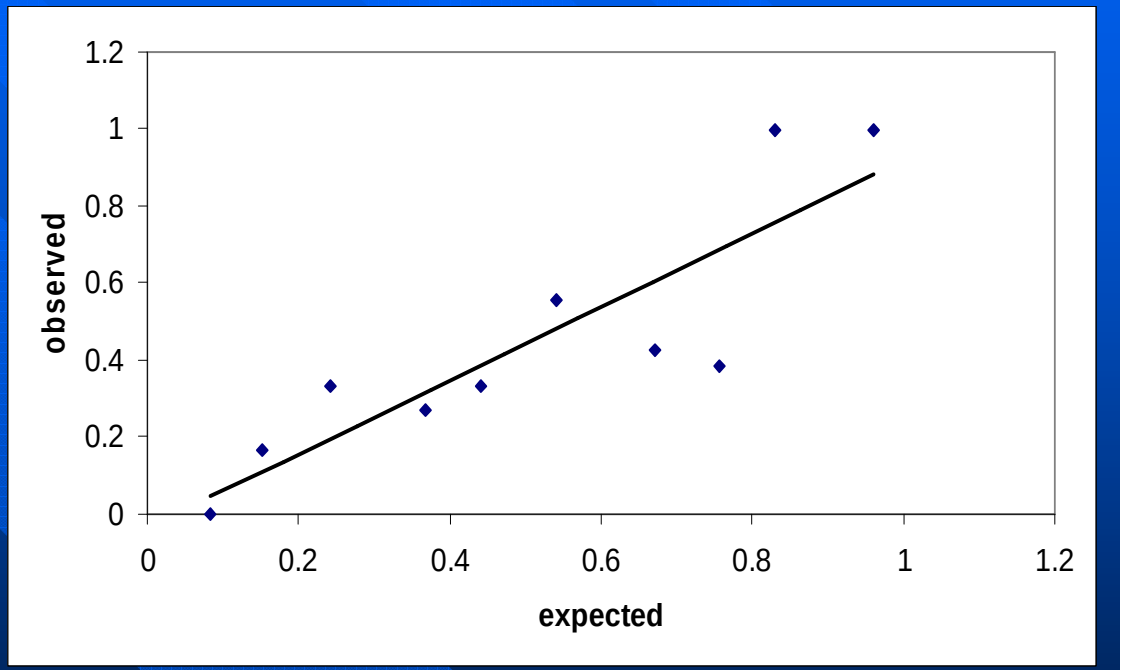
- A nomogram score was calculated for each patient.
  - For the Neo-Adj group – 2 scores:
    - » Tumor size based on pathology.
    - » Tumor size based on Pre-Neo Imaging.
- The MSKCC nomogram was assessed by the area under ROC curve.
- To address the calibration accuracy of the nomogram, a calibration plot was drawn.
- Univariate logistic regression analysis was applied to our database variables.

Results

- 103 patients had positive SLN biopsy.
- 80 patients underwent CALND.
  - 32 (40%) with Non-SLN involvement.
- 23 patients with positive SLN did not undergo CALND. In a mean follow up of 3 years, only 1 of them had distant recurrence with no axillary recurrence.

ROC Curve and Calibration plot: Excluding Neo-Adj Patients





AUC=0.64

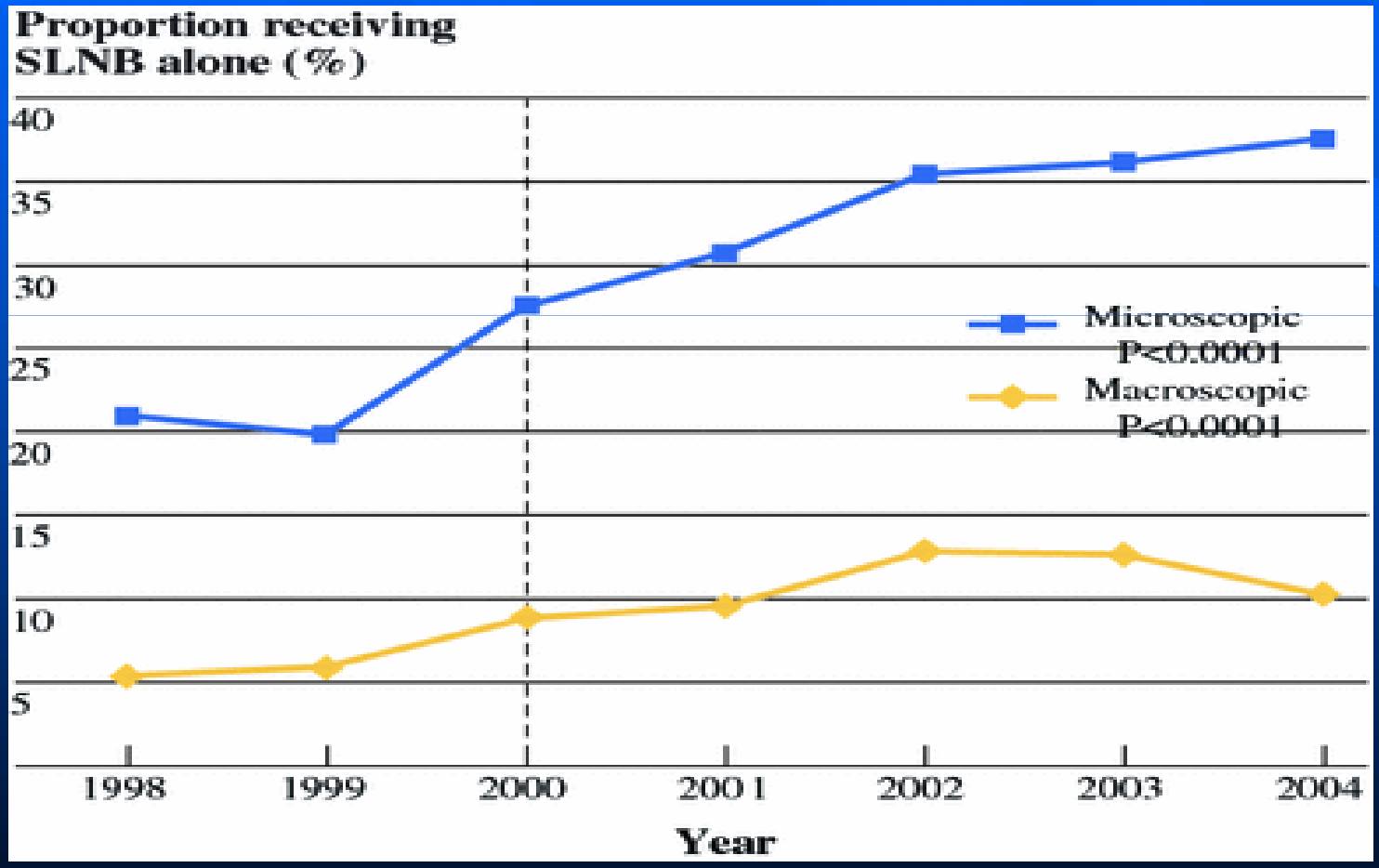
R=0.96

Trends in and outcomes from sentinel lymph node biopsy (SLNB) alone vs. SLNB with axillary lymph node dissection for node-positive breast cancer patients: experience from the SEER database

- NCCN guidelines: completion of axillary dissection for patients with N>0.2 mm
- Approximately 50% - no further metastases
- SEER data 1998-2004: 26,986 patients with a positive sentinel node biopsy and at least 24 months follow-up

Yi et al, Ann Surg Oncol 2010

Trends in and outcomes from sentinel lymph node biopsy (SLNB) alone vs. SLNB with axillary lymph node dissection for node-positive breast cancer patients: experience from the SEER database



Yi et al, Ann Surg Oncol 2010

Trends in and outcomes from sentinel lymph node biopsy (SLNB) alone vs. SLNB with axillary lymph node dissection for node-positive breast cancer patients: experience from the SEER database

Multivariate analysis of factors associated with

Characteristic	Odds ratio (95% CI)	*P* value
Age ≥55	1.4 (1.3–1.5)	<0.0001
Segmental mastectomy	2.8 (2.5–3.0)	<0.0001
T1	1.2 (1.1–1.3)	<0.0001
Micrometastasis	3.8 (3.5–4.1)	<0.0001
Grade: Low/intermediate	1.4 (1.3–1.5)	<0.0001
Estrogen receptor Positive	1.2 (1.1–1.3)	0.001

Completion Axillary Dissection Following Positive Sentinel Node Biopsy

American College of Surgery - Oncology Group (ACOSOG) Z0011 trial – Multicenter study

Aim: Significance of axillary LN dissection for SLN positive (H&E) patients

Randomization: ALND vs. No additional axillary treatment

ACOSOG Z0011- Axillary Dissection vs. No Axillary Dissection in Women With Sentinel Node Metastasis

- non-inferiority: at least 75% 5 year survival in the control arm.
- Study terminated early due to low accrual and low overall mortality
- 20 years of follow-up would be needed to reach a conclusion
- 445 and 446 patients enrolled

- Study design: treatment arm – 80% 5 year overall survival;

Guilliano et al, JAMA 2011

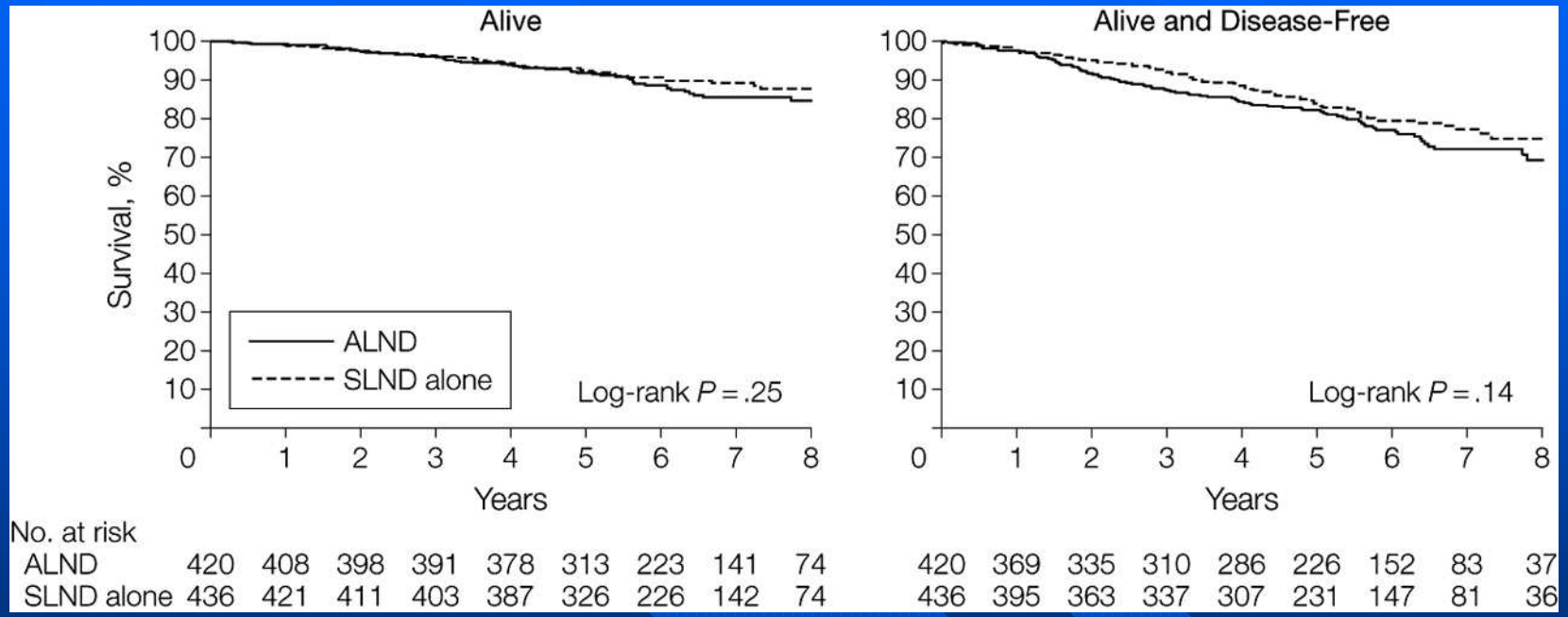
Characteristic	No. (%) ALND (n = 420)	No. (%) SLND Alone (n = 436)
Age, median (range), y	56 (24-92)	54 (25-90)
Missing	7	10
Clinical T stage		
T1	284 (67.9)	303 (70.6)
T2	134 (32.1)	126 (29.4)
Missing	2	7
Tumor size, median (range), cm	1.7 (0.4-7.0)	1.6 (0.0-5.0)
Missing	6	14
Receptor status		
ER+/PR+	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
Modified Bloom-Richardson score		
1	71 (22.0)	81 (25.6)
2	158 (48.9)	146 (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
Lymph node metastases		
0	4 (1.2)	29 (7.0)
1	199 (58.0)	295 (71.1)
2	68 (19.8)	76 (18.3)
3	25 (7.3)	11 (2.7)
≥4	47 (13.7)	4 (1.0)
Missing	77	21

ACOSOG Z0011- Axillary Dissection vs. No Axillary Dissection in Women With Sentinel Node Metastasis

- Results:
- Median follow-up 6.3 years.
- 5 year survival 92%
- rate of wound infections, axillary seromas, and paresthesias for ALND vs. SLND: 70% vs. 25%, $P < .001$
- Lymphedema in the ALND group was significantly more common by subjective report ($P < .001$).

Guilliano et al, JAMA 2011

ACOSOG Z0011- Axillary Dissection vs No Axillary Dissection in Women With Sentinel Node Metastasis



Survival of the ALND Group Compared With SLND-Alone Group

- Median follow-up 6.3 years.
- 5 year survival 92%

Guilliano et al, JAMA 2011

Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis

A Randomized Clinical Trial

- Partial recruitment (intended 1900 vs. 891)
- Mostly T1 (intended: T1 and T2)
- Mostly ER positive
- All patients radiated Tangent
- All patients received Chemo
- Most of the patients SLN metastasis after first surgery
- Short follow up

Prediction of Non-SLN Metastasis With MSKCC Nomogram

	Actual Study Data	Virtual patients	
Pathologic size	1.7	3.7	3.7
Estrogen receptor status	+	-	-
Methods of detection	H&E	FS	FS
Number of positive SLNs	1	2	2
Number of negative SLNs	1	0	0
Tumor type and nuclear grade	Ductal II	Lobular	Ductal II
Lymphovascular invasion	no	yes	no
Calculated percentage	12%	72%	64%

Completion Axillary Dissection

- St Gallen consensus meeting 2011

- Axillary lymph node dissection is recommended if Sentinel Node is positive

- No Axillary lymph node dissection is recommended if Sentinel Node is positive:
  - for isolated tumor cells only (less than 0.2 mm)
  - for micrometastasis (0.2-2mm)

Completion Axillary Dissection

- MD Anderson implementation of Z0011 Data
- No Axillary lymph node dissection is recommended if Sentinel Node is positive:
  - for isolated tumor cells only (less than 0.2 mm)
  - for micrometastasis (0.2-2mm)
  - For 1-2 lymph nodes ER +,PR+ patients but add radiation to the axilla

- Axillary lymph node dissection is recommended if Sentinel Node is positive for
  - Lobular carcinoma
  - ER-,PR- or HER-2 +
  - Post Mastectomy
  - Post Neoadjuvant
- Caution :young age, nodular ratio.

DCIS (Ductal Carcinoma In Situ)

- Most common presentation:
  Clustered microcalcifications
- Mass
- Pathologic nipple discharge
- Incidental findings
- Proliferation of malignant epithelial cells within the mammary ductal lobular system without light microscopy invasion into the surrounding stroma.

  10946 DCIS pts.
- 406 - 3.6% Axillary metastasis

SENTINEL NODE BIOPSY IN BREAST CANCER

DCIS

74 patients (DCIS/DCIS+microinvasion <1mm)

	n	Pos. SLN	Pos. IHC
High-risk DCIS	38	5/38 (13%)	4/5
DCIS with microinvasion	36	5/36 (14%)	5/5

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7 complete axillary lymph node dissection, 1 non-SLN (+)

(High risk = high grade, large tumor palpable, multifocality)

Klauber-DeMore et al. MSKCC, SSO 2000

SENTINEL NODE BIOPSY IN BREAST CANCER

38 pts. with DCIS or with microinvasion

Indications:

1. patient requiring mastectomy 52.6% (n=20)
2. extensive multifocal/multicentric disease 23.6% (n=9)
3. pathology suspicious for microinvasion 10.5% (n=4)
4. presence of microinvasion 7.8% (n=3)
5. mammogram/sonogram suspicious for invasion 2.6% (n=1)
6. low grade lesion >=3cm 2.6% (n=1)

4/38 (10.5%) SLN positive in categories 1,2,3 and 5

Hoover et al. Abs. P78, SSO 2002

SENTINEL NODE BIOPSY for DCIS

PRO

- Mastectomy:
  - Not to lose opportunity if invasive carcinoma is ultimately discovered in their mastectomy specimen.
  - Only a small volume of breast tissue is usually being evaluated
  - Positive SLN can surrogate for invasion.

SENTINEL NODE BIOPSY for DCIS

PRO

- Prevent second operation
  - Palpable DCIS
  - Radiographic involvement more than 4 cm.
  - High nuclear grade
  - Questionable areas of micro invasion.

SENTINEL NODE BIOPSY for DCIS

CON

Surgeon is not a Barber

- Only 1-2% DCIS die of breast cancer ,die of missed Ca in tissue removed.
- 3% micro metastasis, clinical significance?
- 20-25% will have invasive component, unnecessary operation in 75-80%

SENTINEL NODE BIOPSY for DCIS

While DCIS remains a disease without metastatic potential its association and coexistence with invasive carcinoma require a selective approach to staging


Thank you!
Todah!
Merci!
Thank you!
GRACIAS!
ThAnK YoU!
Thank you!


THANK YOU

Reference		Patients(n)	ROC	Correlation(r)
Van Zee et al., USA, 2003		373	0.77	0.97
Kocsis et al., Hungary, 2004		140	0.73§	0.84
Smidt et al., The Netherlands, 2005		222	0.77	~1
Degnim et al., USA, 2005	Mayo Clinic	462	0.72	N/A
	Michigan	89	0.86	N/A
Soni et al., Australia, 2005		149	0.75	N/A
Lambert et al., USA	2006- Full database	200	0.71	0.97
	2007- excluding neoadjuvant patients and incomplete data	141	0.69	0.92
Ponzone et al., Italy, 2006		186	0.71	N/A
Cripe et al., USA, 2006		92	0.82	0.86
Dauphine et al., USA, 2006		39	0.63	N/A
Zgajnar et al., Slovenia, 2007		276	0.72	N/A*
Alran et al., France, 2007		588	0.72	N/A
Pal et al., UK, 2007		118	0.68	N/A
Klar et al., Germany, 2007		98	0.58	N/A

* The nomogram was biased.

§ Published later by Cserni G, Am J Surg 2007

Completion Axillary Dissection Following Positive Sentinel Node Biopsy

MULTICENTER STUDIES

AMAROS: After Mapping of the Axilla: Radiotherapy or Surgery

10981 EORTC

All patients SLND

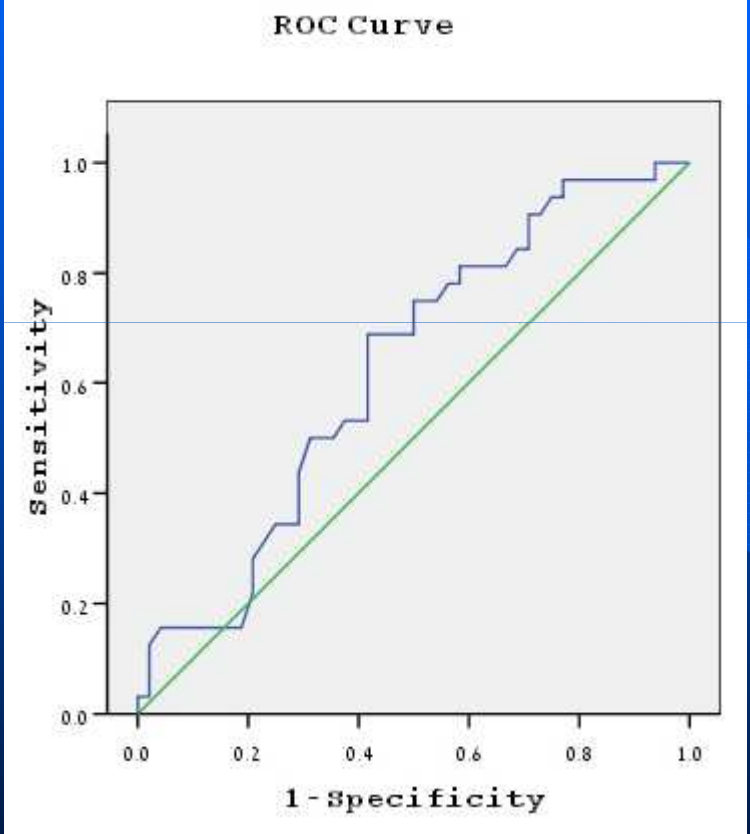
If positive: randomization to surgical treatment vs. radiation therapy

Aim: Importance of CLND vs. Radiation treatment

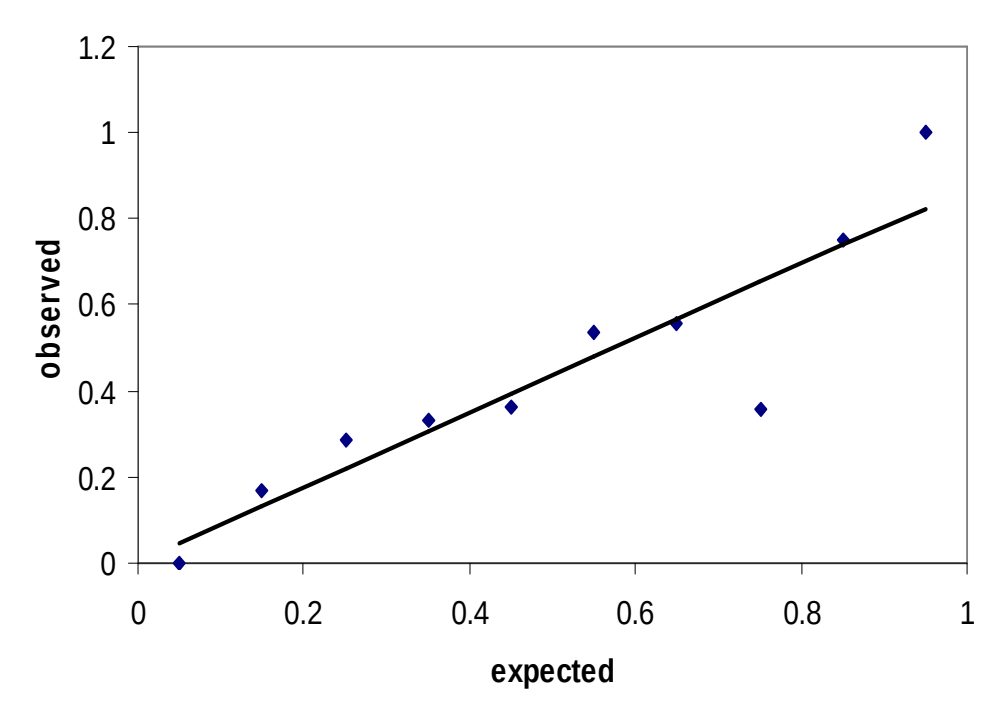
Conclusion – cont.

- Institutional variation in SLN biopsy technique and pathological processing might be responsible for wide range of results.
- Lack of pathological data for Neo-Adj patients impairing the nomogram's prediction ability.
- Cancer centers should test the performance of the MSKCC nomogram on their own population prior to introducing it into clinical use.

ROC curve and calibration plot: The entire population

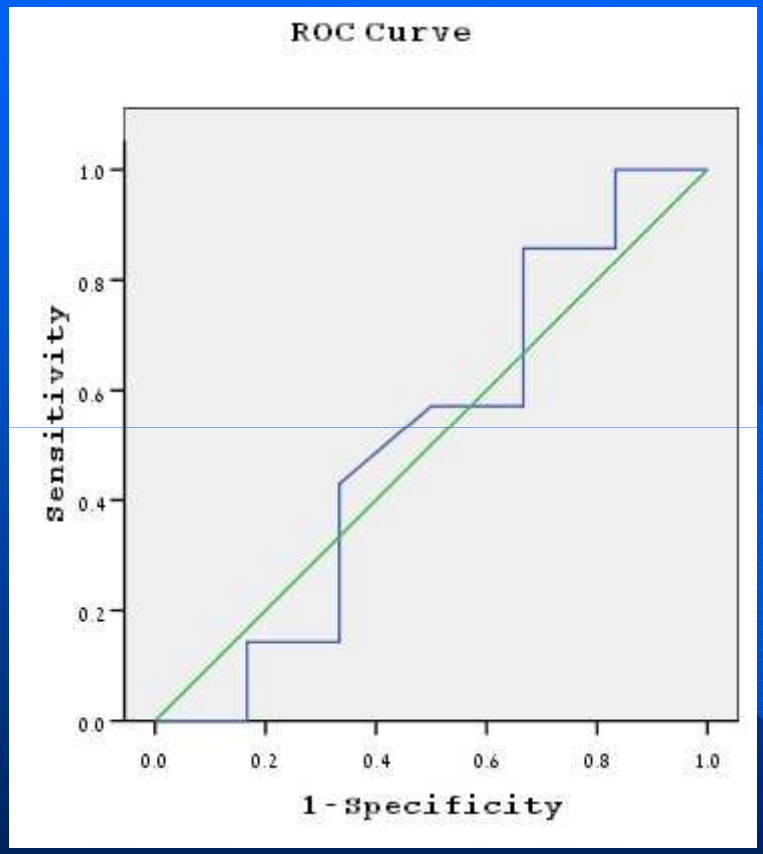


AUC=0.63



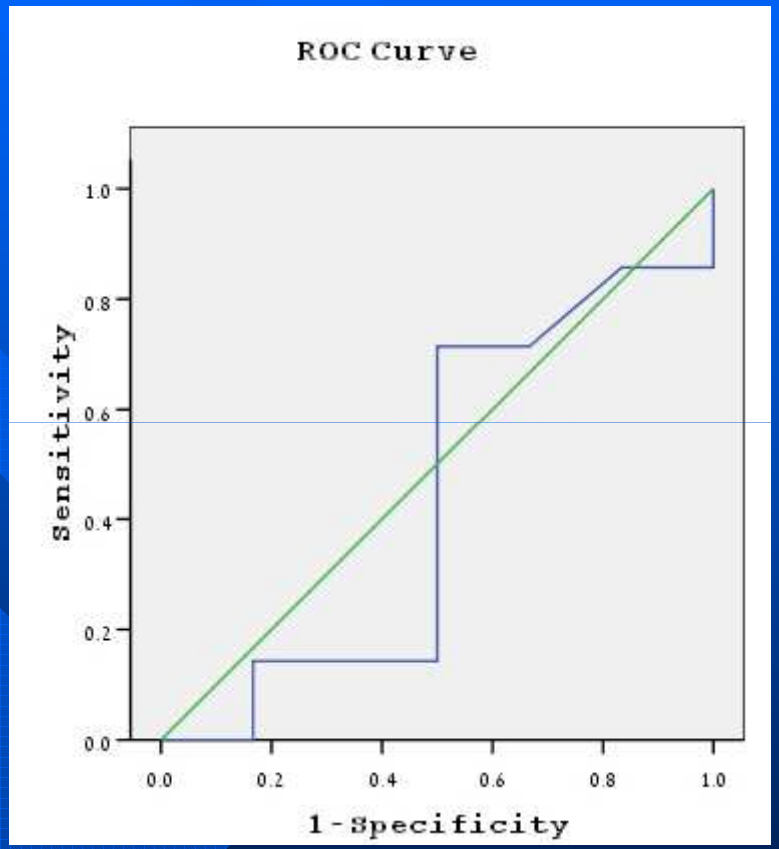
R=0.87

ROC curve for Neo-Adj group



Based on imaging tumor size

AUC=0.51



Based on pathological tumor size

AUC=0.44

Randomized Trial Comparing Axillary Clearance Versus No Axillary Clearance in Older Patients With Breast Cancer: First Results of International Breast Cancer Study Group Trial 10-93

- 1993-2002
- 473 patients age 60 years +, T1-3, clinically node negative
- Randomized to breast surgery with +/- axillary dissection (from 1999 also sentinel node)
- All received adjuvant tamoxifen for 5 years (from 2002 only those with ER+).
- Outcomes: quality of life, disease-free survival, overall survival
- 1,020 patients needed to assess no difference in survival
- In 2000 redesign (430 patients accrued)- difference in quality of life.

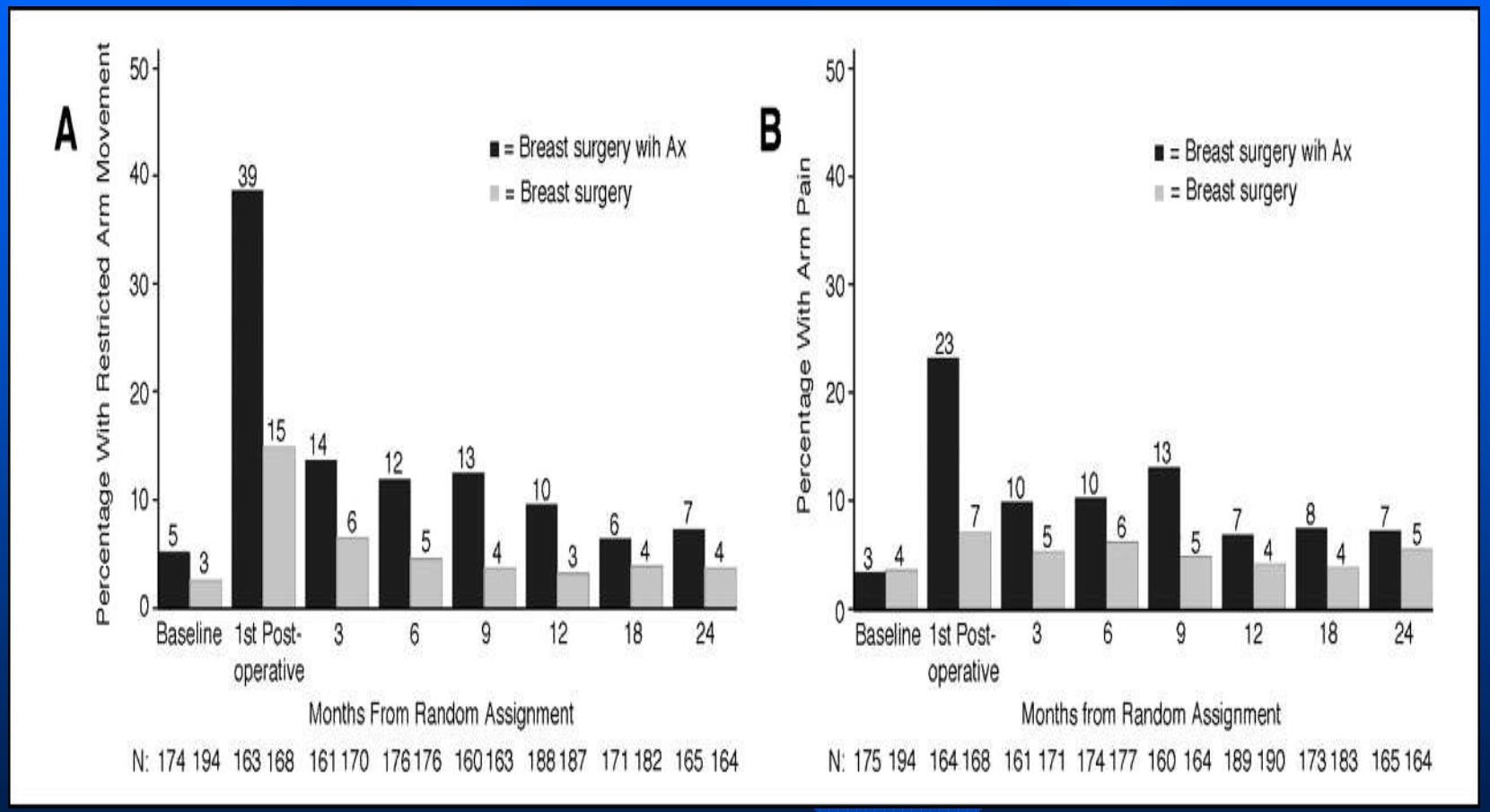
International Breast Cancer Study Group, JCO 2006

Axillary Clearance in Older Patients With Breast Cancer: First Results of International Breast Cancer Study Group Trial 10-93

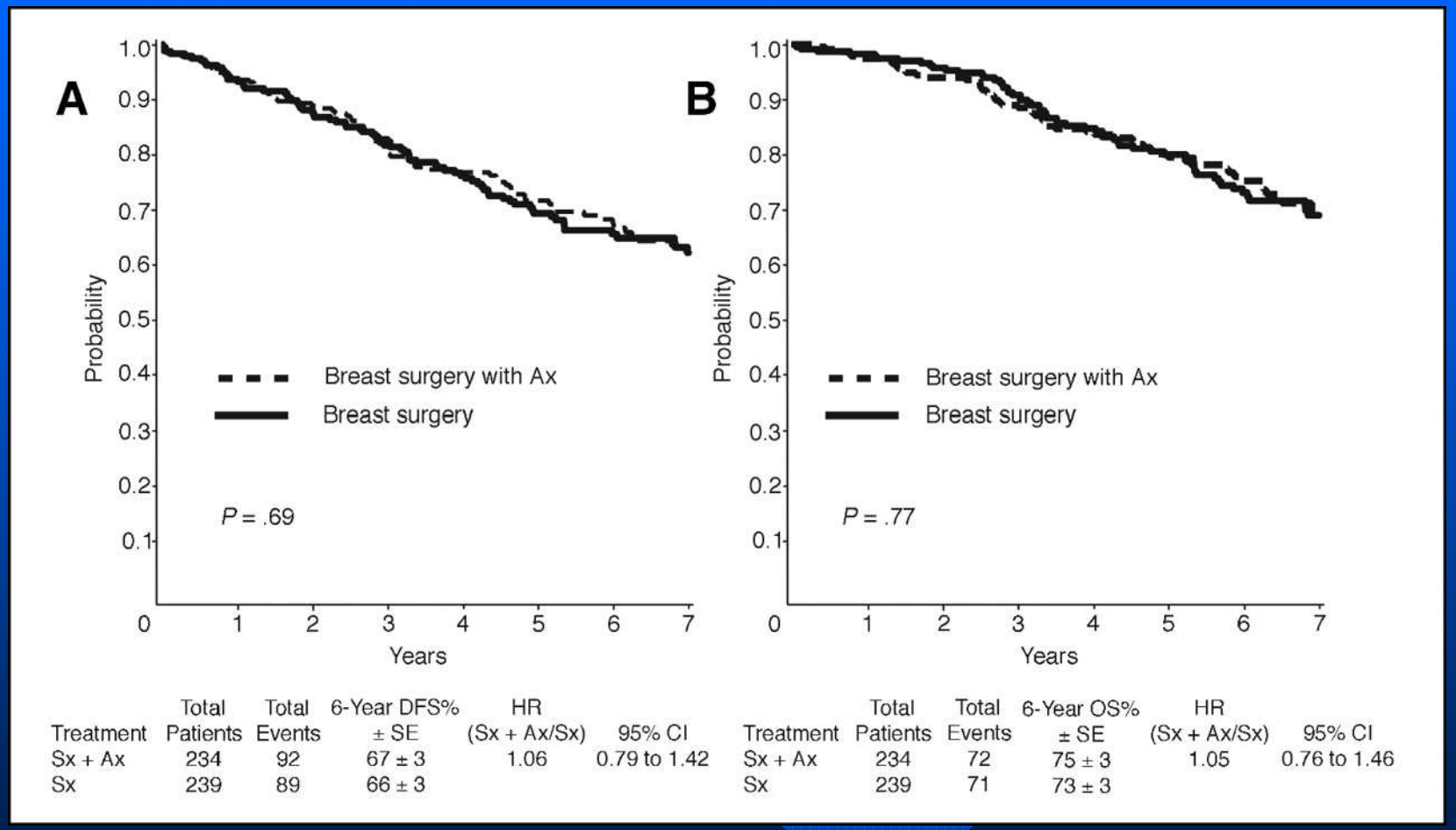
- Median age 74
- 80% ER+ disease.
- 28% node positive (ALND group)

International Breast Cancer Study Group, JCO 2006

Randomized Trial Comparing Axillary Clearance Versus No Axillary Clearance in Older Patients With Breast Cancer: First Results of International Breast Cancer Study Group Trial 10-93



International Breast Cancer Study Group, JCO 2006



Treatment	Total Patients	Total Events	6-Year DFS% ± SE	HR (Sx + Ax/Sx)	95% CI
Sx + Ax	234	92	67 ± 3	1.06	0.79 to 1.42
Sx	239	89	66 ± 3		

Treatment	Total Patients	Total Events	6-Year OS% ± SE	HR (Sx + Ax/Sx)	95% CI
Sx + Ax	234	72	75 ± 3	1.05	0.76 to 1.46
Sx	239	71	73 ± 3		

International Breast Cancer Study Group, JCO 2006

Randomized Trial Comparing Axillary Clearance Versus No Axillary Clearance in Older Patients With Breast Cancer: First Results of International Breast Cancer Study Group Trial 10-93

Conclusions:

- avoiding axillary clearance for older women with clinically node-negative breast cancer who receive adjuvant tamoxifen seems safe and results in early improved quality of life.

International Breast Cancer Study Group, JCO 2006

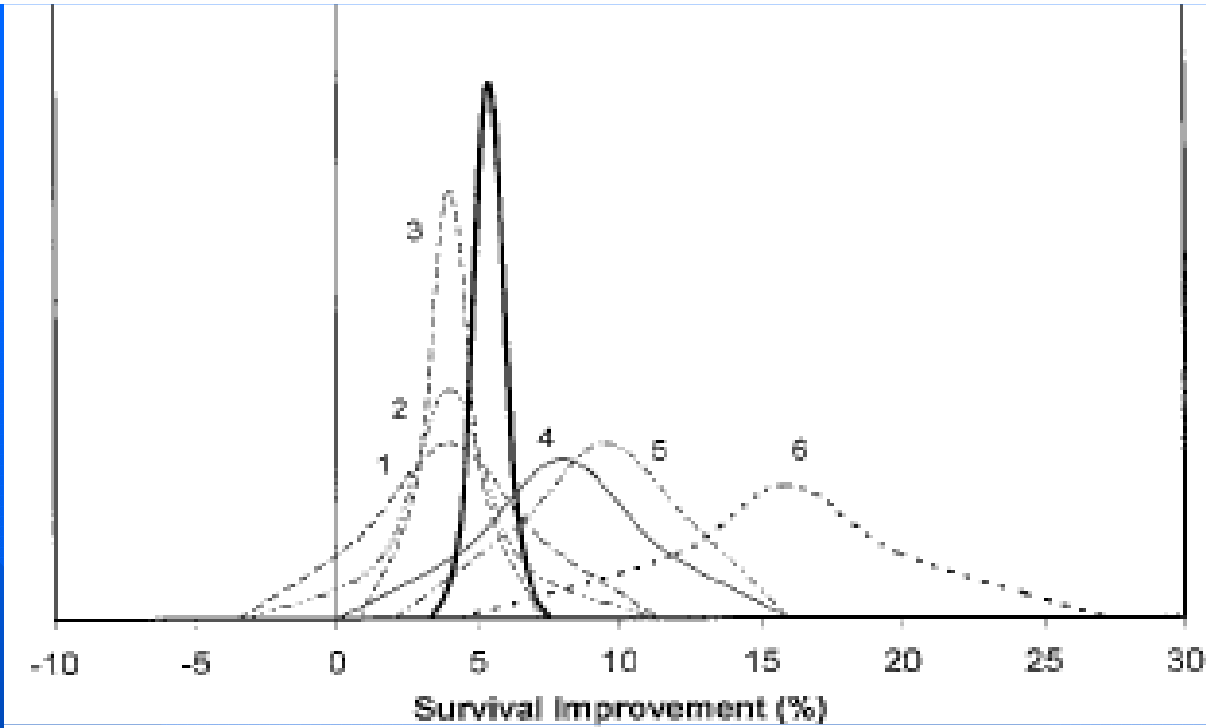


FIG. 2. Bayesian analysis of survival benefit. Black line: results of meta-analysis. Numbers 1-6, individual studies. *1*, Copenhagen; *2*, B-04; *3*, Curie; *4*, Guy's I; *5*, SouthEast Scotland; *6*, Guy's 2.

TABLE 3. *Stage I patients*

Trial	No. patients	% Survival		% Difference	% Reduction	*P* Value
		Control	Treated			
Copenhagen	290	54	59	5	10.9	NS
Guy's I	220	52	58	6	12.5	NS
SES	275	53	71	18	38.3	<.01
B-04	727	54	58	4	8.7	NS
Guy's II	258	57	73	16	37.2	.01
Curie	658	92.6	96.6	4	45.9	.03

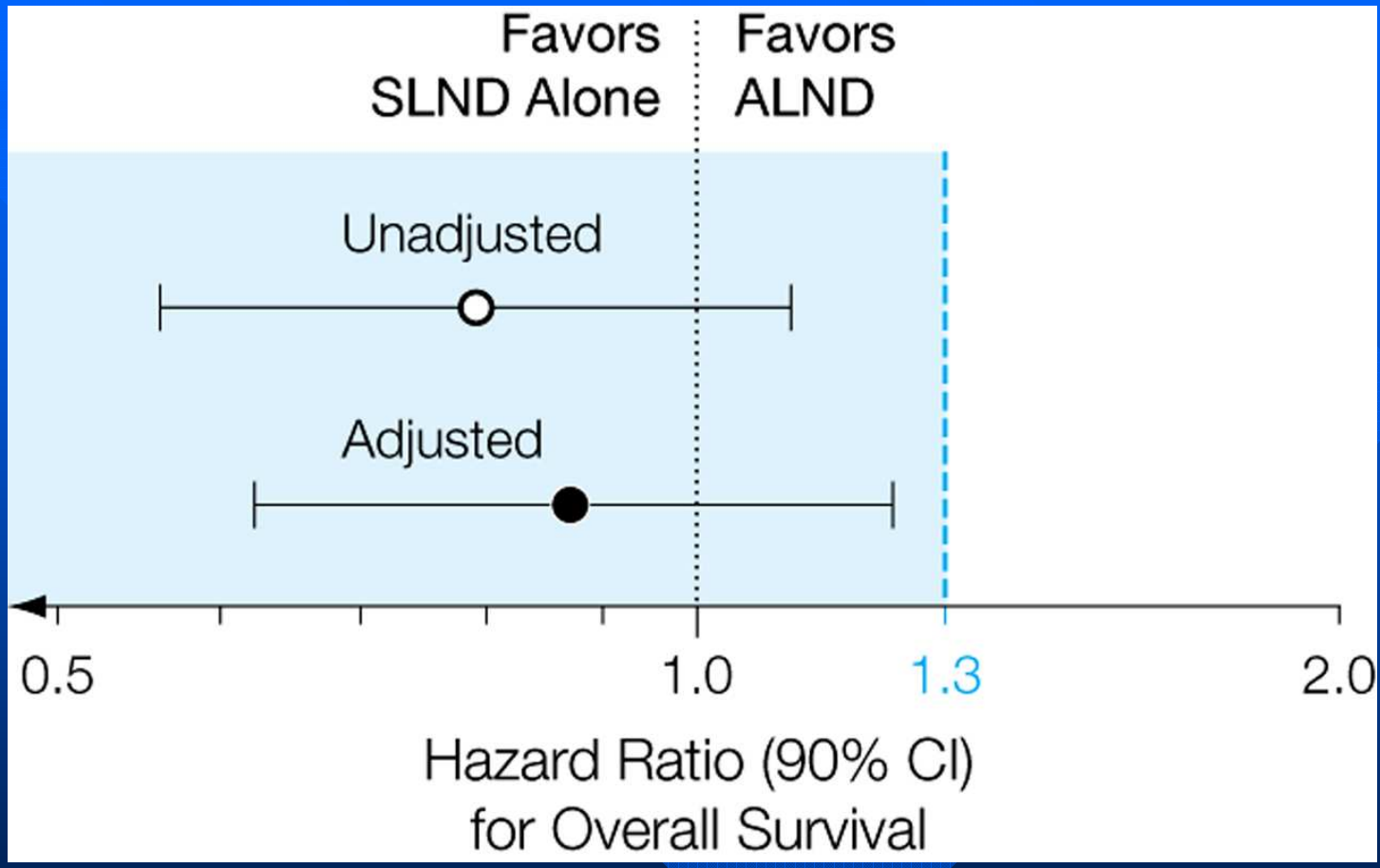
NS, not significant.

ACOSOG Z0011- Axillary Dissection vs. No Axillary Dissection in Women With Sentinel Node Metastasis

- Groups were similar in baseline characteristics
- More nodes removed in the axillary dissection group (median 17 vs. 2)
- Micrometastatic disease (N1mic<2mm) was identified in 45% of SLNB and 38% of ALND (p=0.5)
- Additional metastatic nodes: 27% of patients in the ALND group.
- Patients with micrometastatic disease- 10% had additional disease.
- Similar rates of adjuvant chemotherapy and radiation treatment (whole breast including low axilla).

Guilliano et al, JAMA 2011

ACOSOG Z0011- Axillary Dissection vs. No Axillary Dissection in Women With Sentinel Node Metastasis.



Hazard Ratios Comparing Overall Survival Between the ALND and SLND-Alone Groups

Guilliano et al, JAMA 2011

Trends in and outcomes from sentinel lymph node biopsy (SLNB) alone vs. SLNB with axillary lymph node dissection for node-positive breast cancer patients: experience from the SEER database

- worse disease specific survival for Same overall survival
- patients undergoing ALND-
- Better loco-regional control in patients with macrometastatic disease who had ALND (0.08 vs. 0.2%; HR, 0.30; *P* = 0.02).

Yi et al, JCO 2010

NSABP B-32 randomized phase 3 trial

Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial

David N Krag, Stewart J Anderson, Thomas B Julian, Ann M Brown, Seth P Harlow, Joseph P Costantino, Takamaru Ashikaga, Donald L Weaver,

Eleftherios P Mamounas, Lynne M Jalovec, Thomas G Frazier, Robidoux, Hugh M C Scarth, Norman 'R Dirk Noyes, Andr Wolmark

NSABP B-32 randomized phase 3 trial

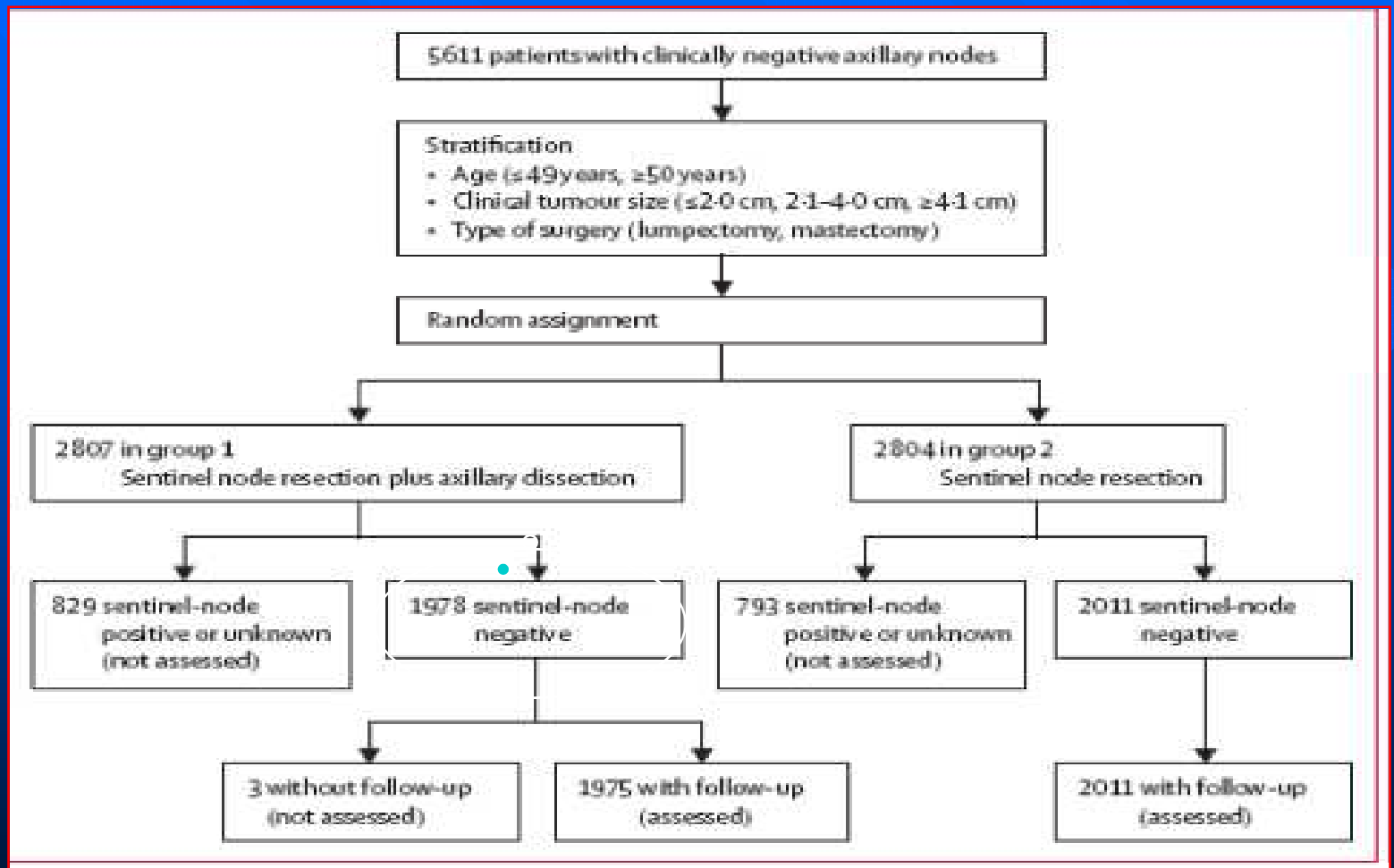


Figure 1: NSABP B-32 trial profile
Group 2 patients in whom a sentinel lymph node (SLN) was not identified received an axillary-lymph-node dissection (ALND).

NSABP B-32 randomized phase 3 trial

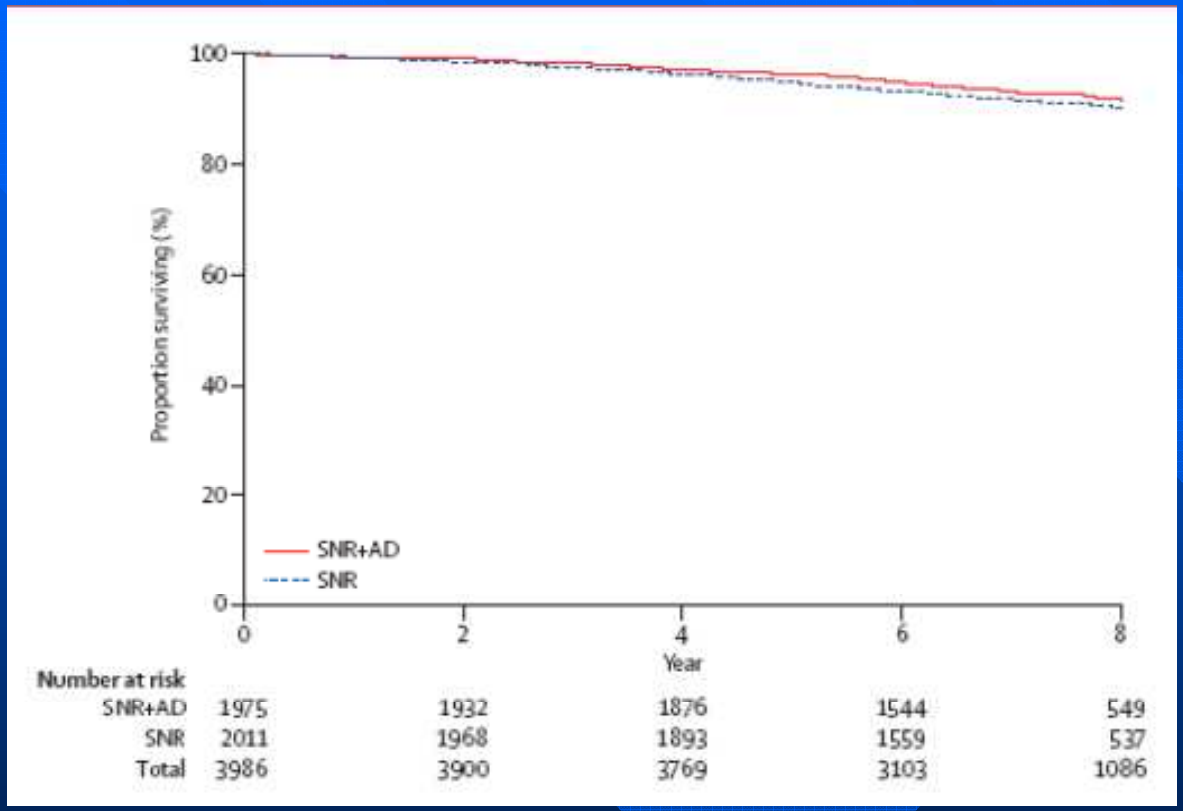


Figure 2: Overall survival for sentinel-node (SLN)-negative patients
Data as of Dec 31, 2009. For sentinal node resection (SNR) plus axillary dissection (AD), N=1975, 140 deaths. For SNR, N=2011, 169 deaths. Hazard ratio 1·20, 95% CI 0·96–1·50; p=0·12.

Univariate Analysis

Parameter	P
Number of positive SLN excised	**0.04**
Number of total SLN excised	**0.04**
Tumor size	*0.06*
Tumor grade	*0.07*
Tumor type	0.16
ER Status	0.27
Neo-Adjuvant treatment	0.27
Lympho-vascular invasion	0.36
PR Status	0.44
Number of negative SLN excised	0.58
Her-2 Status	0.59
Pathological detection method	0.6
Multifocality	0.62
Age	0.67

NSABP B-32 randomized phase 3 trial

	Group 1 (n=1975)	Group 2 (N=2011)
Type of failure		
Local recurrence	54 (2·7%)	49 (2·4%)
Regional node recurrence	8 (0·4%)	14 (0·7%)
Distant metastasis	55 (2·8%)	64 (3·2%)
Opposite breast	56 (2·8%)	44 (2·2%)
Second non-breast cancer	89 (4·5%)	109 (5·4%)
Dead, no evidence of disease	53 (2·7%)	56 (2·8%)
Total first events	315 (15·9%)	336 (16·7%)
Alive, event free	1660 (84·1%)	1675 (83·3%)

Data are number (%).

Table 2: First reported site of treatment failure for sentinel-node (SLN)-negative patients

Completion Axillary Dissection Following Positive Sentinel Node Biopsy

RESTROSPECTIVE STUDIES

Predictors of positive non-SLN

- Stage of primary tumor, SLN metastases size (micro vs. macro), lymphovascular invasion (1)
- Tumor size >1cm, SLN metastases size, extranodal extension, apex L.N. involvement (2)
- SLN metastases size (3)
- Primary tumor size, SLN metastases size, lymphovascular invasion (4)

Conclusion: Pts. With T1a-T1b or G1 tumor should be spared ALND. (4)

1. Weiser et al, SSO 2000
2. Kuijit GP et al. EJSO 2006
3. Fan YG et al. Ann Oncol Surg 2005
4. Gipponi M. et al. EJSO 2006

Completion Axillary Dissection Following Positive Sentinel Node Biopsy

Conclusion

No subgroup could be identified in which axillary dissection may be omitted

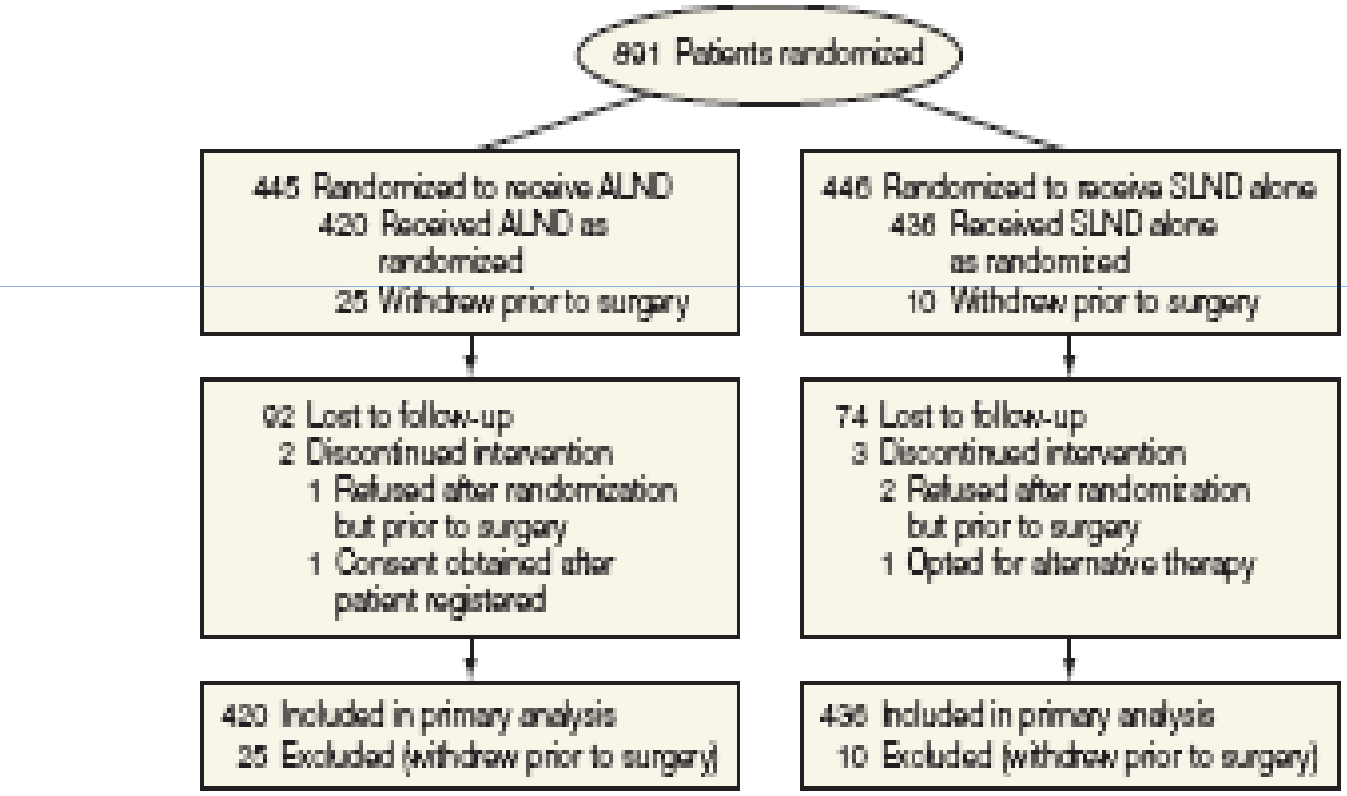
Usually associated with only one axillary L.N. are:

- Tumor size < 1 cm
- Micrometastasis
- No extranodal extension

Kuijit GP et al. EJSO 2006

Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis

A Randomized Clinical Trial



ALND indicates axillary lymph node dissection; SLND, sentinel lymph node dissection.

ACOSOG Z0011- Axillary Dissection vs. No Axillary Dissection in Women With Sentinel Node Metastasis

- Patients with limited metastatic disease in the axilla (stage 2) have very good 5 year survival.

- Limited disease- high rate of micrometastatic disease (only 27% had additional metastatic lymph nodes).
- 2/3 of the patients were randomized after final pathology documented a positive sentinel node.
- Limited follow-up (6.3 years).
- The Z0011 trial did not include patients undergoing mastectomy, lumpectomy without radiotherapy, partial-breast irradiation, neoadjuvant therapy
- 67 and 69% were ER+- Can conclusions be drawn for different subtypes of breast cancer (Her2n+, triple negative?)

Guilliano et al, JAMA 2011

SENTINEL NODE BIOPSY IN BREAST CANCER

NASBP B 04 STUDY

MODIFIED RADICAL MASTECTOMY (MRM)

vs. TOTAL MASTECTOMY (TM)

MRM 38% AXILLARY METASTASIS

TM ONLY 18% REQUIRED AXILLARY DISSECTION

AT 10 YEARS - SAME DFS; OVERALL SURVIVAL

Fisher B et al. NEJM 1988

The Impact of Prophylactic Axillary Node Dissection on Breast Cancer Survival—A Bayesian Meta-Analysis

Richard K. Orr, MD, MPH

TABLE 1. *Baseline characteristics of included trials*

Trial	Years	No. patients	Age (y)	Pre (%)*	Stage I (%)	Size	% T1	% N+
Copenhagen	1951–1957	425	–	–	68	–	–	–
Guy's I	1961–1971	370	61	9	60	3.5	17	54
SES	1964–1971	498	55	69	55	3.7	–	41
B-04	1971–1974	727	56	28	100	3.2	–	39
Guy's II	1971–1975	258	–	–	100	–	38	31
Curie	1982–1987	658	51	60	100	1.5	67	18

* Percentage of premenopausal women in the trial.
N+, node-positive.

Orr RK, Ann Surg Oncol, 1999

Impact of prophylactic axillary dissection on breast cancer survival-metanalysis

TABLE 2. *Uncorrected survival*

Trial	No. patients	Follow-up (y)	% Survival		% Difference	% Reduction	*P* Value
			Control	Treated			
Copenhagen	425	10	46	50	4	7.4	NS
Guy's I	370	10	43.6	51.6	8	14.2	NS
SES	498	10	51.5	61	9.5	19.6	.04
B-04	727	10	54	58	4	8.7	NS
Guy's II	258	10	57	73	16	37.2	.01
Curie	658	5	92.6	96.6	4	45.9	.03

NS, not significant.

axillary dissection confers a survival advantage of 5.4%;(95% CI 5 2.8-8.1),

Orr RK, Ann Surg Oncol, 1999

Impact of prophylactic axillary dissection on breast cancer survival-metanalysis

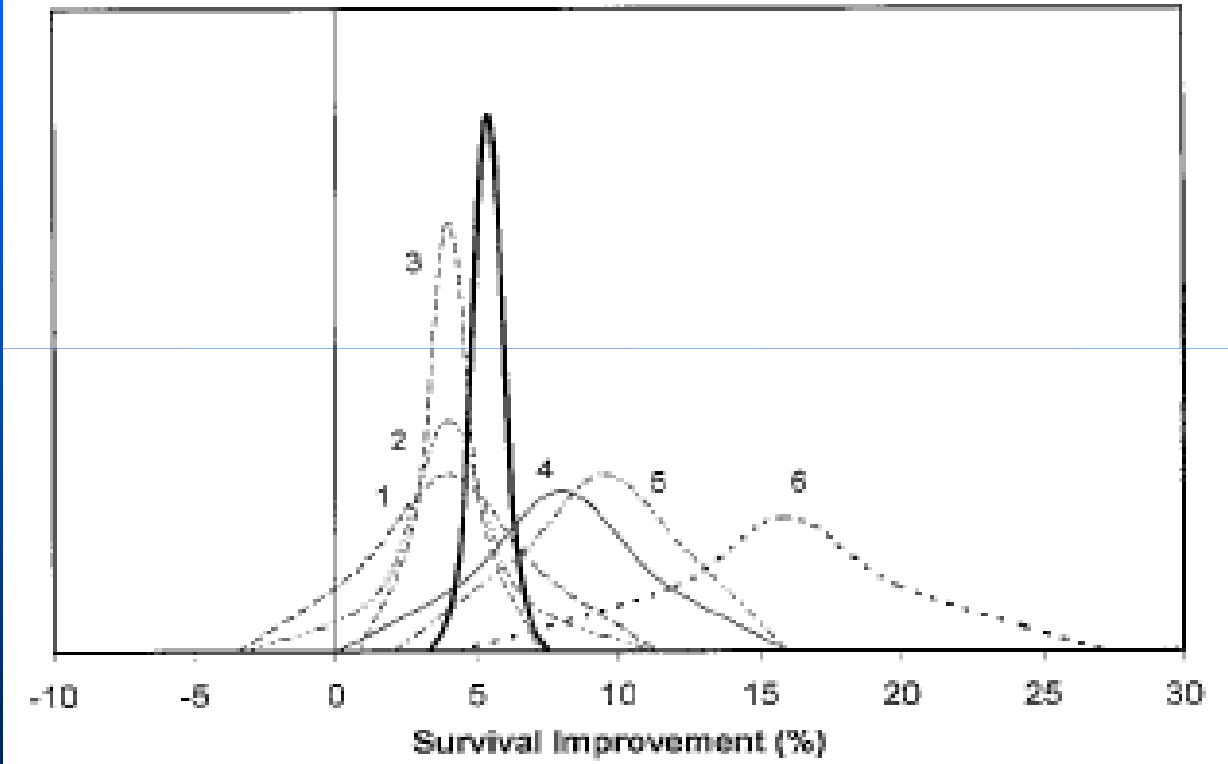


FIG. 2. Bayesian analysis of survival benefit. Black line: results of meta-analysis. Numbers 1-6, individual studies. *1*, Copenhagen; *2*, B-04; *3*, Curie; *4*, Guy's I; *5*, SouthEast Scotland; *6*, Guy's 2.

Editorial

A Survival Benefit From Axillary Dissection: Was Halsted Correct?

Monica Morrow, MD

However, axillary dissection in this group is worthwhile to maintain local control. It is the patient with a more limited regional tumor burden—1 to 3 positive nodes and a small primary tumor—in whom locoregional therapy has the greatest likelihood of improving survival. Sentinel node biopsy, by allowing the reliable identification of nodal metastases, eliminates axillary dissection for patients who will not benefit because of the absence of metastases. For the patient with metastases to the sentinel node, dissection of the remaining nodes remains standard practice, even if the patient has been staged as needing

survival benefit for axillary dissection. However, other data validate the underlying assumption that local therapy does affect the natural history of some breast cancers. If all breast cancers were systemic from the time they became clinically recognizable, screening mammography should have no effect on survival, yet studies clearly demonstrate a 30% reduction in mortality in women aged 50 and older who are screened. The recent

women aged 50 and older who are screened. The recent Danish[6] and British Columbia trials,[7] in which postmastectomy radiotherapy was given to the chest wall, axilla, internal mammary node fields, and supraclavicular node fields of patients with axillary metastases demonstrate a survival benefit when compared to treatment with mastectomy alone. In addition, studies of the long-term outcome of patients with small breast cancers metastatic to 1 to 3 axillary nodes demonstrate that two-thirds of these patients survive after locoregional therapy alone.[8] What

Editorial

A Survival Benefit From Axillary Dissection: Was Halsted Correct?

Monica Morrow, MD

Prediction of Non-SLN Metastasis With MSKCC Nomogram

- Nomogram was examined by Receiver Operating Curve (ROC)
  - The inherent capacity of a test to discriminate a diseased from a nondiseased subject across all possible levels of positivity
  - Area under the ROC:
    - » 0.5 flipping a coin 1.0 perfect test
- 702 patients who underwent complete ALND
  - Area under ROC curve 0.76
- 373 patients prospective group
  - Area under ROC curve 0.77

Van Zee KZ et al. Ann Surg Oncol. 2003

Prediction of Non-SLN Metastasis With MSKCC Nomogram

site	Nijmegen, Netherlands	Bacs-Kiskum County Teaching Hospital, Hungary	Texas M.D. Anderson Cancer Center
No of patients	696		
Positive SLN with completion ALND	229	140	200
Intraopertative method	Frozen section	Touch imprint cytology	Touch imprint cytology
Results : ROC Correlation Obs. to Pred.	0.76	0.84	0.74 0.97
Conclusions:	Nomogram is valid for populations that differ considerably from the population from which it was developed.	Nomogram could not be validated Authors warn against the unvalidated use	Nomogram also accurate for TIC

Prediction of Non-SLN Metastasis With MSKCC Nomogram

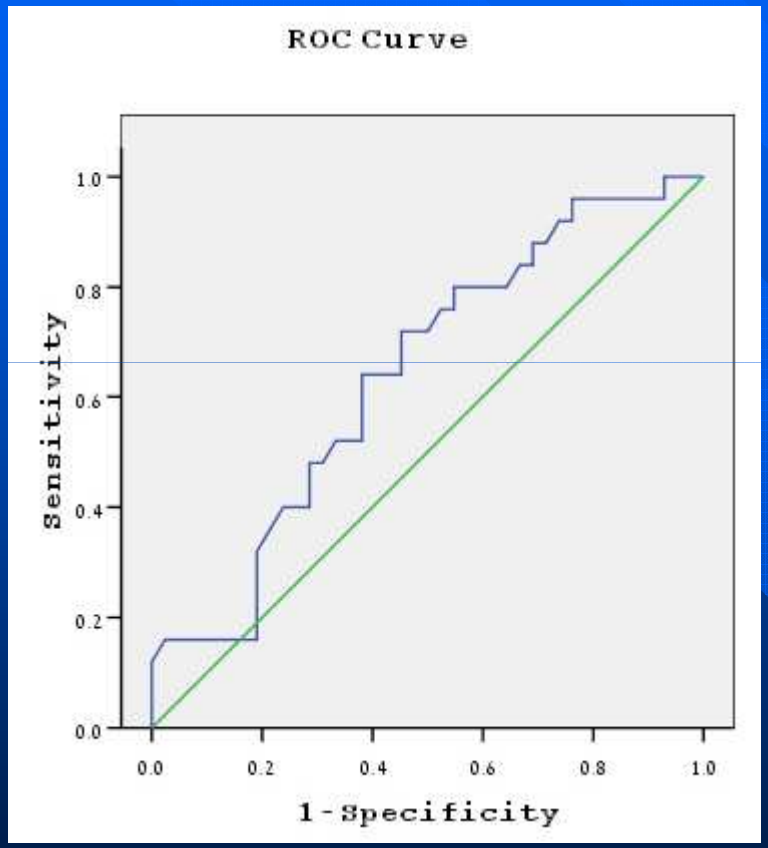
Possible explanation to Bacs-Kiskum results discrepancy

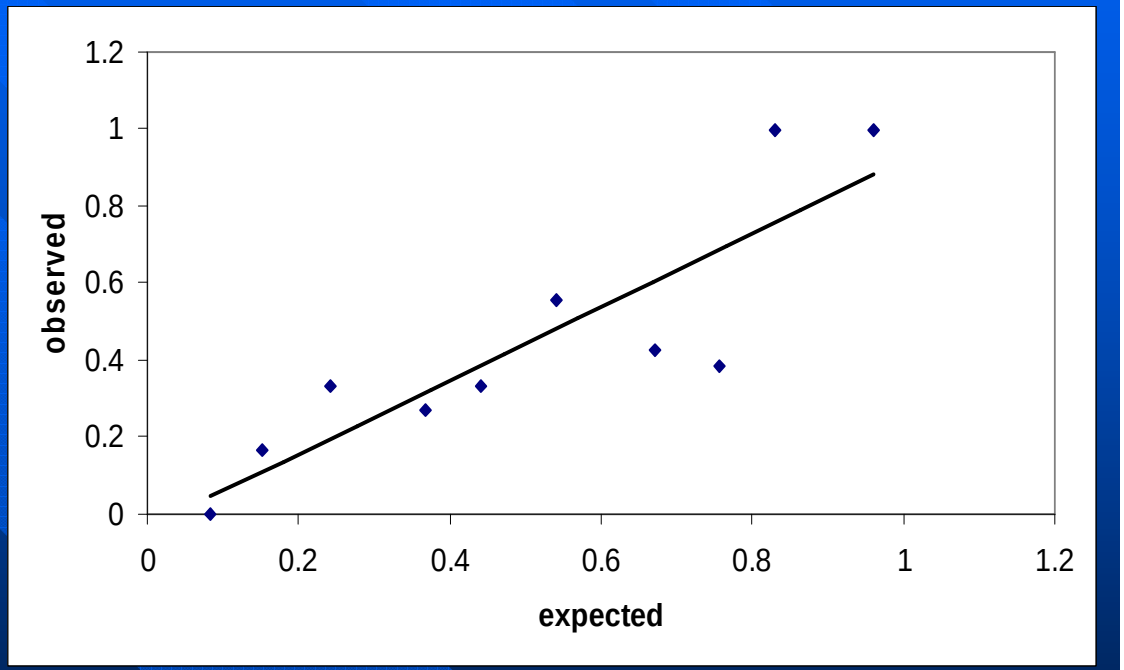
- Number of SLN removed:
  - Removal of maximum 3 (B.K.)
  - Removal of all blue and hot (MSKCC)
  - B.K. – mean 1.3–1.4 SLNs and median 1 SLN
  - MSKCC – mean 2.7 SLNs and median 2 SLNs

Studies show that in 98% of positive SLN the positive node is in the first three nodes. Therefore fewer nodes removed would imply higher number of non SLN positive.

Lampert LA et al. Ann Surg Oncol. 2006

ROC Curve and Calibration plot: Excluding Neo-Adj Patients





AUC=0.64

R=0.96

SENTINEL NODE BIOPSY for DCIS

CON

Surgeon is not a Barber

- Age 55 or younger O.R. 2.19 P=0.024
- Core needle biopsy O.R. 3.76 P= 0.006
- Size DCIS greater than 4 cm
  O.R. 2.92 P= 0.001
- High grade O.R. 3.06 P= 0.002

NOT to PERFORM just because we can

SENTINEL NODE BIOPSY for DCIS

PRO

- Image guided core needle biopsy
  - Identify benign
  - Maybe upstaged
- Prevent second operation
  - Palpable DCIS
  - Radiographic involvement more than 4 cm.
  - High nuclear grade
  - Questionable areas of micro invasion.