Sentinel Node Preoperative or Intraoperative?

Surgical Challenges

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The surgeon, above all in high volume centres, is faced with problems of

Resourses

Availability of operating room

Long waiting list

Limited time of operating room

The guiding principle in his/her profession is obviously absolutely …

What's best for the patient !

Inevitably he/she is forced to consider the resources at his/her disposition

Regarding this topic there are two situations:

Primary Surgery (early breast cancer)

Primary Chemotherapy (T2>3 cm, LABC)

Primary Surgery

The purpose of the pre or intraoperative exam is to determine:

To whom to perform axillary dissection

Primary Chemotherapy

The purpose of the pre or intraoperative exam is to determine:

To whom not to perform axillary dissection

Primary Surgery

SLNB preoperative o intraoperative??

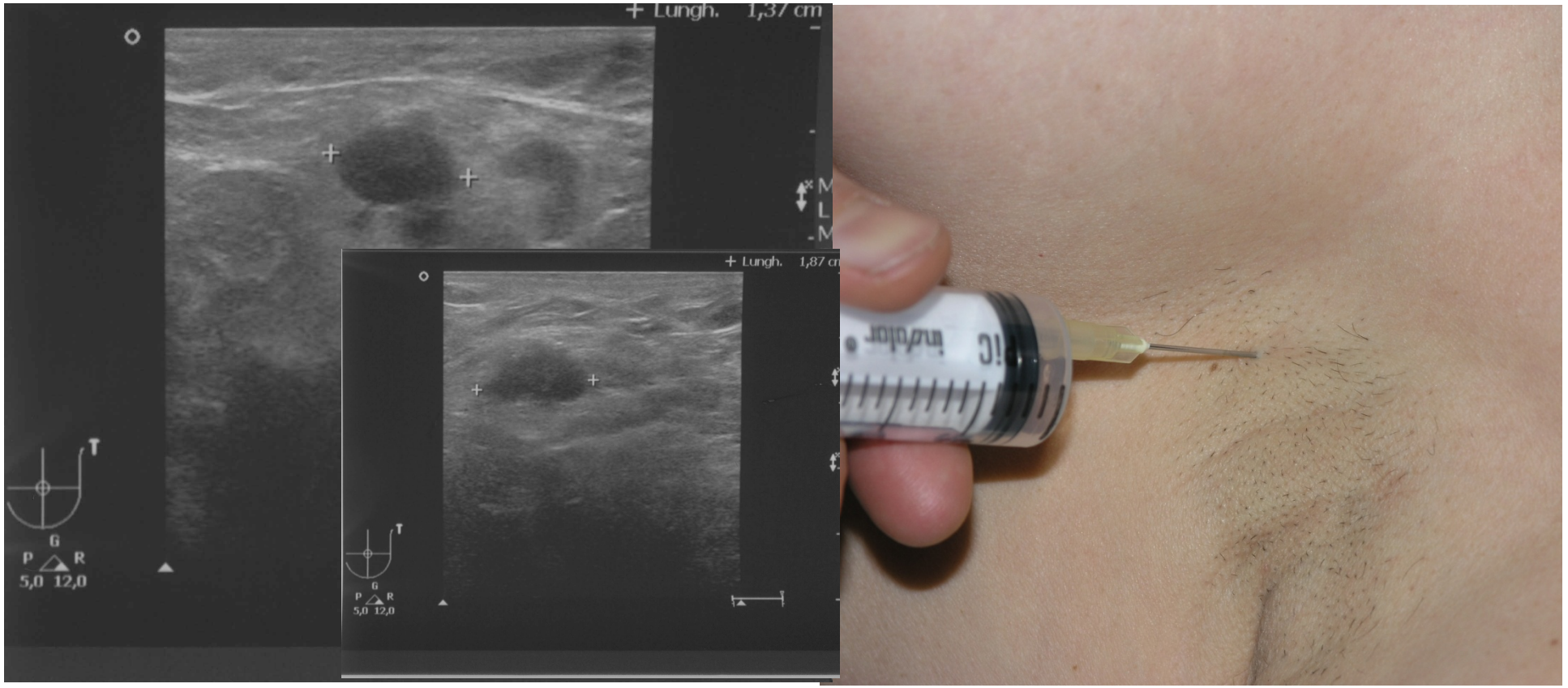
The problem concerns

cN0 patients

After a clinical and ecographic evaluation with FNAC.
If the preoperative diagnosis is N+: AD is indicated

cN0 and doubtful cases

Axillary Ecography and FNAC



Preoperative Sentinel Node Biopsy

In Local Anesthesia

GA is not reccomended due to economic resources, problems of time, availability of OR, 2 GAs in a short period, discomfort for the patients

Contraindications

- obesity
- anxiety

….in local anesthesia

Limits

- Two operations needed
- Experts surgeons (rapid and precise operation)
- Postoperative fibrosis if AD is needed
- Pain
- Organizational problems (availability of dedicated spaces)

Advantages for the Patient

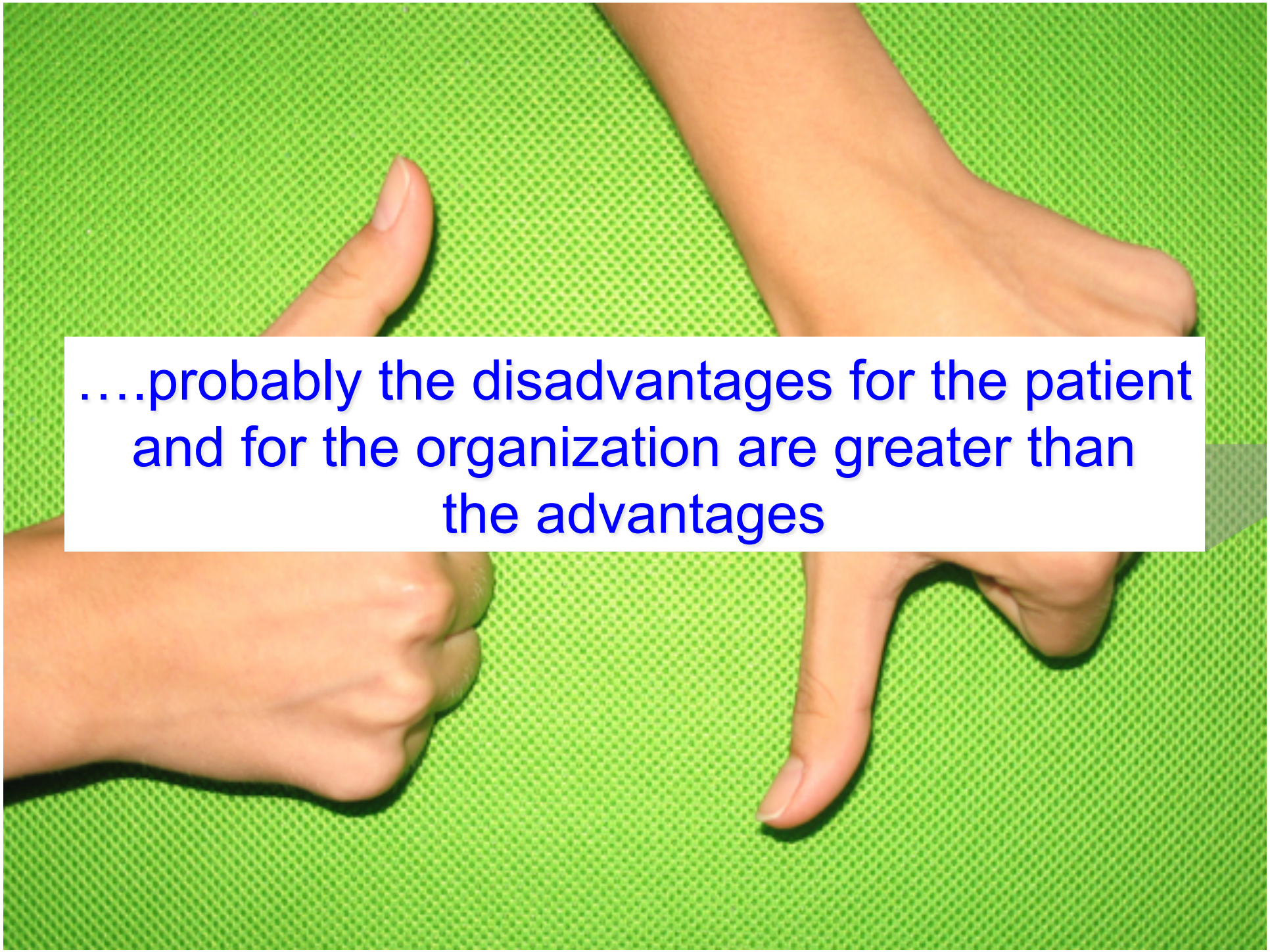
- Complete preoperative staging and the possibility of exactly deciding on surgical program

- Avoiding false negatives

Advantages for the Surgeon

- No loss of time during the operation (oncoplastic)

- SLNB is feasible even where Pathological Anatomy Unit does not exist (Breast Unit)


….probably the disadvantages for the patient and for the organization are greater than the advantages

Intraoperative examination

Different methods:

- Total Examination
- on 3-5 slices *
- OSNA

Advantages

- Axillary dissection in the same operation
- Only one hospitalization
- Low costs
- Psychological compliance for the patient
- Positive effect on waiting list

Disadvantages

- False negative

- Prolonging surgical time, even with the method of 3-5 slices in particular if SN are more than one

Intraoperative examination

What about accuracy?….

Very good for macrometastases (> 90%)

Not so good for micrometastases (20-40%)

ORIGINAL ARTICLE

Effectiveness of Sentinel Lymph Node Intraoperative Examination in 753 Women With Breast Cancer

Are We Overtreating Patients?

Mario Taffurelli, MD, Isacco Montroni, MD,* Donatella Santini, MD,† Monica Fiacchi, MD,* Simone Zanotti, MD,* Giampaolo Ugolini, MD, PhD,* Margherita Serra, MD,* and Giancarlo Rosati, MD, PhD**

Annals of Surgery • Volume 255, Number 5, May 2012

…but when do we still need informations from intraoperative histological examination related to axillary dissection?????

Micrometastases???

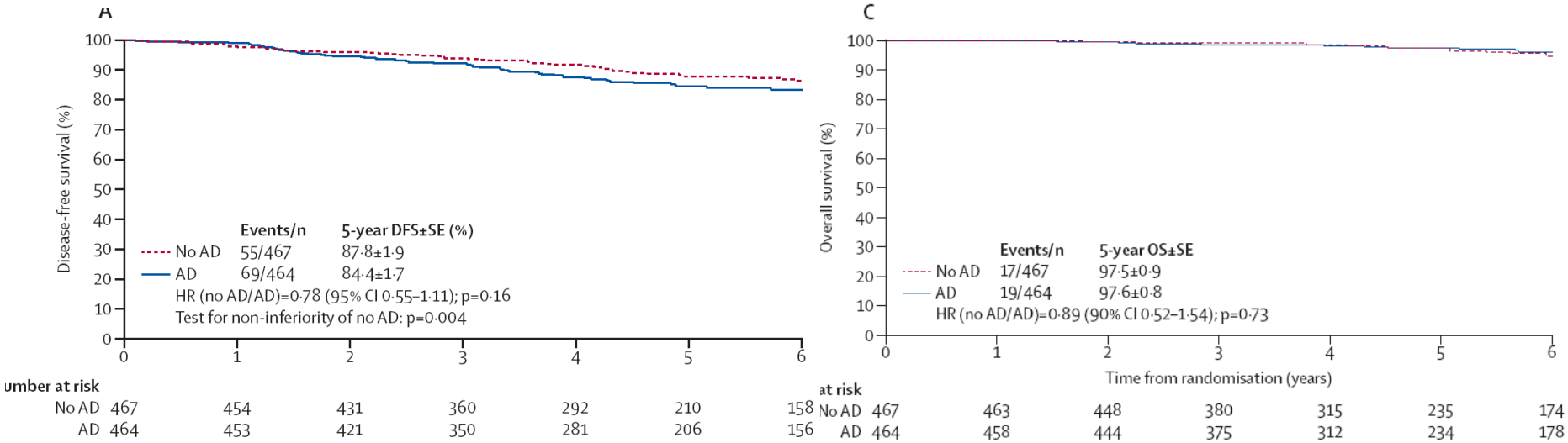
Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23–01): a phase 3 randomised controlled trial

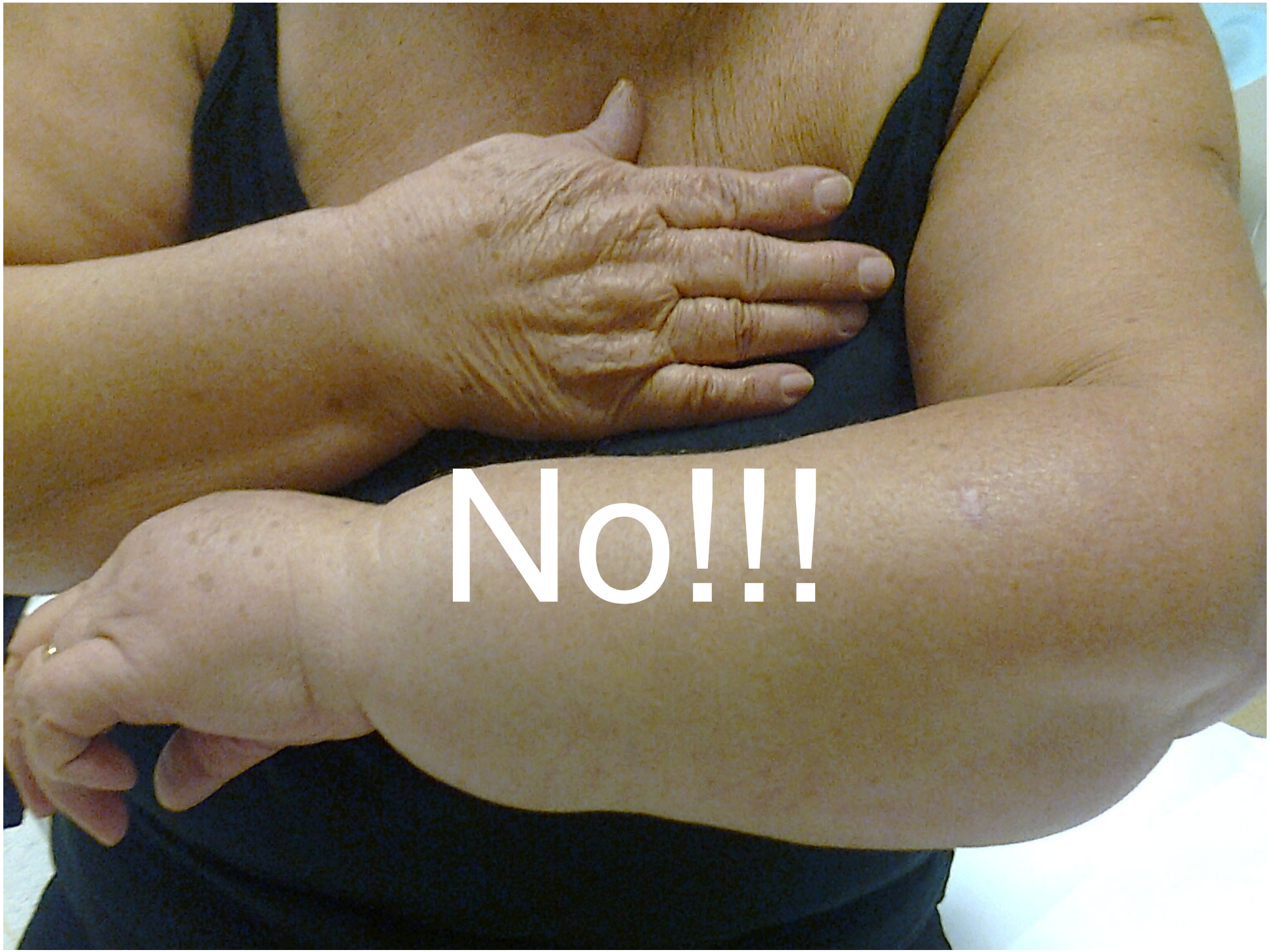
Viviana Galimberti, Bernard F Cole, Stefano Zurrida, Giuseppe Viale, Alberto Luini, Paolo Veronesi, Paola Baratella, Camelia Chifu, Manuela Sargenti, Mattia Intra, Oreste Gentilini, Mauro G Mastropasqua, Giovanni Mazzarol, Samuele Massarut, Jean-Rémi Garbay, Janez Zgajnar, Hanne Galatius, Angelo Recalcati, David Littlejohn, Monika Bamert, Marco Colleoni, Karen N Price, Meredith M Regan, Aron Goldhirsch, Alan S Coates, Richard D Gelber, Umberto Veronesi, for the International Breast Cancer Study Group Trial 23–01 investigators

Summary

Background For patients with breast cancer and metastases in the sentinel nodes, axillary dissection has been standard treatment. However, for patients with limited sentinel-node involvement, axillary dissection might be overtreatment.

Lancet Oncol 2013; 14: 297–305
Published Online




No!!!


Macrometastases????

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

A Randomized Clinical Trial

Armando E. Giuliano, MD
Kelly K. Hunt, MD
Karla V. Ballman, PhD
Peter D. Beitsch, MD
Pat W. Whitworth, MD
Peter W. Blumencranz, MD
A. Marilyn Leitch, MD
Sukamal Saha, MD
Linda M. McCall, MS
Monica Morrow, MD

Context Sentinel lymph node dissection (SLND) accurately identifies nodal metastasis of early breast cancer, but it is not clear whether further nodal dissection affects survival.

Objective To determine the effects of complete axillary lymph node dissection (ALND) on survival of patients with sentinel lymph node (SLN) metastasis of breast cancer.

Design, Setting, and Patients The American College of Surgeons Oncology Group Z0011 trial, a phase 3 noninferiority trial conducted at 115 sites and enrolling patients from May 1999 to December 2004. Patients were women with clinical T1-T2 invasive breast cancer, no palpable adenopathy, and 1 to 2 SLNs containing metastases identified by frozen section, touch preparation, or hematoxylin-eosin staining on permanent section. Targeted enrollment was 1900 women with final analysis after 500 deaths, but the trial closed early because mortality rate was lower than expected.

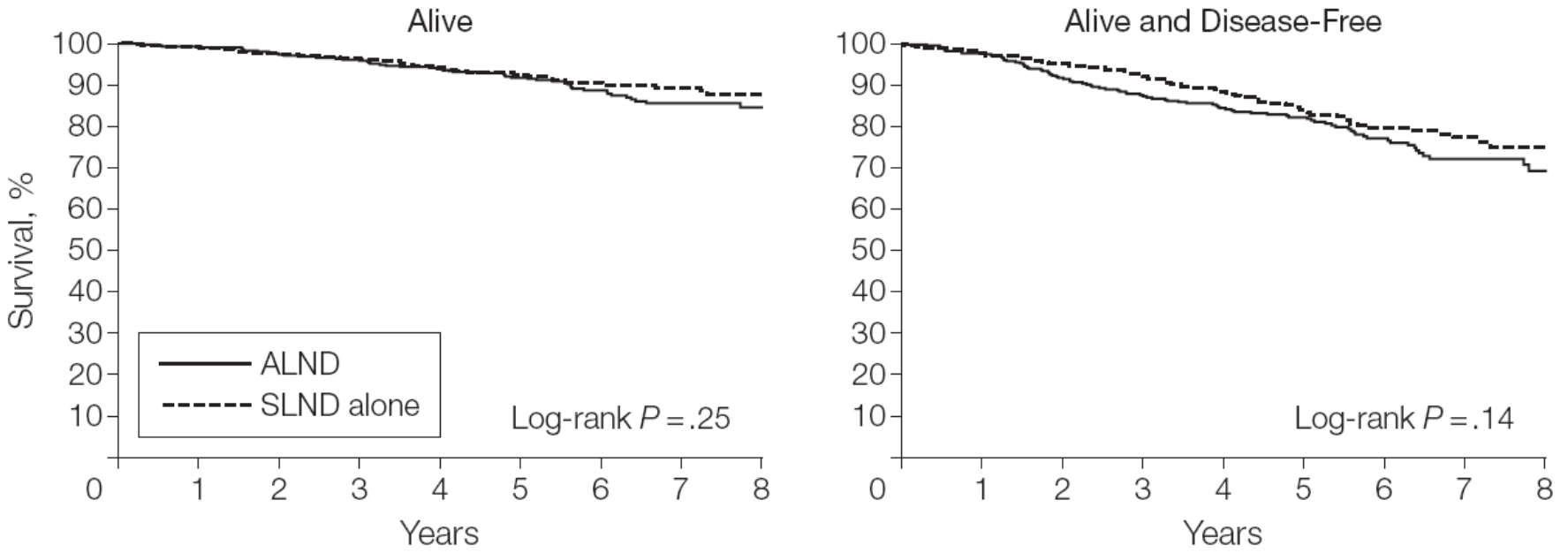
Interventions All patients underwent lumpectomy and tangential whole-breast irra-

…in this setting:

- T1-2 cN0 M0
- Conservative Surgery + Radiotherapiy (WBI)
- 1-2 SLN + (EE)

Random: Axillary Dissection VS No Dissection

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

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

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

Giuliano AE, 2011

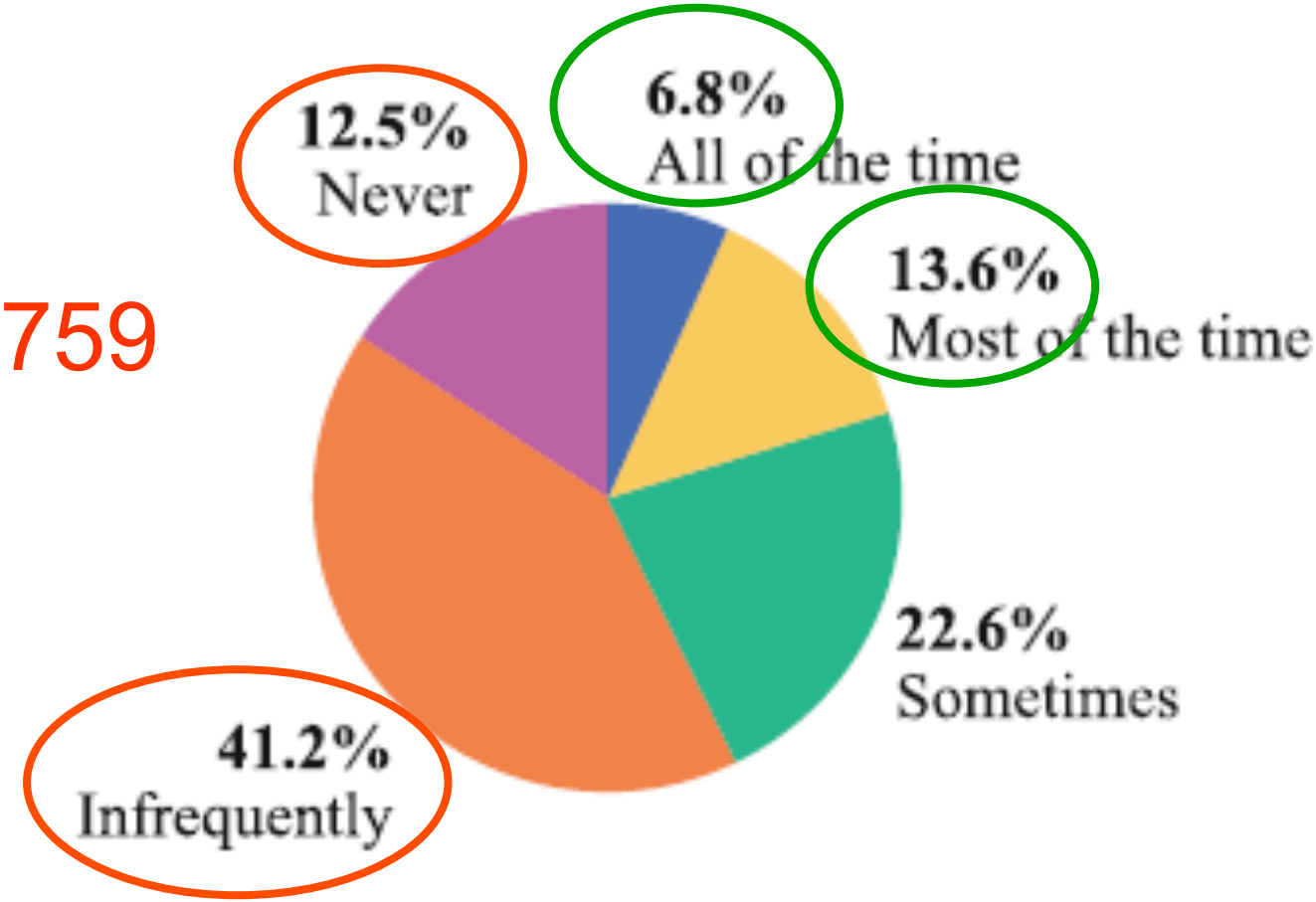
…but when do we still need informations from intraoperative histological examination related to axillary dissection?????

- Macrometastases in patients operated on for Mastectomy

- Macrometastases in patients operated on for Conservative Surgery ?????

Within the Z0011 trial, who still performs an axillary dissection???

849/2759



Gainer SM, 2012

The American Journal of Surgery (2012) 203, 618–622

181 answers

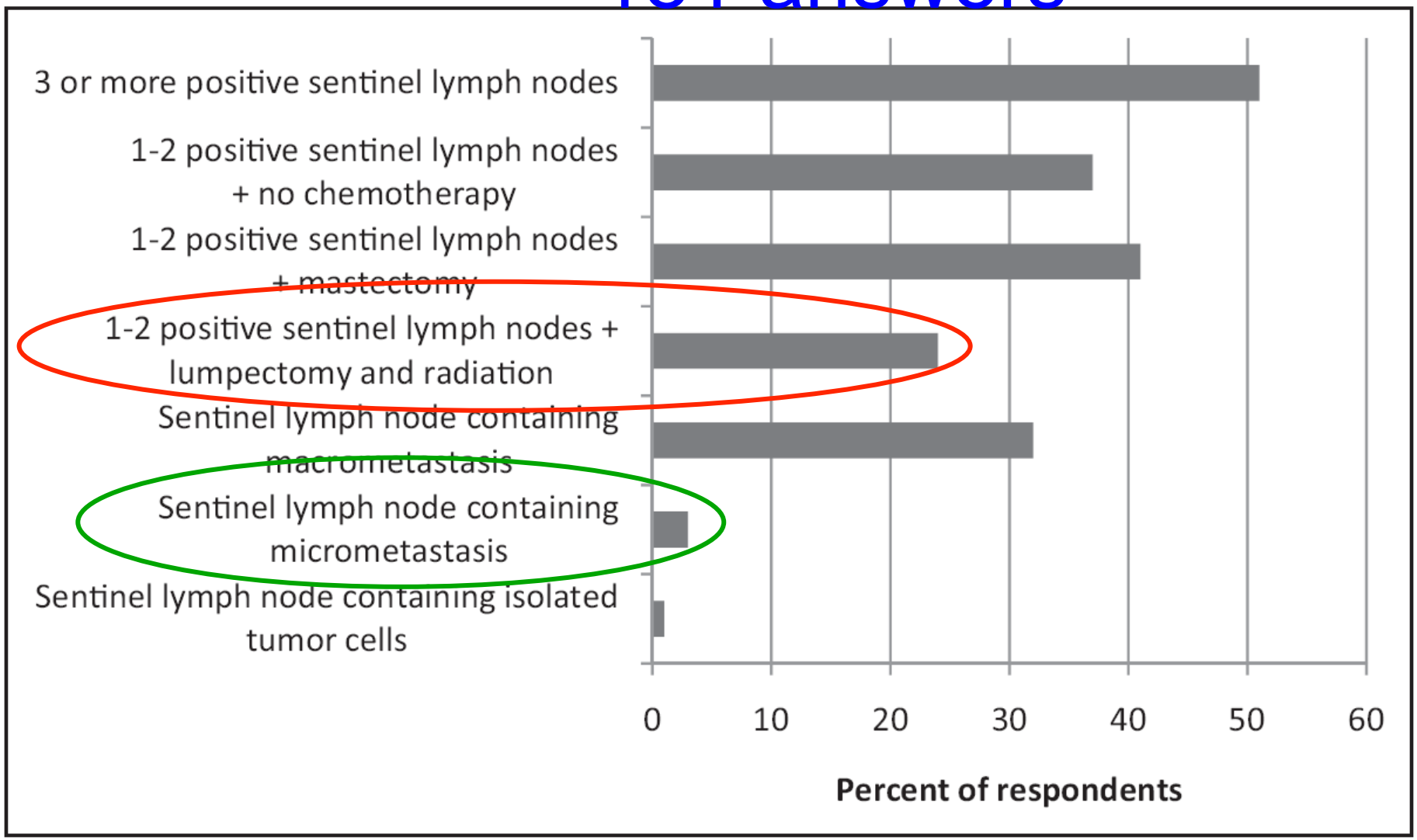


Figure 1 Reported indications for completion axillary dissection.

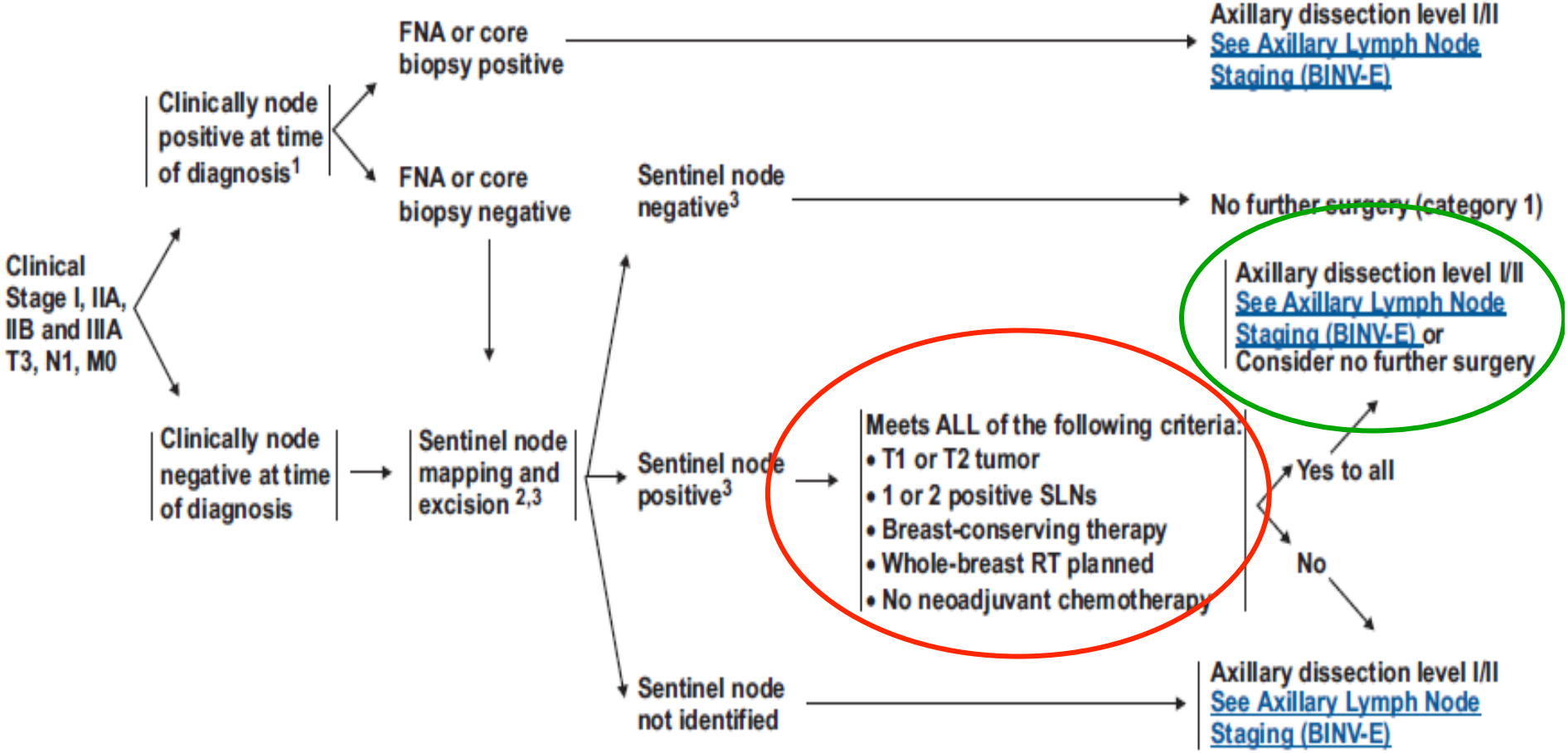
Massimino KP, 2012

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2013
Invasive Breast Cancer

NCCN Guidelines Index
Breast Cancer Table of Contents
Discussion

SURGICAL AXILLARY STAGING - STAGE I, IIA, IIB and IIIA T3, N1, M0



To which patients can we spare Intraoperative examination today???

T1a, T1b (?)

Breast Unit Sant'Orsola-Malpighi Hospital Bologna

(Chief: Prof. M. Taffurelli)

2010-2013: T1N0 513 cases

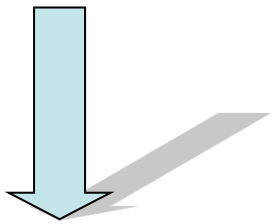
	n.cases	SLNB+ (M)	%
T1a:	42	- (3m)	-
T1b:	197	26 (15m)	13.1 (9.1)
T1c:	274	65 (38m)	23.7 (20)

To which patients can we spare Intraoperative examination today???

Histotypes having a good prognosis (tubular, mucoid, luminal A) and early breast cancer in elderly women

…but at this point, the Surgeon always has to know the biopathological characterization of the tumor, before the operation

Preoperative Core biopsy and biopathological characterization for all cases cN0



Surgery guided by biology

…..But, can we afford it ????

Costs

- Biopathological characterization only in core biopsy or in the whole neoplasia??? (Ki 67, HER 2)
- Organizational problems
- Small tumors

Primary Chemotherapy (NAC)

The goal of SLNB is not to perform axillary dissection

- SLNB in the patients treated with NAC is still a gray area in the surgical treatment of breast cancer

- One of the main reasons about the incertainty of the procedure is that chemotherapy might damage and change the lymphatic drainage from tumors

Four meta-analyses confirm the feasibility and accuracy of SLNB in the NAC setting

(Xing Y, 2006; Kelly AM, 2009;Van Deurzen CH; 2009, Tan VK, 2011)

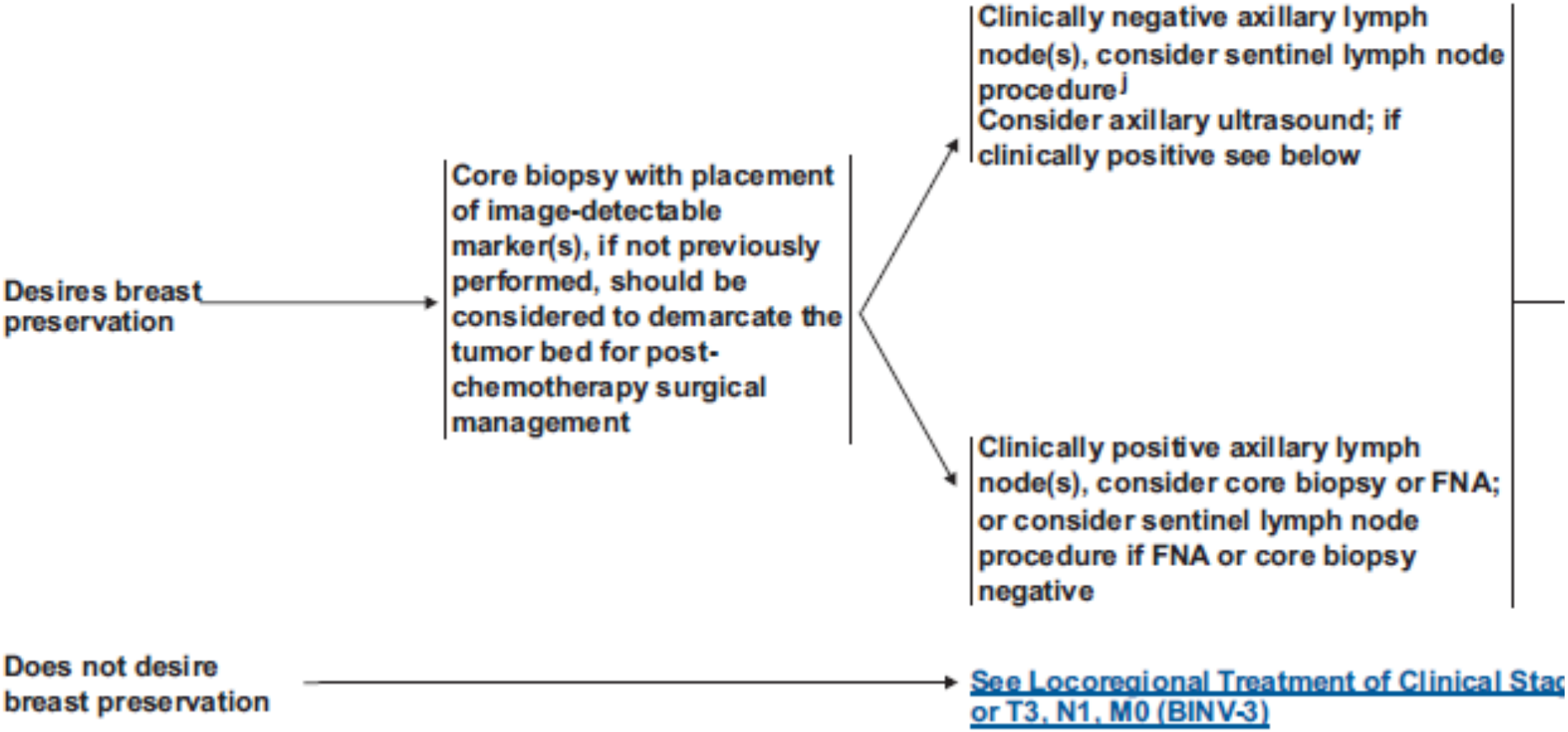
But when???

SLNB before or after NAC with FS?

…and in which patients???

cN0 or cN1 too ??????????

Preoperative Chemotherapy Breast and Axillary Evaluation



SLNB before NAC

(If SLN is negative : no AD; if positive AD)

Few studies, with few patients !!!

Advantages

- High DR (integral lymphatic vessels): 98-100%
- Low False Negative Rate

Ollila DW, 2005; Cox CE, 2006; van Rijk, 2006;Kilbride KE,2008; Schrenk P, 2008; Grube BJ, 2008 ;Menard JP, 2009;

….before

Table 2. Studies on sentinel lymph node biopsy before neoadjuvant chemotherapy

First author[Ref.]	Year	Stage	No. of patients	Identification rate	False-negative rate
Ollila[16]	2005	T2–3, >3.5 cm	21	100%	0%
Cox[17]	2006	Stage II or III, >4.5 cm, N0	47	98%	NS
van Rijk[18]	2006	T2N0	25	100%	NS
Kilbride[19]	2008	T1–4, N0–1	44	98%	NS
Schrenk[20]	2008	T2–3, N0–1	45	100%	0%
Menard[21]	2009	>3.0 cm, N0	31	100%	0%
Grube[22]	2008	Stage I–III, N0	55	100%	NS

ALND, axillary lymph node dissection; NS, not stated

Shimazu K, 2011

SLNB before NAC

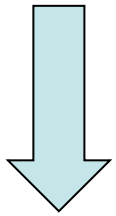
(If SLN is negative : no AD; if positive AD)

Disadvantages

- Two operations
- Delay in starting the CHT
- Loss of those patients with axillary downstaging (20-44%)

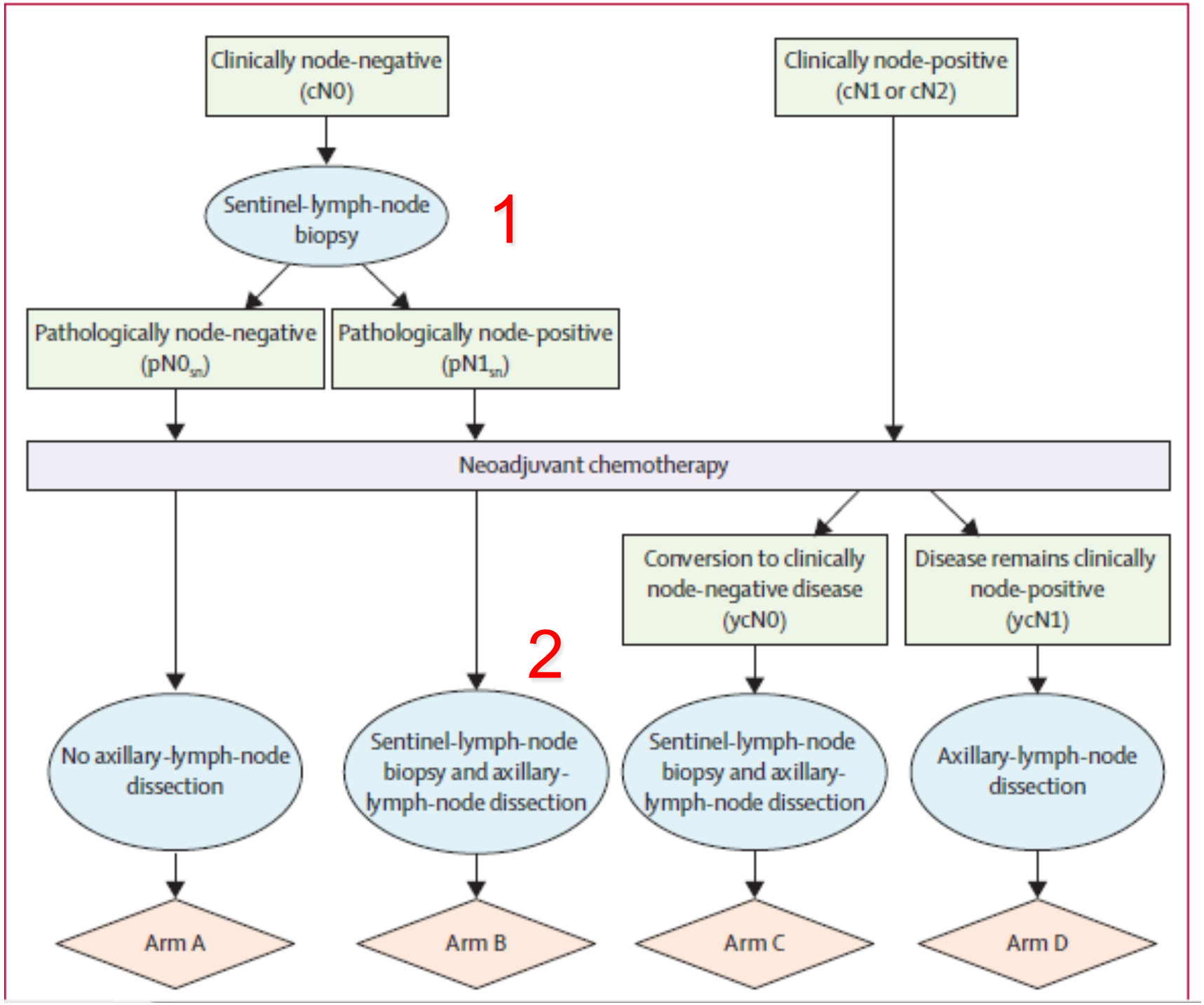
…in order not to lose those patients, performing an inopportune dissection….

Repetition of SLNB after NAC in SN+



SENTINA TRIAL

Kuehn T, 2013


Clinically node-negative (cN0)
Clinically node-positive (cN1 or cN2)
Sentinel-lymph-node biopsy
1
Pathologically node-negative ($pN0_{sn}$)
Pathologically node-positive ($pN1_{sn}$)
Neoadjuvant chemotherapy
Conversion to clinically node-negative disease (ycN0)
Disease remains clinically node-positive (ycN1)
2
No axillary-lymph-node dissection
Sentinel-lymph-node biopsy and axillary-lymph-node dissection
Sentinel-lymph-node biopsy and axillary-lymph-node dissection
Axillary-lymph-node dissection
Arm A
Arm B
Arm C
Arm D

Repeat SLNB after NAC

Low DR (60.8%) ; FNR (51.6%) Arm B

Kuehn T, 2013

Contrasting data !!!

DR: 97%; FNR: 4.5%

Khan A, 2005

SLNB after NAC e FS

(If SN - : no DA)

Is FS also accurate after NAC ?

Few studies! but those inherent to this topic, confirm the accuracy of the FS after NAC

Shimazu K, 2008; Rubio IT, 2010; Komenaka IK, 2010

SLNB after NAC + FS

Advantages

- Only one operation
- Gain of the patients with positive lymph nodes, that become negative after NAC

Disadvantages

- Low DR
- Higt FNR

Mamounas EP, 2005; Xing Y, 2006; Kelly AM, 2009; Van Deurzen CH, 2009; Classe JM, 2009; Hunt KK, 2009

….after

Table 1. Results of sentinel lymph node biopsy after neoadjuvant chemotherapy in meta-analyses and large population studies

First author[Ref.]	Year	No. of patients	Identification rate	False-negative rate
Xing[13]	2006	1273	89.7%	12.0%
Kelly[14]	2009	1799	89.6%	8.4%
van Deurzen[15]	2009	2148	90.9%	10.5%
Mamounas[9]	2005	428	84.8%	10.7%
Classe[10]	2009	195	90.3%	11.5%
Hunt[11]	2009	575	97.4%	5.9%[a]

[a] Eighty-four patients underwent planned axillary lymph node dissection

Shimazu K, 2011

What effect does an FNR have???

Only a little on adjuvant therapies:
the decision on CHT has already been made!!!

No axillary dissection (total number of N+)
affects the decision regarding radiotherapy

Main problem:

These studies on timing are studies of feasability,detection rate and accurancy,

not of FU

in particular in SN negative patients where axillary dissection is not performed!!!


Preoperative or intraoperative SLNB
AVANTI
Multidisciplinary approach!!!

BMJ

BMJ 2012;344:e2718 doi: 10.1136/bmj.e2718 (Published 26 April 2012)

RESEARCH

Effects of multidisciplinary team working on breast cancer survival: retrospective, comparative, interventional cohort study of 13 722 women

Eileen M Kesson *project manager*[1 4], Gwen M Allardice *statistician*[1 4], W David George *school of medicine honorary professor*[2], Harry J G Burns *chief medical officer for Scotland*[3], David S Morrison *director*[4]

Breast Cancer mortality 18% lowrer with Multidisciplinary Care!!!!!

…. Se è vero, come è vero, che il trattamento Multidisciplinare migliora la sopravvivenza del 18%

…If is true, as is true, that multidisciplinary approach increase the survival rate of 18%

For Patients downstaged less radical surgery for
The breast and Axilla

European Journal of Surgical Oncology
Volume 39, Issue 5 , Pages 417-424, May 2013

Timing of the sentinel lymph node biopsy in breast cancer patients receiving neoadjuvant therapy – Recommendations for clinical guidance

Duveken B.Y. Fontein, Willemien van de Water, J. Sven D. Mieog, Gerrit-Jan Liefers, Cornelis J.H. van de Velde

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Accepted 1 February 2013.

Abstract

Neoadjuvant chemotherapy (NAC) is an increasingly important component in the treatment of both locally advanced and early-stage breast cancer. With this, a debate on the timing of the sentinel lymph node biopsy (SLNB) has emerged. At the end of the last century, the SLNB was introduced as an axillary staging modality, and this paper aims to further elucidate this issue in the context of NAC. We compiled available data on the SLNB after NAC and provide clinical guidance for timing the SLNB in this context. On the basis of our findings, we recommend that the SLNB can be performed after NAC in all cases. In patients with a