Why is contouring important?

- **Targets**: Tumors and Nodal stations
- **Normal tissues**:
  - Reduce doses by blocking
  - Choosing beam angles with greatest separation between targets and OARs
  - Understanding dose-volume-toxicity relationships
  - Reducing toxicity
Learning Objectives

1) Understand the need for consistency in normal tissue contouring in the thorax

2) Be able to access atlases developed by radiation oncologists to improve contour consistency

3) Use these atlases as a guide to standardize contours and improve normal tissue sparing
OARs highlighted today

- Heart
- Brachial plexus
- Esophagus
Radiation can cause cardiac toxicity

(Reuters Health) - The radiation that might cure a breast cancer may also raise a woman's risk of having a heart attack or heart disease later in life, according to a new study that looked back at the cases of 2,168 women in Sweden and Denmark.
Radiation can cause cardiac toxicity

**METHODS**
We conducted a population-based case–control study of major coronary events (i.e., myocardial infarction, coronary revascularization, or death from ischemic heart disease) in 2168 women who underwent radiotherapy for breast cancer between 1958 and 2001 in Sweden and Denmark; the study included 963 women with major coronary events and 1205 controls. Individual patient information was obtained from hospital records. For each woman, the mean radiation doses to the whole heart and to the left anterior descending coronary artery were estimated from her radiotherapy chart.

**RESULTS**
The overall average of the mean doses to the whole heart was 4.9 Gy (range, 0.03 to 27.72). Rates of major coronary events increased linearly with the mean dose to the heart by 7.4% per gray (95% confidence interval, 2.9 to 14.5; P<0.001), with no apparent threshold. The increase started within the first 5 years after radiotherapy and continued into the third decade after radiotherapy. The proportional increase in the rate of major coronary events per gray was similar in women with and women without cardiac risk factors at the time of radiotherapy.

Dose effect on the heart

No threshold

Dose effect on the heart

How was dosimetry analyzed?

• Virtual simulation and planning based on CT or manual planning “were used to reconstruct each radiotherapy regimen on the CT scan of a woman with typical anatomy”

• (Virtual) Radiation doses to the structures of interest were then estimated

• In manual planning, the (virtual) doses were estimated on the basis of charts on which isodose curves had been drawn

How was dosimetry analyzed?

- Dose-volume histograms for the whole heart and for the left anterior descending coronary artery were obtained.
- Mean doses were calculated.

Are these results believable?

- In general? Probably
- Specifically? No
  - Reconstructed, hypothesized cardiac doses
  - Not based on reality
What do we know about cardiac toxicity?

The time-course and extent of cardiac damage depends on dose

– In the past, Hodgkin’s survivors were diagnosed with heart disease 1-2 years after radiotherapy (30 Gy+)

– Latency greater for lower doses of RT
## Cardiac toxicity after breast RT

**SEER study of 300,000 women with breast cancer**

<table>
<thead>
<tr>
<th>Years since breast cancer diagnosis</th>
<th>No radiotherapy</th>
<th>Radiotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of deaths left/right</td>
<td>Mortality ratio left versus right &amp; 95% CI</td>
</tr>
<tr>
<td>Heart disease death</td>
<td>2164/1972</td>
<td>1.03 (0.97-1.09)</td>
</tr>
<tr>
<td>&lt; 5 years</td>
<td>1632/1479</td>
<td>1.05 (0.98-1.13)</td>
</tr>
<tr>
<td>5 - 9</td>
<td>806/758</td>
<td>1.01 (0.91-1.11)</td>
</tr>
<tr>
<td>10 - 14</td>
<td>568/524</td>
<td>1.02 (0.91-1.15)</td>
</tr>
</tbody>
</table>

**All other known causes**

|                                     | 14775/13522 | 1.04 (1.01-1.06) | 6911/6516 | 1.01 (0.98-1.05) |
| < 5 years                           | 8009/7863  | 0.97 (0.94-1.00) | 3178/2990 | 1.01 (0.96-1.06) |
| 5 - 9                               | 3472/3343  | 0.99 (0.94-1.04) | 1165/1095 | 1.01 (0.93-1.10) |
| 10 - 14                             | 2106/2040  | 0.98 (0.92-1.04) | 611/560  | 1.04 (0.93-1.17) |

Darby, et al. Lancet Oncology 2005
Rationale for heart avoidance

Table 4. Spectrum of Radiation Damage to the Heart

<table>
<thead>
<tr>
<th>Structure</th>
<th>Abnormality</th>
<th>Natural History</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericardium</td>
<td>Pericarditis</td>
<td>Chronic asymptomatic effusion and/or pericarditis</td>
<td>Fibrous thickening and fluid production</td>
</tr>
<tr>
<td></td>
<td></td>
<td>with symptoms: hemodynamic compromise with either</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>constriction or tamponade</td>
<td></td>
</tr>
<tr>
<td>Myocardium</td>
<td>Myocarditis</td>
<td>Progressive diastolic dysfunction and restrictive</td>
<td>Diffuse interstitial fibrosis/microcirculatory damage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hemodynamics with symptoms: CHF</td>
<td>leading to capillary obstruction/extensive fibrosis</td>
</tr>
<tr>
<td>Endocardium</td>
<td>Valvular damage</td>
<td>Over time, progressive stenosis and regurgitation</td>
<td>Cusp and/or leaflet fibrosis</td>
</tr>
<tr>
<td>Vascular System</td>
<td>Arteritis</td>
<td>Premature CAD/accelerated atherosclerosis</td>
<td>Ostial and proximal stenosis; LAD, RCA, and left main</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pulmonary hypertension</td>
<td>more than left circumflex</td>
</tr>
<tr>
<td>Conduction System</td>
<td>All forms of heart</td>
<td>Fibrosis of the conduction system</td>
<td>Pathology similar to atherosclerosis</td>
</tr>
<tr>
<td>Autonomic Dysfunction</td>
<td>Supraventricular</td>
<td>heart rate variability</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CHF, congestive heart failure; CAD, coronary artery disease; LAD, left anterior descending [coronary artery]; RCA, right coronary artery.
Mechanisms of RT cardiac effects

Dose-volume-toxicity data in other organs

Pneumonitis

Kwa et al, IJROBP 1998

Xerostomia

Dijkema et al, IJROBP 2010
Dose-volume-toxicity data in other organs

Rectal Toxicity

Tucker, et al, IJROBP 2012

Gastric Bleed

Feng, et al, IJROBP 2012
Why haven’t we had similar plots for cardiac damage?

- In the pre-CT era, we could not accurately define the heart
- There is little agreement on how to define the heart
- Additionally, substructures of the heart may have specific importance
The data is hypothesized

Hypothesized curves

How can we move forward?

• We must first understand the relationship between dose and volume of heart (or cardiac substructures) and toxicity

• We can then incorporate these into treatment planning to minimize the risk of cardiac complications
Motivated by the lack of consistency in cardiac delineation, we

– Developed an atlas of cardiac substructure anatomy through a collaboration with cardiology and cardiac radiology

– Validated this atlas using a pre- and post-test study of 7 radiation oncologists
Cardiac atlas

Heart begins just inferior to L pulmonary artery

Non-contrast CT

Feng, et al. IJROBP, 2011
Cardiac atlas

Non-contrast CT

Feng, et al. IJROBP, 2011
Cardiac atlas

Non-contrast CT

Feng, et al. IJROBP, 2011
Cardiac atlas

Non-contrast CT

Feng, et al. IJROBP, 2011
Cardiac atlas

Contrast CT

Feng, et al. IJROBP, 2011
Cardiac atlas

Contrast CT

Feng, et al. IJROBP, 2011
Cardiac atlas

Contrast CT

Feng, et al. IJROBP, 2011
Cardiac atlas

Contrast CT

Feng, et al. IJROBP, 2011
Cardiac atlas

Contrast CT

Feng, et al. IJROBP, 2011
Cardiac atlas

Contrast CT

Feng, et al. IJROBP, 2011
Which of these structures is the LAD?

A  
B  
C  
D
Cardiac atlas

Multi-observer pre-test and post-test study

Pre-test  Post-test
Feng, et al. IJROBP, 2011
Cardiac atlas

Pre-test  Post-test
Feng, et al. IJROBP, 2011
Percent overlap of observer and gold standard contours

<table>
<thead>
<tr>
<th>Structure</th>
<th>Pre-atlas (mean ± SD)</th>
<th>Post-atlas (mean ± SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>79 ± 13</td>
<td>91 ± 4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>L main</td>
<td>10 ± 22</td>
<td>22 ± 20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LAD</td>
<td>35 ± 21</td>
<td>62 ± 16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>R coronary</td>
<td>11 ± 14</td>
<td>24 ± 18</td>
<td>0.002</td>
</tr>
<tr>
<td>Left ventricle</td>
<td>87 ± 11</td>
<td>92 ± 6</td>
<td>0.06</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>65 ± 10</td>
<td>74 ± 8</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Feng, et al. IJROBP, 2011
### Concordance index

<table>
<thead>
<tr>
<th>Structure</th>
<th>Pre-atlas (mean ± SD)</th>
<th>Post-atlas (mean ± SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>0.76 ± 0.11</td>
<td>0.89 ± 0.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>L main</td>
<td>0.05 ± 0.12</td>
<td>0.18 ± 0.16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LAD</td>
<td>0.19 ± 0.11</td>
<td>0.34 ± 0.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>R coronary</td>
<td>0.08 ± 0.10</td>
<td>0.18 ± 0.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left ventricle</td>
<td>0.75 ± 0.06</td>
<td>0.79 ± 0.05</td>
<td>0.04</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>0.55 ± 0.08</td>
<td>0.65 ± 0.08</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Feng, et al. IJROBP, 2011
Mean absolute value dose difference (Gy)

<table>
<thead>
<tr>
<th>Structure</th>
<th>Pre-atlas (mean ± SD)</th>
<th>Post-atlas (mean ± SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>0.88 ± 0.15</td>
<td>0.14 ± 0.14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>L main</td>
<td>1.68 ± 1.53</td>
<td>0.88 ± 1.56</td>
<td>0.005</td>
</tr>
<tr>
<td>LAD</td>
<td>3.90 ± 2.80</td>
<td>2.56 ± 3.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>R coronary</td>
<td>1.15 ± 1.07</td>
<td>0.61 ± 0.39</td>
<td>0.001</td>
</tr>
<tr>
<td>Left ventricle</td>
<td>0.25 ± 0.20</td>
<td>0.15 ± 0.14</td>
<td>0.13</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>1.06 ± 0.73</td>
<td>0.46 ± 0.37</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Feng, et al. IJROBP, 2011
Cardiac summary

- Breast RT may increase the risk of cardiac death many years after treatment.
- Unlike other structures such as the parotid gland, lung, and rectum, the heart’s dose-volume-toxicity profile is not well-understood.
- With a validated, detailed cardiac atlas, we can begin to collect information to elucidate the effect of RT on heart structures.
OARs highlighted today

- Heart
- Brachial plexus
- Esophagus
OARs highlighted today

- Heart
- Brachial plexus
- Esophagus
Importance of the brachial plexus

- Brachial plexus damage could lead to arm weakness or pain
- Commonly used dose limits range from 50 to 60 Gy
- Hot spots in treatment plans can be located in the brachial plexus if careful planning is not used
Brachial plexus on MRI
Brachial plexus on CT

AS = anterior scalene  MS = middle scalene  BP = brachial plexus

Brachial plexus on CT

AS = anterior scalene  MS = middle scalene  BP = brachial plexus

Brachial plexus on CT

AS = anterior scalene  MS = middle scalene  BP = brachial plexus

Brachial plexus on CT

AS = anterior scalene  MS = middle scalene  BP = brachial plexus

Brachial plexus

Which of these structures is the brachial plexus?

A  B  C  D
Brachial plexopathy from RT

Clinical Investigation: Thoracic Cancer

Brachial Plexopathy in Apical Non-Small Cell Lung Cancer Treated With Definitive Radiation: Dosimetric Analysis and Clinical Implications

Michael J. Eblan, MD,* Michael N. Corradetti, MD, PhD,* J. Nicholas Lukens, MD,* Eric Xanthopoulos, MD, JD,* Nandita Mitra, PhD,† John P. Christodoulas, MD, MPH,* Surbhi Grover, MD,* Annemarie T. Fernandes, MD,* Corey J. Langer, MD,‡ Tracey L. Evans, MD,‡ James Stevenson, MD,‡ Ramesh Rengan, MD, PhD,* and Smith Apisarnthanarax, MD*

Departments of *Radiation Oncology, †Biostatistics and Epidemiology, and ‡Medical Oncology, Abramson Cancer Center, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania

Eblan, et al, IJROBP 2012
Brachial plexopathy from RT

Fig. 2. Cumulative rate of RIBP as a function of maximal dose delivered to the IBP.

Eblan, et al, IJROBP 2012
OARs highlighted today

- Heart
- Brachial plexus
- Esophagus
OARs highlighted today

- Heart
- Brachial plexus
- Esophagus
Esophagitis

• Can be a significant side effect of RT, especially if combined with chemotherapy for lung cancer
• Pain affects quality of life and causes patients to lose weight, which reduces the ability to tolerate treatment
• Multiple dose-volume limits have been proposed to minimize esophagitis
Esophageal contours

- RTOG recommends contouring from the cricoid to the GE junction
- Esophageal diameter, shape, and position are variable
- Pay attention for accurate contours
The esophagus starts at the level of cricoid
Esophageal contours

Usually it quickly becomes round

Kong, et al
Esophageal contours

Then it can take a turn to the side

Kong, et al
Esophageal contours

…and flatten out more…

Kong, et al
Esophageal contours

...before it rounds out again and joins the stomach.

Kong, et al
Esophagitis from RT

Kwint, et al, IJROBP 2012
Variability in esophageal contours

A: Esophagus Contour Variants

Kong, et al, IJROBP 2011
Summary

• Accurate OAR contouring is important for treatment planning

• Atlases have been created to improve consistency

• As centers create more uniform OAR contours, data can be compiled to build more realistic models to estimate and minimize toxicity risk
Thanks for your attention