Functional Lung Avoidance with CT-Ventilation

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Functional Lung Avoidance with CT-Ventilation

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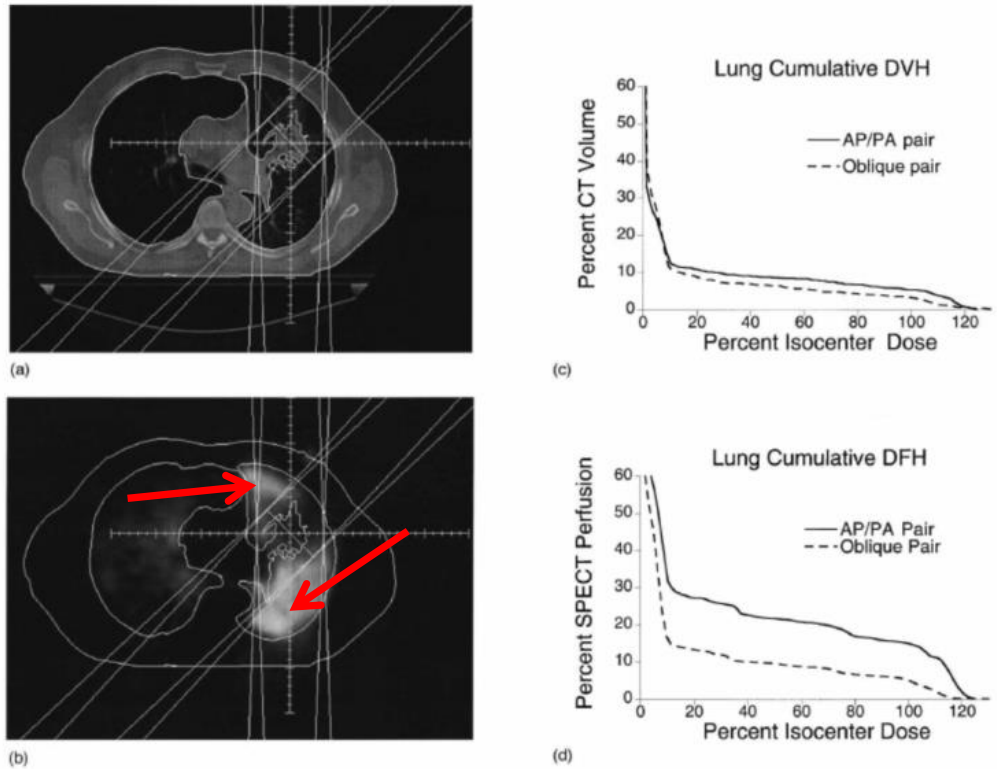
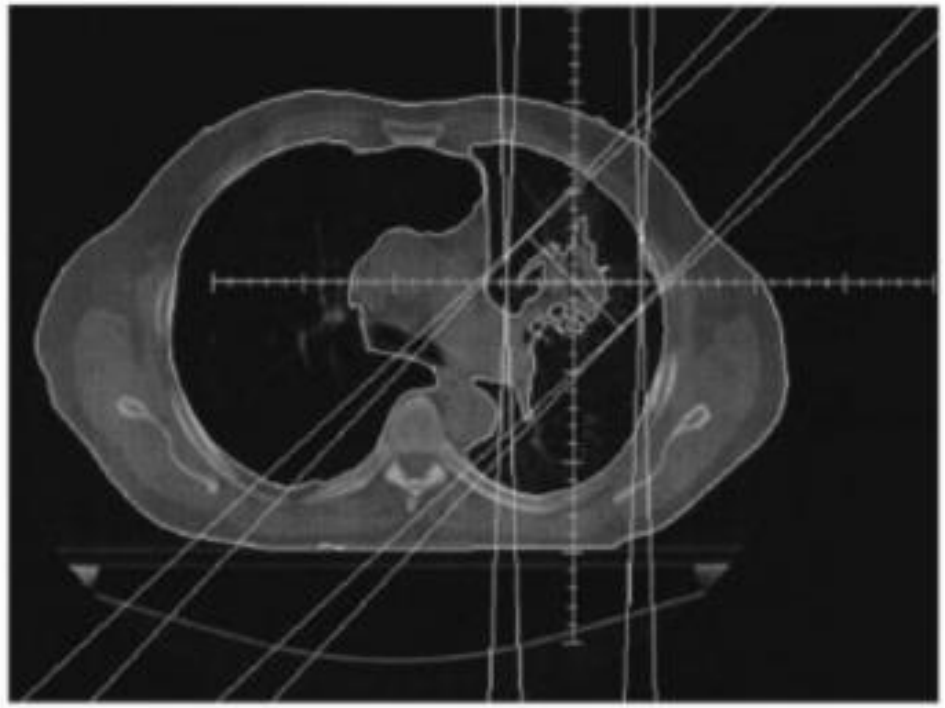
Clinical original contribution

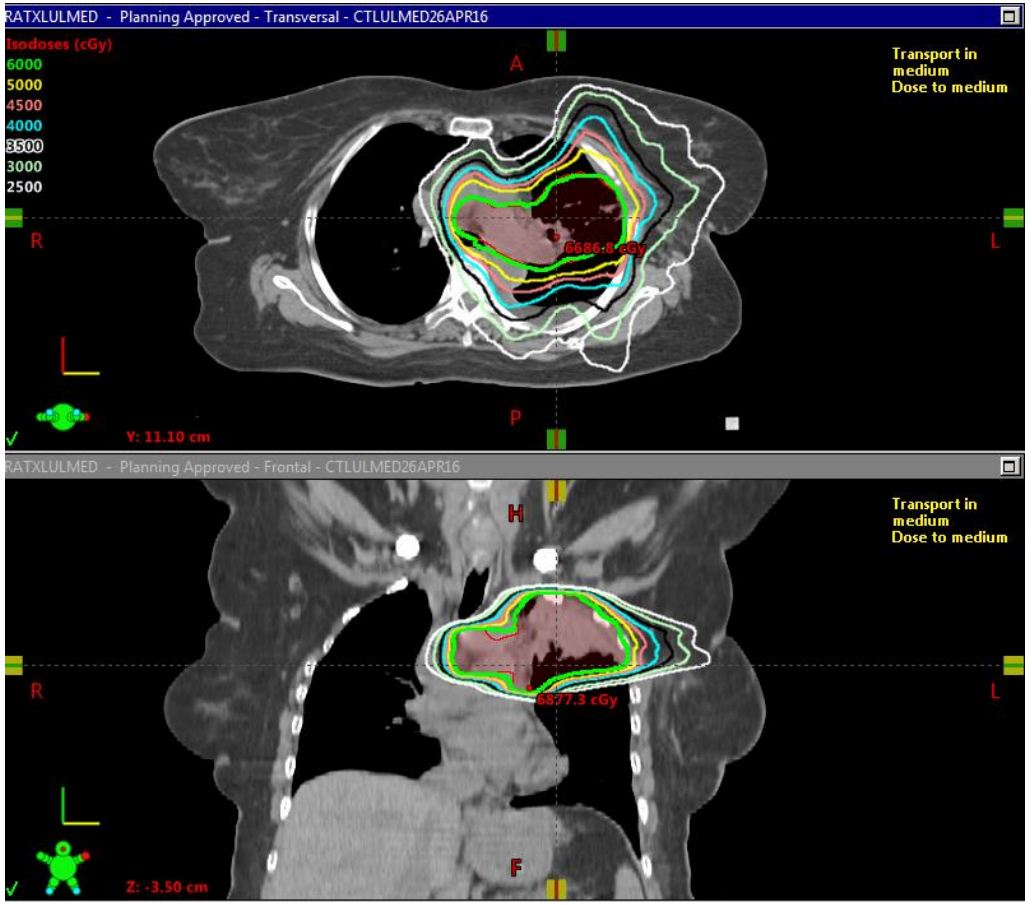
The role of three dimensional functional lung imaging in radiation treatment planning: The functional dose-volume histogram

Lawrence B. Marks, M.D.*, David P. Spencer, Ph.D.*, George W. Sherouse, Ph.D.*, Gunilla Bentel, R.N., R.T.T.*, Robert Clough*, Karen Vann, R.N.*, Ronald Jaszczak, Ph.D.†, R.Edward Coleman, M.D.†, Leonard R. Prosnitz, M.D.*



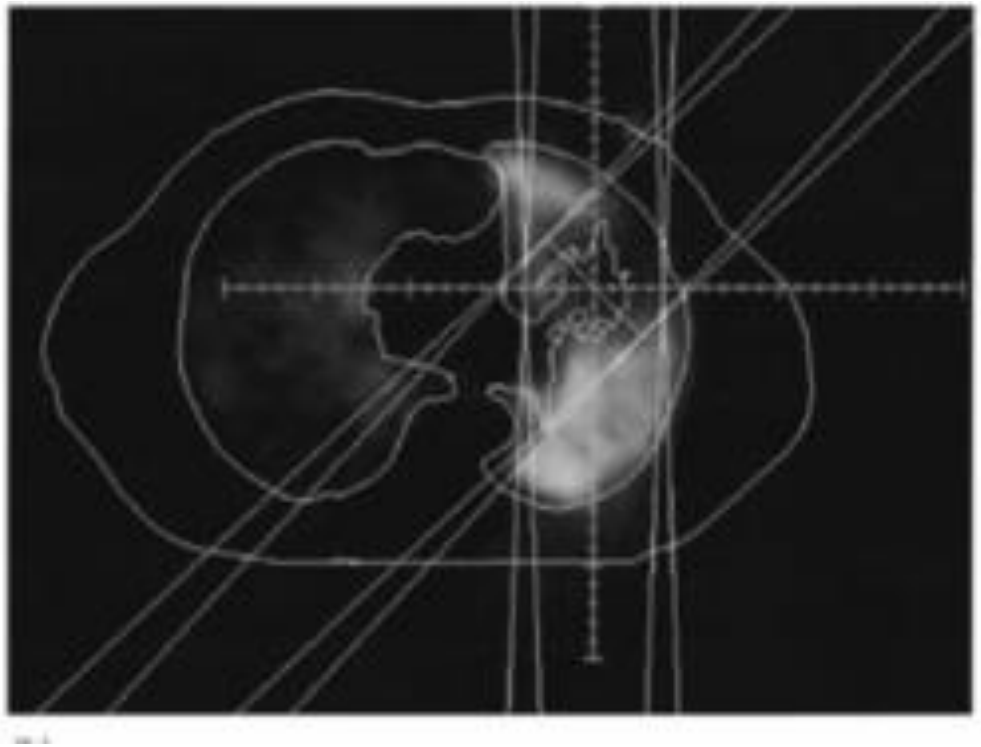
Functional Lung Avoidance with CT-Ventilation



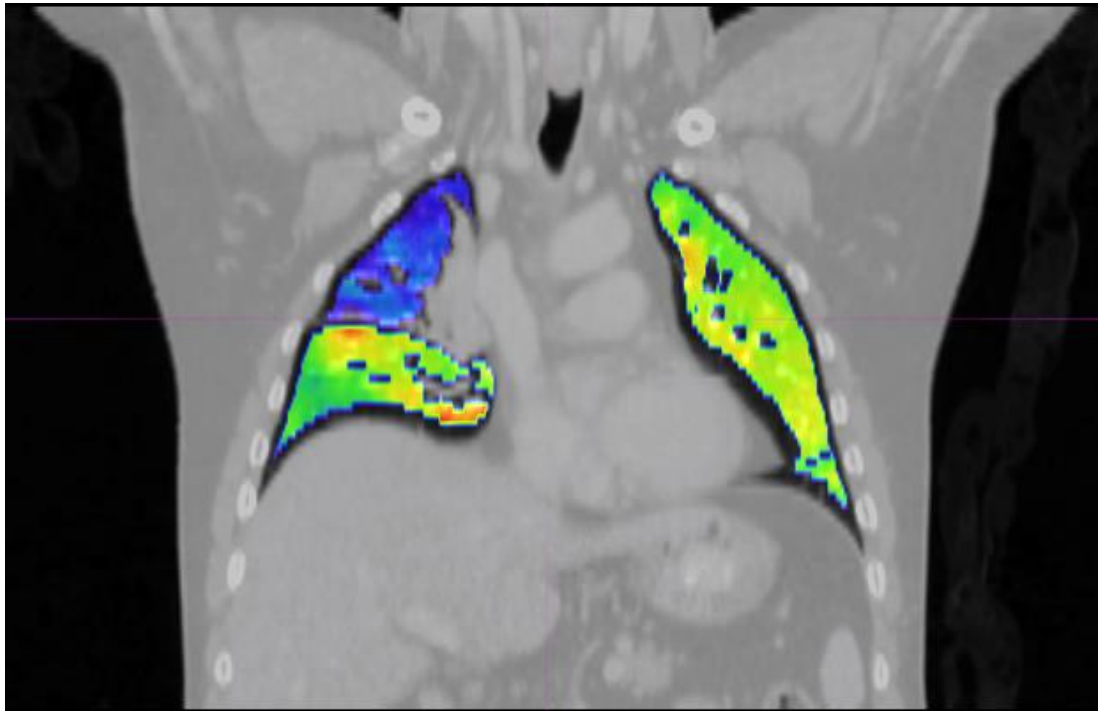


Functional Lung Avoidance with CT-Ventilation

SPECT



4DCT-Ventilation

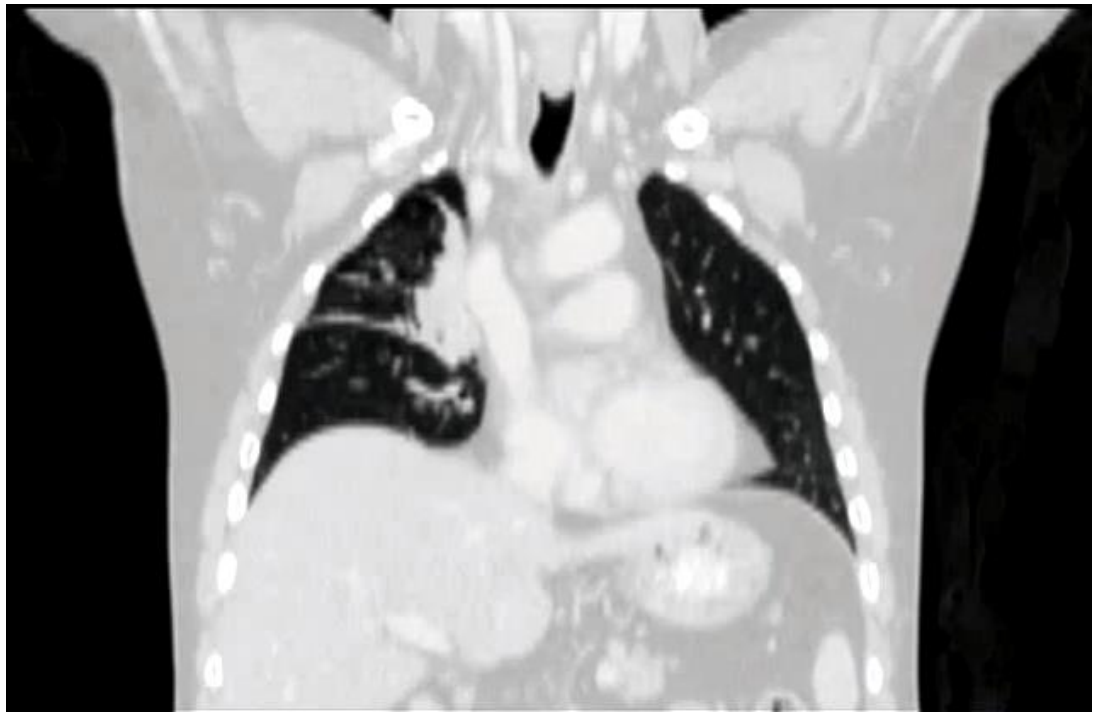


Functional Radiotherapy For Lung Cancer

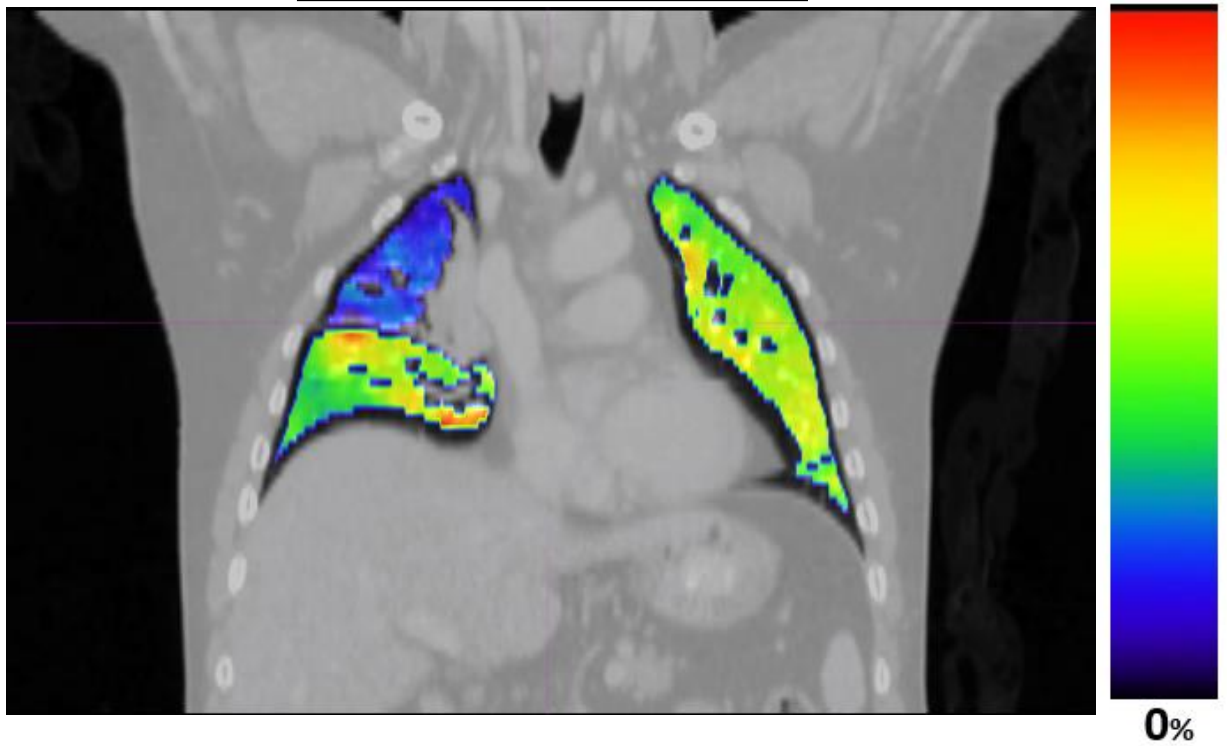
4DCT-Ventilation

- 4DCT acquired for simulation (reduced time, cost, dose)
- Anatomical + Functional information
- Good spatial resolution

4DCT



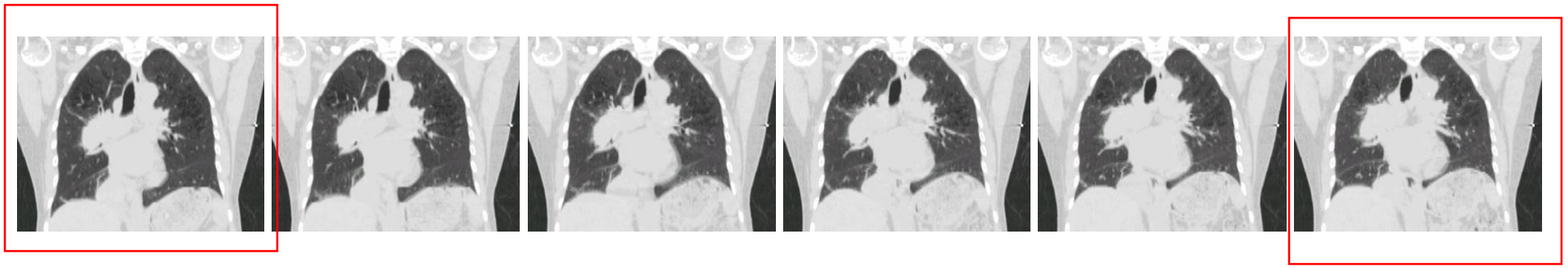
4DCT-Ventilation



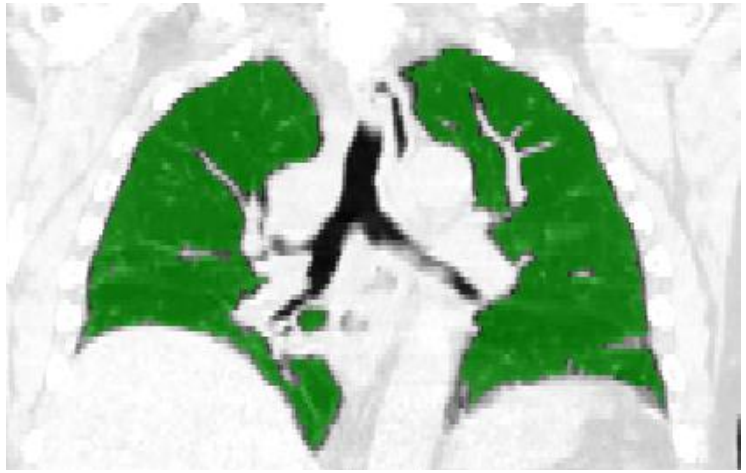
Calculating Ventilation Images

Calculating ventilation maps

4DCT – 10 phases

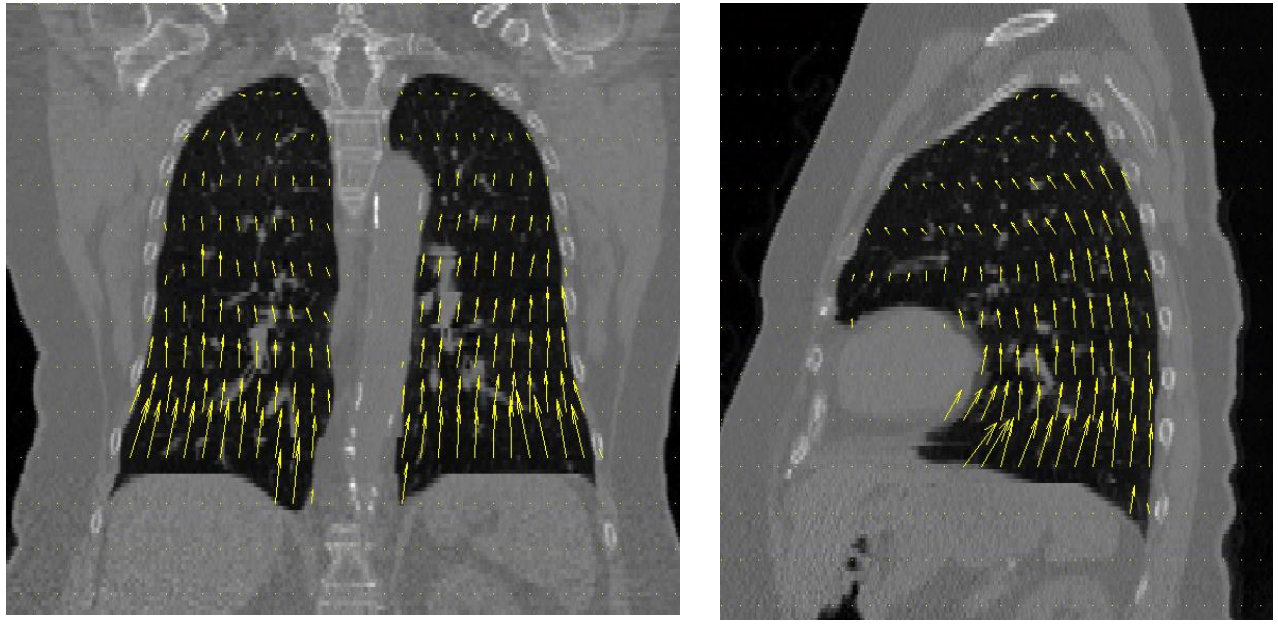


0% 10% 20% 30% 40% 50%



Calculating Ventilation Images

Link lung voxel elements from inhale to exhale using deformable registration

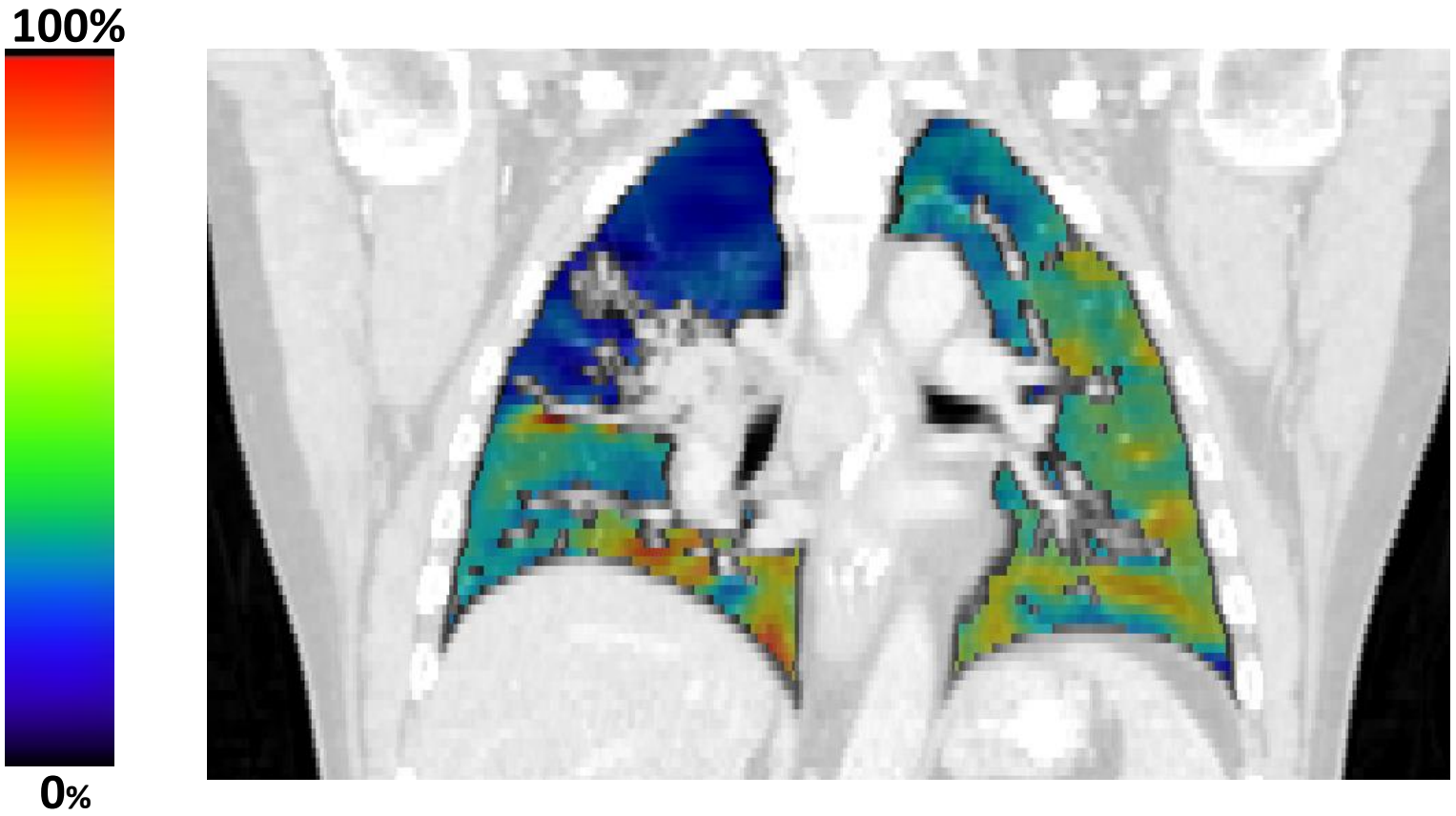


(Castillo et al., 2010)

Apply density-change-based equation

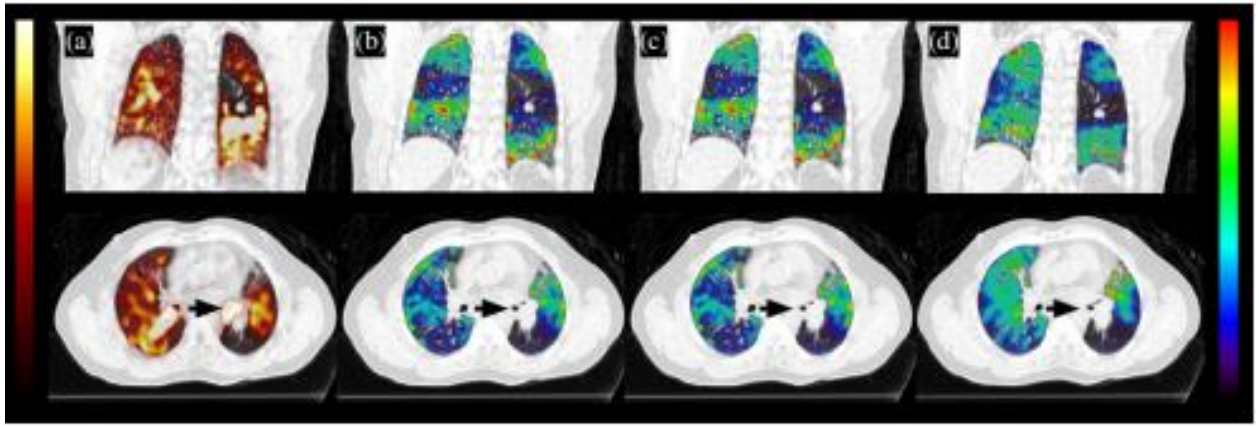
$$\frac{V_{in} - V_{ex}}{V_{ex}} = 1000 \frac{\overline{HU}_{in}^{voi} - HU_{ex}}{HU_{ex}(1000 + \overline{HU}_{in}^{voi})}$$

Calculating Ventilation Images

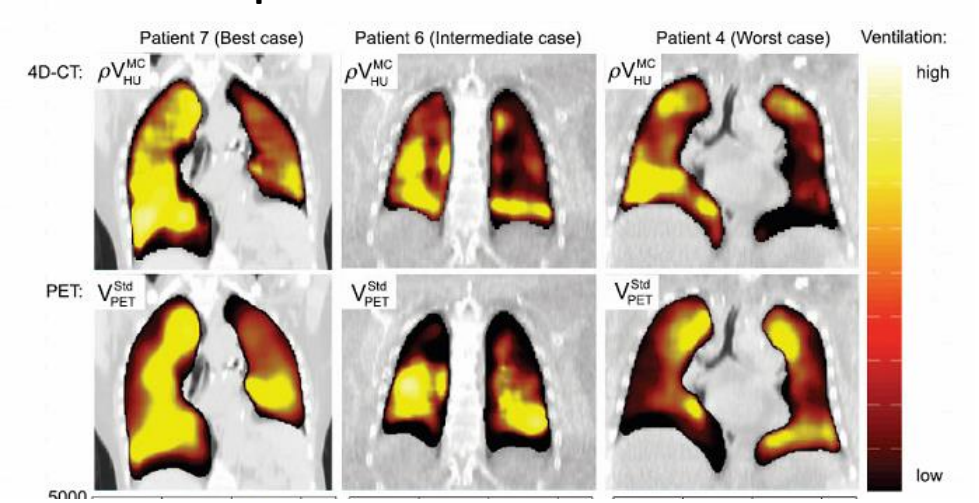


Functional Imaging to Functional Radiotherapy: Validation

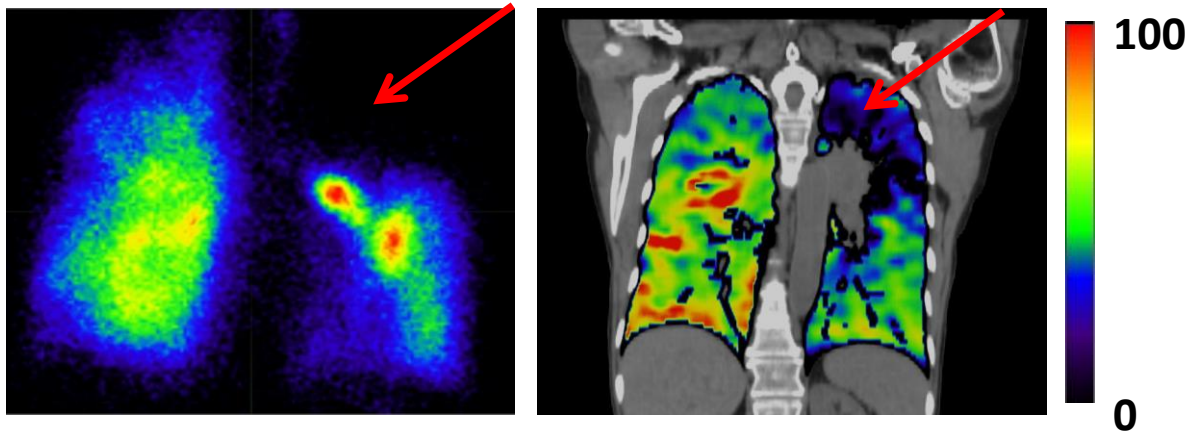
Castillo et al - SPECT



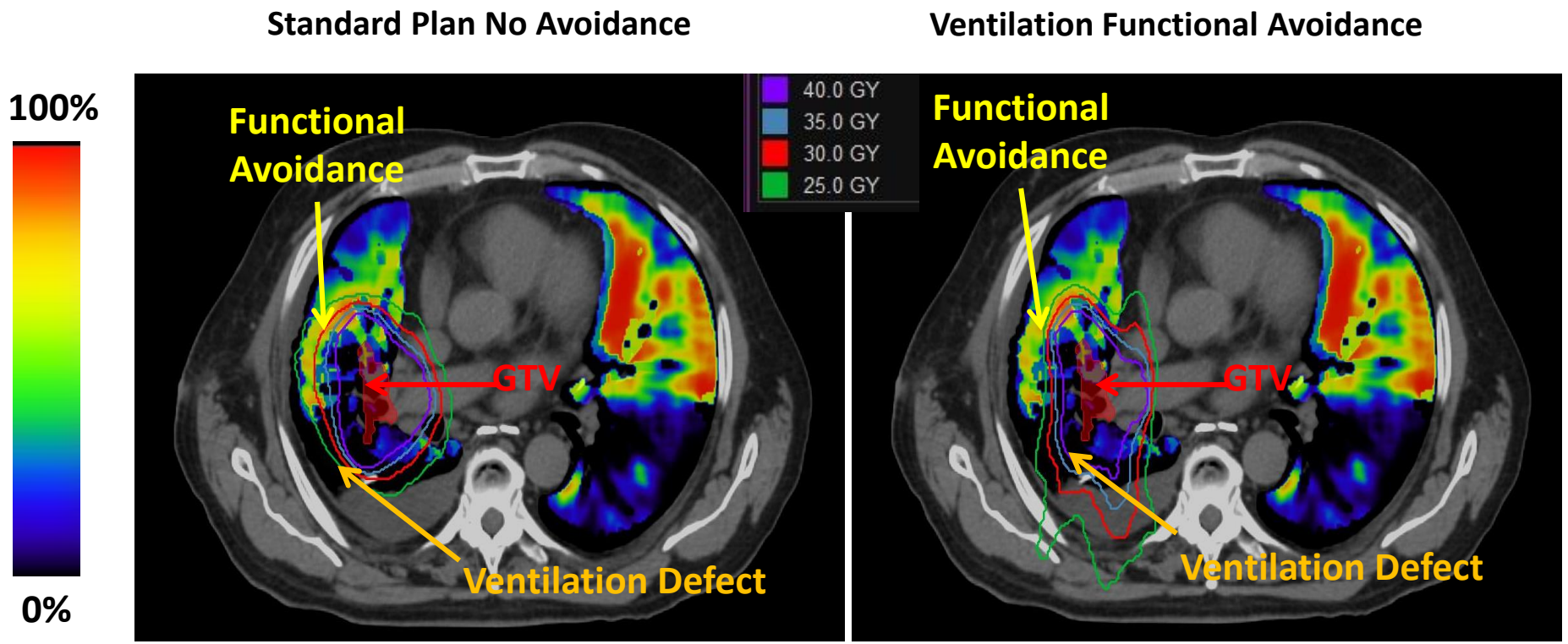
Kipritidis et al – PET 68Ga



Vinogradskiy et al - VQ scans



Functional radiotherapy example with CT Ventilation



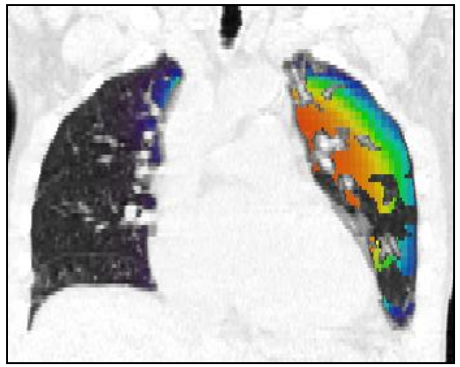
Predicting pneumonitis: dose + function > dose ???

- 96 NSCLC patients
- Radiation pneumonitis toxicity information using CTCAE grading
- Calculated dose metrics
  - Mean lung dose
  - V20 Gy = Volume of lung receiving 20 Gy or higher
- Calculated dose + function metrics
  - Functionally weighted mean lung dose
  - FV20 Gy = Amount of functioning lung getting 20 Gy or higher

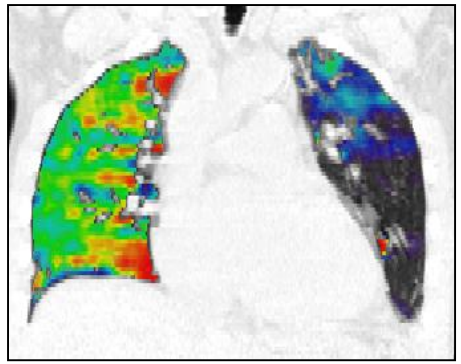
Functional planning

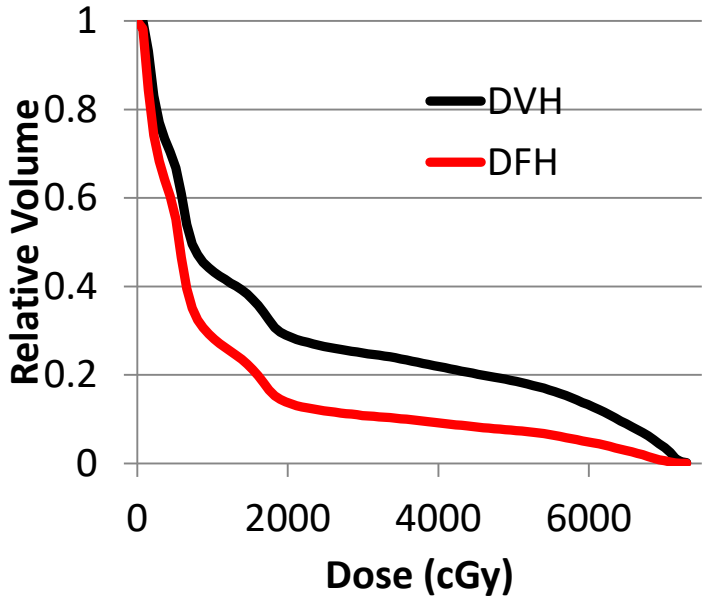
MLD = 22.9 Gy
No pneumonitis

Dose



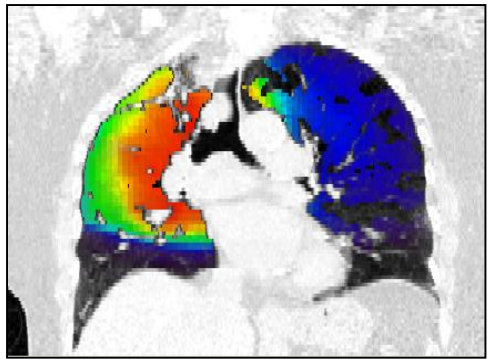
Ventilation



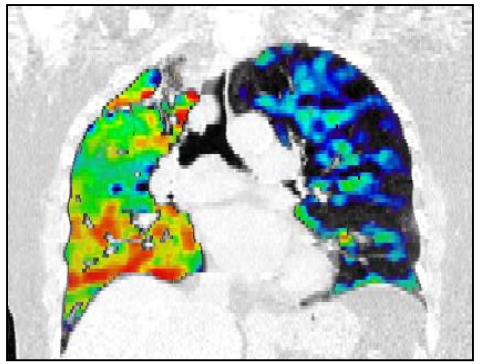


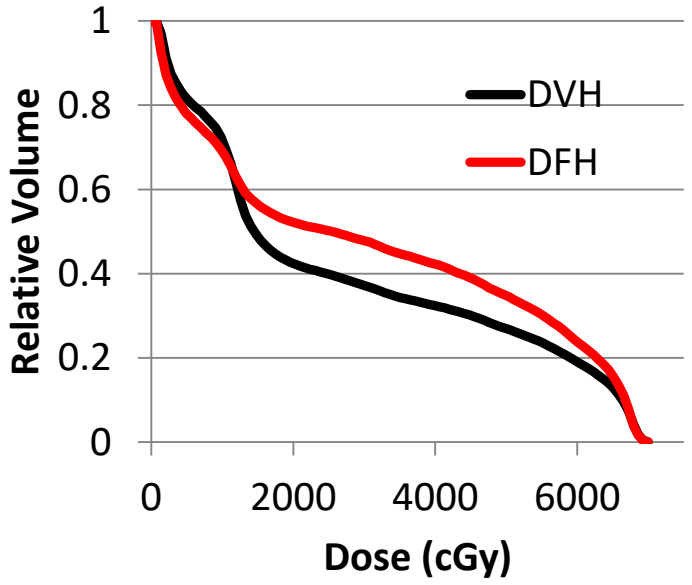
MLD = 23.2 Gy
Grade 3 pneumonitis

Dose



Ventilation





4DCT-ventilation conformal avoidance – Will it work?

Ability of dose and dose + function metrics to predict for grade 3+ radiation pneumonitis: area under the curve (AUC) and logistic regression (Vinogradskiy et al 2013, Faught et al 2017)

MLD	fMLD
AUC=0.55	AUC=0.66

V20	fV20
AUC=0.57	AUC=0.70

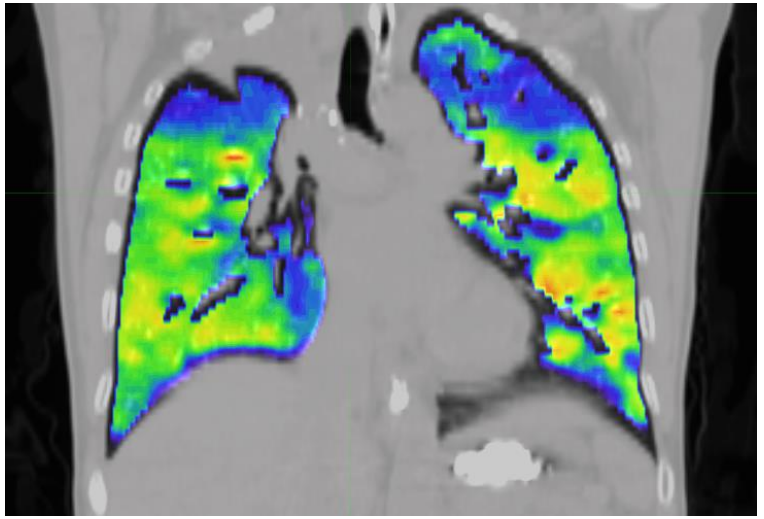
Dose+function >> Dose alone

CT Ventilation Functional Radiotherapy Clinical Trial

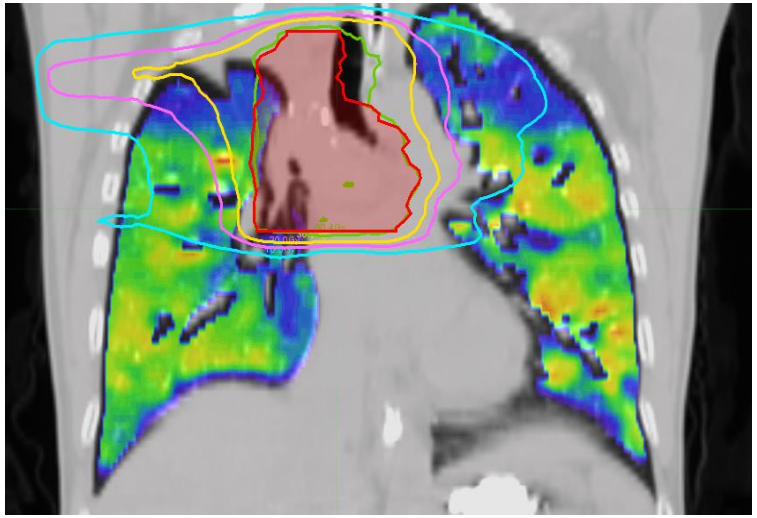
- **67 lung cancer patients at University of Colorado + William Beaumont (NCT02528942)**
- **Use 4DCT to calculate ventilation imaging**
- **Use 4DCT-ventilation to design functional radiation plans**
- **Reduce functional dose metrics using favorable arc geometry + optimization**
- **Single-arm, early phase trial looking at feasibility, safety, toxicity rates to be compared to current standard of care techniques**

4DCT

4DCT-Ventilation



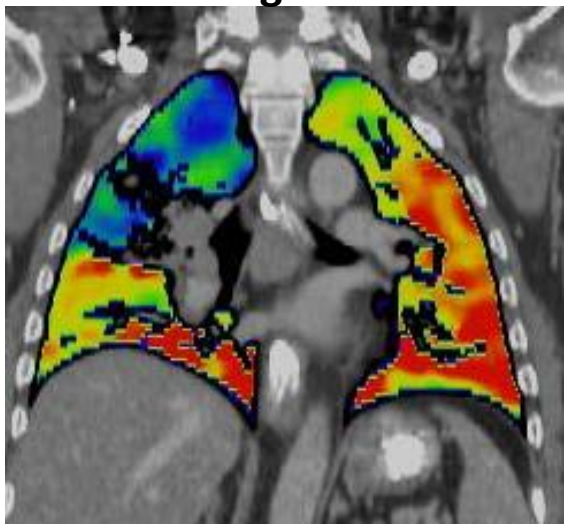
Functional Plan



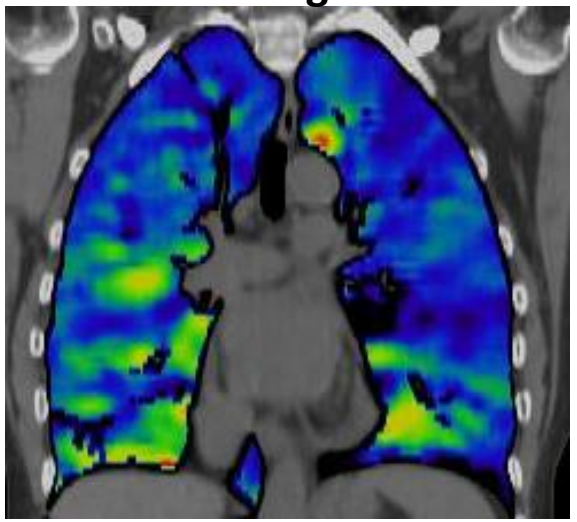
Inclusion/Exclusion Criteria

- **Trial inclusion/exclusion criteria**
  - **No SBRT, No palliative RT**
  - **Definitive Rx dose ≥ 45Gy**
  - **Planned concurrent chemotherapy regimen**
  - **Image heterogeneity criteria**

Eligible



Not Eligible



Trial Design

- **Phase II study, compare functional avoidance against historical control**
- **Primary endpoint: grade ≥ 2 Radiation Pneumonitis**
- **Hypothesis: Rate of grade ≥ 2 Radiation Pneumonitis can be reduced to 12% with functional radiotherapy compared to 25% rate of grade ≥ 2 Radiation Pneumonitis with historical control**
- **Simon's Two-Stage design**
- **67 patient total enrollment, futility analysis at 17 patients**

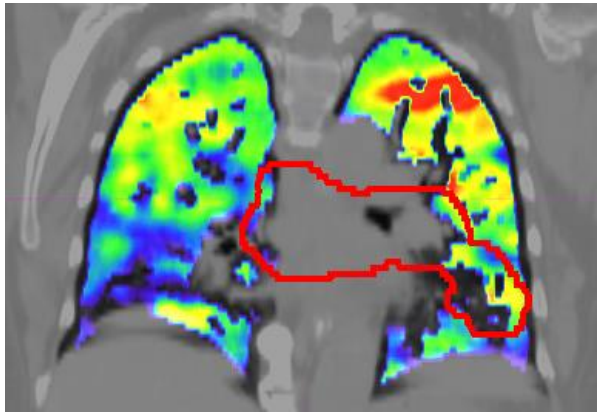
Outcome assessments

- **Assess lung function in a variety of ways**
  - **CTCAE Toxicity (Pulmonary toxicity, pneumonitis, esophagitis)**
  - **PFTs**
  - **QOL Questionnaires**
  - **Imaging: CT, 4DCT-Ventilation, PET, VQ**

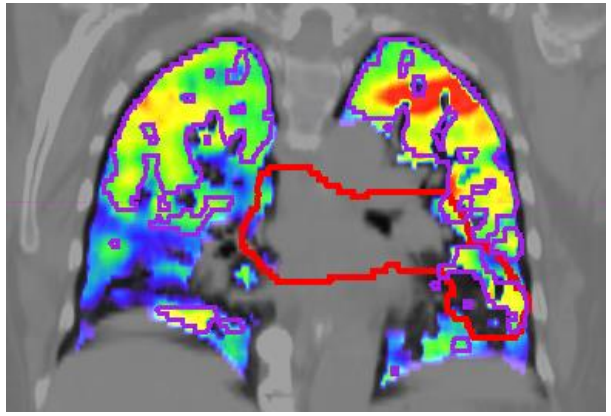
Implementation: Treatment planning

Structure-based treatment planning

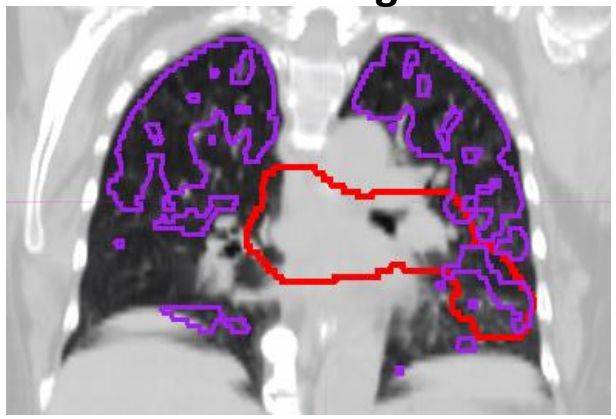
Functional Image



Functional Image + Structure



Functional Planning Structure

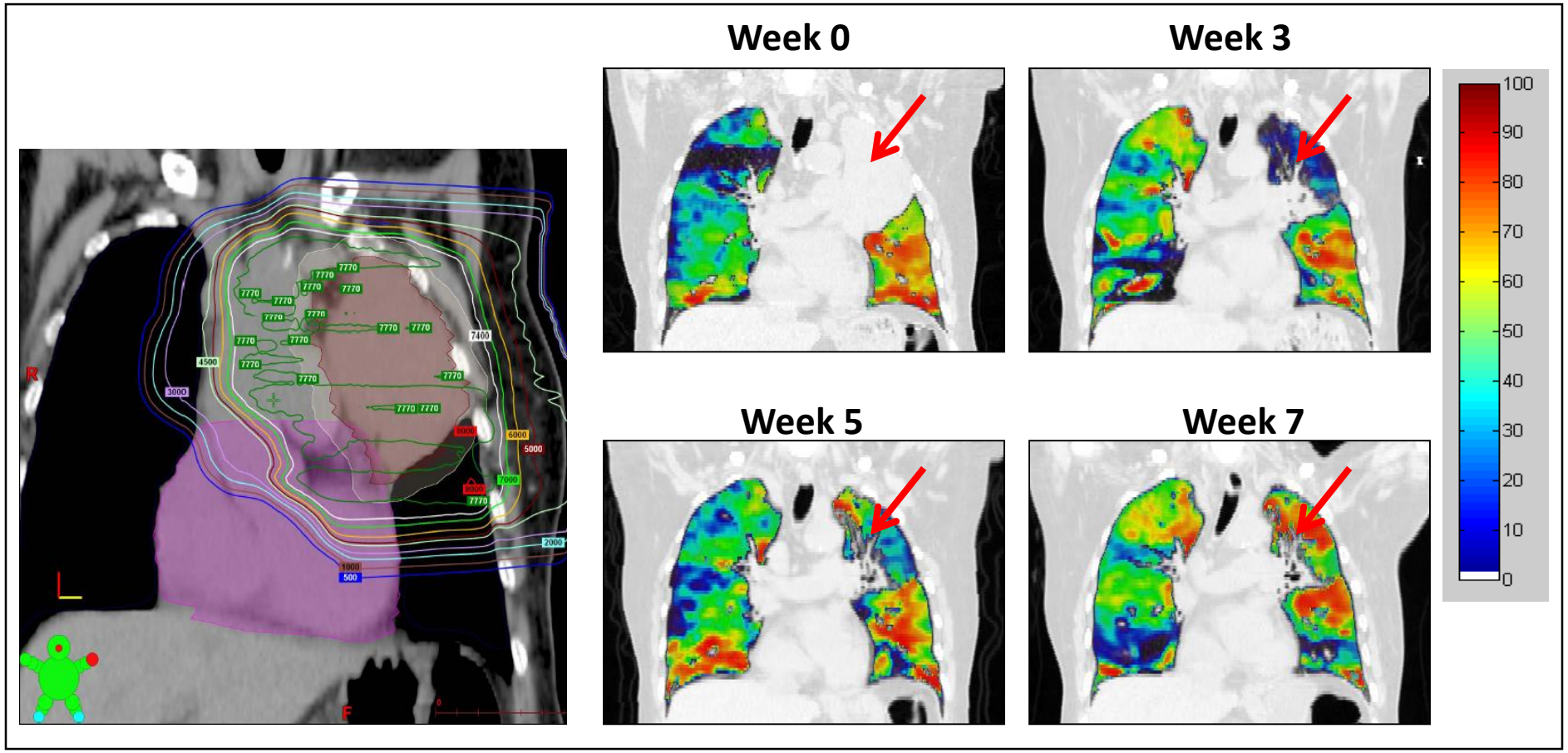


Implementation: Treatment planning

- **Start with standard (non-functional) plan, proceed to functional plan using favorable arc geometry + optimization techniques**
- **Planning priorities 1) Target coverage 2) OAR constraints 3) Reducing dose to functional lung**

Implementation: Adaptive planning

- **Image guidance per institutional protocol (CBCT daily, 4D CBCT @ Beaumont)**
- **Adaptive planning per attending discretion**
- **If an adaptive plan is needed, a 4DCT is done and a functional adaptive plan is made**



Multi (2) – Institution Trial Credentialing

- **Identical versions of CT Ventilation code installed at both institutions**
- **Site Initiation Visits performed at both institutions**
- **CT ventilation physicist (+ backup) identified and trained at both institutions**
- **3 sample CT ventilation cases run at both institutions, evaluated for reproducibility**

Feasibility: Trial Enrollment

- **95 patients consented in ~2.5 years**
- **62 evaluable patients**
- **Trial met futility criteria, progressed with accrual**
- **8 (8.4%) ineligible per imaging criteria**

ELSEVIER

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Volume 102, Issue 4, 15 November 2018, Pages 1357-1365

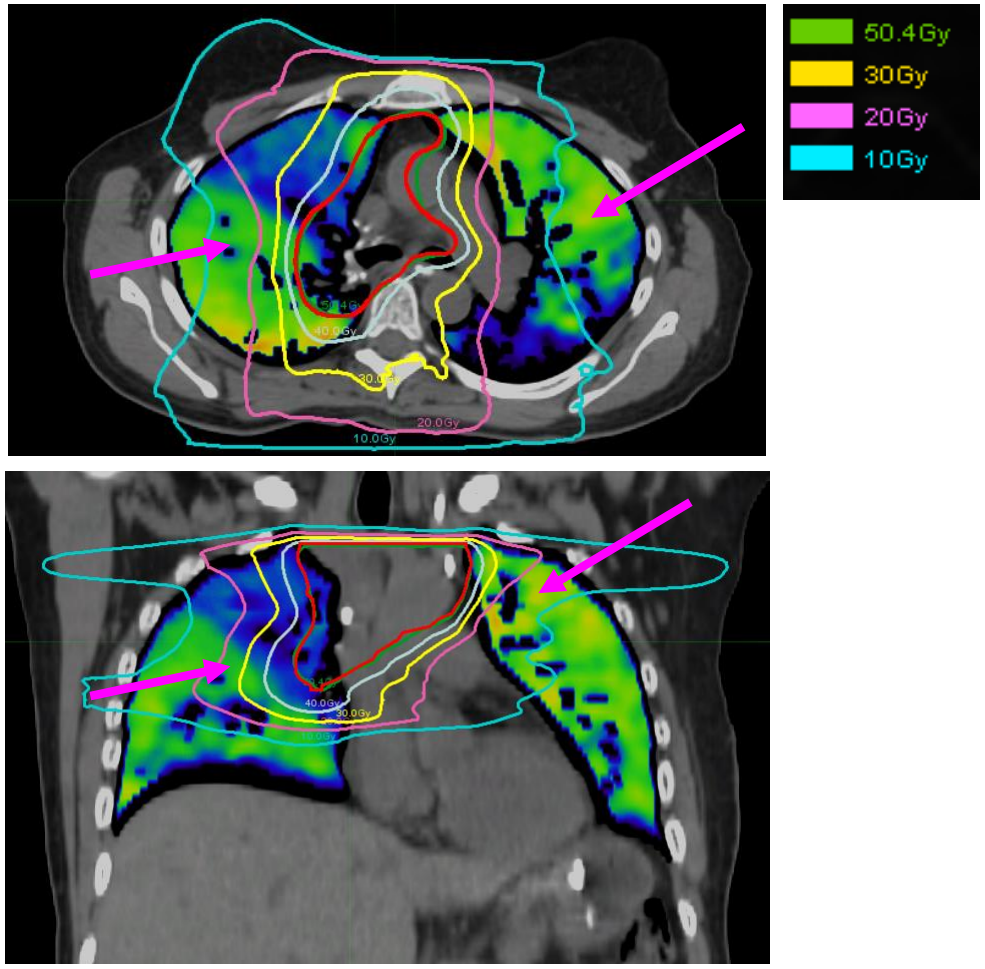
Imaging to Prevent Radiation Sequelae

Interim Analysis of a Two-Institution, Prospective Clinical Trial of 4DCT-Ventilation-based Functional Avoidance Radiation Therapy

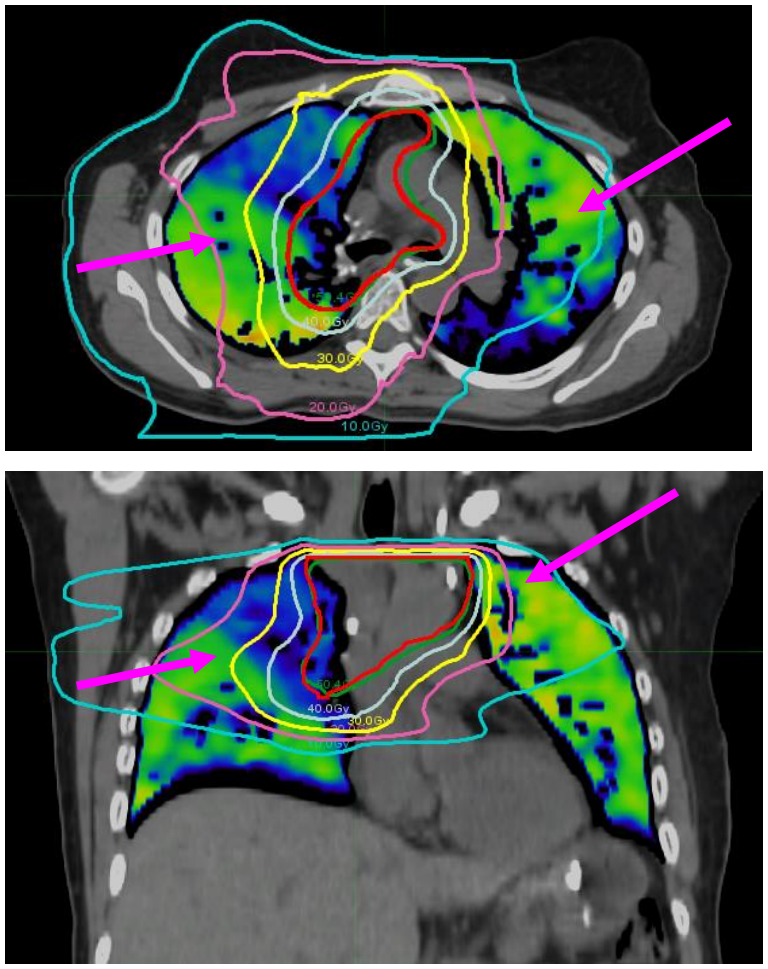
Yevgeniy Vinogradskiy PhD *, Chad G. Rusthoven MD *, Leah Schubert PhD *, Bernard Jones PhD *, Austin Faught PhD †, Richard Castillo PhD ‡, Edward Castillo PhD §, Laurie E. Gaspar MD, MBA *, Jennifer Kwak MD ||, Timothy Waxweiler MD *, Michele Dougherty PhD ¶, Dexiang Gao PhD #, Craig Stevens MD, PhD §, Moyed Miften PhD *, Brian Kavanagh MD, MPH *, Thomas Guerrero MD, PhD §, Inga Grills MD §

Patient plan example

Functional Plan

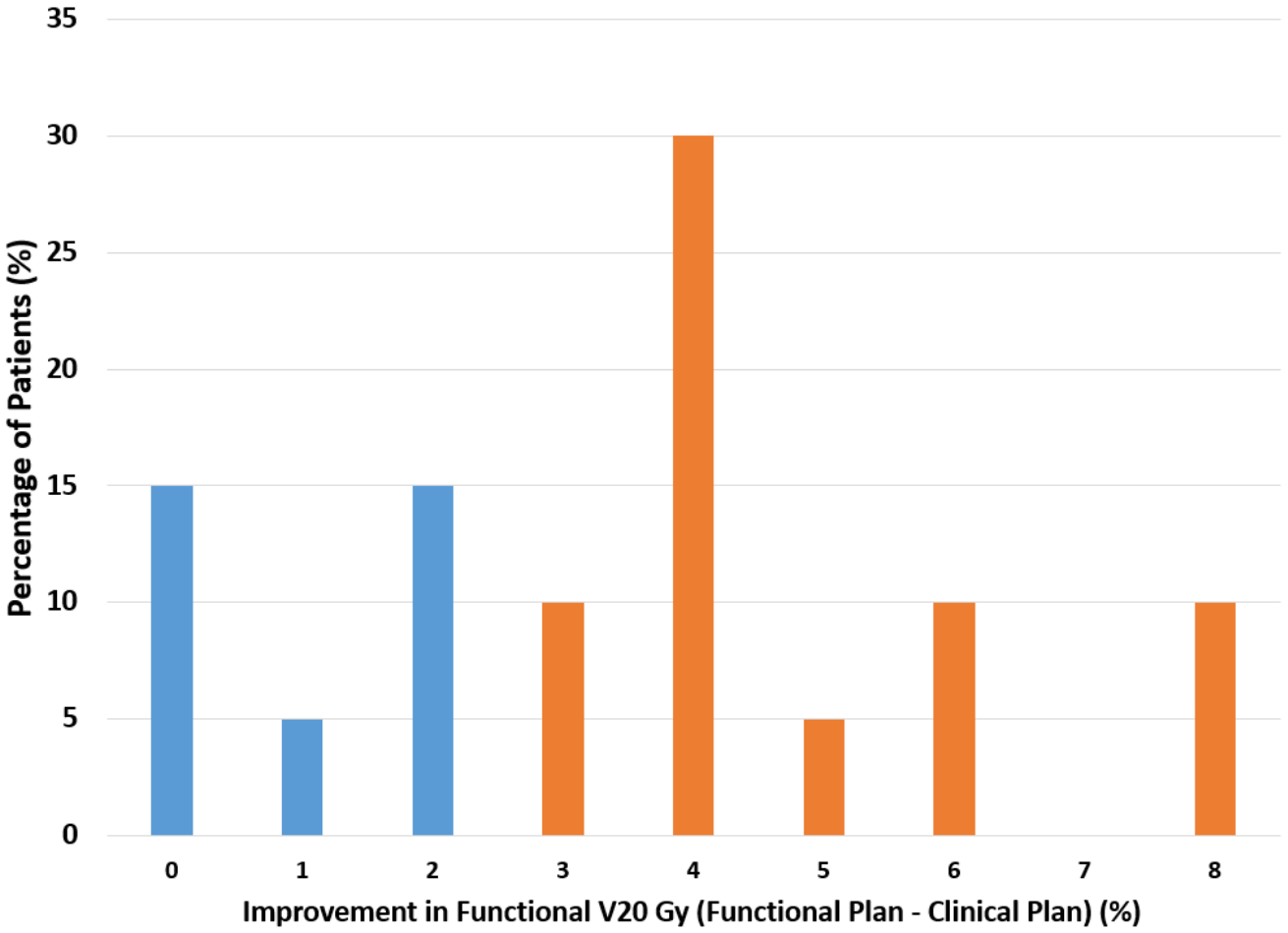


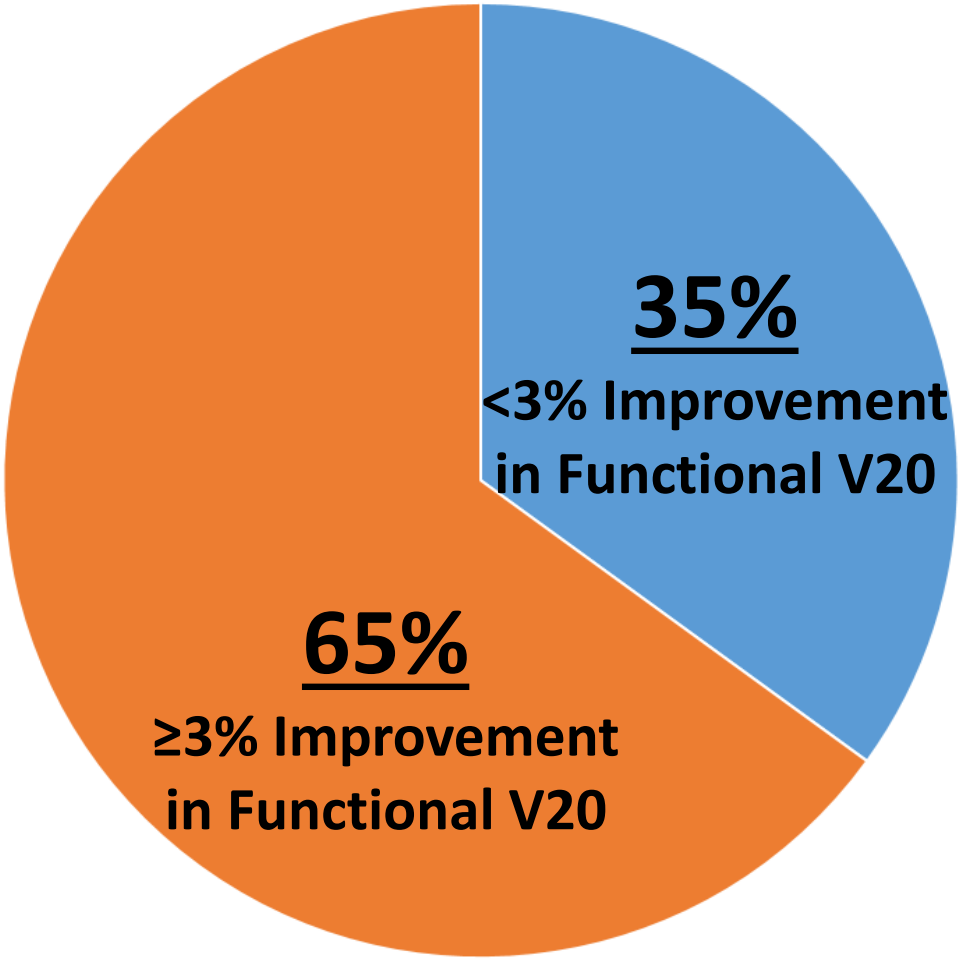
Non-Functional Plan



Functional V20 Trial Dosimetry

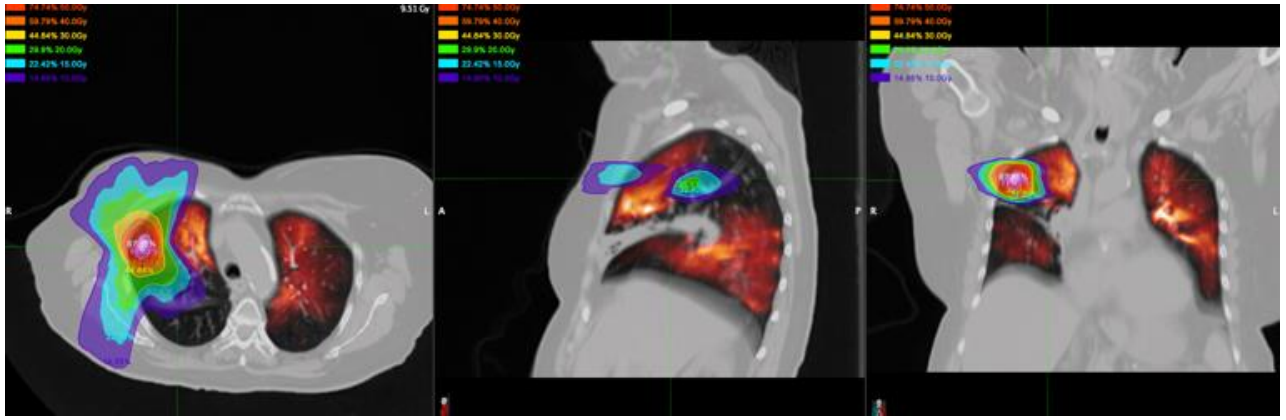
Mean Improvement in Functional V20: 3.2% [0.1% to 7.9%]





Conformal Avoidance: Future/On-going work

SBRT Conformal Avoidance



J Bayouth, T Patton, S Gerard, G Christensen, A Baschnagel, & J Reinhardt. Clinical Application of a Lung Function Planning Technique Designed to Improve Toxicity (2017), Med. Phys., 44: 2721–3318. doi:10.1002/mp.12304

Improved calculation robustness

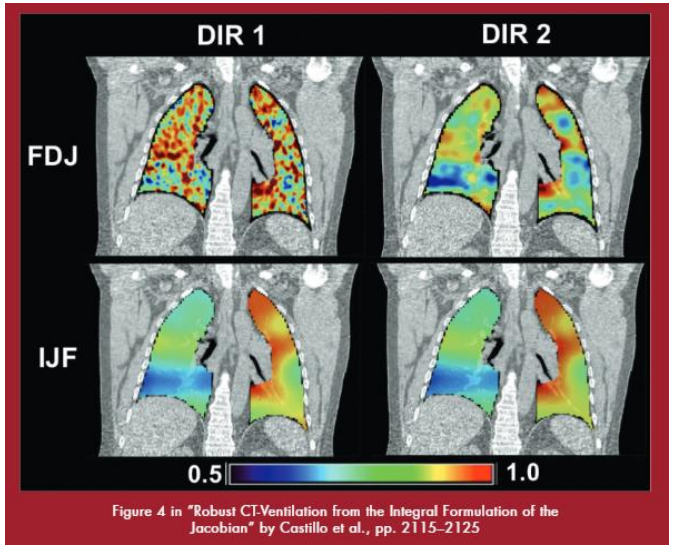
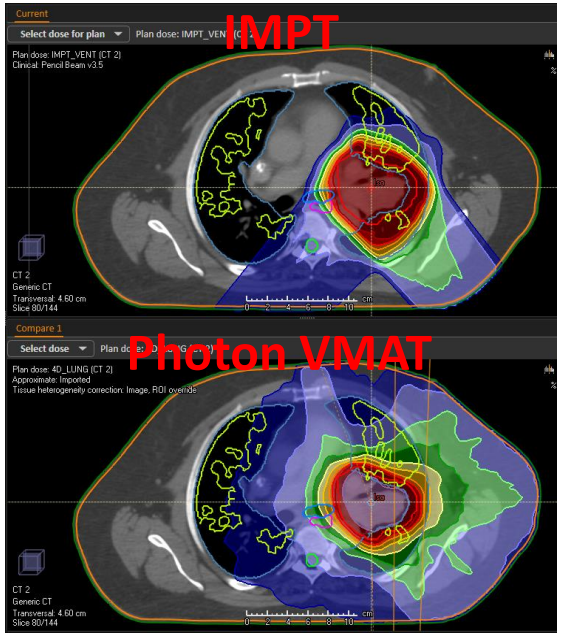


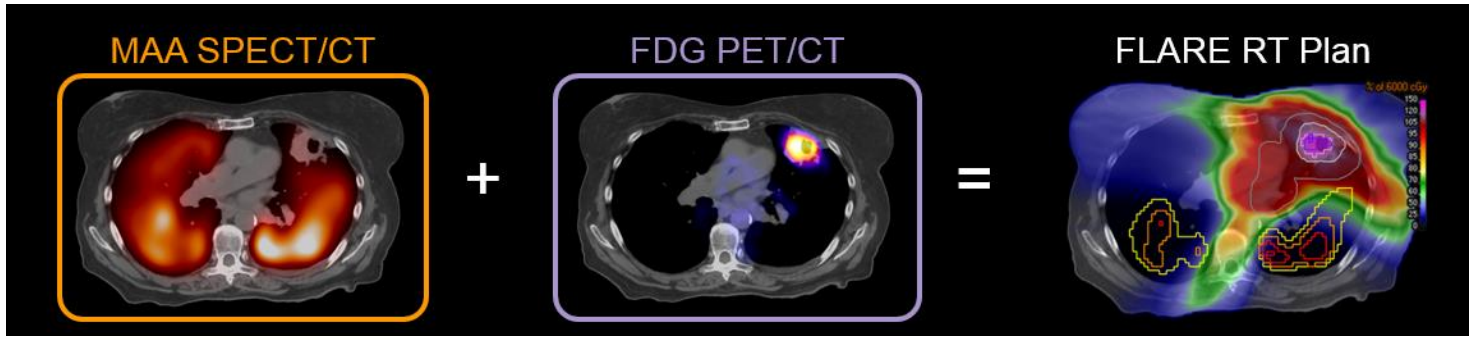
Figure 4 in "Robust CT-Ventilation from the Integral Formulation of the Jacobian" by Castillo et al., pp. 2115–2125

Proton Conformal Avoidance



M Dougherty

Conformal avoidance + PET dose escalation (RTOG 1106)



SR Bowen, J Zeng, University of Washington

Thank you

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