Updates on management of the axilla in breast cancer the surgical point of view

Edwige Bourstyn
Centre des maladies du sein
Hôpital Saint Louis
Paris

- Sentinel lymph node biopsy (SLNB) is the standard of care for axillary staging in early stage clinically node negative infiltrating breast carcinoma regardless of the type of breast surgery performed

- The dual technique (isosulfan blue and radioisotope) is the gold standard for successful identification
- Ultrasound guided needle aspiration or biopsy or TEP scan should be proposed in patients clinically node positive patients

Use of SLNB is still debated

- In multifocal carcinomas
- After primary chemotherapy
- After major breast or axillary surgery
- During pregnancy

Up to 2011 : axillary dissection was mandatory

- In case of sentinel node involvement on multilevel node sectioning with hematoxilyn and eosin staining
- For micrometastasis (≤ 2mm) and macro metastasis (> 2mm)

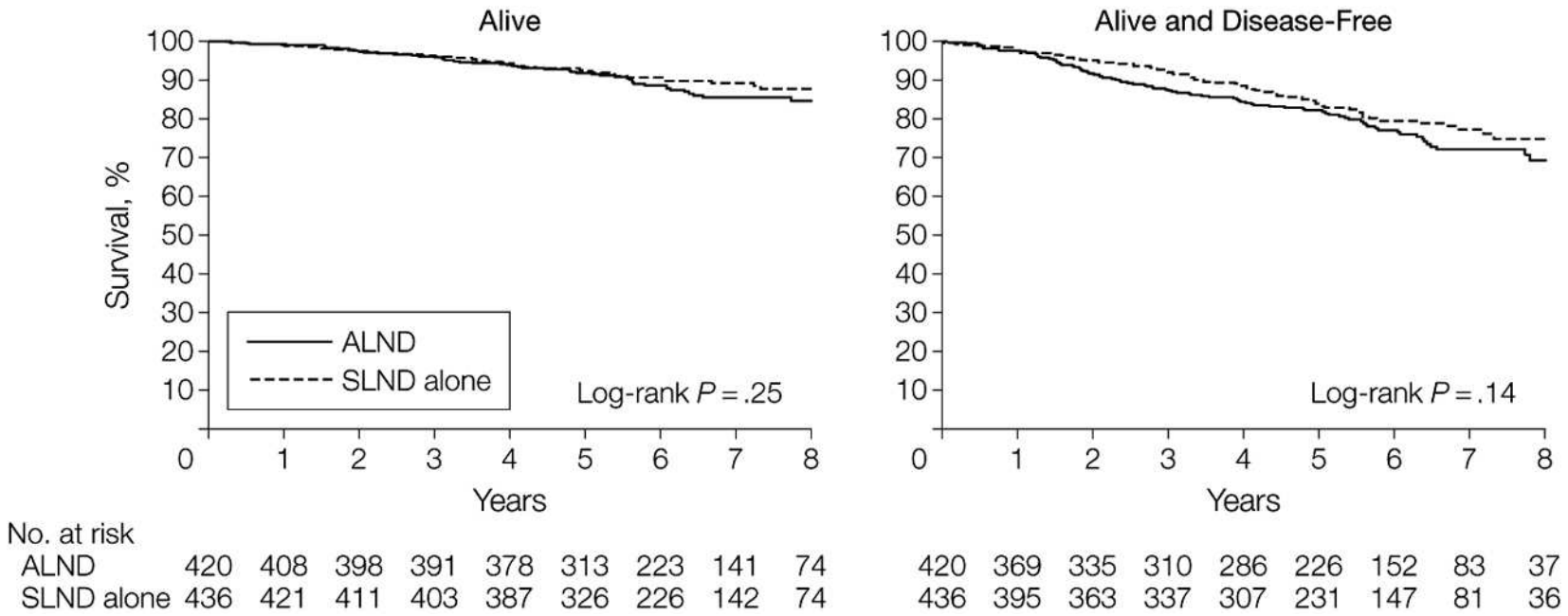
The ACOSOG Z0011 trial

- Giuliano JAMA February 2011
- Enrollment from May 1999 to December 2004 (target 1900 patients) at time of surgery or after pathological results
- 856 patients with 1-2 + SLNB were randomized to receive ALND /SLNB alone
  - All had BC surgery and tangential RT
  - 96%received systemic therapy
- Median FU : 6.3 years
- Cancer recurrence
  - Locoregional (T in breast or ipsilateral supraclavicular,subclavicular, internal mammary or axillary nodes)
  - Distant metastasis

The ASCOSOG Z0011 trial :results

- 5-year overall survival :
  - SLNB alone : 92.5%
  - SLNB + ALND : 91.8%
- 5-year DFS :
  - SLNB alone : 83.9 %
  - SLNB + ALND : 82.2%
- In ALND group 27.3% of patients had additional metastatic nodes removed (10% of those with micro metastasis)

Survival of the ALND Group Compared With SLND-Alone Group



Giuliano, A. E. et al. JAMA 2011;305:569-575

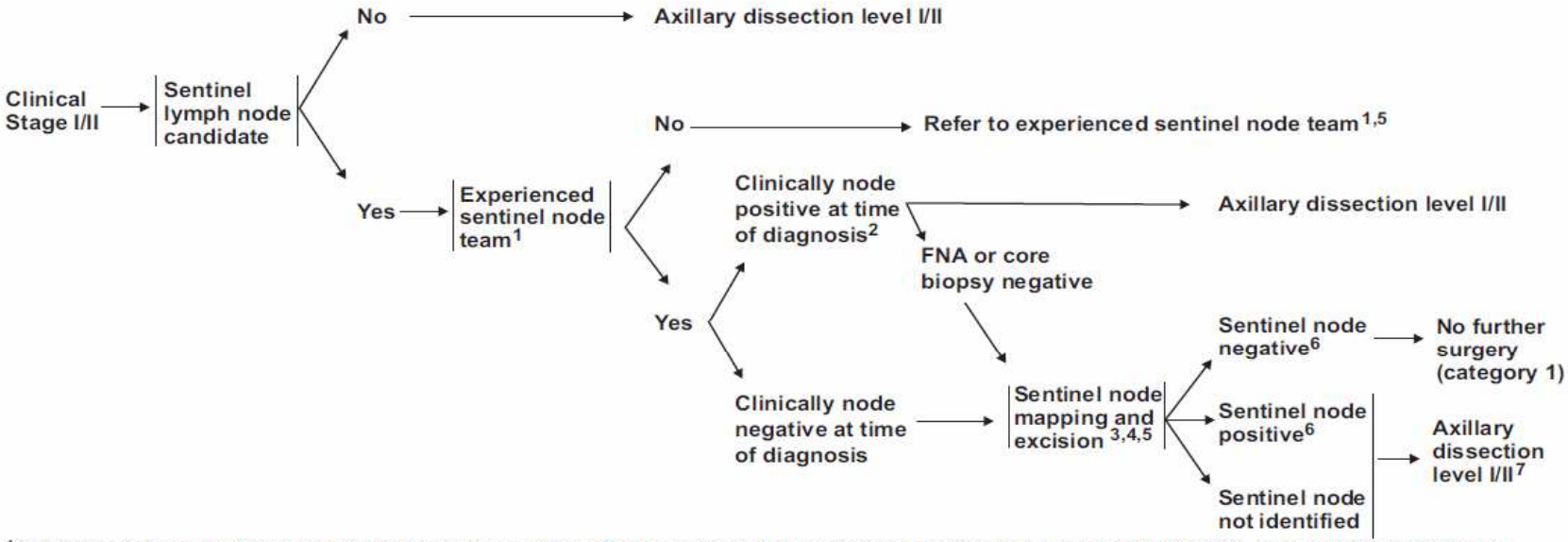
- Publication of this study was followed by a tremendous amount of commentaries in the medical and non medical medias
- Several professionals societies modified their recommendations
  - NCCN
  - Saint Gallen

National Comprehensive Cancer Network®

NCCN Guidelines™ Version 2.2011
Invasive Breast Cancer

NCCN Guidelines Index
Breast Cancer Table of Contents
Staging, Discussion

SURGICAL AXILLARY STAGING - STAGE I, IIA, AND IIB



[1]Sentinel node team must have documented experience with sentinel node biopsy in breast cancer. Team includes surgeon, radiologists, nuclear medicine physician, pathologist, and prior discussion with medical and radiation oncologists on use of sentinel node for treatment decisions.

[2]Consider pathologic confirmation of malignancy in clinically positive nodes using ultrasound guided FNA or core biopsy in determining if patient needs axillary lymph node dissection.

[3]Axillary sentinel node biopsy in all cases; internal mammary sentinel node biopsy optional if drainage maps to internal mammary nodes (category 3).

[4]Sentinel lymph node mapping injections may be peritumoral, subareolar or subdermal. However, only peritumoral injections map to the internal mammary lymph node(s).

[5]Results of randomized clinical trials indicate that there is a lower risk of mobidity associated with sentinel node mapping and excision than with level I/II axillary dissection.

[6]Sentinel node involvement is defined by multilevel node sectioning with hematoxylin and eosin (H&E) staining. Cytokeratin Immunohistochemistry (IHC) may be used for equivocal cases on H&E. Routine cytokeratin IHC to define node involvement is not recommended in clinical decision making.

[7]Data from a single, randomized trial suggests that complete axillary lymph node dissection in women with clinically node negative T1-T2 tumors, fewer than 3 involved sentinel lymph nodes, and undergoing breast-conserving surgery and whole breast radiation results in more morbidity, no improvement in locoregional recurrence rates, and no difference in overall survival compared with sentinel lymph node procedure alone.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Return to Locoregional Treatment (BINV-2)

Saint Gallen 2011

“Isolated tumor cells and metastasis up to 2 mm in a sentinel node does not constitute an indication for axillary dissection regardless of the type of breast surgery performed”

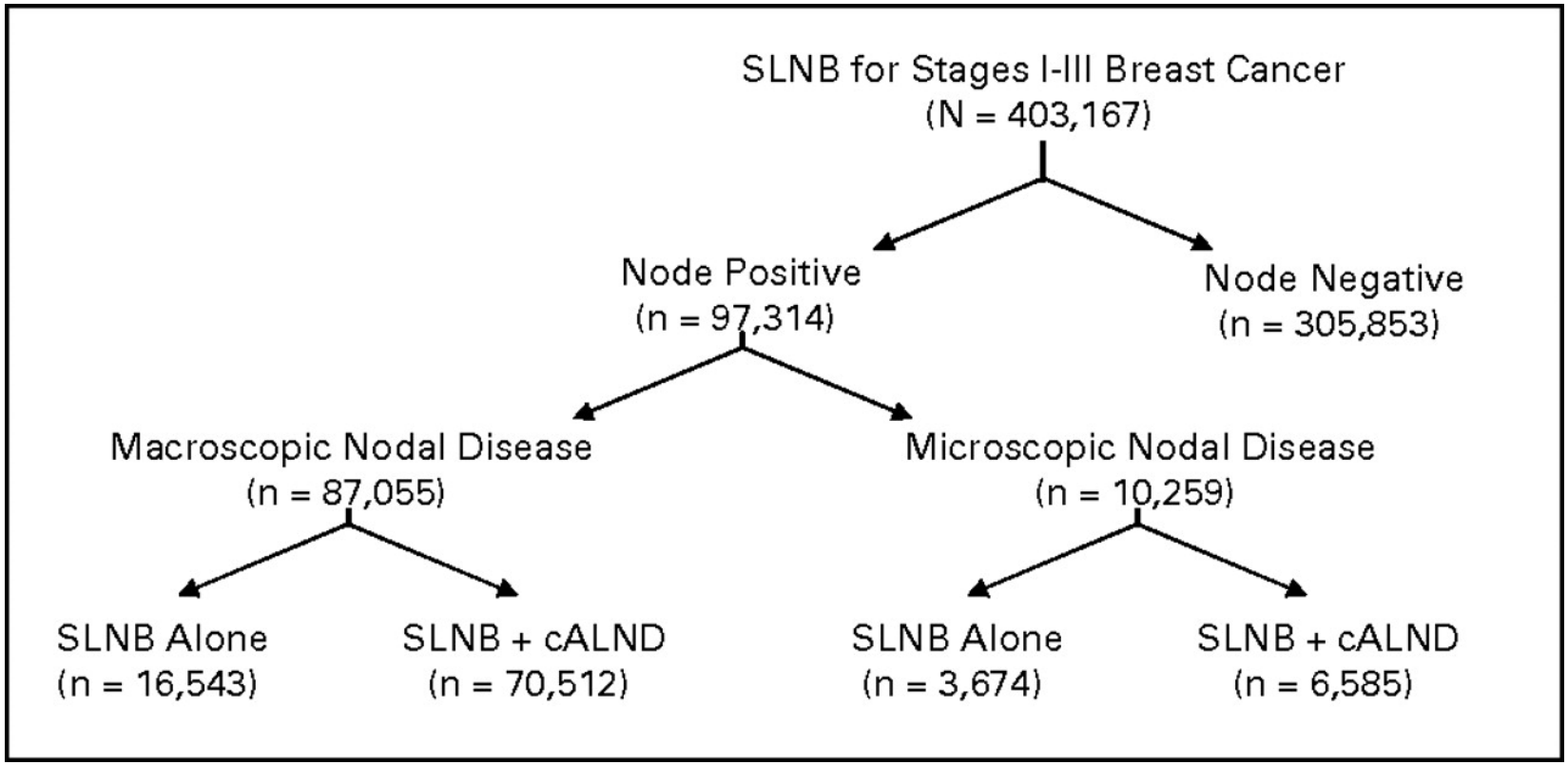
“The Panel accepted the option of omitting axillary dissection for macro metastasis in the context of lumpectomy and radiation therapy for clinically node negative patients with 1 or 2 positive sentinel nodes.

This practice should not be extended to patients undergoing mastectomy, those with involvement more than 2 SN and patients receiving neoadjuvant chemotherapy”

What about individual practices ?

- Karl Y, Bilimore D J Clin Oncol 2009
- National cancer data base
- Evaluation of practices in USA
- 97 314 patients with nodal metastasis on SLND
- 20 217 (28.8%) received SLNB alone
- 77 097 (79.2%) received SLNB +ALND

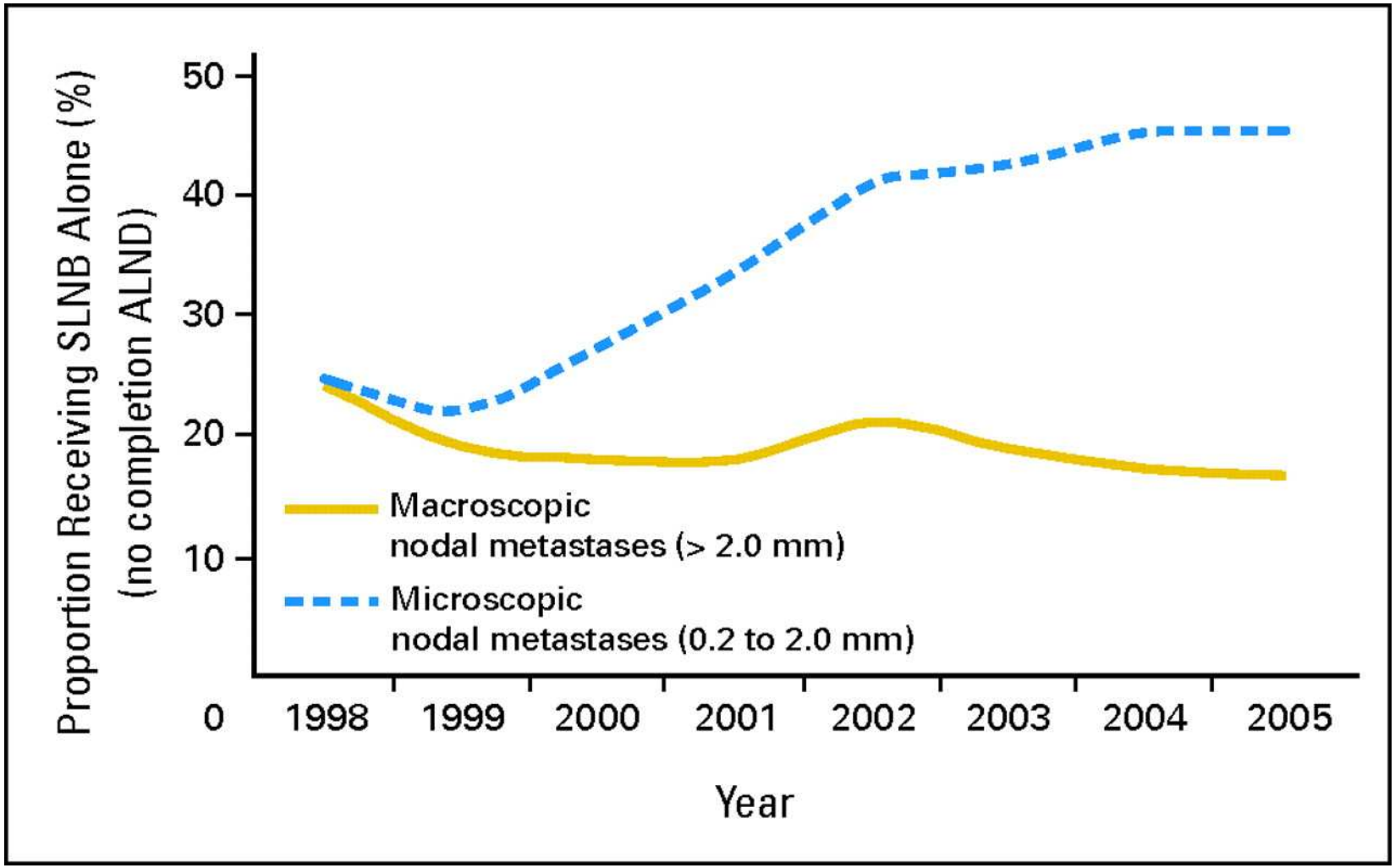
Nodal management of breast cancer in the United States in patients who underwent sentinal lymph node biopsy (SLNB; 1998 to 2005). cALND, completion axillary lymph node dissection.



Bilimoria K Y et al. JCO 2009;27:2946-2953

JOURNAL OF CLINICAL ONCOLOGY

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



Bilimoria K Y et al. JCO 2009;27:2946-2953

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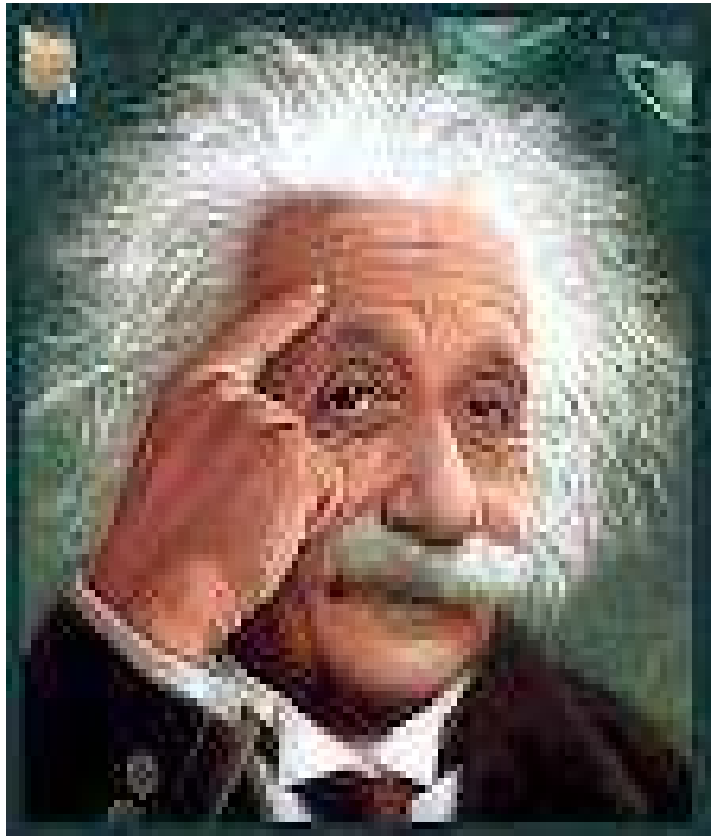
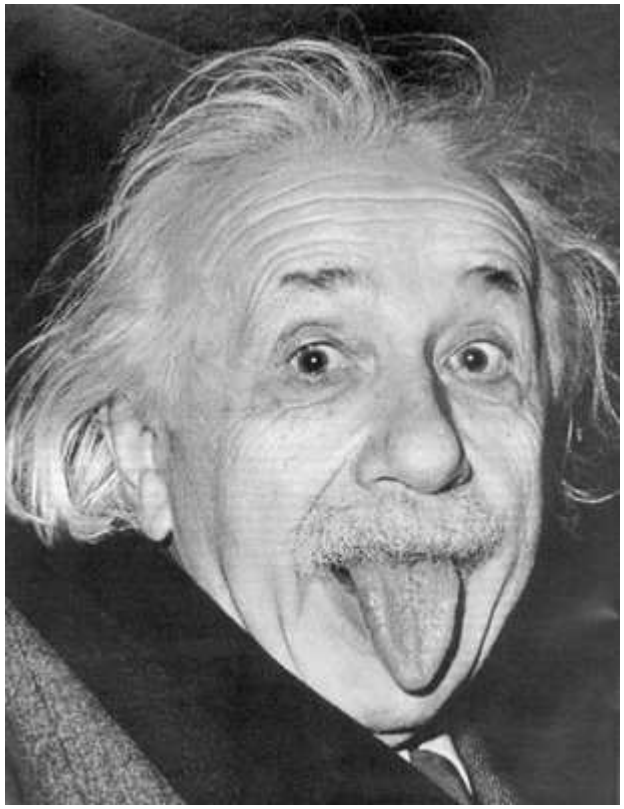
What did you do in your breast unit?



- Elaborate new guidelines as a result of this publication ?
- Discuss all SLNB positive patients patients in multidisciplinary meetings ?
- Wait for more evidence ?

Is the story over ?



The MIRROR retrospective cohort study (Dutch cancer registry)

- Regional recurrences in breast cancer patients with sentinel nodes and micro metastasis Pepels et al Ann Surg January 2012
- 2680 patients 3 cohorts, 2 subgroups in each cohort (SLNB alone or additional axillary therapy by ALND or RT)
  1. Node - after SLNB (n= 857)
  2. Patients with SLNB isolated tumor cells n =795
  3. Patients with SLNB micro metastasis n = 1028
- Median FU : 5.1 years
- 48% of patients received systemic therapy
- Comparison of rates of RR in each group and subgroup (RR could be detected at surgery for breast ipsilateral or contra lateral recurrence)

Results :5 year regional recurrence rate (RRR)

	Number of patients	5 year RRR	HR for RRR
Isolated tumor cells in SLNB	795		
-SLNB alone	345	2%	
-ALND	396	0.9	2.39
-RT alone	54	0	
Micrometastasis in SLNB	1028		**<u>4.39</u>**
-SLND alone	141	5.6%	
-ALND	793	1%	
-RT alone	94	0%	

TABLE 1

Characteristic	N0(i −)(sn)		N0(i +)(sn)		N1(mi)(sn)	
	No Axillary Treatment (N = 732) N (%)	Axillary Treatment (N = 125) N (%)	No Axillary Treatment (N = 345) N (%)	Axillary Treatment (N = 450) N (%)	No Axillary Treatment (N = 141) N (%)	Axillary Treatment (N = 887) N (%)
No. sentinel lymph nodes removed						
Median	2	1	2	2	2	2
Interquartile range	1,2	1,2	1,3	1,2	1,3	1,3
Age at diagnosis, yr						
Median	59	61	58	57	59	56
Range	30–89	34–87	34–93	31–89	36–88	32–89
Tumor size						
≤1 cm	310 (42%)	37 (30%)	91 (27%)	125 (28%)	34 (24%)	197 (22%)
>1 to ≤2 cm	375 (51%)	73 (58%)	201 (58%)	239 (53%)	80 (57%)	539 (61%)
>2 to ≤3 cm	47 (7%)	15 (12%)	53 (15%)	86 (19%)	27 (19%)	151 (17%)
Tumor grade, no. (%)						
1	264 (37%)	54 (44%)	117 (35%)	137 (31%)	41 (30%)	287 (33%)
2	408 (57%)	66 (53%)	211 (62%)	283 (64%)	93 (67%)	543 (62%)
3	45 (6%)	4 (3%)	11 (3%)	22 (5%)	5 (3%)	45 (5%)
Hormone receptor status, no. (%)						
Negative	42 (6%)	9 (8%)	22 (7%)	33 (7%)	11 (8%)	41 (5%)
Positive	661 (94%)	100 (92%)	311 (93%)	407 (93%)	130 (92%)	834 (95%)
Type of breast surgery, no. (%)						
Mastectomy	167 (23%)	57 (46%)	109 (32%)	140 (31%)	40 (28%)	267 (30%)
Breast conserving	565 (77%)	68 (54%)	236 (68%)	310 (69%)	101 (72%)	620 (70%)
Radiation of the breast, no. (%)						
No	185 (25%)	59 (47%)	118 (34%)	136 (30%)	48 (34%)	270 (30%)
Yes	547 (75%)	66 (53%)	227 (66%)	314 (70%)	93 (66%)	617 (70%)
Adjuvant systemic therapy, no (%)						
No systemic therapy	732 (100%)	125 (100%)	260 (75%)	239 (53%)	73 (52%)	283 (32%)
Chemotherapy	0 (0%)	0 (0%)	4 (1%)	14 (3%)	3 (2%)	32 (4%)
Hormonal therapy	0 (0%)	0 (0%)	67 (20%)	143 (32%)	53 (38%)	349 (39%)
Both	0 (0%)	0 (0%)	14 (4%)	54 (12%)	12 (8%)	223 (25%)

Regional Recurrence in Breast Cancer Patients With Sentinel Node Micrometastases and Isolated Tumor Cells.

Pepels, Manon; de Boer, Maaike; Bult, Peter; MD, PhD; van Dijck, Jos; van Deurzen, Carolien; Menke-Pluymers, Marian; MD, PhD; van Diest, Paul; MD, PhD; Borm, George; Tjan-Heijnen, Vivianne; MD, PhD

Annals of Surgery. 255(1):116-121, January 2012.
DOI: 10.1097/SLA.0b013e31823dc616

TABLE 1 . Baseline Characteristics of 2680 Patients With Early Stage Breast Cancer According to Axillary Lymph Node Status

TABLE 2

Variable	N0(i-)(sn)		N0(i+)(sn)		N1(mi)(sn)	
	Hazard Ratio for Regional Recurrence	95% CI	Hazard Ratio for Regional Recurrence	95% CI	Hazard Ratio for Regional Recurrence	95% CI
No axillary treatment	1.08	0.23–4.98	2.39	0.67–8.48	4.39	1.46–13.24
Young age at diagnosis (per year)	1.08	1.02–1.12	1.06	1.00–1.12	1.05	1.00–1.10
Doubling of tumor diameter	1.22	0.48–3.05	3.80	0.74–19.42	7.91	1.36–45.91
Histological grade 2 vs 1	NE		1.60	0.32–7.96	4.90	0.63–38.33
Histological grade 3 vs 1	NE		NE		25.05	1.26–497.18
Negative hormone receptor status	1.23	0.35–4.39	5.92	1.52–23.00	4.96	1.48–16.62
No adjuvant systemic therapy	NE		1.03	0.28–3.85	1.36	0.47–3.99
No breast irradiation	1.96	0.73–5.29	1.54	0.44–5.39	1.01	0.36–2.88

NE indicates not estimable.

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TABLE 2 . Cox Proportional-Hazards Model of the Effect of Variables on Regional Recurrences in Patients With Negative SLNs, Patients With SLN Isolated Tumor Cells, and Patients With SLN Micrometastases

The MIRROR Study

Other risk factors associated with RR in patients not receiving axillary complementary treatment:

- Doubling tumor size
- Histopathological grade 3
- Negative hormonal receptor status
- No adjuvant chemotherapy
- No radiation therapy

Conclusions: towards a tailored surgery for breast cancer

- Surgeons face ethical dilemma between offering to more patients the benefits of a “glamorous” surgery and a long term better security
- Multidisciplinary approaches in specialized breast units for better selection of patients are mandatory
- For individual patients, all factors have to be taken into account to offer most optimal, personalized treatment strategies