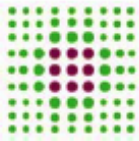


Azienda USL di Bologna
Azienda Ospedaliero-Universitaria di Bologna

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 anatomo-patologiche,
chirurgiche e radioterapiche**

23 settembre 2009

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

La biopsia del linfonodo sentinella nel carcinoma duttale in situ: si,no, forse...

Dott. S.Folli
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Definizione

Il carcinoma duttale *in situ* della mammella è una proliferazione cellulare epiteliale “presumibilmente” maligna, che interessa il sistema duttulo-lobulare senza invasione microscopica, attraverso la membrana basale, dello stroma circostante.

Silverstein MJ. *Ann Surg Oncol*, 1999



Terapia chirurgica DCIS

Mastectomia	20 - 25%
Trattamento conservativo	75 - 80%
Biopsia Linf. Sentinella ?	(20 - 100%)



La biopsia del linfonodo sentinella nel DCIS

ASCO (American Society of Clinical Oncology) Recommendations for SNB in Early-Stage Breast Cancer†

Clinical circumstance	Recommendation for use of sentinel node biopsy	Level of evidence*
DCIS with mastectomy	Acceptable	
DCIS without mastectomy	Not recommended except for large DCIS (>5 cm) on core biopsy or with suspected or proven microinvasion	
axillary nodes		
Older age	Acceptable	Limited
Obesity	Acceptable	Limited
Male breast cancer	Acceptable	Limited
Pregnancy	Not recommended	Insufficient
Evaluation of internal mammary lymph nodes	Acceptable	Limited
Prior diagnostic or excisional breast biopsy	Acceptable	Limited
Prior axillary surgery	Not recommended	Limited
Prior non-oncologic breast surgery (reduction or augmentation mammoplasty, breast reconstruction, etc)	Not recommended	Insufficient
After preoperative systemic therapy	Not recommended	Insufficient
Before preoperative systemic therapy	Acceptable	Limited



La biopsia del linfonodo sentinella nel DCIS

Controindicazioni relative e controverse:

- ✓ **CARCINOMA IN SITU.** Non vi è indicazione assoluta alla biopsia del LS. Nei casi in cui il sospetto di microinvasione sia elevato, ossia grading alto, pattern mammografico ad alto rischio ed estensione superiore a 5 cm, la metodica è consigliata, mentre può essere considerata discrezionale e da discutere con la paziente negli altri casi.

F.O.N.Ca.M 2005



Perché la biopsia del Linfonodo Sentinella nel DCIS ?

- Incidenza delle metastasi linfonodali nel DCIS
- Definizione preoperatoria del T (sottostadiazione)
- Costo / beneficio



La biopsia del linfonodo sentinella nel DCIS

Incidenza delle metastasi linfonodali nel DCIS

Valutazione istologica EE 1- 4%

Valutazione immunoistochimica 12-13%

McMaster KM. *Cancer* 2002
Veronesi P. *The Breast* 2005
Intra M. *Ann. Surg.* 2008



Incidenza delle metastasi linfonodali nel DCIS

Valutazione immunohistochimica 12-13%

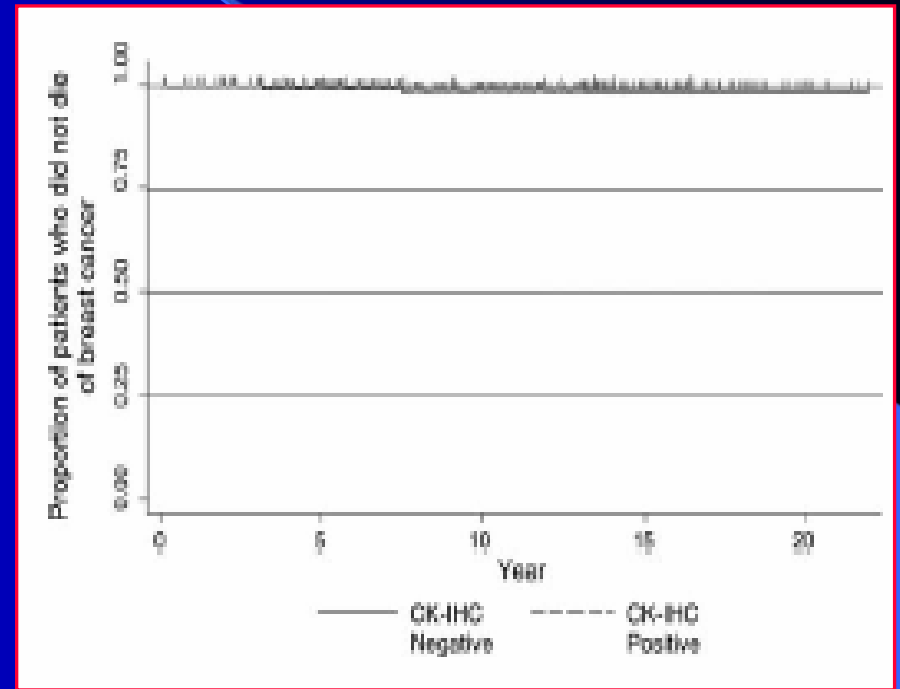
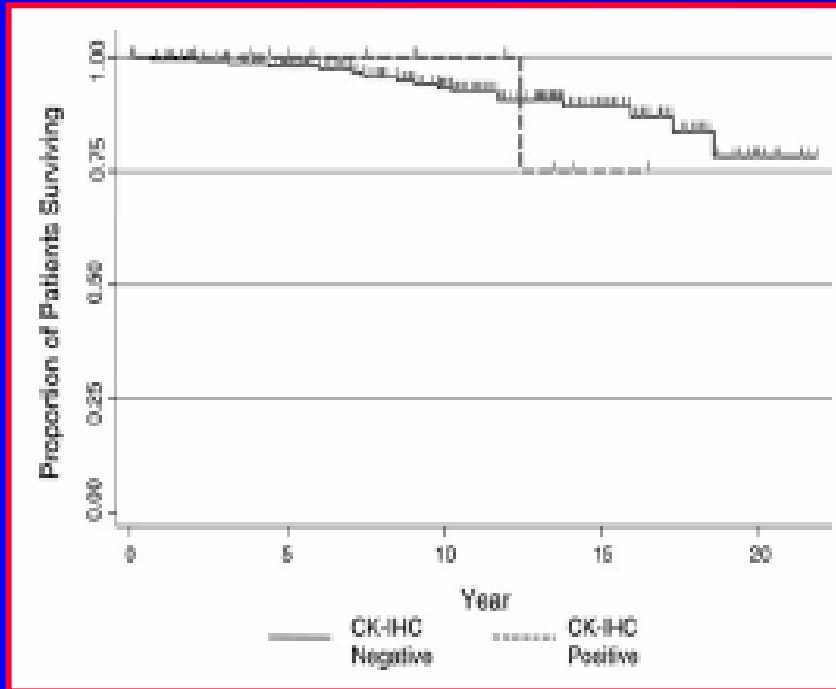
3 studi retrospettivi indicano che nei DCIS le metastasi rilevate soltanto con IHC non hanno significato clinico

Tamhane R. *Ann Surg Oncol* 2002
Lara JF. *Cancer* 2003
El-Tamer M.. *Ann. Surg.Oncol.* 2005



Incidenza delle metastasi linfonodali nel DCIS

Valutazione immunoistochimica 12-13%



El-Tamer M., *Ann. Surg. Oncol.* 2005



Incidenza delle metastasi linfonodali nel DCIS

Valutazione istologica EE 1- 4%

Table 1 – Overview of studies on the sentinel node (SN) biopsy in patients with a final diagnosis of DCIS of the breast

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
Parkas 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			4	0
Leidenius and colleagues ⁴⁴	2006			3	0
Fraile and colleagues ⁴⁵	2006			0	
UMC Utrecht (unpublished)	2006			0	0
Total			91 (4%)	29	0

a Three patients with stromal or lymphovascular invasion and one patient with contralateral breast cancer excluded. It is not mentioned if the one patient with an additional ALND metastasis had invasiveness on retrospective.

b Six patients had ALND and one of them had one additional node involved. They did not mention if these patients had pure DCIS or stromal/lymphovascular invasion.



Incidenza delle metastasi linfonodali nel DCIS

Outcomes for Women With Ductal Carcinoma-in-Situ and a Positive Sentinel Node: A Multi-Institutional Audit

Katrina H. Moore, MS, MBBS,¹ Karl J. Sweeney, MD, FRCSI,¹ Meaghan E. Wilson, BA,¹
Jessica I. Goldberg, BA,¹ Claire L. Buchanan, MD,² Lee K. Tan, MD,³
Laura Liberman, MD,⁴ Roderick R. Turner, MD,⁵ Michael D. Lagios, MD,⁶
Hiram S. Cody III, MD,¹ Armando E. Giuliano, MD,⁷ Melvin J. Silverstein, MD,² and
Kimberly J. Van Zee, MS, MD¹

Ann Surg Oncol 2007

...we conclude that the principal benefit of SNLB to the patient with a definitive diagnosis of DCIS is to identify those with occult invasion.



Perché la biopsia del Linfonodo Sentinella nel DCIS ?

- Incidenza delle metastasi linfonodali nel DCIS
- Definizione preoperatoria del T (sottostadiazione)
- Costo / beneficio



La biopsia del linfonodo sentinella nel DCIS

Annals of Surgical Oncology 14(8):2179–2181
DOI: 10.1245/s10434-006-9300-9

2007

Editorial

Breast Oncology

Sentinel Lymph Node Biopsy for DCIS: Are We Approaching Consensus?

Hiram S. Cody III, MD

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tomy for extensive DCIS.¹⁶ As we have argued before (“Is it really DCIS?”),²² the principal justification for SLN biopsy in DCIS is diagnostic uncertainty. The goal is to identify those patients with unrecognized invasive cancers who might benefit from systemic



La biopsia del linfonodo sentinella nel DCIS

Diagnosi di ca *in situ* sottostadiazione

Metodica:

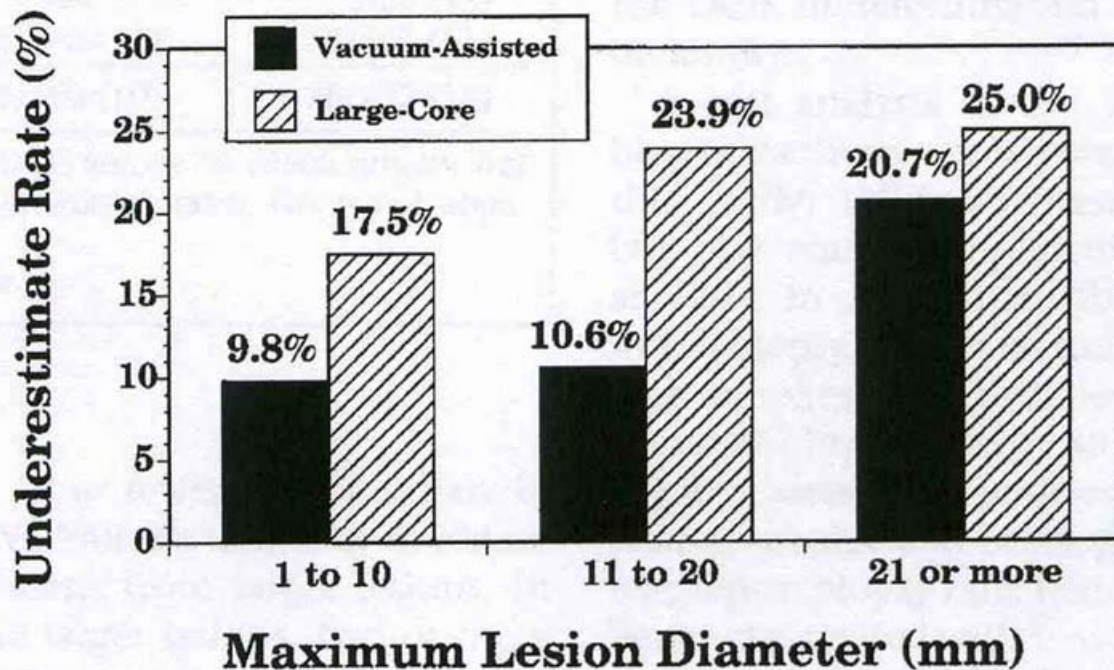
- | | |
|--------------------------|-------|
| ✓ Biopsia escissionale | rara |
| ✓ Core needle-biopsy | 20,4% |
| ✓ Vacuum assisted biopsy | 11,2% |

Jackman RJ. *Radiology* 2001



La biopsia del linfonodo sentinella nel DCIS

Fattori predittivi per la sottostadiazione



Bar graph shows significantly lower underestimation rates for biopsies performed with a vacuum-assisted device, as compared with those performed with a large-core device in lesions with a maximum diameter of 1–10-mm ($P < .004$) or 11–20 mm ($P < .006$) but not for lesions with a maximum diameter of 21 mm or greater ($P > .5$).



La biopsia del linfonodo sentinella nel DCIS

Table 2 – Overview of studies revealing invasion in the resection specimen after a core or vacuum assisted biopsy of DCIS

First author	Year	# Patients	# Patients with invasion in subsequent resection specimen (%)
Jackman and colleagues ⁴⁹	1994	43	8 (19%)
Liberman and colleagues ⁵⁰	1995	15	3 (20%)
Acheson and colleagues ⁵¹	1997	54	10 (19%)
Burbank and colleagues ⁵²	1997	87	9 (10%)
Fuhrman and colleagues ⁵³	1998	84	30 (36%)
Won and colleagues ⁵⁴	1999	40	10 (25%)
Burak and colleagues ⁵⁵	2000	89	10 (11%)
Darling and colleagues ⁵⁶	2000	289	40 (13%)
Lee and colleagues ⁵⁷	2000	59	17 (29%)
Cox and colleagues ⁵⁸	2001	224	23 (10%)
Brem and colleagues ⁵⁹	2001	24	3 (12%)
Jackman and colleagues ⁶⁰			
King and colleagues ⁶¹			
Renshaw and colleagues ⁶²			
Verkooijen and colleagues ⁶³			
Pandelidis and colleagues ⁶⁴			
Crowe and colleagues ⁶⁵			
Hoorntje and colleagues ⁶⁶			
Goyal and colleagues ⁶⁷			
Total			721 (19%)



La biopsia del linfonodo sentinella nel DCIS

Fattori predittivi per la sottostadiazione

- ✓ Comedo – alto grado
- ✓ > 2 cm – 5 cm
- ✓ Mx con opacità
- ✓ Nodulo palpabile
- ✓ Multicentricità
- ✓ Giovane età
- ✓ Mastectomia



La biopsia del linfonodo sentinella nel DCIS

“ Non ci sono fattori predittivi certi per la presenza di focolai invasivi”

Yen TW. *J Am Coll Surg*,2005
Mebry H. *Am J Surg*,2006

“ Indicazione di principio alla BLS”

Pendas S. *Cancer Control*,2004. Sakr R. *IntJ Clin Pract.* 2008
McMaster KM. *Cancer*,2002. Doyle B. *J Clin Pathol.* 2009
Cox CE. *Am Surg*,2001

“ la biopsia del L.S. non è una procedura standard”

Intra M et al. *Ann Surg* 2008



La biopsia del linfonodo sentinella nel DCIS

Meta-analysis of sentinel node biopsy in ductal carcinoma *in situ* of the breast

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Departments of ¹Surgery and Molecular Oncology and ²Pathology, Ninewells Hospital, and ³Department of Epidemiology and Public Health, Dundee University, Dundee, UK

Correspondence to: Mr B. Ansari, Department of Surgery and Molecular Oncology, Ninewells Hospital, Dundee DD1 9SY, UK (e-mail: bijan.ansari@nhs.net)

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. 1.15 to 2.93).

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



Perché la biopsia del Linfonodo Sentinella nel DCIS ?

- Incidenza delle metastasi linfonodali nel DCIS
- Definizione preoperatoria del T (sottostadiazione)
- Costo / beneficio



La biopsia del linfonodo sentinella nel DCIS

Analisi dei costi/benefici

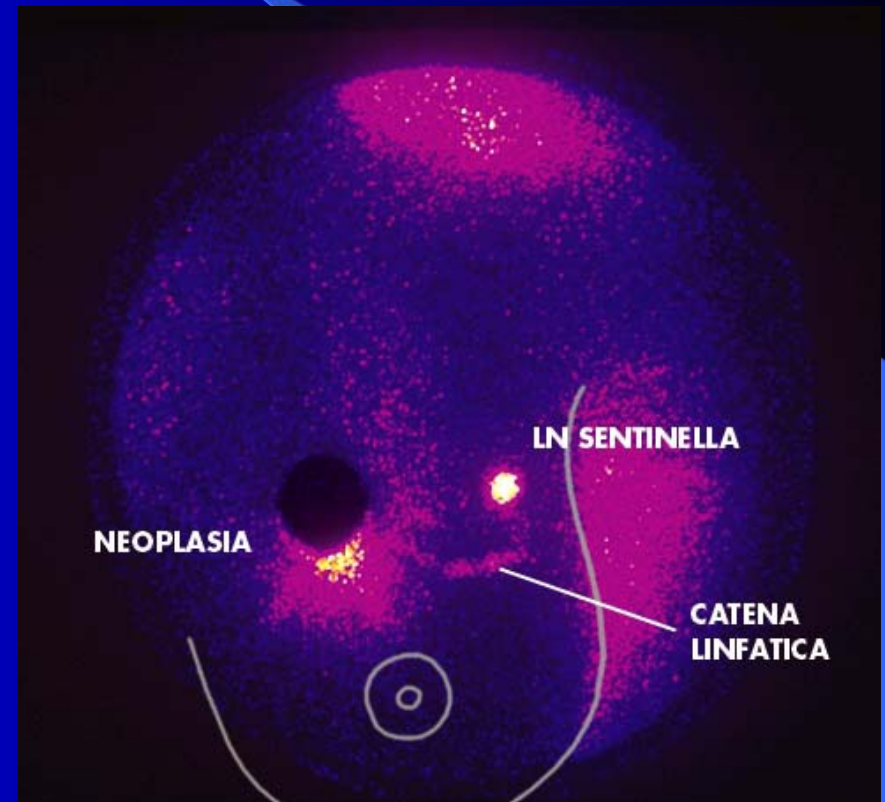
- Morbilità minima ?
possibile re-BLS ?

- 384 dollari

Cox CE et al. Am Surg 2001

- 644 dollari

Soran A et al. Ann Surg Oncol 2006



La biopsia del linfonodo sentinella nel DCIS

Casistica personale

Diagnosi preoperatoria - *FORLÌ* Gennaio 2000 - 2008

CDIS	#	%
"puri"	301	93,2%
<i>G1</i>	55	
<i>G2</i>	104	
<i>G3</i>	132	
<i>C3-C5</i>	10	
"mic"	22	6,8%
Tot	323	

- In 10 casi la diagnosi preoperatoria è stata eseguita con esame citologico



La biopsia del linfonodo sentinella nel DCIS

DIAGNOSI ISTOLOGICA DEFINITIVA		
<i>CDIS "puri" al mammotome = 301</i>		
CDIS "puri"	244	81,1%
CDIS "mic"	14	4,7%
CDI	43	14,3%
Tot	301	

SOTTOSTADIAZIONE: 57/301 casi (18,9%)



La biopsia del linfonodo sentinella nel DCIS

Fattori predittivi per la sottostadiazione

variabile	OR	
Grading G3 vs G1 + G2	4.75 (95% CI 1.58-14.34)	p = 0.006
Mastectomia vs T. Conservativo	3.01 (95% CI 1.58-5.75)	p < 0.001



La biopsia del linfonodo sentinella nel DCIS

218 BLS / 323 paz.

- **Positivo** **11 (5,1%)**
- **Negativo** **207 (94,9%)**
- **In 2 casi di CDIS mic erano presenti cellule tumorali isolate (itc +)**



La biopsia del linfonodo sentinella nel DCIS

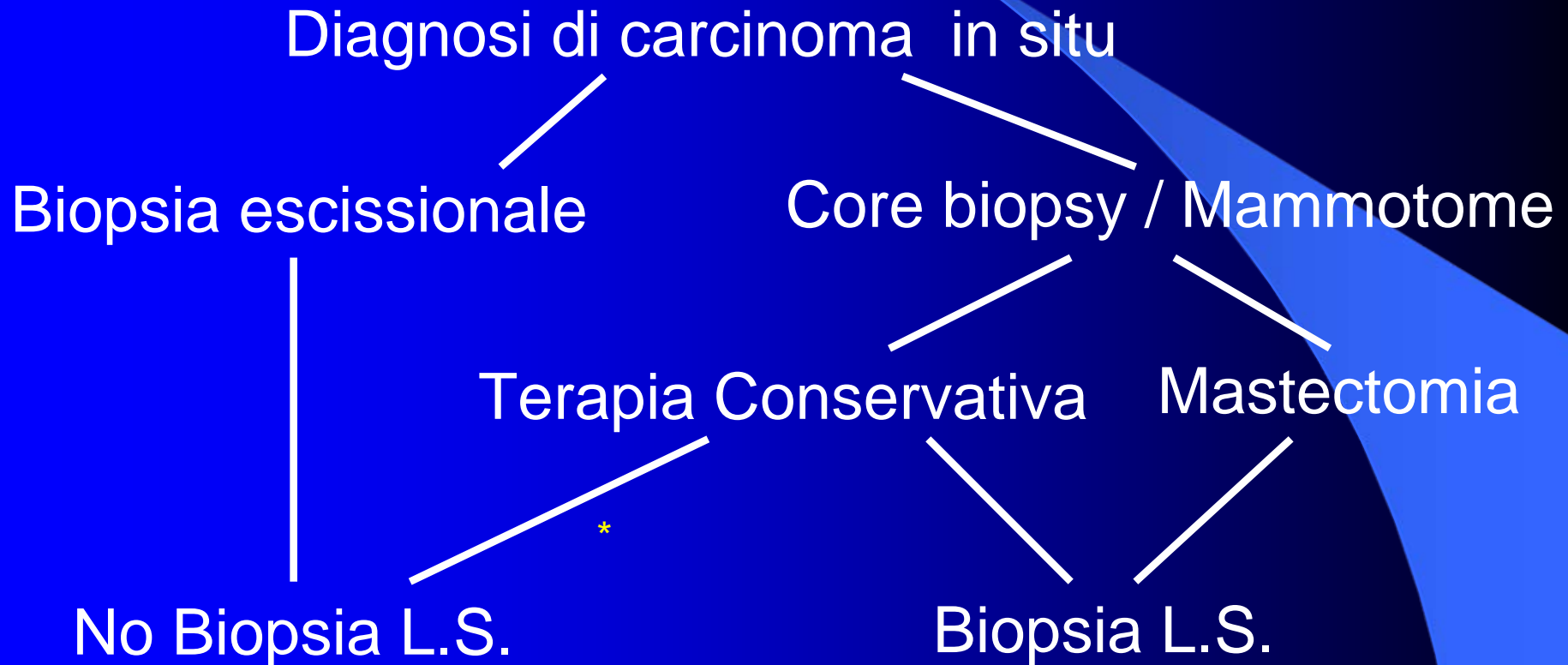
Istologia definitiva nelle paz. con BLS positivo

11/218 (5,1%)

Ca duttale infiltrante	7
DCIS con “mic”	3
DCIS puro	1



Indicazioni alla biopsia del L.S.



* G1, G2 <1 cm, senza nodulo



Conclusioni

La biopsia del Linfonodo Sentinella **“di principio”** nel Ca in situ non è indicata, tuttavia l'incertezza circa l'esatta stadiazione del **“T”** rende al momento non codificabile un comportamento univoco; in letteratura e nella pratica clinica, accanto a criteri di scelta condivisi (**mastectomia, dimensioni >5cm, sospetta mic.**) permangono ancora molti aspetti controversi che giustificano l'eterogenicità dei comportamenti.



Conclusioni

World J Surg (2007) 31:1153–1154
DOI 10.1007/s00268-007-9028-0

World Journal
of Surgery

EDITORIAL

One-step Surgery for Breast Cancer: Back to the Future?

Hiram S. Cody III

the time to weigh their treatment options, I agree entirely with the authors that “one-step surgery” is once again the way to go.

