Comprehensive Breast Planning Techniques with an Emphasis on New Trends in IMPT

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Disclosures

- None
Learning Objectives

• Discuss benefits and limitations of different photon and proton techniques for comprehensive breast planning.

• Discuss proton therapy breast planning techniques employed at MCI

About Miami Cancer Institute

• 440,000 square feet, $430 million center
• 113 patient friendly exam rooms
• 60 infusion rooms / 8 infusion beds
• Alliance with Memorial Sloan Kettering- access to clinical trials, sharing educational resources and new techniques to improve care
• Reaching communities and residents of South Florida, Latin America, the Caribbean and internationally
Technology at MCI

Breast Cancer in Society
Why the Attention?

About 1 in 8 women will develop invasive breast cancer over the course of their lifetime.

American cancer society cancer statistics 2018

Risk Factors

- Female
- Age: most breast cancers are diagnosed after age 50
- Genetics: inherited changes to certain genes such as BRCA1 and BRCA2
- Early menstrual period: women who start their periods before the age of 12 are exposed to hormones longer
- Menopause after the age of 55
- Not being physically active
- Dense breast tissue: having more connective tissue than fatty tissue (can be difficult to see tumors on a mammogram)
- Family history of breast cancer
- Prior XRT to the chest before the age of 30 (Hodgkin’s Lymphoma)

cdc.org
Treatment Options

- Modality
  - Photons: 3D, IMRT, VMAT, Tomo
  - Protons: Passive scattering, uniform scanning, or PBS
  - Electrons: boost
  - Brachytherapy
- Positioning
  - Supine, Prone, Decubitis
- Free Breathing vs DIBH

Staging in Breast Cancer

**TNM Staging System** - based on size of the tumor (T), lymph node involvement (N) and whether the cancer has metastasized (M).

- **T** - tumor can’t be measured or found
- **T** - there isn’t any evidence of the primary tumor
- **T** - cancer is “in situ” (hasn’t started growing into healthy breast tissue).
- **T**, **T**, **T**, **T** - based on the size and the extent to which the tumor has grown into neighboring breast tissue. The higher the number, the more it may have grown into breast tissue.

Breastcancer.org
How Do We Decide?

TxN0M0

Lumpectomy → Mastectomy

Radiation Therapy

1. Opposed tangents
2. Prone
3. Tomotherapy
4. IMRT/VMAT

Opposed Tangents

FIF using static segments/control points to preferentially cool the breast to create a more homogeneous plan

Don’t have to image daily, can do weekly KVs
Coronary Exposure from Conventional RT for Breast Cancer can lead to Coronary Stenosis

Coronary artery radiation exposure

Stenosis of the main left anterior descending (LAD) artery

DIBH vs FB

Tx with DIBH can reduce heart and lung dose
Used primarily with Left-sided breast cancer

Figure 4: Comparison of dose distributions of (a) deep inspiration and (b) free breathing plans for a patient. Radiation exposed Left Anterior Descendent artery (LAD) (yellow color), LAD+5mm (orange color) and heart (green color).
Prone Treatment

- Patients with large or pendulous breasts
- Creates distance between chestwall and breast
- Helps to avoid the heart and provide better cardiac sparing
- Decreases dose to the lungs (especially important for patients who are smokers or have lung issues like COPD)
- Reduce skinfolds decreasing acute and late skin effects
- Potentially improve dose homogeneity

Prone Treatment

Disadvantages:

- Reproducibility in patient setup
- Discomfort/ can the patient tolerate the position?
- Need to image (KVs) every treatment
For Early Stage Breast Cancer, Prone Photon RT is a Good Option to Lower Heart Dose

If a patient has their sim done prone, they will also have a supine SIM for the boost (if applicable). If patient has a nodal component, won’t sim prone, but rather supine

Most patients treated to breast only are suitable for prone setup and will not require Protons

VMAT

Difficulties include:
• Mean Heart dose
• V20 Total Lung
• Contralateral Breast
Tomotherapy

- Combines IMRT with on-board CT scanner
- Delivers dose to breast tumors in full helical 360 degrees
- Beneficial for large, complex tumor volumes or unfavorable anatomy

How Do We Decide?

- TxA+N+M0
- Lumpectomy + Lymph Node Assessment
- Mastectomy + Lymph Node Assessment
- Radiation Therapy
  1. 3-Field +/- IMN
  2. 4-Field +/- IMN
  3. Tomotherapy
  4. IMRT/VMAT
  5. Protons
3D- Multiple Fields (3,4,5F)

A lot of manual manipulation, especially with field set ups.

Moving toward VMAT (NASBP-51, RADCOMP)

Why Protons for Breast Cancer?

- Increasing trend of treating regional nodes, including IMN nodes
- The breast and lymph nodes lie in close proximity to the heart and lungs
- Exposure to the heart and lungs can lead to serious morbidity and mortality
- The majority of women with breast cancer are cured and will live long enough to suffer long term consequences of radiation
- Lower doses to heart and lung with proton therapy may reduce radiation-related toxicity
Protons vs. Photons in Breast Cancer

Excess radiation delivered by X-Rays
- Potential for:
  - Coronary Artery Stenosis
  - Fatal Myocardial Infarction
  - Secondary Cancer
  - Lung Fibrosis

THE PAST: 2011-2012, Before PBS Technique We Used Uniform Scanning for Breast Treatment
Limited Field Size = Requires Multiple Fields and Match Lines
- Long treatment time + 45 min
- Higher skin dose than PBS
- Compensators & Apertures

Marcio Fagundes, MD MCI – Miami Cancer Institute
IMPT Protons

With PBS proton therapy, we are able to generate homogenous plans while maintaining conformality and OAR sparing more so than other modalities in most instances, but not always.

Notice LAD Sparing!

Photons vs. Protons:
A Further Look at Heart Dose

3D, Breath-hold  VMAT, FB  Protons, FB

Mean heart dose

3D: 3.02 Gy  VMAT: 10.75 Gy  IMPT: 0.04 Gy

Slide adapted from Rupesh Kotecha, MD-Miami Cancer Institute
Heart Dose = Cardiac Toxicity

Darby (Breast Cancer)
- Relative risk of major coronary events increased by 7.4% per Gy mean heart dose

Comparison between modalities

Table 4  Organ at-risk median dosimetry for various techniques targeting internal mammary lymph nodes

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Electrons</th>
<th>Photons/ electrons/pelvis</th>
<th>5 FIELD mixed photons/ electrons</th>
<th>IMRT after immediate reconstruction</th>
<th>IMRT photons</th>
<th>IMRT IMRT</th>
<th>Protons (previous series)</th>
<th>Protons (present series)</th>
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<tbody>
<tr>
<td>Heart (mean dose)</td>
<td>NR</td>
<td>7.5 Gy</td>
<td>NR</td>
<td>3.50 Gy</td>
<td>2.18 Gy</td>
<td>2.46 Gy</td>
<td>0.44 Gy (RBE)</td>
<td>1.00 Gy (RBE)</td>
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<tr>
<td>Heart V20 (%)</td>
<td>NR</td>
<td>NR</td>
<td>46.00</td>
<td>NR</td>
<td>31.00</td>
<td>31.00</td>
<td>41.00</td>
<td>41.00</td>
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<tr>
<td>Ipsilateral lung</td>
<td>38.03</td>
<td>NR</td>
<td>65.00</td>
<td>NR</td>
<td>65.00</td>
<td>80.18</td>
<td>65.00</td>
<td>65.00</td>
</tr>
<tr>
<td>V20 (%)</td>
<td>NR</td>
<td>28.00</td>
<td>28.00</td>
<td>NR</td>
<td>34.46</td>
<td>29.49</td>
<td>34.46</td>
<td>29.49</td>
</tr>
<tr>
<td>V5 (%)</td>
<td>NR</td>
<td>65.00</td>
<td>NR</td>
<td>65.00</td>
<td>65.00</td>
<td>65.00</td>
<td>65.00</td>
<td>65.00</td>
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<tr>
<td>Total long V20 (%)</td>
<td>20.30</td>
<td>14.4</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>12.70</td>
<td>7.31</td>
</tr>
</tbody>
</table>

Abbreviations: IMRT = intensity modulated radiation therapy; NR = not reported.
* Forward planned simplified IMRT using opposed lateral beams.
† Extracted from figure in publication.

Recent review of published breast cancer studies from 2003-2013 showed an mean heart dose of 8.4 Gy for left-sided cases and 4.2 Gy for right-sided cases if comprehensive regional nodal irradiation required

PMID: 25754632
Comprehensive Breast Planning with PBS Proton Therapy

- Basic physics
- Machine terminology
- Delivery techniques
- Beam angles
- Optimization strategies

Basic Proton Physics

A single Bragg Peak isn’t very useful clinically because it is small. By modulating the beam and changing the energy, we can make multiple Bragg peaks at different depths. By taking the sum of these individual Bragg Peaks, we get the SOBP.
Basic Proton Physics

Machine Terminology

- The Snout Position (SP) is the distance from the distal edge of the snout to the Isocenter of the beam. It can move either toward or away from the patient.

SP/AG are inter-related.

For PBS, we do not have to worry too much about SP/AG...unless we need a range shifter (superficial targets)
Range Shifters

- Purpose of the range Shifter (RS) is to reduce the entrance energy so that superficial target can be treated. For IBA/Varian, the lowest energy available is 70 MeV. This equates to a minimum ~4 cm depth. This means that the shallowest depth the beam can treat is ~4 cm.

- Shallower targets (e.g. breast), cannot be optimally treated without extreme beam modulation, which will create very high/non-uniform dose.

- The dosimetric effect of the RS is to add “virtual” tissue in front of the target, making it look as if the target is deeper, thus “shifting” the range.
Range Shifters

- RS also increases the Spot Size because it scatters the beam (magnitude depends on snout position). The beam is not as “sharp” meaning there is an increase in the lateral penumbra.

Effect of Air Gap and Spot Size

- 7.5cm RS with 5cm air gap
- 7.5cm RS with 28cm air gap

Dose Difference
Determining the Air Gap

At CT Sim, we ask for a reconstructed CT with a FOV of about 70cm.

Planning CT at 50cm FOV  
CT at 70cm FOV

Air Gaps in TPS

Visual representation of the snout with range shifters to check for clearance.

Keep isocenter as inferior as possible to help ensure clearance and avoid collisions with the patient!

Be aware of collisions with immobilization devices as well.

Always good to do a “Dry-Run”.

Try and keep the air gap as small as possible!
Advanced Proton Delivery

PBS Delivery Techniques

SFO (SFUD)
- FieldDose = TotalDose / #Of Beams. Each field has a weighting, and is independent and the dose is \(~\text{uniform}\) for each field.

MFO (IMPT)
- All spots from all fields are optimized simultaneously, whereas in SFO, all spots within each field are optimized separately. \(~\text{Non-uniform}\) dose from each field.

SFO vs. MFO

Looking at the composite doses for each plan, they look very similar. What about single beam dose?
SFO vs. MFO

SUMMARY:

- In general, but not always, SFO plans are more robust because there is less modulation per field. MFO can be highly modulated, as seen in previous example.
- MFO can potentially spare OARs better.
- SFO is better suited for targets that are more uniform in shape.
- SFO is used for most of cases because robust optimization is now available, planning with MFO seems to be more common.

Photon Vs Proton Beam Arrangement

Tangents  VMAT
Photon Vs Proton Beam Arrangement

AP  En Face

Proton beam arrangement

What About Target Motion Due to Respiration?

Motion is minimal with Protons with En Face beam
Motion along the beam has little effect on dose distribution
What About Target Motion Due to Respiration?

10 phases from 4D Ct

How Do We Decide?

Depends on patient anatomy.
Tangential Effects, need for a gradient?
Are we avoiding Hardware?

What are your first thoughts, 1 beam? 2 beams? SFO or MFO?
How Do We Decide?

At first glance, this looks reasonable…but is it?

Evaluating the dose from each beam, we see the AP beam is much hotter medially and the En Face beam is much hotter laterally... up to 135% hot spot.
How Do We Decide?

“Heavy-weighted” spot right on the surface, possibly slightly outside the body

The Solution

By splitting the target in the chest wall, we can create a gradient to make a homogenous plan. Ended up treating the superior nodes more SFO.
Creating the Gradient

MFO technique using gradients to treat sub targets, 2 beams

How do we go about planning this case? Create beam blocks!

Create a contour that we don’t want the AP beam to treat.

Creating the Gradient

Let’s do the same thing for our En Face beams!

Create a contour that we don’t want the En Face beams to treat.
Dose Distribution

Dose from AP beam

Dose from En face beam

Spot Placement

Spots from AP beam

Spots from En face beam
How Important is Spot Placement?

No Spot Blocker  Spot Blocker

Another Example of Spot Placement

“Heavy” Weighted spots...
How Can We Improve Treatment Plans for Breast Patients?

Improving the Patients Quality of Life

1. OBJECTIVES

1.1 Study Design.
This is a pragmatic randomized clinical trial in which patients with locally advanced breast cancer will be randomized to either proton or photon therapy and followed longitudinally for cardiovascular morbidity and mortality, health-related quality of life (HRQOL), and cancer control outcomes. We hypothesize that proton therapy, as part of multi-modality curative treatment for locally-advanced breast cancer, reduces major cardiovascular events (MCE), is non-inferior in cancer control, and improves HRQOL compared to photon therapy, the current standard treatment.

1.2 Primary Objective
To assess the effectiveness of proton vs. photon therapy in reducing major cardiovascular events (MCE), defined as atherothrombotic coronary heart disease or other heart disease death, myocardial infarction, coronary revascularization, or hospitalization for major cardiovascular event (heart failure, valvular disease, atrial fibrillation, or unstable angina or other major cardiovascular event).

1.3 Secondary Objectives
- To assess the non-inferiority of proton vs. photon therapy in reducing splintered breast cancer local-regional recurrence and in reducing any recurrence, defined as the first reported breast cancer recurrence of any type (local-regional or distant or cancer-specific mortality).
- To assess the effectiveness of proton vs. photon therapy in improving patient-reported body image and function, fatigue and other measures of health-related quality of life (HRQOL) (anxiety, social roles, financial toxicity, general satisfaction) and adverse events.
- To develop predictive models to examine the association of radiation dose distribution (to heart and other normal tissues) and MCE and HRQOL outcomes.
- To assess longer-term rates of breast cancer specific and overall survival and development of second malignancies.

Here is our approach..
Intact Breast- Skin Sparing and Rib Rind (CW) Sparing

CTV breast Opti (cyan)
Skin 5mm rind (orange)
Rib rind (red)
Rib rind opti (purple)

Intact Breast- Skin Sparing and Rib Rind (CW) Sparing

Skin and Rib Sparing
No Sparing
Intact Breast- Skin Sparing and Rib Rind (CW) Sparing

Example Case: Chest Wall Sparing with IMC Escalation

Post-Mastectomy-3mm Skin Rind, Rib Rind sparing (5mm) and SIB IMC boost to 56 Gy
Case Study

RC, 83 y.o. female patient with bilateral breast cancer with post bilateral mastectomy, axillary dissection:

PMHx: CAD, smoking x 17 yrs, COPD- cardiac sparing is very important

Recommendation:
50.4 Gy to bilateral chest wall, axilla, scbav regions and right IMC

Goal was to achieve a proton plan:
- Target coverage
- OAR sparing
- Efficient delivery
- Robust

Adapted from slides by Marcio Fagundes, MD – Miami Cancer Institute

Monoisocentric IMPT Plan with Gradient Junction Using 3- Fields

3 Field Composite Dose

Adapted from slides by Marcio Fagundes, MD – Miami Cancer Institute
### IMPT Plan and Gradient Junction

**RAO**

**AP**

**LAO**

Gradient junction

Adapted from slides by Marcio Fagundes, MD – Miami Cancer Institute

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### How Did We Do?

<table>
<thead>
<tr>
<th></th>
<th><strong>IMPT</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Target coverage:</td>
<td>D99 50.4 Gy</td>
</tr>
<tr>
<td>Heart: Mean</td>
<td>0.06 Gy</td>
</tr>
<tr>
<td>LAD: D1 Mean</td>
<td>0.47 Gy</td>
</tr>
<tr>
<td></td>
<td>Mean 0.09 Gy</td>
</tr>
<tr>
<td>Total lung: V20</td>
<td>8%</td>
</tr>
<tr>
<td>V5</td>
<td>21%</td>
</tr>
<tr>
<td>Esophagus: D1</td>
<td>29.8 Gy</td>
</tr>
<tr>
<td>Mean</td>
<td>4.2 Gy</td>
</tr>
</tbody>
</table>

Adapted from slides by Marcio Fagundes, MD – Miami Cancer Institute
Robust Evaluation

- 8 scenarios: 6 Pt setup errors (5mm, ±x, ±y, ±z) &
- 2 range uncertainties (±3.5%)
- Nominal and 2 worst case scenarios are illustrated:

Coverage was maintained D99CTV > 95% of prescribed dose

Adapted from slides by Marcio Fagundes, MD – Miami Cancer Institute

Quality Control Scans During Treatment

Maintained target coverage while reproducing similar OAR doses.

Adapted from slides by Marcio Fagundes, MD – Miami Cancer Institute
Side Note About QA CTs

Check for changes in anatomy and weight loss

<table>
<thead>
<tr>
<th>Statistics</th>
<th></th>
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<tbody>
<tr>
<td>Start Weight</td>
<td>59.70 kg</td>
</tr>
<tr>
<td>Min Weight</td>
<td>59.70 kg</td>
</tr>
<tr>
<td>Max Weight</td>
<td>78.30 kg</td>
</tr>
</tbody>
</table>

How Do We Setup the Patient, Image, and Monitor Motion?

- **C-RAD**
  - Patient treatment setup and monitoring

- **Orthogonal X-rays**
  - Surface BBs for correlation

- C-RAD- SIG
- CBCT- if we have clearance
- KV/KV imaging with skin surface fiducials

Adapted from slides by Marcio Fagundes, MD – Miami Cancer Institute
C-RAD
Patient Treatment Setup and Monitoring

Treatment fraction completed in 21 minutes
Highly efficient pre-treatment imaging and delivery

Skin Tolerance

Evidence of midline junction skin sparing

32.4 Gy

41.4 Gy

50.4 Gy

1 Week after Tx

Adapted from slides by Marcio Fagundes, MD – Miami Cancer Institute
Tomotherapy Backup Plan

Fortunately, the patient completed her proton treatment without any downtime.

<table>
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<th>TOMO</th>
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<tr>
<td>V5</td>
<td></td>
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What are Some of the Technical Challenges in Treating Bilateral Breast Cancer with IMPT?

- Patient setup (posture correction-arms) C-RAD
- Field Junctions IMPT
- Intrafraction Motion monitoring C-RAD
- Daily reproducibility Daily KV/C-RAD
- Treatment time Monoisocenter
- Changing Anatomy Weekly QA CT
What are Some of the Planning Challenges in Treating Bilateral Breast Cancer with IMPT?

- Creating substructures when choosing the technique you need to plan with - Very much based on patient anatomy
- Mean Heart/LAD dose under 1 Gy if treating IMNs in some cases
- Robustness in the IMN - such a small target
- Esophagus Dose - max dose of 40 Gy!
- Robustness in the SCLV - D95>95 with 5mm shift!
Conclusion

- More than one way to achieve a great plan
- Patient anatomy dictates the delivery method and technique used
- Intact breast- 5mm skin/rib rind sparing (try and maintain D95/95, D90/90 worse case scenario)
- Chest wall patients= 3mm skin rind (try and keep hot spots off the skin)
- Patients planned with CTV robustness (3.5% RU, 5mm shifts)
- Weekly QA CTs
- Be Creative!

Thank You