

Azienda USL di Bologna
Azienda Ospedaliero-Universitaria di Bologna

collaborazione con:
*Assessorato Politiche per la salute
Regione Emilia-Romagna*



SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA

Seminario di studio

**Analisi dei dati sulla qualità del
trattamento dei tumori della
mammella screen-detected nella
Regione Emilia-Romagna:
problematiche anatomico-patologiche,
chirurgiche e radioterapiche**

23 settembre 2009

**Auditorium Via Aldo Moro n. 18
Bologna**



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

**BREAST UNIT
OSPEDALE RAMAZZINI - CARPI
UNITA' OPERATIVA DI CHIRURGIA**

LA BIOPSIA DEL LINFONODO SENTINELLA NEL CARCINOMA IN SITU: SI', NO, FORSE

CONTRO

Maria Grazia Lazzaretti



SNB IN DCIS

WORTH

Sakr 2006

Lee 2007

Van La Parra 2008

Doyle 2009

NO SENSE

Buttarelli 2004

Wilkie 2005

Moran 2005

Yen 2005

Mabry 2006

Katz 2006

Farshind 2007

Zavagno 2007

Julian 2007

Intra 2008

Fentiman 2008

Bergkvist 2008

Murphy 2008

Ranijeesingh 2009

Rubio 2009

Buonomo 2009

Simpson 2009



DCIS

“A neoplastic intraductal lesion characterized by increased epithelial proliferation, subtle to marked cellular atypia and an inherent but not necessarily obligate tendency for progression to invasive breast cancer, without any evidence of invasion through the basement membrane of the duct.”



ENTITA' DEL PROBLEMA

DALLA LETTERATURA

Author	No. Patients	No. Axillary Dissections	No. Positive Nodes
Ashikari, et al.	112	113	1
Brown, et al.	40	21	1
Carter and Smith	38	26	1
Fisher, et al.	78	78	0
Gump, et al.	70	64	1
Lagios, et al.	87	87	2
Patchefsky	51	51	3
Recht, et al.	40	13	0
Rosner, et al.	210	210	8
Schuh, et al.	52	52	1
Silverstein, et al.	319	319	2
Sunshine, et al.	70	61	0
Von Rueden, et al.	53	32	0
Total	1220	1127	20

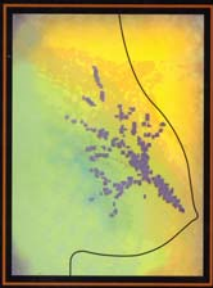
1.8%

ENTITA' DEL PROBLEMA

DALLA LETTERATURA

First author	Year	# Patients with DCIS	# Patients with positive SN (%)	#SN positive patients undergoing ALND	# Patients with ALND metastases (%)
Klauber De More and colleagues ²⁶	2000	72 ^a	5 (7%)	Unknown ^b	Unknown
Kelly and colleagues ²⁷	2003	41	1 (2%)	1	0
Farkas and colleagues ²⁸	2003	46	0 (0%)	0	
Trisal and colleagues ²⁹	2004	15	0 (0%)	0	
Buttarelli and colleagues ³⁰	2004	41	3 (7%)	4	0
Zavagno and colleagues ³¹	2005	102	1 (1%)	0	0
Mittendorf and colleagues ³²	2005	34	6 (18%)	2	0
Giard and colleagues ³³	2005	55	1 (2%)	0	
Yen and colleagues ³⁴	2005	99	3 (3%)	1	0
Schrenk and colleagues ³⁵	2005	29	0 (0%)	0	
Wilkie and colleagues ³⁶	2005	559	27 (5%)	Unknown	Unknown
Camp and colleagues ³⁷	2005	25	1 (4%)	0	
Veronesi and colleagues ³⁸	2005	508	9 (2%)	8	0
Torok and colleagues ³⁹	2006	40	2 (5%)	0	
Cserni and colleagues ⁴⁰	2006	36	4 (11%)	4	0
Katz and colleagues ⁴¹	2006	110	8 (7%)	2	0
Mabry and colleagues ⁴²	2006	171	10 (6%)	0	
Sakr and colleagues ⁴³	2006	39	4 (10%)	4	0
Leidenius and colleagues ⁴⁴	2006	74	5 (7%)	3	0
Fraille and colleagues ⁴⁵	2006	92	1 (1%)	0	
UMC Utrecht (unpublished)	2006	8	0 (0%)	0	0
Total		2196		29	0

EE: 0.8-2.6%



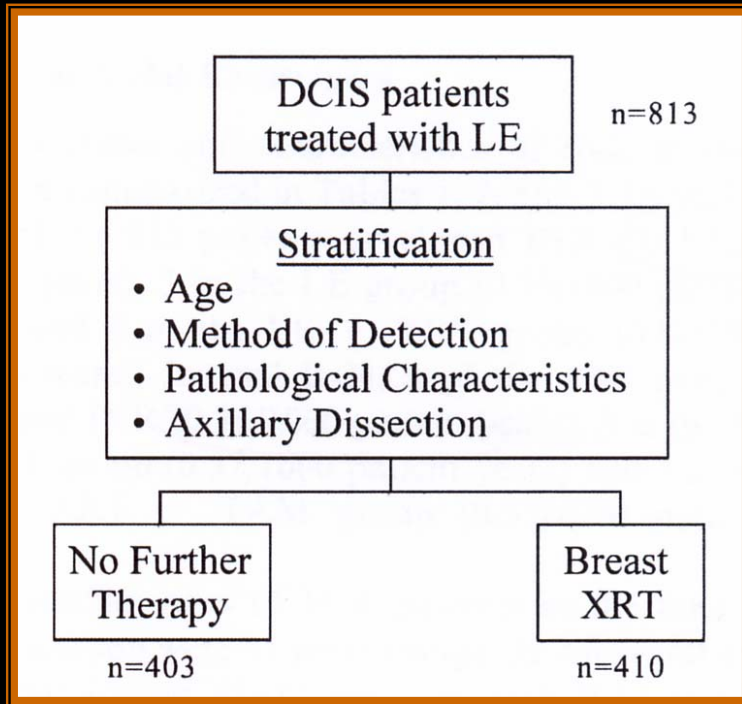
MORTALITA'

AUTHOR	NO. OF PATIENTS	FOLLOW-UP (yr)	LOCAL RECURRENCE	DEAD FROM BREAST CANCER
Archer (1994)	52	11.1	0	0
Arnesson (1989)	28	6.4	0	0
Ashikari (1971)	110	1-10	2	1
Brown (1976)	39	1-15	0	0
Carter (1977)	38	6.2	0	1
Ciatto (1990)	210	5.5	3	1
Farrow (1970)	181	2-20	2	4
Fentiman (1986)	76	4.8	1	1
Fisher (1991)	28	7.1	0	1
Kinne (1989)	101	11.5	1	1
Lagios (1982)	53	3.7	2	1
Rosner (1980)	182	5	—	3
Schuh (1986)	51	5.5	0	1
Silverstein (2002)	326	6.1	2	0
Simpson (1992)	34	17.7	0	0
Sunshine (1985)	68	10	0	3
Von Reuden (1984)	47	1-22	0	0
Westbrook (1975)	60	5-25	1	0
TOTAL	1684	7.7	14 (0.9%)	18 (1.1%)

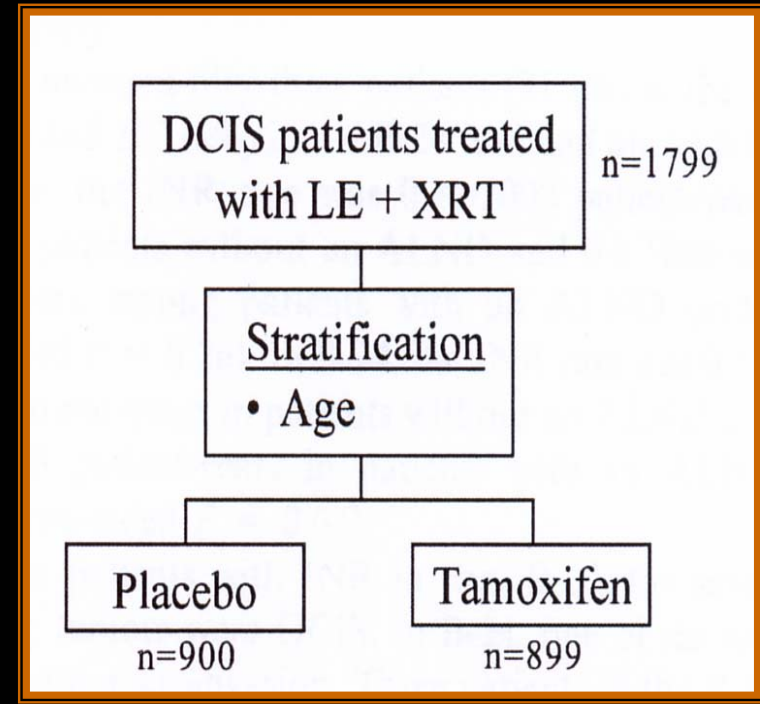
14 (0.9%)

18 (1.1%)

NSABP B-17 e B-24



F.U. 15.3 yrs



F.U. 11.5 yrs

I.N.R. = 0.83/1000 pts-years
0.36/1000 pts-years



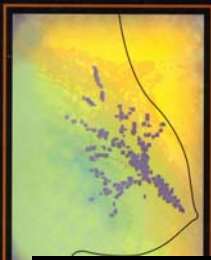
SN POSITIVITY

Lagios M.D. 2001, Bleiweiss I. 2004

“...the small clusters observed in SLNs of patients with DCIS represent artifacts of the procedure rather than true clonagens capable of distant spread and growth.”

Julian T.B. 2007

“...iatrogenic transport of benign epithelial cells can account for some of the positive SNs.”



SOTTOSTIMA IDC

Author	Pts	Upstaged	Sig. predictors of IDC	Non sign. predictors of IDC
Moran 2007	62	20 (32)	High grade DCIS > 2.5 cm or if mastectomy was required	
Rutstein 2007	254	21 (8.3)	Fewer than 12 core samples (size 11–14 G); comedo necrosis	
Meijnen 2007	171	45 (26.3)	Palpable lesion; mammographic mass; intermediate grade; poorly differentiated tumour grade	
Goyal 2006	587	220 (37.5)	Clinically palpable mass; mammographic mass; size of clinically palpable mass and mammographic mass significant predictors on univariable analysis but not on multivariable analysis	High grade, younger age, microinvasion and comedo necrosis were not predictors of invasive cancer
Huo 2006	200	41 (20.5)	Mass lesion on imaging; lesion > 1.5 cm; high nuclear grade; presence of lobular cancerization	Architectural pattern; presence of necrosis; periductal fibrosis or lymphocytic infiltrate; number of cores; extent of DCIS in cores
Wilkie 2005	675	66 (9.8)	High-grade DCIS; mammographic mass; microinvasion	
Mittendorf 2005	30	6 (20)	Diagnosis by core-needle biopsy	Palpable lesion; grade; presence or absence of necrosis
Yen 2005	398	80 (20.1)	Age ≤ 55 years; mammographic size ≥ 4 cm; grade 3 DCIS; diagnosis by core-needle biopsy	Palpable mass; pathological size; presence of comedo necrosis
Hoorntje 2003	255	41 (16.1)	Grade 3 DCIS; periductal inflammation in core biopsies; large area of calcification	Periductal stromal fibrosis
Renshaw 2002	91	17 (19)	Comedo DCIS with cribriform/papillary pattern; DCIS > 4 mm with lobular extension	Nuclear grade; comedo necrosis; histological pattern
Jackman 2001	1326	183 (13.8)	Diagnosis by core-needle biopsy; mammographic mass; ≥ 10 cores per lesion	
Cox 2001	240	30 (12.5)	None	Nuclear grade; comedo necrosis; histological pattern; core biopsy <i>versus</i> excisional biopsy
King 2001	140	36 (25.7)	Mass on breast imaging	
Wahedna 2001	140	61 (43.6)	None	Neither mammographic features nor grade were predictive
Lee 2000	59	17 (29)	Inflammatory infiltrate	Nuclear grade; comedo necrosis; desmoplasia; histological pattern; no. of core biopsies, 11-G <i>versus</i> 14-G cores, size of lesion, level of suspicion, distribution and morphology of calcifications showed no difference between vacuum-assisted core and surgical biopsy

CB = 16-43%

VAB = 0-19%

SNB IN DCIS

Modified from Ansari B. et Al.; Br J Surg 2008; 95: 547



UTILIZZO SELETTIVO DELLA SNB

INDICAZIONI SNB

BCS

- QSE (Silverstein 2004)
- sempre se CB dubbia per DCISmic
- sempre se DCIS G3 alla CB
- paziente a rischio di infiltrazione (età, CB, diametro, G3) (Yen TWF J Am Coll Surg 2005)

MASTECTOMIA

- sempre



RACCOMANDAZIONI

FONCaM 2005

- SNB solo nel ca infiltrante
- DCIS controindicazione relativa alla SNB

ASCO 2005

- no SNB in DCIS
- yes for mastectomy patients

GERMAN SOCIETY OF SENOLOGY 2005

- optional for mastectomy patients

NCCN 2009

- NO SNB for pure DCIS
- MAYBE in mastectomy patients or when surgery may compromise performance of future SNB



RACCOMANDAZIONI

GIVOM 2005

- SNB SI' per mastectomia
- tumori del QSE
- $T > 3$ cm

ITT 2006

- SNB solo in caso di mastectomia

R.E.R. 2007

- SNB SI' per mastectomia
- G3
- $T > 3$ cm



SNB AT FIRST SURGERY

WHY?

Krag D. 1998, Borgstein P.J. 1998

- significantly higher lymphatic mapping failure after excisional biopsy
- the lymphatic channels may possibly become transected

Ohtake E. 2005, Trifiro G. 2006

- previous breast surgery does not prohibit efficient sentinel lymph node localization
- SNB can correctly stage the axilla in these patients



SINGLE STAGE SURGERY

...**BUT**...

*“...SINGLE STAGE SURGERY, WHERE POSSIBLE, WILL **USUALLY** BE FAVOURED BY PATIENTS.”*

Moran C.J. Et Al.; EJSO 2005; 31: 1105

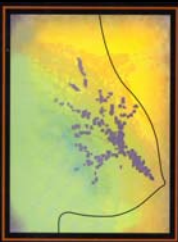


THE RIGHT BALANCE



**SIDE EFFECTS OF
AXILLARY SAMPLING**

**RISK OF A SECOND
OPERATION**



POSITIVE SN: UNANSWERED QUESTIONS

DALLA LETTERATURA

- /// WHAT THE MEANING (i+ only in 70-80% of cases)
- /// WHETHER TO COMPLETE WITH AXILLARY DISSECTION
- /// WHETHER TO PROCEED WITH SYSTEMIC THERAPY

/// **DCIS IS NOT ONE DISEASE**
(Wilkie C. 2005)

MULTIDISCIPLINARY SETTING



SNB: PRO E CONTRO

PROs

- /// SOTTOSTIMA IDC 20-30%
- /// *PREGRESSA CHIRURGIA*
- /// *MIGLIOR STADIAZIONE*

CONs

- /// METASTASI RARE
- /// METASTASI DI INCERTO SIGNIFICATO
- /// *PREGRESSA CHIRURGIA NON CONTROINDICAZIONE ALLA SNB*
- /// MORBIDITA'
- /// *PRECLUDE UN'ULTERIORE SNB SE RECIDIVA*
- /// CHE FARE SE SN+
- /// RISCHIO DI SNB PER UNA PATOLOGIA BENIGNA



METAANALYSIS OF SENTINEL NODE BIOPSY IN DUCTAL CARCINOMA IN SITU OF THE BREAST

Background: The need for sentinel lymph node (SLN) biopsy in patients with a preoperative diagnosis of ductal carcinoma *in situ* (DCIS) is debated. Advocates recommend such biopsy based on a high incidence of SLN involvement in some series. Opponents discourage SLN biopsy based on a perceived low incidence of nodal involvement in this setting. These contradictory arguments are generally based on small studies. The present study is a meta-analysis of the reported data on the incidence of SLN metastasis in patients with DCIS.

Methods: A search of electronic databases identified studies reporting the frequency of SLN metastases in DCIS. The random-effects method was used to combine data.

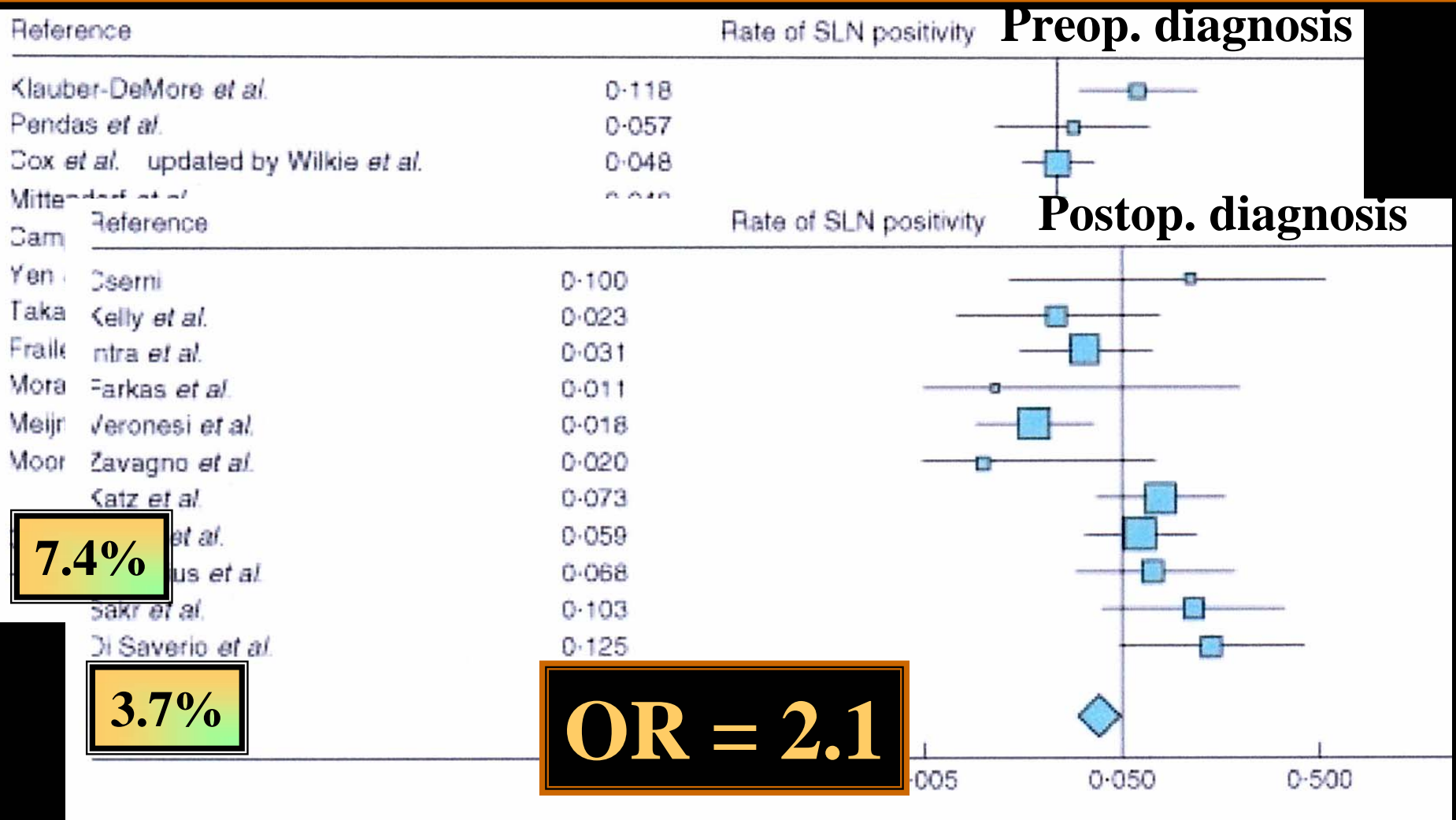
Results: Twenty-two published series were included in the meta-analysis. The estimate for the incidence of SLN metastases in patients with a preoperative diagnosis of DCIS was 7.4 (95 per cent confidence interval (c.i.) 6.2 to 8.9) per cent compared with 3.7 (95 per cent c.i. 2.8 to 4.8) per cent in patients with a definitive (postoperative) diagnosis of DCIS alone. This was a significant difference with an odds ratio of 2.11 (95 per cent c.i. 1.1 to 4.1).

Conclusion:

Patients with a preoperative diagnosis of DCIS should be considered for SLN biopsy.



METAANALYSIS OF SENTINEL NODE BIOPSY IN DUCTAL CARCINOMA IN SITU OF THE BREAST



SNB IN DCIS



??? RCT ???

R

**LYMPHATIC
MAPPING**

NO MAPPING

END-POINTS:

- /// **FINAL DIAGNOSIS**
- /// **CHANGES IN TREATMENT
DECISIONS**
- /// **MORBIDITY**
- /// **MORTALITY**
- /// **LONG-TERM-COSTS**



? SURGEON'S RESISTENCE ?

Morrow M. et Al.; CA Cancer J Clin 2002; 52 5): 256

“ Axillary surgery took place despite core biopsy and even open biopsy diagnosis of DCIS, emphasizing the need for greater education of surgeons in this regard.”

Morrow M.; Ann Surg Oncol 2008, DOI

“When tempted to use SNB in a majority of patients with DCIS just to be safe, it's worth remembering that a fool with a tool is still a fool.”



...grazie...

