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
- Medical Oncologists
- Radiation Oncologists
- 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\} micorosscopic 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

Curative

- Post Mastectomy
- Post Lumpectomy
- Post Chemotherapy

ADVANCED BREAST CANCERS

Palliative
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
Comparative 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

**Any first recurrence**

- **Women with pN0 disease (n=7287)**
  - 10-year gain 15.4% (SE 1.1)
  - RR 0.49 (95% CI 0.45–0.55)
  - Log-rank 2p<0.00001
  - BCS 31.0%
  - 15.6% BCS+RT
  - 22.5%
  - 10.6%

- **Women with pN+ disease (n=1050)**
  - 10-year gain 21.2% (SE 3.4)
  - RR 0.53 (95% CI 0.44–0.64)
  - Log-rank 2p<0.00001
  - BCS 63.7%
  - 42.5% BCS+RT
  - 53.7%
  - 31.1%

**Breast cancer death**

- **Women with pN0 disease (n=7287)**
  - 15-year gain 3.3% (SE 1.3)
  - RR 0.83 (95% CI 0.73–0.95)
  - Log-rank 2p=0.005
  - BCS 20.5%
  - 17.2% BCS+RT
  - 5.5%
  - 12.7%
  - 4.6%
  - 10.9%

- **Women with pN+ disease (n=1050)**
  - 15-year gain 8.5% (SE 3.4)
  - RR 0.79 (95% CI 0.65–0.95)
  - Log-rank 2p=0.01
  - BCS 51.3%
  - 42.8% BCS+RT
  - 22.4%
  - 34.2%
  - 19.8%
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

<table>
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<tr>
<th>T stage</th>
<th>No LNs</th>
<th>1-3 LNs</th>
<th>4-9 LNs</th>
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<tr>
<td>T1</td>
<td>6%</td>
<td>7%</td>
<td>9%</td>
<td>17%</td>
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<tr>
<td>T3</td>
<td>29%</td>
<td>29%</td>
<td>31%</td>
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</table>
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%
Local Recurrence

EBCCTG

pN0

5-year gain 2.8% (SE 1.0)

Mast+AC 5.8%
Mast+AC+RT 2.4%

pN1-3

5-year gain 15.7% (SE 1.2)

Mast+AC 24.7%
Mast+AC+RT 5.3%

pN4+

5-year gain 22.3% (SE 2.0)

Mast+AC 40.6%
Mast+AC+RT 12.9%
OVERALL SURVIVAL

EBCCTG

pN0

% 60
50
40
30
20
10
0

0  5  10  15  years

Mast+AC+RT 26.6% 26.0%
Mast+AC 11.2
10.9
20.5
19.8

15-y loss 0.6% (SE 2.5)
Logrank 2p > 0.1; NS

pN1-3

% 60
50
40
30
20
10
0

0  5  10  15  years

Mast+AC 50.9%
43.3%
Mast+AC+RT 24.3
22.8
36.6

15-y gain 7.6% (SE 1.9)
Logrank 2p = 0.002

pN4+

% 60
50
40
30
20
10
0

0  5  10  15  years

Mast+AC 76.4%
69.5%
Mast+AC+RT 69.1
50.3
46.6

15-y gain 6.9% (SE 1.9)
Logrank 2p = 0.0008
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
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

Couch
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
Dashed line is used when too much lung or heart is seen.
TREATMENT PLANNING
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

- Local failure
- Change in breast appearance

Local failures <5%

Dose (Gy)/# wks:
- 40/3wk qd
- 50/5wk qd
- 39/5 wk qd
- 41.6/5 wk qd
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
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

<table>
<thead>
<tr>
<th>Category</th>
<th>Mean cardiac dose (Gy)*</th>
<th>Events/Women</th>
<th>Radio. events</th>
<th>Ratio of annual event rates</th>
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<td></td>
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<td>15+</td>
<td>17</td>
<td>125/1140</td>
<td>72/1185</td>
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<td>Unknown</td>
<td>10</td>
<td>162/5019</td>
<td>157/5045</td>
<td>12.7</td>
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</table>

Test for trend: $\chi^2 = 4.4; 2p = 0.04$
Risk ratio per 10 Gy cardiac dose*: 1.31 SE 0.07; 2p < 0.00001

Total: 669/15573 516/15588 66.3 268.5

- 93% or (>) 95% CI

Radio. better | Radio. worse
Treatment effect 2p = 0.00005, adverse

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

- **Risk factors**
  - Radiation
  - Lymphedema

- **Treatment**
  - Excision, radiation
The Evolution of Radiation Therapy

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

First Linac

Computerized 3D CT treatment planning

IMRT dose-painting

Particle Therapy


Standard collimator

Shaped electron fields

Multileaf collimator

High resolution IGRT

Stereotactic Radiotherapy

Courtesy Gillies McKenna
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