Leveraging advanced technologies for improved cardiac sparing

Carri Glide-Hurst, PhD, DABR, FAAPM
Director of Translational Research, Radiation Oncology
Henry Ford Cancer Institute

Director, Radiation Oncology Physics, Department of Human Oncology,
University of Wisconsin Madison
Disclosures

- Research funding provided by:
  - NIH R01CA204189 (PI: Glide-Hurst)
  - Philips Healthcare

- Collaborations with Modus Medical Devices, ViewRay (unrelated to the current work)

- Many of these slides are compliments of the recently minted Dr. Eric Morris (HFCI/WSU—>UCLA)
How is the heart like bowling?
Clinical Motivation: Cardiac Dose

- Radiation dose to the heart may be fatal\(^1\)
- Hodgkin’s lymphoma\(^2\)
  - Myocardial infarction
- Esophageal\(^3\)
  - Heart failure
- Advanced stage lung\(^4\) and breast\(^1\)
  - Coronary artery disease: Left > Right

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Slide Credit: Eric Morris, PhD
Deep-inspiration Breath Hold (DIBH)

- Surface monitoring (RPM, AlignRT, bellows, SDX)
- Spirometry (ABC)

Rong et al, Plos One, 2014
Limitations in Heart Dose/Volume Metrics

- RTOG 0617: 74 Gy (2 Gy fx) w/ concurrent chemo was not better than 60 Gy
  - Might be potentially harmful (!!!)
- RTOG 0617 heart dose-volume thresholds for treatment planning:
  - Heart V33% < 60 Gy; V66% < 45 Gy; V100% < 40 Gy
- Lowest priority among all normal tissues
- QUANTEC endpoint: <10% of heart receives >25 Gy for long-term cardiac mortality endpoints

Whole-heart Dose Metrics are not Sensitive

Basic Original Report

The Meaningless Meaning of Mean Heart Dose in Mediastinal Lymphoma in the Modern Radiation Therapy Era

Bradford S. Hoppe, MD, MPH,a,* James E. Bates, MD,b,c Nancy P. Mendenhall, MD,b,c Christopher G. Morris, MS,b,c Debbie Louis, CMD, b Meng Wei Ho, MS,b Richard T. Hoppe, MD,d Marwan Shaikh, MD,e Zuofeng Li, DSc,b,c and Stella Flampouri, PhD,b,c

"Mayo Clinic Florida, Department of Radiation Oncology, Jacksonville, Florida; "University of Florida Health Proton Therapy Institute, Jacksonville, Florida; "Department of Radiation Oncology, University of Florida College of Medicine, Gainesville, Florida; "Department of Radiation Oncology, Stanford University, Palo Alto, California; and "Department of Hematology/Oncology, University of Florida College of Medicine"
Clinical Motivation: Cardiac Substructure Doses

- RTOG 0617 sub-analysis suggests dose to substructures were more strongly associated with overall survival than standard of care whole-heart dose estimates\(^1\)
- Left atrium/ventricle (LA/LV) & left anterior descending artery (LADA) have prognostic inferences, such as: **Risk of cardiomyopathy, CAD, ischemic diseases, etc.\(^2\)**
- Recent dose constraints to substructures have been introduced\(^3\)

<table>
<thead>
<tr>
<th>Structure</th>
<th>Constraint</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Heart</td>
<td>Mean Heart Dose</td>
<td>&lt; 2.5 Gy</td>
</tr>
<tr>
<td>LV</td>
<td>LADA-V40</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>LV</td>
<td>Mean LV Dose</td>
<td>&lt; 3 Gy</td>
</tr>
<tr>
<td>LADA</td>
<td>LV-V5</td>
<td>&lt; 17%</td>
</tr>
<tr>
<td>LADA</td>
<td>LADA maximum dose</td>
<td>&lt; 10 Gy</td>
</tr>
</tbody>
</table>

Substructure Atlas Generation & Application in MIM

- 20 left-sided breast cancer patients, cardiac T2-weighted MRI at 3T and TPCTs
- 15 patients in the atlas, 5 test subjects
- Compared (1) single-atlas, (2) majority vote (MV), and (3) simultaneous truth & performance level estimation (STAPLE)
- Atlas subject selected via mutual information, then contours deformably registered
- Multi-atlas matches iterated (1, 3, 5, 10, and 15)

Morris et al, IJROBP, 2019
Single Validation Patient: ST10 vs. Ground Truth Contours

- DSC > 0.75
- DSC < 0.55
- Paired MRI/CT data for 25 patients were placed into separate image channels to train network
- **Novel Deep Learning Contributions**: Multi-channel (MRI/CT) inputs, deep supervision, 3D adaptation on original 2D U-Net, and hyperparameter optimization

1. Morris et al, MedPhys, 2020
2. Ronneberger et al., MICCAI, 2018
Results: Worst Case

Mid-Line
Superior

Ground Truth

2D Axial

DL Prediction

Sagittal
Coronal

3D Rendering

LV  RV  LA  RA  SVC  IVC  PV  PA  AA  RCA  LADA
Results: Comparison to Multi-Atlas Method

Deep Learning vs. Multi-Atlas:

~14 seconds (DL) vs. ~10 minutes (multi-atlas)

Cardiac Substructure

Morris et al, MedPhys, 2020
Cardiac Substructure Motion During Respiration

Cardiac Substructure Shifts During Respiration

Centroid Displacement (mm)

Substructure

Heart LV LA RV RA AA PA SVC IVC PV LMCA LADA RCA

PO-GeR: I-96
Miller, C. et al.
**Dose Variations During Respiration**

- Note small variations for the whole heart (red), mean dose < 0.5 Gy (not sensitive!!)
- Superior vena cava mean dose > 5 Gy difference

PO-GeP-M-96
Miller, C. et al.
Substructure Spared Planning, IMRT

- Exceptional sparing to the LADA
- New beam arrangements possible with 4/16 patients

Morris et al., Under Revision JACMP, 2020
Negligible increase in estimated delivery time with re-optimized plans (0.1 ± 1.3 min) with 12/16 plans having <100 MU change
Substructure spared planning: VMAT, Protons

VMAT
2-4 Arcs

CARDIAC SPARED VMAT
2-4 Arcs

PROTONS
2-3 beams IMPT

60 Gy
45 Gy
30 Gy
Cardiac Displacement Visualized in MR-guided RT

LADA
Superior-Inferior

Axial
Patient 6 Simulation
Patient 6 Fraction 3

Substructure | SIM | Fx3 | Dose (Gy)
---|---|---|---
Heart | | | 45
RV | | | 40
LV | | | 30
RA | | | 20
LA | | | 10
AA | | | 5
LADA | | | 
RCA | | | 
PV | | | 

MO-F-TRACK 2-1*
Morris, E. et al.
Clinical Impact & Conclusions

▪ Radiation therapy dose to the heart is avoidable and modifiable: we can (and should!) do better
▪ Becomes of even greater importance with dose escalation, hypofractionation, etc.
▪ Applying advanced technologies will help us keep our patients safer from acute and late cardiac toxicities