A new Kind of Ray:
The last 100 Years

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A Brief History of Radiation

- Wilhelm Roentgen discovered *X-rays* on November 8, 1895, while experimenting with a gas-filled cathode tube
  - He noted an image of the bones of his hand projected on a screen when placed between the tube and the fluorescent screen
  - He wrote a carefully reasoned explanation of the phenomenon within two months

Early radiograph taken by Roentgen, January, 1896.

Brief History of Radiation Therapy

- The first patient was treated with radiation in 1896, two months after the discovery of the X-ray.
- Back then, both doctors and non-physicians treated cancer patients with radiation.
- Rapid technology advances began in the early 1950s with cobalt units followed by linear accelerators a few years later.
- Recent technology advances have made radiation more effective and precise.

Breast Cancer

Case presentation/ Breast

- 63 yof, MMG/US - Cluster of numerous heterogeneous micro calcification at UOQ of lt.breast, 1.8 cm, core bx. + IDC/HG DIC comedo, LVI +, ER+/PR-, Her 2neu +

William Halsted 1907

ORIGINAL MEMOIRS.

THE RESULTS OF RADICAL OPERATIONS FOR THE CURE OF CARCINOMA OF THE BREAST.*

BY WILLIAM STEWART HALSTED, M.D.,
OF BALTIMORE, MD.,
Surgeon to Johns Hopkins Hospital.

The Operation.—Though the area of disease extend from cranium to knee, breast cancer in the broad sense is a local affection, and there comes to the surgeon an encouragement to greater endeavor with the cognition that the metastases to bone, to pleura, to liver, are probably parts of the whole, and that the involvements are almost invariably by process of lymphatic permeation and not embolic by way of the blood. Extension,

First hypothesis

- William S. Halstead – Radical Mastectomy
  - Breast cancer is a loco regional dz
  - Step by step extension via lymph system leads to metastatic dz

- Cure requires enblock dissection of
  - Breast tissue including tumor
  - Regional lymphatic and LNs.

Haagensen and Stout 1943

- Retrospective review of 21 different prognostic factors analyzed in RM pts.

Clinical features	**# of patients**	**5 yr LF (%)**	**5 yr cure (%)**
Cancer during pregnancy/lactation	20	30	0
Extensive edema of skin over breast	41	65.9	0
Satellite nodules of skin over breast	7	57.1	0
Intercostal/parasternal nodules	1	0	0
Edema of arm	3	66.7	0
Supraclavicular metatasis	12	58.3	0
Inflammatory breast cancer	20	50	0
Distant metastasis	7	14.3	0

Ann Surg 1951 Aug;134(2):unknown

Haagensen and Stout 1943

Concls:

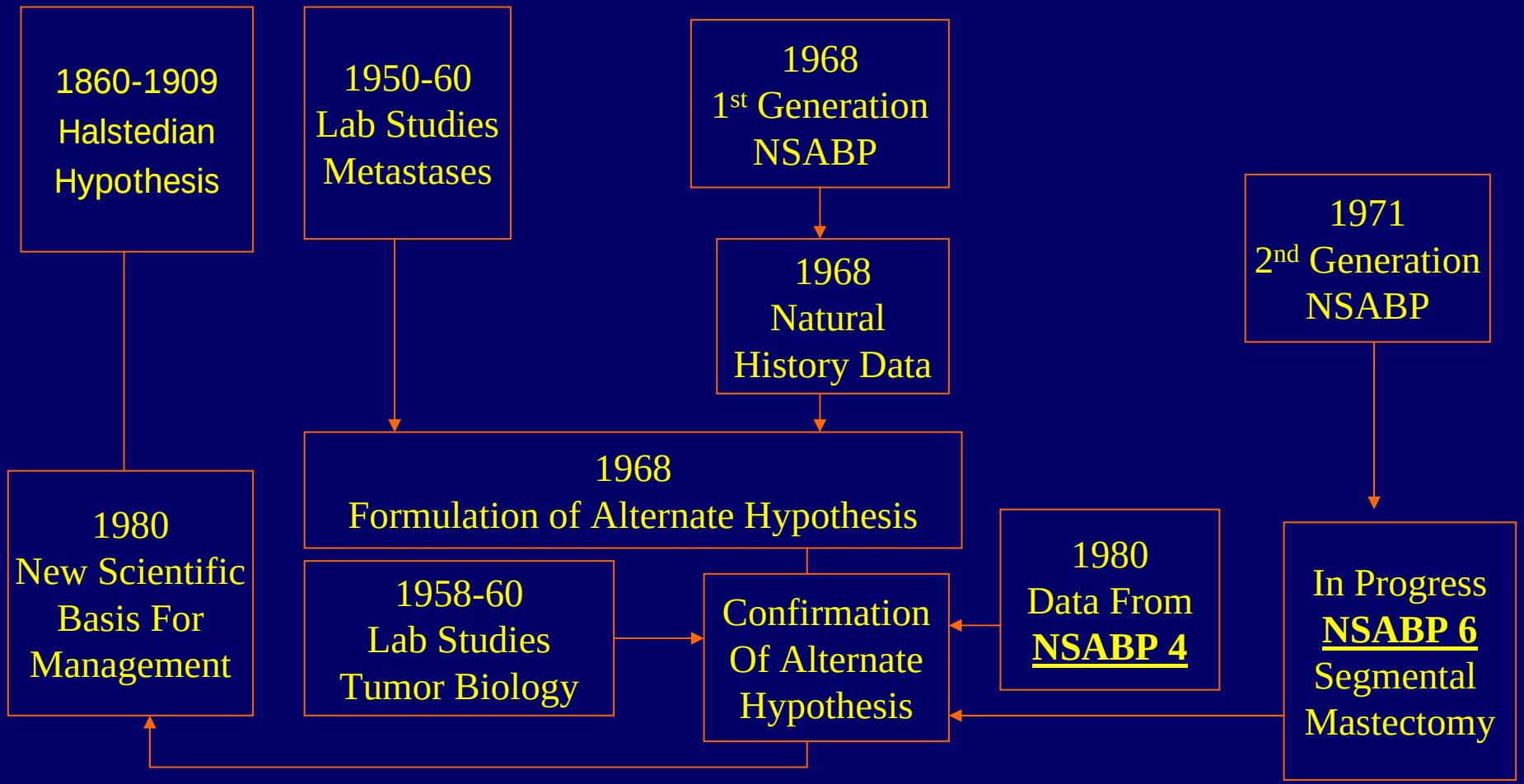
- These pts. Should not have received RM, recommend RT.

Ann Surg 1951 Aug;134(2):unknown

Next 40 years

- Following this landmark publication Radiation Therapy alone became the treatment of choice for BC pts for a long time, specifically for the LABC pt

Second hypothesis/Bernard Fisher 1980



Second hypothesis/Bernard Fisher 1980

Series of lab/clinical studies formulated a new Breast cancer hypothesis

- Breast cancer is a systemic dz
- Blood and lymphatic are interrelated
- Systemic treatment needed to improve cure

Bernard Fisher 1981/ NSABP 4

- 1971-1974, 1655 pts, operable breast ca
- RM vs SM+RT vs SM(+LND)

- 10 yrs result

	LF/ N0	OS/ N0	LF/ N1	OS/ N1
	(%)	(%)	(%)	(%)
RM	2	57	1	38
SM + RT	2	57	12	38
SM (+LND)	18	57	not ran	not ran

- Concl
- No difference in OS in any groups

Cancer 48:1863-1872, 1981

Bernard Fisher 1995/ NSABP 6

- 1843 pts, stage I, II, randomized
- MRM vs lumpectomy+ALND vs Lumpectomy +ALND+RT
- 12 yrs result

	LF	LF/ N0	LF/ N1	OS
	(%)	(%)	(%)	(%)
MRM	59			60
Lump + LND	35	32	41	60
Lump + LND + RT	10	12	5	62

- Concl
- OS is independent of mastectomy vs lumpectomy
- RT reduces local failures and is crucial for BCT

NEJM 333:1456-1461, 1995

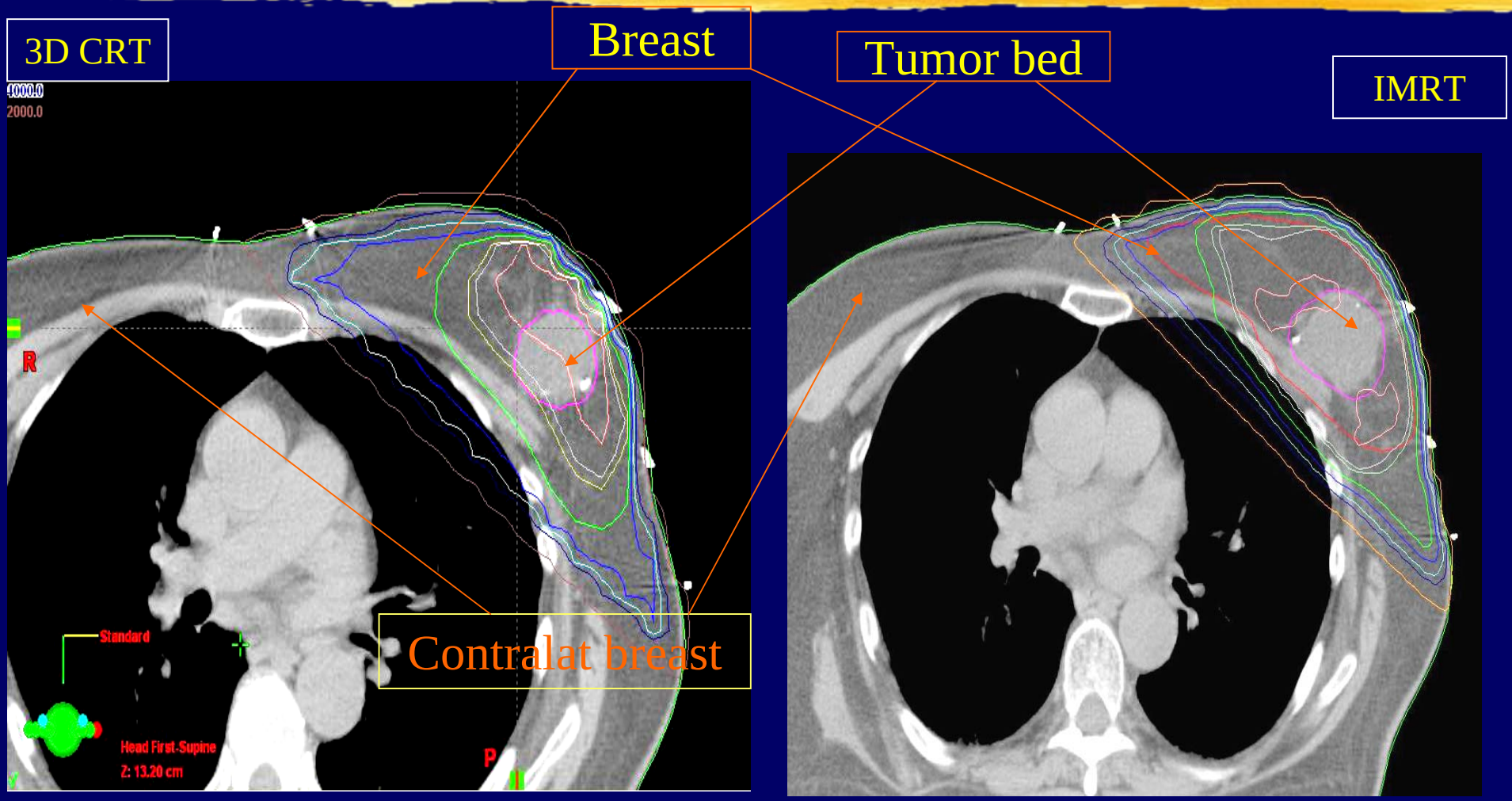
Over the last 100 yrs

- Halstedian concept of RM does not improve OS
- Breast cancer is a systemic dz and systemic therapy was introduced to cure pts
- RT is essential for LC and is a critical part of multimodality management for breast cancer pts

Case presentation/ Breast Tx 2007

- Under went lumpectomy and SLN bx
- Received AC x4, Taxol x4, on HTx and receiving Herceptin
- Post-op RT to whole breast to 50 Gy, followed by tumor bed boost to 61.2 Gy utilizing IMRT technique

Case presentation/ Breast Tx 2007



Case presentation/ Breast Tx 2007

3D CRT

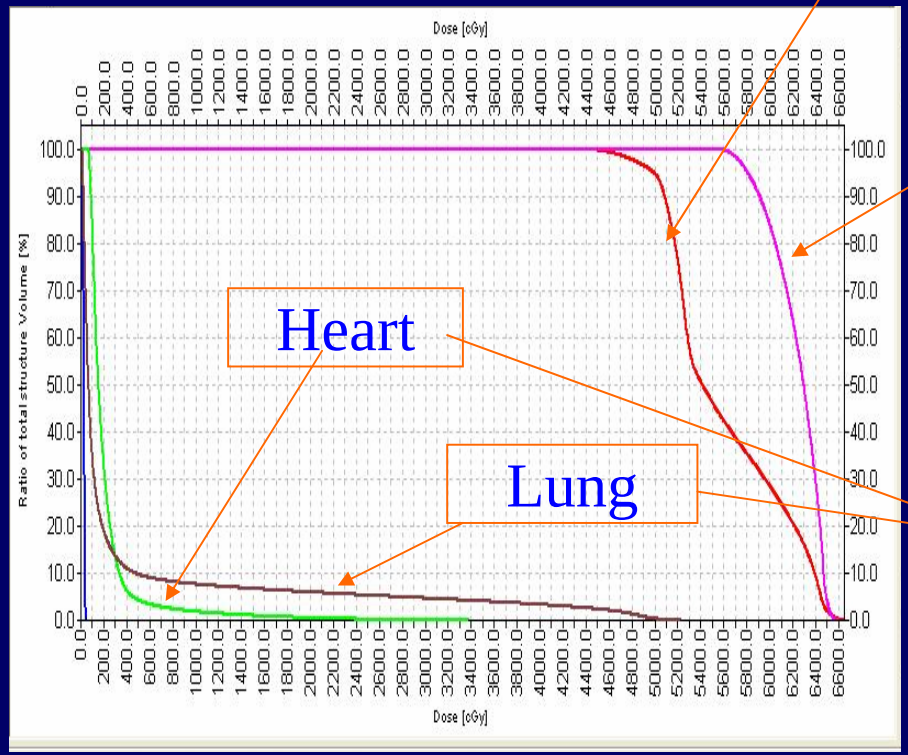
IMRT

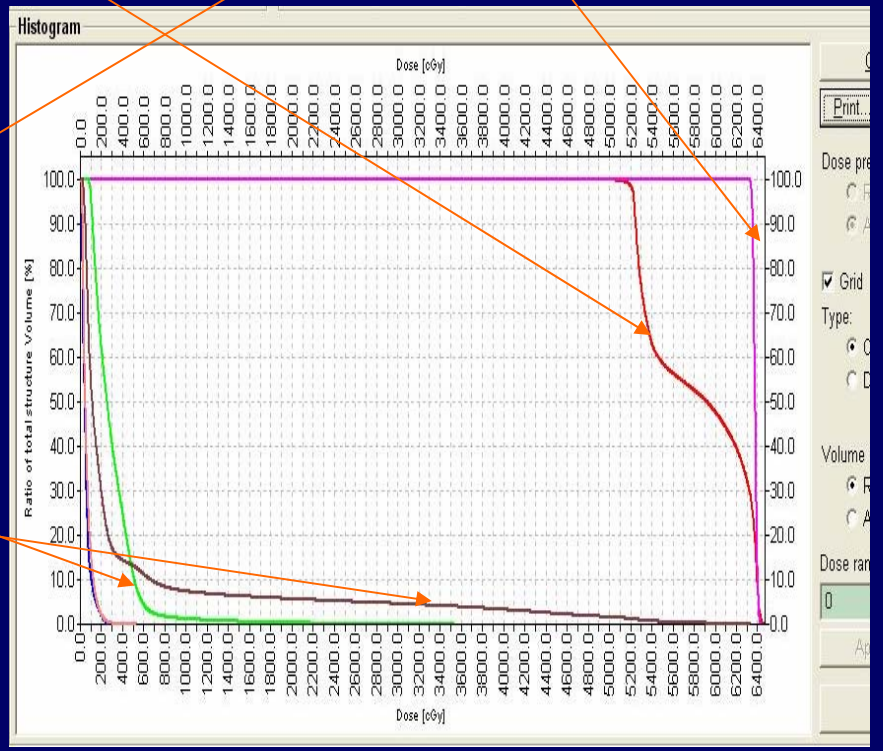
Breast

Tumor bed

Heart

Lung

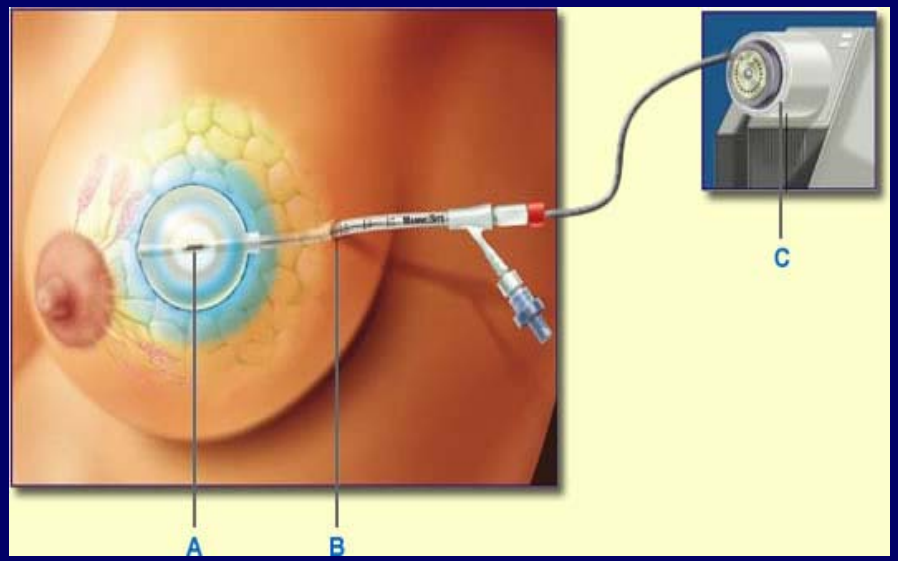




Brachytherapy for Breast Ca

- Mammosite
  - **<u>BID radiation over 1 week</u>**

- High-Dose-Rate (HDR)
  - High energy source delivers the dose in a matter of minutes rather than days
    - > Gynecologic, breast and some prostate implants may use use high-dose-rate brachytherapy



HDR brachytherapy for breast cancer using MammoSite catheter (B) with an Iridium-192 source (A) and a high-dose-rate afterloader (C). This is an example of a temporary high-dose-rate implant.

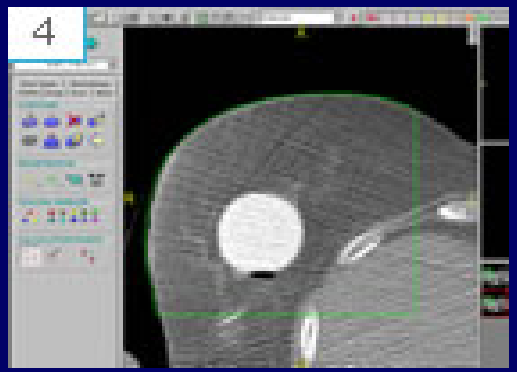
BID RT over 1 week for Breast Cancer

1

2

3

4



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BID RT over 1 week for Breast Cancer

- There have been several clinical studies since the MammoSite® Radiation Therapy System received FDA clearance in 2002.

- **5-year results from the initial 43-patient MammoSite clinical trial show:** No local recurrences and 82% of patients had good/excellent cosmetic results.[7]

- Five hundred and eighty patients have been enrolled in a manufacturer-sponsored registry trial designed to determine the technical reproducibility and acute toxicity involved in the large scale use of the device. This registry is now managed by the American Society of Breast Surgeons. The registry contains 81 sites (36 sites are enrolling patients) and 94 surgeons.

Keisch M, Vicini F, Kuske RR, et al: Int J Radiat Oncol Biol Phys 55:289-293, 2003.

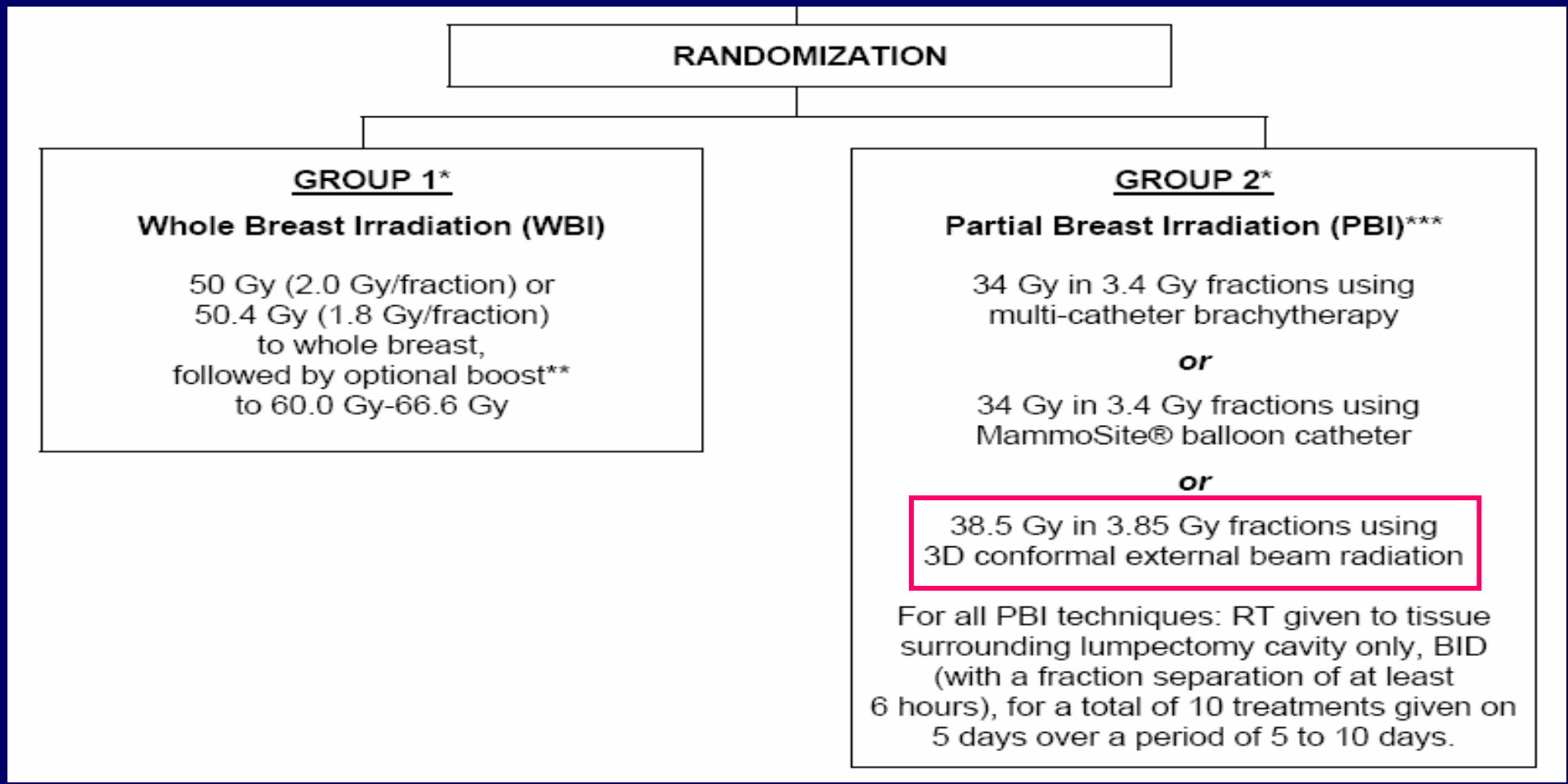
Ongoing Clinical Trial

NSABP PROTOCOL B-39
RTOG PROTOCOL 0413

A Randomized Phase III Study of Conventional Whole Breast Irradiation (WBI) Versus Partial Breast Irradiation (PBI) for Women with Stage 0, I, or II Breast Cancer

National Surgical Adjuvant Breast and Bowel Project (NSABP)
Radiation Therapy Oncology Group (RTOG)

RTOG PROTOCOL 0413/ BID RT over 1 week



RTOG PROTOCOL 0413/ BID RT over 1 week

Figure 2. Whole breast contour

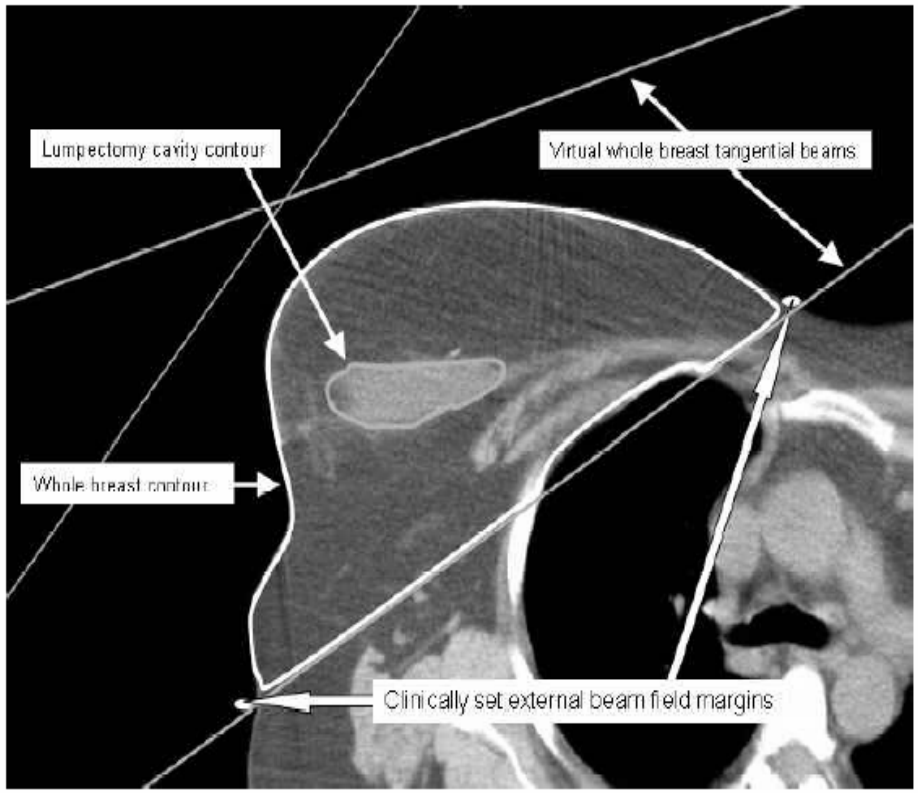
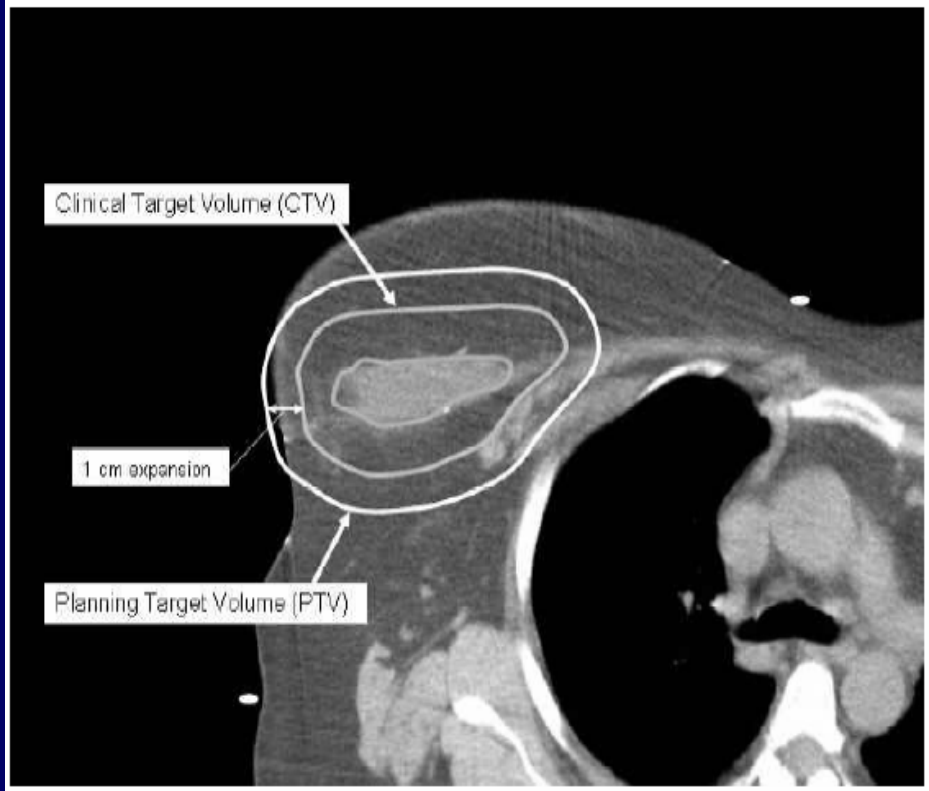
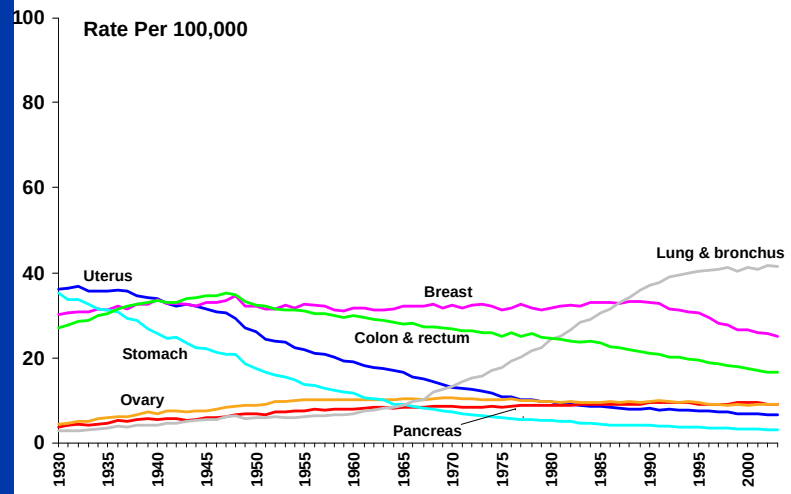


Figure 5. 3D-CRT



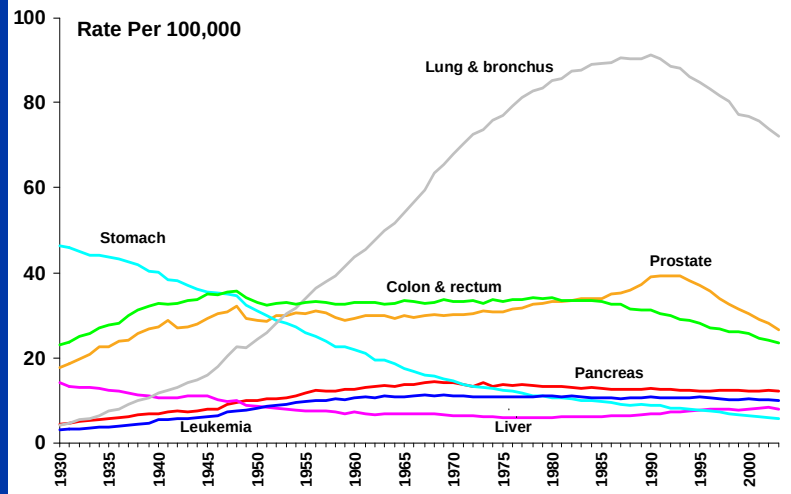
Cancer death rates 1930-2003

Cancer Death Rates*, for Women, US,1930-2003



*Age-adjusted to the 2000 US standard population.
Source: US Mortality Public Use Data Tapes 1960-2003, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2006.

Cancer Death Rates*, for Men, US,1930-2003



*Age-adjusted to the 2000 US standard population.
Source: US Mortality Public Use Data Tapes 1960-2003, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2006.

Conclusions/ Breast

- Breast cancer is a systemic dz, requires systemic Rx
- RT is a critical component of the multi-modality management for the breast cancer
- IMRT can reduce heart, lung, contralat breast and skin dose for breast cancer pts

Conclusions/ Breast

- New RT technique with brachytherapy given BID over 1 week for selected breast cancer patient is a safe and effective Tx

- Phase III clinical trial underway to determine
  - whether PBI limited to the region of the tumor bed following lumpectomy provides equivalent local tumor control in the breast compared to conventional WBI in the local management of early stage breast cancer.
  - We are now enrolling patients with early stage breast cancer in local clinical trial at the local hospital in Panama City, FL.

Conclusions

- IMRT is the latest radiation technique
- X-rays have come a long way in last 100 yrs, now actively contributing to cure of cancers

The End

Thanks

- Dr. Buchholz, MD Anderson Can Cnt
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