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Review Article

Changing Trends in Axillary Management of Early Breast Cancer: From Radical to Conservative

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ABSTRACT

Background: In the last decade, surgical management of breast cancer has evolved from more extensive procedures like radical mastectomy to less invasive breast conserving surgery. Increasing evidence suggests that surgical removal of the axillary lymph nodes (ALN) in early breast cancer yields no advantage in terms of either overall or disease free survival. Significance of sentinel lymph node biopsy (SLNB) in neoadjuvant chemotherapy (NACT) is currently under discussion. A risk of non – sentinel lymph node (non-SLN) involvement is always present despite negative SLN biopsy . There are various tumour characteristics and patients' factors that are associated with increased risk of non-SLN involvement.

Methods: A literature search was performed in the PubMed Database for relevant articles on the role of axillary dissection in node positive early breast cancer, the role of SLNB, SLNB after NACT and the factors affecting involvement of axillary lymph nodes

Results: The available literature increasingly cast doubt on the putative therapeutic benefit of axillary lymph node dissection (ALND) as a part of routine multimodal treatment strategy for breast cancer. Various clinicopathological features like lymphovascular invasion (LVI), tumour size, ER, PR, HER-2 status are associated with increased incidence of non –SLN involvement so ALND should be limited to patients with these characteristics inspite of negative SLNB.

Conclusion: Current evidence indicates that the radicality of lymph node surgery in the treatment of breast cancer can be reduced, even if the node status is positive.LVI, increased tumour size , Infiltrating ductal carcinoma(IDC), Grade II&III and ER , PR, HER-2 overexpression significantly associated with positive axillary status .

Keywords: Axillary lymph node dissection (ALND), Neoadjuvant chemotherapy (NACT), SLND (sentinel lymph node biopsy), Tumour size.

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INTRODUCTION

Until the beginning of the last decade, axillary dissection was an established part of breast cancer surgery, alongside surgical removal of the primary tumour[1]. The main role of axillary dissection at present is to provide staging and prognostic information with a secondary function of providing local control of axillary disease. ALND carries a significant risk of complications as demonstrated in many studies in literature. A recent systemic review found the incidence of self- reported lymphedema after axillary dissection to be 28%.[2]

Because the diagnostic accuracy of sentinel lymph node biopsy in establishing lymph node status is comparable to that of axillary dissection, sentinel lymph node biopsy is now the standard procedure for axillary staging of breast cancer, if performed according to standard, quality assured procedure, the accuracy of SLNB in staging is high (more than 90%)[3] and morbidity is significantly reduced.[4,5]

The value of sentinel node biopsy after neoadjuvant therapy has not yet been unambiguously established. Reliable data is only available for SLNB detection rates (feasibility, diagnostic accuracy) before systemic therapy. Sentinel node biopsy after neoadjuvant chemotherapy could reduce the axillary dissection rate, because 20- 40% of node positive patients are node negative after chemotherapy.

REVIEW OF LITERATURE

Factors Affecting Involvement of Axillary Lymph Nodes in Breast Cancer

It must be noted that in western series, 30%-40% of all invasive breast cancers are node positive. Therefore, approximately two third of patients have histologically negative nodes. To determine the factors for lymph node dissection three retrospective studies were carried out in different parts of the world between 2000-2010. Various factors like patient's age, histopathological type, histological grade and ER, PR status were correlated with ALN positivity. Largest among these was a retrospective study of 1325 female patients with invasive breast cancer conducted at Changua Christian Hospital between Jan 2004 to Jan 2010.[6] In this study 742 patients had axillary lymph node metastasis. Tumour size (with p< 0.0001), poor histological grade (with p =0.0002) and presence of LVI (with p<0.0001) were significantly associated with

positive axillary status. Progesterone receptor positivity (p=0.0032) and HER-2 overexpression (p=0.002) were also associated with ALN metastasis (Table 1).

Another study Yenidunya et al included 210 breast carcinoma patients who underwent breast conserving surgery and ALND (level I and II) or Modified radical mastectomy (MRM) in Faith University Hospital between March 2004 and august 2010.[7] Axillary lymph node metastasis was found in 55% (n=116) of the study group. Tumour size (p=0.001) and lymphovascular invasion (p<0.001), multicentric disease, epithelial hyperplasia and perineural invasion were found to be significantly associated.

Ashturkar et al showed strong association between histological grade, ER, PR status with axillary lymph node status positivity. No correlation was observed between tumour size and patients age with axillary metastasis. On histological typing of breast cancer, 68 cases were infiltrating ductal carcinoma (IDC). Tumours like DCIS, tubular carcinoma and mucinous carcinoma showed less tendency for axillary metastasis compared to IDC.[8]

In study by Gurleyik et al tumour size was not found to be an important factor for axillary involvement. Axillary metastasis was significantly associated with LVI (p<0.001).[9]

Nomogram score were assigned to all patients based on criteria specified in Memorial Sloan Kettering Cancer nomogram. Lower score predict a lower risk of further positive nodes on Completion axillary lymph node Dissection (CALND). Those who had scoreless than 10%, chance of having additional non -SLN involvement based on their nomogram scores is low and more likely to undergo SLNBs only, compared to those with a greater than 10% chance. (Table 2)

Axillary Dissection in Cases of Positive Sentinel Lymph Node Biopsy:

The axillary recurrence rate after ALND in invasive breast cancer is less than 1%.[10] 16 studies were carried out that described patients with macrometastatic disease in SLN, in whom ALND had not been performed. A total of 3268 patients were identified, with a median follow up of 43 months (range 1-142 months), 24 axillary recurrences were observed (0.7%). In this group the median age was 58 years (53-64 years).The national database study by Yi et al[11] showed axillary recurrence (AR) of 0.1% in 1473 patients with macrometastatic disease. In case of macrometastatic disease in the sentinel node, 6 studies reported that patients had been treated with axillary radiotherapy in 2%-63% of the patients. In majority of the patients who developed axillary recurrences (n=24) details regarding the type of surgery of the primary tumour is lacking (Table 3).

Table 1: Factors Affecting Involvement of Axillary Lymph Nodes in Breast Cancer

Variables	Wu JL et al		Ashturkar et al		Gurleyik et al		Yenidunya et al	
No.of patients	n=1325		n=95		n=59		n=210	
	Node –ve	Node +ve	Node –ve	Node +ve	Node –ve	Node +ve	Node -ve	Node +ve
Age(mean)	51.12	51.43	Mean : 49.32		-	-	55.8	51.7
p value	p=0.6154		p>0.05		-		p=0.020	
Tumour size								
T1	458	211	17	9	34	5	52	34
T2	246	286	22	24	12	8	37	62
T3	38	86	09	14	-	-	04	09
T4							0	10
p value	p<0.0001		p>0.05		p=0.022		p=0.001	
Grade								
I	143	72	16	5	15	2	19	24
II	415	320	25	24	25	7	37	32
III	184	191	9	14	6	4	31	55
p value	p=0.0002		p<0.001		p=0.139		p=0.091	
Pathological Factors								
ER +ve	486	406	21	37	35	7	-	-
PR +ve	451	400	16	29	31	8	-	-
ER -ve	256	177	27	10	11	6	-	-
PR -ve	291	183	32	18	15	5	-	-
Her 2neu +ve	126	139	-	-	-	-	-	-
Her2neu –ve	616	444	-	-	-	-	-	-
p value	p=0.0019		p<0.002		p=0.467		-	
LVI								
No	585	167	-	-	37	3	69	64
Yes	157	416	-	-	9	10	22	50
p value	p<0.0001		-		p<0.001		p <0.001	
Histological type								
DCIS			04	00				
IDC			32	36				
ILC			07	07				
IDC & ILC			01	02				
Mucinous	-	-	02	00	-	-	-	-
Tubular			01	00				
Metaplastic			00	01				
Medullary			01	01				
p value			P<0.046					

Table 2: Patients with MSKCC nomogram scores below and above 10% in a study of about 194 patients

Nomogram Scores	No. Of patients	No. (%) of Pts who underwent CALND	P value
< 10 %	64	19(32.2)	0.004
>10 %	130	67(54.9)	

CALND= completion axillary lymph node dissection

Table 3: Sentinel node status: Macrometastatic disease (>2.0mm)

Source	Year	Pts	Age	T1%	LV	BCt	Ct/Ht	RT to axilla	F/U mth	AR
Yi et al [11]	2010	1473	61	69	NM	79	NR	NM	50	3 (0.1%)
Giuliano et al[12]	2010	199	54	70	36	100	60/48	NM	76	2
Takei et al [13]	2010	32	55	30	78	92	19/77	52	58	0
Yegiyants et al [14]	2010	14	57	66	43	100	92/76	0	79	1
Bilimoria et al[15]	2009	1458	58	63	NM	81	71/74	NM	64	18
Zakaria et al[16]	2008	17	62	62	29	60	53/87	19	30	0
Hwang et al[17]	2007	39	56	72	22	69	56/27	58	30	0
Schulze et al[18]	2006	1	64	100	0	74	3/68	NM	49	0
Haid et al[19]	2006	2	59	77	NM	87	32/93	NM	47	0
Swenson et al[20]	2005	4	59	82	NM	75	42/58	NM	33	0
Schrenk et al[21]	2005	4	59	61	NM	29	NR	0	48	0
Fan et al[22]	2005	11	53	71	28	NM	NR	63	31	0
Chagpar et al[23]	2005	1	57	89	2	86	33	NM	40	0
Carlo et al[24]	2005	2	57	84	NM	92	100	NM	60	0
Guenther et al[25]	2003	7	62	67	NM	NM	100	2	32	0
Fant et al[26]	2003	4	NM	81	NM	NM	100	3	30	0

SLNB=sentinel lymph node biopsy, LVI= Lymphovascular invasion, RT = Radiotherapy, NR= Not Reported, NM= Not Mentioned; BCt= breast conservation therapy, Ct/Ht= Chemotherapy/ Hormone Therapy;F/U= Follow up ; AR= axillary recurrence Pts= Patients, SN= Sentinel node

Table 4: Comparison of the ACOSOG Z0011 and IBCSG 23-01 trials

Variable	ACOSOG Z0011	IBCSG 23-01
No of patients randomised	891(target = 1900)	934(target =1960)
No of patients enrolled	856	931
Years of accrual	5/99-12/04	4/01-2/10
Number of institutions	115	27
Primary aim	Overall survival	Disease free survival
Median follow up	6.3yrs	5yrs
Patients age , median	54-56	53-54
ER positive	82.7%	75.9%
T1 tumour	69.3%	69.4%
Micrometastasis	41.2%	97.8%
Single positive LN	67.7%	96.0%
Solitary positive LN	65.2%	88.0%
Breast conservation with radiation	89%	88.4%
Breast conservation with partial breast radiation only	0	19.3%

Table 5: Comparing Group A and Group B

Variable	Group A(SLNB alone)	GroupB(SLNB+ALND)
5yrs OS	94.6%	95.8%
5 yrs DFS	86.4%	89.2%
5yrs distant DFS	89.7%	92.5%

MAJOR TRIALS EVALUATING ALND IN CLINICALLY NODE NEGATIVE PATIENTS:

- **ACOSOG Z0011 trial:**

ACOSOG Z0011 (The American College of Surgeons Oncology Group Z0011) was published in 2010-11 has led to significant shift from routine use of ALND in women with positive SLN.[12,27] (Fig 1)

ALND is indicated for SLN positive patients outside ACOSOG Z0011 entry criteria specifically:

i. T3 disease
ii. A clinically positive axilla & biopsy proven
iii. Positive SLN with disease requiring mastectomy
iv. >2 positive SLN or matted nodes

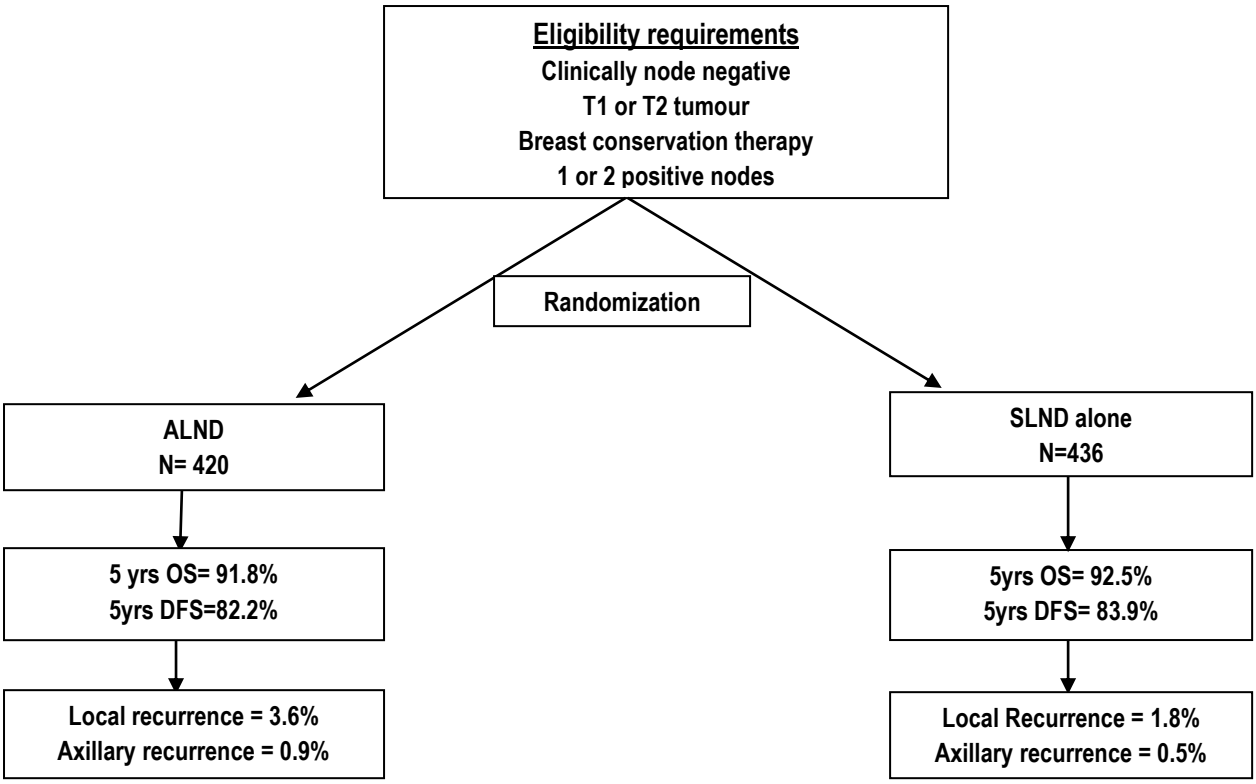

Fig 1: Schema of ACOSOG Z0011 trial[12,27]. The ACOSOG Z0011 trial was designed to determine whether there was a difference in overall survival or locoregional recurrence in early breast cancer with one or two positive sentinel lymph nodes who underwent axillary lymph node dissection versus those that had no further axillary therapy. OS= overall survival, DFS= Disease free survival

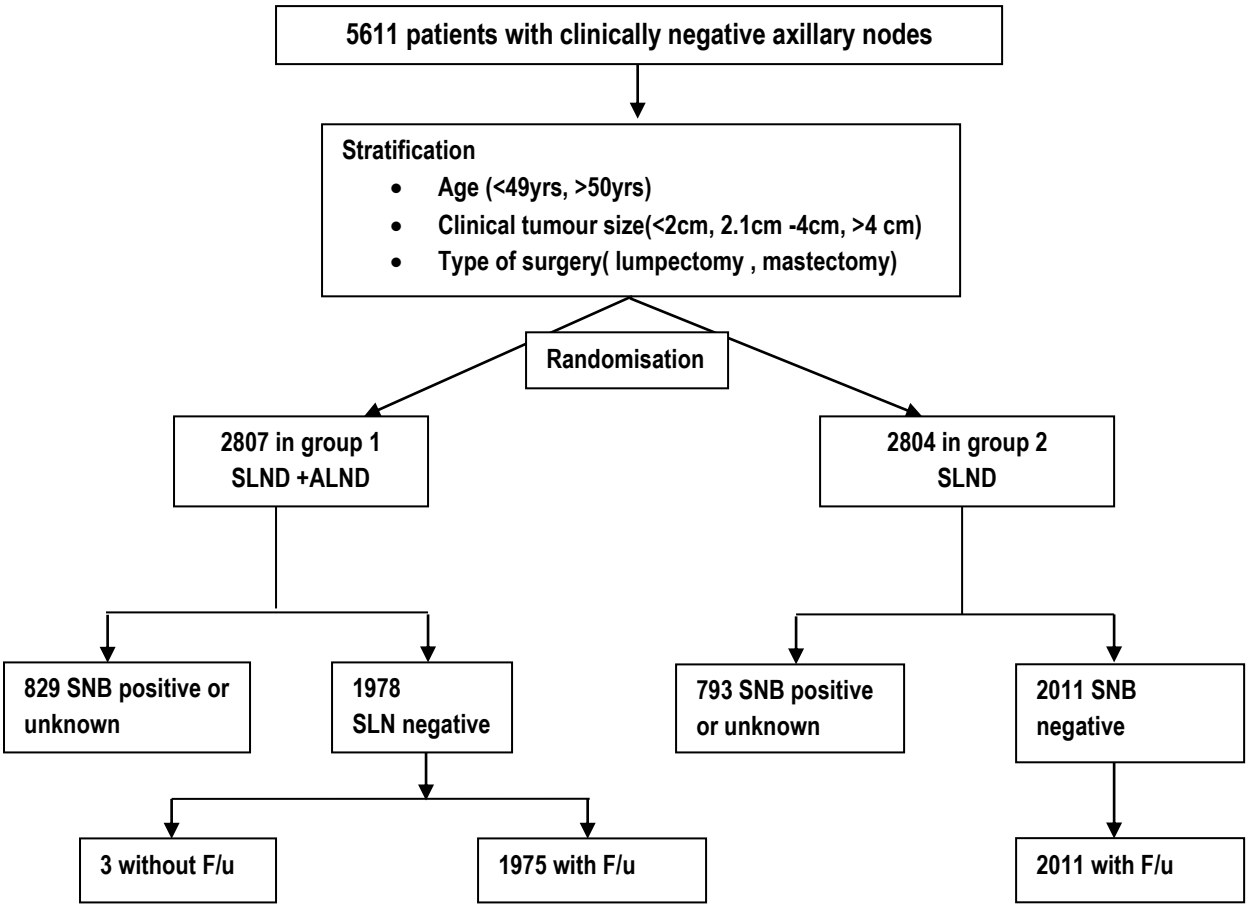

Fig 2: NSABP B-32 Trial Profile

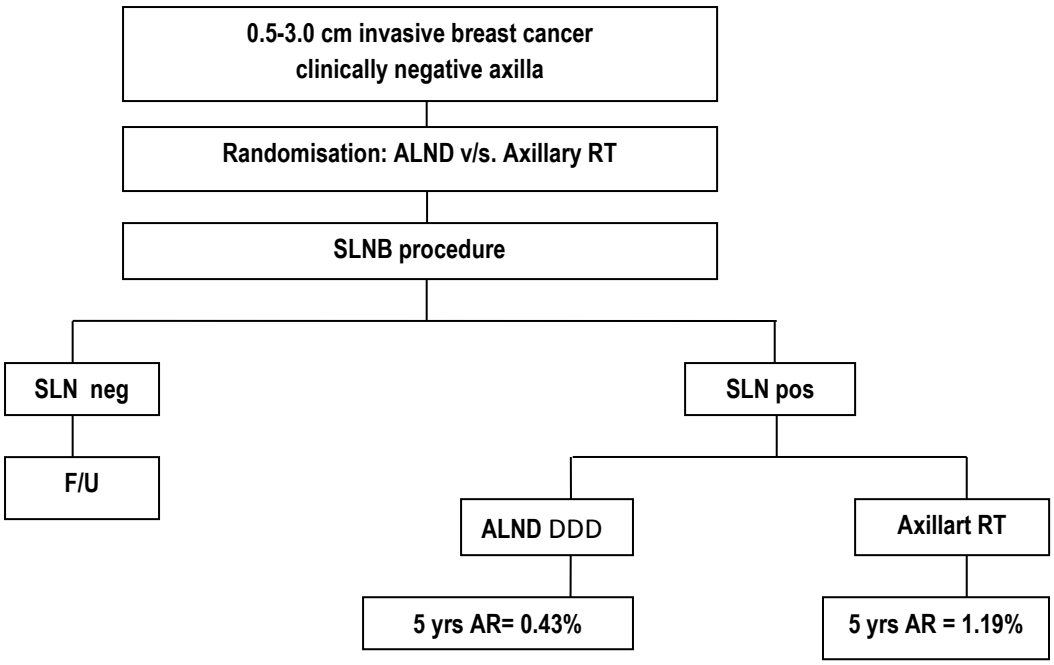

Fig 3: Study design of AMAROS trial

Since ACOSOG Z0011 trial found no evidence of a therapeutic benefit for axillary dissection in patients with positive SLN status, the value of surgical lymphadenectomy for breast cancer patients has been questioned increasingly critically.[12]

- **IBCSG 23-01 Trial**

This trial randomly assigned participants to receive either ALND or no further axillary surgery. Most of the patients received radiation or chemotherapy or both. It was activated in April 2001 & accrued patients through Feb 2010 randomising those patients with micrometastasis & ITC in the SLN based on HPE pathology evaluation, to ALND or no ALND. In many ways, IBCSG 23-01 results are very similar to the findings from ACOSOG Z0011 study. Similar to the ACOSOG Z0011, study also closed early after meeting less than 50% of its targeted accrual goal. The results of IBCSG 23-01 study, in which 95.6% of patients who had only one positive SLN limited to ITC s or micro metastatic disease, local control and disease free survival were not different with or without ALND after a median follow up of 5 yrs (Table 4). One of the important differences between the two studies is that IBCSG 23-01 study did allow enrolment of 86 patients undergoing mastectomy accounting for just 9% of each arm. Therefore, this number (42patients without ALND) is really too small to allow extrapolation of the trial results to patients that did not undergo breast conservation surgery and radiation therapy. Another interesting aspect of IBCSG 23-01 study is that 19% of patients received partial breast radiotherapy and again this is too small (80 patients with SLN only) and the follow up too short to draw meaningful conclusions about the suitability of omission of ALND for patients with micro metastases or ITCs undergoing adjuvant partial versus whole breast radiation.[28] (Table 4)

- **National Surgical Adjuvant Breast and Bowel Project (NSABP)- 32 Trial**

This study evaluated the suitability of SLN biopsy alone for SLN – negative clinically node negative patients, by comparing SLN negative patients undergoing SLN biopsy followed by ALND, suggests there is a significant survival disadvantage, after a median 8 yrs of follow up, for women with occult nodal disease.[29] (Fig 2) In this study 15.9% of patients who were SLN negative by conventional histology had their SLNs re-evaluated with immunohistochemistry by a central pathology lab, and were found to be node positive. Only 0.4% of patients had macro metastatic disease, while 4.4% had micro metastases and 11.1% ITCs. 85% of patients in this study received adjuvant systemic therapy. The 8-year median follow up in the B-32 study is longer than that reported for Z0011 and IBCSG 23-01.[30,31] This study adds to the totality of evidence in breast cancer patients by definitely demonstrating that there is no significant difference in survival between axillary dissection and sentinel node surgery alone in patients with negative sentinel nodes. (Table 5)

- **AMAROS trial - After mapping of the axilla: Radiotherapy or Surgery**

This multicentric trial was specifically designed to compare local and regional control & morbidity with axillary radiation therapy versus axillary surgery. (Feb 2001-April 2010)[32,33] (Fig 3) Results are in accordance with findings from 2 randomised trials i.e. NSABP- B04 trial and InstitutCurie in which authors compared ALND with axillary RT.

- **ALMANAC Trial: Axillary Lymphnode Mapping Against Nodal Axillary Clearance**

This trial found that women who underwent SLNB alone experienced less lymphedema and sensory deficit than women who underwent ALND. Women who underwent SLNB alone were also able to resume their normal activity more quickly than women who underwent ALND.[34]

All the above major studies concluded that there is no significant difference in disease free survival, overall survival & locoregional recurrence rate between ALND and no ALND group in clinically node negative & SLN positive patients.

Isolated Tumour Cells / Micrometastasis & Axillary Dissection

Isolated tumour cells & micrometastasis were the new definitions for nodal staging in addition to macrometastasis. Isolated tumour cells were defined as cell clusters less than 0.2 mm in diameter or tumour cells fewer than 200 in number. On the other hand micrometastasis refer to malignant cell clusters between 0.2-2 mm in size or cells more than 200 in number. When the size of metastasis is more than 2mm, it is called macrometastasis. Presence of isolated tumour cells in an axillary LN is staged as N0 whereas micrometastasis and macrometastasis were accepted as N1.ITCs are not distinguishable by H&E staining but detected only with IHC or molecular methods.[37]

Surgeons first started to avoid axillary dissection in patients with isolated tumour cells or micrometastasis in sentinel lymph nodes. IBCSG 23-01 study randomised 934 patients with micrometastasis to either axillary dissection or no further surgical treatment. DFS and overall survival were similar in both groups after a median 5 year follow-up. Patients treated with breast conserving surgery received radiotherapy whereas almost all patients were treated with systemic therapy mostly hormonal treatment in this study.[28]Locoregional recurrence rate in ALND arm is 2.4% whereas in no ALND arm it is 2.8%. In a meta-analysis, 30 studies including patients with positive SLNB and without completion axillary dissection were reviewed.[35] In these studies, 3568 patients with micrometastatic disease in SLNB were included. After a median follow up time of 42 months, only 0.3% of the patients developed an axillary recurrence. (Table 6) Another study, including patients from surveillance, epidemiology and End results database reported even less regional recurrence rate of 0.1% among 1767 patients with micrometastatic disease & no further axillary dissection.[36] Bilimoria et al evaluating the patients in the United States National Cancer data base reported an axillary recurrence rate of 0.6% in 530 patients with micrometastatic disease.

Axillary Management In Case Of Sentinel Lymph Node Negativity

Main objective of SLNB is to prove that clinically and radiologically negative axilla is actually tumour free after histopathological examination. Previous prospective randomised trials reported false negativity of <10% with SLNB.[40] These results encouraged the surgeons not to perform axillary dissection in cases with negative SLNB. 5 yrs axillary recurrence rate changes between 0.5%-1.5% in patients with negative SLNB.[41,42] It continues to be low even after 10 yrs.[43] In meta- analysis of 48 studies including 14959 patients, axillary recurrence rate was reported as 0.3% after a median follow –up time of 34 months.[44] According to the results of previously mentioned studies, currently axillary dissection is not performed in patients with a negative SLNB result to avoid possible morbidity due to dissection.

Sentinel Lymph Node Biopsy after Neoadjuvant Chemotherapy

During the last few years there have been a number of clinical trials on the effectiveness and role of SLNB after Neo adjuvant chemotherapy (NAC). Reliability of SLNB following NAC for patients with initial nodal disease has been questioned, as the only available data has been from small series, reporting false negative rates ranging from 7% to 25%. Currently, ALND after NAC in patients with FNAC proven node positive disease at presentation is recommended. However, the ALN metastasis may have been eradicated by the chemotherapy in certain patients who could consequently be spared ALND. Several reasons for avoiding SLNB after NAC have been suggested. Anatomical alteration of the lymph node drainage may occur by disruption of the lymphatic vessels by the tumour inflammation or fibrosis of lymphatic duct or blockage by necrotic and/or apoptotic cells. In addition, NAC can induce a non-uniform tumour regression in the axillary nodes.[46-48] i.e. the order of response of the nodes in the axilla is not known, the sentinel lymph node may respond to treatment and become free of tumour regardless of whether or not other axillary node still harbour the disease.

The National Surgical Adjuvant Breast and Bowel Project (NSABP) B-27 trial is one of the largest studies published to date on SLNB after NAC.[49] A total of 428 patients underwent SLNB with concomitant ALND after NAC with an identification rate of 84.8% and false negative rate (FNR) of 10.7%.

In addition a meta-analysis of 21 studies, involving a total of 1273 patients who received NAC followed by SLNB and ALND indicated an average identification rate of 91% and an FNR of 12 %.[50]

The *ACOSOG Z1071 trial* was designed to test the hypothesis that SLND performed with a standardised surgical approach would accurately assess nodal response after chemotherapy. The study enrolled women with clinical T0-4N1-2 M0 breast cancer with nodal metastases confirmed by needle biopsy.

After completing neoadjuvant chemotherapy, enrolled patients underwent SLND followed by completion ALND in order to assess the FNR. The FNR of SLNB after NAC in patients with cN1 breast cancer (with at least two SLNs identified at the time of surgery) was 12.6% higher than the expected threshold of 10 %.[51] (Fig 4)

SENTINA (SENTinelNeoAdjuvant) multicentre study was designed to investigate the value of SLNB before and after neoadjuvant chemotherapy.[52]

There are four arms in the trial: (a) clinically node negative patients who underwent SLND before NACT, a portion of whom were then moved to arm (b)if they had a positive SLN and then had a second SLND after NACT. The third arm (c) consisted of clinically node positive patients who converted to clinically negative after NACT and then underwent SLND to restage the axilla followed by ALND. The remaining arm (d) consisted of clinically node positive patients who remained clinically positive after NACT and underwent ALND.

In contrast to ACOSOG Z1071 trial, patients in the SENTINA trial didn't have nodal metastases confirmed by needle biopsy. The authors showed that SLNs could be detected in 99.1% before NACT (arm A); However among patients who had nodal metastases identified by a SLND prior to NACT , a second SLND procedure (Arm B) was only successful in 60.8% demonstrating that patients should only undergo one SLN procedure for staging. Arm C focused on the possibility of accurately restaging the axillary nodes after NACT in clinically node positive patients. (Fig 5).

The authors reported an overall FNR for SLND in these patients of 14.2% with findings similar to the Z1071 trial are the FNR was lower when more SLN s were retrieved . The FNR for SLND in the 149 patients who had biopsy confirmed metastases was 19 % compared to 12.3% in 443th patients who were classified as node positive without pathological confirmation.[52] (Table 7, 8)

Table 6: Describes the Incidence & Prognostic Impact of ITCs in sentinel node biopsies

Authors	No of patients	ITC (%)	Outcome
Herbert et al	514	16	No effect
Reed et al [38]	1255	25	No effect
De Boer et al[39]	2707	819	HR= 1.5
Barbosa et al	1000	43	No effect
Anderson et al	3369	107	No effect
Leidenium et al	1390	63	⇩5 yrs survival

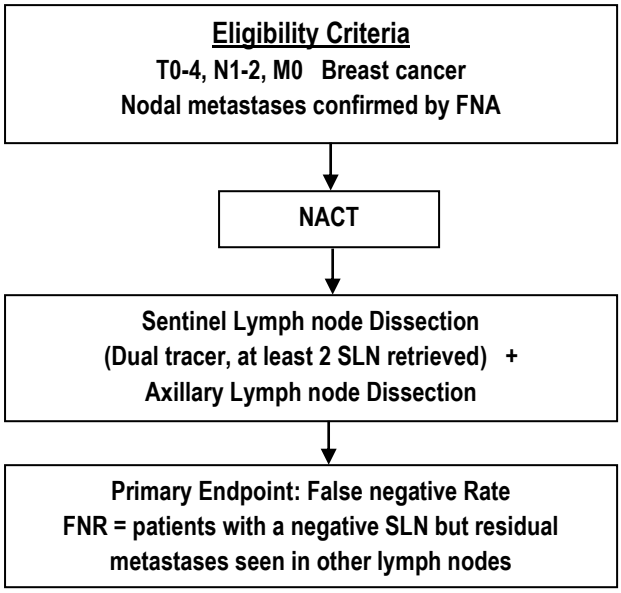

Fig 4: ACOSOG Z1071 Trial[51]

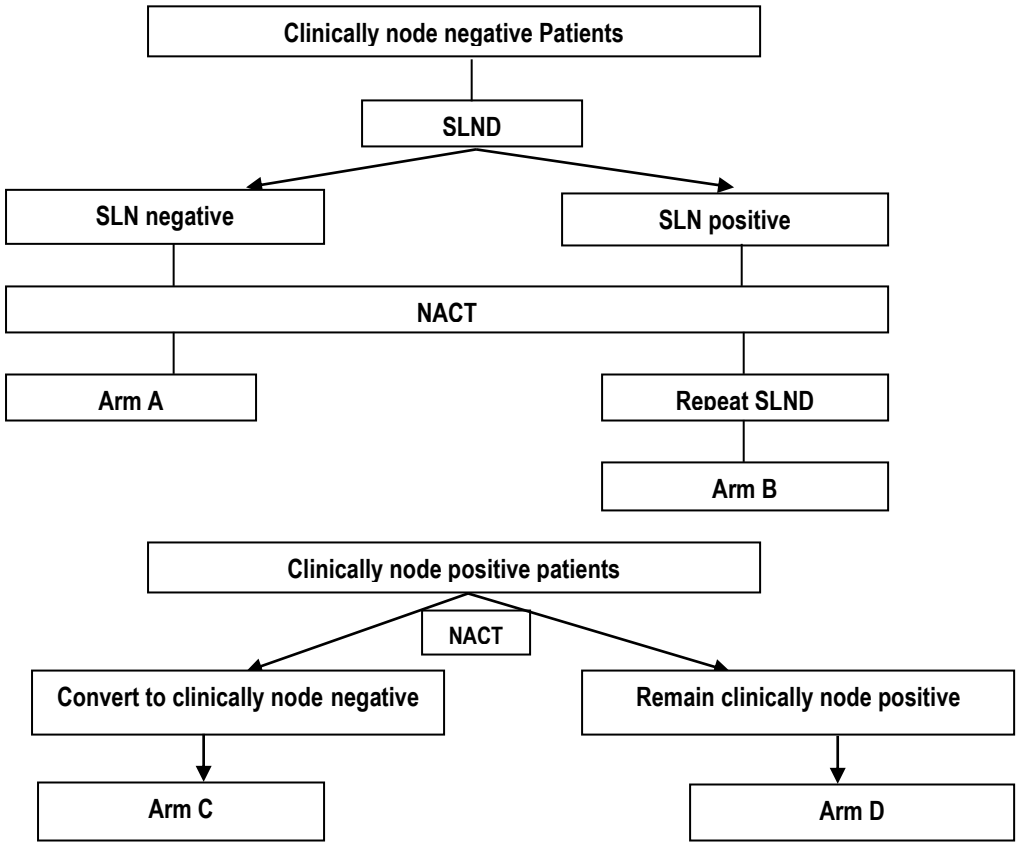

Fig 5: SENTINA trial[52]

Table 7: Diagnostic performance of sentinel lymph node biopsy after neoadjuvant chemotherapy according to the number of retrieved SLN in a study of 89 patients

No. of retrieved nodes	No of cases	Status of SLNB, No (%)		
	N= 89	True positive	True negative	False negative
1	19	12(63.2%)	7(100)	0
2	16	11(68.8%)	5(100)	0
3	21	19(90.5%)	1(50)	1(50)
>4	28	22(78.6%)	5(83.3)	1(16.6)
Not found	5			

Table 8: Diagnostic Performance of SLNB after neoadjuvant chemotherapy in patients with initial cytology proven nodal disease at presentation

Findings of SLN	No.(%)
SLN identification rate after NAC	115/120(95.8)
No. of nodes retrieved	3(1-7)
No residual axillary metastases	18/89(20.2)
Residual axillary metastases	71/89(79.8)
Residual metastases limited to SLNs	27/70(38.6)
Falsely negative SLNs	2/20(10.0)

CONCLUSIONS

The evaluation and management of axillary lymph nodes is critical in breast cancer with impact on loco regional as well as survival outcomes. ALND can be extremely morbid for patients and adversely impact on quality of life. Current evidence indicates that the radicality of lymph node surgery in the treatment of breast cancer can be reduced, even if the node status is positive. Various factors i.e. LVI, increased tumour size, infiltrating ductal carcinoma (IDC), grade II&III and ER, PR, HER-2 overexpression are significantly associated with positive axillary status so ALND should be considered.

The omission of ALND in clinically node negative patients with nodal metastases discovered by SLND has been incorporated broadly into clinical practice, although it is unclear if the inclusion of axillary radiotherapy adds substantial benefit.

Moving forward, the safety and efficacy of selective omission of ALND among patients who convert from biopsy proven node positive breast cancer to pathologic negative disease after NACT must be systemically studied.

REFERENCES

1. GiulianoAE, Haigh PI, Brennan MB, et al.: Prospective observational study of sentinel lymphadenopathy without further axillary dissection in patients with sentinel node negative breast cancer . J Clin Oncol 2000;18:2553-9.

2. M.Goker, N.Devogdt, G.Vandeputte et al, "Systematic review of breast cancer related lyphedema: making a balanced decision to perform axillary clearance ", Facts, Views and Vision in Obgyn, Vol 5, no.2, p.p.106-115, 2013.

3. Kuehn T, Vogl FD, Helms GV, et al .: Sentinel Node Biopsy is a reliable method for axillary staging in breast cancer ; results from a large prospective German multiinstitutional trial. Eur J Surg Oncol 2004;30:252-9.

4. Fleissig A, FallowfieldLJ, Langridge CI, et al .: Postoperative arm morbidity and quality of life . Results of the ALMANAC randomised trial comparing sentinel node biopsy with standard axillary treatment in the management of patients with early breast cancer . Breast Cancer Res Treat 2006; 349:546-53.

5. Veronesi U, Pagnelli G , Viale G, et al. :A randomised comparison of sentinel node biopsy with routine axillary dissection in breast cancer . N Engl J Med 2003;349:546-53.

6. Wu J-L ,Tseng H, Yang L, Wu H et al .: Prediction of axillary lymph node metastases. Med Sci Monit2014;20: 577-581.

7. Yendunya, Bayrak R, Haltas H et al. Predictive value of histopathological and immunohistochemical parameters for axillary lymph node metastasis in breast carcinoma. Diagnostic Pathology 2011, 6: 18. http://www.diagnosticpathology.org/content/6/1/18

8. Ashturkar A, Pathak G, Deshmukh S, et al .:"Factors predicting the axillary lymph node metastasis in Breast cancer" : Is axillary node clearance indicated in every breast cancer patient.Indian J Surg(Sept-Oct 2011);73(5):331-335

9. Gurleyik G, Aker F, Aktekin A et al .: Tumour characteristics influencing Non- sentinel lymph node involvement in clinically node negative patients with breast cancer . J breast cancer 2011 June ; 14(2):124-128.

10. Palesty JA, Foster JM, Hurd TC, Watroba N.,Rezaishiraz H, Edge S B: Axillary recurrence in women with a negative sentinel lymph node and no axillary dissection in breast cancer . J Surg Oncol 2006; 93 : 129-32.

11. Yi M, Giordano SH, Meric-Bernstam F, et al . Trends in and outcomes from sentinel lymph node biopsy (SLNB) alone vs SLNB with axillary lymph node dissection for node positive breast camcer patients: experience from the SEER database. Ann Surg Oncol 2010;17: S343-51.

12. Giuliano AE, McCall L , Beitsch P, et al . Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: ACOSOG Z0011randomised trial. Ann Surg .2010;252: 426-32.

13. Takei H, Kurosumi M, Yoshida T, et al . Axillary lymph node dissection can be avoidd in women with breast cancer with intraoperative, false negative sentinel lymph node biopsies. Breast Cancer .2010;17: 9-16.

14. Yegiyants s, Romero LM , Haigh PI, et al . Completion axillary lymph node dissection not required for regional control in patients with breast cancer who have micrometastases in a sentinel node. Arch Surg. 2010; 145: 564-9.

15. Bilimoria KY, Bentrem DJ, Hansen NM, et al. Comparison of sentinel lymph node biopsy alone and completion axillary lymph node dissection for node positive breast cancer. J Clin Oncol.2009; 27: 2946-53.

16. Zakaria S, Pantvaidya G, Reynolds CA, et al. Sentinel node positive breast cancer patients who do not undergo axillary dissecton: are they different? Surgery.2008; 143: 641-7.

17. Hwang RF, Gonzalez – Angulo A, Yi M, et al . Low locoregional failure rates in selected breast cancer patients with tumour positive sentinel lymph nodes who do not undergo completion axillary dissection. Cancer. 2007; 110:723-30.

18. Schulze T, Mucke J, Markwardt J, et al. Long term morbidity of patients with early breast cancer after sentinel lymph node biopsy compared to axillary lymph node dissection. J Surg Oncol.2006;93: 109-19.

19. Haid A, Knauer M, Koberle-Wuhrer R, et al. Medium – term follow up data after sentinel node biopsy alone for breast cancer. Eur J Surg Oncol. 2006; 32:1180-5.

20. Swenson KK, Mahipal A, Nissen MJ, et al. Axillary disease recurrence after sentinel lymph node dissection for breast carcinoma. Cancer.2005;104:1834-9.

21. Schrenk P, Konstantiniuk P,Wolfl S, et al. Prediction of non- sentinel lymph node status in breast cancer with a micrometastatic sentinel node. Br J Surg. 2005;92:707-13.

22. Fan YG, Tan YY, Wu CT, et al . The effect of sentinel node tumour burden on non-sentinel node status and recurrence rates in breast cancer. Ann Surg Oncol. 2005;12:705-11.

23. Chagpar A, Middleton LP, Sahin AA, et al. Clinical outcome of patients with lymph node negative breast carcinoma who have sentinel lymph node micrometastases detected by immunohistochemistry. Cancer.2005;103:1581-6.

24. Carlo JT, Grant MD, Knox SM, et al. Survival analysis following sentinel lymph node biopsy: a validation trial demonstrating its accuracy in staging early breast cancer. Proc(Bayl Univ Med Cent).2005;18:103-7.

25. Guenther JM, Hansen NM, DiFronzo LA, et al. Axillary dissection is not required for all patients with breast cancer and positive sentinel nodes. Arch Surg. 2003;138:52-6.

26. Fant JS, Grant MD, Knox SM, et al. Preliminary outcome analysis in patients with breast cancer and a positive sentinel lymph node who declined axillary dissection . Ann Surg Oncol. 2003;10:126-30.

27. Guiliano A, Hunt K, Ballman K, Beitsch P, Whitworth P, Blumencranz P, et al. Axillary dissection vs no axillay dissection in women with invasive breast cancer and sentinel node metastasis: a randomised clinical trial. JAMA.2011;305:569-75.

28. Galimberti V, Cole BF, Zurrida S, et al . Axillary dissection versus no axillary dissection in patients with sentinel –node micrometastases (IBCSG 23-01) ; a phase 3 randomised controlled trial. Lancet Oncol 2013;14:297-305.

29. Weaver DL, Ashikaga T, Krag DN, et al. Efftect of occult metastases on survival in node -negative breast cancer. NEnglJMed2011;364:412-21.

30. Krag DN, Julian TB, Harlow SP, et al . NSABP-32: Phase III, randomised trial comparing axillary resection with sentinel lymph node dissection : A description of the trial . Ann Surg Oncol 2004;11:208S-10S.

31. Land SR , Kopec JA , Julian TB, et al . Patient –reported outcomes in sentinel –node negative adjuvant breast cancer patients receiving sentinel node biopsy or axillary dissection : National Surgical Adjuvant Breast and Bowel Project Phase III Protocol B-32 . J Clin Oncol 2010;28:3929-3936.

32. D.J. Rutgers, M. Donker, M.E. Strauer, P. Meijnen, C.J.H. Vande Velde & R.E.Mansel. Radiotherapy or surgery of the axilla after a positive SLN in breast cancer patients: Final analysis of the EORTC AMAROS trial(10981/22023)". Journal of clinical oncology, vol.31,no.15, supplement, Article IDLBA 1001,2013.

33. Rutgers EJ, Meijnen P, Bonnefoi H. Clinical trials update of the European Organisation for Research and Treatment of Cancer Breast Cancer Group. Braest Cancer Res.2004;6:165-9 .

34. R.E Mansel, L. Fallowfield , M Kissin et al, "Randomised multicentre trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer : ALMANAC trial". Journal of the National Cancer Institute, vol.98, no.9, p.p.599-609,2006.

35. Francissen CM, Dings PJ, van Dalen T, Strobbe LJ, van Laarhoven HW, de Wilt JH. Axillary recurrence after a tumour positive sentinel lymph node biopsy without axillary treatment ; a review of the literature .Ann Surg Oncol 2012;19:4140-4149[PMID : 22890590 DOI : 10.1245/s10434-012-2490-4]

36. Yi M, Giordano SH, Meric- Bernstam F, Mittendorf EA, Kuerer HM, Hwang RF, Bedrosian I, Rourke L, Hunt KK. Trends in and outcomes from sentinel lymph node biopsy (SLNB) alone vs. SLNB with axillary lymph node dissection for node – positive breast cancer patients: experience from the SEER database. Ann Surg Oncol 2010;17 Suppl 3:343-351[PMID : 20853057 DOI: 10.1245/s10434-010-1253-3]

37. Bilimoria KY, Bentrem DJ, Hansen NM, Bethke KP, Rademaker AW, Ko CY, Winchester DP, Winchester DJ. Comparison of sentinel lymph node biopsy alone and completion axillary lymph node dissection for node positive breast cancer. J Clin Oncol 2009;27:2946-2953 [PMID: 19364968 DOI : 10.1200/JCO.2008.19.5750]

38. Reed J , Rosman M, Verbanac KM, et al . Prognostic implications of isolated tumour cells and micrometastases in sentinel nodes of patients with invasive breast cancer: 10- year analysis of patients enrolled in the prospective East Carolina University / Anne Arundel Medical Centre sentinel node multicentre study . J Am Coll Surg .2009;208:333-340.

39. De Boer M, van Deurzen C, van Dijck J. et al . Micrometastases or isolated tumour cells and the outcome of breast cancer. N Engl J Med. 2009; 361:653-63.

40. Krag Dn, Anderson SJ, Julian TB, Brown AM, Harlow AM, Harlow SP, Ashikaga T. Technical outcomes of sentinel lymph node resection and conventional axillary lymph node dissection in patients with clinically node negative breast cancer : results from the NSABP-B32 randomised phase II trial. Lancet Oncol 2007;8:881-888.

41. Naik AM, Fey J, Gemignani M, Heerdt A, Montgomery L, Petrek J, Port E, Sacchini V, Sclafani L, VanZee K, Wagman R, Borgen PI, Cody HS. The risk of axillary relapse after sentinel lymph node biopsy for breast cancer is comparable with that of axillary lymph node dissection : a follow up study of 4008 procedures. Ann Surg 2004;240:462-468; discussion 462-468.

42. Bergkvist L, de Boniface J, Jonsson PE, Ingvar PC, Liljegren G, Frisell J. Axillary recurrence rate after negative sentinel node biopsy in breast cancer :three year follow up of the Swedish Multicentre Cohort Study. Ann Surg 2008;247:150-156.

43. Veronesi U, Orecchia R, Zurrida S, Galimberti V, Luini A, Veronesi P, Gatti G, D'aiuto G, Cataliotti L, Paolucci R, Piccolo P, Massaioli N, Sismondi P, Rulli A, Lo Sardo F, Recalcati A, Terribille D, Acerbi A, Rotmensz N , Maisonneuve P. Avoiding axilllary dissection in breast cancer surgery : a arndomised trial to assess the role of axillary radiotherapy . Ann Oncol2005;16:383-388.

44. van der Ploeg IM, Nieweg OE, van Rijk MC, Valdes Olmos RA, kroon BB. Axillary recurrence after a tumour negative sentinel node biopsy in breast cancer patients : A systematic review and meta-analysis of the literature . Eur J Surg Oncol 2008; 34: 1277-1284.

45. Park J, Fey JV, Naik AM, et al. A declining rate of completion axillary dissection in sentinel lymph node positive breast cancer patients is associated with the use of a multivariate nomogram . Ann Surg 2007;245:462-8.

46. Charfare H, Limongelli S, Purushotham AD. Neoadjuvant chemotherapy in breast cancer . Br J Surg 2005;92:14-23.

47. Nason KS, Anderson BO, Byrd DR, Dunnwald LK, Eary JF, Mankoff DA, et al. Increased false negative sentinel node biopsy rates after preoperative chemotherapy for invasive breast carcinoma. Cancer 2000;89:2187-94.

48. Pecha V, Kolarik D, Kozevnikova R, Hovorkova K, Hrabetova P, Halaska M, et al . Sentinel Lymph node biopsy in breast cancer patients treated with neoadjuvant chemotherapy. Cancer 2011;117:4606-16.

49. Mamounas EP, Brown A, Anderson S, Smith R, Julian T, Miller B, et al . Sentinel node biopsy after neoadjuvant chemotherapy in breast cancer : results from National Surgical Adjuvant Breast and Bowel Project Protocol B-27. J Clin Oncol 2005;23:2694-702.

50. Xing Y, Foy M, Cox DD, Kuerer HM, Hunt KK, Cormier JN. Meta-analysis of sentinel lymph node biopsy after preoperative chemotherapy in patients with breast cancer. Br J Surg 2006;93:539-46.

51. Boughey JC, Suman VJ, Mittendorf EA , Ahrendt GM, Wilke LG, Taback B, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial . JAMA 2013;310:1455-61.

52. Kuehn T, Bauerfeind I, Fehm T, Fleige B, Haussild M, Helms G , et al. Sentinel lymph node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA) : a prospective , multicentre cohort study . Lancet oncol.2013;14:609-18.

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