Sentinel Lymph Node Biopsy for Breast Cancer

Registrar Tutorial

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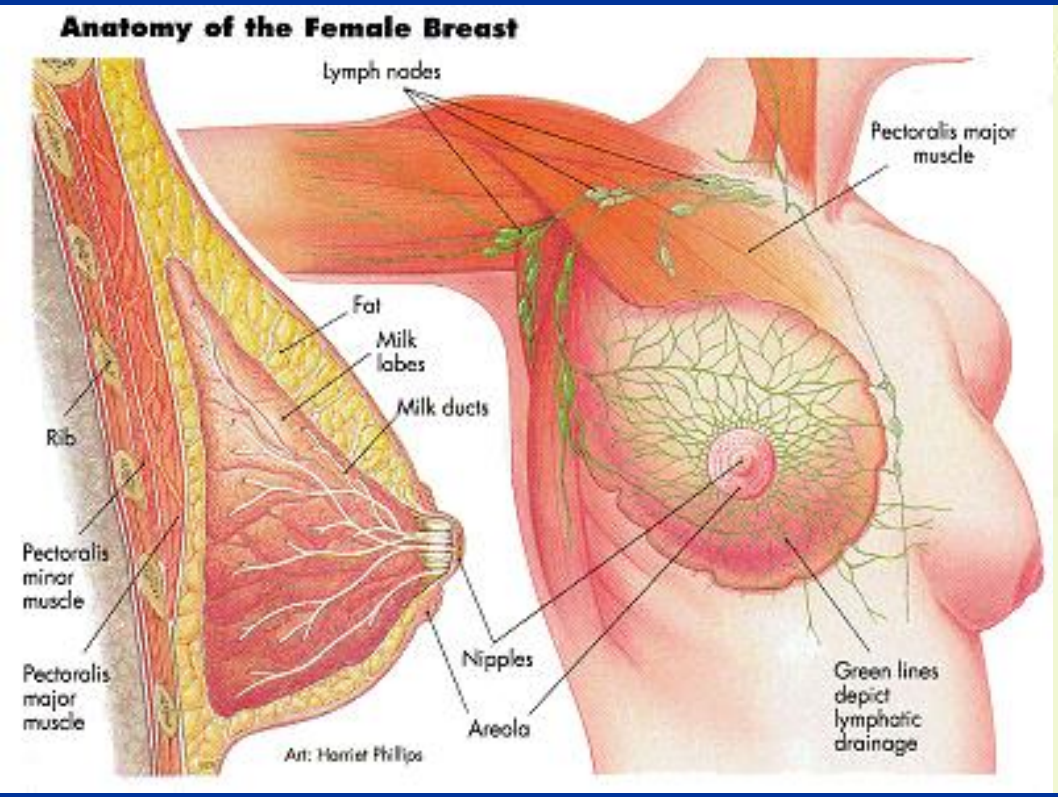
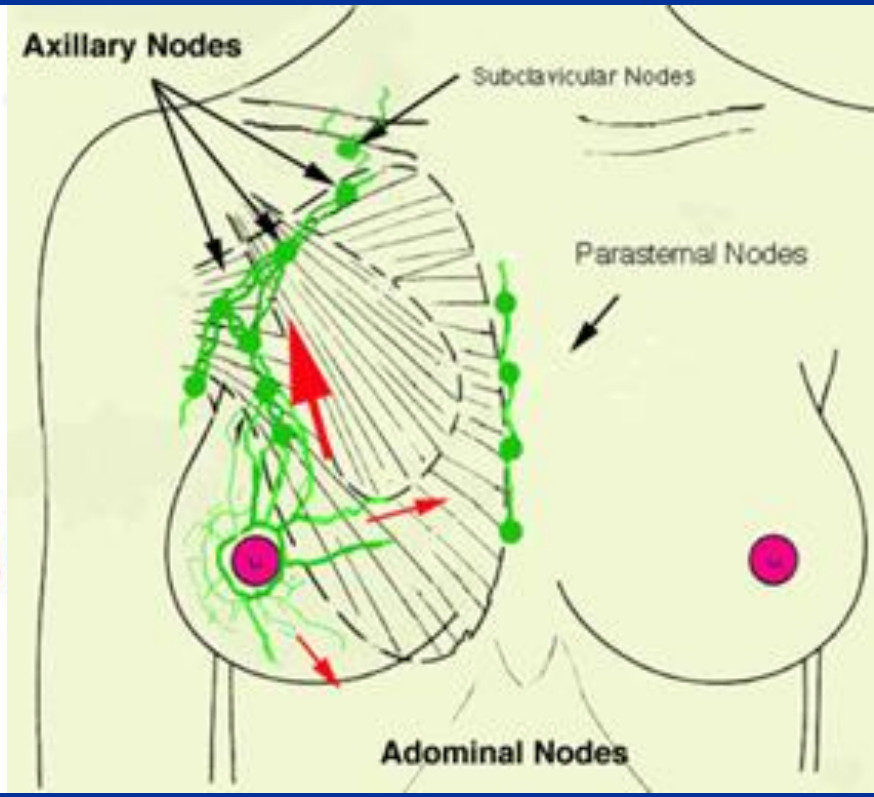
Sentinel Lymph Node Biopsy

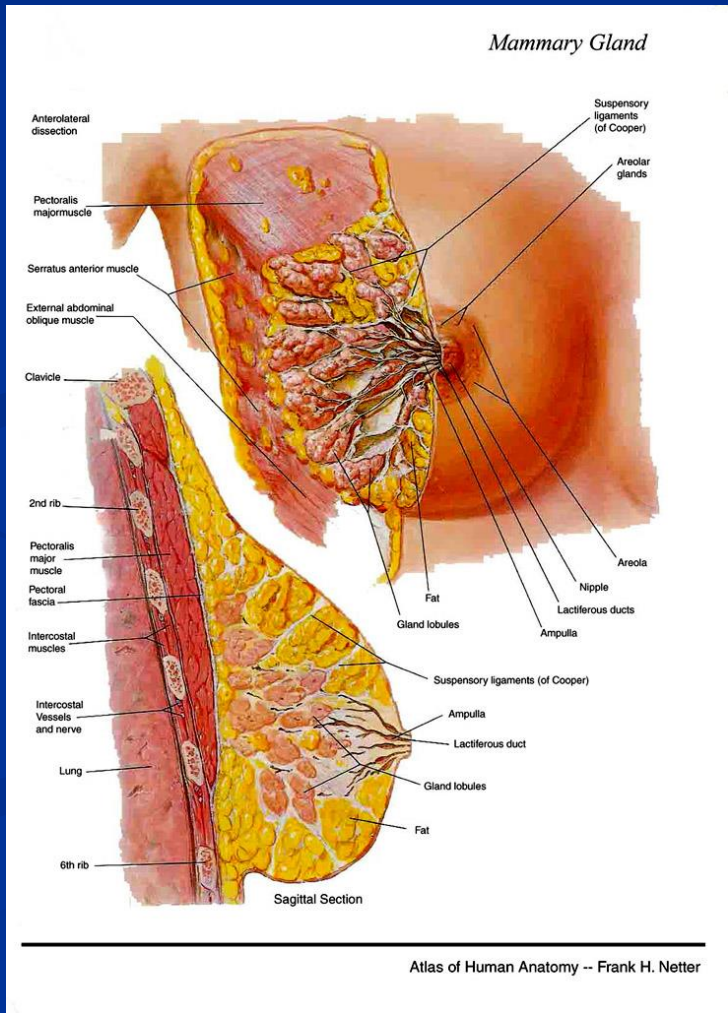
- Axillary LN status important prognostic factor
- Axilla receives 85% of lymphatic drainage from breast





Sentinel Lymph Node Biopsy

- Likelihood of axillary nodal involvement related to:
  - Tumour size
  - Tumour location
  - Histologic grade
  - Presence of lymphatic invasion



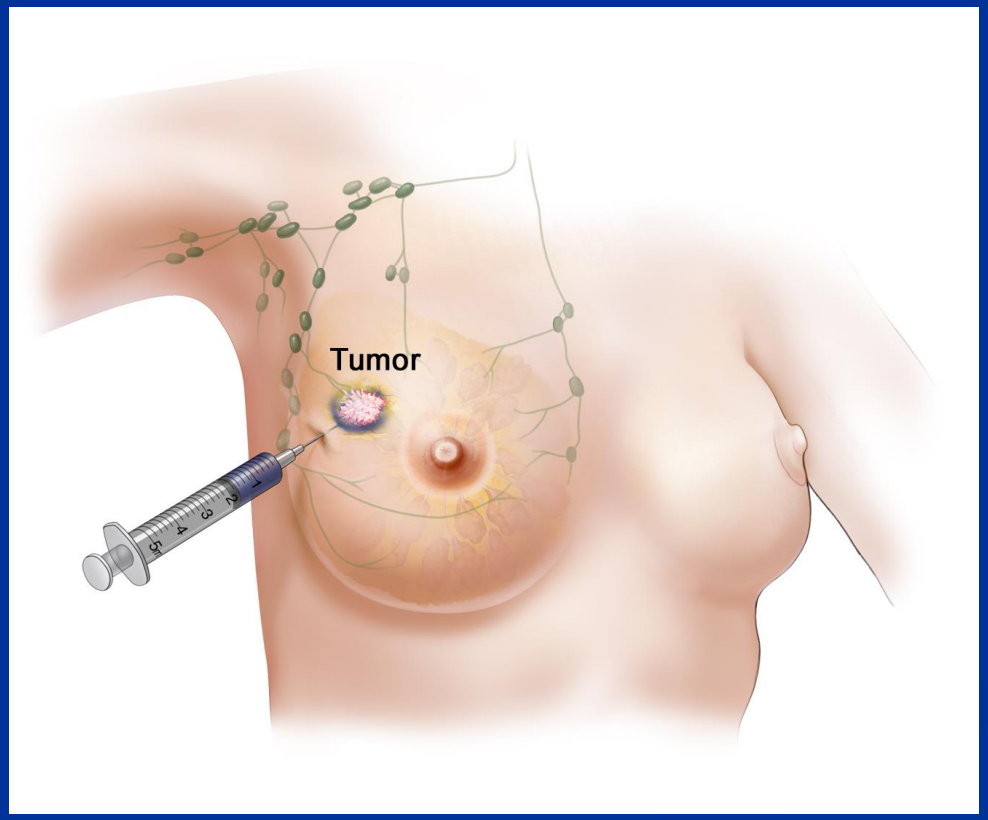
Sentinel Lymph Node Biopsy

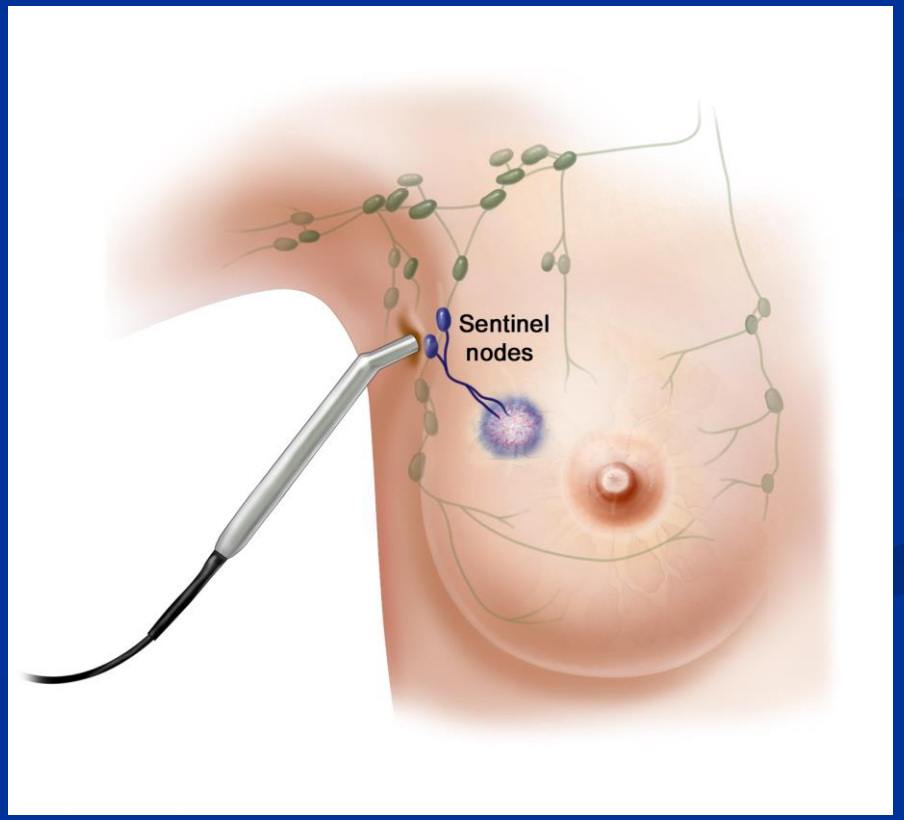
- ALND remains standard for positive nodes

- ALND associated with significant morbidity:
  - Seroma
  - Sensory loss
  - Lymphoedema
  - Impaired shoulder function

Sentinel Lymph Node Biopsy

- Tumour cells migrate to one or few LNs before others
- Sentinel lymph node biopsy (SLNB)





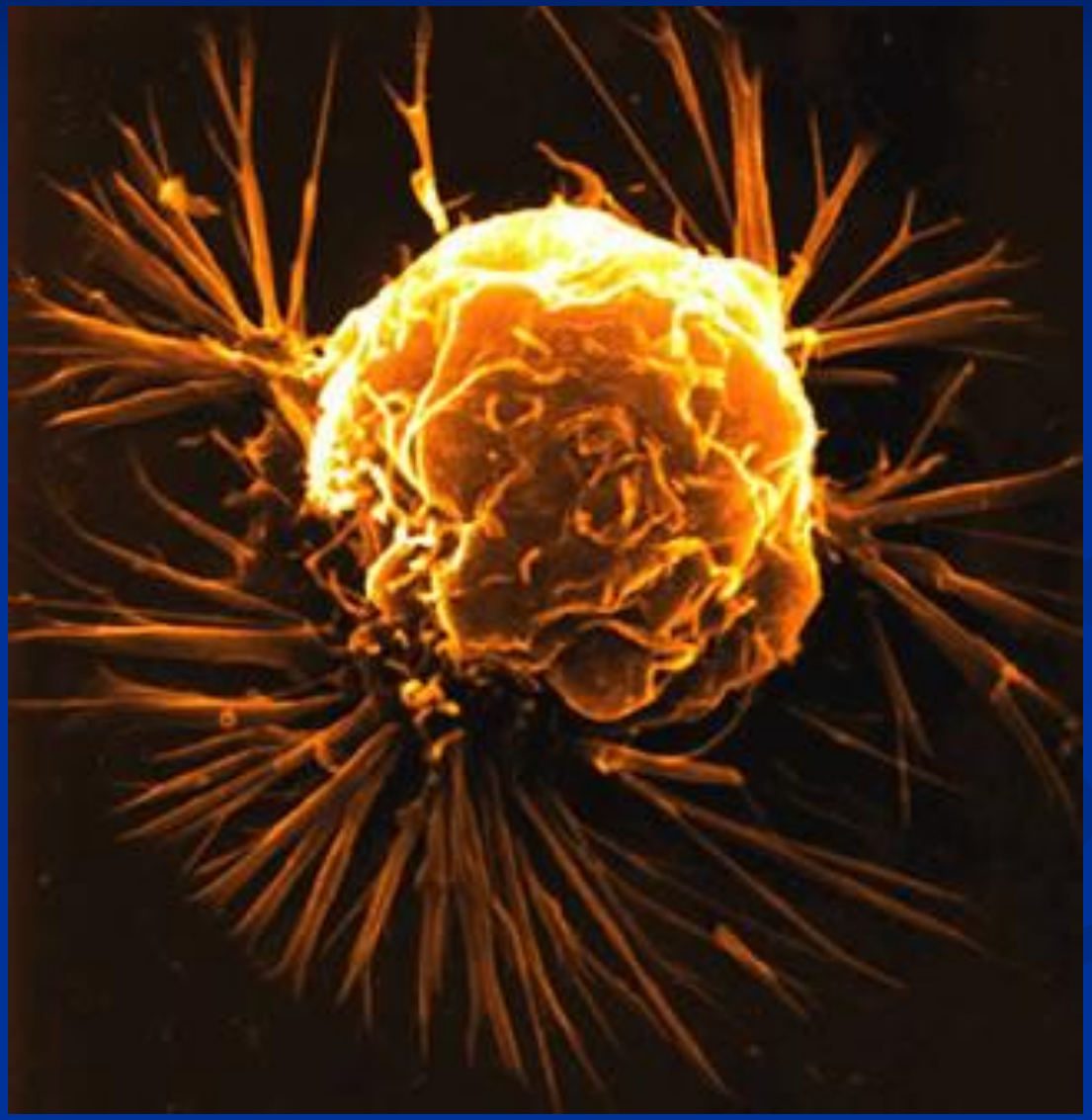
Sentinel Lymph Node Biopsy

- SLN identified in ~96%
- Predicts status of remaining axillary LNs in ≥95%
- False negative rate 5 – 10%
- Axillary recurrence low after –ve SLNB (0 – 4.5%)
- Lower false –ve rate with radiocolloid + blue dye

Sentinel Lymph Node Biopsy

- No difference cf. ALND:
  - Regional control
  - Overall survival
  - Disease-free survival
- Clinically node negative invasive breast cancer
- Omit if ≥70 yrs + small (<2 cm) + ER positive
- ~40% with +ve SLN have residual disease in axilla

Isolated Tumour Cells



Isolated Tumour Cells

- Small clusters of cells not greater than 0.2 mm
- Designated as pN0(i+)
- Not indication for axillary surgery, RT or systemic Rx

Micrometastases

- >0.2 mm & ≤2.0 mm (pN1mi)
- Most studies show no reduction in survival
- Debate about prognostic value of size of micromets
- ASCO & NCCN recommend completion ALND
- Completion ALND controversial

Macrometastases

- >2 mm
- Routine completion ALND
- Indications for ALND if <3 +ve SLNs controversial

IHC & PCR

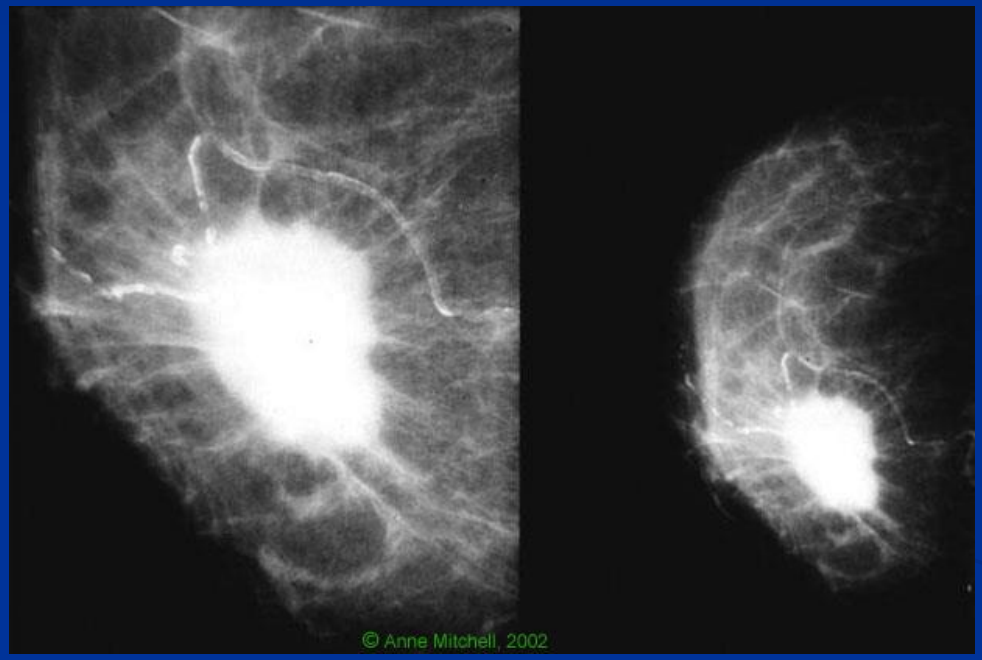
- 'Occult' micrometastases = mets not seen with H&E
- Detected by IHC or PCR

- ACOSOG Z0010 trial
- IHC-detected mets no impact on overall survival

- Routine IHC or PCR not recommended

Locally Advanced Breast Ca

- SLNB accurate in T3 tumours



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- Wong, SL, Chao, C, Edwards, MJ, et al. Accuracy of sentinel lymph node biopsy for patients with T2 and T3 breast cancers. Am Surg 2001; 67:522.

Locally Advanced Breast Ca

- SLNB contraindicated if T4 or inflammatory breast Ca

- False negative rate high with inflammatory breast Ca

- Hidar, S, Bibi, M, Gharbi, O, et al. Sentinel lymph node biopsy after neoadjuvant chemotherapy in inflammatory breast cancer. Int J Surg 2009; 7:272.
- Singletary, SE. Surgical management of inflammatory breast cancer. Semin Oncol 2008; 35:72.
- Lyman, GH, Giuliano, AE, Somerfield, MR, et al. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol 2005; 23:7703.
- Kaufmann, M, Morrow, M, von Minckwitz, G, et al. Locoregional treatment of primary breast cancer: consensus recommendations from an International Expert Panel. Cancer 2010; 116:1184

Neoadjuvant Chemotherapy

- Optimal timing of SLNB debated
- Efficacy of SLNB after chemo similar to no chemo
- Consider SLNB if good tumour response

Multicentric Disease

- Studies show all areas of breast drain into same LNs
- SLNB successful in 91%
- SLNB false negative rate 4%
- ASCO recommends SLNB as appropriate

- Klimberg, VS, Rubio, IT, Henry R, et al. Subareolar versus peritumoral injection for location of the sentinel lymph node. Ann Surg 1999; 229:860.
- Borgstein, PJ, Meijer, S, Pijpers, RJ, van Diest, PJ. Functional lymphatic anatomy for sentinel node biopsy in breast cancer: echoes from the past and the periareolar blue method. Ann Surg 2000; 232:81.
- McMasters, KM, Wong, SL, et al. Dermal injection of radioactive colloid is superior to peritumoral injection for breast cancer sentinel lymph node biopsy: results of a multiinstitutional study. Ann Surg 2001; 233:676.
- Schrenk, P, Wayand, W. Sentinel-node biopsy in axillary lymph-node staging for patients with multicentric breast cancer. Lancet 2001; 357:122.
- Kern, KA. Concordance and validation study of sentinel lymph node biopsy for breast cancer using subareolar injection of blue dye and technetium 99m sulfur colloid. J Am Coll Surg 2002; 195:467.
- Knauer, M, Konstantiniuk P, Haid, A, et al. Multicentric breast cancer: a new indication for sentinel node biopsy – a multi-institutional validation study. J Clin Oncol 2006; 24:3374.

Prior Breast Surgery

- Feasibility of SLNB after breast surgery unclear
- No recommendations due to insufficient data
- Preoperative lymphoscintigraphy essential

- Lyman, GH, Giuliano, AE, Somerfield, MR, et al. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol 2005; 23:7703.

Prior Axillary Surgery

- SLN not identified in 25%
- ASCO recommends against SLNB
- Reports of successful 2nd SLNB after local recurrence
- Preoperative lymphoscintigraphy essential

- Port, ER, Fey, J, Gemignani, ML, et al. Reoperative sentinel lymph node biopsy: a new option for patients with primary or locally recurrent breast carcinoma. J Am Coll Surg 2002; 195:167.
- Lyman, GH, Giuliano, AE, Somerfield, MR, et al. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol 2005; 23:7703.
- Intra, M, Trifiro, G, Viale, G, et al. Second biopsy of axillary sentinel lymph node for reappearing breast cancer after previous sentinel lymph node biopsy. Ann Surg Oncol 2005; 12:895.
- Taback, B, Nguyen, P, Hansen, N, et al. Sentinel lymph node biopsy for local recurrence of breast cancer after breast-conserving therapy. Ann Surg Oncol 2006; 13:1099.
- Newman, EA, Cimmino, VM, Sabel, MS, et al. Lymphatic mapping and sentinel lymph node biopsy for patients with local recurrence after breast-conservation therapy. Ann Surg Oncol 2006; 13:52.

Internal Mammary Nodes

- Clinical relevance controversial
- Difficult to sample
- Usually included in radiation field if +ve axillary LNs
- Diagnosis of +ve IM LNs may influence adjuvant Rx

Milan Trial

- Milan, Italy
- Veronesi, et. al.
- New England Journal of Medicine, 2003
- 516 patients
- Single-centre randomised controlled trial

Milan Trial

- SLNB vs ALND
- Tumour ≤2 cm
- SLN +ve in 32.3% (ALND) & 35.5% (SLNB)

- SLNB vs ALND
  - Overall accuracy 96.9%
  - Sensitivity 91.2%
  - Specificity 100%
  - False –ve rate 8.8%
  - Less pain & better arm mobility

Milan Trial

- Median follow-up 46 months
- No difference in recurrence or overall survival
- No axillary recurrence

ALMANAC Trial

- United Kingdom
- Mansel, et. al.
- Journal of the National Cancer Institute, 2006
- 1031 patients
- Multicentre randomised controlled trial

ALMANAC Trial

- SLNB vs ALND
- 25% in ALND group underwent 4 node sampling
- Outcomes at 12 months

ALMANAC Trial

- SLNB vs ALND
  - Lymphoedema 5% vs 13% ($p<0.001$)
  - Sensory loss 11% vs 31% ($p<0.001$)
  - Drain usage lower ($p<0.001$)
  - Length of hospital stay shorter ($p<0.001$)
  - Return to normal activity shorter ($p<0.001$)
  - Quality of life better ($p=0.001$)
  - Arm functioning better ($p<0.001$)
  - No increase in anxiety levels

- Same local recurrence rate & overall survival

NSABP B-32

- USA & Canada
- Krag, et. al.
- The Lancet Oncology, 2007
- 5611 patients
- Multicentre randomised controlled trial

NSABP B-32

- SLNB vs ALND
- SLN successfully removed in 97.2%
- 1.4% of SLNs outside axillary levels I & II
- Accuracy of SLNB 97.1%
- False –ve rate 9.8%

NSABP B-32

- The Lancet Oncology, 2010
- Mean follow-up at 95.6 months
- No significant difference in:
  - Overall survival
  - Disease-free survival
  - Regional control

NSABP B-32

- New England Journal of Medicine, 2011
- 3887 patients with –ve SLNs on H&E
- 'Occult' metastases detected by IHC
- Occult metastases detected in 15.9%

NSABP B-32

- Significant difference between occult vs no mets in:
  - Overall survival (p=0.03)
  - Disease-free survival (p=0.02)
  - Distant disease-free survival (p=0.04)
- Magnitude of difference at 5 yrs small (1.2%)
- 5 yr survival 94.6% vs 95.8%
- No clinical benefit of IHC analysis

SNAC 1

- Australia
- Gill, et al.
- Annals of Surgical Oncology, 2008
- 1088 patients
- Multicentre randomised controlled trial

SNAC 1

- SLNB vs ALND
- Tumour ≤3 cm, unifocal
- Outcomes at 12 months

SNAC 1

- SLNB vs ALND
  - Increase in arm volume 2.8% vs 4.2% ($p=0.002$)
  - Less arm swelling ($p<0.001$)
  - Less symptoms ($p<0.001$)
  - Less dysfunctions ($p=0.02$)
  - No difference in disabilities ($p=0.5$)

- SLN found in 95% (SLNB) & 93% (ALND)
- SLN +ve in 29% (SLNB) & 25% (ALND)
- SLNB false –ve rate 5.5%

SNAC 2

- Multicentre randomised controlled trial
- SLNB vs ALND
- Invasive breast cancer, unifocal or multifocal, any size
- Outcomes:
  - Loco-regional recurrence
  - Distant disease-free survival
  - Overall survival

ACOSOG Z0010

- USA
- Prospective, multicentre observational study
- 5539 patients
- Significance of SLN & bone marrow (BM) mets

ACOSOG Z0010

- Women with T1/T2 N0 M0 breast cancer
- BM & histologically –ve SLN evaluated with IHC
- IHC detected additional 10.5% with SLN mets
- BM mets identified by IHC in 3.0%

ACOSOG Z0010

- BM IHC +ve predicted ↓ overall survival (p=0.015)
- SLN IHC +ve no impact on overall survival (p=0.53)
- Examination of SLN by IHC not supported

ACOSOG Z0011

- USA
- Giuliano, et. al.
- Journal of American Medical Association, 2011
- 891 patients
- Multicentre randomised controlled trial

ACOSOG Z0011

- SLNB vs ALND
- Inclusion criteria:
  - T1/T2 breast cancer
  - Lumpectomy & irradiation
  - No palpable lymphadenopathy
  - 1 or 2 SLNs containing mets
- Randomised to ALND or no further axillary Rx

ACOSOG Z0011

- Median follow-up 6.3 years
- 27.3% additional mets removed by ALND
- SLNB vs ALND
  - 5-year overall survival 92.5% vs 91.8% (p=0.97)
  - 5-year disease-free survival 83.9% vs 82.2% (p=0.52)
- SLNB equivalent survival to ALND if limited mets