

Surgical Issues in Pre-operative Therapy

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Advantages of Neoadjuvant Therapy

- Convert inoperable to operable
- Convert mastectomy to lumpectomy
- Allow smaller, more cosmetic lumpectomy
- Assess tumor sensitivity to new therapies
- Collection of paired tissue samples before and after treatment

BUT:

- No improvement in survival
- Not yet able to tailor treatment to response

Surgical Challenges with the Neoadjuvant Approach

- Patient selection for neoadjuvant therapy
- Imaging studies to guide surgery
- Extent of lumpectomy
- Axillary staging – sentinel node issues
- Coordination of radiation and reconstruction for mastectomy patients

Selection of Patients for Neoadjuvant Therapy

Good candidates: may improve surgical options

- Inoperable, locally advanced
- Inflammatory cancer
- Single large mass
- Central, superficial lesions, larger medial lesions

Selection of Patients for Neoadjuvant Therapy

Poor candidates: not likely to avoid
mastectomy

- Multiple primary tumors
- Extensive calcifications
- Direct nipple involvement
- ?Large invasive lobular cancers

Neoadjuvant vs. Adjuvant Chemotherapy: NSABP B-18

- 1988-1993 1523 patients, T1-3, N0-N1
- Randomization:
 - AC x 4 followed by surgery
 - Surgery followed by AC x 4
- Findings:
 - No difference in overall or disease-free survival
 - More breast conservation with pre-op AC

9-year Breast Preservation and Local Recurrence NSABP B-18

- More lumpectomies with neoadjuvant:
 - Pre-op AC 67.8%
 - Post-op AC 59.8%
- No significant increase of in-breast recurrence:
 - Pre-op AC 10.7% p=NS
 - Post-op AC 7.6%

JNCI Monograph 2001 30:96-102

Breast Conservation ECTO trial

Gianni Proc. ASCO 21: Abst 132, 2002

Tumors >2 cm randomized:

Pre-op AT-CMF



Surgery



71%

Breast Conservation

P<0.001

Surgery



A-CMF or AT-CMF



35%

Breast Conservation

MD Anderson: Lumpectomy After Neoadjuvant Rx JCO 22:2303 2004

- 340 cases lumpectomy and radiation after neoadjuvant chemotherapy 1987-2000
- Stage I (4%), Stage II (58%), Stage III (38%)
- Excision of residual disease, not initial volume
- At 60 months:
 - 5% ipsilateral breast recurrence
 - 9% locoregional recurrence

MD Anderson: Lumpectomy After Neoadjuvant Rx JCO 22:2303 2004

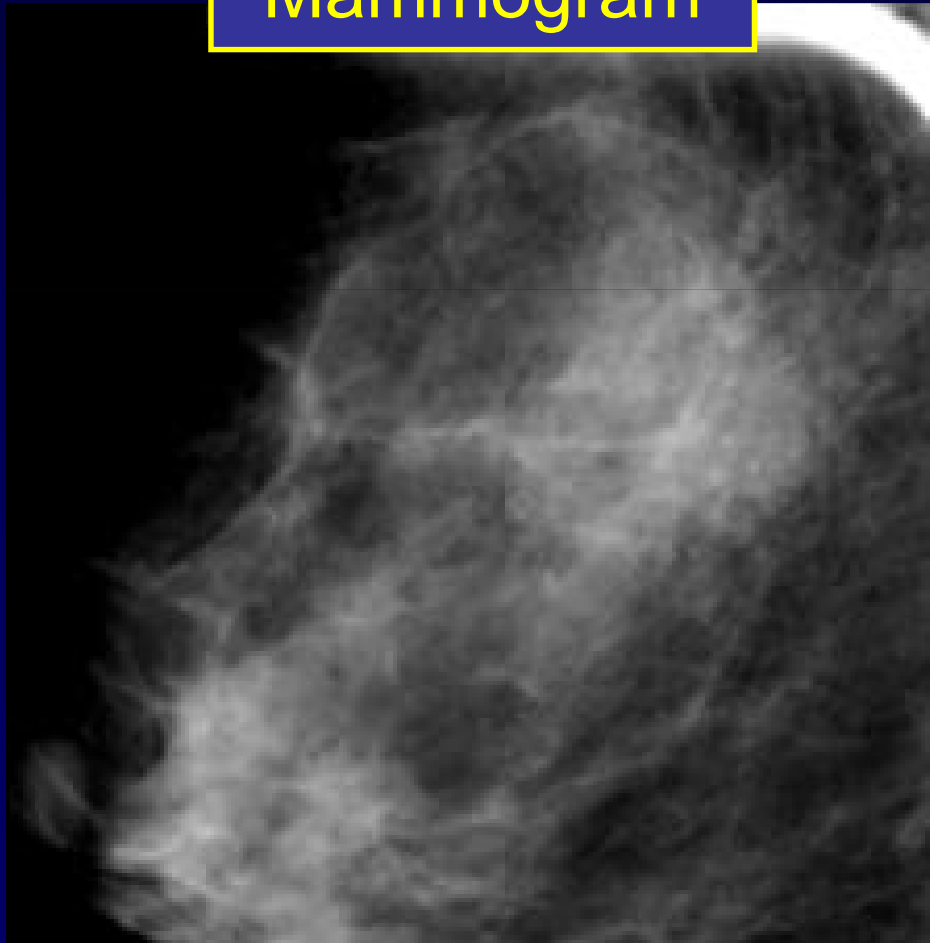
- Higher local recurrence rates with
 - N2-N3 disease
 - >2 cm residual tumor on pathology
 - Multifocal residual disease
 - LVI- lymphatic vessel invasion
- No difference local recurrence with T1-2 vs. T3-4 primaries (4% vs 8% p=.19)

Neoadjuvant Imaging Considerations

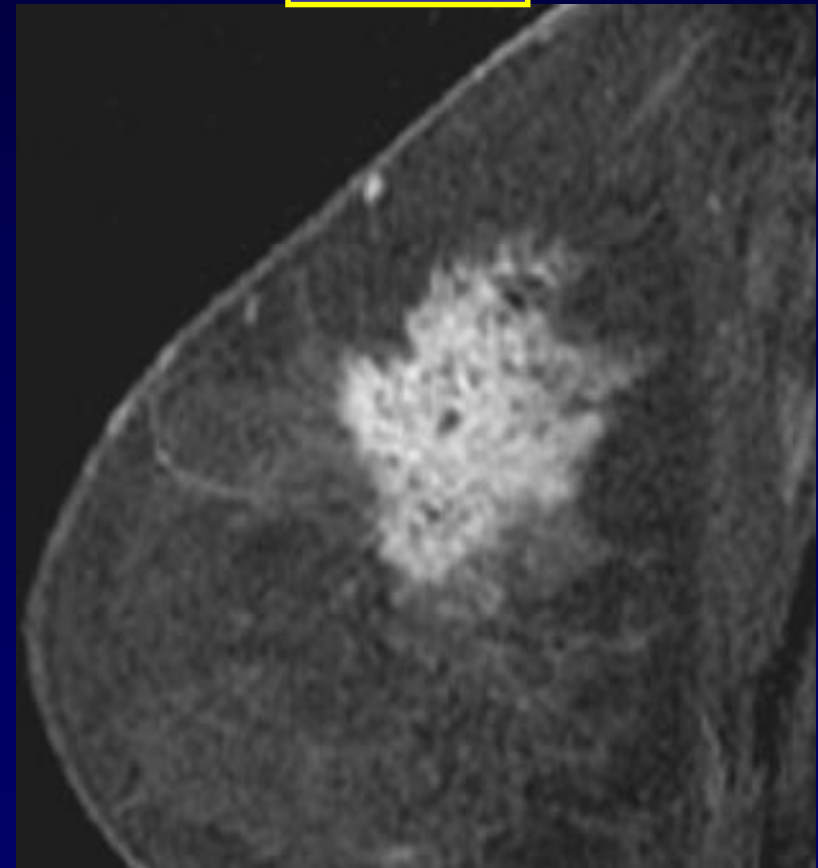
- Place clip in lesion before treatment
 - 10-25% complete response rate
 - Identify tumor site for lumpectomy
- Imaging before treatment to assess size
 - Mammogram, ultrasound and MRI
- Repeat best imaging method after chemo
 - Check eligibility for lumpectomy

MRI defines some tumors more accurately than mammography

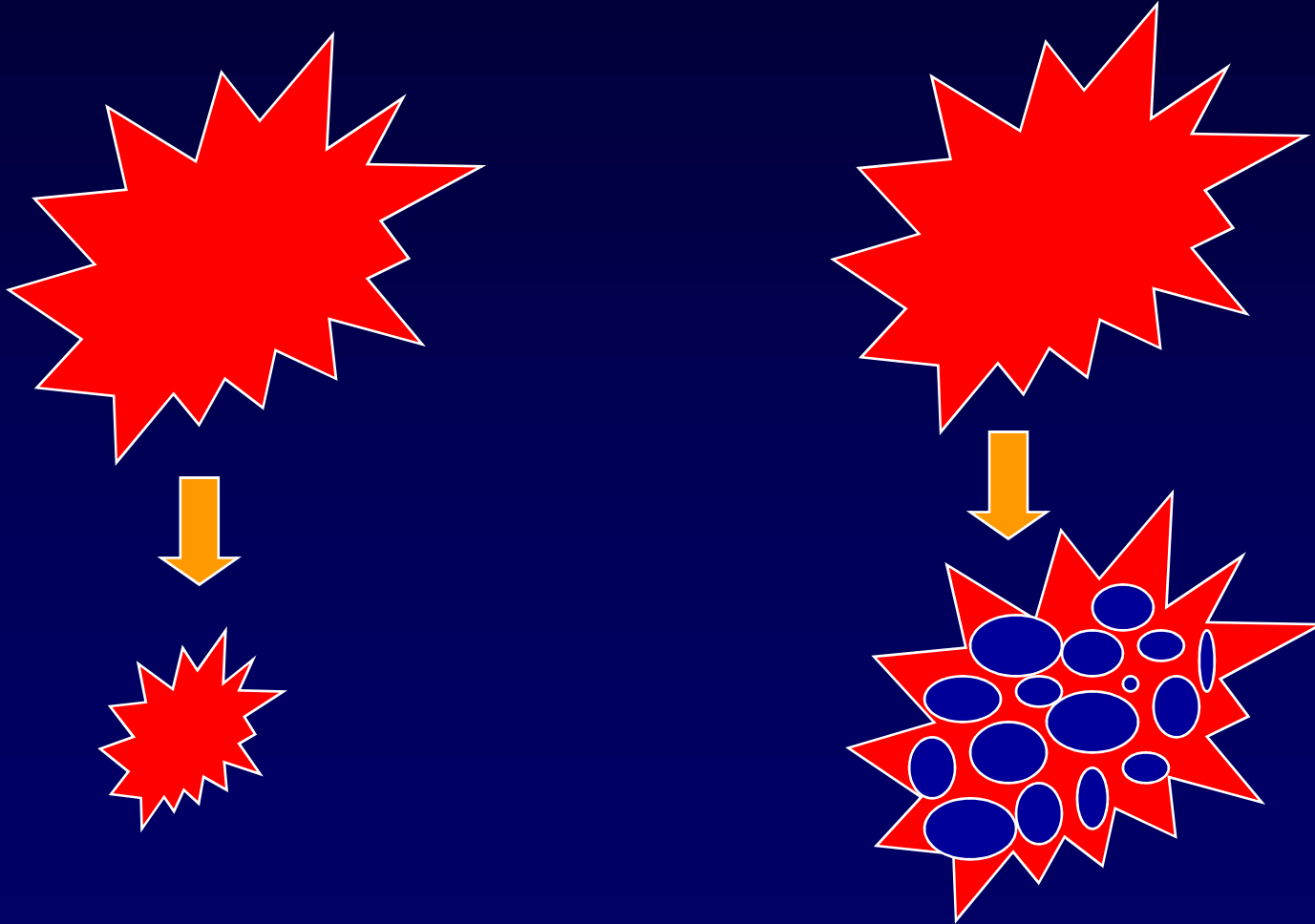
Mammogram



MRI



Will lumpectomy be possible?
Overall diameter of tumor may not decrease
with neoadjuvant therapy



Breast Conservation After Neoadjuvant Therapy

- Imaging to assess residual tumor
- Excise residual tumor volume, not original size
- Clean margins – 2-3 mm
- Use of multiple localizing wires for larger lesions or extensive calcifications
 - 77% lumpectomy success with large lesions and multiple wires - Kirstein JACS 2008

Neoadjuvant Therapy: Axillary Staging Issues

- Many patients now receiving neoadjuvant therapy will have negative nodes
- Morbidity of axillary dissection may offset benefits of neoadjuvant approach
- Can SNB replace axillary dissection for patients undergoing neoadjuvant therapy?

Sentinel Node Biopsy

- Lymphatic drainage is to a specific “sentinel” node
- A negative sentinel node predicts with high accuracy that remaining nodes are negative
- Reduces complications of axillary staging
 - Lymphedema <1% MGH series
 - Only rare chronic pain or reduced mobility
- Has become standard of care for clinically node negative

Expanded Eligibility for Sentinel Node Biopsy

- T1-T3 tumors, direct skin involvement
- Neoadjuvant systemic therapy
- Multifocal tumors
- Prior breast surgery
- Prior axillary surgery
- Prior sentinel node biopsy
- Prior breast radiation

Not Eligible for Sentinel Node

- Palpable suspicious nodes
 - Palpable, ?reactive nodes
 - Fine needle biopsy of node, if (-) → SNB
- Inflammatory cancer
- Positive supraclavicular nodes
- Distant metastases

Sentinel Node Before Neoadjuvant Systemic Therapy

- Advantages:
 - Initial pathologic nodal status known
 - Helpful for radiation planning
 - Node negative may avoid extra treatment
 - Highest mapping success rates
- Disadvantages:
 - Additional surgical procedure
 - Impact of treatment on nodal disease not known

Sentinel Node After Neoadjuvant Systemic Therapy

- Advantages:
 - Can assess impact of systemic therapy
 - Avoids surgical procedure before treatment
 - Node positives converted to node negative by treatment avoid axillary dissection
- Disadvantages:
 - Lower mapping success rates – 80-85%
 - No nodal status data for planning systemic therapy
 - Most radiation algorithms based on initial node status

SNB After Neoadjuvant Therapy

		# pts / stage	% success mapping	False negative rate
B-27	2005	428 II-III	84.8%	10.7%
Julian	2002	34 I-IIIA	91.2%	0% (0/13)
Miller	2002	35 I-IIIB	86%	0% (0/9)
Stearns	2002	34 T3-T4	85%	14% (3/16)
Breslin	2000	51 II-III	84.3%	12% (3/25)

SNB Before or After Neoadjuvant Therapy

T2-T4 Tumors - Jones JL Am J Surg 190:517 2005

	N	SNB mapping success	False (-)
SNB before	52	100%	n/a
SNB after	36	80.6%	11%
Initial N0	17	94%	10%
Initial N1	19*	68%	13%

* 26% of initially N1 had negative nodes on dissection after chemotherapy

False Negative SNB – Why?

- Lymphatics occluded by tumor
- Lymphatics occluded by treatment-induced changes
- Uneven tumor clearance rates in initially positive axillary nodes
- Multiple drainage patterns for large tumors
- Careful palpation intraoperatively to avoid leaving positive nodes after SNB

SNB Before or After?

- SNB before neoadjuvant – for smaller tumors
 - Clinical N0 to avoid dissection
 - If results will alter systemic therapy
 - If results will alter radiation
 - If results will alter reconstruction plans
- SNB after neoadjuvant
 - RT planned, systemic decided, can assess response and prognosis, avoid extra surgery
 - If not done before treatment and no palpable nodes
 - ?Initially palpable now node negative, RT planned

Special Cases

- Locally advanced tumors sometimes drain to contralateral axilla
- Repeat mapping possible after prior sentinel node or prior axillary dissection
 - Higher success if fewer nodes previously removed, longer interval since surgery
 - Lower mapping success
 - If successful, appears accurate

Special Considerations after Neoadjuvant Chemotherapy

- Repeat staging studies if limited response
 - Rule out metastases
- Allow recovery from chemotherapy before surgery
 - 2-4 weeks for recovery of blood counts
 - Avastin: 6+ weeks - wound healing problems, seromas, tissue expander complications
 - Herceptin: long half life but no peri-operative cardiac issues seen

Importance of the Oncoplastic Approach after Neoadjuvant Chemotherapy

- Large lumpectomy defects require creative oncoplastic closure
- Careful selection of lumpectomy incision in case mastectomy ultimately required
- Optimum reconstruction approach for the patient and her additional planned treatments
 - More chemotherapy, post mastectomy radiation

Bilateral Nipple-sparing mastectomies after neoadjuvant chemotherapy



