# Breast Cancer Update

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2019

# Disclosure Slide

## Slide 1

- **Speaker: Ralph George**

- **Relationships with commercial interests:**
  - **Grants/Research Support:** AbbVie, Immode (supplies and training)
  - **Speakers Bureau/Honoraria:** Alleragan, Roche, AbbVie
  - **Consulting Fees:** AbbVie, Genomic Health
  - **Other:** Medical Legal Fees-Apotex

  - Advocacy Groups: CBCF, IDEOM, CHSF
  - Non Industry Trial: RUBY, PET ABC
  - Industry Funded Trial: SHARPE

# Disclosures

- Roche — Speakers Fees
- AbbVie — Speakers Fees / infomercial fees
  Consultancy Fees
- Genomic Health — Consultancy Fees
- Apotex — Medical Legal Fees
- Immode — Equipment / Research / Training
- Allergan — Speaker fees / training

Advocacy groups: -CBCF (Board, SAC )
-CHSF (Board)
-IDEOM

Ruby, PETacb, SHARPE

# The Breast Cancer Update

**Objectives in Program**:

- "Changes in breast cancer treatment"

  -axillary dissection/surgery/radiation

- "Medications for risk reduction"

# Breast Cancer Update

- Risk and risk reduction
- What's new with genetics
- What's new with screening

- What's new  in surgery
- What's new in adjuvant

- *Evolving indications for Neo-adjuvant

SURVIVORSHIP

# Breast Cancer Update

- **What's New?**

- More and more women are being cured!
- More and more women are alive who have had breast cancer

- 2017 90% 5YS
- 2017 99% 5YS (stage I or II)

- In Canada
- 250,000 women
- Alive now
- Dx of Breast Cancer

survivorship

# Risk Factors for Breast Cancer

- Age
- Race
- Menarche*
- Menopause*
- Nulliparity*
- first pregnancy*
- hormonal therapy*

- Prior breast cancer
- Family history
- Prior breast problems or procedures

- ***Radiation exposure**

Non Modifiable Risk factors

# Breast Cancer Update: Risk

Modifiable:

-obesity—age dependent

-exercise

-alcohol use

-type II diabetes (hyperinsulinism)

Weaker data: diet, pesticides, melatonin

# Risk and Modern Lifestyle

- Menarche > 15
- Normal weight
- Abstain from alcohol
- > 5 children
- Breast feed > 10 years

…major portion of breast cancer risk today is accounted for by a lack of these factors alone.

**Performance of Common Genetic Variants in Breast-Cancer Risk Models.**
Wacholder, et al. N Engl J Med 2010; 362:986-993 March 18, 2010

# Breast Cancer Update-Risk

- Multiple factors
- Family History

- Putting it together
- IBIS*

https://bcrisktool.cancer.gov/

25% qualify genetic testing / HROBSP
20-25% -private testing / enhanced screening
Chemoprevention

# Breast Cancer Update-Risk

- Chemoprevention:
- Includes high risk by IBIS
- Also high risk pathology*

- LIN I
- LIN II
- LIN III

*Atypias: ADH, ALH, FEA, LCIS

EVOLVING TERMINOLOGY

# Breast Cancer- Risk

Risk reduction: (average)

- Exercise
- Weight
- Alcohol
- (Diet)

Risk reduction: (20-25%)

- Clinical Trials
- Tamoxifen
- Aromatase inhibitors
- Raloxifene

# Breast Cancer Update- Risk

- Solution: uptake/adherence?
- YES

- LOW DOSE tamoxifen:
- TAM01 5mg
- 52% reduction

JCO 2019 DeCensi et al

# Reduction Strategies

Prophylactic Surgery -high risk mutation carriers

- Oophorectomy

49% reduction in risk of breast cancer, Rebbick,NEJM,2002

- Bilateral mastectomy (with reconstruction)

90% reduction in risk of breast cancer,Hartman,NEJM,1999

# WHO

- **Induced abortion does not increase breast cancer risk**


"Therefore, results from epidemiological studies are reassuring in that they show no consistent effect of first trimester induced abortion upon a woman's risk of breast cancer later in life." (WHO web site.)

## The Pill and increased cancer risk


For 10,000 women:
-2 additional breast cancers- pill **before** first full-term pregnancy
-1 additional breast cancer - pill **after** first full-term pregnancy
(CCS web site).

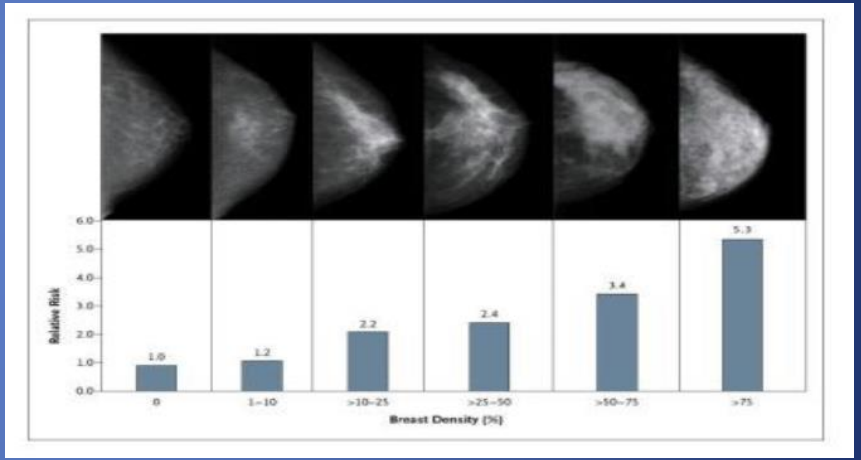
# Risk Reduction Summary

- Average risk: (etoh, obesity, exercise, (diet) )
- Moderate Risk: (enhanced surveillance, medical chemo prevention)
- High Risk: (add MRI, medical chemo prevention)
- Mutation carriers: (prophylactic surgery)

Radiation exposure: lymphoma

# One Final Point on Risk-DENSITY

- Independent risk factor
- Does not add to existing familial or genetic risk




Santen RJ, Mansel R. N Engl J Med 2005;353:275-285.

# Breast Cancer Update -Genetics

- HROBSP
- IBIS

- CCO – now recommending all triple neg <61 yrs
- ASBrS-now recommending all breast cancer

Affordability private testing:
breast cancers, moderate risk

# Reduce your Risk

- Limit alcohol
- Don’t smoke
- Control your weight
- Be physically active
- Breast feed
- Limit dose/duration HRT
- Avoid radiation exposure/environmental pollution

Mayoclinic.org

# Screening

- Controversial
- Varied recommendations

# Comparison of Guidelines

| Organization | Mammography | | | Breast Self Exam | Clinical Breast Exam |
|---|---|---|---|---|---|
| | *40 – 49 years* | *50 – 74 years* | *75 + years* | | |
| **CTFPHC (2011)** | Recommend against routine screening. Individual decision. | Every 2-3 years | No recommendation | Recommend against | Recommend against |
| **Previous CTFPHC (1994; 1998; 2001)** | No recommendation (2001) | Every 1-2 years (age 50 – 69) (1998) | No recommendation (1994) | Recommend against (age 40 – 69) (2001) | Every 1 – 2 years (age 50 – 69) (1998) |
| **USPSTF (2009) USA** | Recommend against routine screening. Individual decision. | Mammography every 2 years | Insufficient evidence | Recommend against | Insufficient evidence |
| **BreastScreen Australia** | No active recruitment | Every 2 years (age 50 – 69) | No active recruitment | N/A | N/A |
| **NHS screening program, United Kingdom** | No active recruitment* | Recruited every 3 years until age 70 | Women over 70 not routinely recruited* | Not recommended | Not recommended |

* The National Health Service (NHS) is phasing in an extension to their breast cancer screening program that will extend screening Mammography every three years to women aged 47-73 years

Canadian Task Force on Preventive Health Care

# Screening Discussion

## What is AGREED:

- All major endorse screening age 50-74.
- None endorse screening before 40
- Most accept that benefits increase with age.
- Absolute age divisions are arbitrary
- 50 meant to be a surrogate for pre and post menopausal women.
- Screening can not benefit an individual who is in their last 5-7 years of life.

# Same data with different emphasis

**Table 2.** Relative Risk of Death from Breast Cancer, Number Needed to Invite to Screening, and Rates of False Positive Results, According to Age.*

| Age | No. of Trials | Relative Risk of Death (95% CI) | Number Needed to Invite to Screening (95% CI)† | Rate per 1000 Women Screen | | | |
|---|---|---|---|---|---|---|---|
| | | | | True Positive Rate | | False Negative Rate | False Posi Rate |
| | | | | *Invasive* | *DCIS* | | |
| 39–49 yr | 8‡ | 0.85 (0.75–0.96) | 1904 (929–6378) | 1.8 | 0.8 | 1.0 | 97.8 |
| 50–59 yr | 6§ | 0.86 (0.75–0.99) | 1339 (322–7455) | 3.4 | 1.3 | 1.1 | 86.6 |
| 60–69 yr | 2¶ | 0.68 (0.54–0.87) | 377 (230–1050) | 5.0 | 1.5 | 1.4 | 79.0 |
| 70–79 yr | 1‖ | 1.12 (0.73–1.72) | Not available | 6.5 | 1.4 | 1.5 | 68.8 |

* Data are from a meta-analysis of randomized breast-cancer screening trials, performed by the U.S. Preventive Servic from the Breast Cancer Surveillance Consortium (for data in the five columns at the right) and are based on a single CI denotes confidence interval, and DCIS ductal carcinoma in situ.

# Screening 40-49

Meta-analysis RR 0.85

- Absolute benefit per individual screened is lower in this age group (lower cancer incidence, decreases sensitivity, higher false positive screen)

- Benefit for individual found to have cancer is greater (quality life year saved)

Cost 40-80 years $35,000 to $47,000

# Patient

- 43 female, Caucasian, active and healthy.
- No breast symptoms
- Menarche 13
- First child at 28, P2.
- Paternal aunt with breast cancer
- best friend diagnosed with metastatic breast cancer

What can we advise her?

# Our Patient

- 1 in 80  in 10 years (1.2%)
- Screening  improve her chance of surviving cancer15% (RR 0.85)
- 40% chance call back for additional views over 10 years
- 3% chance of having a negative biopsy

Warner NEJM 2011

CPSTF  2018:  40 – 49 “conditional…relative value benefits and harms…”

# Screening: elderly

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# Screening and the elderly

- CCO 2013
- 70-74 (oldest group included)

- Increase detection
- Increase ppv
- Decrease recall rate

USA population study 403,488
-subset 70-79
-increased sensitivity
-increased specificity
-increased ppv
-Increased detection rate
-decreased recall rate (Sinclair,AJR, 2011))

# Screening and the Elderly

Lag time to benefit 10.7 years (Lee BMJ,2013)

- health/comorbidity impact screening benefit
- Observational/decision model studies

Support screening

- Good to moderate health 75-85
- Excellent health over 85
- Predicted models (Charlson Comorbidity Index)

Braithwaite, Clin Interv Aging, 2016

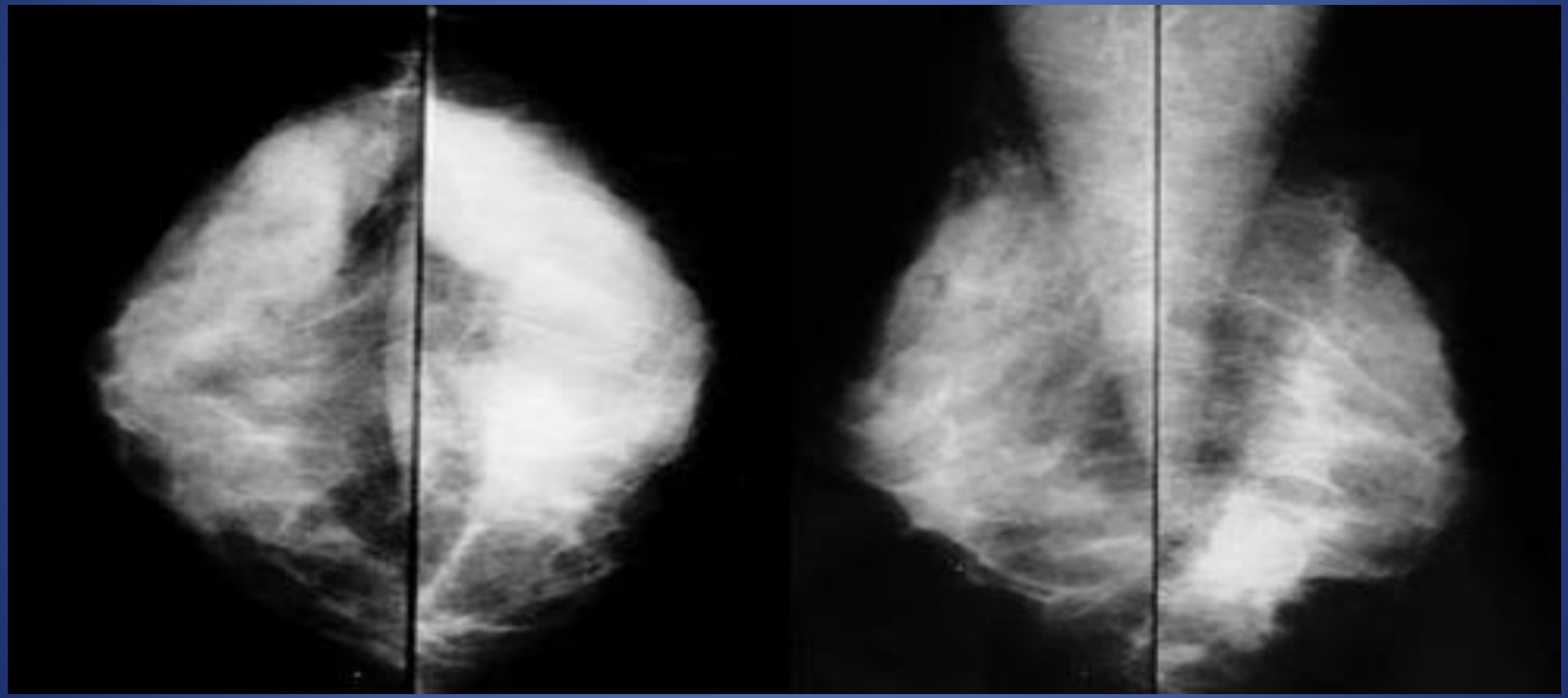
# Screening and the Elderly

- American Geriatrics society
- ACOG
- ACS

- All recommend a consideration of life expectancy in decision to screen:
- Over 85 should be in excellent health
- 75 to 85 good to moderate health.

(Charlson CoMorbidity Index / readily calculated on line)

# Density limits mammography



# Breast imaging: density

- Dense breast independent risk factor
- Decreases sensitivity
- Supplemental ultrasound (C, D categories)
- Annual mammography

CAR position statement July 2019

# Ultrasound/ DBT Screening

- Approximately 4 cancers per 1000 women are detected only by ultrasound. (ACRIN Study 42838 women)
- Over 90% of these were in dense breasts
- 9-11 mm and 91% node negative

  (JAMA 2008)

Tomosynthesis and ultrasound:
-3231 dense normal mammogram
-4/1000 DBT
-7/1000 US
(JCO 2016)

# Radiation

- Digital
- Benefits exceed risk (100 fold)

- O.4 milliesieverts
- 1.3/ 100,000  age 40
- 0.1/ 100,000  age 80

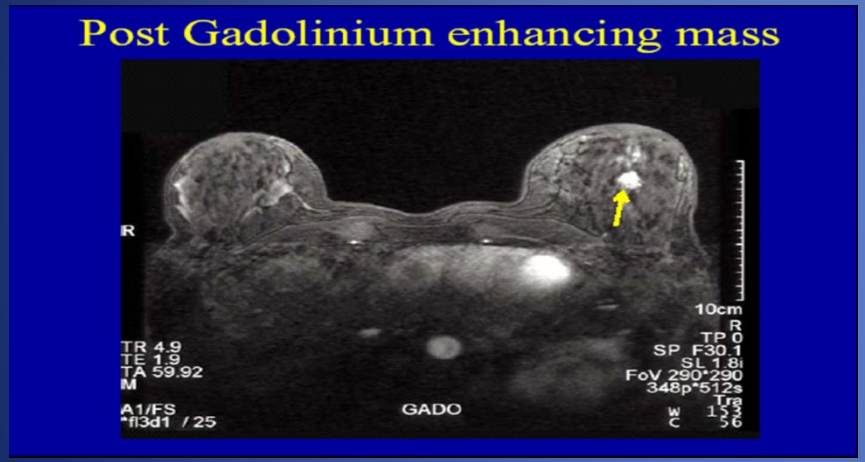
-2 months background
-flight calgary
-CT abd 25 x

# Gadolinium

- Chuck Norris law suit

- Retention body brain
- FDA alert

# Summary-MRI indications




- Unknown primary
- Density (ultrasound)*
- Cancer in very dense
- Post-op margin/scar
- High risk screening
- Implant assessment
- Suspected multi focal
- Lobular carcinoma*
- Neoadjuvant response
- (Severe Mastalgia)

ALCL – ultrasound seroma like collection

# Surveillance: post breast cancer

- Annual imaging
- Mammography

- Ultrasound / Dense
- High risk / MRI
- Genetics / IBIS

Re constuction post mastectomy

# Summary-Screening

- Mammogram
- Tomosynthesis
- Ultrasound

- MRI

- 40-49 (individualize)
- 50-74 (q2-3)
- ELDERLY (Benefit Health)

Density- add ultrasound
Highrisk-add MRI

# What’s New in Surgery

# What's new Surgery-De-escalation

- NSABP B-04
- NSABP B-32

- Z-11
- AMAROS

- SSO/ASTRO margin

# Evolving concept: systemic treatment impacts local control

| | | |
|---|---|---|
| B14 | 4.3% (tam) | 14.7 (placebo) |
| B13 | 2.6 (cmf) | 13.4 (no tx) |
| B31 | 1.7 (add H) | 2.8 |

De-escalation surgery = appropriate systemic tx and radiation

# How far can De-Escalation Go?

- SOUND (European Institute of Oncology)
- INSEMA (German/Austrian)

Include radiation arms without any nodal surgery

# What's New in Chemotherapy

- OncoType DX
- ER positive

- TaylorX (NEJM 2018)
- 10,273 women

Reliably select women who do not need chemotherapy

# What's new in Chemotherapy

- Extended Hormonal therapy
- Higher risk (high grade, node positive, younger age)

MA-17, NSABP B33

# What's new in Chemotherapy?

## HER2 therapy/NeoAdjuvant setting

| Important trials | pCR | pCR | |
|---|---|---|---|
| NOAH | 26.3 | 60 | 2010 Lancet/2013 ASCO |
| B-41 | 60.2 (T+L) | | 2012 ASCO |
| NeoAltto | 51.3 (T+L) | | 2012 Lancet |
| TRYPHAENA | 61.6 (T+P) | | 2013Lancet |

Highest pCR's ER- subgroup

## Response to NeoAdjuvant

| Tumour Type | pCR (%) |
|---|---|
| ER+/HER2- | 10% |
| TNBC | 30-45% |
| HER2+/ER+ | 33% |
| HER2+/ER- | 50-60% |

# What's New Chemotherapy? Incomplete responders

- CREATE-X (HER2 negative) NEJM 2017
- KATHERINE (HER2 positive) NEJM 2019
- Role additional tx residual disease

False negative rate of SN

# Sentinel node after Neoadj

## ACOSOG Z1071 trial (JAMA 2013/ JCO 2015)

- 9.1 % (if 3 nodes identified)

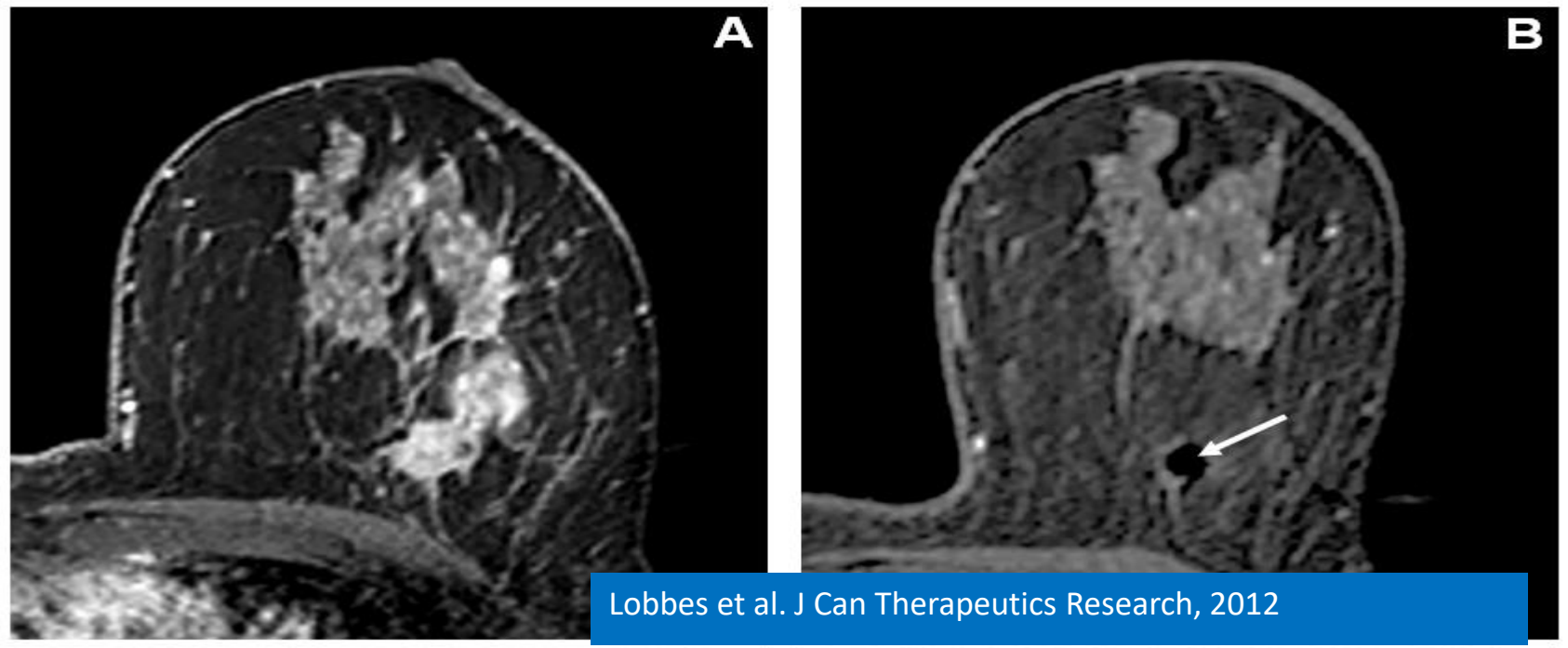
## Sentina (Lancet Oncol 2013)

- FNR less than 10% with 3 nodes identifies
- Combination localization higher detection rate

## Boileau (JCO 2015) FNR 8.4 %

TAD FNR 1.7% (Caudle JCO 2016)

# What's new chemo-Does this patient even need Surgery?




Lobbes et al. J Can Therapeutics Research, 2012

Nsabp B51 and Alliance A011202 initial are steps in that direction

# What's Next

- Eliminating surgery
- Exceptional responders

- MD Anderson /NCI
- T1-2  N0-1

- At least 12 cores no residual IDC or DCIS

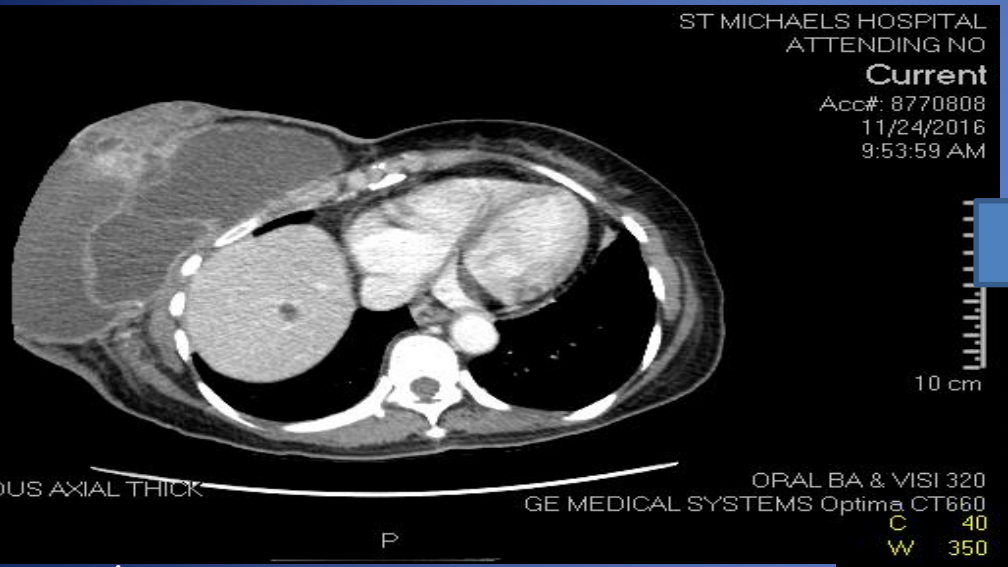
Netherlands, Germany, UK

# Neo adjuvant: Conclusion-Surgeons perspective

- Inoperable  to operable
- Mastectomy to lumpectomy
- Improve Aesthetics Lumpectomy
- Lowers ALND


- Exceptional responders

# Neo Adj Conclusion: Expanded Role



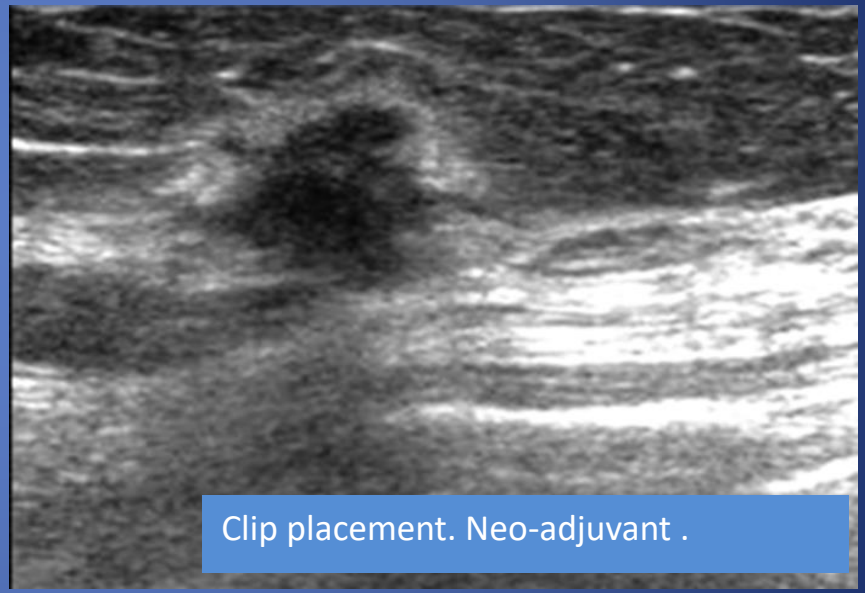


- Extended mastectomy / latisimus flap
- Axilla negative and margins clear

# Neo-adj conclusion: expanded role

- 29 year old
- Self detected (visible)
- Rapid growth

- ER/PR negative
- HER2+
- cT1cN0



Clip placement. Neo-adjuvant .

Radiological /pCR

# What’s new Radiation?

# Metastatic breast cancer cured?

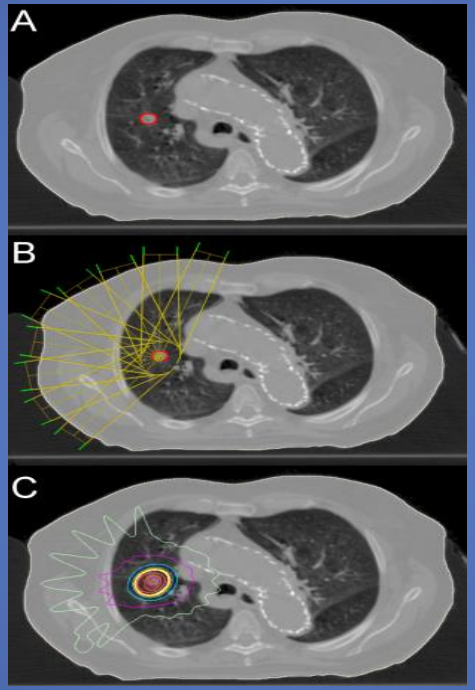
**Table 1. Lines of Evidence Suggesting Metastatic Breast Cancer Is Curable**

| |
|---|
| Adjuvant therapy cures micrometastasis |
| Adjuvant therapy after isolated local-regional recurrence improves survival |
| Chemotherapy for overt metastatic disease produces long-term survivors |
| Exceptional responders with novel agents |
| Treatment of low-volume metastatic disease with surgery and radiation produces long-term survivors |

Sledge J of OP 2016

- Burgeoning options
- Anti HER2 (trastuzamab, lapatinib, pertuzamab)
- CLEOPATRA (NEJM 2015)
- TRYPHAENA (Ann Oncol 2013)
- PALOMA-1 (Breast Cancer Res 2016)
- (Stage IV ER+HER2-)  PFS p=0.0004
- Check point inhib (PD-1, PD-L1 TNBC) (SABCS 2015 Adams)

# Stereotactic body radiotherapy: A critical review for nonradiation oncologists

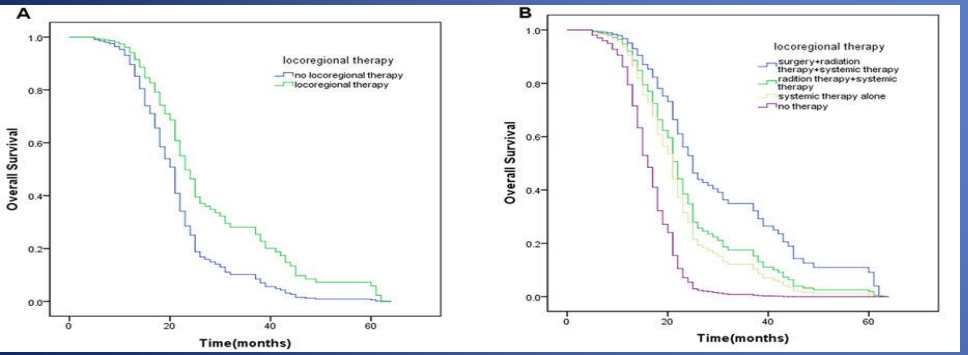



**Cancer**
Cancer V120, pages 942-954, 30 DEC 2013 DOI: 10.1002/cncr.28515
http://onlinelibrary.wiley.com/doi/10.1002/cncr.28515/full#cncr28515-fig-0003

# oligometastasis

- Median OS
- CR 62 vs 25 (p=0.005)
- PR 22 vs 18
- SD 18 vs 15

Yi Yan et al reports 2016



- It’s tough to make predictions, especially about the future.


Yogi Berra

Anti HER2 therapy, checkpoint immunotherapy TNBC, CDK 4/6 inhib ER +.

New Therapies for every Br Ca subtype

# Randomized Oligo metastatic

NCI/NRGBR-002

- 1 or two sites
- Standard of care vs added STRS or surgery
- CONTROL of primary required

- Accrual 2014
- OS and PFS primary end points
- Anticipated results 2022.

# Local surgery/radiation: in setting of Stage IV

## Conclusion

- Palliation in appropriately selected

- Curative intent setting oligmetastastic *

*-Younger, reserve, performance status, limited tumour burden, 1 or 2 sites.
-Optimal systemic (targeted) tx
-Local treatment to mets

Otherwise controlled with targeted systemic therapy!

# Beyond Breast Cancer

Survivorship

# Beyond Breast Cancer

- Statistics
- 26,300 women 230 men
- 1 in 8 lifetime risk
- 1 in 31 die of breast cancer

Targeted therapies/ early detection mean 250,000 alive with dx

# Beyond breast Cancer - Survivorship

- Chronic condition
- Recurrence
- New primary Breast
- Second primary cancers (other than breast)

# Beyond breast Cancer - Survivorship

- Chronic state in survivors
- Sexuality / fertility
- Heart disease
- Bone health
- Cognition
- Emotional / mental health

# Beyond Breast Cancer- Survivorship

Sexuality

- Hormonal and Chemotherapy
- Hot flashes, vaginal dryness, mood swings, depression
- Loss of libido, arousal, dyspareunia, organism

# Beyond breast Cancer - survivorship

Cognition (35%)

- Concentration
- Executive function
- Memory
- Depression

# Beyond Breast Cancer Survivorship

- Bone Health
- Athralgia
- Osteopenia
- Fracture Risk

# Survivorship

- Come LONG way
- Cure rates high
- 250,000
- Living having been treated
- Unique social / medical needs

# Survivorship

- Survivor initiatives
- Adherence to endocrine tx
- No tobacco
- 30 minutes exercise
- BMI
- Healthy Diet

# Survivorship

- Health professionals
- Aware
- Cardiac, bone, emotional, sexual

Bone Density
-Bisphosphonates
-Denosumab

# Survivorship

- We HAVE come long way
- All have role moving forward
- Research better and EASIER treatments
- Aware and care for the chronic affects in growing population BREAST CANCER SURVIVORS

# Breast Cancer Update

- Highlights:
- Screening / density
- Availability genetics
- De-escaltion of surgery
- Remarkable systemic advances
- Above advanced neoadjuvant

Survival new issues around survivorship