Journey to the Top: Thorax

Breast repositioning can reduce breast dose in mediastinal radiotherapy for Lymphoma

C. Hornby, T.Kron, E.Muir, A. Wirth
Welcome to Peter Mac

Colin Hornby
Head of Planning - Clinical Services
Australia’s only Hospital dedicated solely to Cancer

Main campus is situated on the edge of Melbourne CBD
PMCC Radiation Therapy Services located across 5 sites

- Main campus in central Melbourne
- 3 Metropolitan sites (20 - 45 mins)
- 1 Regional campus (2.5 hours)
Peter Mac’s New Home
Peter Mac RTS in the future

Peter Mac new main campus
RTS Machine Hardware

16 Linacs - all Varian

5 CT Widebore scanners - Philips

2 Acuity simulators - Varian

1 PET-CT - GE

4 Orthovoltage (1 SXRT only) – Pantak, Xstrahl

2 x HDR afterloader - Nucletron

1 Intraoperative - Intrabeam
RTS Software Systems

2 Treatment Planning Systems (main) - XiO
  - Eclipse

26 Full TPS workstations - 13 XiO
  - 13 Eclipse

21 Contouring / Plan review terminals - 18 Focal
  - 3 Somavision

1 Stereotactic TPS - iPlan

1 HDR - Oncentra

1 Seeds - Variseed

2 MU redundancy check S/W – Rad Calc, Monitor U

Radiation Oncology Information System (RV), Mosaiq

PACS – Siemens Syngo
6 Dual Energy Linacs - all Varian (2100iX, Trilogy, Truebeam)

4 x OBI + CBCT

1 Stereotactic Linac – Varian True Beam STX

1 CT Widebore scanners – Philips 16 SL

Bellows Gating + Varian RPM

1 Acuity simulator - Varian

1 PET-CT – GE 8 SL (includes Varian RPM)

1 Orthovoltage – Pantak

2 x HDR afterloader - Nucletron

1 Intraoperative - Intrabeam
East Melb Software Systems

2 Treatment Planning Systems (main) - XiO
- Eclipse

9 Full TPS workstations - 4 XiO, 5 Eclipse

8 Contouring / Plan review terminals - 7 Focal, 1 Somavision

1 Stereotactic TPS – Brainlab iPlan

1 HDR - Oncentra

1 Seeds - Variseed

1 MU redundancy check S/W – Monitor U

Radiation Oncology Information System - Mosaiq (paperless)

PACS – Siemens Syngo Server
Radiation Oncology Workforce

Current Effective Full Time Staff

Total Peter Mac Staff = 2610
Rad Therapists / Dosimetrists = 167
Radiation Oncologists = 35
Physicists = 16 Snr, 14 Jnr / registrars
RT Nursing = 20
Peter Mac Cancer Treatment Profile

20,000 pts annually
RT New Cases = 6,500 per year

Cancer Treatment Profile
Radiation Therapy = 120,000 treatments / year
Medical Oncology = 9,499 chemotherapy episodes
Surgery = 4,743 oncology surgical procedures annually
Breast repositioning can reduce breast dose in mediastinal radiotherapy for Lymphoma.

A pilot study into breast repositioning for [female] lymphoma patients and the associated out-of-field dosimetry.
Outline

• Background
• Rationale
  – Low doses
  – Equipment
  – Tissue relocation
• Study methods
• Repositioning results
• TLD – TPS dose results
• Conclusions

The graph shows the relative risk and 95% confidence interval for cancer according to weighted breast tissue dose in Sv. The units 1 Sv ≈ 1 Gy are used.
What defines a secondary malignancy or second cancer?

- Historically described by Cahan (1948)

1. the second tumor occurs in locations irradiated by primary or secondary therapeutic beams,
2. the histology of the second tumor is different from that of the original disease so a metastasis is excluded,
3. the existence of a latency period, typically of several years,
4. the second tumor was not present at the time of radiation treatment and
5. the patient does not have a cancer-prone syndrome

2° Breast cancer in RT Lymphoma pts ✅
Why do we want to be concerned about the dose out of the field?

- Contributes to stochastic effects
- Has become more relevant as treatment outcomes have become better
- Needs to be considered in addition to imaging dose (imaging increasing in RT)
- May interact with other treatment modalities
- Because others are...
INTENSITY-MODULATED RADIATION THERAPY, PROTONS, AND THE RISK OF SECOND CANCERS

Eric J. Hall, D.Phil., D.Sc.

Center for Radiological Research, Columbia University Medical Center, College of Physicians and Surgeons, New York, NY

Intensity-modulated radiation therapy (IMRT) allows dose to be concentrated in the tumor volume while sparing normal tissues. However, the downside to IMRT is the potential to increase the number of radiation-induced second cancers. The reasons for this potential are more monitor units and, therefore, a larger total-body dose because of leakage radiation and, because IMRT involves more fields, a bigger volume of normal tissue is exposed to lower radiation doses. Intensity-modulated radiation therapy may double the incidence of solid cancers in long-term survivors. This outcome may be acceptable in older patients if balanced by an improvement in local tumor control and reduced acute toxicity. On the other hand, the incidence of second cancers is much higher in children, so that doubling it may not be acceptable. IMRT represents a special case for children for three reasons. First, children are more sensitive to radiation-induced cancer than are adults. Second, radiation scattered from the treatment volume is more important in the small body of the child. Third, the question of genetic susceptibility arises because many childhood cancers involve a germline mutation. The levels of leakage radiation in current Linacs are not inevitable. Leakage can be reduced but at substantial cost. An alternative strategy is to replace X-rays with protons. However, this change is only an advantage if the proton machine employs a pencil scanning beam. Many proton facilities use passive modulation to produce a field of sufficient size, but the use of a scattering foil produces neutrons, which results in an effective dose to the patient higher than that characteristic of IMRT. The benefit of protons is only achieved if a scanning beam is used in which the doses are 10 times lower than with IMRT. © 2006 Elsevier Inc.

Intensity-modulated radiation therapy, Passive modulation, Pencil beams, Protons, Second cancers.
## Estimate of risk for secondary cancers (Hall 2006)

<table>
<thead>
<tr>
<th></th>
<th>Hall and Wuu (4)</th>
<th>Kry et al. (5)</th>
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<tbody>
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<td>1.7</td>
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<td>IMRT 6 MV</td>
<td>3.0</td>
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<td>IMRT 15-MV Varian</td>
<td>3.4</td>
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**Abbreviations:** IMRT = intensity-modulated radiation therapy; MV = megavoltage; RT = radiation therapy.
Long-term mortality from heart disease and lung cancer after radiotherapy for early breast cancer: prospective cohort study of about 300 000 women in US SEER cancer registries

Sarah C Darby, Paul McGale, Carolyn W Taylor, Richard Peto

Lancet Oncology 2005

Summary
Background Radiotherapy for early breast cancer can decrease breast cancer mortality but increase other mortality, mainly from heart disease and lung cancer. The mean cardiac dose from irradiation of a left-sided breast cancer can be two or three times that for a right-sided breast cancer. The mean ipsilateral (ie, on the same side as the breast cancer) lung dose can also be two or three times the mean contralateral lung dose. Particularly during the 1970s, when typical heart and lung exposures were greater than now, the laterylity of an irradiated breast cancer could measurably affect cardiac mortality and mortality from cancer of the right or the left lung decades later. This study aimed to assess the hazards in the general US population from routine cancer-registry and death-certificate data.

Methods We analysed data for 308 861 US women with early breast cancer of known laterality (left-sided or right-sided) who were registered in the US Surveillance Epidemiology and End Results (SEER) cancer registries during 1973–2001 and followed prospectively for cause-specific mortality until Jan 1, 2002.

Findings 115 165 (37%) received radiotherapy. Among those who did not, tumour laterality was of little relevance to subsequent mortality. For women diagnosed during 1973–82 and irradiated, the cardiac mortality ratio (left versus right tumour laterality) was 1.20 (95% CI 1.04–1.38) less than 10 years afterwards, 1.42 (1.11–1.82) 10–14 years afterwards, and 1.58 (1.29–1.95) after 15 years or more (trend: 2p=0.03). For women diagnosed during 1983–92 and irradiated, the cardiac mortality ratio was 1.04 (0.91–1.18) less than 10 years afterwards and 1.27 (0.99–1.63) 10 or more years afterwards. For women diagnosed during 1993–2001 and irradiated the cardiac mortality ratio was 0.96 (0.82–1.12), with none yet followed for 10 years. Among women irradiated for breast cancer who subsequently developed an ipsilateral or contralateral lung cancer, the lung cancer mortality ratio (ipsilateral versus contralateral) for women diagnosed during 1973–82 and irradiated was 1.17 (0.62–2.19), 2.00 (1.00–4.00), and 2.71 (1.65–4.48), respectively, less than 10 years, 10–14 years, and 15 or more years afterwards (trend: 2p=0.04). For women irradiated after 1982 there is, as yet, little information on lung cancer risks more than 10 years afterwards.

Interpretation US breast cancer radiotherapy regimens of the 1970s and early 1980s appreciably increased mortality from heart disease and lung cancer 10–20 years afterwards with, as yet, little direct evidence on the hazards after more than 20 years. Since the early 1980s, improvements in radiotherapy planning should have reduced such risks, but the long-term hazards in the general populations of various countries still need to be monitored directly.
Study Summary

- SEER database: 300,000 breast cancer patients
- 115,000 with RT:
  - Cardiac mortality is higher in patients with left sided breast cancer
  - Ipsilateral lung and breast cancer risk higher in patients who had radiotherapy
  - Effect is less (or not even detectable?) with modern RT
- For patients treated 1970’s and 1980’s increased risk of lung cancer 10 to 20 years after RT
More recent reviews...


Is breast dose in Lymphoma relevant in the USA?

### Lymphoma 2014 USA Incidence

<table>
<thead>
<tr>
<th>Lymphoma 2014 USA Incidence</th>
<th>Projected Total</th>
<th>Male</th>
<th>Female</th>
<th>Est. Female % Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total All types</td>
<td>79,990</td>
<td>43,340</td>
<td>36,650</td>
<td>75.4%</td>
</tr>
<tr>
<td>Hodgkins</td>
<td>9,190</td>
<td>5,960</td>
<td>4,120</td>
<td>87.6%</td>
</tr>
<tr>
<td>Non- Hodgkins</td>
<td>70,800</td>
<td>38,270</td>
<td>32,530</td>
<td>73.9%</td>
</tr>
</tbody>
</table>

**Mortality**

| Mortality | 20,190 | 11,140 | 9,030 |
Age dependence of cancer risk

Does knowledge of out-of-field dose help us to improve RT?

- Linac selection
Sources of radiation

1) scattered radiation inside the patient body
2) scattered radiation from the head of the accelerator where collimators are located
3) leakage radiation from other parts of the accelerator

N.B. neutrons occur if photon energy high enough
Estimate of risk for secondary cancers
(Hall 2006)

Table 3. Estimated risk of fatal radiation-induced malignancies after RT for prostate cancer (%/Sv)

| Method                        | Risk  
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Abbreviations: IMRT = intensity-modulated radiation therapy; MV = megavoltage; RT = radiation therapy.
Does knowledge of out-of-field dose help us to improve RT?

- Linac selection
- Field size /selection
- Beam weighting
- External blocks
Breast Dose from Lymphoma techniques

PMCC Study showed breast dose decreased as field size decreased
Does knowledge of out-of-field dose help us to improve RT?

- Linac selection
- Field size / selection
- Beam weighting
- External blocks
- Technique selection?
Technique impact on dose to Breast tissue

Campbell, Hornby et al; Annals Oncol 2012
Why not just do more sophisticated dosimetry?

6MV EBRT

6MV IMRT
More sophisticated techniques require more imaging

- Scatter is very significant (>50% of dose)
- Dose is higher closer to surface of the phantom
- Dose in bone up to 4 times higher
- Dose cannot be accounted for in planning
If low doses to breast are important ...

- More monitor units with IMRT/VMAT increases scatter dose
- Out of field scatter/leakage dose may not be accurately reflected in routine dosimetry
Does knowledge of out-of-field dose help us to improve RT?

- Linac selection /energy
- Field size /selection
- Beam weighting
- External blocks
- Technique selection

- Move the tissue away?
Basis for Organ relocation

- If you don’t beam through the tissue, it won’t get as much dose
  - remember exit & entrance dose

**Dosimetry study: Tangents v 5FId IMRT v 9 FId IMRT**

Heart Dose: 2.63Gy, 4.04Gy, 4.3Gy
Contralateral Breast: 0.58Gy, 0.70Gy, 2.08Gy
Basis for Organ relocation

- If you don’t beam through the tissue, it won’t get as much dose
  - remember exit & entrance dose

- Historically proven concept
  - Brachytherapy / IORT
Basis for Organ relocation

- If you don’t beam through the tissue, it won’t get as much dose
  - remember exit & entrance dose

- Historically proven concept
  - Brachytherapy / IORT

- Well established approach in EBRT
  - Bellyboards, H&N biteblocks, gonad strapping etc.
There are various methods of breast relocation . . . but how reproducible are they on a daily basis?
Do what you can, with you have, where you are

- Theodore Roosevelt
Mr Ms Drape
Learning curve mitigation through practice
Pilot Study patient data

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Separation</th>
<th>Dose/fx</th>
<th>No. Fields</th>
<th>Indicative Field size (cm)</th>
<th>Nipple Day 1</th>
<th>Nipple Repositioned</th>
<th>Nipple Day 1</th>
<th>Nipple Repositioned</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>DISTANCE (cm) SUP-INF</td>
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<td>DISTANCE (cm) LEFT- RIGHT</td>
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<tr>
<td>1</td>
<td>28</td>
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(Units: cm, Gy, cm)
Total breast displacement for Left & Right breasts
Does breast relocation really work?

Breast repositioning can be done reproducibly with a thermoplastic drape
Does breast relocation reduce the OAR dose?

TLDs placed on Day 1 (no drape), and Days 2 & 3 (with drape)

Could we have used the TPS calculated dose to find out?
Dose ratio compared to breast repositioning distance

Repositioning distance didn’t correlate to rel % of dose reduction
Dose reduction due to repositioning

Repositioning location did correlate to absolute dose reduction
Dose reduction as a function of Field size
"The dose algorithm, ….. is the most unique, critical, and complex piece of software in a computerized planning system. The dose algorithm underpins many clinical decisions taken”.

Van Dyke, Barnett & Battista

- Eclipse TPS used for all calcs
- PBC algorithm used for all cases
Dose: TPS vs Measured

XiO dose calculations Collapsed Cone Convolution

relative reading (% of CAX dose)

distance from field edge (cm)

field centre

ionchamber

TERMA4

TERMA10

3%
Ratio of Calc’d : Measured doses - plotted against Dose / Fx
 Expanded plot of Calc’d:Measured dose ratio against Dose / Fx

Systematic under-prediction of out-of-field dose by TPS <0.03 Gy
"The dose algorithm, ..... is the most unique, critical, and complex piece of software in a computerized planning system. The dose algorithm underpins many clinical decisions taken".
Van Dyke, Barnett & Battista

PBC v AAA?

PBC contains adjustments for transmission that AAA doesn’t (at commissioning)

AAA only calcs scatter to 18-19cm outside beam
How did measured and doses calculated on a modern TPS compare?

- Measured & Calc’d consistent when in or near beam edge
- Error in matching TLD point & TPS calc point ~ biggest issue
However . . . Out-of-field doses are a different story

- PBC & AAA consistent under-prediction for nipple – AAA worse
- AAA consistent over-prediction for lateral breast tissue
Summary Conclusions

- To ensure truly optimal RT we need to consider low dose out of field
- Hard to quantify risk, but patients are relatively young and deserve the effort
- Simple breast repositioning is feasible
- Thermoplastic drapes can be used for breast repositioning - well tolerated
- Patients and clinicians want to know
Summary Conclusions

- Accurate TPS calculations for dose outside the field remains a dosimetry challenge.

- TPS calcs should not be relied upon when precise assessment of dose is important – invtro dosimetry.

- We need to also consider dose from imaging to normal tissue – increasingly important (and kV not yet available on TPS).
Thank you!