

# Sentinel lymph node examination with three different approaches

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4<sup>th</sup>

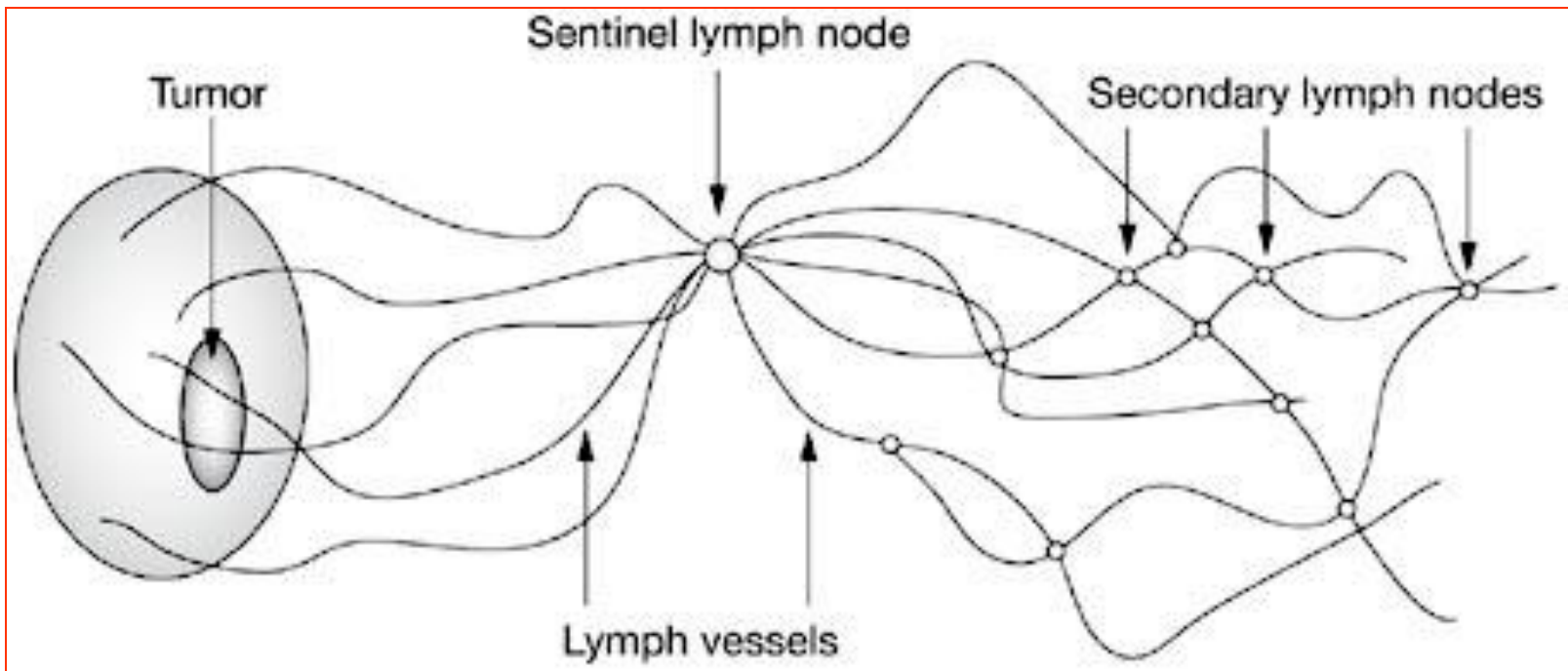
International Congress  
of Breast Disease Centers

2014

THE BREAST CENTER:  
A MODEL TO IMPROVE PATIENT CARE



# SLN in breast cancer: rationale



# SLN in breast cancer: background

ANNALS OF SURGERY  
Vol. 220, No. 3, 391-401  
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Lymphatic Mapping and Sentinel

THE LANCET

**Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph-nodes**

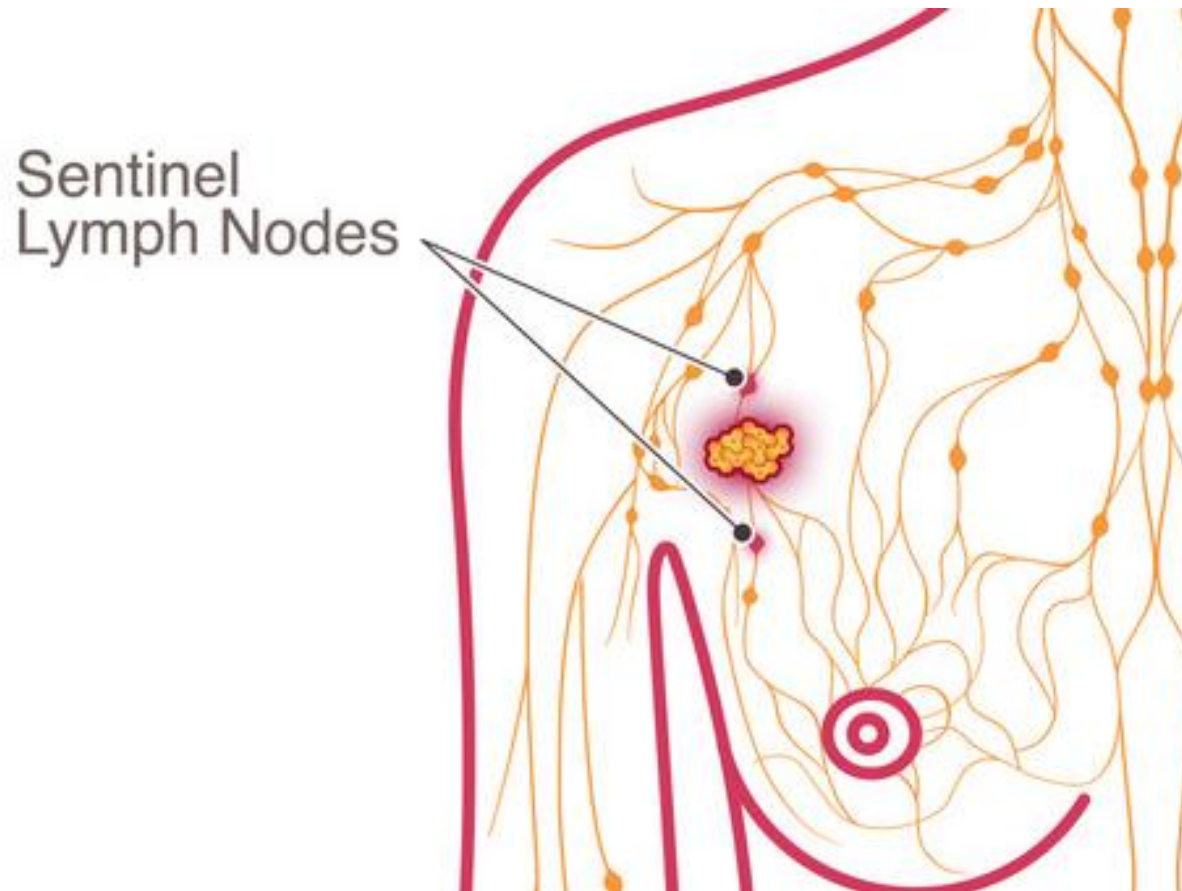
**Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis**

*The* NEW ENGLAND JOURNAL of MEDICINE

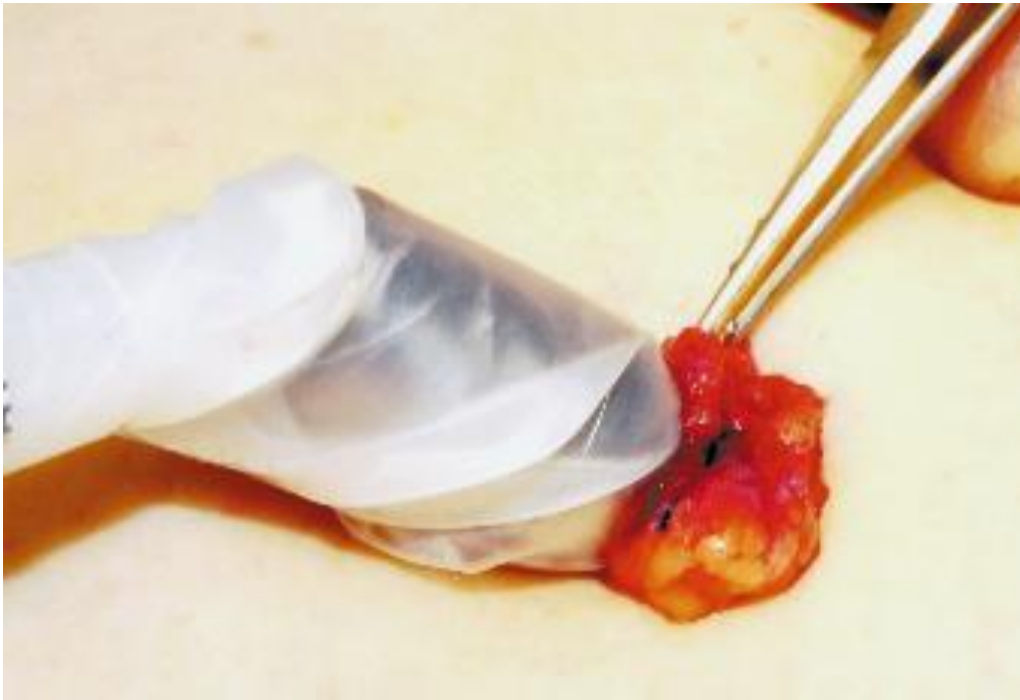
ORIGINAL ARTICLE

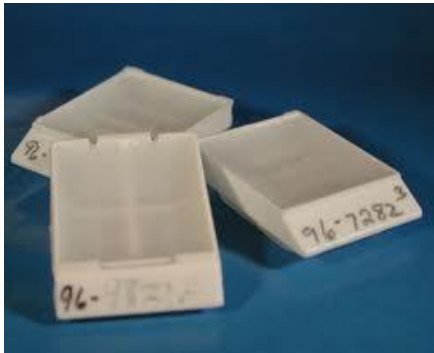
**Effect of Occult Metastases on Survival in Node-Negative Breast Cancer**

# SLN in breast cancer: standard of care



# SLN in breast cancer: current situation





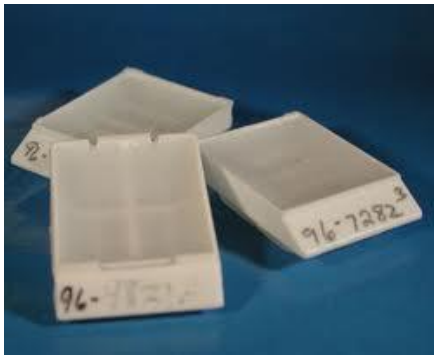
# SLN on FFPE tissue

[Formalin Fixed Paraffin Embedded]

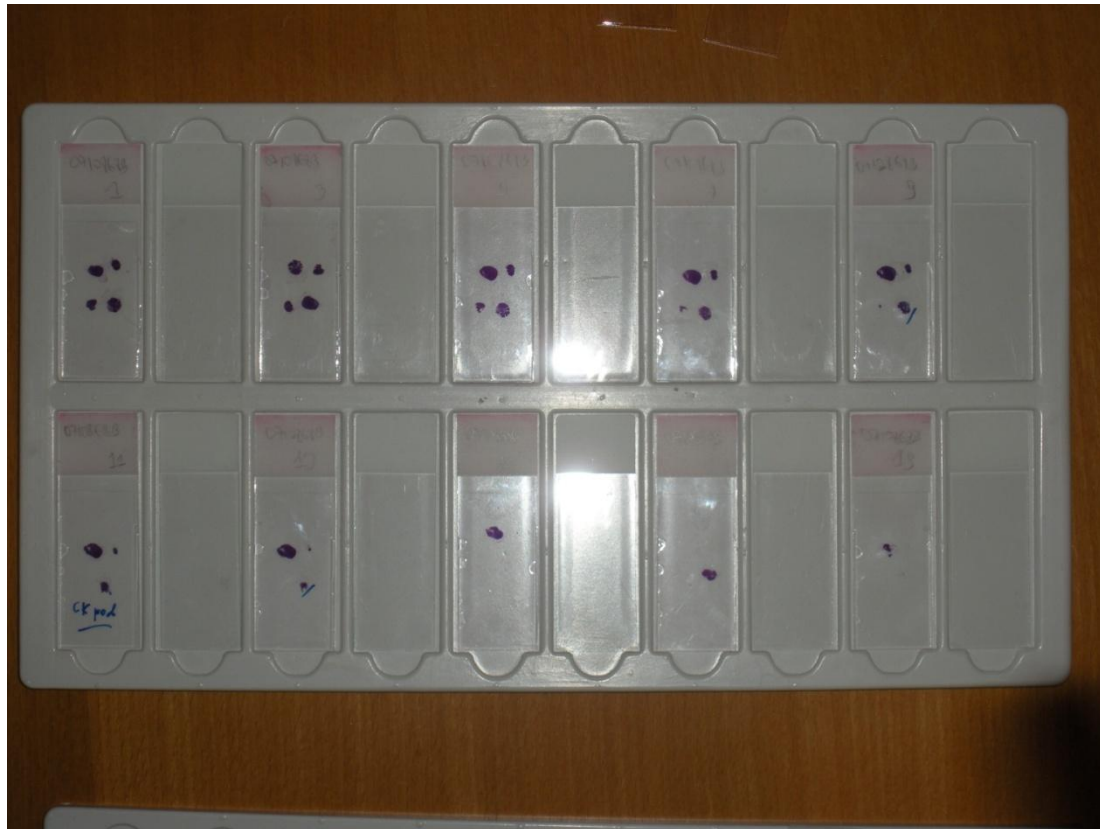


# SLN on FFPE tissue

[Formalin Fixed Paraffin Embedded]



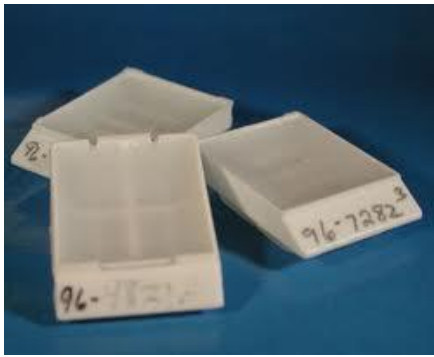
- Unstained sections



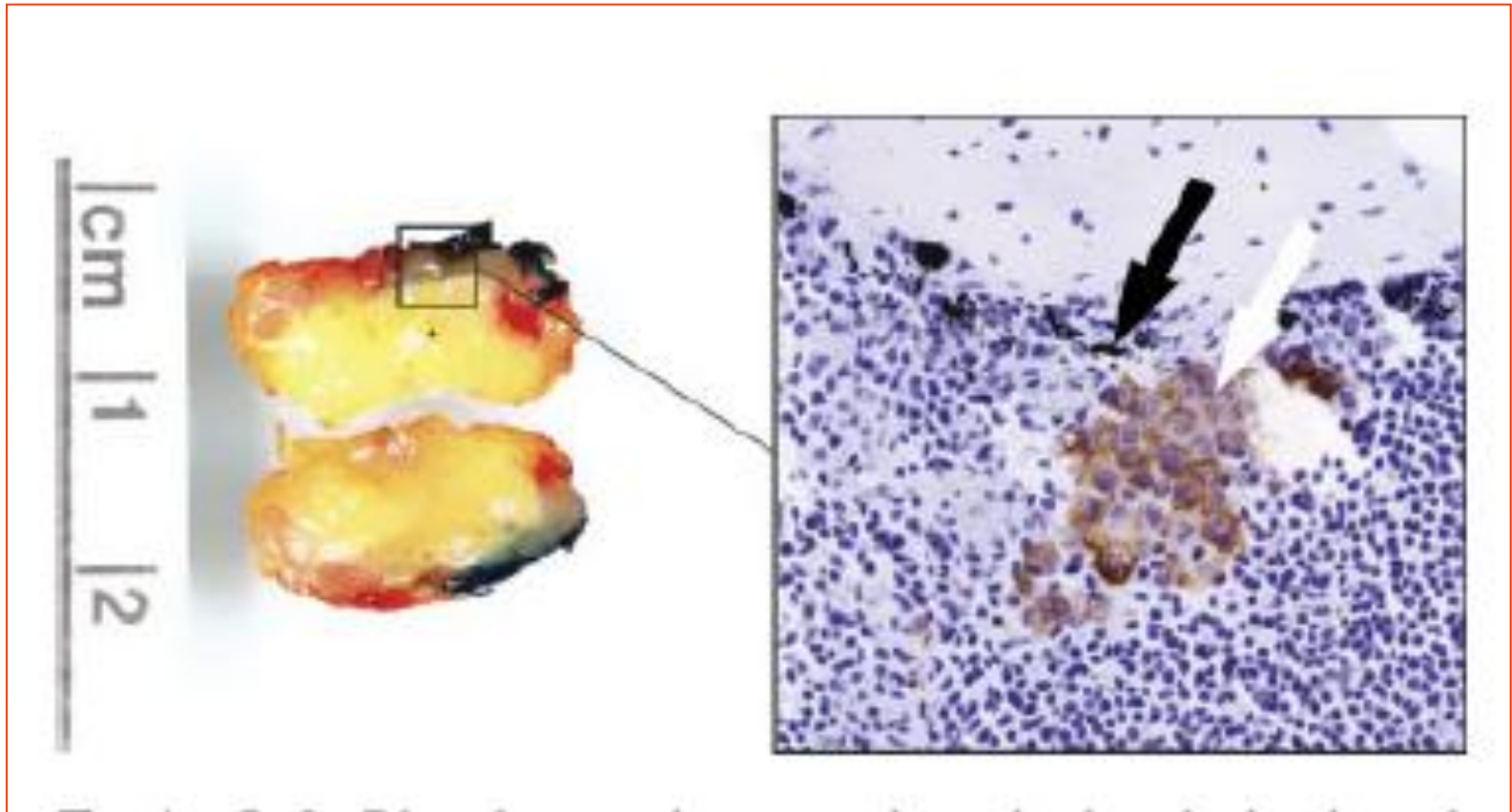


# SLN on FFPE tissue

[Formalin Fixed Paraffin Embedded]



- Immunohistochemistry

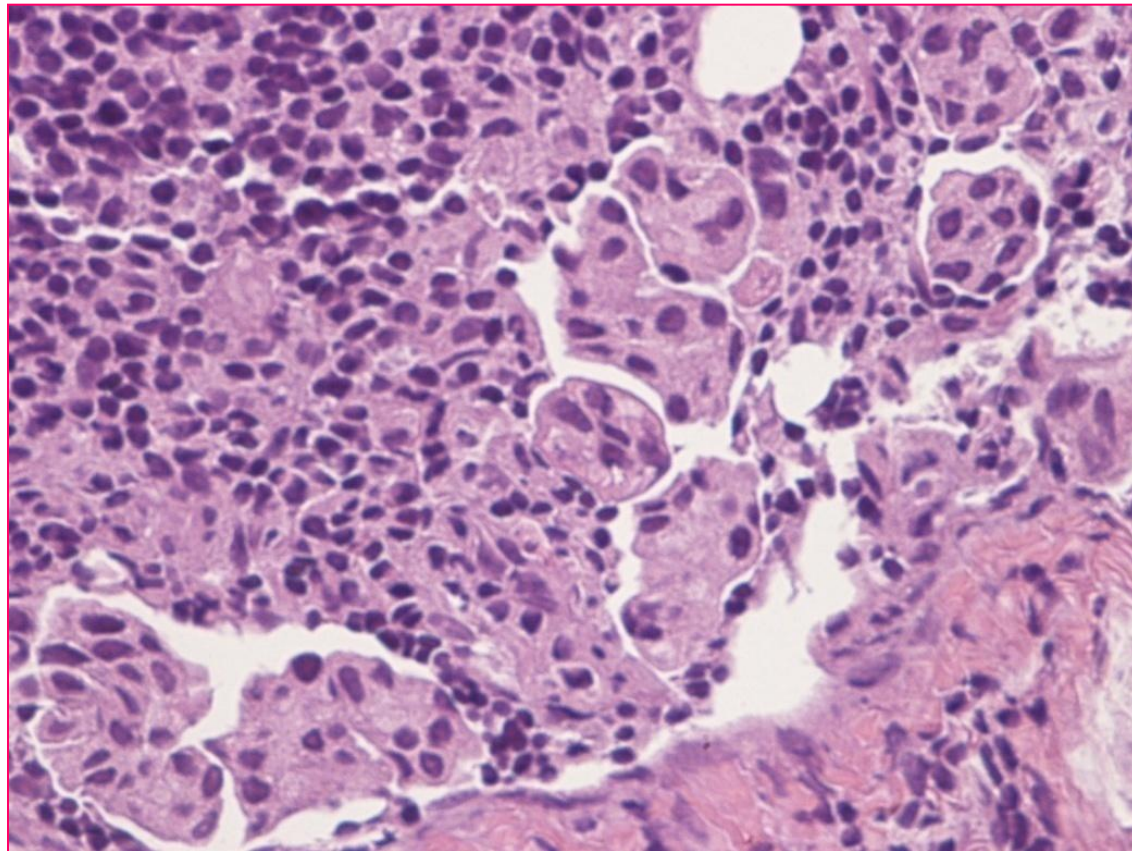
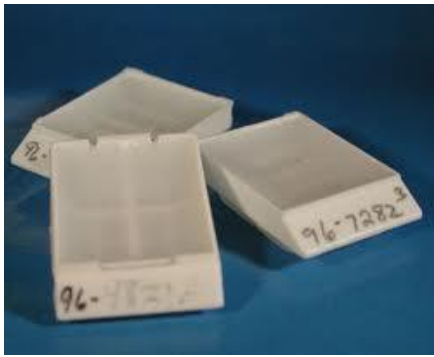




# SLN on FFPE tissue

[Formalin Fixed Paraffin Embedded]

- Collegial discussion/revision



# SLN on FFPE tissue: ICH experience (2000-2008)

- Data from 01-01-2000 to 31-12-2005
- 540 patients
- 648 SLN (mean: 1,2; range: 1-5)

# SLN on FFPE tissue: ICH experience

- SLN+: 162/540 (30%)
  - macromets: 100 (61%)
  - micromets: 62 (38%)



- SLN+/ALND+: 53/162 (33%)
  - macromets: 43/100 (43%)
  - micromets: 10/62 (16%)



SLN on FFPE tissue:  
the gold standard ?





SSLN Noon FFS E it is use e  
[Formalin [Fixed] Resection [Embedded]



# SLN on FS: ICH experience (2009-2011)

- Data from 01-01-2009 to 31-12-2009
- 390 patients
- 507 SLN (mean: 1,3; range: 1-5)



# SLN on FS: ICH experience

- SLN+: 87/390 (22%)
  - macromets: 64 (74%)
  - micromets: 23 (26%)



- SLN+/ALND+: 27/87 (31%)
  - macromets: 23/64 (36%)
  - micromets: 4/23 (17%)



# FFPE vs. FS: ICH experience

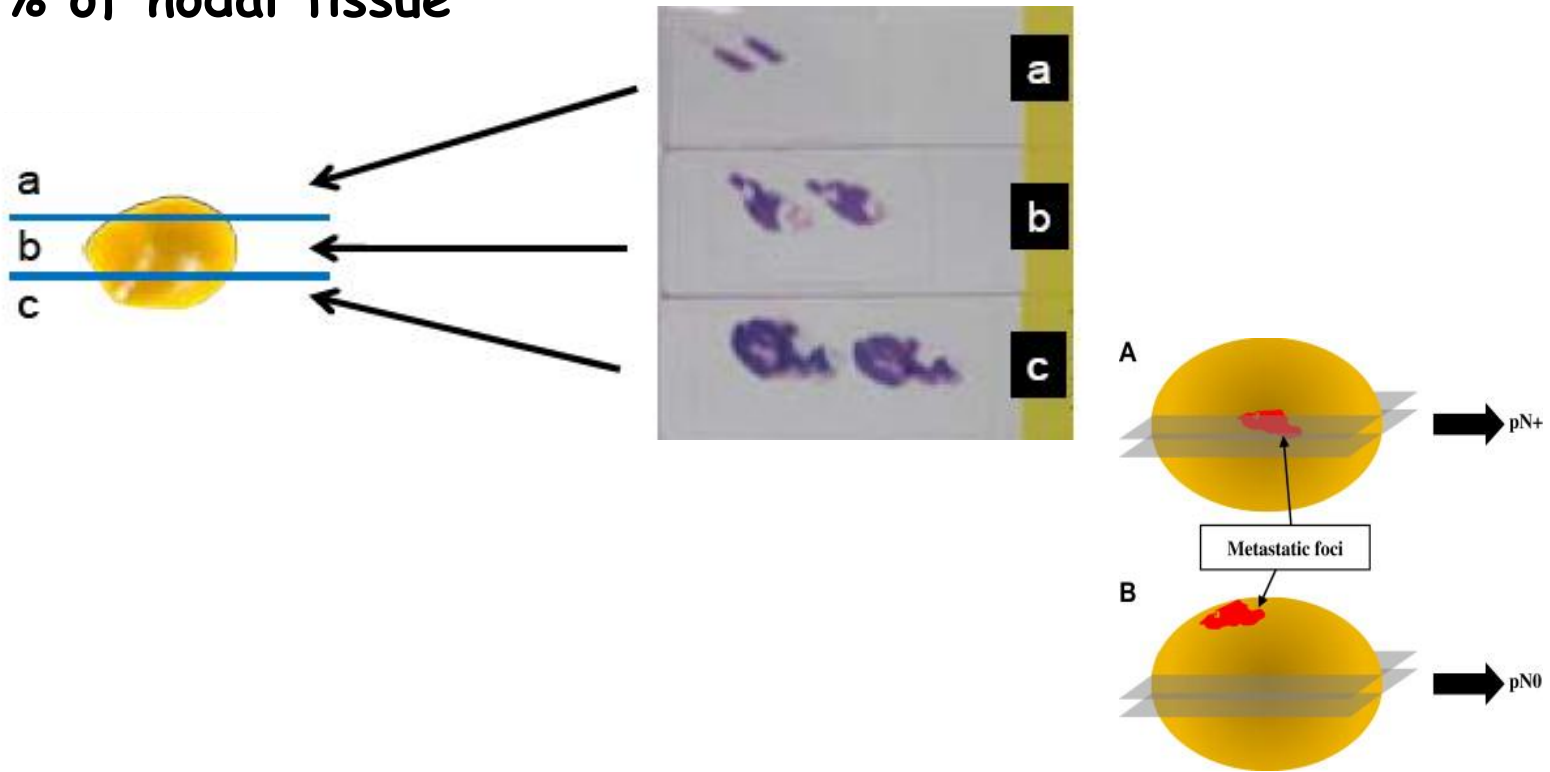
	FFPE	FS
SLN+	30%	22%
SLN+/ALND+	33%	31%

The table compares the percentage of SLN+ and SLN+/ALND+ cases between FFPE and FS methods. A red double-headed arrow is positioned between the 30% and 22% values in the SLN+ row. A blue dashed oval encircles the 33% and 31% values in the SLN+/ALND+ row.

# Morphology (FFPE & FS) limits

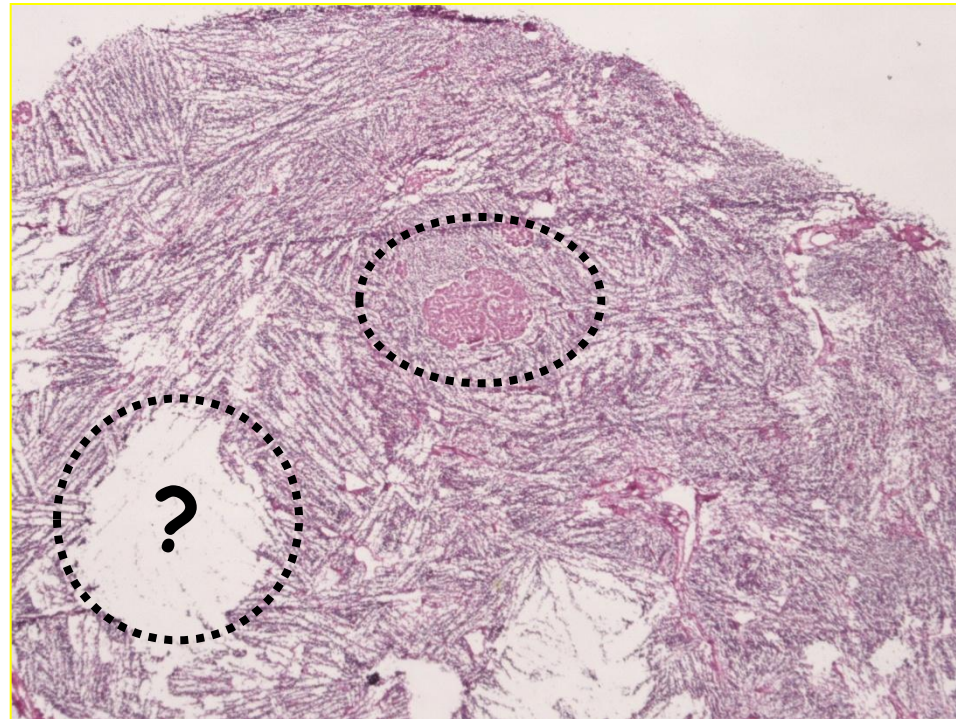
5 mm SLN thickness; 1 section each 50 $\mu$ m

1 % of nodal tissue

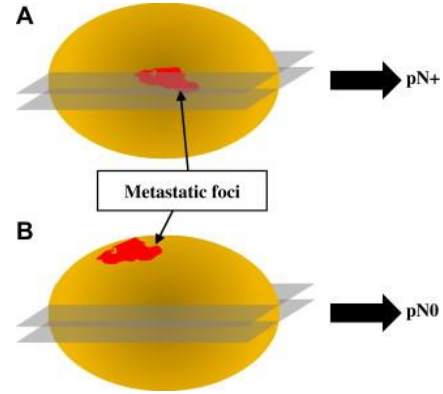
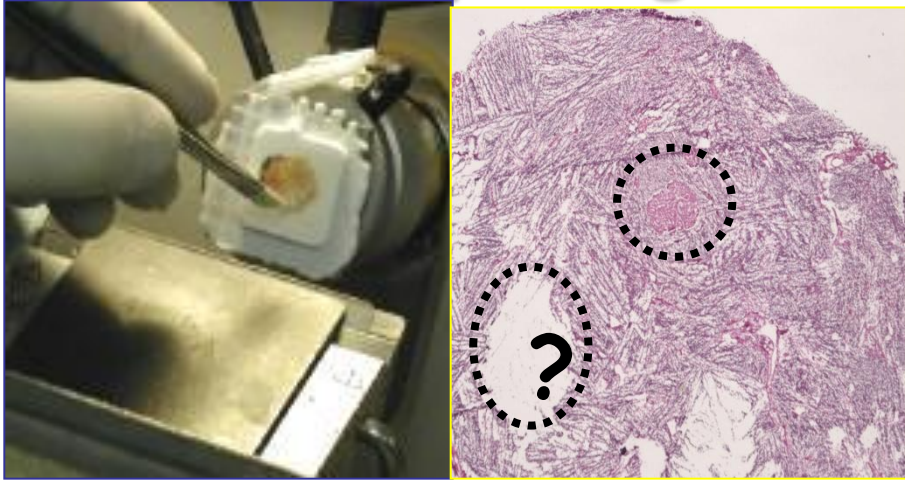


# Morphology (mainly FS) limits

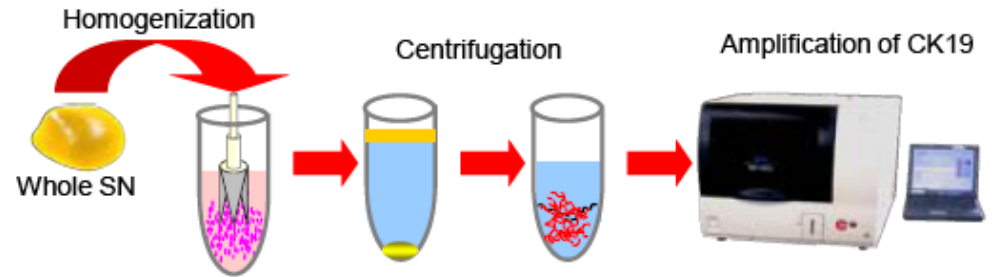
- technician/physician experience



# From morphological...



...to molecular era.





## REVERSE TRANSCRIPTION-POLYMERASE CHAIN REACTION ASSAY FOR MULTIPLE mRNA MARKERS IN THE DETECTION OF BREAST CANCER METASTASES IN SENTINEL LYMPH NODES

Michela MANZOTTI<sup>1</sup>, Patrizia DELL'ORTO<sup>1</sup>, Patrick MAISONNEUVE<sup>2</sup>, Stefano ZURRIDA<sup>3</sup>, Giovanni MAZZAROL<sup>1</sup> and Giuseppe VIALE<sup>1\*</sup>

<sup>1</sup>*Department of Pathology, European Institute of Oncology and University of Milan School of Medicine, Milan, Italy*

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<sup>3</sup>*Department of Senology, European Institute of Oncology, Milan, Italy*

TABLE IV – CORRELATIONS BETWEEN RT-PCR ASSAYS AND HISTOPATHOLOGY OF SLNS

	Histologically negative SLNs (no.)		Histologically positive SLNs (no.)		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Overall concordance (%)
	PCR -ve	PCR +ve	PCR -ve	PCR +ve					
Maspin	94	7	23	22	48.9	93.1	75.9	80.3	79.5
CK19	82	19	12	33	73.3	81.2	63.5	87.2	78.8
CEA	91	10	20	25	55.6	90.1	71.4	82.0	79.5
MUC-1	101	0	30	15	33.3	100.0	100.0	77.1	79.5
MG1	87	14	10	35	77.8	86.1	71.4	89.7	83.6
Any	67	34	2	43	95.6	66.3	55.8	97.1	75.3
Maspin/CK/MG1 <sup>1</sup>	93	8	9	36	80.0	92.1	81.8	91.2	88.4

<sup>1</sup>Maspin/CK/MG1: Expression of two of the maspin, cytokeratin 19 and mammaglobin 1 mRNA markers.



# **One-step Nucleic Acid Amplification for Intraoperative Detection of Lymph Node Metastasis in Breast Cancer Patients**

Masahiko Tsujimoto, Kazuki Nakabayashi, Katsuhide Yoshidome, et al.

*Clin Cancer Res* 2007;13:4807-4816. Published online August 15, 2007.

*Virchows Arch* (2009) 454:203–210

DOI 10.1007/s00428-008-0703-9

ORIGINAL ARTICLE

## **One-step nucleic acid amplification—a molecular method for the detection of lymph node metastases in breast cancer patients; results of the German study group**

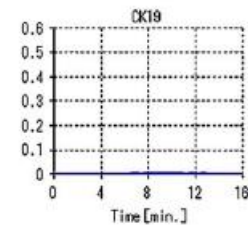
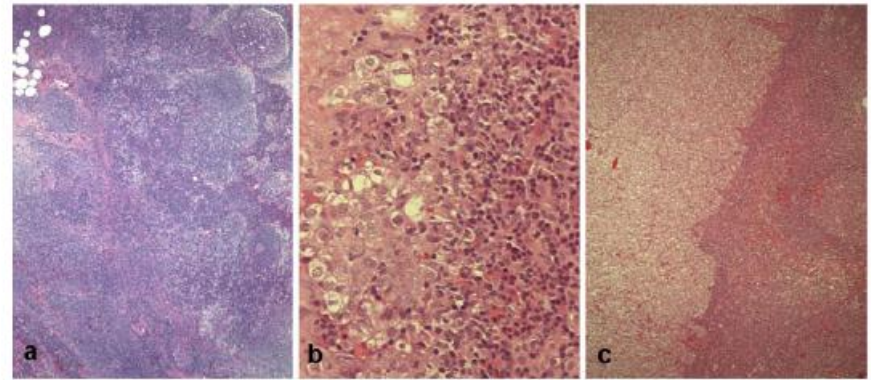
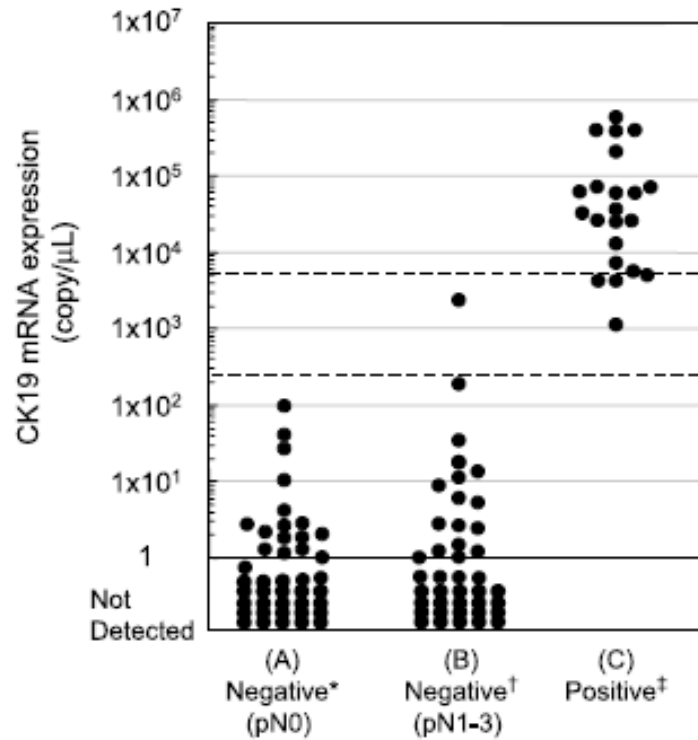
# **Molecular Detection of Lymph Node Metastases in Breast Cancer Patients: Results of a Multicenter Trial Using the One-Step Nucleic Acid Amplification Assay**

Yasuhiro Tamaki, Futoshi Akiyama, Takuji Iwase, et al.

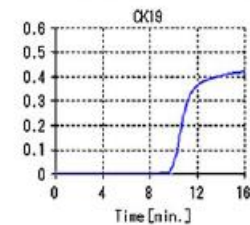
*Clin Cancer Res* 2009;15:2879-2884. Published online April 7, 2009.

A Novel Automated Assay for the Rapid Identification of Metastatic Breast Carcinoma in Sentinel Lymph Nodes *Cancer* 2011;117:2599–607.

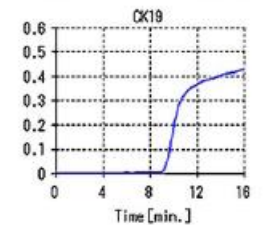
# OSNA method



Time	ND	[min.]
Copies	$<2.5E+02$	[copies/ $\mu$ L]
Qualitative	(-)	

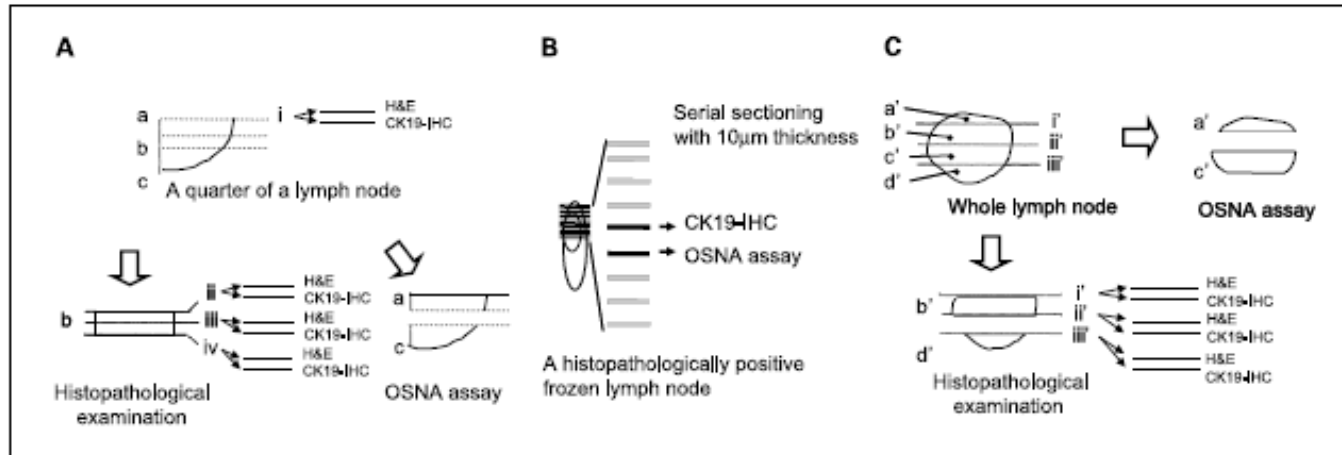


Time	10.3	[min.]
Copies	$4.0E+05$	[copies/ $\mu$ L]
Qualitative	(++)	



Time	9.7	[min.]
Copies	$2.1E+07$	[copies/ $\mu$ L]
Qualitative	(++)	

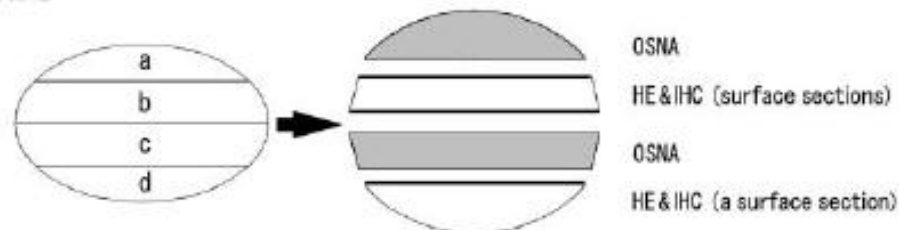
# OSNA vs morphology



## A Trial 1



## B Trial 2



# OSNA: reliability

- Does it recognize all positive SLN?
- Does it separate micro from macro mets?
- Does it overestimate the probability of additional axillary lymph node (ALN) mets?

# SLN with OSNA: ICH experience

- From 01-10-2011 to 30-09-2013
- 803 Patients
- 920 SLN (mean 1.1, range 1-4)
- Pts with SLN+: 222 (222/803, 27%)
  - metastasis: 150 (10/222, 68%)
  - micrometastasis: 72 (72/222, 32%)

# Does OSNA recognize all positive SLN?

	FFPE [6 yrs]	FS [1 yr]	OSNA [2 yr]
Pts with SLN+	162/540 (30%)	87/390 (22%)	222/803 (28%)

Predicting the Risk for Additional Axillary Metastases in Patients With Breast Carcinoma and Positive Sentinel Lymph Node Biopsy

Viale et al *Annals of Surgery* • Volume 241, Number 2, February 2005

• Do recognize all positive SLN?

SLN+: 1228/4207 (29.2%)

**YES**



# Does OSNA separate micro from macro mets?

	FFPE [6 yrs]	FS [1 yr]	OSNA [2 yr]
Metastasis	100 (61%)	64 (74%)	150 (68%)
Micrometastasis	62 (38%)	23 (26%)	72 (32%)

Predicting the Risk for Additional Axillary Metastases in Patients With Breast Carcinoma and Positive Sentinel Lymph Node Biopsy

*Viale et al Annals of Surgery* • Volume 241, Number 2, February 2005

Macromets 794/1228 (64.6%)

Micromets 318/1228 (26%)

[ITC not reported]

•Do separate  
micro from macro  
mets?

**YES**

# Does OSNA overestimate the probability of additional axillary lymph node (ALN) mets?

Pts with SLN+/ALND+: 40 (40/117\*, 34%)

1° yr OSNA

with SLN+ metastasis:	30 (30/57, 52%)
with SLN+ diluted:	5 (5/24, 20%)
with SLN+ micrometastasis:	6 (6/36*, 16%)

\* 2 pts with micro did not undergo ALND

Pts with SLN+/ALND+: 28 (28/85\*, 33%)

2° yr OSNA

with SLN+ metastasis:	19 (19/39, 48%)
with SLN+ diluted:	5 (5/26, 19%)
with SLN+ micrometastasis:	4 (6/20, 16%)

\* 1 pts with SLN+ met, 3 with SLN+ diluted and 14 with SN+ micro did not undergo ALND

# Do OSNA overestimate the probability of additional axillary lymph node (ALN) mets?

	FFPE [6 yrs]	FS [1 yr]	OSNA [2 yr]
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Pts SLN+/ALND+	53/162 (33%)	27/87 (31%)	68/202 (33%)
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SLN+ metastasis	43/100 (43%)	23/64 (36%)	59/145 (41%)
SLN+ micrometastasis	10/62 (16%)	4/23 (17%)	10/56 (17%)

Predicting the Risk for Additional Axillary Metastases in Patients With Breast Carcinoma and Positive Sentinel Lymph Node Biopsy

*Viale et al Annals of Surgery • Volume 241, Number 2, February 2005*

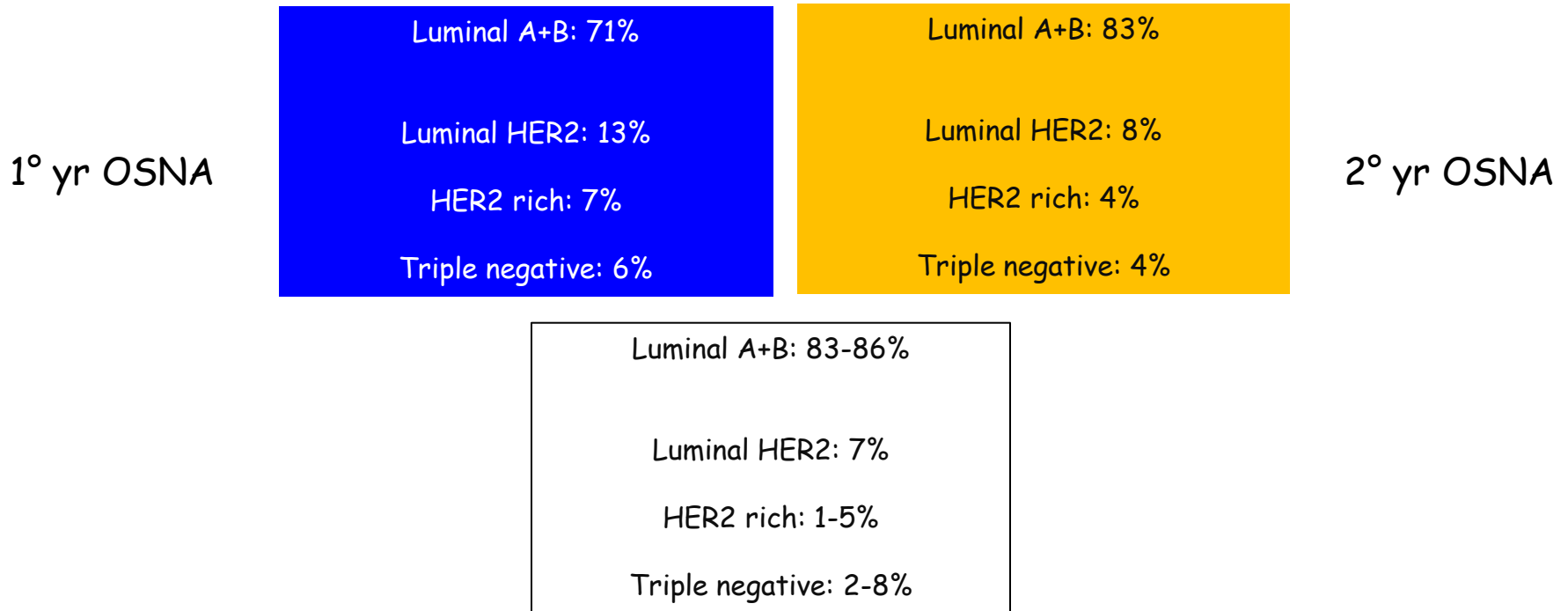
• Do overestimate tumor load?

Macromets 399/794 (50.4%)

Micromets 68/318 (21.4%)

**NO**

# Molecular subclasses of cases with SLN+: OSNA vs morphology



## Morphology

(Reyal et al; PLOS one 2012)

Luminal A [ER and/or PgR +, Ki67<14%; HER2 -]; Luminal B [ER and/or PgR +, Ki67>15%; HER2 -];  
Luminal HER2 [ER /PgR +, HER2 +]; HER2 rich [ER/PgR -; HER2 +]; Triple negative [ER -, PgR -, HER2 -].

# Cost of SLN examination

## Morphology

Materials: 25 euro/SLN

Technician: 15 euro/SLN

Physician: 50 euro/SLN

FINAL COST: 90 euro/SLN

## 1° yr OSNA

Materials: 137.000 euro

Technician: 15 euro/SLN

Physician: none

FINAL COST: 300 euro/SLN

## 2° yr OSNA

Materials: 65.000 euro

Technician: 15 euro/SLN

Physician: none

FINAL COST: 200 euro/SLN

# CONCLUSIVE REMARKS



A new skyline

Women's health

Don't be afraid of the frontier  
Get the best from it





**Thank you for  
your attention!**