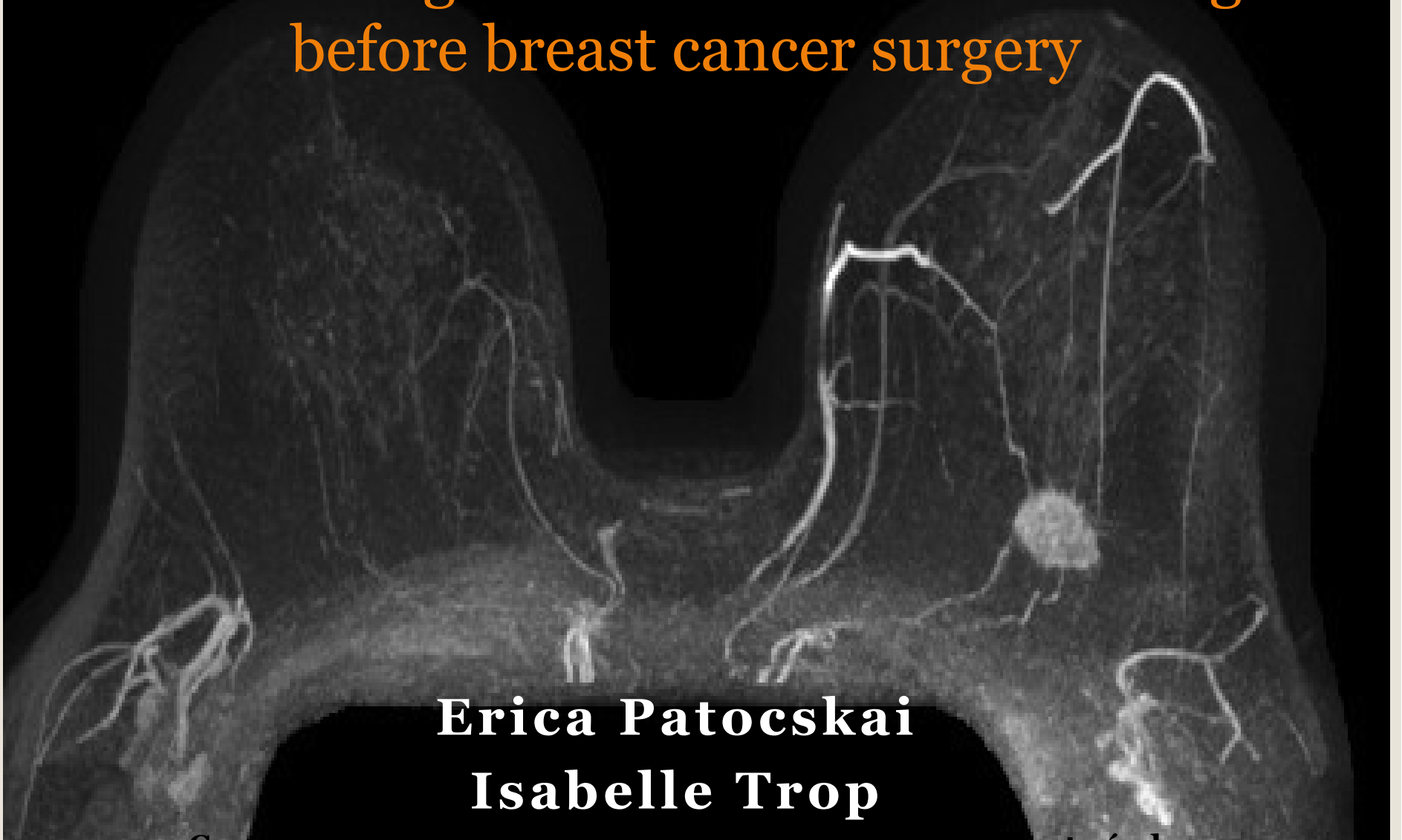


What the surgeon wants from the radiologist before breast cancer surgery



Erica Patocskai
Isabelle Trop

Centre Hospitalier de l'université de Montréal
CAR, April 2013

Plan



- What is the role of MRI for breast cancer preoperative evaluation ?
- How can radiology help in the evaluation of women treated with neoadjuvant chemotherapy?
- In the post-Z0011 era, does it remain relevant to evaluate the axillary region ?

A few facts



- **Mastectomy = local excision + radiation**
for lesions < 2cm

Fisher, NEJM 2002
Veronesi, NEJM 2002

- YES, in terms of **mortality** at 20 years:

- ✦ 41.7% local excision vs 41.2% mastectomy

- NO, in terms of **local recurrence**:

- ✦ 30/352 (8.5%) local excision vs 8/349 (2.3%) mastectomy (p<0.001)

- Prognosis worse in women with late recurrence

→ **Strive for complete excision of tumor with clean margins**

- The local recurrence rate after conservative surgery is **significantly lower** than the rate of additional disease at MRI

- 10-20% additional disease vs 1.8-4% recurrence rate at 8 years

Solin. JCO 2008; 26:386.

Hwang. Ann Surg Oncol 2009; 16:3000.

A few more facts



- **Positive margins**

- Not uncommon
- Frequency depends on definition

- 1648 ♀

- ✦ 14% positive margins
- ✦ 17% close (< 1 mm) margins
- ✦ 17% re-excision → 33% residual tumor

Kurniawan, Ann Surg Oncol 2008

- With **positive margins**, odds of local recurrence 2.4 X ↑ (p<0.01)

Houssami. EJC 2010; 46:3219.

→ **Strive for fewer interventions with positive margins and fewer re-excisions**

Comparative effectiveness of MRI in breast cancer (COMICE) trial: a randomised controlled trial

Lindsay Turnbull, Sarah Brown, Ian Harvey, Catherine Olivier, Phil Drew, Vicky Napp, Andrew Hanby, Julia Brown

Lancet 2010

First randomized prospective study evaluating preop breast MRI

**1623 women eligible for breast-conserving surgery after triple assessment (clinical, mammo and US workup)
45 centers in the United Kingdom**

	MRI group n = 816	No MRI group n = 807
First-intention mastectomy	58 (7%)	10 (1%)
Repeat tumorectomy within 6 mos	85 (10%)	90 (11%)
Overall mastectomy rate	106 (13%)	71 (9%)
Overall reoperation rate at 6 mos	153 (19%)	156 (19%)

Should we dispense with preoperative breast MRI?

Elizabeth A Morris

Department of Radiology, Sloan-Kettering Cancer Center,

1. In COMICE, 38% of recommended mastectomies were false+
 - Suspicious lesions at MRI were not evaluated prior to surgery, surgery was widened without pathologic proof of disease.
 2. The rate of re-intervention for + margins (10%) is quite low
 - Wider surgeries were performed, diminishing the potential benefit of MRI in precisely delineating multifocal disease.
 3. 70% of women were menopausal and 77% were ≥ 50 yo
 - Likelihood of added benefit of MRI over MG-US is lower.
 4. Radiologist-surgeon expertise issue
 - 14% of surgeons enrolled 1-2 patients per year
 - Rate of contralateral cancer detection: 1.6%, half of expected value.
- Long-term benefits on recurrence rate and mortality were not evaluated

Sardanelli: These results only reveal the performance of suboptimal MRI!



Preoperative Magnetic Resonance Imaging in Breast Cancer: Meta-Analysis of Surgical Outcomes



Annals of Surgery:
February 2013 – 257:249–255

- 9 studies (2 randomized trials, 7 cohorts)

	Preop MRI	no MRI	Adjusted OR
TOTAL n=3112			
Initial mastectomy	16.4%	8.1%	3.06 (p<0.001)
Re-excision rate	11.6%	11.4%	0.95 (p=0.71)
Overall mastectomy	25.5%	18.2%	1.51 (p<0.001)
Inf Lobular CA n=766			
Initial Mastectomy	31.1%	24.9%	2.12 (p=0.008)
Re-excision rate	10.9%	18.0%	0.56 (p=0.09)
Overall mastectomy	43.0%	40.2%	1.64 (p=0.034)

Optimizing use of preop MRI



- Added value in women with **dense breast parenchyma**
 - ✦ 7% re-excision rate with preop MR vs 26% without
 - ✦ 17% positive margins with MRI vs 53% without
- Added value in **women 39-49 yo**
 - ✦ Re-excision rates were halved from 60% to 30% with MRI

Philpotts, RSNA 2011

A practical approach to manage additional lesions at preoperative breast MRI in patients eligible for breast conserving therapy: results

Lotte E. Elshof · Emiel J. Th. Rutgers ·
Eline E. Deurloo · Claudette E. Loo · Jelle Wesseling ·
Kenneth E. Pengel · Kenneth G.A. Gilhuijs

L. E. Elshof · E. E. Deurloo · C. E. Loo ·
K. E. Pengel · K. G.A. Gilhuijs (✉)
Department of Radiology, The Netherlands Cancer Institute,
Antoni van Leeuwenhoek Hospital, Plesmanlaan 121,
1066 CX Amsterdam, The Netherlands
e-mail: k.gilhuijs@nki.nl

Prospective study of 690 women undergoing breast MRI prior to surgery

- 141 additional lesions in 121 women (17.5%)
 - ✦ 62 (44%) were pathology-proven malignant
 - ✦ 81 women had *Unidentified Bright Objects* without correlation at ultrasound (11.7% of population)
 - If within 3cm of the index cancer, margins were widened
 - 77.5% at surgery were malignant
 - If multicentric or contralateral, MRI follow-up (n=44)
 - No malignancies after mean follow-up of 57.1 months
- No change in surgical management should occur without pathologic proof

Elshof, Br Ca Res Tr 2010

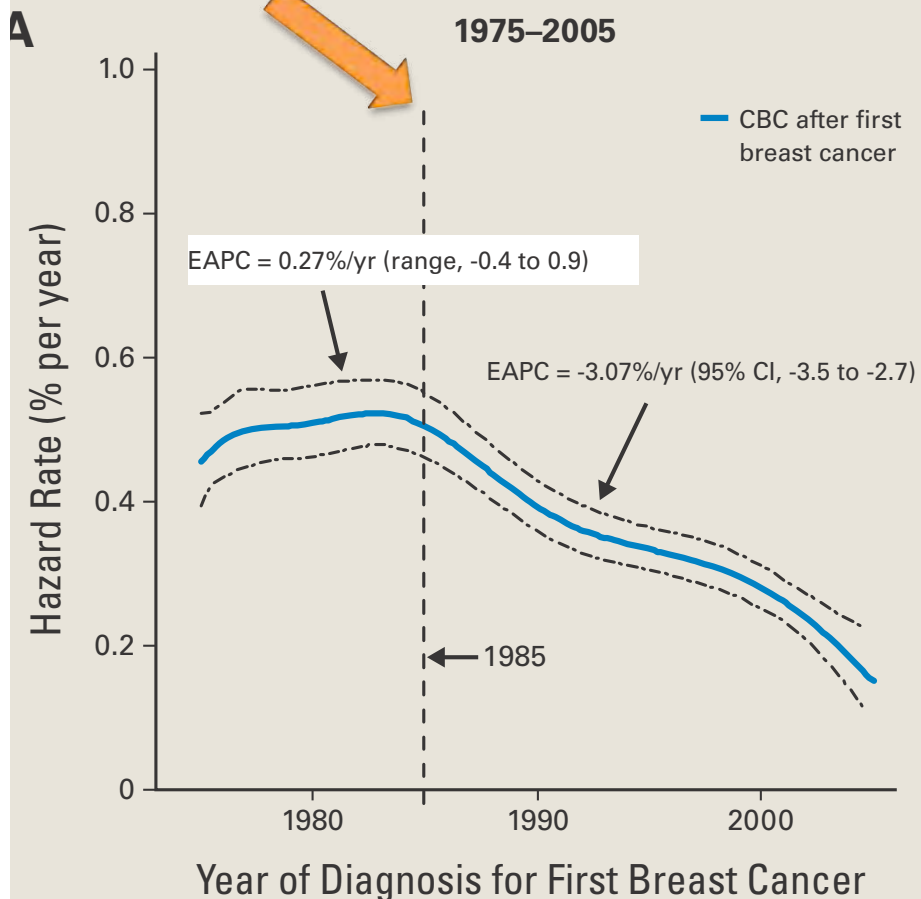
Optimizing use of preop MRI



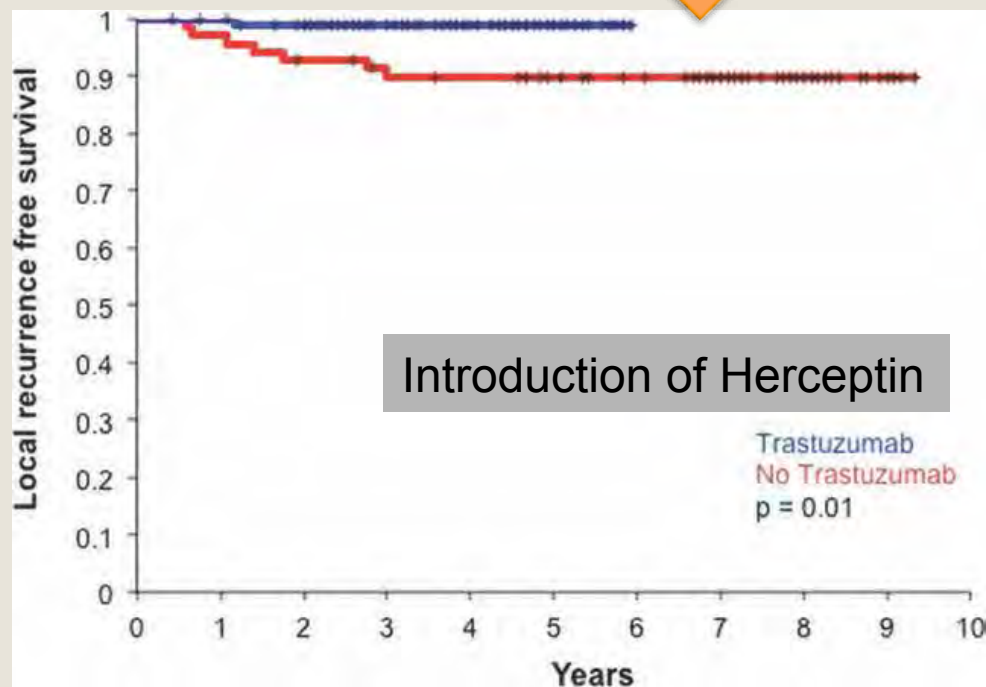
- At the CHUM, preoperative MRI for
 - Clinico-radio-path discordance
 - Young women
 - Dense breast parenchyma
 - Strong family Hx
 - Candidates for neoadjuvant chemotherapy
- Second-look ultrasounds/mag views as needed
- MRI-guided biopsies
 - in 2012, 88 lesions/1800 MRI (4.9%)

Shift in breast cancer

1985 marks introduction of Tamoxifen



- Decrease in incidence of contralateral cancer since mid-80s
- Decrease in locoregional recurrence with targeted therapies



Kiess. Cancer 2012; 118:1982.

Shift in breast cancer management



Morrow. RSNA 2012.

The era of effective multimodality therapy obviates the need to surgically eradicate all microscopic disease in both the breast and the axillary nodes.

Outcome is largely determined by biology and the availability of targeted therapy.

Neoadjuvant chemotherapy



**HOW CAN RADIOLOGY HELP THIS SUBGROUP
OF WOMEN IN THE EVALUATION OF
TREATMENT RESPONSE AND SURGICAL
PLANNING ?**

Neoadjuvant chemotherapy



- Neoadjuvant chemotherapy is **used increasingly** preoperatively for women with breast cancer
 - With **similar locoregional control** and survival, decrease tumor bulk to allow for **conservative surgery**.
- More protocols are available
 - **Not generally recommended for** tumors <2cm, strongly expressing hormonal receptors, or of low-grade.
 - Not for ILC, DCIS
- Rate of **complete pathologic response**
 - As high as 40-67% in her2+ subpopulations

Evaluation of tumor response



Complete pathologic response = no residual invasive CA (+- DCIS)

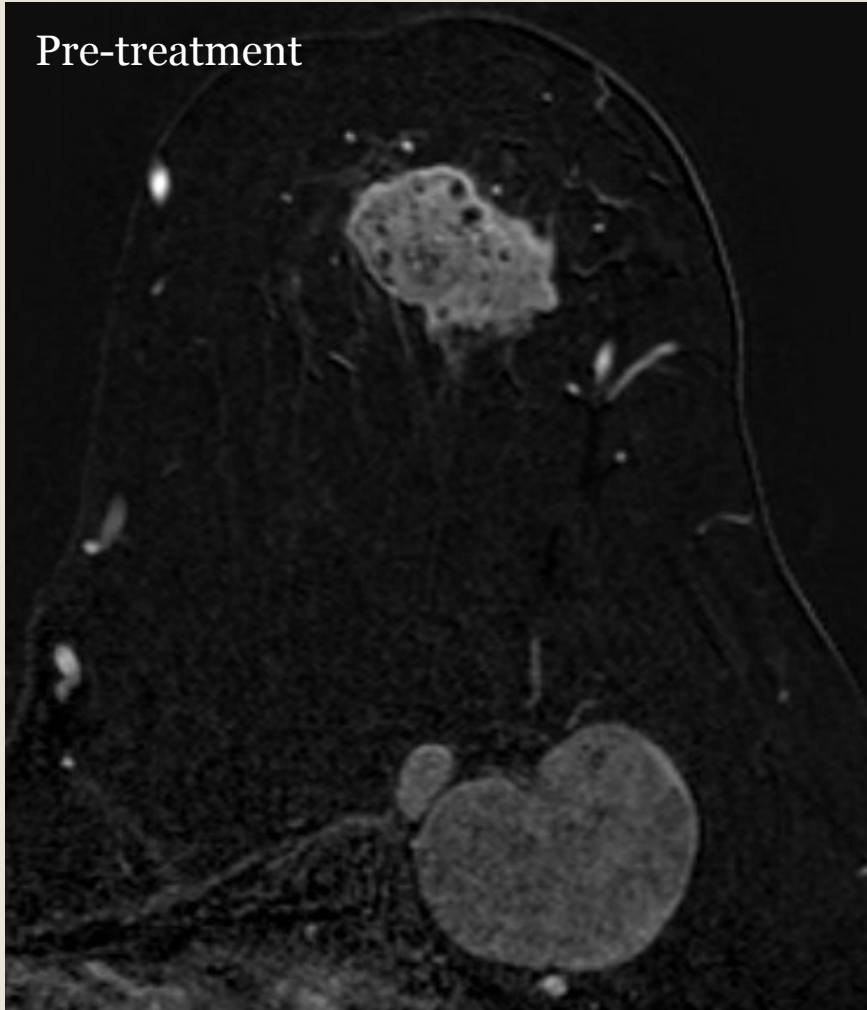
Must be able to **correctly assess response** to treatment, including DCIS, to limit the extent of surgery

- Clinical exam, mammo and US are imperfect for tumor assessment
 - ✦ Ultrasound still best for lymph node evaluation
 - ✦ Radiologic evaluation is opportunity to **deploy clip** at cancer site
 - Local control 98.6% with clip, vs 91.7% without
- **Highest sensitivity is MRI**, but with limitations

Assessing chemotherapy response at MRI



Pre-treatment



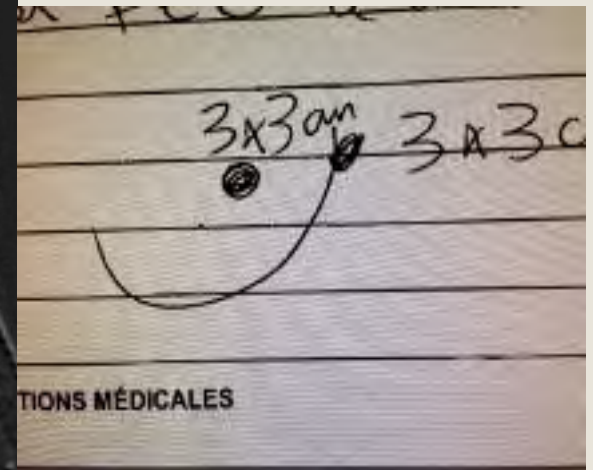
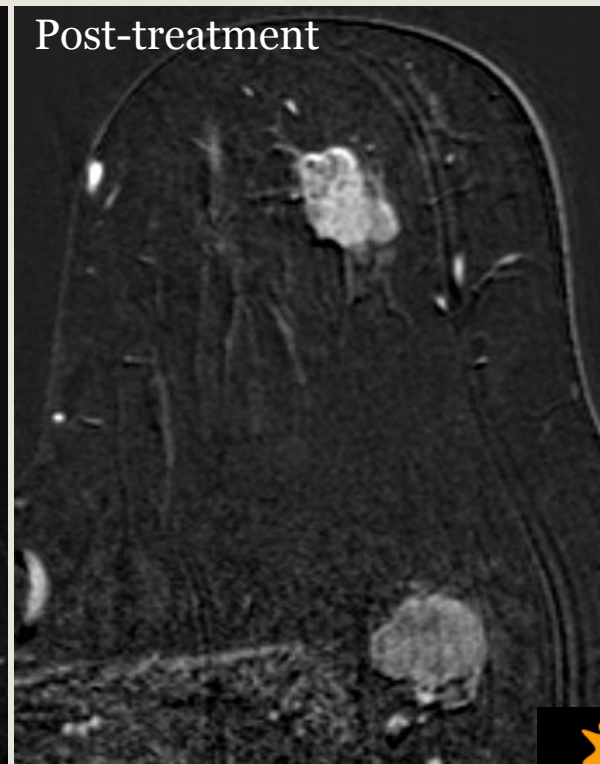
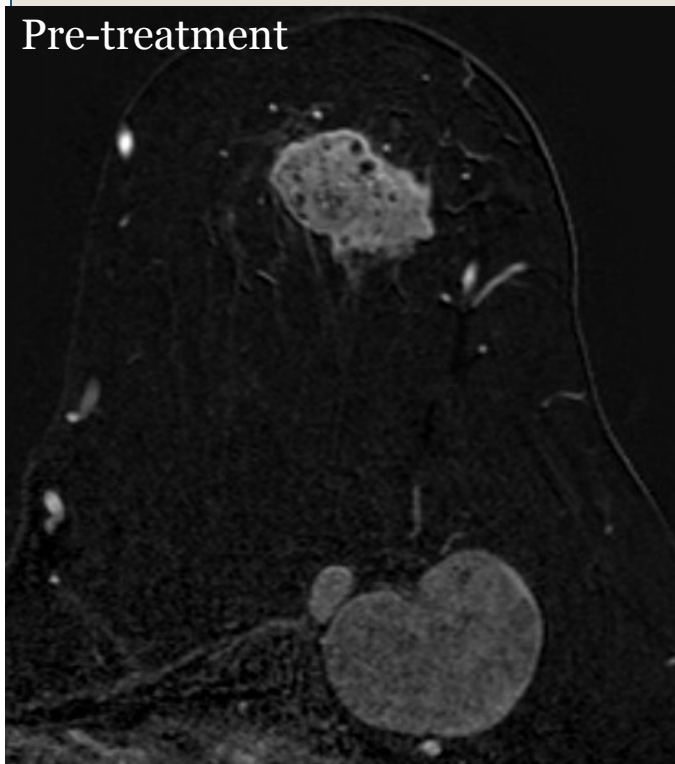
62 yo woman.
6.1 X 5.8 cm high-grade infiltrating
ductal carcinoma with
5.5 cm axillary metastasis
ER- PR- her2-
(Triple negative tumor).

Taxol X 12; FEC X 4

Assessing chemotherapy response at MRI

Partial response to treatment, with size decrease (4.6 down to 2.7 cm) for intramammary tumor, and axillary metastasis (5.8 down to 3 cm).

Surgery: partial mastectomy and axillary dissection - T2 N1 disease.

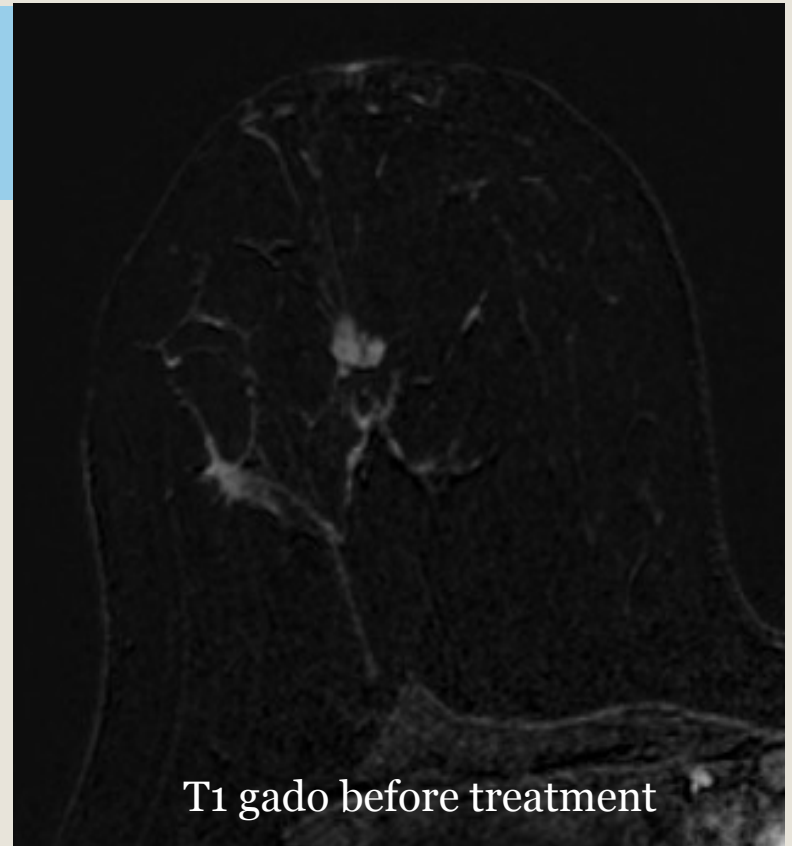
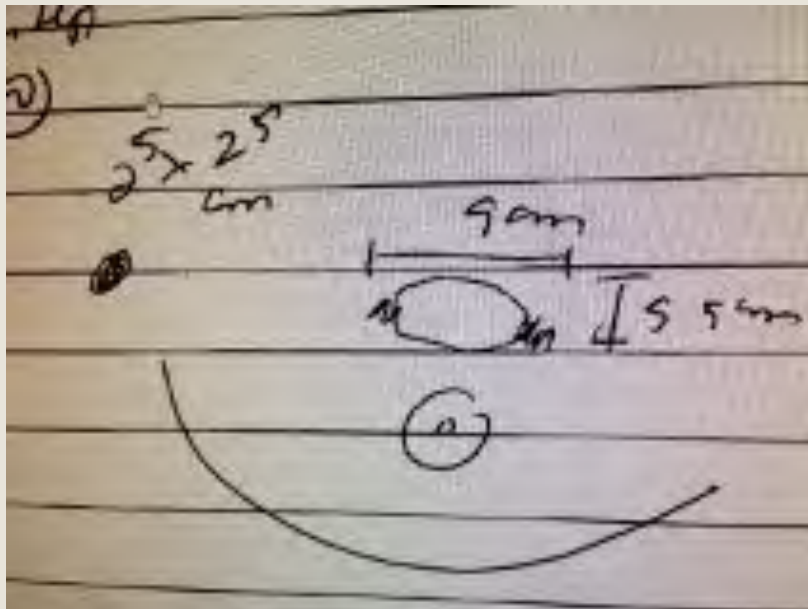


MRI **correlates** well with **pathology size** for enhancing **masses**.
MRI's ability to evaluate for complete response better for **high grade** lesions

Assessing chemotherapy response at MRI



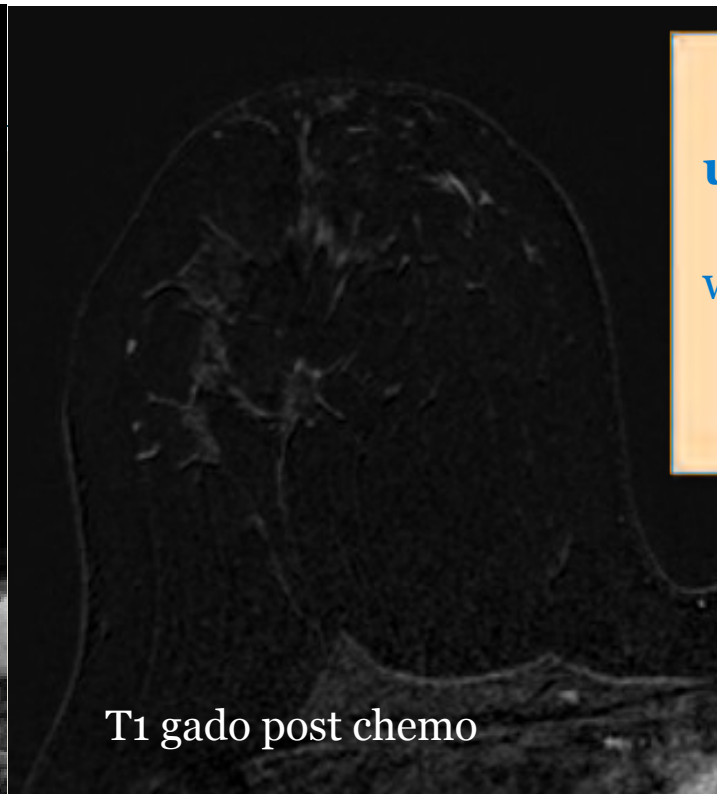
30 yo woman, no family history
Multifocal Grade 2 infiltrating ductal carcinoma
ER+ PR+ Her2- (Luminal A subtype)



T1 gado before treatment

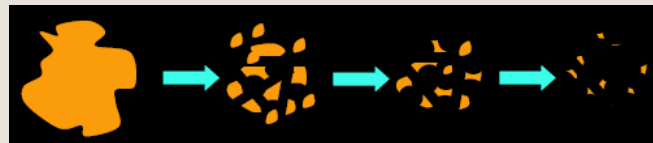
Taxol X 12; FEC X 4

Assessing chemotherapy response at MRI



MRI often **underestimates** residual disease when dealing with **non-mass enhancement**.

Clinically, residual 3.1 X 2.6 cm mass; no palp node.
At MRI: enhancing masses have resolved, spiculated mass and distortion remain.



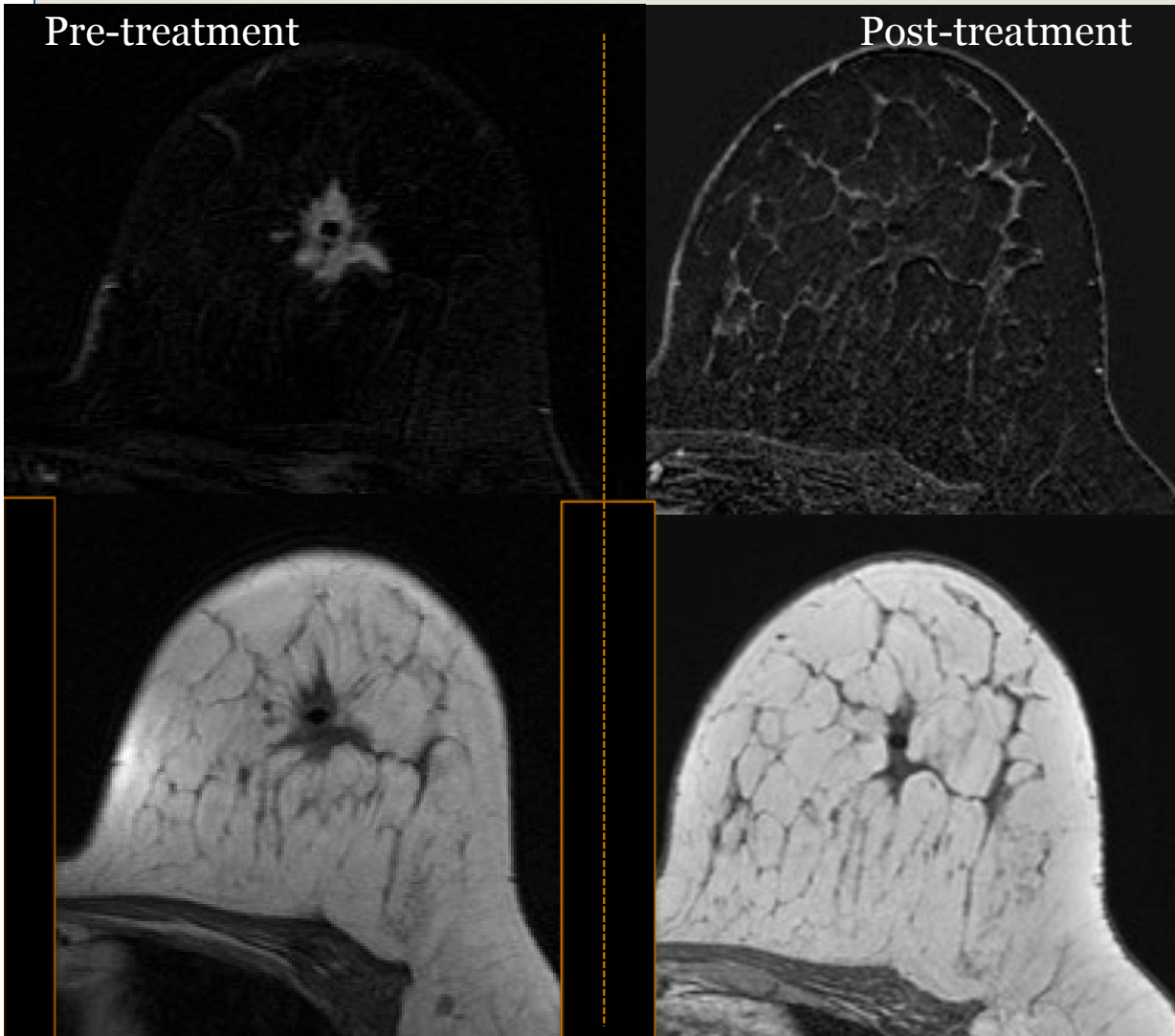
Surgery: modified radical mastectomy with skin preservation and DIEP flap.
Surgical pathology revealed **partial response**, with discontinuous residual disease (largest IDC measuring 2 cm); 7/12 nodes +.

Assessing chemotherapy response at MRI

43 yo woman with 3.5 x 1.3 cm Grade 3 IDC;
ER+ PR- Her2+ (Her2-enriched tumor)
Treated with AC X 4, T + H

Pre-treatment

Post-treatment



MRI reveals no residual enhancement, **suggestive of complete response**. Partial mastectomy and sentinel node performed. Final pathology revealed 2 mm **residual focus of ductal carcinoma in situ**, 0/3 lymph nodes

MRI is limited in cases of **DCIS**, and for **multifocal** disease

MRI as predictor of tumor response

	Sens	Spec	NPV	PPV	Accuracy
Total	83%	47%	47%	83%	74%

567 women, reported by De Los Santos et al. Cancer 2013.

- MRI's predictive ability depends on cancer subtype, reflecting
 - Type and Frequency of response to chemotherapy
 - MRI appearance of tumour
 - ✦ Radiologic complete response for NME and low-grade cancers should be interpreted with caution
- Management changes based on MRI will require further improvements in our ability to correctly assess for pathologic complete response at imaging
 - ✦ Diffusion-weighted imaging
 - ✦ Tumour bed biopsy?

Once Imaging Complete Individualizing surgery for each woman



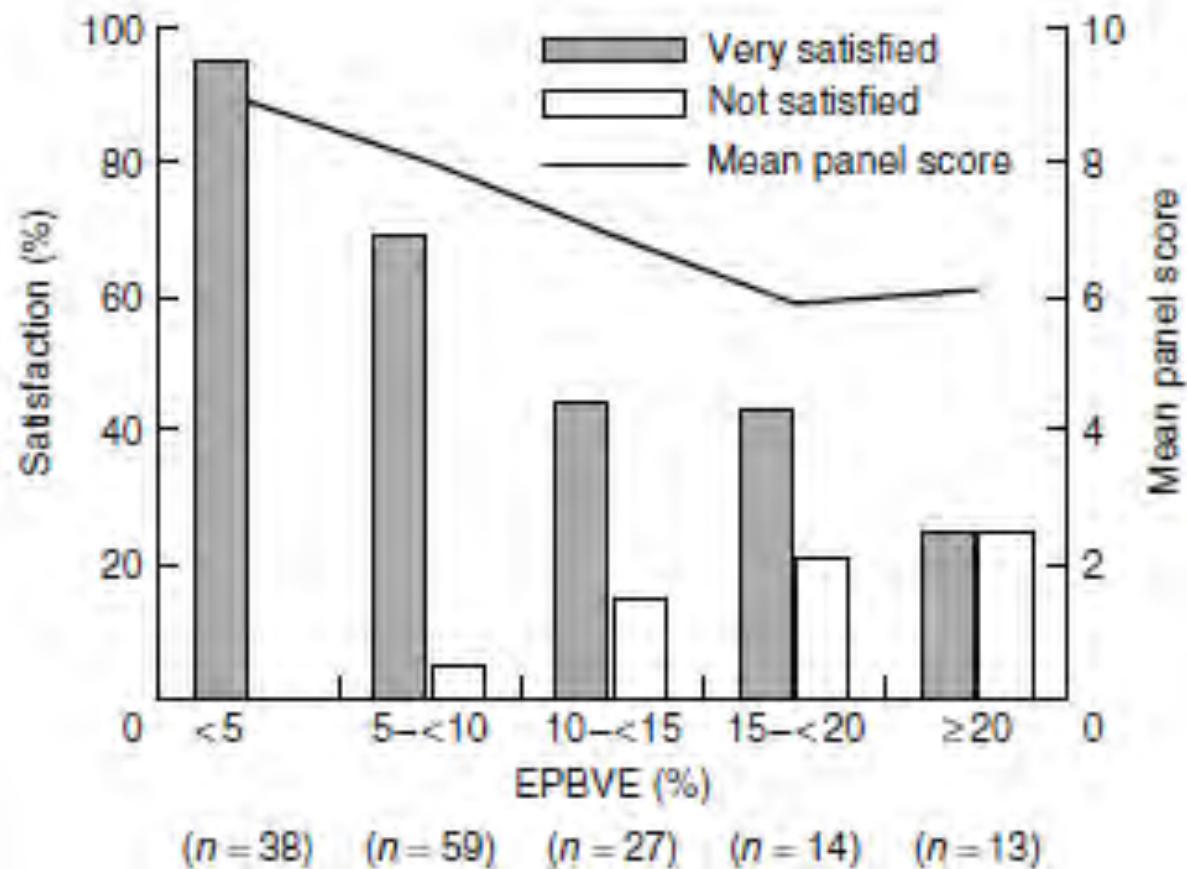
Optimal Lumpectomy Candidates:

- Tumors < 5 cm, limited to one quadrant
- Breast size/tumor size ratio permitting lumpectomy with acceptable cosmetic result
- No contraindications to breast XRT

Cosmesis and satisfaction after breast-conserving surgery correlates with the percentage of breast volume excised

R. A. Cochrane, P. Valasiadou, A. R. M. Wilson, S. K. Al-Ghazal and R. D. Macmillan

Nottingham City Hospital Breast Unit, Nottingham, UK



Surgical considerations after partial mastectomy



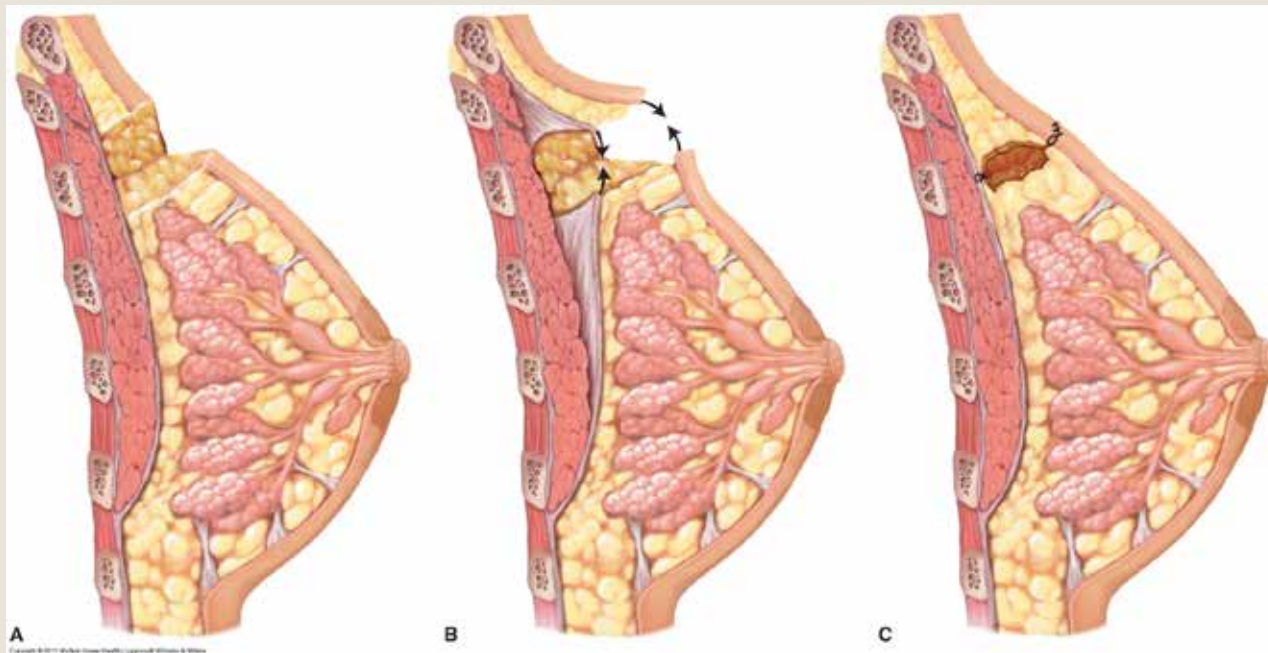
Which women are candidates for oncoplastic reconstruction:

- Excision of more than **20%** of breast volume
- Non favorable **localisation** (central, inferior, medial)
- **Large breasts** or important **ptosis** and desire reduction

When more than 20% excised...



- The goal is to **obliterate the residual cavity** to avoid a seroma by remodeling with **displacement of adjacent breast tissue**
- Undermining of skin and separation of breast tissue from pectoral muscle & **reapproximation** of breast tissue



Musculocutaneous flap post partial mastectomy



- If not enough residual breast tissue available a musculocutaneous flap may be used
- Latissimus dorsi most frequent
- Preoperative imaging essential because if positive margins....very difficult problem



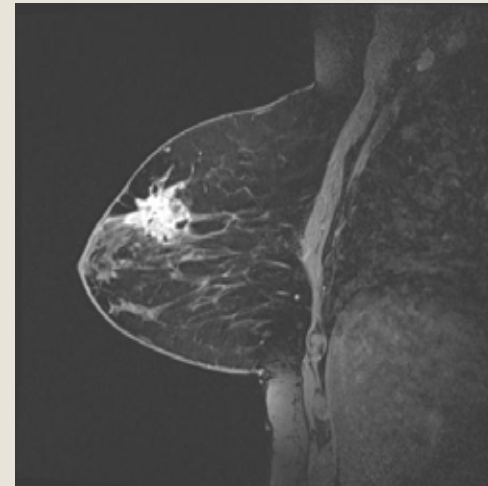
Non favorable location (Inferior)



Non favorable location (Inferior)



Partial mastectomy with reduction



Images from S. Willey

Partial mastectomy with reduction



Images from S. Willey

Immediate Reconstruction post Mastectomy

With or without neoadjuvant chemotherapy



Delayed Reconstruction



Immediate Reconstruction post Mastectomy

The main advantage is skin preservation

Delayed Reconstruction



Immediate Reconstruction



Skin sparing mastectomy & Immediate reconstruction with expander



Preservation of the nipple-areola complex is becoming more widespread



Nipple Sparing Criteria

Not Typically Performed after Neoadjuvant Chemotherapy



Optimal Nipple-sparing mastectomy Candidates:

- Tumor < 3 cm
- Tumour at least 2 cm from the nipple-areola complex
- Absence of multicentricity
- No malignant calcifications extending to nipple-areola complex
- Negative intraoperative biopsy of nipple-areola complex

Spear SL, et al. Plast Reconstr Surg 2009
Golshan M. Diseases of the Breast 2009

Axillary evaluation prior to surgery



Does it remain relevant to evaluate the axillary region after the results from the ACOSOG Z11 trial have been released ?

Until recently...



Abnormal lymph node on U/S → FNA &
axillary dissection if +

Normal lymph nodes on U/S → sentinel lymph node
biopsy &
axillary
dissection if +

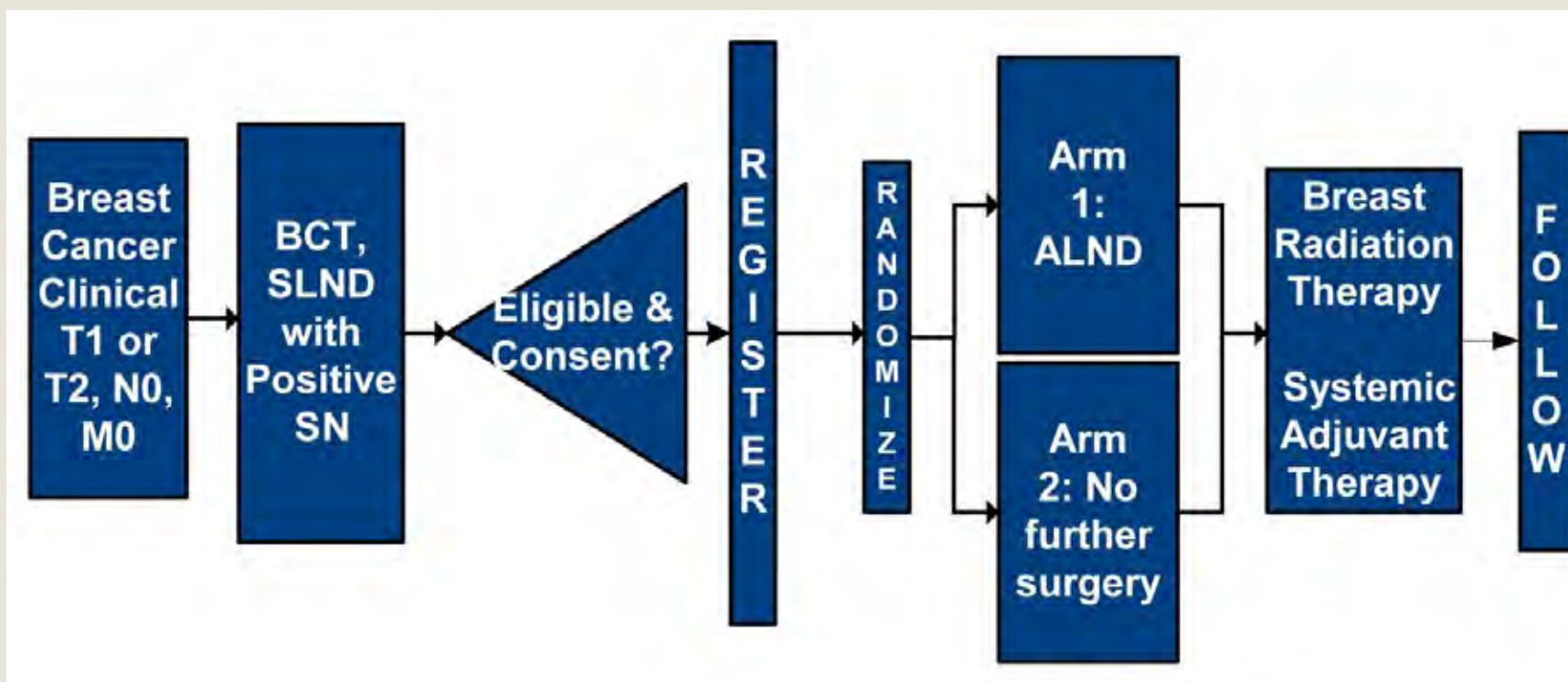
Now



- **Radiologists** not sure when to biopsy abnormal lymph nodes
- **Surgeons** not sure when to ask for a frozen section and when to do axillary dissection
- **Radio-oncologists** now see patients with positive sentinel nodes without dissections
- **Patients** have to make important decisions based on a widely criticised trial

ACOSOG Z0011

Phase 3 non-inferiority trial conducted at 115 sites



ACOSOG Z0011



Eligible

- Clinical T1 T2 No breast cancer
- H&E-detected metastases in SN
- Lumpectomy with whole breast irradiation
- Adjuvant systemic therapy by choice

Ineligible

- Clinical N1 or T3
- Extracapsular extension
- Bilateral breast cancer
- Total mastectomy
- Preoperative chemotherapy
- Nodal irradiation or PBI
- Metastases in SN detected by IHC

Patient Characteristics Z11



- Median age: 55 years
- 70% T1 tumors
- HR (+) >80% in both groups
- Equal number of patients with systemic therapy (96-7%)
 - 58 % chemotherapy & 46% hormone therapy

Patient Characteristics Z11



- 70% had only one positive node
- 40% with micrometastases and 60% macrometastases

Results



- No significant difference in **Locoregional Recurrence** between patients treated with SLN (2.8%) or ALND (4.1%)
- No significant difference in **Disease-Free Survival** between patients treated with SLN (83.9%) or ALND (82.2%)
- No significant difference in **Overall Survival** between patients treated with SLN (92.5%) or ALND (91.8%)

Criticisms



- Mainly older ER positive patients with very favorable prognosis (how many 5 cm tumors?)
- 70% had only one + lymph node
- Don't know HER 2 status of patients
- How many patients HER 2+ or triple – which confer a worse prognosis?

Methodological Shortcomings



- Targeted enrollment of 1900 with final analysis after 500 deaths
- 891 (47%) patients accrued
- Trial closed early because mortality rate (94 deaths) lower than expected
- Protocol violations (no radiotherapy in 11%, no lymph node metastasis (7% vs 11 % in SNB only))
- Analysis based on *intent to treat* in a trial of noninferiority

Methodological Shortcomings



- **Missing data**

- Histological grade 25%
- Lymphovascular invasion 25%
- Size of metastasis 15%
- Hormone receptor status 9%
- Lost to followup 19% (22% vs 17%)

Radiotherapy



- Details of the radiation not in database
- The degree to which the radiation oncologists biased the field edge superiorly to cover more of the axilla is currently undocumented
- It is probable that the majority of patients received adequate dose to the Level I and a portion of Level II to control microscopic disease

Conclusions of INESS (Institute of Excellence in Health and Social Services)



- Z11 does not provide sound statistical proof that omission of axillary dissection after positive sentinel node biopsy is not inferior to axillary dissection
- Prudence has to be applied when applying the results to patients with a more aggressive tumor who are underrepresented in z11
 - Young patients
 - T2
 - More than 1 LN with a macrometastasis
 - Grade 3
 - HER 2+ or triple –

What we do in the CHUM (mostly)...



Should radiologists continue to perform FNA of suspicious nodes?



- Yes, almost all of the time...to avoid SNB
- Not only for T3 or N1
- How do you know if the surgeon will use z11 criteria?
- How do you predict that patient will not request or require mastectomy (if additional foci found)?
- How do you predict whether the patient will not receive preoperative chemotherapy?

Always Follow Z11 Criteria



Axillary dissection:

- Total mastectomy
- Neoadjuvant chemotherapy
- Partial breast radiotherapy

We often follow Z11 Criteria



No dissection:

- T1/T2
- One or two positive SLNs without extracapsular extension
- Whole-breast radiotherapy
- Receiving systemic therapy

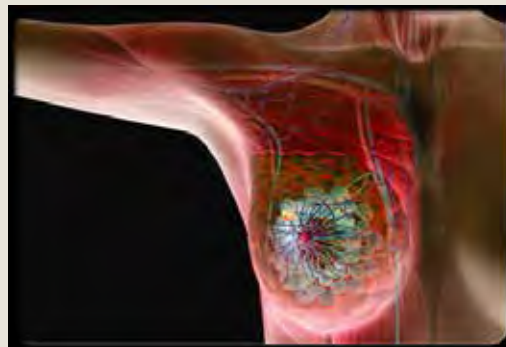
*Almost always when older patient with hormone receptor + disease

In the CHUM...



In patients at higher risk of locoregional recurrence
the complexities of z11 are explained and informed
decision is obtained

« Risk-benefit ratio is patient specific »



What about regional node irradiation??



**TRADING ONE
TREATMENT FOR
ANOTHER**

What happens to all these patients that we don't dissect??



Radiooncologists generally include level 1 and 2 in their fields of treatment if no axillary dissection

Suggested Approach for Radiation Field with SN + but no Axillary Dissection

Table 1. Suggested Approach for Radiation Field Design in Patients With Sentinel Node-Positive Disease Not Undergoing Axillary Lymph Node Dissection

Clinical Scenario	No. of Positive Sentinel Nodes	Total No. of Sentinel Nodes Sampled	Probability of Additional Nodes* (%)	Probability of Additional Nodes† (%)	Probability of Four or More Nodes Involved‡ (%)	Field Design
IDC, 1.0 cm, ER positive, LVI negative	1 (IHC only)	3	3	8	< 1	Tangents only
IDC, 1.8 cm, G3, ER positive, LVI negative, unifocal	1 (macro)	2	27	24	2	High tangents
IDC, 2.0 cm, ER negative, LVI positive	2 (macro)	2	63	55	30	High tangents/consider full nodal treatment
ILC, 4.0 cm, ER positive, multifocal, LVI negative	2 (macro)	2	77	64	40	High tangents/consider full nodal treatment
IDC, 3 cm, ER negative, LVI positive, multifocal	3 (macro with ENE)	3	78	95	80	Full nodal treatment

Abbreviations: ENE, extranodal extension; ER, estrogen receptor; G, grade; IDC, infiltrating ductal carcinoma; IHC, immunohistochemistry; ILC, infiltrating lobular carcinoma; LVI, lymphovascular invasion; macro, macroscopic.

*On the basis of the Memorial Sloan-Kettering Cancer Center nomogram.¹⁹

†On the basis of the MD Anderson Cancer Center nomogram.¹⁸

‡Katz et al.²³

Haffty B et al. JCO 29, 34, 2011
MD Anderson, Dana Farber, Cancer Institute of New Jersey

AMAROS EORTC 10981

(After Mapping of the Axilla Radiotherapy or Surgery)



- 4827 Total Patients
- Tumor < 5 cm
- Mastectomy or BCS
- Opened in 2001-ongoing
- SLN-Positive randomized to RT vs ALND
- Main objective: prove equivalent locoregional control and reduced morbidity for ART

Straver et al. Ann Surg Onc & J Clin Onc 2010

New Trials

?Abandoning SLN



- Sentinel node vs. Observation after axillary UltrasouND (SOUND)
- N=1,560
- European Institute of Oncology, Milan
- Eligibility: <2 cm, negative preop axillary US, breast conservation

Gentilini & Veronesi, *Breast* 2012



Photomosaic of 32,000 Barbies
Chris Jordan, « Close encounters: facing the future »
Katzen art centre, Massachusetts.