

Update on the Axilla in Breast Cancer

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Management of the Axilla in Breast Cancer

- The pathological status of the axillary nodes is one of the most important prognostic indicators for recurrence and survival in patients with breast cancer
- Before the 1990's when Sentinel Node biopsy was introduced, the standard of care was an Axillary Node Dissection (Level I and II) (ALND) in all women with invasive breast cancer.

Management of the Axilla in Breast Cancer

Axillary Node Dissection gives maximal axillary local control and staging information.

However, there is a significant morbidity including pain, nerve injury and lymphedema (13-77%).

With screening mammography cancers are now detected at a much earlier stage and 70% of women will not have any nodal disease.

Sentinel Node Biopsy (SLNB) has now become the accepted care for axillary staging. (Lymphedema 0-13%)

Early stage Breast Cancer



Management of the Axilla in Breast Cancer

Topics to cover

- 1) Axillary surgery in the primary treatment of breast cancer
- 2) Axillary management after neoadjuvant chemo +/- radiation
- 3) Axillary management in Recurrent Breast Cancer

Primary Surgery-Clinically Positive Axilla

1) Palpable suspicious nodes

2) Suspicious nodes seen on ultrasound

Routine MRI and PET not recommended

Fine needle aspirate suggested and if positive,
patient needs an ALND

Primary Surgery-Clinically Negative Axilla

No palpable nodes

No suspicious nodes seen on ultrasound

ASCO 2006:

SLNB sufficient unless there is an evidence of node positivity at surgery in the axilla

Recurrence in axilla in negative SLNB is 0-1.6%

ALND is 0-5%

Recurrence in Axilla after a negative SLNB

	Number of patients	Recurrence rates	Length of follow up
Marrazo Italy 2006	233	0%	33 mos
Veronisi Italy 2003	259	0%	60 mos
Pugliese NY (MSK) 2010	76	0%	6.4 yrs
Kiluk Florida 2010	1530	4 in axilla (0.26%) 54 in breast/chest 24 metastatic	63 mos

Primary Surgery-
how many nodes to remove?

SLNB- How many nodes to remove

	Number of patients	Accuracy with hottest node only	Accuracy with 2 nd or more	Accuracy if < 10% hottest
Low (NSW) 2006	113	86.9%	97%	
Lim (SF) 2008	332	81.7%	Added up to 18.3%	6.4% more
Martin MSK NY 2001	1566	80%	Hottest -ve and others positive in up to 20%	

Optimal number of nodes

Table 1. Summary of Published Literature on Number of Sentinel Lymph Nodes Removed

Lead author, year	Technique	n	Mean	Range	Accuracy (%)
Krag, 1993 ¹²	Tc-SC	22	3.4	NA	100
Veronesi, 1997 ²⁵	Tc-alb	163	1.4	1-3	98
Krag, 1998 ²⁶	Tc-SC	443	2.6	1-4	97
Offodile, 1998 ²⁴	Tc-dex	41	3.0	1-7	100
Borgstein, 1998 ²⁷	Tc-alb	130	1.5	1-3	99
Winchester, 1999 ²⁸	Tc-SC	180	3.1	NA	NA
Giuliano, 1994 ²⁹	Blue dye	174	1.8	NA	96
Giuliano, 1997 ³⁰	Blue dye	107	1.8	1-8	100
Flett, 1998 ³¹	Blue dye	68	1.2	NA	95
Barnwell, 1998 ³²	Blue dye + Tc-alb	38	1*	1-3	100
Bass, 1999	Blue dye + Tc-SC	700	2.0	NA	99
Hill, 1999 ⁸	Blue dye + Tc-SC	500	2.1	1-8	NA

Optimal number of nodes

Table 4. Number and Percentage of Patients with Metastasis to Sentinel Lymph Nodes by Site Examined

Number of SLN sites examined	Number of patients with a positive SLN	Cumulative percentage with a positive SLN
1	338	75.3
1 or 2	417	92.9
1, 2 or 3	440	98.0
1, 2, 3, or 4	445	99.1
1, 2, 3, 4, or 5	447	99.6
1-8	449	100

SLN, sentinel lymph node.

Relation between # nodes removed and Lymphedema

- Two papers from MSK NY with mean of 5 year follow up
- Overall lymphedema rate in SLNB was 5% with 3% more having perceived lymphedema
- No correlation to number of nodes removed
- Only factor in multivariate analysis to increased rate was increasing BMI
- If > 10 nodes removed, no lymphedema
- ?global disruption of node basin more important than # nodes removed

Conclusion # nodes

Aim for 97% + accuracy

If all the hot nodes are removed to up to 10% count of the hottest node and remove all blue (if using), this seems to give the best result.

In most series, ideal is somewhere between 2 and 4 nodes

10 nodes is usually too many

SLNB is going to be Positive in 30%-what to do?

- Role of Frozen Section?
- Do you re-operate on all?
- Selective re-operation-who?
- Will the treatment by oncologists change?
- Will you have good local control?

Accuracy of Frozen Section

	Touch imprint cytology	Frozen section	Rapid IHC
Memar 2010 Iran	71%	87.5%	
Franzc 2010 Hungary	69.4%	53.3%	68.5%
Liu 2010 SF		60.6%	
Lumachi 2011 Italy		73.7%	
Geetsma 2010 Netherlands		63.7%	No change Rx if ALND done
Pechlavides 2010 Greece	63%	75%	85% (takes 20 min)

Role of Frozen Section

- about 30% of SLNB will be positive for cancer
- 65% of those women may be able to go on to ALND within their primary surgery
- Time added to each case for frozen section is at least 20 min
- 80% of cases will have used 2x as much surgery time for SLNB if frozen not done
- Many of those with +ve SLNB will not need completion ALND
- Morbidity and cost savings are not obvious

SLNB positive for cancer when to do an ALND

	Number of patients	Number negative nodes	Number positive nodes	Percent more nodes positive after ALND
Staver EORTC 2010	1888	65%	34%	Macro 41% Micro 18% ITC 18%
Pugliese 2010MSK NY	171	76	95 (IHC positive only)	18%

SLNB - frozen section and ALND

Weibe (MSK NY) 2008 reviewing practice

“are ALND and frozen section becoming obsolete?”

Standard of care is ALND if node +ve on frozen and if +ve on routine histology

7648 pts reviewed between 1997-2006

Rate of frozen section decreased from 100 – 62%

ALND after +ve node decreased from 84% to 78%

Gradual reduction in ALND in SLNB +ve patients (especially in low volume disease)

Is ALND necessary in all cases after
Positive nodes are found on SLNB?

Veronisi study from 2003

- Randomized 516 women to SLNB only or SLNB followed by ALND
- 257 women had ALND after SLNB (83 - 32.3% had positive SLN)
- 259 had SLNB only (92 - 35.5% had a positive SLN)
- Less pain and morbidity in SLNB only group

Comparison of SLNB only with SLNB followed by ALND (Veronisi 2003)

Table 4. Unfavorable Events and Deaths in the Two Study Groups.

Event	Axillary-Dissection Group (N=257)	Sentinel-Node Group (N=259)
	<i>no. of events</i>	
Events other than death		
Axillary metastasis	0	0
Supraclavicular metastasis	2	0
Recurrence in ipsilateral breast	1	1
Cancer in contralateral breast	2	3
Distant metastasis	10	6
Other primary tumor	6	3
Total	21	13
Death due to breast cancer	2	1
Death from other causes	4	1

ASCOG Z0011 Trial

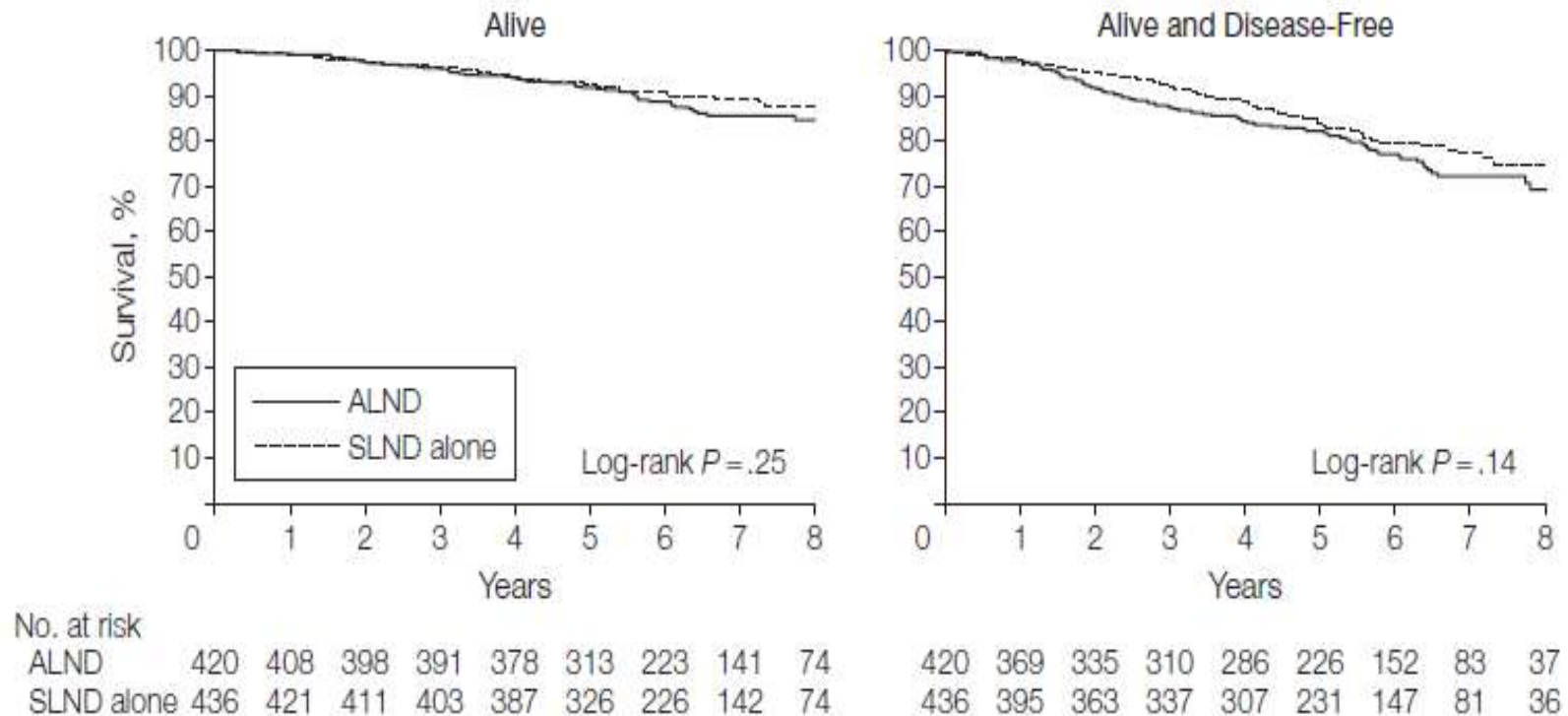
- Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastases
- Published Feb 2011
- Am College of Surgeons Oncology group at 115 sites
- 1999 to 2004
- T1 T2 tumors with 1 – 2 positive SLN
- 445 ALND 446 SLNB only
- Chemo and radiation as discretion of treating physician

ASCOG Z0011 Trial

- Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastases
- Trial closed early because mortality was less than expected
- Median survival at 5 years was 91.8% with ALND and 92.5% with SLNB alone

ALND or no ALND after SLNB positive (Giuliano 2011)

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



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

HE vs IHC

ASCOG 20010 trial

- Observational trial 3904 women
- 349 (10.5%) had micromets on immunohistochemical exam
- 5 year survival 95.7% for occult mets
- 5 year survival 95.1% for those who did not
- Disease free survival 92.2% vs 90.4%
- With adjuvant chemo 91.4% vs 91%

- Do we need to do routine IHC studies ??

Do we need IHC?

- NSABP B₃₂
- Clinically node neg. ALND vs SLNB –no survival difference
- 16% node neg were +ve on IHC (mostly micromets)
- 1.2% survival difference
- ALND made no difference in survival

- Routine IHC not recommended

SLNB only for Node Positive Disease

- Spiguel et al Dept of Surgery Chicago 2011
- Follow up up 123 pts
- 12 year experience with mean follow up 7.9 yrs
- 1 axillary recurrence, 2 in breast recurrence
- 87% survival
- Most had micromets and less than 3 nodes +ve
- Literature review 2003 -2005 with mean of 3.5 yr follow up shows axillary recurrence of 0-2.6% . 11/16 had 0% . 3 less than 1.5% and 2 over 2%.

Conclusion ALND after Positive SLNB

- In most patients it is safe to omit ALND after a positive SLNB. (ASBS official statement)

(Studies are limited to early stage disease with 1-3 nodes positive)

Not yet recommended for mastectomy patients, more than 3 nodes positive or partial breast radiation .
Radiation is given to the low axilla with breast conservation.

Sentinel Node Biopsy in DCIS

- Generally not recommended
- 1-2% will have node metastases
- However, if DCIS extensive and mastectomy done is a reasonable option as cannot do later if a small amount of invasion is found on the final pathology. Especially recommended if mastectomy is followed by immediate reconstruction.

Sentinel Node Biopsy in DCIS

Yen (Houston) 2004

398 pts with DCIS

20% had Invasive disease on final pathology

141 (35%) had SLNB at original operation

103 had core bx only and 30% had IBC on final path -
10% had positive SLN

14 women had positive SLN and 11 /14 had IBC on final path

Only predictor of +ve SLN was palpable mass

Axillary Surgery after neoadjuvant chemotherapy +/- radiation

SLNB after Neoadjuvant Chemotherapy

- Accuracy average 91% with 100% at MD Anderson
- Gives results of residual disease and guides radiotherapy
- ? Suitable for those with positive nodes diagnosed pre chemo
- ?same local control rates
- Felt by many to still be investigational

SLNB after Neoadjuvant Chemo

- Reitsame et al Salzburg 2010
- 185 pts 160 chemo 25 endocrine therapy
- All had SLNB followed by ALND
- Complete response in 15.2% with chemo and 0% with endocrine therapy
- Nodes positive in 55.2% after chemo and 59.1% after endocrine therapy
- Identification are 81.1%

Management of axilla after NAC

	# Patients	Ident rate	False neg if node + pre op	False neg if node -ve pre op
Shimazu 2004 Osaka	47	94%	15.8%	1%
Gimberques 2008 France	129	93%	29.6%	0%
Ollo-Aquire 2010 Granada Spain	88	92%	8.3% both groups together	
	All patients clinically node neg after NAC	In 69.4% sentinel node was the only	Positive node	

Conclusion SLNB after NAC

- If the axilla is clinically node negative prior to neoadjuvant chemotherapy, then it would seem that SLNB alone is very reliable
- If the axilla is node positive pre therapy, then surgically should consider ALND or SLNB plus ALND

Treatment of the Axilla

Breast cancer recurrence

SLNB in operations for Recurrent Breast Cancer

	Number of patients	Previous operation	% identification of Sentinel Node
Axelson 2008 Denmark	50	ALND in 47 of 50	51% 7 had +ve nodes 16% treatment change
Palit 2008 Belgium	287 Review 1999-2007 16 reports	37.7% ALND 62.3% SLNB	73% Aberrant in 32.4% 8/17 in contralat axilla -47.1% +ve
Maaskant-Braat 2011 Netherlands	88 36 hospitals	31 BCS +SLNB 44 BCS +ALND 13 Mast +SLNB or ALND	65.9% 33/58 after ALND 36 aberrant Treatment change in 9%

Reoperative SLNB after Previous Mastectomy

- Karam –Mem Sloan Kettering NY 2008
- 20 patients (1996-2007)
- Injection into mastectomy flap at area of recurrence
- SLNB success was 45.5% with prev ALND
 - 100% with prev SLNB
 - 80% with no previous axillary surg
 - 55.6% with prev implant recon
 - 33.3% with prev tram recon
- Conclusion was that it was possible and may add prognostic information

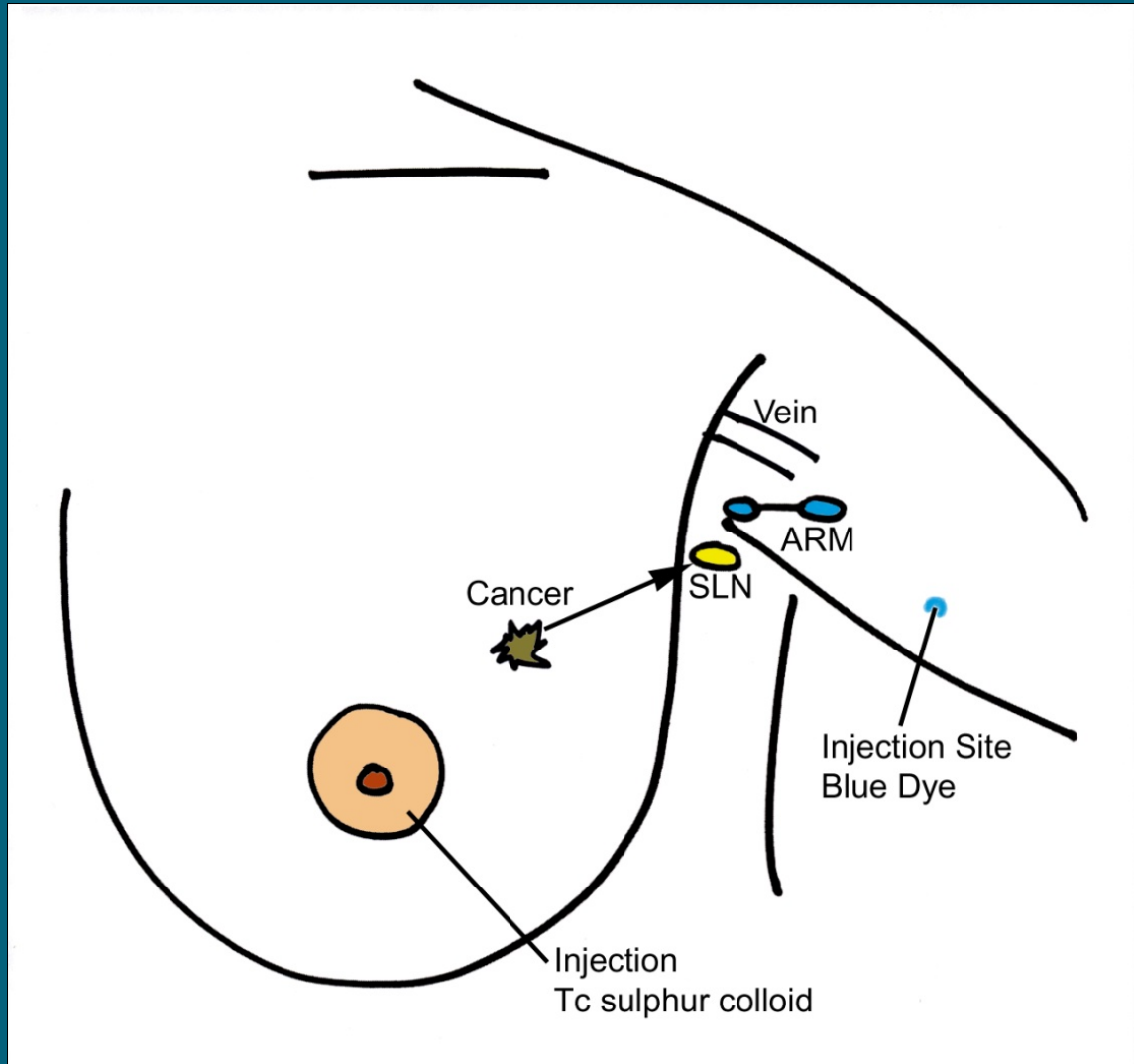
SLNB after prev axillary surgery

- How reliable is the information:
 - has the tumor always drained there
 - is a negative node reliably predictor of disease free
 - should non axillary nodes be pursued as many now have drainage to internal mammary or contralateral nodes.

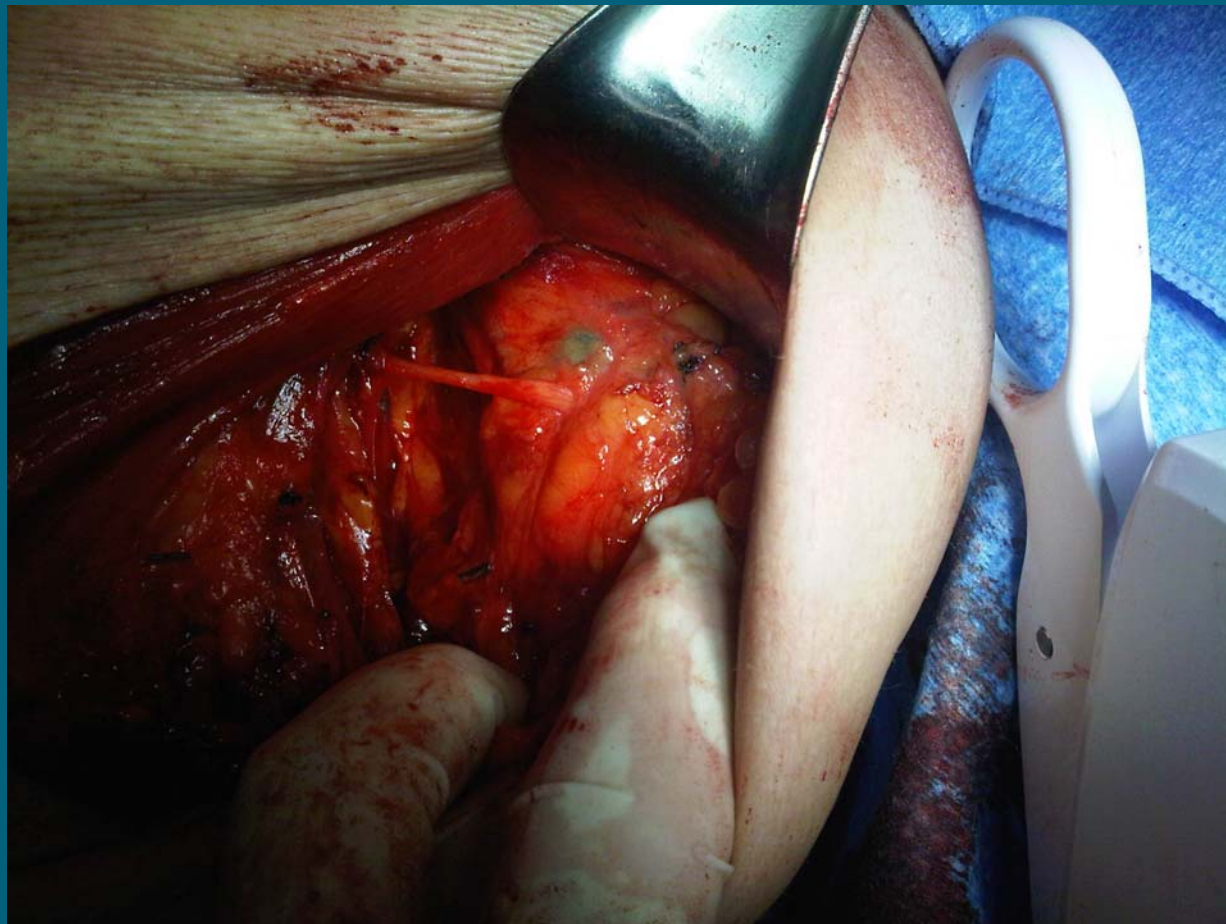
Axillary Reverse Mapping

- Research to try and reduce the risk of lymphedema by
- “separating” lymphatic drainage from the arm and the breast

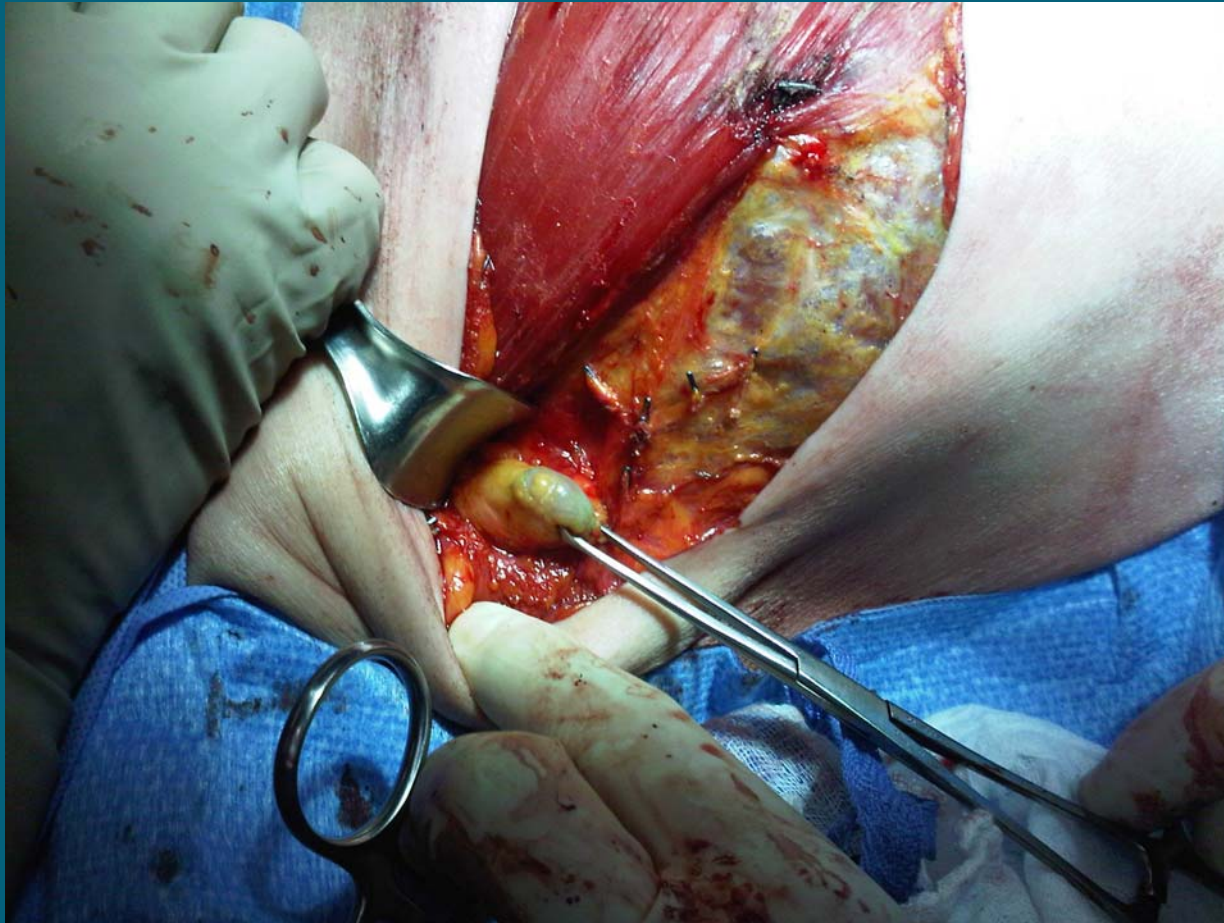
Diagram of Procedure



Blue Node after SN taken



Cross over-SLNB



Lymphedema

ARM results published Mar 2011 from UMAS, Little Rock, AR with median follow up 12 months showed 3.5% lymphedema in SLNB and 7% in ALND measured by volume change

Conclusions ARM

Technique is safe and easy to do

Arm and Axillary lymph nodes can be separately identified most of the time

There is cross over identified which may potentially identify those women at risk for lymphedema

Overall Conclusions

- SLNB is the preferred treatment of the axilla in most patients:
 - clinically and radiographically node negative disease
 - this can also apply to patients after neoadjuvant treatment
- ALND is the preferred treatment:
 - if nodes are known positive either in primary treatment or after neoadjuvant treatment

Conclusions

- The role of ALND after a positive SLNB is still an appropriate treatment depending on the patient characteristics, number of nodes positive ,etc
- However, most women can omit this treatment (especially if less than 2 nodes are positive)
- ALND may be regarded as a means of local control rather than staging

Conclusions

- The role of SLNB after previous surgery is uncertain
- Technically this can be done in over 50% of patients but the outcome is unclear for any improvement in patient care