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Global Breast Cancer Conference 2011

October 6 ~ 8, 2010 Sheraton Grande Walkerhill Seoul, Korea

Recent Advance and Controversial Issues in Sentinel Node Biopsy

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TAIWAN

President, Taiwan Breast Cancer Society (2004~2007)

Controversial Issues

1). What are the indications of SLNB?

2). Should a complete axillary dissection be performed when the SLNB is positive?

3). Can lymphedema occur after SLNB?

4). What is the accuracy of SLNB in patients who have received neoadjuvant therapy prior to surgery?

5). Technical considerations about SLNB

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The indications of SLNB 2005 ASCO guideline

Indications

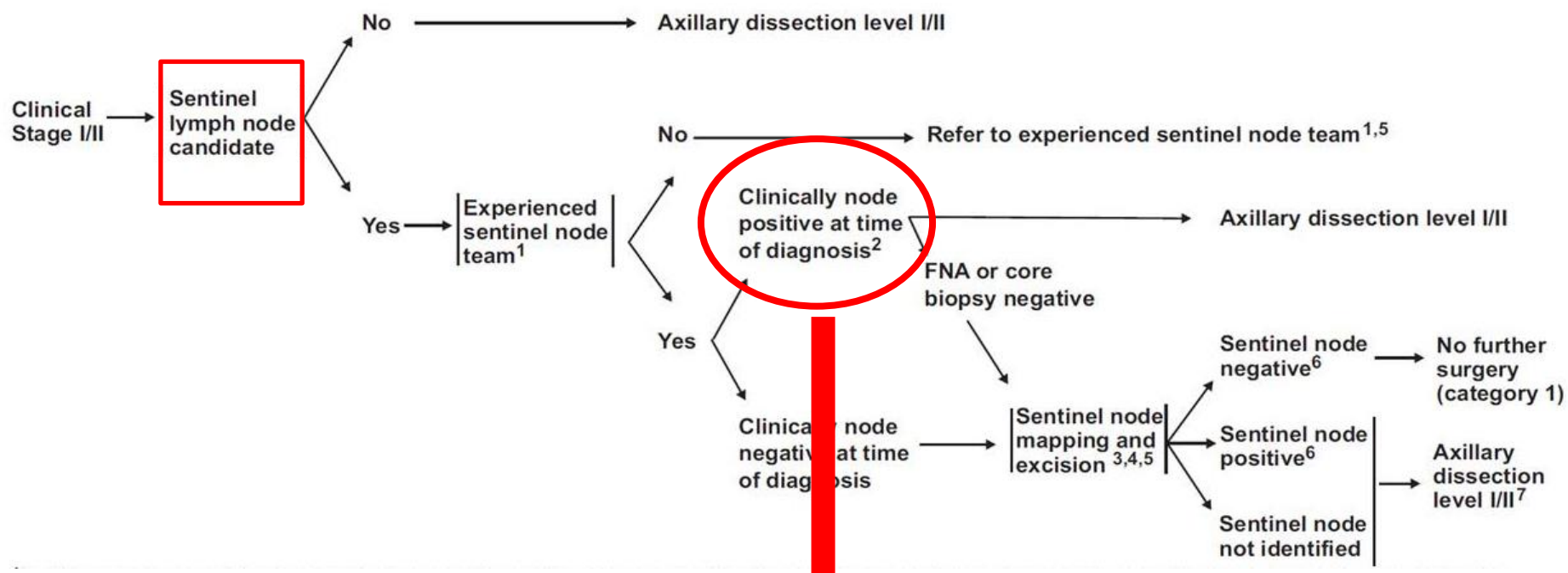
- T1 and T2 tumors
- The older age, obesity, and male breast cancer are acceptable
- DCIS with mastectomy
- The evaluation of internal mammary nodes(IMNs) by SLNB is acceptable

Contraindications

- **T3,T4 or inflammatory cancers.**
- **Previous axillary and breast surgery, neoadjuvant systemic and obvious palpable axillary nodes are considered relative contraindications.**
- **Pregnancy women due to lack of safety data.**

J Clin Oncol 23:7703-7720.2005

SURGICAL AXILLARY STAGING - STAGE I, IIA, AND IIB



Stage I, II

?

Patients with palpable axillary nodes Clinically palpable : Contraindication??

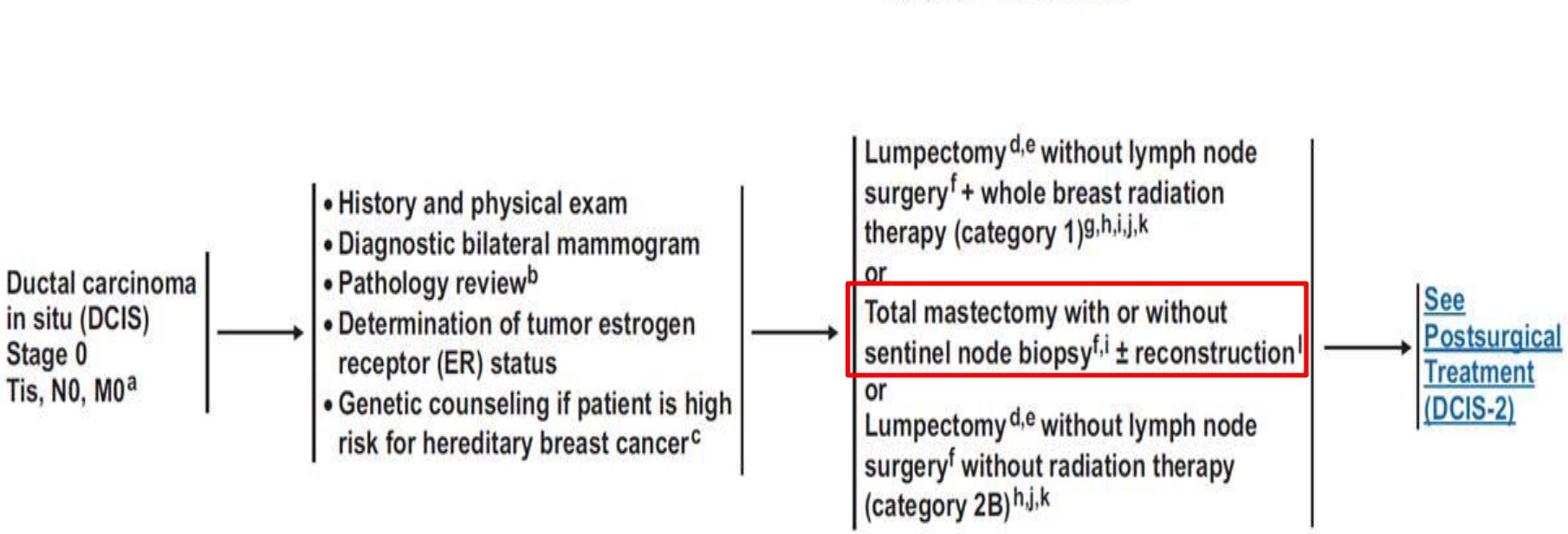
- **Positive predictive rates:64–82%, negative predictive rate: 50–63%, overall accuracies: 63–68%.**
- **2,027 SLNB procedures: two experienced surgeons, clinical examination of the axilla was inaccurate in 41% .**
- **No clinically significant difference in node size between normal and metastatic nodes, and the fact that subcentimeter lymph nodes can contain micrometastases**

Imaging guiding node diagnosis

- ***SLNB should not be performed if patients have histologically confirmed positive axillary nodal involvement.***

Cutler SJ, Surg Gynecol Obstet 1970;131:41–52.
Specht MC J Am Coll Surg 2005;200:10–4.
Lanng C. Eur J Surg Oncol 2007;33:281–4.
Eur J Nucl Med Mol Imaging (2011) 38:562–575

NCCN Guidelines™ Version 2.2011
Ductal Carcinoma in Situ



[a] See NCCN Breast Cancer Screening and Diagnosis Guidelines.

[b] The panel endorses the College of American Pathology Protocol for pathology reporting for all invasive and non-invasive carcinomas of the breast. http://www.cap.org

[c] See NCCN Genetic/Familial High-Risk Assessment: Breast and Ovarian Guidelines.

[d] Re-resection(s) may be performed in an effort to obtain negative margins in patients desiring breast conserving therapy. Patients not amenable to margin-free lumpectomy should have total mastectomy.

[e] See Margin Status in DCIS (DCIS-A).

[f] Complete axillary lymph node dissection should not be performed in the absence of evidence of invasive cancer or proven metastatic disease in women with apparent pure DCIS. However, a small proportion of patients with apparent pure DCIS will be found to have invasive cancer at the time of their definitive surgical procedure. Therefore, the performance of a sentinel lymph node procedure may be considered if the patient with apparent pure DCIS is to be treated with mastectomy or with excision in an anatomic location compromising the performance of a future sentinel lymph node procedure.

Risk of pathologic underestimation of needle biopsy for DCIS

	Study	No.	With invasion	underestimation, %
Mammography-guided	Jackman et al	54	8	14.8
	Won et all	40	10	25
	Lee et al	59	17	28.8
	Brem et al	34	3	8.8
	Pandelidis et al	91	12	13.2
	Dillon et al	57	12	21.1
	Miyake T	26	6	23.1
Sonography-guided*	Crowe et al	33	17	51.5
	Yen et al	260	66	25.4
	Dillon et al	23	11	47.8
	Miyake T	77	31	40.3

Underestimate rate :24.3 %

(Mam:21.2% vs Sono: 31.3%)

Predictors of invasive components in patients with preoperatively diagnosed DCIS

Study	Total no. of patients	No. of patients upstaged to invasive cancer (%)	Significant predictors of invasive component
Meijnen et al	171	45 (26.3)	Palpable lesion; mass; intermediate –high grade;
Goyal et al			
Huo et al			
Wilkie et al			
Yen et al			
Hoorntje et al			
Renshaw et al			
Jackman et			
King et al			
Miyake T			

- Large tumors
- High-grade tumors
- Tumors with comedo-type necrosis
- Diagnosis by core needle biopsy
- Presence of a palpable mass
- A mass that is visible on imaging studies

Miyake T, The American Journal of Surgery, Vol 202, No 1, July 2011

Conclusion of SLNB for DCIS

- SLNB for patients diagnosed preoperatively with DCIS should be planned according to the risk for upstaging to IDC, and can be omitted for patients with a final pathologic diagnosis of pure DCIS.
- However, prospective studies involving larger numbers of patients are required to fully establish the necessity of SLNB for patients with DCIS.

Controversial Issues

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For and against ALND when the SN is positive

FOR

- About 50% of patients have additional positive nodes
- Total number of involved nodes is important prognostic information guiding adjuvant treatment decisions
- Possibility of therapeutic effect

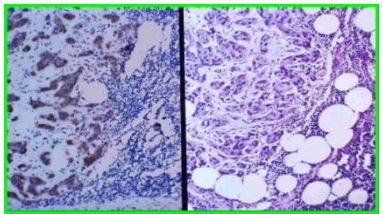
AGANIST

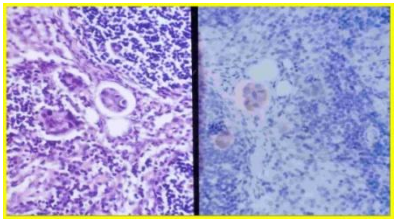
- About 50% of SN (+) patients have no additional axillary involvement
- Most pts receive adjuvant systemic therapy
- Breast RT includes
- Nomograms can predict non-sentinel nodal involvement
- No survival benefit
- ALND associated with higher morbidity

FREQUENCY OF NON-SENTINEL NODE METASTASES IN SN

SLN metastases	Tumor size	No. of patients	Incidence of non-SLN metastases (%)
Macrometastasis	T1	40	46~50
	T2-3	49	46~87
Micrometastasis	T1	18	0~21
	T2-3	15	13~80
Isolated tumor cells	T1	794	15
	T2-3	63	19

isolated tumor cells (ITC, pN0(i)<0.2 mm)
micrometastases (pN1mi 0.2 to 2.0 mm)
macrometastases (pN1a>2.0 mm)





Chu KUAnn Surg 1999;229:536–41.
Reynolds C, J Clin Oncol 1999;17:1720–6.
Viale GAm Surg 2005;241:319–25.
Menes TSJ Am Surg 2005;200:323–7
Viale GCancer 2001;92:1378–84.
den Bakker MA J Clin Pathol 2002;55:932–5.
M. Noguchi EJCO (2008)

The impact of prophylactic axillary node dissection on breast cancer survival — a Bayesian meta-analysis

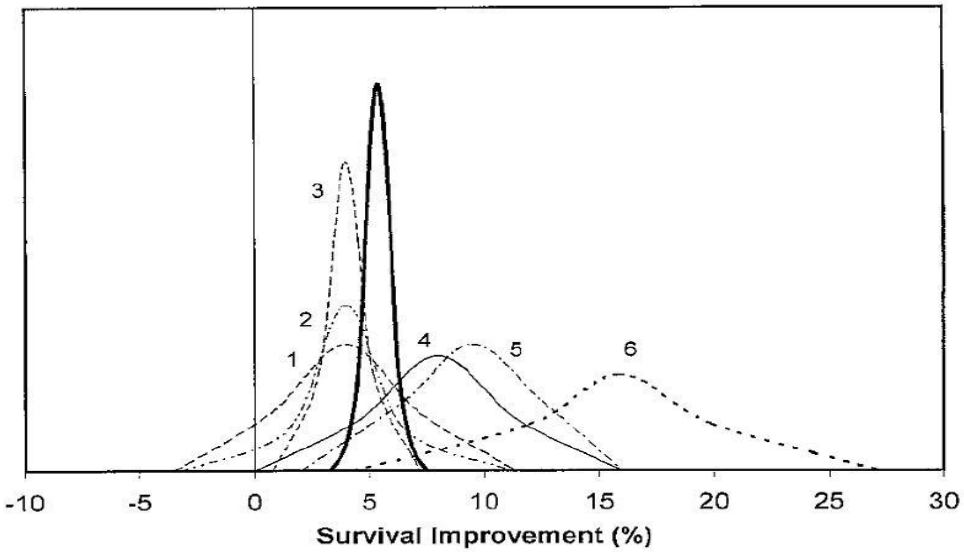
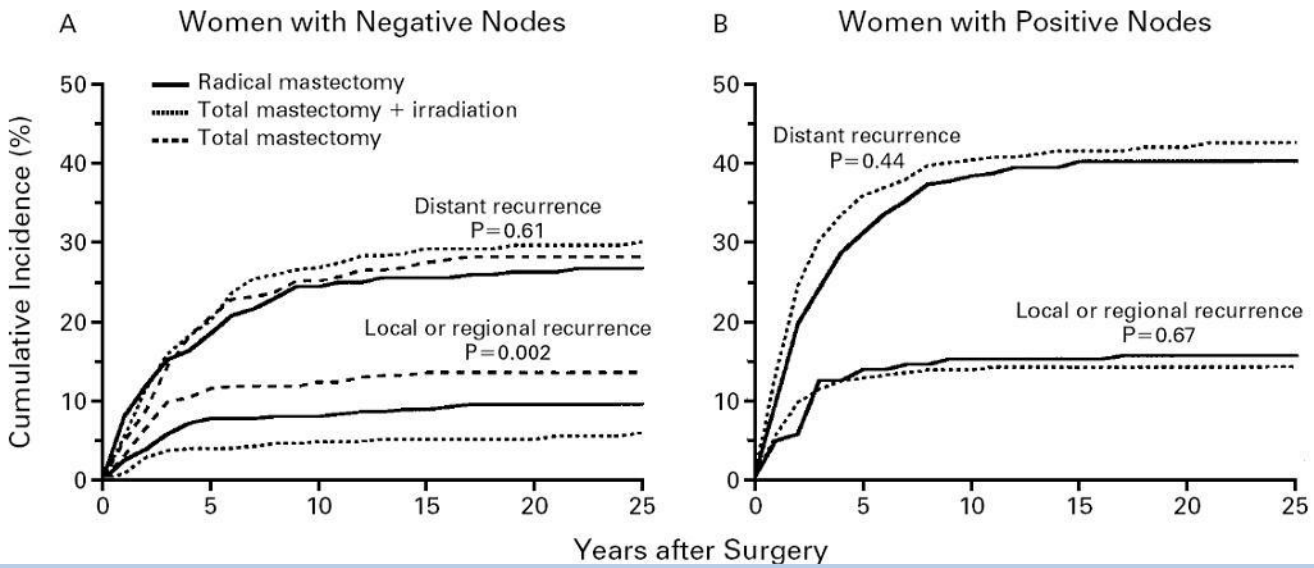


FIG. 2. Bayesian analysis of survival benefit. Black line: results of meta-analysis. Numbers 1-6, individual studies. *1*, Copenhagen; *2*, B-04; *3*, Curie; *4*, Guy's I; *5*, SouthEast Scotland; *6*, Guy's 2.

All six trials showed that prophylactic axillary node dissection improved survival, ranging from 4% to 16%, corresponding to a risk reduction of 7%-46%. Combining the six trials showed an average survival benefit of 5.4%

Orr RK.. *Ann Surg Oncol* 1999;6:109-16.

TWENTY-FIVE-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL COMPARING RADICAL MASTECTOMY, TOTAL MASTECTOMY, AND TOTAL MASTECTOMY FOLLOWED BY IRRADIATION NSABP B-4



Although ALND provides little survival advantage, it has traditionally been performed to access axillary nodal status and control regional disease in the axillae

Fisher B N Engl J Med 2002;347(8):567–75
Noguchi M. Breast Cancer 1997;4:143–53

Studies on Sentinel Lymph Node Dissection Alone for Node-Positive Disease

First author	Year	n	Follow-up, mo, mean (range)	Axillary recurrence, %

Those studies showed lower (0% to 2.6%) axillary recurrence rate with median F/U of 2 to 2.5 years in those patients with a tumor-positive SN who do not undergo completion axillary dissection

Spiguel L J Am Coll Surg 2011;213:122–129.

Lymph Node Micrometastases in Breast Cancer

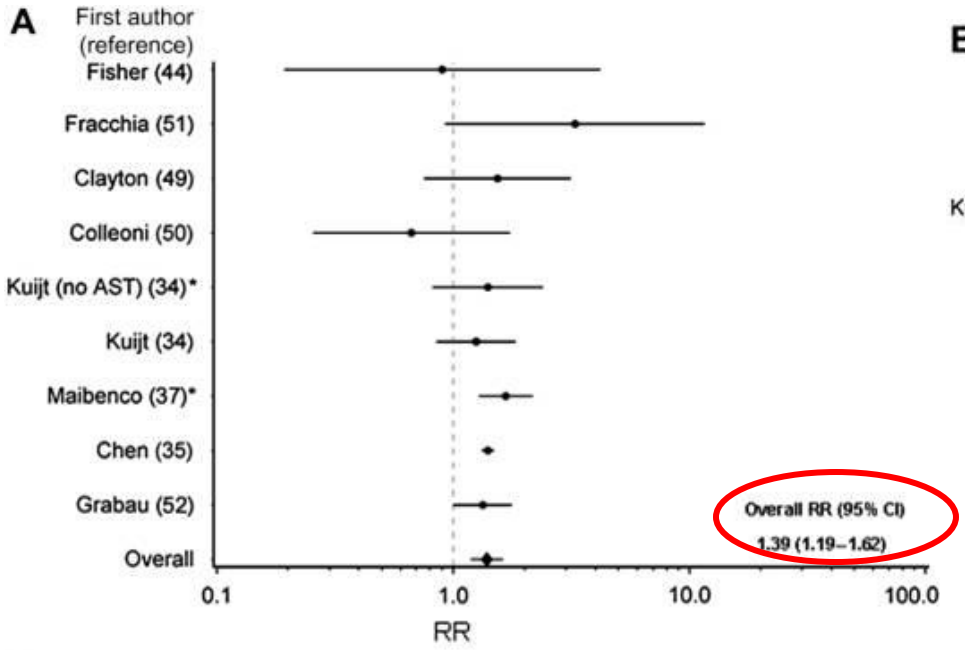
Study	Detection of Occult Mets	Change In DFS	Change In OS
Pickeren, et al (1961)	22%	NS	NS
Rosen, et al (1982)	32%	NS	NS
Trojani, et al (1990)	14%	p=0.0025	p=0.02
Bettelheim, et al (1990)	9%	p=0.003	p=0.002
Nasser, et al (1993)	17%	NS	NS
McGuckin, et al (1996)	25%	p=0.021	p=0.007
Cote, et al (1999)	20%	NS	NS
Langer, et al (2003)	12%	NS	NS

Several early large studies suggest that Micrometastases impact a survival disadvantage, But no conclusion

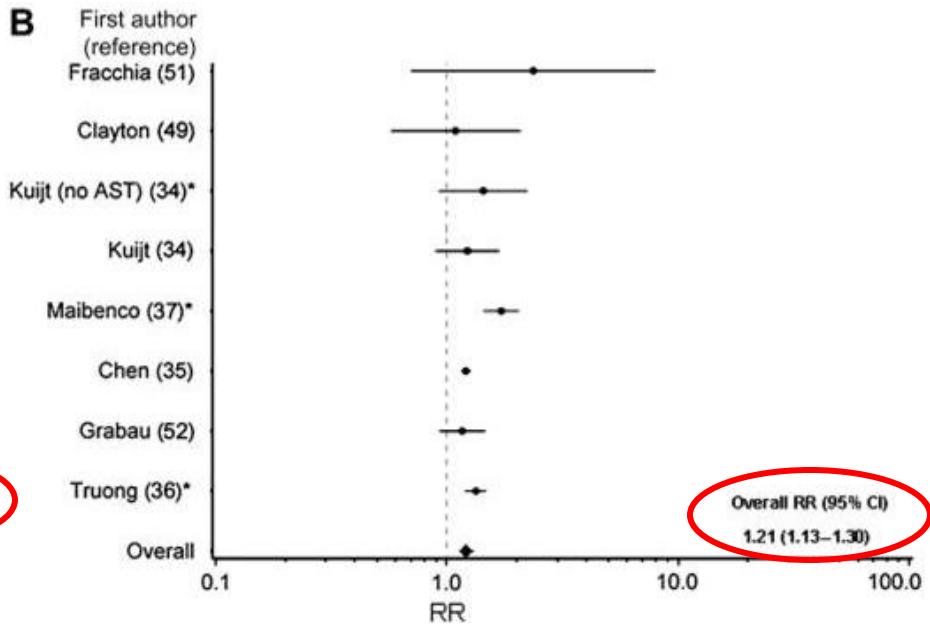
POOR Prognosis (DFS & OS) in Occult Lymph Node Metastases, Isolated Tumor Cells, and Micrometastases (<2mm) groups

1997~2008 **metanalysis** 58 studies (No= 297 533)

DFS



OS



The presence (vs the absence) of metastases of 2 mm or less in diameter in axillary lymph nodes detected on single-section examination was associated with *poorer disease-free and overall survival*

de Boer M et al, J Natl Cancer Inst 2010;102:410–425

NSABP B-32

- **5611 patients**
- **H&E negative evaluated with IHC at 2 levels (blinded)**
  - **2807 SLND plus ALND**
    - » **300 occult metastases**
  - **2804 SLND alone**
    - » **300 occult metastases**

Occult metastases were detected in 15.9% of 3,887 patients: 11.1% with ITC clusters, 4.4% with micrometastases, and 0.4% with macrometastases.

Weaver DL, Ashikaga T, Krag DN et al (2011). N Engl J Med 364:412–421

NSABP B-32
5-Year Results Occult Metastases (IHC stain)

	Yes	NO	P Value
OS	94.6%	95.8%	0.03
DFS	86.4%	89.2%	0.02
DDFS	89.7%	92.5%	0.04

Occult metastases were an independent prognostic variable; however, the magnitude of the difference in OS at 5 years was **small** (94.6%vs 95.8%).

The **identification** of occult metastases does **not** appear to be clinically **useful** for patients with newly diagnosed disease in whom systemic therapy can be recommended on the basis of the characteristics of the primary tumor.

Weaver DL, Ashikaga T, Krag DN et al (2011). N Engl J Med 364:412–421

US National Cancer Data Base women with a positive SN treated 1998-2005 Median follow-up 63 months

VOLUME 27 · NUMBER 18 · JUNE 20 2009
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Comparison of Sentinel Lymph Node Biopsy Alone and Completion Axillary Lymph Node Dissection for Node-Positive Breast Cancer

Karl Y. Bilimoria, David J. Bentrem, Nora M. Hansen, Kevin P. Bethke, Alfred W. Rademaker, Clifford Y. Ko, David P. Winchester, and David J. Winchester

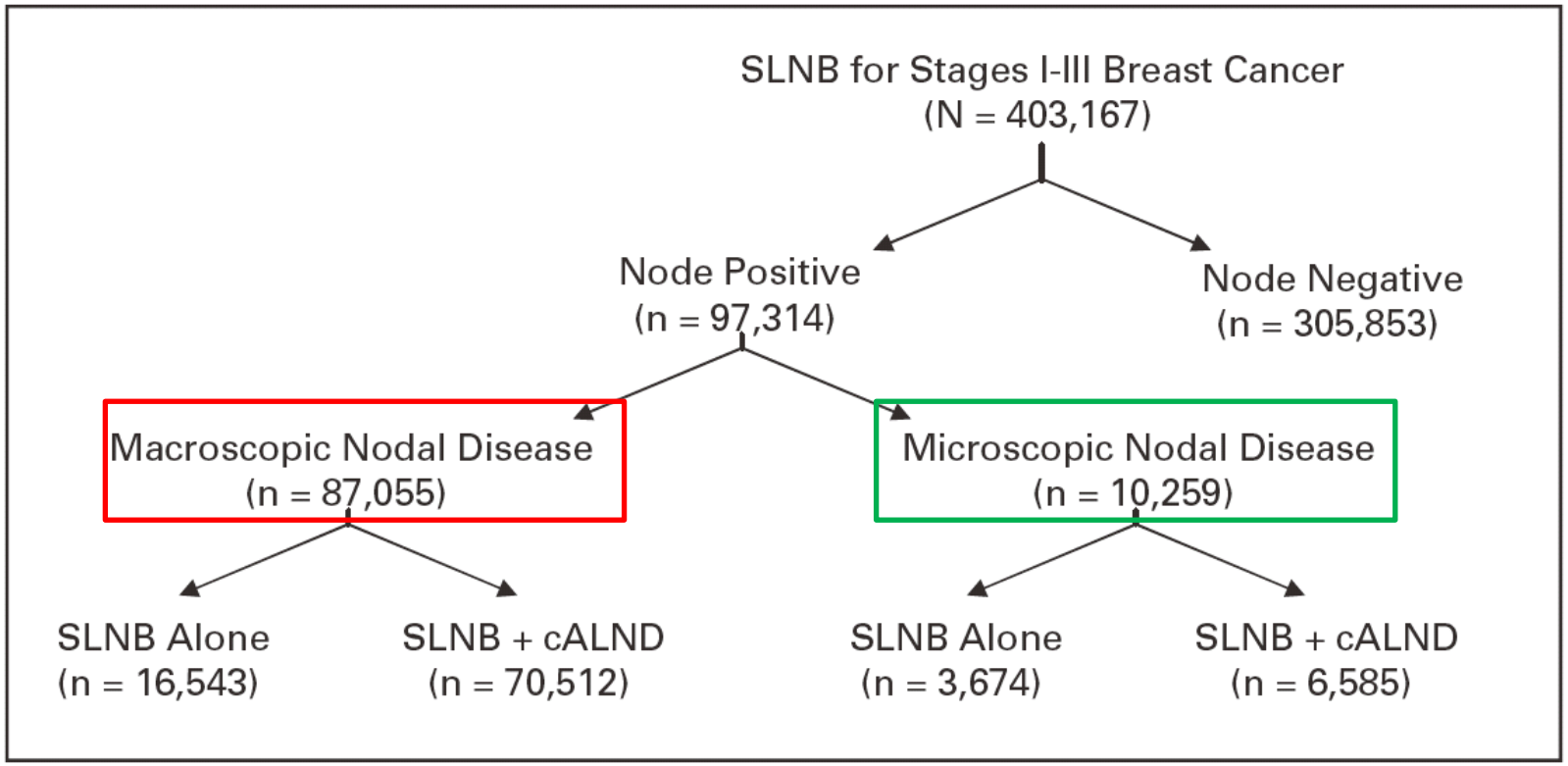


Fig 1. Nodal management of breast cancer in the United States in patients who underwent sentinal lymph node biopsy (SLNB; 1998 to 2005). cALND, completion axillary lymph node dissection.

Bilimoria et al JCO2009

Conclusions (National Cancer Data Base)

Variable	Reported Nodal Evaluation			Nodal Evaluation With Lymph Node Count Thresholds*		
	SLNB Alone	SLNB With Completion ALND	*P*	SLNB Alone†	SLNB With Completion ALND‡	*P*
No. of patients	802	2,357		530	1,673	
Axillary recurrence						
Rate, %	0.4	0.2	.18	0.6	0.2	.063
95% CI	0.0 to 0.8	0.0 to 0.4		0.0 to 1.3	0.0 to 0.4	
Unadjusted hazard ratio§	—	—		—	—	
95% CI						
Adjusted hazard ratio§‖	—	—		—	—	
95% CI						
5-Year survival						
Relative, %¶	99.0	97.8	.81	98.5	98.2	.72
95% CI	96.5 to 100	96.4 to 99.3		95.1 to 100	96.5 to 99.9	
Observed, %	90.3	90.3	.98	88.6	90.9	.16
95% CI	88.1 to 92.6	88.9 to 91.6		85.6 to 91.6	89.3 to 92.4	
Unadjusted hazard ratio	1.0**	1.00	.98	1.0**	0.79	.16
95% CI		0.71 to 1.32			0.57 to 1.10	
Adjusted hazard ratio§	1.0**	0.95	.75	1.0**	0.84	.33
95% CI		0.70 to 1.27			0.60 to 1.19	

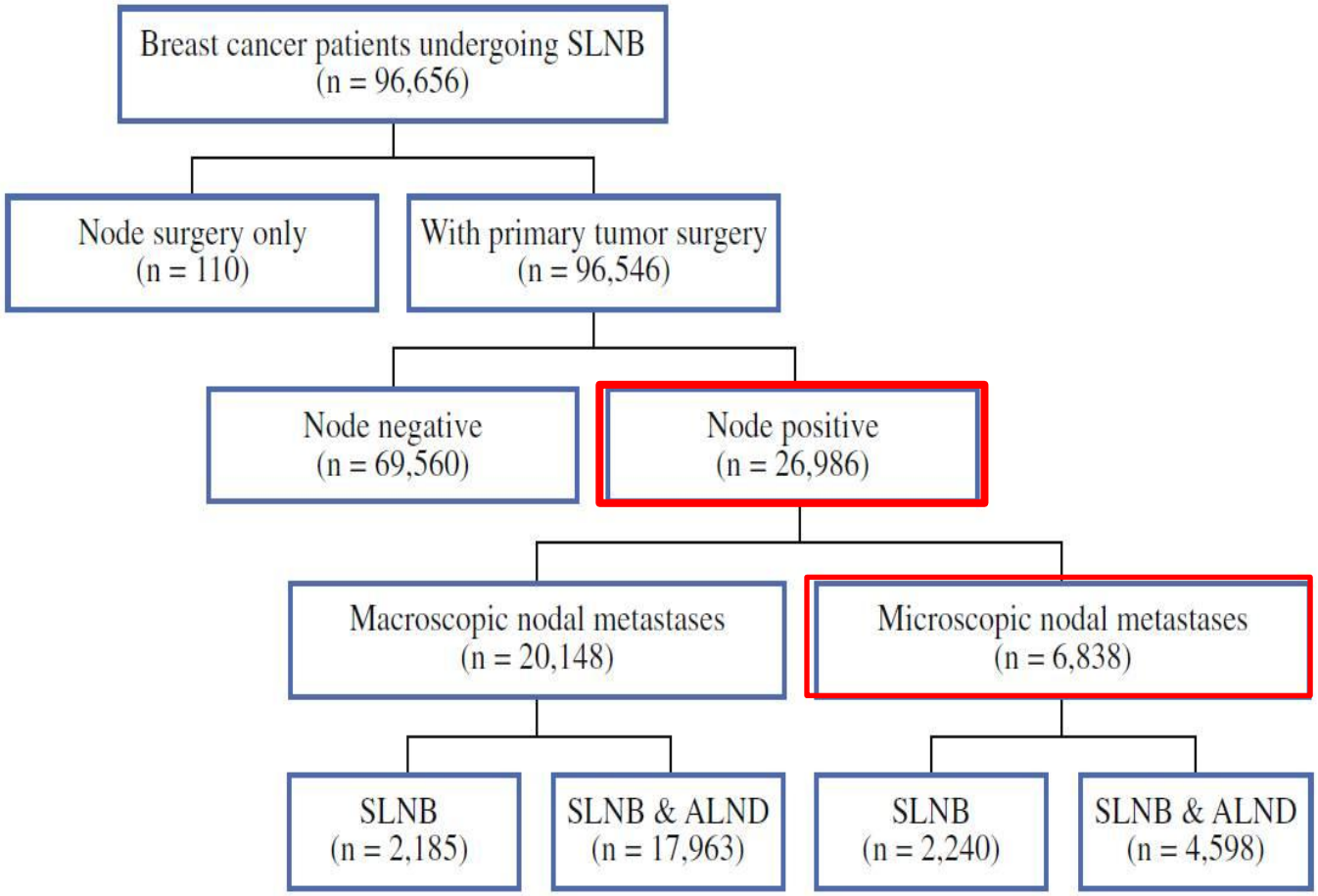
ALND did not improve outcomes in pts with microscopic SN , However there was a non-significant trend to better outcomes for AD (v SNB alone) in those with macroscopic disease

Ann Surg Oncol (2010) 17:S343–S351
DOI 10.1245/s10434-010-1253-3

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

Trends in and Outcomes from SLNB Alone vs. SLNB with ALND for Node (+): SEER Database

FIG. 1 Nodal management of breast cancer patients in the Surveillance, Epidemiology, and End Results Program (SEER) database who underwent SLNB and/or complete ALND, during the period 1998–2004



YiM. Ann Surg Oncol (2010) 17:S343–S351

TABLE 4 Results of Cox proportional hazard analyses of OS and breast cancer-specific survival

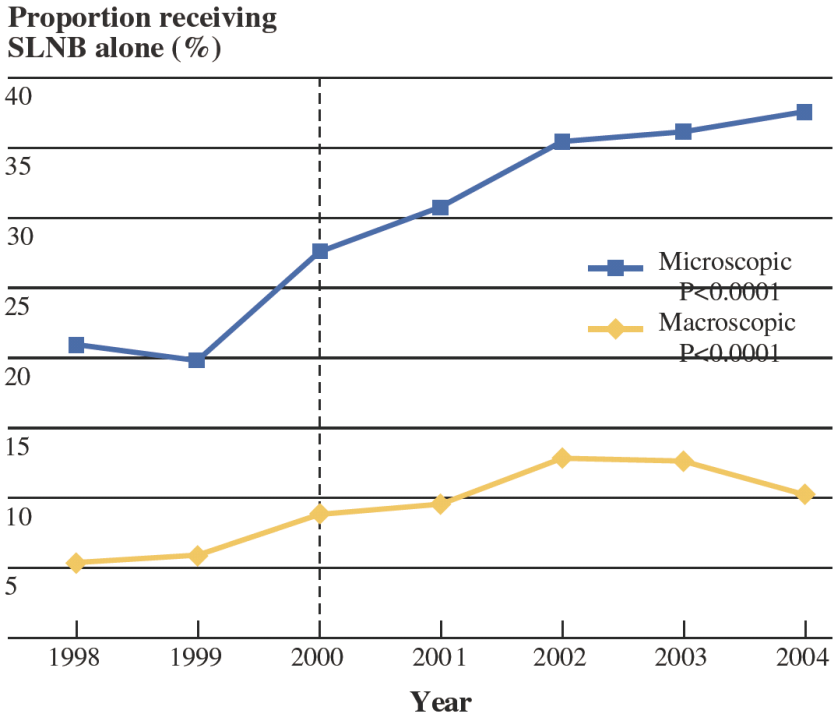
Variable	OS survival			Breast cancer-specific survival in all patients			Breast cancer-specific survival in patients with micrometastasis		
	HR	*P*	95% CI	HR	*P*	95% CI	HR	*P*	95% CI
LN category									
Micrometastasis (>0.2–2.0 mm)	Reference			Reference					
Macrometastasis (>2.0 mm)	1.2	<0.0001	1.1–1.4	1.5	<0.0001	1.3–1.8			
Grade									
Low/intermediate	Reference			Reference			Reference		
High	1.5	<0.0001	1.3–1.8	2.9	<0.0001	2.2–3.8	2.4	0.004	1.3–4.4
Axillary LN surgery									
SLNB only	Reference			Reference			Reference		
SLNB and ALND	1.0	0.6	0.9–1.2	1.3	0.003	1.1–1.6	1.2	0.3	0.9–1.7
Age (years)	1.04	<0.0001	1.04–1.05	1.01	<0.0001	1.01–1.02	[illegible]	0.001	1.01–1.03
T stage									
T1							[illegible]ference		
T2								<0.0001	1.8–3.2
T3								0.005	1.3–5.0
Estrogen receptor status									
Positive							[illegible]rence		
Negative								<0.0001	1.4–3.3
Progesterone receptor status									
Positive							[illegible]rence		
Negative								0.05	1.0–2.2
No. of positive LNs								<0.0001	1.1–1.2

SLNB sentinel lymph node bi[illegible] hazard ratio; *95% CI* 95% confidence interval

Worse OS in macrmeta group

Completion ALND does not seem to be associated with improved survival for breast cancer patients with micrometastasis in the sentinel lymph nodes

Use over time of SNB alone for SN+



Ann Surg Oncol (2010) 17:S343–S351

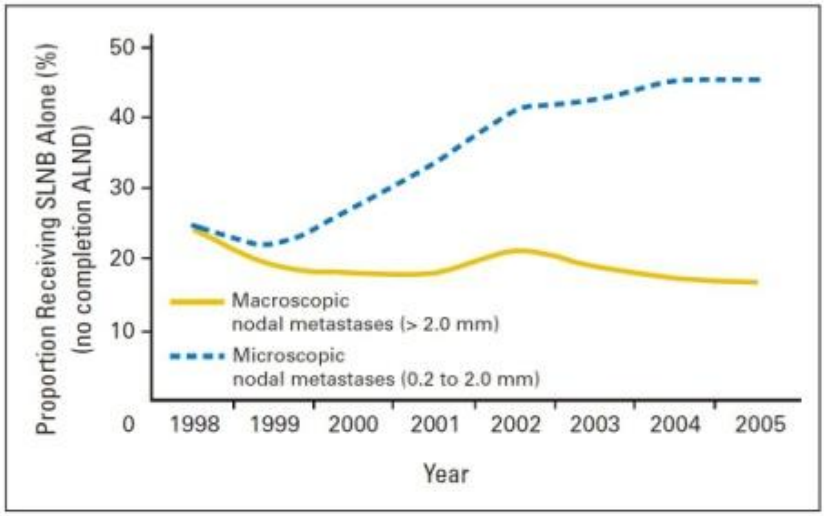


Fig 2. Utilization over time of sentinel lymph node biopsy (SNLB) alone without completion axillary lymph node dissection (ALND) for node-positive breast cancer.

Bilimoria et al JCO2009

More SLNB alone performed in micrometa group

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 13, 2009 VOL. 361 NO. 7

Micrometastases or Isolated Tumor Cells and the Outcome of Breast Cancer

MIRROR Study

(Micrometastases and Isolated tumor cells: Relevant and Robust or Rubbish

- **Retrospective study, identified all Dutch patients who had SNB before 2006 with favorable tumor characteristics and only micro-metastases of ITC in axilla (Note: axilla not just SN)**
- **Compared use and non-use of adjuvant therapy (usually systemic; less often axillary)**

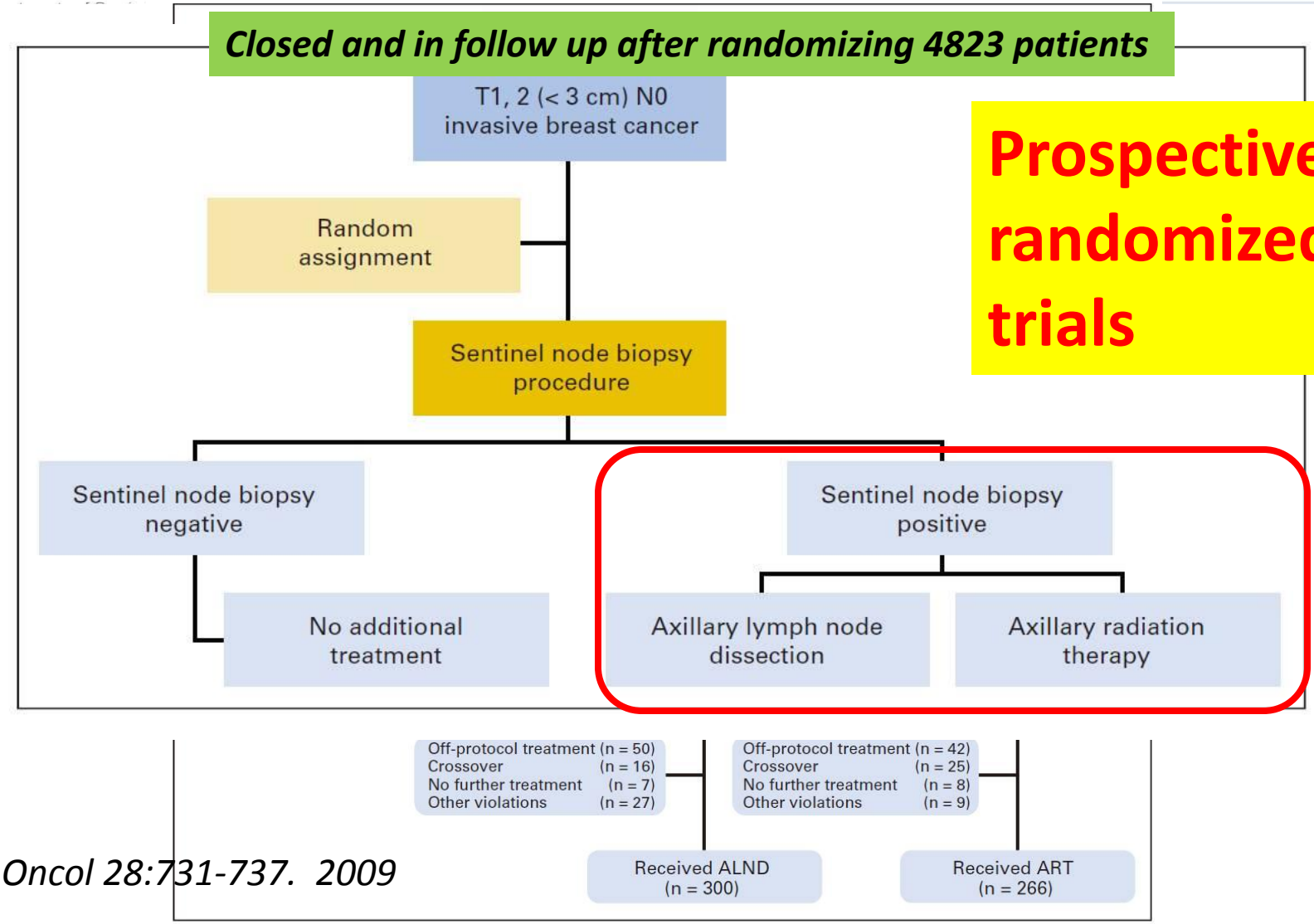
✓ ***Patients with micrometastases/ ITC and no adjuvant therapy had significantly worse DFS than those with adjuvant therapy, even after adjusting for potential confounders.***

✓ ***Whether of not AD was performed had no influence on outcomes.***

VOLUME 28 · NUMBER 5 · FEBRUARY 10 2010
JOURNAL OF CLINICAL ONCOLOGY
ORIGINAL REPORT

The After Mapping of the Axilla: Radiotherapy or Surgery? (AMAROS) phase III study compares axillary lymph node dissection (ALND) and axillary radiation therapy (ART) in early breast cancer patients with tumor-positive sentinel nodes.

Closed and in follow up after randomizing 4823 patients



Prospective randomized trials

J Clin Oncol 28:731-737. 2009

Conclusions of AMAROS Trial

- ✓Knowledge of further nodal involvement does not influence treatment decisions in adjuvant systemic therapy

- ✓Administration of systemic adjuvant therapy is mainly based on tumor and patient characteristics(**age, tumor grade, multifocality, and size of the sentinel node metastasis**)

J Clin Oncol 28:731-737. 2009

International Breast Cancer Study Group

Trial 23-01

(Closed 02/2010 at n=934)

T≤ 5cm cN0

↓

SNB

↓

MICROMETASTASES

R

↙ ↘

FOLLOW UP

AXILLARY DISSECTION

Galimberti V (2006) International Breast Cancer Study Group Trial of sentinel node biopsy. J Clin Oncol

Prospective randomized trials

Result : not yet

American College of Surgeons Oncology Group Z0011

ORIGINAL ARTICLES

Locoregional Recurrence After Sentinel Lymph Node Dissection With or Without Axillary Dissection in Patients With Sentinel Lymph Node Metastases

The American College of Surgeons Oncology Group Z0011 Randomized Trial

Armando E. Giuliano, MD, Linda McCall, MS,† Peter Beitsch, MD,‡ Pat W. Whitworth, MD,§ Peter Blumencranz, MD,¶ A. Marilyn Leitch, MD,‖ Sukamal Saha, MD,** Kelly K. Hunt, MD,†† Monica Morrow, MD,‡‡ and Karla Ballman, PhD§§*

Trial Z0011

(Closed 12/04 at n=891)

165 investigators / 177 institutions
50 investigators with 5 or more patients

Clinical T1-2, N0, M0 breast cancer,

Positive SN by H&E staining

Prospective randomized trials

R

Arm 1
AD

Arm 2
No further axillary treatment

Breast radiation therapy and/or Systemic adjuvant therapy

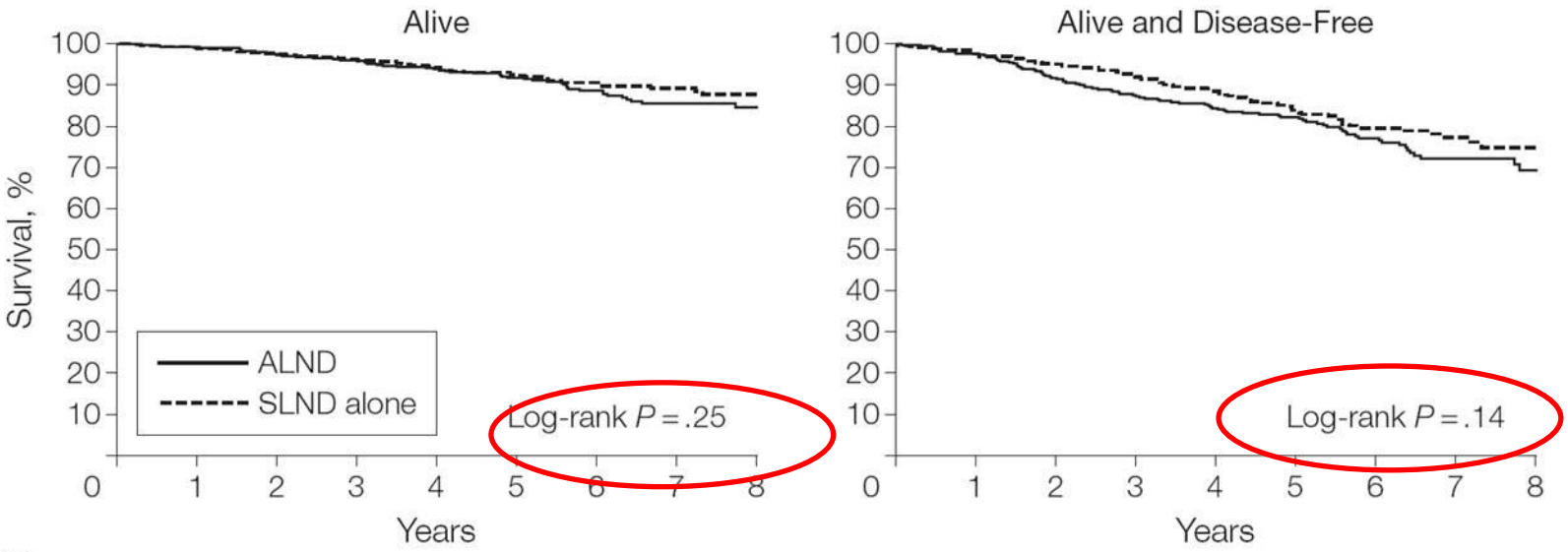
Follow up

Ann Surg 2010;252: 426–433

Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancerand Sentinel Node Metastasis A Randomized Clinical Trial

Armando E. Giuliano, MD

Figure 2. Survival of the ALND Group Compared With SLND-Alone Group



No. at risk

ALND	420	408	398	391	378	313	223	141	74
SLND alone	436	421	411	403	387	326	226	142	74

ALND	420	369	335	310	286	226	152	83	37
SLND alone	436	395	363	337	307	231	147	81	36

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

NS in OS and DFS between ALND group vs SLND-Alone group

JAMA, February 9, 2011—Vol 305, No. 6 569

Summary of Z0011 Trial

- **No significant difference in DFS between patients treated with SLND (83.9%) or ALND (82.2%)**
- **No significant difference in OS between patients treated with SLND (92.5%) or ALND (91.8%)**
- **Only age, ER, and use of adjuvant systemic therapy – not type of operation –were associated with OS by mutivariable analysis.**

Z0011 trial does not support the routine use of ALND for some women with early nodal metastatic breast cancer

SLND alone provides excellent locoregional control and survival comparable to completion ALND in patients with T1 or T2 breast cancers with SN metastasis treated with whole breast irradiation and adjuvant systemic therapy.

JAMA, February 9, 2011—Vol 305, No. 6 **569**

Z0011 Concerns

- **Single study**
- **6.3-year follow-up inadequate**
- **Mainly ER-positive patients (83%)**
- **Mainly older women (24~92 mean:56)**
- **Did not reach target accural (early close)**

Summary of recent large studies

			DFS	OS	
De Boer	2010	Occult	Worse	Worse	
NSABP	2011	Occult	Worse	Worse	Small
NCDB	2009	Micro	NS	NS	
		Macro	Trend	Trend	
SEER	2010	Micro	NS	NS	
		Macro	Worse	Worse	
MIRROR	2009	Micro, ITC	Worse	Worse	No adjuvant
AMOROS	2009	RT vs ALND	-	-	No affect CT
Trial 23-1	2011	Micro	-	-	
Z0011	2011	ALND vs SLN	NS	NS	

In view of new and pre-existing data the role of axillary dissection must be reconsidered and should not be routinely performed

Prospective randomized clinical trials comparing axillary lymph node dissection versus no axillary surgery

	Pts.	*N*	Follow-up (mo)	Axillary recurrences	DFS	OAS
Rudenstam [54]	>60 y, pT1-2[a] cN0,	473	78	0.9 vs. 2.5%	67 vs. 66% *P* = .7	75 vs. 73%; *P* = .8
Martelli [55]	>65 y, pT1 cN0, Tam	219	60	0 vs. 1.8%	95% both *P* = .9	96% both *P* = .9
Veronesi [56]	>45 y, Tumor <1.2 cm, cN0,	435	63	0.5 vs. 1.5%	97 vs. 95% *P* = .19	99 vs. 97% *P* = .23

The results of all three studies showed a very *low rate* of axillary recurrences, even in the arms without axillary surgery, and comparable disease-free and overall survival (Old age)

Rudenstam CM, Zahrieh D, Forbes JF et al (2006) J Clin Oncol 24:337–344
Martelli G, Boracchi P, De Palo M et al (2005) Ann Surg 242:1–6
Veronesi U, Orecchia R, Zurrida S et al (2005) Ann Oncol 16:383–388

2011 St gallen Consensus in Axillary Surgery

New results from clinical trials supported the safety of omitting axillary dissection not only in patients with a negative sentinel node biopsy but also in patients with a clinically node negative axilla but pathological macrometastatic involvement of one or two sentinel nodes in the context of breast-conserving surgery with tangential field radiation therapy . This continues a trend of reduced surgical extent without loss of efficacy, which dates back to the breast-conserving approaches pioneered by Veronesi and Fisher .

Krag DN NSABP B-32 Lancet Oncol 2010; 11: 927–933.
Giuliano AE JAMA 2011; 305: 569–575
Veronesi U N Engl J Med 1981; 305: 6–11.
Fisher B N Engl J Med 1985; 312: 665–673.

National Comprehensive Cancer Network®

NCCN Guidelines™ Version 2.2011
Invasive Breast Cancer

NCCN Guidelines Index
Breast Cancer Table of Contents
Staging, Discussion

AXIL

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Current NCCN guidelines

consider the performance of ALND as optional in patients who have particularly favorable tumors, in patients for whom the selection of adjuvant systemic therapy is unlikely to be affected, for the elderly, or those with severe comorbid conditions .

There is no clear statement in the NCCN guidelines in which patients the SLNB can be avoided

Optional:
- Favorable tumors,
- Old age,
- Unaffected selection of adjuvant therapy,
- Serious comorbid,

Suggestion

Who May Avoid ALND

- **T1 T2, N0 with:**
  1. **Only 1 or 2 involved SN**
  2. **Micrometastases**
  3. **ITC**
  4. **US identified metastases but only 2 or less involved SLN**
  5. **Old age**
  6. **Favorable type**

Who Should Have ALND

- Clinical T3
- Clinical N1
- Neoadjuvant therapy
- Mastectomy
- APBI/Prone radiotherapy

Controversial Issues

1). What are the indications of SLNB?

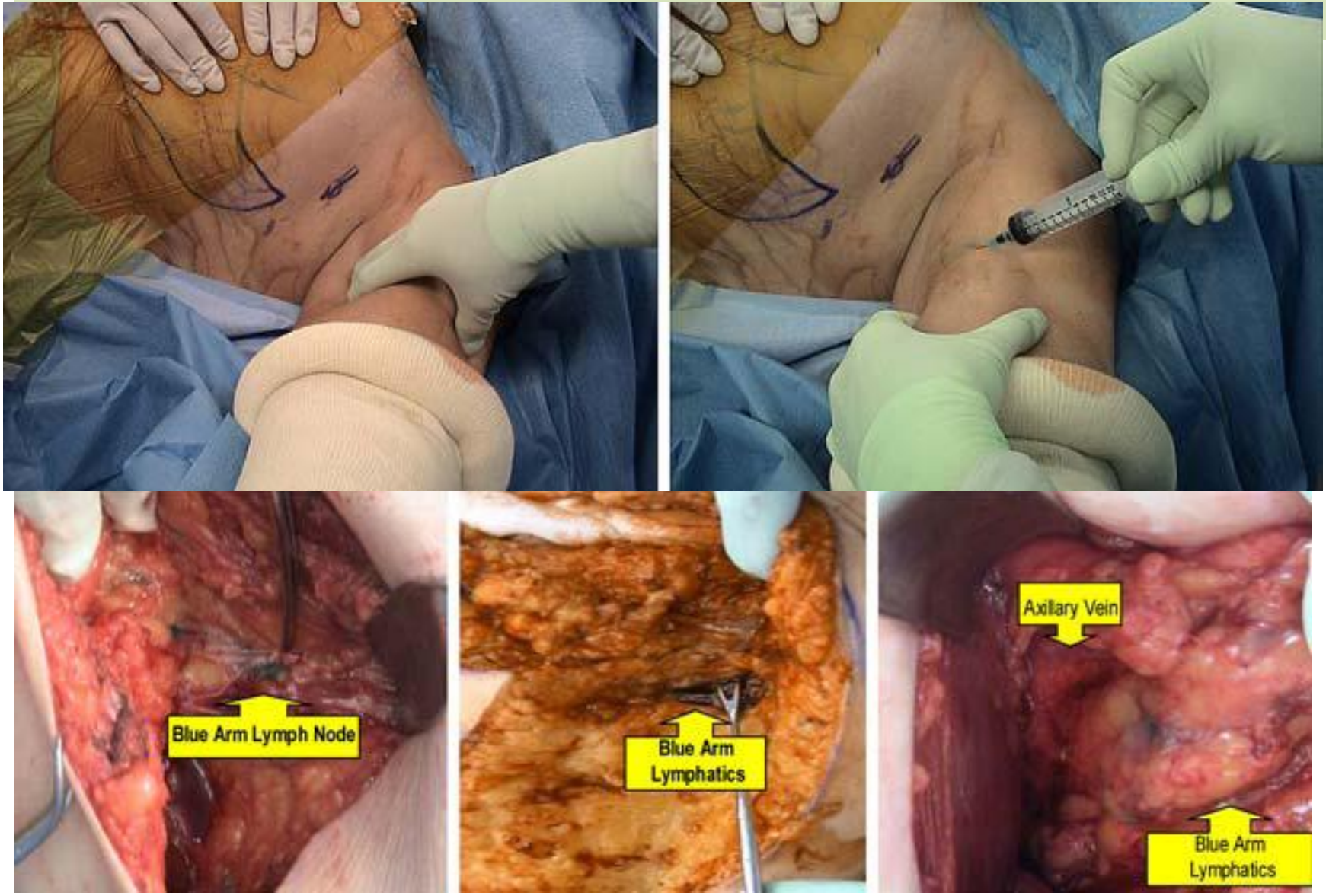
2). Should a complete axillary dissection be performed when the SLNB is positive?

3). Can lymphedema occur after SLNB?

4). What is the accuracy of SLNB in patients who have received neoadjuvant therapy prior to surgery?

5). Technical considerations about SLNB

Axillary Reverse Mapping (ARM): A New Concept to Identify and Enhance Lymphatic Preservation



Thompson M .Annals of Surgical Oncology 14(6):1890–1895 2007

The Involvement of ARM Nodes in Patients Who Underwent ALND With Removal of ARM Nodes

References	No. of patients	No. of patients with ARM involvement	% of ARM involvement
Thompson et al.	7	0	0
Boneti et al.	7	0	0
Nos et al.	10	0	0
Nos et al.	21	3	14
Ponzone et al.	27	3	11
Kang et al.	101	9	8.9
Bedrosian et al. 13.6%	11	2	18
Noguchi et al.	7	3	43
Noguchi et al.	34	11	32

13.6% of ARM nodes involvement

The Concordance of SLN and ARM Nodes in Patients Who Underwent SLN Biopsy and ARM Procedure

References	No. of patients	No. of patients with converged SLN-ARM node	Rates of convergence (%)
Boneti et al.	220	6	2.2
Britton et al.	15	2	13
Kang et al.	96	19	18.9
Noguchi et al.	14	2	14
Noguchi et al.	96	27	28

Kang SH Cancer Res 2009;69:87

Rates of convergence:12.7%

CONCLUSIONS of Axillary Reverse Mapping (ARM)

- **Lower convergence rate and involvement rate of ARM node (12,7%; 13.6%)**
- **There were no complete accurate : differentiating the arm and breast lymphatic pathways.**
- **Therefore, it may be possible to spare the ARM nodes during ALND only in patients with clinically uninvolved nodes.**

Need more studies

Controversial Issues

1). What are the indications of SLNB?

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5). Technical considerations about SLNB

Use of SLNB to stage the axilla after NAC is controversial.

- CT induces fibrosis of lymphatics while eradicating tumor, thus impeding the flow of mapping agents to the SLNs.
- The potential differential sterilization of sentinel and non-SLNs may also render SLNs no longer representative of the entire nodal basin
- Single or multi-institutional studies of limited numbers

Nason KS Cancer 2000;89:2187–2194. 33.
Shen J Cancer 2007;109:1255–1263

The Feasibility and Accuracy of Sentinel Lymph Node Biopsy in Clinically Node-Negative Patients After Neoadjuvant Chemotherapy for Breast Cancer Four large Meta-Analysis

	Patients	Identification rate	False negative rate
Xing et al	1273	90%	12%
Kelly et al	1799	90%	8.4%
van Deurzen et al	2148	90.9%	10.5%
K.M. TAN et al.	449	94%	7.4%

Acceptable identification rate
Higher false negative rate

Xing Y.Br J Surg 2006;93:539–546.
Kelly AMAcad Radiol2009;16:551–563.
van Deurzen CH.Eur J Cancer 2009;45:3124–3130
K.M. TAN . VKMJ. Surg. Oncol. 2011;104:97–103.
Yu JC Ann Surg Oncol 2007;14:174–180

SLN biopsy Before neoadjuvant CT

First author[Ref.]	Stage	No. of patients	Identification rate	False-negative rate	Patient criteria for ALND
Ollila[16]	T2–3, >3.5 cm	21	100%	0%	T2 or node-positive cases
Cox[17]	Stage II or III, >4.5 cm, N0	47	98%	NS	Only node-positive cases
van Rijk[18]	T2N0	25	100%	NS	Only node-positive cases
Kilbride[19]	T1–4, N0–1	44	98%	NS	Only node-positive cases
Schrenk[20]	T2–3, N0–1	45	100%	0%	All cases
Menard[21]	>3.0 cm, N0	31	100%	0%	All cases
Grube[22]	Stage I–III, N0	55	100%	NS	Only node-positive cases

Similar Identification Rate and False negative rate

Surg Today (2011) 41:311–316

Sentinel Lymph Node Biopsy Before Neoadjuvant Chemotherapy

Contrary to the high number of studies reporting SLNB after NAC, only a few studies have reported the results of performing SLNB before NAC.

The advantage of SLNB before NAC is that it provides an accurate assessment of initial axillary nodal

The disadvantage of SLNB before NAC is that patients with a positive SLN are not able to avoid axillary surgery at the time of breast surgery after NAC, even if NAC has eradicated the axillary disease.

Chung MH.Ann Surg Oncol 2001;8(9):688–92.
Bedrosian I, Cancer 2000;88(11):2540–5.
Surg Today (2011) 41:311–316

Intraoperative Assessment of Sentinel Lymph Nodes After Neoadjuvant Chemotherapy

- **The sensitivity, specificity, and accuracy of FS analysis of SLNs were 74%, 100%, and 88%, respectively, for the NAC-treated patients, which were similar to the corresponding values of 71%, 99%, and 90% for the non-NAC-treated patients.**

Surg Today (2011) 41:311–316

Repeat Sentinel Lymph Node Biopsy After Neoadjuvant Chemotherapy

- **One-third** of patients who were initially node(+) were subsequently proven to be node(-), allowing for the avoidance of ALND
- **Higher** identification rate in the pretreatment group (100%) than in the post-treatment group (81%).
- The optimal **timing** for SLNB in the neoadjuvant setting remains controversial.

Jones JL Am J Surg 2005;190(4):517–20.
Goldhirsch A Ann Oncol 2009;20(8):1319–29
Surg Today (2011) 41:311–316

Summary of SLN biopsy for NAC

- Meta-analyses and many single-institution experiences have strongly suggested the feasibility and accuracy of SLNB after NAC.
- Further follow-up studies on patients with a negative SLN after NAC, who did not undergo ALND, are required to firmly establish the utility of SLNB after NAC.
- Several studies have suggested that both SLNB before NAC and repeat SLNB are promising, the data are insufficient.
- Further studies on large populations are required to evaluate the feasibility and accuracy of SLNB in these settings

Controversial Issues

1). What are the indications of SLNB?

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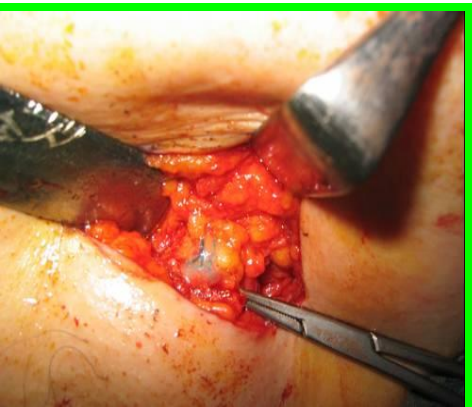
5). Technical considerations about SLNB

Technical considerations in SLNB

- Radiotracer
- Blue dye injection
- Preoperative scintigraphic imaging
- Intraoperative gamma probe localization

No consensus regarding how the procedure should be performed.




Radioactive agents

- **99mTc-sulfur colloid (US commercial product lymphoscintigraphic SLN detection**)
  Unfiltered particles sizes (15–5,000 nm average 305–340 nm)
  0.22-µm filter (100 nm - 220 nm)
- **99mTc-Nanocolloidal albumin (Nanocoll) (Europe,5–100 nm)**
- **99mTc-Antimony trisulfide (Canada,Australia,3–30 nm)**
- **Lymphoseek** (7 nm, a dextran backbone with multiple glucose and mannose molecules attached to DTPA and 99mTc,is not yet used widely)

Small particles are drained and cleared first and large particles are drained and cleared last, and may be retained virtually indefinitely at the injection site

Additionally, particles smaller than 4–5 nm may penetrate the capillary membranes without adequate retention in the lymph nodes. It is believed that a particle size range of 100–200 nm are the best compromise between the need for efficient and fast lymphatic drainage (for scintigraphic visualization) and the need for satisfactory retention in SLN (for subsequent intraoperative detection with a gamma probe)

Mariani G J Nucl Med 2001;42:1198–215.1998;39:1185–90.
Glass EC. Semin Nucl Med 1999;29:57–68.

Vital dyes

- **Patent blue V (is also referred to as sulfan blue, sulphane blue, patent blue, patent blue violet,patent pure blue, etc.),isosulfan blue, methylene blue dyes.**
- **Interfere with pulse oximetry**
- **Various safety concerns for the use of blue dyes in pregnant women.**
- **More frequently associated with side effects (in 1–3%) skin necrosis, angioedema, infectious cellulitis, inflammatory change of the skin , and even anaphylaxis.**

Masannat Y Eur J Surg Oncol 2006;32:381–4
Weng PW Eur J Cancer Care 2007;16:390–1.
Jaffer U Breast J 2008;14:508–9.
Bleicher RJ . J Surg Oncol 2009;99:356–60.
Scherer K Ann Allergy Asthma Immunol 2006;96:497–500..

Optimal Injection methods : active debate

Two categories

- **deep (subcutaneous or parenchymal, PT, subtumoral, intratumoral)**
- **Superficial (epidermal or dermal, intradermal, subdermal, PA, SA)**

The location of the injection does not significantly affect the identification of SLN

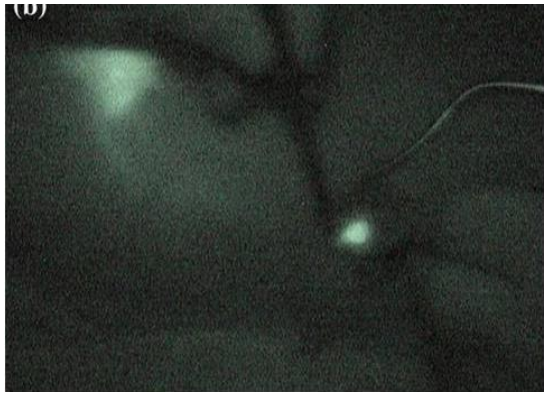
[63]	456	Subareolar	Radiotracer	98.0	NA	Peritumoral	Radiotracer	96.0	NA
		Subareolar	Combined	98.0	NA	Peritumoral	Combined	97.0	NA

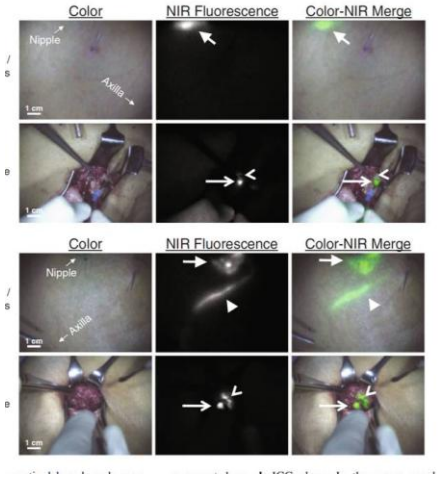
- **Radiotracers results in a higher SLN identification rate than the use of blue dyes, regardless of the injection method (PT or SA/PA) .**
- **Only two randomized prospective clinical trials have been published , and the results are inconclusive.**

[19]	449	Periareolar	Combined	99.1	NA	Peritumoral	Combined	99.1	NA
		Periareolar	Radiotracer	98.2	NA	Peritumoral	Radiotracer	96.0	NA
		Periareolar	Vital dye	95.6	NA	Peritumoral	Vital dye	93.8	NA
[38]	400	Intradermal	Radiotracer	100.0	NA	Intrapar			
		Subareolar	Radiotracer	95.0	NA				

Rodier J J Clin Oncol 2007;25:3664–9.
Noguchi M J Surg Oncol 2009;100:100–5.
Cheng G. Eur J Nucl Med Mol Imaging (2011) 38:562–575
Povoski SP, Ann Surg Oncol 2006;13:1412–21.

Indocyanine green vs near-infrared fluorescence





Raman spectroscopy

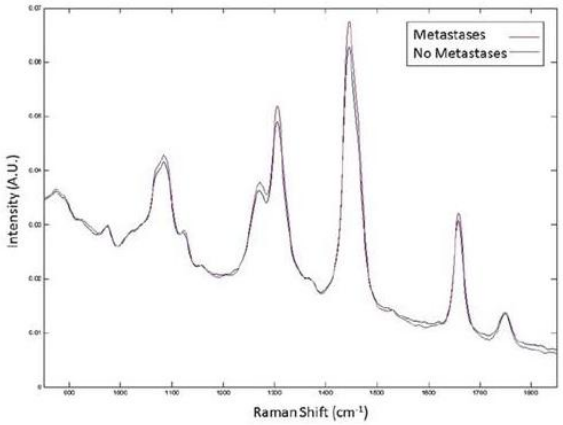
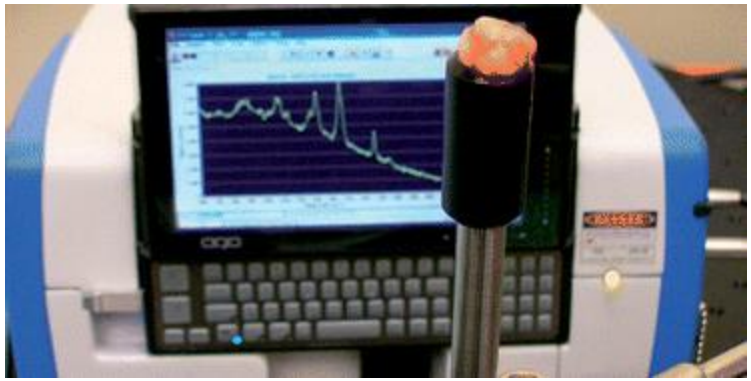


Fig. 1 Mean normalised spectra of 13 positive nodes (metastases) and 25 negative nodes (no metastases).



Hirche C. et al. Breast Cancer Res Treat (2010) 121:373–378
Breast Cancer Res Treat (2011) 127:163–170
Analyst, 2010, 135, 3042–3047

Controversial Issues

1). What are the indications of SLNB? More

2). Should a complete axillary dissection be performed when the SLNB is positive? subgroup

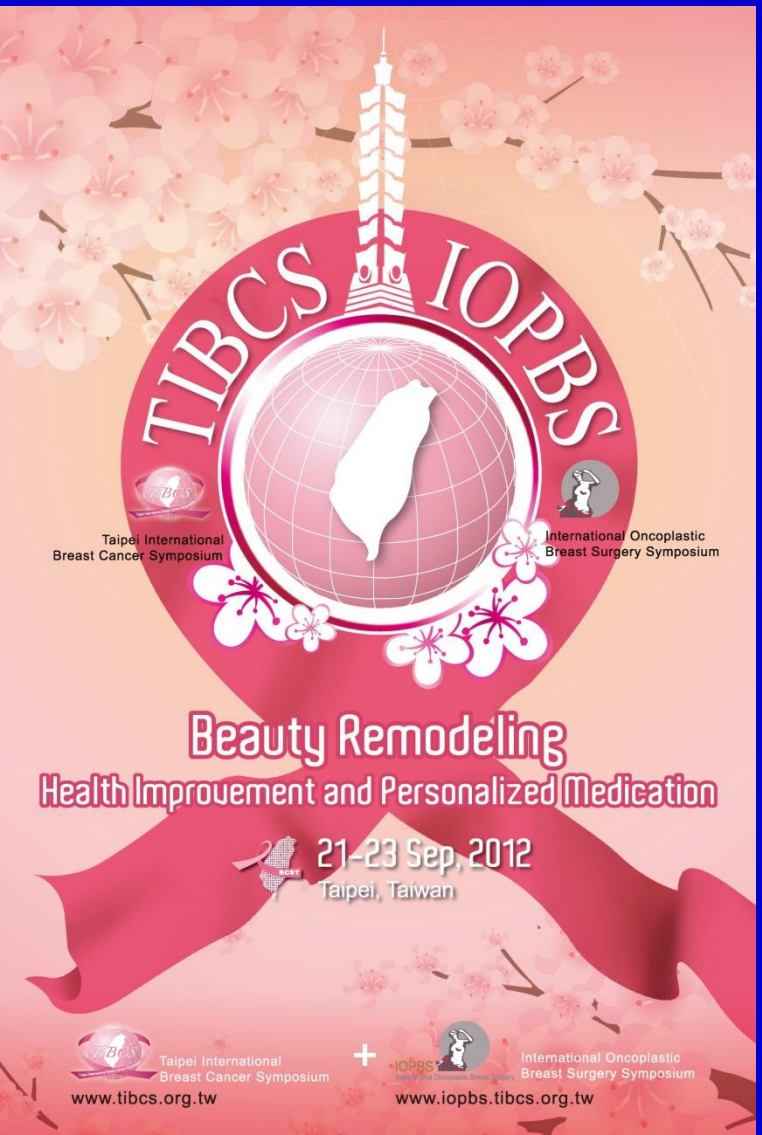
3). Can lymphedema occur after SLNB? Validate new procedure

4). What is the accuracy of SLNB in patients who have received neoadjuvant therapy prior to surgery? Need trial

5). Technical considerations about SLNB? Difficult to establish standard procedure

2012

Taipei International Breast Cancer Symposium & the 4th International OncoPlastic Breast Surgery Symposium



Theme:

Beauty Remodeling, Health Improvement and Personalized Medication

Date:

September 21-23, 2012

Venue:

Taipei International Convention Center, Taiwan

Hosted by:

The Breast Cancer Society of Taiwan


Welcome To Taiwan

Koahsiung 高雄 2011 TAIWAN

Thank you

Welcome to TAIWAN

Formosan rock-monkey