Azienda USL di Modena
in collaborazione con
Regione Emilia-Romagna
Assessorato politiche per la salute

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA

La sorveglianza epidemiologica dello screening dei tumori della mammella nella Regione Emilia-Romagna

Seminario di studio

Bologna, 30 marzo 2017

Sala 20 maggio 2012
Viale della Fiera 8 – Bologna

Seconda sessione:
nodi strategici e sviluppi
Moderatori: Mario Taffurelli, Dolores Santini

14.30 **La procedura del linfonodo sentinella nel PDTA del tumore della mammella**
Maria Grazia Lazzaretti

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale di Modena

Ospedale Ramazzini – Carpi
Unità Operativa Chirurgia Generale
(Unità semplice di Chirurgia Senologica)

LA PROCEDURA DEL LINFONODO SENTINELLA NEL PDTA DEL TUMORE DELLA MAMMELLA

Maria Grazia Lazzaretti

ESEMPIO DI MULTIDISCIPLINARIETA'

Centro Interregionale Screening Oncologia

CDS Bologna
CPO Torino
CSPO Firenze

Workshop CHIRURGHI: NUOVE TECNOLOGIE per gli OPERATORI degli SCREENING ONCOLOGICI

Il workshop è rivolto a medici specialisti coinvolti nel trattamento del carcinoma mammario.

29 Novembre 1999

Per informazioni e iscrizioni rivolgersi a:

CSPO Presidio per la Prevenzione Oncologica
Azienda Ospedaliera Careggi - Firenze
Tel. 055- 5012218 - Fax 055- 5001623
E-mail: ajcro@tin.it

PRESIDIO PER LA PREVENZIONE ONCOLOGICA (CSPO)
Centro di Riferimento Regionale per la Prevenzione Oncologica
Centro Interregionale Screening Oncologia (CISO)
AZIENDA OSPEDALIERA CAREGGI - FIRENZE
V.le Volta, 171 - 50131 Firenze
Tel: 055/5012218 - Fax.: 055/5001623 - E Mail ajcro@tin.it

WORKSHOP - 29 NOVEMBRE '99

CHIRUGHI: NUOVE TECNOLOGIE

Direttore del Corso	**Dr. Vito Distante**
Sede del Corso	Firenze, presso la CISL Studium Via della Piazzola,71 (055/5032111) Raggiungibile dalla stazione con il bus n. 7 (scendere a Camerata)
Segreteria organizzativa	Dr.ssa Isabel de Maurissens - Maria Mereu Tel. 055/5012218

PROGRAMMA DELLA GIORNATA

9.00 - 9. 15	Introduzione e presentazione della giornata	V.Distante
9.30 - 10.30	Stato dell'arte ed indicazione all'uso della biopsia del linfondo sentinella	M.Mano
10.30 - 11.00	*Coffee Break*	
11.00 - 11.45	Il ruolo del medico nucleare	F.Briganti
11.45 - 12.45	Ricerca intraoperatoria radioimmunoguidata	A.Luini
12.45 - 13.30	Ricerca intraoperatoria con il metodo del colorante	G.Canavese
13.30 - 14.30	*Pranzo*	
14.30 - 15.30	Il ruolo del patologo La problematica delle micrometastasi	S.Bianchi
15.30 - 16.00	Centratura radioguidata delle lesioni non palpabili	A.Luini
16.00 - 16 30	Omologazione del metodo e linee guida	L.Cataliotti
16.30 - 17.00	Discussione e chiusura del Corso	

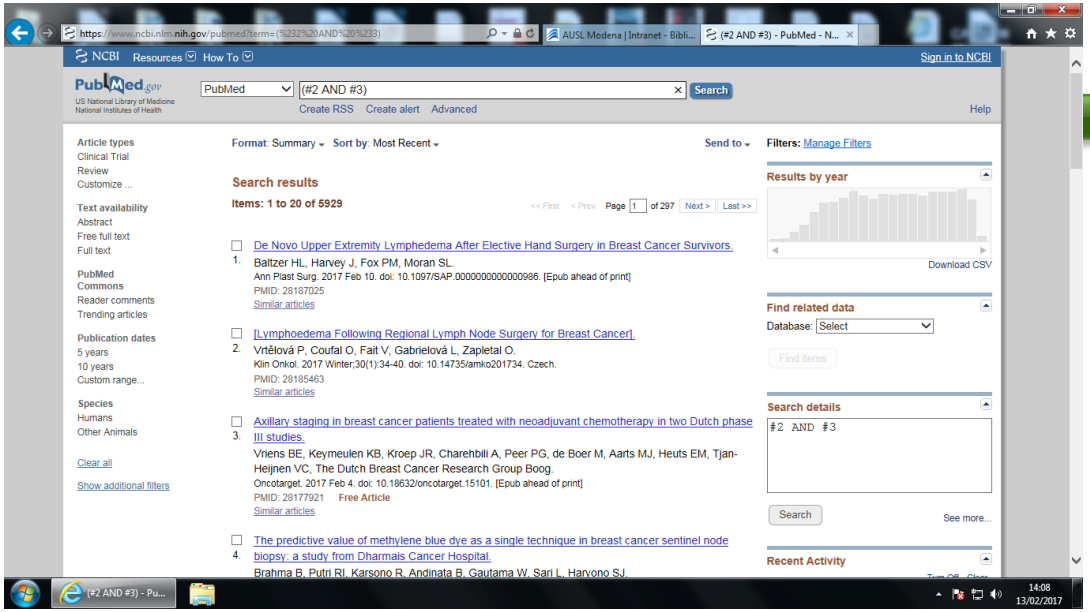
VALUTAZIONE ASCELLA

- **PROGNOSI**

- **RACCOMANDAZIONI PER LA TERAPIA ADIUVANTE**

…NONOSTANTE MECCANISMI MOLECOLARI…

MEDLINE SEARCH



5929 ARTICOLI

101 FULL TEXT

1° FRASE DI INTRODUZIONE:

- **critical role as a staging procedure**
- **prognostic indicator**
- **integral role as a staging tool**
- **a guide to adjuvant therapy**
- **critical role in loco-regional control**
- **crucial role in staging systems**
- **significant prognostic factor**

STANDARD NELLA STADIAZIONE DELL'ASCELLA

…MA…:

- **NON SERVE PER ALCUNE PAZIENTI**
- **SE POSITIVO, NON SEMPRE NECESSARIA UNA D.A.**
- **SE FNAC+ PRE-INTERVENTO: SEMPRE D.A.?**

TROUBLESHOOTING SENTINEL LYMPH NODE BIOPSY IN BREAST CANCER SURGERY

No

Consider blue dye injection and lymphoscintigraphy

Yes

Has prior

radi
bre

- Ensure gamma probe i
- Inject additional fluid (massage
- Search for extramamm
- Ensure sufficient dose surgery or 2.5 mCi if i
- Contact nuclear medic concern

- Interro
- Palpat
- Consi
- Consi

Cons

Consider contacting the nuclear medicine department to use unfiltered radioactive colloid*

N

Remove any node with a count >10% of the hottest node

No

If the previous steps are completed and the surgeon is still concerned, consider axillary ultrasound to locate any lymph nodes

N

Overlap between injection site and axilla (i.e. cannot isolate sentinel lymph node)

Have you made adjustments to reduce shine-through ?

No

- Angle gamma probe away from injection site and toward axilla
- Adjust probe settings to reduce background noise
- Use collimator
- Retract breast downward and medially

Yes

Did you utilize a peritumoral injection technique?

Yes

Proceed with lumpectomy or mastectomy and then re-evaluate the axilla

No

Consider dual tracer with blue dye

Proceed with incision

- Recheck axilla with gamma probe
- Advance gamma probe into axillary fat to increase additional distance

S.N.B. = AN OUTDATED PROCEDURE?

1. **INVASIVE PROCEDURE**
2. **AXILLARY SURGERY NOT THERAPEUTIC**
3. **IMPORTANCE OF STAGING DECREASING**

…BUT….:

"…enormous investment in health care resources."

Cyr AE et Al; J Am Coll Surg 2016

LINEE GUIDA

Senonetwork Italia Onlus

ASCO® American Society of Clinical Oncology

NCCN

ASTRO
TARGETING CANCER CARE

RAO

AIOM
Associazione Italiana di Oncologia Medica

AGO
ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.
KOMMISSION MAMMA

NICE National Institute for Health and Care Excellence

A.N.I.S.C.
Associazione Nazionale Italiana Senologi Chirurghi

SENTINEL LYMPH NODE BIOPSY WITH EARLY-STAGE BREAST CANCER: AMERICAN SOCIETY OF CLINICAL ONCOLOGY CLINICAL PRACTICE GUIDELINE. UPDATE

BOTTOM LINE 2014

Guideline Questions

How should the results of sentinel node biopsy (SNB) be used in clinical practice? What is the role of SNB in special circumstances in clinical practice? What are the potential bene

Target Population

Medical oncologists, radiation oncologists, pa

Target Audience

Medical oncologists, surgical oncologists, hos

Methods

An Expert Panel was convened to determine w from the medical literature.

Recommendations

Recommendation 1. Clinicians should not recommend axillary lymph node dissection (ALND) for women with early-stage breast cancer who do not have nodal m Strength of recommendation: strong).

Recommendation 2.1. Clinicians should n or two sentinel lymph node metastase whole-breast radiotherapy (Type: evid recommendation: strong).

Recommendation 2.2. Clinicians may offer SNB specimens who will receive mast Strength of recommendation: weak).

Recommendation 3. Clinicians may offer circumstances:

3.1. Multicentric tumors (Type: evidenc recommendation: moderate).

3.2. Ductal carcinoma in situ when mas Evidence quality: insufficient. Strength of recommendation: weak).

3.3. Prior breast and/or axillary surgery (Type: evidence based; benefits outweigh harms. Evidence quality: intermediate. Strength of recommendation: strong).

3.4. Preoperative/neoadjuvant systemic therapy (Type: evidence based; benefits outweigh harms. Evidence quality: intermediate. Strength of recommendation: moderate).

Recommendation 4. There are insufficient data to change the 2005 recommendation that clinicians should not perform SNB for women who have early-stage breast cancer and are in the following circumstances:

4.1. Large or locally advanced invasive breast cancers (tumor size T3/T4) (Type: informal consensus. Evidence quality: insufficient. Strength of recommendation: weak).

4.2. Inflammatory breast cancer (Type: informal consensus. Evidence quality: insufficient. Strength of recommendation: weak).

4.3. Ductal carcinoma in situ when breast-conserving surgery is planned (Type: informal consensus. Evidence quality: insufficient. Strength of recommendation: strong).

4.4. Pregnancy (Type: informal consensus. Evidence quality: insufficient. Strength of recommendation: weak).

184 pubblications

8 full text articles

Consistent with 2014 recommendations

CAUTION:

- **T > 5 cm**
- **large or bulky sentinel node mts**
- **gross extranodal extension**

BOTTOM LINE 2017

Guideline Question

- How should the results of sentinel node biopsy (SNB) be used in clinical practice? What is the role of SNB in special circumstances ed with SNB?

gy nurses, patients/caregivers, and guideline implementers.

d an Update Committee was convened to review the evi- ecommendations and strength of evidence is provided in the

- Recommendation 1: Clinicians should not recommend axillary lymph node dissection (ALND) for women with early-stage breast cancer who do not have nodal metastases. Type: evidence based; benefits outweigh harms. Evidence quality: high. Strength of recommendation: strong.

mmend ALND for women with early-stage breast cancer who have one or two breast-conserving surgery (BCS) with conventionally fractionated whole-breast weigh harms. Evidence quality: high. Strength of recommendation: strong.
D for women with early-stage breast cancer with nodal metastases found on SNB ed; benefits outweigh harms. Evidence quality: low. Strength of recommendation:

r women who have operable breast cancer who have the following circumstances: benefits outweigh harms. Evidence quality: intermediate. Strength of recommen-

ectomy is performed. Type: informal consensus; benefits outweigh harms. Evi- ndation: weak.
idence based; benefits outweigh harms. Evidence quality: intermediate. Strength

Type: evidence based; benefits outweigh harms. Evidence quality: intermediate.

- Recommendation 4: There are insufficient data to change the 2005 recommendation that clinicians should not perform SNB for women who have early-stage breast cancer and are in the following circumstances:
- 4.1: Large or locally advanced invasive breast cancers (tumor size T3/T4). Type: informal consensus. Evidence quality: insufficient. Strength of recommendation: weak.
- 4.2: Inflammatory breast cancer. Type: informal consensus. Evidence quality: insufficient. Strength of recommendation: weak.
- 4.3: DCIS when breast-conserving surgery is planned. Type: informal consensus. Evidence quality: insufficient. Strength of recommendation: strong.
- 4.4: Pregnancy. Type: informal consensus. Evidence quality: insufficient. Strength of recommendation: weak.

Qualifying Statements

- Clinicians may perform SNB for DCIS diagnosed by minimally invasive breast biopsy: one, when mastectomy is planned, because this precludes subsequent SNB at a second operation; two, when physical examination or imaging shows a mass lesion highly suggestive of invasive cancer; or three, the area of DCIS by imaging is large (≥ 5 cm). SNB may be offered before or after neoadjuvant systemic therapy (NACT), but the procedure seems less accurate after NACT. This update deleted a recommendation for patients having undergone prior nononcologic breast surgery or axillary surgery because of insufficient data to inform a recommendation.

Cochrane Library
Cochrane Database of Systematic Reviews

COCHRANE LYBRARY

Axillary treatment for operable primary breast c… (Review)

26 RCTs

No Ax surgery vs ALND	10 trials	3849 …	…oderate quality evidence
Ax sampling vs ALND	6 tri…	…59 pts	Low quality evidence
SLNB vs ALN…	…ls	9426 pts	Moderate quality evidence
R…	4 trials	2585 pts	High quality

"ALND of the clinically and radiologically uninvolved axilla is no longer acceptable practice in people with breast cancer."

LES… SURGERY vs ALND: < OS (HR=1.08)
> LR (HR 1.53)

Low quality evidence suggests increased risk of lymphoedema with ALND

Bromham N et Al; Cochrane Collaboration 2017

Cochrane Library
Cochrane Database of Systematic Reviews

COCHRANE LYBRARY

Axillary treatment for operable primary breast cancer (Review)

Comparison 5 Less surgery versus ALND, Outcome 4 Local recurrence

Study or subgroup	Less surgery n/N	More surgery n/N	Hazard Ratio	Weight
1 axillary sampling vs ALND				
Cape Town (1)	8/232			
Cape Town (2)	9/173			
Cardiff	31/99			
Edinburgh 1	15/234			
Subtotal (95% CI)	**738**			
Heterogeneity: Chi² = 2.01, df = 3 (P = 0.57); I² =0.0%				
Test for overall effect: Z = 1.67 (P = 0.095)				
2 SLNB vs ALND				
Milan (3)	4/259			
Subtotal (95% CI)	**259**			
Heterogeneity: not applicable				
Test for overall effect: Z = 0.08 (P = 0.93)				
3 radiotherapy vs ALND				
Manchester	41/1113			
NSABP B-04 (4)	42/2025			
NSABP B-04 (5)	18/3896			
SE Scotland (6)	21/2204			
SE Scotland (7)	17/878			
WSSA Glasgow (8)	13/483			
WSSA Glasgow	1/41			
Subtotal (95% CI)	**10640**	**11616**		**76.5 %**
Heterogeneity: Chi² = 4.34, df = 6 (P = 0.63); I² =0.0%				
Test for overall effect: Z = 2.07 (P = 0.038)				
Total (95% CI)				**100.0 %**
Heterogeneity: Chi² = 12.34, df = 11 (P = 0.34); I² =11%				
Test for overall effect: Z = 1.05 (P = 0.30)				
Test for subgroup differences: Chi² = 5.99, df = 2 (P = 0.05), I² =67%				

0.01 0.1 1 10 100
Favours less surgery | Favours more surgery

Comparison 5 Less surgery versus

Study or subgroup	Less surgery n/N	More su
1 no axillary surgery vs ALND		
Milan 2	9/110	
NSABP B-04	107/365	10
Subtotal (95% CI)	**475**	
Heterogeneity: Chi² = 1.66, df = 1 (P = 0.20); I² =40%		
Test for overall effect: Z = 0.59 (P = 0.55)		
2 axillary sampling vs ALND		
E'dburgh Sample/Clear	53/203	5
Subtotal (95% CI)	**203**	
Heterogeneity: not applicable		
Test for overall effect: Z = 0.27 (P = 0.79)		
3 radiotherapy vs ALND		
NSABP B-04 (1)	127/294	12
NSABP B-04 (2)	111/365	10
Subtotal (95% CI)	**659**	
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.95); I² =0.0%		
Test for overall effect: Z = 0.96 (P = 0.34)		
Total (95% CI)		
Heterogeneity: Chi² = 1.69, df = 4 (P = 0.79); I² =0.0%		
Test for overall effect: Z = 1.15 (P = 0.25)		
Test for subgroup differences: Chi² = 0.02, df = 2 (P = 0.99), I² =		

Comparison 5 Less surgery versus ALND, Outcome 7 Lymphoedema. Increase in arm volume at 12 months postop.

Study or subgroup	Less surgery n/N	More surgery n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 no axillary surgery vs ALND					
Addenbrookes (1)	6/53	12/45		4.2 %	0.35 [0.12, 1.03]
Guy's (2)	0/91	6/104		2.2 %	0.08 [0.00, 1.49]
Institut Bergonie (3)	3/258	41/274		14.4 %	0.07 [0.02, 0.22]
NSABP B-04 (4)	48/312	177/577		38.5 %	0.41 [0.29, 0.59]
Subtotal (95% CI)	**714**	**1000**		**59.4 %**	**0.31 [0.23, 0.43]**
Total events: 57 (Less surgery), 236 (More surgery)					
Heterogeneity: Chi² = 9.68, df = 3 (P = 0.02); I² =69%					
Test for overall effect: Z = 7.29 (P < 0.00001)					
2 axillary sampling vs ALND					
Cardiff (5)	11/45	20/40		5.9 %	0.32 [0.13, 0.81]
Subtotal (95% CI)	**45**	**40**		**5.9 %**	**0.32 [0.13, 0.81]**
Total events: 11 (Less surgery), 20 (More surgery)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.40 (P = 0.016)					
3 SLNB vs ALND					
GIVOM Sentinella (6)	15/336	30/341		10.4 %	0.48 [0.26, 0.92]
Milan (7)	0/100	12/100		4.6 %	0.04 [0.00, 0.60]
SNAC (8)	29/544	47/544		16.3 %	0.60 [0.37, 0.96]
Subtotal (95% CI)	**980**	**985**		**31.3 %**	**0.48 [0.33, 0.69]**
Total events: 44 (Less surgery), 89 (More surgery)					
Heterogeneity: Chi² = 4.06, df = 2 (P = 0.13); I² =51%					
Test for overall effect: Z = 3.92 (P = 0.000090)					
4 radiotherapy vs ALND					
SE Scotland	5/100	10/100		3.5 %	0.47 [0.16, 1.44]
Subtotal (95% CI)	**100**	**100**		**3.5 %**	**0.47 [0.16, 1.44]**
Total events: 5 (Less surgery), 10 (More surgery)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.32 (P = 0.19)					
Total (95% CI)	**1839**	**2125**		**100.0 %**	**0.37 [0.29, 0.46]**
Total events: 117 (Less surgery), 355 (More surgery)					
Heterogeneity: Chi² = 16.78, df = 8 (P = 0.03); I² =52%					
Test for overall effect: Z = 8.64 (P < 0.00001)					
Test for subgroup differences: Chi² = 3.25, df = 3 (P = 0.36), I² =8%					

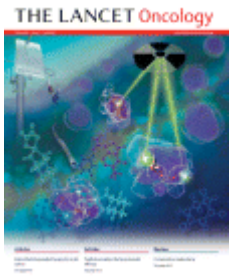
p < 0.00001

0.001 0.01 0.1 1 10 100 1000
Favours less surgery | Favours more surgery

TREATMENT OF THE AXILLA IN PATIENTS WITH PRIMARY BREAST CANCER AND LOW BURDEN AXILLARY DISEASE: LIMITATIONS OF THE EVIDENCE FROM RANDOMIZED CONTROLLED TRIALS

1. ***Is there a need for ALND in SLN negative patients?***
   - **NSABP-B32: good level I evidence**
2. ***Is there a need for ALND in SLN micrometastasis?***
   - **IBCSG-23-01: non practice changing**
3. ***Is there a need for ALND in SLN macrometastasis?***
   - **ACOSOG Z0011: critical limitations, critically flawed**
4. ***Is axillary radiotherapy equivalent to ALND in patients with SLN macrometastasis?***
   - **AMAROS TRIAL: underpowdered, low risk population**
5. ***Does regional nodal irradiation add to whole breast irradiation after BCS for women with node positive or high risk node negative breast cancer treated with adjuvant systemic therapy?***
   - **MA20: important in interpreting Z0011 results**

Robertson JFR et Al; Crit Rev Oncol Hemat 2017



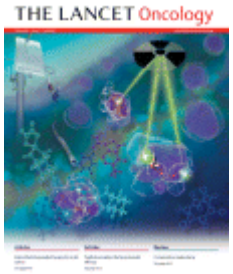
KYOTO BREAST CANCER CONSENSUS CONFERENCE 1 DE-ESCALATION OF AXILLARY SURGERY IN EARLY BREAST CANCER

35 MULTIDISCIPLINARY PANEL MEMBERS

TREND TO DE-ESCALATION

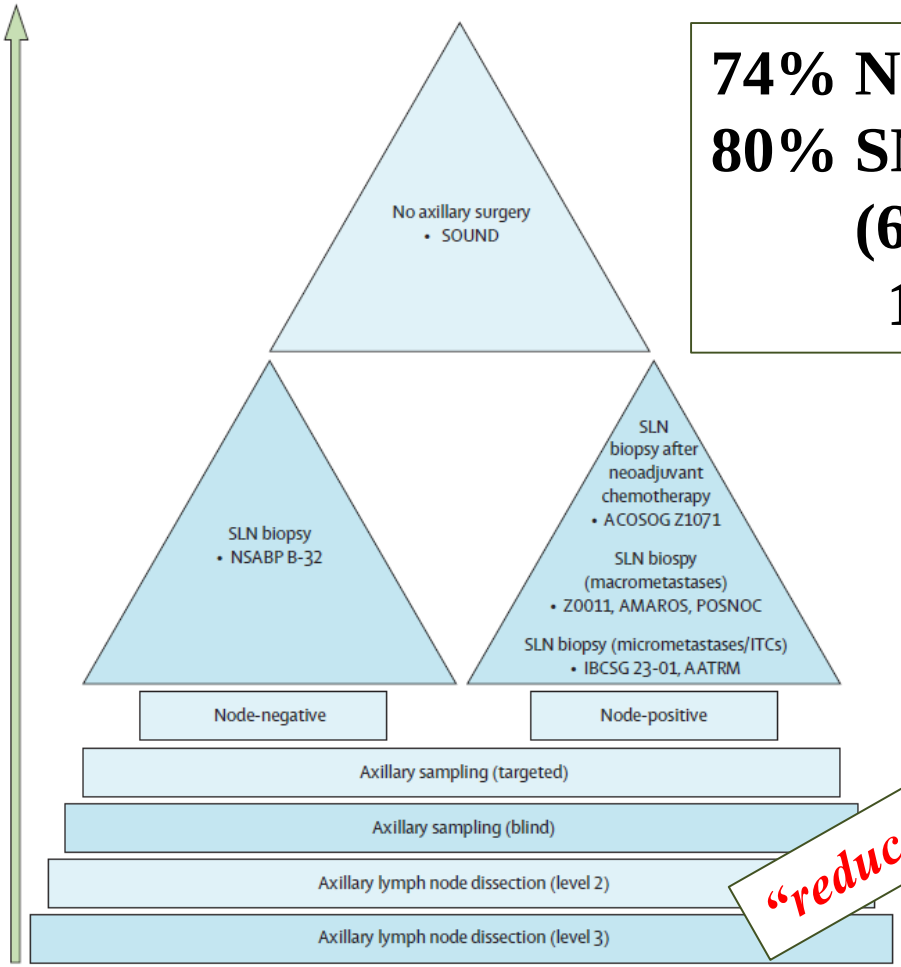
1. **advent of sentinel node biopsy**
2. **improvements in adjuvant therapies**
3. **down-staging of disease with neo-adjuvant approaches**
4. **predictive biomarkers superseding nodal status as prime determinants of eligibility for adjuvant systemic therapy**

Jatoi I et Al; Lancet Oncol 2016



KYOTO BREAST CANCER CONSENSUS CONFERENCE 1 DE-ESCALATION OF AXILLARY SURGERY IN EARLY BREAST CANCER

35 MULTIDISCIPLINARY PANEL MEMBERS



74% No ALND in low volume +SNs
80% SNB after NACT
(60% >2 nodes removed
17% placed a marker)

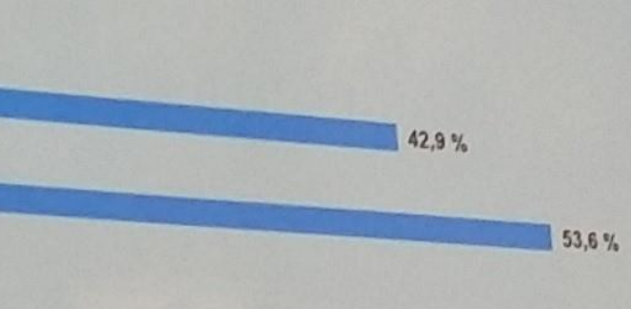
"reduced morbidity and enhanced quality of life"

Jatoi I et Al; Lancet Oncol 2016

st.gallenoncology conferences

Surgery of the Axilla following Neo-Adjuvant Chemotherapy

20. In a patient who is clinically node-positive at diagnosis and who downstages after chemotherapy: Is SN biopsy appropriate with 1-2 LN detected?



15th St.Gallen International Breast Cancer Conference 2017 Consensus

BCC 2017

st.gallenoncology conferences

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onference 2017

Consensus

BIG
International Group

IBCSG
International Breast Cancer Study Group

THE INTERPLAY BETWEEN HOSPITAL AND SURGEON FACTORS AND THE USE OF SENTINEL LYMPH NODE BIOPSY FOR BREAST CANCER

LIKELIHOOD OF RECEIVING SLNB

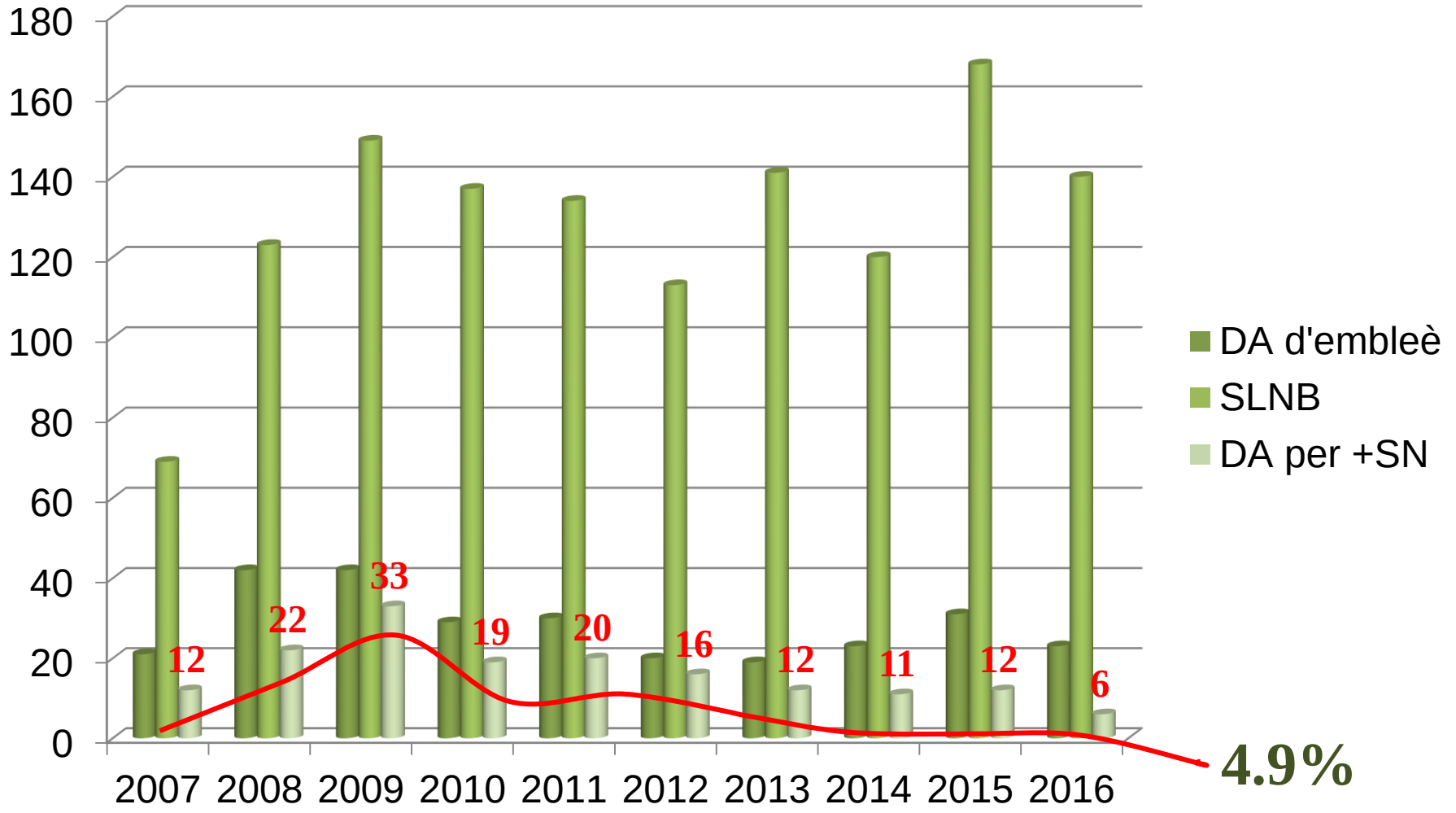
HIGH vs LOW VOLUME HOSPITALS	➢ OR = 1.66
HIGH COMMITMENT TO CANCER CARE	➢ OR = 1.36
NON URBAN AREAS	➢ OR = 0.43
HIGH vs LOW VOLUME SURGEONS	➢ OR = 1.90

SURGEONS DEVOLVING AT LEAST 10% OF THEIR WORK-TIME

- OR = 2.56 in low volume hospitals
- 1.78 in high volume hospitals

Yen TWF et Al; Medicine 2016

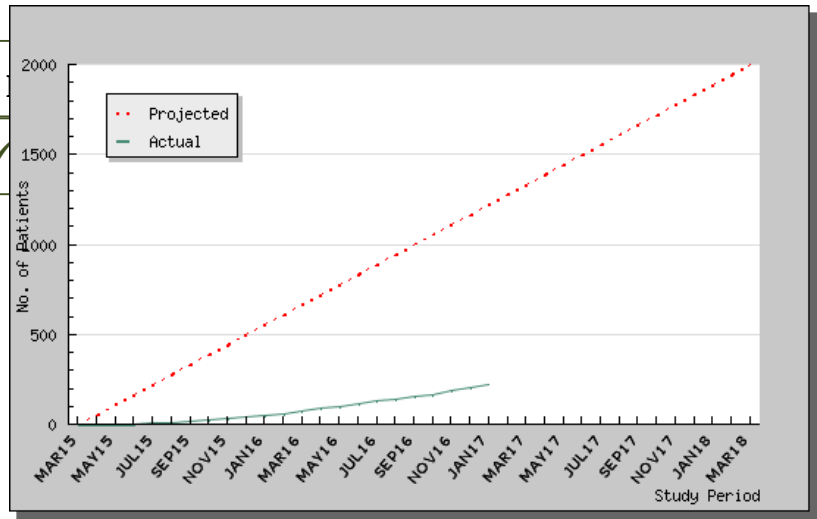
CASISTICA 2007 - 2016



CASISTICA 2007 - 2016

PROTOCOLLI INTERNI

	2007	2015
INDICAZIONI	✓ cN0 (EOL, US, FNAC) ✓ T< 3cm ✓ unicentrico	✓ cN0 (EOL, US, FNAC) ✓ CTNA ✓ multicentrico ✓ recidiva dopo SNB
CONTROINDICAZIONI	✓ recidiva ✓ CTNA ✓ > 3cm	✓ cN+ ✓ infiammatorio
SNB+	✓ DA anche per	



POST-MASTECTOMY RADIOTHERAPY: AN AMERICAN SOCIETY OF CLINICAL ONCOLOGY, AMERICAN SOCIETY FOR RADIATION ONCOLOGY, AND SOCIETY OF SURGICAL ONCOLOGY FOCUSED GUIDELINE UPDATE

FOCUSED GUIDELINE UPDATE QUESTIONS

Question 1: Is PMRT indicated in patients with T1 ... with one to three positive axillary lymph nodes ... D?

Question 2: Is PMRT indicated in pati... ors and a positive SNB who do not ... ALND?

Question 3: Is PMRT ind... presenting with clinical stage I or ... received NAST?

Question 4: Sho... internal mammary (IMNs) and/or ... ary apical nodes when PMRT is

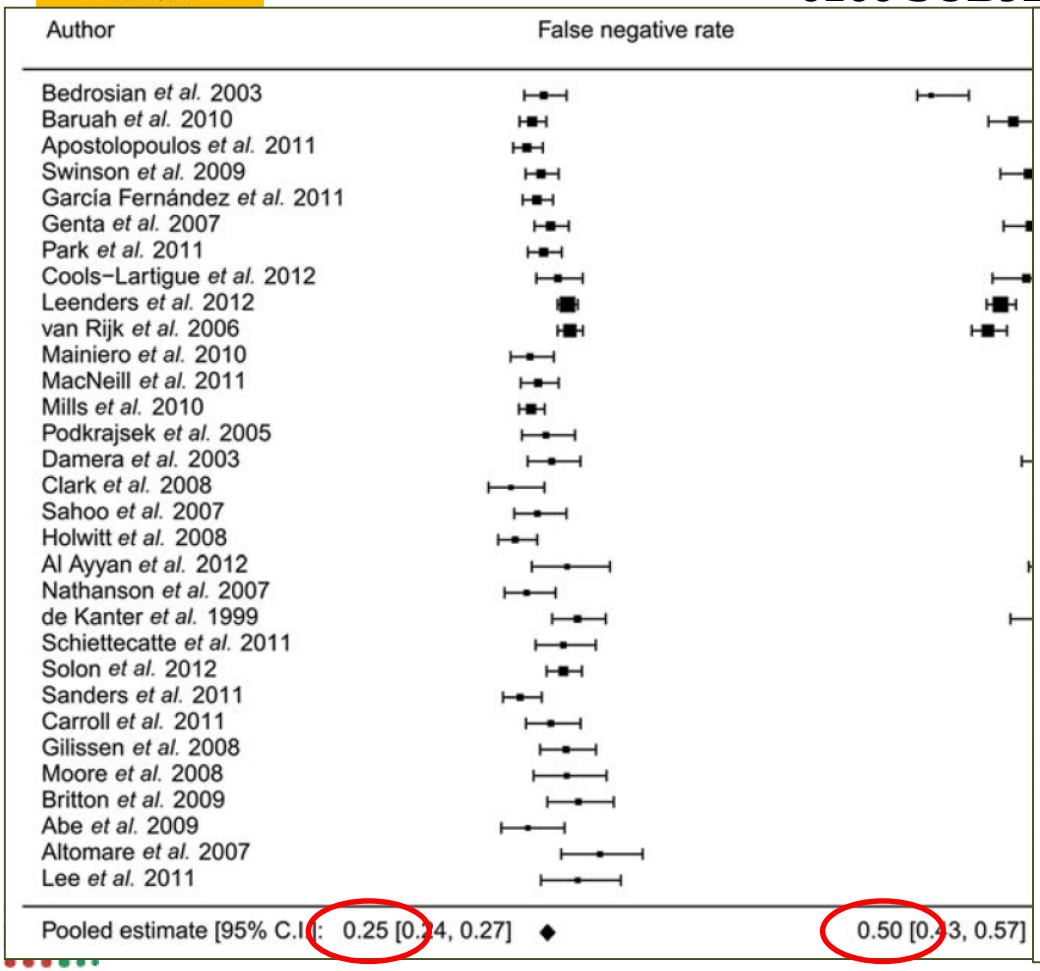
"...input from all clinicians as well as the patient is needed to yield the best results from PMRT."

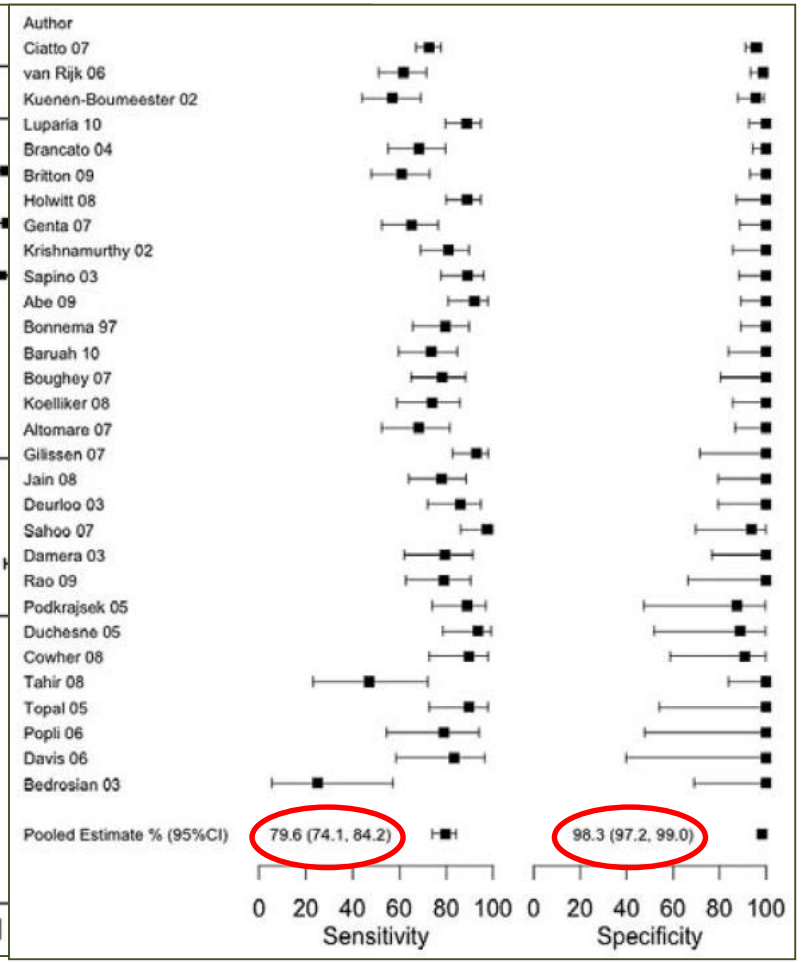
"Would I re... RT for this patient if she had undergone simultaneo... there were no additional nodal metastases in the non-sentine...? If the answer is no, ALND should be performed. This discussion should ideally occur before surgery, expecially because this could guide patient decision making about reconstruction choices if reconstruction is desired."

Recht A et Al; JCO 2016

CLINICAL UTILITY OF ULTRASOUND-NEEDLE BIOPSY FOR PREOPERATIVE STAGING OF THE AXILLA IN INVASIVE BREAST CANCER

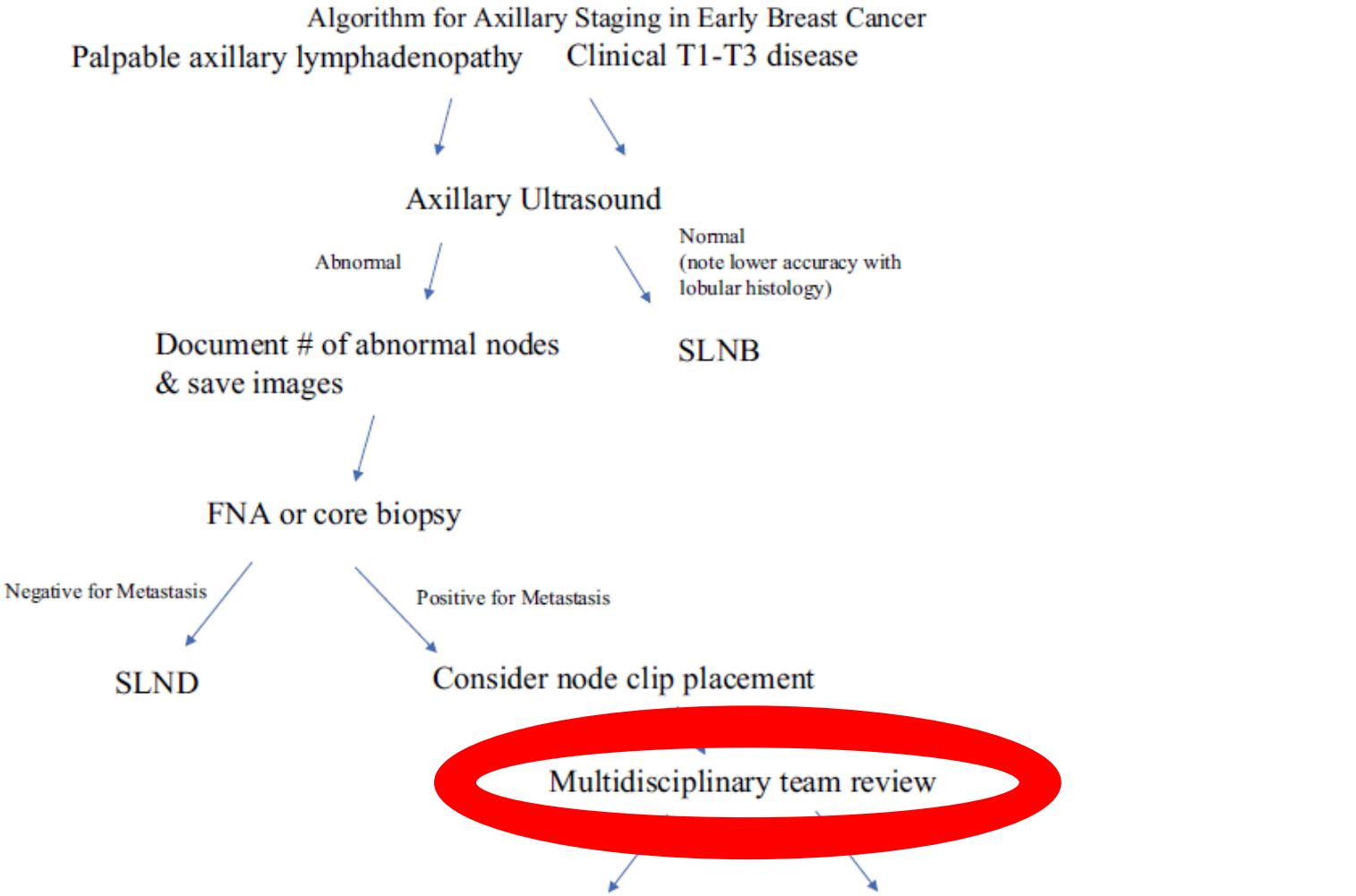
31 STUDIES
6166 SUBJECTS





Diepstraten SCE et Al; Ann Surg Oncol 2014

SNB & I RADIOLOGI



Black D; Ann Surg Oncol 2017

SNB & I RADIOLOGI

A POSITIVE NODE ON ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION PREDICTS HIGHER NODAL BURDEN THAN A POSITIVE SENTINEL LYMPH NODE BIOPSY IN BREAST CARCINOMA

Total patients	$n = 1315$	SLNB positive group	P value
Total patients proceeding to ALND	$n = 974$		
% Females	99.8 %		
	USFNAC-positive group		

Total patients	$n = 1315$ USFNAC-positive group	SLNB-positive group	P value (Mann–Whitney test)
Patients proceeding to ALND	439	535	
Total number of nodes excised	23	21	<0.001
Level 1	15	13	<0.001
Level 2	4	3	<0.001
Level 3	3	3	0.81
Total number of positive nodes	3	1	<0.001

"…patients with a positive US-FNAC are likely to require an ALND and represent a different cohort of patients than those with a positive SLNB who could potentially avoid such an intervention."

Oestrogen receptor positive	81.1 %	88.8 %	<0.001
HER 2 positive	25 %	12.6 %	<0.001
Number of patients receiving neoadjuvant chemotherapy	169 (38.5 %)	28 (5.2 %)	<0.001

MR et Al; World J Surg 2016

PREDICTING THE EXTENT OF NODAL DISEASE IN EARLY-STAGE BREAST CANCER

	US (one to two suspicious lymph nodes) ($N = 149$)	SLND ($N = 518$)	p value
Mean number of positive lymph nodes	3.6	2.2	<0.001
Number of positive lymph nodes			
1	44 (30)	290 (56)	<0.001
2	38 (26)	127 (25)	
3	20 (13)	43 (8)	
≥4	47 (32)	58 (11)	
Largest lymph node	13.4	5.3	<0.0001

"…having metastases identified by US was the strongest predictor of having more than three positive lymph nodes (OR = 3.80)."

"…lobular histology was also predictive of having more than three positive lymph nodes (OR = 1.77)."

Caudle AS et Al; Ann Surg Oncol 2014

SNB & TUMOUR LOAD

TOTAL TUMOUR LOAD ASSESSED BY ONE-STEP NUCLEIC ACID AMPLIFICATION ASSAY AS AN INTRAOPERATIVE PREDICTOR FOR NON-SENTINEL LYMPH NODE METASTASIS IN BREAST CANCER

	OR (95% CI) Univariate	*P* Univariate	OR (95% CI) Multivariate	*P* Multivariate
Age (years)	0.99 (0.94–1.05)	0.711		
Tumor size (mm)	1.08 (1.00–1.16)	0.047	1.06 (0.98–1.15)	0.168
Log TTL (copies/μL)	3.56 (1.57–8.09)	0.002	2.67 (1.06–6.70)	0.036
SLN macrometastases	4.64 (1.55–13.92)	0.006	2.63 (0.94–7.36)	0.066
Histologic type				
Invasive ductal carcinoma	1	0.974		
Invasive + ductal carcinoma in situ	0.97 (0.09–10.26)			
Invasive lobular carcinoma	0.58 (0.06–5.51)			
Invasive papillary carcinoma	–			
Histological tumor grade				
I	1	0.069		
II	0.15 (0.02–1.05)			
III	1.14 (0.18–7.28)			
Lymphovascular invasion (yes vs no)	1.60 (0.45–5.74)	0.471		
ER (positive vs negative)	2.33 (0.26–21.17)	0.451		
PR (positive vs negative)	6.28 (0.75–52.90)	0.091		
HER2 (positive vs negative)	0.71 (0.13–3.94)	0.699		
Multifocality (yes vs no)	2.78 (0.53–14.48)	0.226		

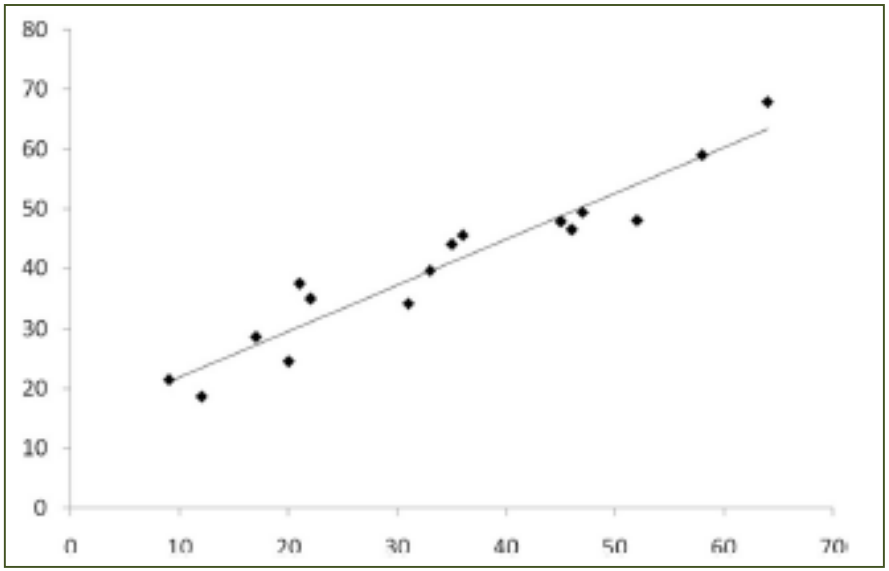
TTL only independent predictor of non SN metastases (OR = 2.67)

Nabais C et Al; The Breast 2016

SNB & TUMOUR LOAD

Journal of Experimental & Clinical Cancer Research

ELABORATION OF A NOMOGRAM TO PREDICT NONSENTINEL NODE STATUS IN BREAST CANCER PATIENTS WITH POSITIVE SENTINEL NODE, INTRAOPERATIVELY ASSESSED WITH ONE STEP NUCLEIC ACID AMPLIFICATION: RETROSPECTIVE AND VALIDATION PHASE



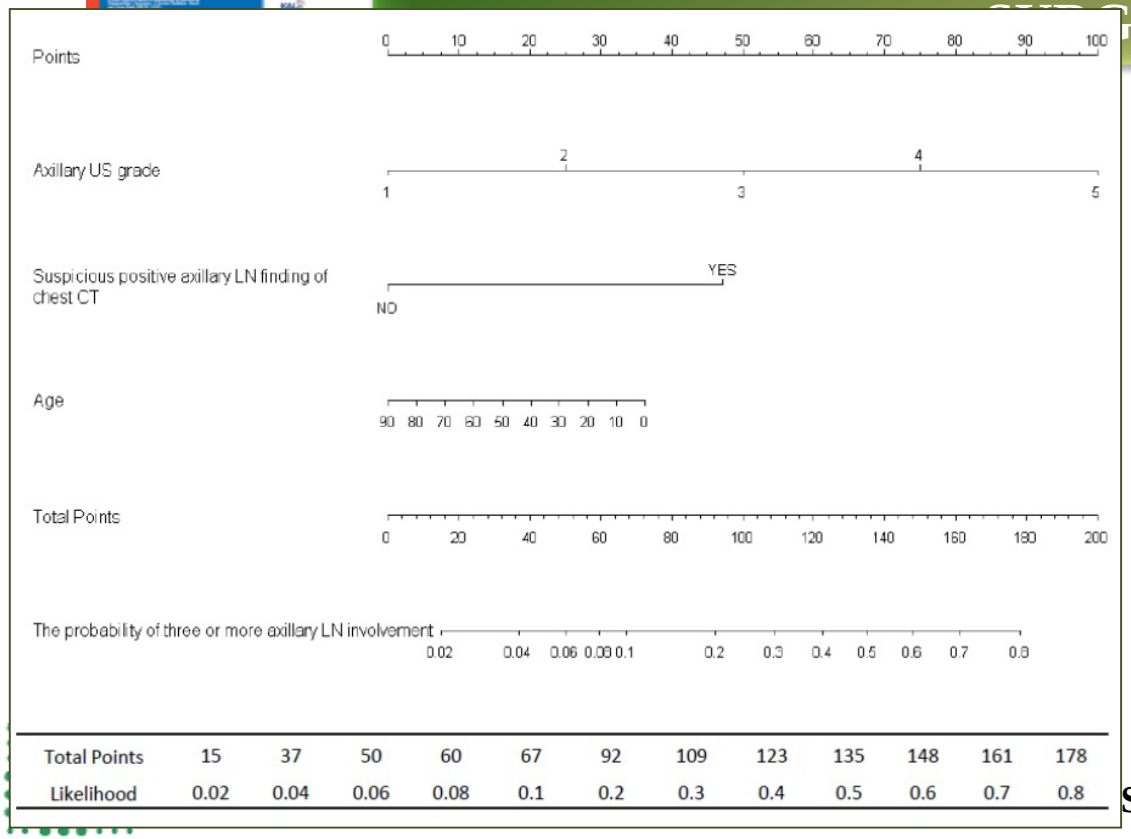
1495 pts

- **choice of the right treatment during the operation**
- **avoidance of a second surgery procedure**

Di Filippo F et Al; J Exp & Clin Cancer Res 2016

SNB & I PATOLOGI E CHIRURGHI

CAN WE SKIP INTRAOPERATIVE EVALUATION OF SENTINEL LYMPH NODES? – NOMOGRAM PREDICTING INVOLVEMENT OF THREE OR MORE AXILLARY LYMPH NODES BEFORE BREAST CANCER SURGERY



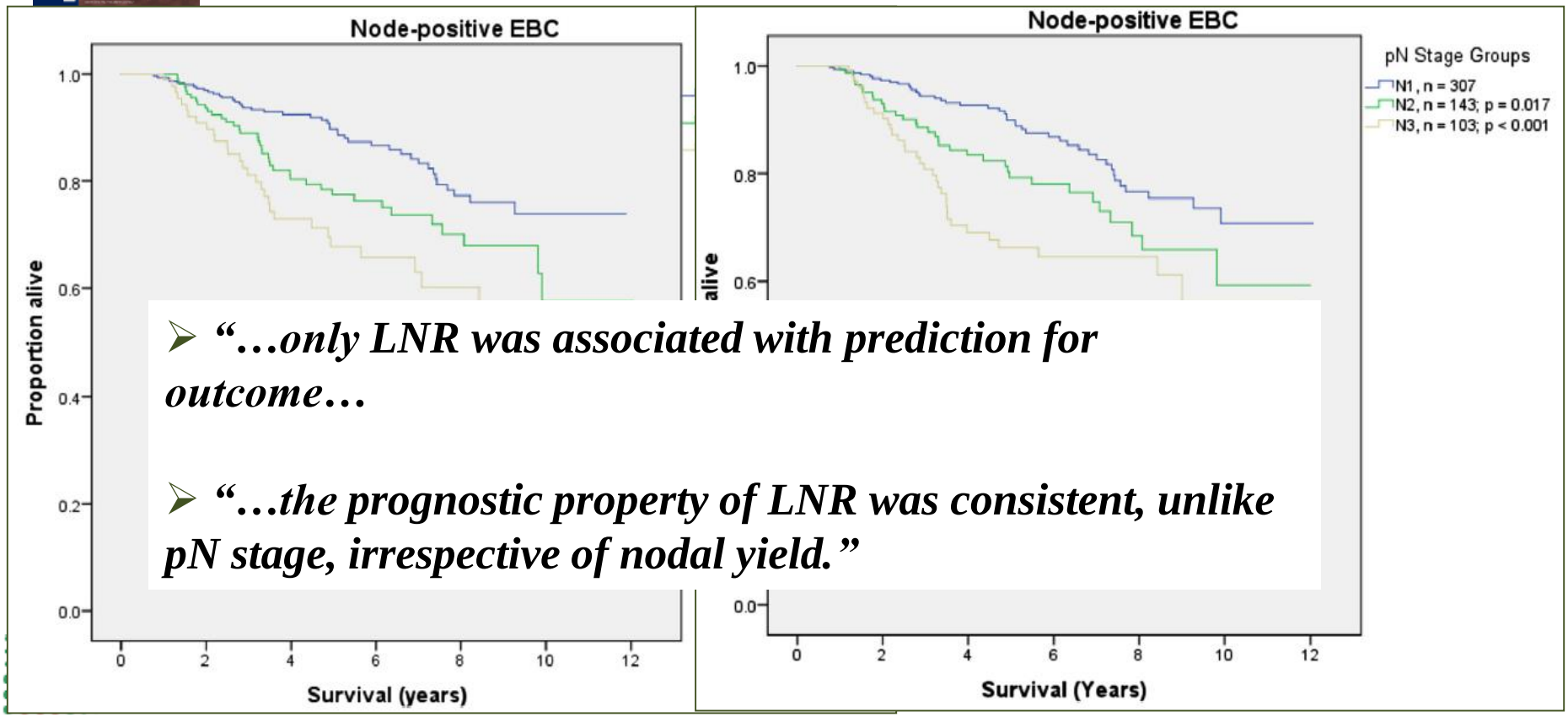
Total Points	15	37	50	60	67	92	109	123	135	148	161	178
Likelihood	0.02	0.04	0.06	0.08	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8

- **reoperation rate < 5%**
- **FNR of FS = 14-43%**

SK et Al; Cancer Res and Treat 2017

…CHE DICONO GLI ONCOLOGI

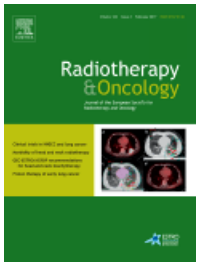
LYMPH NODE RATIO IN SENTINEL LYMPH NODE BIOPSY ERA: ARE WE LOSING PROGNOSTIC INFORMATION?



- ***"…only LNR was associated with prediction for outcome…***
- ***"…the prognostic property of LNR was consistent, unlike pN stage, irrespective of nodal yield."***

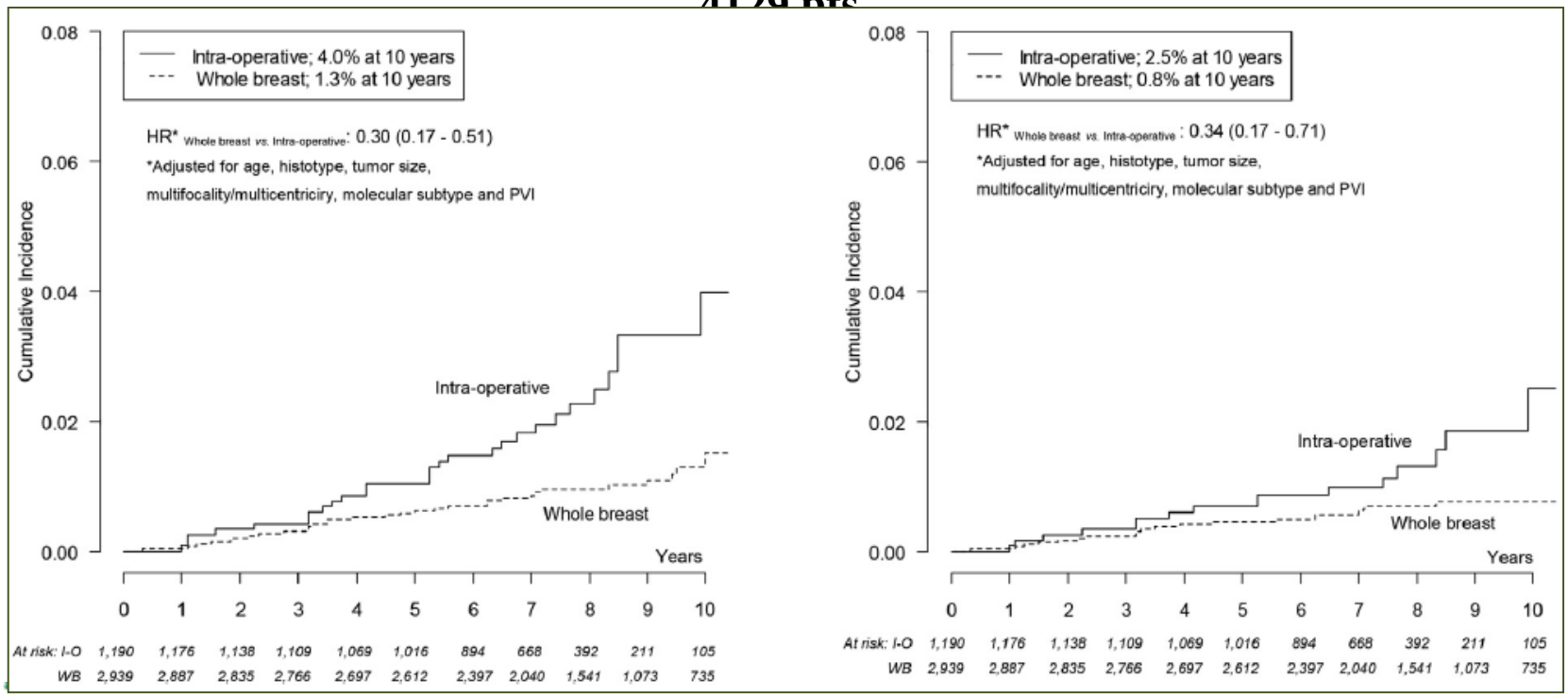
Quintyne KI et Al; Clin Breast Cancer 2016

…& I CHIRURGHI E RADIOTERAPISTI



IPSILATERAL AXILLARY RECURRENCE AFTER BREAST CONSERVATIVE SURGERY: THE PROTECTIVE EFFECT OF WHOLE BREAST RADIOTHERAPY

4129 pts

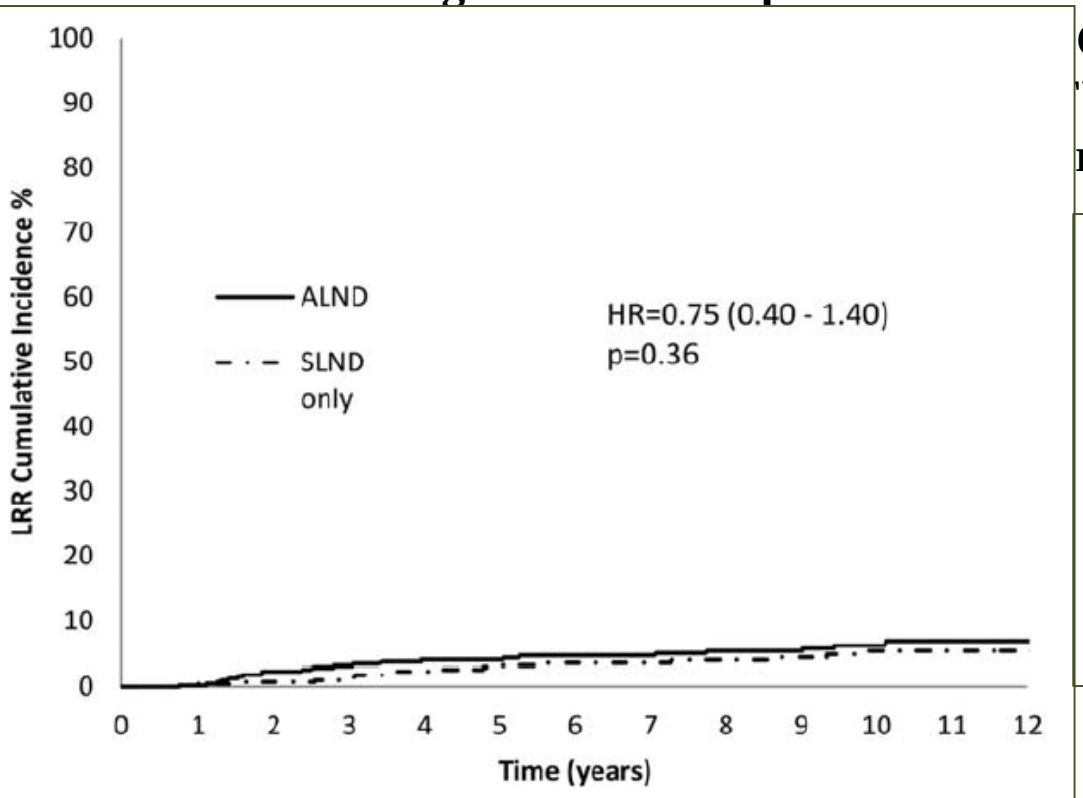


Gentilini O et Al; Rad & Oncol 2017

…& I CHIRURGHI E RADIOTERAPISTI

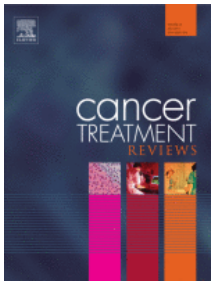
LOCOREGIONAL RECURRENCE AFTER SENTINEL LYMPH NODE DISSECTION WITH OR WITHOUT AXILLARY DISSECTION IN PATIENTS WITH SENTINEL LYMPH NODE METASTASES

Long-term follow-up from the American College of Surgeons Oncology
G Z0011 Randomized trial
'U 9.25 yrs
recurrences 39



- **LR at 10 yrs 5.6% in the ALND arm vs 3.8% in the SNB arm (p=0.13)**
- **axLR at 10 yrs 0.5% in the ALND arm vs 1.5% in the SNB arm**

Giuliano AE et Al; Ann Surg 2016



OMISSION OF AXILLARY DISSECTION AFTER A POSITIVE SENTINEL LYMPH-NODE: IMPLICATIONS IN THE MULTIDISCIPLINARY TREATMENT OF OPERABLE BREAST CANCER

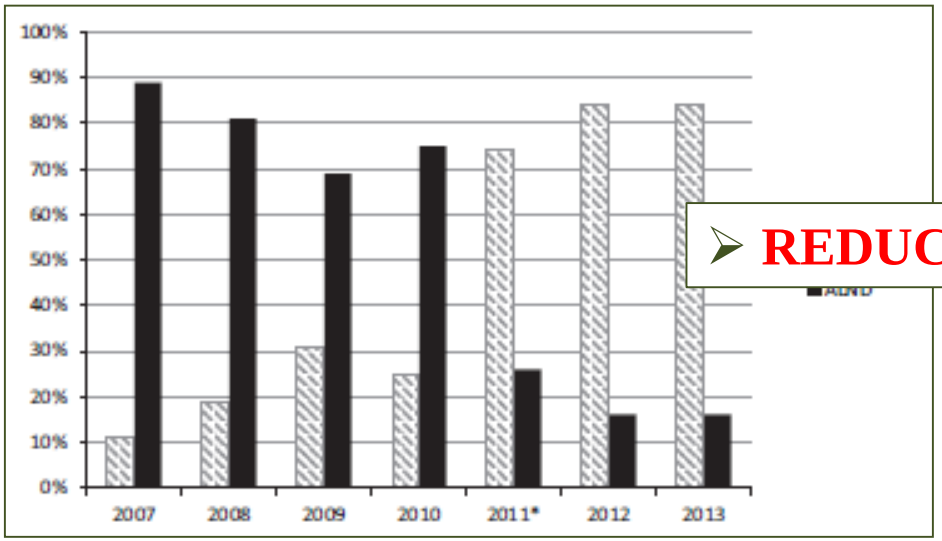
Nomogram		Patient feature		Tumor features						Sentinel lymph nodes features						
Reference n°	**Website**	**Age**	**Size**	**Type**	**G**	**LVI**	**ER**	**Her2**	**MF**	**Method of MTS detection**	**N° SLN**	**N° Positive**	**N* Negative**	**Proportion positive**	**Size of MTS**	**ECI**
MSKCC[32]	https://www.mskcc.org/teaser/prediction-tools-01		Yes	Yes	Yes	Yes	Yes		Yes	Yes		Yes	Yes			
MD Anderson[33]	http://www3.mdanderson.org/app/medcalc/bc_nomogram2/index.cfm?pagename=nsln		Yes			Yes						Yes			Yes	Yes
Tenon[34]	http://www.meducator3.net/algorithms/content/tenon-axillary-scoring-system-barranger-et-al-predicting-metastasis-status-non-sentinel		Yes											Yes	Yes	
Mayo[35]		Yes	Yes									Yes	Yes		Yes	Yes
Stanford[36]	http://www.meducator3.net/algorithms/content/model-kohrt-et-al-predicting-non-sentinel-lymph-node-status-woman-breast-cancer-and-positive		Yes												Yes	
Cambridge[37]					Yes									Yes	Yes	
Turkish[38]						Yes								Yes	Yes	
Helsinki University Central Hospital nomogram[39]													Yes		Yes	Yes
Shanghai Cancer Center Non-SLN nomogram[40]						Yes						Yes	Yes		Yes	

"ANCILLARY TOOLS"

"…none of them appears totally reliable."

Ponzone R et Al; Cancer Treat Rev 2016

HEALTHCARE COSTS REDUCED AFTER INCORPORATING THE RESULTS OF THE AMERICAN COLLEGE OF SURGEONS ONCOLOGY GROUP Z0011 TRIAL INTO CLINICAL PRACTICE



➢ **REDUCTION OF ALND FROM 78 TO 21%**

	2010 (*N* = 12)	2011 (*N* = 16)	2012 (*N* = 12)	2013* (*N* = 6)	Correlation coefficient
Average overall cost per patient, mean (SD)	$55,148 ($16,149)	$46,113 ($12,831)	$42,439 ($13,289)	$42,248 ($17,110)	*r* = 0.991
Rate of ALND	75%	26%	16%	16%	
Reduction in overall cost from 2010		−16%	−23%	−22%	

➢ **REDUCTION OF OVERALL COSTS 9940$/PTS**

➢ **REDUCTION OF FS PERFORMANCE FROM 95 TO 66%**

(COST REDUCTION FROM 4319 TO 2036$/PTS)

J 2016

…& TERAPIE ADIUVANTI

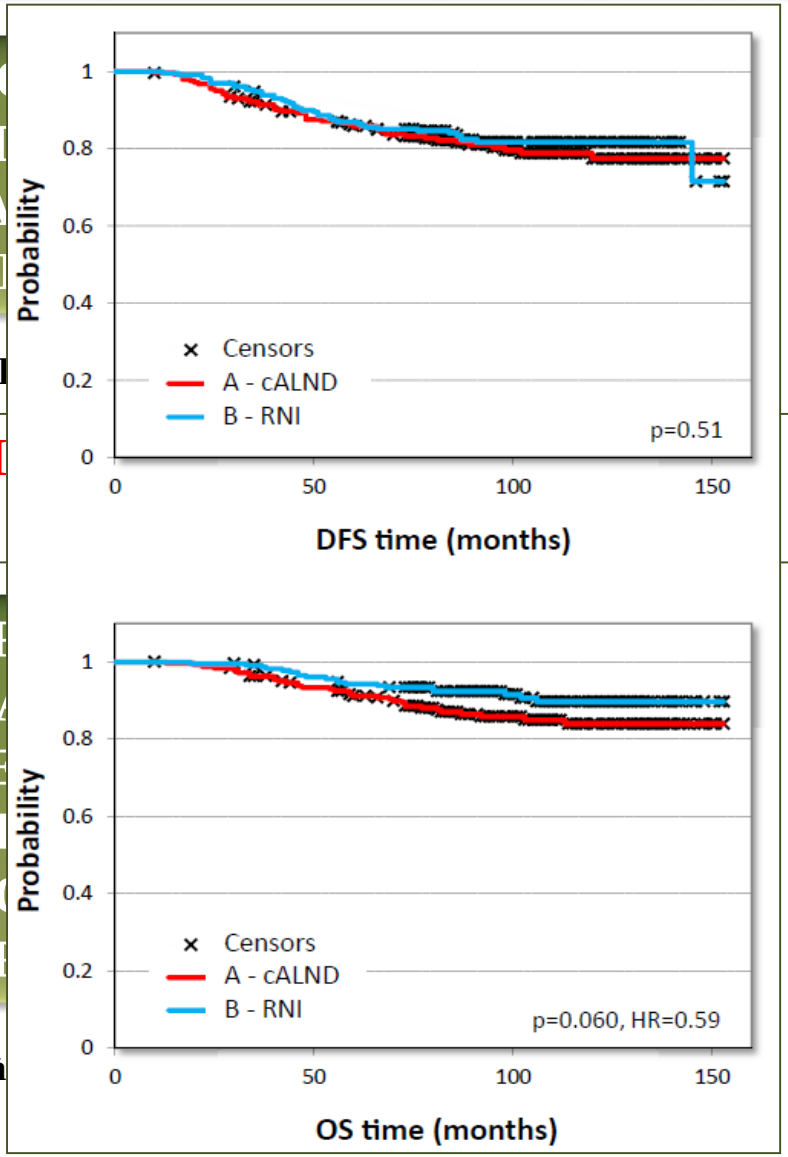
DOES THE RESULT OF C… LYMPH NODE DISSECT… RECOMMENDATION FOR A… SENTINEL LYMPH-NOD…

Sàvol…

➢ **NO MAJOR IMPACT ON ADMINISTRATI… THERAPY**

Axillary recurrence and survival.

Treatment arm	Arm A	Arm B	p
Axillary recurrence			
Total number (%)	5 (2.0)	4 (1.7)	1.00
Isolated number (%)	1 (0.4)	2 (0.8)	0.61
Survival at 8 years			
Overall survival number (%)	190 (77.9)	195 (84.8)	0.060
Disease-free survival number (%)	176 (72.1)	178 (77.4)	0.51
Alive with recurrence number (%)	14 (5.7)	17 (7.0)	
Died of breast cancer number (%)	34 (13.9)	20 (8.7)	
Died of other cause number (%)	20 (8.2)	15 (6.5)	



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OUTCOMES OF POST-MASTECTOMY RADIATION THERAPY IN PATIENTS RECEIVING AXILLARY LYMPH NODE DISSECTION AFTER POSITIVE SENTINEL LYMPH NODE BIOPSY

"Should PMRT be offered to avoid lymph node dissection in women with a positive sentinel lymph node after mastectomy?"

"The potential for additional tumour control benefit must then be weighed against the risk of cardiac events, the operative implications, and the risk of development of lymphoedema."

Stauder MC et Al; Int J Rad Oncol Biol Phys 2016

…& LA TERAPIA SISTEMICA PRIMARIA

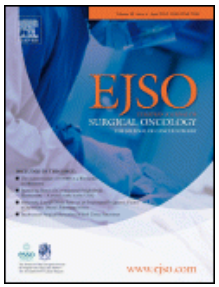
SENTINEL NODE BIOPSY PERFORMANCE AFTER NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED BREAST CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

72 eligible studies
7451 pts
IR 89.6%
FNR 14.2%

…BUT…:

Mocellin S et Al; Int J Cancer 2016

- **no survival benefit**
- **no therapeutic role of AD**
- ***role of minimal residual disease?***



SENTINEL NODE BIOPSY AFTER NEOADJUVANT TREATMENT IN BREAST CANCER: FIVE YEAR FOLLOW-UP OF PATIENTS WITH CLINICALLY NODE-NEGATIVE OR NODE-POSITIVE AXILLARY DISEASE BEFORE TREATMENT

- **FNR irrilevant**
- **AD has no effect on outcomes**

Galimberti V et Al; EJSO 2016

…& E RECIDIVE

META-ANALYSIS OF ABERRANT LYMPHATIC DRAINAGE IN RECURRENT BREAST CANCER

7 included studies
1053 pts
IR 63.3% by lymphoscintigraphy (DA vs SNB OR = 2.97)
IR 59.6% by intraoperative search

- **ABERRANT IDENTIFICATION: 25.7% BY LYMPHOSCINTIGRAPHY (previous SNB vs ALND OR = 0.27)**
- **7.6% BY INTRAOPERATIVE SEARCH**
- **METASTATIC RATE IPSILATERAL AXILLA vs ABERRANT OR = 6.31**

1. **ALMOST 50% OF PATIENTS COULD AVOID ALND**
2. **TARGETED VISUALIZATION OF METASTATIC SNs**

Alteration of adjuvant treatment plan (systemic therapy/radiotherapy)
…BUT… CALOR trial results

Ahmed M et Al; Br J Surg 2016

SNB REDUNDANT?

AXILLARY ULTRASOUND AND FINE-NEEDLE ASPIRATION CYTOLOGY IN THE PREOPERATIVE STAGING OF AXILLARY NODE METASTASES IN BREAST CANCER PATIENTS

Gipponi M et Al; The Breast 2016

PREOPERATIVE ULTRASOUND STAGING OF THE AXILLA MAKES PEROPERATIVE EXAMINATION OF THE SENTINEL NODE REDUNDANT IN BREAST CANCER: SAVING TISSUE, TIME AND MONEY

Van Berckelaer C et Al; Eur J Obst & Gynecol &Reprod Biol 2016

OVEREXPLORING AND OVERTREATING THE AXILLA

Galimberti V et Al; The Breast 2016

"If surgical staging of the axilla proves unnecessary, what is the role of preoperative axillary imaging?"

"…tailor more than to omit lymph node treatment…." **Poortmans 2016**