Model-based selection of breast cancer patients for proton therapy

Anne Crijns, MD, PhD
Department of Radiation Oncology
University Medical Center Groningen
Groningen
The Netherlands
## Disclosures

<table>
<thead>
<tr>
<th></th>
<th>COI status</th>
<th>Names of companies / organizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>①</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>②</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>③</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>④</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>⑤</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>⑥</td>
<td>YES</td>
<td>Department of Radiation Oncology has research collaborations with IBA, RaySearch, Siemens and Mirada</td>
</tr>
<tr>
<td>⑦</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>
CASE 1

- BC patient of 61 years
  - No cardiac risk factors
  - Breast conserving surgery of the left breast + sentinel node: pT1cN1mi(sn)M0 invasive carcinoma
  - Parasternal uptake on scintigraphy

- Treatment
  - Locoregional RT including internal mammary chain
CASE 2

- BC patient of 40 years
  - Cardiac risk factor: BMI >30
  - Breast conserving surgery of the left breast + SN: pT1bN0(i+)M0 invasive carcinoma

- Treatment
  - Local RT
CASE 3

• BC patient of 63 years
  - Cardiac risk factors: BMI >30, diabetes, hypertension, hypercholesterolemia
  - Breast conserving surgery of the left breast + SN: pT1cN1ma(sn)M0 invasive carcinoma

- Treatment
  - Locoregional RT
Indication for proton therapy?

- Proton therapy is an expensive treatment
- Limited available in the Netherlands

➤ Model-based selection of breast cancer patients for proton therapy based on model for acute coronary events (ACE)

Source: National Indication Protocol Proton Therapy Breast Cancer (The Netherlands, 2018)
Model for acute coronary events

• Relative risk increases linearly by 7.4% / Gy MHD
  • No dose threshold
  • < 5 years after RT

How to translate the relative risk of 7.4% / Gy into an excess risk for an individual patient?

Darby, N Engl J Med 2013
Risk on ACE
Excess risk in relation to baseline risk Dutch population

![Graph showing excess risk in relation to baseline risk for different genders and risk factors.](image-url)
Risk on ACE
Excess risk in relation to baseline risk Dutch population

- Male with risk factors
- Female without risk factors

<table>
<thead>
<tr>
<th>Baseline risk</th>
<th>If dose = 10 Gy</th>
</tr>
</thead>
<tbody>
<tr>
<td>21%</td>
<td>Excess risk: 15.6%</td>
</tr>
<tr>
<td>5%</td>
<td>Excess risk: 3.8%</td>
</tr>
</tbody>
</table>

Mean heart dose (Gy)
How does model-based selection work?

According to the National Indication Protocol National Indication Protocol Proton Therapy Breast Cancer (The Netherlands, 2018), the model-based selection process for photon or proton therapy is as follows:

1. **Plan comparison**:
   - Photons: MHD PHOTON plan
   - Protons: MHD PROTON plan

2. **NTCP-model**:
   - Graph showing NTCP (Normal Tissue Complication Probability) model with different risk factors for male and female patients.

3. **Selection**:
   - If ∆NTCP ≥2% according to criteria National Indication Protocol, then:
     - Yes: Protons
     - No: Photons

Source: National Indication Protocol Proton Therapy Breast Cancer (The Netherlands, 2018)
CASE 1
pT1cN1mi(sn)M0 invasive carcinoma

Calculator for excess ACE-risk

<table>
<thead>
<tr>
<th>AGE:</th>
<th>61 Years</th>
<th>MHD PHOTONS</th>
<th>6.39 Gy</th>
<th>MHD PROTONS</th>
<th>0.37 Gy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factors ACE?</td>
<td>(0=NO, 1=Yes)</td>
<td>0</td>
<td>No risk factors for ACE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sexe</td>
<td>(0=Female, 1=Male)</td>
<td>0</td>
<td>Female</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RESULT PLANNING COMPARISON

Pre-selection tool (based on photon plan only)

Lifetime Excess Risk ACE with photons 2.2% YES Indication for planning comparison

Planning comparison

Lifetime Excess Risk ACE with photons

2.2% 0.1% 2.1% YES Indication for proton therapy

Photons

Protons

1 Age <40 years always fill in 40, Age >70 years always fill in 70.
CASE 2
pT1bN0(i+)M0 invasive carcinoma

<table>
<thead>
<tr>
<th>Calculator for excess ACE-risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fill in part: only fill in red boxes</strong></td>
</tr>
<tr>
<td><strong>AGE:</strong></td>
</tr>
<tr>
<td><strong>MHD PHOTONS:</strong></td>
</tr>
<tr>
<td><strong>MHD PROTONS:</strong></td>
</tr>
<tr>
<td><strong>Risk factors ACE?</strong></td>
</tr>
<tr>
<td><strong>Sex:</strong></td>
</tr>
</tbody>
</table>

**Pre-selection tool (based on photon plan only)**

<table>
<thead>
<tr>
<th>Lifetime Excess Risk ACE with photons</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>YES</strong> indication for planning comparison</td>
</tr>
</tbody>
</table>

**Planning comparison**

<table>
<thead>
<tr>
<th>Lifetime Excess Risk ACE with photons</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>YES</strong> indication for proton therapy</td>
</tr>
</tbody>
</table>

**Photon vs. Protons**

- Photon: 2.2% lifetime excess risk ACE
- Proton: 0.13% lifetime excess risk ACE

Note: Age ≤50 years always fill in 46; Age >50 years always fill in 70.
CASE 3
pT1cN1ma(sn)M0 invasive carcinoma
Model-based selection protons

- Model for ACE will be further optimized
- Models for other late (cardiac) complications
  - Heart failure
  - Pneumonitis
  - Secondary tumors

Better selection of BC patients for proton therapy
Acknowledgements

Department of Radiation Oncology
Prof. Hans Langendijk, MD, PhD
John Maduro, MD, PhD
Marleen Woltman, MD
Dianne Busz, MD
Max Beijert, MD
Olga Chouvalova, MD
Gertjan Stiekema, PA
Estelle Batin, ir, PhD
Erik Korevaar, ir, PhD
a.p.g.crijns@umcg.nl

Julius Center Utrecht
Ewoud Schuit, PhD

National Platform Radiotherapy
Breast Cancer

National Platform Proton Therapy

Jan Hietkamp
Patrick Kalk