National Cancer Institute

Preoperative Therapy in Invasive Breast Cancer

Reviewing the State of the Science and Exploring New Research Directions

Special Issues in Locally Advanced Breast Cancer – Surgical Perspective

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Disclosures

- None

LABC – Definition by Stage Grouping – AJCC 6th Ed.

Stage Grouping

		Stage	T	N	M
☐	☐	0	Tis	N0	M0
☐	☐	I	T1[7]	N0	M0
☐	☐	IIA	T0	N1	M0
			T1[7]	N1	M0
			T2	N0	M0
☐	☐	IIB	T2	N1	M0
			T3	N0	M0
☐	☐	IIIA	T0	N2	M0
			T1[7]	N2	M0
			T2	N2	M0
			T3	N1	M0
			T3	N2	M0
☐	☐	IIIB	T4	N0	M0
			T4	N1	M0
			T4	N2	M0
☐	☐	IIIC	Any T	N3	M0
☐	☐	IV	Any T	Any N	M1

LABC: Clinical T Stage – AJCC 6th Ed

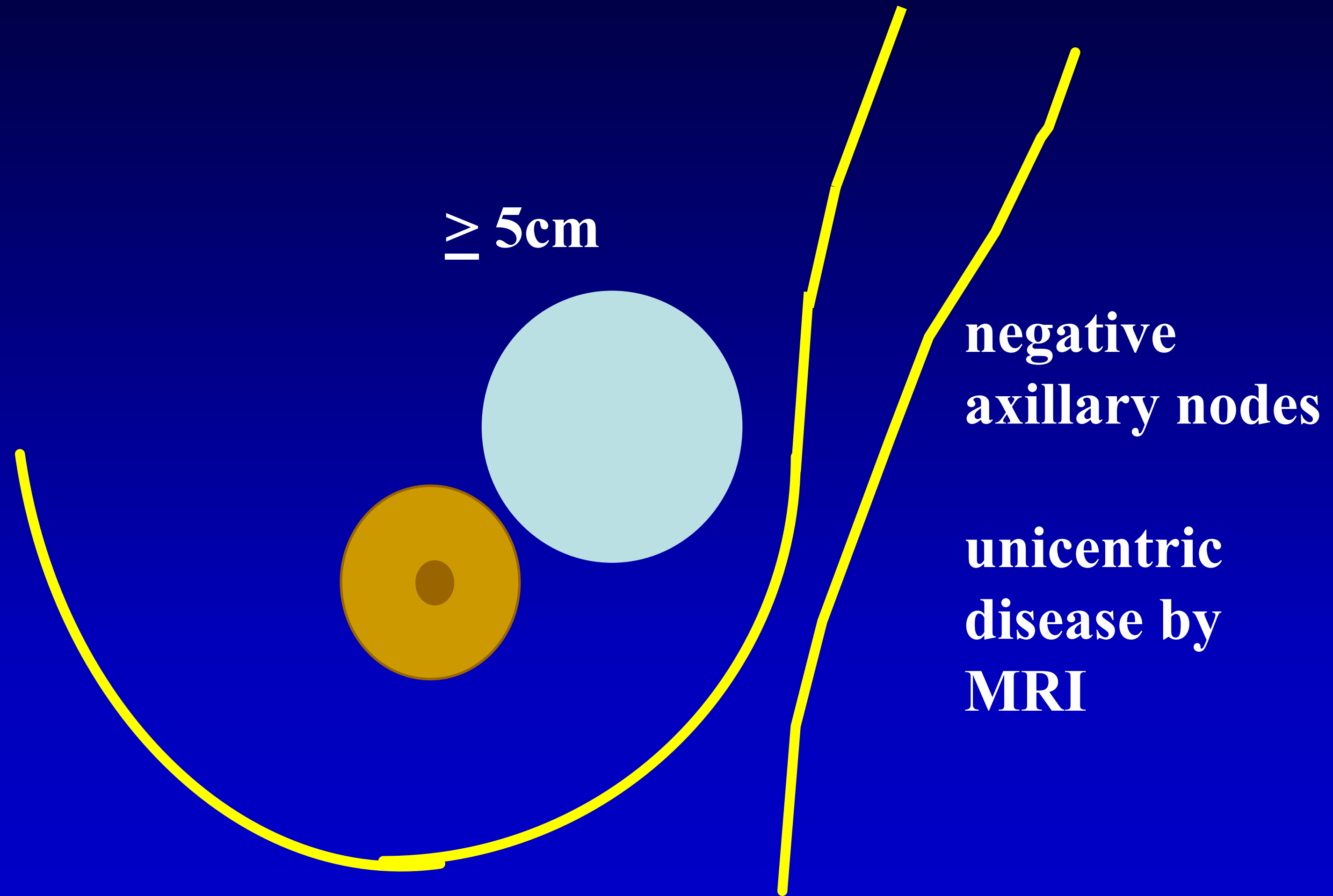
☐	☐	T3	Tumor more than 5 cm in greatest dimension
☐	☐	T4	Tumor of any size with direct extension to (a) chest wall or (b) skin, only as described below.
☐	☐	T4a	Extension to chest wall, not including pectoralis muscle
☐	☐	T4b	Edema (including peau d'orange) or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast
☐	☐	T4c	Both T4a and T4b
☐	☐	T4d	Inflammatory carcinoma

yTNM – AJCC 6th Ed

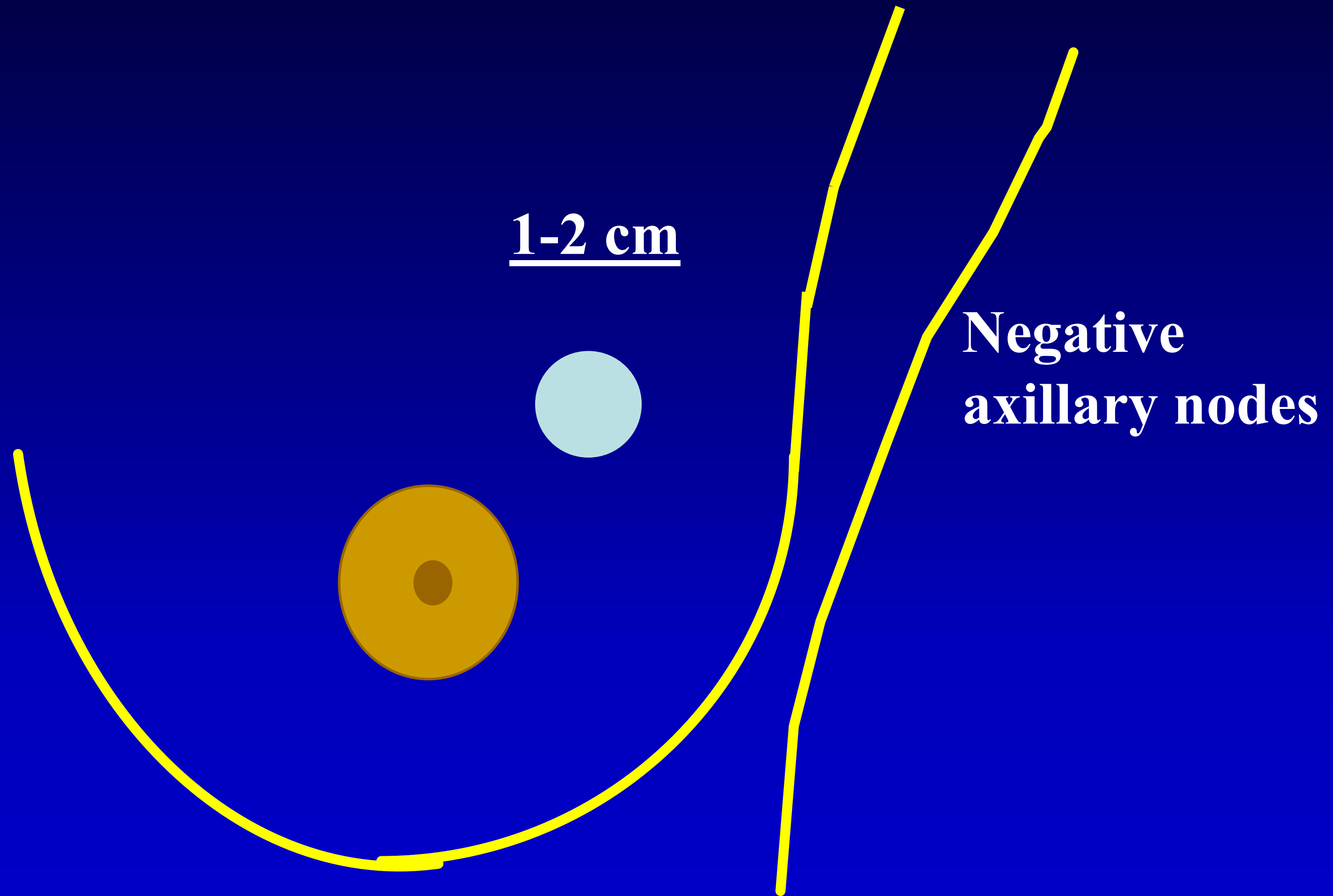
- "y" designates the stage of the residual tumor after neoadjuvant therapy
- Includes both the primary tumor and regional lymph nodes
- AJCC 7th Ed breast task force (Dr. Daniel Hayes) has subcommittee focused on neoadjuvant therapy (Dr. Monica Morrow)

Surgical Issues by T Stage

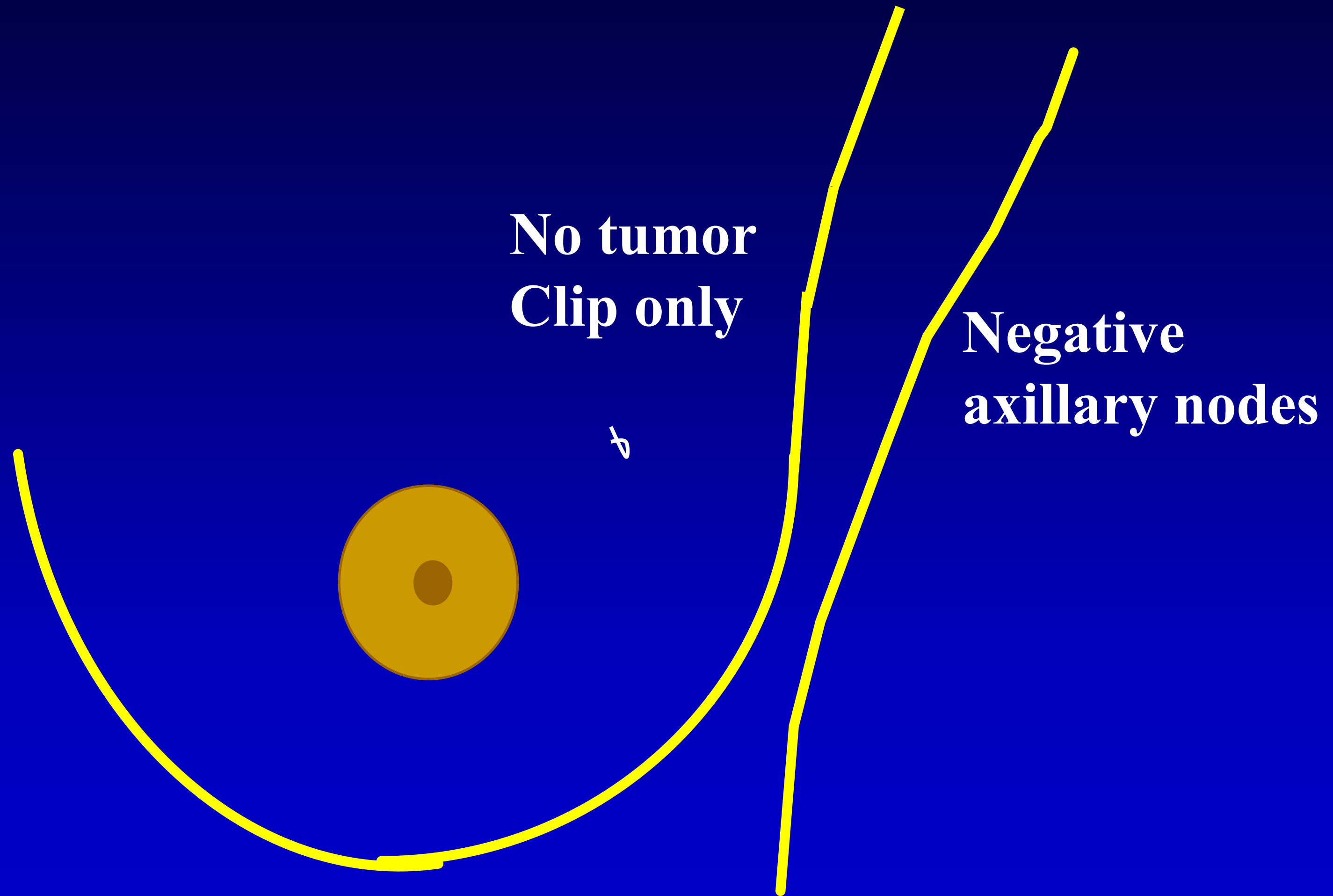
Clinical Stage T3N0 - Operable



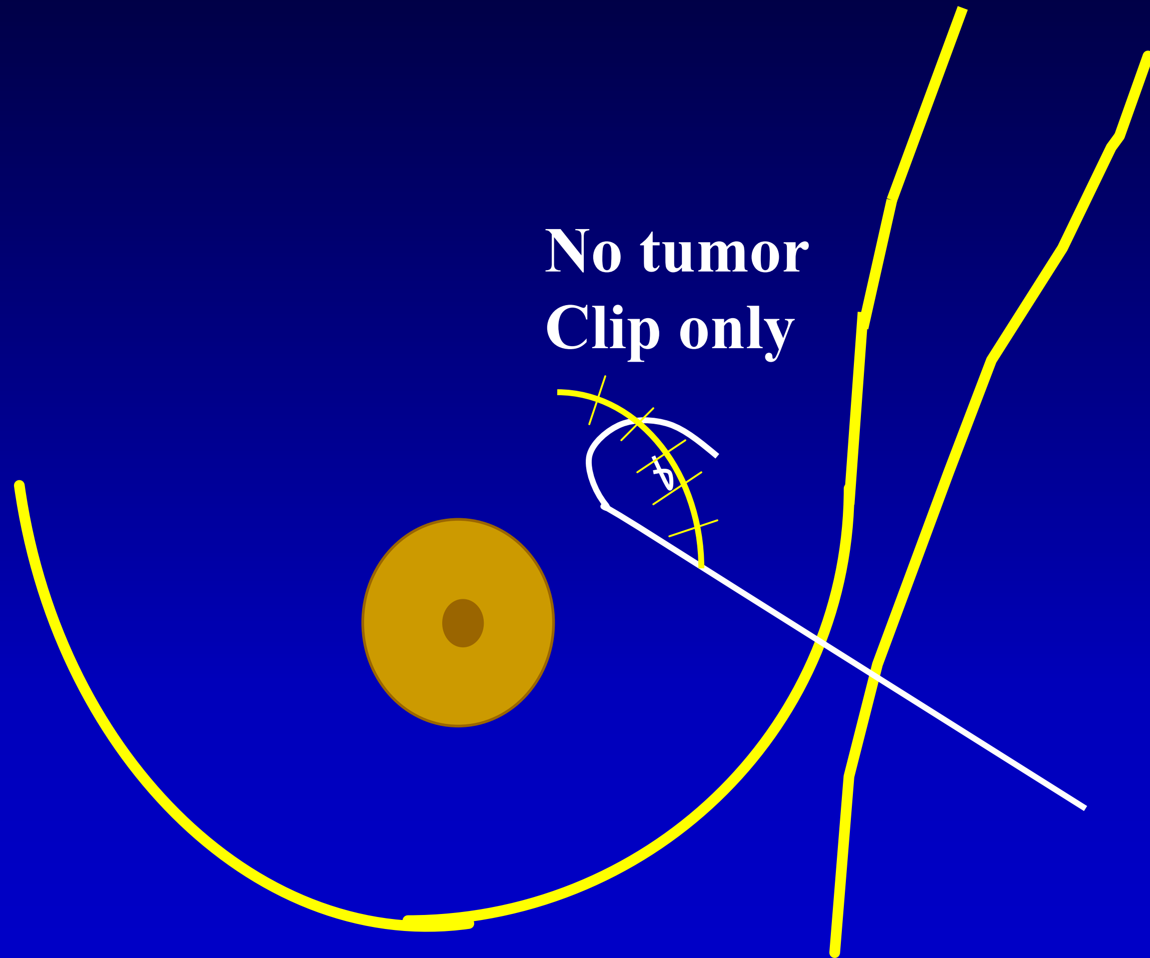
Clinical Stage T3N0 – Clinical Partial Response (cPR)



Clinical Stage T3N0 – Clinical Complete Response (cCR)

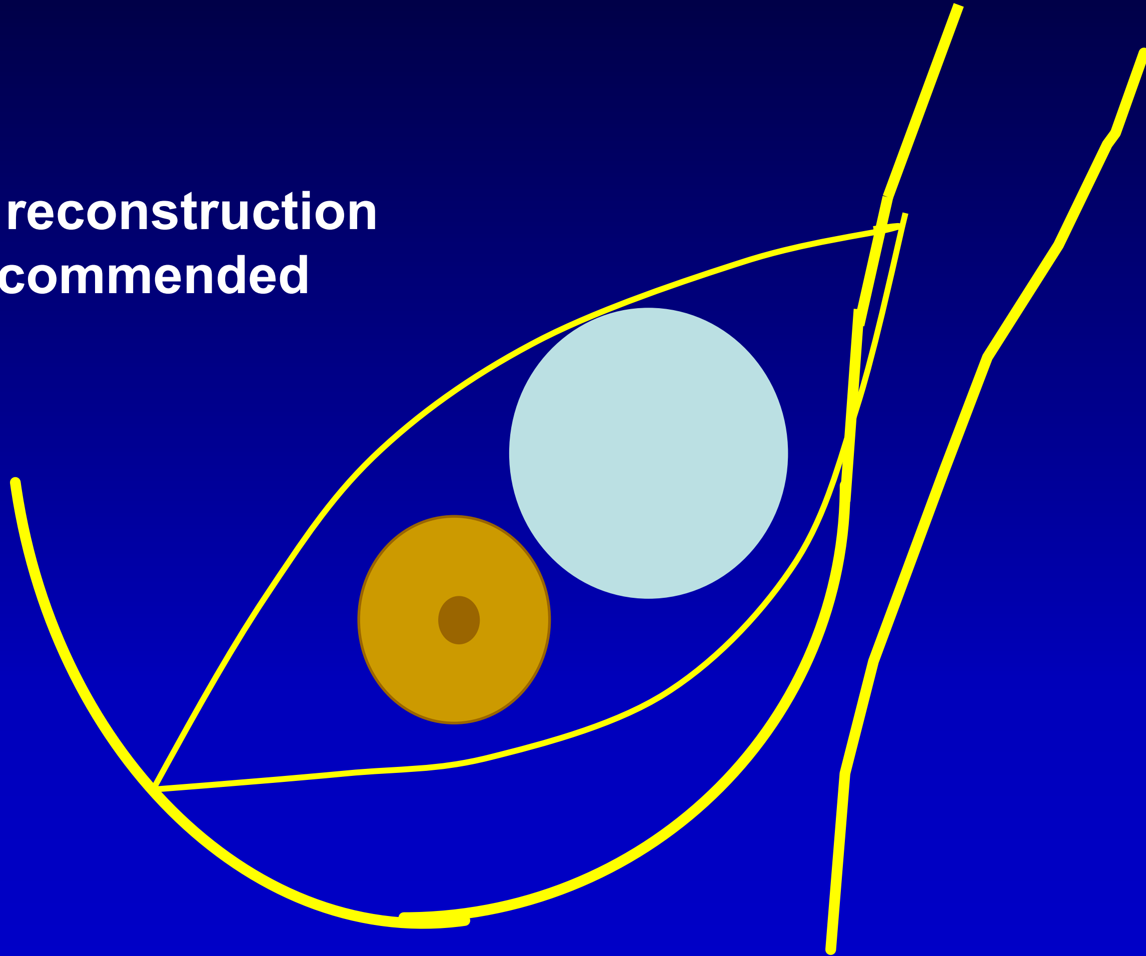


Breast Conservation: Wire-Localized Partial Mastectomy



Mastectomy for Residual Large Primary

No immediate reconstruction since RT recommended



Clinical Stage T4 – non-inflammatory – skin or chest wall

- Mastectomy with wide skin margins 1-2 cm
- BCT feasible and safe in selected patients with cPR or cCR to chemotherapy

BCT for T4, non-inflammatory Tumors – M.D. Anderson

33 patients (IIIB = 23, IIIC = 10), mean age=52, all with skin involvement

	Pre-treatment	post-treatment	
Median size	7 cm	2 cm	
		Path tumor size:	
		pCR	8(24%)
		resid >1cm	21(64%)
		resid ≤1cm	4(12%)
		Skin involvement:	
		yes	4(12%)
		no	29(88%)
Clinical node status		Path node status	
N0	5(15%)	ypN0	15(55%)

-Shen, et al. Ann Surg Onc 11(9):854-860, 2004

BCT for T4, non-inflammatory Tumors – M.D. Anderson-Results

- 29 pts (88%) skin changes resolved (pt selection)
- Median f/u = 91 mos.
  - O.S. = 78%
  - DFS = 70%
- Ipsilateral breast local recurrence = 6%
- Conclusion – mastectomy not mandatory in all patients with T4 skin involvement

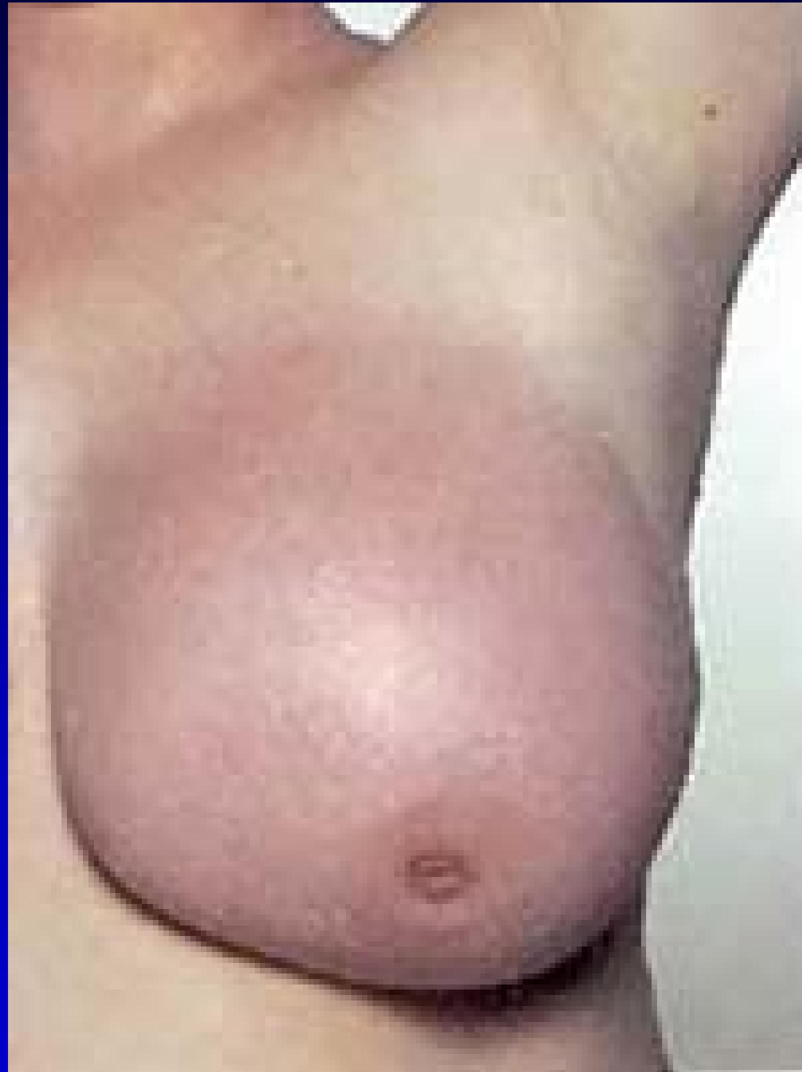
-Shen, et al. Ann Surg Onc 11(9):854-860, 2004

IBC – Working Clinical Definition

Acute and rapid onset of breast symptoms including skin erythema, edema (peau d’orange), erysipeloid border, warmth and tenderness, and breast enlargement, involving at least 1/3 or more of the breast.

Breast mass often not palpable. Dermal lymphatic metastases may or may not be identified

Inflammatory Breast Carcinoma

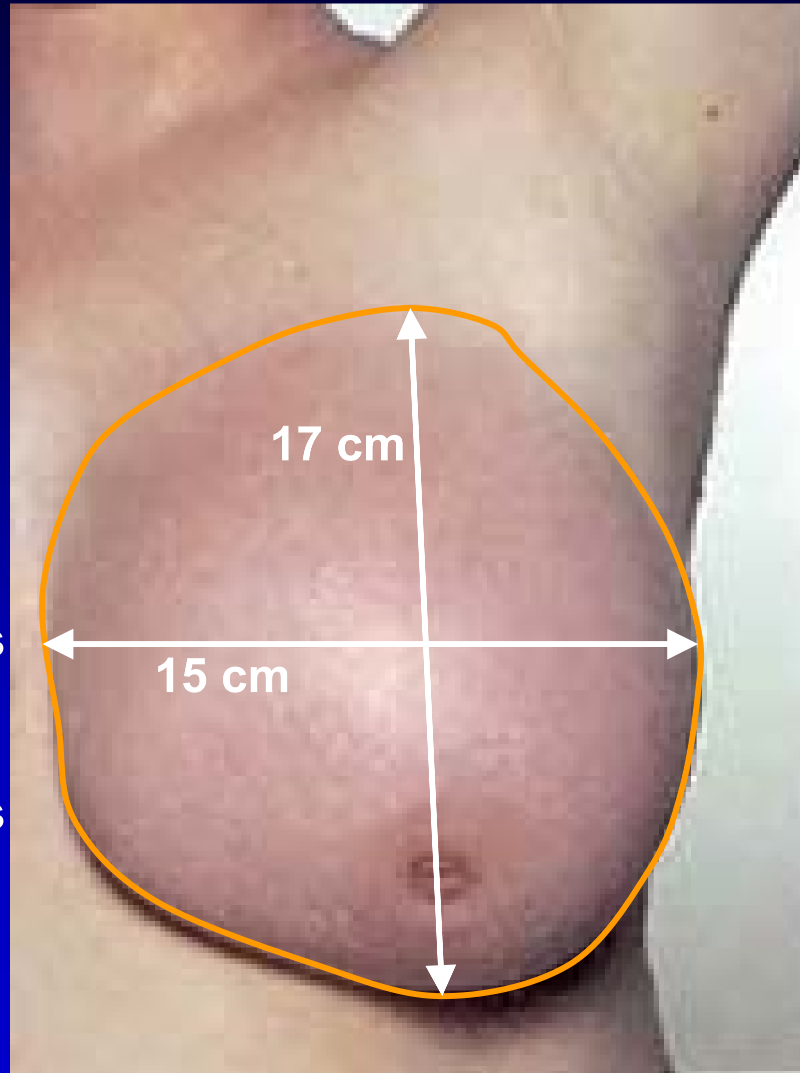


Pre-Treatment Documentation of Skin Involvement

Special notes:

?dimensions
?cross midline
?beyond the confines of the breast
?satellite lesions – erythematous patches or nodules

Consider digital photos and/or drawings, border tatoos



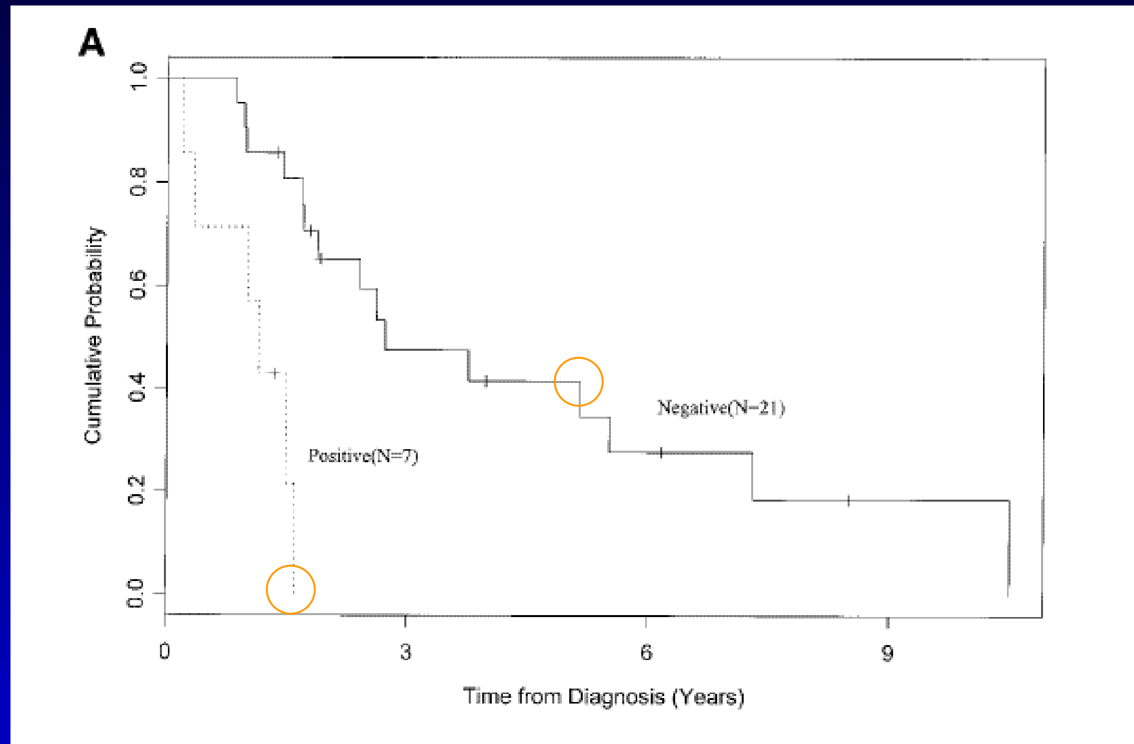
IBC – Breast Surgery after Preoperative Chemotherapy

- Mastectomy:
  - primary closure based on initial extent and skin findings after chemotherapy
    - Skin punch biopsies of discordant findings may be helpful
  - Goal is negative skin and peripheral margins
    - Frozen section of skin margins not helpful
  - May require skin pedicle reconstruction
    - Counsel patient toward chest wall reconstruction and not breast reconstruction
- Breast Conservation is not indicated

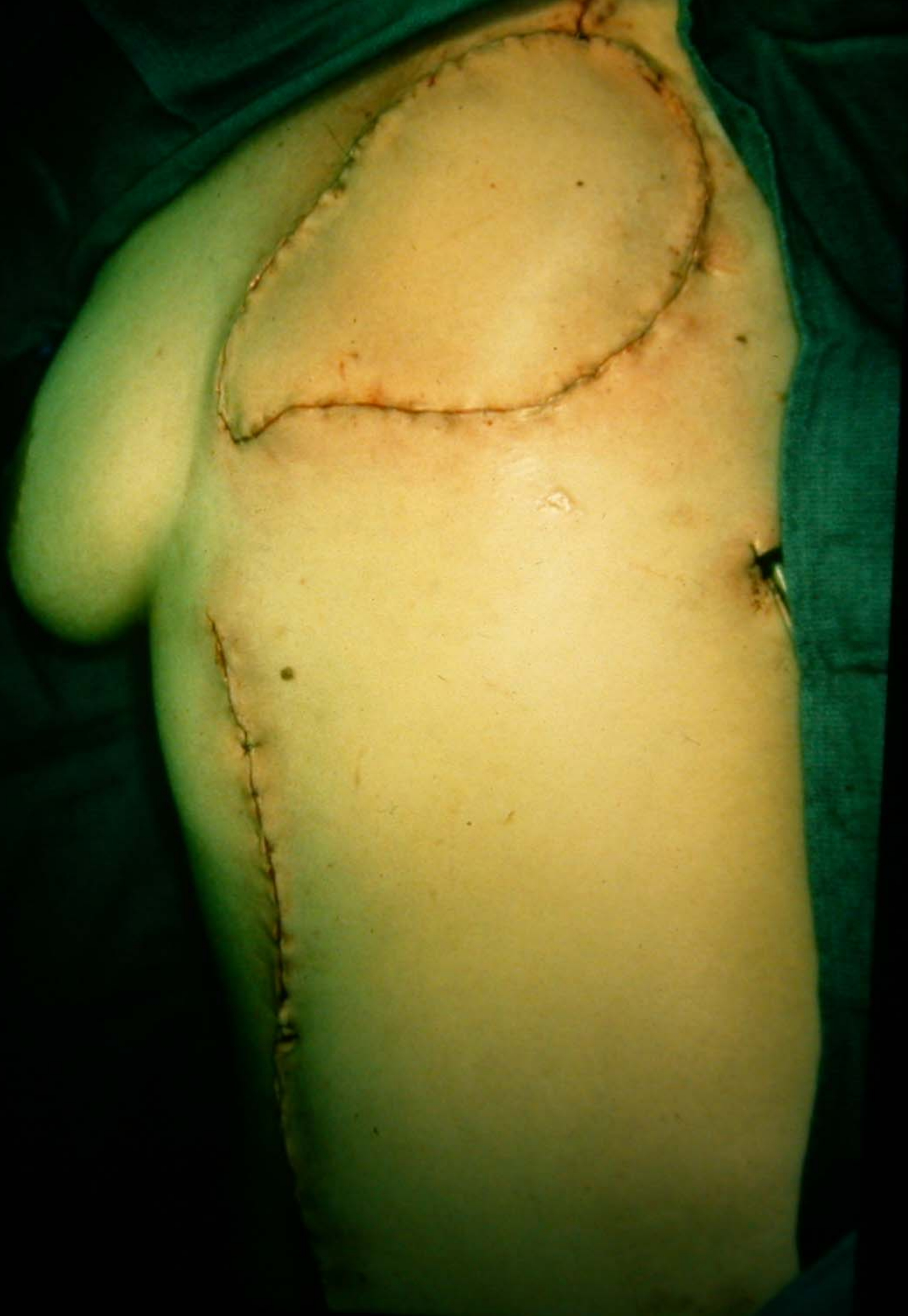
Post-Mastectomy Margin Significance in IBC

Stage IIIB, n=28

Overall Survival



-Curcio, et al. Ann Surg Oncol 1999; 6(3):249-254



Summary - Breast Surgery by T Stage

- T3 – mastectomy if minimal or no response. BCT if clinical cPR or cCR. Long-term local recurrence is unknown
- T4 (non-inflammatory) – mastectomy. BCT possible for selected patients with cCR with skin response
- T4 (inflammatory) – mastectomy with wide skin margins

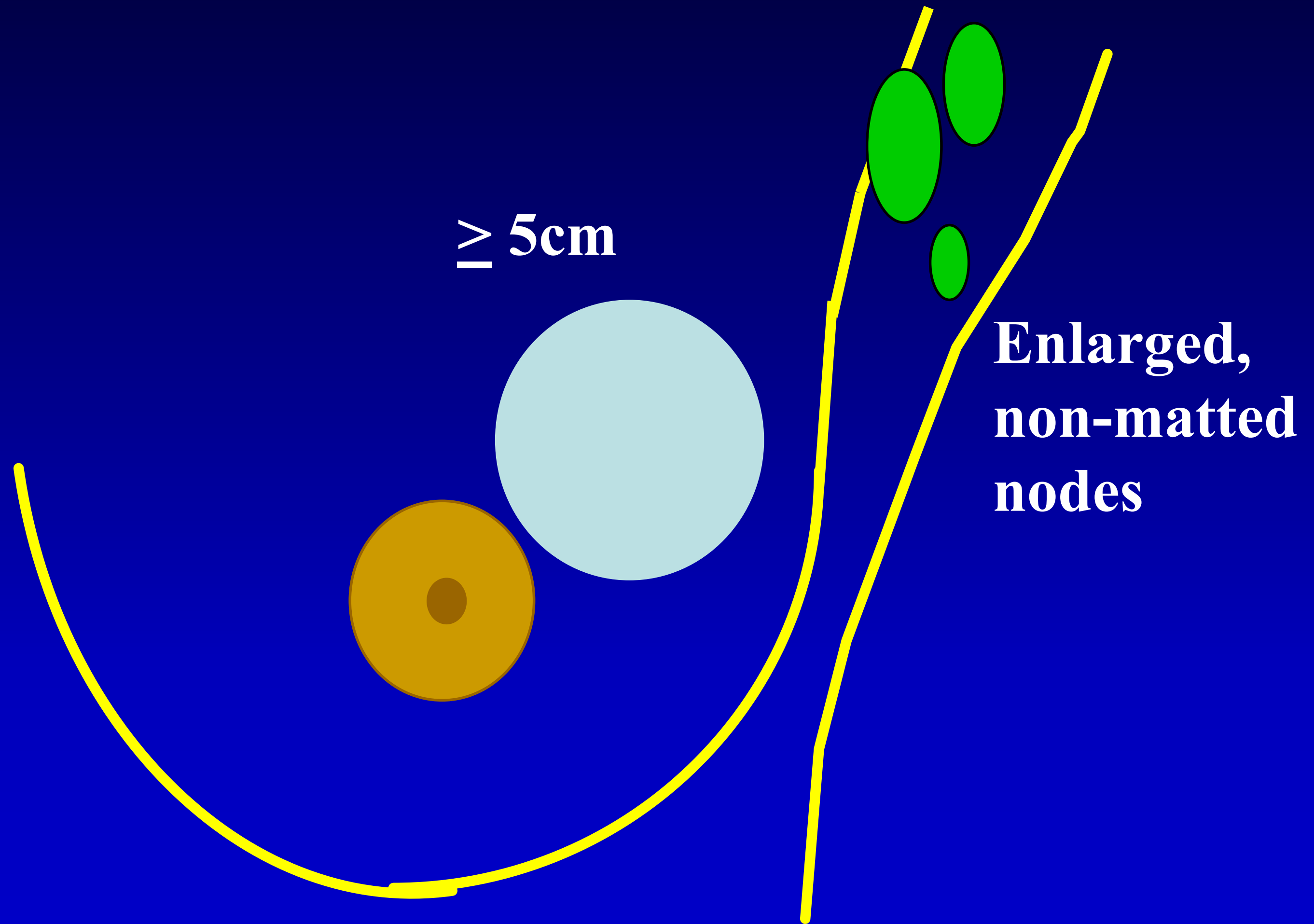
Surgical Issues by N Stage

LABC: Clinical N Stage – AJCC 6th Ed.

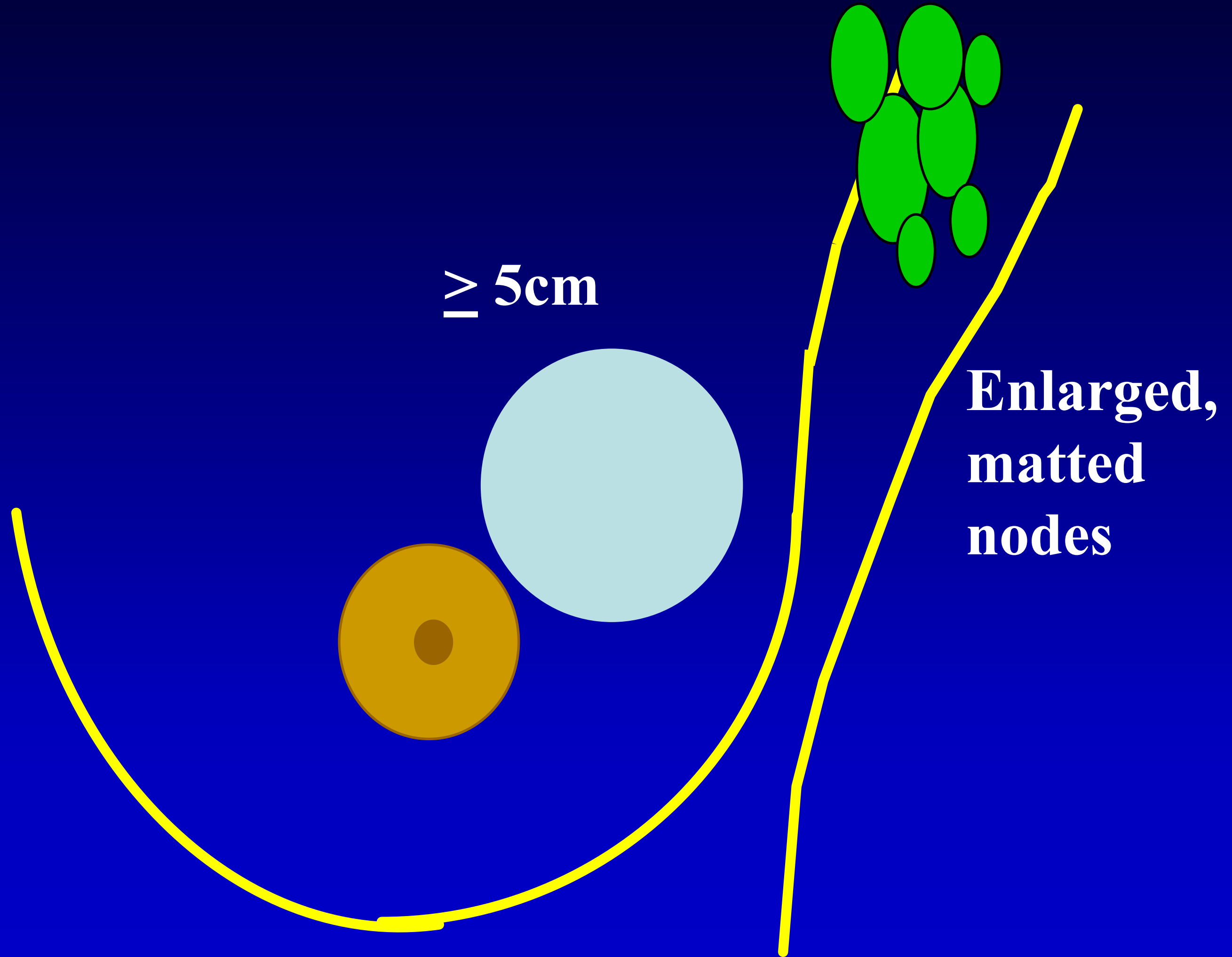
☐	N1	Metastasis in movable ipsilateral axillary lymph node(s)
☐	N2	Metastases in ipsilateral axillary lymph nodes fixed or matted, or in clinically apparent[1] ipsilateral internal mammary nodes in the *absence* of clinically evident axillary lymph node metastasis

☐	N3	Metastasis in ipsilateral infraclavicular lymph node(s) with or without axillary lymph node involvement, or in clinically apparent[1] ipsilateral internal mammary lymph node(s) and in the *presence* of clinically evident axillary lymph node metastasis; or metastasis in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement

Clinical Stage T3N1



Clinical Stage T3N2



Treatment of Clinical N1,2

- Standard of care is axillary lymph node dissection, regardless of response
- Patients with a pCR in the breast have up to 85% chance of axillary node sterilization – not identified by current techniques

LABC – Clinical N0 Disease

- Pathologic nodal staging may influence both systemic therapy and regional nodal irradiation
- Most T3, T4 primary tumors are node positive – 60-85%
- Axillary U/S + biopsy should be considered prior to SLND

LABC – Clinical N0 Disease

- What is the role of SLND?
- What is the management of a positive SLN before or after preop chemo?

SLND before Preoperative Chemotherapy for T3, T4 Tumors

	n	false negative rate
• T3 primary:		
– Bedrosian (>3cm)	56 (T3=16)	1/34 (3%)
– Chung	41	1/31 (3%)
– Stearns	23	1/16 (6%)
• T4/IBC:		
– Stearns	8	2/5 (40%)

Bedrosian, et al. Cancer 2000;88:2540
Chung, et al. Ann Surg Oncol 2001;8(9):688-693
Stearns, et al. Ann Surg Oncol. 9(3):235-243, 2002

SLND after Preop Chemotherapy

TABLE 3. *Studies reporting on SLN mapping after treatment with neoadjuvant chemotherapy*

Author	Year	No. of patients	T status	Average tumor size (cm)	Failure to identify an SLN (%)	FNR (%)
Tafra[17]	2001	29	1, 2	1.4	2/29 (7)	0
Miller[18]	2002	35	1–3	3.5 median	5/35 (14)	0
Haid[19]	2001	33	1–3	3.3	4/33 (12)	0
Julian[20]	2002	31	1–3	< 4	3/34 (9)	0
Brady[21]	2002	14	1–3	–	1/14 (7)	0
Balch[22]	2003	26	2–4	–	1/26 (4)	7
Schwartz[14]	2003	21	2–4	> 3	0/21 (100)	9
Lang[16]	2004	53	–	4.5	3/53 (5.7)	9
Kang[15]	2004	54	2–4	> 3	15/54 (28)	11
Mamounas[23]	2002	428	1–3	–	65/428 (15)	11
Breslin[24]	2000	51	2, 3	5 median	9/51 (18)	12
Stearns[25]	2002	34	3, 4	> 5	5/34 (15)	14
Piato[26]	2003	42	1, 2	< 5	1/42 (2.4)	17
Fernandez[27]	2001	40	1–4	–	4/40 (10)	20
Nason[28]	2000	15	2, 3	5	2/15 (13.3)	33

SLN, sentinel lymph node; FNR, false-negative rate.

-Cox, et al Ann Surg Oncol 2006;13(4):483-490

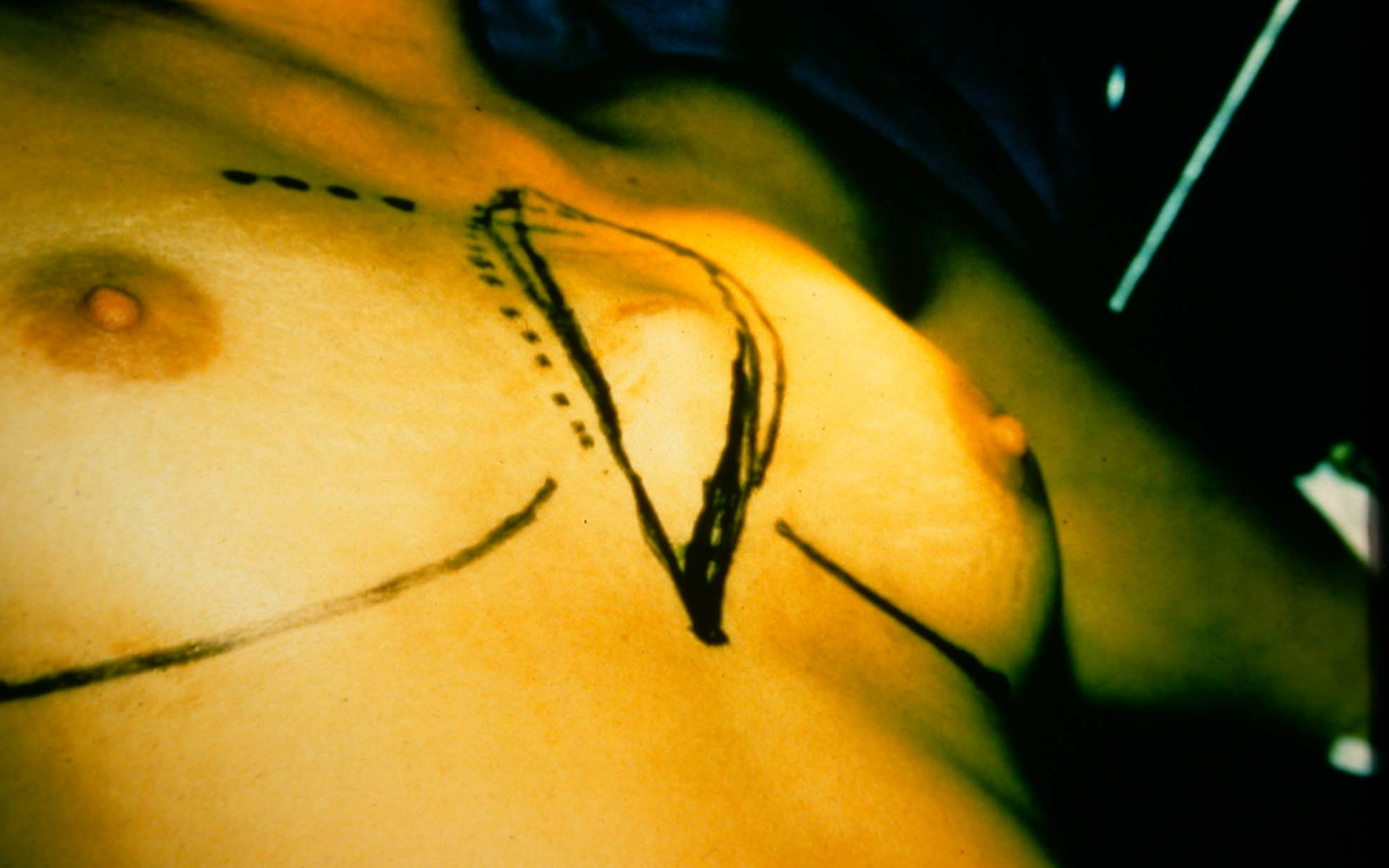
Summary - SNB in LABC

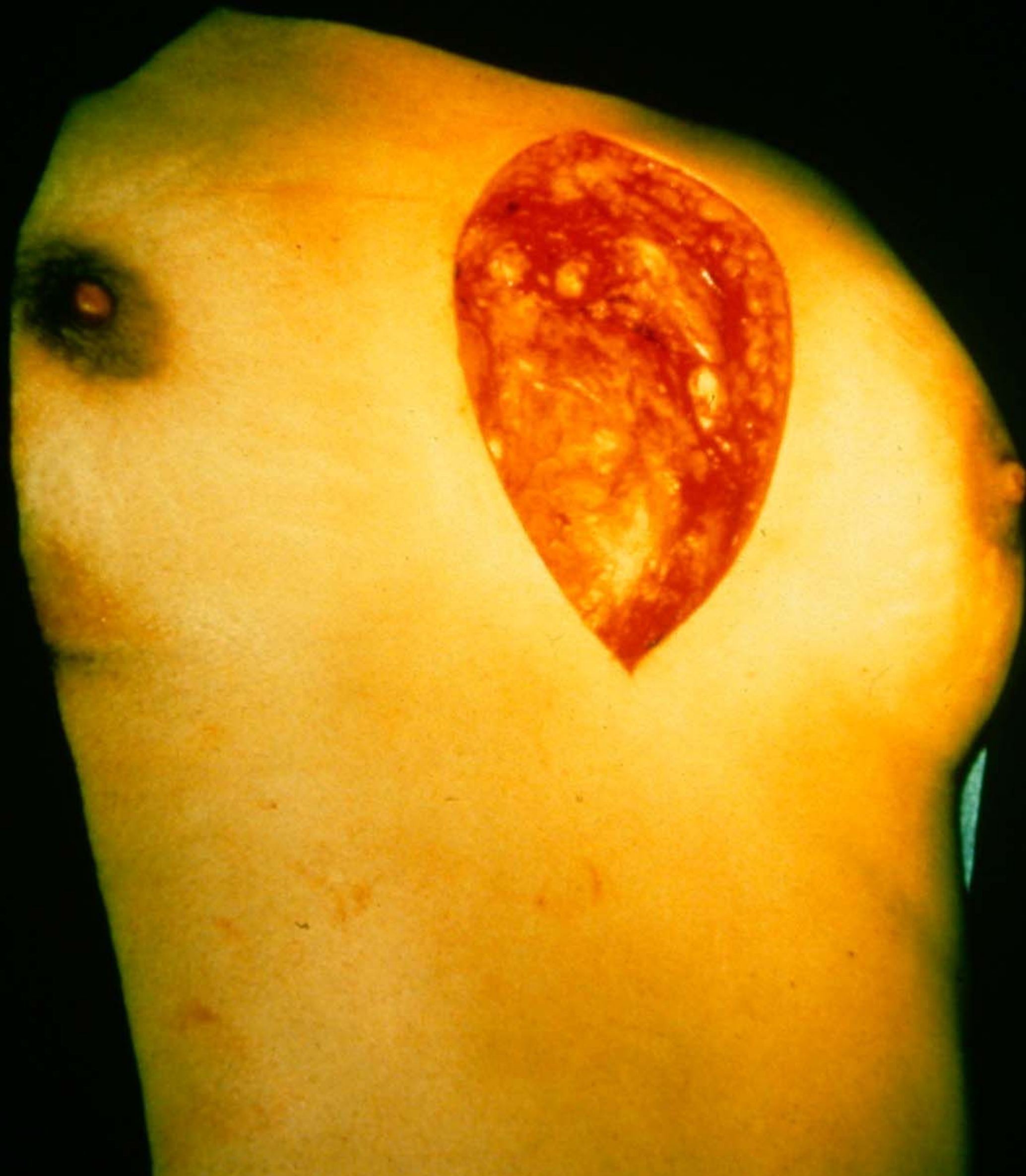
- Pre-treatment SNB may be accurate for T3, selected T4 tumors, NOT for IBC
- SNB post-treatment – insufficient data to recommend. Clinical significance of a false negative SLN more relevant as the denominator of node positive patients becomes larger

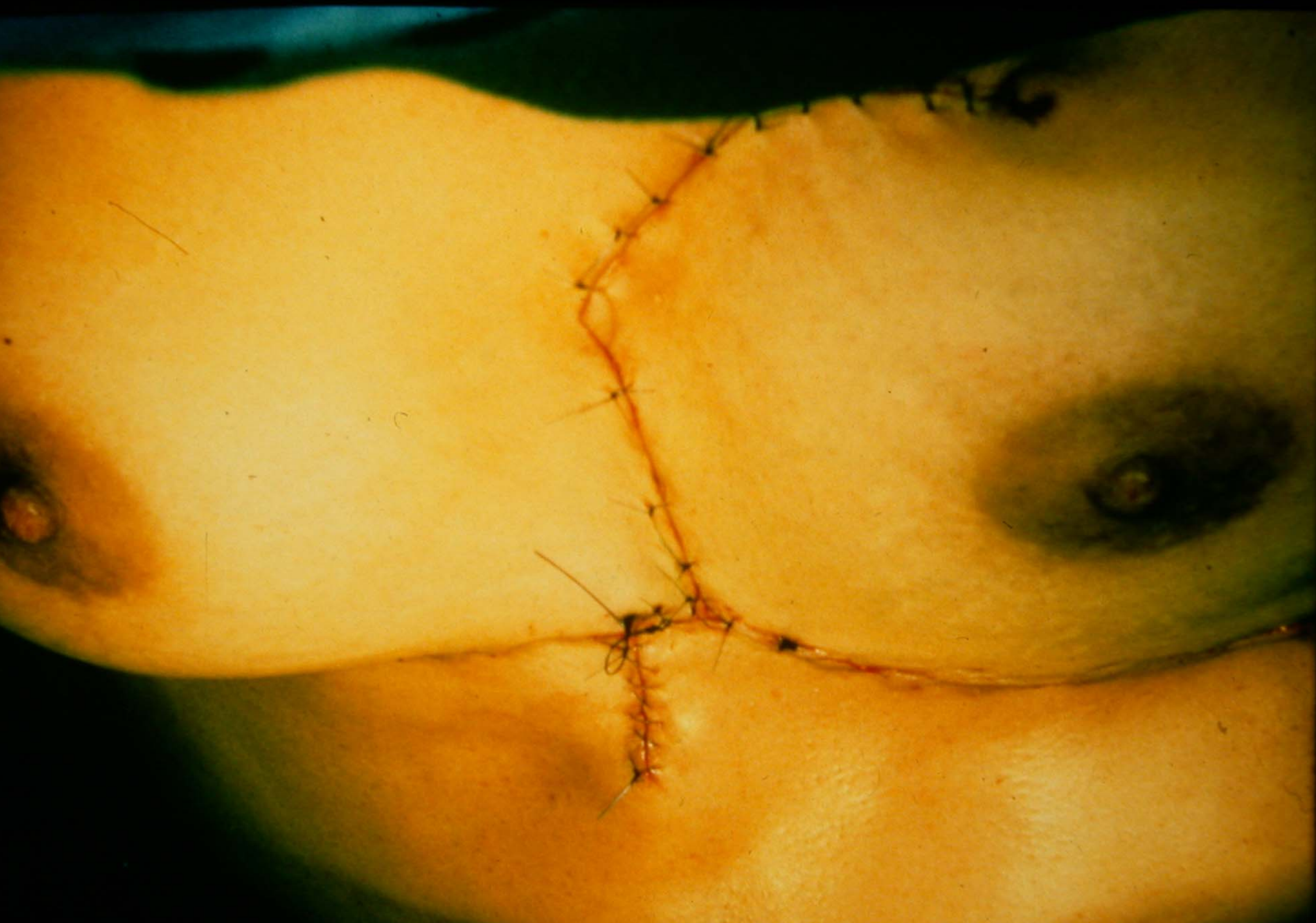
The "Take home" Nodal Message in LABC

- Any patient found to have axillary nodal metastases by any technique, pre- or post-chemotherapy, should receive a completion axillary node dissection
- Current data are insufficient to identify patients who do not need axillary specific treatment

Clinically Positive IMN Disease







Summary – Surgical Issues in LABC

- surgeon involved in multidisciplinary decision up front
- surgeon involved in clinical evaluation during response
- BCT is option in selected patients
  - imaging may help evaluate response and residual disease - U/S, MRI, PET
- decide on axillary management pre-Rx

Surgery in LABC – Unresolved Questions

- How do we evaluate the extent of residual primary tumor to increase successful BCT?
- Can we identify patients with positive nodes (micro- or macro-) before neoadjuvant treatment who do not need axillary-specific treatment?
- What group will design and fund clinical trials that address locoregional treatment?