



Montefiore Montefiore Einstein
Center for Cancer Care

Breast Cancer 2018: Innovations and Advances

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Discussion Topics

- Philosophy of Care
- Optimizing Breast Conservation, Oncoplastics
- Mastectomy Overuse
- Intraoperative Radiation
- Tumor Ablation
- Lymphedema Prevention
- Intraductal therapy
- Supportive care

Disclosure

- As a physician, surgeon, educator and researcher; my training stressed that scientific proof is fundamental to demonstrate efficacy of all treatment modalities. Through my life experience, I now know and fully accept that there are fundamental truths that cannot be validated scientifically. This is a major philosophical shift which may or may not allow health care professionals to fully embrace their full potential as healers.

Why Montefiore?

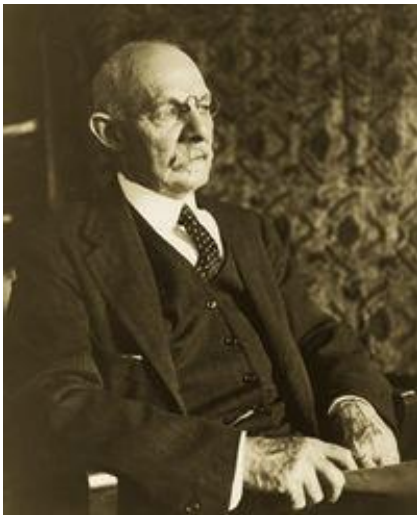
- Socially progressive medical model fully aligned with my personal values
- Potential to bring innovative therapies to large at risk underserved patient population
- Strong multidisciplinary team in place with opportunity to provide leadership
- Opportunity to help elevate breast cancer care standards throughout the Montefiore system
- Opportunities for collaboration with Einstein basic science researchers

Philosophy of Care

- Single standard of care clinic/private
- Compassionate patient centered individualized care by coordinated multidisciplinary team
- Prompt minimally invasive diagnostic workup and treatment
- Achieve lowest mortality with least morbidity, pain or functional change
- DE-ESCALATION of therapy; Minimal effective NOT Maximal tolerated
- Maintenance of normal appearance
- Integration of resident/student education and clinical trials

History of Breast Cancer Treatment

- 1882 - Age of Halsted
 - Cancer spreads centrifugally by direct extension
 - Patients with advanced disease
 - Radical surgery
 - Skin graft reconstruction

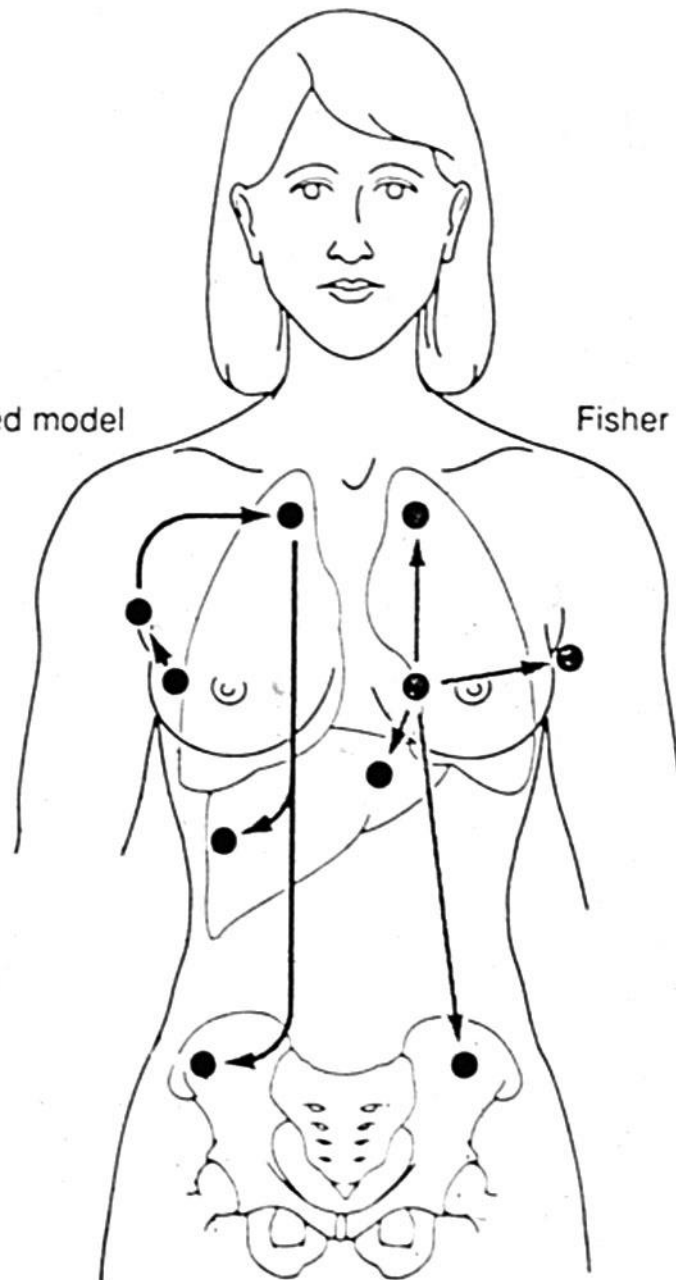


William Halsted



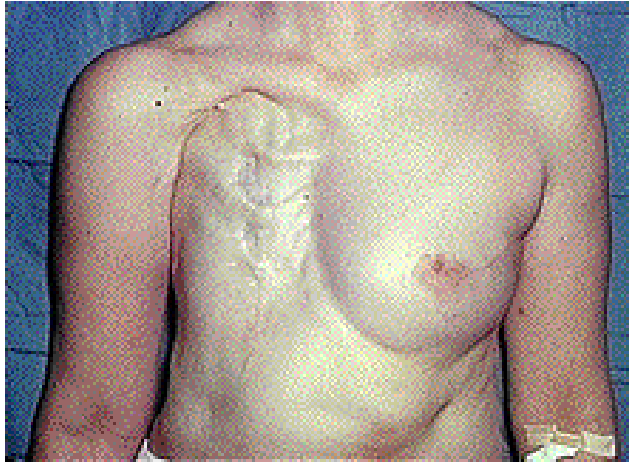
Halsted model

Fisher model



SIGNIFICANT PROGRESS

Radical mastectomy



1975

Nipple sparing mastectomy
With DIEP Flap



2005

Many battles over 30 years by
determined advocates to effect this
change including breast surgeons,
plastic surgeons and patients!!

AWARENESS



THINK PINK

October is
Breast Cancer
Awareness Month!

SUPPORT
THE
FIGHT!

PARANOIA?



TWENTY-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL COMPARING TOTAL MASTECTOMY, LUMPECTOMY, AND LUMPECTOMY PLUS IRRADIATION FOR THE TREATMENT OF INVASIVE BREAST CANCER

BERNARD FISHER, M.D., STEWART ANDERSON, PH.D., JOHN BRYANT, PH.D., RICHARD G. MARGOLESE, M.D., MELVIN DEUTSCH, M.D., EDWIN R. FISHER, M.D., JONG-HYEON JEONG, PH.D., AND NORMAN WOLMARK, M.D.

TOTAL MASTECTOMY VERSUS LUMPECTOMY

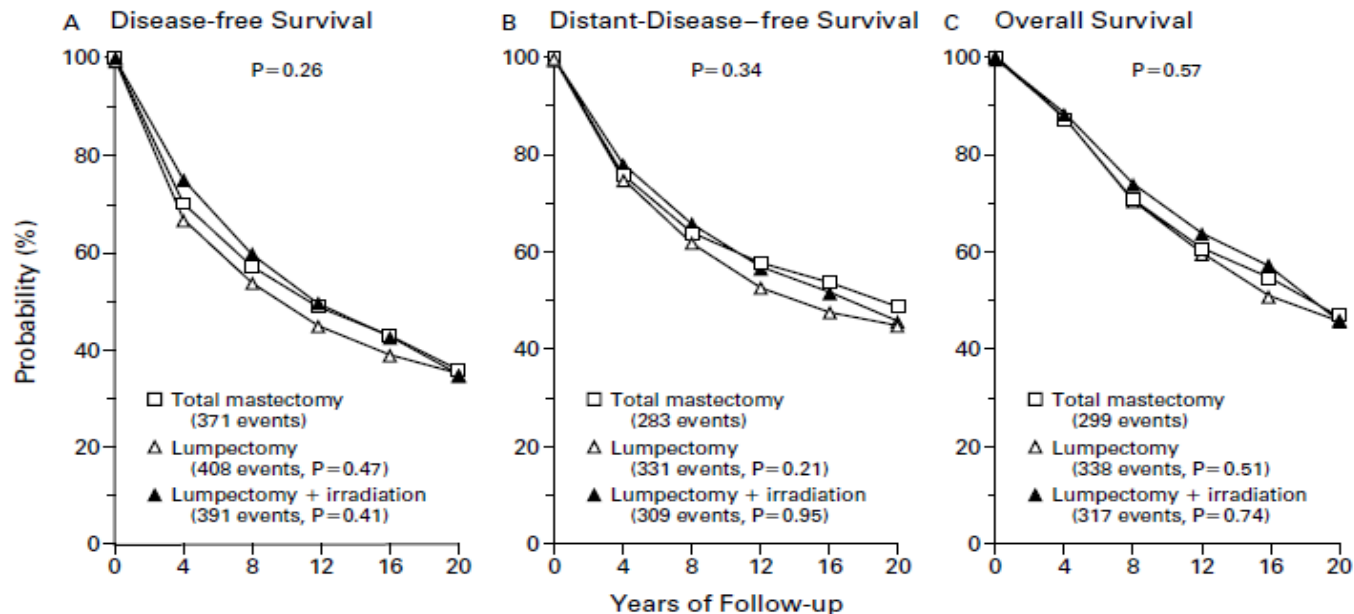


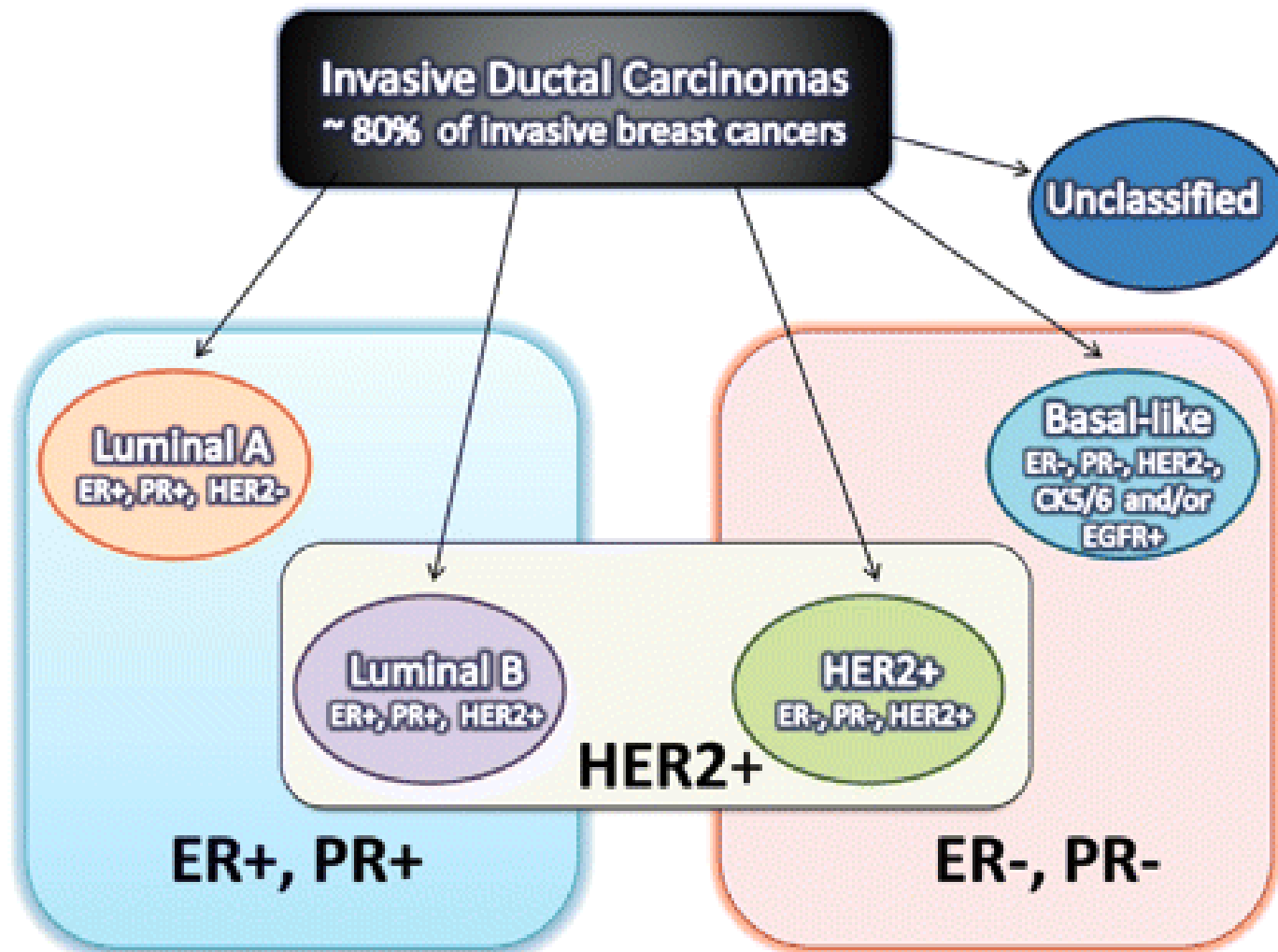
Figure 2. Disease-free Survival (Panel A), Distant-Disease-free Survival (Panel B), and Overall Survival (Panel C) among 589 Women Treated with Total Mastectomy, 634 Treated with Lumpectomy Alone, and 628 Treated with Lumpectomy plus Irradiation.

In each panel, the P value above the curves is for the three-way comparison among the treatment groups; the P values below the curves are for the two-way comparisons between lumpectomy alone or with irradiation and total mastectomy.

Contraindications to Breast Conservation

- Multicentric (not multifocal) cancer
- Radiation concern-prior RT, active collagen vascular disease, pregnancy
- Inflammatory breast cancer
- Unfavorable tumor/breast size-feasible after preoperative chemo/hormonal Rx
- Nipple involvement-central lumpectomy
- Strongly + family hx; deleterious mutation, BRCA, PALB 2, etc.

Breast Cancer Phenotypes



Neoadjuvant(preop) systemic therapy

- 48yo,G1P1, premenopausal, 4cm R breast mass, neg fam hx, mammo dense, FNA=grade 3 IDC,ER/PR-,her-2-neu 3+
- Desires breast conservation/ unfavorable tumor/breast size ratio
- Workup-PET/CT–suspicious right axilla,no disease elsewhere
- Preop chemo; Complete pathological response
- Lumpectomy and sentinel node biopsy. NO RESIDUAL CANCER! (up to 70% ER-PR- her-2neu+)

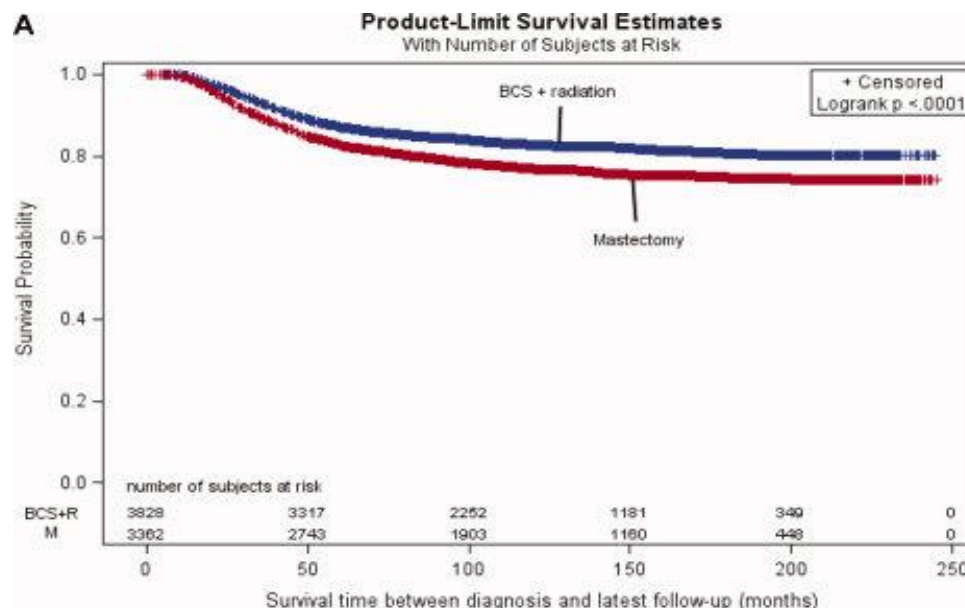
Nationwide Trends in Mastectomy for Early-Stage Breast Cancer

- NCDB review >1.2 million women 1998-2011
- 35.5% mastectomy
- 34% increase mastectomy in BCS eligible pts last 8 years
- Greatest increase in mastectomy with clinically node negative and DCIS
- Bilateral mastectomy for unilateral disease increased from 1.9%(1998) to 11.2%(2011)

Reasons for choosing mastectomy

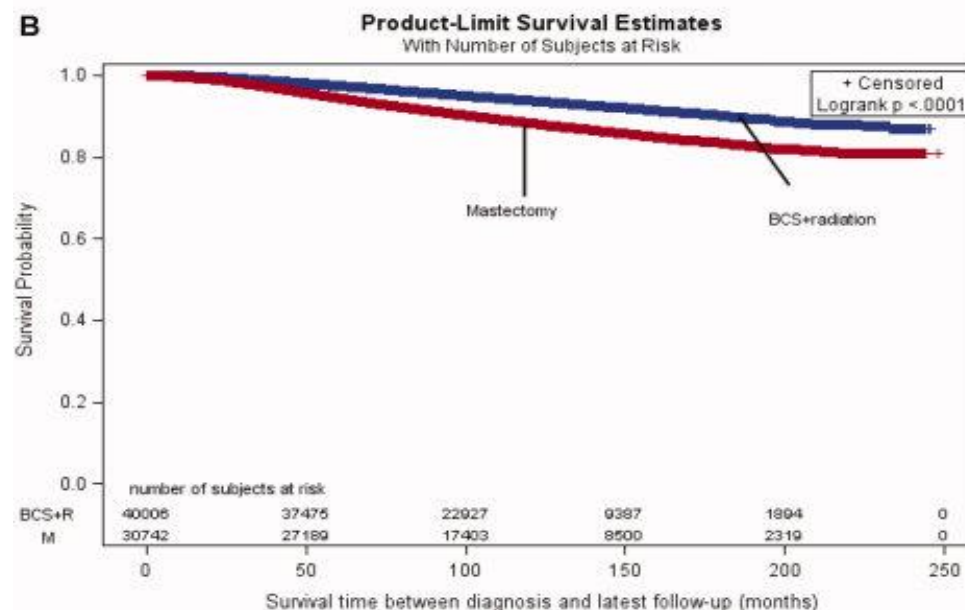
- Increased use of skin sparing and nipple sparing mastectomy with immediate reconstruction
- Peace of mind-if bilateral, better symmetry, NO MORE MAMMOGRAMS/MRI
- Patients are more proactive, and are given information through support groups, media, and the internet
- Breast MRI
- HOWEVER: BREAST CANCER SPECIFIC SURVIVAL MAY ACTUALLY BE WORSE!!

Survival after lumpectomy and mastectomy for early stage invasive breast cancer



112,154 pts
From 1990-2004

Age < 50 ER-



Age > 50 ER+

How can breast conservation have a better survival than mastectomy?

- Mastectomy does not remove all breast tissue
- Radiation can treat larger region of breast tissue completely
- MA 32 trial suggests comprehensive radiation may improve survival
- Complex since tumor subtype and targeted systemic therapy major impact on local control
- Consider current trials with no surgery after neoadjuvant chemotherapy and clinical CPR

Should patients with early breast cancer still be offered the choice of breast conserving surgery or mastectomy?

- Unless clear contraindication to BCT or deleterious gene mutation- discourage mastectomy! BEST WAY TO PREVENT UNNECESSARY CONTRALATERAL PROPHYLACTIC MASTECTOMY!!!
- Mastectomy- lower body image, lower sexual functioning, lymphedema risk(management axilla), increased chronic pain issues, increased health dollars(with reconstruction)-UK not covered!!

Johs EJSO 2016,Tsai ASO 2009,Engel Breast J 2004

Factors Associated with increase in contralateral prophylactic mastectomy(CPM)

- Younger age, educated, well insured
- Tumor factors- Multicentric disease, lobular histology, or extensive DCIS in the ipsilateral breast
- BRCA + gene or genetic testing
- Anxiety about cancer and desire to reduce cancer risk
- Plans for immediate breast reconstruction
- Optimal cosmesis with best symmetry
- Approaching 25%

Balch, et al. "Mastectomies on the rise for breast cancer: The tide is changing." Ann Surg Oncol 2009 16: 2669- 2672

“Providers should provide the following CPM information to every patient considering for unilateral breast cancer, (excluding high risk patients like BRCA carriers).”

Contralateral Prophylactic Mastectomy Consensus Statement from American Society of Breast Surgeons: Framework for Shared Decision Making

ANNALS SURG ONC 2016, BOUGHEY et al

CPM Discussion Guide

- For most women, the estimated risk of cancer in the opposite breast is 2-6% over the next 10 years. This means you have a 94-98% chance of not getting cancer in your opposite breast over the next 10 years or more.
- CPM is not 100% protective against cancer forming in your other breast.
- CPM will not improve your cure rate for your known cancer.

CPM Discussion Guide

- CPM will not reduce your risk of cancer returning from your known cancer
- CPM will not reduce your need for other cancer treatments for your known cancer (adjuvant therapy), if indicated
- The risk of surgical complications at the surgical site is approximately twice as high when CPM is performed.

CPM Discussion Guide

- CPM results in permanent numbness of the chest wall (and nipple if preserved).
- CPM with reconstruction will result in an increased number of operations
- Complications from CPM may delay treatment of your known cancer, including chemotherapy and radiation
- CPM may be associated with negative impact on physical, emotional and sexual well-being.

Impact of CPM on Overall Survival and Disease-Free Survival

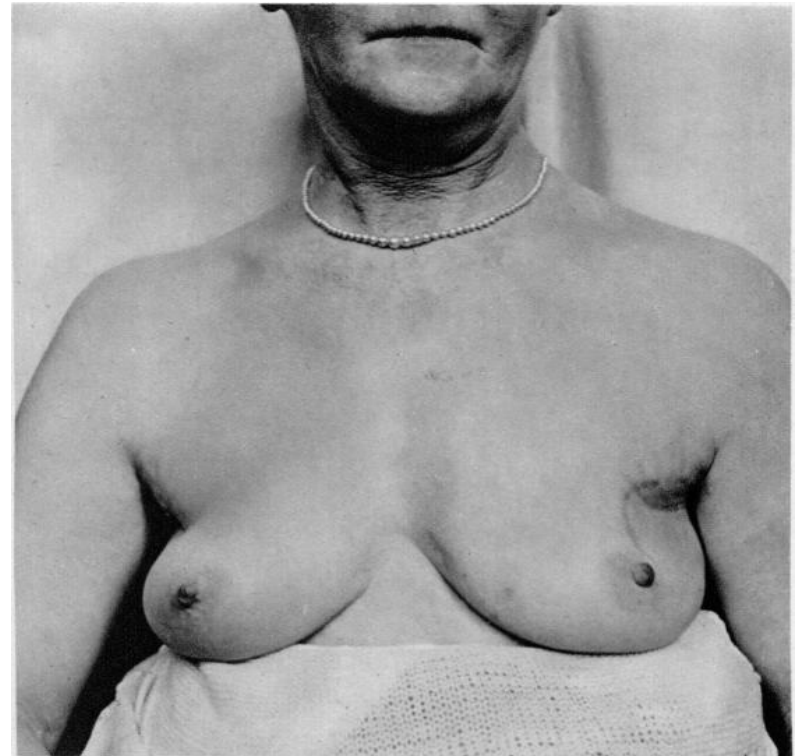
- “There are no prospective studies on the impact of CPM on overall survival (OS) and disease-free survival (DFS). In view of this, all published studies comparing OS and DFS for woman undergoing CPM with those not undergoing CPM have to be interpreted with caution, as they are retrospective and may contain known and unknown biases”
- CPM does not appear to be associated with a survival benefit, with the possible exception of BRCA carriers

Changes in Surgery

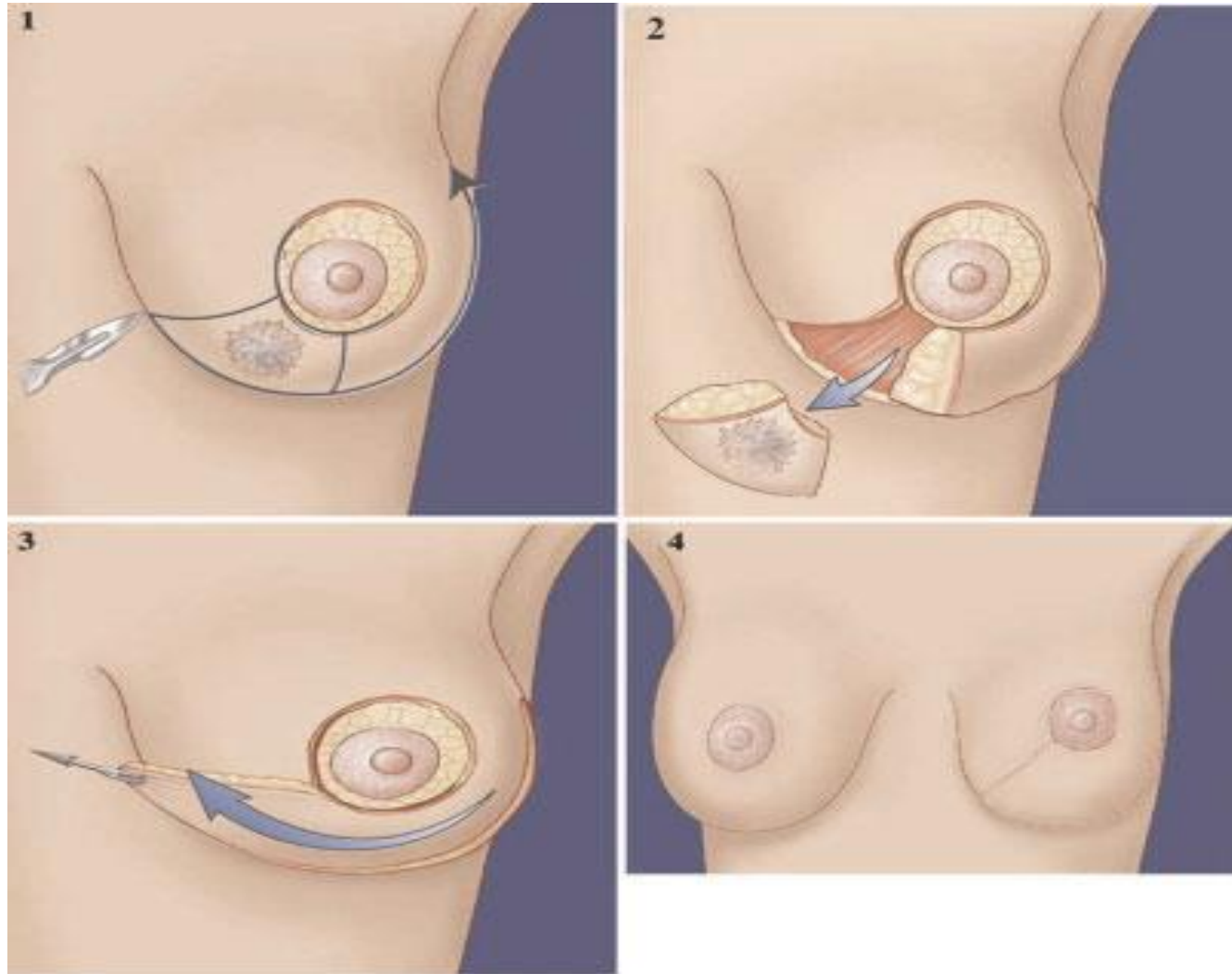


- 1948 - David Patey
 - Modified Radical Mastectomy
- 1966 - Shapiro, Strax & Venet
 - Screening mammography

- 1932 – Geoffrey Keynes
 - Breast conservation therapy with radiation



Oncoplastic Approach



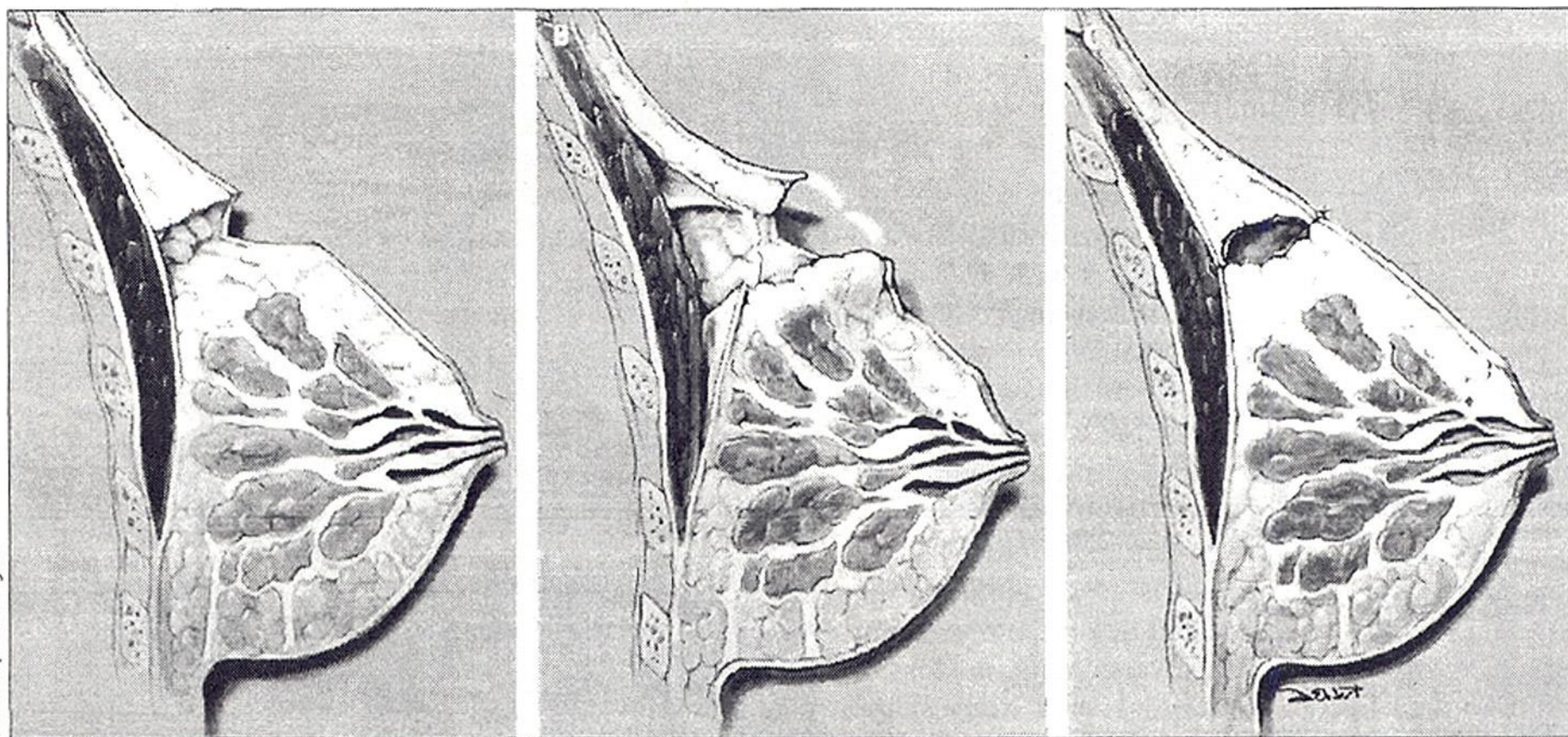
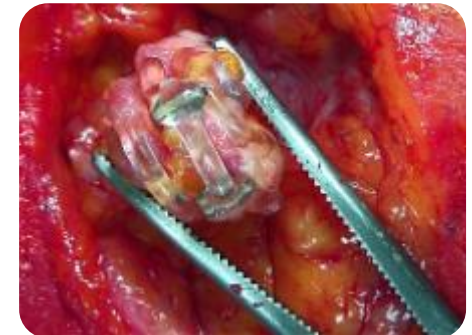


Figure 2: Closure of breast-flap mastopexy advancement in oncoplastic partial mastectomy resection

(A) Resection at full thickness from pectoralis fascia to skin, with an overlying skin island to allow proportional reduction in skin and fibroglandular tissue. (B) Fibroglandular tissue lifted off the pectoralis muscle to allow its advancement over the chest wall. (C) Closure of defect.

BioZorb

- Unique 3 dimensional marker
 - Implanted at surgery
 - Bioabsorbable framework
 - Clips remain for follow up
 - Clearly marks site of tumor removal
- Support of tissue during healing¹
 - Allows tissue in-growth within the framework
 - Minimizes fibrosis and scarring



¹Kaufman CS, et al. Clinical use of a three-dimensional tissue marker to target post lumpectomy radiation. *J Clin Oncol* 33, 2015 (suppl 28S; abstr 53)

BioZorb Implants

Spiral Design

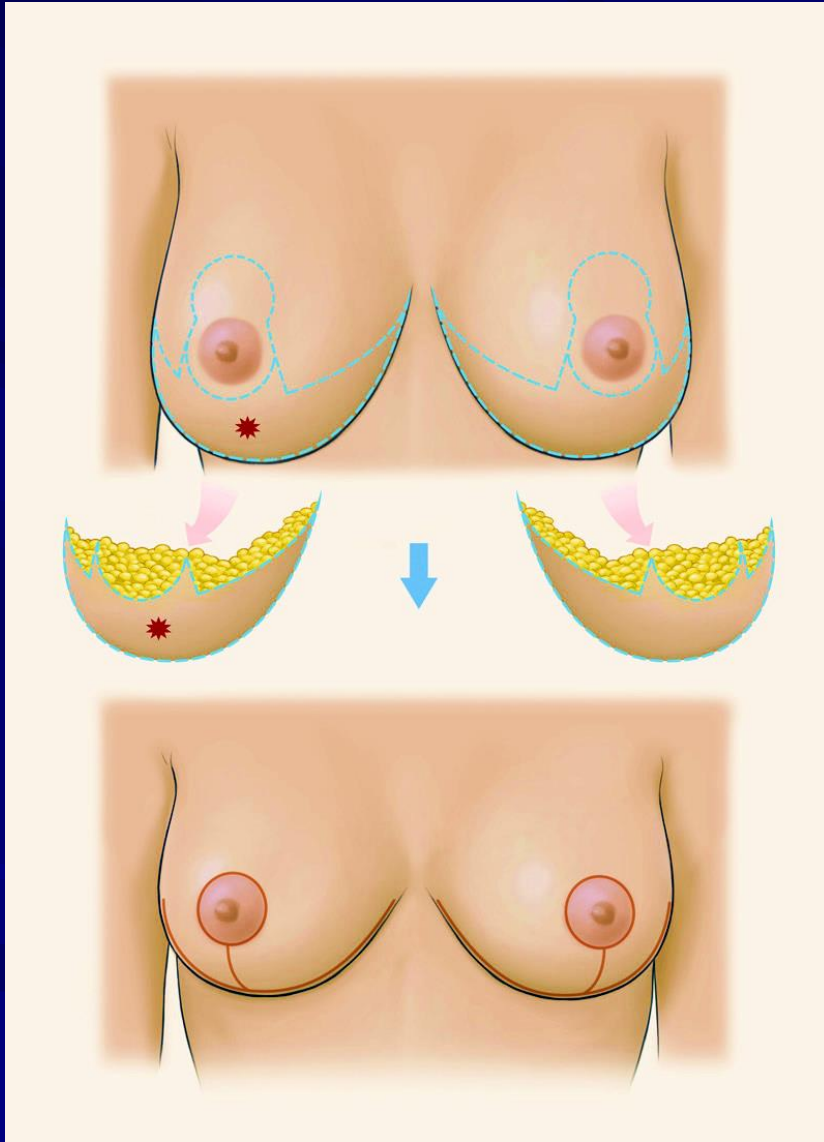


Low Profile Design*



*To accommodate smaller surgical tissue sites

Cosmesis: oncoplastic surgery



- An acceptable cosmetic appearance to the patient is an important goal of breast conservation
- Oncoplastic surgery combines cancer excision with reconstruction and symmetry
- This technique may be used in women previously unsuitable for conservation, such as large tumors or tumors in the lower pole of the breast

Breast Conservation Therapy

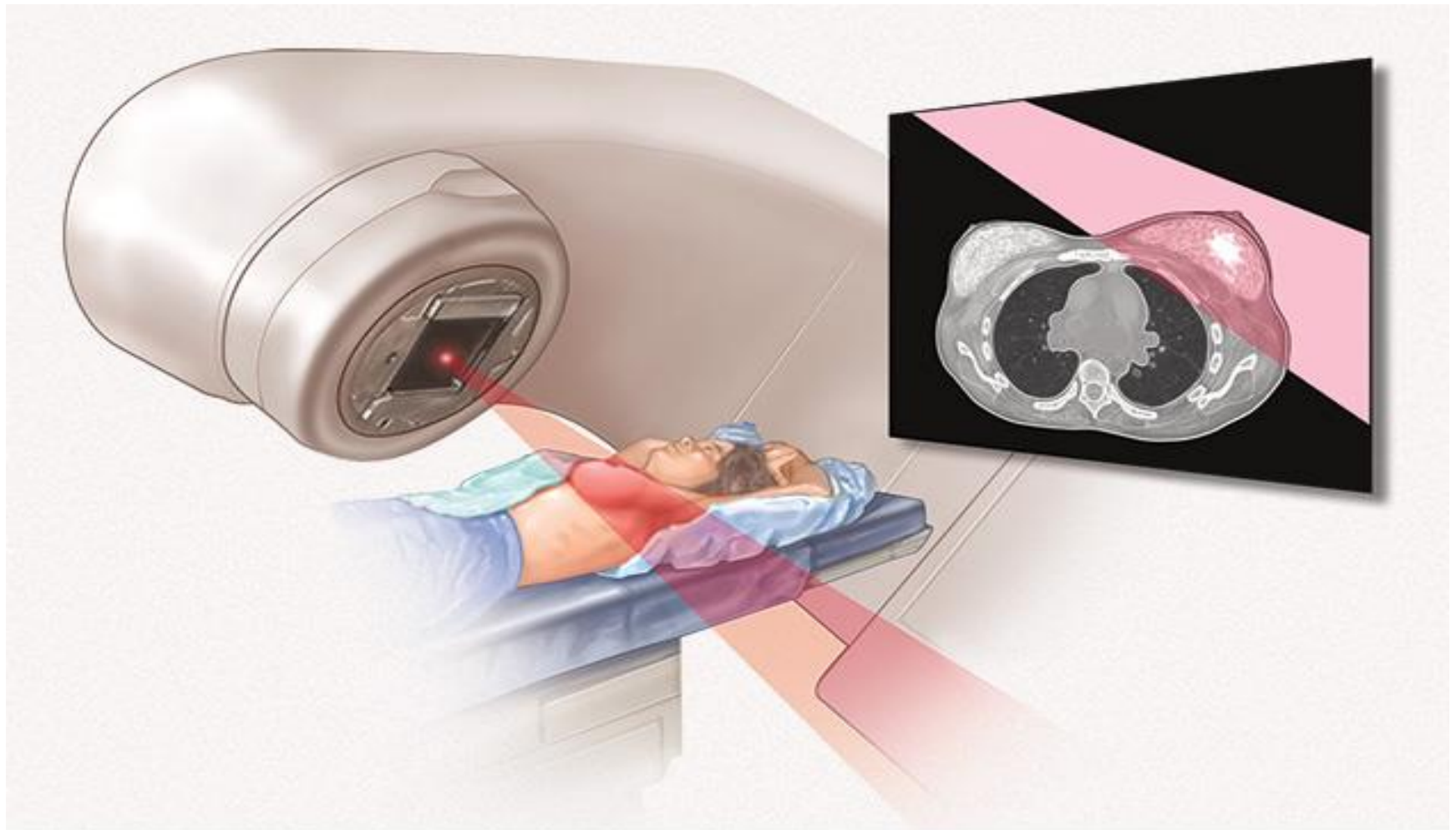
- BCT = Lumpectomy + whole breast RT; Standard of care for early stage Breast Cancer/DCIS
- RT typically 3- 6 weeks
- Mastectomy or Lumpectomy w/o RT remains common
- Access to care-COMPLIANCE ISSUES!!
- Length of treatment
- Distance to treatment – as distance increases, BCT decreases

82% <10miles

69% 50-75 miles

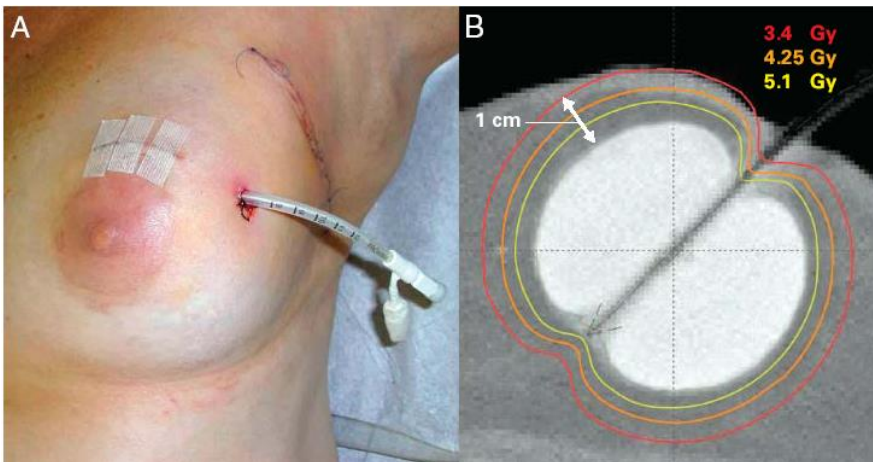
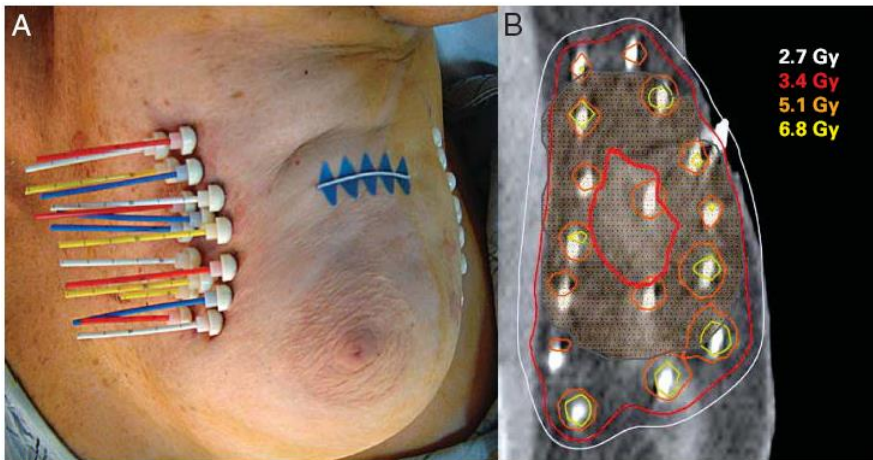
42% if >100 miles

Traditional whole breast radiation



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Partial Breast Irradiation (PBI)



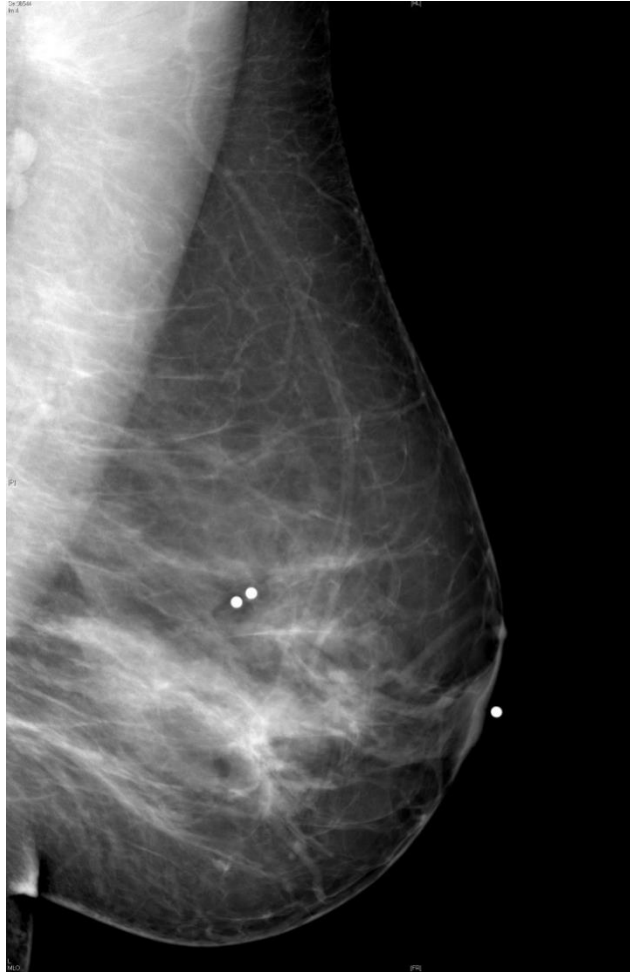
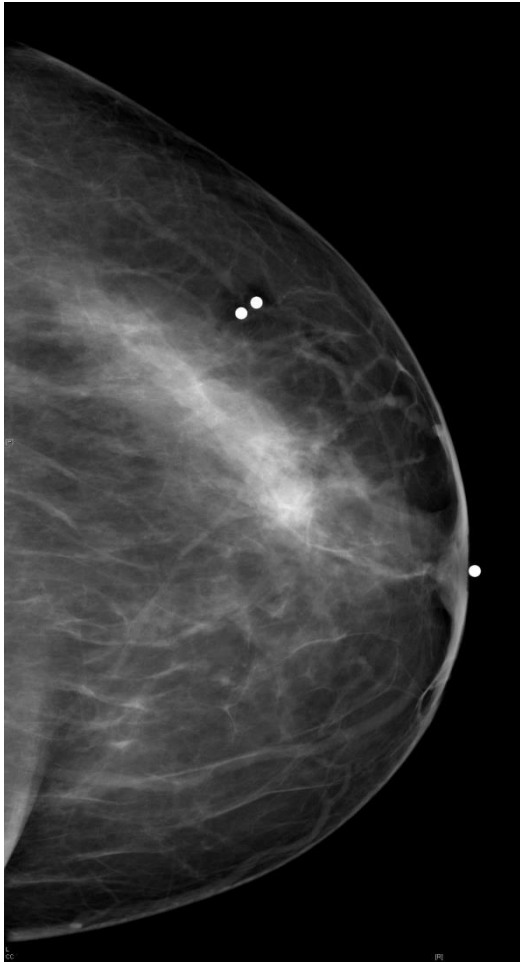
- **Larger radiation dose/fraction**
- **Brachytherapy or external beam**
- **Complete RT in 0-5 days instead of 6-7 weeks**

What is Intraoperative Radiation(IORT)?

- Technique developed since 1998
- IORT delivers dose of radiation directly to the tumor bed in the operating room
- Single dose is higher than that delivered during conventional radiation therapy, but cumulative amount of radiation is similar to conventional treatment
- Been shown to give results equivalent to weeks of whole breast radiation therapy at 6 years

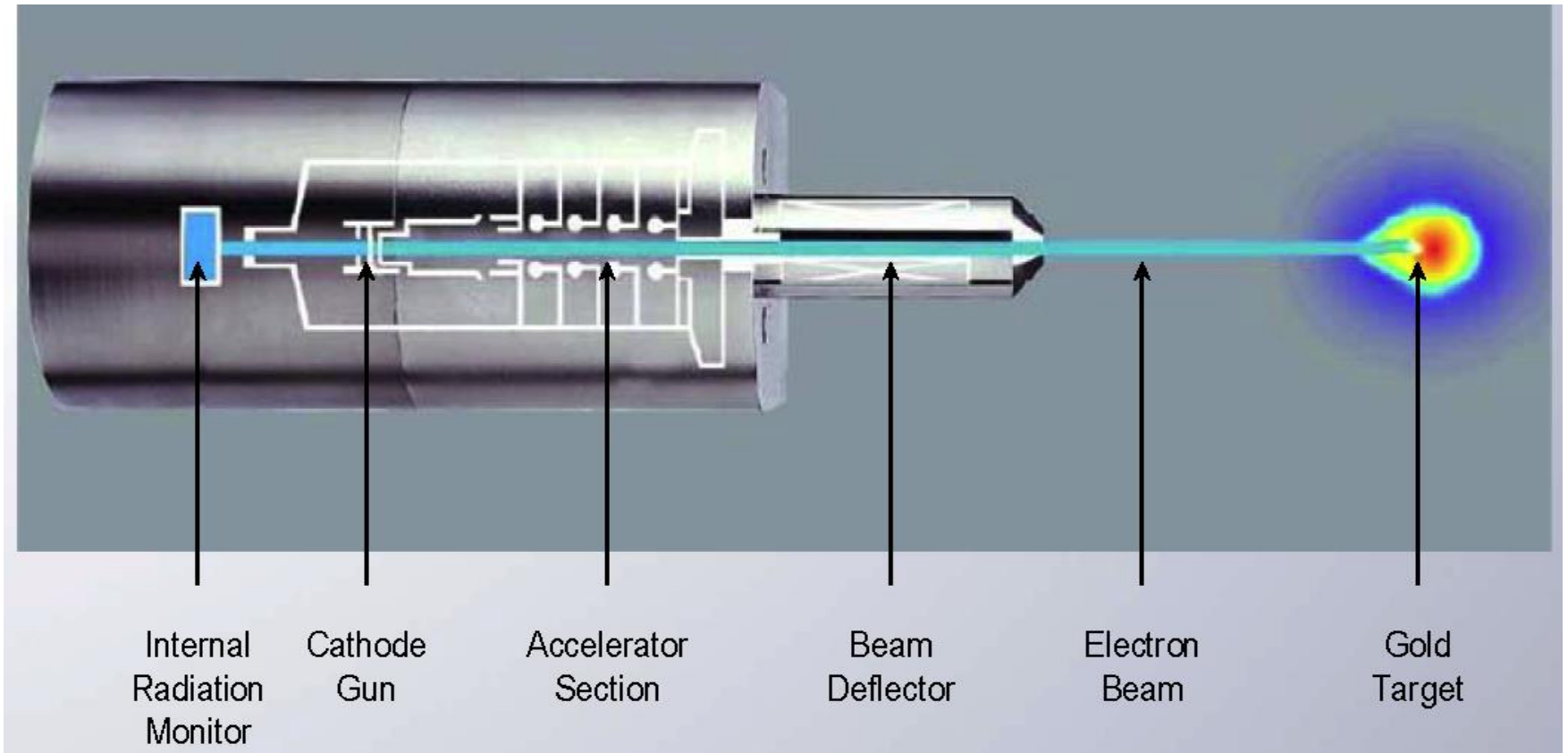
Clinical Example

- 55yo woman noted left breast mass
- Mammo/sono 1cm mass corresponding
- Sono guided core bx = invasive ductal cancer-estrogen receptor positive
- Radiation oncology consultation preop
- Outpatient surgery; lumpectomy with IORT oncoplastic repair and sent node bx
- Pathology; 1cm tumor, clean margin, node ok
- Medical oncology consult for anti-estrogen Rx



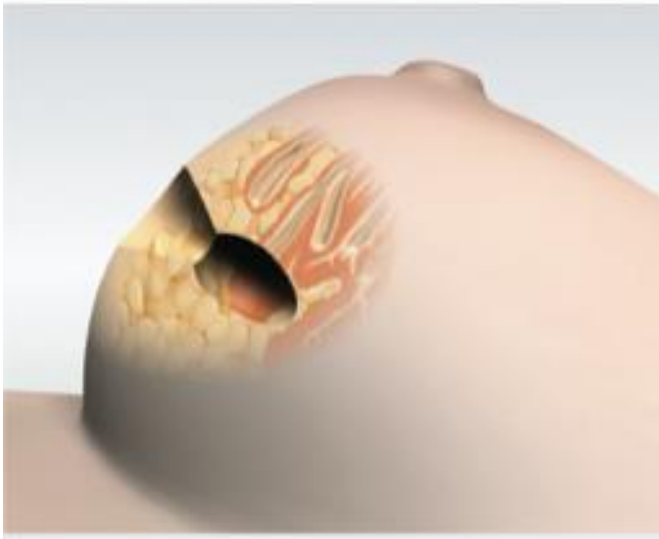


- Generates and delivers a high dose of low energy (50KeV) x-rays in a precise, spherical distribution pattern around a point source



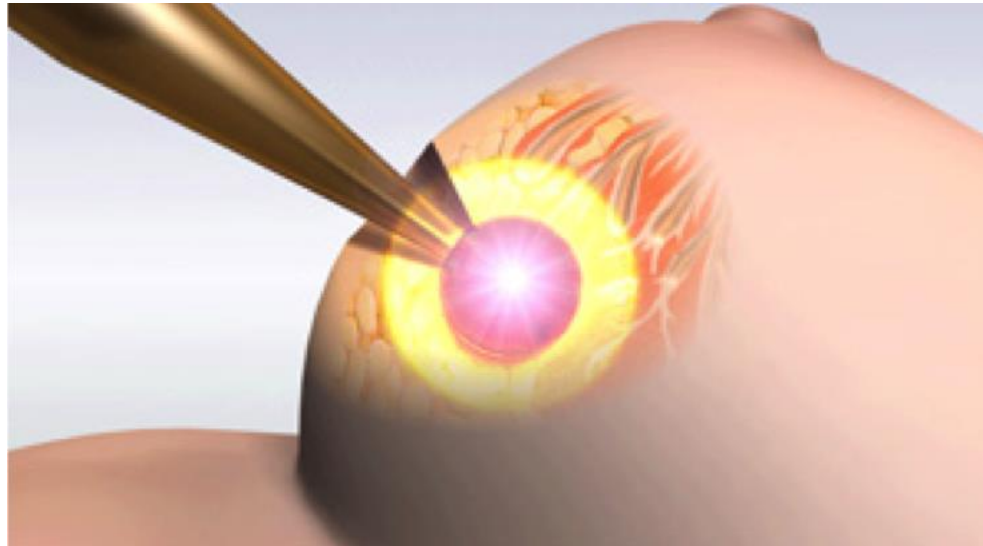


IORT Procedure in the OR

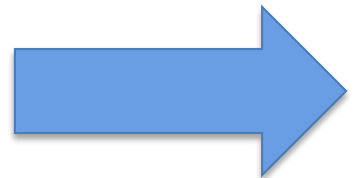


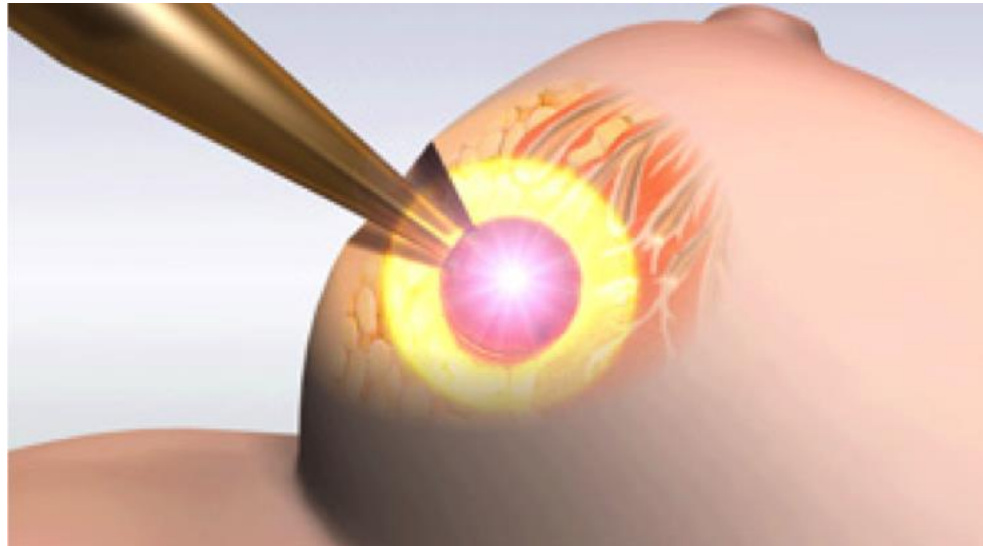
First the surgeon removes the tumor
and measures the cavity to decide
which sized applicator will be
appropriate for treatment





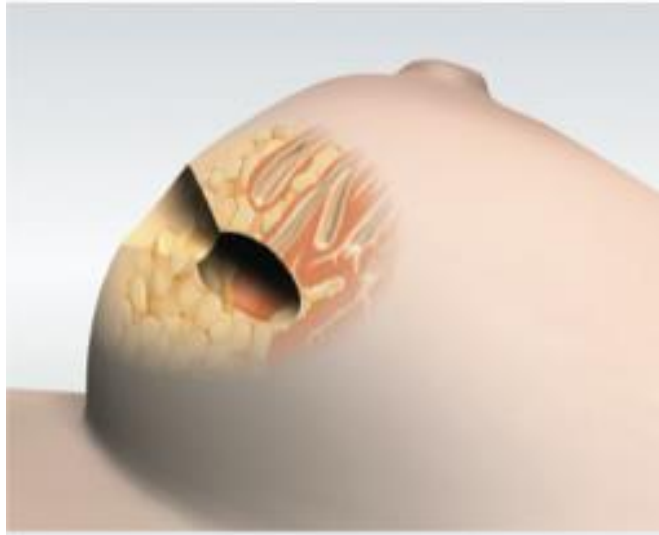
Next, the applicator is positioned within the tumor cavity.





Radiation therapy is then delivered, focused on the tumor cavity and minimizing exposure to healthy tissue.





Following treatment, the applicator is removed and the surgeon closes the cavity.

IORT with Intrabeam System

- Single procedure(lumpectomy, repair breast defect and sentinel nodebx,IORT (ONE AND DONE)
- RT compliance-logistics-travel issues resolved
- Patient centered- high satisfaction
- Robust research platform
- Financial obstacles to implementation

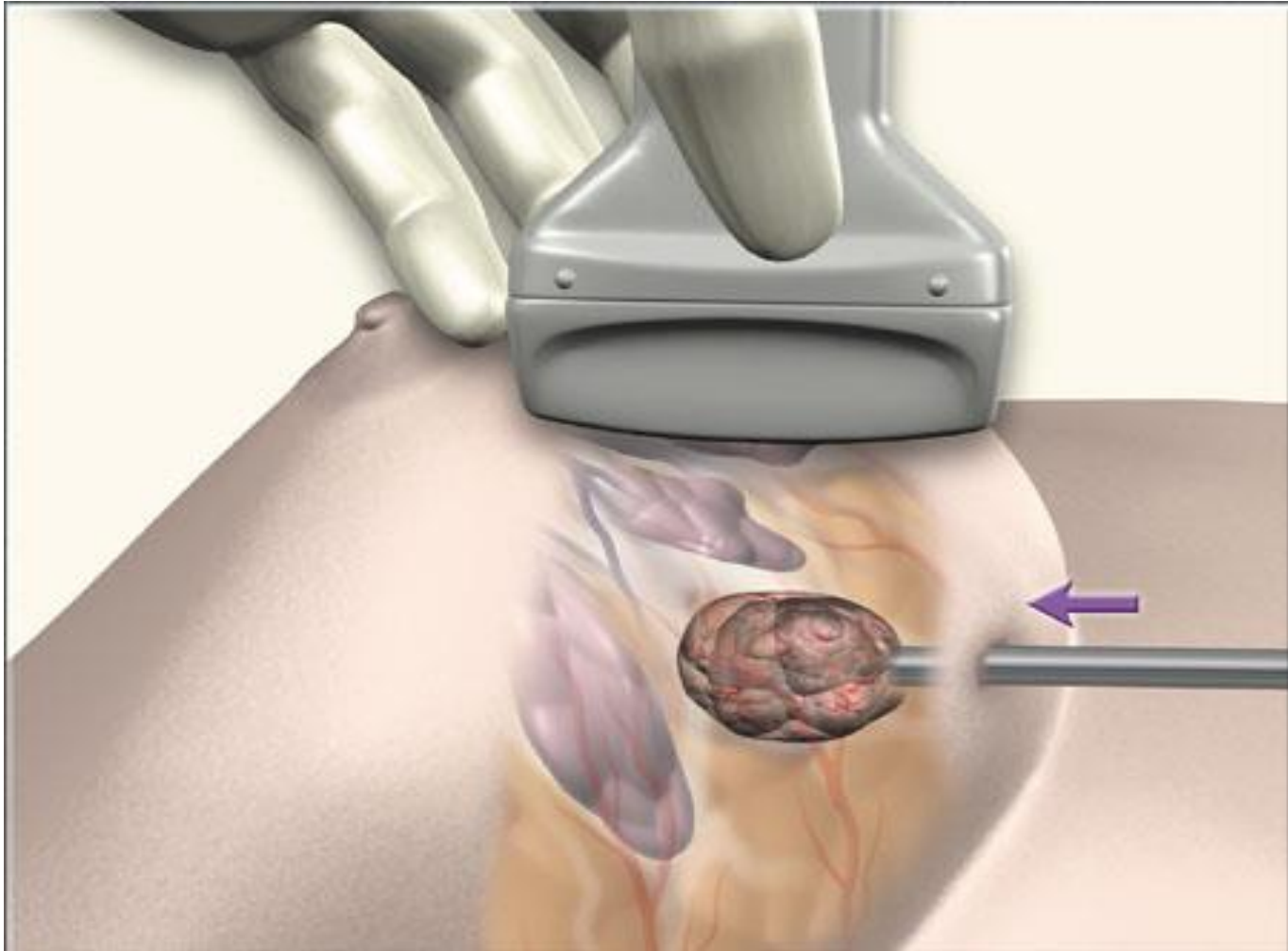
Systemic Benefit of IORT?

- Abscopal Effect: radiation makes residual tumor cells visible to immune system
- Autovaccination?
- Supportive evidence melanoma and prostate cancer
- Would effect be larger with preop stereotactic radiation or cryoablation

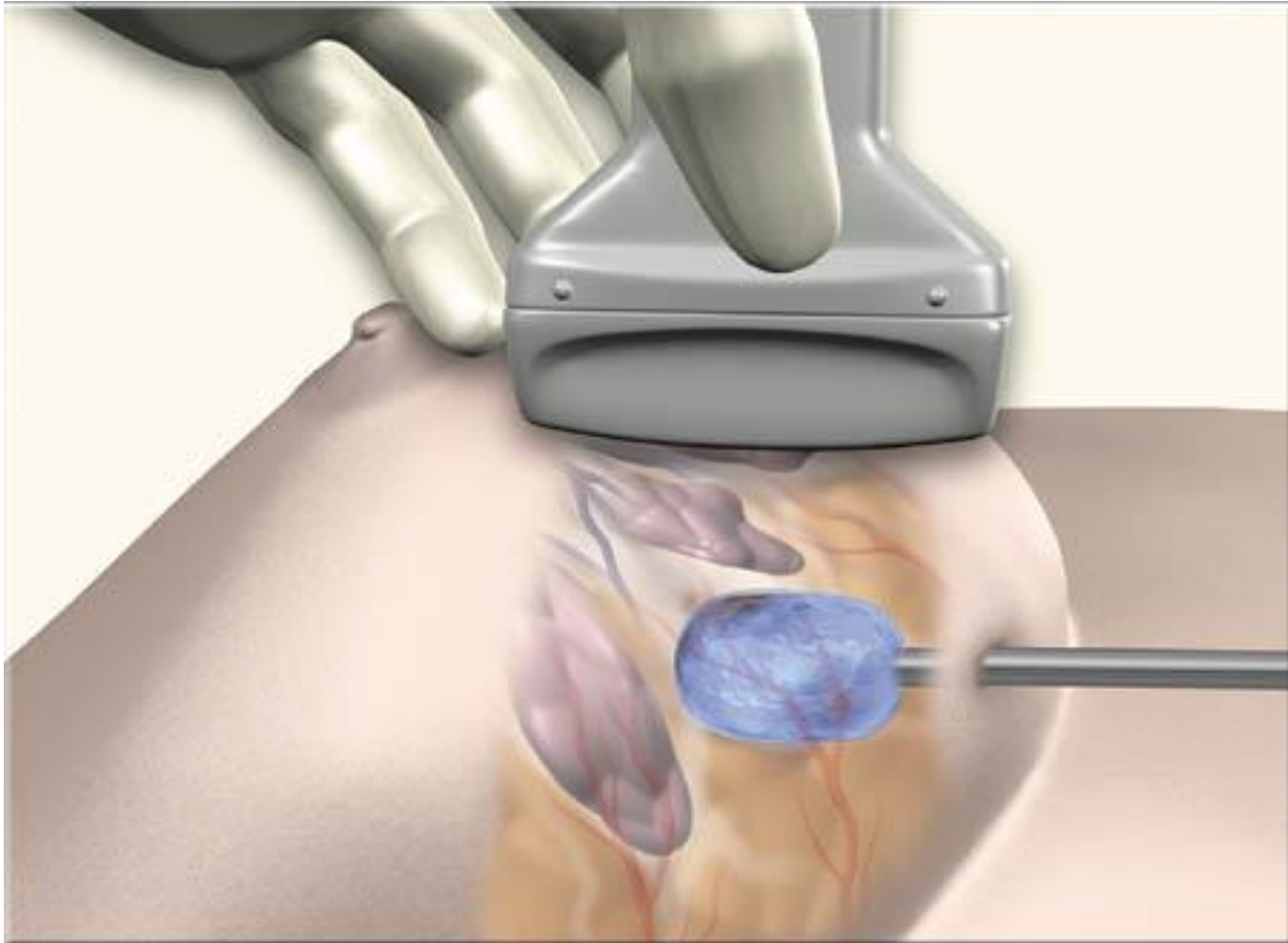
Rationale for Tumor Ablation

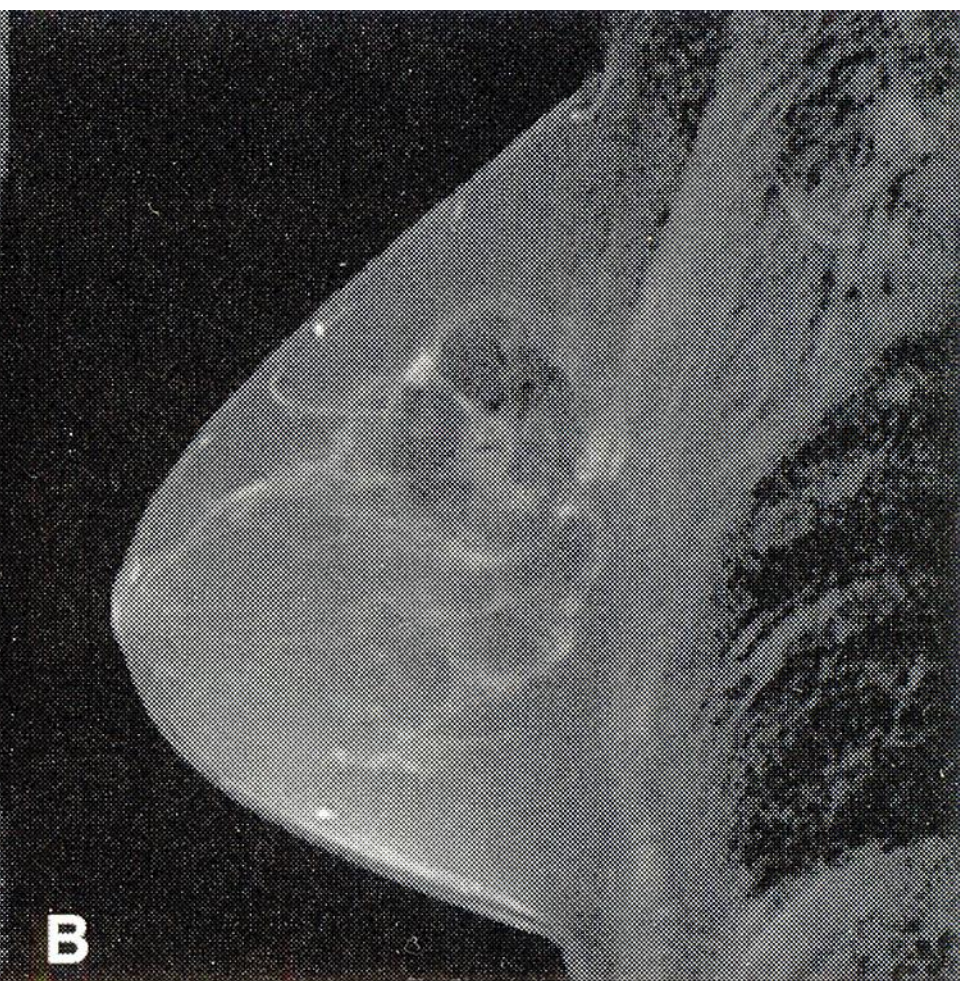
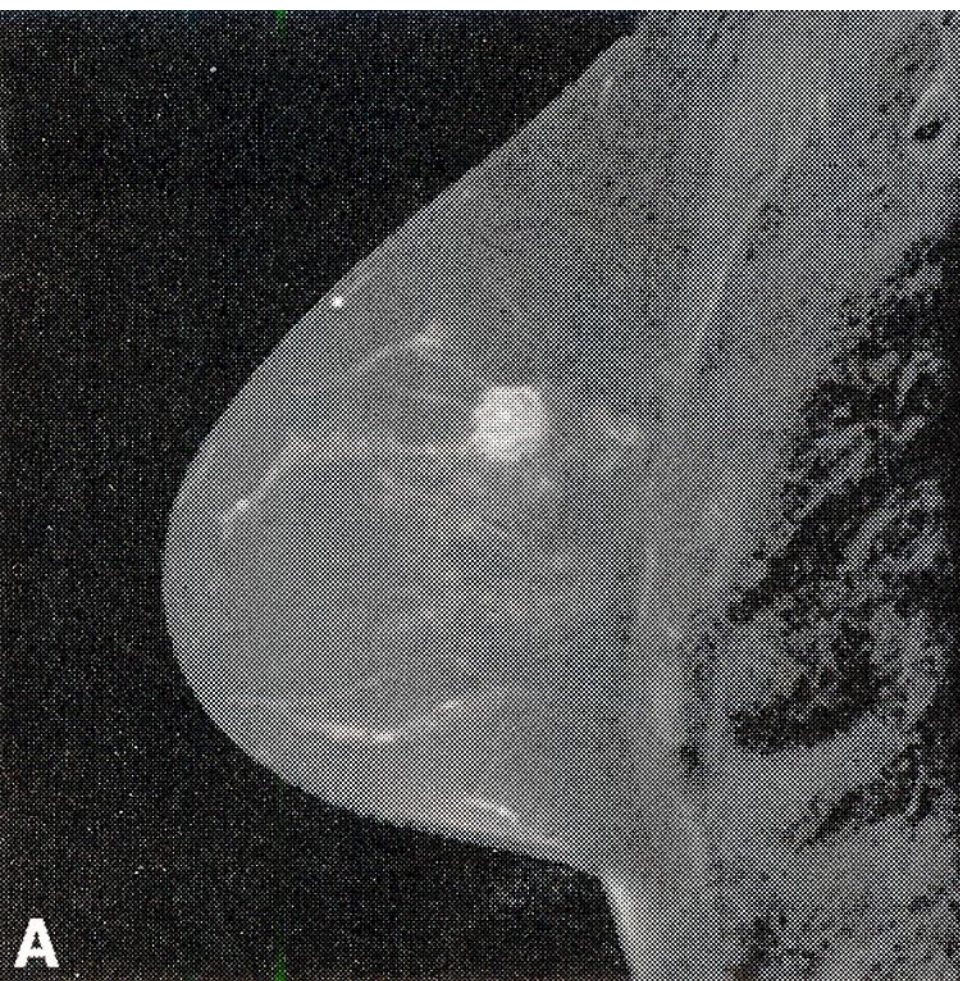
- Improved screening-more small cancers
- Favorable phenotype confirmed by core bx
- Patients prefer scarless, effective minimally invasive treatment
- Rapid advances with novel technology; laser, RFA, cryo, HIFU(Ultrasound), microwave
- Ablation dangerous targets(brain-gamma knife) routine. The breast should be easy!
- Injure tumor- leaks proteins(antigens) stimulates immune system; combine with immunotherapy to treat ALL sites of disease

CRYOABLATION



CRYOABLATION





ICE CURE CRYOSURGERY TRIAL

- Office based cryotherapy with local anesthesia
- Eligibility: age >50yo, Invasive ductal less than 1.5cm, low to intermediate grade, ER+. Tumor clearly visualized by ultrasound
- MRI, radiation, sentinel node bx optional
- Aromatase inhibitor therapy encouraged
- Mammo and ultrasound f/u q 6 months for 1 year then annually

HIFU



Patient Safety

- Non-invasive therapy
- No radiation or ionization
- Patient motion detection
- Skin cooling system

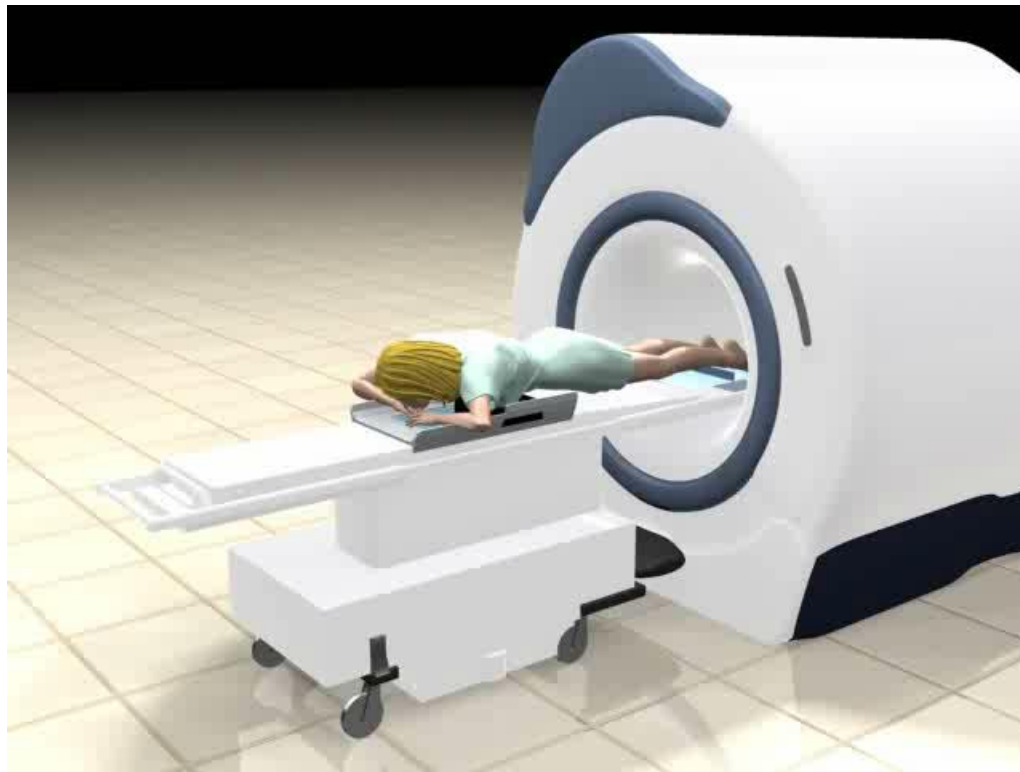
Great Accuracy

- Millimetric accuracy of dose-delivery
- High ultrasound image quality

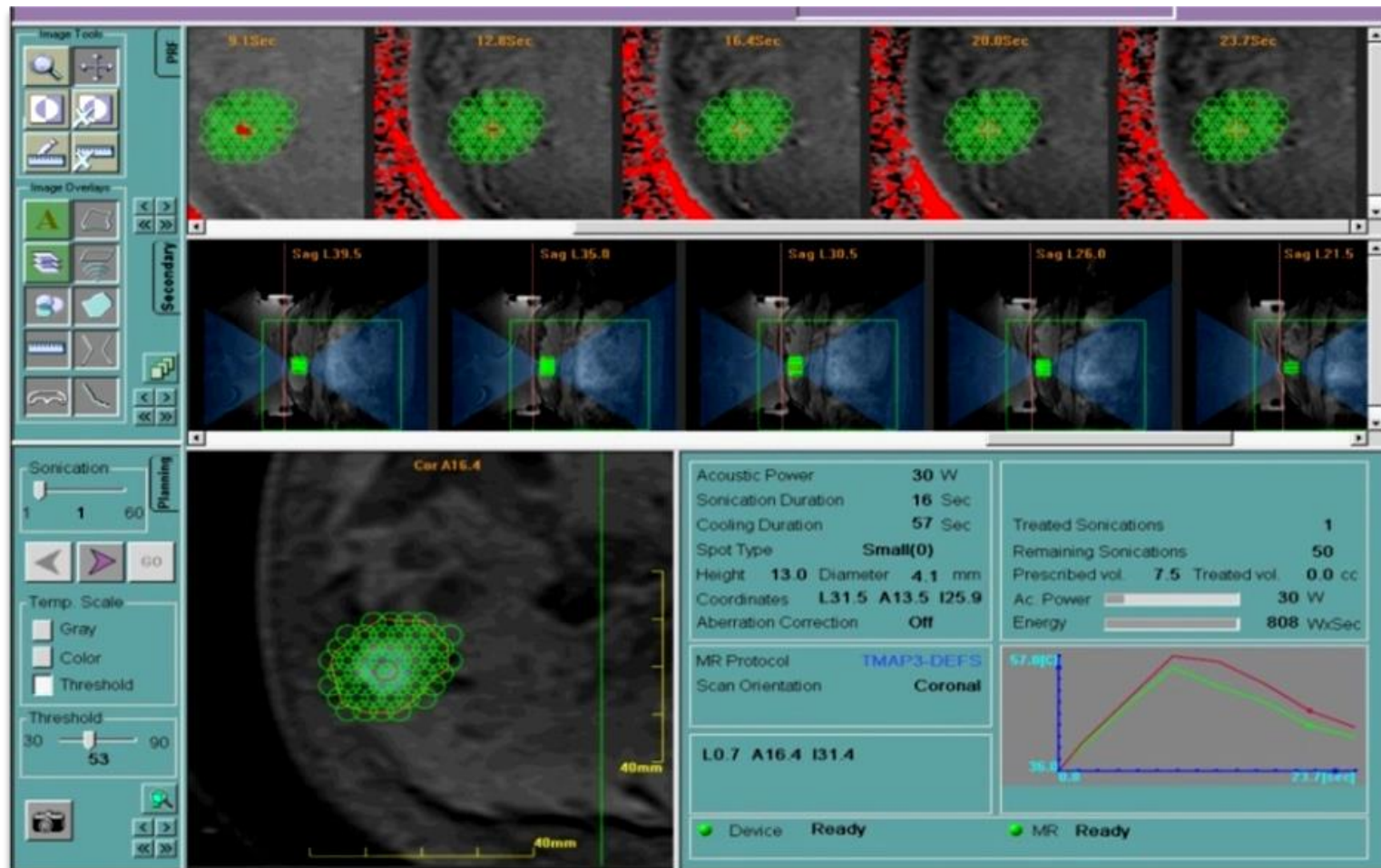
HIFU ABLATION TRIAL FOR FIBROADENOMAS

- Office based ablation with local anesthesia
- Eligibility; symptomatic fibroadenoma(painful), less than 4cm in maximum diameter
- Requires preop core biopsy to confirm diagnosis
- Ultrasound f/u q 6 months for 2 years
- Approved modality in Europe
- This is pivotal US trial

MRI-GUIDED FOCUSED ULTRASOUND ABLATION OF BREAST CANCER



MR-G HIFU ABLATION PLANNING STAGE



X-ray Irradiation

Directly Treated
Tumor

Secondary
"Abscopal"
Tumor

APC

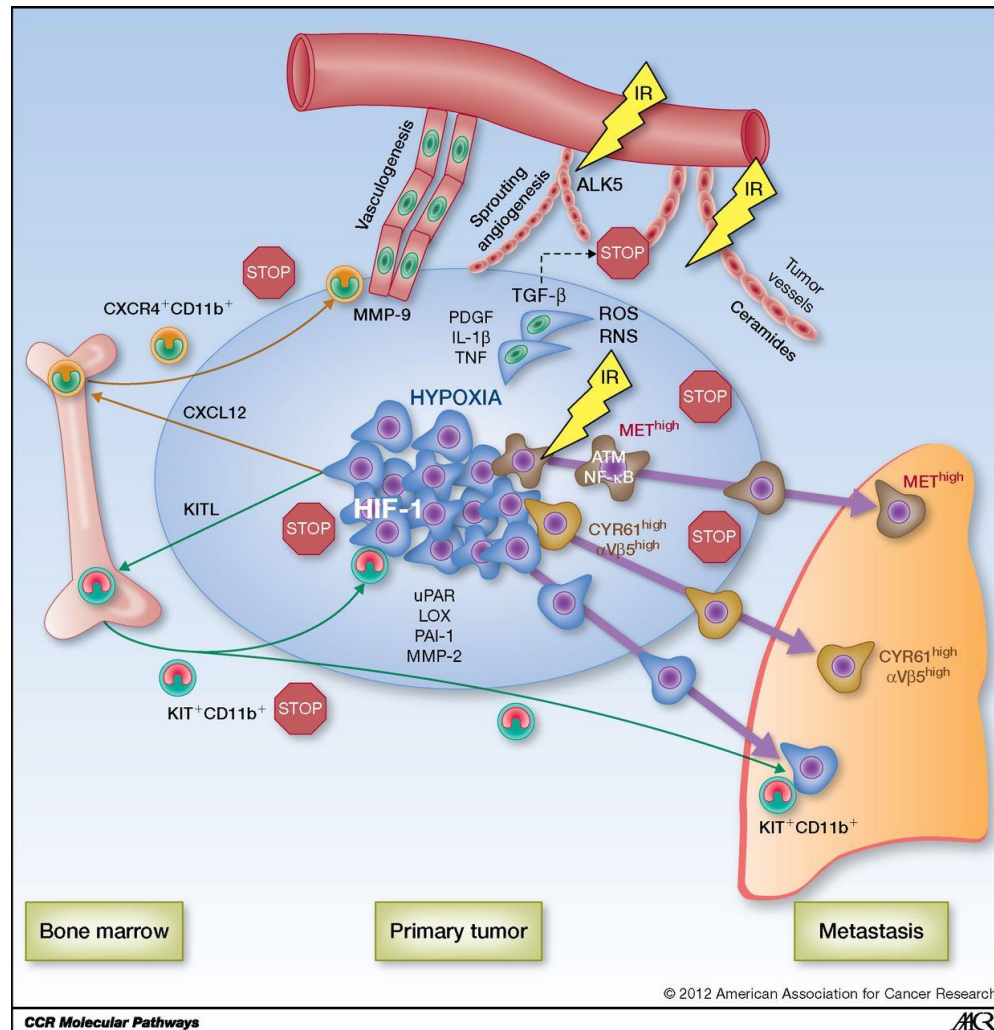
CD8

CD8

CD8

CD8

Emerging pathways mediating growth, invasion, and metastasis of tumors progressing after radiotherapy.

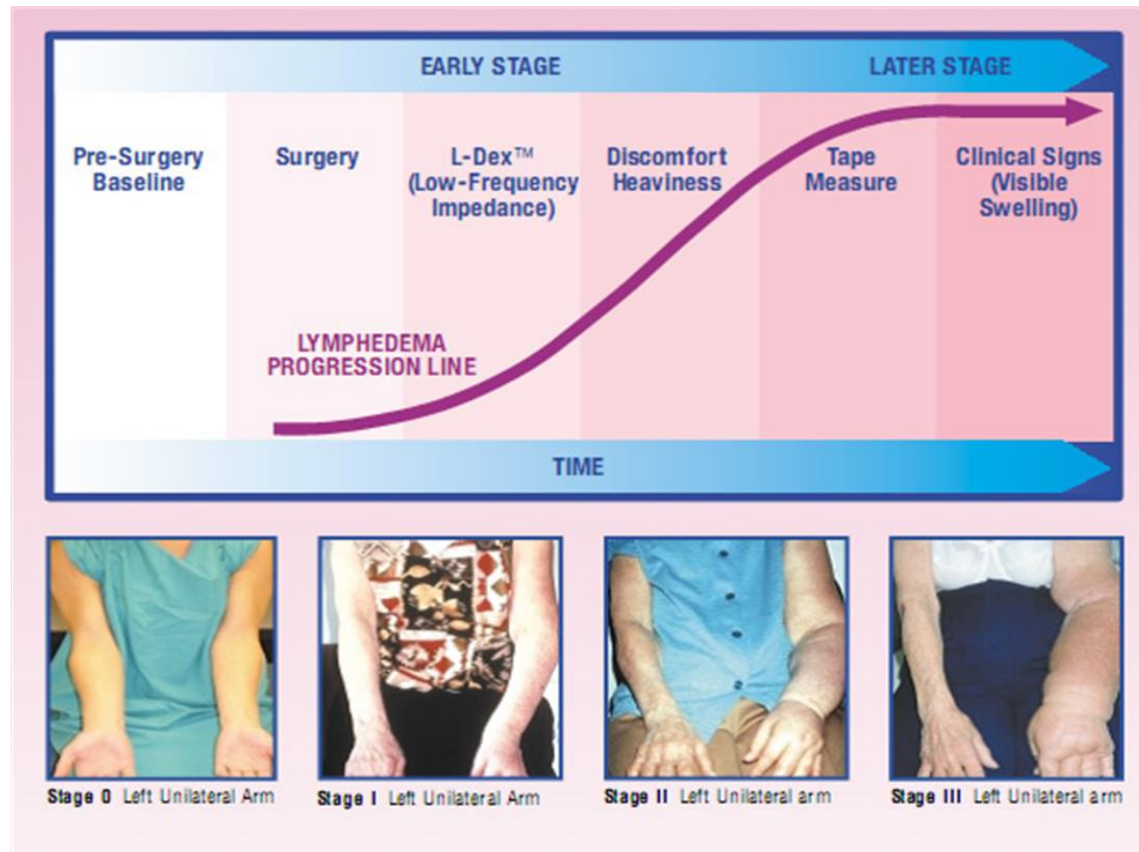


Kuonen F et al. Clin Cancer Res 2012;18:5196-5202

OVERVIEW OF LYMPHEDEMA ISSUE

- Major morbidity of breast cancer treatment
- Impacts quality of life and survivorship
- Often life long chronic therapy
- Many patients poorly controlled- infectious complications and secondary malignancy
- Risk factors; number nodes removed, BMI>30 radiation, advanced age, limited ROM
- Incidence 40% high risk group

EARLY DETECTION LIMB VOLUME CHANGES



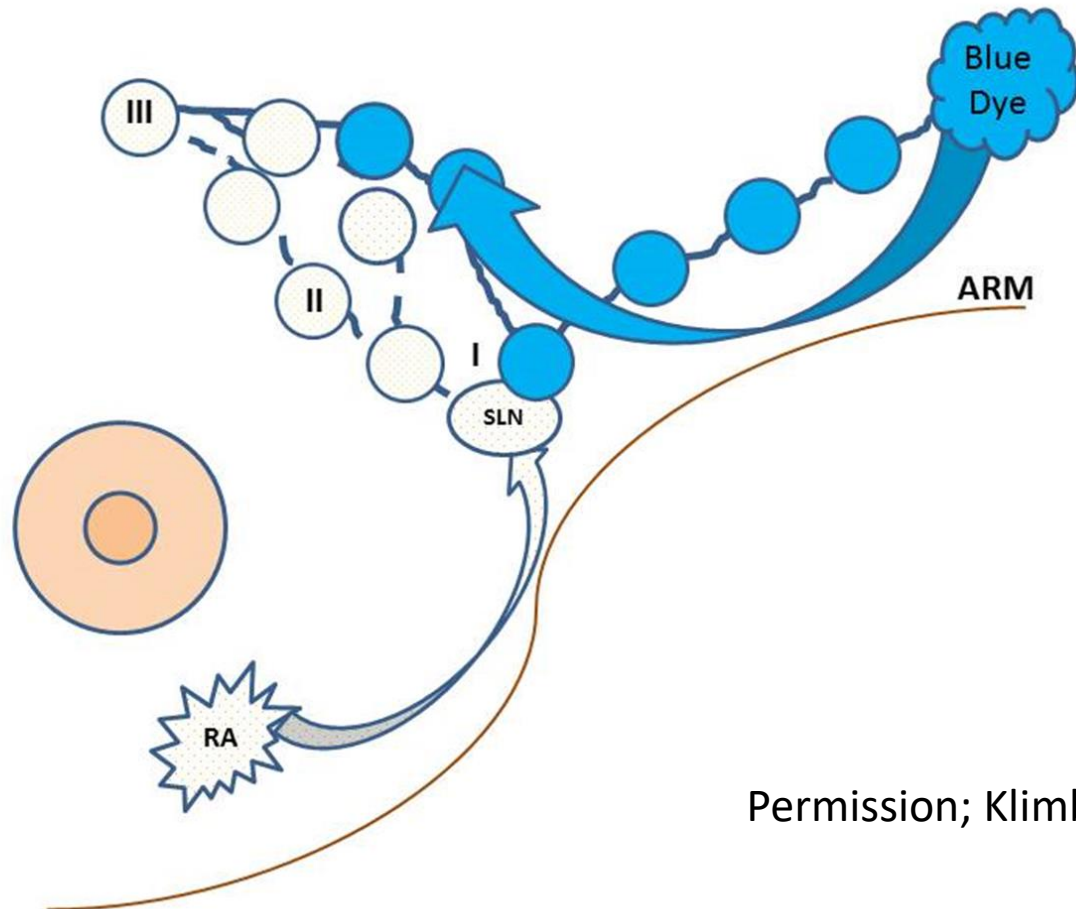
Minimize Lymphedema Risk

- Less axillary surgery- sentinel node bx, preop chemotherapy for node + patients
- No sentinel node bx if will not effect systemic Rx
- Preserve Arm nodes with mapping technique
- LYMPHA procedure if extensive residual disease requiring complete axillary dissection
- Monitor for pre-clinical volume increase with bioimpedence spectroscop[y(L-Dex)
- Patient education and awareness key
- Early physical therapy

Taking a Measurement with L-Dex^(R) U400 Bioimpedance Spectroscopy

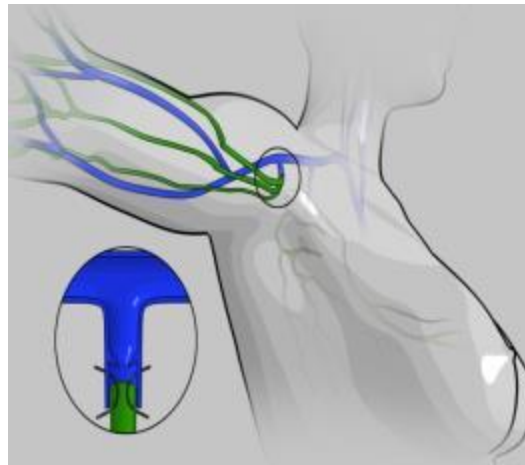
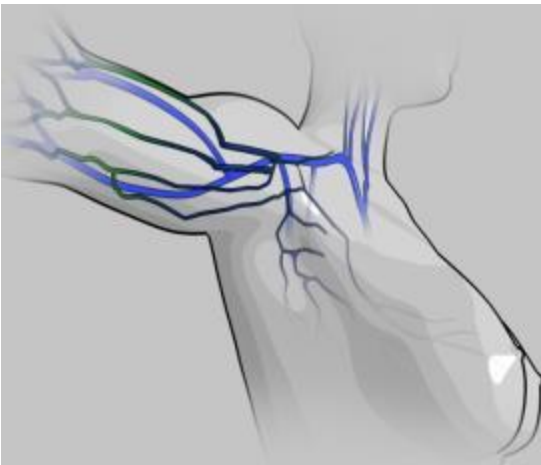
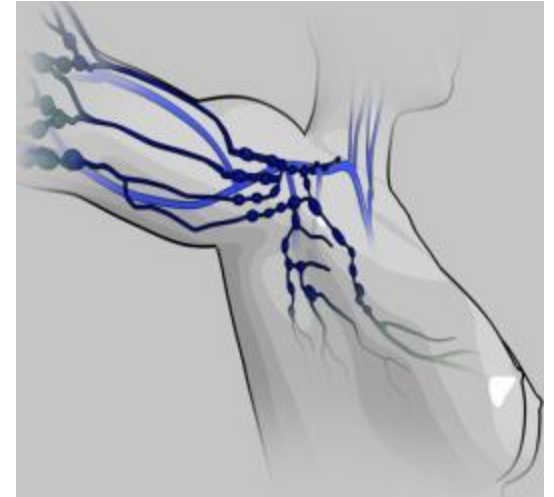
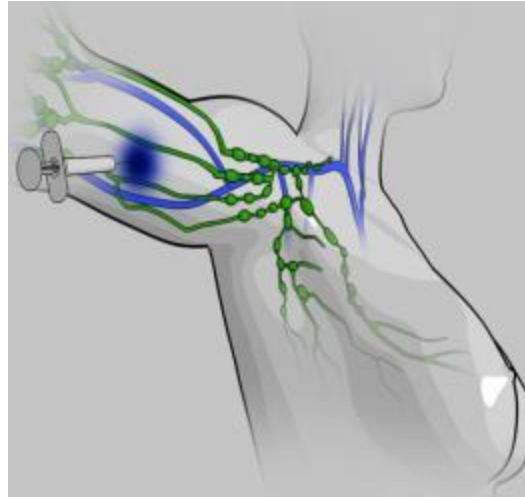
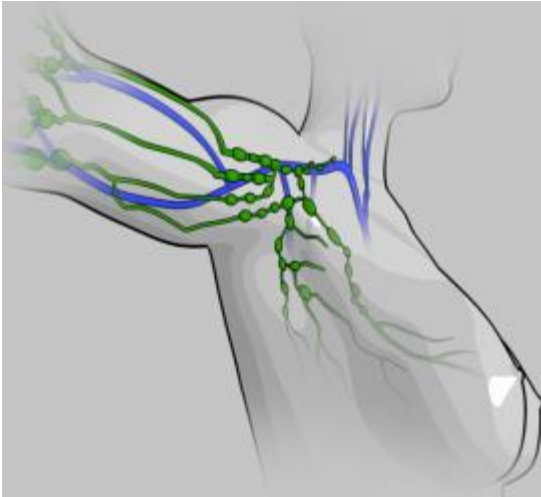


AXILLARY REVERSE MAPPING



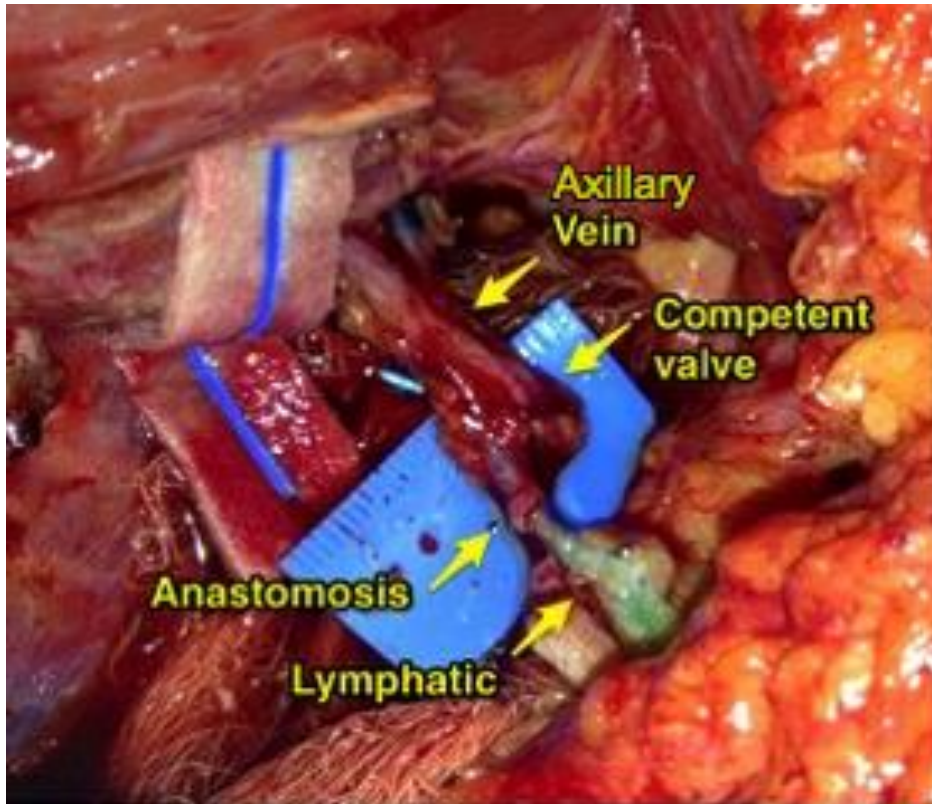
Permission; Klimberg

Lymphatic-venous anastomosis



Illustrated by Peter Kuempel.

LYMPHA PROCEDURE



- Average diameter of anastomosed vessels was 1-2 mm.



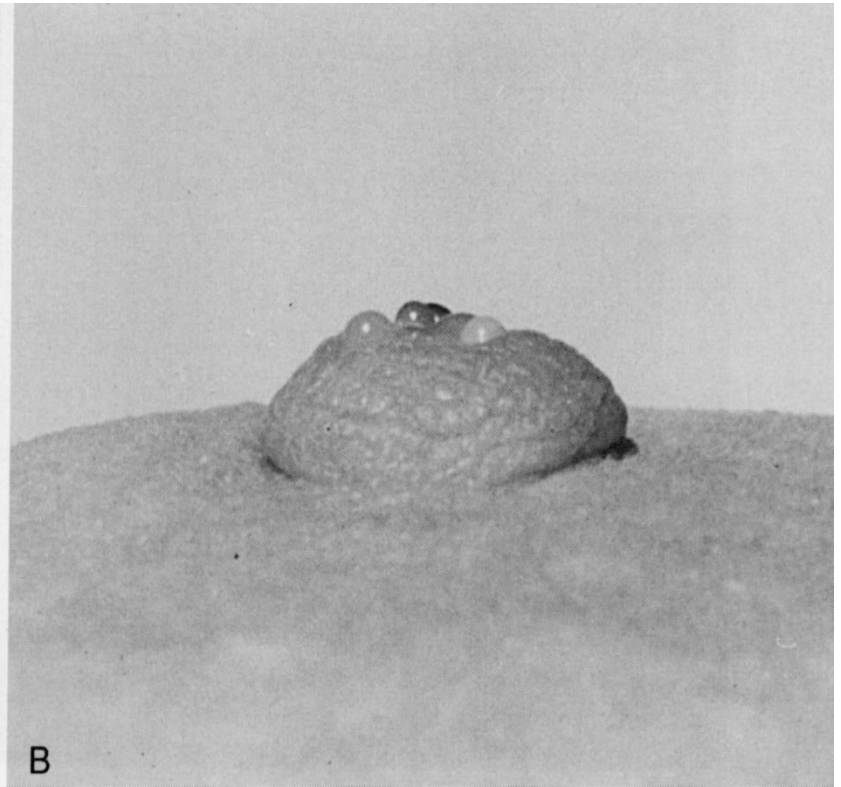
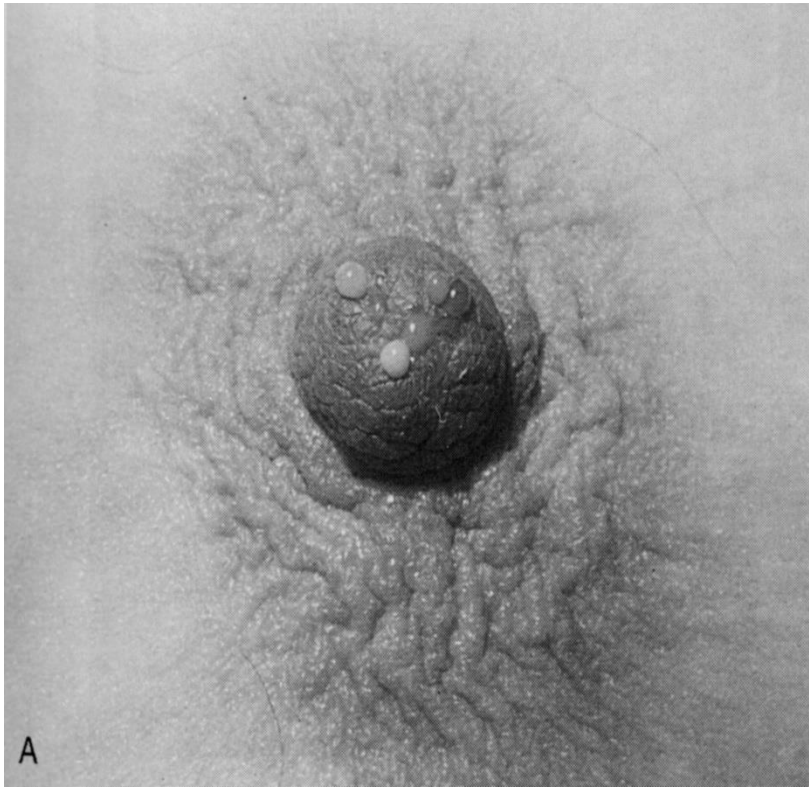
- LYMPHA added about 45 minutes of OR time.
- Study patients experienced no LVA-related complications.

Access to Where Cancer Starts has Great Potential : Pap smear model

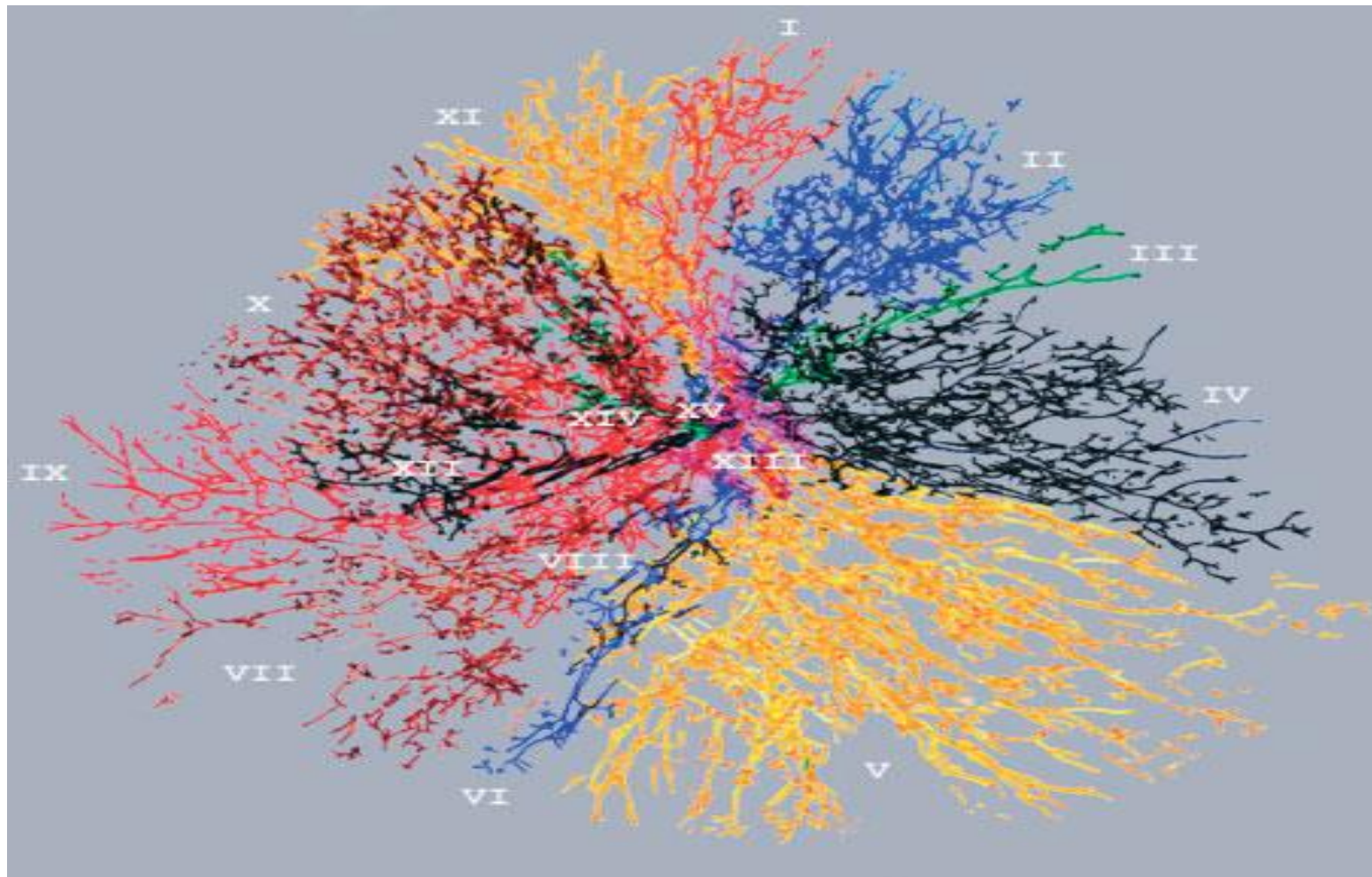
- Screening for markers in fluid and/or exfoliated cells
- Intraductal Prevention and Therapy
- Monitoring of Risk



Nipple Aspirate Fluid (NAF)

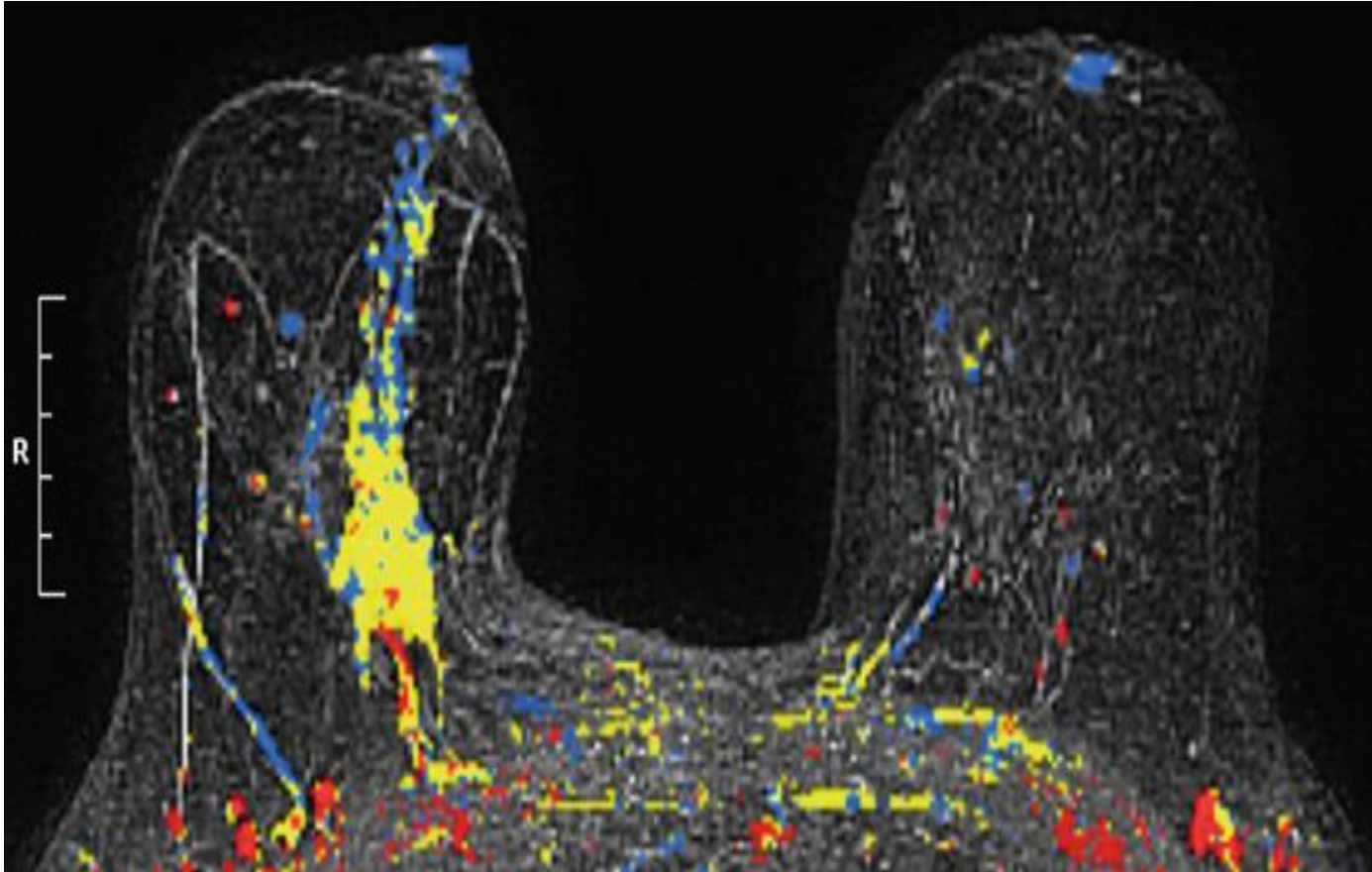


Ductal anatomy reconstruction;autopsy mastectomy; thin serial sections

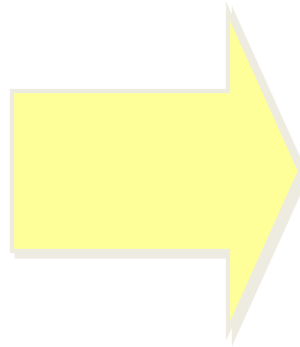
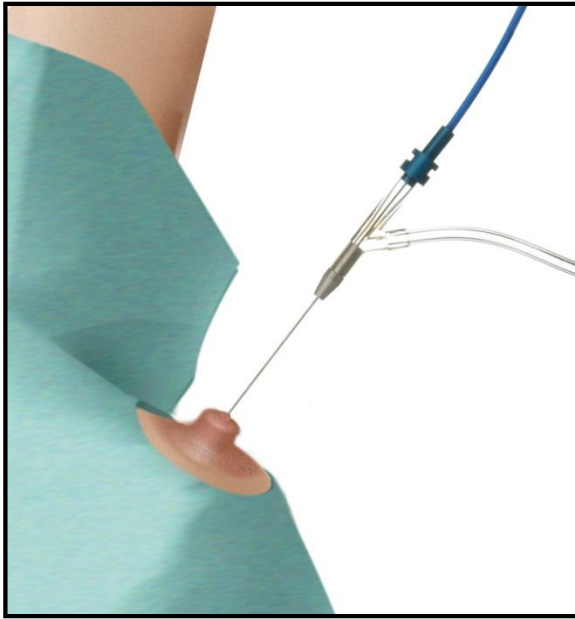


SICK LOBE HYPOTHESIS(TOT)

MRI HIGH GRADE DCIS SHOWS LOBAR PATTERN(Tabar 2008)



Breast Endoscopy



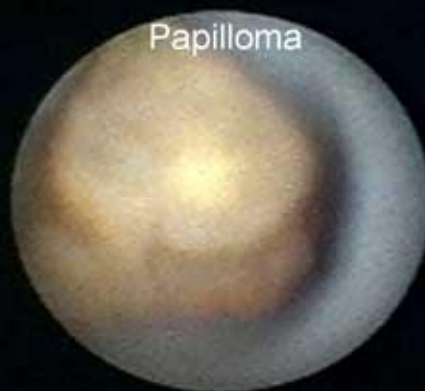
Imaging system magnifies the image 60 times actual size (resolution is 0.1 mm).

Clean duct with bifurcation

Bifurcation



Papilloma



Papillomas



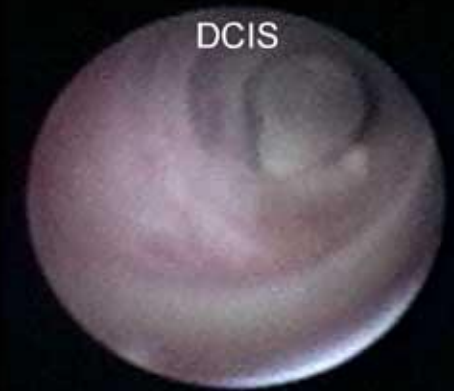
Low Grade DCIS



DCIS



DCIS

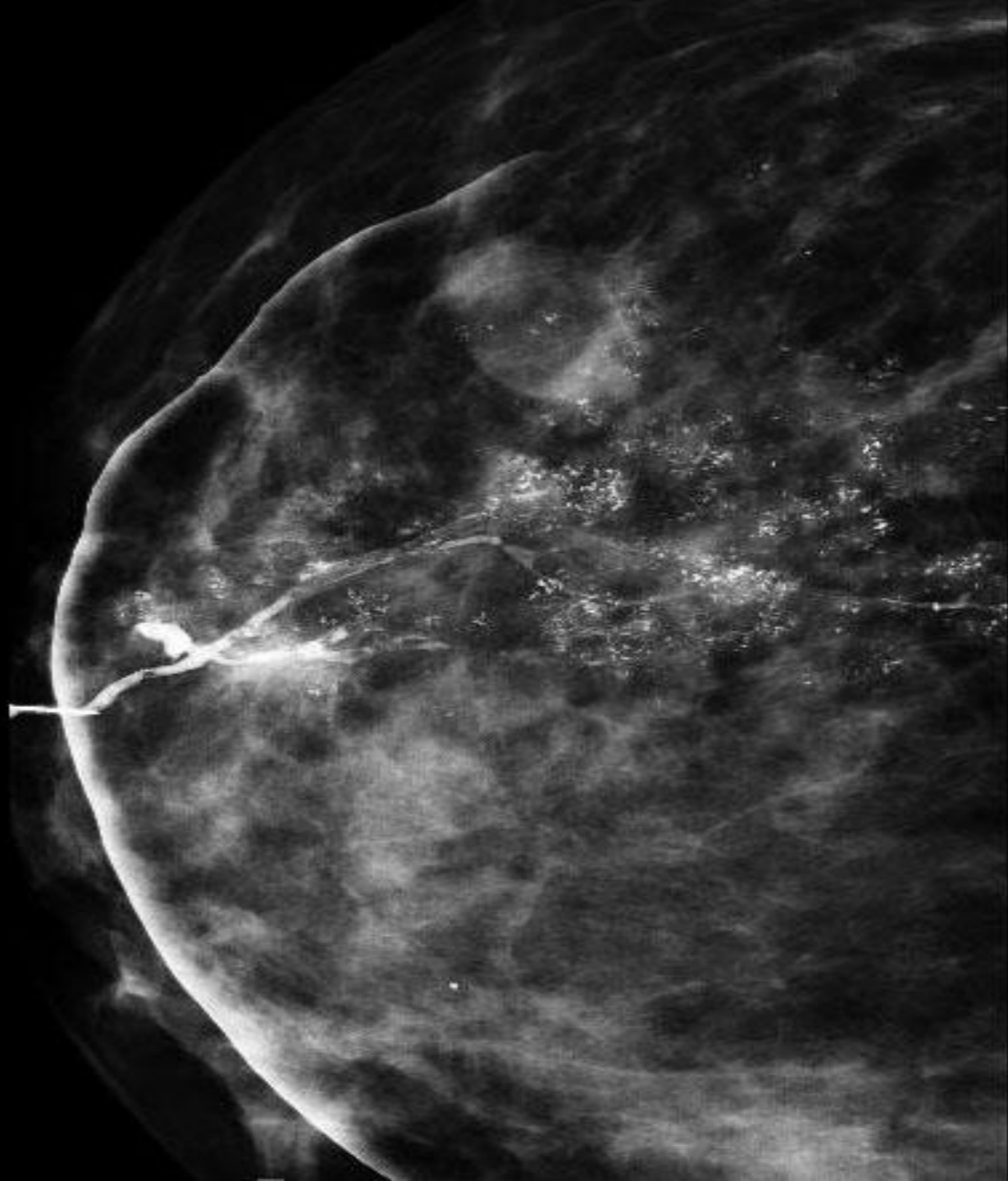


High Grade DCIS



High Grade DCIS





Intraductal Chemotherapy

- Direct access to the site of disease
- Epithelial ductal ablation
- Prevent cancer
- No systemic effects
- Alternative to risk reducing mastectomy

Intraductal Therapy for Prevention and Treatment

- Phase 1 Chinese clinical trial(4/08-AACR),60-300 mg carbo intraductal(2-5 ducts) 2-4 days premastectomy-(Love)
- Phase 1 –intraductal pegylated doxorubicin in patients pre-mastectomy-Stearns-
- Intraductal doxil; mice with BRCA mutation to prevent cancer-Sukumar-Hopkins
- Intraductal fulvestrant-1 month preop ER+ opening at Montefiore

Dose Escalation Premastectomy Intraductal Therapy Study: WHM China

- 30 women had from 5-7 ducts dry cannulated for drug installation under nipple block
- Phase 1 Chinese clinical trial: 60-300 mg carbo intraductal(2-5 ducts) 2-4 days premastectomy-w/o sig adverse events
- Love et al;Cancer Prevention Res 2013



Intraductal Presurgical Trial(Montefiore- SF PI)

- 30 patients with Stage 0-2 ER+ breast cancer undergoing BCT or mastectomy
- Pre-surgical trial; 30 days preop intraductal fulvestrant(500mg) injected in all cannulated ducts(up to 5- dose divided)
- Pathology; histological changes and Ki67
- Tissue and serum drug levels

Questions to be answered

- Efficacy
- Whole breast treated?
- Which drugs/dose/combinations
- Stem cells die?
- Side effects(long term?)
- Duration of effect- how to monitor?

“BREAST SPARING” MASTECTOMY

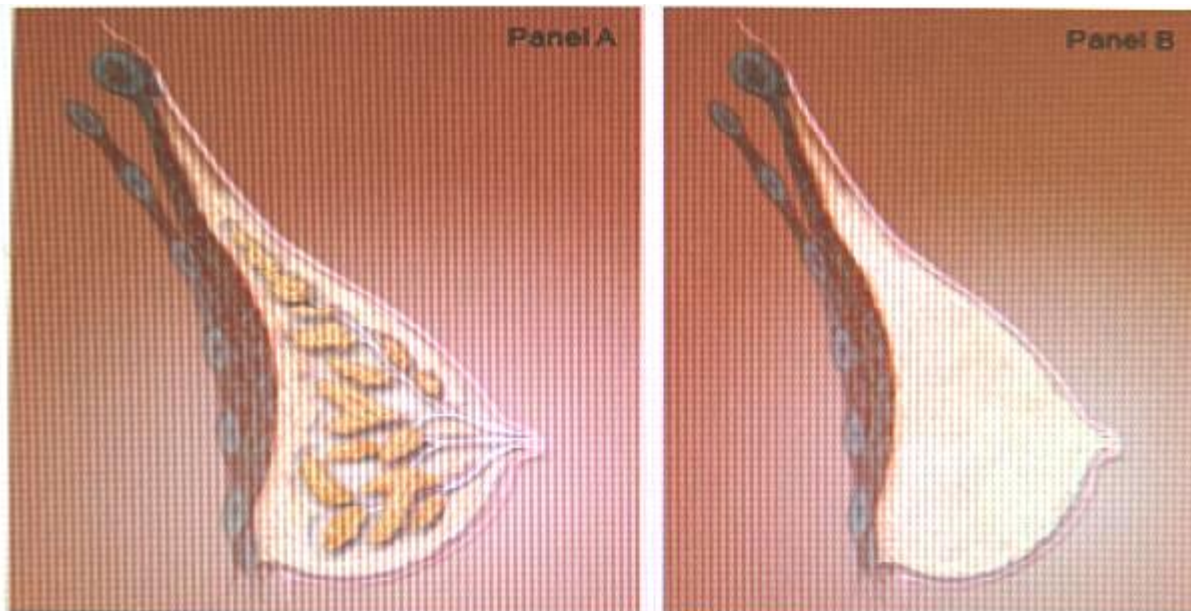
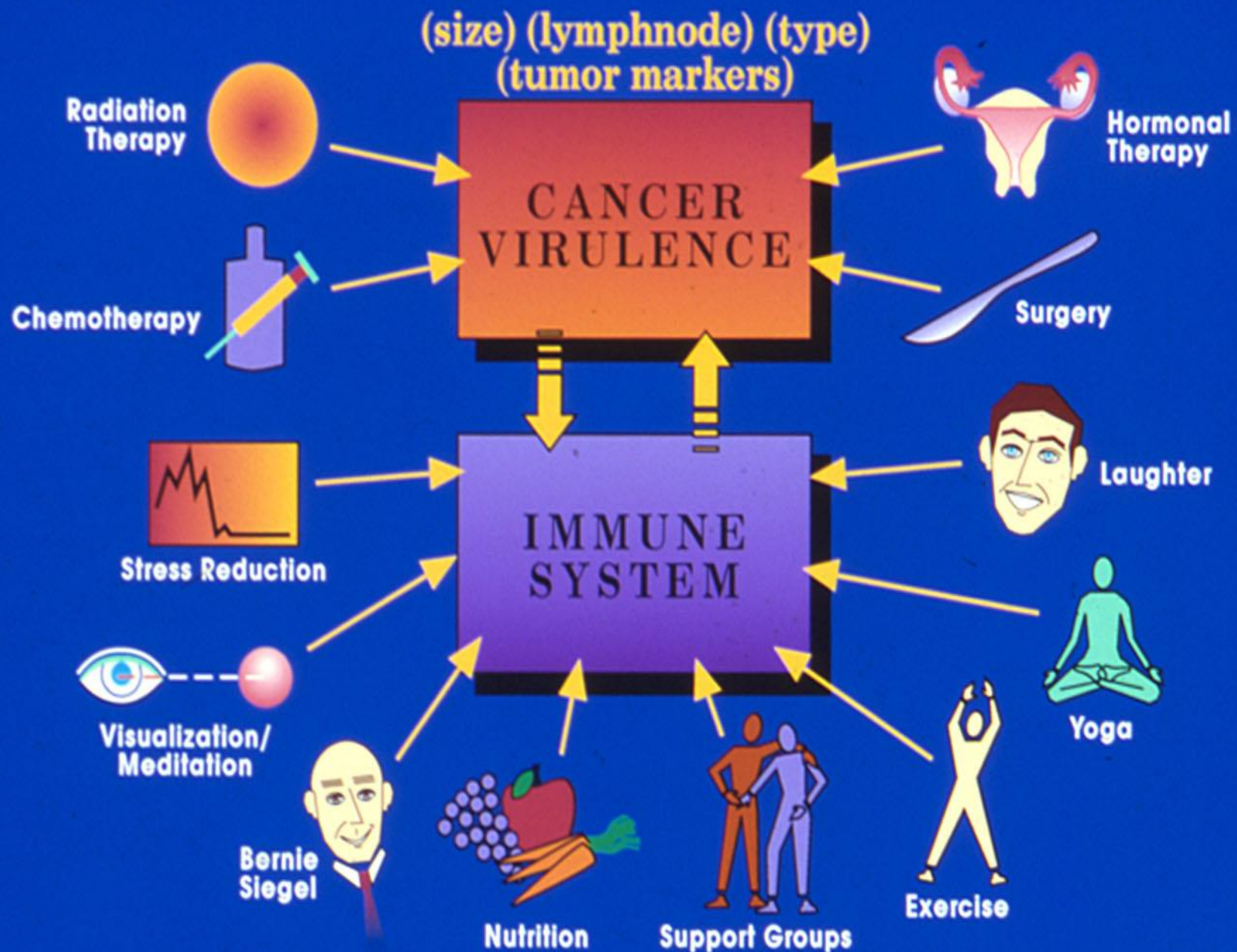


Figure 1: Ductal cells are the Site of Origin of Breast Cancer.

Panel A: Over 95% of breast cancers begin in the epithelial cells lining the milk ductal system. **Panel B:** Ablation of the mammary epithelium may prevent tumor formation while keeping the breast structure.



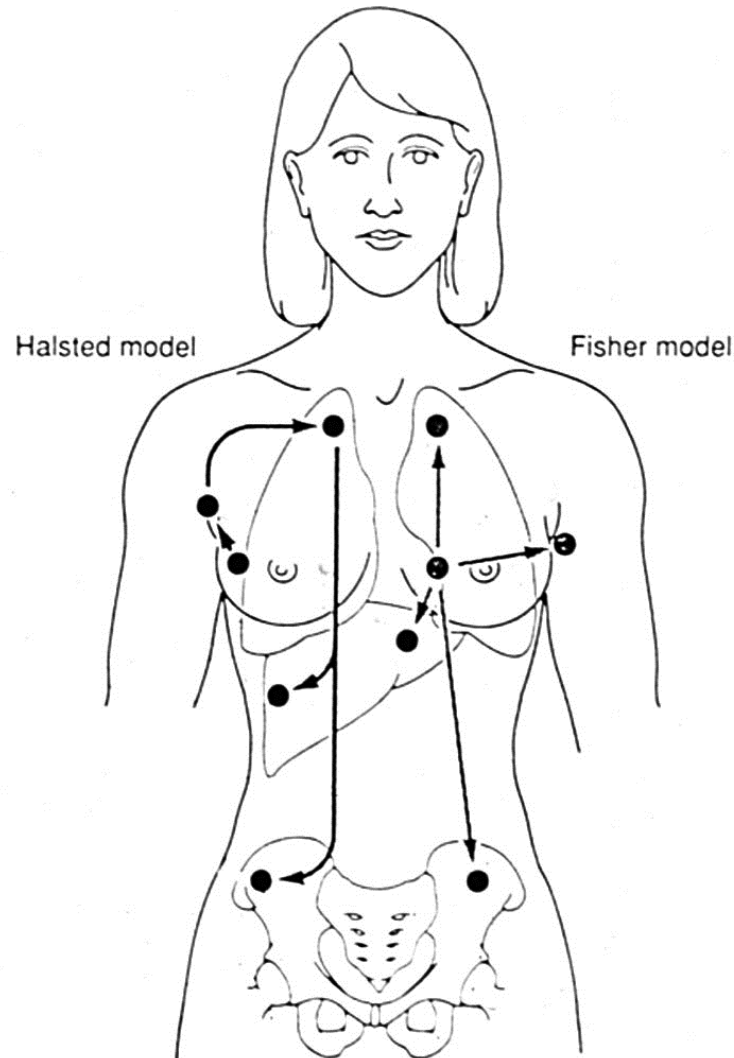
SEED AND SOIL HYPOTHESIS

*“The seeds of a plant are carried in all directions;
but they can only live and grow if they fall on
congenial soil”*

– Paget 1889

The successful growth of metastatic cells depends on the interactions and properties of cancer cells (seeds) and their potential target organs (soil)

PREVENTION OF METASTASES





BRONX ONCOLOGY LIVING DAILY (BOLD) PROGRAM OF THE INTEGRATIVE ONCOLOGY PROGRAM

A Cancer Wellness Program—
Where Mind, Body and Spirit are Nurtured

PROGRAMA DE ONCOLOGÍA VIVIENDO
A DIARIO EN EL BRONX (BOLD) PROGRAMA
DE ONCOLOGÍA INTEGRADA

Un proyecto de bienestar a la salvo para pacientes de
cáncer dónde se nutre el cuerpo, la mente y el espíritu

Montefiore Einstein
Center for Cancer Care

Montefiore
DOING MORE™



BOLD BUDDY PROGRAM

Would you like to speak with someone who has been through cancer and understands? Peer support by English- and Spanish-speaking cancer survivor volunteers is available to those with any type or stage of cancer. BOLD Buddies can provide treatment companionship, supportive phone calls, as well as hope, compassion, and encouragement during these challenging times. BOLD Buddy volunteers receive ongoing training, supervision, and education in patient navigation.



PSYCHOSOCIAL ONCOLOGY SERVICES

Individual counseling and support groups for cancer patients, survivors and family members are available in English and Spanish. Services are provided by Psychosocial Oncology interns who are supervised by a licensed health psychologist. This support service can teach you methods to cope with sadness, anxiety, isolation, relationship stresses, treatment side-effects and making healthy lifestyle changes.



SOCIAL WORK SERVICES

Oncology social workers are licensed and masters level clinicians who provide supportive counseling and education to patients, families and caregivers. They offer assistance in identifying barriers to quality care, individual and group counseling and referrals to community resources. Social workers are located in each oncology clinic and inpatient unit with the goal of advocating for those affected by cancer.

COLD CAP- AVOID CHEMOTHERAPY INDUCED HAIR LOSS



Current Trends; Future Directions

- Axillary Node Dissection- replaced by systemic therapy and radiation
- Sentinel node biopsy-staging-replaced by genomics
- DCIS-active surveillance, local topical and intraductal therapies replace surgery
- Tumor ablation causing autovaccination coupled with immunotherapy will be highly effective!
- No surgery after neoadjuvant chemotherapy with evidence of a complete pathological response
- Liquid biopsy(blood test) will allow be paradigm shifting; only treat when necessary, avoid overtreatment, real time response to therapy

"ARRIVING IN 40 YEARS."
THAT CAN'T BE RIGHT..



Wabeeja
Medawagse
Mersi
unalchéesh
Tingki
Komapsumnida
Shukuria
Paldies
Hatur
Tashakkur
Maketai
hui
Sanco
bolzün
Maake
Denkauja
gozaimashita
Fakaaue
Spasibo
Ekhmet
Mehrbani
Nenachalhya
Baiika
Yuspagaràtam
Minmonchar
Atto
Gaejtho
Yaqhanyelay
Efcharisto
Dankscheen
Arigato
suksama
ekoju
Tavtapuch
Maiteka
Sikomo
Gui
Gracias
Merci
Shukria
lah
Merastawhy
Dhanyabaad
Chaltu
Biyan
Grazie
Snachalhuya
Juspa
Thank
YOU