Consideration for Further Pulmonary Toxicity Reduction with 4DCT Derived Functional Avoidance Intensity Modulated Proton Therapy

Jingjing Michele Dougherty, PhD

Department of Radiation Oncology
Mayo Clinic, Rochester MN

Conflict of Interest

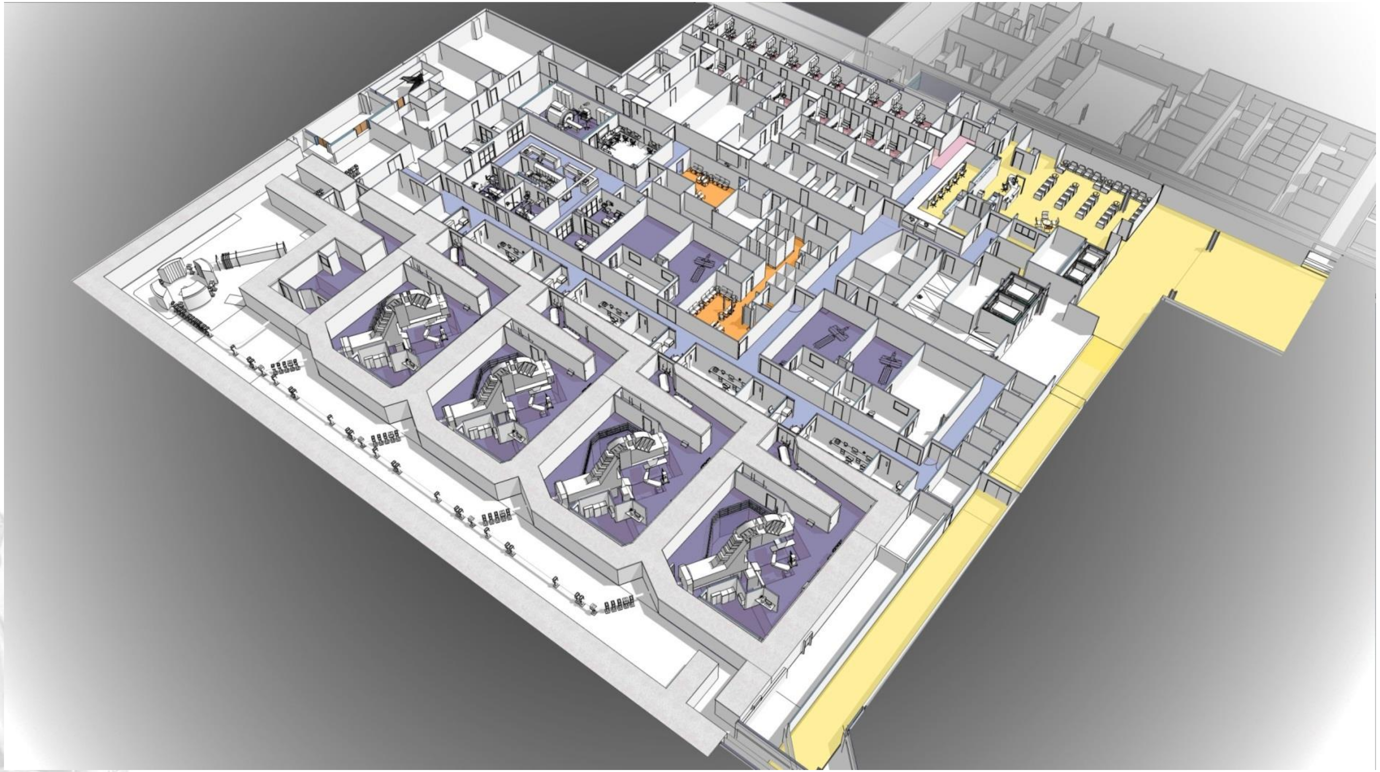
- **Nothing to declare**

AAPM 2019 JUL 14–18

61ST ANNUAL MEETING & EXHIBITION | SAN ANTONIO, TX

BUILDING **BRIDGES.** **CULTIVATING** SAFETY. GROWING **VALUE.**

Mayo Jacobson Proton Center



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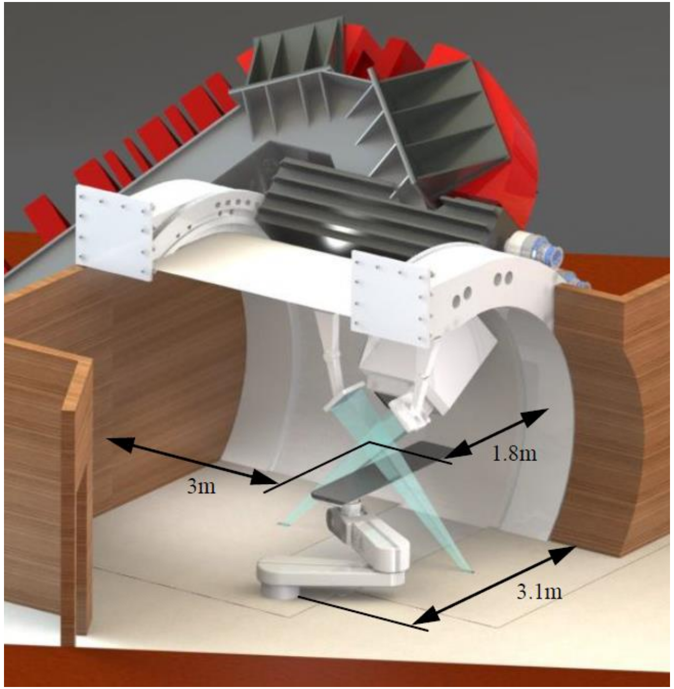
Mayo Jacobson Proton Center



Half Gantry

CT on Rails

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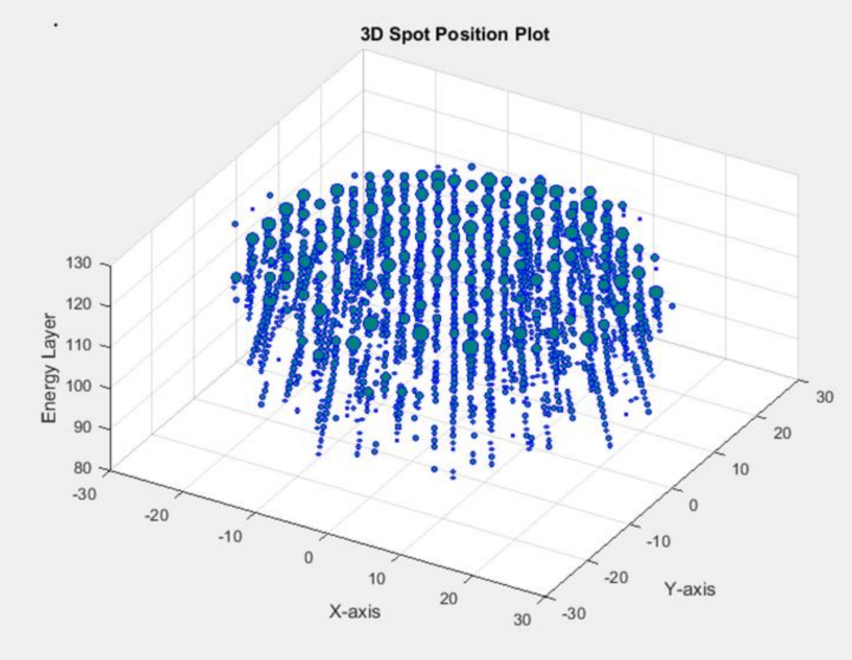
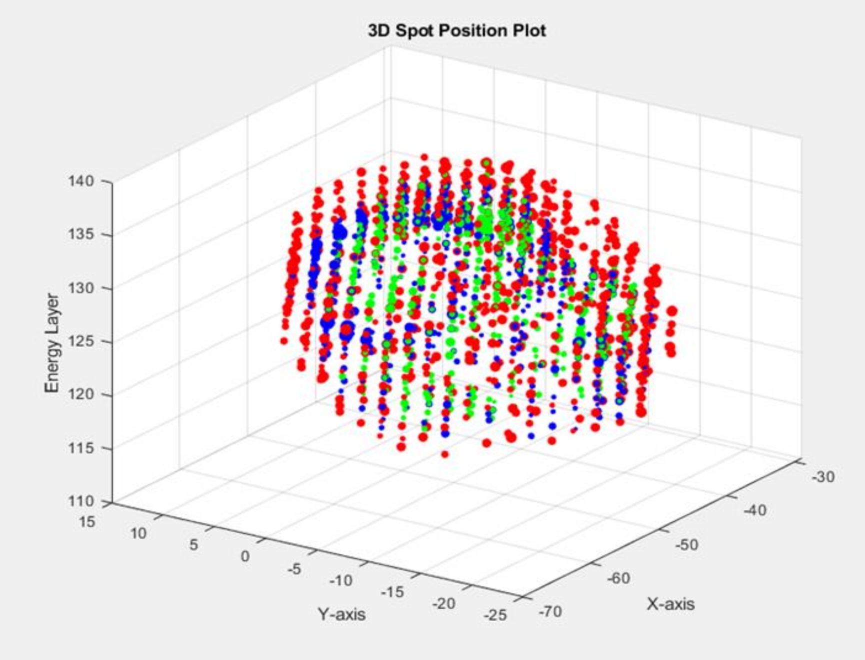
Spot Scanning Proton Treatment Planning

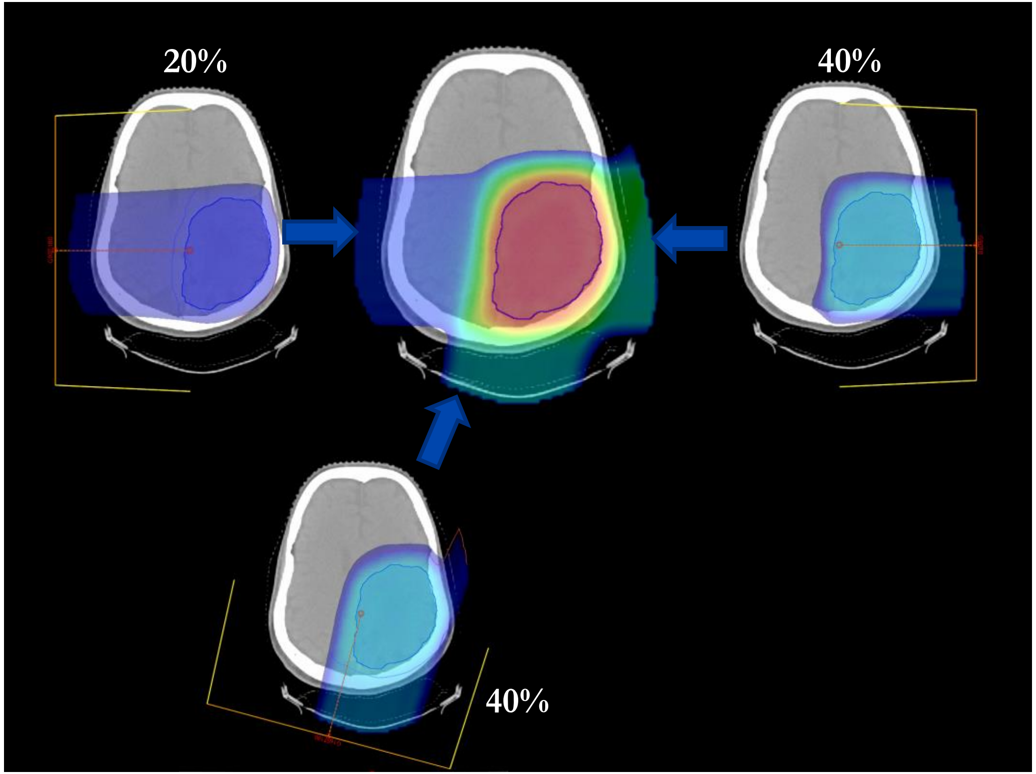


Single Proton Field



Three Proton Fields

Spot Scanning Proton Treatment Planning



- SFO: Single Field Optimized
- Each field uniformly covers target volume
- May include concomitant boost volumes
- More robust than MFO
- Less ability to sculpt dose around critical structures

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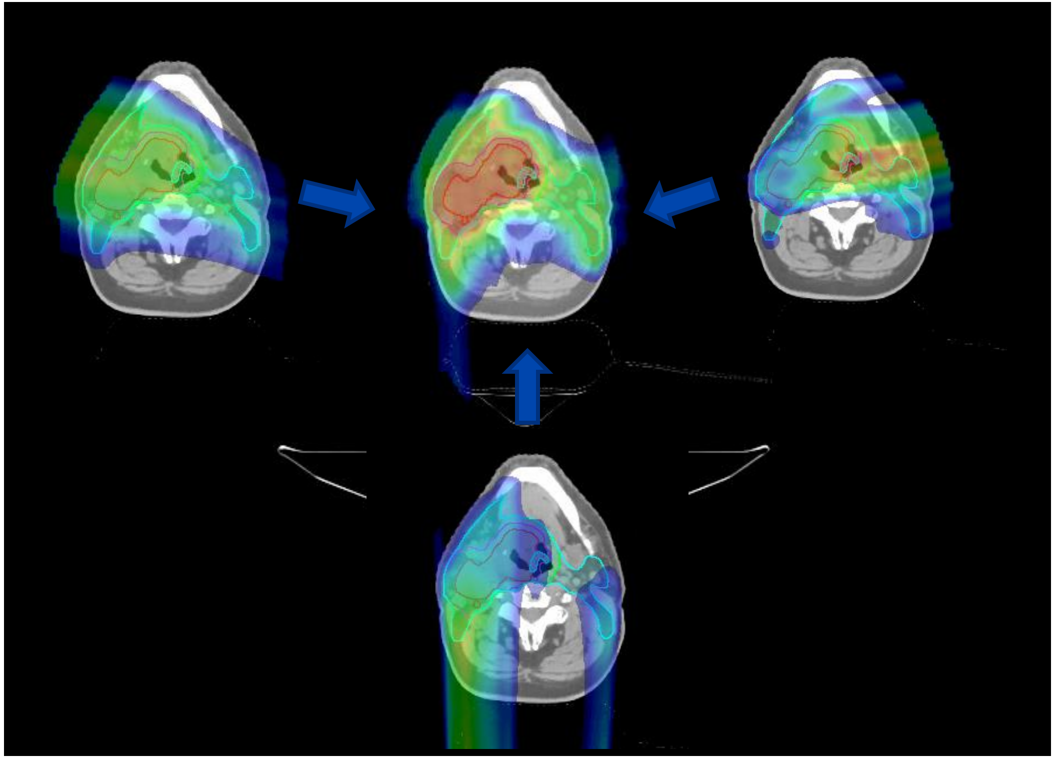
Spot Scanning Proton Treatment Planning



- MFO: Multi Field Optimized
- Fields don't necessarily deliver uniform dose to target
- Hot and cold spots from various beams compensate each other
- May be less robust than SFO
- More flexibility

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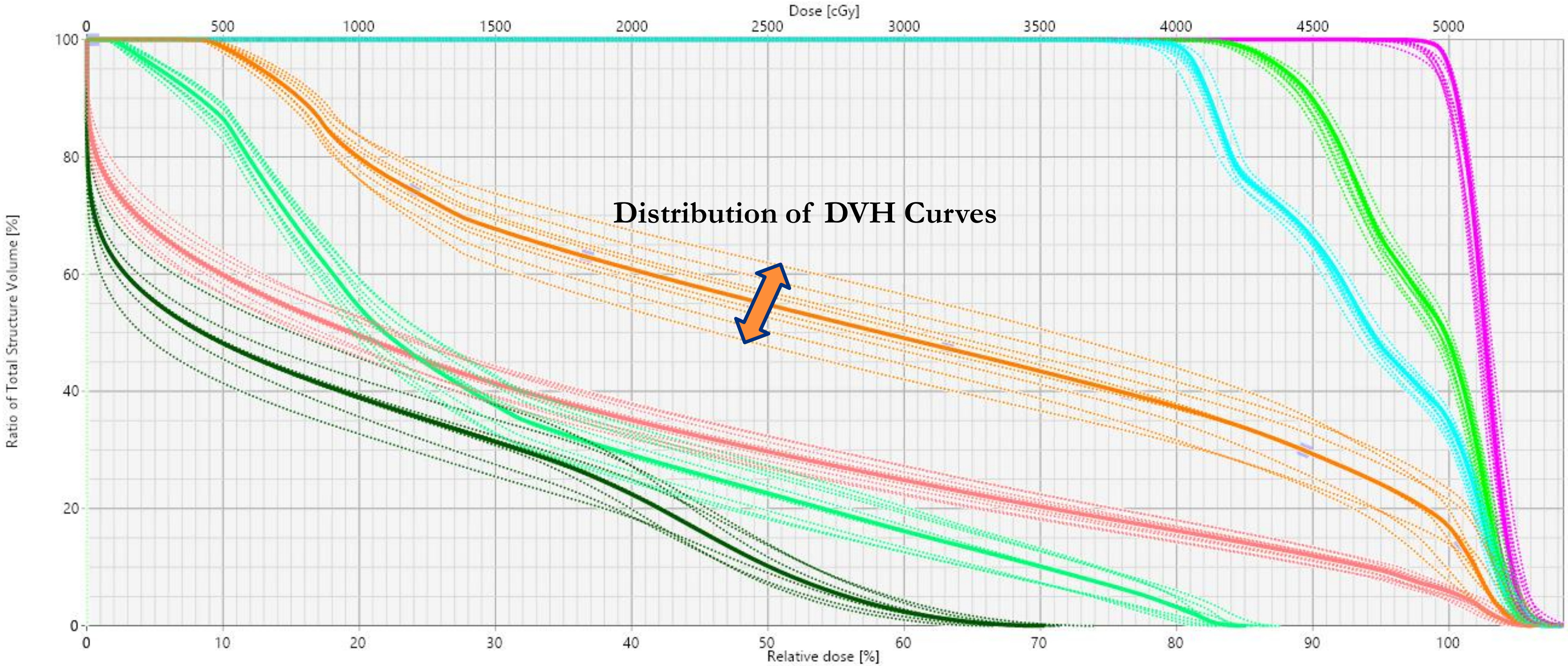
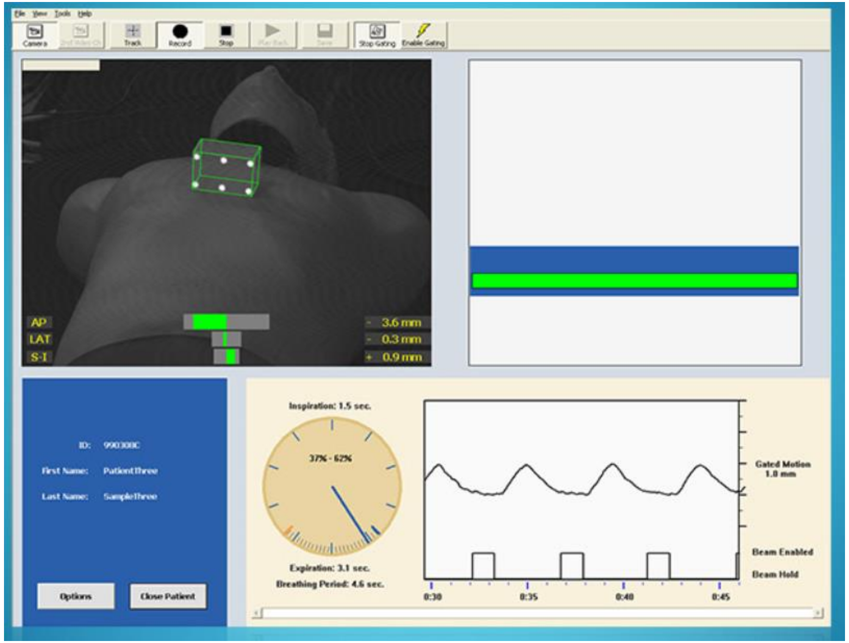
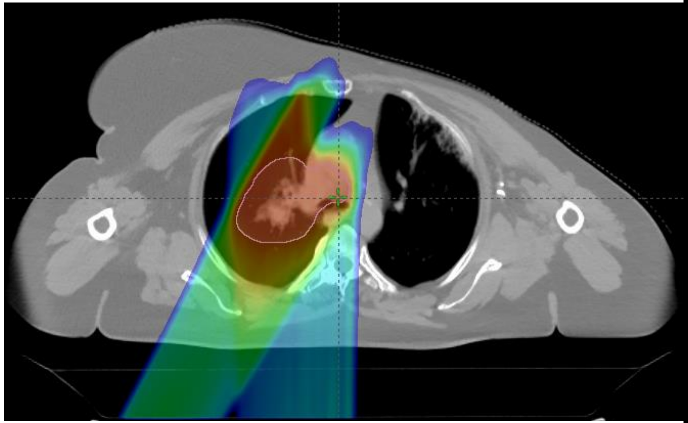
Robust Optimization with IMPT



Proton Simulation for Lung Patients



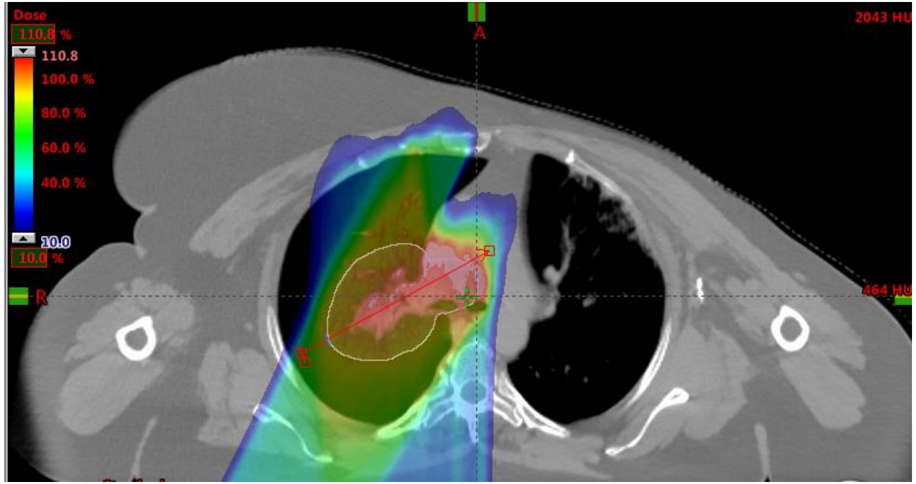
IMPT Treatment Planning for Lungs

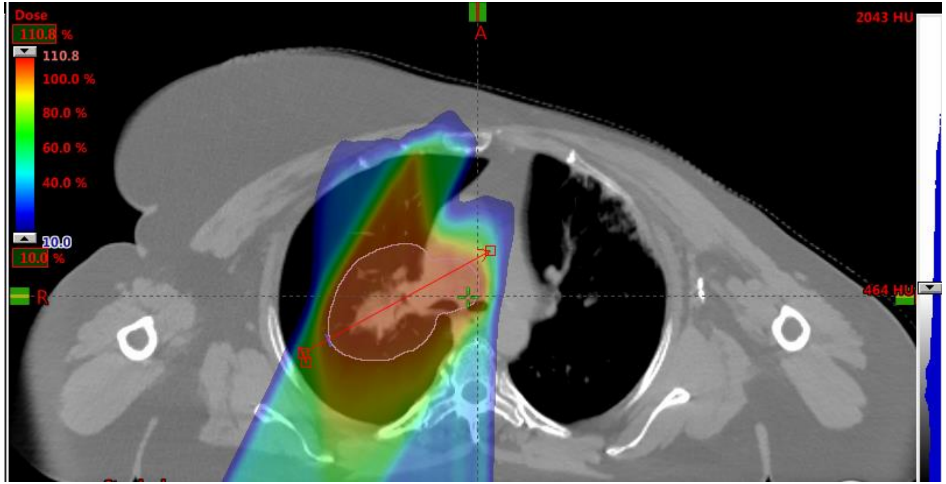


Two-field MFO Plan

Jon Kruse

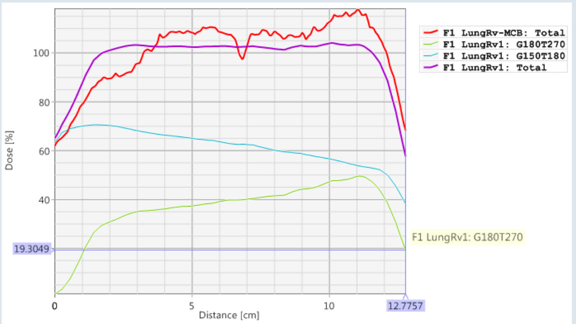
Robust Lung Plan Evaluation: Monte Carlo Dose





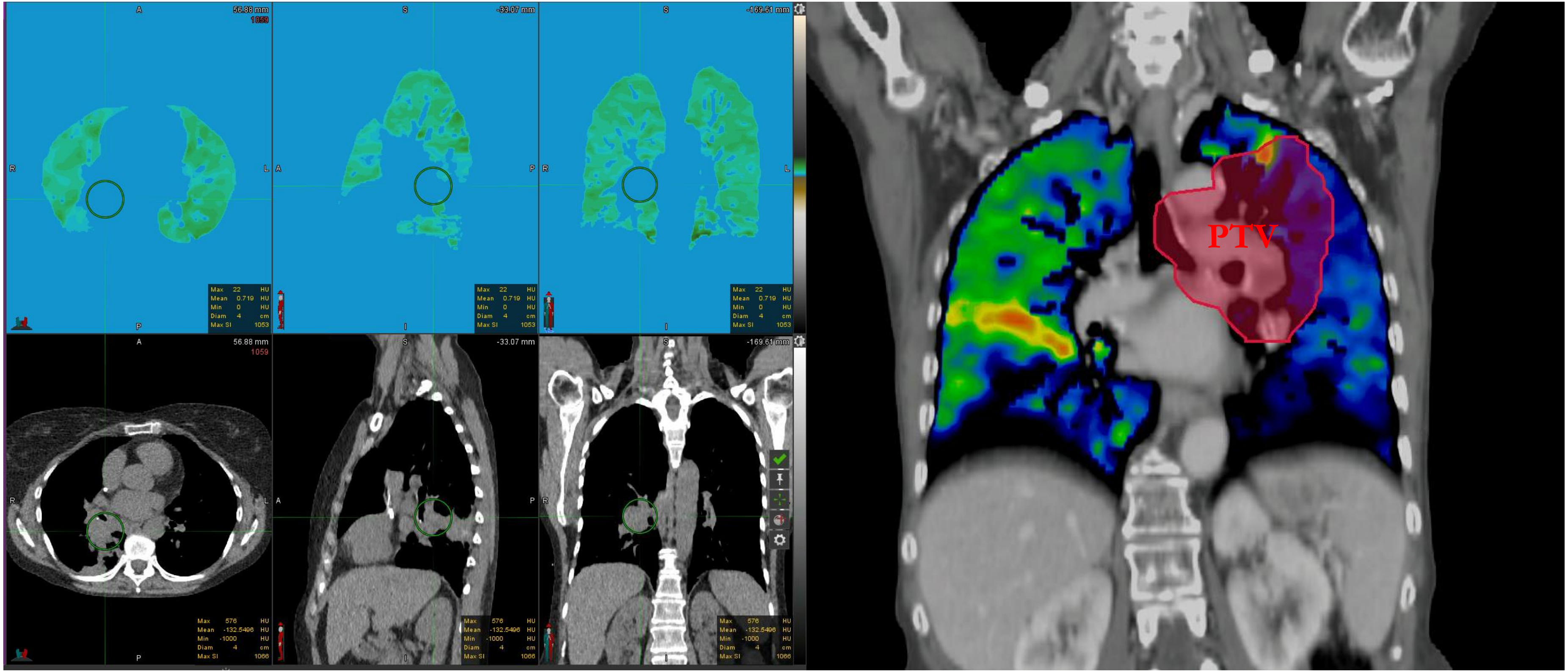
Monte Carlo Dose

Eclipse Dose



Jon Kruse

Virtual Histology of the Human Lung Tissue



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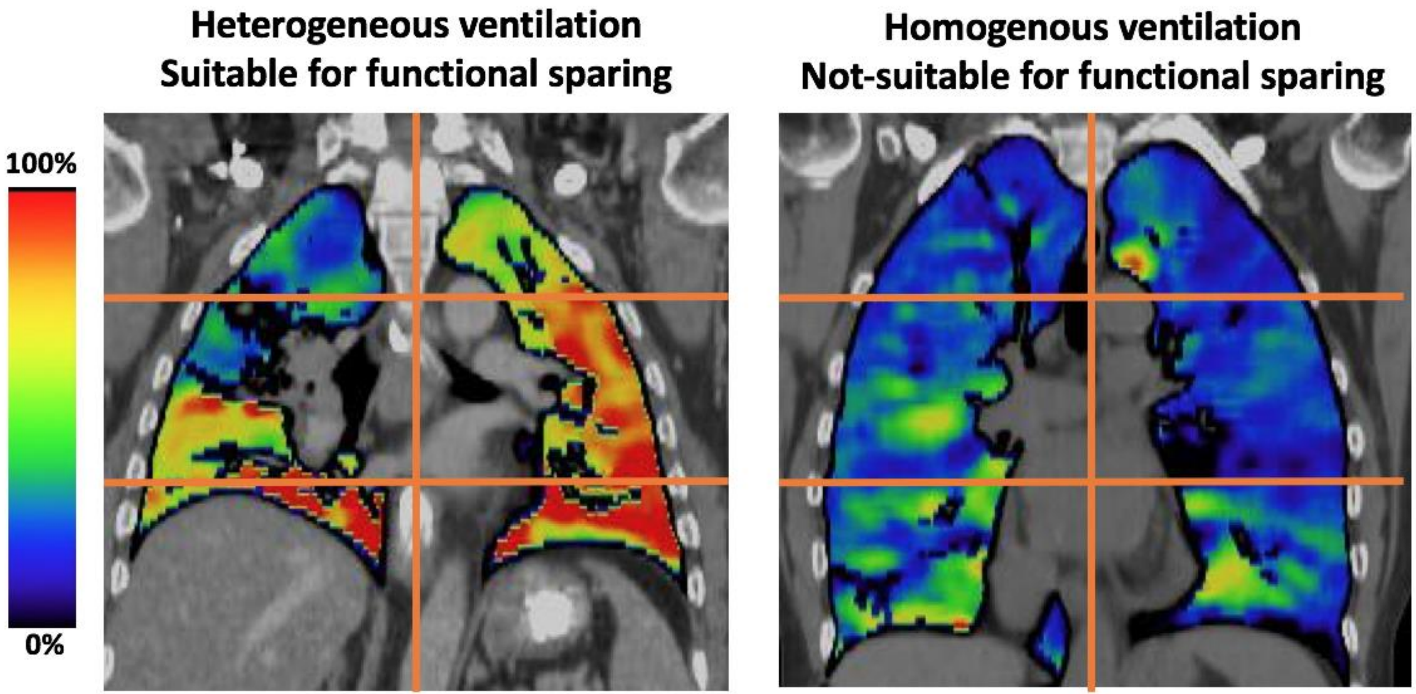
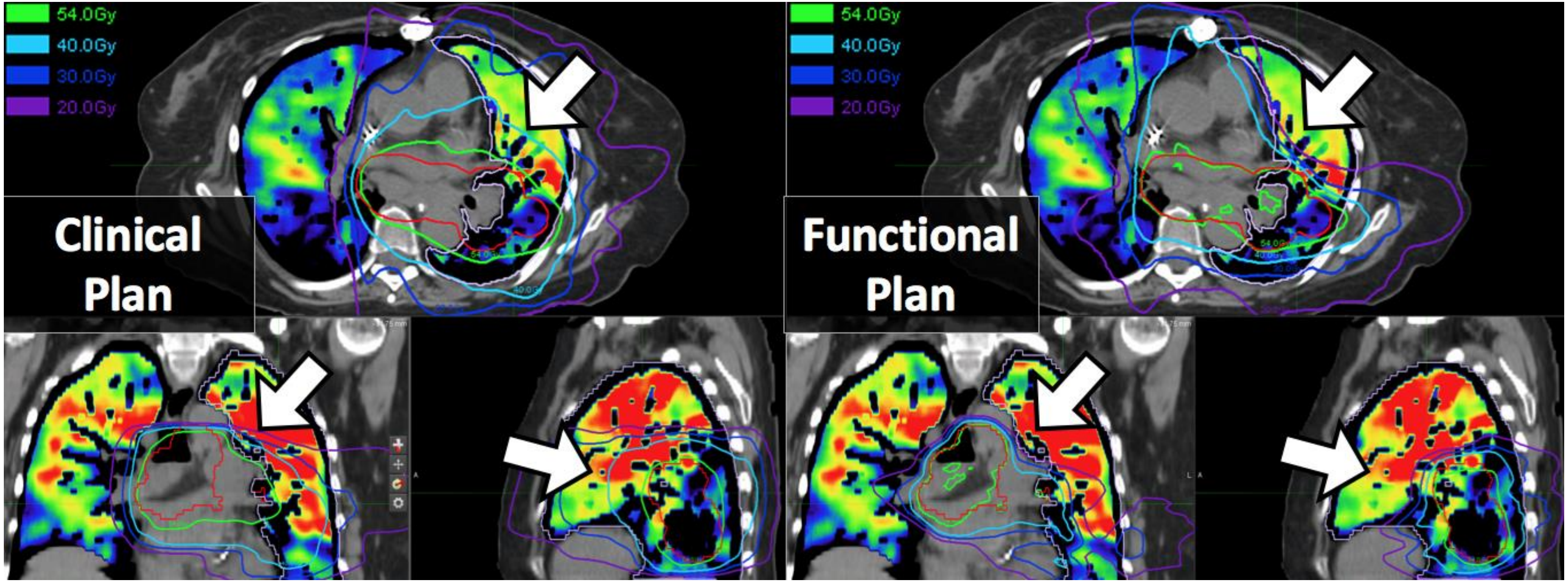
4DCT Derived Functional Pulmonary Ventilation Map



Yevgeniy (Jenia) Vinogradskiy

Pulmonary Functional Avoidance based Treatment Planning with VMAT



Yevgeniy (Jenia) Vinogradskiy

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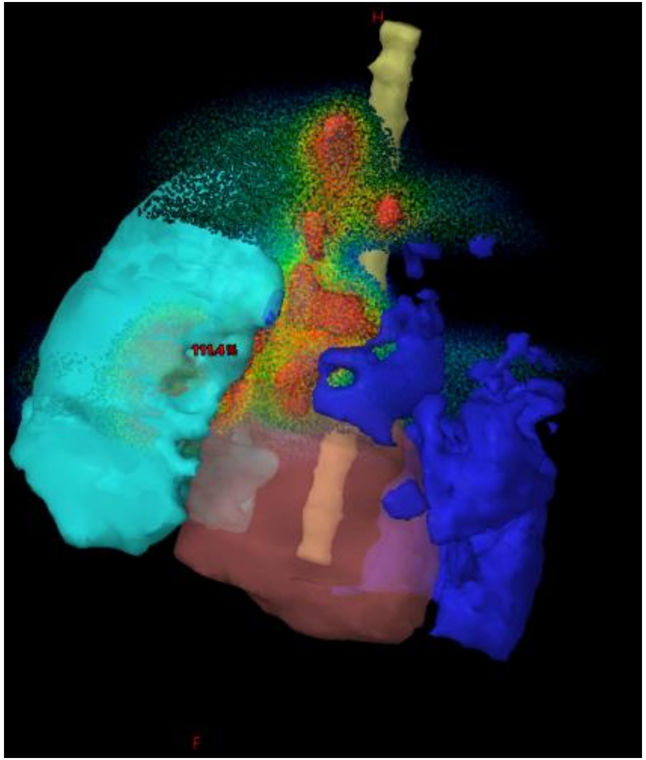
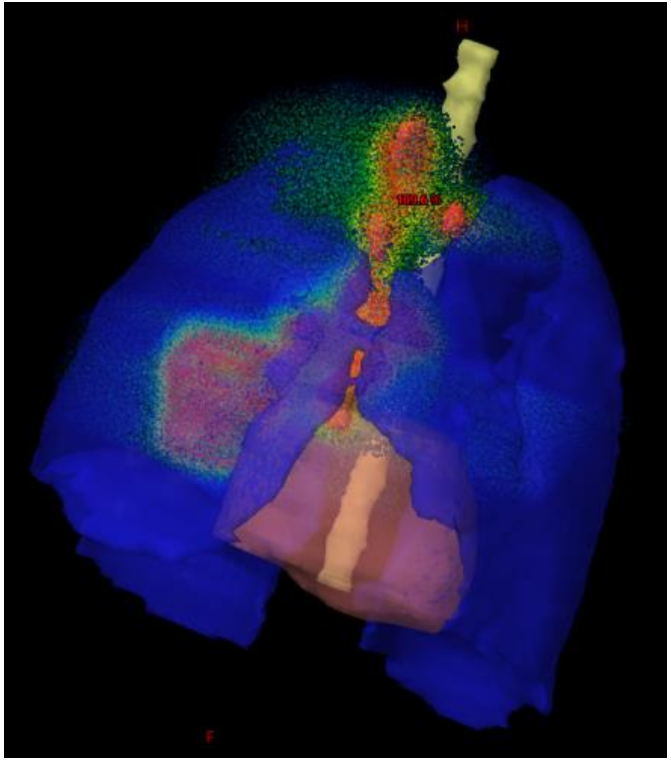
Functional Lung Structures vs Normal Lung Structures



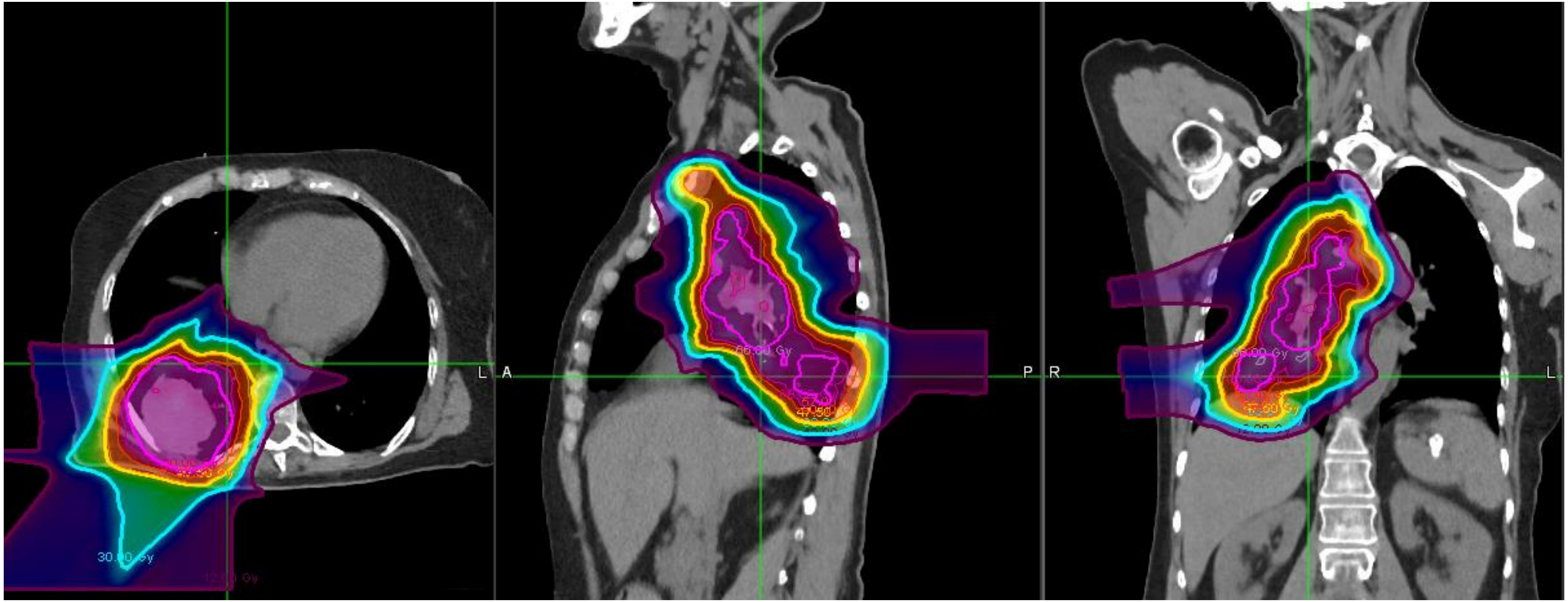
Functional Lungs



Total Lungs

Clinical Lung Treatment Plans with IMPT

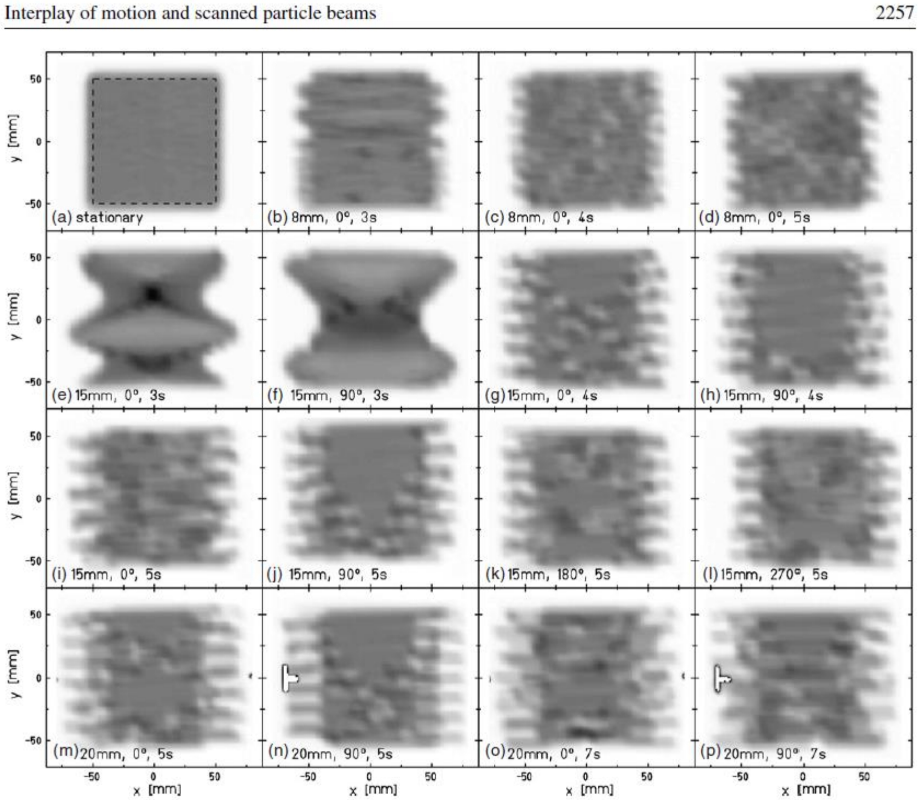
20% to 70% Phase Gated Lung Plan



Tumor Motion Evaluation in MIM

zzMotion 1	
Max Centroid Motion in X (R/L) Direction (cm)	0.26
Max Centroid Motion in Y (A/P) Direction (cm)	0.12
Max Centroid Motion in Z (S/I) Direction (cm)	0.55
Max Radial Motion Vector (cm)	0.62
zzMotion 2	
Max Centroid Motion in X (R/L) Direction (cm)	0.15
Max Centroid Motion in Y (A/P) Direction (cm)	0.23
Max Centroid Motion in Z (S/I) Direction (cm)	0.64
Max Radial Motion Vector (cm)	0.7
zzMotion 3	
Max Centroid Motion in X (R/L) Direction (cm)	0.13
Max Centroid Motion in Y (A/P) Direction (cm)	0.27
Max Centroid Motion in Z (S/I) Direction (cm)	0.34
Max Radial Motion Vector (cm)	0.45

Interplay Effects



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Bert et al., PMB 53 (2008) p. 2253

Experimentally Measured Synchrotron Timing

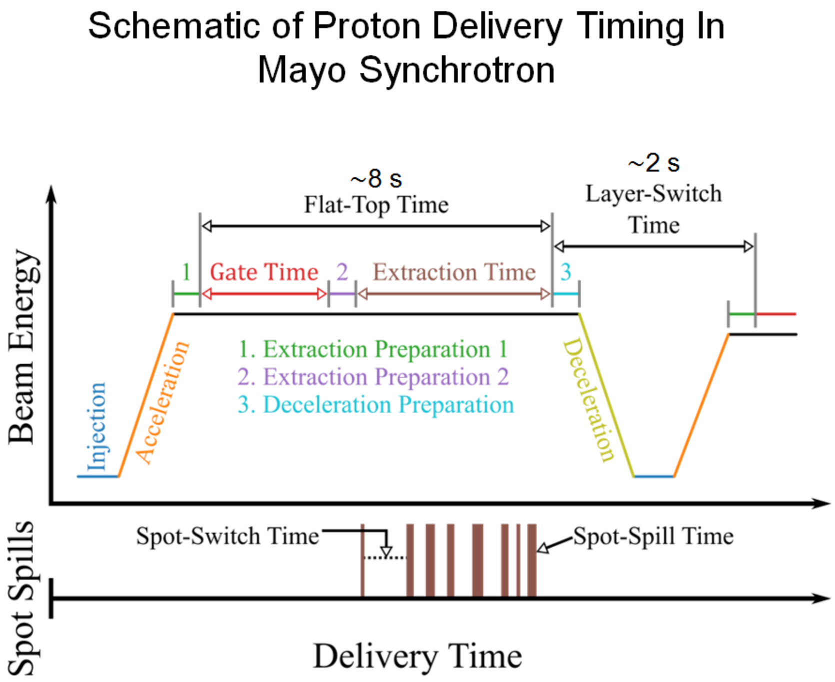

TABLE II. The vendor-provided (nominal) and experimentally determined parameters used as the input for the model to calculate the beam delivery time.

Parameter	Nominal values	Experimental values
Total charge (nC)	2	2.0 ± 0.4
Flat top time (s)	8	7.87 ± 0.07
Extraction time (s)	7.93	7.80 ± 0.07
Layer switch time (s)	1.905	1.90; E<200.4 MeV 2.05; E=200.4 MeV 2.00; E>200.4 MeV
Effective magnet scanning speed, V_x (m/s)	6	5.0; high E group 5.7; medium E group 7.0; low E group
Effective magnet scanning speed, V_y (m/s)	10	17.1; high E group 18.2; medium E group 22.2; low E group
Magnet preparation/verification time (ms)	2.2	1.93 ± 0.02
Proton spill rate (MU/s)[a]	–	9.8; high E group 8.1; medium E group 8.5; low E group

[a]Vendor did not give a specific proton spill rate. Experimentally measured proton spill rates were also used as the nominal values.

Shen et al

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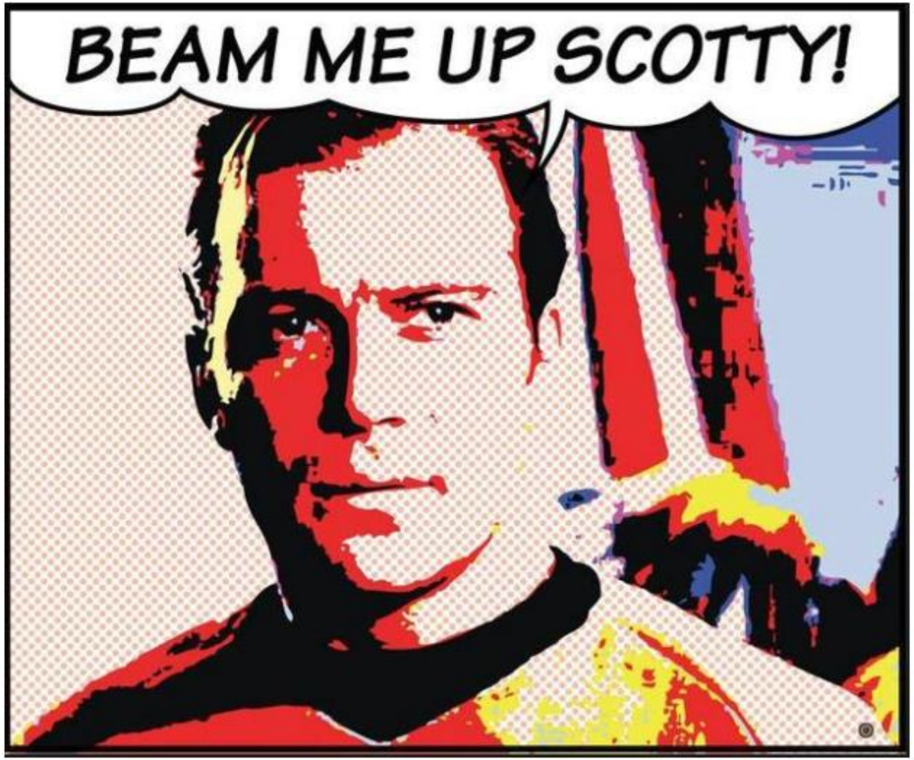
Mayo 4D Dynamic Dose Simulator - SCOTTY

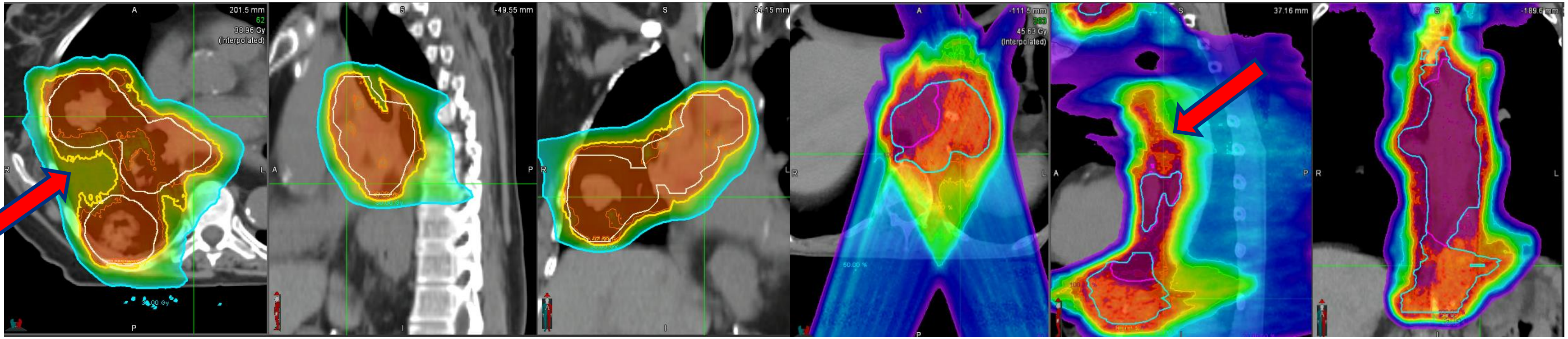
```
[dougherty@enterprise tools]$ vim scotty_inputs.txt
[dougherty@enterprise tools]$ scotty_master.sh
===========================================================
++~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~++
~~                                                       ~~
++  SS  SS           Scotty (beta)               $$  $$  ++
++    SS    Mayo's GPU-Based 4D-Dose Calculator    $$    ++
~~                                                       ~~
++~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~++
===========================================================

scotty_master - Beam us up, Scotty!
                Aye Aye Sir, starting the calculation!
scotty_master - Working on archiveScotty.sh
     -> Preparing
     -> Running 'archiveScotty.sh -dataDirectory /data/dougherty/cu
eMapping 0 1 2 3 4 5 6 7 8 9 -log files'
     -> Completed
scotty_master - Working on Generate4DSpockCommandFiles.py
     -> Preparing
     -> Running 'Generate4DSpockCommandFiles.py -dataDirectory /dat
Phases4DCT 10 -folderPhaseMapping 0 1 2 3 4 5 6 7 8 9 -spockSeed -1
/usr/lib/python2.7/site-packages/dicom/__init__.py:53: UserWarning:
This code is using an older version of pydicom, which is no longer
maintained as of Jan 2017.  You can access the new pydicom features
by installing `pydicom` from PyPI.
See 'Transitioning to pydicom 1.x' section at pydicom.readthedocs.c
for more information.

  warnings.warn(msg)
```



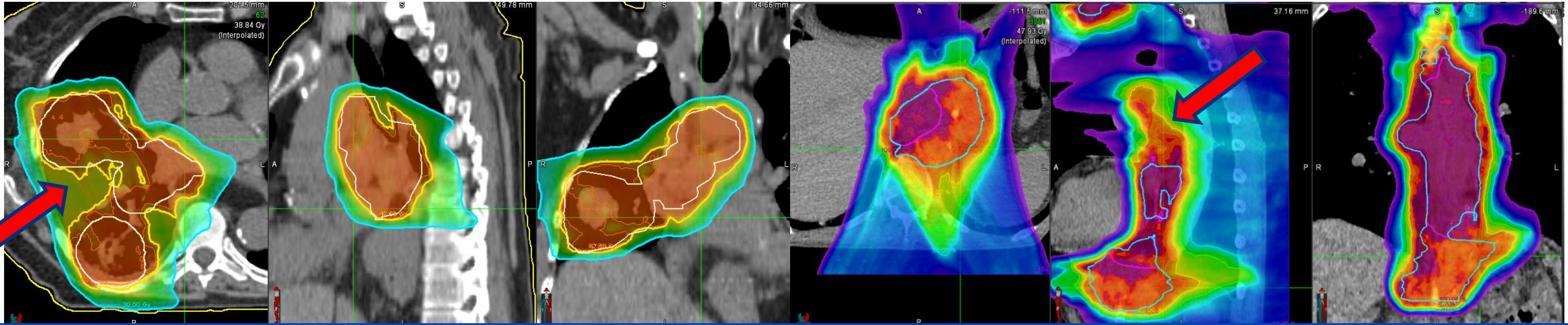
Pepin et al

Proton Interplay Effect Dose Degradation

Original Planning Dose – Monte Carlo



4D Dynamic Dose – Monte Carlo



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Lung Case

Esophagus Case

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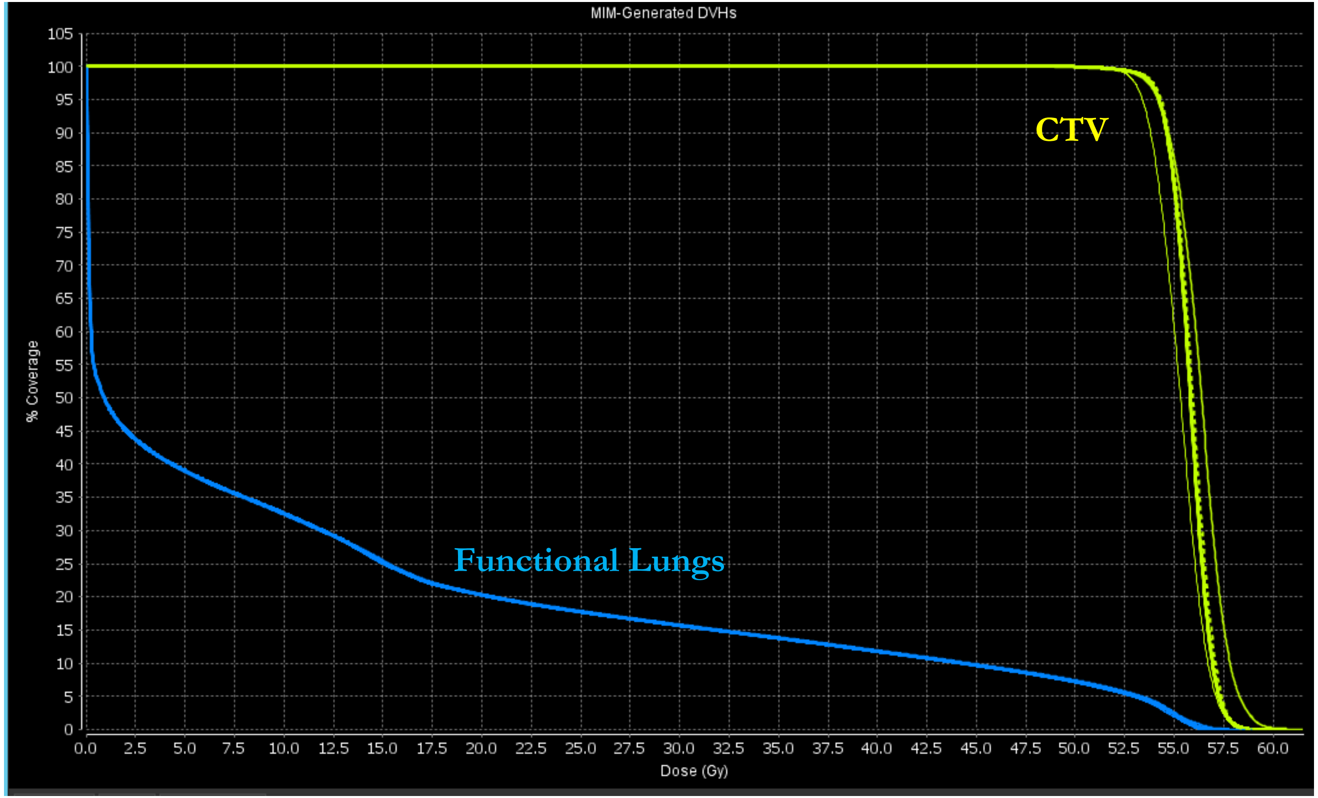
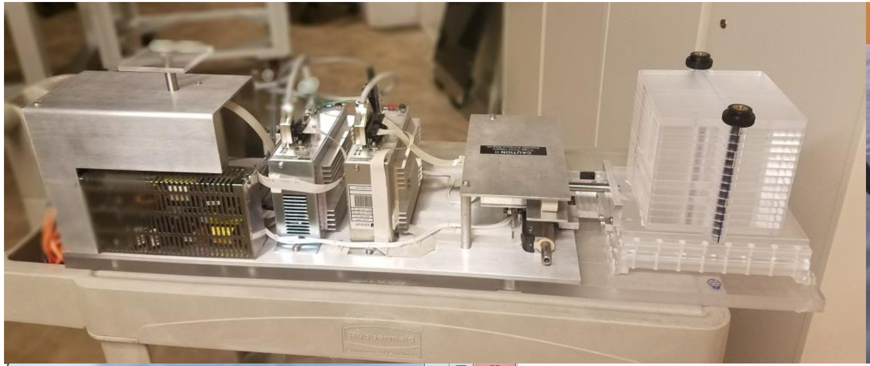
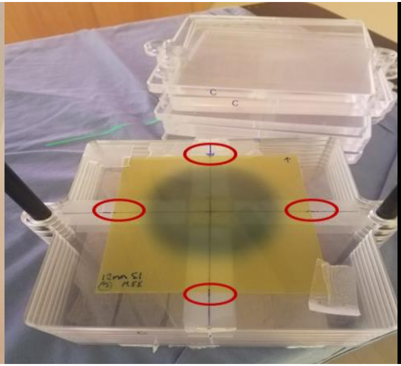
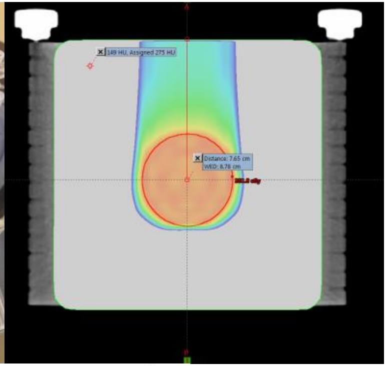
Interplay Effect Causing Dose Distribution Uncertainty

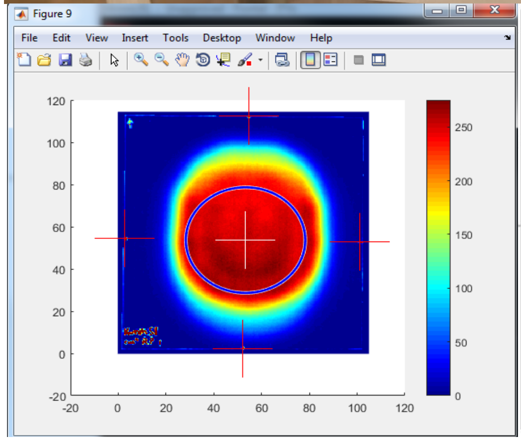


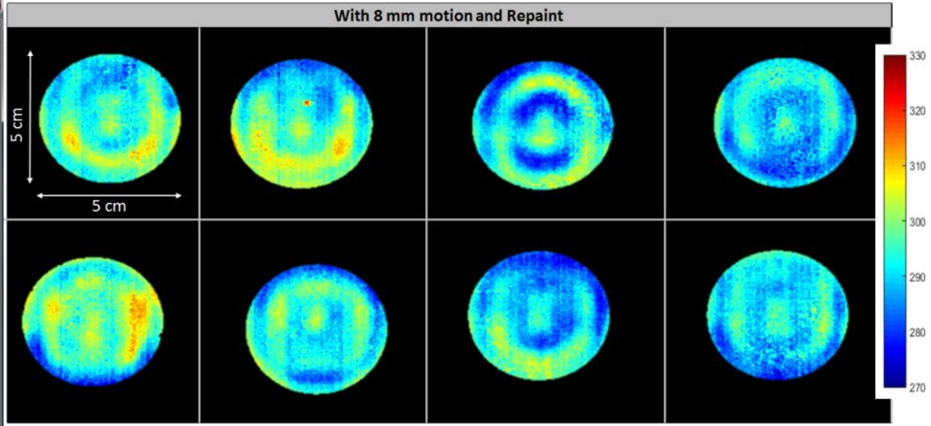
Experimental Validation with EBT3 Films









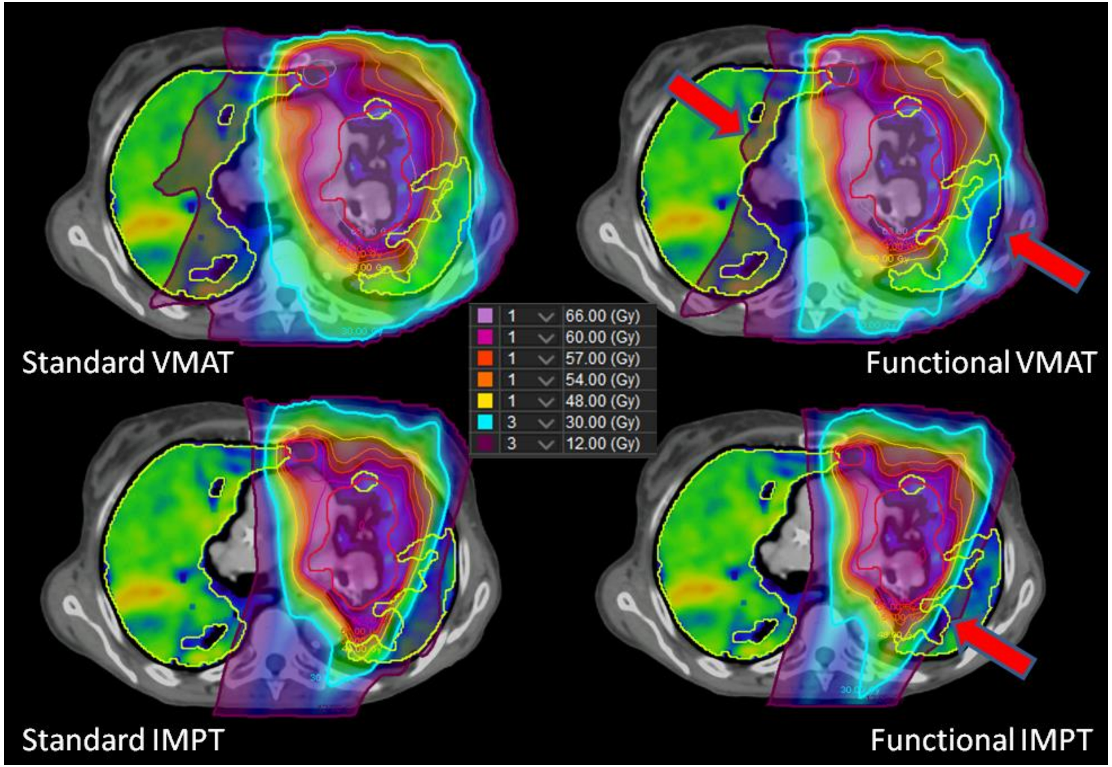


El-Sherif et al

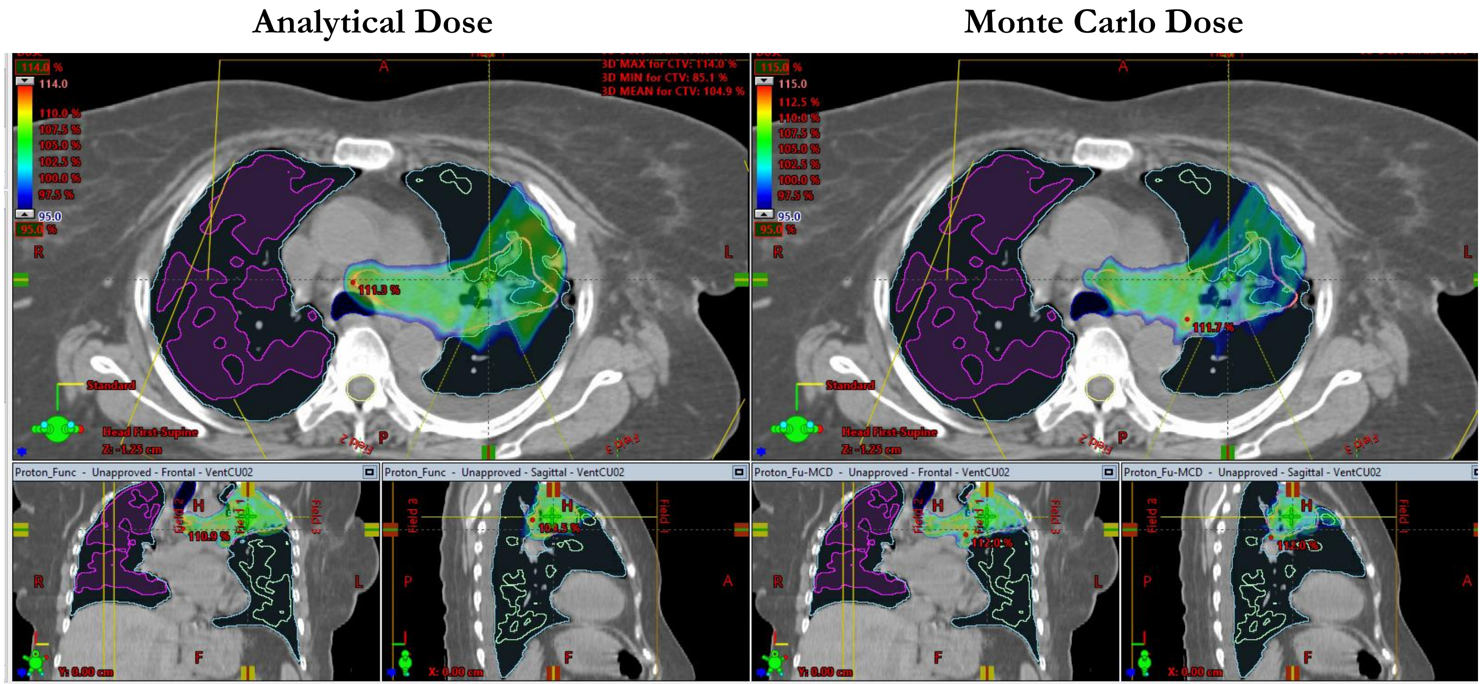
Dosimetric Comparison with VMAT plans

- 31 clinical trial (NCT02528942) patient data
- IMPT plans were created (standard and functional)
- 192 plans were reviewed (eclipse dose and MC dose)
- Motion evaluation
- 4D dynamic dose evaluated for selected patients

Dosimetric Comparison with VMAT plans



Dosimetric Considerations



Dosimetric Comparison with VMAT plans

	Volumetric Arc Therapy			Intensity Modulated Proton		
	Standard Plan	Functional Plan	P- Value	Standard Plan	Functional Plan	P- Value
CTV Metrics						
CTV max (RBE[Gy])	70.93 (16)	71.45 (15.9)	0.1	62.09 (12.4)	62.86 (12.6)	<0.000
Conformity Index	2.22 (0.7)	2.15 (0.7)	<0.000	1.79 (0.4)	1.71 (0.4)	0.002
Homogeneity Index	1.22 (0.3)	1.23 (0.3)	0.02	1.10 (0.2)	1.11 (0.2)	0.001
OAR Metrics						
Total MLD (RBE[Gy])	16.14 (2.7)	15.28 (2.9)	<0.000	9.73 (3.3)	8.78 (2.9)	<0.000
Total Lung V20 (%)	27.57 (5.7)	25.50 (6.1)	<0.000	19.54 (6.8)	17.06 (5.7)	<0.000
Total Lung V5 (%)	66.8 (11.2)	64.89 (12.9)	0.005	29.80 (9.2)	27.67 (8.5)	<0.000
Esophagus Mean (RBE[Gy])	24.79 (8.2)	24.10 (8.6)	0.005	19.57 (10.0)	19.56 (10.1)	0.92
Heart Mean (RBE[Gy])	11.90 (6.2)	11.88 (6.4)	0.92	4.62 (2.9)	4.77 (3.5)	0.75
Cord Max (RBE[Gy])	36.18 (8.4)	36.72 (8.4)	0.46	31.84 (9.9)	33.57 (8.8)	0.1

	Volumetric Arc Therapy			Intensity Modulated Proton		
	Standard Plan	Functional Plan	P- value	Standard Plan	Functional Plan	P- value
Functional Lung Metrics						
Ipsilateral						
MLD (RBE[Gy])	24.38 (7.2)	22.49 (7.0)	<0.000	17.65 (7.6)	14.72 (6.7)	<0.000
Lung V5 (%)	77.9 (17.6)	76.5 (18.3)	0.005	53.81 (18.2)	48.10 (17.9)	<0.000
Lung V20 (%)	51.6 (17.1)	45.57 (16.9)	<0.000	35.83 (16.2)	28.05 (13.7)	<0.000
Lung V30 (%)	34.9 (16.1)	30.75 (14.8)	<0.000	26.70 (14.2)	21.25 (12)	<0.000
Contralateral						
MLD (RBE[Gy])	9.26 (3)	7.99 (2.7)	<0.000	1.75 (2.4)	1.66 (2.2)	0.74
Lung V5 (%)	69.6 (14.2)	66.08 (15.3)	0.015	8.24 (11.1)	6.88 (8.9)	0.002
Lung V20 (%)	5.79 (6.6)	4.10 (5.5)	<0.000	2.68 (4.7)	1.66 (3.1)	0.004
Lung V30 (%)	1.68 (3)	1.34(2.6)	0.013	1.02 (2.3)	0.75 (1.7)	0.015
Total Lung						
MLD (RBE[Gy])	16.05 (3.3)	14.49 (3.3)	<0.000	8.82 (3.9)	7.31 (3.3)	<0.000
Lung V5 (%)	73.7 (11.5)	71.06 (13.3)	0.003	28.78 (11.6)	25.40 (10.3)	<0.000
Lung V10 (%)	52.8 (13.7)	43.92 (12.8)	<0.000	24.47 (10.4)	20.20 (8.4)	<0.000
Lung V20 (%)	**26.38 (8.3)**	**22.66 (8.2)**	**<0.000**	**17.59 (8.4)**	**13.48 (6.6)**	**<0.000**
Lung V30 (%)	**16.31 (6.9)**	**14.30 (6.6)**	**<0.000**	**12.49 (6.9)**	**9.89 (5.7)**	**<0.000**
Lung V40 (%)	10.54 (6.0)	9.28 (5.7)	<0.000	9.01 (5.7)	7.32 (4.9)	<0.000
Lung V50 (%)	5.95 (4.2)	5.44 (4.2)	0.006	5.78 (4.1)	4.82 (3.6)	<0.000

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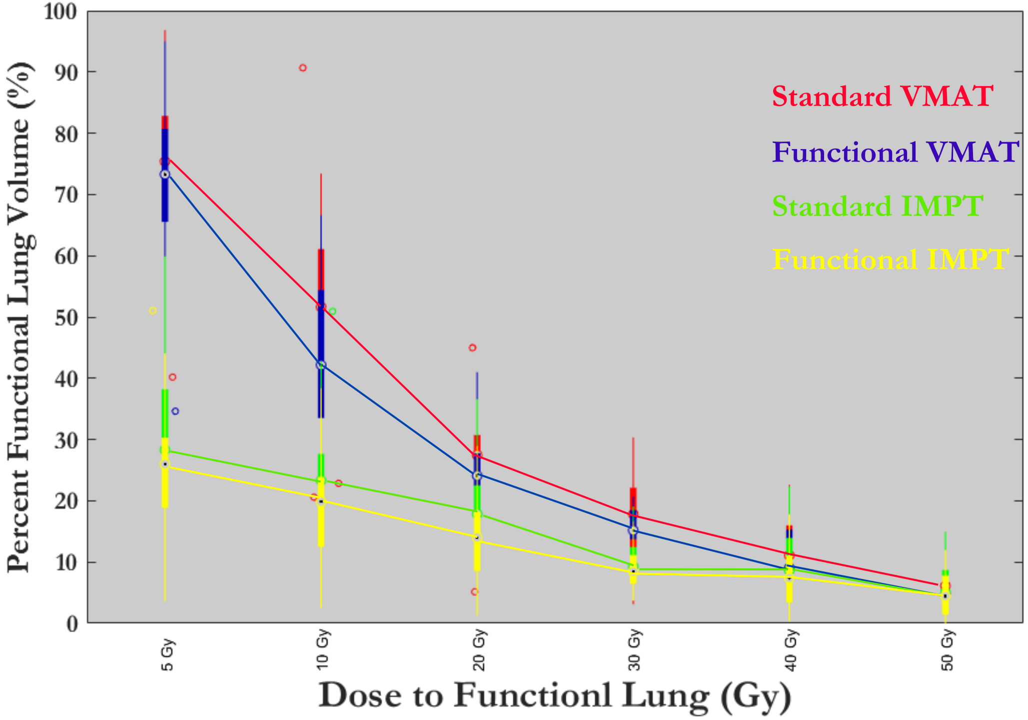
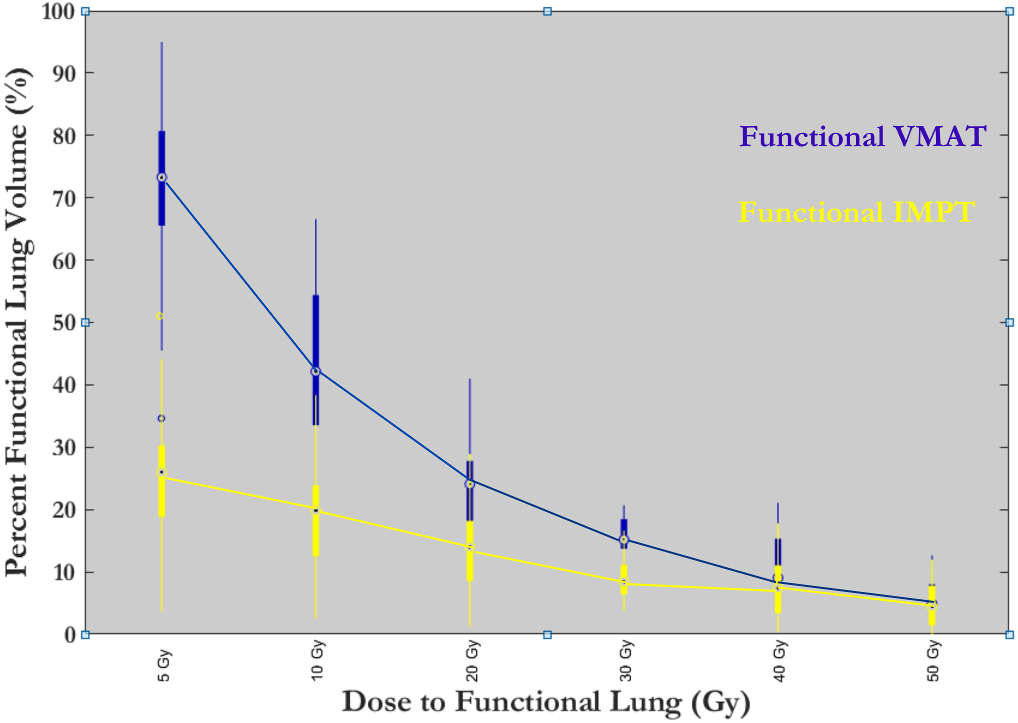
Dose to Functional Lung Comparison



Dose to Functional Lung Comparison



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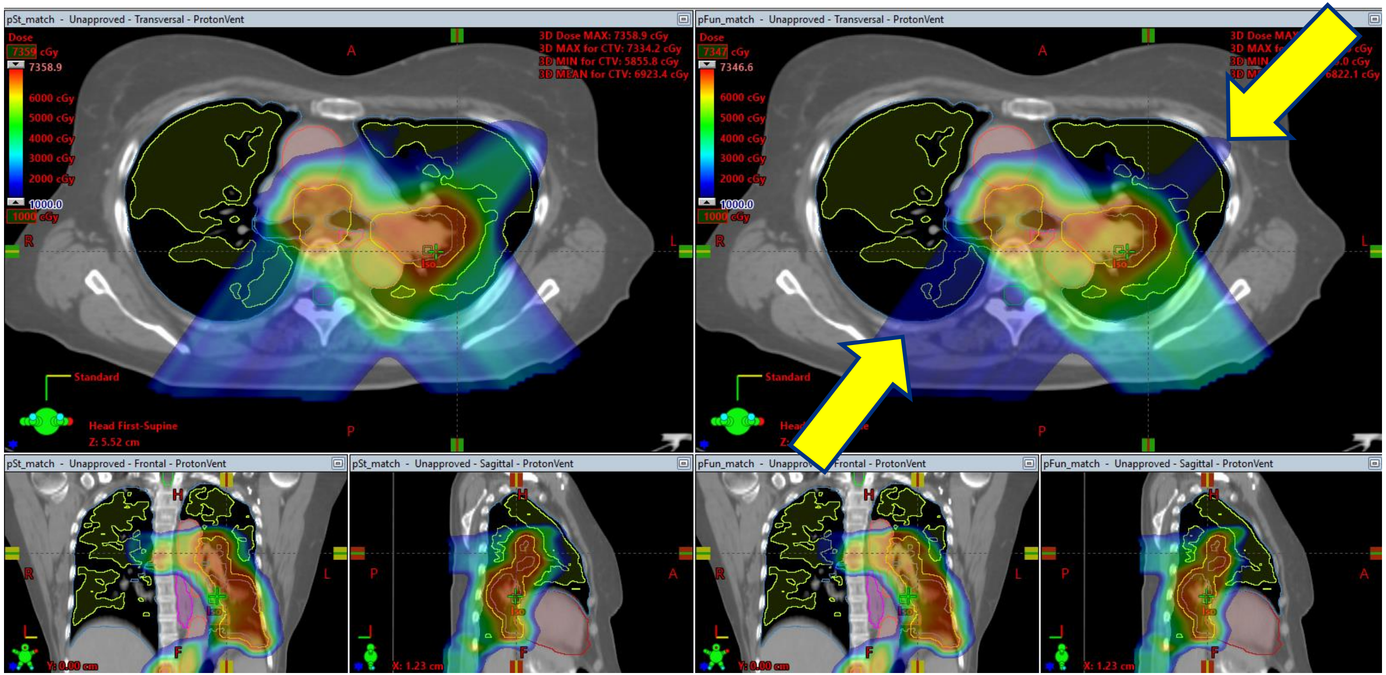
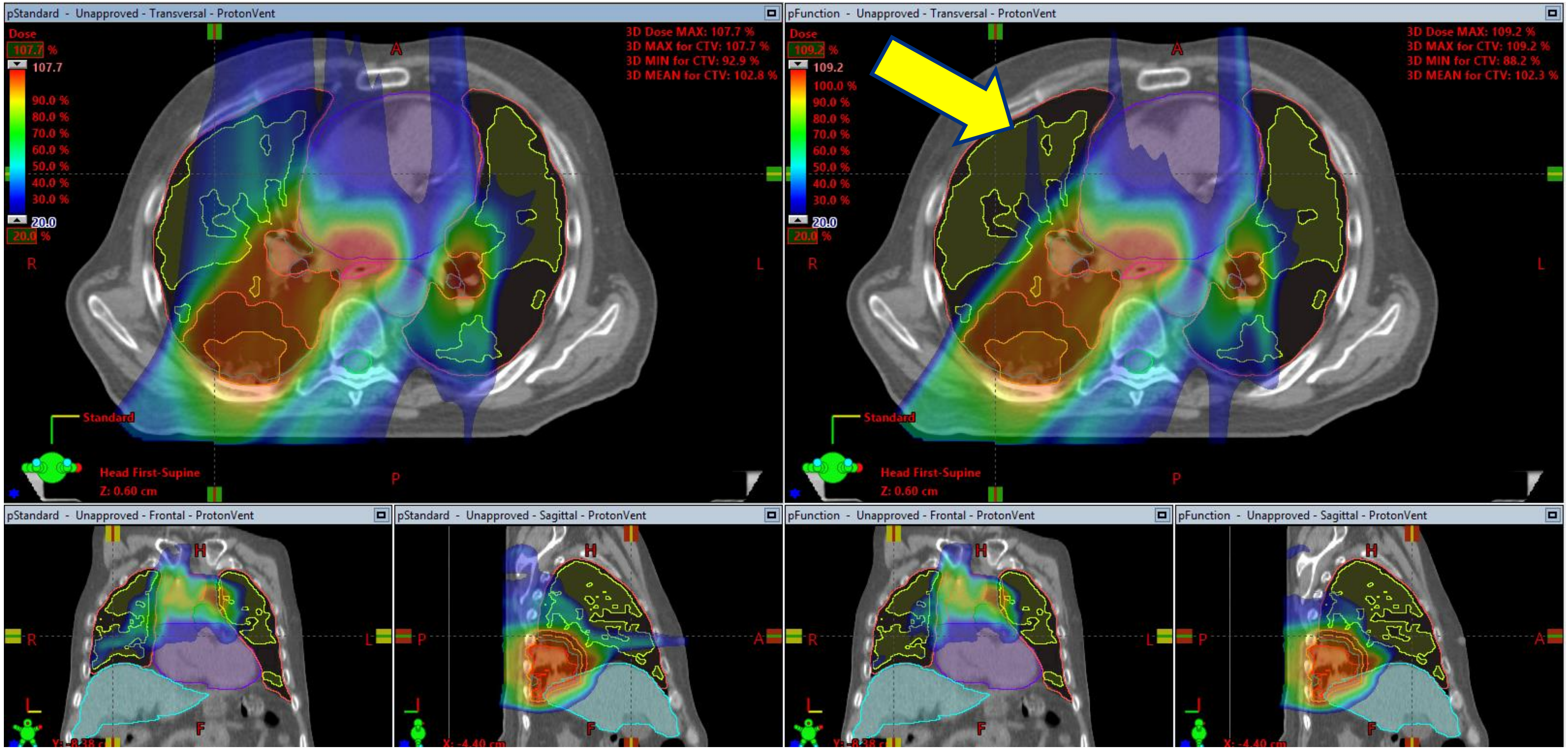
Functional Sparing Comparisons

- **Where does the functional dose sparing come from?**



Standard IMPT **Functional IMPT**

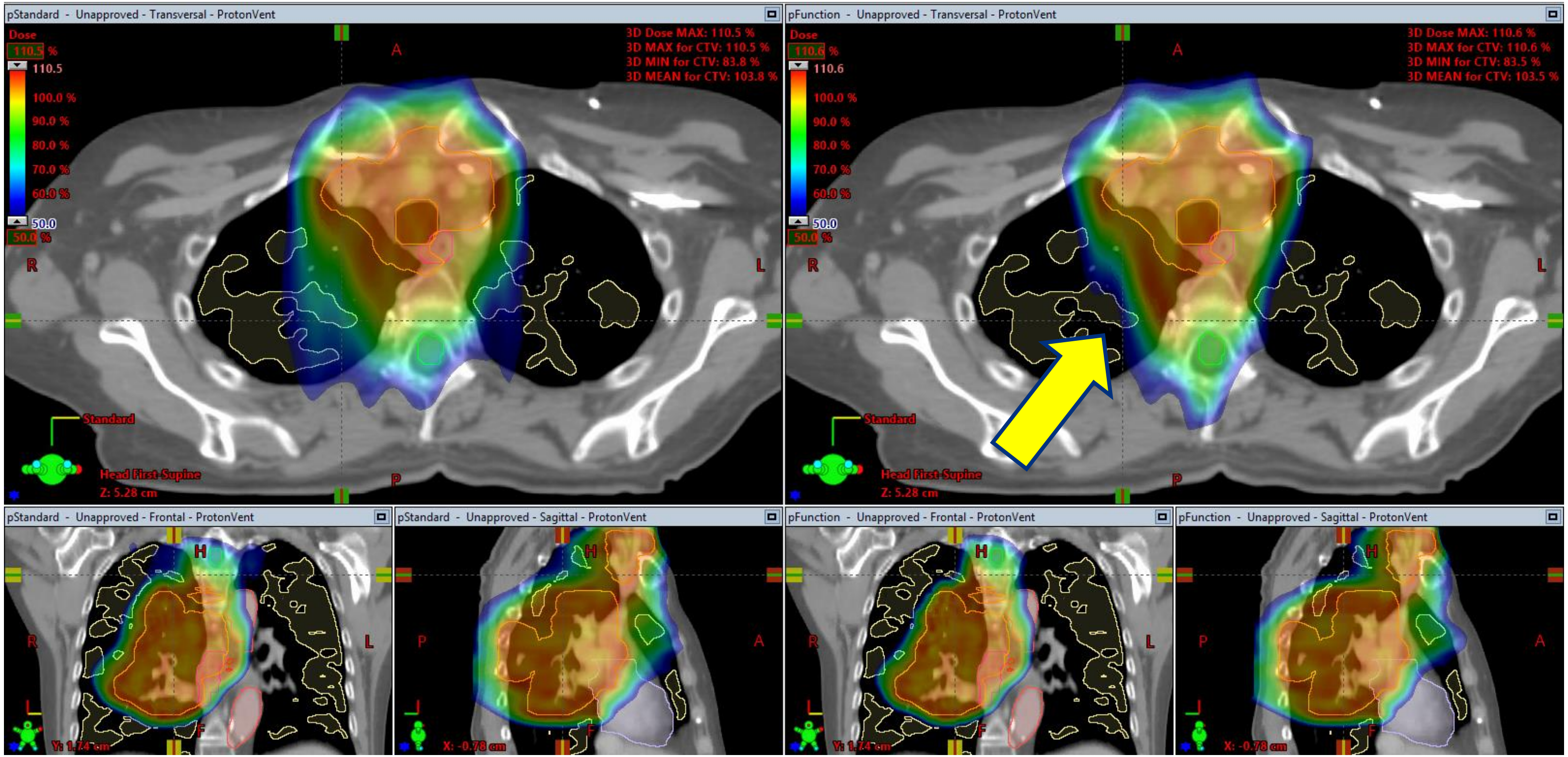
Functional Sparing Comparisons



Standard IMPT

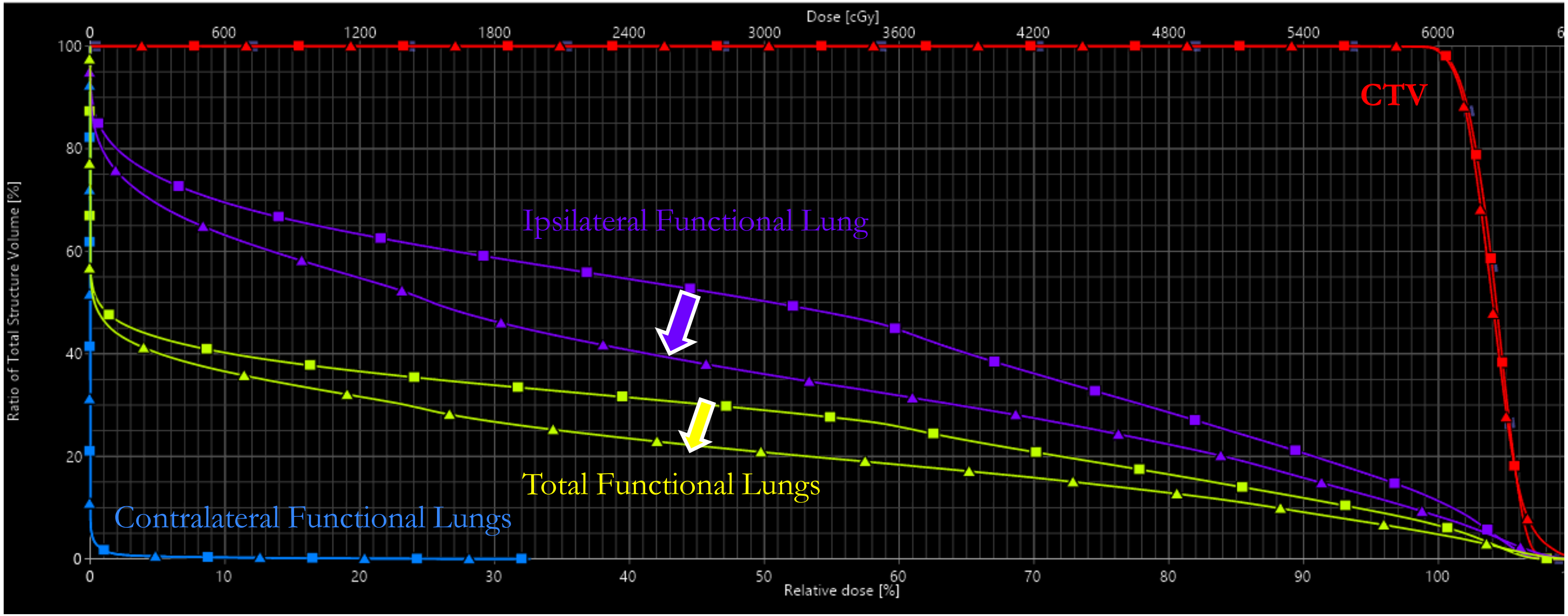
Functional IMPT

Functional Sparing Comparisons



Standard IMPT **Functional IMPT**

Functional Sparing Comparisons



Prediction for Radiation Pneumonitis

International Journal of Radiation Oncology*Biology*Physics
Volume 86, Issue 2, 1 June 2013, Pages 366-371

Physics Contribution

Use of 4-Dimensional Computed Tomography-Based Ventilation Imaging to Correlate Lung Dose and Function With Clinical Outcomes

Yevgeniy Vinogradskiy PhD [*], Richard Castillo PhD [†], Edward Castillo PhD [‡,§], Susan L. Tucker PhD [‖], Zhongxing Liao MD [‡], Thomas Guerrero MD, PhD [‡,§], Mary K. Martel PhD [†]

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https://doi.org/10.1016/j.ijrobp.2013.01.004

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International Journal of Radiation Oncology*Biology*Physics
Volume 99, Issue 2, 1 October 2017, Pages 325-333

Physics Contribution

Evaluating the Toxicity Reduction With Computed Tomographic Ventilation Functional Avoidance Radiation Therapy

Austin M. Faught PhD [*], Yuya Miyasaka BS [†], Noriyuki Kadoya PhD [†], Richard Castillo PhD [‡], Edward Castillo PhD [§], Yevgeniy Vinogradskiy PhD [*], Tokihiro Yamamoto PhD [‖]

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https://doi.org/10.1016/j.ijrobp.2017.04.024

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Toxicity Reduction Analysis

Grade 2+ Toxicity			
Dose Metric for NTCP	Toxicity Probability of the Mean - VMAT Standard	Toxicity Probability of the Mean - VMAT Functional	Absolute Reduction [Range of Reduction]
fV20Gy	31.3% [5.9%-67.8%]	25.1% [5.5%-60.2%]	6.2% [-0.1%-13.1%]
fV30Gy	24.5% [9%-50.1%]	21.5% [8.5%-45.8%]	3% [0.1%-7.4%]
fVMLD	24.1% [11.9%-33.4%]	21.8% [11.4%-31.5%]	2.3% [-0.1%-5.5%]
Dose Metric for NTCP	Toxicity Probability of the Mean - IMPT Standard	Toxicity Probability of the Mean - IMPT Functional	Absolute Reduction [Range of Reduction]
fV20Gy	17.6% [4.4%-51.3%]	12.7% [3.9%-36.1%]	5.70% [0%-26%]
fV30Gy	19% [7.9%-47.5%]	15.7% [7.3%-35.9%]	3.30% [0%-15.3%]
fVMLD	14.6% [7.7%-25.4%]	12.9% [7.4%-21.3%]	1.80% [0%-5.9%]

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Toxicity Reduction Analysis

Grade 3+ Toxicity			
Dose Metric for NTCP	Toxicity Probability of the Mean - VMAT Standard	Toxicity Probability of the Mean - VMAT Functional	Absolute Reduction [Range of Reduction]
fV20Gy	15.5% [2.9%-40.4%]	12.1% [2.7%-34.2%]	3.4% [-0.1%-8.1%]
fV30Gy	11.3% [3.6%-27.8%]	9.7% [3.4%-24.7%]	1.6% [0%-4.4%]
fVMLD	11.1% [4.9%-16.4%]	9.8% [4.7%-15.3%]	1.3% [0%-3%]
Dose Metric for NTCP	Toxicity Probability of the Mean - IMPT Standard	Toxicity Probability of the Mean - IMPT Functional	Absolute Reduction [Range of Reduction]
fV20Gy	8.4% [2.2%-27.7%]	6% [2%-18.1%]	2.4% [0%-15.4%]
fV30Gy	8.4% [3.1%-25.9%]	6.7% [2.9%-18%]	1.7% [0%-10.2%]
fVMLD	6.2% [3.1%-11.8%]	5.4% [2.9%-9.6%]	0.8% [0%-3.2%]

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Summary

- **4DCT based lung functional avoidance proton therapy is clinically feasible**

- **Further dosimetric gains to functional lungs**

- **Reduce lung toxicity**

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Thank you