

INCONTRO ITALO-FRANCESE
SUL CARCINOMA MAMMARIO:
problematiche attuali

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4

INCONTRO ITALO-FRANCESE
SUL CARCINOMA MAMMARIO:
problematiche attuali

Coordinatori del convegno:
Cynthia Aristei
Bruno Cutuli
Elisabetta Perrucci

CON IL PATROCINIO DI

AOn
Associazione Italiana
di Oncologia Medica

AIRO
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di Radioterapia Oncologica

SCO

SEGRETERIA SCIENTIFICA
Antonio Rulli
Lorenzo Falchini
Bisetta Palumbo

SEGRETERIA ORGANIZZATIVA
CONSULTA UMBRIA s.r.l.
Via R. Gallenga, 2
06127 Perugia
tel. 075 5200066
fax 075 5154166
congressi@consultaumbria.com

Hotel Giotto
Assisi
22/23 novembre 2013

**Problematiche nella diagnosi e terapia
della malattia a livello ascellare**

Analisi molecolare intraoperatoria: la soluzione del problema?

Isabella Castellano

Dipartimento di Scienze Mediche
Università degli studi di Torino
Anatomia Patologica
(Direttore: Prof. A. Sapino)
Città della Salute e della Scienza-Presidio
Molinette, Torino

Tecniche diagnostiche a disposizione per l'analisi del linfonodo sentinella (LS)

**ESAME
ESTEMPORANEO
INTRAOPERATORIO**

**ESAME SU LS FISSATO IN
FORMALINA ED INCLUSO
IN PARAFFINA**

**TECNICHE
MOLECOLARI
OSNA**

CHIRURGHI



**ANATOMO-
PATOLOGI**



COSTO



PERCHE' L'ANALISI MOLECOLARE DEL LS

QUALI SONO GLI SVANTAGGI

LA NOSTRA SOLUZIONE MOMENTANEA

PERCHE' L'ANALISI MOLECOLARE DEL LS

- 1. FORNIRE UN DATO INTRAOPERATORIO**
- 2. FORNIRE UN DATO RIPRODUCIBILE**

INTRAOPERATIVE SLN ASSESMENT

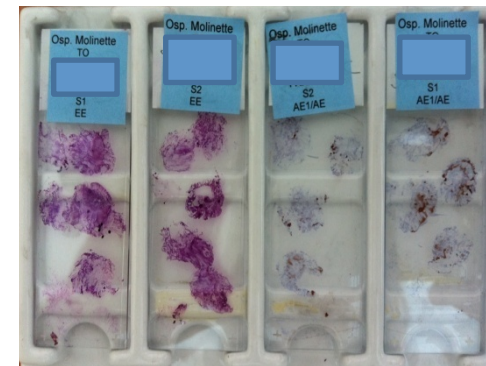
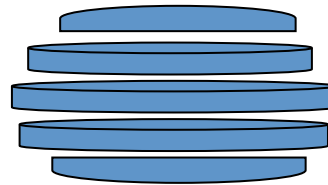
Conduce all'immediata dissezione del cavo ascellare evitando il secondo reintervento



SEZIONI CRIOSTATICHE



IMPRINT CITOLOGICO



Con o senza immunocitochimica rapida

MA....

Intraoperative assessment of sentinel lymph nodes in breast cancer

D. M. Layfield¹, A. Agrawal³, H. Roche² and R. I. Cutress¹

British Journal of Surgery 2011; 98: 4–17

SNL frozen section analysis

SNL imprint cytology analysis

	Permanent section methods	Sensitivity (%)	Specificity (%)
Pooled data from 31 studies included in Tew <i>et al.</i> ²⁵	Various	Total 63 Macro 81 Micro 22	Total 99
Barranger <i>et al.</i> ²⁶	3-mm sections, each analysed 4 times; 150-µm levels; H&E + IHC (AE1–AE3)	Total 33 Macro 75	Total 98
Chicken <i>et al.</i> ²⁷	Sections at 3 levels; H&E + IHC (AE1/AE3)	Total 73	Total 100
Cox <i>et al.</i> ²⁸	Single section; further sections taken if initial section negative; H&E + IHC (CK)	Total 53 Macro 69.3 Micro 6.4	Total 99
Contractor <i>et al.</i> ²⁹	Single section; H		

Reference	No. of patients	Permanent staining methods	Sensitivity (%)	Specificity (%)
Veronesi <i>et al.</i> ¹⁸ (1997)	107	Paraffin; 3 levels from one half; H&E stain	Total 64	Total 100
Weiser <i>et al.</i> ¹⁹ (2000)	890	Paraffin; half node section at 50 µm; 3 sections H&E stain and 2 sections IHC (CAM5.2 AE1/AE3)	Total 58 Macro 92 Micro 17	Total 99
Rahusen <i>et al.</i> ²⁰ (2000)	100	Paraffin; initial single level; if negative, additional 4 levels; H&E stain; IHC (CAM5.2)	Total 57 Macro 84 Micro 27	Total 100
Zurrada <i>et al.</i> ²¹ (2000)	192	Paraffin; 3 levels from each half; H&E stain	Total 68	Total 100
Tanis <i>et al.</i> ²² (2001)	262	Paraffin; H&E stain from 3 levels; IHC	Total 74	Total 99
			6 0 1	Total 100
				NA

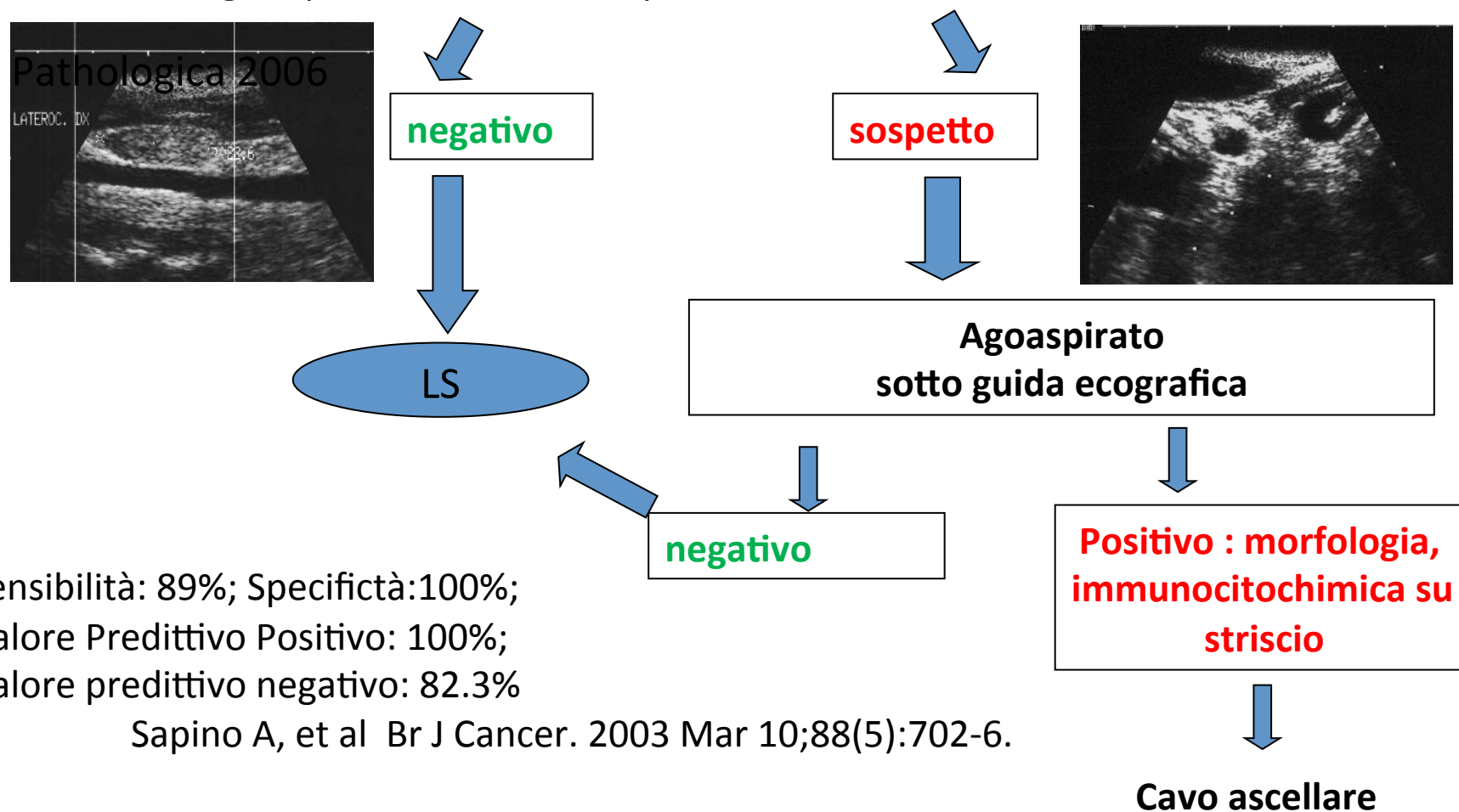
Sensibilità varia dal 33% to 84% indipendentemente dal metodo utilizzato: rischio di FALSI NEGATIVI

PROPOSTA DI PROTOCOLLO DI TRATTAMENTO DEL LINFONODO SENTINELLA IN PATOLOGIA MAMMARIA DELLA SIAPEC REGIONE PIEMONTE

F. PIETRIBIASI¹, G. DE ROSA², R. ARISIO³, R. BAGNATO⁴, N. RAVARINO⁵, M. PAVESI⁶, G. CANAVESE⁷, I. CASTELLANO⁸, A. SAPINO⁸ E SIAPEC PIEMONTE

No all'esame estemporaneo

Sì ad un accurato esame ecografico pre-chirurgico del cavo ascellare con eventuale agoaspirato su nodo sospetto



PERCHE' L'ANALISI MOLECOLARE DEL LS

- 1. FORNIRE UN DATO INTRAOPERATORIO**
- 2. FORNIRE UN DATO RIPRODUCIBILE**

The **lack of universally adopted protocols** has resulted in a wide heterogeneity in gross- and micro-sectioning procedures used in different institutions



POOR REPRODUCIBILITY OF THE SNL DIAGNOSIS

ORIGINAL ARTICLE

Discrepancies in current practice of pathological evaluation of sentinel lymph nodes in breast cancer. Results of a questionnaire based survey by the European Working Group for Breast Screening Pathology

G Cserni, I Amendoeira, N Apostolikas, J P Bellocq, S Bianchi, W Boecker, B Borisch, C E Connolly, T Decker, P Dervan, M Drijkoningen, I O Ellis, C W Elston, V Eusebi, D Faverly, P Heikkila, R Holland, H Kerner, J Kulka, J Jacquemier, M Lacerda, J Martinez-Penuela, C De Miguel, J L Peterse, F Rank, P Regitnig, A Reiner, A Sapino, B Sigal-Zafrani, A M Tanous, S Thorstenson, E Zozaya, G Fejes, C A Wells

J Clin Pathol 2004;57:695-701. doi: 10.1136/jcp.2003.013599

VARIABILITY IN GROSS AND MICRO-SECTIONING
VARIABILITY IN THE USE OF IMMUNOHISTOCHEMISTRY
VARIABILITY IN THE RESULT INTERPRETATION
VARIABILITY IN PERFORMING INTRAOPERATIVE DIAGNOSIS

LA STADIAZIONE DEL LINFONODO SENTINELLA GUIDA
L'EVENTUALE
CLEARANCE DEL CAVO ASCELLARE

pN0

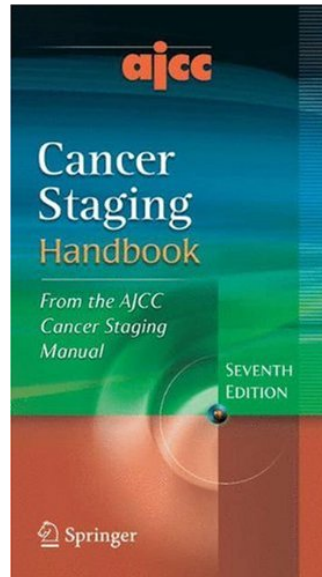


FOLLOW UP
ASCELLARE

No regional lymph node metastasis
histologically, no additional
examination for isolated tumor cells

pN0(i-) No regional lymph node metastases
histologically, negative IHC

pN0(i+) Malignant cells in regional lymph
node(s) not greater than 0.2 mm or single
tumor cells, or a cluster of fewer than 200 cells
in a single histologic cross-section (detected by
H&E or IHC including ITC)



Based on AJCC/
UICC TNM, 7th
edition
**October
2009**

pN1



ASPORTAZIONE DEL
CAVO ASCELLARE

pN1mi: MICROMETASTASES

(greater than 0.2 mm and/or more than 200 cells,
but none greater than 2.0 mm).

pN1 a: METASTASES in 1 to 3 axillary lymph
nodes, at least 1 metastasis greater than 2.0 mm

TNM Classification for Breast Cancer from the AJCC Cancer Staging Manual, 7th Edition

pN0: No regional lymph node metastasis histologically, no additional examination for isolated tumor cells

(i) è usato per indicare le ITC

pN0(i-) No regional lymph node metastases histologically, negative IHC

pN0(i+) Malignant cells in regional lymph node(s) not greater than 0.2 mm or single tumor cells, or a cluster of fewer than 200 cells in a single histologic cross-section (detected by H&E or IHC including ITC) #

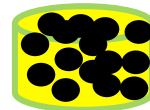
Nodes containing only ITCs are excluded from the total positive node count for purposes of N classification but should be included in the total number of nodes evaluated.

pN0 (mol-): No regional lymph node metastases histologically, negative molecular findings (reverse transcriptase polymerase chain reaction [RT-PCR])

pN0 (mol+): Positive molecular findings (RT-PCR), but no regional lymph node metastases detected by histology or IHC

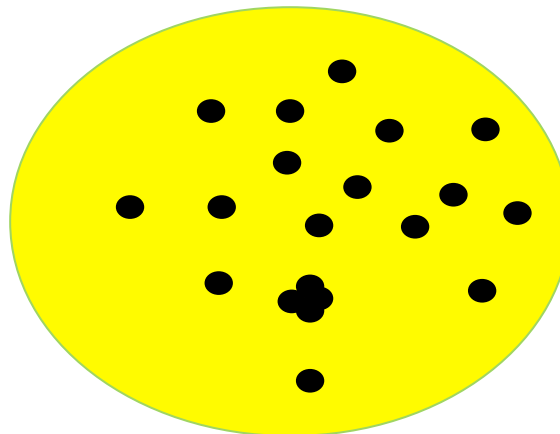
Approximately 1000 tumor cells are contained in a 3-dimensional 0.2-mm cluster. Thus, if more than 200 individual tumor cells are identified as single dispersed tumor cells or as a nearly confluent elliptical or spherical focus in a single histologic section of a lymph node, there is a high probability that more than 1000 cells are present in the node. In these situations, the node should be classified as containing a micrometastasis (pN1mi). Cells in different lymph node cross sections or longitudinal sections or levels of the block are not added together; the 200 cells must be in a single node profile even if the node has been thinly sectioned into multiple slices. It is recognized that there is substantial overlap between the upper limit of the ITC and the lower limit of the micrometastasis categories because of inherent limitations in pathologic nodal evaluation and detection of minimal tumor burden in lymph nodes. Thus, the threshold of 200 cells in a single cross-section is a guideline to help pathologists distinguish between these 2 categories.

Cluster tridimensionale
di 0,2 mm



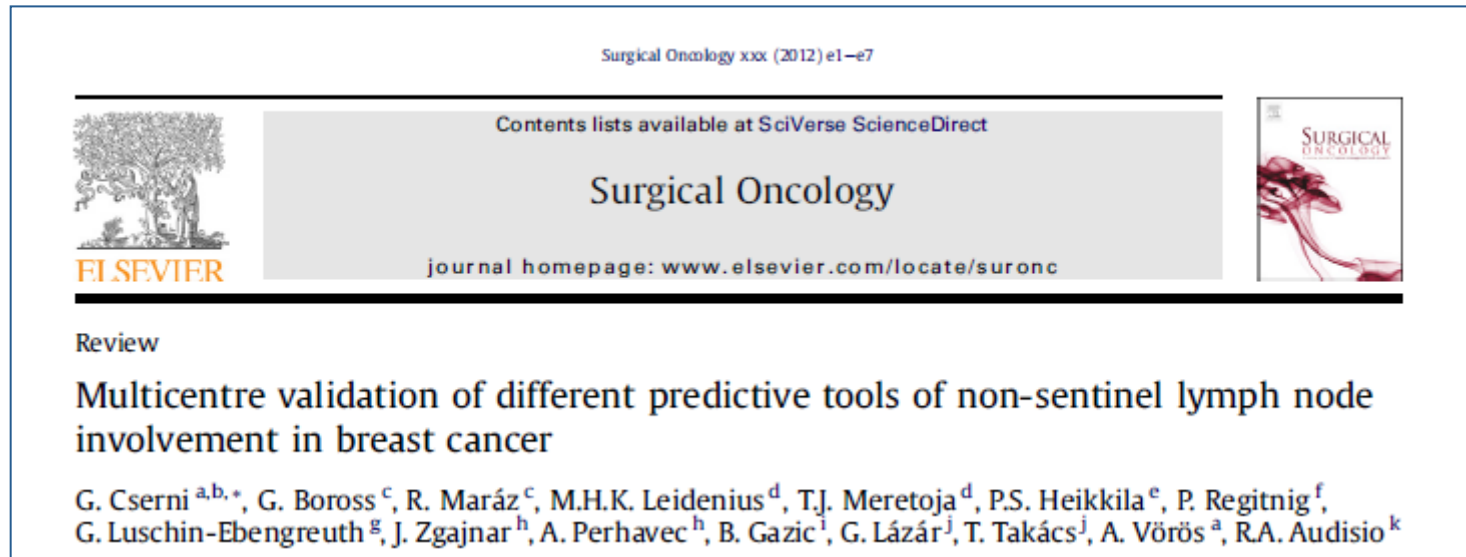
1000 cellule

Se più di 200 cellule in una
singola
sezione istologica

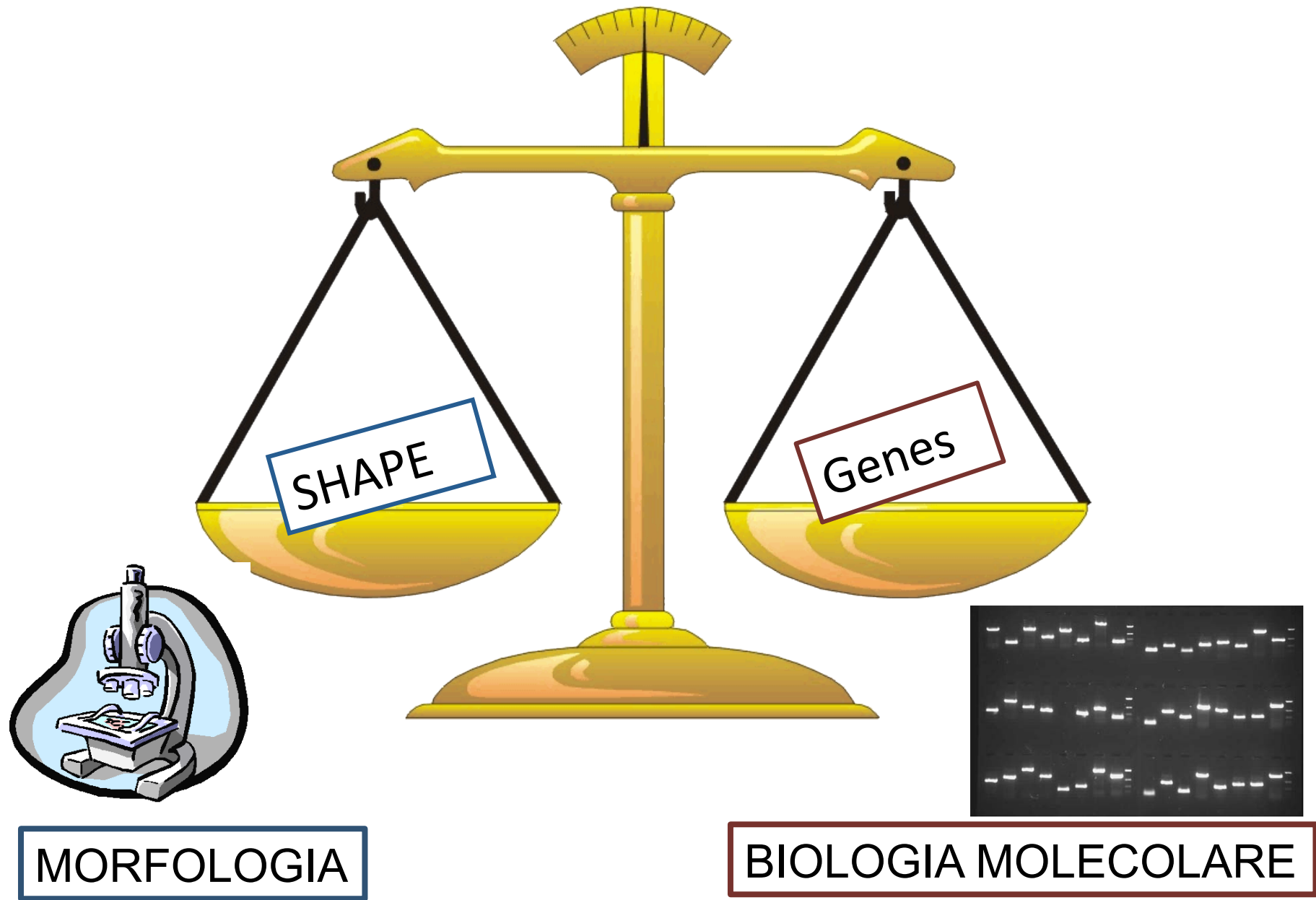


pN1mi

I FALSI NEGATIVI SI RECUPERANO MA.....



Noi crediamo che le differenti applicazioni dei protocolli su LS possano creare differenze anche nei risultati degli studi sulla predittività dello stato ascellare



Biologia molecolare: PCR

J Clin Oncol. 1998 Aug;16(8):2632-40.

Ann Surg. 2008 Jan;247(1):136-42.

Perché non si è divulgata?

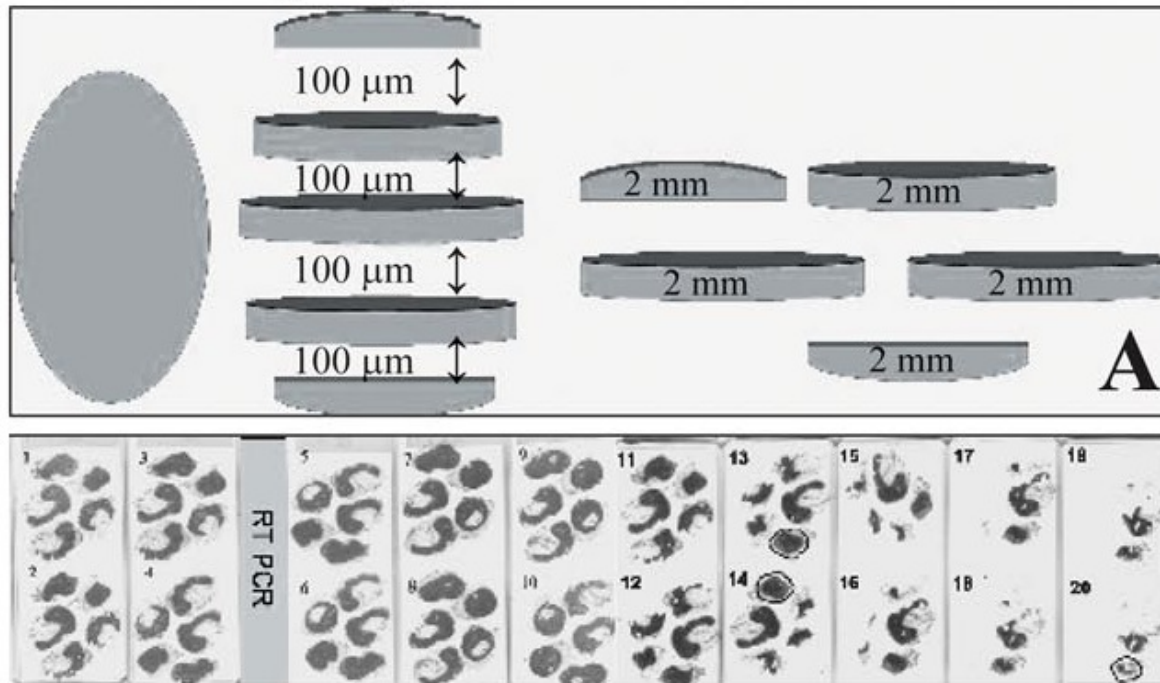
Technical limits of comparison of step-sectioning, immunohistochemistry and RT-PCR on breast cancer sentinel nodes: a study on methacarn fixed tissue.

Daniele et al. J. Cell. Mol. Med. Vol 12, No 5, 2008 pp. 1-9

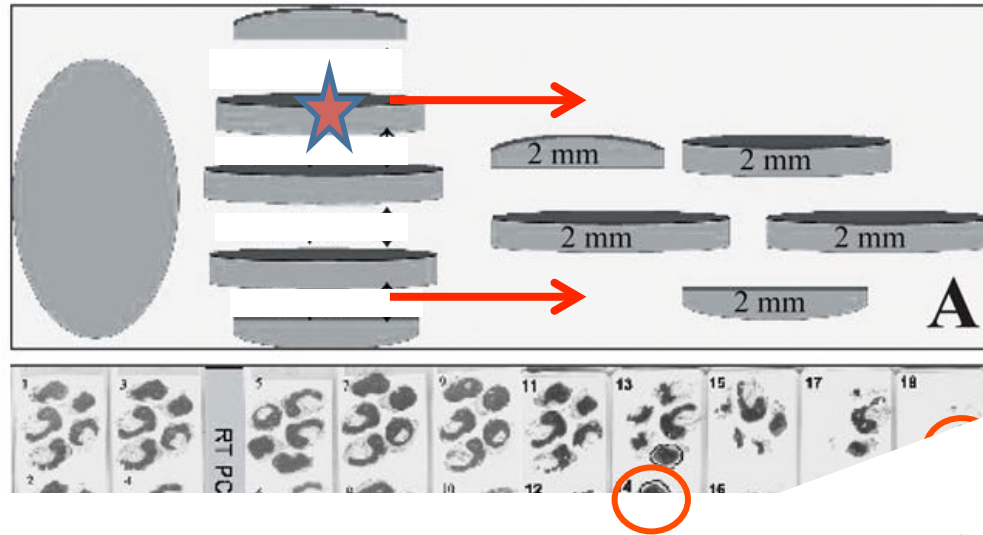
74 LS fissati in methacarn

Geni usati per RT-PCR: Mammaglobina, CEA e CK19.

Daniele et Al. 2007 Figure 1 Top



Daniele et Al. 2007 Figure 1 Top

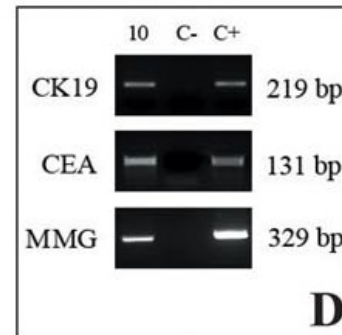
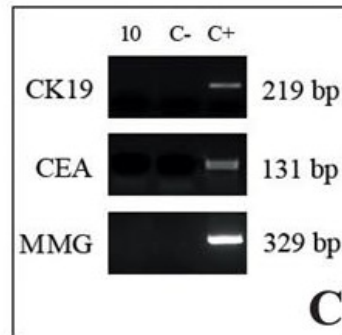


RT-PCR è specifico

all'

bias

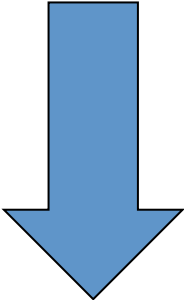
METODICA COSTOSA
METODICA CHE RICHIEDE TEMPO: NO INTRAOPERATORIA



Febbraio 2009



OSNA



A TORINO



Clin Cancer Res 2007;13(16) August 15, 2007

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

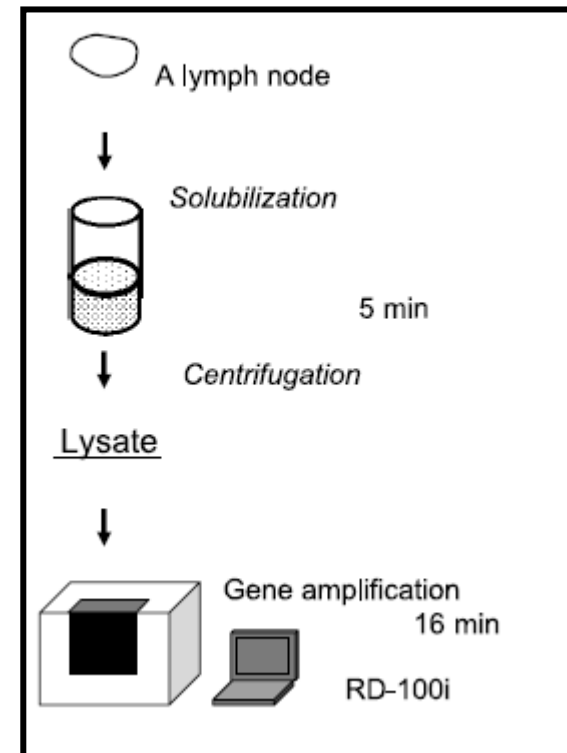
Tsujimoto et al

OSNA assay è un sistema automatizzato a ciclo chiuso per l'individuazione rapida della quantità di mRNA (citocheratina19 (CK19) mediante l'utilizzo di una reverse transcription loop-mediated isothermal amplification (**RT-LAMP**)

SLNs sono omogenati in 4 ml lysis buffer per 90 s

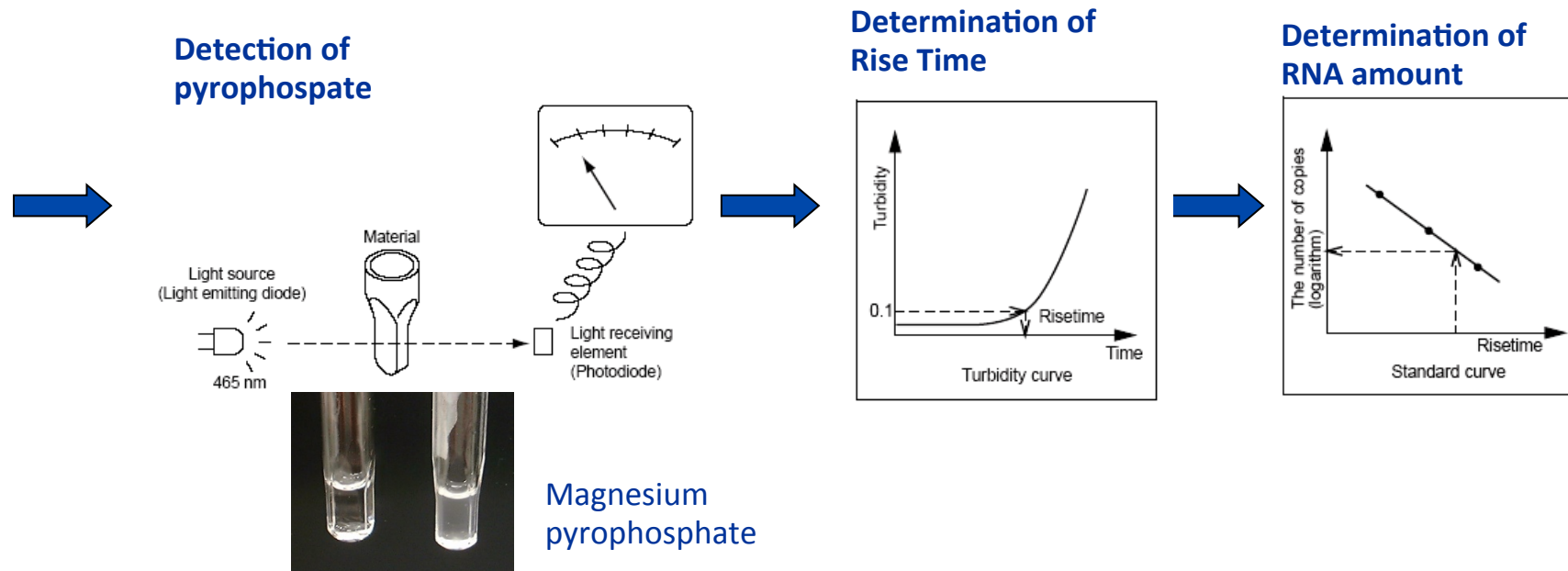
L'omogenato viene poi centrifugato a 10,000 x g a temperatura ambiente per un minuto

20µl di aliquota vengono usati per la reazione di RT-LAMP al fine di determinare i livelli di mRNA CK19 nello strumento RD-100i (Sysmex, Kobe, Japan)



Tsujimoto et al. CCR (2007)

RT-LAMP REACTION

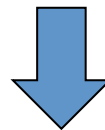


I risultati sono espressi in numero di copie di mRNA di CK19/ μ l
 Il carico metastastico viene attribuito in base a cut off prestabiliti

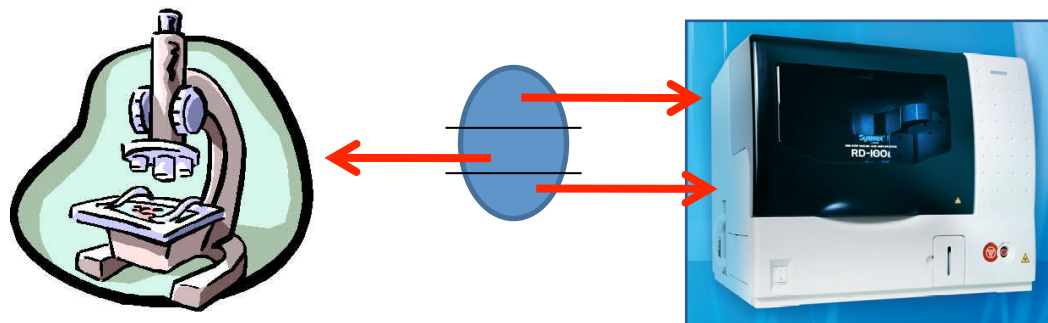
Size of metastasis	CK19 mRNA
Macro-Metastasis	++ >5.000 copies mRNA/ μ L – CK19(1.0×10^8)
Micro-Metastasis	+ 250 - 5000 copies mRNA/ μ L – CK19 (5.0×10^6)
ITC / background	< 250 copies mRNA/ μ L – CK19 (5.0×10^6)

Tsujimoto et al.
 CCR (2007)

Tsujimoto et al 2007 - Clinical Cancer Research
Visser et al 2008 - Int J Cancer
Schem et al 2009 - Virchows Arch
Tamaki et al 2009 – Clinical Cancer Research



Sensitivity: 95- 98.1%
Specificity: 94.7-100%



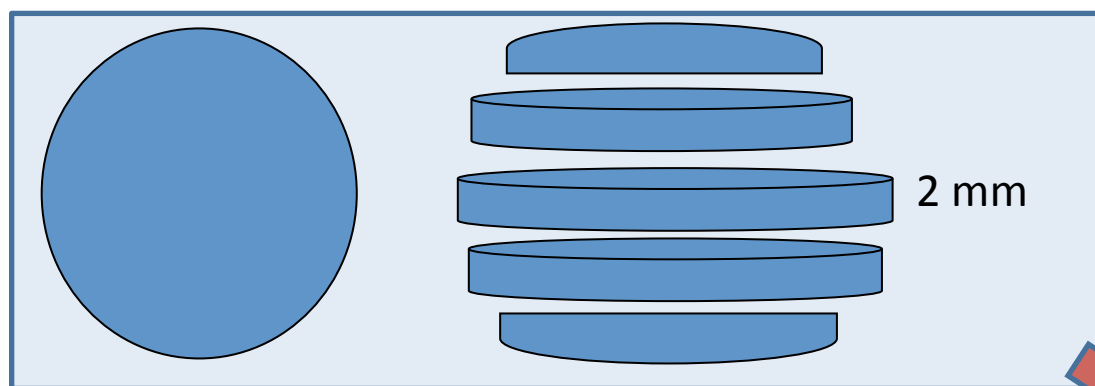
Quale risultato è quello di cui mi devo fidare?

Le micrometastasi individuate con la metodica molecolare devono essere sommate a quelle diagnosticate con la metodica istologica?

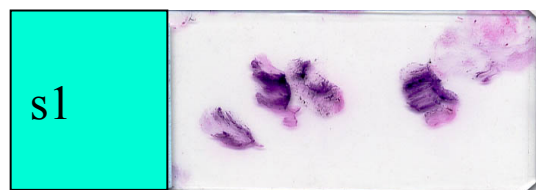
METODO UTILIZZATO E PROPOSTO AL NOSTRO COMITATO ETICO INTERAZIENDALE

Tumori CK 19 + all'esame pre-operatorio

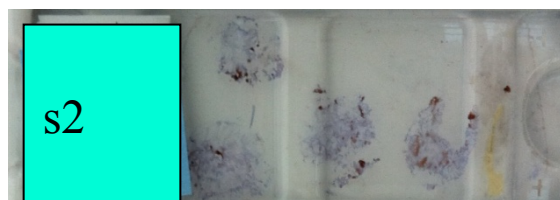
1) LS viene sezionato tradizionalmente



2) Citologico su IMPRINT (due strisci)



Ematossilina-Eosina



Immunoistochimica
rapida
AE1-AE3

3) OSNA (LS intero)



Reliability of Whole Sentinel Lymph Node Analysis by One-Step Nucleic Acid Amplification for Intraoperative Diagnosis of Breast Cancer Metastases

Isabella Castellano, MD,† Luigia Macrì, MD,*† Cristina Deambrogio, MD,* Davide Balmativola, MD,*
Riccardo Bussone, MD,†‡ Ada Ala, MD,†‡ Claudio Coluccia, MD,†‡ and Anna Sapino, MD*†*

Annals of Surgery • Volume 00, Number 00, 2011

COMPARING OSNA AND TRADITIONAL HISTOLOGICAL RESULTS

	TOTAL CASES		NEGATIVE and ITC				MICROMETS		MACROMETS	
	OSNA(%)	NON OSNA(%)	OSNA	NON OSNA			OSNA (%)	NON OSNA (%)	OSNA (%)	NON OSNA (%)
			Neg (%)	Neg (%)	ITC (%)	Neg + ITC (%)				
<i>Number of cases</i>	110 (100)	169 (100)	78 (71)	112 (66)	11 (7)	123 (73)	20 (18)	13 (8)	12 (11)	33 (20)

OSNA negative cases were comparable with the negative cases determined by standard histology (negative + ITC)

OSNA Micrometastases were higher than that determined by the standard procedure (χ^2 7.0; $P < 0.01$)

OSNA Macrometastases were lower but was not significantly different from that determined by histology

It could be an overestimation of the macro- versus micrometastases by histology. In general, we avoided OSNA in case of macroscopic appearance of metastasis in SLN

RESULTS 2

COMPARING OSNA AND TRADITIONAL HISTOLOGICAL RESULTS

	TOTAL CASES		NEGATIVE and ITC				MICROMETS		MACROMETS	
	OSNA(%)	NON OSNA(%)	OSNA	NON OSNA			OSNA(%)	NON OSNA (%)	OSNA (%)	NON OSNA (%)
			Neg (%)	Neg (%)	ITC (%)	Neg + ITC (%)				
Number of cases	110 (100)	169 (100)	78 (71)	112 (66)	11 (7)	123 (73)	20 (18)	13 (8)	12 (11)	33 (20)
Vascular invasion										
Absent	80	118	65 (81)	92 (78)	6 (5)	98 (83)	13 (16)	8 (7)	2 (3)	12 (10)
Present	30	51	13 (43)	20 (39)	5 (10)	25 (49)	7 (23)	5 (10)	10 (33)	21 (41)

Macrometastases in both protocols correlated with **vascular invasion** (χ^2 21.34; $P < 0.01$ and 21.79; $P < 0.01$)

RISULTS 3

AXILLARY STATUS

SNL	OSNA	Technology
Macrometastases	5/12 (42%)	33(45%)
Micrometastases	2/9 (22%)	2/9 (22%)

The metastatic axillary assessment in non SLN, using OSNA, did not show differences in comparison to histological additional method

OSNA: Test molecolare altamente sensibile e specifico

OSNA sites in Italy

1.	<u>Roma - IFO Regina Elena</u>	2008
2.	Erba (Co) - Osp. Fatebenefratelli	2009
3.	<u>Sanremo - Ospedale Civile</u>	2009
4.	Milano Ospedale Luigi Sacco	2009
5.	<u>TORINO - A.O. Molinette</u>	2009
6.	Conegliano V.to - A.O de' Gironcoli	2010
7.	Novara -A.O. Maggiore della carità –	2010
8.	Aviano - CRO	2010
9.	<u>Roma -S. Filippo Neri</u>	2010
10.	Napoli - Pascale	2011
11.	Brescia - Clinica Sant'Anna	2011
12.	Rozzano (MI) - Humanitas	2011
13.	Bergamo -Gavazzeni Humanitas	2011
14.	Udine – Università	2011
15.	Roma -Osp. Fatebenefratelli	2012
16.	Prato – Ospedale Misericordia	2012
17.	<u>Bergamo – Ospedali Riuniti</u>	2012
18.	Milano – Clinica Pio X	2012
19.	Cosenza – S. Annunziata	2012
20.	Bari – Policlinico	2012
21.	Como - Valduce	2012
22.	San Giovanni rotondo - Casa Sollievo della Sofferenza	2012
23.	Catania – Cannizzaro (not in routine yet – demo)	2012
24.	Andria - _BAT	2012
25.	Bari - S. Paolo	2012
26.	Foggia – Ospedale Riuniti	2012
27.	Perugia- Ospedale S. Maria della Misericordia	2012
28.	Alba- Ospedale S. Lazzaro	2012
29.	Pisa - AUO Pisana	2012
30.	Palermo – ARNAS civico	2013



33 sites in routine use (March 2013)

18 new sites in the last year

NCBI Resources How To Sign in to NCBI

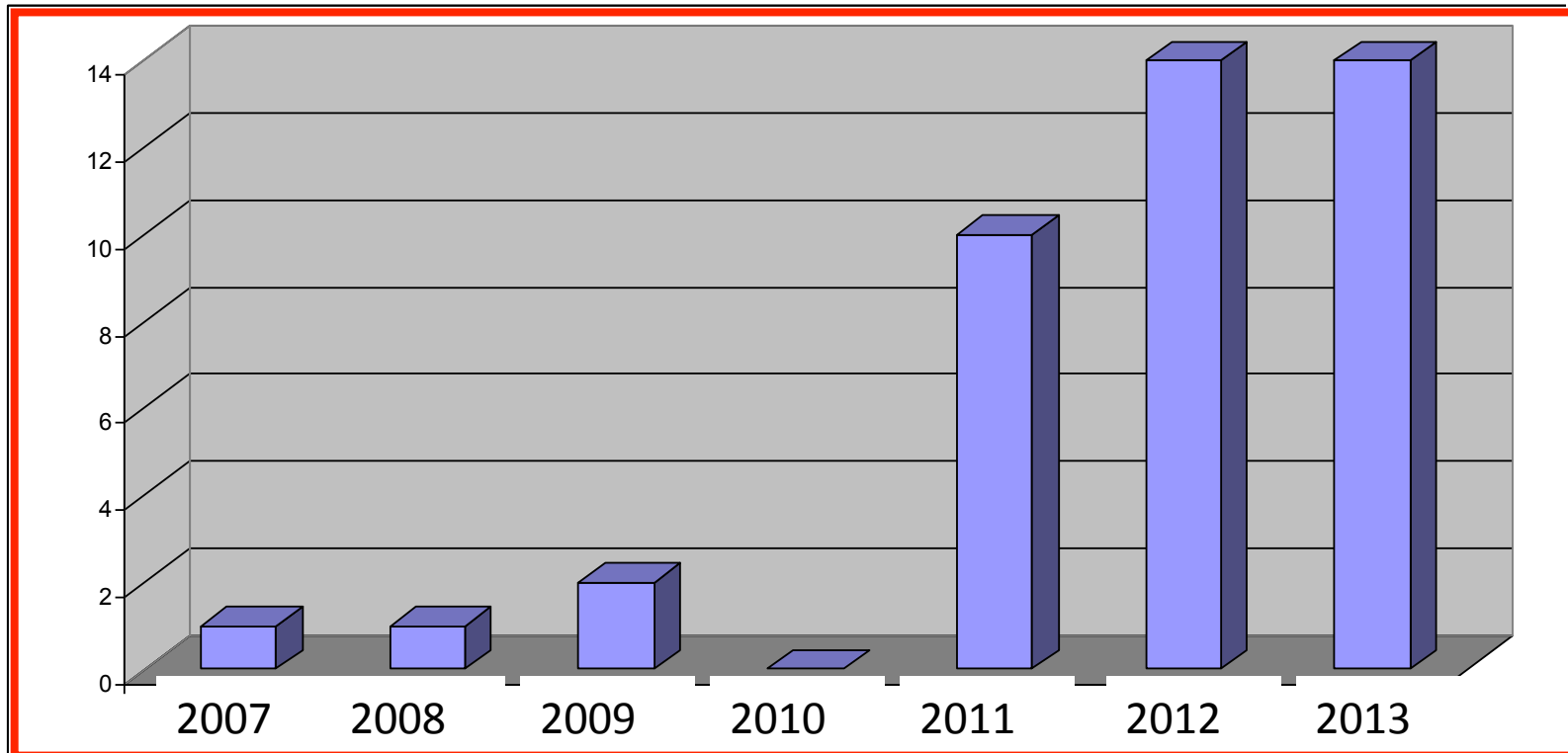
PubMed.gov OSNA AND BREAST Search

US National Library of Medicine
National Institutes of Health

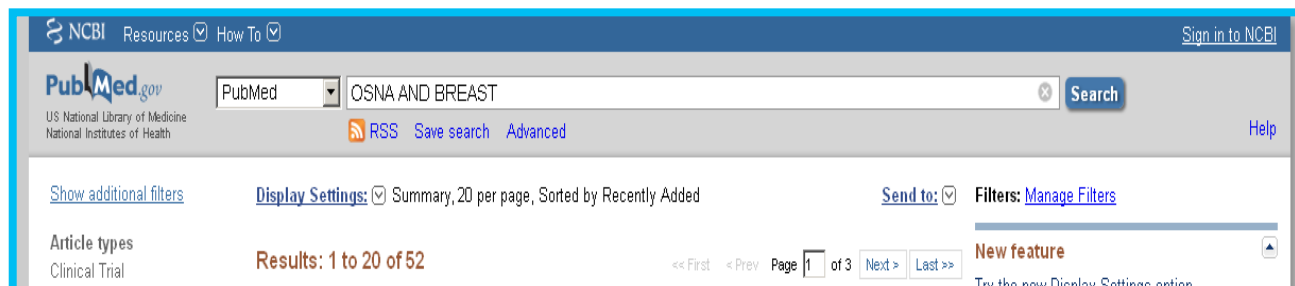
RSS Save search Advanced Help

Show additional filters Display Settings: Summary, 20 per page, Sorted by Recently Added Send to: Filters: Manage Filters

Article types Results: 1 to 20 of 52 Clinical Trial << First < Prev Page 1 of 3 Next > Last >> New feature



TEMI TRATTATI RIGUARDO L'UTILIZZO DI OSNA NELLA ROUTINE DIAGNOSTICA



AFFIDABILITA' DELLA METODICA

UTILIZZO DELLA CK19 SU CORE BIOPSY PREOPRATORIA PER IDENTIFICARE PAZIENTI DA SOTTOPORRE A TALE METODICA

UTILIZZO DI OSNA DOPO CHEMIOTERAPIA NEOADIUVANTE

RICERCA DI UN CUT OFF DI COPIE mRNA -CK19 UTILE NELL'IDENTIFICARE PAZIENTI CON MICROMETASTASI SENZA ALTRI LINFONODI COINVOLTI

Tumori negativi alla CK19: 1-2%

Histopathology 2002, 40:403–39

La mancata espressione di CK19 in IHC non necessariamente coincide con la presenza dell'mRNA del gene stesso

Virchows Arch. 2013 Jul;463(1):7-15.

I Tumori negativi alla CK19 hanno di solito un immunofenotipo basale. Tale immunofenotipo metastatizza ai linfonodi meno frequentemente dell'immunofenotipo luminale

Table 3 Multiple Regression Analysis for the Lumpectomy Model with Respect to Odds Ratios for Risk of Axillary Lymph Node Involvement

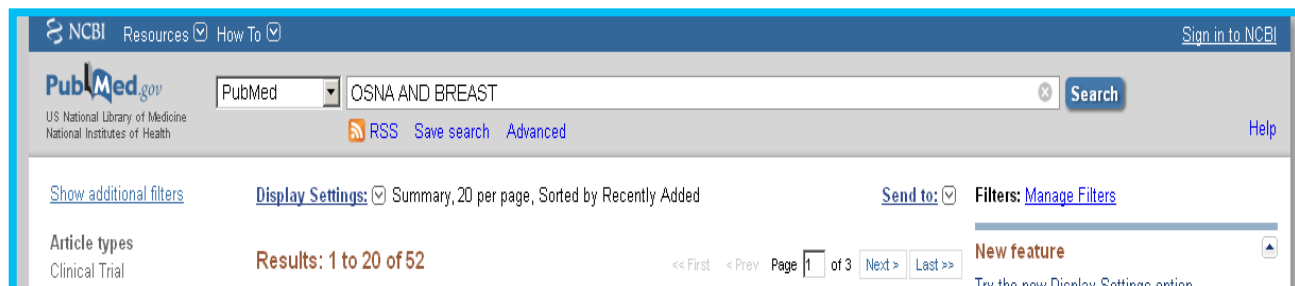
Variable	Node Negative (n = 1800)	Node Positive (n = 1361)	Odds Ratio (95% CI)	P Value
Age, Years				
Molecular Subtype				
Luminal	1397	1000	1.00	2.67 × 10 ⁻³
Luminal/HER2-positive	95	115	1.04 (0.741-1.44)	
HER2-positive/ER-negative/PgR-negative	109	131	1.19 (0.872-1.63)	
Basal	199	115	0.607 (0.453-0.812)	

Clinical Breast Cancer, Vol. 8, No. 3, 249-256, 2008;

TABLE 2 Tumor and patient characteristics by subtype^a

Clinicopathologic variable	Luminal A	Luminal B	HER-2	Basal	P value ^b
<i>N</i>	4336	476	368	892	
Age					
No. missing	0	0	0	0	
Mean	58	52	53	54	<0.0001
Tumor size					
No. missing	134	19	32	44	
Mean (cm)	1.68	1.97	2.22	2.25	<0.0001
Nodal involvement					
No. missing	0	0	0	0	
% ≥1 positive LN	43%	52%	57%	44%	<0.0001
% ≥4 positive LN	11%	20%	28%	14%	<0.0001

TEMI TRATTATI RIGUARDO L'UTILIZZO DI OSNA NELLA ROUTINE DIAGNOSTICA



AFFIDABILITA' DELLA METODICA

UTILIZZO DELLA CK19 SU CORE BIOPSY PREOPRATORIA PER IDENTIFICARE PAZIENTI DA SOTTOPORRE A TALE METODICA

UTILIZZO DI OSNA DOPO CHEMIOTERAPIA NEOADIUVANTE

RICERCA DI UN CUT OFF DI COPIE mRNA -CK19 UTILE NELL'IDENTIFICARE PAZIENTI CON MICROMETASTASI SENZA ALTRI LINFONODI COINVOLTI

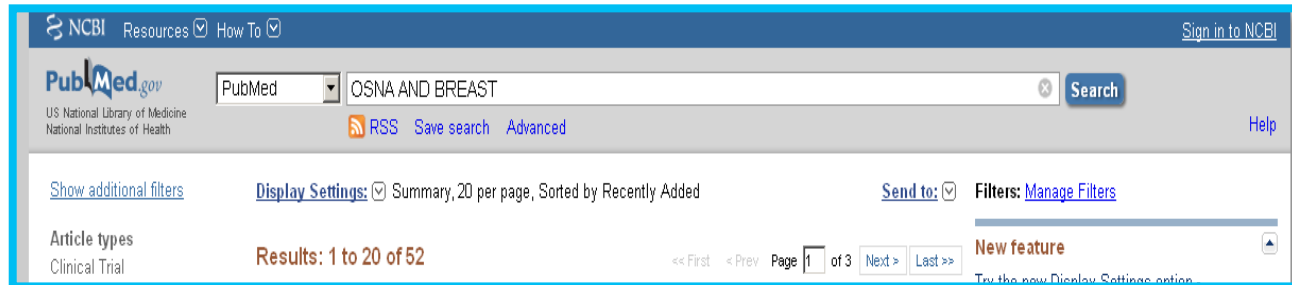
Conclusions: Intraoperative SLNB using OSNA in women with clinically negative axillary lymph nodes at initial presentation who received NAC could predict axillary status with high accuracy. Also it allows us to take decisions about the indication or not to perform an axillary dissection at the moment, thus avoiding delay in the administration of chemotherapy and benefiting the patients from a single surgical procedure

J. Navarro-Cecilia et al. / EJSO 39 (2013) 873e879

Conclusion: The OSNA assay can detect the residual tumour burden as accurately as conventional pathology, although chemotherapy-induced histological changes are present.

British Journal of Cancer (2013) 109, 1693–1698

TEMI TRATTATI RIGUARDO L'UTILIZZO DI OSNA NELLA ROUTINE DIAGNOSTICA



AFFIDABILITA' DELLA METODICA

UTILIZZO DELLA CK19 SU CORE BIOPSY PREOPRATORIA PER IDENTIFICARE PAZIENTI DA SOTTOPORRE A TALE METODICA

UTILIZZO DI OSNA DOPO CHEMIOTERAPIA NEOADIUVANTE

RICERCA DI UN CUT OFF DI COPIE mRNA -CK19 UTILE NELL'IDENTIFICARE PAZIENTI CON LS+ SENZA ALTRI LINFONODI ASCELLARI COINVOLTI

Prediction of non-sentinel lymph node metastasis in early breast cancer by assessing total tumoral load in the sentinel lymph node by molecular assay

M. Espinosa-Bravo ^{a,*}, I. Sansano ^b, S. Pérez-Hoyos ^c, M. Ramos ^d, M. Sancho ^e, J. Xercavins ^a, I.T. Rubio ^a, V. Peg ^{b,f}

EJSO 39 (2013) 766–773

Sentinel node tumour burden quantified based on cytokeratin 19 mRNA copy number predicts non-sentinel node metastases in breast cancer: Molecular whole-node analysis of all removed nodes

Tomo Osako ^{a,b,*}, Takuji Iwase ^c, Kiyomi Kimura ^c, Rie Horii ^b, Futoshi Akiyama ^a

European Journal of Cancer (2013) 49, 1187–1195

OPEN ACCESS Freely available online

March 2013 | Volume 8 | Issue 3 | e58823

Quantitative Molecular Analysis of Sentinel Lymph Node May Be Predictive of Axillary Node Status in Breast Cancer Classified by Molecular Subtypes

Simonetta Buglioni ^{1*}, Franco Di Filippo ², Irene Terrenato ³, Beatrice Casini ¹, Enzo Gallo ¹, Ferdinando Marandino ¹, Carlo L. Maini ⁴, Rossella Pasqualoni ⁴, Claudio Botti ², Simona Di Filippo ², Edoardo Pescarmona ¹, Marcella Mottolese ¹

PERCHE' L'ANALISI MOLECOLARE DEL LS

QUALI SONO GLI SVANTAGGI

LA NOSTRA SOLUZIONE MOMENTANEA

SVANTAGGI:



- Costo
- Addestramento specifico del personale
- Dati di follow-up
- Codifica del TNM (pN0(mol+))



pN0 (mol-): No regional lymph node metastases, biologically, negative molecular findings (reverse transcription-polymerase chain reaction [RT-PCR])

pN0 (mol+): Positive molecular findings (RT-PCR), but no node metastases detected by histology or IHC

NUOVE TENDENZE



QUANDO PENSAVAMO DI AVERE TUTTE LE
RISPOSTE....
CI HANNO CAMBIATO TUTTE LE DOMANDE!

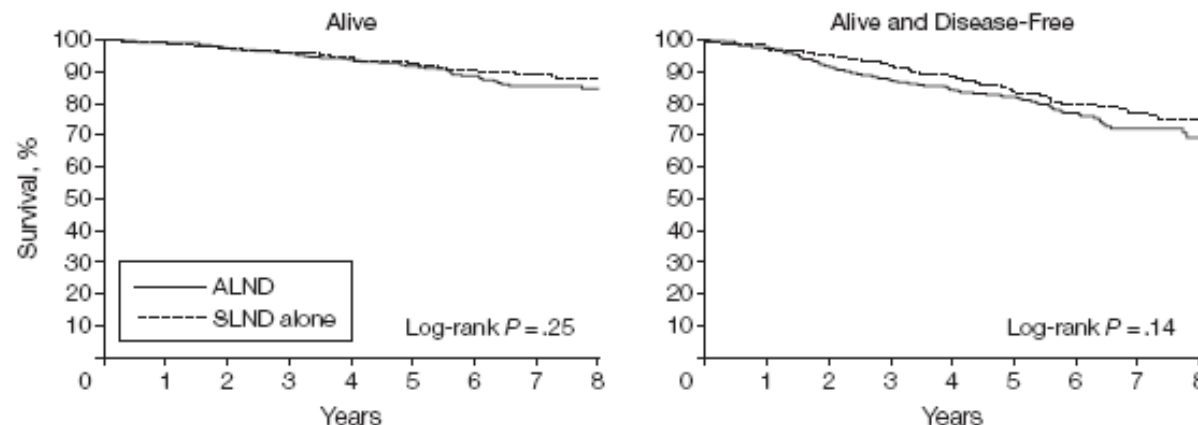
Z0011

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

A Randomized Clinical Trial

JAMA, February 9, 2011—Vol 305, No. 6

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



No. at risk	0	1	2	3	4	5	6	7	8	0	1	2	3	4	5	6	7	8
ALND	420	408	398	391	378	313	223	141	74	420	369	335	310	286	226	152	83	37
SLND alone	436	421	411	403	387	326	226	142	74	436	395	363	337	307	231	147	81	36

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

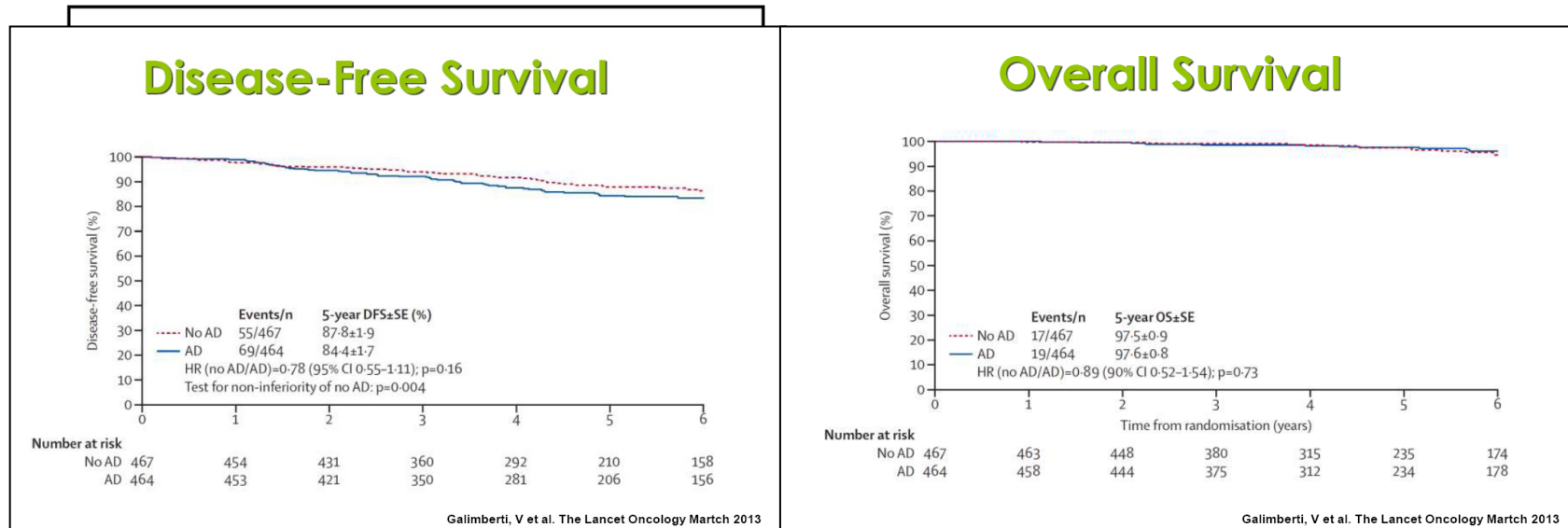
- 1900 patients
- T1-T2 cancers
- without clinical involvement of the axilla
- 1 or 2 metastatic lymph nodes

Conclusion Among patients with limited SLN metastatic breast cancer treated with breast conservation and systemic therapy, the use of SLND alone compared with ALND did not result in inferior survival.

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 Zurrada, 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

[Lancet Oncol.](#) 2013 Apr;14(4):297-305.



**FOLLOW UP
467 pts**

**AXILLARY
DISSECTION
464 pts**

ORIGINAL ARTICLE – BREAST ONCOLOGY

Sentinel Node Identification Rate and Node-Positive Rates in the EORTC 10981-22023 AMAROS Trial

0.5–3.0cm invasive breast cancer
clinically negative axilla

Randomized
ALND vs. axillary radiotherapy

ASCO
American Society of Clinical Oncology Annual Meeting
June 1-3, 2013
McCormick Place, Chicago, IL

Follow-up
Survival (1, 3, 5, 10 years)
Quality of life questionnaire (1, 2, 3, 5, 10 years)
Shoulder function (1, 3, 5, 10 years)

Shoulder function (1, 3, 5, 10 years)

Quality of life questionnaire (1, 2, 3, 5, 10 years)
Shoulder function (1, 3, 5, 10 years)

Axillary Radiotherapy Gives Good Local Control, Lowers Lymphedema Rates in Node-Positive Breast Cancer
Dr. Rutgers

Analysis of the AMAROS trial patients with a tumor-positive axilla who were randomly treated with ART compared with ALND. Results of axillary control and arm and

Personalizing the treatment of women with early breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013

A. Goldhirsch^{1*}, E. P. Winer², A. S. Coates³, R. D. Gelber⁴, M. Piccart-Gebhart⁵, B. Thürlimann⁶ & H.-J. Senn⁷ Panel members[†]

Annals of Oncology 24: 2206–2223, 2013
doi:10.1093/annonc/mdt303

WHEN NOT TO DO ALND

In patients with one or two positive sentinel nodes following breast-conserving surgery **when** whole breast radiation therapy is planned.

WHEN WE DO NOT KNOW (The Panel was equally divided)

In patients undergoing mastectomy followed by radiotherapy

WHEN TO DO ALND

If no radiotherapy was planned.

In patients with three or more involved sentinel nodes or with nodes that were clinically involved before surgery and confirmed by biopsy.



IL PARADOSSO ITALIANO

The Breast 21 (2012) 678–681

Contents lists available at SciVerse ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Viewpoints and debate

Trial SOUND

A new trial in
Sentinel node vs

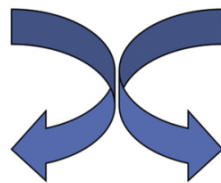
Sentinel node vs Observation after axillary Ultra-souND



- 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



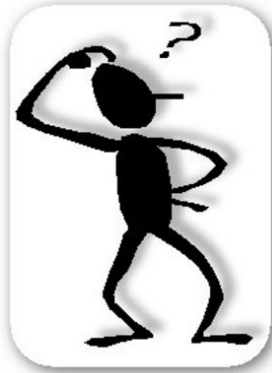
SNB policy No axillary surgery



33 sites in routine use

18 new sites in the last year

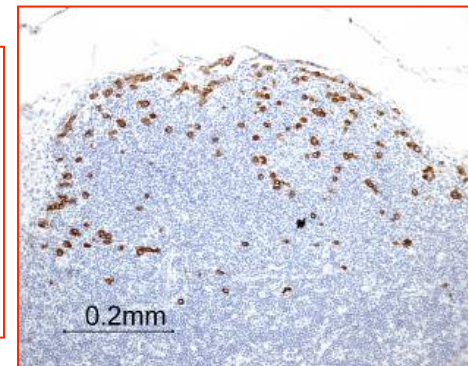
2013: COSA DOBBIAMO FARE??



Metodica molecolare altamente sensibile e specifica anche nei confronti di piccoli depositi tumorali nel linfonodo sentinella



Metodo tradizionale, meno rigorosa ma sufficiente a prendere una decisione mirata sull'ascella?



PERCHE' L'ANALISI MOLECOLARE DEL LS

QUALI SONO GLI SVANTAGGI

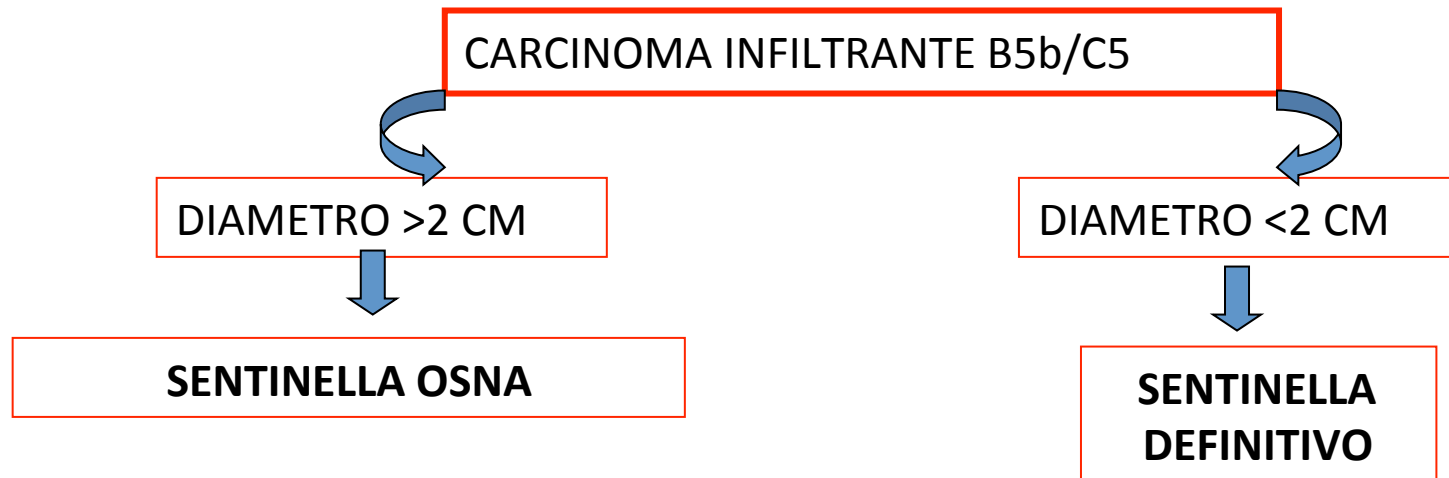
LA NOSTRA SOLUZIONE *MOMENTANEA*



LA NOSTRA SOLUZIONE *MOMENTANEA*



INCONTRI MULTIDISCIPLINARI lunedì pomeriggio
DISCUSSIONE DI TUTTI I CASI PRE-OPERATORI



Perche' il diametro?

Table 1

Variables included in the different predictive models tested.

G. Cserni et al. *Surgical Oncology* 21 (2012) 59-65

Variables	MSKCC nomogram	MD Anderson score	Tenon score	Mayo nomogram	Louisville clinical prediction rule	Stanford nomogram	French micrometastasis nomogram	Masaryk nomogram
Age	-	-	-	+	-	-	-	-
Tumour size	+	+	+	+	+	+	+	+
Categorical	-	+	+	-	+	-	+	+
Continuous	+	-	-	+	-	+	-	-
Tumour type	+	-	-	-	-	-	+	+
Nuclear grade	+	-	-	-	-	-	-	-
LVI	+	+	-	-	-	+	+	+
ER status	+	-	-	-	-	-	-	-
Triple negativity	-	-	-	-	-	-	-	-
Multifocality of the primary tumour	+	-	-	-	-	-	-	+
Tumour location	-	-	-	-	-	-	-	-
Number of positive SNs	+	-	-	+	+	-	-	+
Number of negative SNs	+	-	-	+	-	-	-	+
Number of SNs	-	+	-	-	-	-	-	-
Proportion of positive SNs	-	-	+	-	+	-	-	-
Detection method of SN metastasis	+	-	-	-	-	-	+	-
Size of SN metastasis	-	+	+	+	-	+	-	+
Categorical	-	+	+	-	-	+	-	+
Continuous	-	-	-	+	-	-	-	-
Extracapsular spread	-	-	-	+	-	-	-	+

Il diametro del tumore primitivo è strettamente correlato alla metastatizzazione ed è utilizzato in tutti i nomogrammi che predicono il rischio di ulteriori linfonodi metastatici nel cavo ascellare

I NOSTRI DATI

DA MARZO 2013 A OGGI

	LS negativo	LS micro	LS macro	Totale
>20 mm	31	13	16	60
<20 mm	53	6	9	68

CONCLUSIONI

La prognosi del tumore alla mammella dipende maggiormente dalla biologia del tumore che dal coinvolgimento linfonodale.

METASTASI LINFONODALE = EPIFENOMENO

J Clin Oncol 2010 28:3271–3277,

J Clin Oncol 2010 28:1684–1691,

Breast Cancer Res Treat 2009 117:199–204,

Semin Radiat Oncol 2009 19:204–210



La storia e le scelte storiche vanno sempre contestualizzate..

**LE MODERNE METODICHE MOLECOLARI
SICURAMENTE RAPPRESENTANO UN TENTATIVO
DI UNIFORMARE E STANDARDIZZARE
LA DIAGNOSTICA DEL LS...ALMENO FINO A
QUANDO QUESTA METODICA NON
TRAMONTERA' DEL TUTTO...**

**GRAZIE A TUTTI PER
L'ATTENZIONE**