Leveraging advanced technologies for improved cardiac sparing

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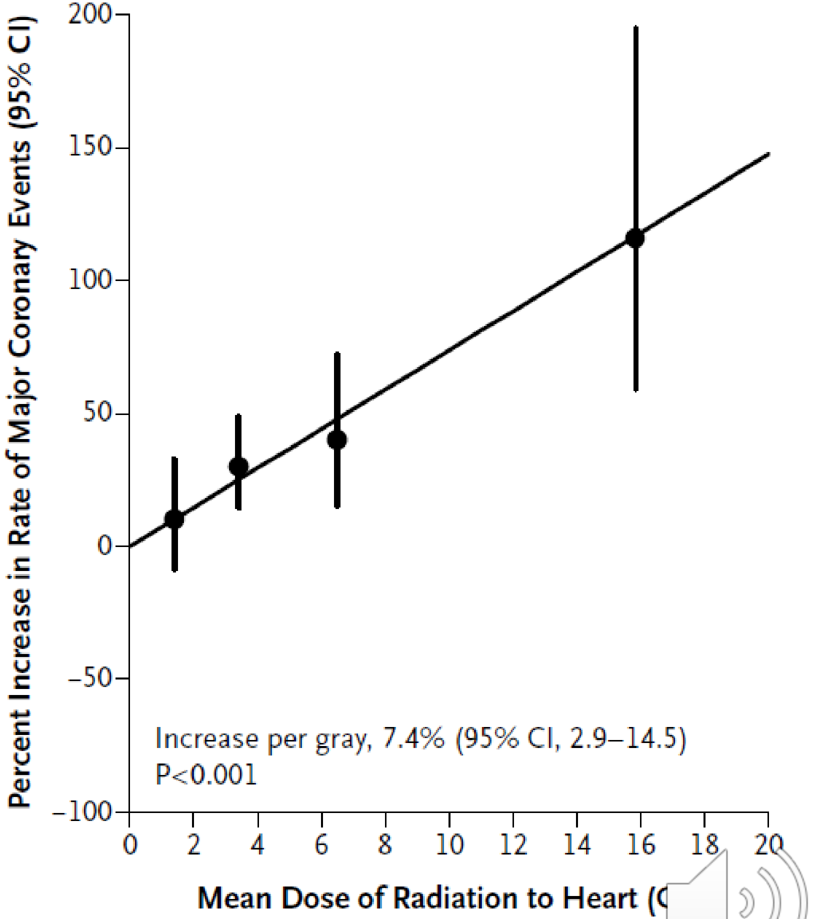
- Many of these slides are compliments of the recently minted Dr. Eric Morris (HFCI/WSU—>UCLA)

How is the heart like bowling?

Clinical Motivation: Cardiac Dose

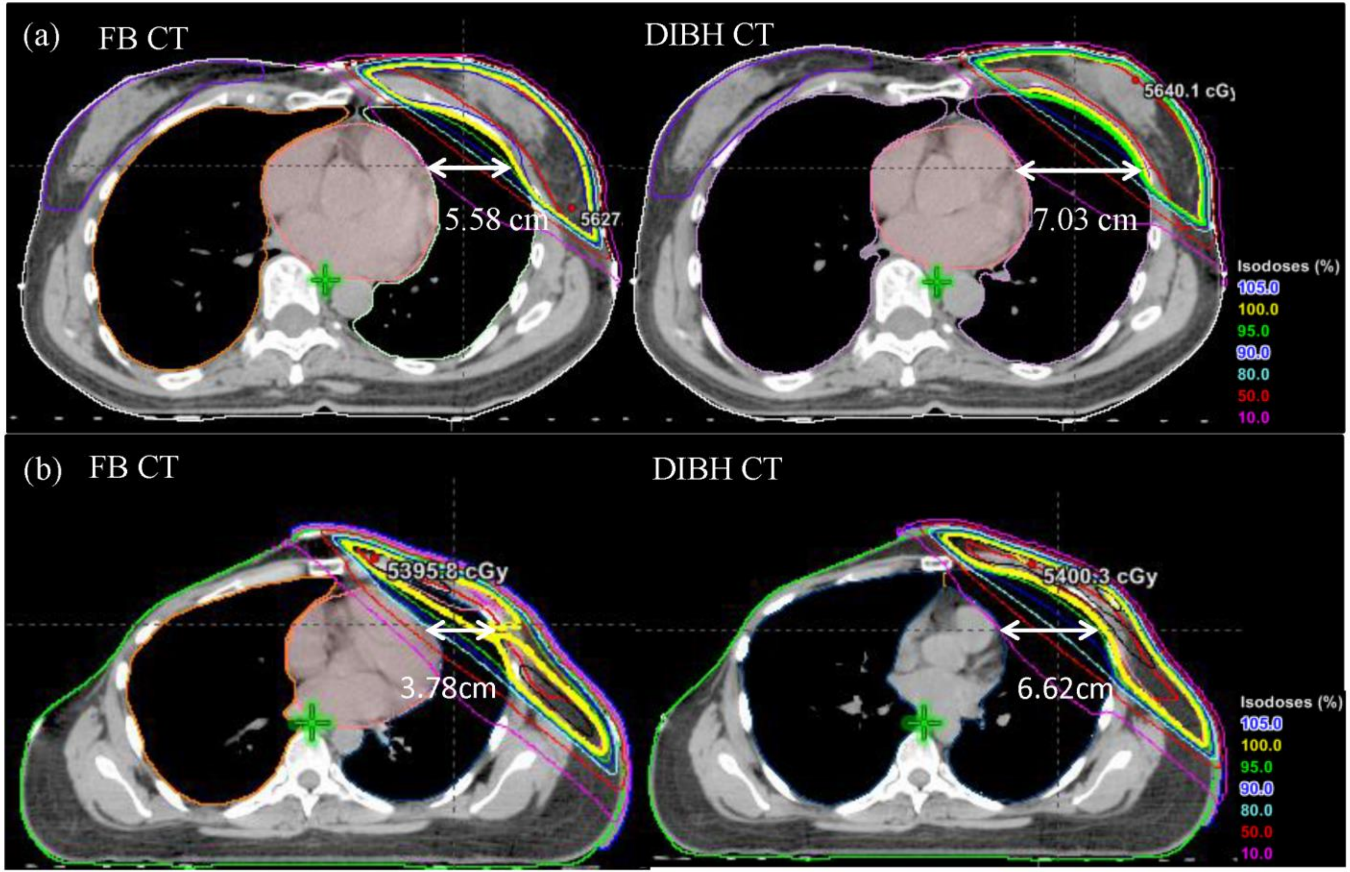
- Radiation dose to the heart may be fatal[1]
- **Hodgkin's lymphoma[2]**
  - Myocardial infarction
- **Esophageal[3]**
  - Heart failure
- **Advanced stage lung[4]** and **breast[1]**
  - Coronary artery disease: Left > Right



1 . Darby et al., NEJM, 2013; **2.** Ng et al., BrJH, 2011; **3.** Beukema et al., RO, 2015; **4.** Hardy et al., AO, 2010.

Slide Credit: Eric Morris, PhD

Deep-inspiration Breath Hold (DIBH)



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

Rong et al, Plos One, 2014

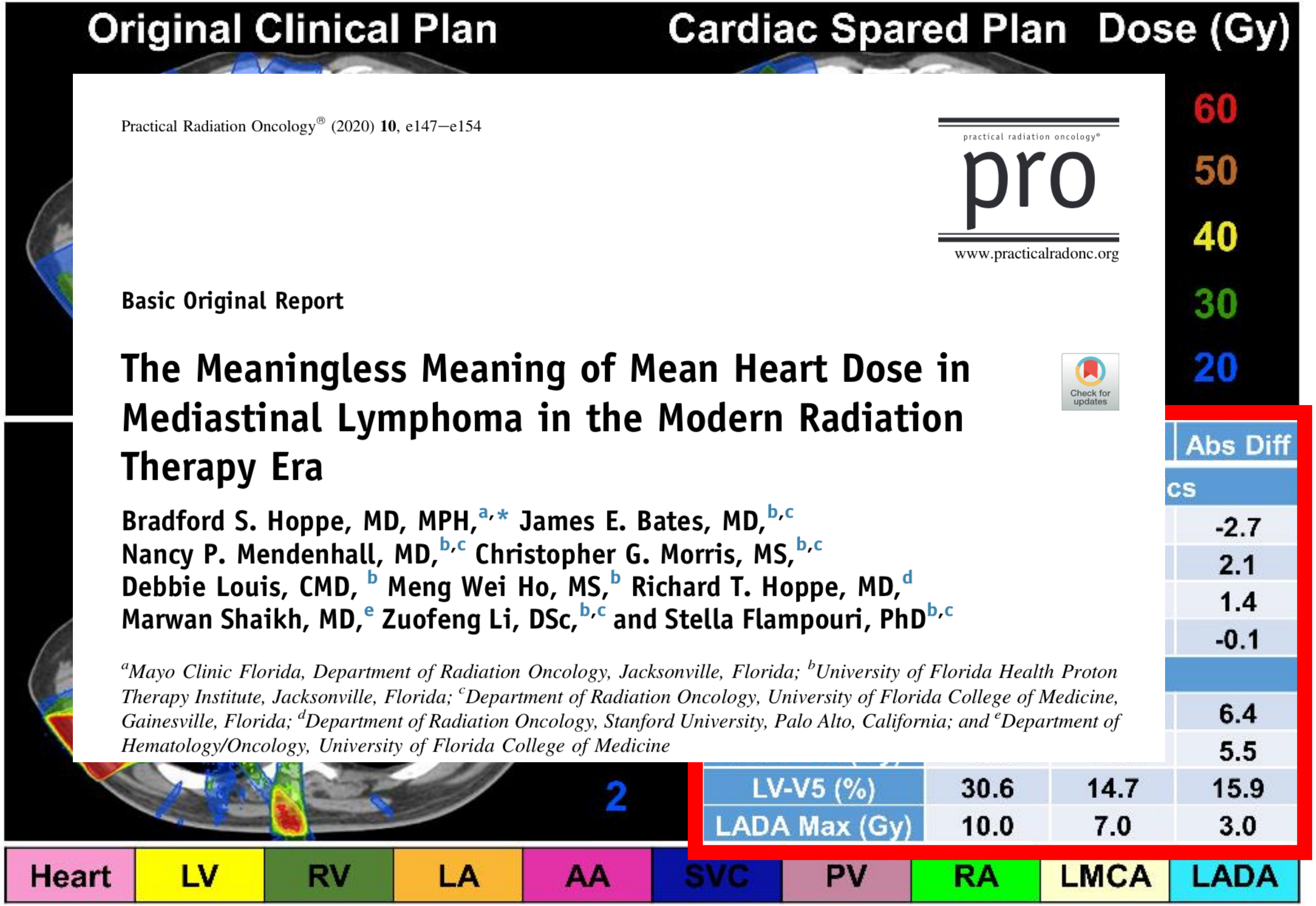
Limitations in Heart Dose/Volume Metrics

- RTOG 0617: 74 Gy (2 Gy fx) w/ concurrent chemo was **not** better than 60 Gy
  - Might be **<u>potentially harmful</u> (!!!)**
- 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

Lancet Oncol. 2015 Feb; 16(2): 187–199.

Whole-heart Dose Metrics are not Sensitive



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Basic Original Report

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

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Morris et al., Under Revision JACMP, 2020

Clinical Motivation: Cardiac Substructure Doses

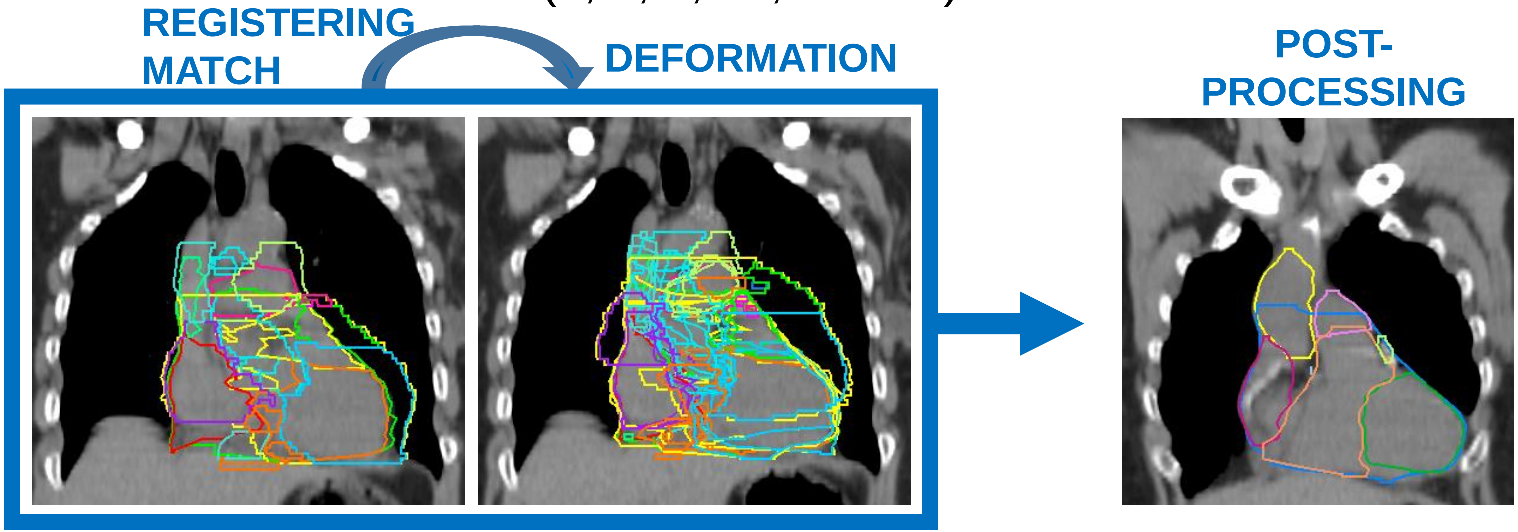
- RTOG 0617 sub-analysis suggests dose to substructures were more strongly associated with overall survival than standard of care whole-heart dose estimates[1]
- Left atrium/ventricle (LA/LV) & left anterior descending artery (LADA) have prognostic inferences, such as: **Risk of cardiomyopathy, CAD,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

Structure	Constraint	Value
Whole Heart	Mean Heart Dose	< 2.5 Gy
LV	LADA-V40	< 1%
	Mean LV Dose	< 3 Gy
LADA	LV-V5	< 17%
	LADA maximum dose	< 10 Gy

1. Thor et al., IJROBP, 2018; **2.** Vivekanandan et al., IJROBP, 2017; **3.** Van den Bogaard et al., ASCO, 2017

Substructure Atlas Generation & Application in MIM

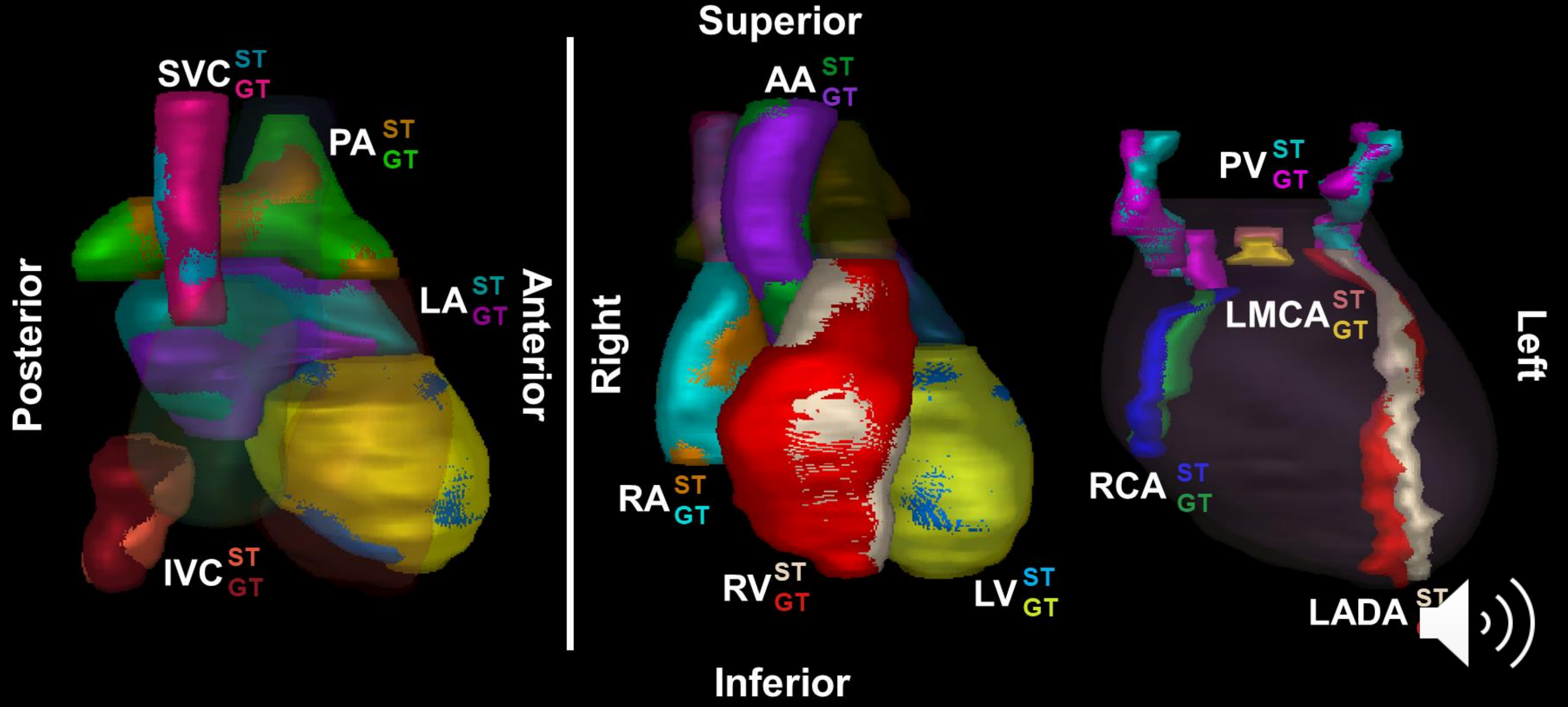
- 20 left-sided breast cancer patients, cardiac T2-weighted MRI at 3T and TPCTs
- 15 patients in the atlas, 5 test subjects
- Compared (1) single-atlas, (2) majority vote (MV), and (3) simultaneous truth & performance level estimation (STAPLE)
- Atlas subject selected via mutual information, then contours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



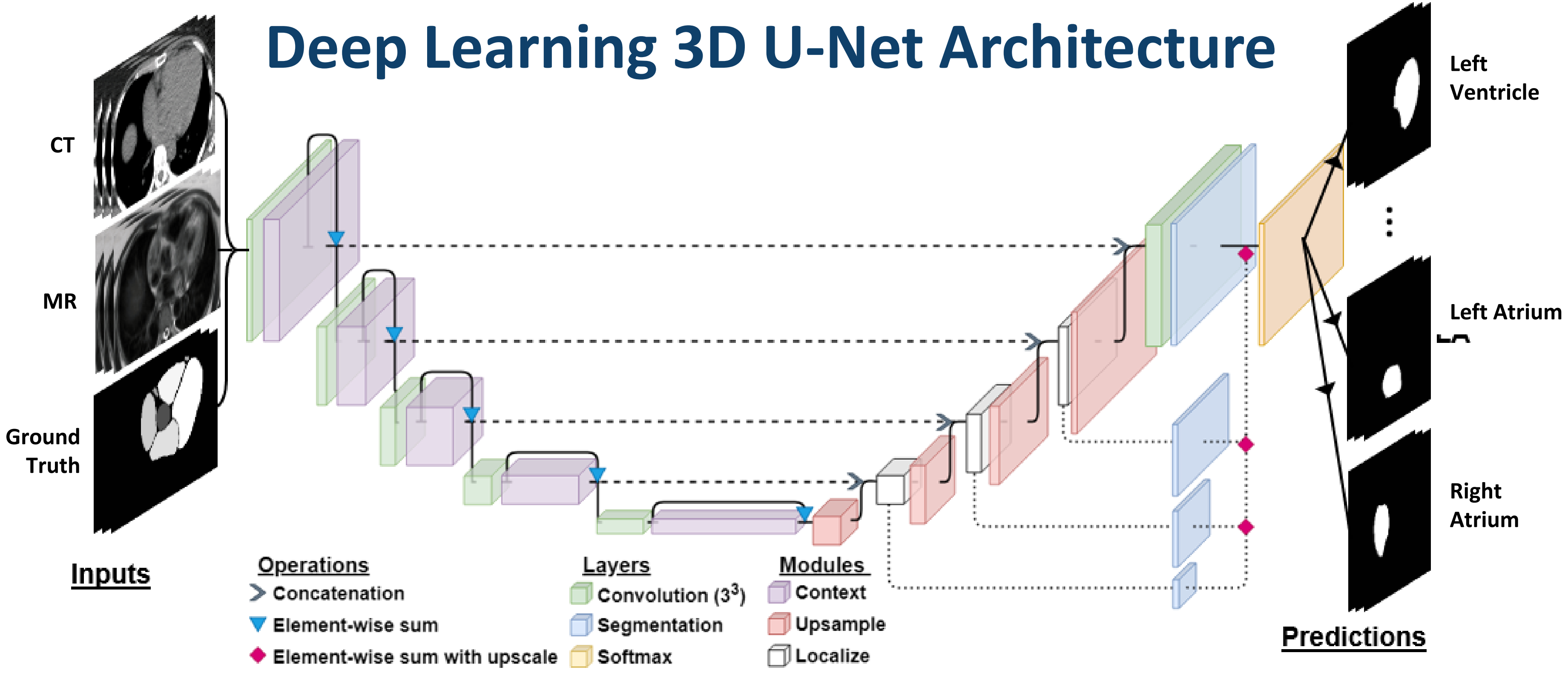
Morris et al, IJROBP, 2019

Single Validation Patient: ST10 vs. Ground Truth Contours

DSC > 0.75 | **DSC < 0.55**



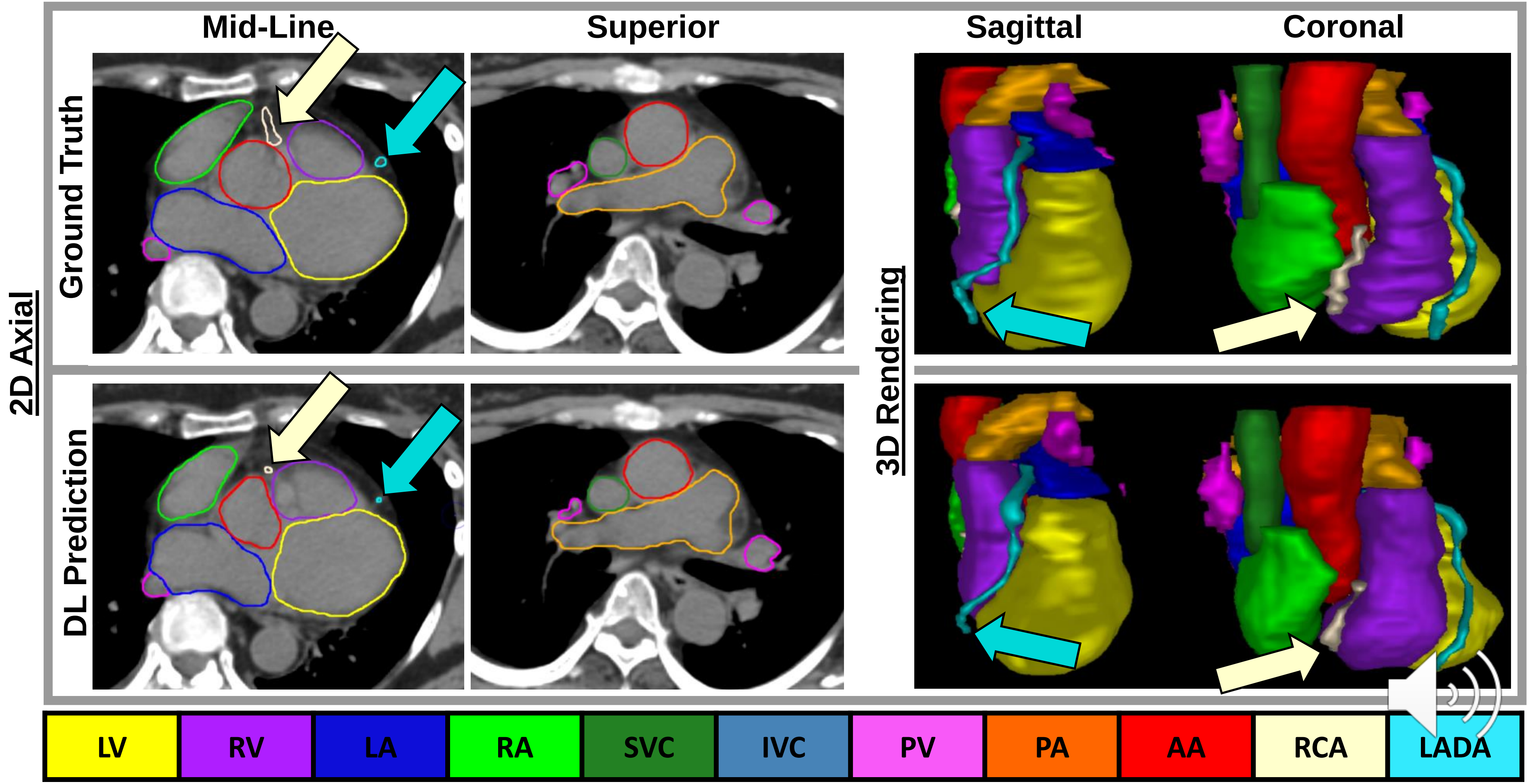
Deep Learning 3D U-Net Architecture



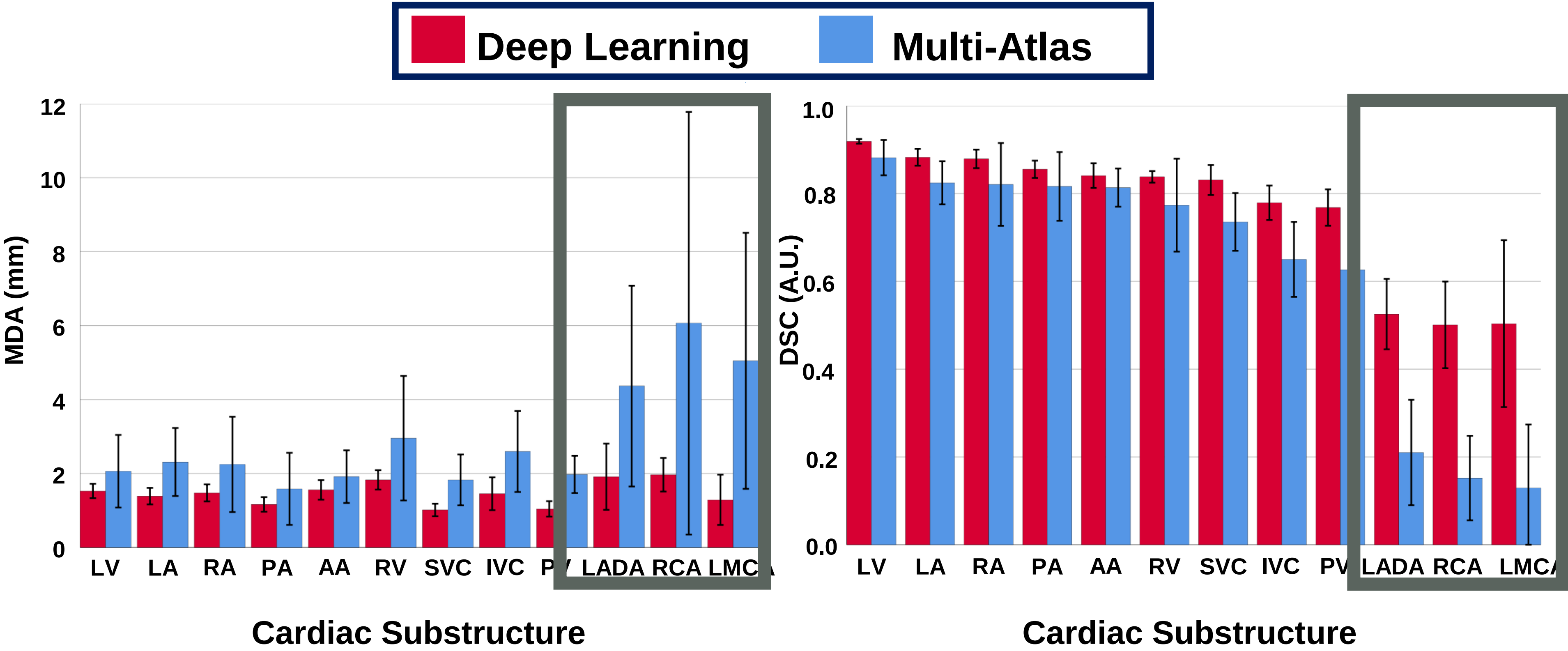
- Paired MRI/CT data for 25 patients were placed into separate image channels to train network
- **Novel Deep Learning Contributions[1]:** Multi-channel (MRI/CT) inputs, deep supervision, a 3D adaptation on original 2D U-Net[2], and hyperparameter optimization

1. Morris et al, MedPhys, 2020 2. Ronneberger et al., MICCAI, 2018

Results: Worst Case



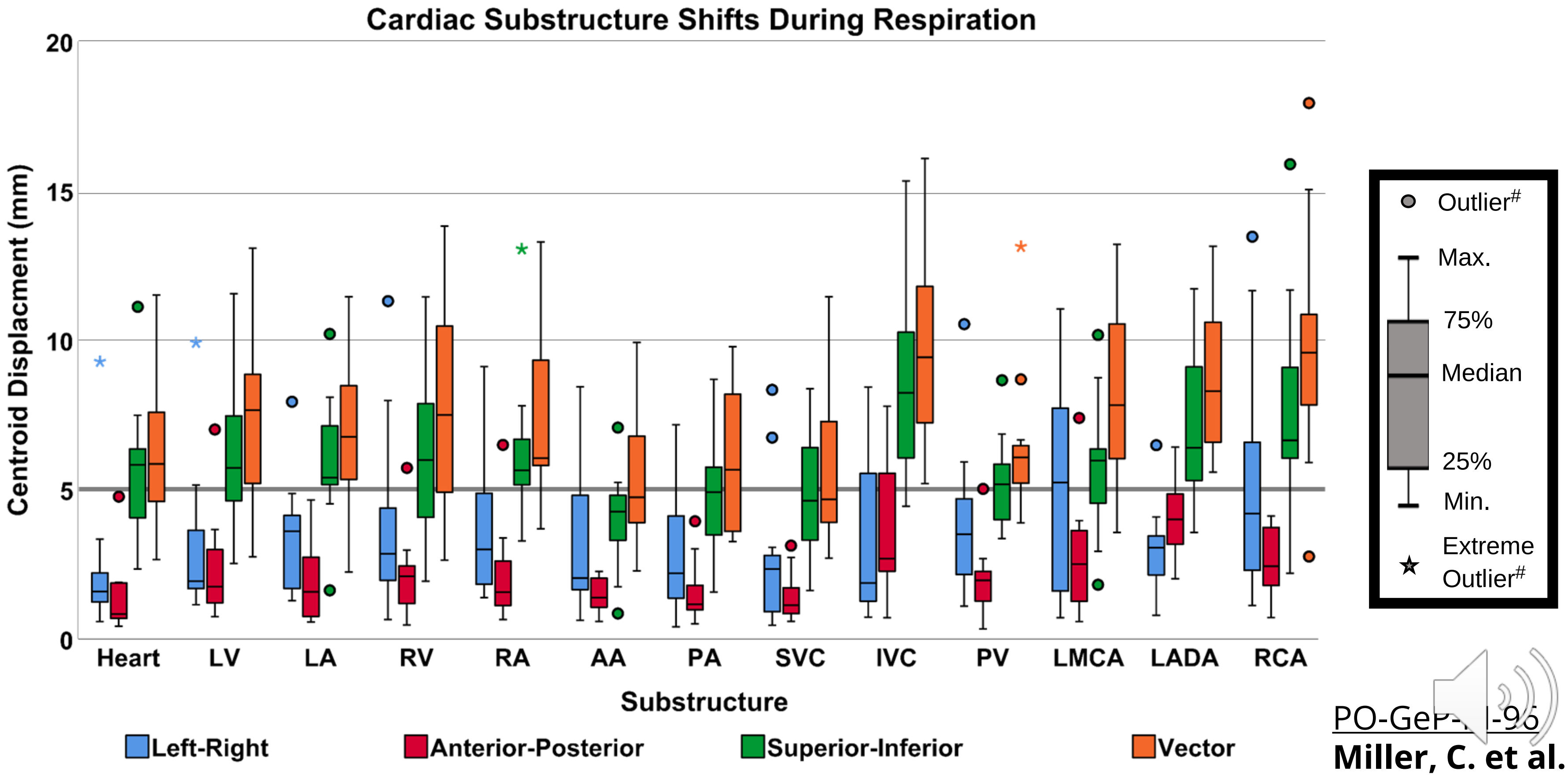
Results: Comparison to Multi-Atlas Method



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

Morris et al, MedPhys, 2020

Cardiac Substructure Motion During Respiration



PO-GeP-?-96

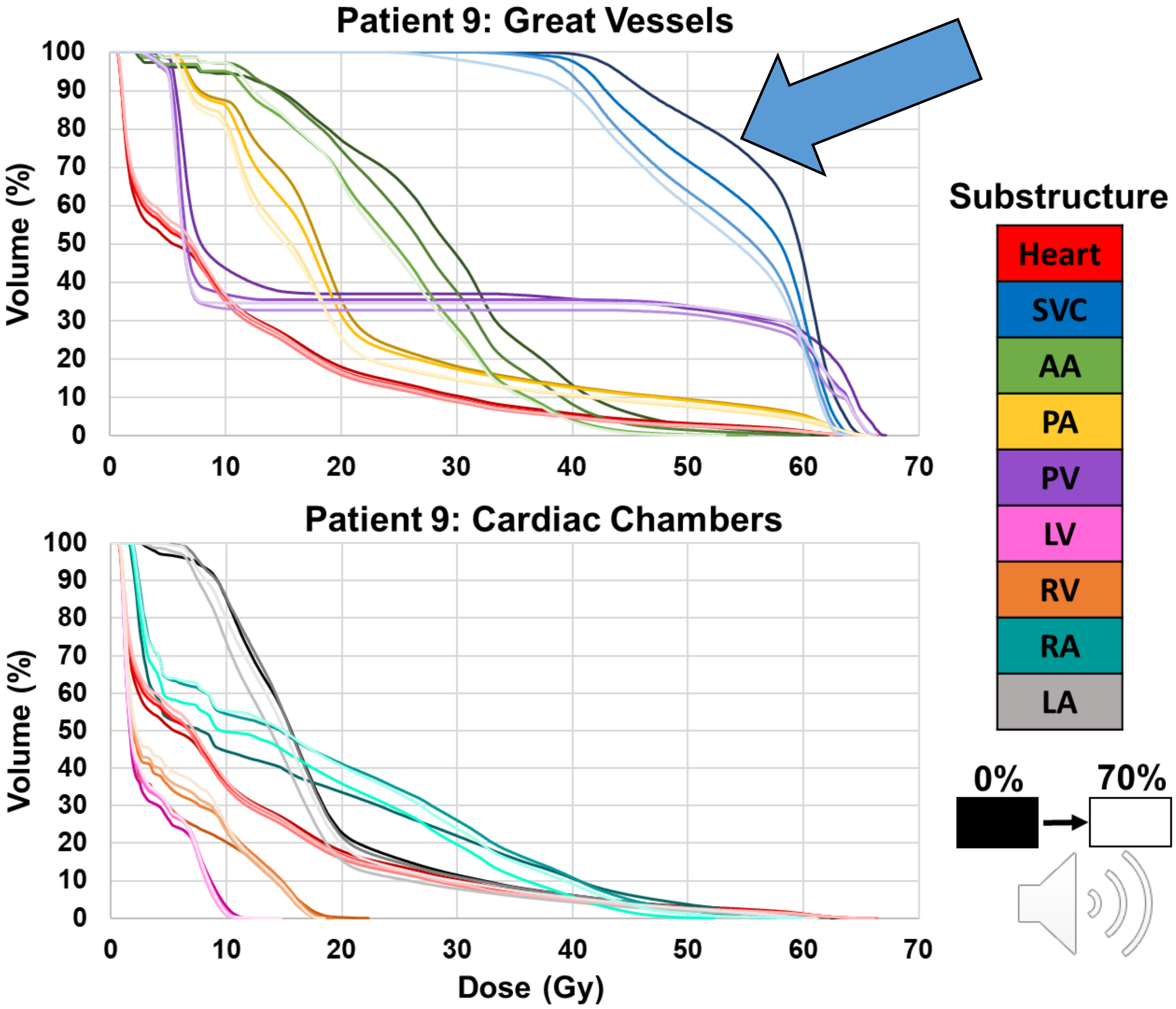
Miller, C. et al.

Dose Variations During Respiration

- Note small variations for the whole heart (red), mean dose < 0.5 Gy

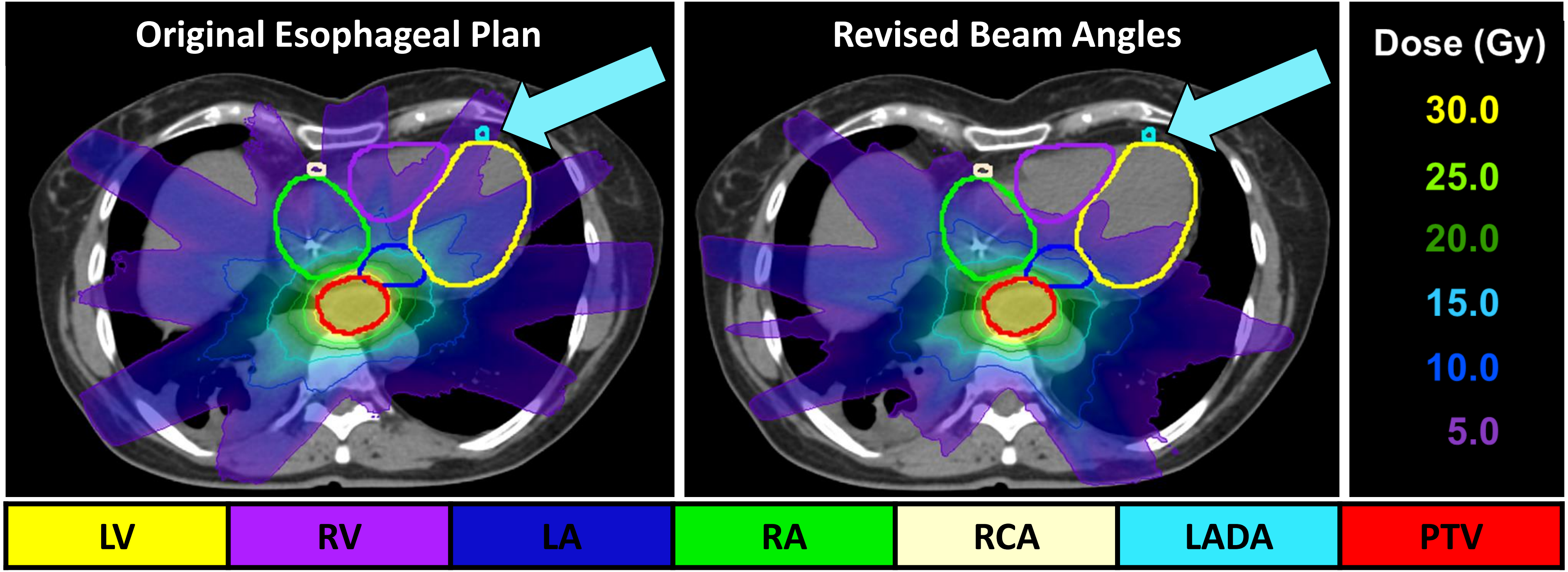
  (not sensitive!!)

- Superior vena cava mean dose > 5 Gy difference



PO-GeP-M-96
Miller, C. et al.

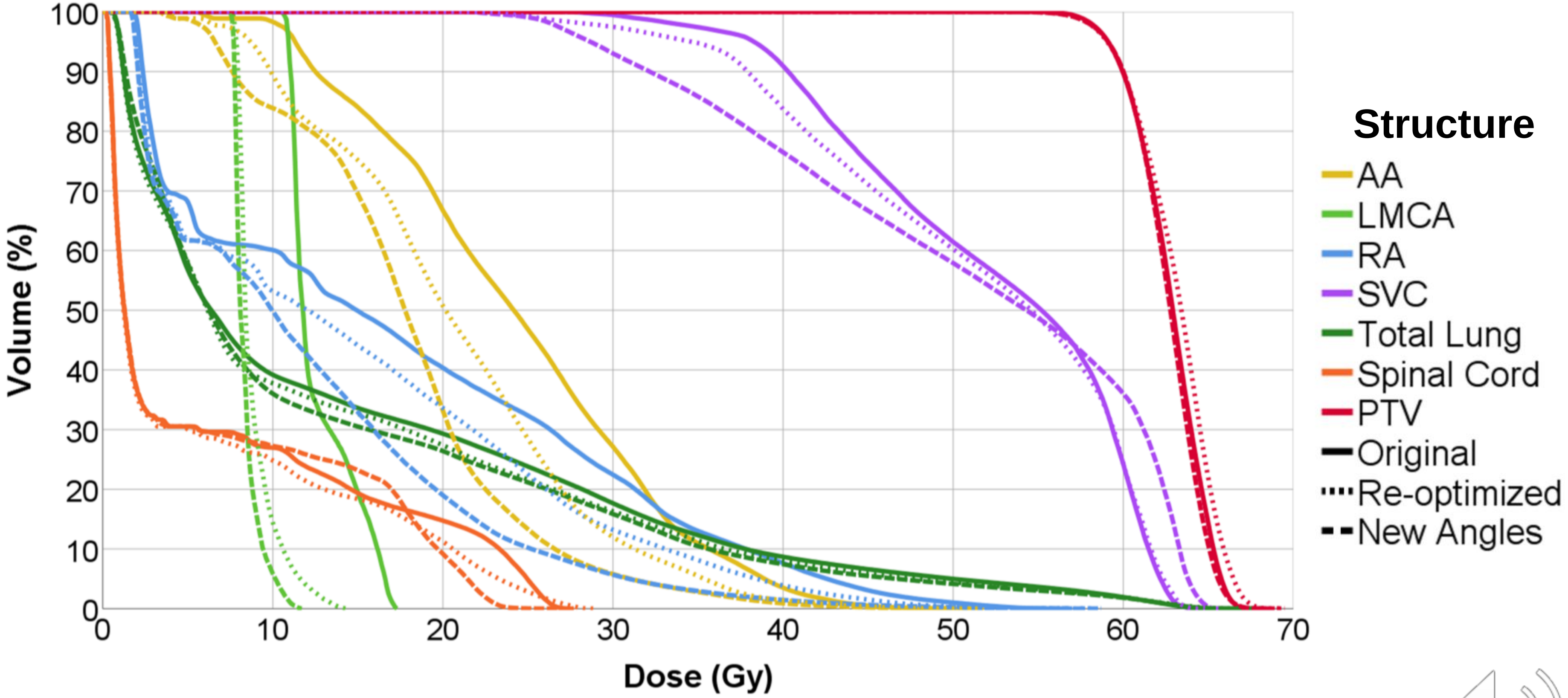
Substructure Spared Planning, IMRT



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

Morris et al., Under Revision JACMP, 2020

Results: Patient DVH with Beam Modification



- Negligible increase in estimated delivery time with re-optimized plans (0.1 ± 1.3 min), with 12/16 plans having <100 MU change

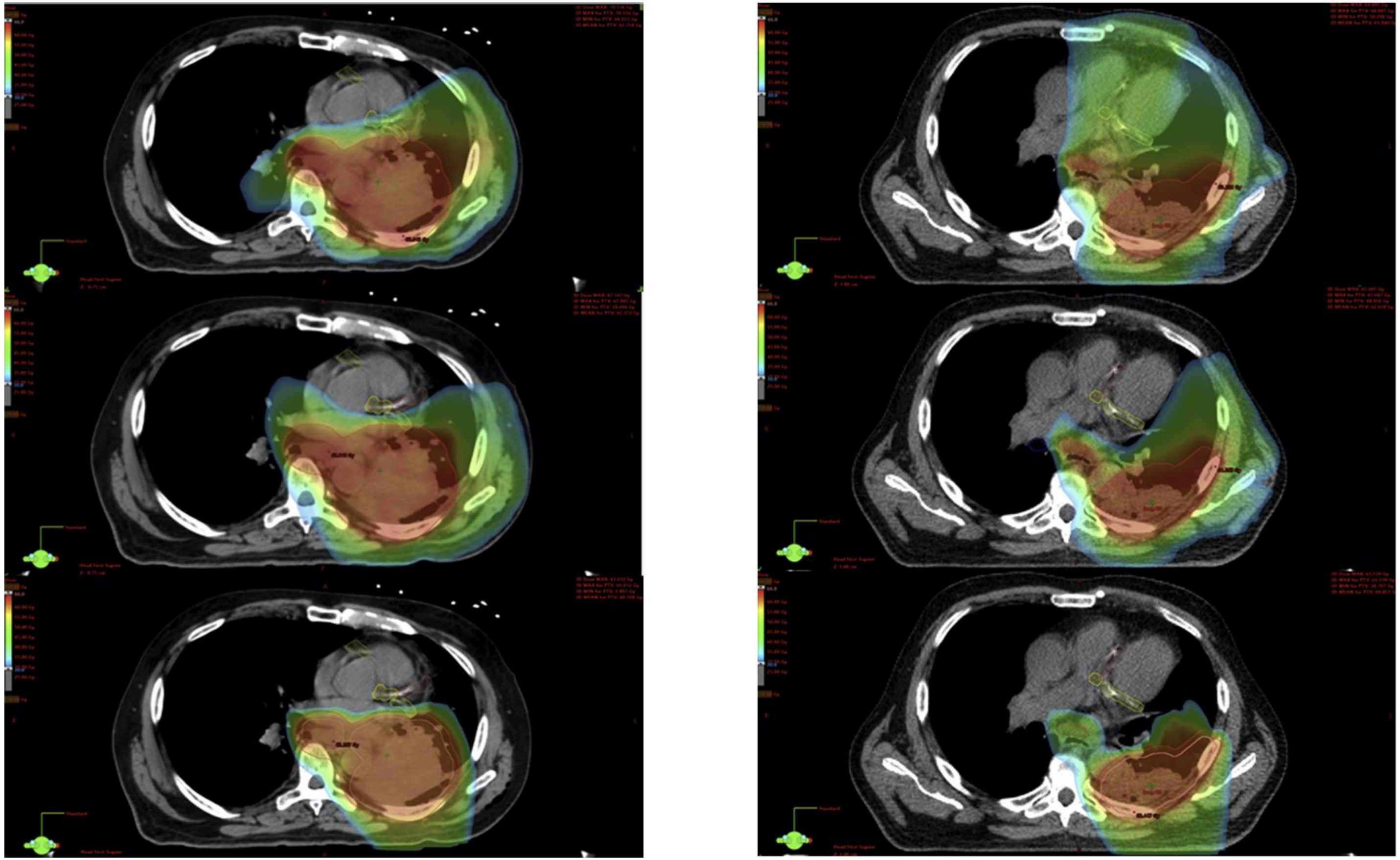
Morris et al., Under Revision JACMP, 2020

Substructure spared planning: VMAT, Protons

VMAT
2-4 Arcs

CARDIAC SPARED VMAT
2-4 Arcs

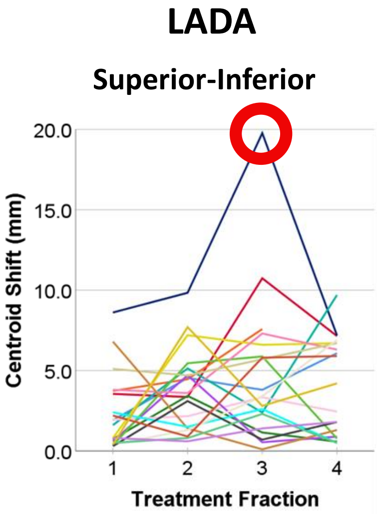
PROTONS
2-3 beams IMPT

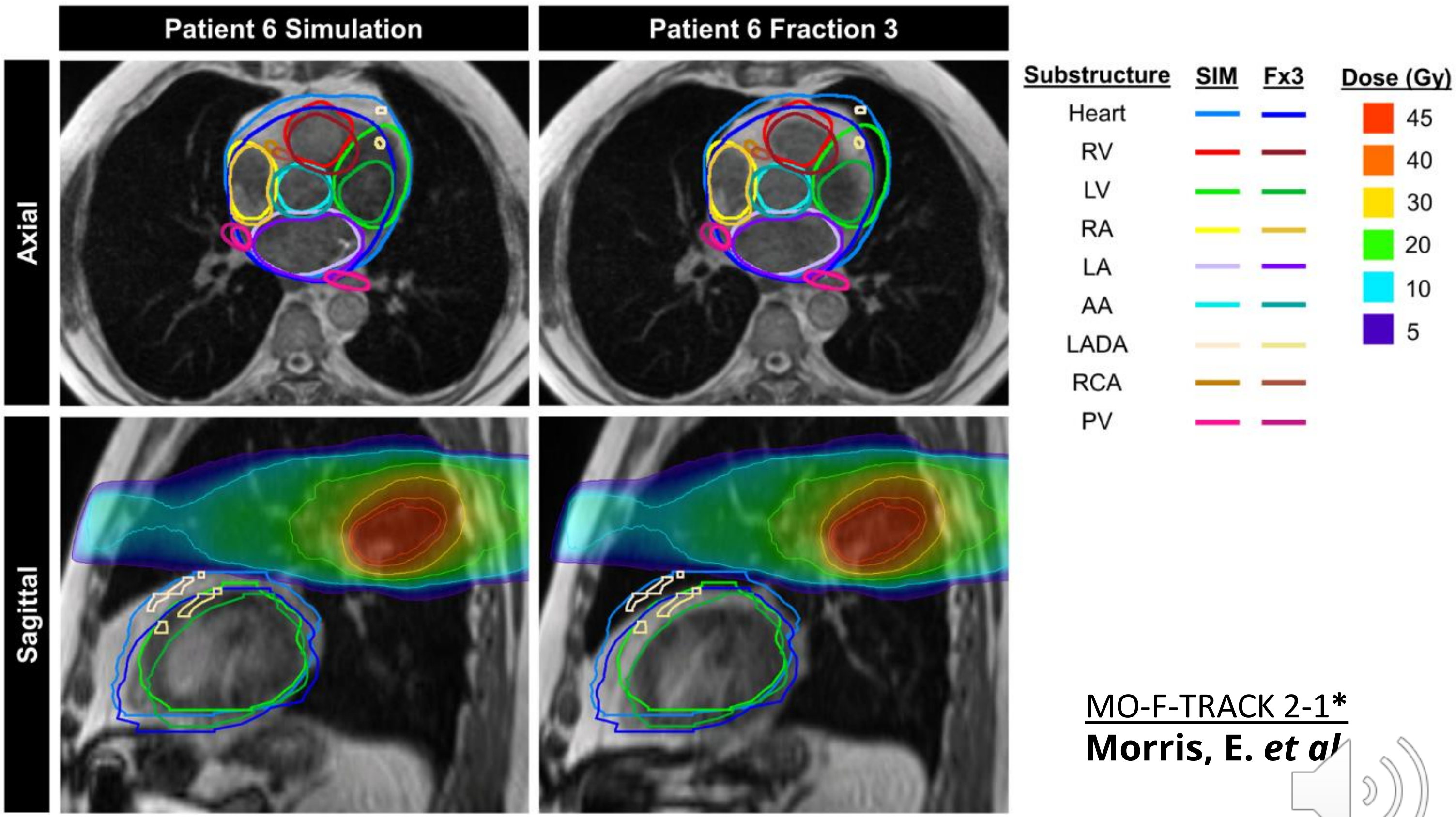


60 Gy
45 Gy
30 Gy

Fer[illegible] al.,
PRO, 2[illegible]19

Cardiac Displacement Visualized in MR-guided RT





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

all for you