Automating Treatment Planning Process: Stanford Experience

Nataliya Kovalchuk, PhD

Yong Yang, PhD

Eric Simiele, PhD

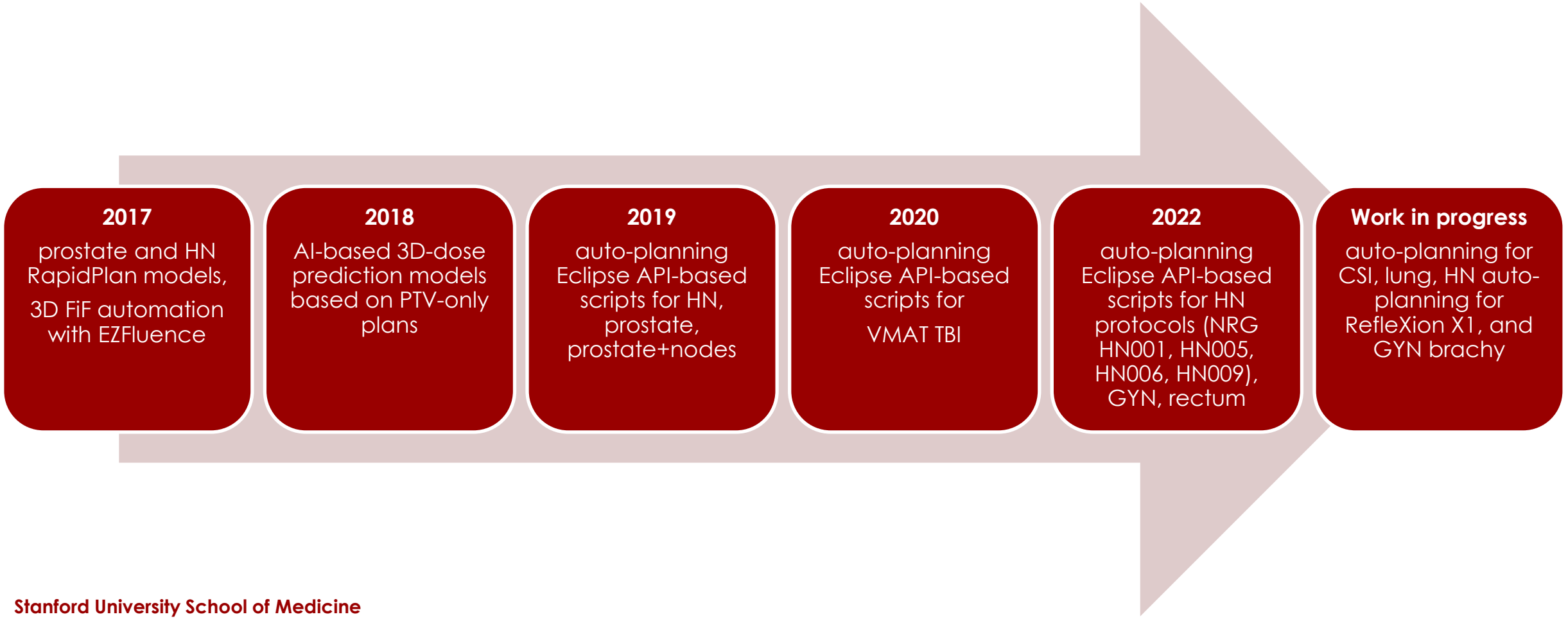
Nataliya Kovalchuk, PhD, Yong Yang, PhD, and Eric Simiele, PhD

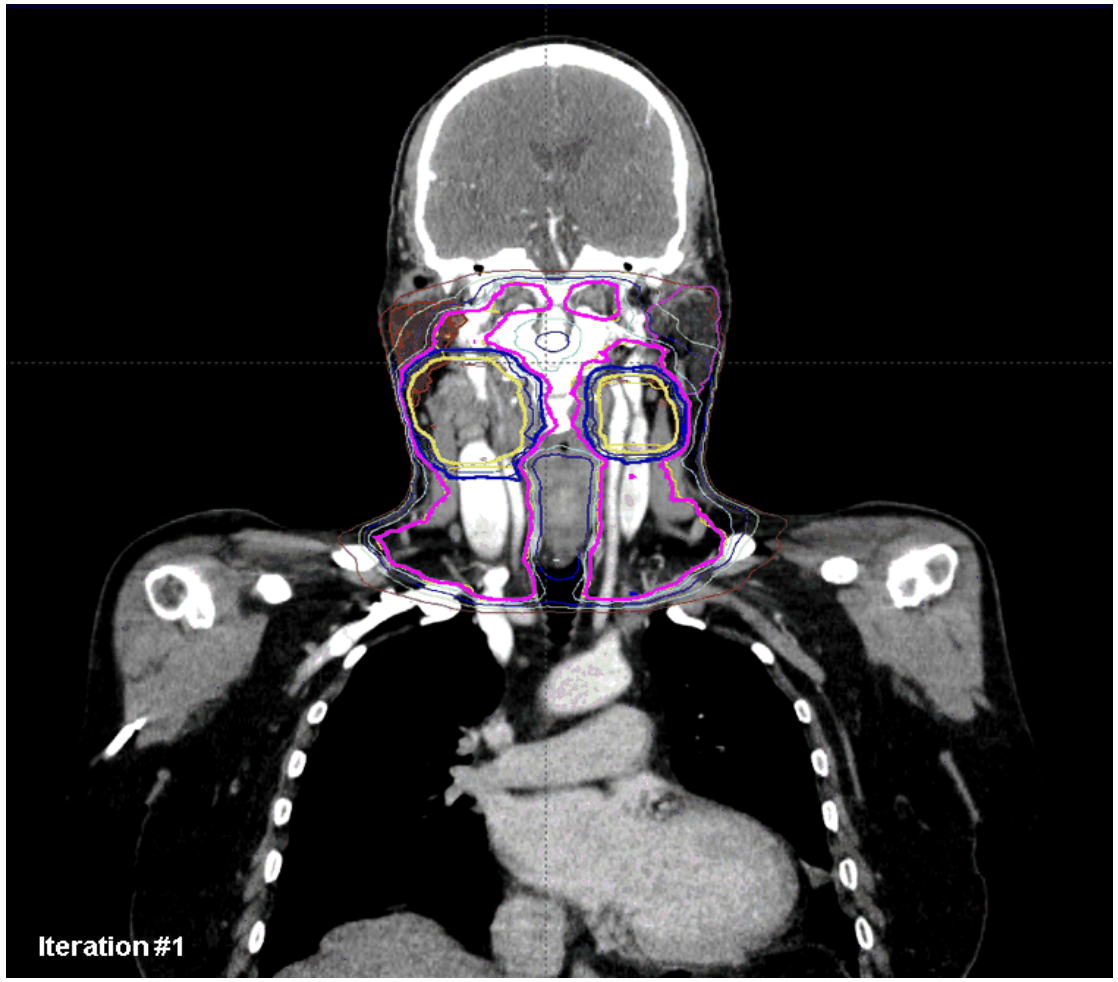
Stanford University School of Medicine

Disclosures

- None

Stanford's Path to Auto-Planning





Automating Prostate/HN/GYN/Rectum Planning

3D Dose Prediction using Deep CNN

Physics in Medicine & Biology

PAPER

Incorporating dosimetric features into the prediction of 3D VMAT dose distributions using deep convolutional neural network

Ming Ma[1], Nataliya Kovalchuk[1], Mark K Buyyounouski[1], Lei Xing[1] and Yong Yang[1]

Published 20 June 2019 • © 2019 Institute of Physics and Engineering in Medicine

Physics in Medicine & Biology, Volume 64, Number 12

Citation Ming Ma *et al* 2019 *Phys. Med. Biol.* **64** 125017

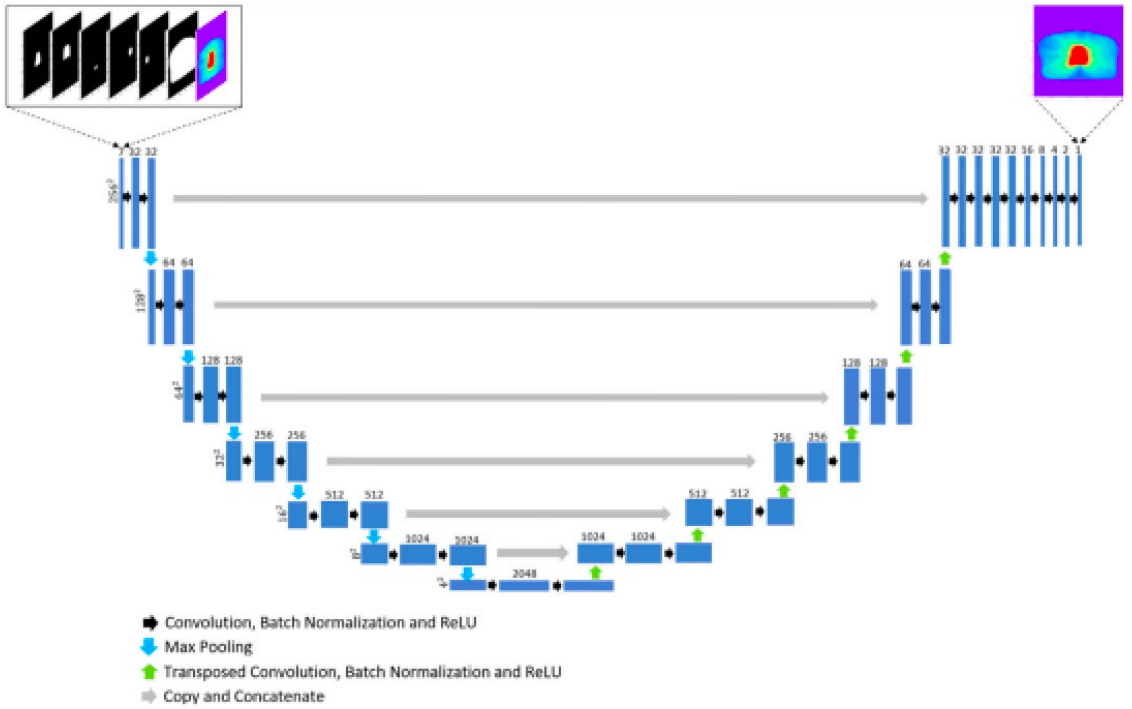
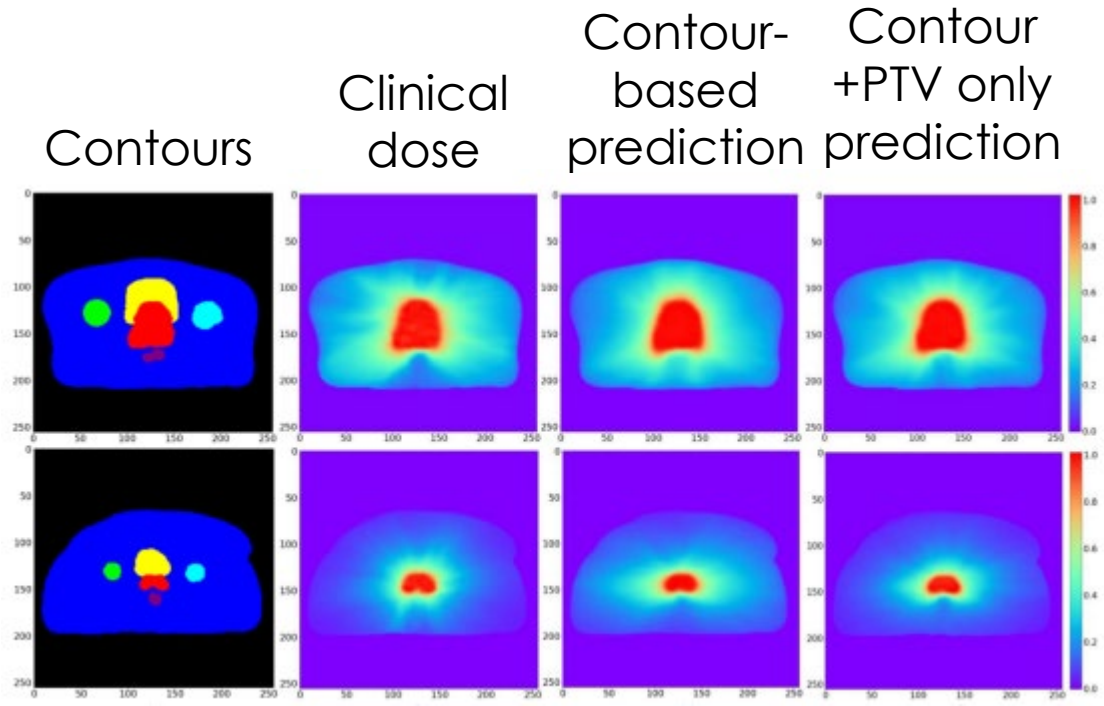


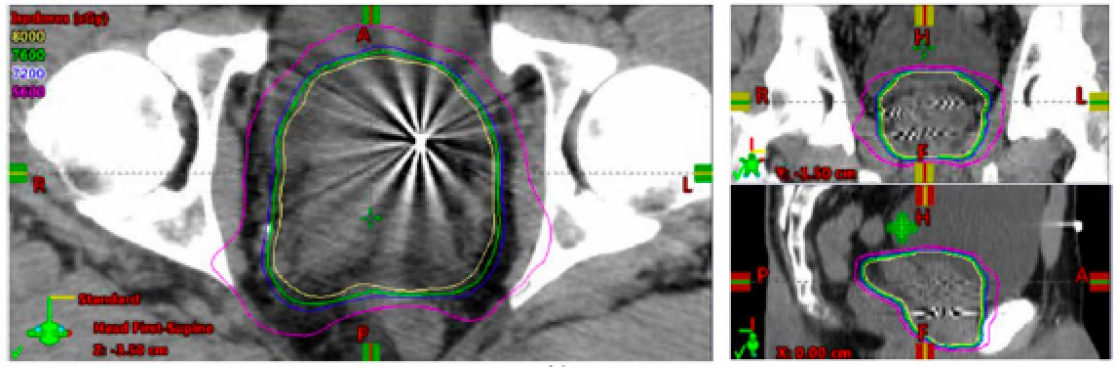
Figure 1. The architecture of the deep CNN for dose prediction.

3D Dose Prediction using Deep CNN

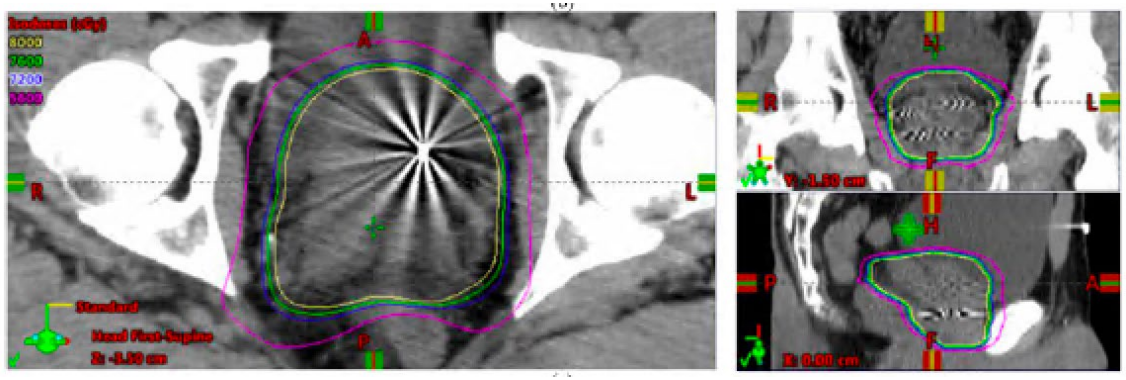


Mean Sum of Absolute Residuals (SARs) for DVHs

Organ	Contour-based prediction	Contour+PTV only prediction
PTV	0.036	0.007
Bladder	0.047	0.035
Rectum	0.068	0.067



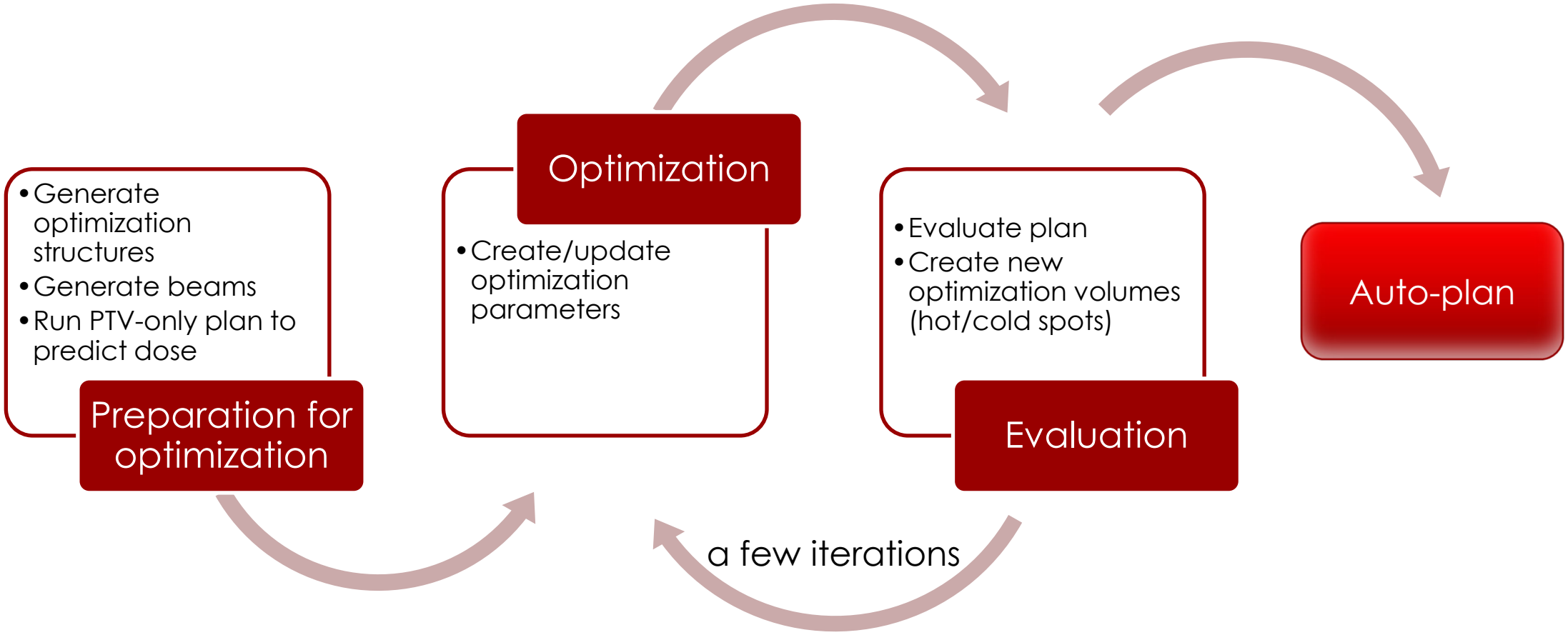
Clinical plan



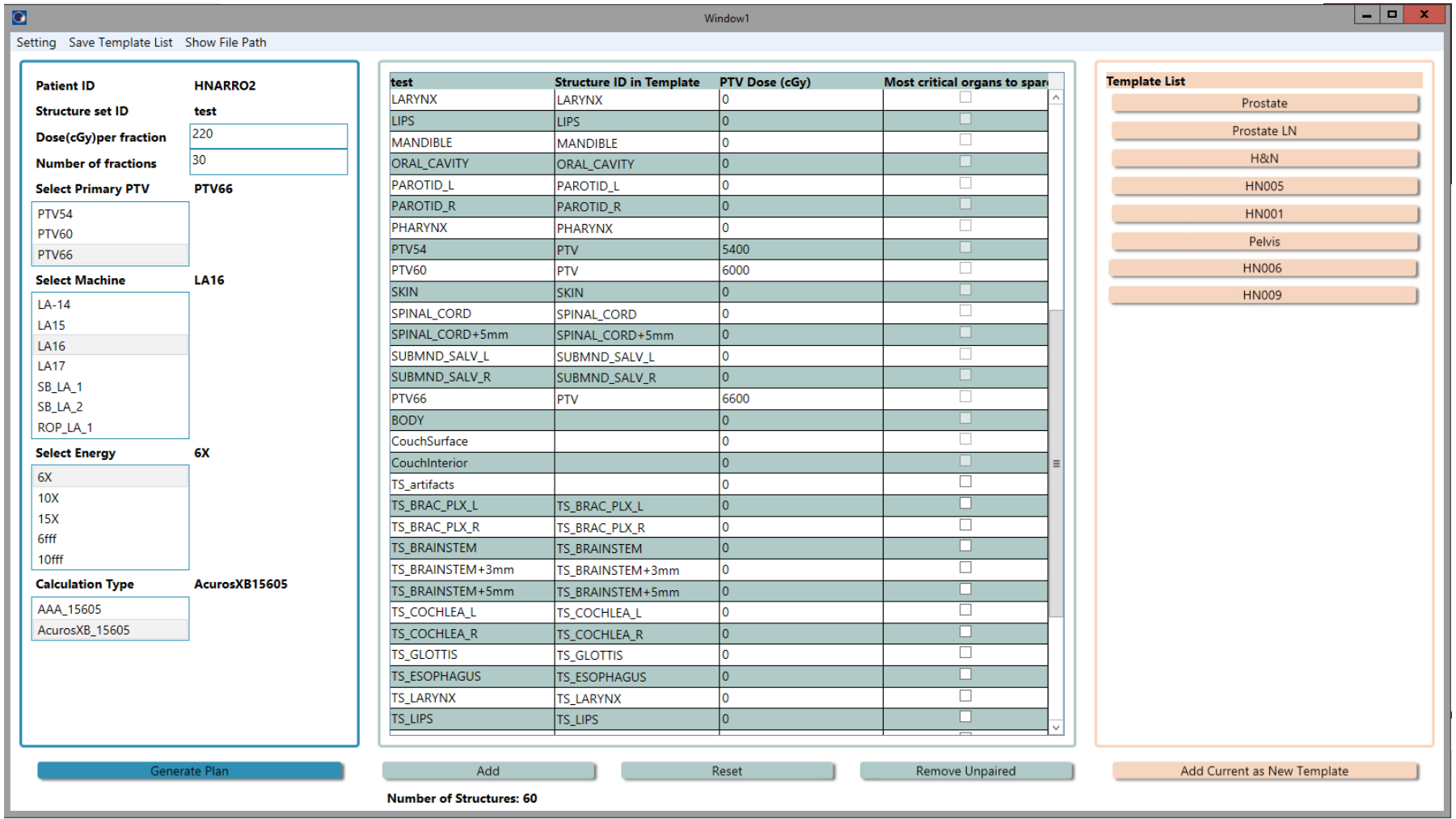
Predicted plan

Ma et al, (PMB 2019)

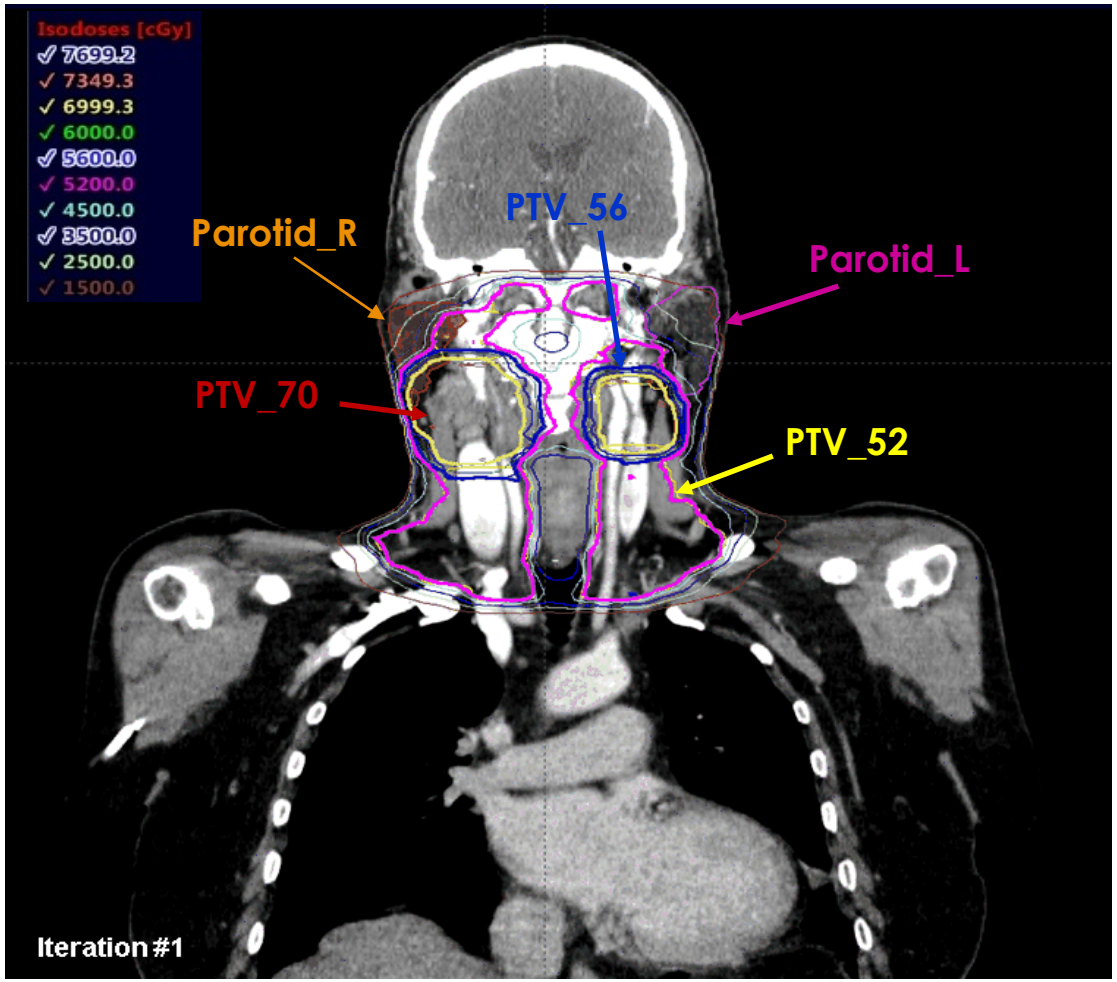
Stanford Auto-planning Solution



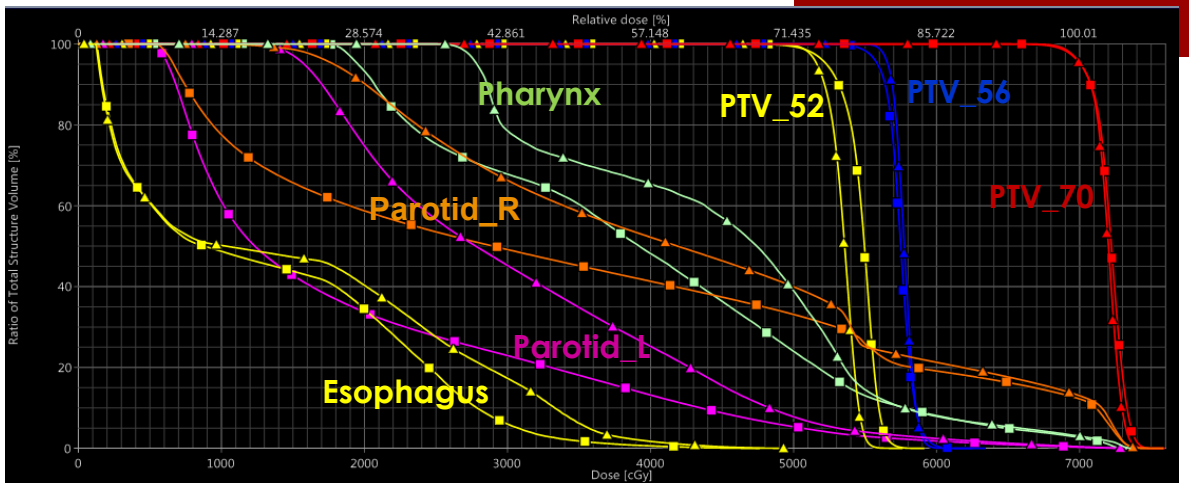
Auto-planning Script GUI

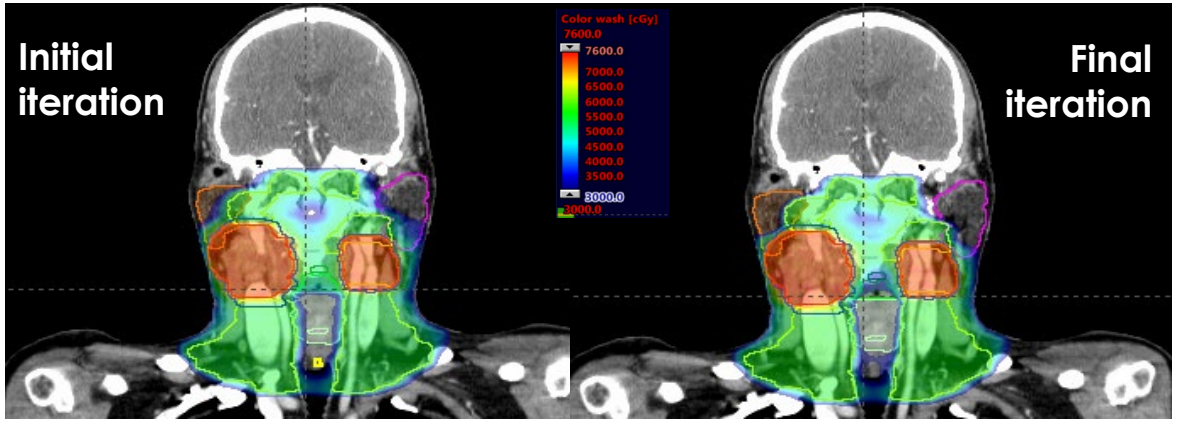


Head and Neck Plan Example



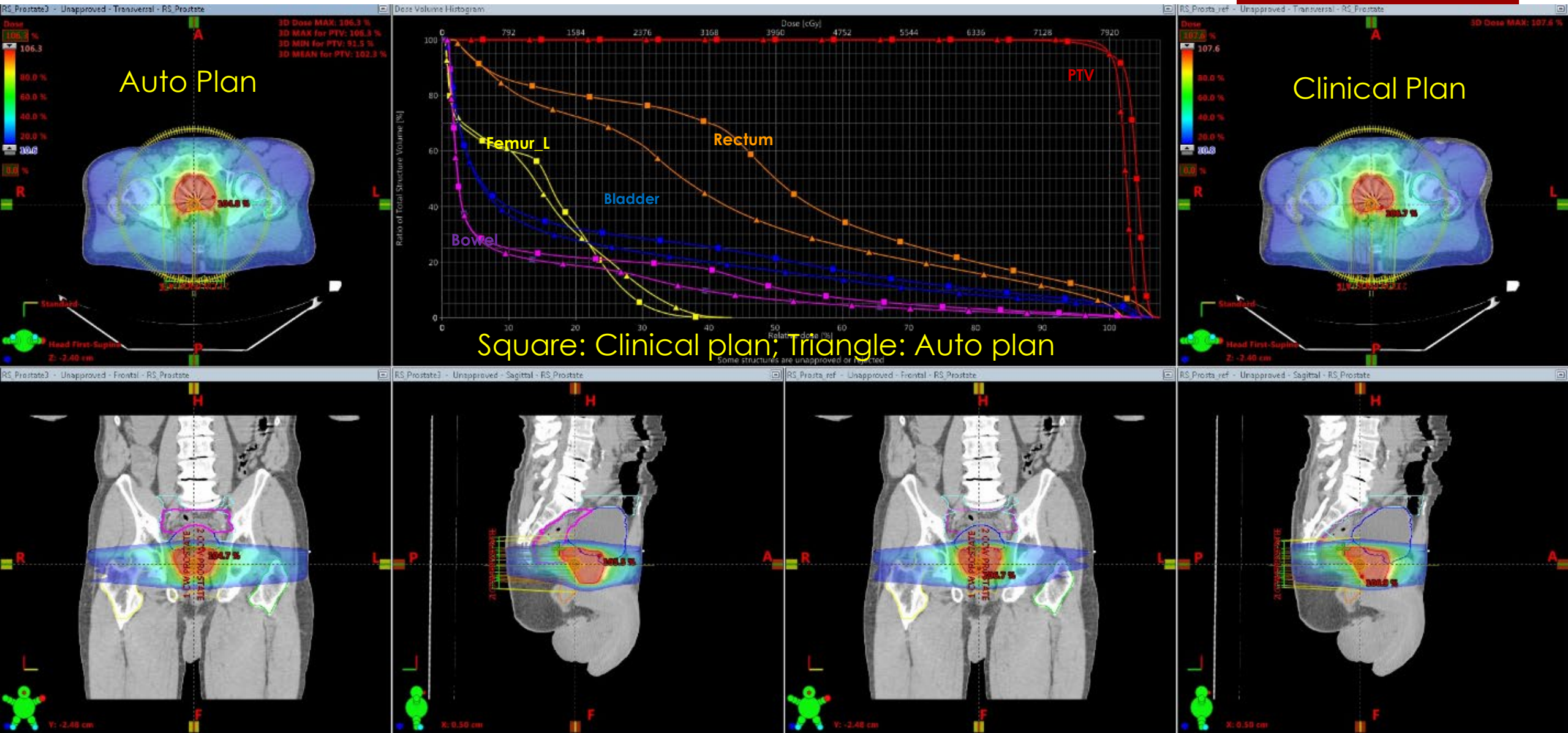
Isodose improvements with successive iterations



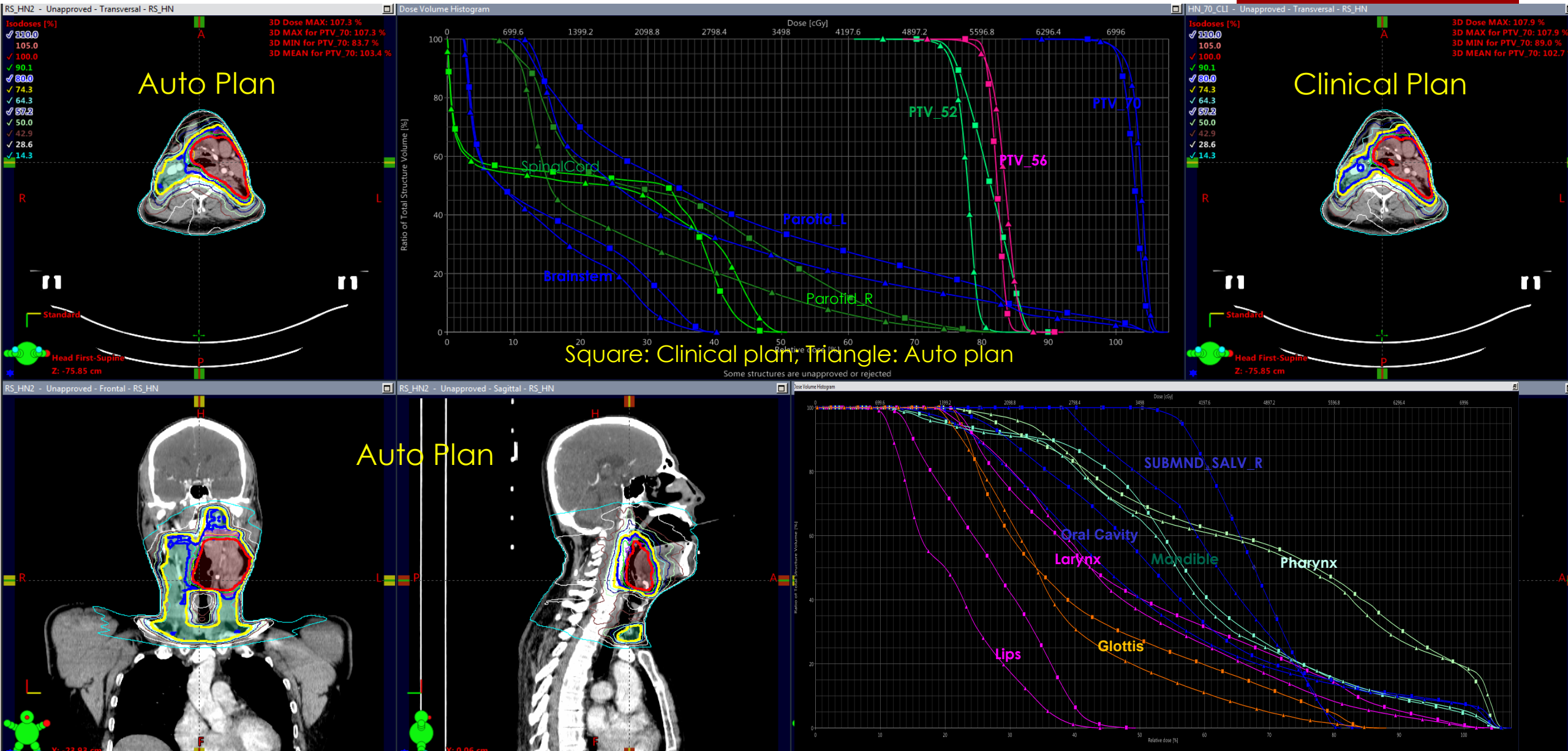


DVH (top) and isodose comparison between initial and final optimization results

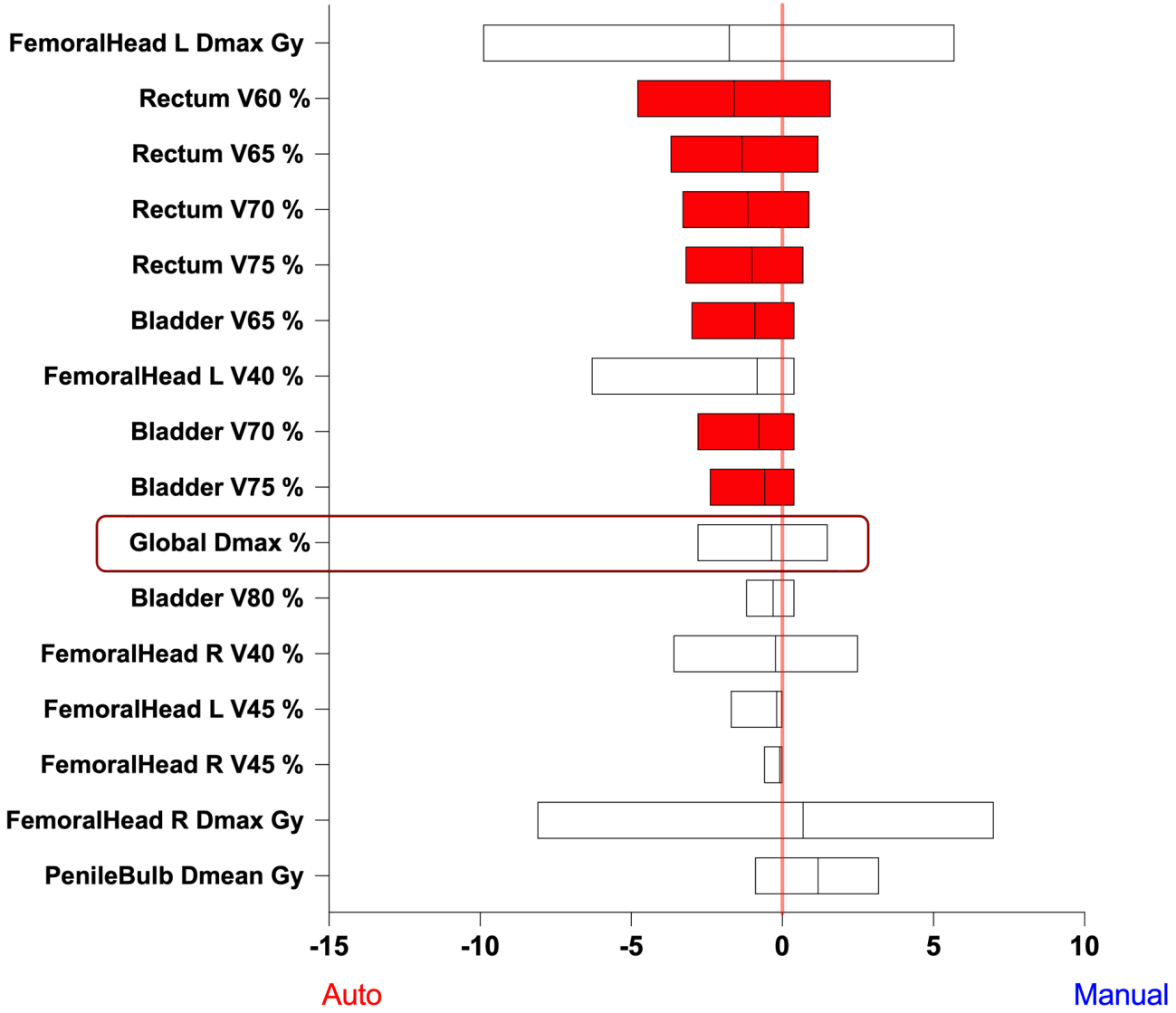
Prostate Plan Comparison: Auto vs Manual Clinical



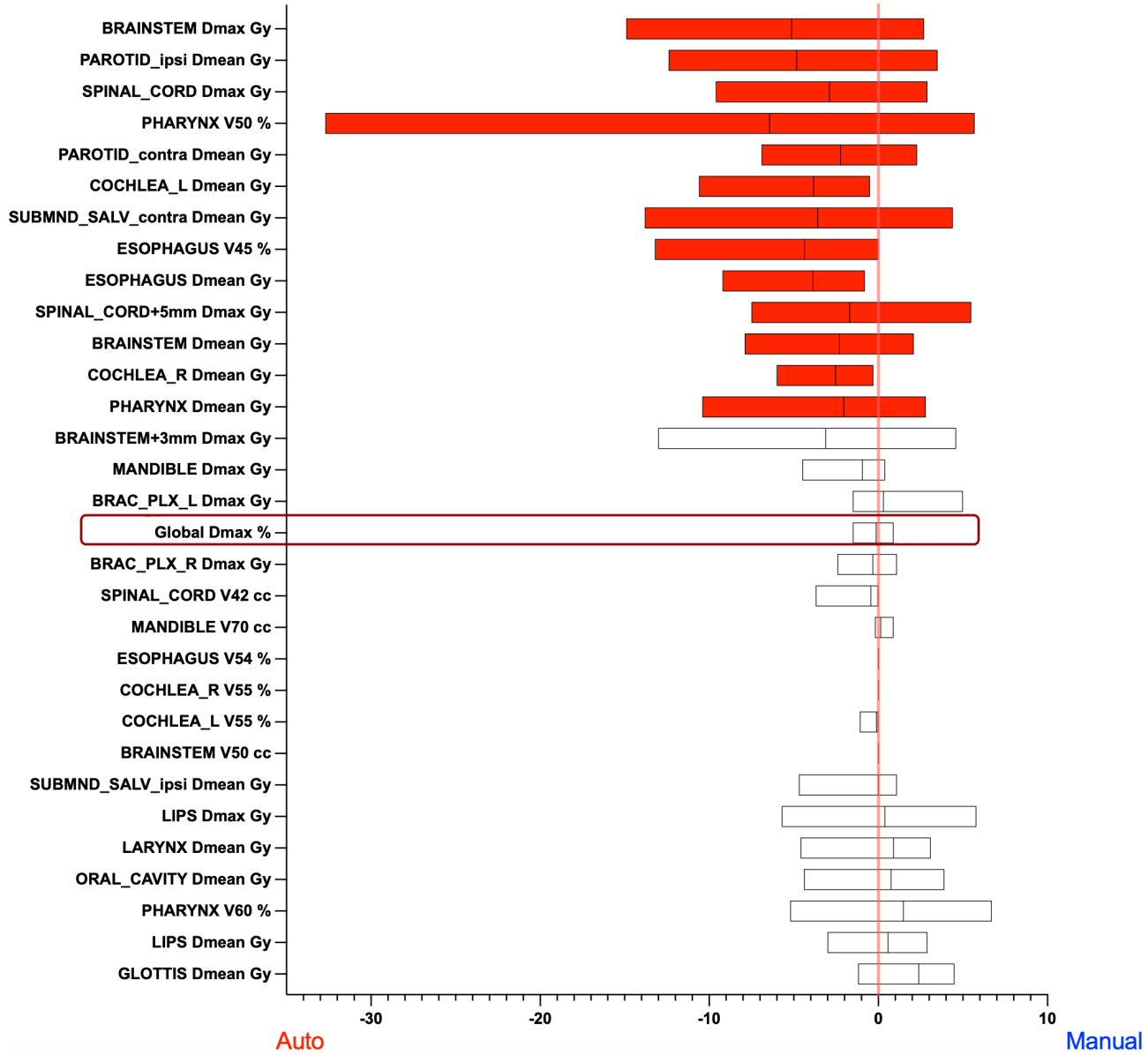
HN Plan Comparison: Auto vs Manual Clinical



Evaluation of Prostate Auto-plans

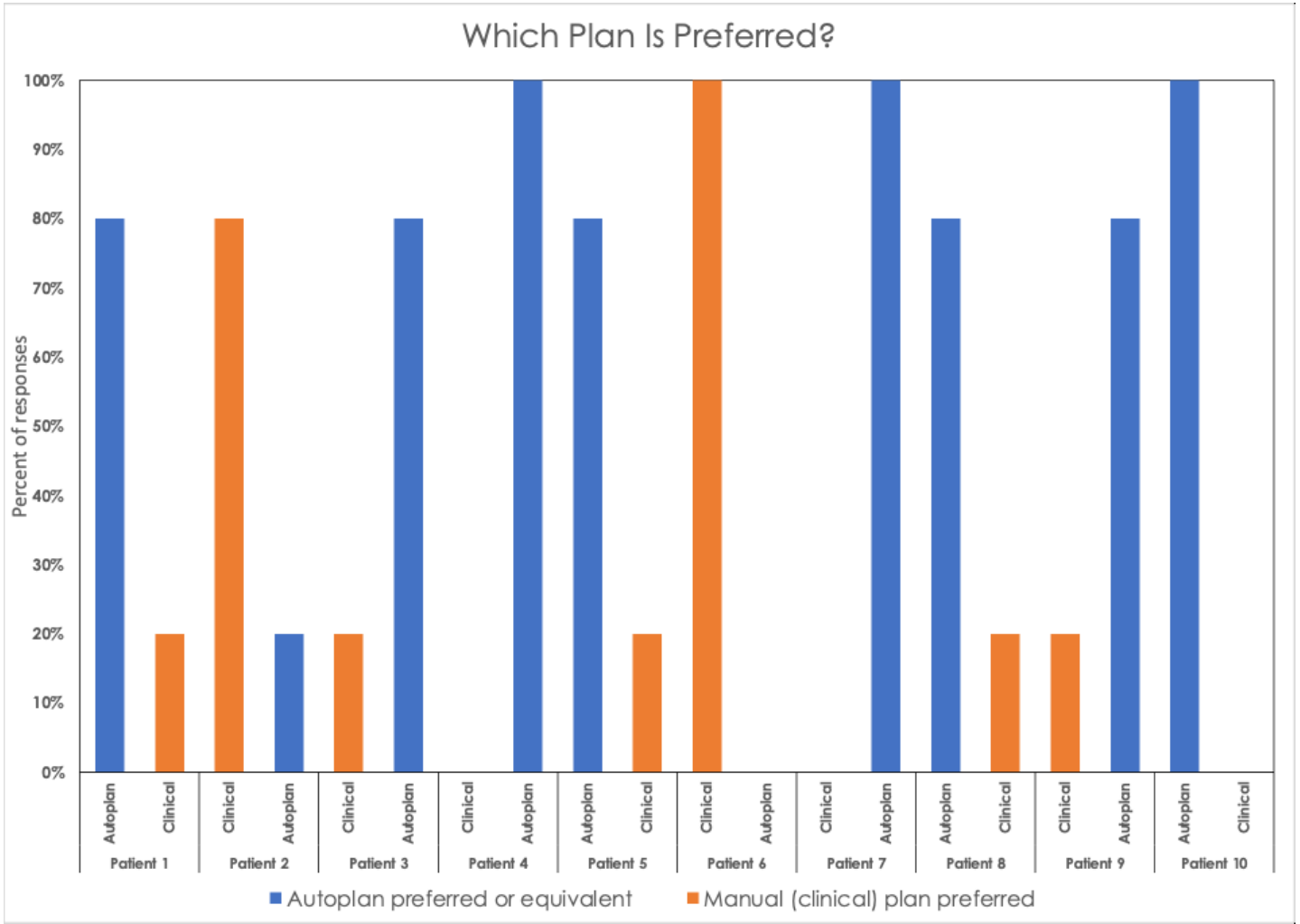


Evaluation of HN Auto-plans

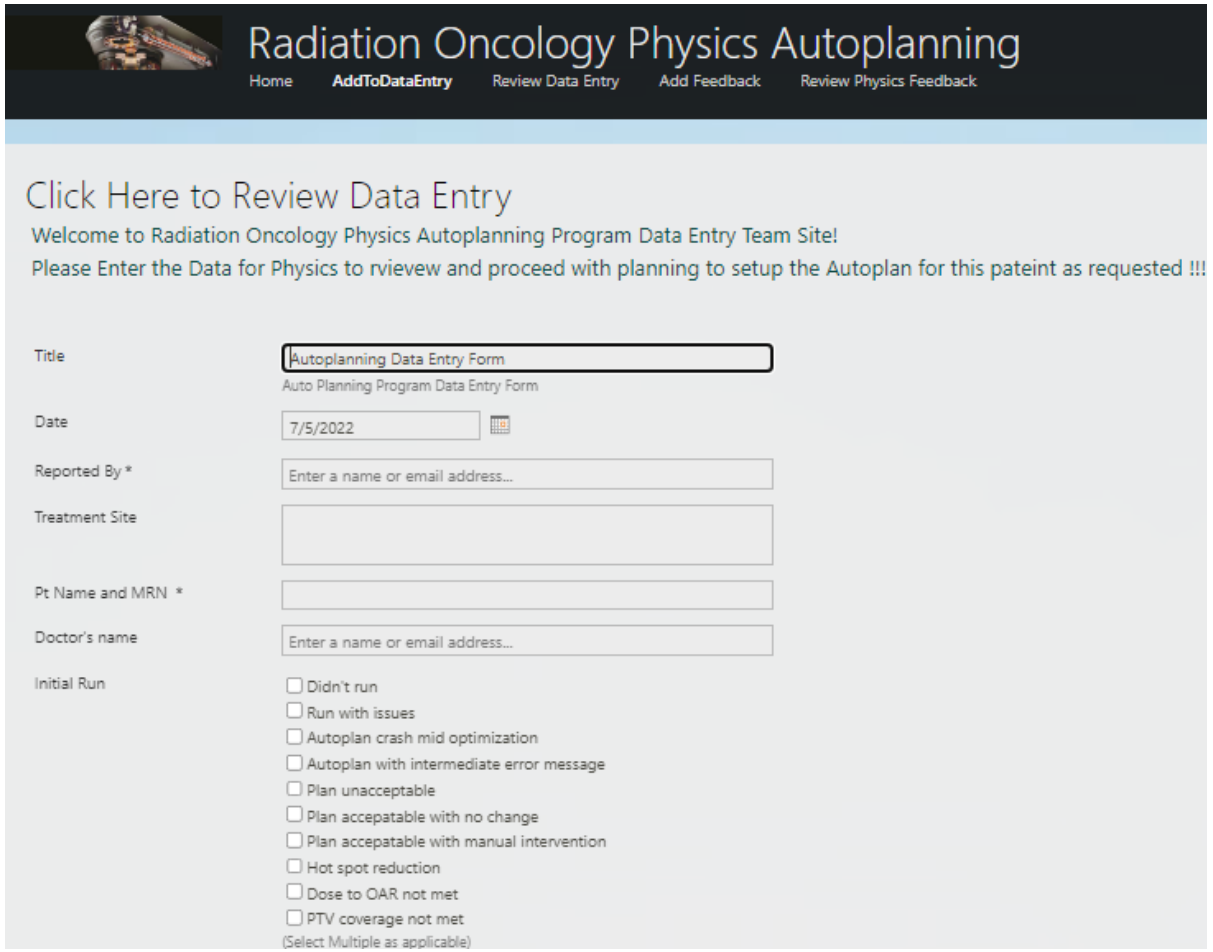


Physicians HN Plan Evaluation Results

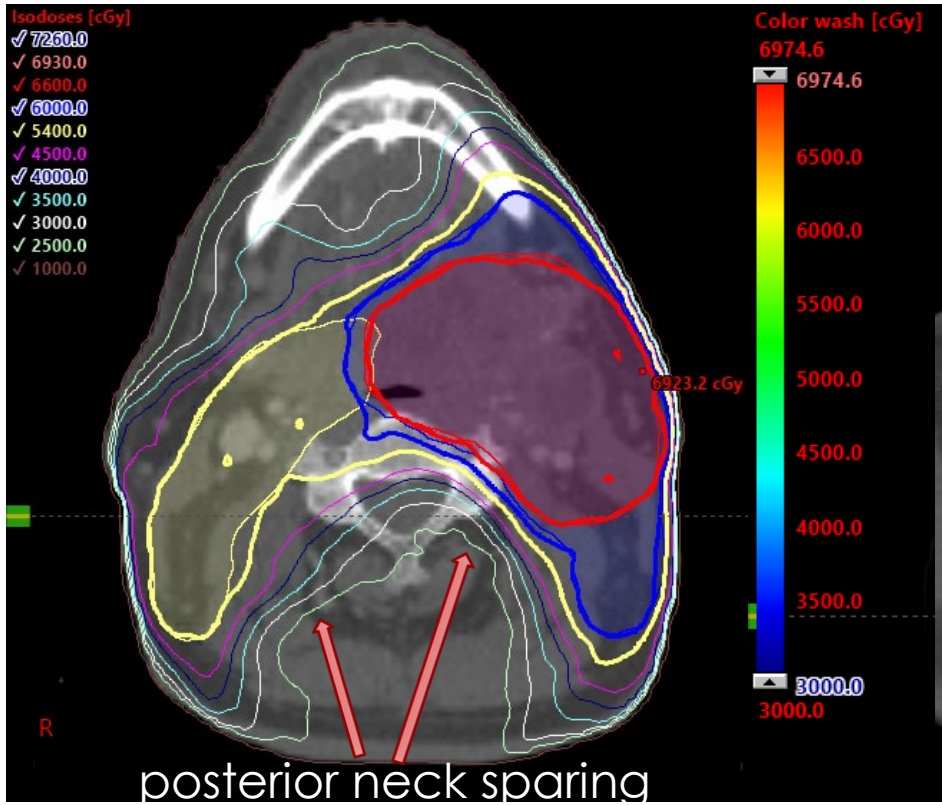
- 20 anonymized HN plans (10 auto-planned and 10 manually planned) were evaluated by 5 physicians for 10 patients
- Clinical Acceptability:
  - Auto-plans: 47 (94%) – yes, 3 – no
  - Manual clinical plans: 43 (86%) – yes, 4 – no, 3 - borderline
- Preference to use for treatment:
  - 7 auto-plans
  - 1 equivalent
  - 2 manual clinical plans



Updating Auto-planning Scripts following Physician/Dosimetrist Feedback

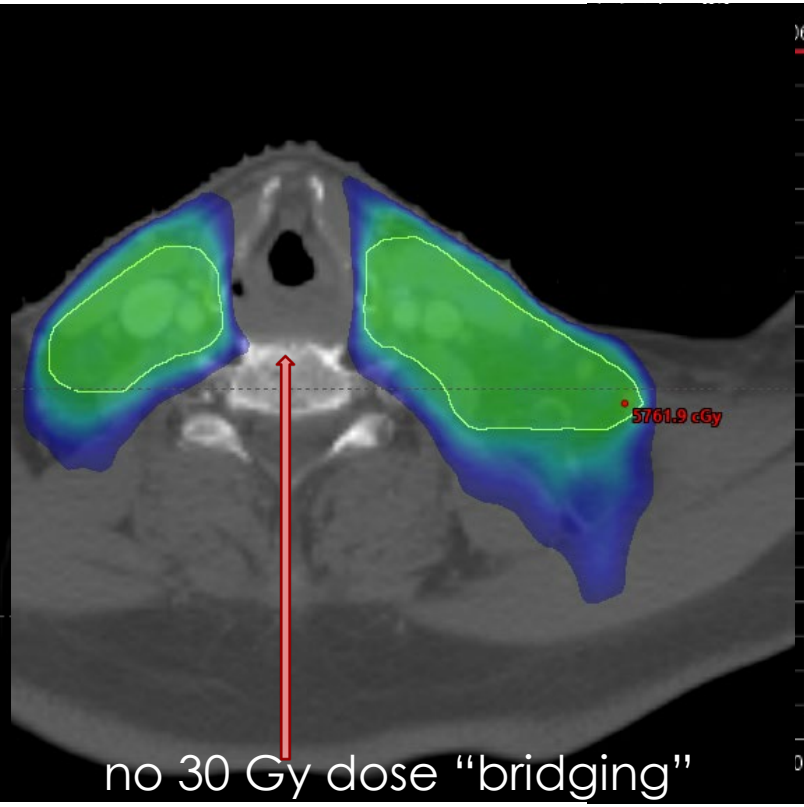


Incorporated All MDs Requests into One Approach



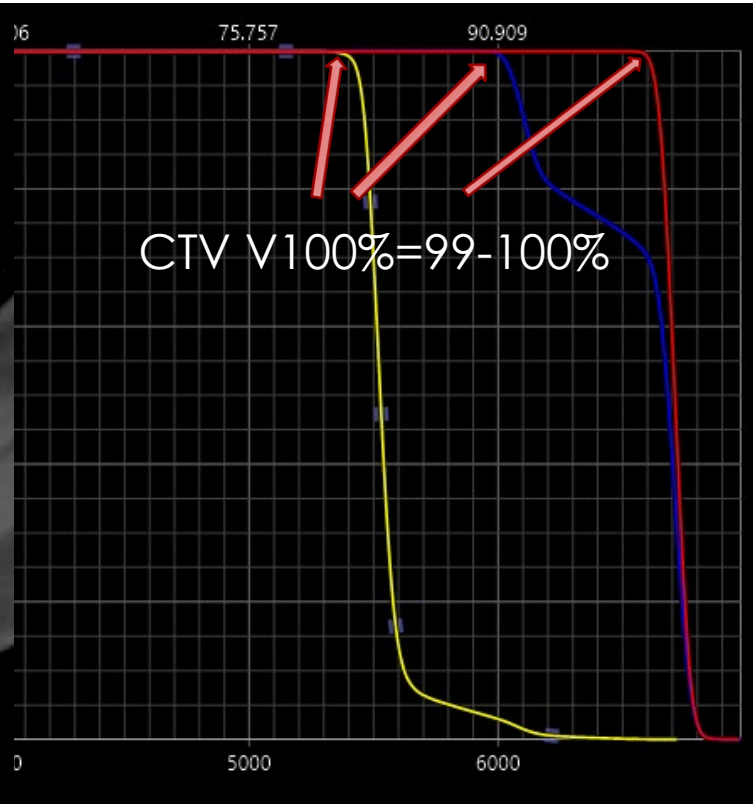
posterior neck sparing

Physician 1



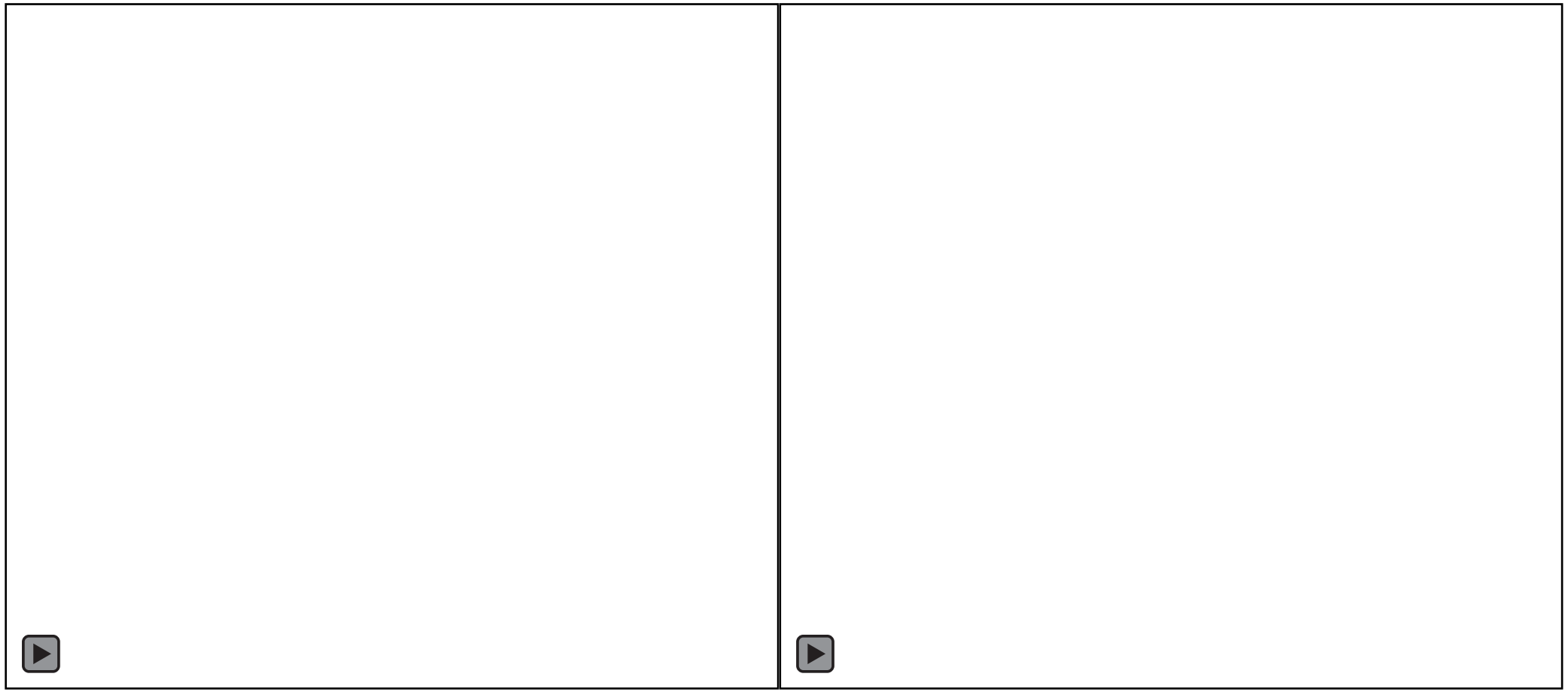
no 30 Gy dose "bridging"

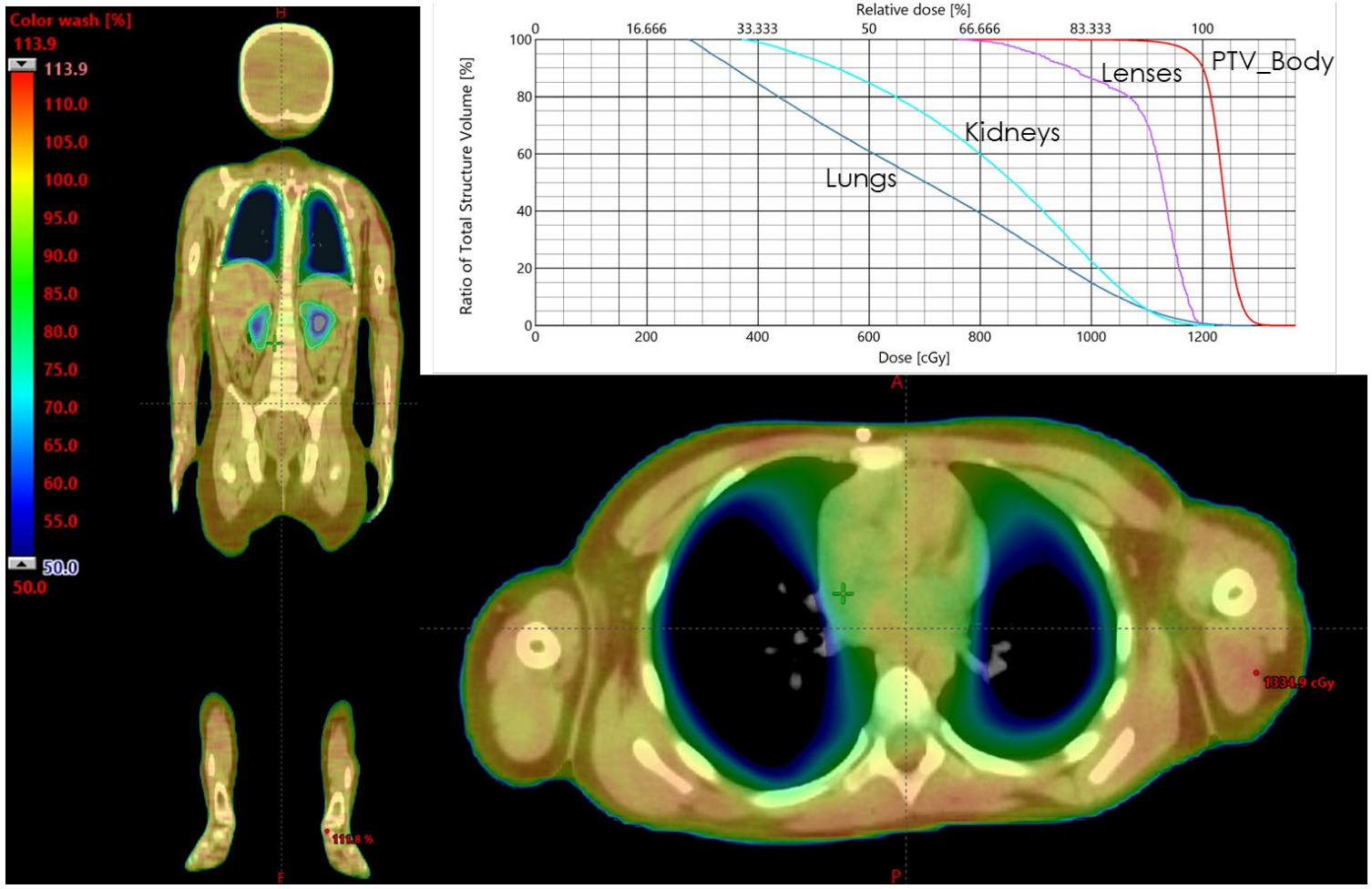
Physician 2



Physician 3

NRG HN Trials Auto-planning: HN001, HN005, HN006, HN009

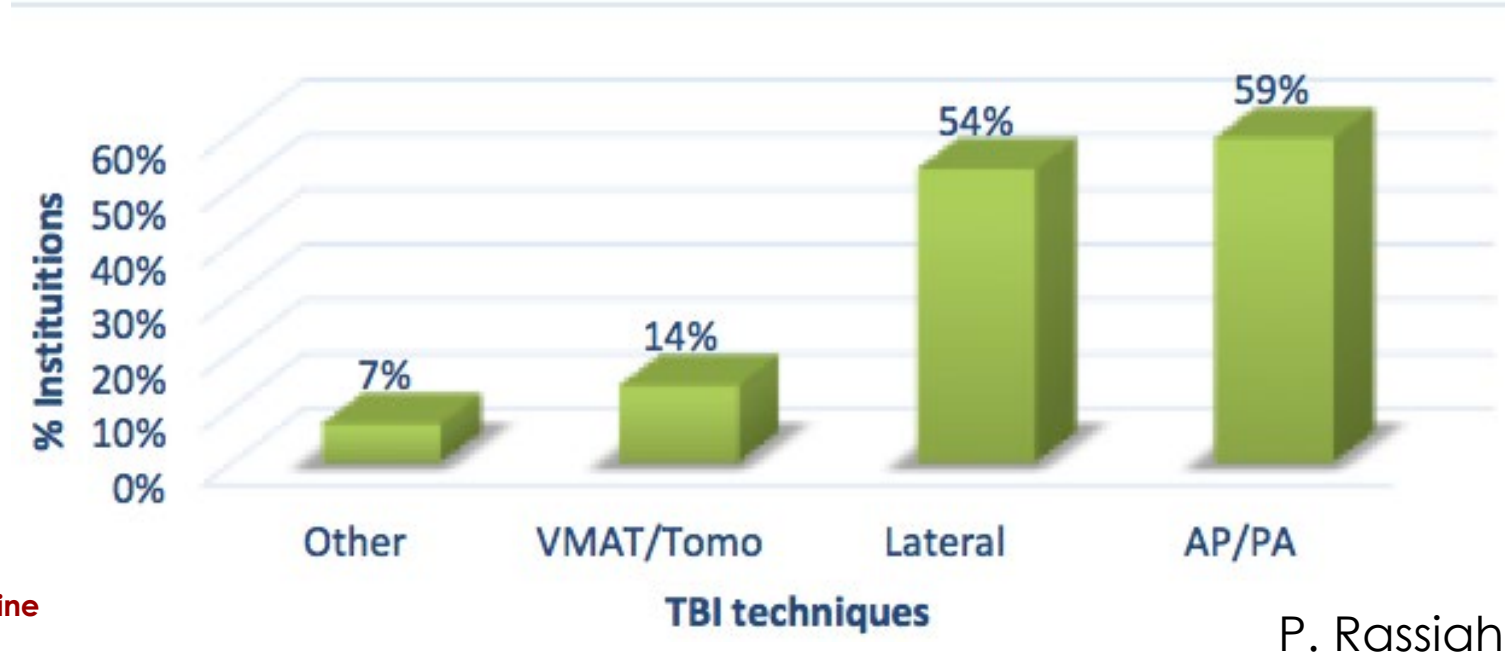




Automating VMAT TBI

Children's Oncology Group (COG) survey

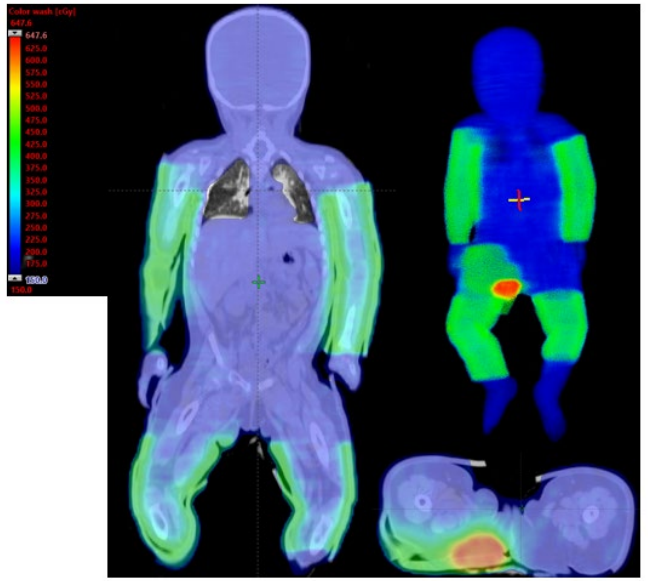
- In 2020-2021, COG TBI workgroup conducted survey of 152 institutions on TBI techniques for physicists and physicians
- 100% of physicians would like to reduce the lung dose for myeloablative regimens
- 75% of physicians (n=85) would like to introduce VMAT or Tomo TBI in their clinics
- Only 7 US institutions adapted VMAT TBI and 3 institutions adapted Tomo TBI

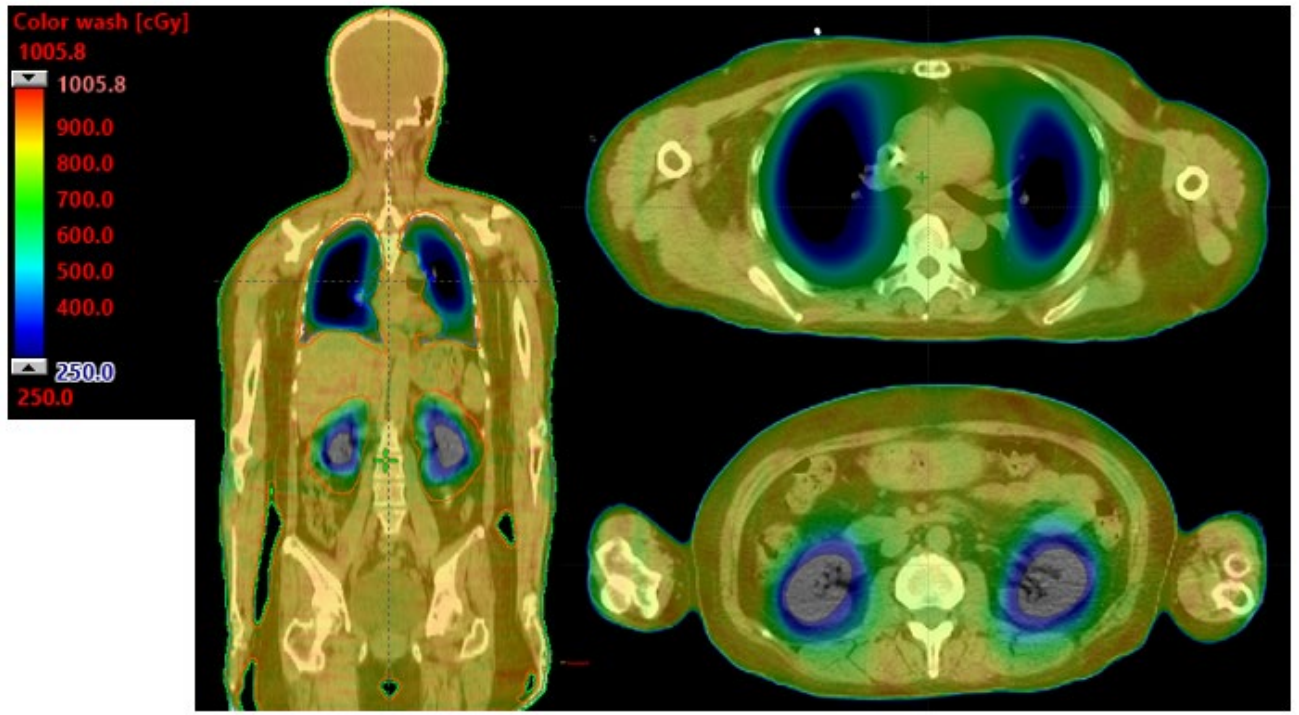


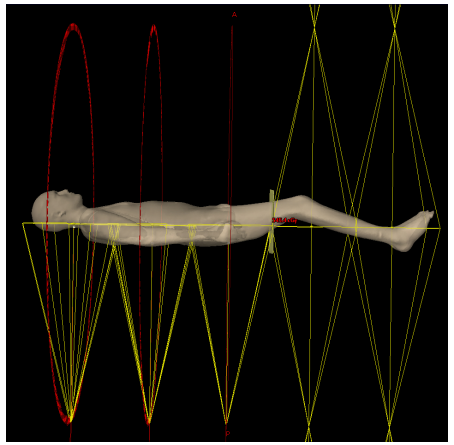
P. Rassiah et al (IJROBP 2021)

Stanford VMAT TBI Experience

- Introduced VMAT TBI in Oct 2019
- In 2020 created automated planning scripts and shared with the public
- Treated >50 VMAT TBI patients to date







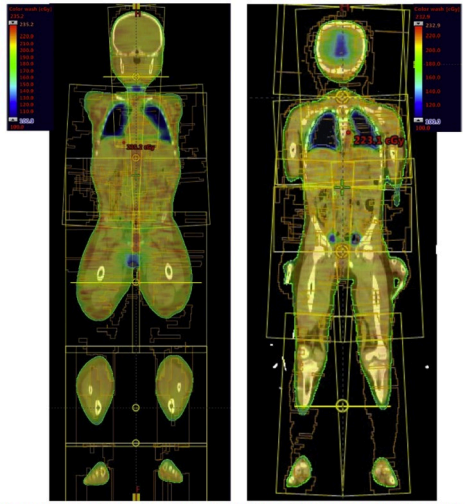
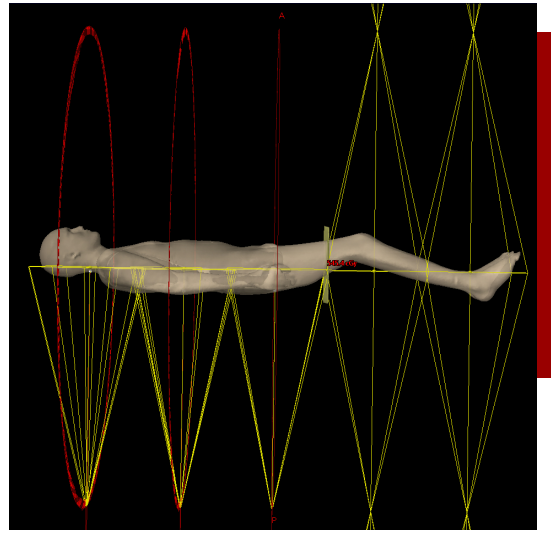


Figure 1 Volumetric modulated arc therapy (VMAT) total body irradiation (TBI) beam arrangement and dose distribution (color wash) on coronal view for boy (*left*) and girl (*right*).



Stanford VMAT TBI: SIM

- Full body scan in whole body bag on Siemens PET/CT scanner with 4-5 mm slice thickness
- Knee fix, foot fix, arms tight to the body
- Matchline b/w HFS and FFS determined at SIM:
  - Patient height ≤ 115 cm – VMAT only (3 isocenters)
  - Patient height > 115 cm – VMAT (3 isocenters) + AP/PA(1-2 isocenters) on Spinning Manny

Figure 1. In-house developed rotational couch-top enabling patient position transition from HFS to FFS.

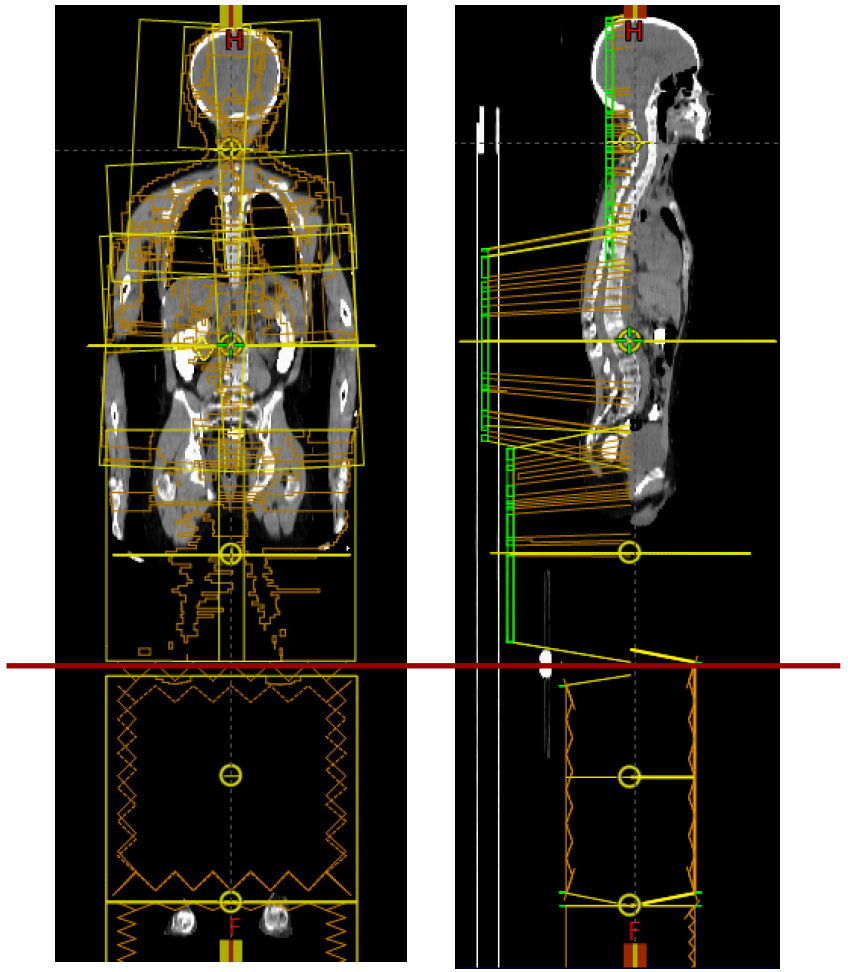
Stanford VMAT TBI: Contouring

- **Myeloablative regimen (12-13.2Gy):** sparing lungs, kidneys, lenses
- **Reduced Intensity Conditioning (2-4Gy):** sparing lungs, kidneys, lenses, brain, thyroid, ovaries/testes
- PTV_Body = (Body-3 mm) – (Lungs+3 mm) – Kidneys – [other OARs]
- 5 mm flash/bolus is added during optimization

Name of Structure	Description
Human_Body	Search BODY in Eclipse
Human_Body-0.3cm	0.3 cm inner margin
Lungs	Lungs, remove tiny islands
Lungs_Eval	Lungs – 1cm
Lungs-2cm	Lungs – 2cm
Kidney_R/L, Kidneys	Kidneys, remove tiny islands
Kidneys-1cm	Kidneys-1cm
Ovary_R/L	Ovaries
Scrotum, Testes	Scrotum, testes
Brain	Brain, remove tiny islands
Brain-0.5cm	Brain-0.5cm
Brain_Eval	Brain-1cm
Brain-2cm	Brain-2cm
Brain-3cm	Brain-3cm
PTV_Body	(Human_Body-0.3cm) – Kidneys– (Lungs+0.3cm) – (Ovaries+1cm include bone) or (Scrotum+2cm) – (Brain-0.5cm)
Matchline	Plane at the level of pivot bolt center
TS_PTV_VMAT	Cut PTV_Body at matchline, crop 0.5cm from skin
Bowel	Bowel bag
Lens_R/L	Lenses
Skin	3mm from Human Body

Stanford VMAT TBI: Beam Placement

- 3 VMAT isocenters in HFS – 6MV/10MV (head, chest, pelvis)
- 1-2 AP/PA isocenters in FFS – 6MV (upper legs, lower legs)
- Pelvis VMAT iso and Upper Leg AP/PA iso's are equidistant from matchline
- >=2-5 cm overlap in junctions for VMAT
- Head iso (3-4 arcs)
- Chest iso (3-4 arcs)
- Pelvis iso (2-4 arcs)
- Skin match for AP/PA
- AP/PA fields have 90^0 coll for FiF



Stanford VMAT TBI: Optimization

- FiF for AP/PA
- Set AP/PA dose as base for VMAT optimization
- Optimizer auto-feathers beam junctions in VMAT
- Dose rate at 100-200 MU/min for Head/Chest iso to keep average dose rate <20 cGy/min for lungs
- AAA v15.6, 2.5mm dose grid

Structure	Dosimetric parameter	Limit (2 Gy Rx)	Limit (12 Gy Rx)
PTV_Body	D90%>=	200 cGy (100%)	1200 cGy (100%)
	Dmax<=	240 cGy (120%)	1440 cGy (120%)
	V110%<=	5%	5%
Lungs_Eval (Lungs-1cm)	Dmean<=	80 cGy (40%)	480 cGy (40%)
Lungs	Dmean<=	110 cGy (55%)	660 cGy (55%)
Kidneys	Dmax<= Dmean<=	210 cGy (105%) 120 cGy (60%)	1260 cGy (105%) 720 cGy (60%)
Bowel	Dmax<=	210 cGy (105%)	1260 cGy (105%)
Lenses	Dmax<=	180 cGy (90%)	1080 cGy (90%)
Testes/ovaries	Dmean<= Dmax<=	50 cGy (25%) ALARA (required <100 cGy)	
Brain_Eval (Brain-1cm)	Dmean<=	150 cGy (75%)	
Thyroid	Dmean<=	150 cGy (75%)	

Stanford VMAT TBI: Dose Distribution

- PTV D90%=100%
- PTV Dmax = 114.6%
- PTV D1cc = 111.5%
- Lungs Dmean = 41.8%
- Ovaries Dmean = 30%
- Kidneys Dmean = 64.1%
- Brain Dmean = 74.9%

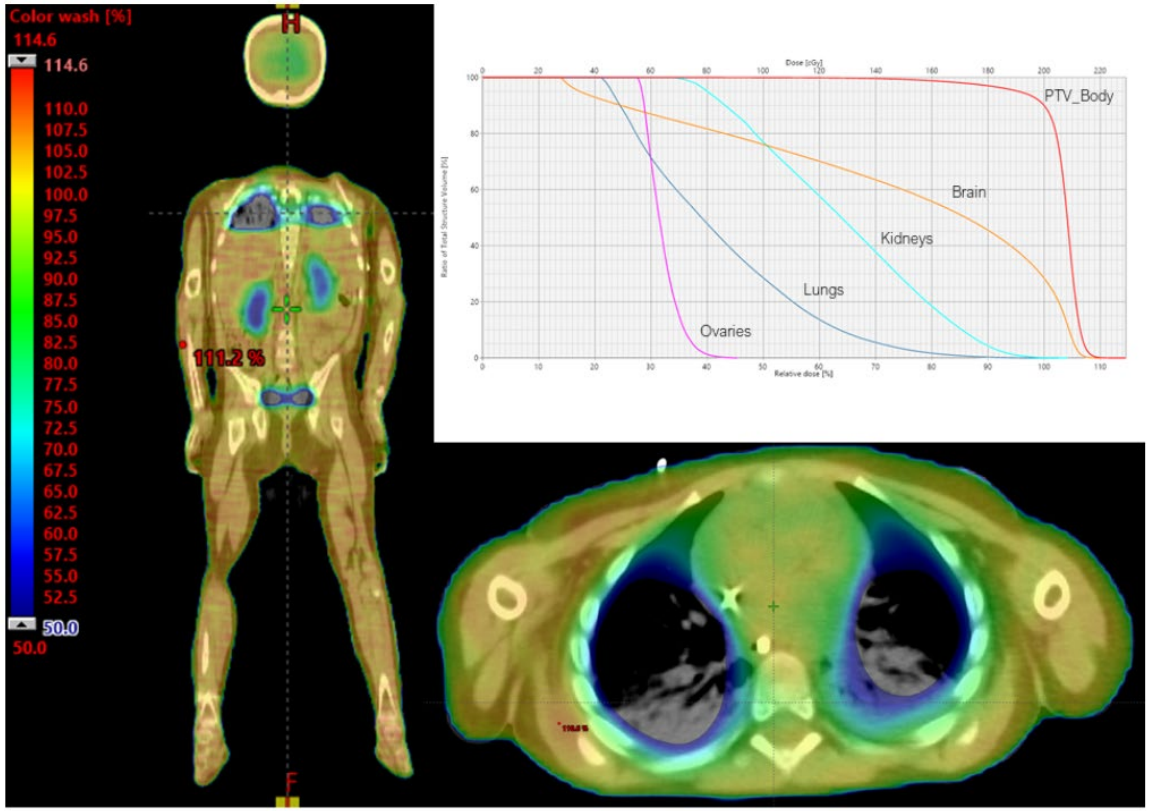


Figure 2: Dose volume histogram (upper right) and dose distribution in coronal (left) and axial (lower right) planes for pediatric VMAT TBI patient diagnosed with congenital agranulocytosis and treated to 2 Gy.

Kovalchuk et al, (PRO, 2022)

Automation of the treatment planning process for VMAT TBI using the Eclipse API framework

https://github.com/esimiele/VMAT-TBI

Eric Simiele, PhD

Stanford University School of Medicine

Plan comparison

Planned 10 VMAT TBI cases manually and with developed scripts:

- Dosimetric indices:
  - Global D_{max}, PTV V110%, lungs and lungs-1cm D_{mean}, kidneys D_{mean}, and bowel D_{max}
  - Paired t-test
- Approximate planning time
- Blinded physician review (60 total responses)

Table 1: Achieved plan quality for each metric considered in this work for the a) manual and b) auto treatment plans. All dose and volume values in a) and b) are expressed as a percentage of the prescription dose and PTV volume, respectively. A plan quality value of N/A indicates that this organ was not considered for sparing in this patient.

(a)

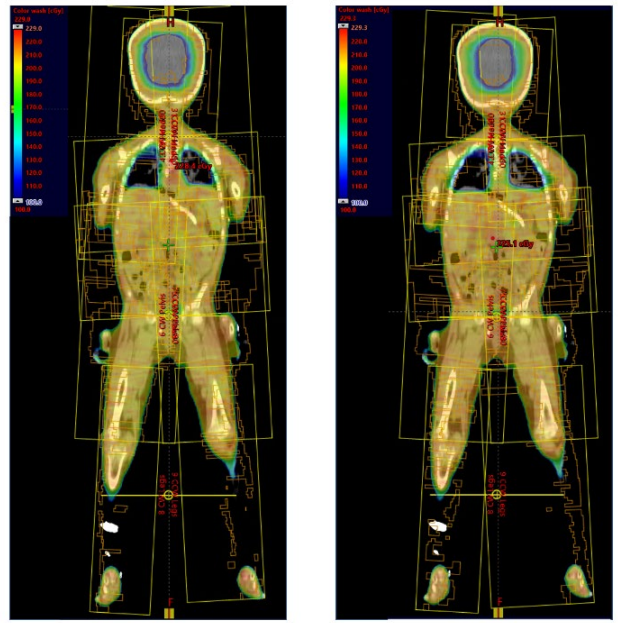
Manual treatment plans						
Patient No.	D_{max}	V110%	Lungs D_{mean}	Lungs-1cm D_{mean}	Kidneys D_{mean}	Bowel D_{max}
1	114.5%	0.2%	55.7%	31.8%	67.6%	111.9%
2	121.0%	1.4%	56.7%	41.2%	65.0%	106.1%
3	119.5%	6.2%	55.0%	45.7%	N/A	N/A
4	116.5%	0.1%	60.0%	44.6%	N/A	110.3%
5	114.0%	0.0%	75.0%	60.6%	N/A	108.1%
6	122.5%	2.5%	65.0%	42.8%	60.0%	111.5%
7	128.5%	4.5%	60.4%	45.4%	66.3%	116.0%
8	121.5%	1.6%	62.5%	40.0%	72.5%	111.2%
9	116.0%	0.6%	65.0%	47.0%	70.0%	112.8%
10	113.9%	0.0%	58.3%	36.5%	65.0%	110.0%

(b)

Auto treatment plans						
Patient No.	D_{max}	V110%	Lungs D_{mean}	Lungs-1cm D_{mean}	Kidneys D_{mean}	Bowel D_{max}
1	114.6%	0.1%	41.8%	26.6%	64.1%	110.0%
2	120.5%	2.2%	58.3%	37.3%	64.2%	111.2%
3	120.3%	2.9%	52.5%	40.3%	N/A	N/A
4	114.7%	0.3%	54.4%	34.1%	N/A	102.5%
5	117.5%	0.5%	54.6%	35.8%	N/A	112.4%
6	121.0%	0.9%	59.4%	36.5%	65.3%	111.6%
7	127.3%	5.3%	59.8%	45.7%	73.3%	114.2%
8	120.4%	1.6%	59.9%	37.5%	72.6%	115.0%
9	117.2%	1.8%	53.4%	35.8%	64.9%	112.3%
10	114.2%	0.1%	56.4%	35.3%	68.4%	103.3%

Table 2: Mean and standard deviation, σ, of the difference in percent between the auto and manual treatment plans. In addition, the calculated p-value from a one-sided t-test is shown for each evaluated metric. A p-value < 0.05 was considered to be statistically significant in this study.

	D_{max}	V110%	Lungs D_{mean}	Lungs-1cm D_{mean}	Kidneys D_{mean}	Bowel D_{max}
Mean	0.0%	-0.1%	-6.3%	-7.1%	0.6%	-0.5%
σ	1.6%	1.3%	6.9%	7.2%	3.7%	4.3%
p-value	0.969	0.750	0.018	0.013	0.598	0.703



(a) (b)

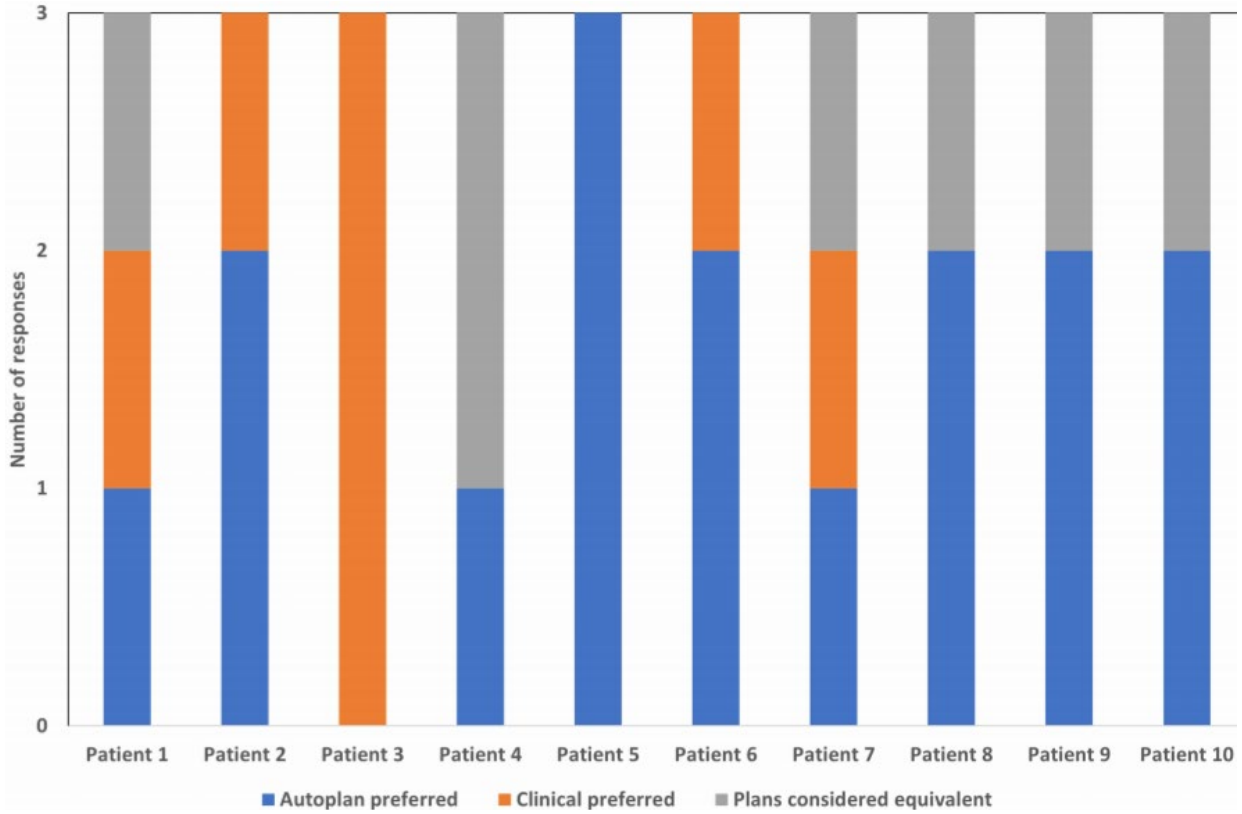
Figure 3: Resulting coronal dose distributions for patient 1 for the a) manual plan and b) autoplan. The prescription for this patient was 2 Gy in one fraction where lungs, kidneys, bowel, gonads, brain, and lenses were selected for sparing.

Simiele et al, PRO 2021

Plan comparison

- 20 plans for 10 patients were reviewed by 3 physicians
- Overall, the autoplans were marked as equivalent or superior to the manual plans 77% of the time

Which plan should be used?



Simiele et al, PRO 2021

Plan preparation

- Another script – Automated Plan Checker – automates the physics plan check by inspecting >150 plan elements and outputs the DVH constraints metrics

External Beam Treatment - Plan Quality Metrics Report

[redacted] - C1 Body - 2 Pelvis

CTP Note Constraints: VMAT_TBI_1fx

Structure	Dosimetric Constraint	Dose/Volume From Plan	Pass/Fail
PTV_Body	D95% ≥ Rx [Gy]	2 Gy	PASS
Bowel	Dmax < 2.1 Gy	2.2 Gy	PASS
Brain	Dmean < 1.5 Gy	0.0 Gy	PASS
Kidneys	Dmax < 2.1 Gy	1.9 Gy	PASS
Kidneys	Dmean < 1.3 Gy	1.2 Gy	PASS
Lenses	Dmax < 1.8 Gy	0.0 Gy	PASS
Lungs	Dmean < 1.2 Gy	0.1 Gy	PASS
Testes	Dmax < 1.0 Gy	0.6 Gy	PASS
Testes	Dmean < 0.3 Gy	0.4 Gy	PASS

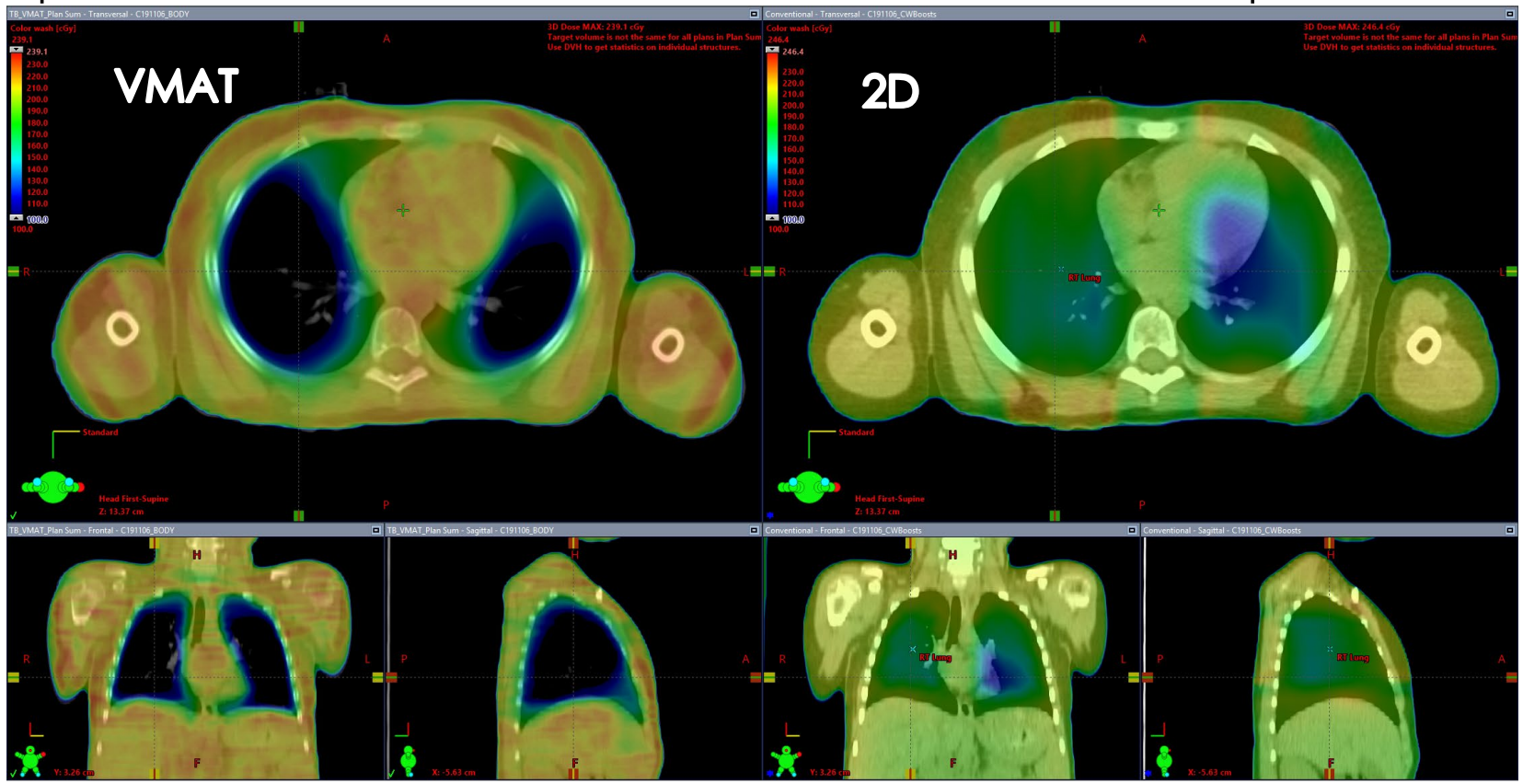
External Beam Treatment - Physics 2nd Check Report

[redacted] - C1 Body - 2 Pelvis - Plan type: VMAT/Conformal Arc

Prescription Approval	PASS	Rx is approved by MD.
Prescription Dose Per Fraction	PASS	Planned dose per fraction matches linked Rx.
Prescription Fractionation	PASS	Plan fractionation matches linked Rx.
Prescription Dose	PASS	Planned total dose matches linked Rx.
Prescription Energy	PASS	Planned energy matches linked Rx.
Prescription Bolus	PASS	Presence of bolus on all Tx fields if bolus included in Rx.
Planning Approval	PASS	Plan is planning approved by MD.
Implanted Cardiac Device	PASS	Plan complies with implanted cardiac device policy if applicable.
Current Plan CT	PASS	Plan CT date <= 14 days from plan creation.
Patient Orientation	PASS	Tx orientation is same as CT orientation.
User Origin	PASS	User origin is not set to(0, 0, 0).
Prescribed Dose Percentage	PASS	Rx dose % is set to 100%.
CTP note	PASS	CTP note exists for current plan and has been approved by MD.
Target Volume	PASS	Target volume does not contain "TS" & contains "PTV".
Gating	PASS	Gating is consistent with Rx.
Plan Normalization (VMAT)	WARN	Plan normalization: 100% covers 95% of Target Volume.
Course Name	PASS	Names are not blank after 'C' character.
Single Active Course	PASS	All courses except for current are completed.
Machine Constancy	PASS	All fields have same Tx machine.
Machine Scale	PASS	Machine IEC61217 scale is used for CCPA & CCSB; Varian IEC for CCEB.
Setup Field MLC	PASS	Setup fields do not contain MLCs.
Arc Field Name (VMAT)	PASS	ARC field names consistent with direction.
Setup Fields Presence (Photon)	PASS	4 cardinal angle setup fields provided.
Setup Field Name	PASS	Setup fields named according to gantry angles.
MLC Check (VMAT/confArc)	PASS	MLC is 'VMAT' or 'Arc Dynamic'.
Setup Field Bolus	PASS	Setup fields do not have bolus linked.
Field Isocenter	PASS	All isocenter coords. for fields match.
Collimator Angle Check (VMAT)	PASS	Coll angle is not 90 or 0.
MU nonzero	PASS	Treatment fields should have nonzero MU.
Adequate Tx Time	PASS	Minimum tx time is met.
Dose Rate	WARN	Maximum dose rates are set.
Tolerance Table	PASS	Non-empty value.
Dose Algorithm	PASS	Photon dose calc. is AAA_15605 or AcurosXB_15605, Electron dose calc is EMC_15605.
Couch Structure (3D/VMAT)	PASS	Correct couch structure is included in plan.
Jaw Max	PASS	Each jaw does not exceed 20.0cm.
Jaw Min	PASS	Each jaw X & Y >= 3.0cm (3D plan) or 1.0cm (VMAT).
Jaw Limit (VMAT)	WARN	X <= 14.5cm (CLINACs); Y1 & Y2 <= 10.5cm (TrueBeam HD MLC).
Table Top (VMAT)	PASS	Table height < 21.0cm.
MU Factor	PASS	Total MU < 4x Rx dose per fraction in cGy.
Reference Point	PASS	Ref. pt tracking correctly & Tolerance Dose vals set accordingly.
Scheduling Fractions	WARN	Status of 1 or more fractions is not set to 'TREAT'.
Scheduling Images	WARN	Status of 1 or more images is not set to 'SCHEDULE'.
DRR Presence (Photon)	PASS	High resolution DRRs present for all fields.
Couch Parameters	PASS	CouchLng & CouchLat not empty; CouchVrt difference is 0 mm from -11cm.
Couch Parameters (Isocentric)	PASS	Couch Parameters match for all isocentric fields.
Imager Position	PASS	Imager position is set to (-50,0,0) for CCPA & CCSB, or (60,0,0) for Pleasanton.
Shift Note in Journal	WARN	Journal shift note was not found.

Comparison between 2D and VMAT TBI

- For 10 patients treated with VMAT TBI conventional 2D TBI plans were created



Ngo et al, (under review, Advances in RO)

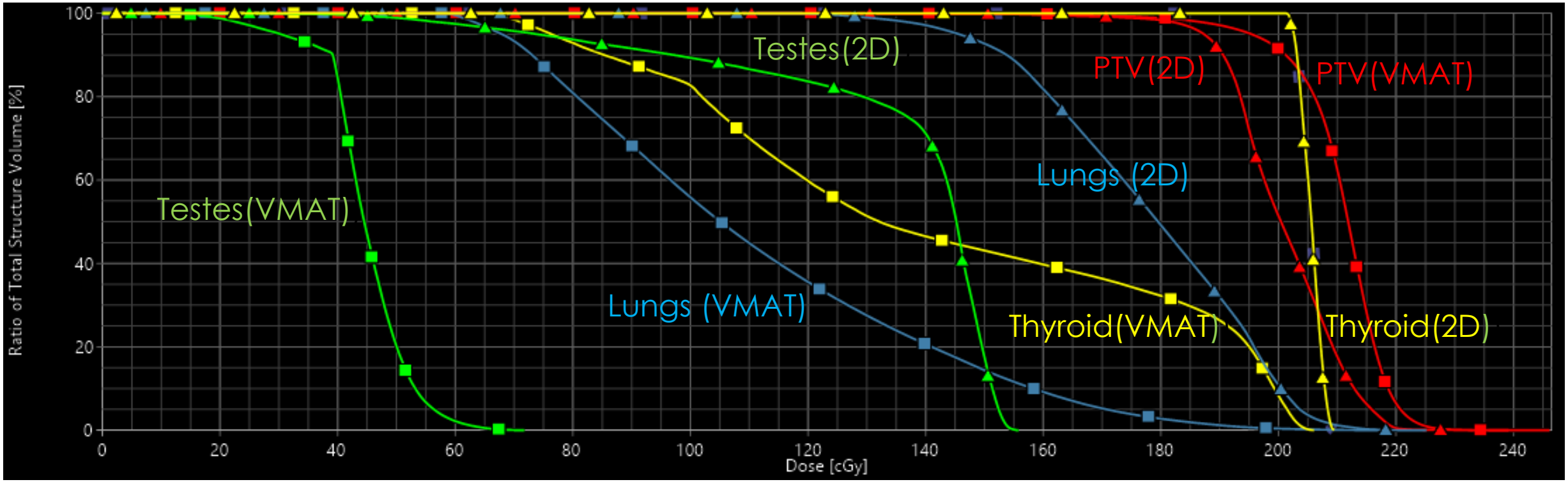
Comparison between 2D and VMAT TBI

- Overall, the coverage was compromised for 2D plans
- On average, mean lung dose with 2D plans was 25.6%±11.5% higher than that with VMAT TBI plans
- Additionally, VMAT TBI plans spared kidneys, brain, thyroid, testes/ovaries where 2D plans delivered prescription dose

Patient	PTV D90	PTV Dmax	PTV V100%	Lungs Dmean	Lungs-1cm Dmean
Patient 1	6.2%	-7.4%	-1.3%	-48.2%	-49.3%
Patient 2	8.8%	-2.0%	1.5%	-28.4%	-44.8%
Patient 3	4.7%	-2.9%	2.4%	-36.5%	-43.7%
Patient 4	10.0%	-3.8%	-0.1%	-27.5%	-38.9%
Patient 5	6.6%	4.8%	-1.4%	-26.2%	-34.6%
Patient 6	4.3%	5.4%	0.7%	-16.0%	-26.1%
Patient 7	5.0%	14.5%	3.5%	-12.2%	-18.4%
Patient 8	7.4%	9.4%	1.6%	-12.1%	-23.7%
Patient 9	1.5%	-1.0%	-6.8%	-30.8%	-33.6%
Patient 10	6.6%	3.1%	0.1%	-17.8%	-28.1%
Mean	6.1%	2.0%	0.0%	-25.6%	-34.1%
σ	2.4%	6.7%	2.9%	11.5%	10.1%
p-value	8.11E-06*	0.226	0.444	2.96E-05*	1.02E-06*

Ngo et al, (under review, Advances in RO)

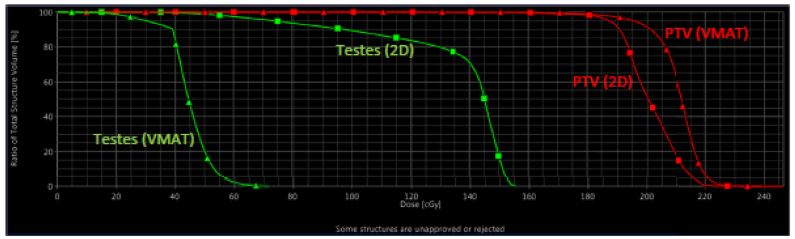
Comparison between 2D and VMAT TBI



Blomain, Kovalchuk et al, PRO 2020

Gonadal sparing: 2D vs VMAT

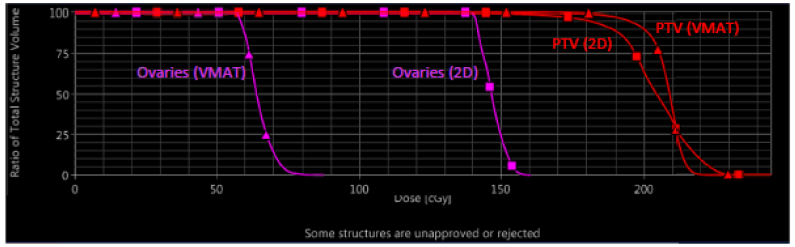
A



B

Structure	Dosimetric parameter	2D conventional plan	VMAT plan
PTV_Body	D90%=	1.9 Gy (95.3%)	2 Gy (100%)
	Dmax=	2.5 Gy (123.2%)	2.4 Gy (117.5%)
	V110%=	0.5%	5%
Testes	Dmean= Dmax=	1.36 Gy (67.8%) 1.56 Gy (78%)	0.44 Gy (22.3%) 0.72 Gy (35.9%)

C



D

Structure	Dosimetric parameter	2D conventional plan	VMAT plan
PTV_Body	D90%=	1.9 Gy (95.3%)	2 Gy (100%)
	Dmax=	2.33 Gy (116.5%)	2.4 Gy (117.5%)
	V110%=	9.2%	0.2%
Ovaries	Dmean= Dmax=	1.47 Gy (73.5%) 1.60 Gy (80%)	0.65 Gy (32.4%) 0.88 Gy (43.9%)

Figure 2 Dosimetric comparison between 2D and VMAT TBI plans for the boy as shown in dose volume histograms (VMAT plan in *triangles*, 2D plan in *squares*) (**A**) and tabulated form (**B**), and for the girl (**C** and **D**).

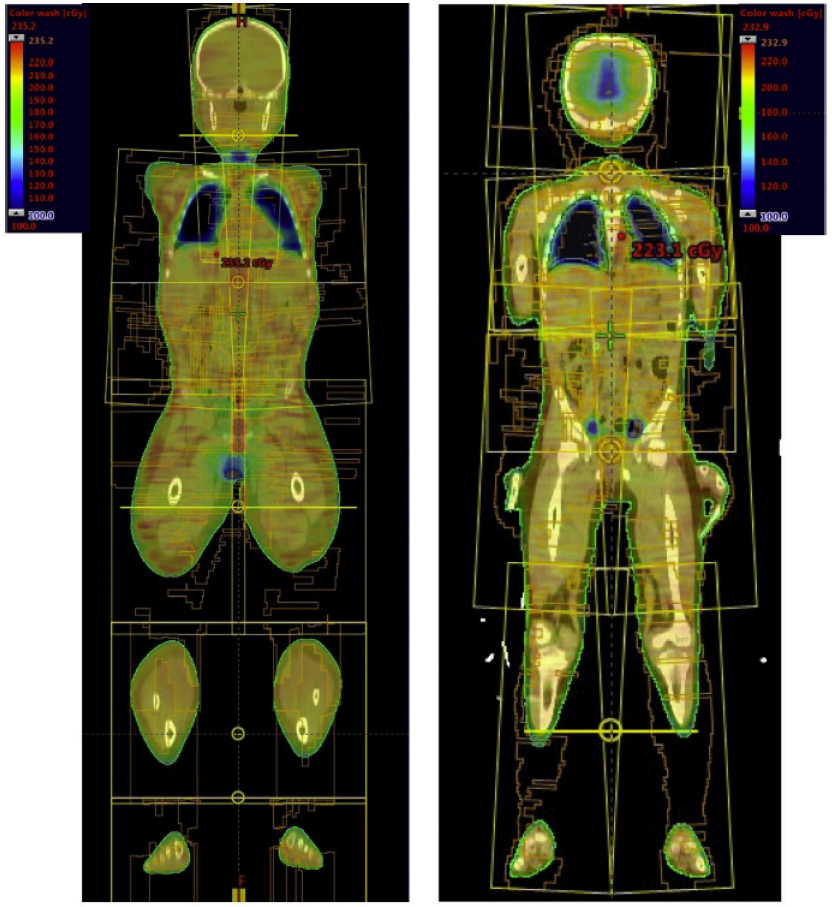
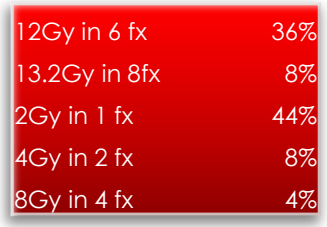


Figure 1 Volumetric modulated arc therapy (VMAT) total body irradiation (TBI) beam arrangement and dose distribution (color wash) on coronal view for boy (*left*) and girl (*right*).

Blomain, Kovalchuk et al, PRO 2020

Patient Outcomes

- 38 ped/young adult patients treated with VMAT TBI from Oct 2019 to Dec 2021
- 38 ped/young adult patients had follow-up 3-20 mo (mean of 10.3 mo):
  - Age: 1 yr – 27 yr (mean of 7.2 yr)
  - Non-myeloablative – 56%; Myeloablative – 44%



- Overall survival at last follow-up: **89.5%**
- Relapse-free survival at last follow-up: **94.7%**
- Toxicity:
  - Pneumonitis (1 (4%); Grade 2; present before RT)
  - Nephrotoxicity (1 (4%); Grade 1; present before RT)
  - Diarrhea - 40%; Grade 3: 1(2.6%)
  - Fatigue – 55%; Grade 3: 0(0%)
  - Nausea – 68%; Grade 3: 1(2.6%)
  - Mucositis - 84%; Grade 3+: 15(39.5%)
  - Skin Toxicity - 16%; Grade 2: 0(0%)

O. Marquez, C. Hui, Ped Blood Cancer, 2022

Conclusions

- Auto-planning scripts are loved in the clinic. They reduce treatment planning time and improve the quality of plans. VMAT TBI scripts are shared with the public at **https://github.com/esimiele/VMAT-TBI**
- Automating treatment planning for VMAT TBI enabled us to switch to more modern TBI technique which offers:
  - possibility of organ sparing (lungs, kidneys, gonads, brain, thyroid, lenses) and SIB boosts
  - accurate dose calculation and image-guided delivery
  - more comfortable patient positioning
  - ability to treat TBI patient is small size vaults

Future Directions

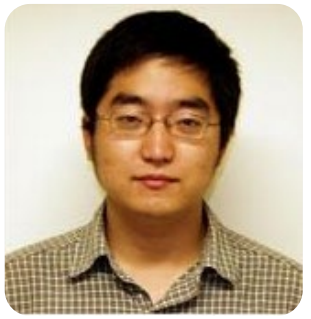
- Children Oncology Group is interested in setting up a multi-institutional trial to show the efficacy of VMAT TBI technique; We are planning on investigating the use of the auto-planning scripts as explorative objective
- Expanding the auto-planning scripts to other sites: CSI, lung, GYN brachy, HN for RefleXion X1
- Planning on implementing reinforcement learning plan optimizer

Acknowledgements

- **Physicians:**
  - Susan Hiniker, MD
  - Richard Hoppe, MD
  - Erik Blomain, MD
  - Caressa Hui, MD
  - Beth Beadle, MD
  - Quynh Le, MD
  - Michael Gensheimer, MD
- **Physicists:**
  - Yong Yang, PhD
  - Nataliya Kovalchuk, PhD
  - Eric Simiele, PhD
  - Peng Dong, PhD
  - Lawrie Skinner, PhD
- **Dosimetrists:**
  - Nic Ngo, CMD
  - Jonathan Lewis, CMD
  - Nicole Howell, CMD
  - Daniel Pham, CMD

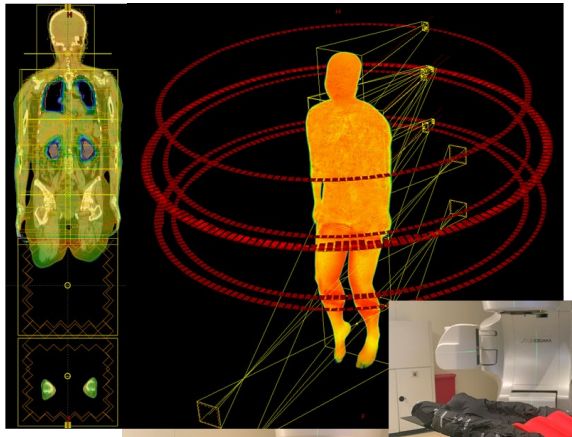
Yong Yang

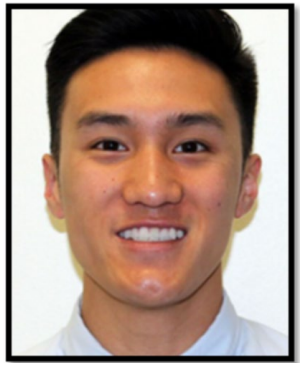
Eric Simiele



Peng Dong

- **Engineer:**
  - Manny Villegas
- **All Stanford RTTs**





Nic Ngo

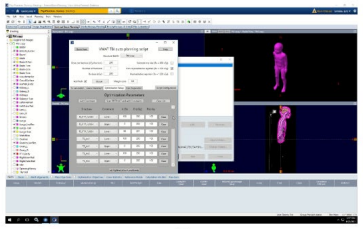
Susan Hiniker

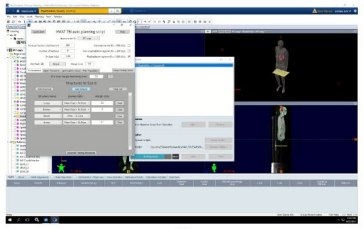
Caressa Hui

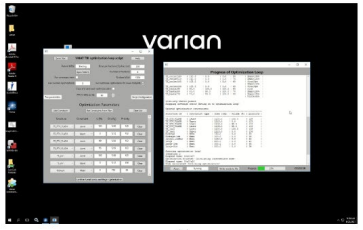
Erik Blomain

Thank you!

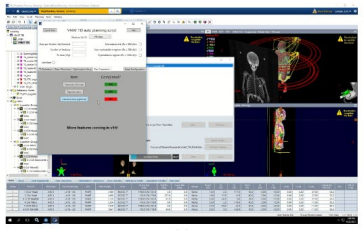
The scripts are shared with the public at https://github.com/esimiele/VMAT-TBI

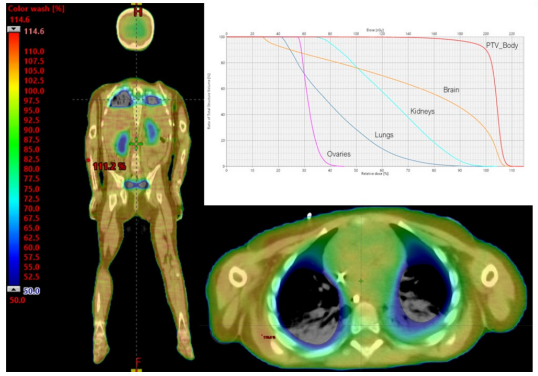

(a)

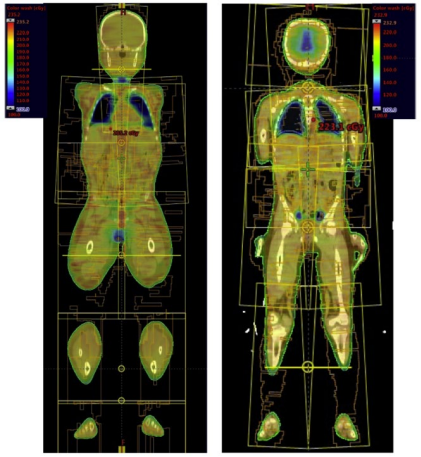

(b)

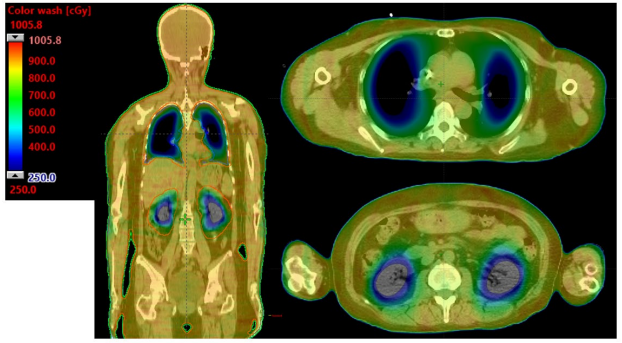


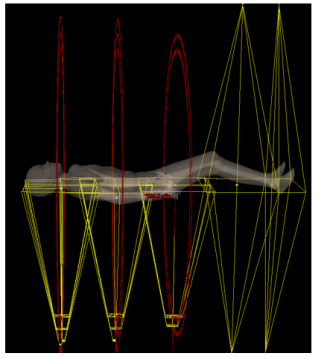
(c)

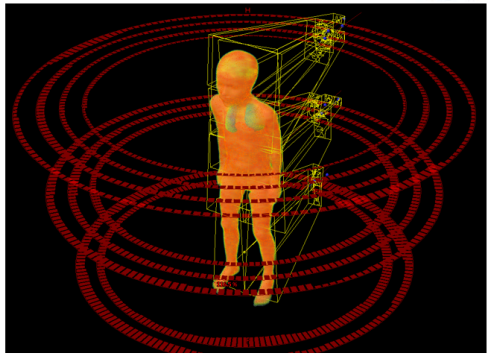

(d)

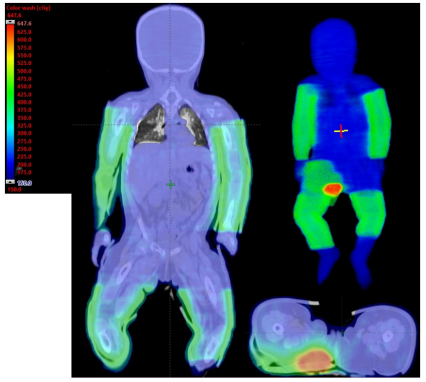












Stanford University School of Medicine