



Current challenges in breast cancer surgery (part I)

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Paris, February 2013

Current challenges in breast cancer surgery

Contents

- **From scalpel to pills?**
- **Approach to the axilla**
- **Mastectomy trends**
- **Nipple-areola Skin Sparing Mastectomy (NASSM)**

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**Surgery for breast cancer will soon be
replaced by personalized systemic
treatment-only**

¿True or False?

Current challenge for the breast surgeon

TO KEEP THE JOB?

Locoregional treatment of breast cancer: LINEAR THINKING

Overtreatment

**Radical
Mastectomy**

**Modified
Radical
Mastectomy**

**Breast
conservation**

**Sentinel
lymph node
biopsy**

**NO ALND
NO RT**

1900

1950

1990

2000

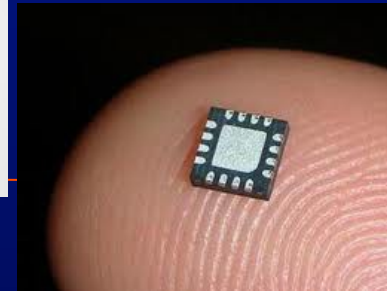
2013

Undertreatment

History of computer technology? LINEAR THINKING

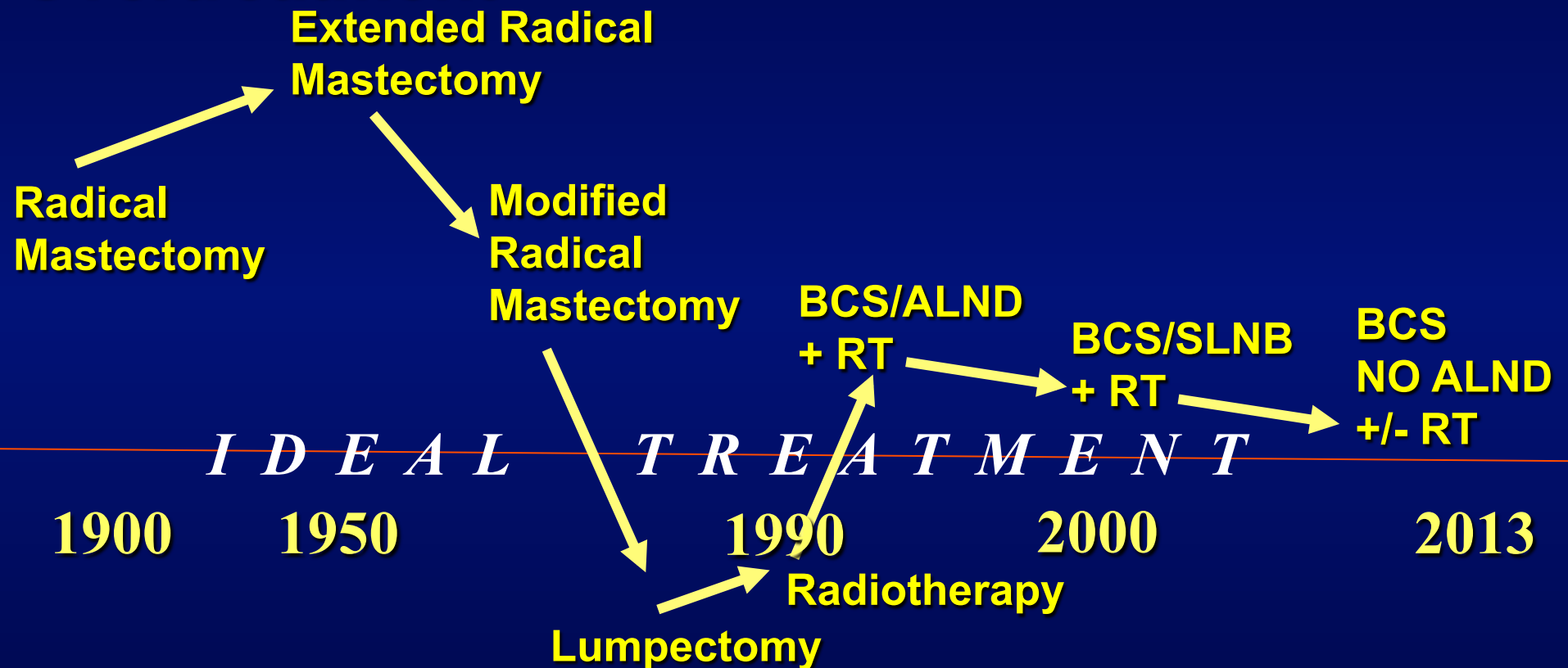


Plate no. ENRAC digital computer in the U.S.A., showing a bank of magnetic tape storage units on the right



Locoregional treatment of breast cancer: GLOBAL THINKING

Overtreatment



Undertreatment

Why is it that the role of surgery has been overshadowed?

- **1990s role of local control was minimized**
- **BC = systemic disease since its inception (Fisherian concept)^{1,2}**
- **Positive results of clinical trials on adjuvant systemic therapies³**

1. Fisher B. Int J Radiat Oncol Biol Phys 1977; 2:989–92

2. Fisher B. World J Surg 1977; 1:354–6

3. EBCTCG. Lancet 1992; 339: 1–15

Systemic BOOM!

Chemo

- CMF¹
- Anthracyclines¹
- Taxanes²

Hormonal

- Tamoxifen¹
- Anastrozol, Letrozol, Exemestane
- Triptorelin, Goserelin

Immune therapy

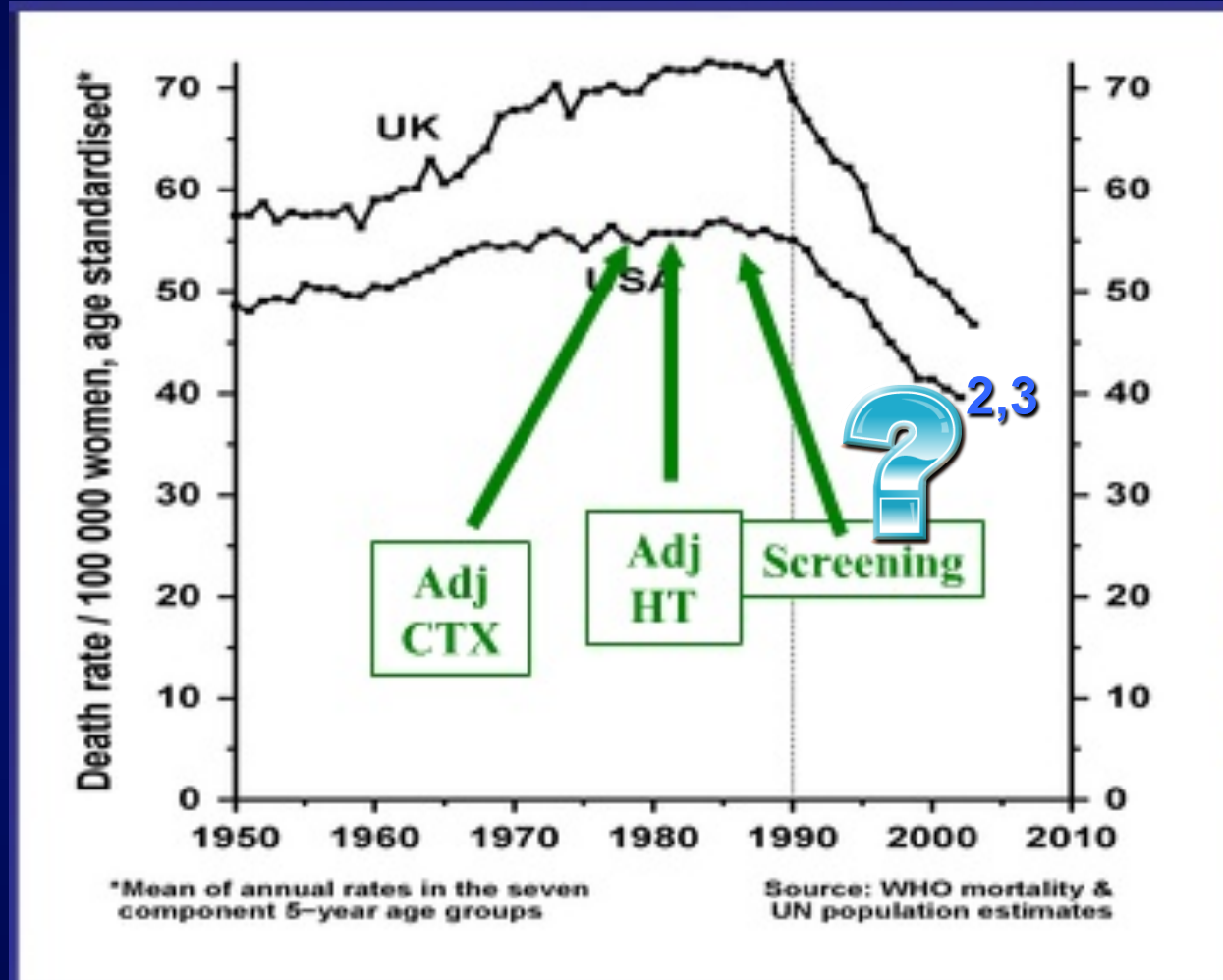
- Trastuzumab
- Bevacizumab

... and the story continues

1. EBCTCG. Lancet 2005;365:1687-717

2. Holmes FA. J Natl Cancer Inst 1991;83:1797-805

Decrease in BC mortality in UK and USA age 35-69 years¹



1. Modified from Peto R et al. Lancet 2000; 355(9217):1822
2. Kalager M. N Engl J Med 2010;363:1203-10
3. Bleyer A. N Engl J Med. 2012;367(21):1998-2005

Goal of systemic agents + COMBINED

Lapatinib
Triptorelin
Trastuzumab
Bevacizumab
Anastrozole
Exemestane
Letrozole
Goserelin
Paclitaxel
Docetaxel
Tamoxifen
Epirubicin
Metotrexate
Doxorubicin
Cyclophosphamide
5-FU

+ Surgical excision

Importance of local control

Dec 2005 EBCTCG¹:

- Meta-analysis of 78 RCTs
- >42,000 patients

**Improvement
of local control
5 years**



**Significant
improvement
BCS & OS
15 years**

**Updated meta-analysis EBCTCG
confirms findings²**

1. EBCTCG. Lancet 2005;366:2087–106
2. EBCTCG. Lancet 2011;378:1707–16

**Importance of
local control**



**Importance of
Surgery & RT**

1. EBCTCG. Lancet 2005;366:2087–106
2. EBCTCG. Lancet 2011;378:1707–16

Not so near future

We may identify a subset of tumors that could be managed by some type of non-surgical ablation (likely small subset)

SURGERY WILL STILL REPRESENT THE ONLY TREATMENT MODALITY WITH A CURATIVE ATTEMPT FOR MOST CASES

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Approach to the axilla

- **Controversial issue for the last three decades^{1, 2}**
- **Treatment, staging?**

1. Harris, J.R. Br. Cancer Res. Treat. 1985;5:17

2. Fisher B. NSABP-04. N Engl J Med 2002;347:567-75

Background

- **SLNB is a reliable method for staging the axilla¹⁻⁴**
- **Axillary recurrence is a rare event in patients with (+)SLNB who undergo ALND¹⁻⁴**

1. Kim T. Cancer 2006;106:4–16

2. Krag DN. Lancet Oncol 2010;11: 927–33

3. Veronesi U. Ann Surg 2010;251(4):595-600

4. Naik AM. Ann Surg 2004;240:462–471

Background

- **Seminal studies have shown that axillary recurrence is much lower than expected in patients with (+) axillary status who forgo ALND¹**
- **NSABP-32 axillary recurrence <1%²**
- **Long standing question:
Could ALND be omitted in patients with (+)SLN?**

1. Fisher B. NSABP-04. N Engl J Med 2002;347:567-75
2. Krag DN. Lancet Oncol 2010;11:927-33

FREQUENCY OF NON-SENTINEL NODE METASTASES IN MACROMETASTASIS TO SN

Author	Tumor size	No. of patients	Frequency of non-SN metastases (%)
Chu et al. (1999)	T1	40	48
	T2-3	49	59
Reynolds et al. (1999)	T1	18	50
	T2	15	87
Viale et al. (2005)	T1-2	794	50
Menes et al. (2005)	T1-3	63	46

FREQUENCY OF NON-SENTINEL LYMPH NODE METASTASES IN MICROMETASTASIS TO SN

Author	Tumor size	No. of patients	Frequency of non-SN metastases (%)
Chu et al. (1999)	T1	46	4
	T2-T3	23	13
Reynolds et al. (1999)	T1	18	0
	T2	9	67
Viale et al. (2001)	T1-2	93	22
	T2	17	24
den Bakker et al. (2002)	T1	22	14
	T2-3	10	80
Viale et al. (2005)	T1-2	318	21
Menes et al. (2005)	T1-3	30	20

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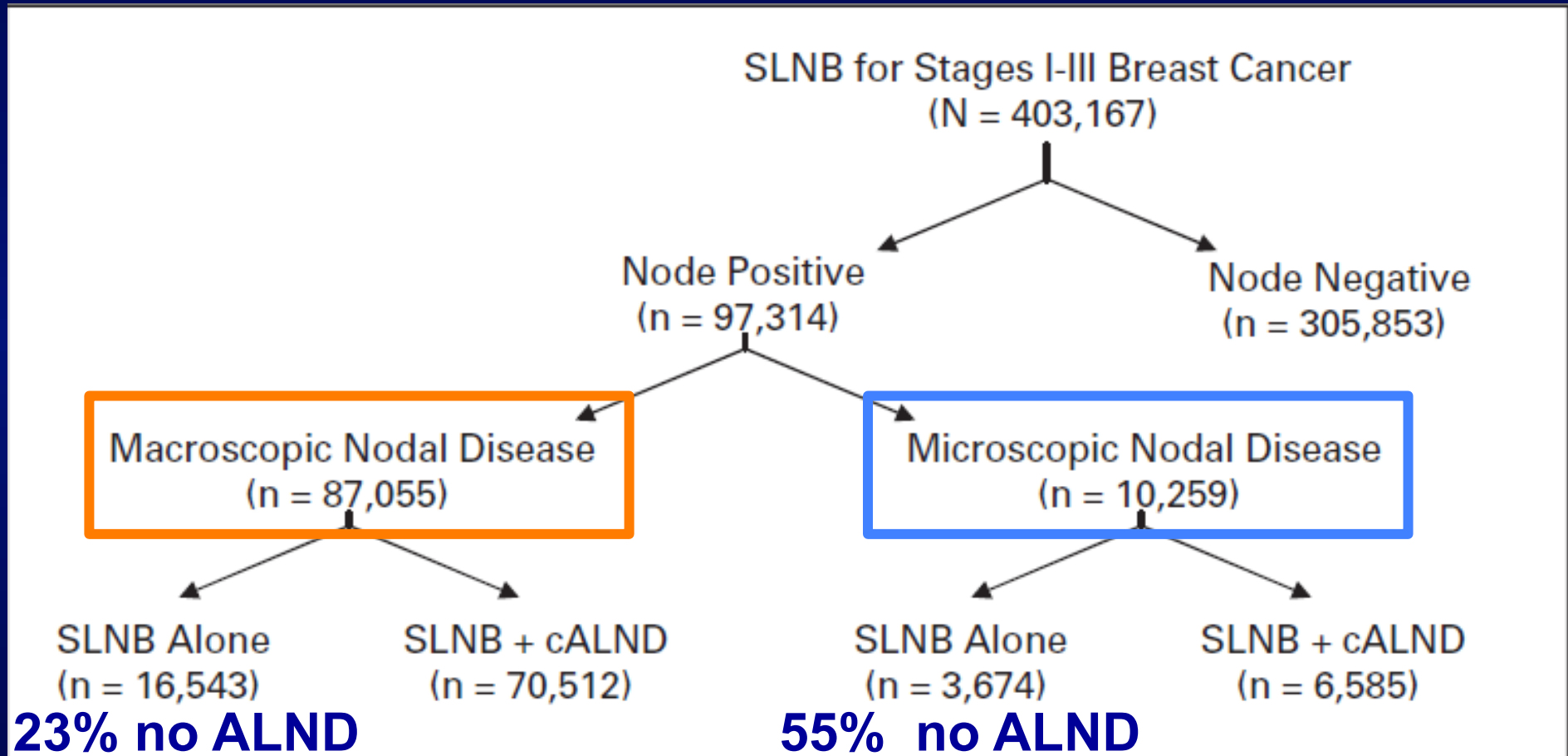
ORIGINAL REPORT

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

**Bilimoria KY. J Clin Oncol 2009;27(18):2946-53
US National Cancer Database**

US National Cancer Data Base (NCDB) Women with +SN 1998-2005 Median follow-up 63 months



Bilimoria KY. J Clin Oncol 2009;27(18):2946-53
US National Cancer Database

(+) SLN ± ALND

	Axillary Recurrence	5-yr relative survival
Micromets to SLN (≤ 2 mm)		
SLNB-only (N = 802)	0.4%	99%
SLNB + ALND (N = 2,357)	0.2%	98%
<i>P</i>	0.18	0.81
Macromets to SLN (> 2 mm)		
SLNB-only (N = 5,596)	1.0%	90%
SLNB + ALND (N = 22,591)	1.1%	89%
<i>P</i>	0.86	0.18

**Bilimoria KY. J Clin Oncol 2009;27(18):2946-53
US National Cancer Database**

**US National Cancer Data Base (NCDB)
Women with +SN 1998-2005
Median follow-up 63 months**

**ALND did not improve outcomes in pts with
micromets to SN**

**However, there was a non-significant trend
to better outcomes for ALND (vs SNB alone)
in those with macroscopic disease to the SN
(HR for axillary recurrence 0.58, 95% CI 0.32-1.06; overall
survival 0.89, 95% CI 0.76-1.04)**

**Bilimoria KY. J Clin Oncol 2009;27(18):2946-53
US National Cancer Database**



IBCSG

International Breast Cancer Study Group

Trial 23-01

(Closed 02/2010 at
n=934)

T ≤ 5 cm cN0

SNB

MICROMETASTASES

R

FOLLOW UP

**AXILLARY
DISSECTION**

IBCSG trial 23-01

Sites of first failure

**Very low number of locoregional
events in both groups**

(official report still pending)

IBCSG trial 23-01

(official report still pending)

	5y-DFS	5y-OS
SLNB-only (N = 467)	88.4%	98%
SLNB + ALND (N = 464)	87.3%	98%

Trial Z0011

(Closed 12/04 at n=891)

Clinical T1-2, N0, M0

+SN by H&E staining

R



Arm1

ALND

Arm2

NO ALND

**BCS & Whole breast RT ±
systemic adjuvant therapy**

Follow up

ACOSOG

American College of Surgeons Oncology Group

Giuliano A. Ann Surg 2010;252:426-433

Giuliano A. JAMA 2011;305:569-75

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§§*

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

A Randomized Clinical Trial

**(+) SLN ± AD
(Z0011)
median f/u 6.3y**

	Locoregional Recurrence¹	Axillary Recurrence¹	Overall Survival²
SLNB-only (N = 425)	2.8%	0.9%	92.5%
SLNB + ALND (N = 388)	4.1%	0.5%	91.8%

1. Giuliano A. Ann Surg 2010;252:426-433

2. Giuliano A. Oral presentation Z0011. ASCO 2010

Z0011

“Despite the widely-held belief that AD improves survival” no significant survival differences were found between ALND and non ALND groups in SN-positive women

Z0011

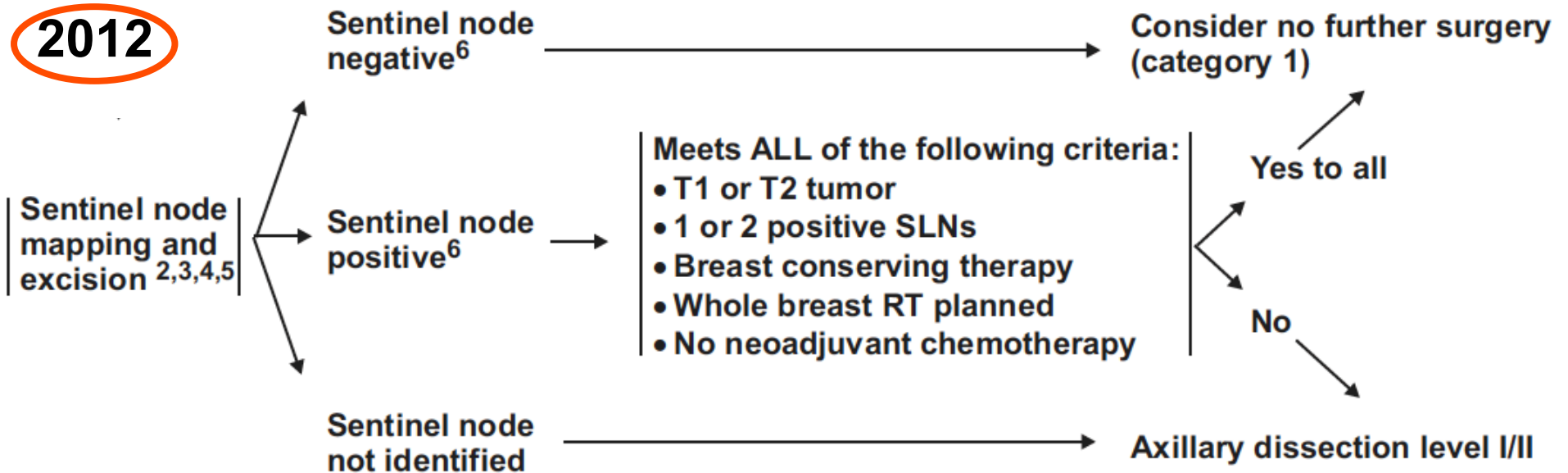
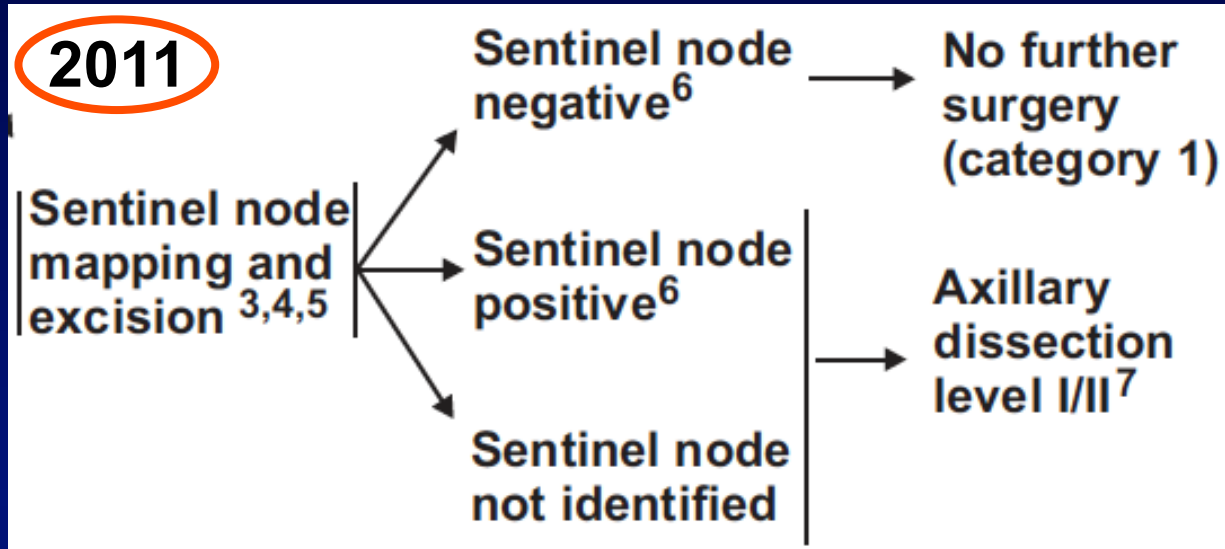
Change of practice Approach to the axilla

- **MSKCC, September 2010¹**

- **MDACC, early 2011²**

1. Morrow M. SSO Meeting, March 2011
2. Caudle AS. Ann Surg Oncol. 2011 Sep;18(9):2407-12

Axillary Staging after Z0011



Have you changed your practice?

To keep in mind from Z0011

- **Mostly cases with small to medium size tumors (~70% T1)**
- **All underwent BCS with WBRT**
- **SNL(s) only site of metastasis in 73% of cases**
- **Burden of axillary disease in cases with positive non-SLNs was very low**

To keep in mind from Z0011

ALND = USELESS?



What it really tells us:

- **In patients with small tumors**
- **No axillary disease**
- **Or very low disease burden in the axilla**
- **ALND offers no advantage**

ALND after (+)SLNB MUST STILL be performed:

- **$\geq T3$**
- **Mastectomy is planned (therefore, not receiving postoperative RT)**
- **Using any type of accelerated partial-breast irradiation (APBI)**
- **Neoadjuvant systemic therapy**
- **≥ 3 (+)SLNs on permanent section (ALND at a second operation)**

Some caveats with Z0011

Underrepresented groups:

- **Very young patients (~65% >50y)**
- **Large tumors (≥ 4 cm) (~70% T1)**
- **ER(-) tumors (16%)**

Longer follow-up (?)

Most patients received chemotherapy (97%)

Z0011

... application in Europe?

- **pN1 \neq chemotherapy (not necessarily)**
- **Same locoregional control without systemic therapy?**
- **Lack of information about remaining nodes in the axilla may interfere with treatment decisions**
- **Omission of AD may fail the indication of ACT in some patients with ER(+)/HER2(-) tumors (16%)¹ (European context)**

AXILLARY SURGERY THE FUTURE

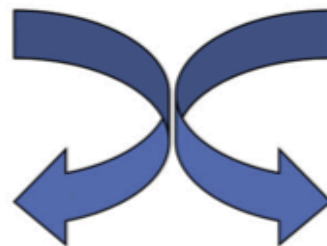
Trial SOUND

Sentinel node vs Observation after axillary Ultra-souND

- Patients with breast cancer ≤ 2.0 cm
 - Any age
- Candidates to Breast Conserving Surgery
- Negative preoperative axillary assessment
(negative ultra-sound of the axilla or negative FNAC of a single doubtful axillary lymph node)



Randomization



SNB policy

No axillary surgery

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THANK YOU