Making sense of Radiation Therapy in Breast Cancer

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Disclosure

- **Relationships with commercial interests:**

- None

Objectives

- List the indications for radiation after lumpectomy and after mastectomy
- List the indications for radiation of the regional lymph nodes
- Explain when is radiation indicated in patients with metastatic breast cancer
- Describe the overall benefit from adjuvant radiation therapy
- Briefly describe the process of radiation therapy
- List management strategies for acute and late effects of radiation

Multidisciplinary

- Family Physicians
- Radiology
- Pathology
- Surgeons
- Medial Oncologists
- Radiation Oncologist's
- HCP

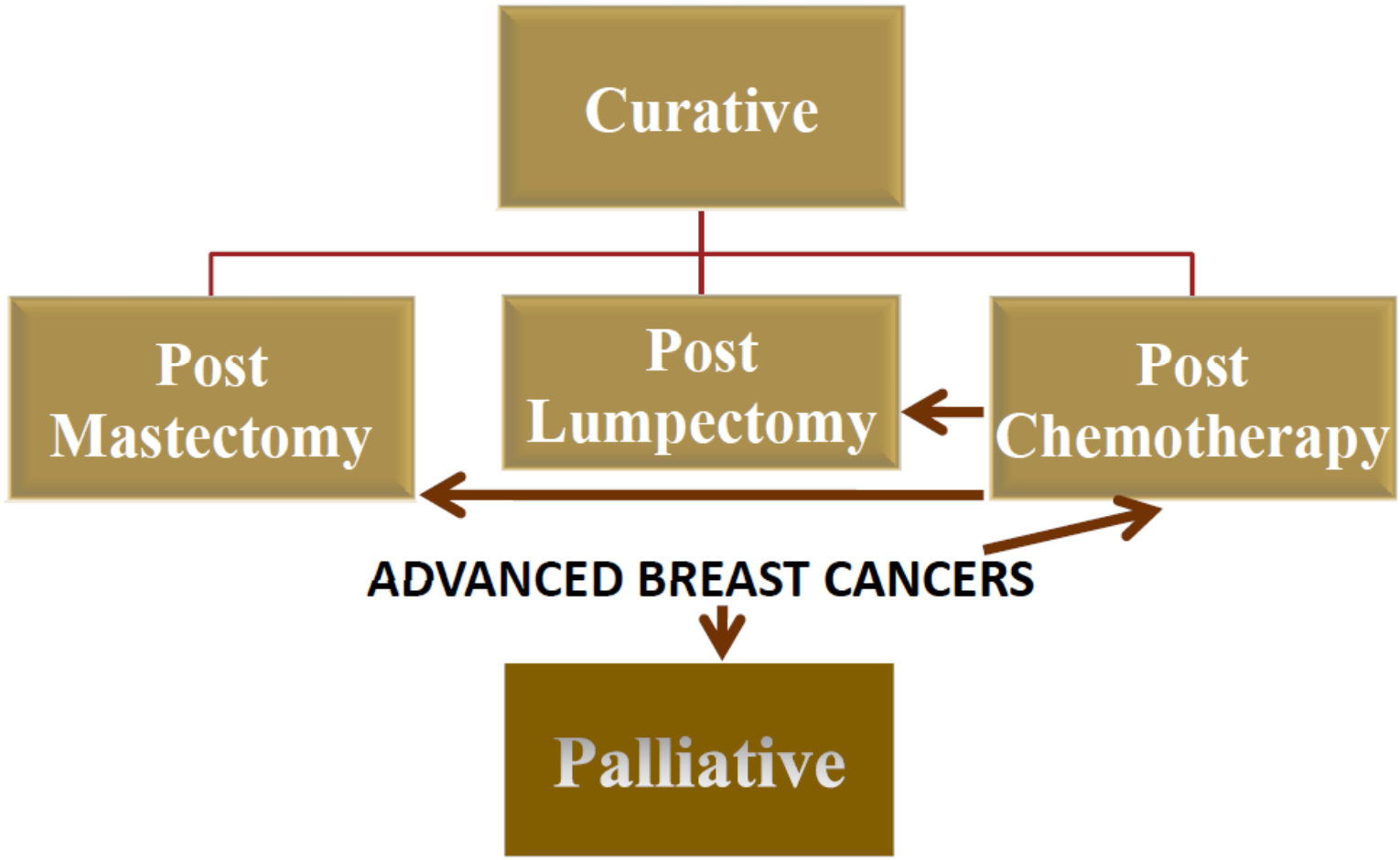
Staging

- Tumor
  - Tis: in situ
  - T1: <2cm
  - T2: 2-5cm
  - T3: >5cm
  - T4: invasion of skin or chest wall
- Node
  - N1: 1-3 axillary nodes or int mam node
  - N2: 4-9 axillary nodes or palpalbe int mam node
  - N3: >10 nodes or combo of axillary and int mam nodes
  - {*mic* micoroscopic posivitiy, *mol* molecular positivity
- Metastasis

Role of Radiotherapy in breast cancer

- 1) Adjuvant
- 2) Palliative
- 3) Neo Adjuvant

Role of radiation therapy in breast cancer



List the indications for radiation after lumpectomy and after mastectomy

List the indications for radiation of the regional lymph nodes

Describe the overall benefit from adjuvant radiation therapy

70-80% of patients with stage I or II disease are candidates for BCT

MRM Vs BCT

Randomized trials

Meta-analysis

↓

Comparable local control, Overall survival

Better cosmetic outcome

EBCTCG, 2011

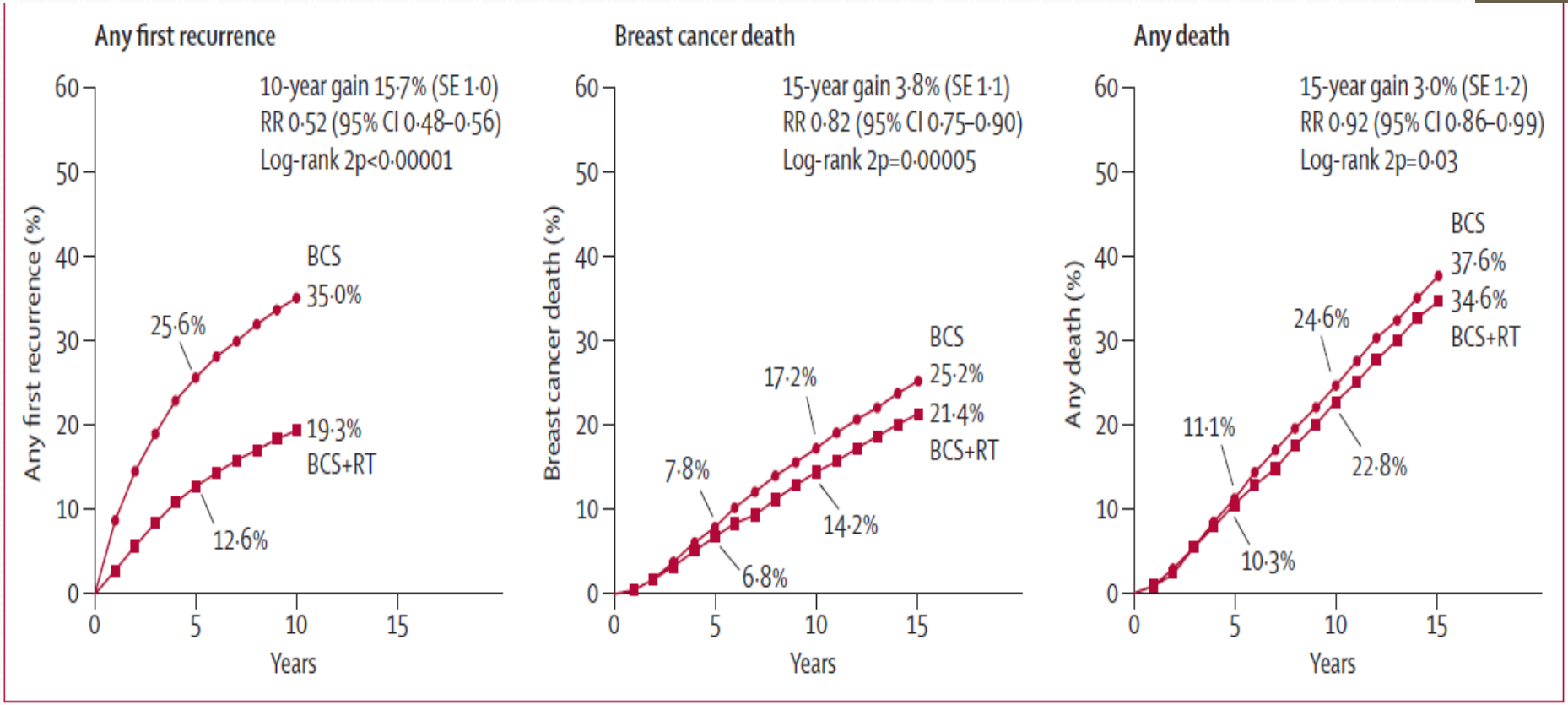
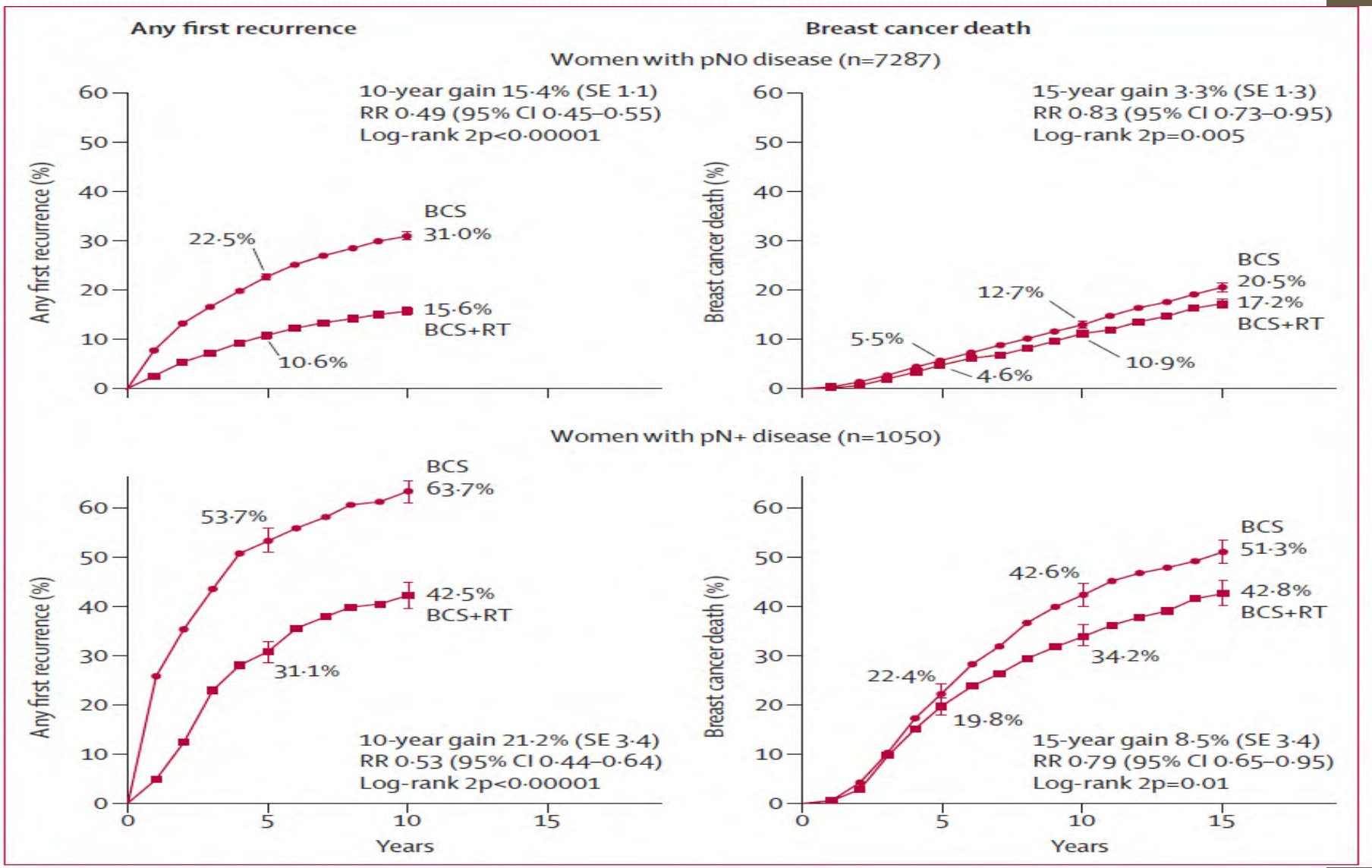


Figure 1: Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on 10-year risk of any (locoregional or distant) first recurrence and on 15-year risks of breast cancer death and death from any cause in 10 801 women (67% with pathologically node-negative disease) in 17 trials

Further details are in webappendix p 5. RR=rate ratio. Rate ratios in this figure include all available years of follow-up.

Node positive/Node Negative



Surgery alone without RT?

- One possible subset where RT maybe omitted
- Patients > 70 years of age
  - with small Node neg ER+ tumors/G1or 2/No adverse risk factors
  - who will get systemic treatment
  - No survival benefit with RT

Timing of RT (chemo)

- Radiation is usually withheld until after the systemic therapy is complete
- Delay of up to 4-6 months from surgery generally not considered a problem
- Possible problem with inflammatory cancer or other locally aggressive cancers
- Hypofractionated schemes may allow for early RT while waiting for Oncotype

Timing of RT (Hormones)

- RT is started post surgery 4 to 6 weeks
- Timing of hormones is unclear
- During or post RT

Conclusions

- RT post BCT is highly effective in reducing recurrence in both N0 and N+ pts
- Also improves OS, impact on mortality is seen late
- One breast cancer death avoided for every 4 recurrence avoided
- Most patients after BCT will be recommended to have adjuvant RT
- RT maybe omitted for a selected group of patients

PMRT

Some breast cancers recur in chest wall
Or RLN despite mastectomy
Not all can be salvaged
Preventing Local relapse has an impact on OS

Locoregional recurrence after mastectomy & adriamycin-based chemotherapy (MDAH)

10 yr actuarial rate of isolated LRF by tumor size and nodal status

T stage	No LNs	1-3 LNs	4-9 LNs	10+ LNs
T1	6%	7%	9%	17%
T2	11%	12%	23%	17%
T3	29%	29%	31%	29%

Postmastectomy Radiotherapy

Intermediate Risk disease

- T2 tumor with multiple adverse features
  - High grade, LVI+, ER-
- 1-3 lymph nodes
- Age < 45 years

- LRR 10 -18% postmastectomy
- LRR 5% post Locoregional radiotherapy

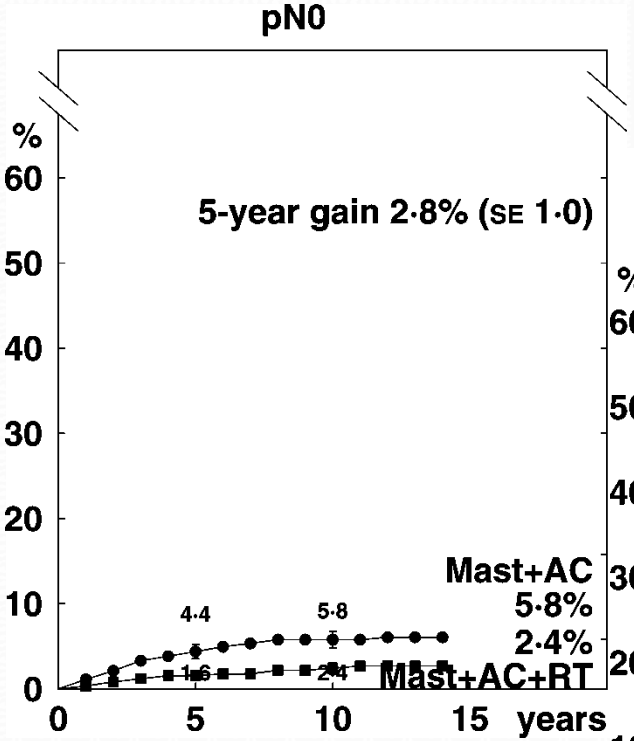
Postmastectomy Radiotherapy

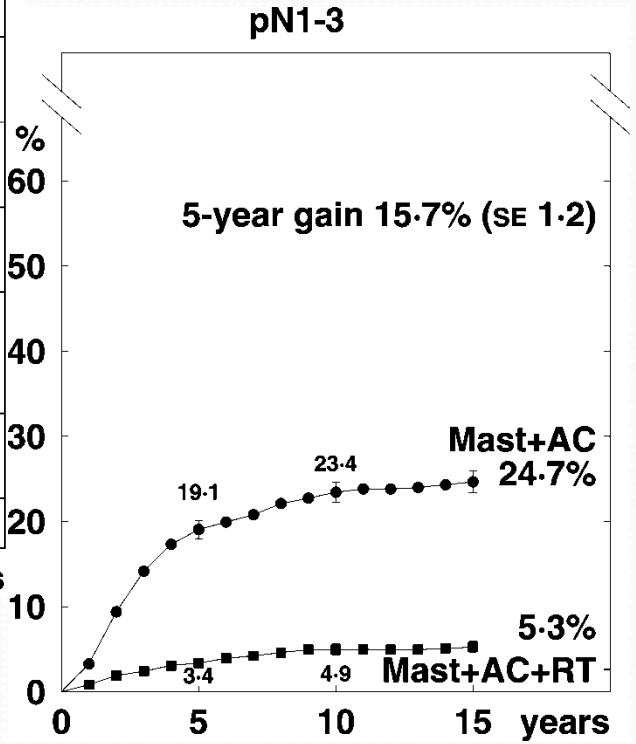
Standard for High Risk disease

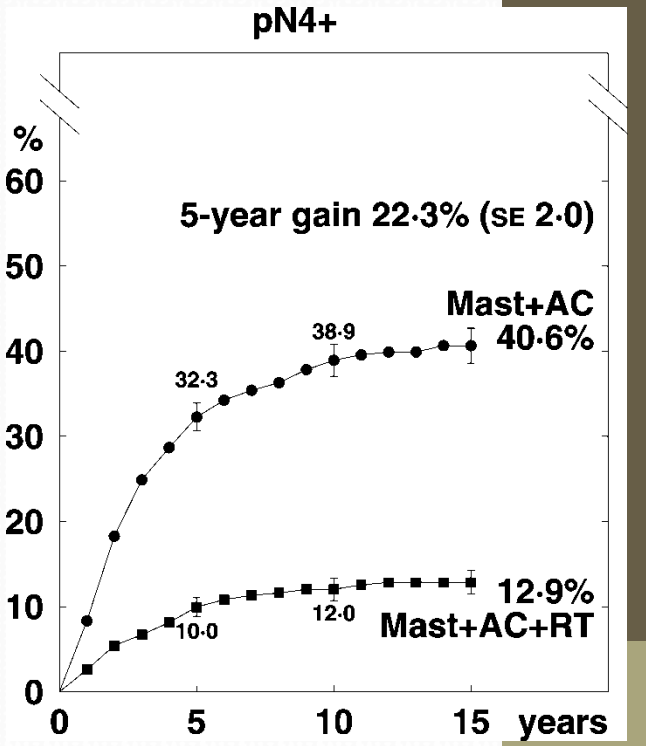
- Tumor > 5cm (T3)
- Tumor involves skin or chest wall (T4)
- 4 or more lymph nodes

  - LRR 25-30% postmastectomy
  - LRR 5- 10% post Locoregional radiotherapy
  - OS improves 5%

EBCCTG

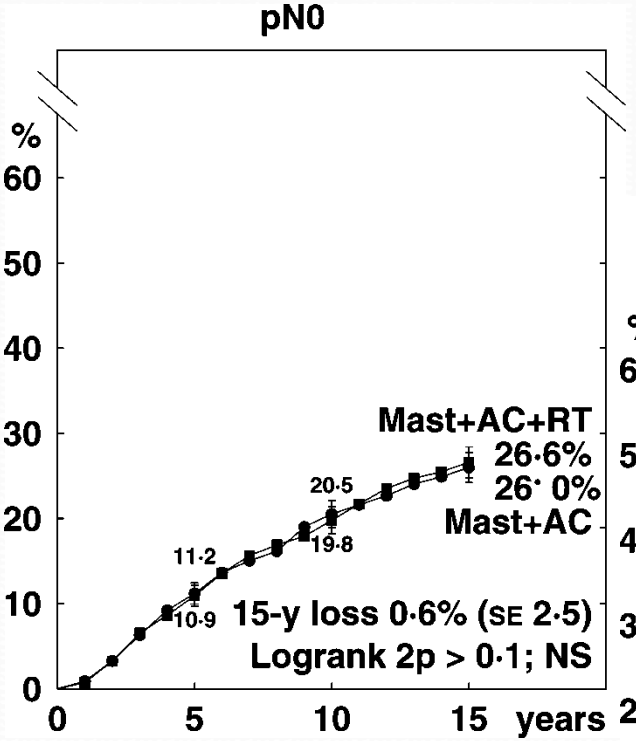


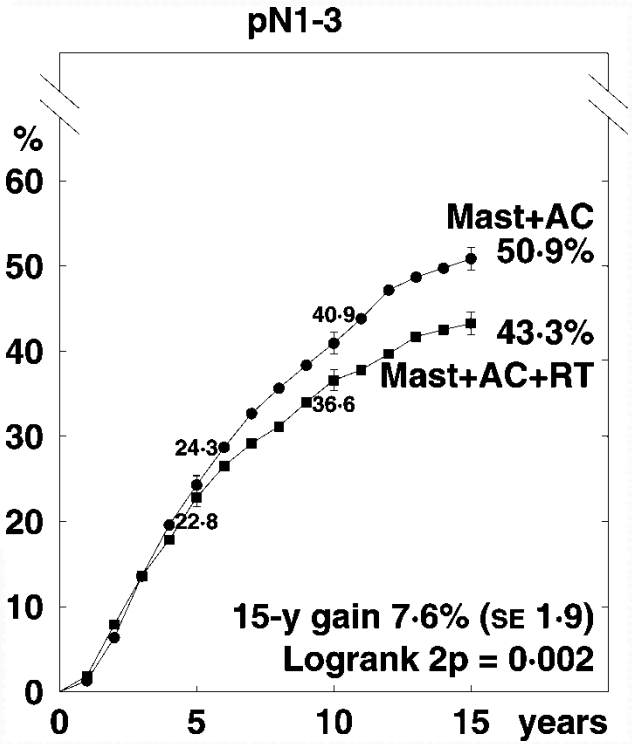


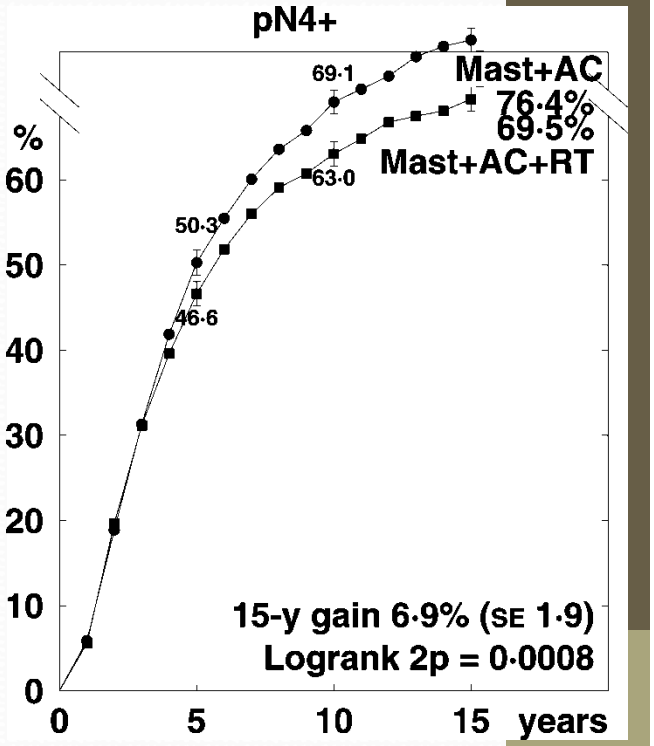


Local Recurrence

EBCCTG





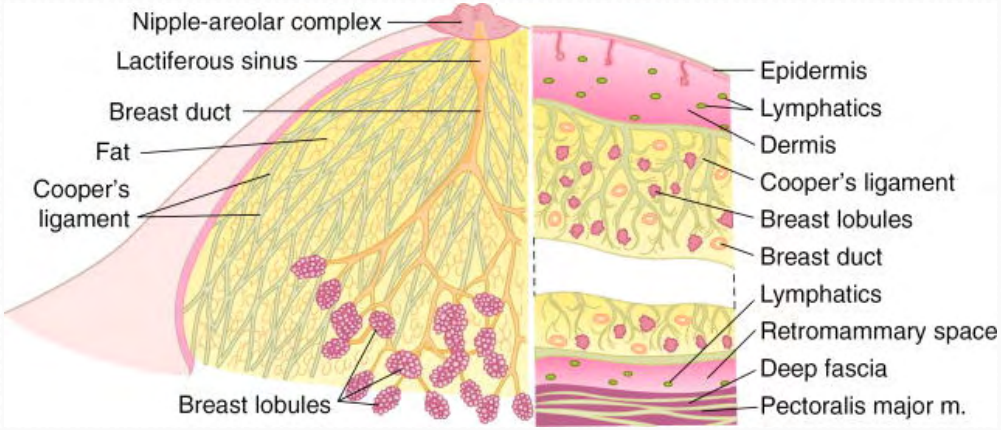


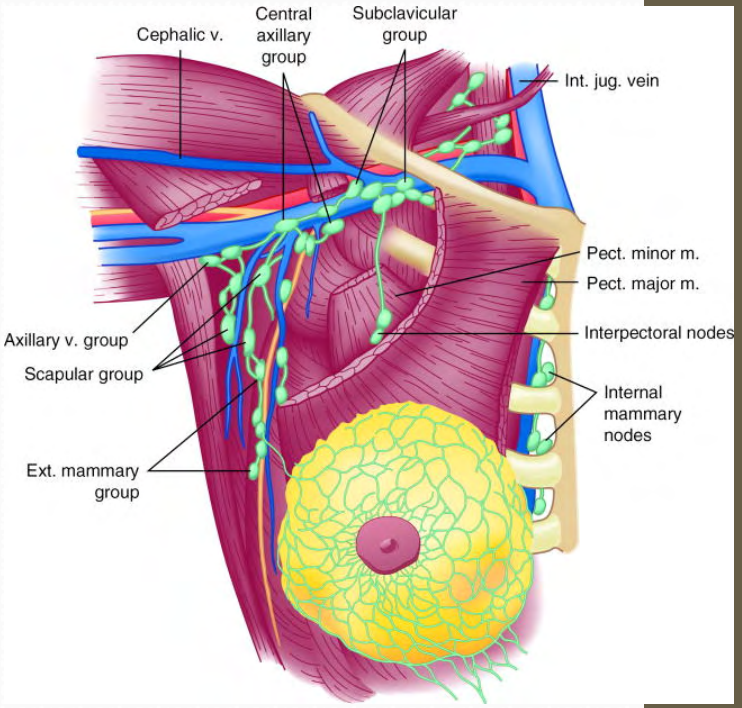
OVERALL SURVIVAL

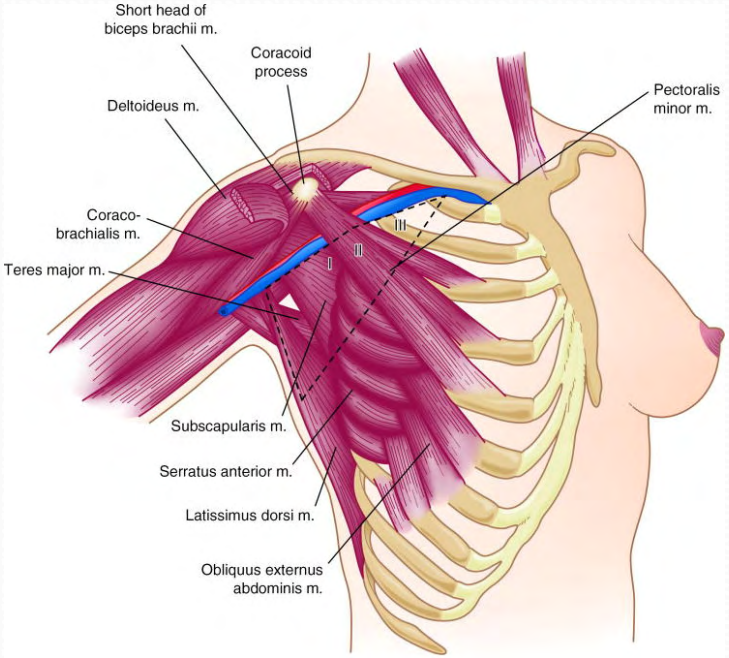
Conclusions

- PMRT improves significantly both OS and LR especially in Node positive pts
- Pts who receive PMRT are generally node positive
- Treating the chest wall alone in node negative patients is not common unless there are positive margins and clinical concern of high risk of recurrence

RT to RLN







75% of lymphatics flow to axilla

RT to RLN

- There has been an increasing trend to treat RLN
- Due to introduction of SLN
- Less number of pts having ALND
- Trials showing benefit in OS and LR even in 1-3 node positive patients

Briefly describe the process of radiation therapy

Radiotherapy

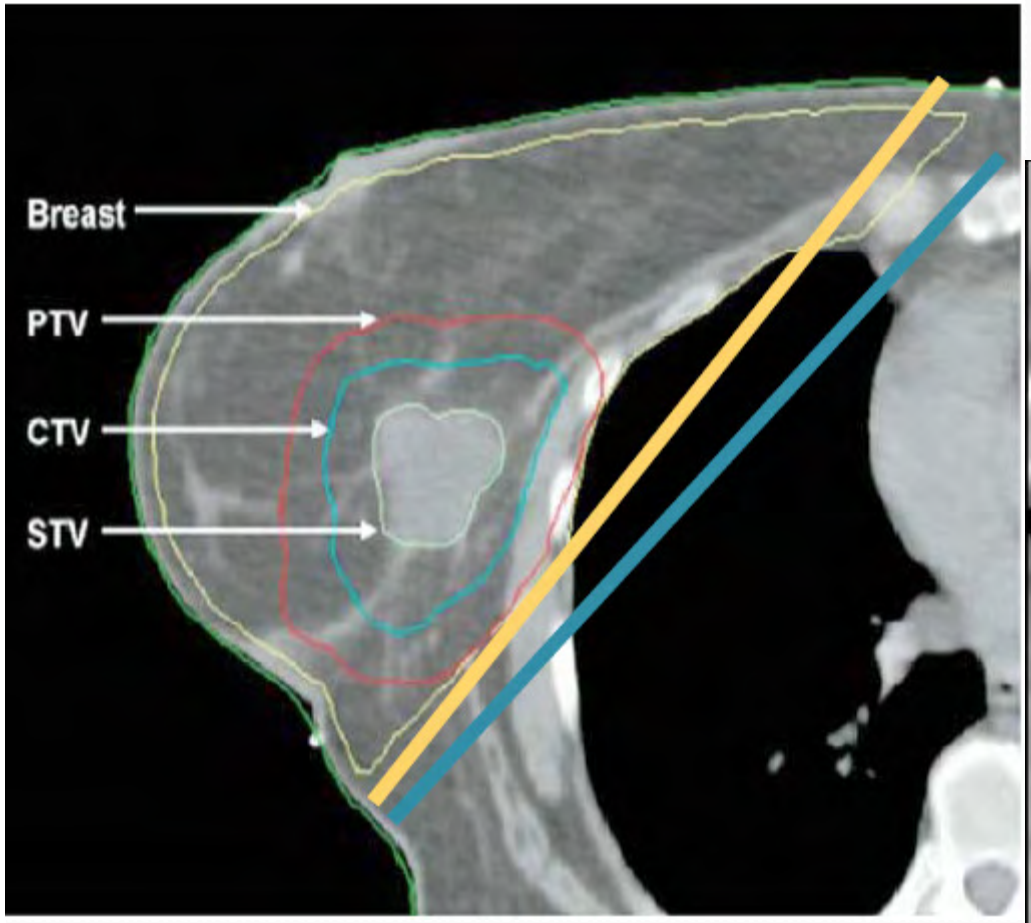
- Local treatment
- Control of the tumor depends on the volume of tumor and the dose of RT
- The treatment target has to be well defined
- Immobilization
- Imaging

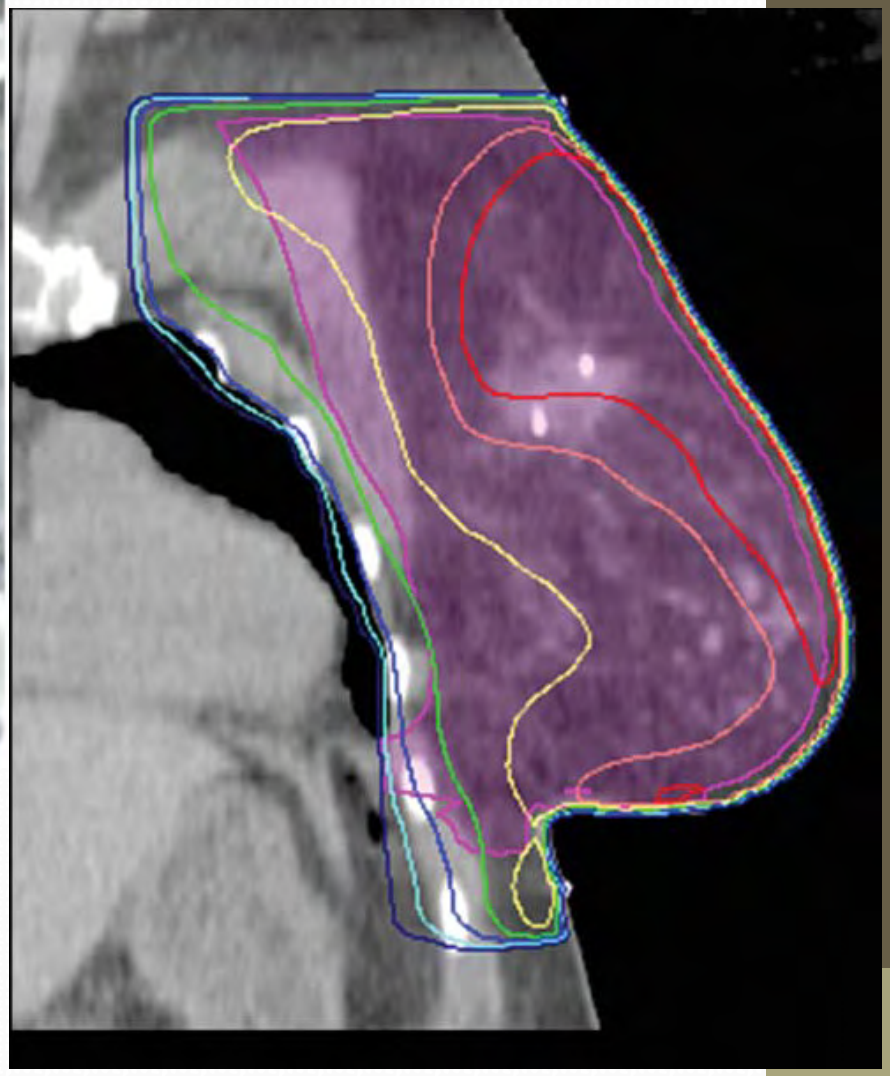
RT process

- Seen in RO clinic
- Consent and counseling
- CT sim date for planning
- Generally take 10 working days before RT start
- Daily treatment form 3 ½ weeks to 5/12 weeks
- Weekly imaging on treatment
- Weekly FU in clinic
- FU 6 weeks post RT

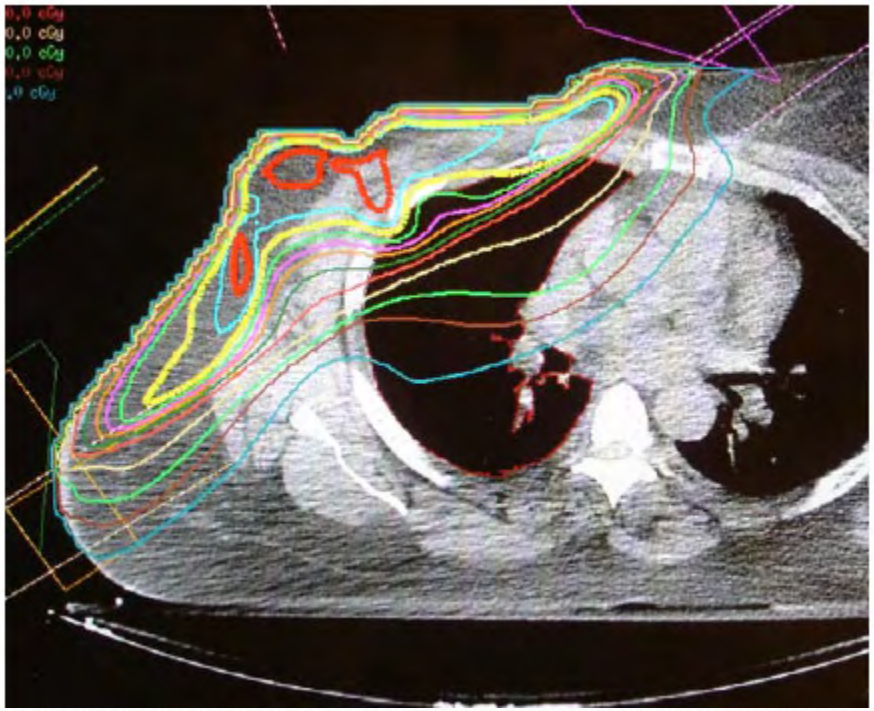
CT Simulator

CT Planning BCT

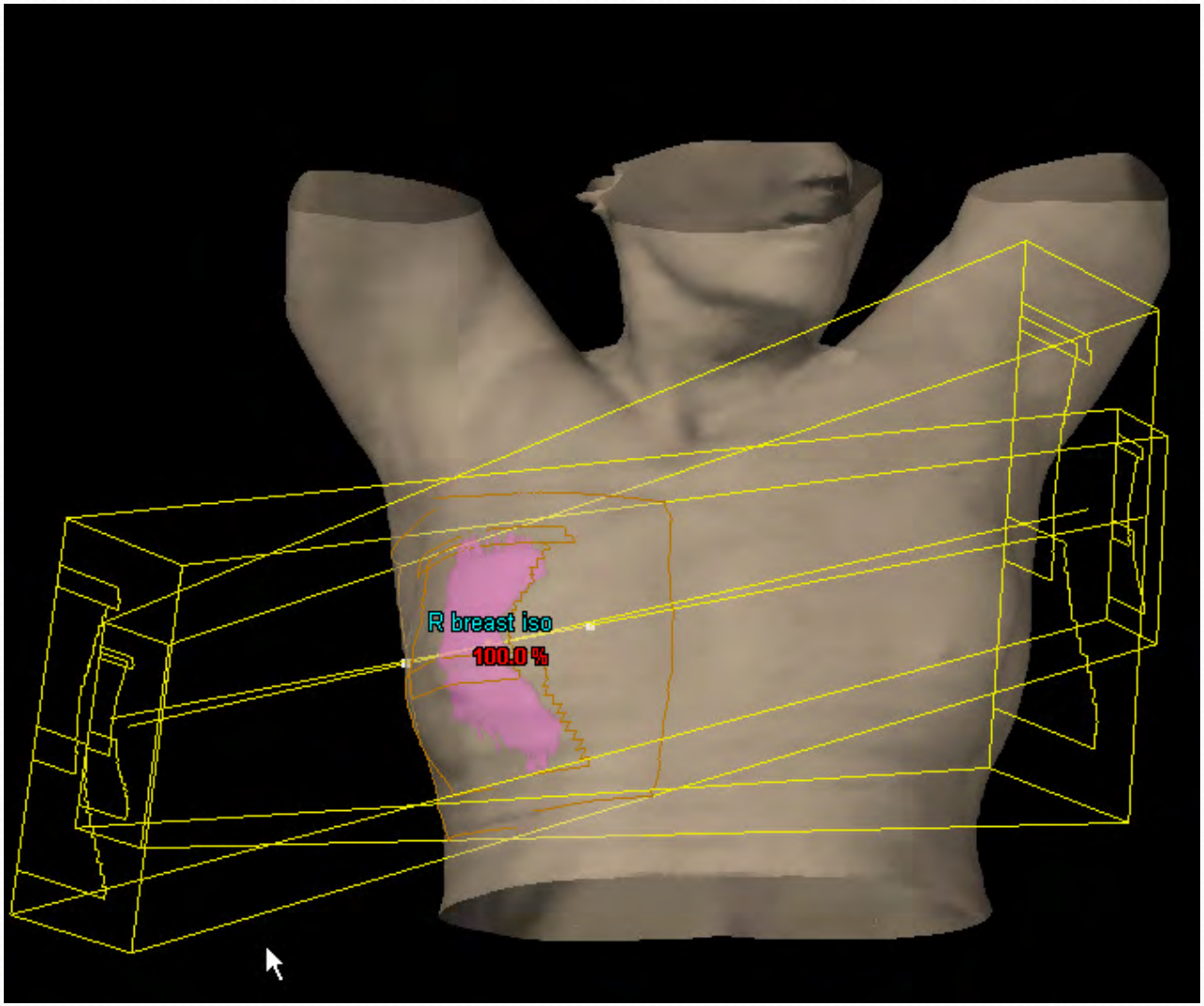


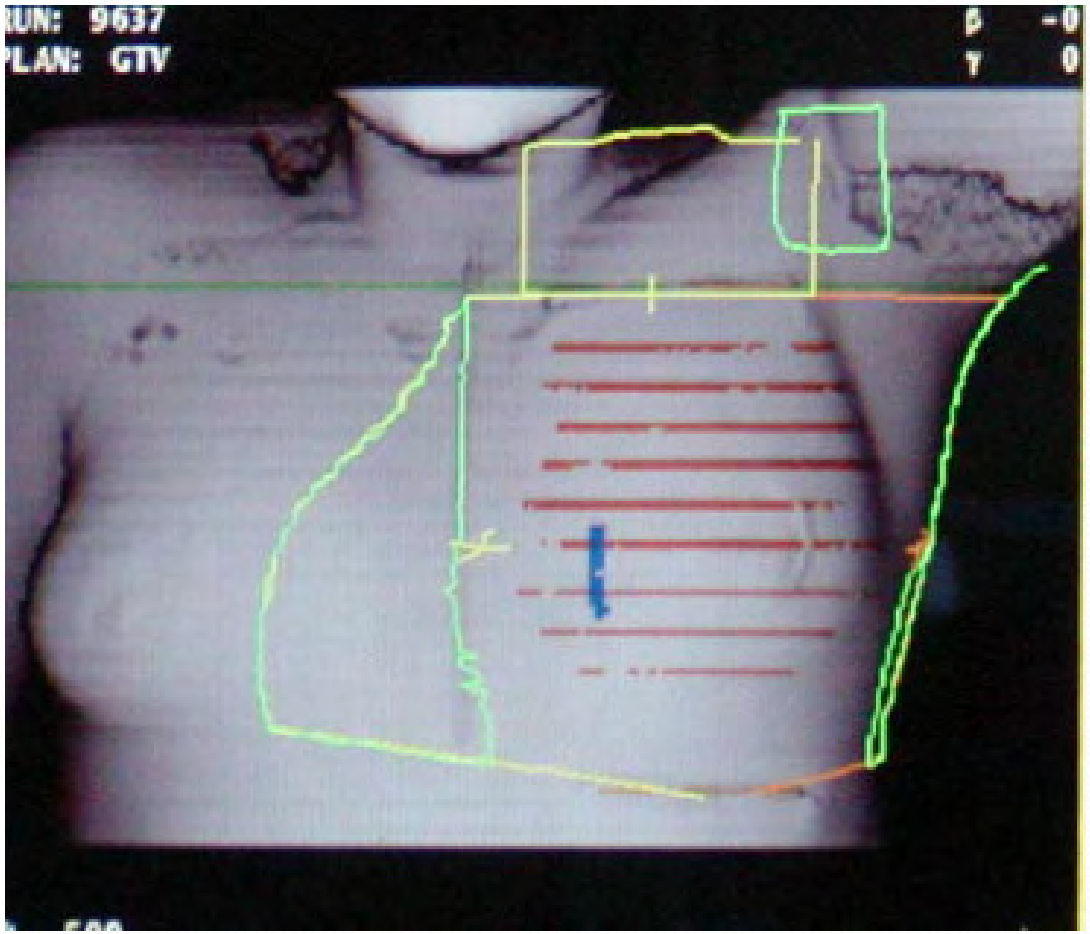


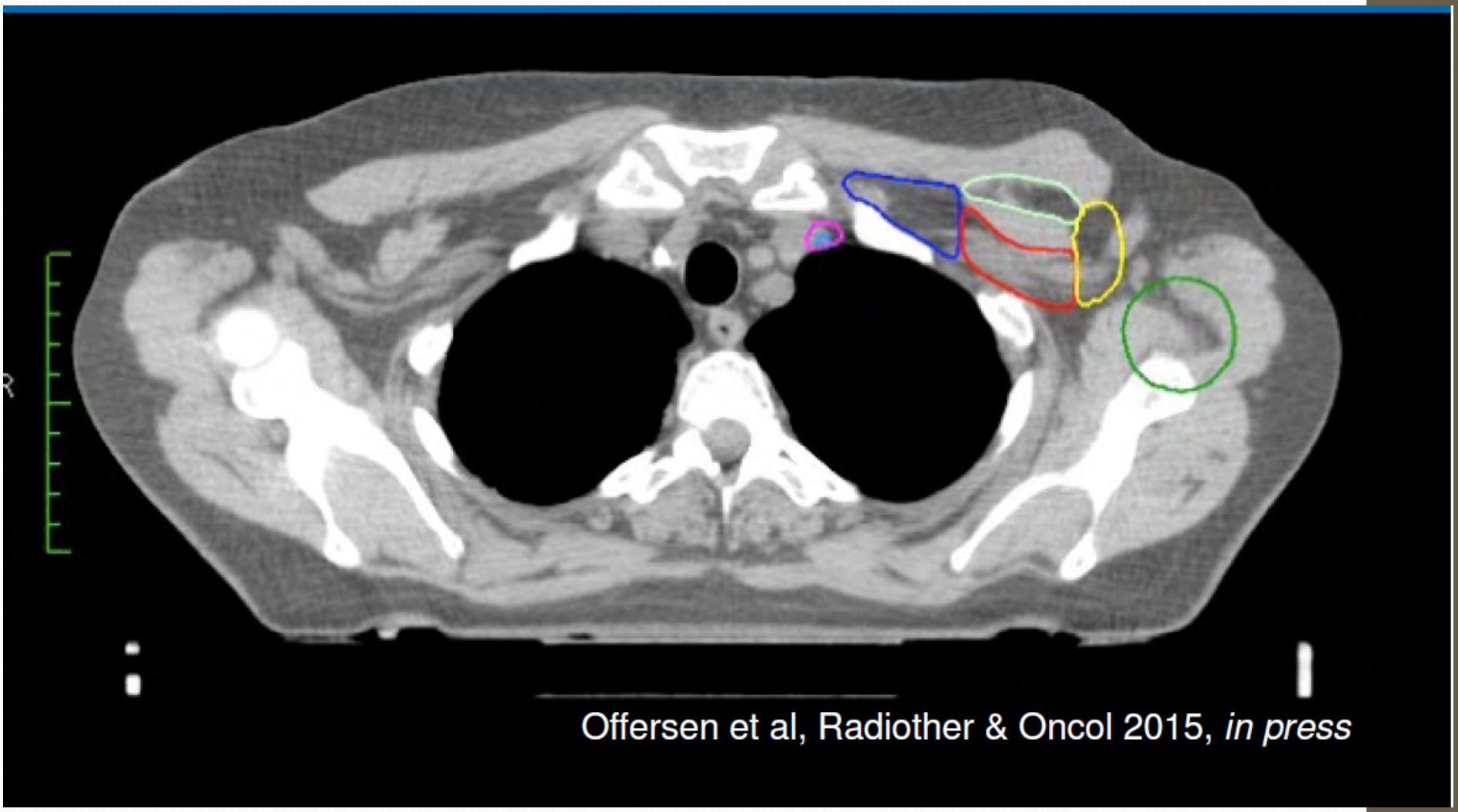
Radiopaque markers on medial
Lateral boarders and on the surgical scar

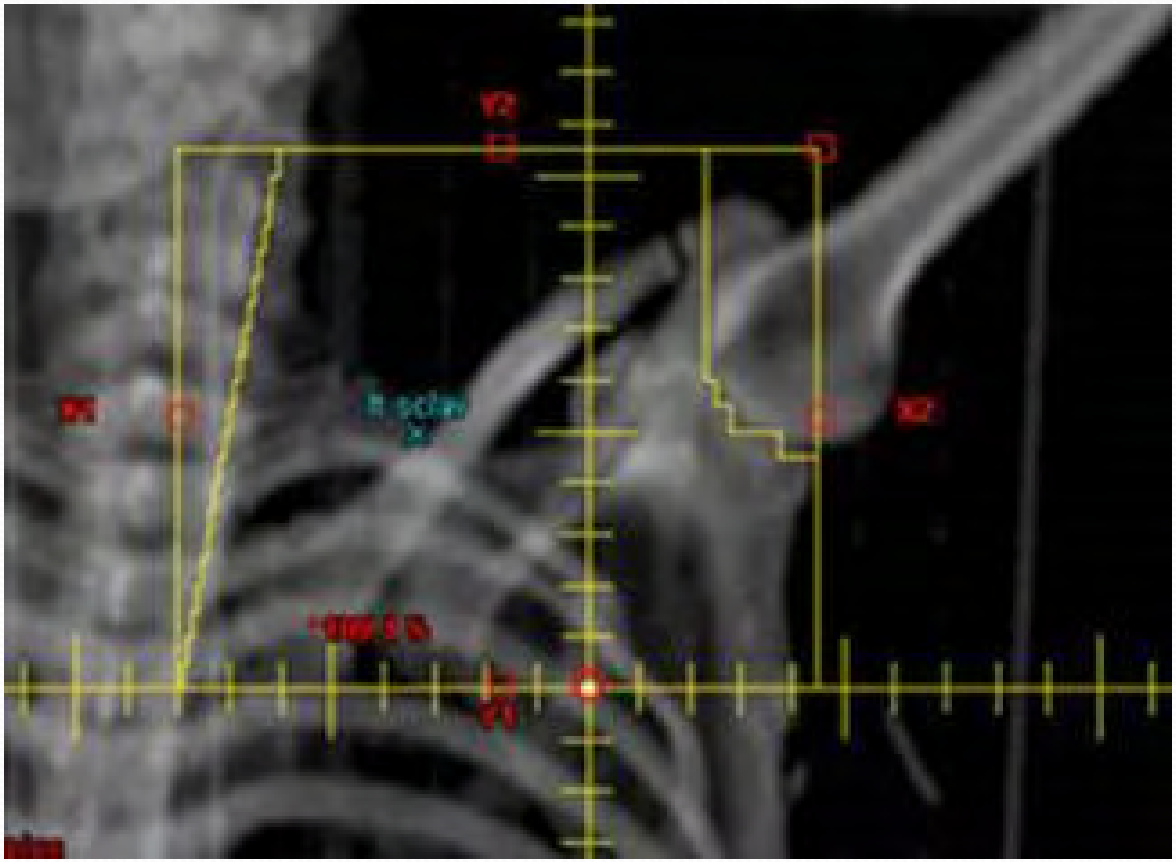


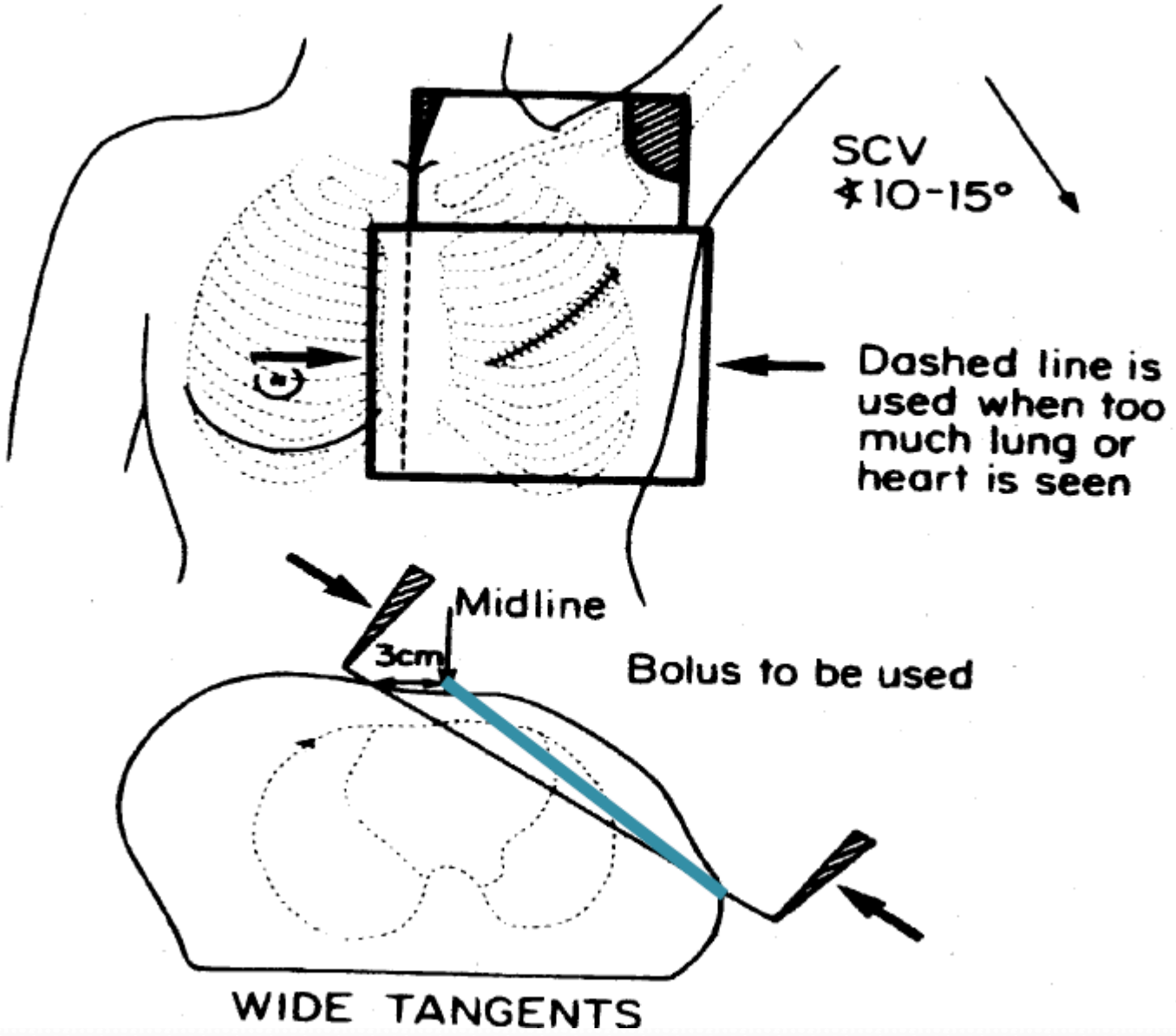
The entire surgical scar is included
Drain sites are generally included
Bolus on the skin


R breast iso
100.0 %

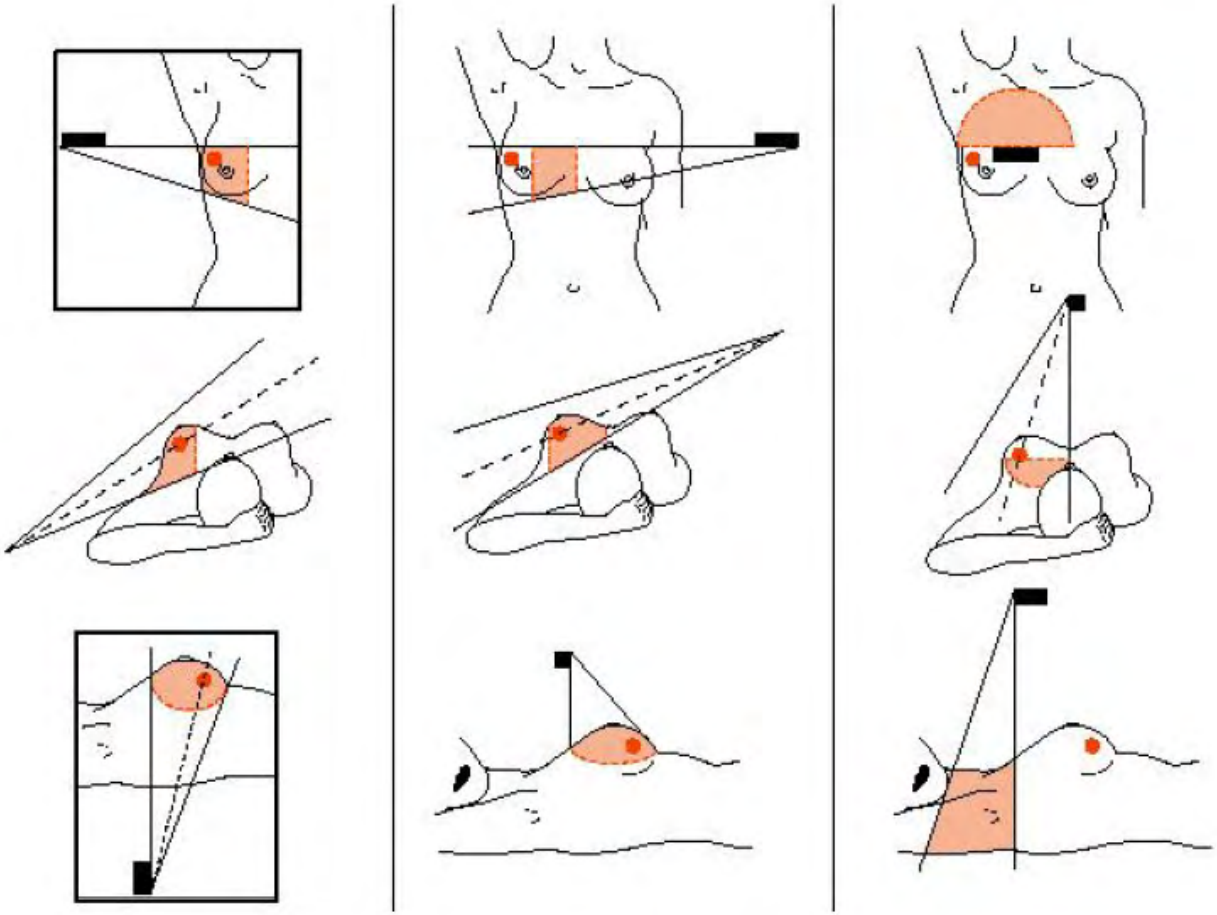

RUN: 9637
PLAN: GTV

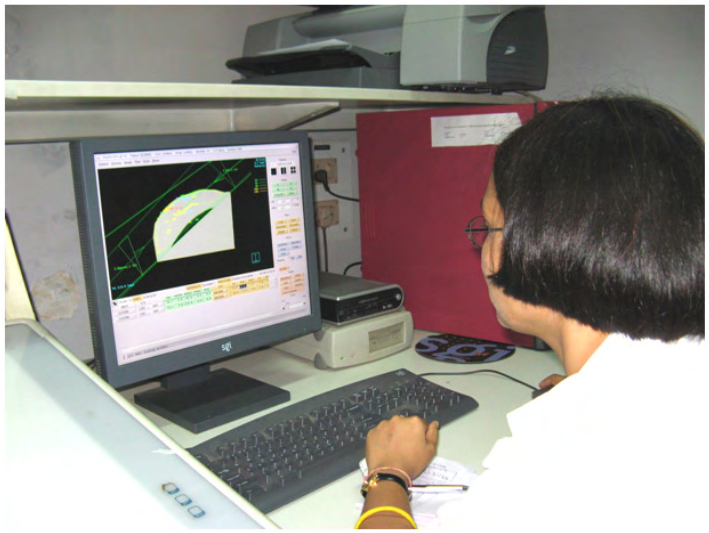

Offersen et al, Radiother & Oncol 2015, *in press*

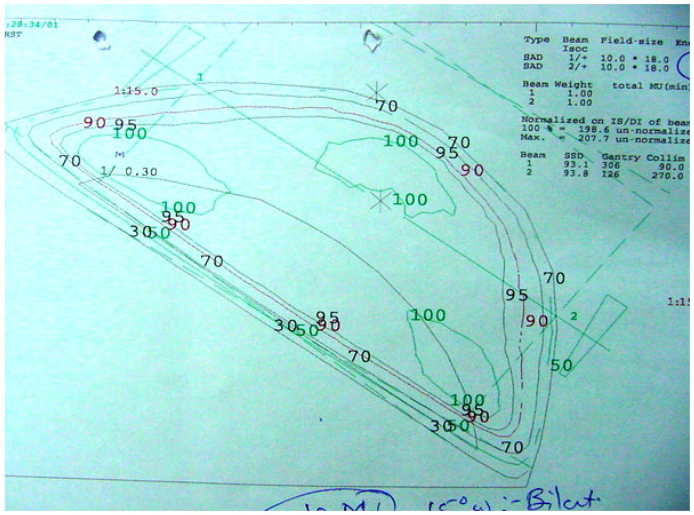



SCV
10-15°
Dashed line is used when too much lung or heart is seen
Midline
3cm
Bolus to be used
WIDE TANGENTS

TREATMENT PLANNING






Type Beam Field-size
Isoc
SAD 1/+ 10.0 • 18.0
SAD 2/+ 10.0 • 18.0
Beam Weight total MU(min
1 1.00
2 1.00
Normalized on IS/DI of bea
Max. = 207.7 un-normalize
Beam SSD Gantry Collim
1 93.1 306 90.0
2 93.8 126 270.0
1:15.0
1/ 0.30
90 95
100
70
95
90
50
Bilat.


VARIAN

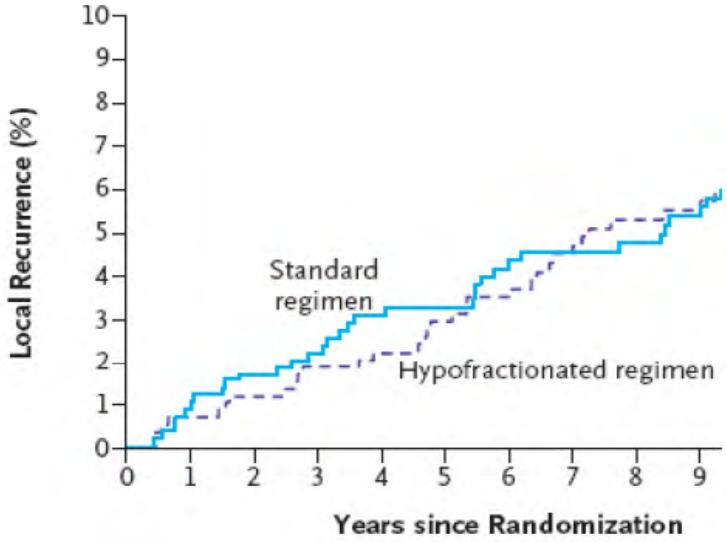
Radiation Technique/Dose

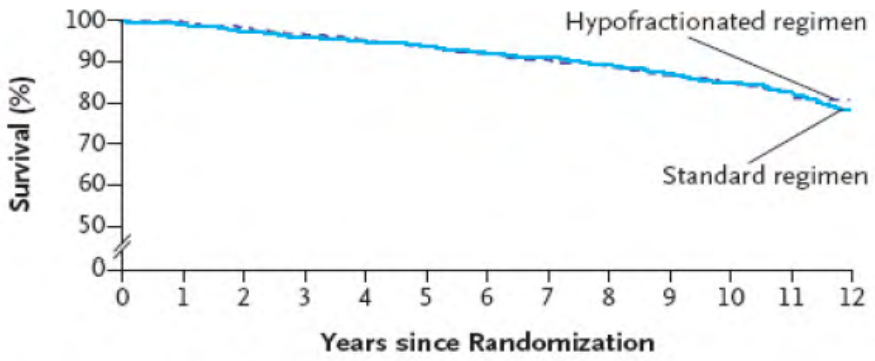
- Opposed tangential fields
- Breast only
- Boost optional
- 50 Gy in 25-28 fractions
- 42.5 Gy in 16 fractions
- For Breast and RLN tangential and 2 or 1 ant field
- Dose generally 50/25

Ontario Clinical Oncology Group Study: 10 year followup

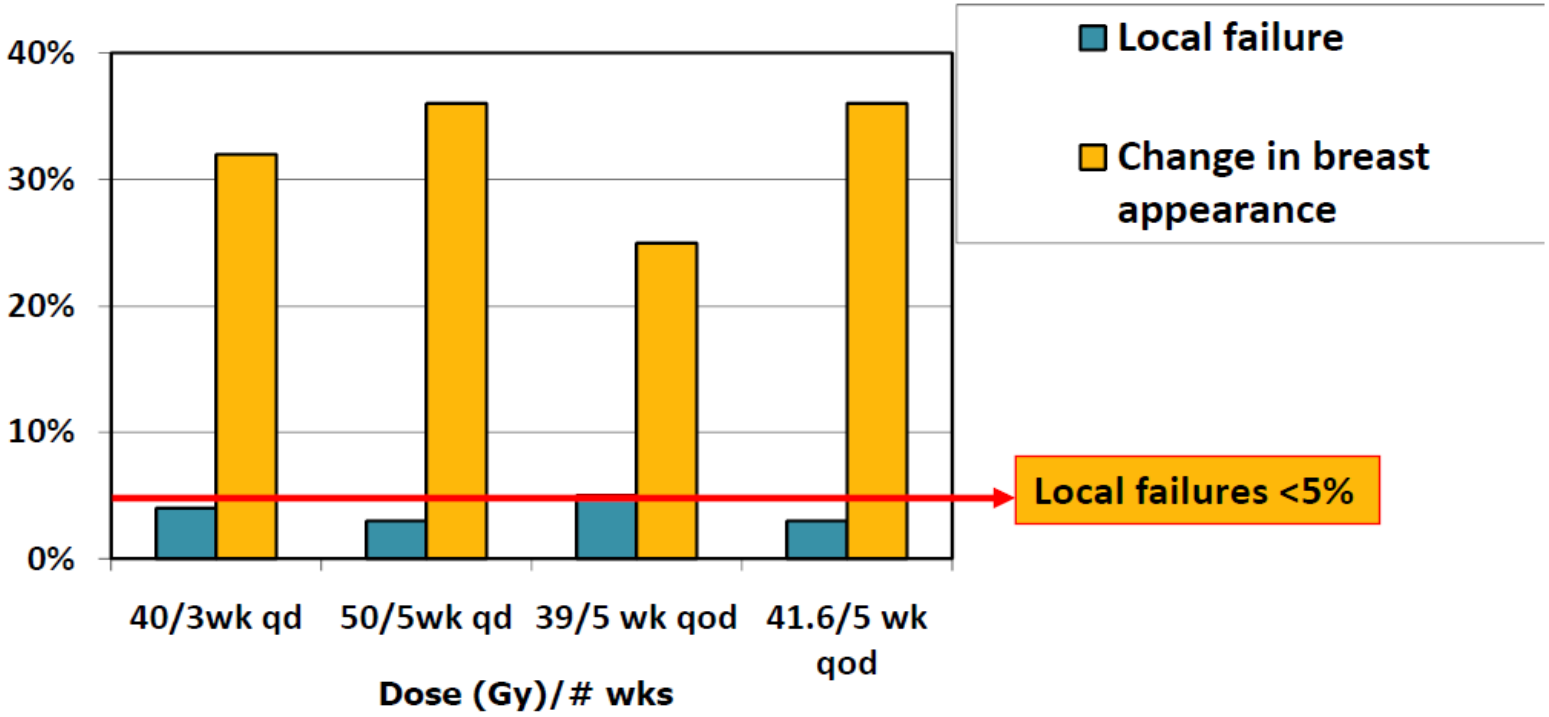
(Whelan, NEJM 2010)

1234 patients randomized to 50 Gy in 5 wks versus 42.5 Gy in 3 wks





START TRIAL results



Radiation Toxicity

- Acute

  Start during RT and can last up to 6 weeks post RT

- Late

  Number of months and years down the line

Acute Effects

- Fatigue
- Skin reaction
- Breast/Chest wall swelling
- Cough

Skin Reaction

- The most common side effect we tend to see
- Mainly in pendulous breast
- Effects generally the inframammary and axilla folds
- Less occurrence with modern techniques

Management

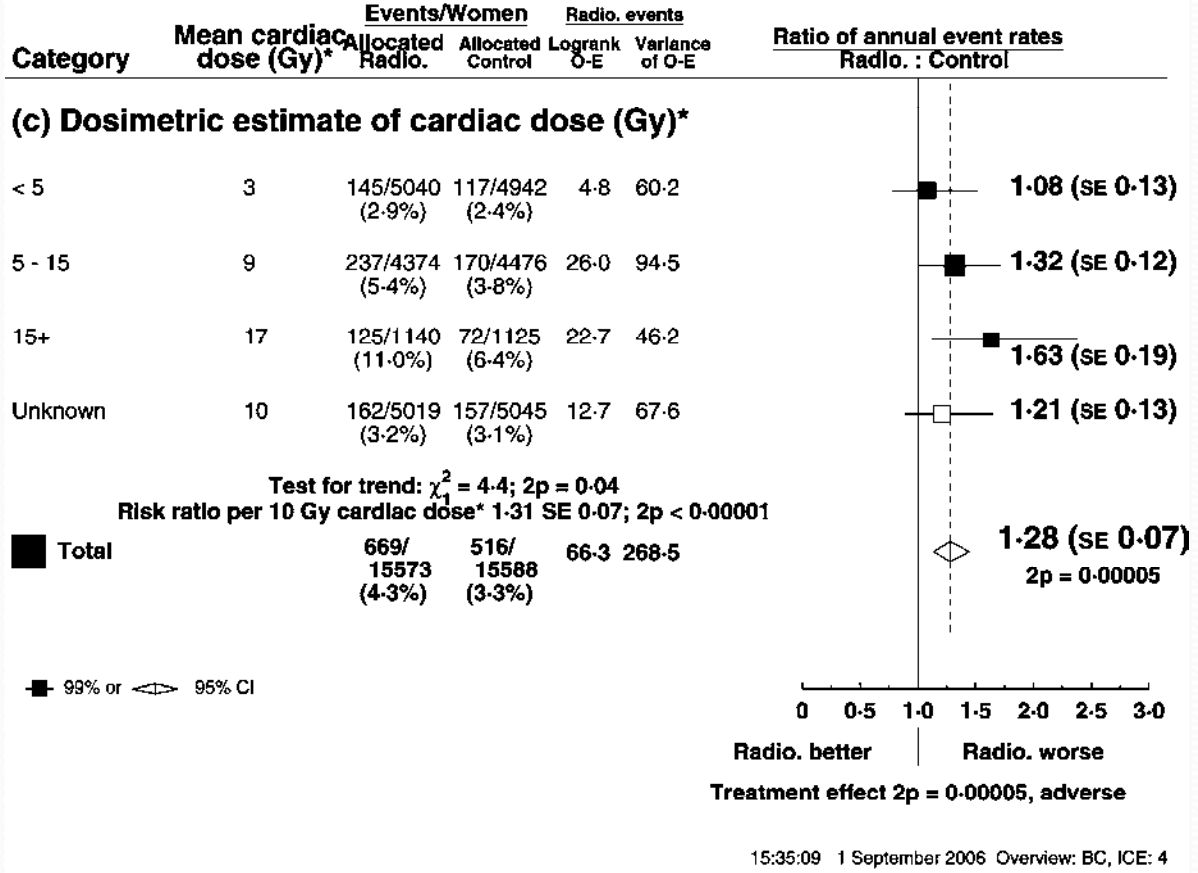
- Pt education and written information
- Weekly seen in the review clinic
- Generally treated with topical lubricants
- May need topical antibiotics occasionally to prevent secondary infections
- CCMB guidelines


b

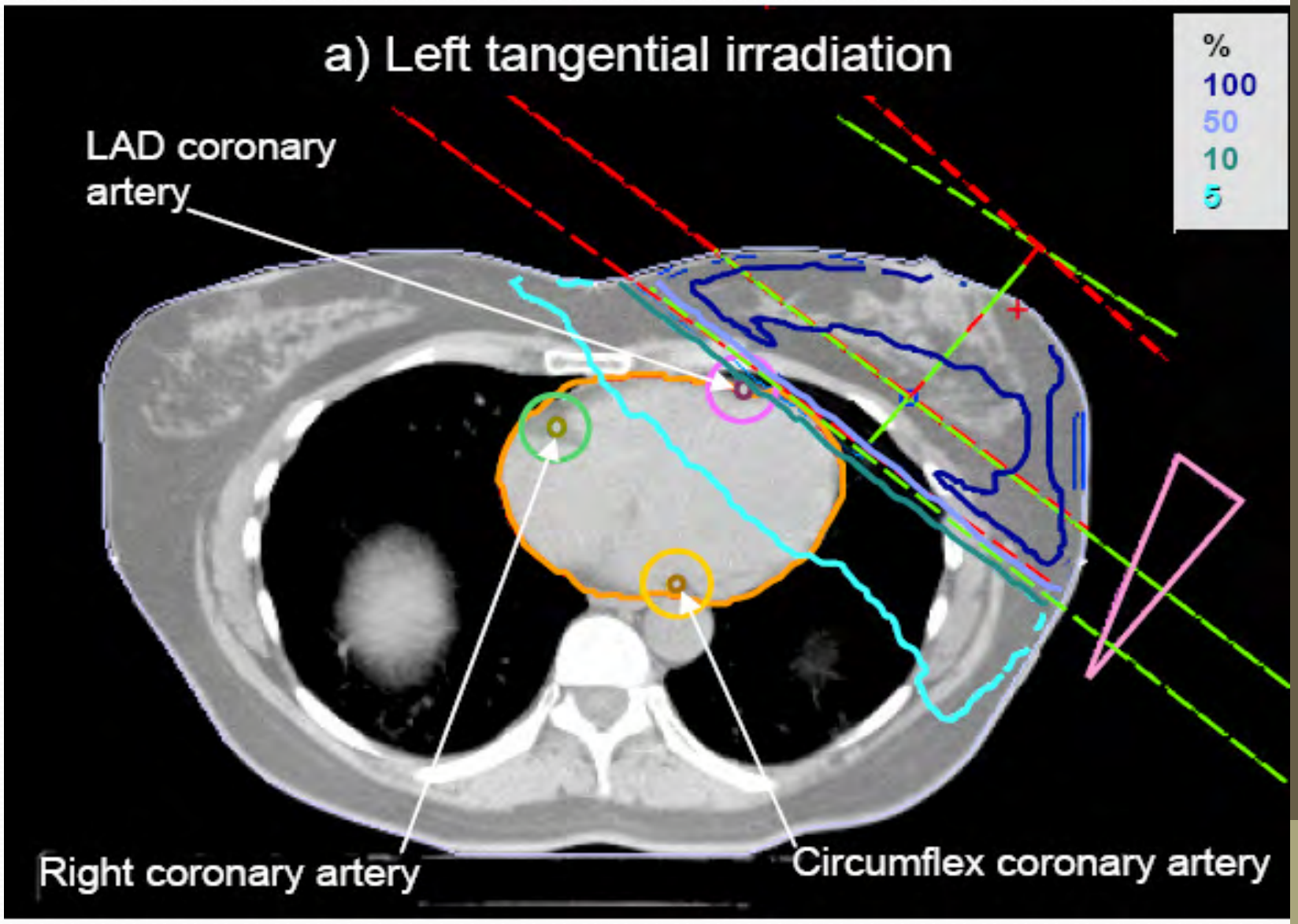
Late Effects

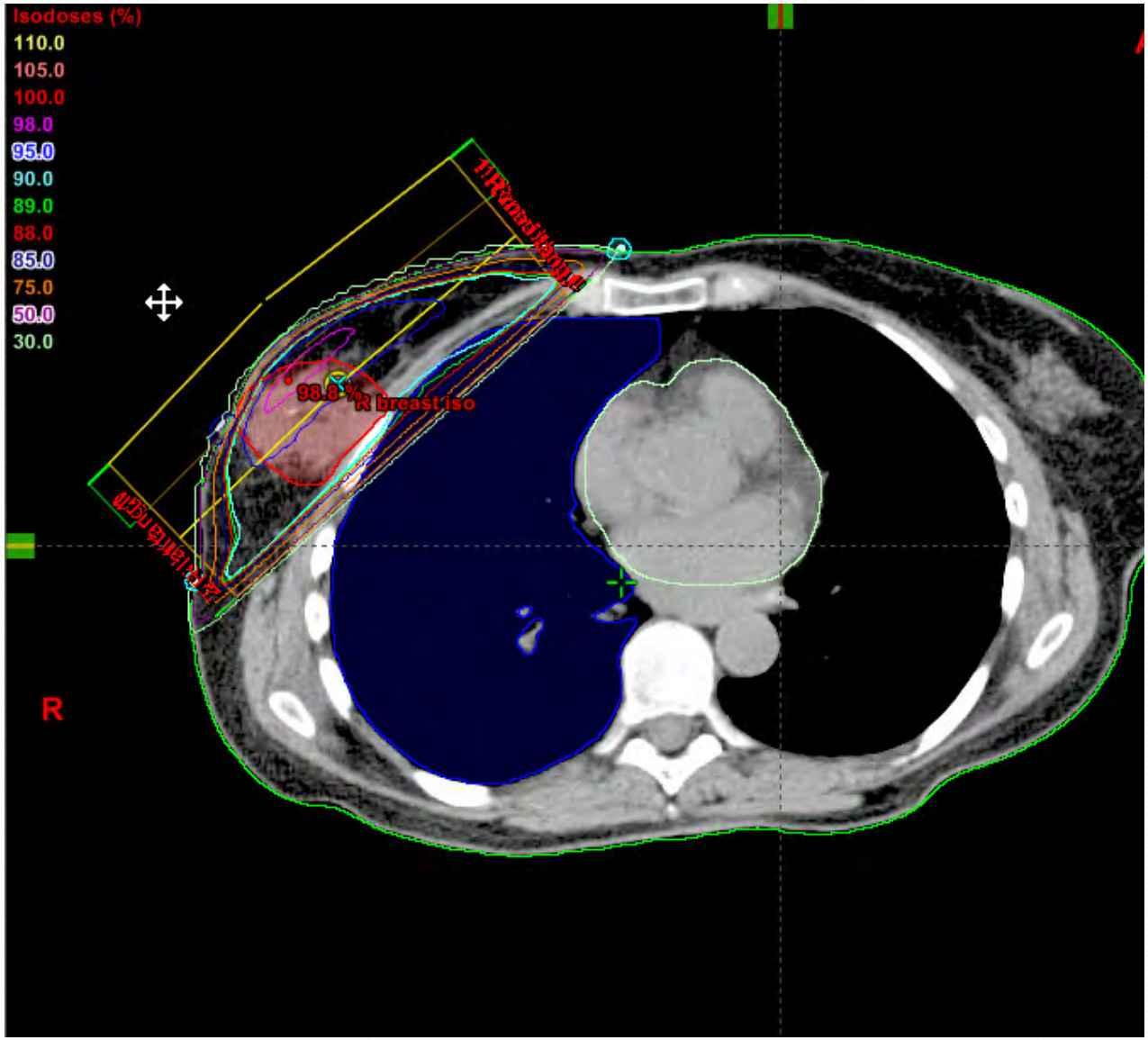
- Lymphedema
  - After full axillary dissection + RT - 37%
  - Level I/II dissection + RT - 7%
- Rib fracture - 1.8%
- Pneumonitis - 1-5%
- Cardiac toxicity - avoidable
- Radiation-induced sarcoma
  - 0.78% at 30 yrs.

Mean Heart Dose: Radio. given vs. no Radio given
HEART DEATHS

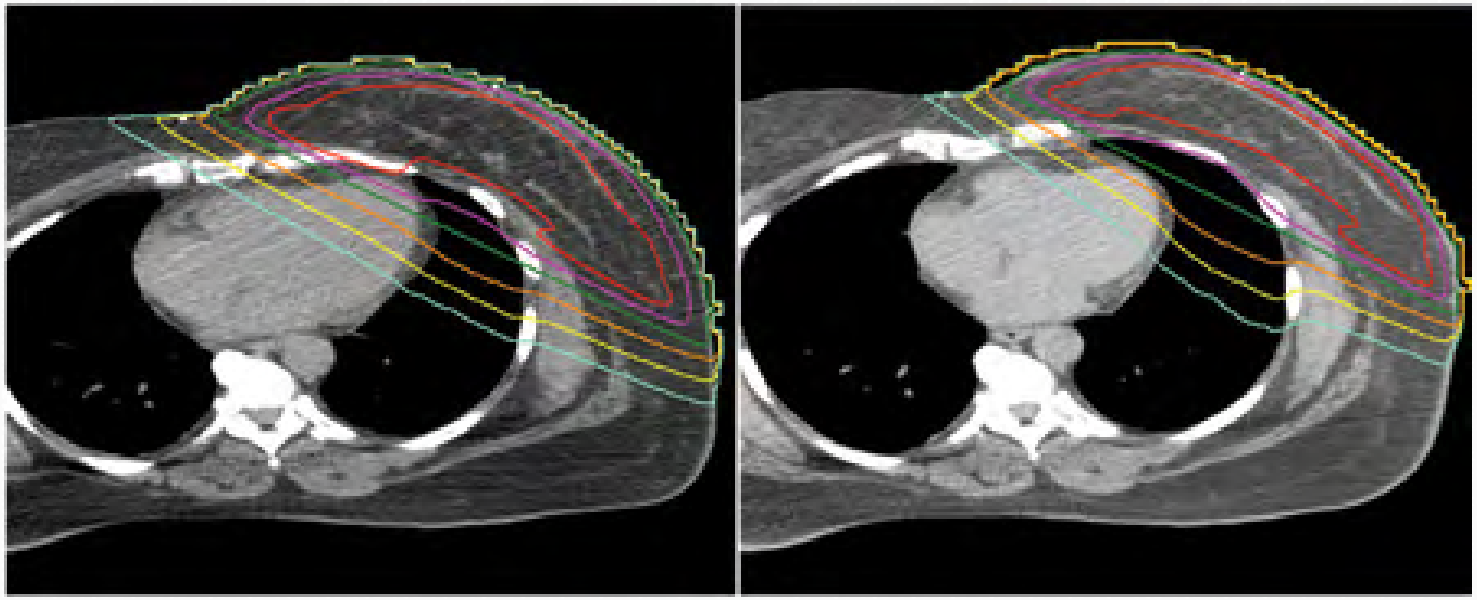


15:35:09 1 September 2006 Overview: BC, ICE: 4


a) Left tangential irradiation
%
100
50
10
5
LAD coronary artery
Right coronary artery
Circumflex coronary artery


Isodoses (%)
110.0
105.0
100.0
98.0
95.0
90.0
89.0
88.0
85.0
75.0
50.0
30.0
98.8 %
R breast iso
R

DIBH



Angiosarcoma

- Risk factors
  - Radiation
  - Lymphedema
- Treatment
  - Excision, radiation

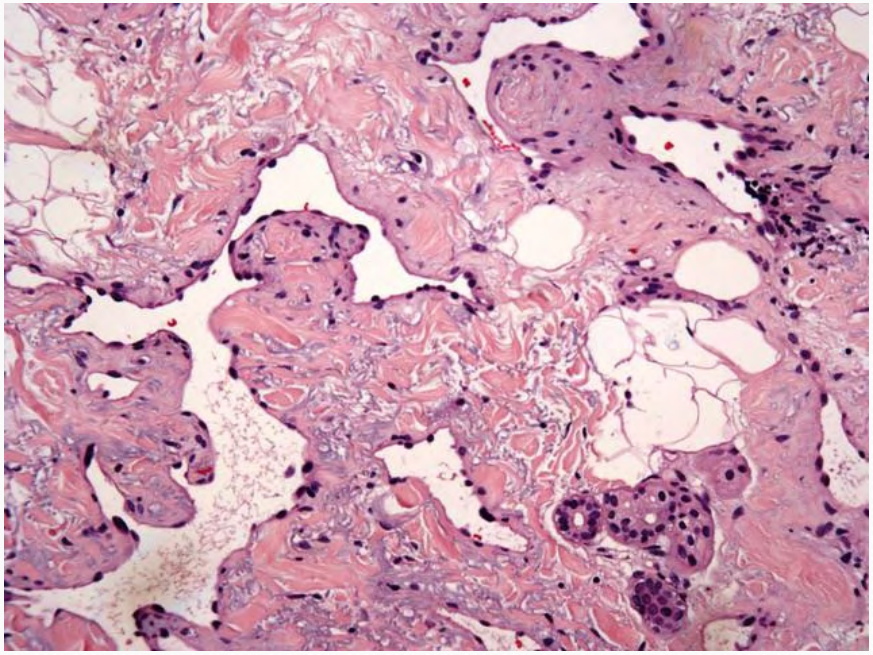
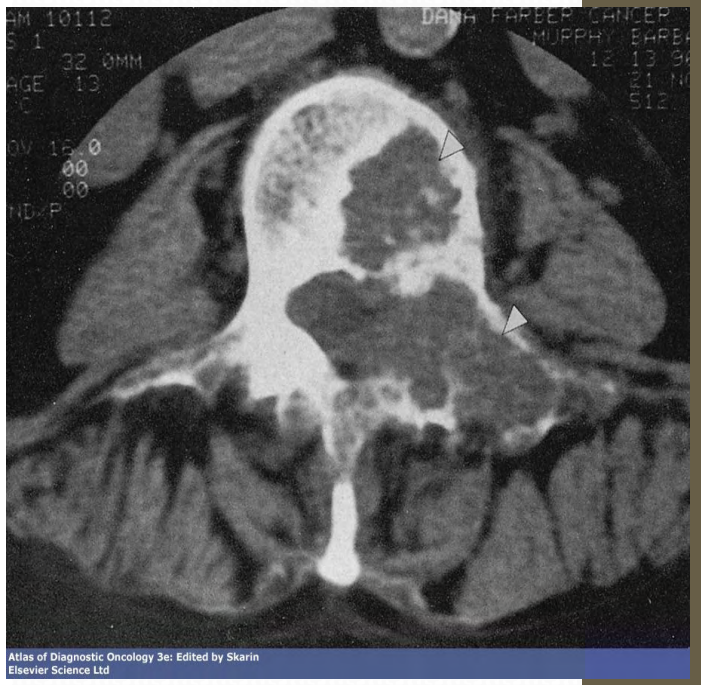
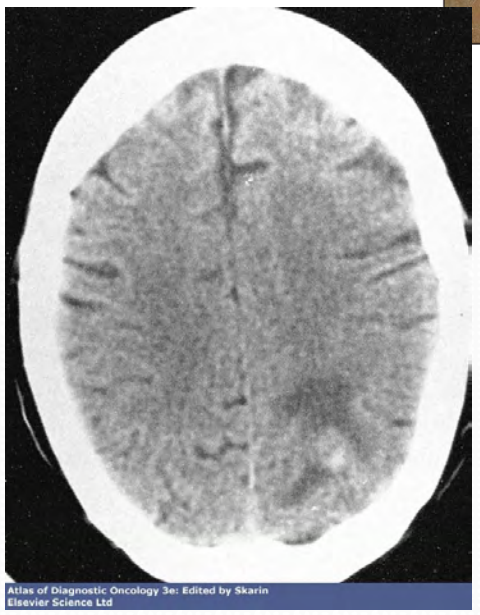


Figura 1 - Notar mastectomia e linfedema no membro superior esquerdo ipsilateral, associado à lesão vinhosa no terço superior.


Atlas of Diagnostic Oncology 3e: Edited by Skarin
Elsevier Science Ltd


Atlas of Diagnostic Oncology 3e: Edited by Skarin
Elsevier Science Ltd


Atlas of Diagnostic Oncology 3e: Edited by Skarin
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Courtesy Gillies McKenna

The Evolution of Radiation Therapy

Drive to increase conformal delivery to irregular tumour targets And reduce toxicity

First Linac

Cerrobend blocks

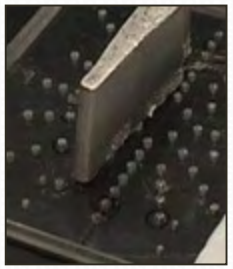
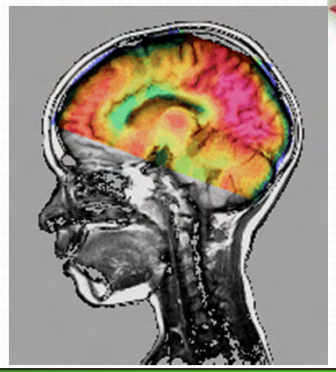
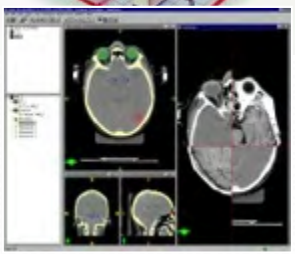


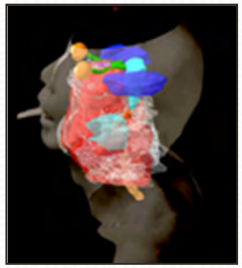
Image Fusion

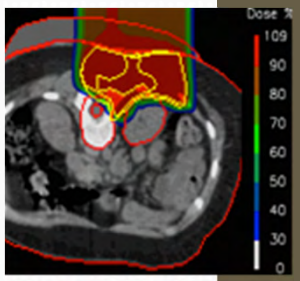


Computerized 3D CT treatment planning



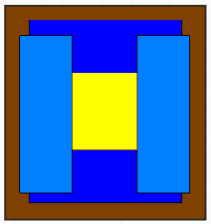
IMRT dose-painting





Particle Therapy

1960 1970 1980 1990 2000 2010

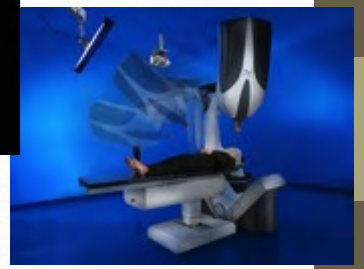


Standard collimator

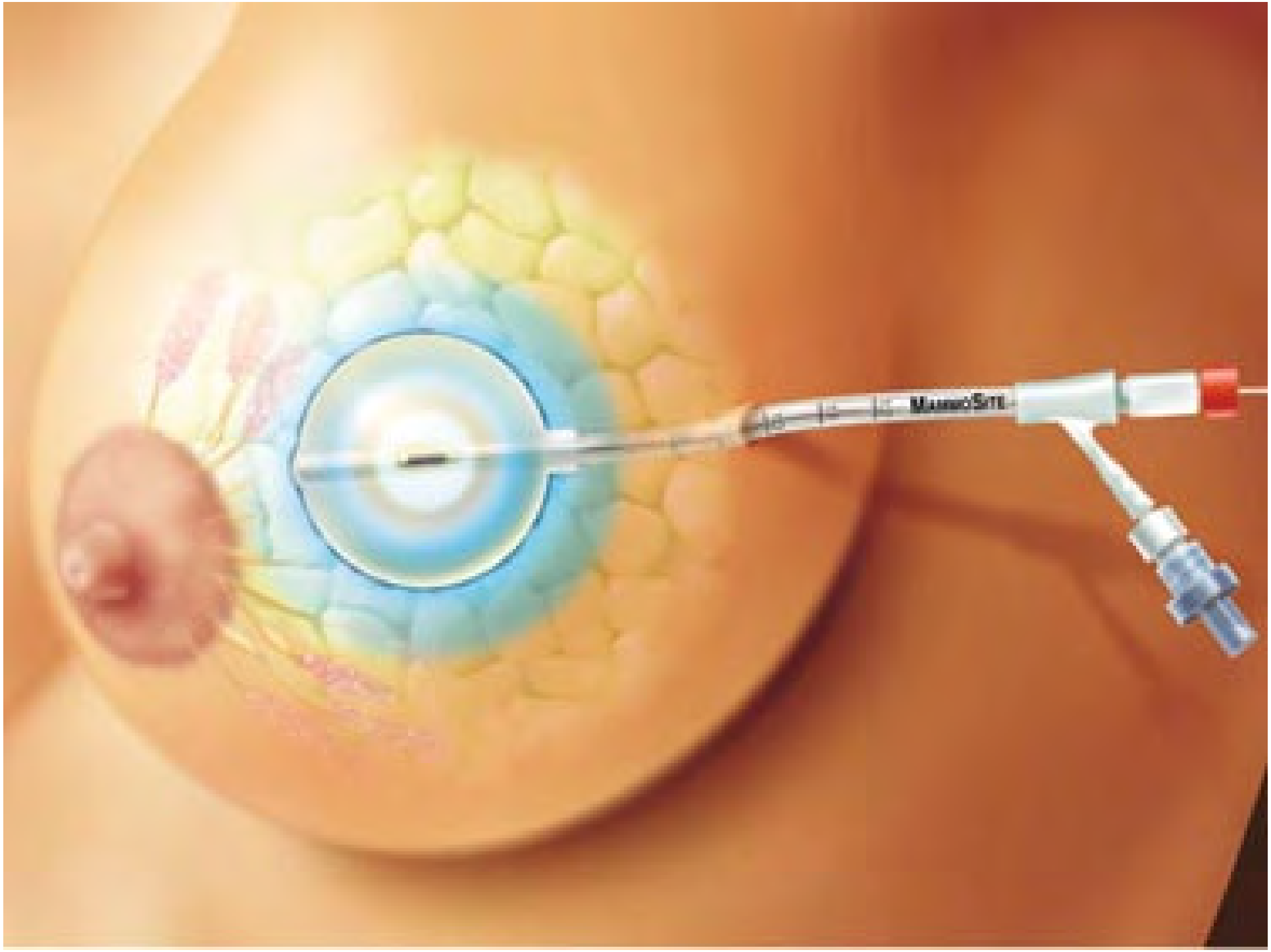
Shaped electron fields

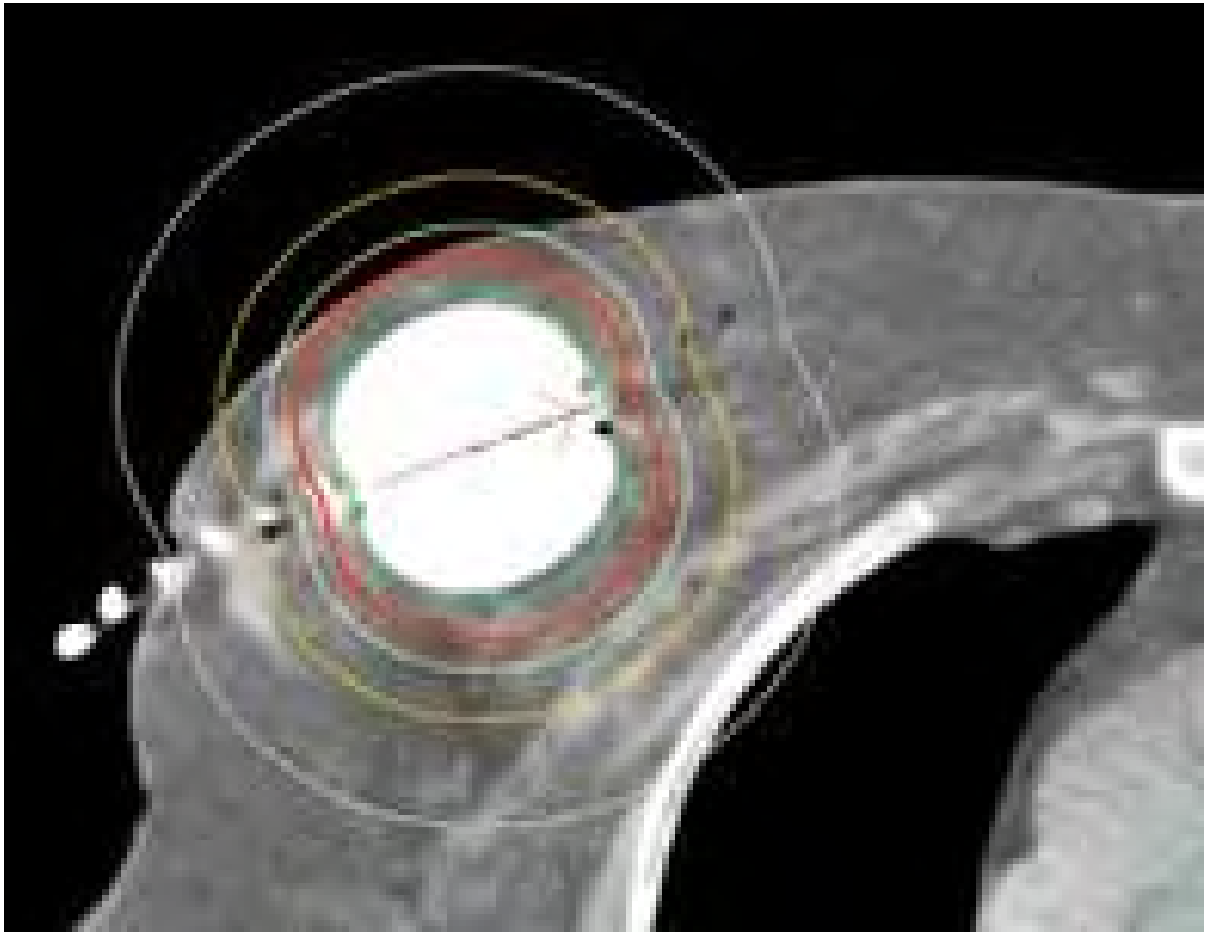
Multileaf collimator

High resolution IGRT



Stereotactic Radiotherapy


MammoSite



A dose of 34 Gy was delivered at a depth of 1 cm over the course of 5 days. CT scans were used to assess the conformance of the resection cavity tissue to the MammoSite® RTS balloon.

Balloon on CT

Conclusion

- Radiotherapy has an important role in management of breast cancer
- Has significant benefit in LC as well as OS
- Side effects from RT are minimal
- New Rt techniques will further reduce the long term side effects