Radiation Oncology Update 2014

Breast Focus

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First Radiation & Oncology Group

RADIATION ONCOLOGY MILESTONES

1895 — William Roentgen Discovers X-rays

1920

1930

1940

1950 — First Linear Accelerator at Stanford

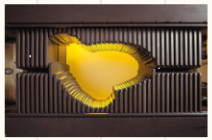
1960

1970 — Gamma Knife by Leksell

1980

1990 — CyberKnife by Adler

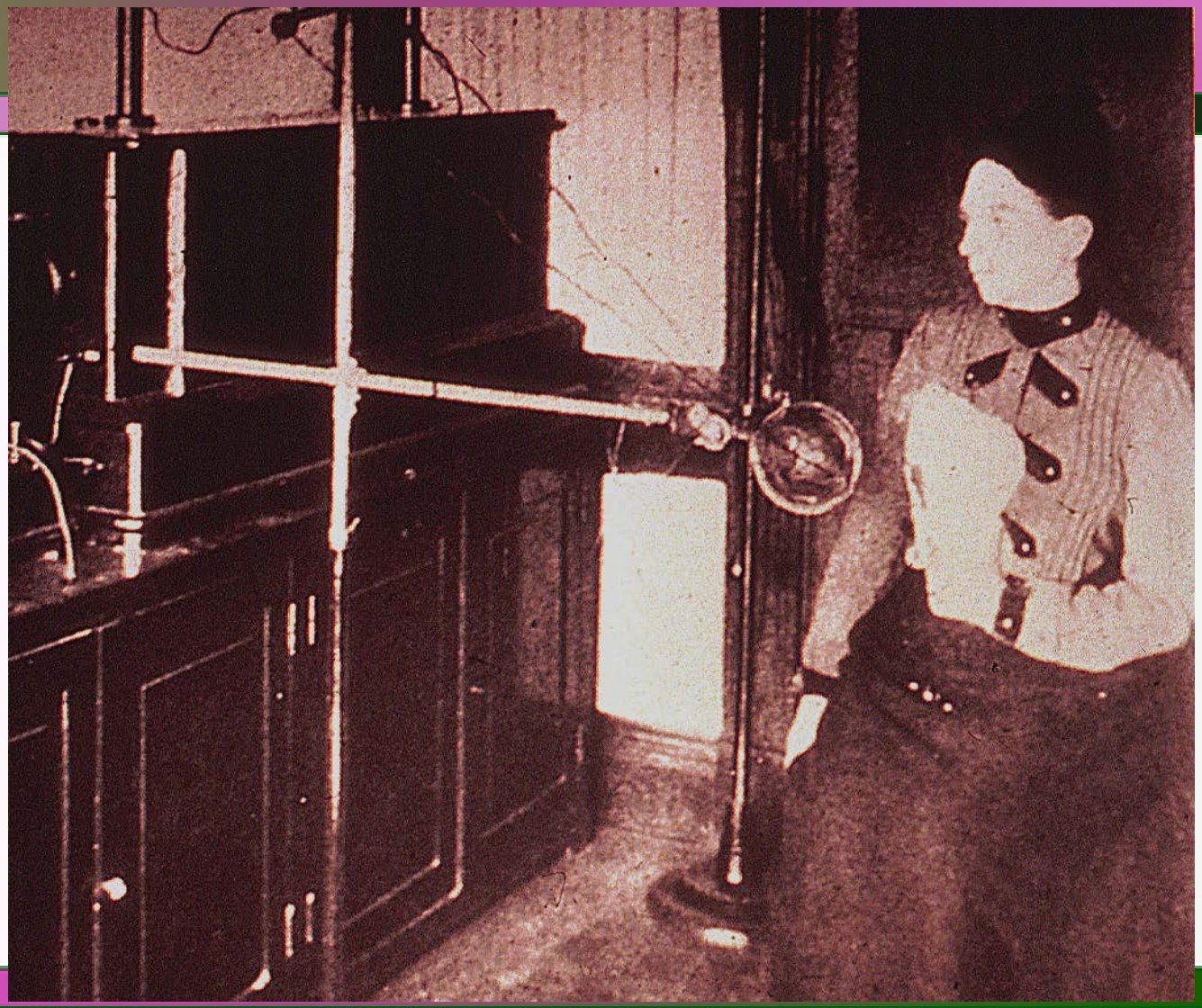
2000 — IMRT Codes Approved



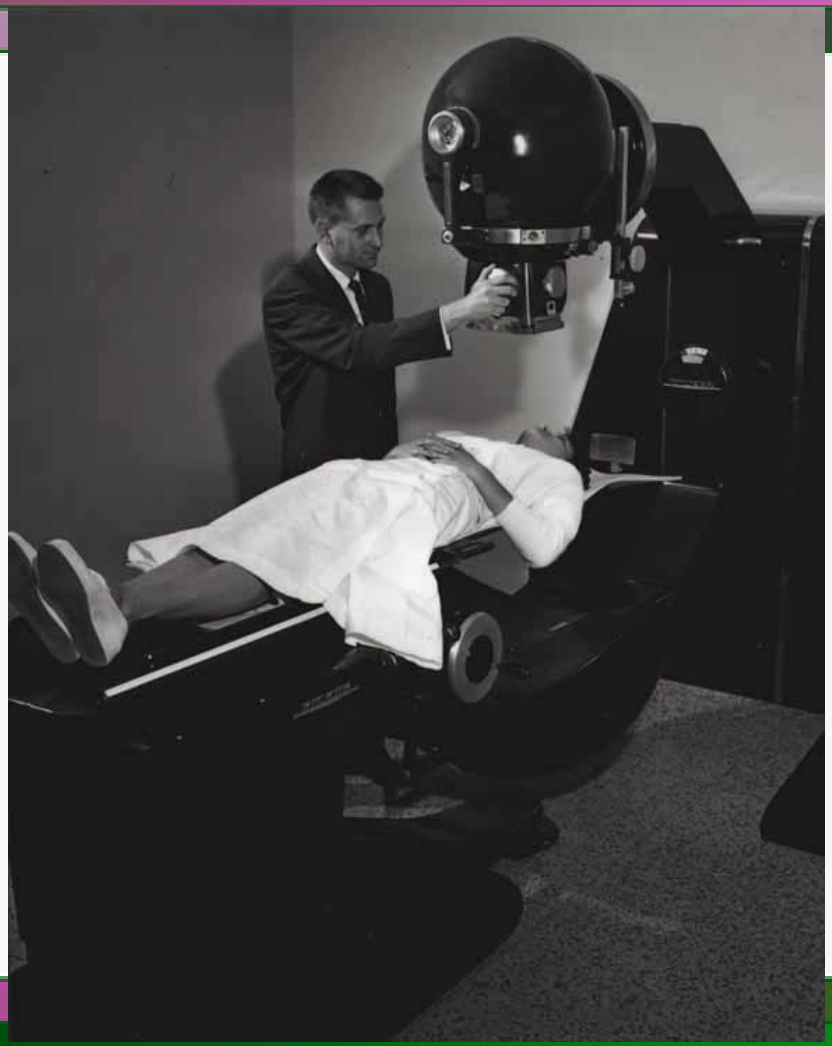
2010 — IGRT Codes Approved

2020

Radiotherapy for breast cancer 1909



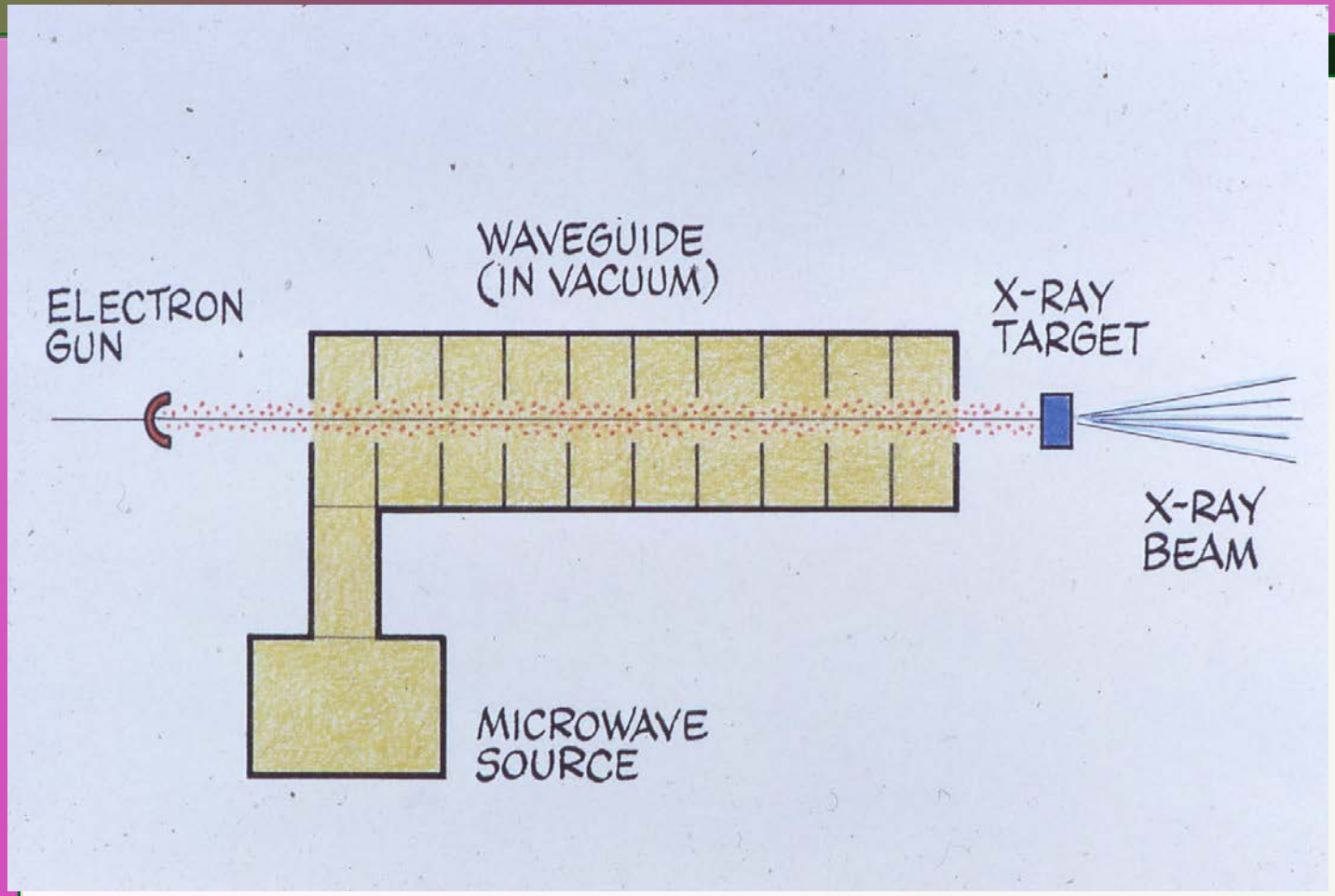
Cobalt-60 Therapy First Unit in 1951



University of Saskatchewan
Harold Johns

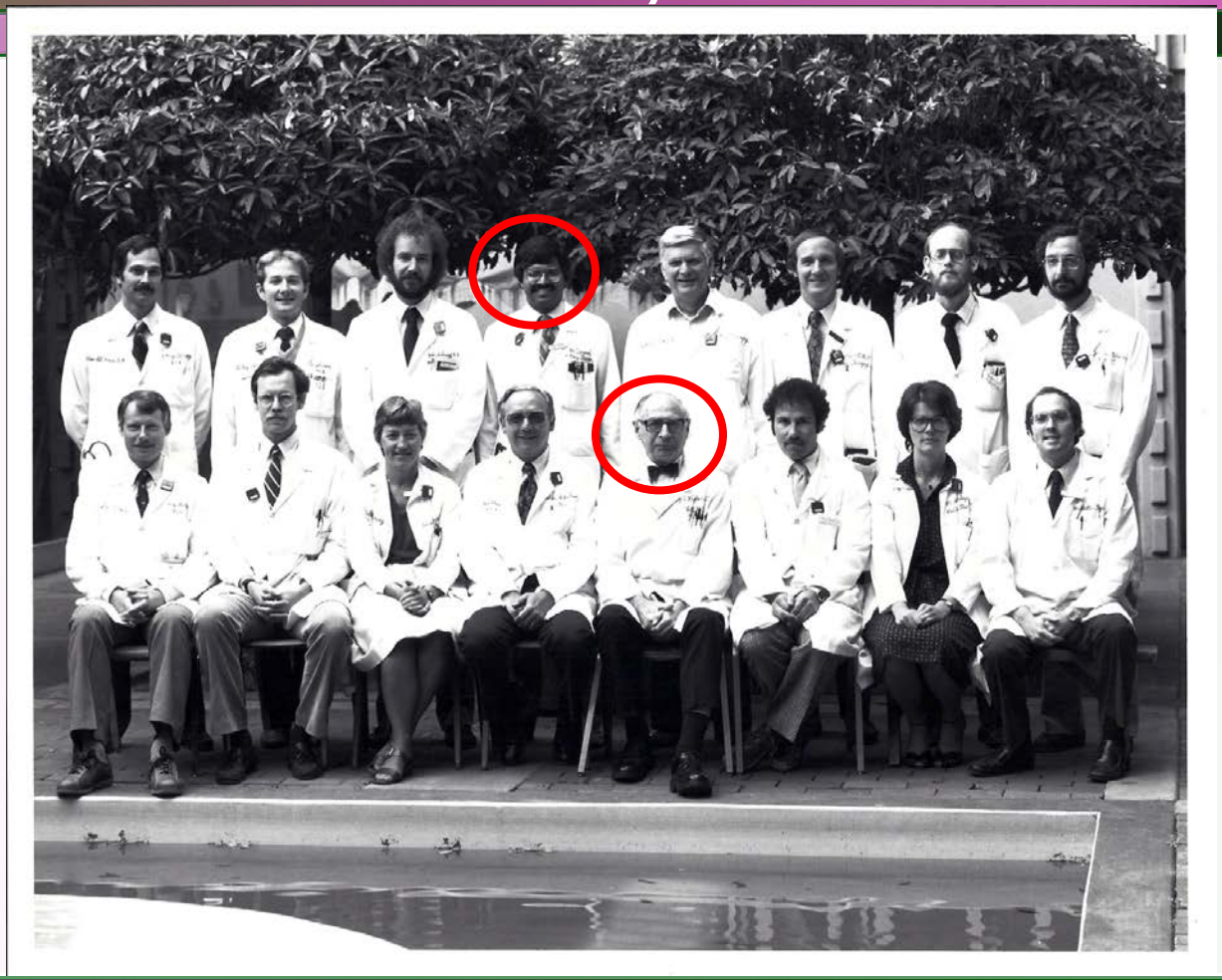
Russell and Sigurd Varian:
Klystron they invented at Stanford (1930)

Linear Accelerator: Single source of power



The First US Linac- 1955 Stanford Hospital Henry Kaplan MD

HENRY KAPLAN
Stanford, 1980



Intensity Modulated Radiation Therapy (IMRT-2000)

- High-precision EBT
- Computer-controlled x-ray accelerators deliver precise doses
- Doses conform to the 3-D shape of the tumor by modulating the beam
- Focuses a higher radiation dose to the tumor and minimizes exposure of normal tissues
- Higher and more effective radiation doses can safely be delivered to tumors with fewer side effects

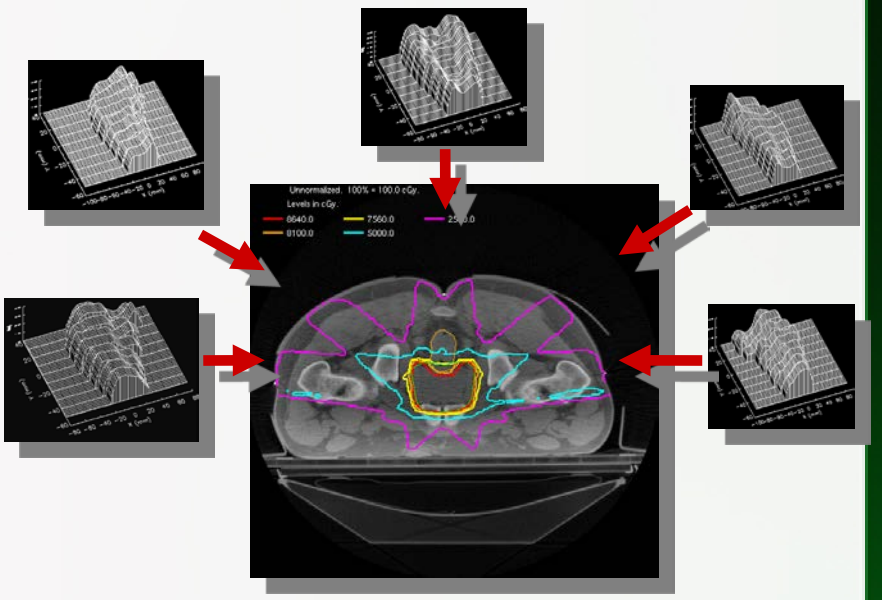


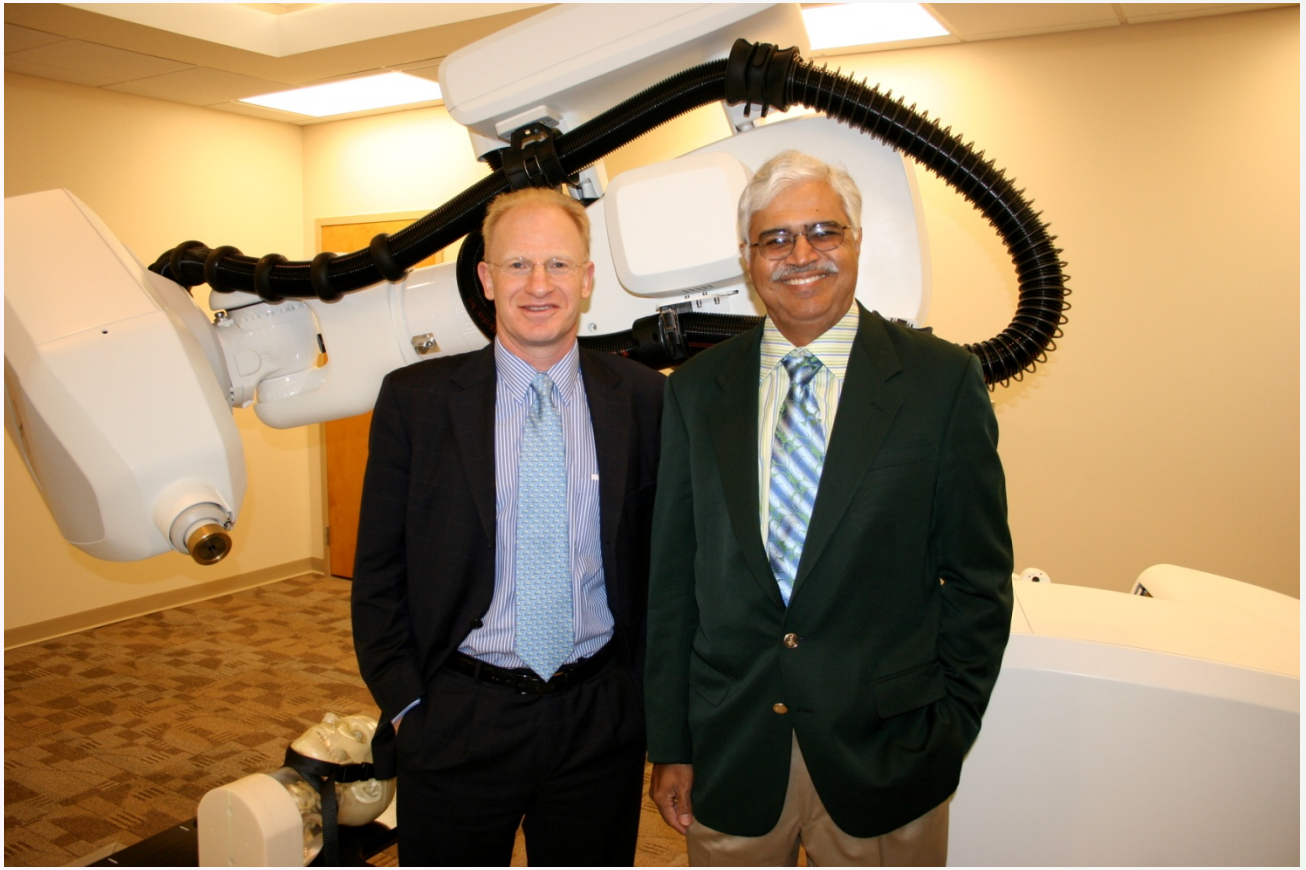
Image-Guided Radiation Therapy (IGRT-2007)

- IGRT uses imaging to direct radiation beams (IMRT) targeted to tumors while avoiding normal issues
- IGRT treatment includes:
  - Ultrasound
  - Stereoscopic X-Rays
  - Computerized Tomography (CT)
  - Stereotactic Radiosurgery (SRS)

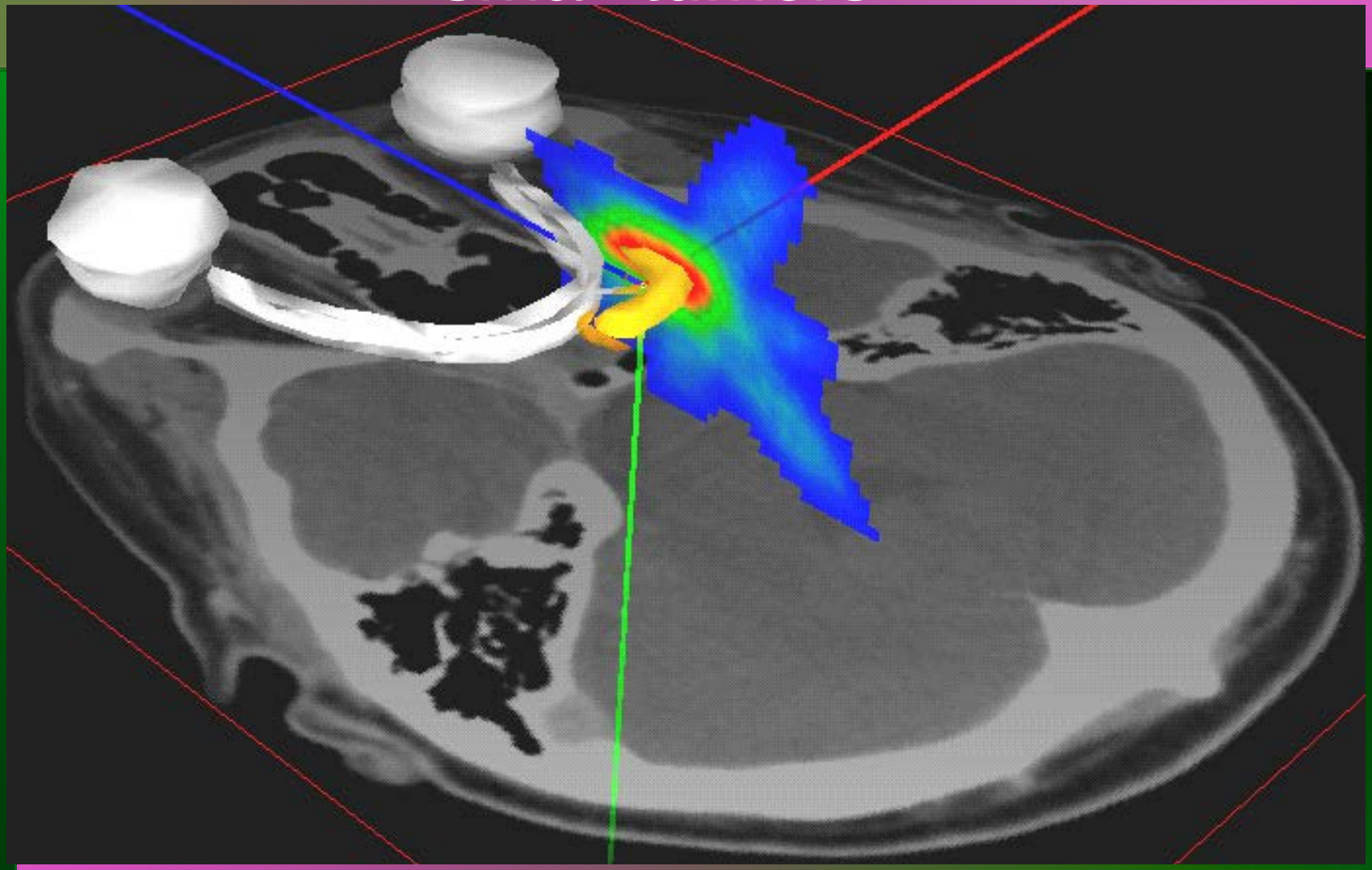
CyberKnife® Robotic Radiosurgery

- Targeting accuracy
  - Continual image guidance throughout the treatment
  - Automatically track, detect, and correct for intra-fraction target movements
- Unhindered non-coplanar treatment delivery
- Flexibility to deliver both isocentric and non-isocentric beams
- Unlimited reach throughout the body

John Adler, Inventor of CK Memorial Cyberknife (2006)



Pencil-thin beams used to target small tumors



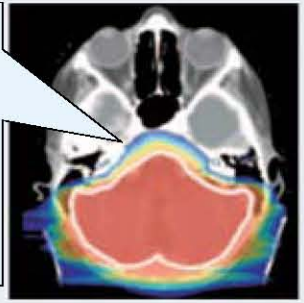
PROTONS

Proton beam therapy is a relatively well-known yet still nascent form of radiation therapy. While the physical properties – and, thus, theoretical clinical benefits – of proton particles have engendered immense support for the use and proliferation of proton therapy in the U.S., the current state of clinical literature has yet to substantiate a concrete improvement in long-term clinical outcomes stemming from proton therapy as compared to those afforded by photon RT. Nonetheless, the physical advantages of proton particles which enable delivery of an equivalent relative biological effect as photons with less dose delivered to healthy tissue as well as early evidence from meta-analyses of existing clinical trials of both photon and proton RT have underpinned the acceptance and use of this modality to date.

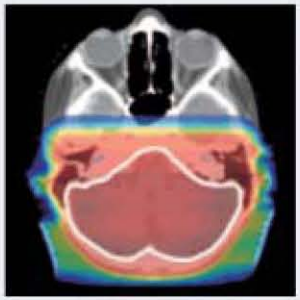
Protons Afford Potential to Achieve More Conformal Dose Deposition

Sharper dose falloff (Bragg Peak) affords tighter dose conformality around tumor

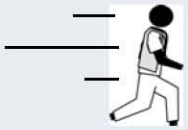
Protons



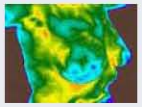
Photons



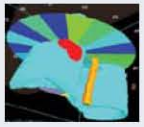
Greater Healthy Tissue Sparing Offers Potentially Significant Benefits to Patient



Potentially Lower Risk of Complications, Morbidities



Potentially Lower risk of Secondary Malignancies

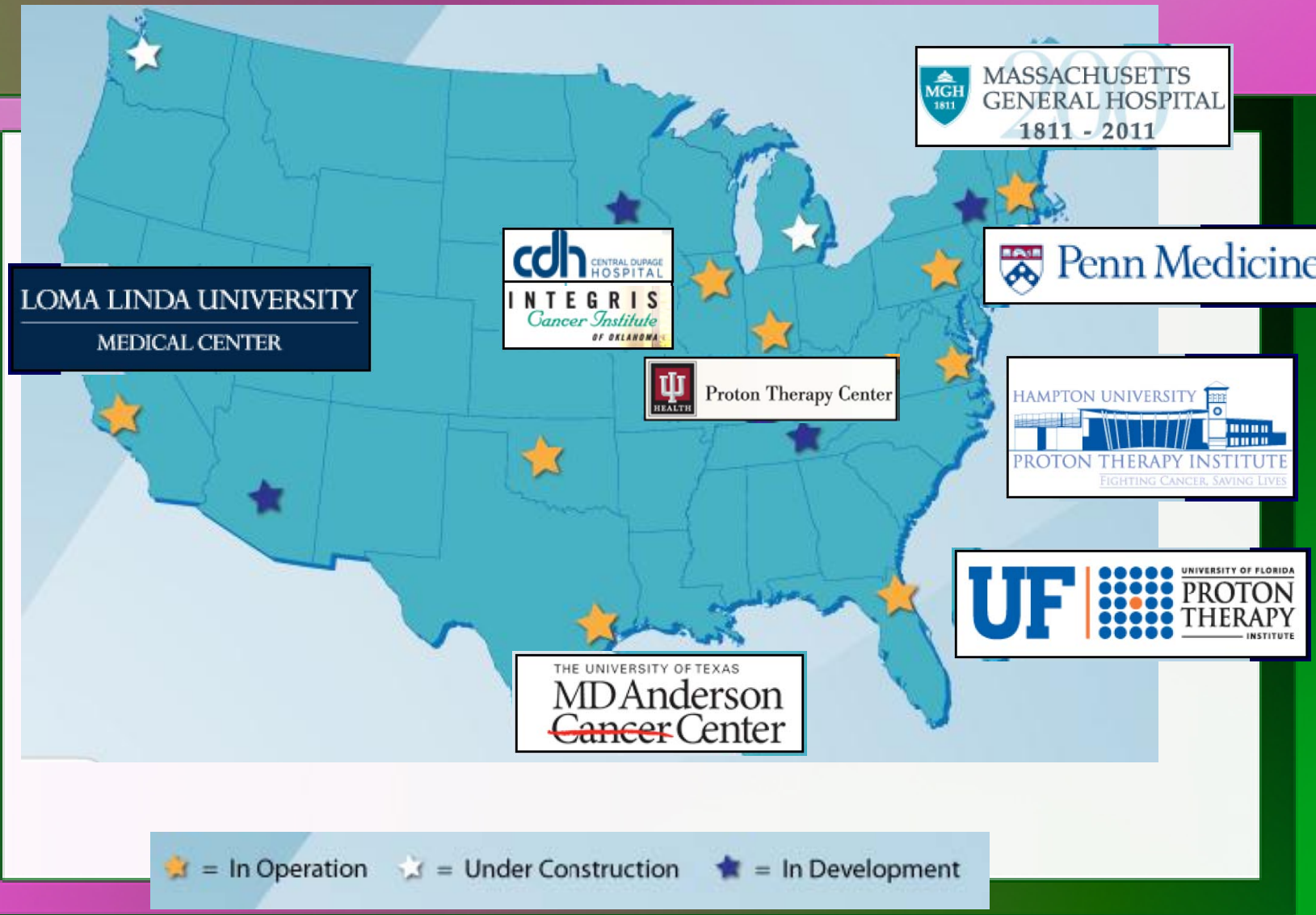


Potentially Safer Dose Escalation

However, Dearth of Evidence Indicating Superiority of Outcomes with Protons

Tumor Site	Number of Studies	Number of Patients	Results
Head and Neck	2	9	No firm conclusions
Prostate	3	1,751	Similar results to photons
Ocular	10	7,798	Potentially advantageous[1]
Gastro-intestinal	5	369	No firm conclusions
Lung (non-small cell)	3	156	No firm conclusions
CNS	10	839	Similar results to photons
Chordomas of the skull base	3	302	Potentially advantageous[1]
Sarcomas	1	47	No firm conclusions
Pelvis	3	80	No firm conclusions

PROTON CENTERS



Jacksonville AccuBoost Installation

Jessica Bahari-Kashani, MD

- Medical School- University of Minnesota
- Residency-UC Irvine
- Director, Southside Cancer Center, 2012

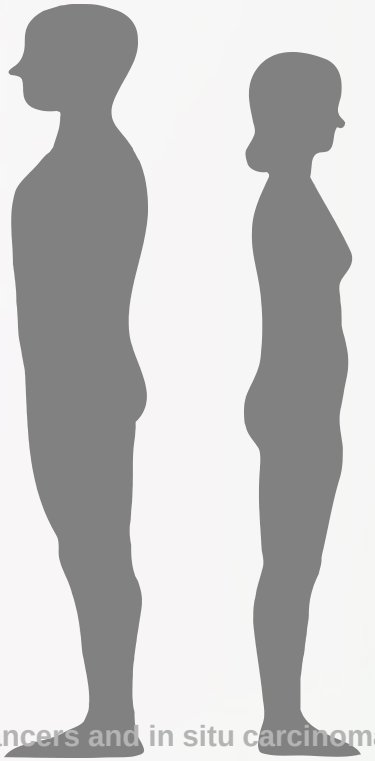
Outline

- *Epidemiology*
- *Screening Guidelines*
- *Risk Factors*
- *Radiation Treatment Options*

Estimated US Cancer Cases

Breast Cancer Incidence : 226,870
1 in every 8 women

Men 848,170		Women 790,740	
Prostate	29%	29%	Breast
Lung and bronchus	14%	14%	Lung and bronchus
Colon and rectum	9%	9%	Colon and rectum
Urinary bladder	7%	6%	Uterine corpus
Melanoma of skin	5%	5%	Thyroid
Kidney	5%	4%	Non-Hodgkin lymphoma
Non-Hodgkin lymphoma	4%	4%	Melanoma of skin
Leukemia	3%	3%	Ovary
Oral Cavity	3%	3%	Kidney
Pancreas	3%	3%	Pancreas
All Other Sites	18%	20%	All Other Sites

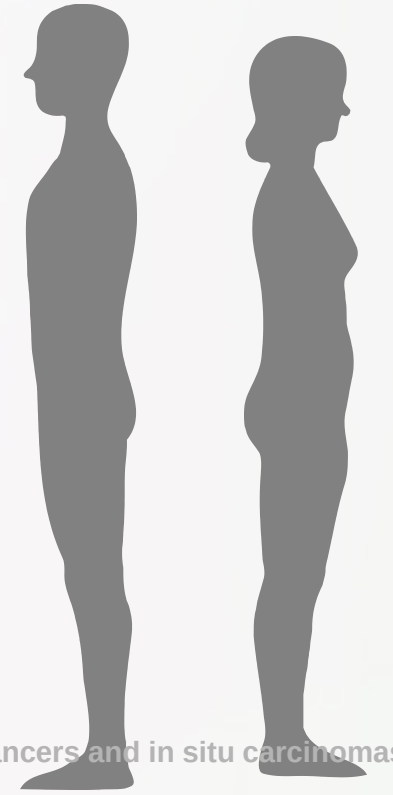


*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.

Estimated US Cancer Deaths

~14% of all cancer deaths = 39,510 deaths

Men 301,820		Women 275,370	
Lung and bronchus	29%	26%	Lung and bronchus
Prostate	9%	14%	Breast
Colon and rectum	9%	9%	Colon and rectum
Pancreas	6%	7%	Pancreas
Liver/intrahepatic bile duct	5%	6%	Ovary
Leukemia	4%	4%	Leukemia
Esophagus	4%	3%	Non-Hodgkin lymphoma
Non-Hodgkin Lymphoma	3%	3%	Uterine corpus
Urinary bladder	3%	2%	Liver/intraheaptic bile
Kidney	3%	2%	Brain
All other sites	25%	22%	All other sites



*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.

EPIDEMIOLOGY

TABLE G–1 Chances of Being Diagnosed with Breast Cancer at Different Age Intervals

From Age	To Age 30	40	50	60	70	80	90	Ever
0	1:2525	1:217	1:50	1:24	1:14	1:10	1:8	1:8
30		1:233	1:50	1:23	1:13	1:9	1:8	1:8
40			1:63	1:26	1:14	1:10	1:8	1:8
50				1:41	1:17	1:11	1:9	1:9
60					1:28	1:14	1:11	1:10
70						1:24	1:16	1:14

Most frequent diagnosed cancer in US women and second most frequent cause of cancer death

Lifetime risk 12.5% (1/8) and mortality 3.0% (1/33)

Screening Guidelines

Screening Guidelines for the Early Detection of Breast Cancer, American Cancer Society

- Women should know how their breasts normally feel and report any breast changes promptly to their health care providers. Breast self-exam is an option for women starting in their 20s.
- A clinical breast exam should be part of a periodic health exam, about every three years for women in their 20s and 30s, and every year for women 40 and older.

Screening Guidelines for the Early Detection of Breast Cancer, American Cancer Society

- Yearly mammograms starting at age 40 and continuing for as long as a woman is in good health.
- Women at increased risk should talk with their doctors about the benefits and limitations of starting mammography screening earlier, having additional tests (i.e., breast ultrasound and MRI), or having more frequent exams.

What's increased risk?

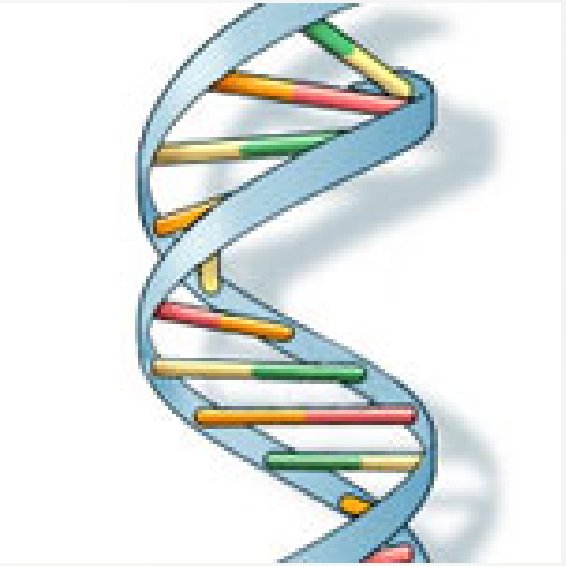
- **HIGH RISK**
  - BRCA1/BRCA2 gene mutation in first-degree relative
  - Li-Fraumeni syndrome, Cowden syndrome
  - Radiation Therapy to the chest between ages of 10 to 30 years
  - Lifetime breast cancer risk 20-25% or greater according to risk tools
    - Gail model: http://www.cancer.gov/bcrisktool

What's increased risk?

- **MODERATE RISK**
  - Personal history of: DCIS (ductal carcinoma in situ), LCIS (lobular carcinoma in situ), ADH (atypical ductal hyperplasia) or ALH (atypical lobular hyperplasia)
  - Extremely dense breasts or unevenly dense breasts when viewed by mammograms
  - Lifetime breast cancer risk 15-20% according to risk tools

BRCA1 & BRCA 2 Gene mutations

- Most common cause of hereditary breast cancer
- In normal cells, help prevent cancer by maintaining normal growth
- Inherited mutated copy of either gene, you have a high risk of developing breast cancer during your lifetime, up to 80%
- *BRCA* mutations more common in Jewish women of Ashkenazi (Eastern Europe) origin than in other racial and ethnic groups, but they can occur in any racial or ethnic group



Breast cancer risk factors you cannot change

- **Gender:** 100 times more common among women than men
- **Aging:** risk of developing breast cancer increases as you get older.
- **Genetic risk factors:** 5% to 10% thought to be hereditary
- **Family history of breast cancer**: 2-3x fold if first-degree relative
  - Most (85%) women who get breast cancer *do not* have a family history of this disease.

Breast cancer risk factors you cannot change

- **Personal history of breast cancer:** 3-4x fold increased risk
- **Menstrual periods:** More menstrual cycles
  - Menstruating early (before age 12) and/or went through menopause later (after age 55). The increase in risk may be due to a longer lifetime exposure to the hormones estrogen and progesterone.
- **Diethylstilbestrol (DES) exposure**
  - From the 1940s through the early 1970s some pregnant women were given an estrogen-like drug called *DES* because it was thought to lower their chances of losing the baby (miscarriage).

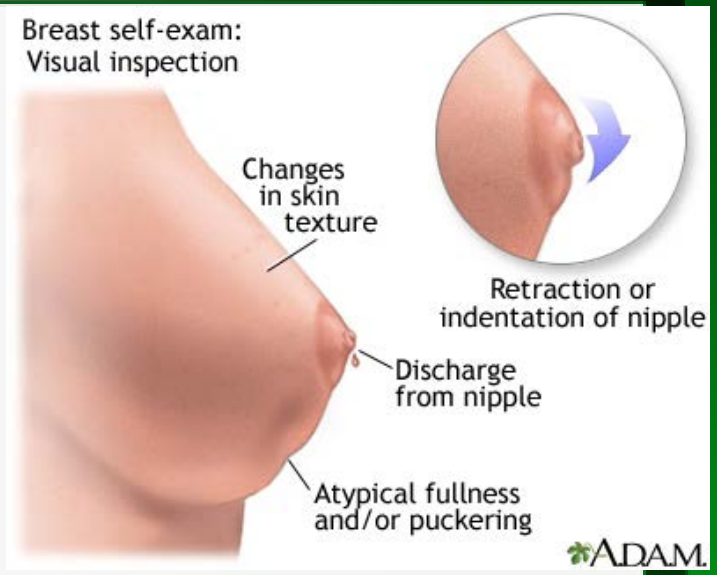
Life-style related risk factors

- **Alcohol:** Risk increases with the amount of alcohol consumed
  - One alcoholic drink a day have a very small increase in risk but 2 to 5 drinks daily increase risk 1½ times compared to non-drinkers
- **Being overweight or obese**
  - Having more fat tissue after menopause can increase your chance of getting breast cancer by raising estrogen levels
- **Physical activity**
  - In one study from the Women's Health Initiative, as little as 1¼ to 2½ hours per week of brisk walking reduced a woman's risk by 18%. Walking 10 hours a week reduced the risk a little more.
  - To reduce your risk of breast cancer: 45 to 60 minutes of intentional physical activity 5 or more days a week.

Signs and symptoms

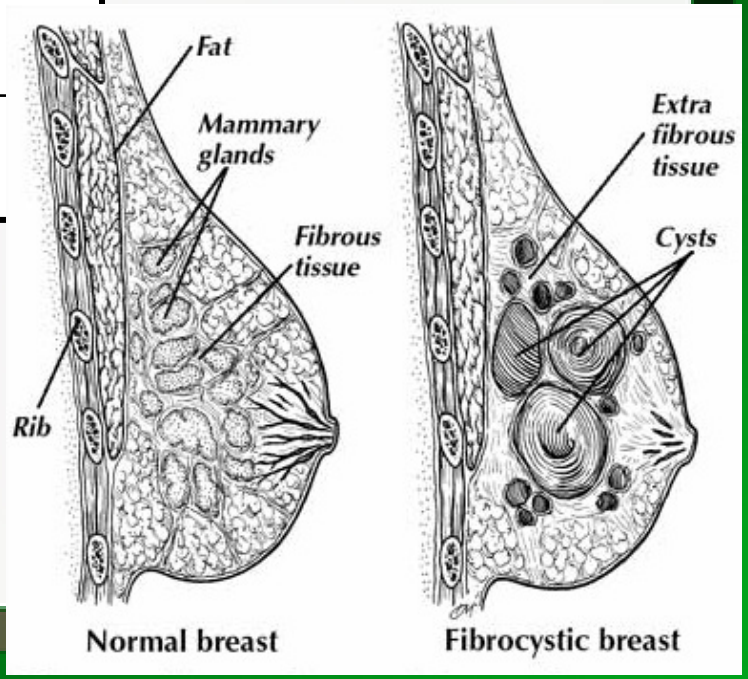
- The most common symptom of breast cancer is a new lump or mass.

- Other signs:
  - Swelling of all or part of a breast
  - Skin irritation or dimpling
  - Breast or nipple pain
  - Nipple retraction
  - Redness, scaliness, or thickening
  - Nipple discharge other than breast milk
  - Sometimes a breast cancer can spread to lymph nodes and cause a lump, even before the original tumor in the can be felt.



What is it?

Age	Chance of Breast mass being malignant	Fibroadenomas	Fibrocystic Disease
25-40	10%	25%	55%
35-55	35%	10%	30%
> 55	85%	N/A	N/A



TREATMENTS

General types of treatment for

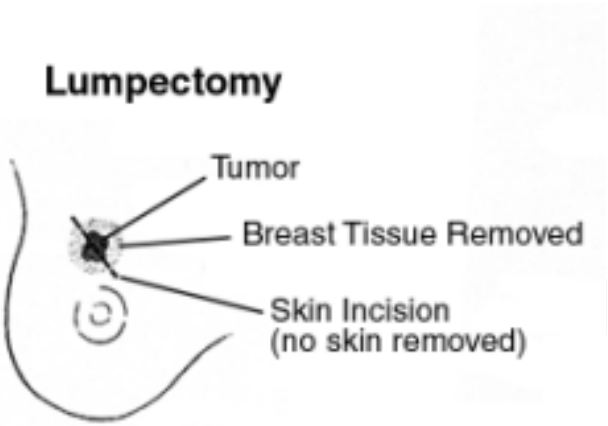
Surg

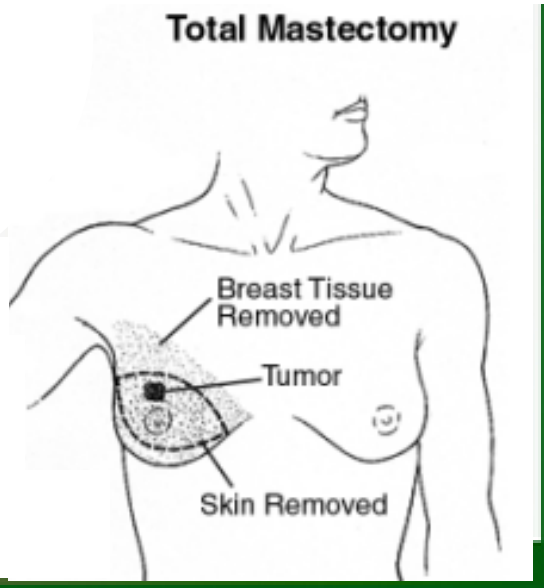
notherapy
none therapy
eted therapy

Surgical Options

Breast Conserving Surgery:
Breast Intact
-Lumpectomy with Sentinel LN Biopsy or Axillary Dissection

Mastectomy:
Entire Breast Removed
-Total / Simple / Modified Radical
-Skin-Sparing: for immediate reconstruction





How can lumpectomy and mastecomy both be options?

- Radiation therapy is required for both DCIS and invasive breast cancer if breast conserving therapy (lumpectomy) is the chosen treatment
- NSABP-06 randomized 1800 women to modified radical mastectomy vs. lumpectomy alone vs. lumpectomy plus radiation
  - Significantly fewer local failures with MRM and lumpectomy WITH radiation (up to 30% local failure with lumpectomy only)
  - NO difference in overall survival
  - The two treatments were judged equal

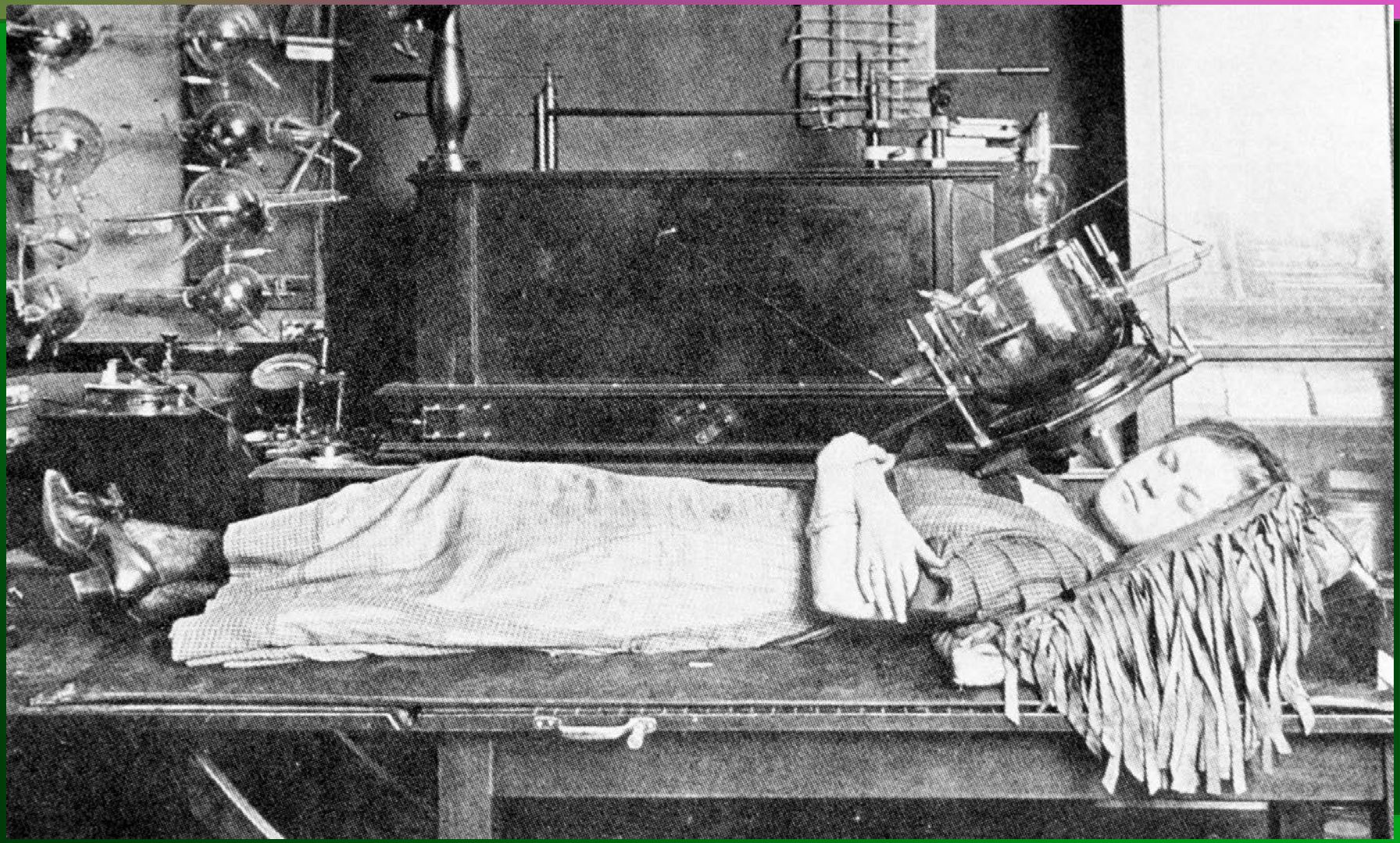
RADIATION THERAPY

- **Do I need radiation after a mastectomy?**

  It depends…

- **Irradiation after Mastectomy**
  - Close or positive chest wall margin
  - 4 or more positive lymph nodes
  - Tumor > 5cm
  - Skin involvement

Radiation…in the past

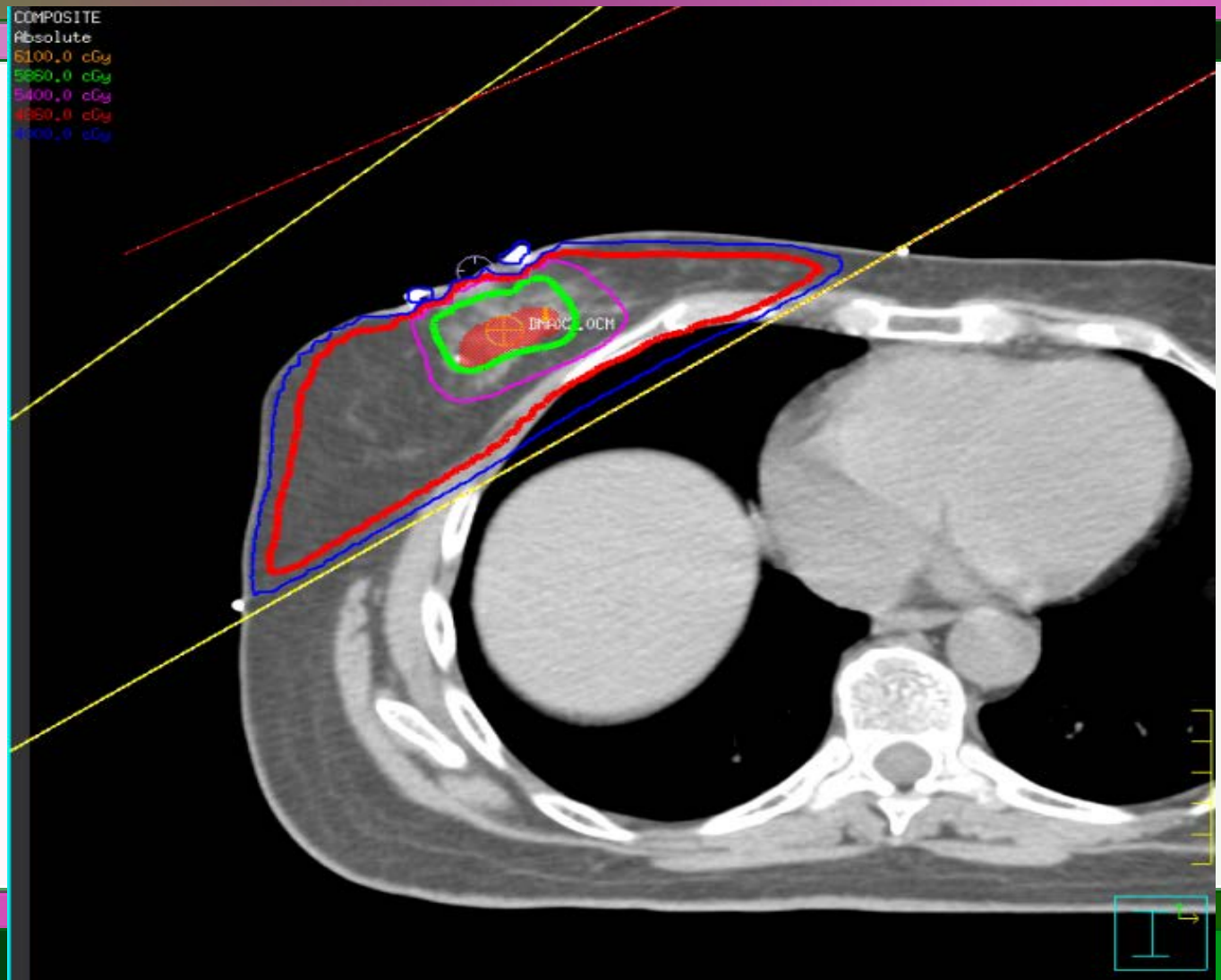


RADIATION TECHNIQUES

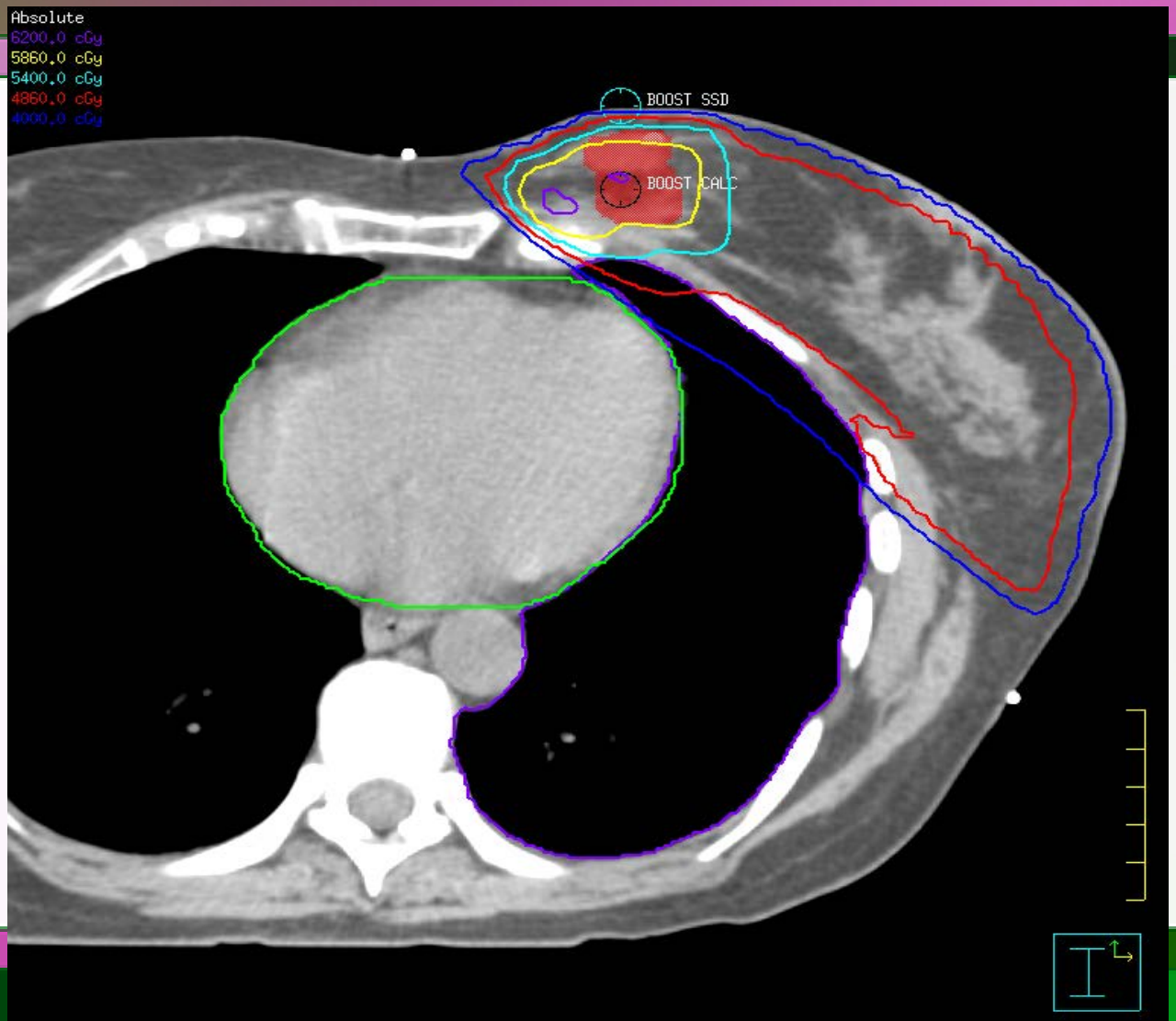
- External Beam Radiation Therapy
  - Delivery of high energy X-rays externally with a treatment machine called a linear accelerator
- Catheter Therapy (Mammosite, Contura, Savi)
  - Delivery of lower energy X-rays internally through placement of radiation sources inside the patient to treat the site of the tumor directly
- Accuboost
  - Delivery X-rays utilizing Mammogram for accurate localization
- Intrabeam
  - Inside the operating room

External Irradiation therapy

Beam angles

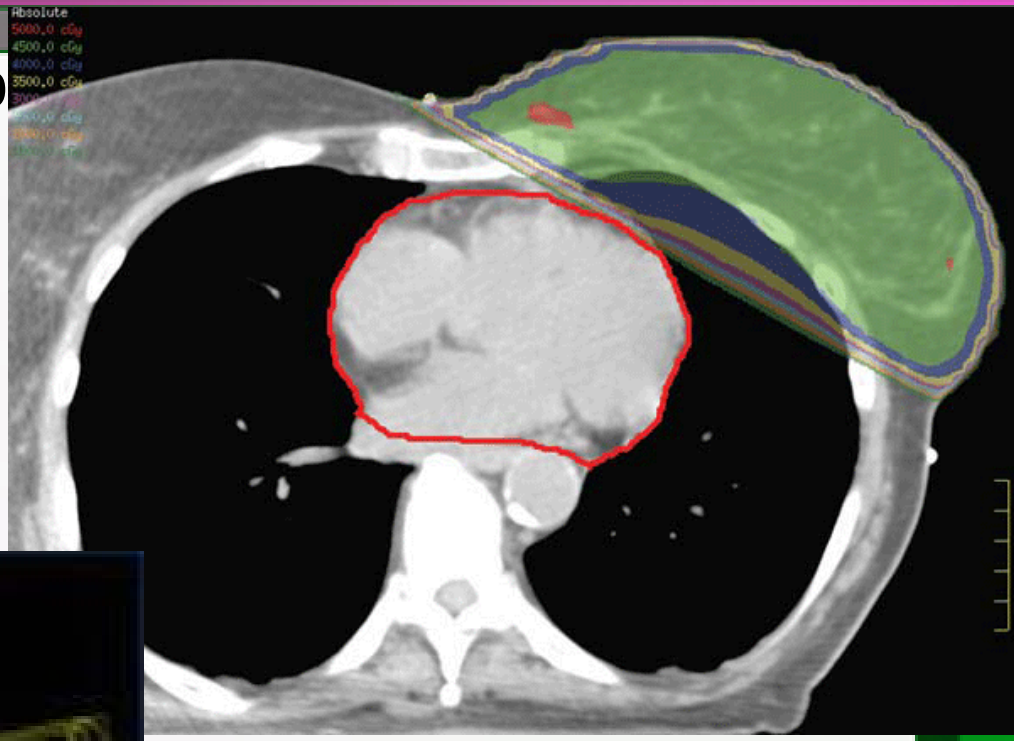


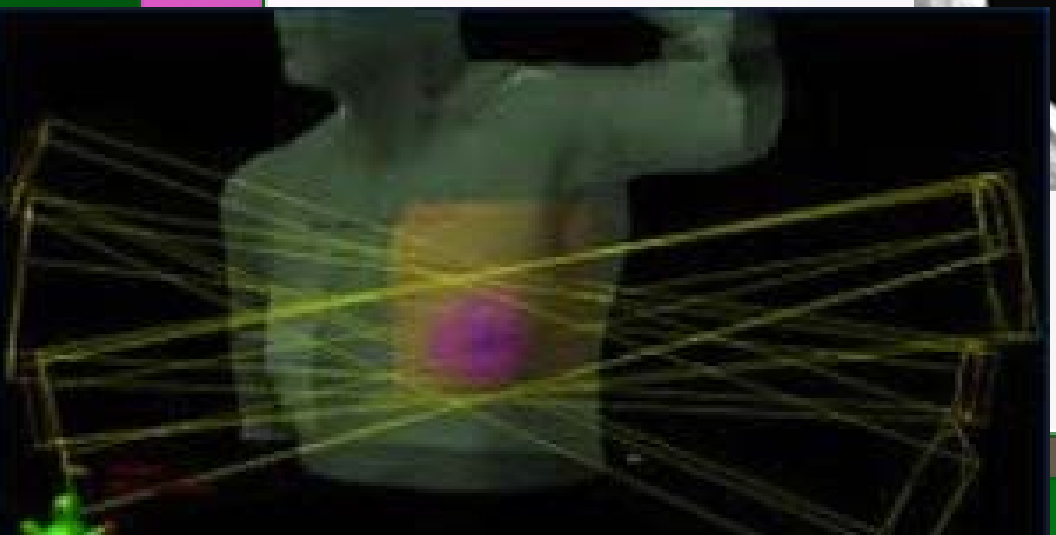
Isodose lines



External Beam

- Standard: ~7 weeks o treatment (Monday-Friday daily treatments)
- Whole breast then extra radiation boost to lumpectomy cavity

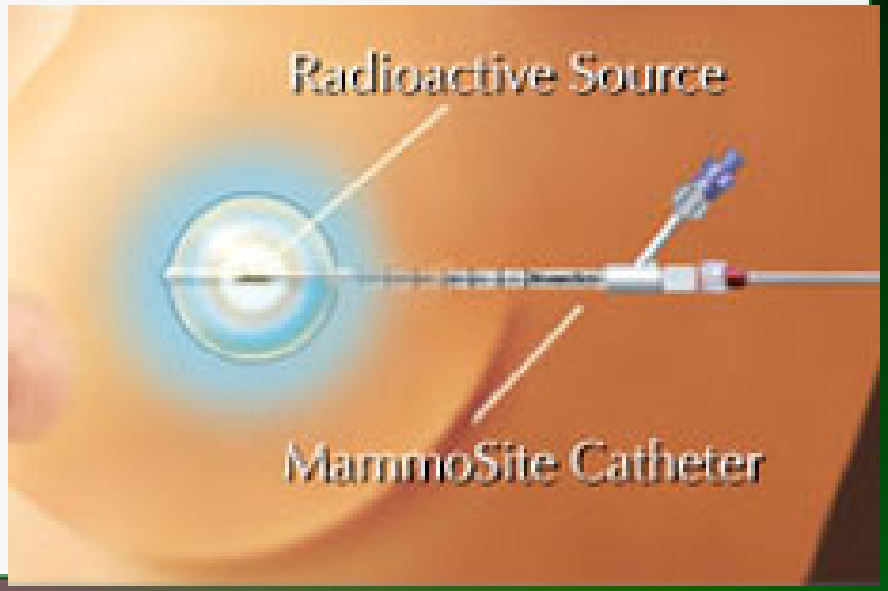




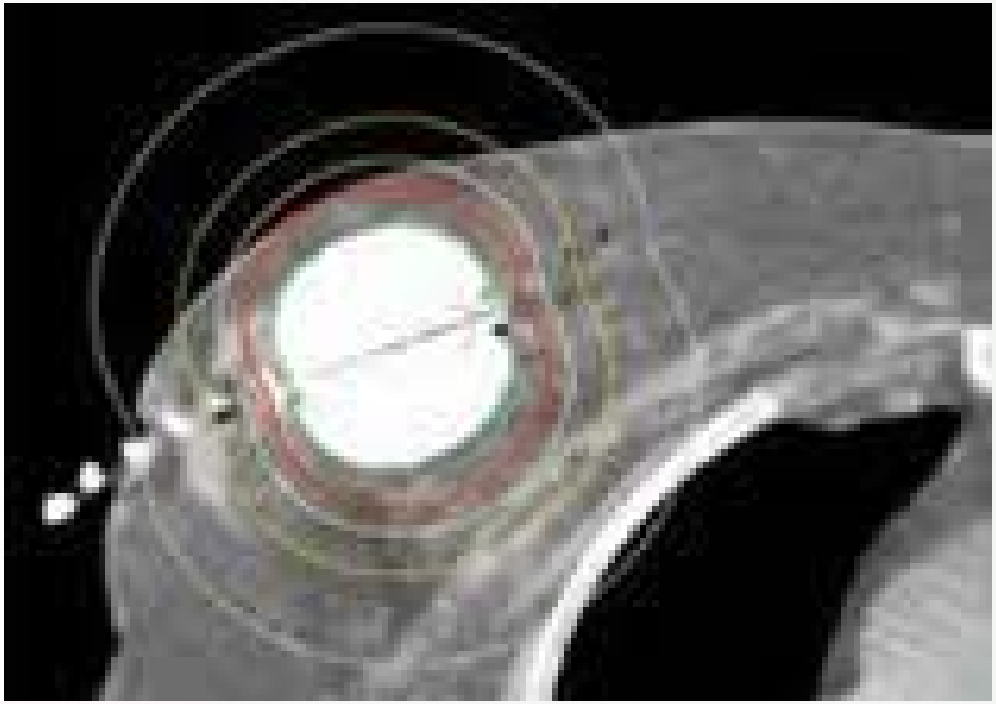
Research Trials

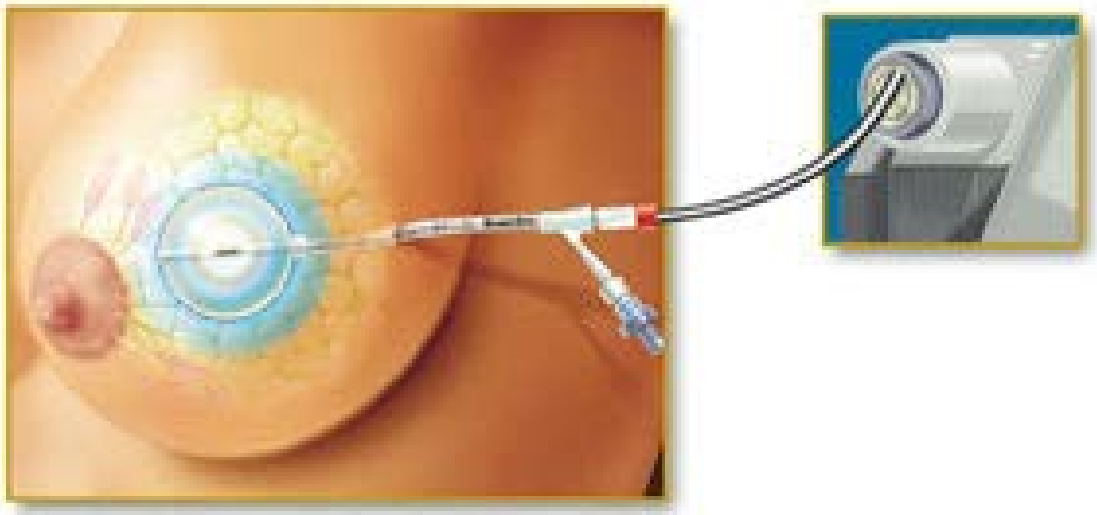
- RTOG 1005
  - Early stage breast cancer
  - Radiation ~3 weeks versus ~7 weeks
  - 3 week: whole breast with concurrent boost
  - 7 week: whole breast then boost

Temporary Internal Radiation HDR



Mammosite/Contoura/Savi



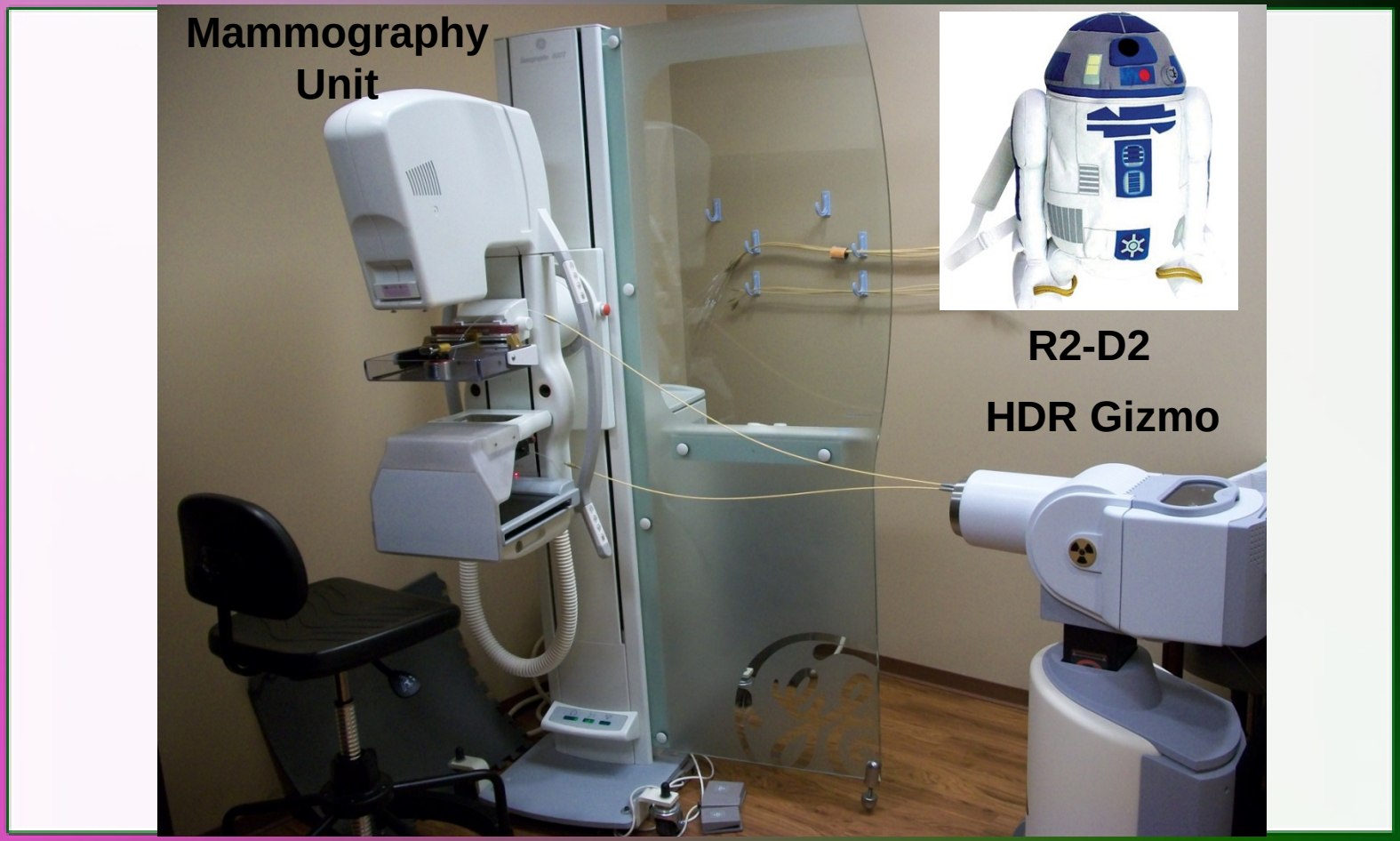


Temporary Internal Radiation HDR

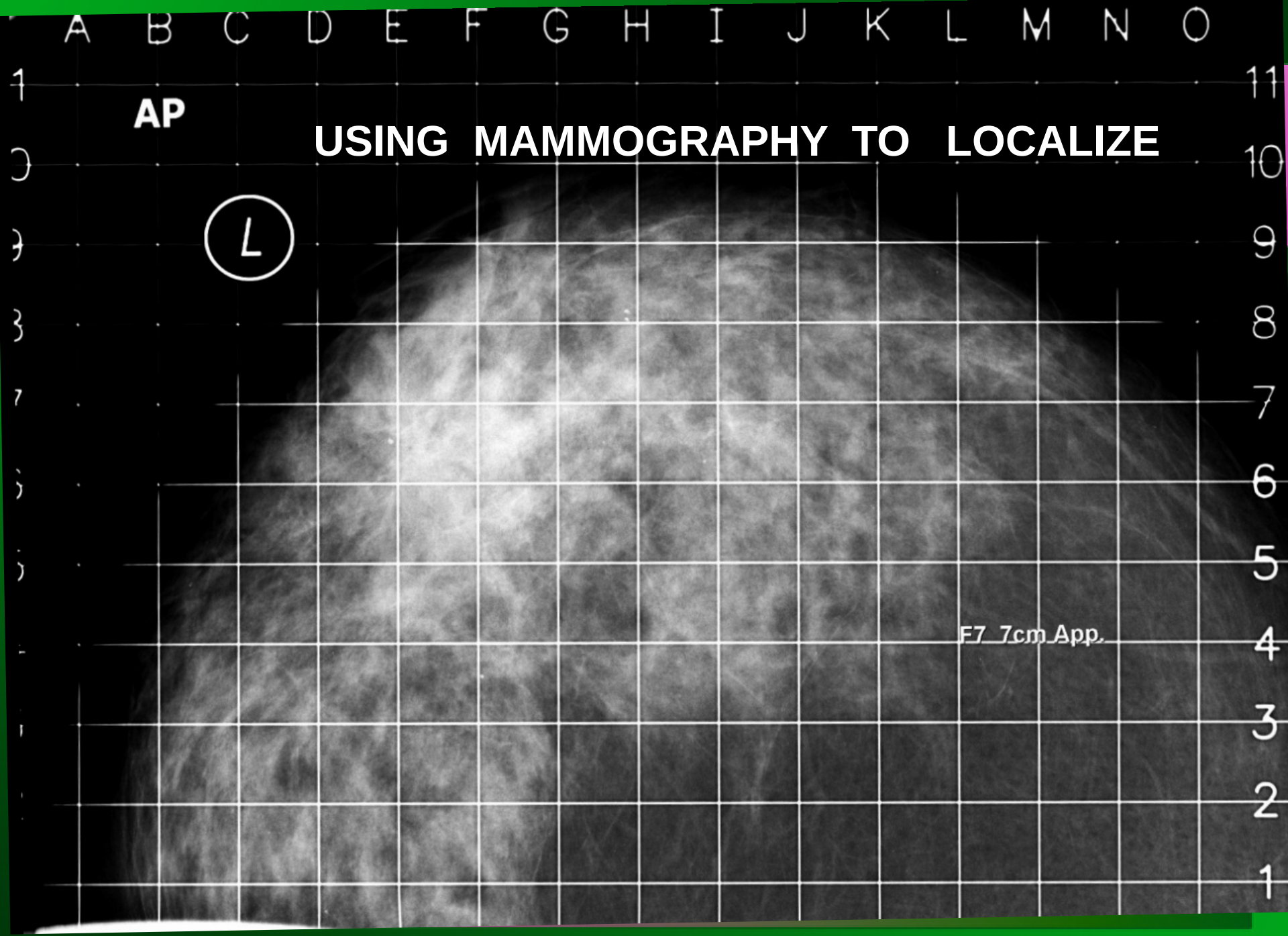
R2-D2

Nucleotrons HDR Gizmo

The Accuboost system



USING MAMMOGRAPHY TO LOCALIZE



Lumpectomy Image

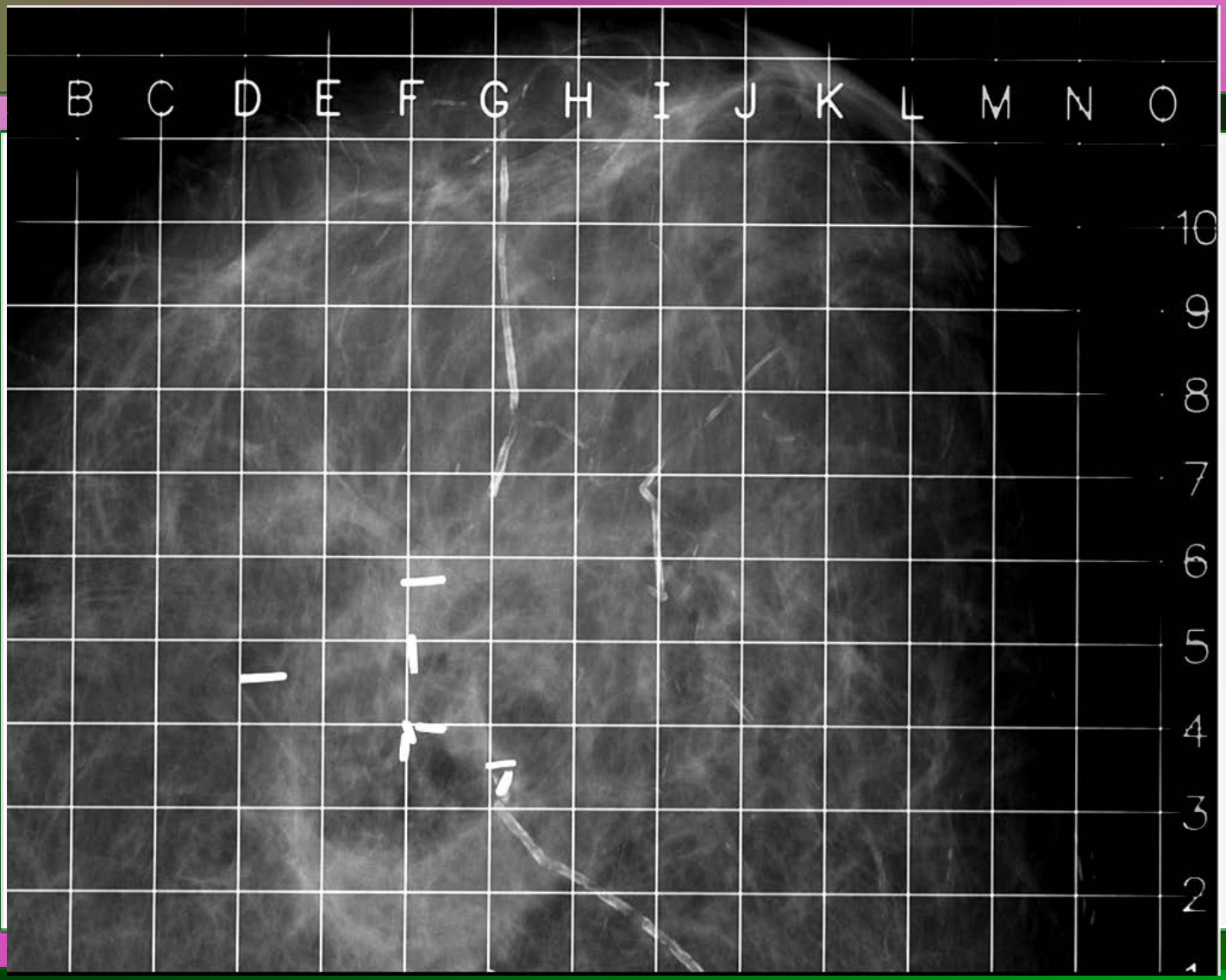
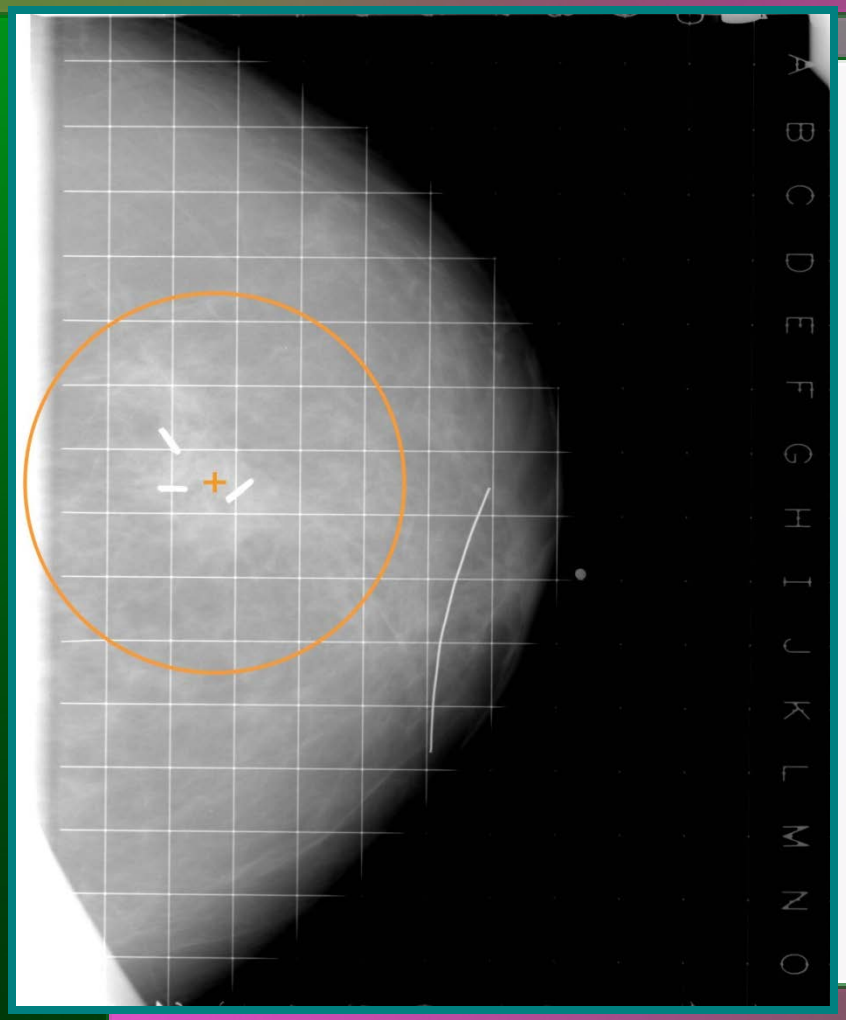
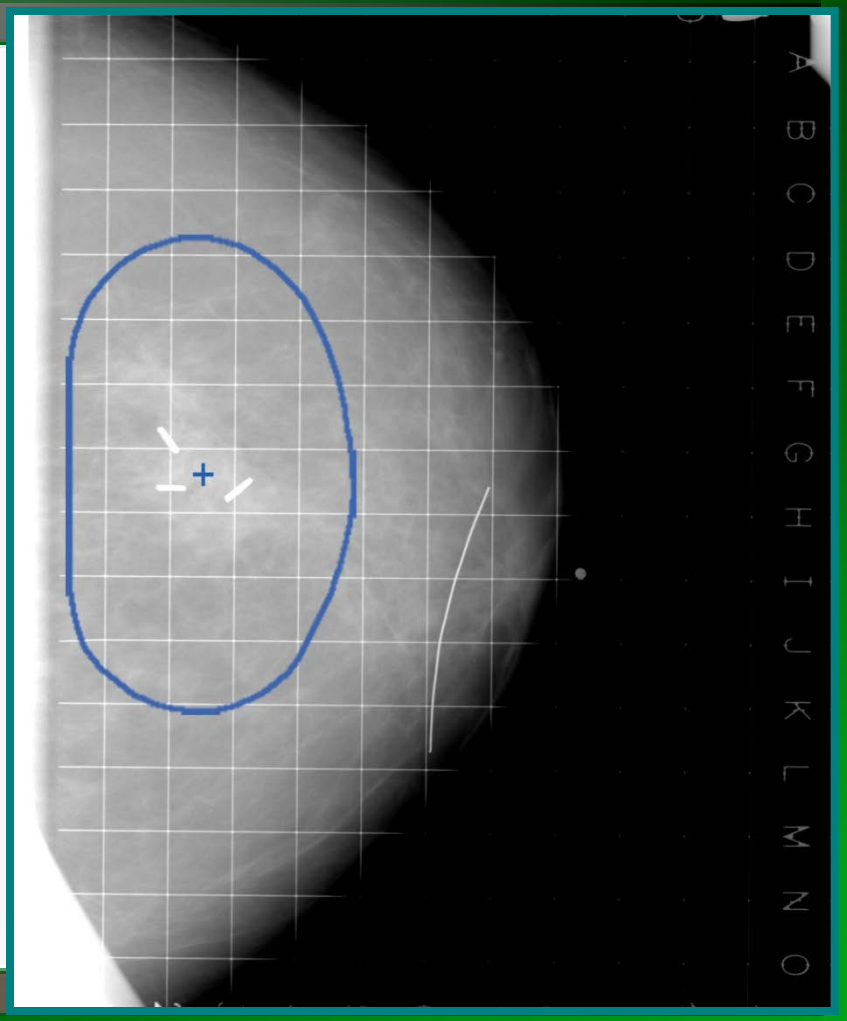


Image guided tailored treatment

Our Surgeons “clip” tumor bed
Mammogram to locate, stabilize & select Applicator shape & size: Circular or D



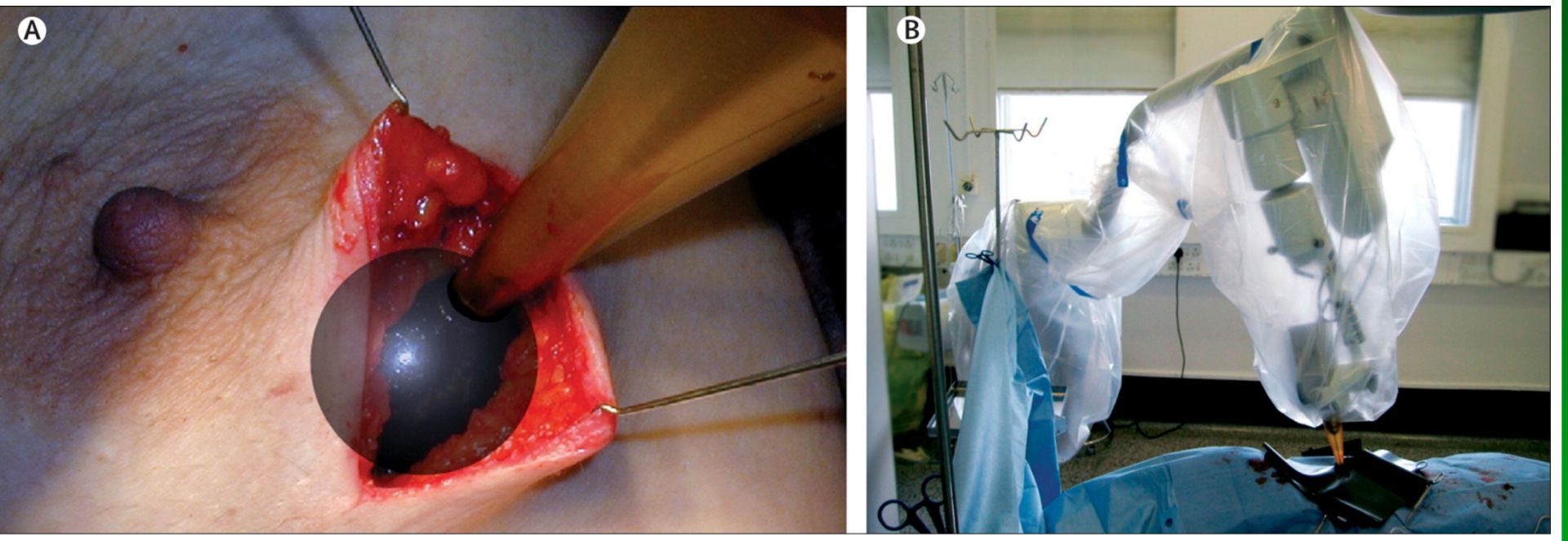


Major Breast Cancer Innovation
Accuboost : External HDR

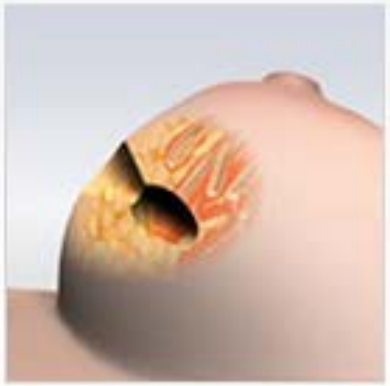
In the operating room:

Figure 1

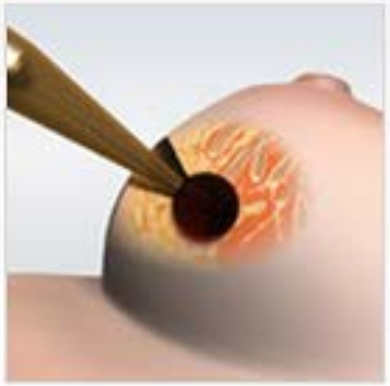
Intrabeam IORT
Intra Operative Radiation Therapy



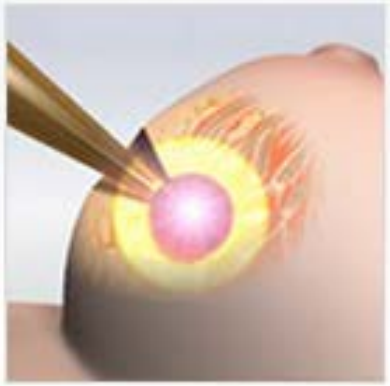
Source: The Lancet 2010; 376:91-102 (DOI:10.1016/S0140-6736(10)60837-9)



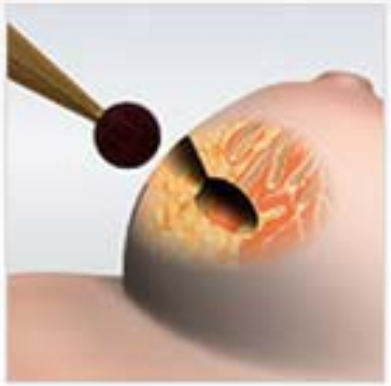
Step 1: INTRABEAM IORT is delivered during the lumpectomy procedure, immediately following tumor removal.



Step 2: After the surgeon has removed the tumor, the radiation oncologist positions the INTRABEAM applicator in the area of the breast where the tumor was located.



Step 3: Low energy radiation is delivered locally to the targeted tissue in the tumor bed, minimizing healthy tissue exposure to radiation.



Step 4: After 20-30 minutes of radiotherapy, the applicator is removed and the surgeon then closes the incision.

Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): an international, prospective, randomised, non-inferiority phase 3 trial

Jayant S Vaidya, PhD, David J Joseph, MD, Jeffrey S Tobias, FRCR, Max Bulsara, PhD, Frederik Wenz, MD, Christobel Saunders, FRCS, Michael Alvarado, MD, Henrik L Flyger, MD, Samuele Massarut, MD, Wolfgang Eiermann, MD, Mohammed Keshtgar, PhD, John Dewar, FRCR, Uta Kraus-Tiefenbacher, MD, Marc Sütterlin, MD, Laura Esserman, MD, Helle MR Holtveg, MD, Mario Roncadin, MD, Steffi Pigorsch, MD, Marinos Metaxas, PhD, Mary Falzon, FRCPath, April Matthews, BSc, Tammy Corica, PGDPH, Norman R Williams, PhD and Michael Baum, FRCS

The Lancet
Volume 376, Issue 9735, Pages 91-102 (July 2010)
DOI: 10.1016/S0140-6736(10)60837-9

RADIATION SUMMARY

- Breast Conservation Therapy is considered equal to Mastectomy if radiation therapy is included following surgical removal of the tumor
- New evidence proves that not only can radiation reduce the risk of tumor recurrence, it can also prolong survival

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Guest Speaker: Melissa Ross

Local Radio Personality from *First Coast Connect*,


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Girls