

# RADIOTHERAPY

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# Radiation Therapy : Primer

- The use of radiation to eradicate a tumor
  - Optical light: a few eV
  - Diagnostic x-rays: 20 – 80 keV;  $< \frac{1}{4}$ " of Pb
  - Therapeutic x-rays: 1 – 6 MeV; 2 ft of concrete, 7" of Pb
- Always try to kill the tumor but not the patient
- Conform dose to the target
- Fractionation: Delivery of dose over several weeks for better normal tissue repair
- Accuracy requirements: 5% change in dose can result in observable biological response

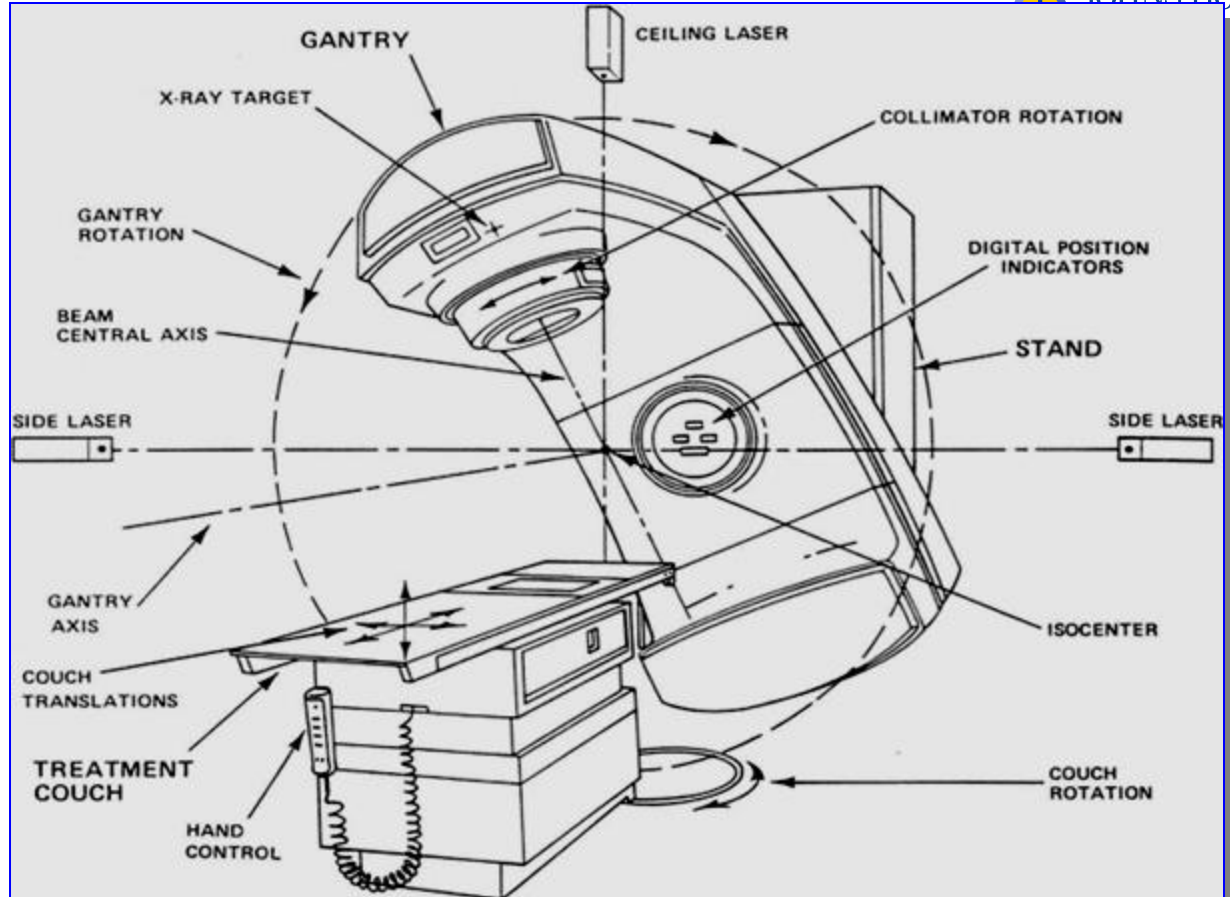
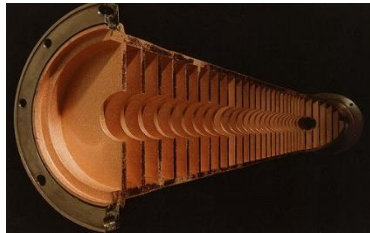


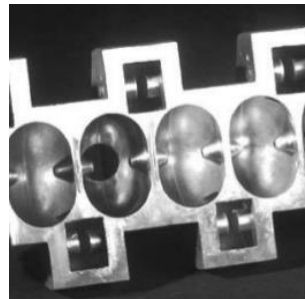
FIGURE 12-1 · Schematic view of a treatment unit emphasizing the geometric relationship of the linac and treatment couch motions. A pedestal type couch is illustrated.

# Major Linac Components

- Electron gun: filament emits electrons into the waveguide
- Accelerating waveguide: uses high-energy microwaves to accelerate electrons to within 0.03% of the speed of light
- Bending magnet: steers high-energy electrons from a “waveguide” toward the patient



Travelling wave



Standing wave

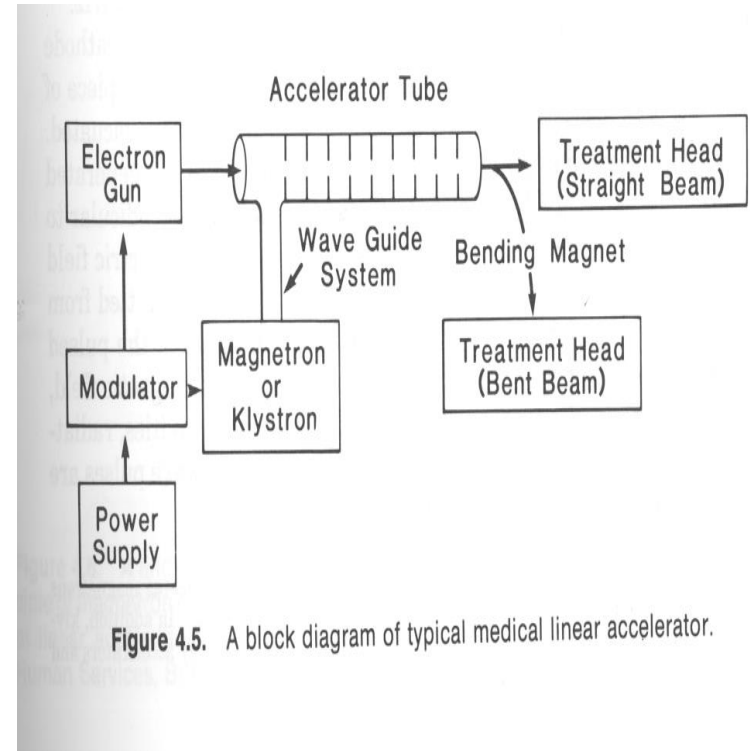


Figure 4.5. A block diagram of typical medical linear accelerator.



# Major Linac Components

- **X-ray target:** heavy-metal target that absorbs electron energy to create photons via bremsstrahlung radiation
- **Carousel:** electron scattering foils and photon flattening filters for each beam energy
- **Monitor ion chambers:** measure the amount of radiation emitted from the carousel

## Photons

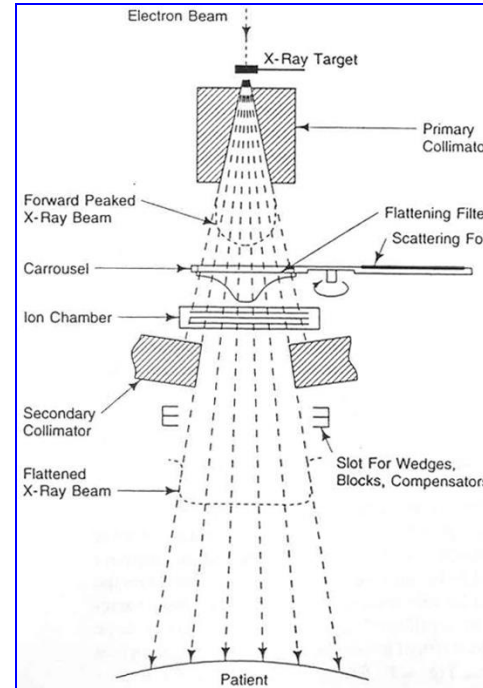


FIGURE 8-6 · Beam subsystem for x-ray beam therapy. Cross section view including central axis of the beam.

## Electrons

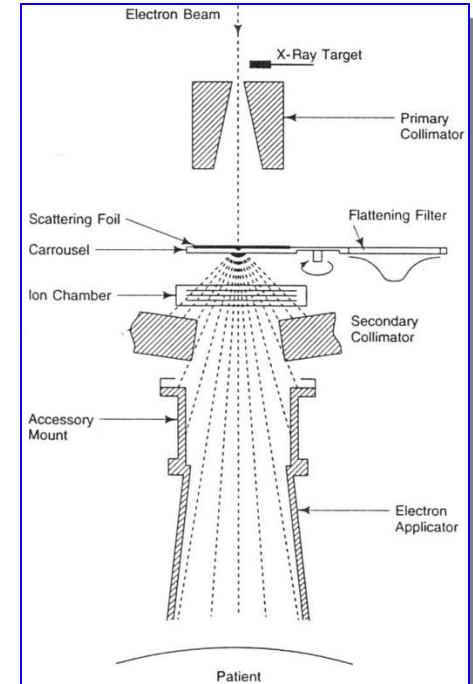
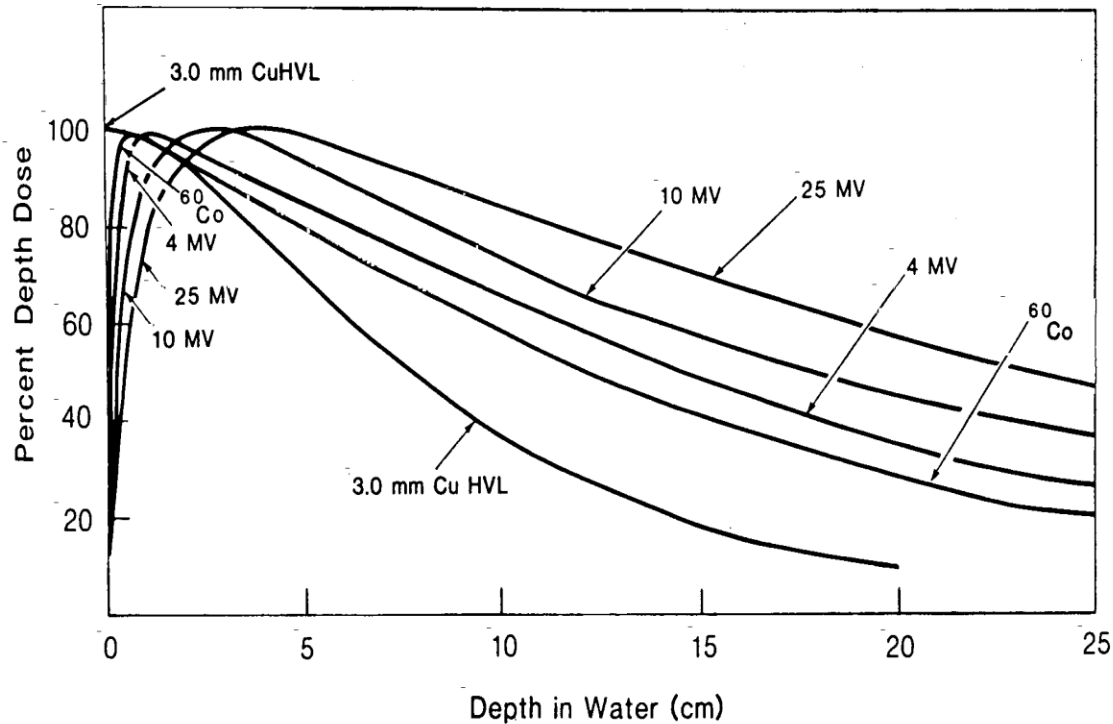


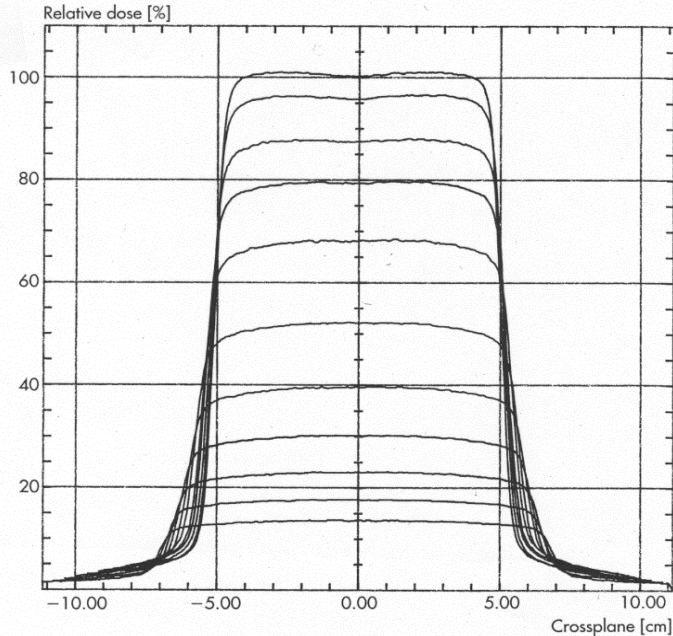
FIGURE 8-4 · Beam subsystem for electron beam therapy. Cross section view including central axis of the beam.

# Photon Dose vs Depth, Energy/Beam Quality



- Higher energy ~ Greater penetrating power ~ Higher PDD
- Build up is deeper with higher energy

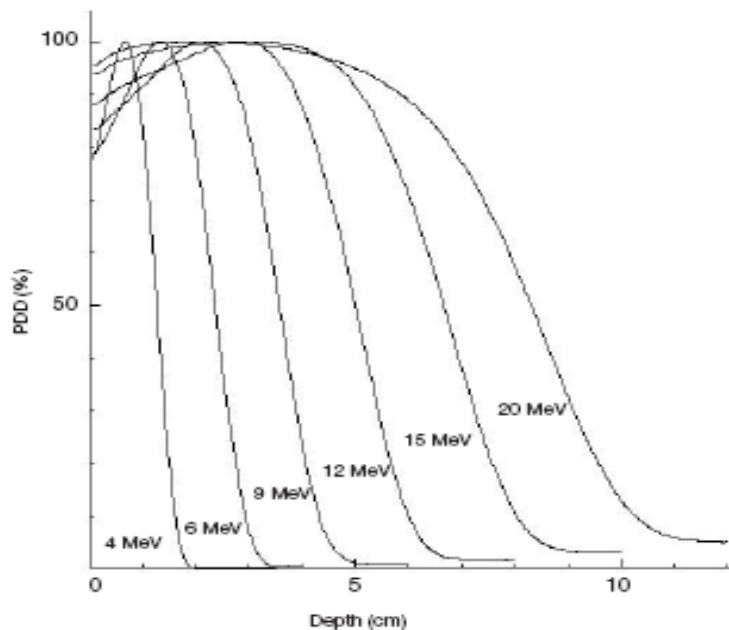
# Family of photon beam profiles



**Figure 11-1** Graphic representation of several measured beam profiles of the type often entered into a treatment planning computer. The illustration shows a number of profiles made along lines perpendicular to the central axis at several depths in a water phantom.

- Dose greatest @ CAX
- Dose decreases @ beam edge
- “Horns” common near surface of accelerator beams
- Dose fall of near beam edge
  - Geometric penumbra
  - Reduced scatter

# Electron Energy Dependence



- Lower surface dose (quick buildup) for lower energy beam
- Dose gradient steeper for lower energy electron
- More x-ray contamination for higher energy beams

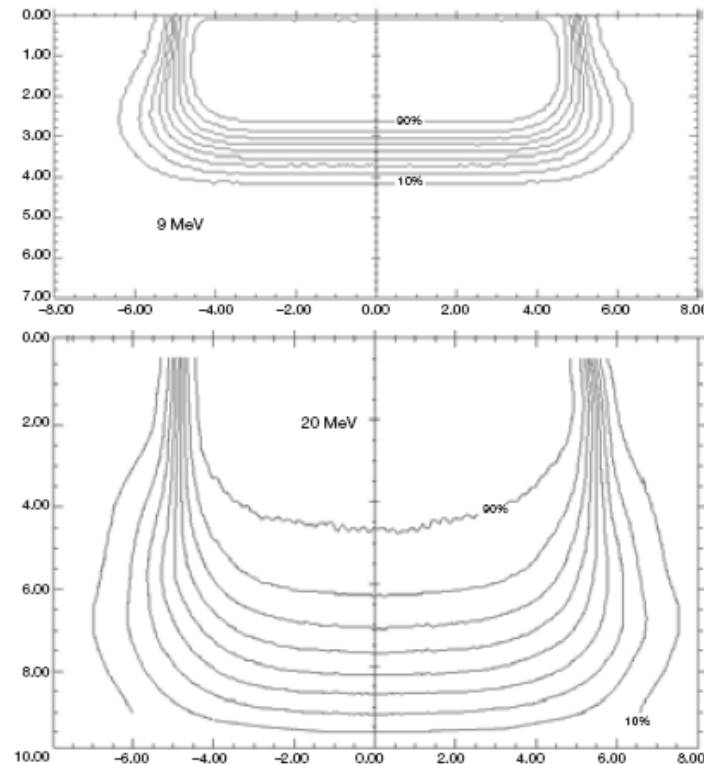
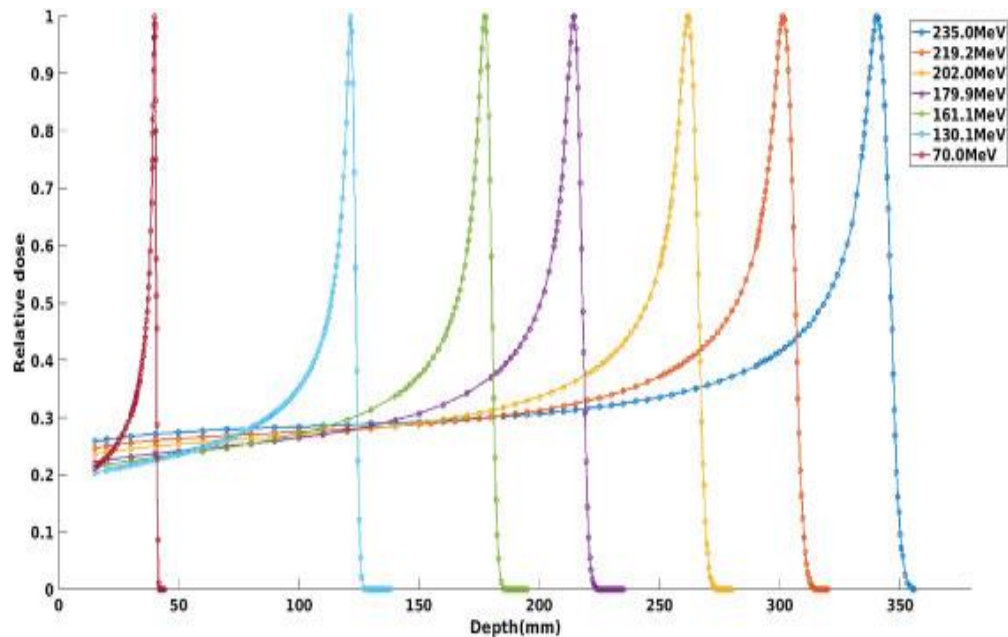


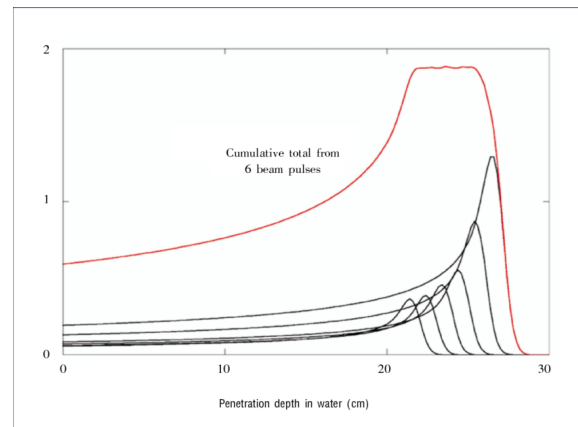
FIG. 8.7. Measured isodose curves for 9 and 20 MeV electron beams. The field size is  $10 \times 10 \text{ cm}^2$  and  $\text{SSD} = 100 \text{ cm}$ . Note the bulging low value isodose lines for both beam energies. The 80% and 90% isodose lines for the 20 MeV beam exhibit a severe lateral constriction. The abscissa and the ordinate represent distance from the central axis and depth in a water phantom, respectively, measured in centimetres.

# Proton depth dose

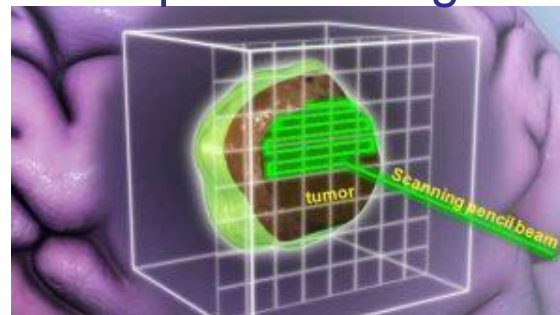
## Bragg Peak vs Energy



## Spread out Bragg Peak

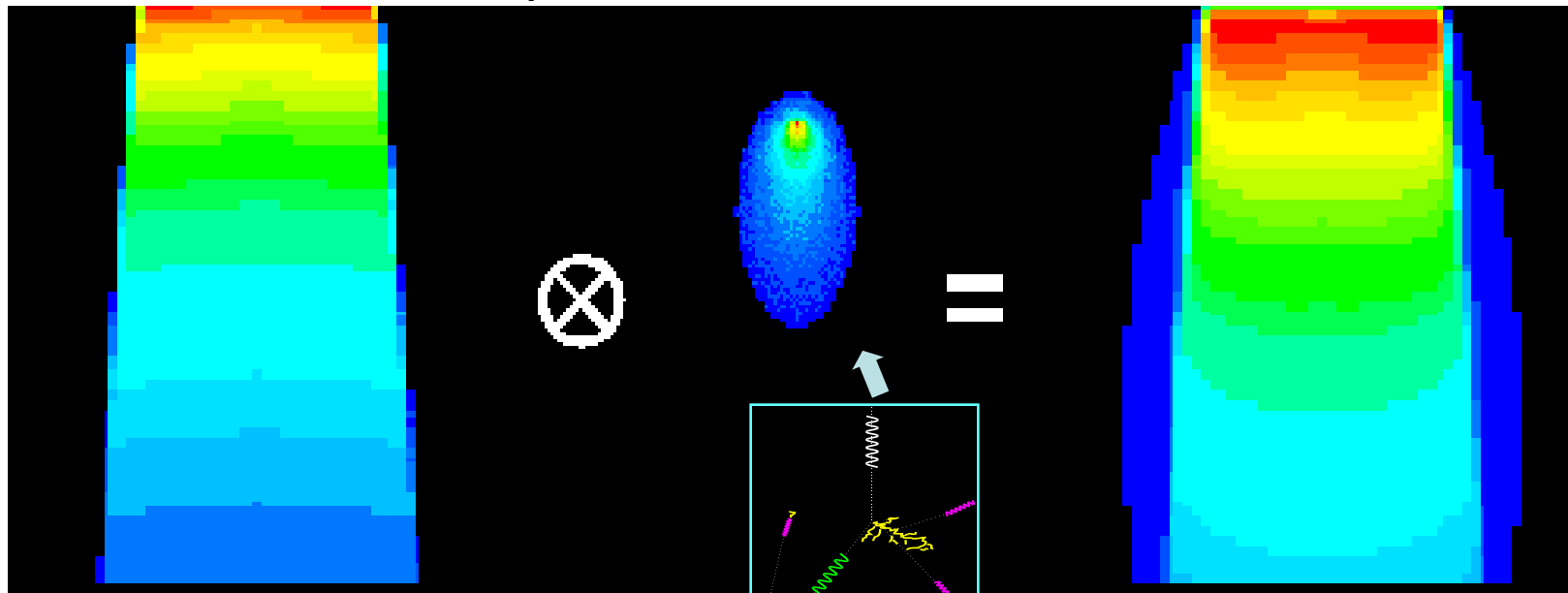


## Spot scanning



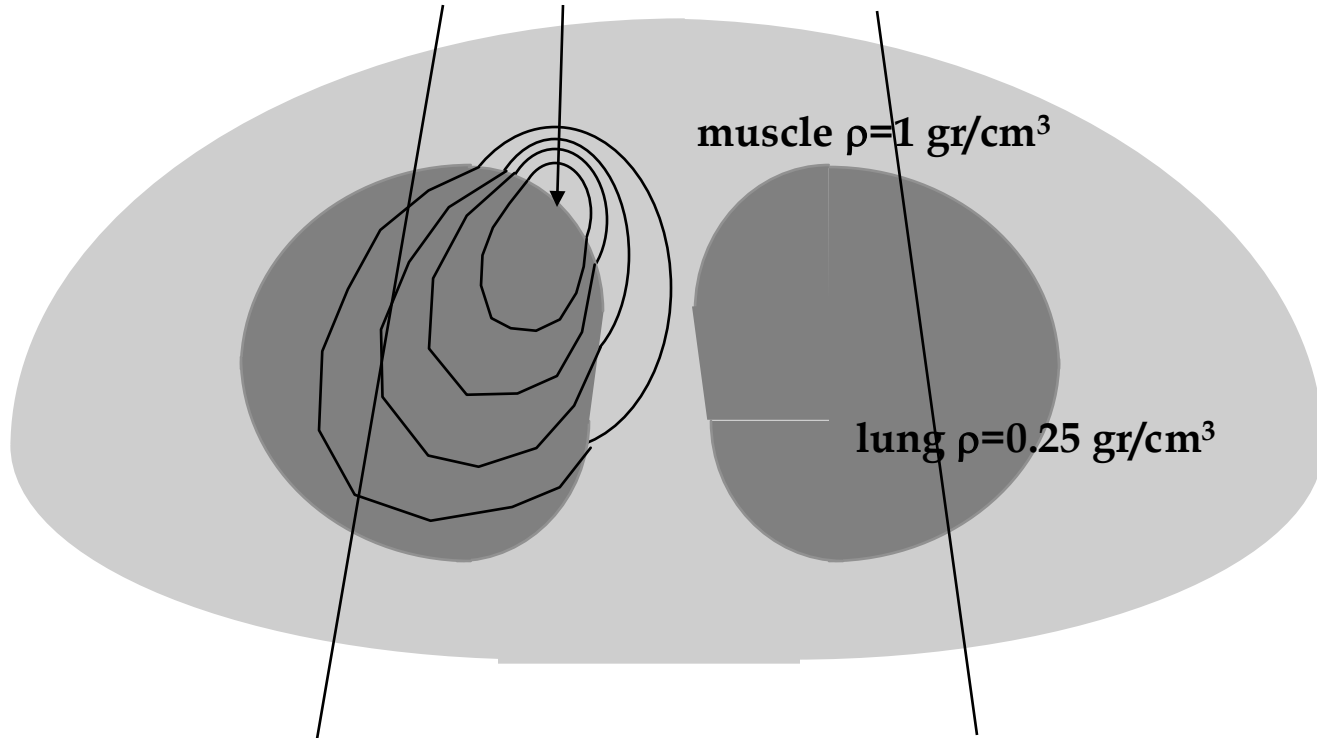
# Method: Convolution/Superposition

$$D(\vec{r}) = \int_{\mathcal{V}} T(\vec{r}') \cdot A(\vec{r} - \vec{r}') d^3 r'$$



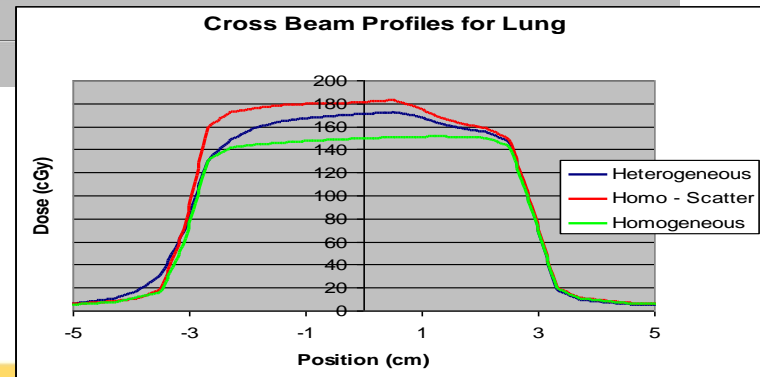
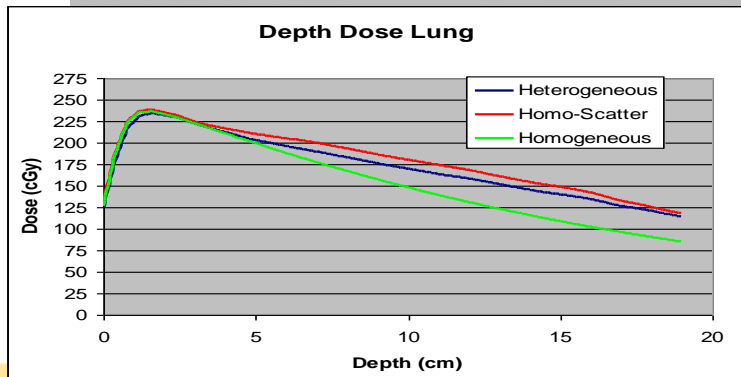
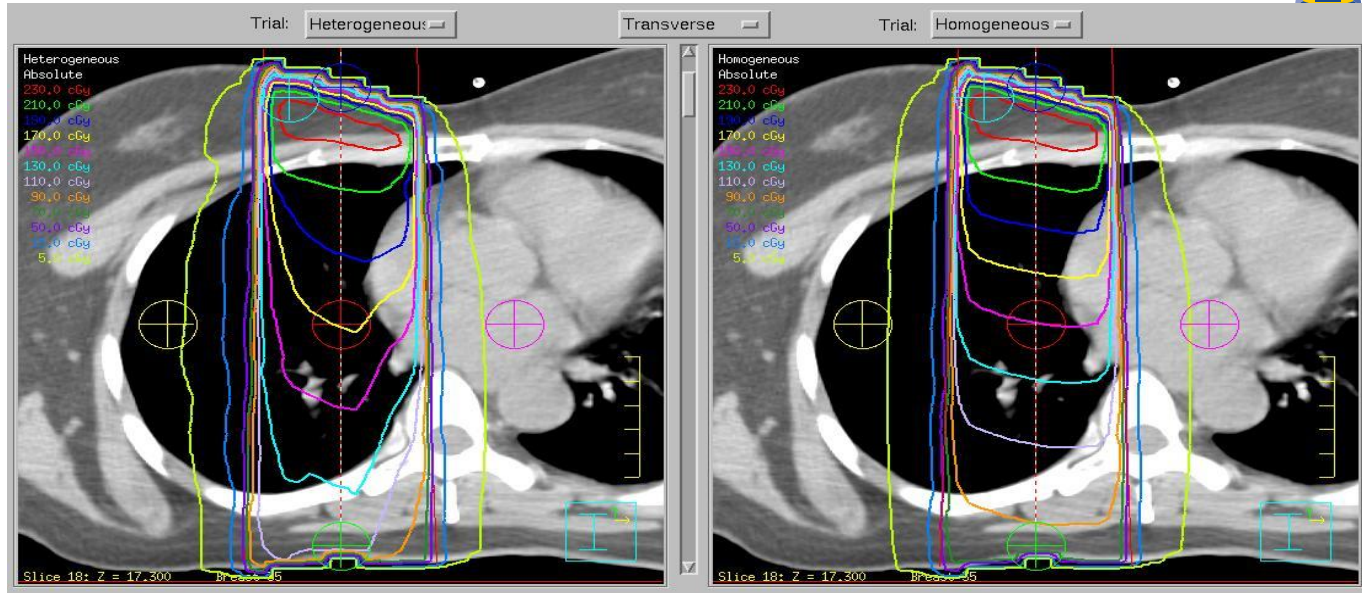
Monte Carlo Simulation

# Convolution/Superposition: Heterogeneities





# Open anterior beam

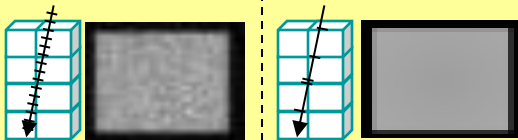
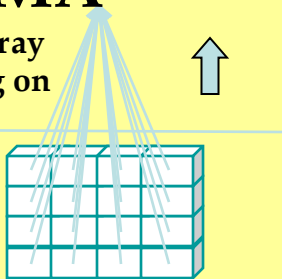




# Fast Convolution/Supersposition Dose Computation on GPU

## TERMA

Invert ray casting on GPU



old

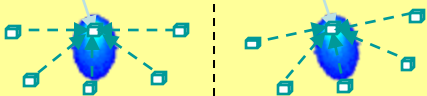
new

Stepwise beam hardening

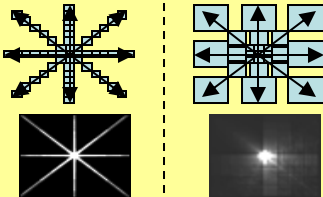
## Superposition

Not Tilted

Tilted



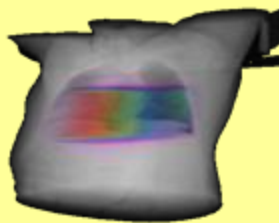
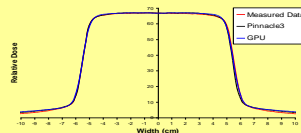
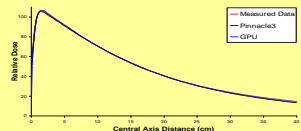
Mipmap kernel ray tracing



## Performance

Engine	Kernel Type	Rays	64 <sup>3</sup>			128 <sup>3</sup>	
			Time (s)	VPS	Speedup	Time (s)	Speedup
GPU	CCK, Tilting*	72	0.198	5.051	41.8x	2.801	33.7x
GPU	CCK, Non-tilting	80	0.159	6.289	52.0x	2.254	41.9x
GPU	CCK, Tilting*	32	0.086	11.628	96.1x	1.246	75.8x
GPU	CCK, Multi-Reso	80	0.097	10.309	85.2x	0.963	98.1x
GPU	CCK, Multi-Reso	32	0.042	23.810	N/A	0.411	N/A
Pinna	CK, Non-tilting	80	8.268	0.121	1.0x	94.51	1.0x

## Accurate



# Target and Clinical Structure Definition

- Planning begins by defining the regions of interest within the patient

## Manual Tools

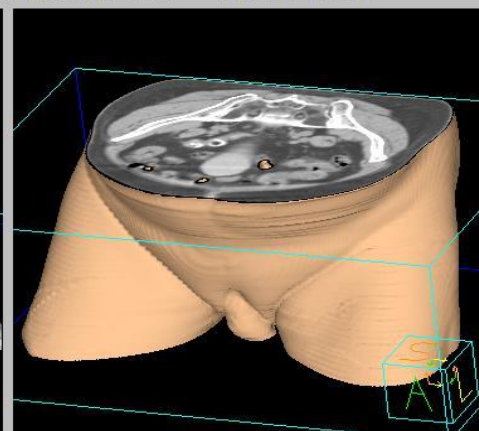
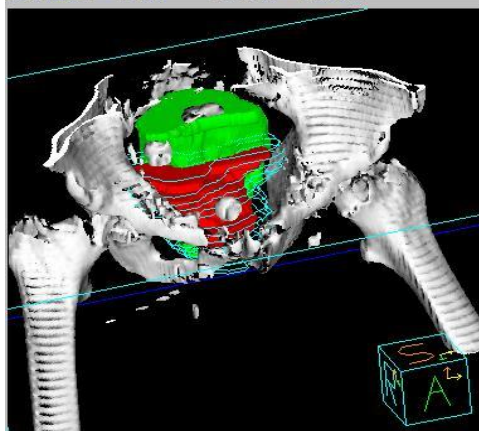
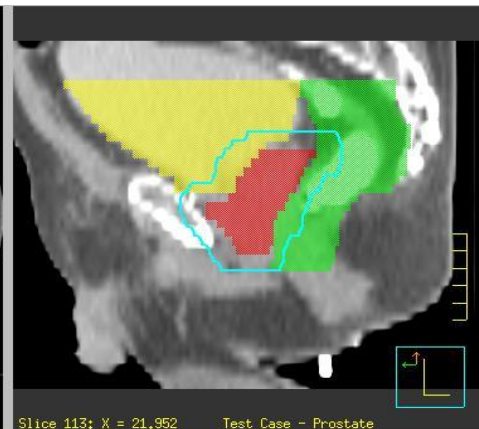
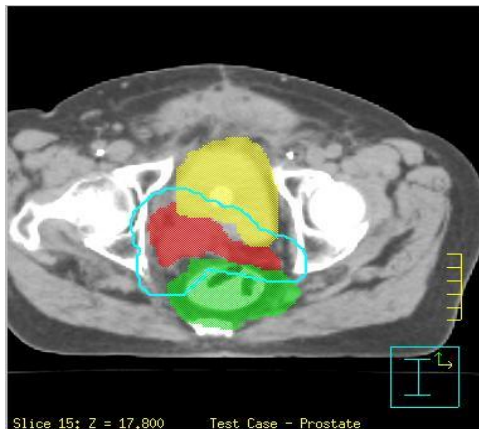
- Line Drawing
- Paint Brush
- 3D tools

## Auto Contouring

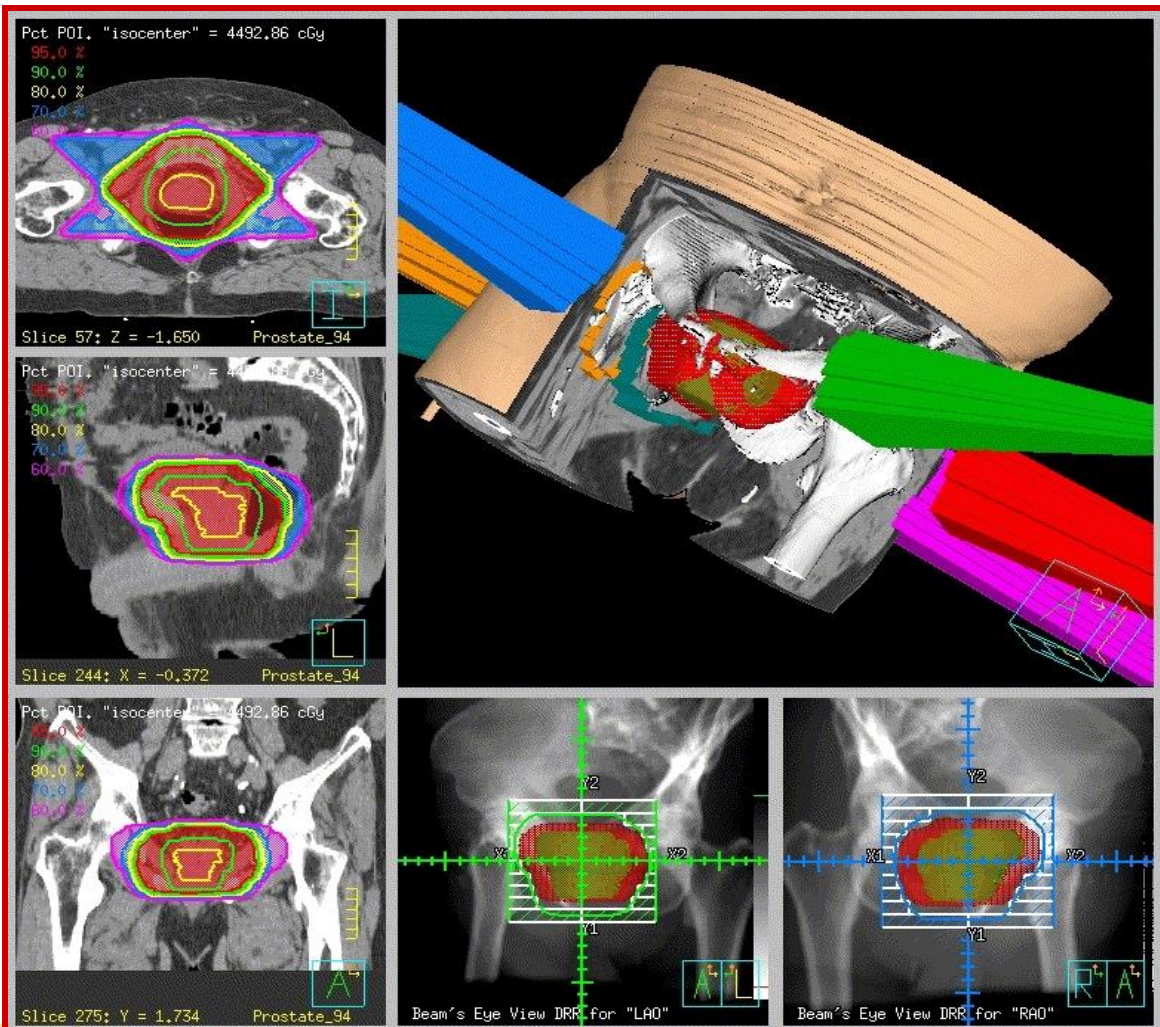
- Threshold
- Gradient/Edge detection
- Model based

## Display

- Contours
- Colorwash
- Polygons (2D and 3D)

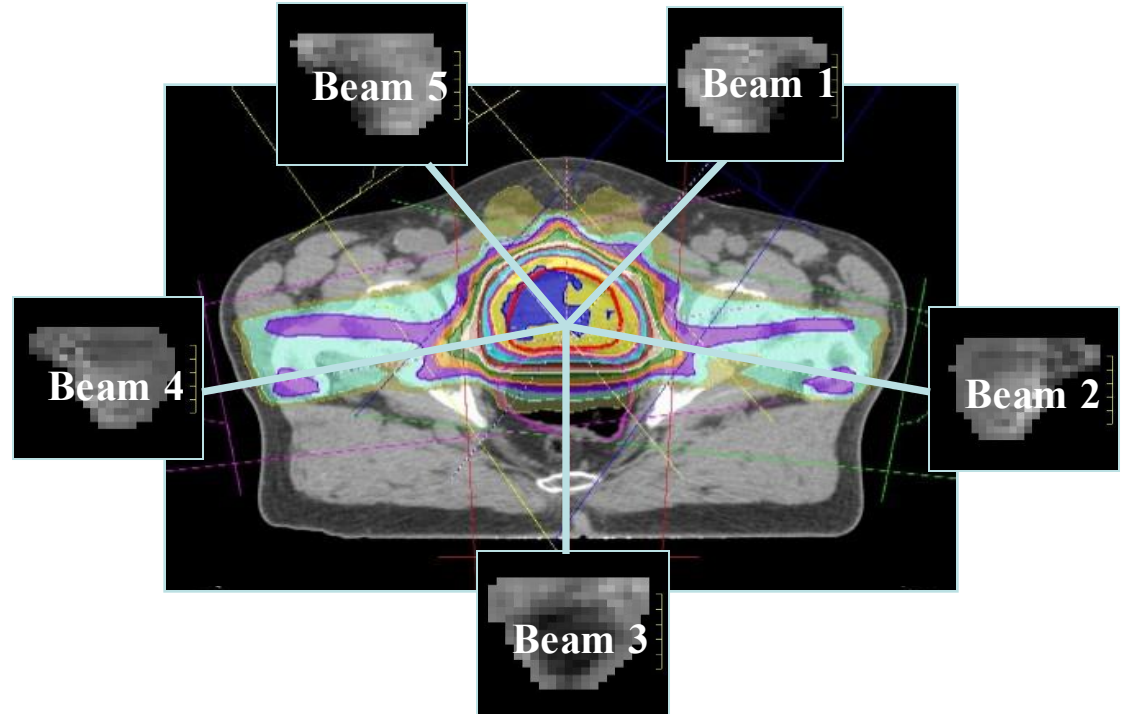
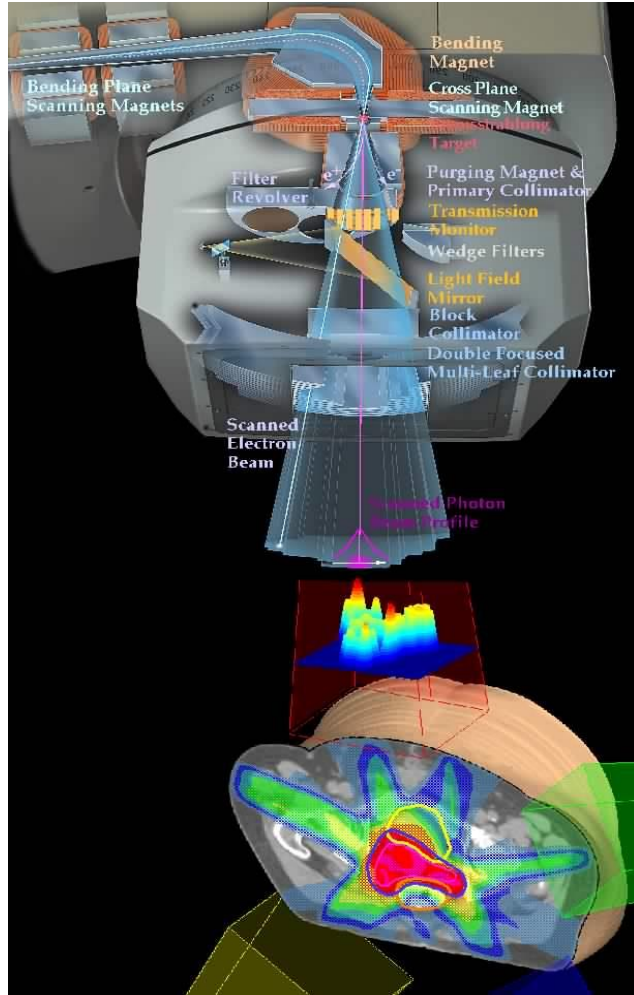


# 3D



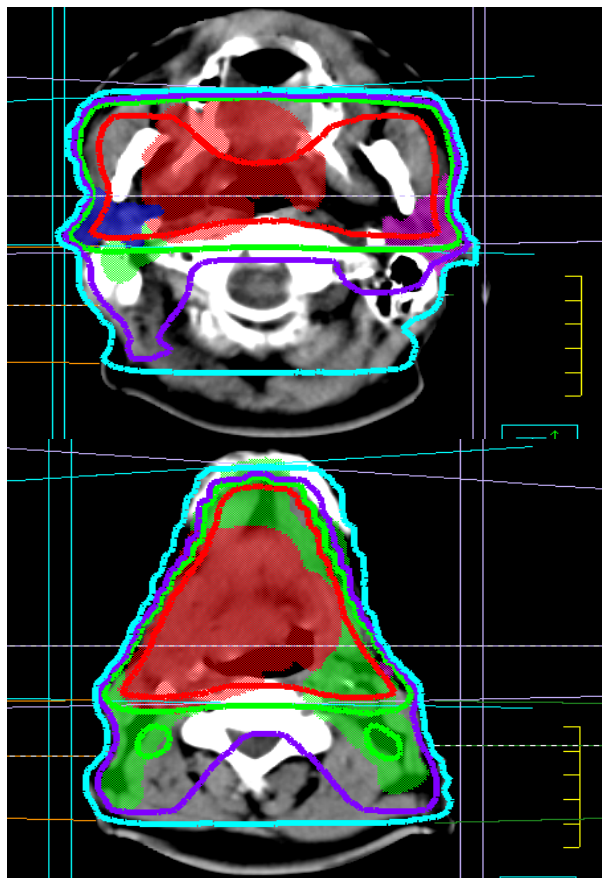


# Modern Medical Accelerator and Intensity Modulation (IMRT)

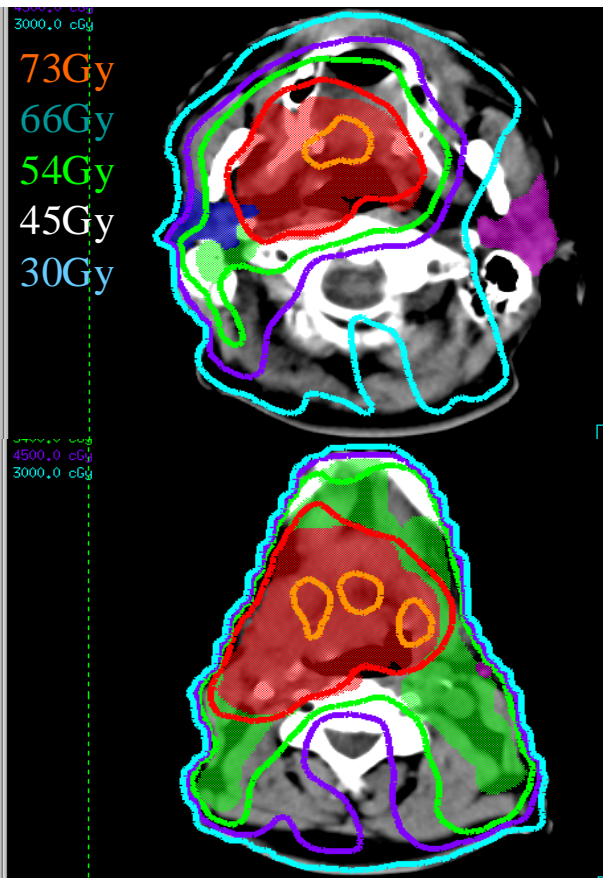


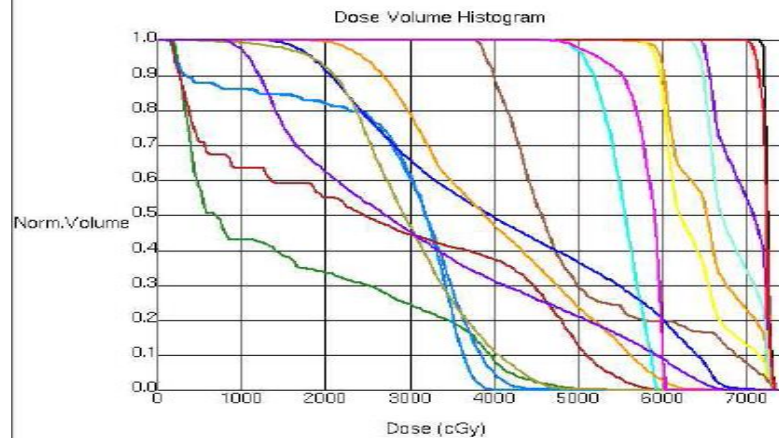
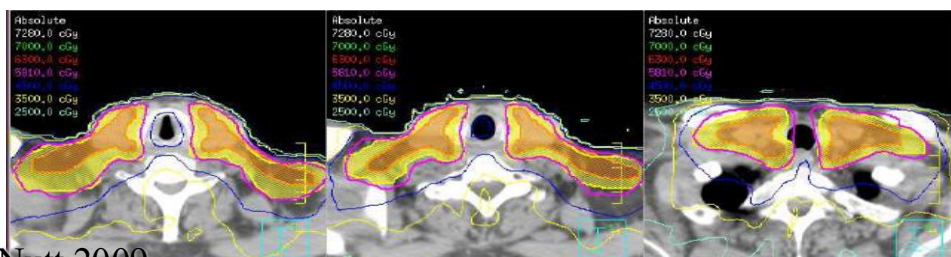
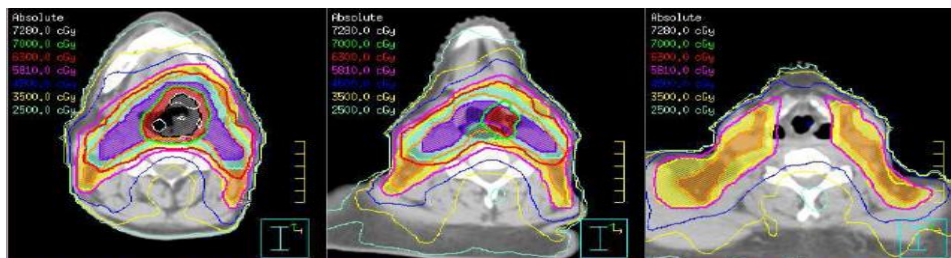
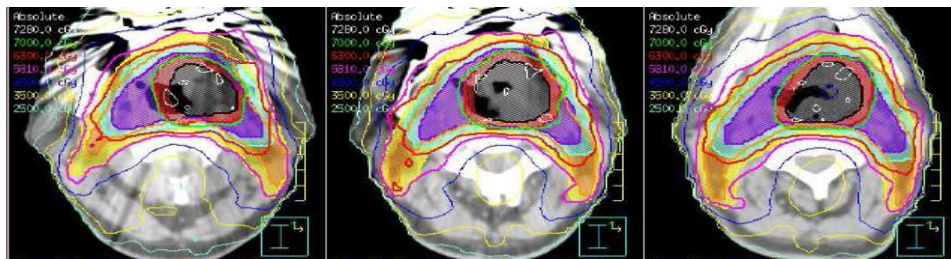
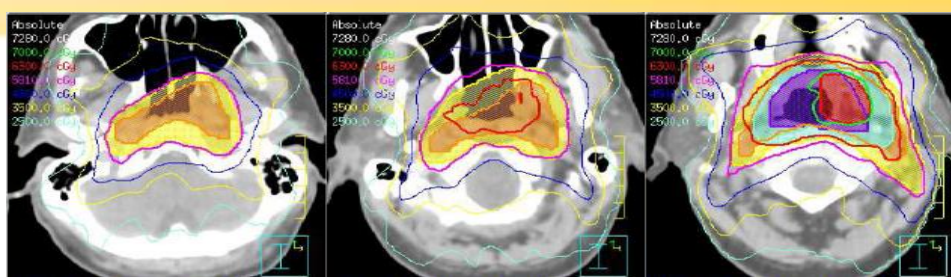
# Isodose Lines Comparing 3D and IMRT

## Conventional



## IMRT



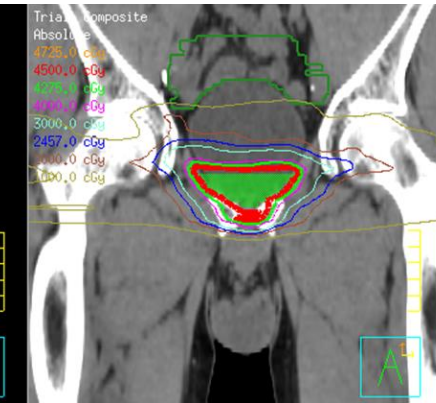
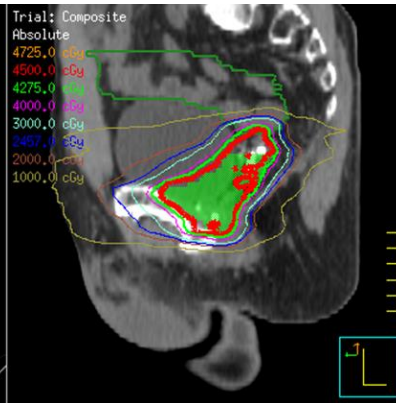
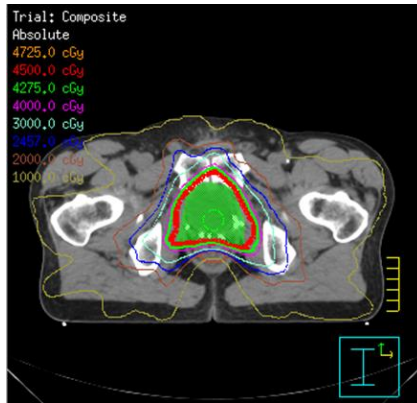
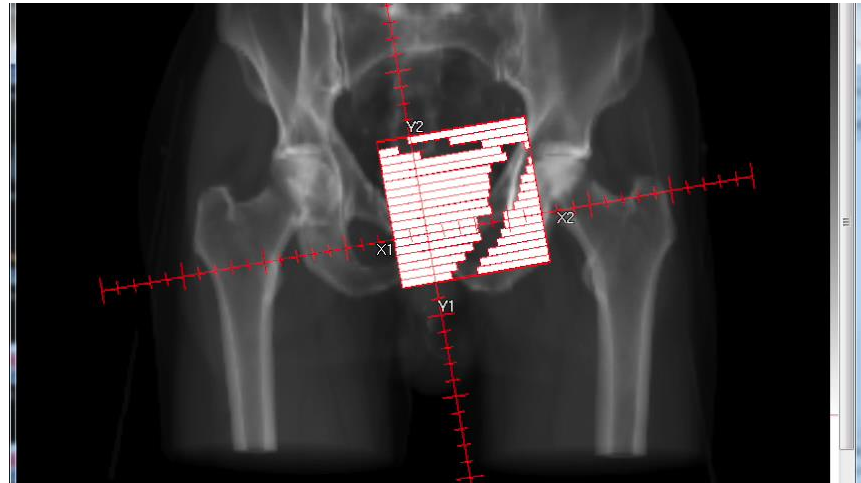
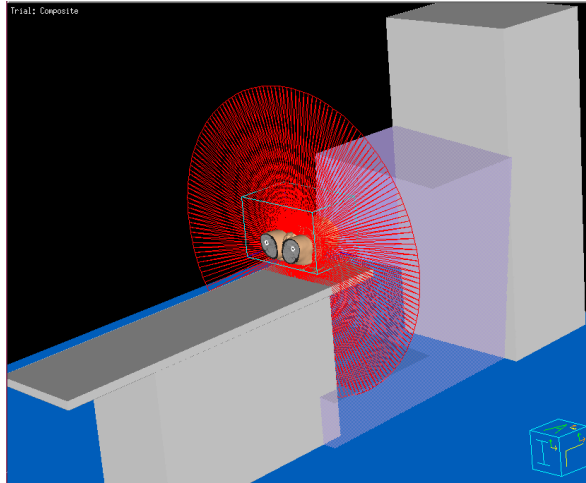


- CTV58.1
- CTV63
- CTV70
- PTV58.1
- PTV63
- PTV70
- brainstem
- cord
- cord+4mm
- esophagus
- larynx for edema
- lt brachial plexus
- lt parotid
- non-targ mand
- oral mucLmt
- rt brachial plexus
- rt parotid

**Dose Volume Histograms** are used to analyze treatment plan quality by determining what percent of a region of interest receives how much dose.

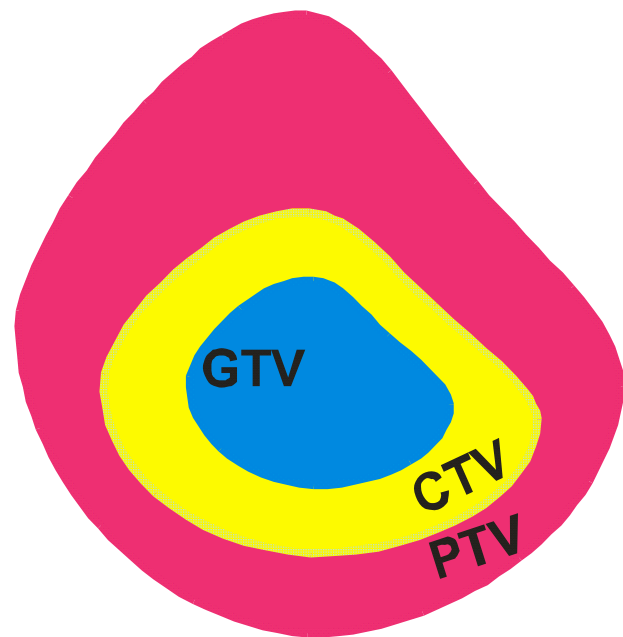


# VMAT – Volumetric Modulated Arc Therapy



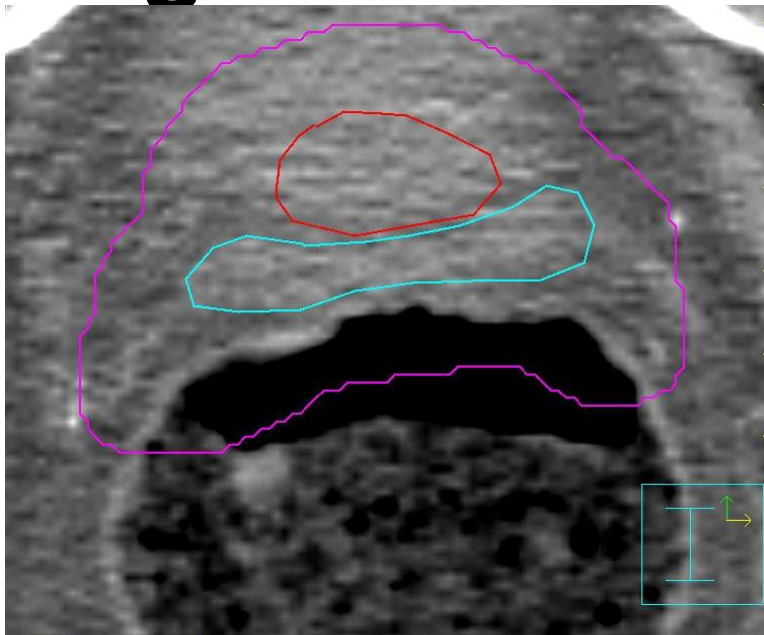
# Target Volume Specification (*late 80's*)

- GTV - Gross Tumor Volume
- CTV - Clinical Target Volume
- PTV - Planning Target Volume
  - Accounts for internal organ motion and patient setup variations during the course of treatment.
- All 'TVs are a statement of the uncertainties (or our ignorance)
  - research opportunities

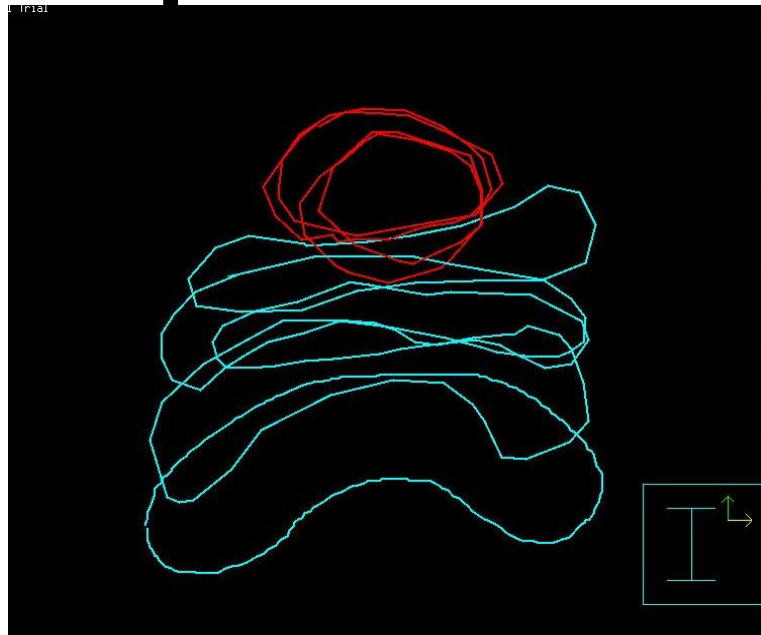




# Organ Motion : Repeat CTs



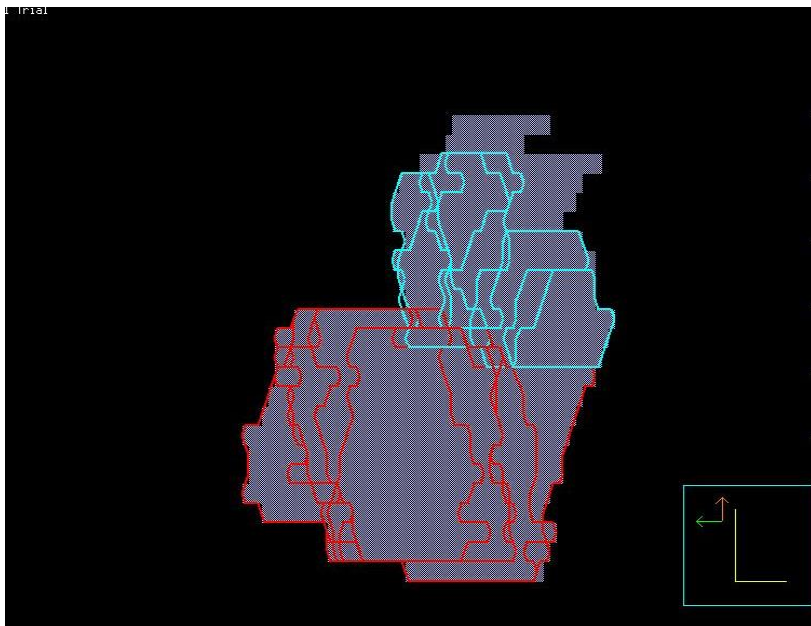
PTV prescribed  
with 1st day CT



Organ motion detected  
on first 5 days

# Patient Specific cl-PTV after 5 days

Original PTV :CTV + 1.0 cm



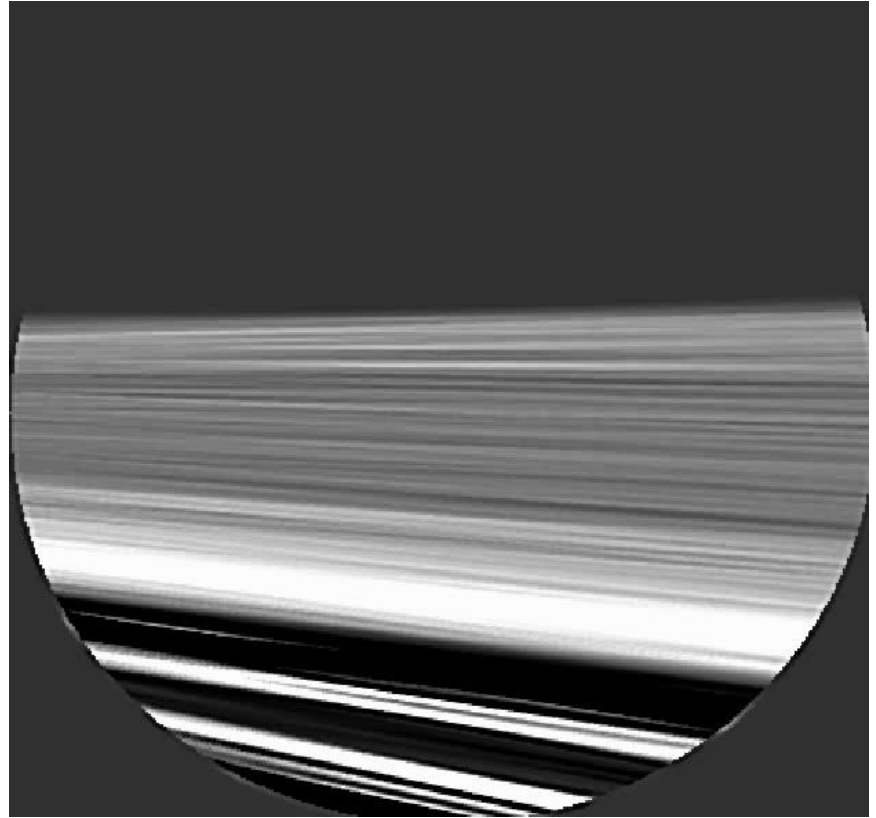
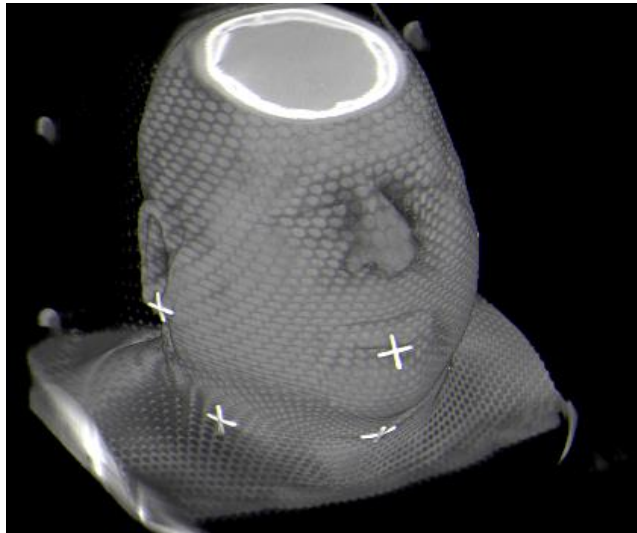
Convex-hull to account for organ motion



Final PTV (setup and organ motion)

# Cone Beam CT Accelerator for On-line intervention









# Adaptive Planning Prototype

File Options Utilities View **CINE** **4D** **PLAN EVAL** **MOTION** **REPLAN** **Models** **IMRT** **InvPlan** Patient: ART\_206,, Predicted WBH 12-19 Help  
Plan: Demo30Frac

## 4 D Plan Evaluation

Plan type: **4D Plan** Create 4D Plan

Current Fraction # Date MU Delivered Fraction Group

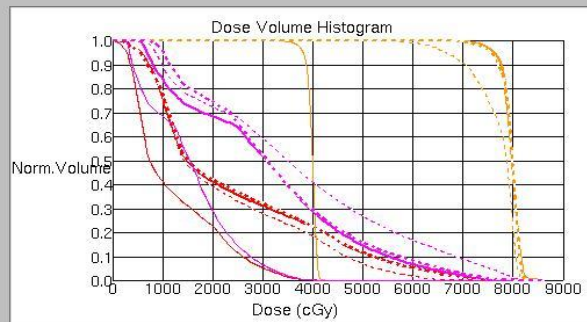
Current Fraction #	Date	MU	Delivered	Fraction Group
1	12/19/03	253€	✓	Delivered
2	12/20/03	253€	✓	Delivered
3	12/21/03	253€	✓	Delivered
4	12/22/03	253€	✓	Delivered
5	12/24/03	253€	□	Predicted
6	12/27/03	253€	□	Predicted
7	12/28/03	253€	□	Predicted
8	12/29/03	253€	□	Predicted

Add Fraction Delete Current Fraction Accumulate Fractionated Dose Copy Current Predicted to Delivered

Dose volume histogram

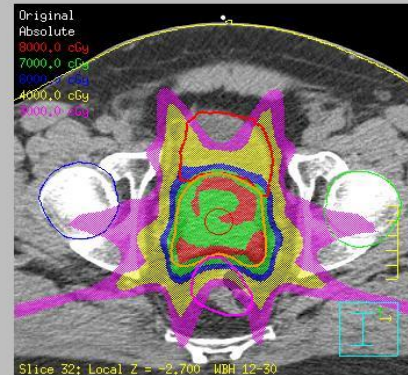
Biological response

Trials ROIs

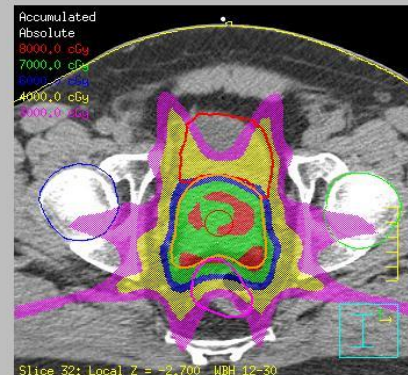


<input checked="" type="checkbox"/>	Original	Medium Solid
<input checked="" type="checkbox"/>	ReoptAccumul	Medium Dash
<input checked="" type="checkbox"/>	Accumulated	Thin Dashed
<input checked="" type="checkbox"/>	Delivered	Thin Solid
<input type="checkbox"/>	Predicted	Thin Solid

## Original Trial



## Planned Trial



Transverse

# Commercial on-line adaptive



(a) MRIdian (ViewRay, Cleveland, OH, US)



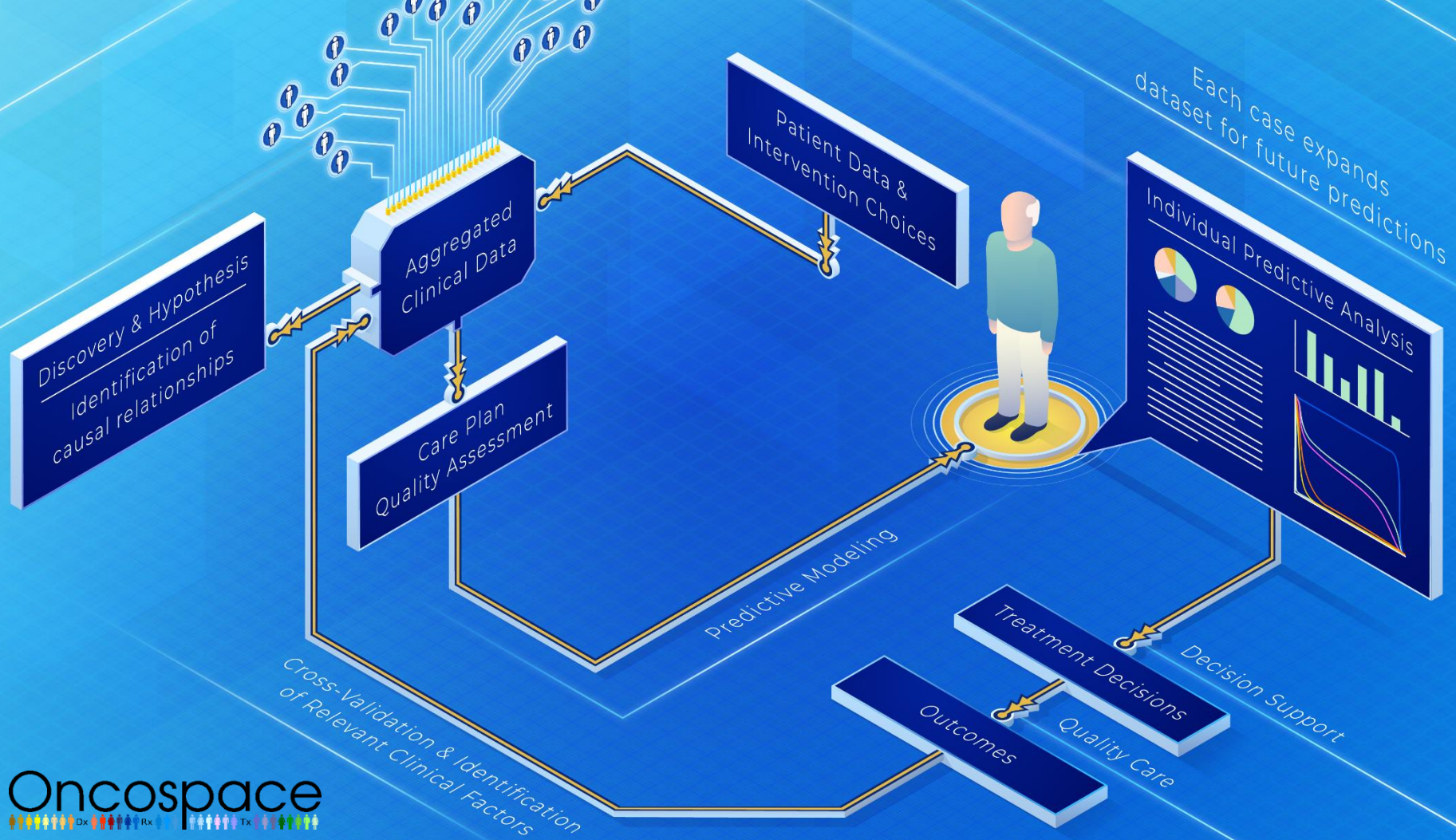
(b) Unity (Elekta AB, Stockholm, Sweden)



(c) Ethos (Varian Medical Systems, Palo Alto, CA, US)

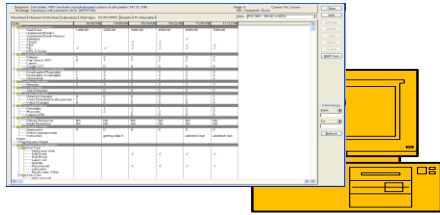
Commercial online adaptive radiotherapy systems. a MRIdian (ViewRay, Cleveland, OH, USA), b Unity (Elekta AB, Stockholm, Sweden), c Ethos (Varian Medical Systems, Palo Alto, CA, USA)



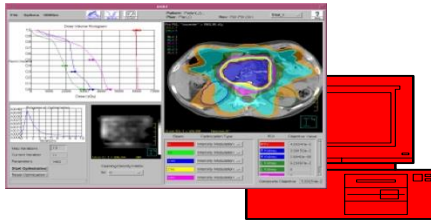




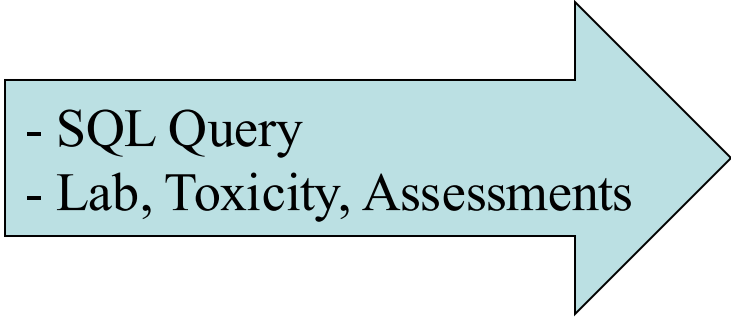
# Extract, Transform, Load

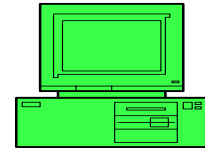


**MOSAIQ**



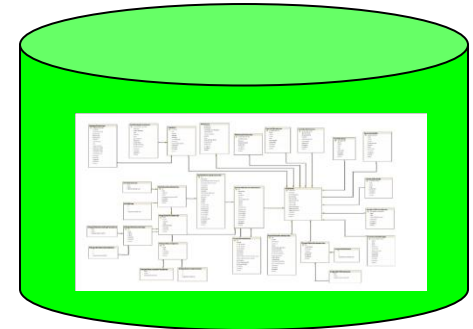
**TPS**

- 
- SQL Query
  - Lab, Toxicity, Assessments



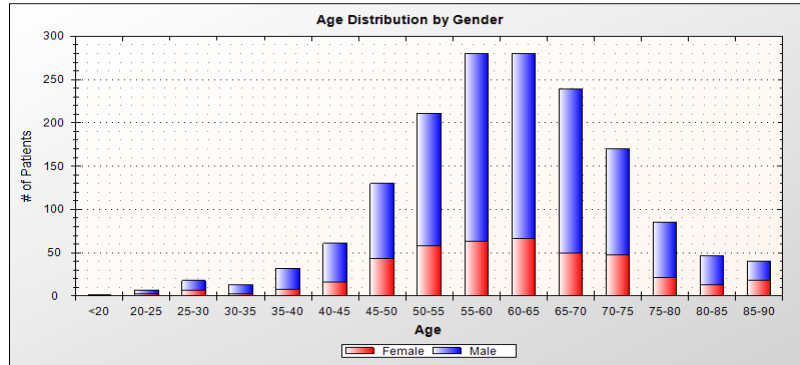
**Oncospace**

- 
- Scripts, Python, DICOM
  - DVH, OVH, Shapes



# Head and Neck Inventory

## Age Distribution



Totals:  
418 female  
1195 male  
1613 total

## Targets

ptv_6300	723
ptv_7000	556
ptv_6000	435
ptv_5400	390
ptv_5425	234
ptv_6800	233
ptv_5810	230
ptv_6240	117
ptv_5940	115
ptv_5520	105
ptv_6720	97
ptv_6120	75
ptv_7200	70
ptv_5760	66
ptv_6996	60
ptv_5600	56

## Normals

cord	1512	l_ear_inner	932
brainstem	1499	esophagus	879
mandible	1457	cricopharyngeal_muscle	827
l_parotid	1448	r_ear_middle	758
r_parotid	1437	oral_cavity	756
r_eye	1436	l_ear_middle	746
l_eye	1431	soft_palate	688
brain	1411	cord_avoidance	637
r_lens	1382	glottis	600
l_lens	1373	constr_muscle_pharyngeal	575
chiasm	1358	ctv_6300	567
l_optic_nerve	1317	comb_parotids	566
r_optic_nerve	1314	l_cochlea	558
l_submandibular	1131	r_cochlea	543
r_submandibular	1108	endolarynx	527
thyroid	1022	midline_avoidance	493
		sublingual	476

**Select assessments:**

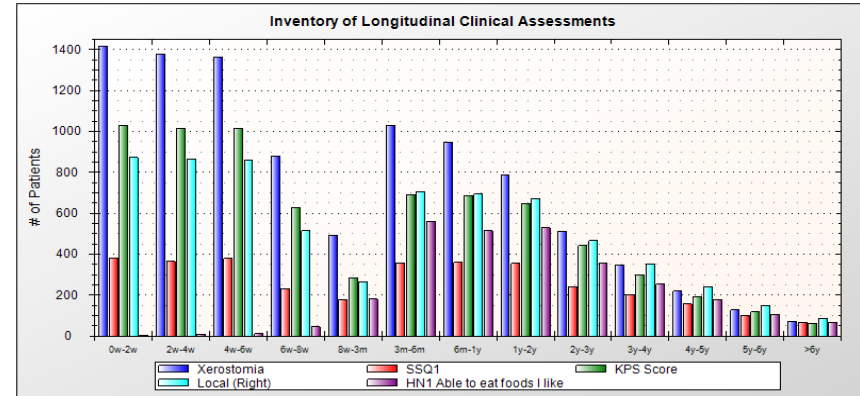
- \$Esophagitis: NCI
- \$Voice Changes
- 4-D/CT
- Abs Lymphocyte Count
- Absolute Lymph Count(JH)
- Absolute Neut Count(JH)
- Act Partial Thromboplastin Tim
- Adenovirus NAT(JH)
- Admission Reason
- Admitted
- Admitted - Y/N
- AER Microscopic Exam(JH)

Reset

**Select assessments to view:**

- Xerostomia
- SSQ1
- KPS Score
- Local (Right)
- HN1 Able to eat foods I like

Clear Selection    Update



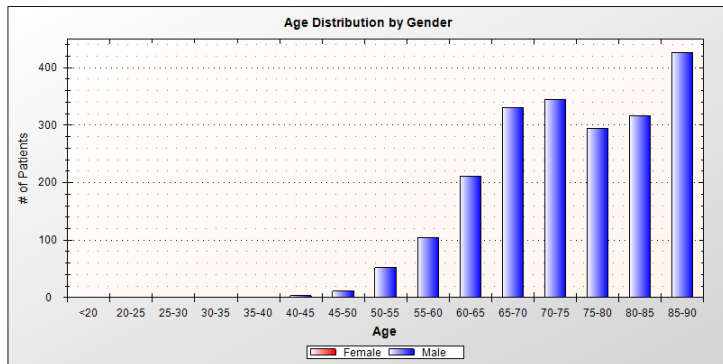
Total: 29579 assessments shown

>6 yrs

# Prostate Inventory

~2100 pts - ~1500 with dose

## Age Distribution



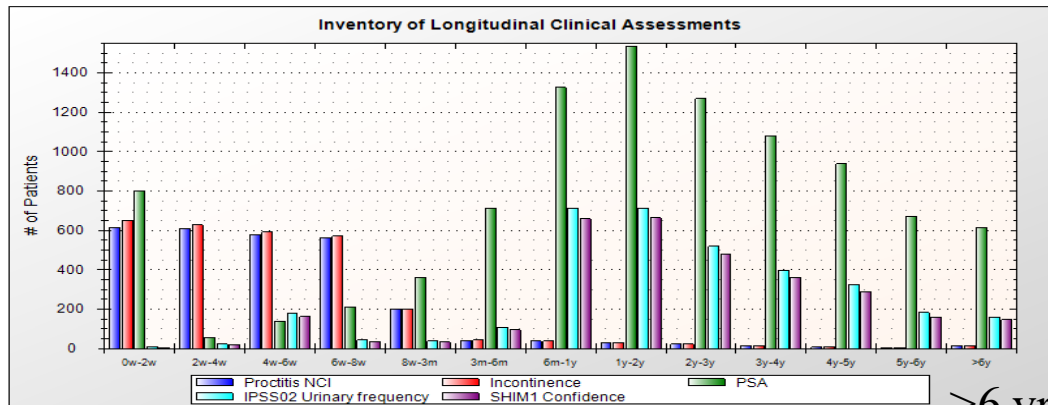
Totals:  
0 female  
2096 male  
2096 total

## Targets

ptv_prostate_sv	568
ptv_prostate_bed	448
ptv_prostate	387
ptv_nodes	349
ptv_prostate_brachy	237
ptv_prostate_bed_cd	207
ptv_prostate_sv_nodes	150
ptv_prostate_bed_nodes	87

## Normals

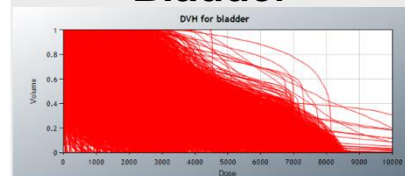
rectum	1798
bladder	1472
l_head_femur	1418
r_head_femur	1414
bowel	817
penile_bulb	511



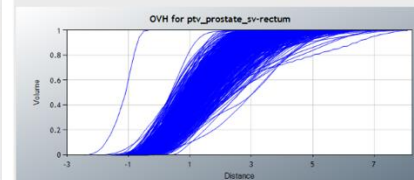
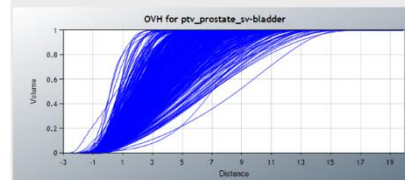
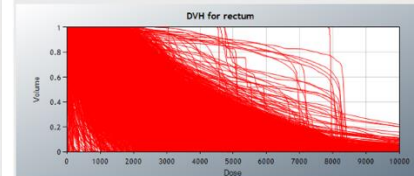
Total: 21743 assessments shown

>6 yrs

## Bladder



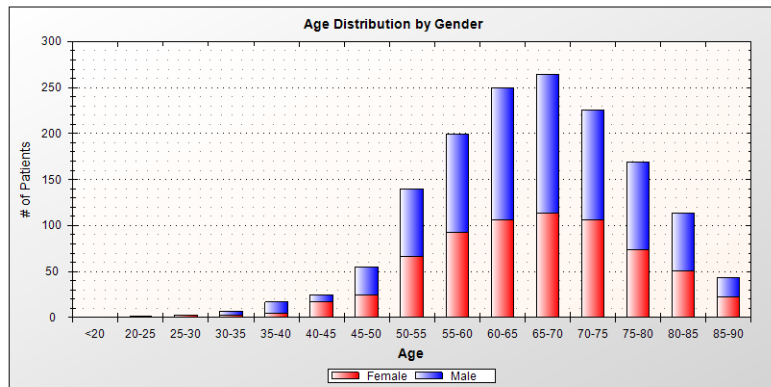
## Rectum



# Thoracic Inventory

~1700 pts

## Age Distribution



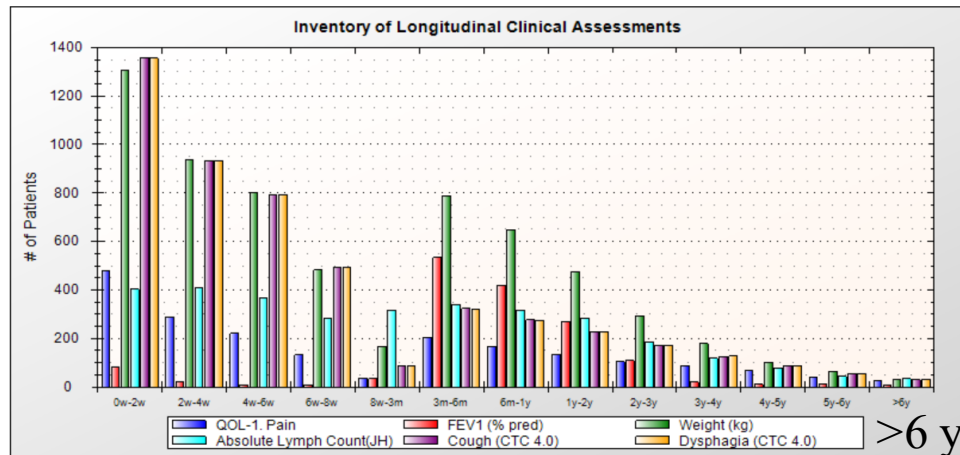
Totals:  
682 female  
831 male  
1513 total

## Targets

gtv_fb	675
gtv_0pct	549
PTV	418
ptv_final	323
gtv_60pct	311
gtv_50pct	215
GTV	211
ptvexp	178
ptv_5mm_exp	164
gtvrol	148
gtv_min	83
gtv_max	83

## Normals

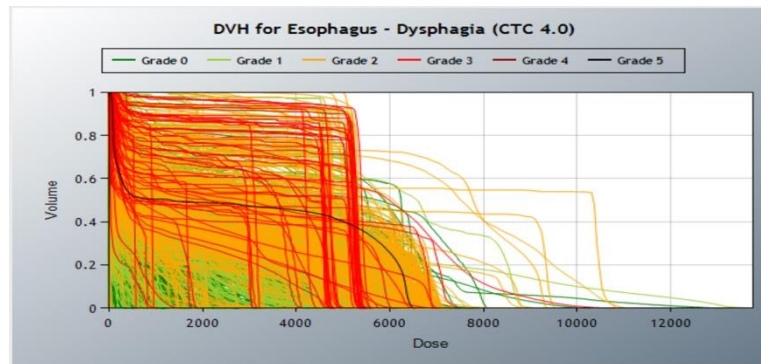
R_Lung	1633
L_Lung	1629
Esophagus	1452
Lungs	1385
Trachea	1322
Heart	836
SpinalCord	823
Pericardium	711
Liver	349
R_Kidney	267
L_Kidney	264
Thyroid	135



Total: 22894 assessments shown

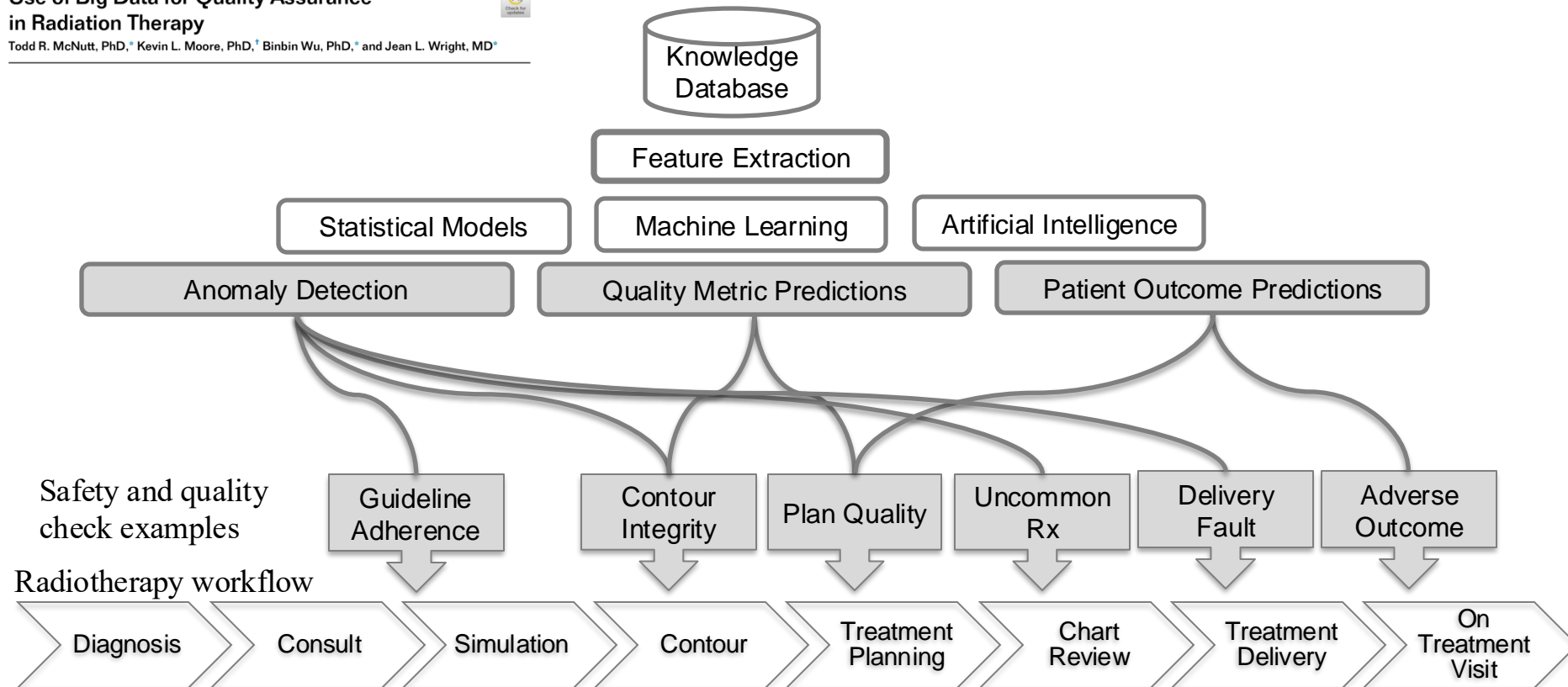
>6 yrs

## Esophagus DVH vs Dysphagia CTCAE

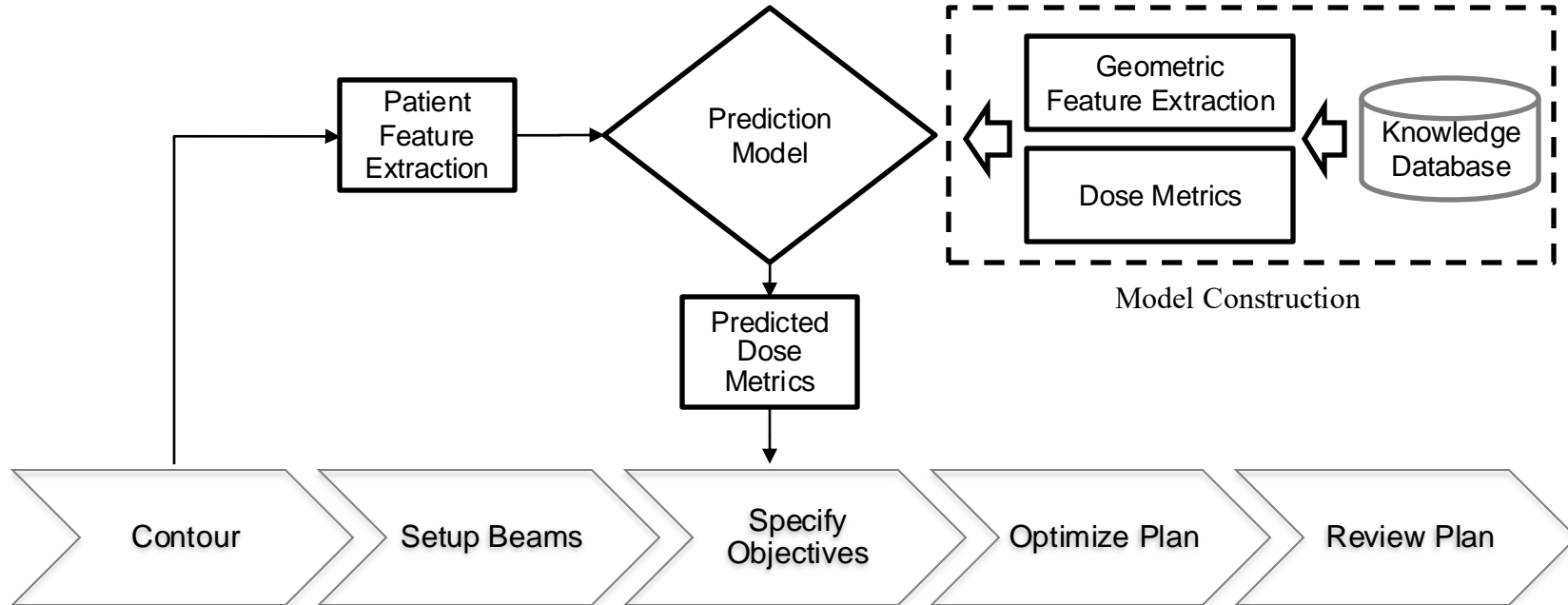


## Use of Big Data for Quality Assurance in Radiation Therapy

Todd R. McNutt, PhD,\* Kevin L. Moore, PhD,<sup>†</sup> Binbin Wu, PhD,\* and Jean L. Wright, MD\*

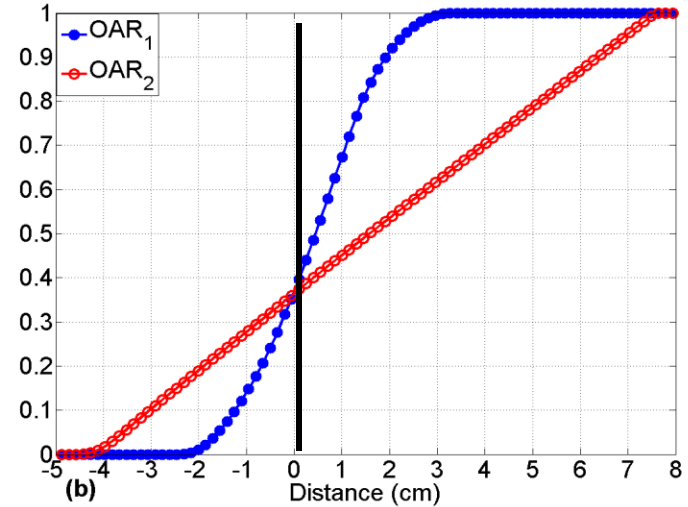
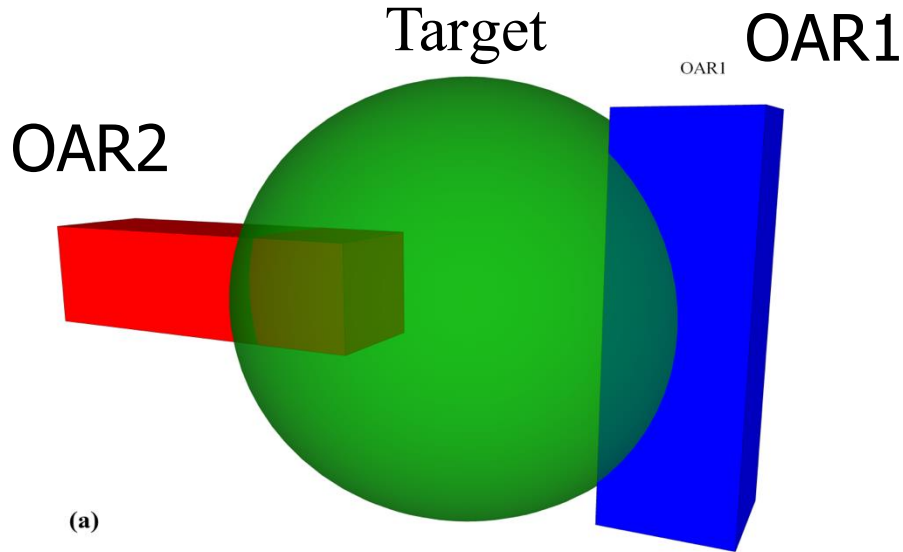


# Knowledge based planning



# Overlap Volume Histogram

OVH: serial vs parallel (Wu, Taylor, Kazhdan, Simari, McNutt)

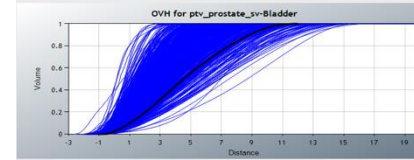
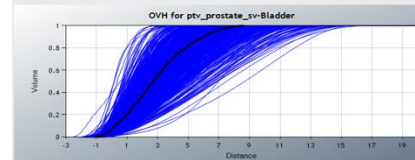
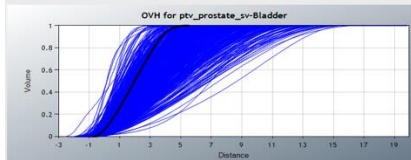
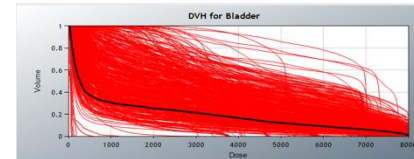
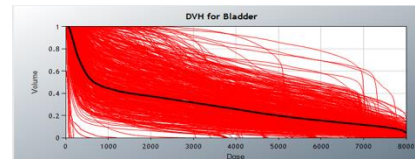
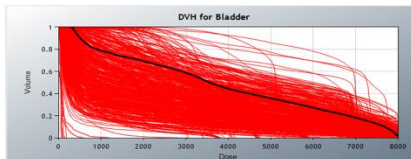


For parallel organs, **OAR2** is more easily spared.  
 For serial organs, **OAR1** is more easily spared.

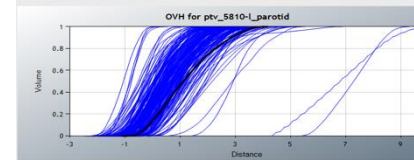
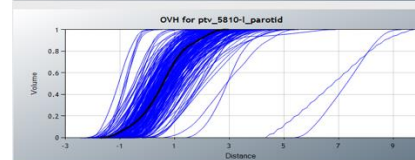
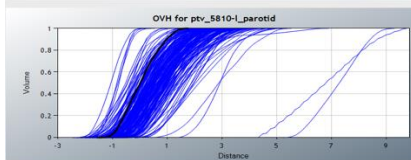
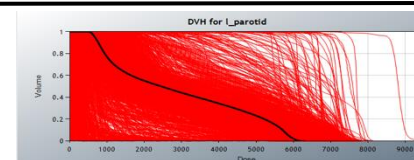
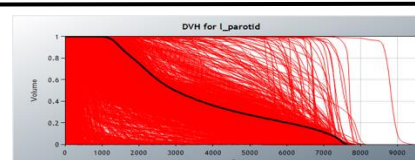
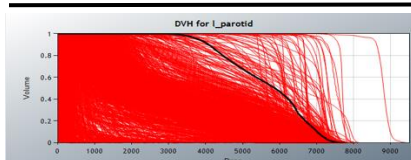


# OVH vs DVH

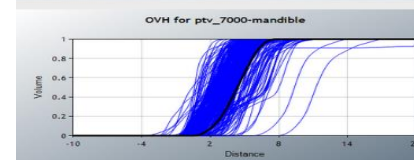
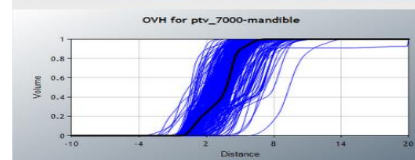
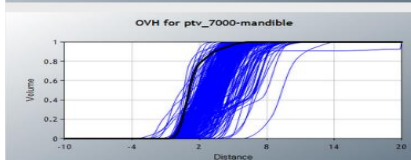
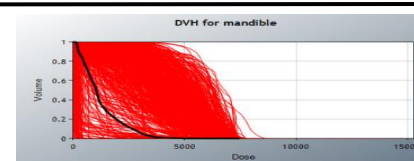
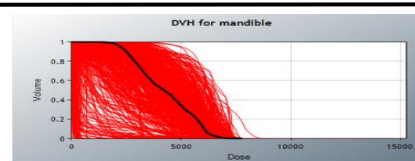
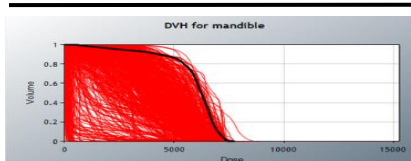
Bladder vs ptv\_prostate\_sv



Left parotid vs ptv\_5810



Mandible vs ptv\_7000

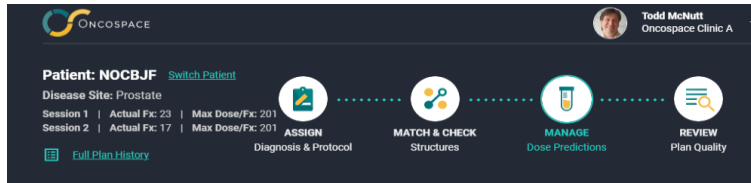




# New model predictions with Random Forest

Features: OVH-xyz, OVH-xy, OVH-z, PTV-Volume, PTV-Concavity...

**Lowest achievable** = Predicted median of the 5th percentile of doses given a set of input features at each %  
**Expected** = Predicted value of prior similar plans



**Patient: NOCBJF** [Switch Patient](#)

Disease Site: Prostate

Session 1 | Actual Fx: 23 | Max Dose/Fx: 201  
 Session 2 | Actual Fx: 17 | Max Dose/Fx: 201

**ASSIGN** (Diagnosis & Protocol) → **MATCH & CHECK** (Structures) → **MANAGE** (Dose Predictions) → **REVIEW** (Plan Quality)

[Full Plan History](#)

← Back Last updated: Jun 8, 2020, 11:38:29 PM

Next →

## Manage Dose Predictions

[PLAN VIEWER](#)

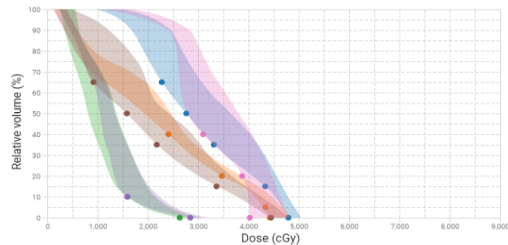
Course

**Plan: initial**

View protocol goals

Plan: conedown

- Bladder
- Bowel\_Bag
- L\_Head\_Femur
- PenileBulb
- R\_Head\_Femur
- Rectum
- Sigmoid\_Colon



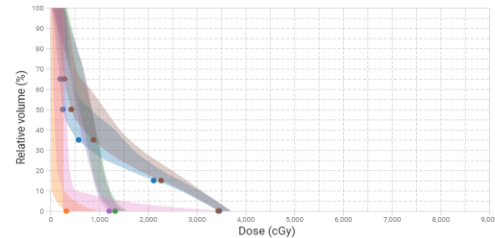

**Manage Dose Predictions** [PLAN VIEWER](#)

Showing:

Plan: conedown

View protocol goals

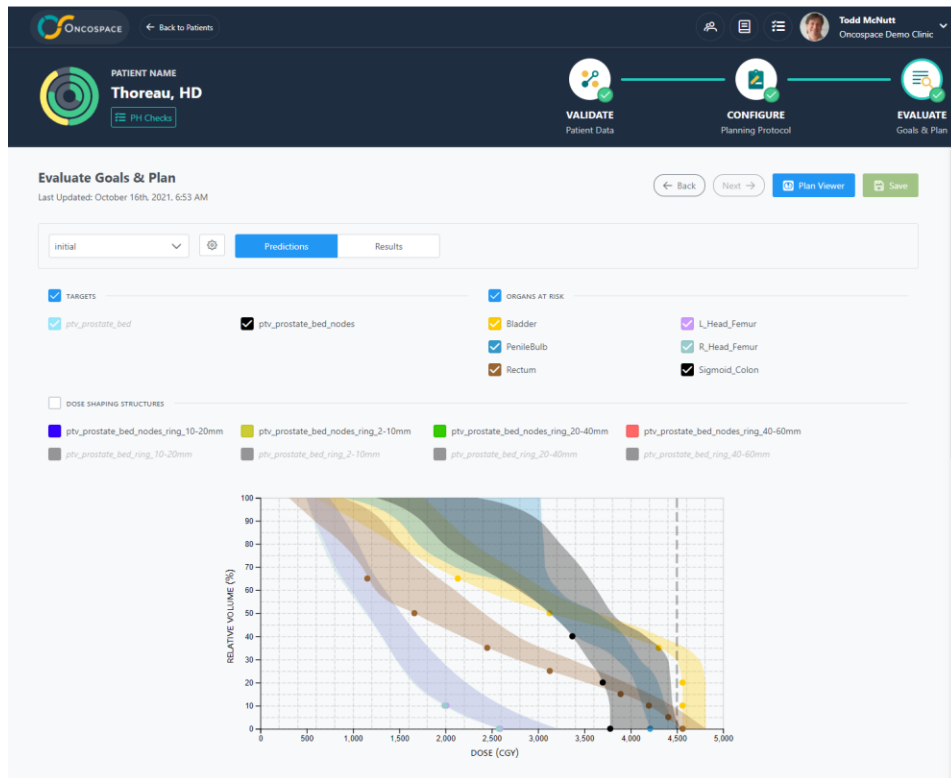
- Bladder
- Bowel\_Bag
- L\_Head\_Femur
- PenileBulb
- R\_Head\_Femur
- Rectum
- Sigmoid\_Colon



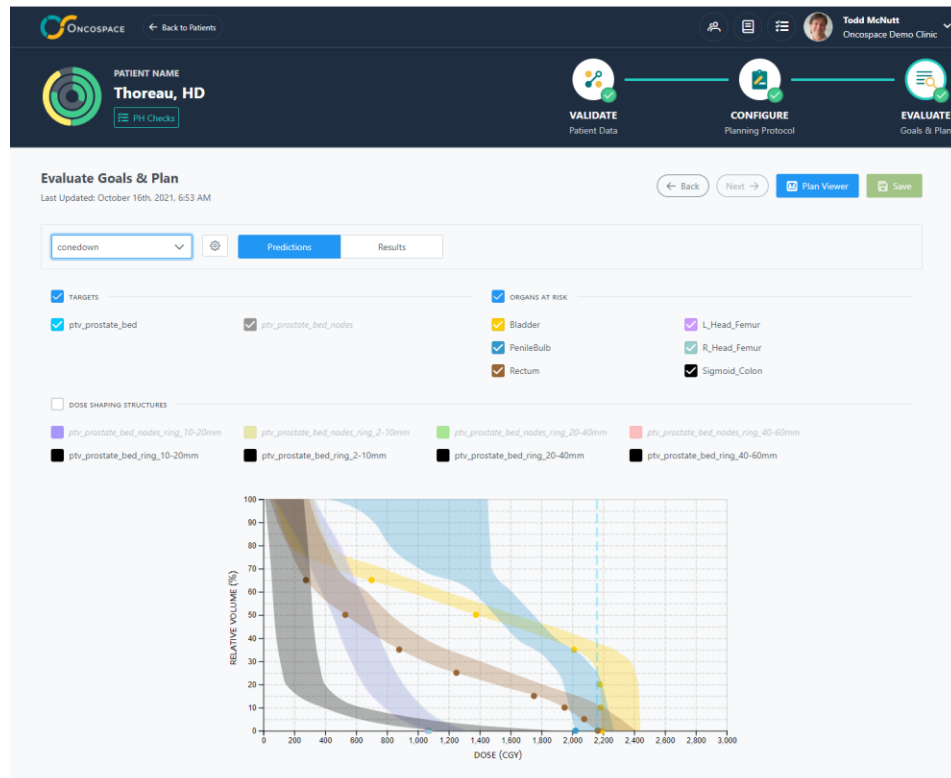
### Bladder

Goal ↓	Protocol	Best Achievable	Expected
Max dose to 65% volume (cGy)	2000	200	399
Max dose to 50% volume (cGy)	2500	254	828
Max dose to 35% volume (cGy)	3000	577	1515
Max dose to 15% volume (cGy)	3400	2118	2669
Max dose to 0% volume (cGy)	3600	3462	3565

# Predicted Plan objectives

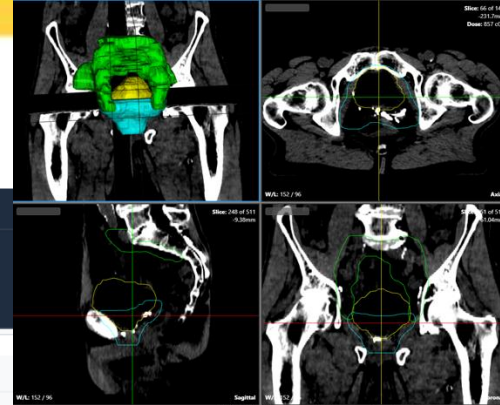


December 3, 2024



38

# Course Predictions



ONCOSPACE ← Back to Patients

Todd McNutt  
Oncospace Demo Clinic

PATIENT NAME  
**Thoreau, HD**  
PH Checks

VALIDATE Patient Data    CONFIGURE Planning Protocol    EVALUATE Goals & Plan

ONCOSPACE ← Back to Patients

Todd McNutt  
Oncospace Demo Clinic

PATIENT NAME  
**Thoreau, HD**  
PH Checks

Evaluate Goals & Plan  
Last Updated: October 16th, 2021, 6:53 AM

← Back    Next →    Plan Viewer    Save

Clinical Goals    Predictions    Results

TARGETS

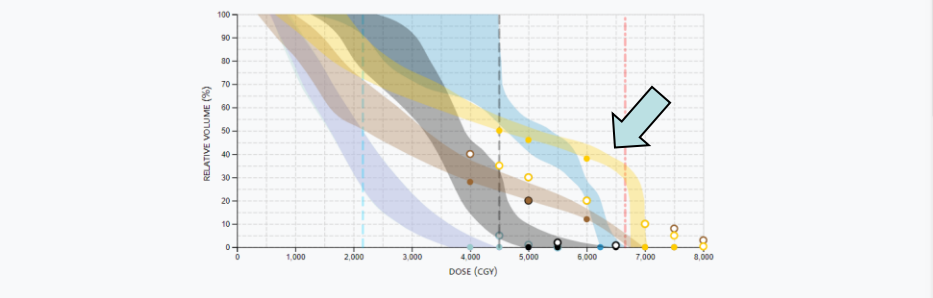
- ptx\_prostate\_bed
- ptx\_prostate\_bed\_nodes

ORGANS AT RISK

- Bladder
- PenileBulb
- Rectum
- L\_Head\_Femur
- R\_Head\_Femur
- Sigmoid\_Colon

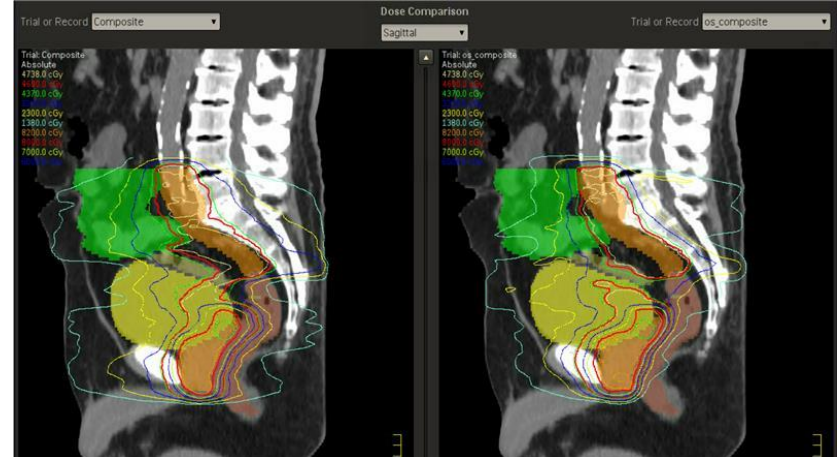
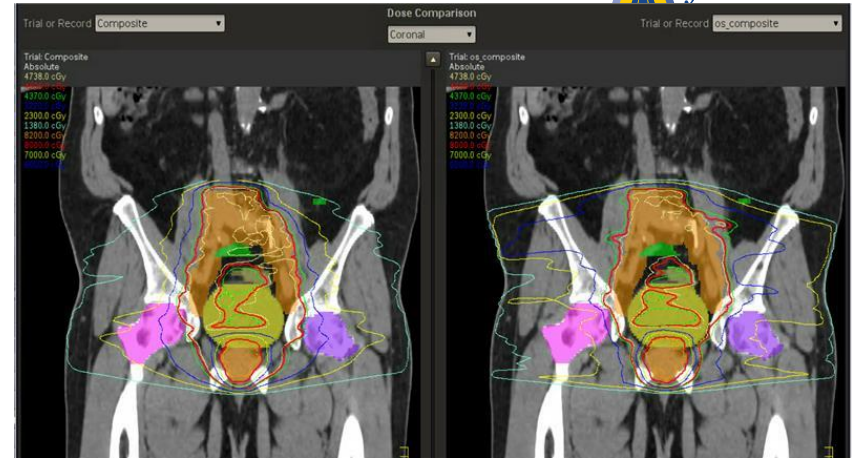
DOSE SHAPING STRUCTURES

- ptx\_prostate\_bed\_nodes\_ring\_10-20mm
- ptx\_prostate\_bed\_nodes\_ring\_2-10mm
- ptx\_prostate\_bed\_nodes\_ring\_20-40mm
- ptx\_prostate\_bed\_nodes\_ring\_40-60mm
- ptx\_prostate\_bed\_ring\_10-20mm
- ptx\_prostate\_bed\_ring\_2-10mm
- ptx\_prostate\_bed\_ring\_20-40mm
- ptx\_prostate\_bed\_ring\_40-60mm



Goal	Protocol	Predicted Range	Visual Progress
<b>Bladder</b>			
V8000cGy[cc]	≤ 1-7.5 cc	0 - 0	[Progress bar]
V4500cGy[%]	≤ 35-55%	50 - 56	[Progress bar]
V5000cGy[%]	≤ 30-50%	46 - 51	[Progress bar]
V6000cGy[%]	≤ 20-40%	38 - 44	[Progress bar]
V7000cGy[%]	≤ 10-30%	0 - 2	[Progress bar]
V7500cGy[%]	≤ 5-25%	0 - 0	[Progress bar]
<b>L_Head_Femur</b>			
<b>PenileBulb</b>			
<b>R_Head_Femur</b>			
<b>Rectum</b>			
V4000cGy[%]	≤ 40-50%	28 - 38	[Progress bar]
V5000cGy[%]	≤ 30-40%	20 - 28	[Progress bar]
V6000cGy[%]	≤ 20-30%	12 - 17	[Progress bar]
V7000cGy[%]	≤ 10-20%	0 - 0	[Progress bar]
V7500cGy[%]	≤ 8-15%	0 - 0	[Progress bar]
V8000cGy[%]	≤ 3-7%	0 - 0	[Progress bar]

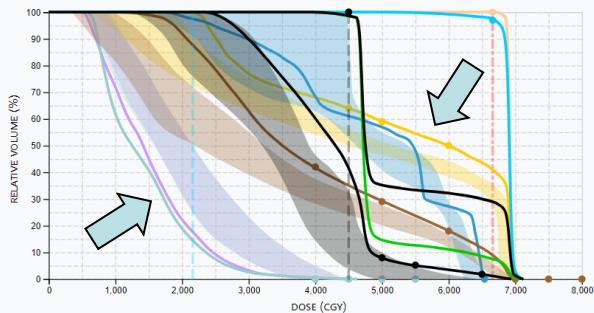
# Autoplan result



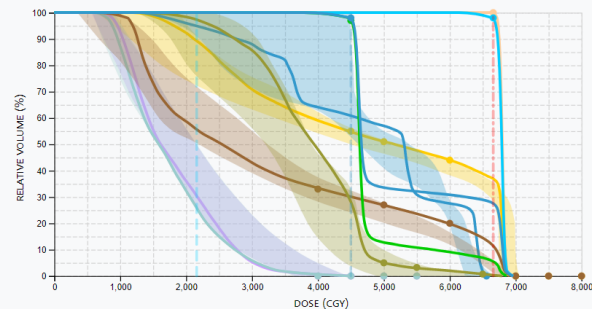
# Comparison

## Clinical Plan

- Bladder
- PenileBulb
- Rectum
- L\_Head\_Femur
- R\_Head\_Femur
- Sigmoid\_Colon



## Predictive Plan



Goal ↑↓	Protocol ↑↓	Predicted Range ↑↓	Plan Value ↑↓	Comparison
Bladder				
V8000cGy(cc)	≤ 1-7.5 cc	0 - 0	0	
V4500cGy(%)	≤ 35-55%	50 - 56	64	
V5000cGy(%)	≤ 30-50%	46 - 51	59	
V6000cGy(%)	≤ 20-40%	38 - 44	50	
V7000cGy(%)	≤ 10-30%	0 - 2	1	
V7500cGy(%)	≤ 5-25%	0 - 0	0	

Goal ↑↓	Protocol ↑↓	Predicted Range ↑↓	Plan Value ↑↓	Comparison
Bladder				
V8000cGy(cc)	≤ 1-7.5 cc	0 - 0	0	
V4500cGy(%)	≤ 35-55%	50 - 56	55	
V5000cGy(%)	≤ 30-50%	46 - 51	51	
V6000cGy(%)	≤ 20-40%	38 - 44	44	
V7000cGy(%)	≤ 10-30%	0 - 2	0	
V7500cGy(%)	≤ 5-25%	0 - 0	0	

# AI prostate planning results

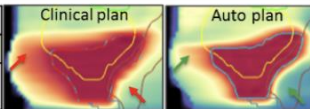
Song, Ennis, Showalter

RadOnc A, High Risk Patient #1

APFLDO (P1 High) Feature Ratings (1 worst – 5 best)				JCLHD (P1 High) Feature Ratings (1 worst – 5 best)			
Category	Feature	Score	Ave cat.	Category	Feature	Score	Ave cat.
Overall	overall quality	3	3	Overall	overall quality	4	4
Targets	tumor coverage	5	5	Targets	tumor coverage	5	5
	tumor homogeneity	5		OARS	tumor homogeneity	5	
OARS	bladder sparing	2	4.2	OARS	bladder sparing	3	4.4
	rectum sparing	4		OARS	rectum sparing	4	
	femur head sparing	5		OARS	femur head sparing	5	
	bowel sparing	5		OARS	bowel sparing	5	
	penile bulb sparing	5		OARS	penile bulb sparing	5	
Non-ROIs	dose outside ROIs	2	2	Non-ROIs	dose outside ROIs	3	3
Plan clinically acceptable?		marginal		Plan clinically acceptable?		yes	
Comments: Dose extends anterior to pubic symphysis				Comments: Better than APFLDO, but high dose fully includes pubic bone			

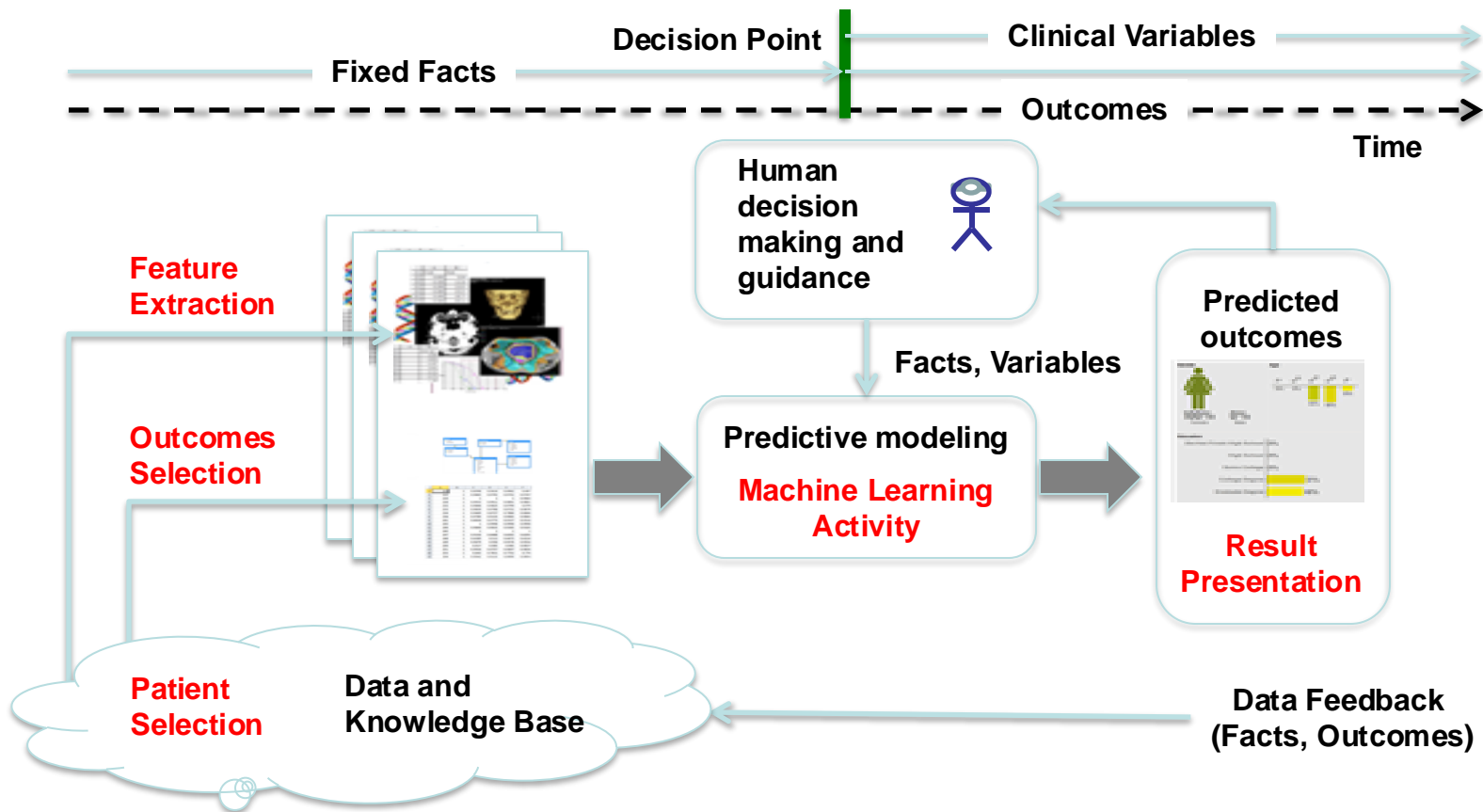
Comparison of plan APFLDO vs JCLHD (P1 High)		
Which plan is preferable?	JCLHD	
Which aspect was most relevant in that selection?	Lower dose rectal volumes better; less anterior coverage beyond pubic bone	



**Figure 13.** Example of ratings and overall preference for the pair of plans for high risk patient #1. Dose overlay indicates the advantages of the auto plan commented on in green.

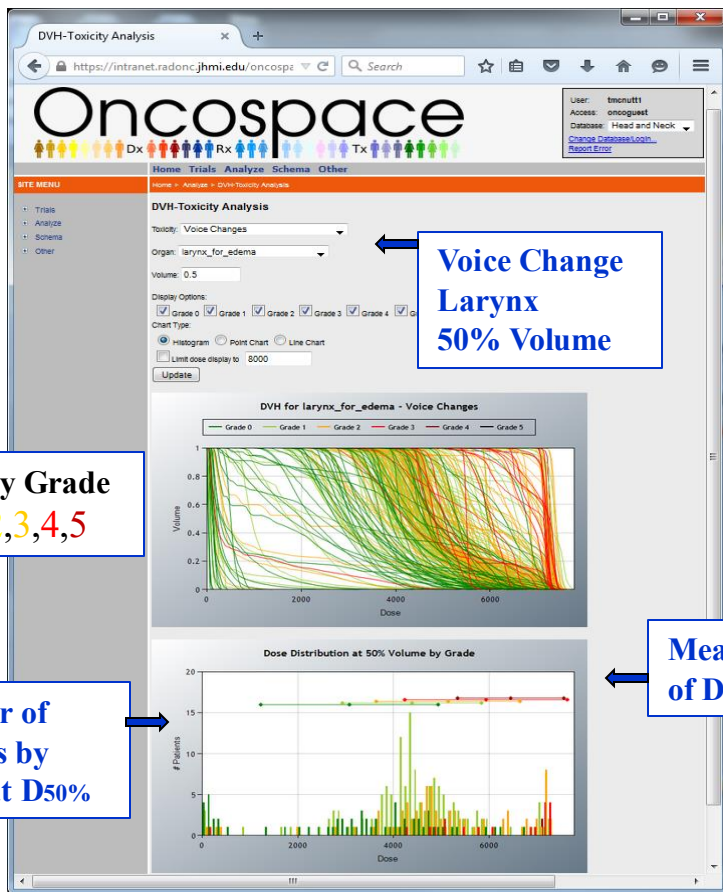
	Clinical Acceptability of Plan						Preferable Plan				
	RadOnc A		RadOnc B		RadOnc C		RadOnc A	RadOnc B	RadOnc C	Overall	
	Auto	Clin	Auto	Clin	Auto	Clin					
<b>Pilot</b>											
P1 Low	Yes	Yes	Yes	Yes	Marginal	Yes	Clin	Auto	Clin	Clin	
P1 Int	No	No	No	No	Marginal	Yes	Clin	Auto	Clin	Clin	
P2 Int	Yes	Marginal	Yes	Yes	Yes	Yes	Auto	Clin	Auto	Auto	
<b>Test</b>											
P2 Low	Yes	Marginal	Yes	Yes	Yes	Yes	Auto 12-0	Auto 10-2	Auto 9-3	<b>Auto 12-0</b>	
P3 Low	Yes	Yes	Yes	Yes	Yes	Yes	Auto	Auto	Clin	<b>Auto</b>	
P4 Low	Yes	No	Yes	No	Yes	No	Auto	Auto	Auto	<b>Auto</b>	
P3 Int	Yes	Yes	Yes	Yes	Yes	Yes	Auto	Auto	Clin	<b>Auto</b>	
P4 Int	Yes	Yes	Yes	Yes	Yes	Marginal	Auto	Auto	Auto	<b>Auto</b>	
P5 Int	Yes	Yes	Yes	Yes	Yes	Yes	Auto	Auto	Auto	<b>Auto</b>	
P1 High	Yes	Marginal	Yes	No	Marginal	Marginal	Auto	Auto	Clin	<b>Auto</b>	
P2 High	Yes	Yes	Yes	Yes	Yes	Yes	Auto	Clin	Auto	<b>Auto</b>	
P3 High	Yes	Yes	Yes	Yes	Yes	Yes	Auto	Clin	Auto	<b>Auto</b>	
P4 High	No	No	No	No	Marginal	No	Auto	Auto	Auto	<b>Auto</b>	
P5 High	Yes	Marginal	Yes	Yes	Yes	Yes	Auto	Auto	Auto	<b>Auto</b>	
P6 High	Yes	Marginal	Yes	Yes	Yes	Yes	Auto	Auto	Auto	<b>Auto</b>	

# Learning health system – Decision Support





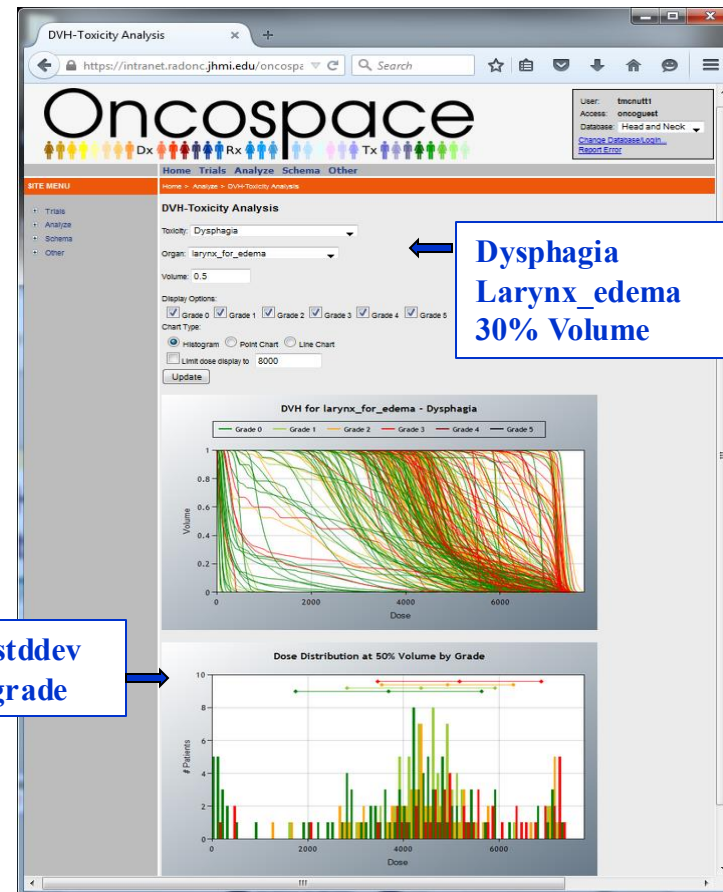
# DVH, Toxicities and Grade distributions



Voice Change  
Larynx  
50% Volume

Toxicity Grade  
0,1,2,3,4,5

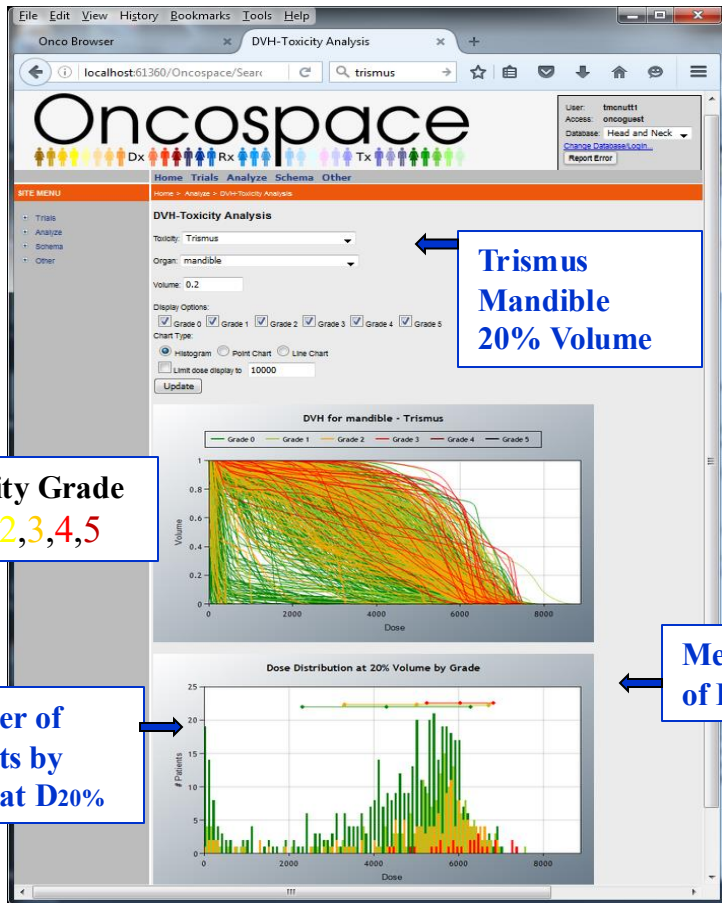
Number of patients by grade at D50%



Dysphagia  
Larynx\_edema  
30% Volume

Mean and stddev of Dx% at grade

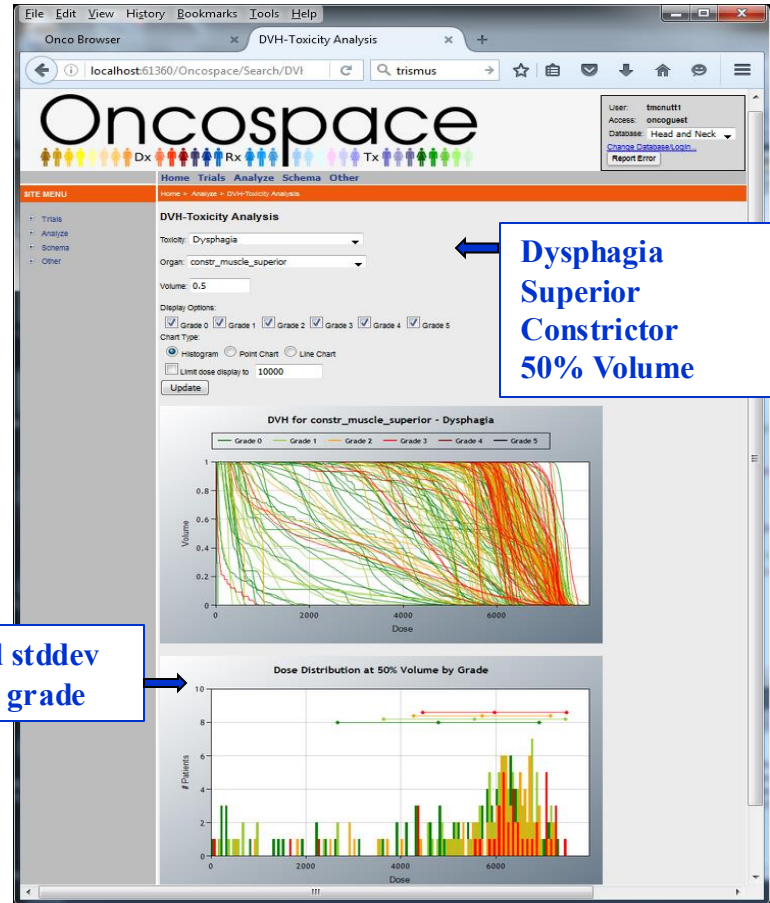
# DVH, Toxicities and Grade distributions



Trismus  
Mandible  
20% Volume

Toxicity Grade  
0,1,2,3,4,5

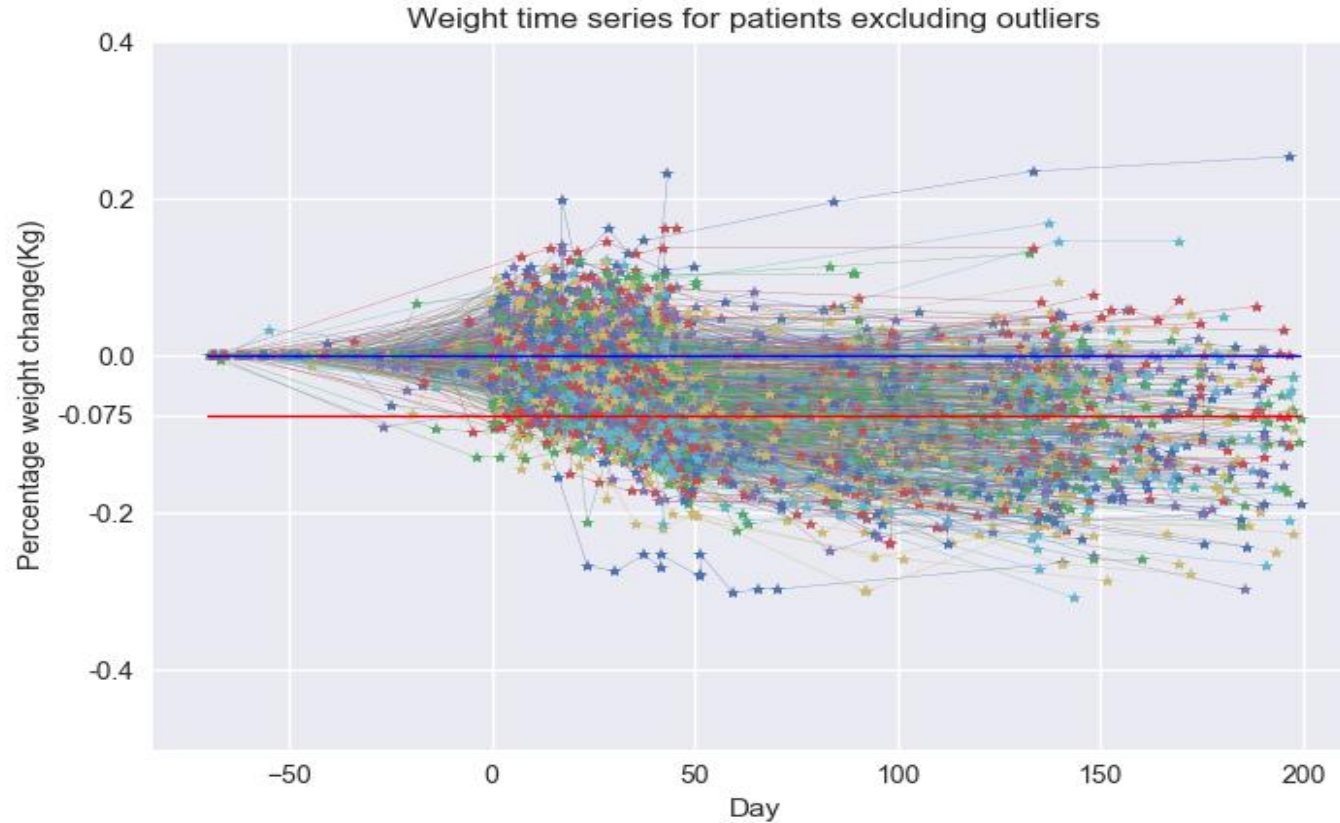
Number of  
patients by  
grade at D20%



Dysphagia  
Superior  
Constrictor  
50% Volume

Mean and stddev  
of Dx% at grade

# Longitudinal measures

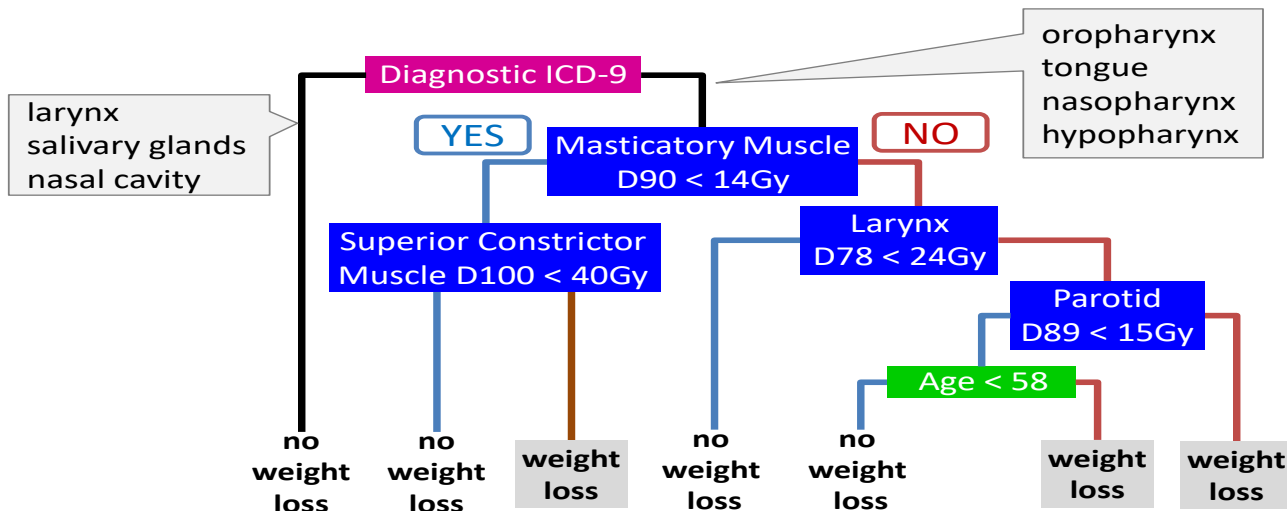


# Results: Weight loss prediction at planning

Endpoint: > 5kg loss at 3 months post RT

- Predictors:
  - (1: **Diagnosis**) ICD-9 code
  - (2: **Dosimetry**) dose to swallowing muscles, larynx, parotid
  - (3: **Patient**) age
- Prediction result: High negative predictive value
  - The model can screen out patient without weight loss
  - Physicians can focus on patients with high probability of weight loss

Sierra Zhi Cheng MD MS  
Minoru Nakatsagawa PhD



## Prediction result

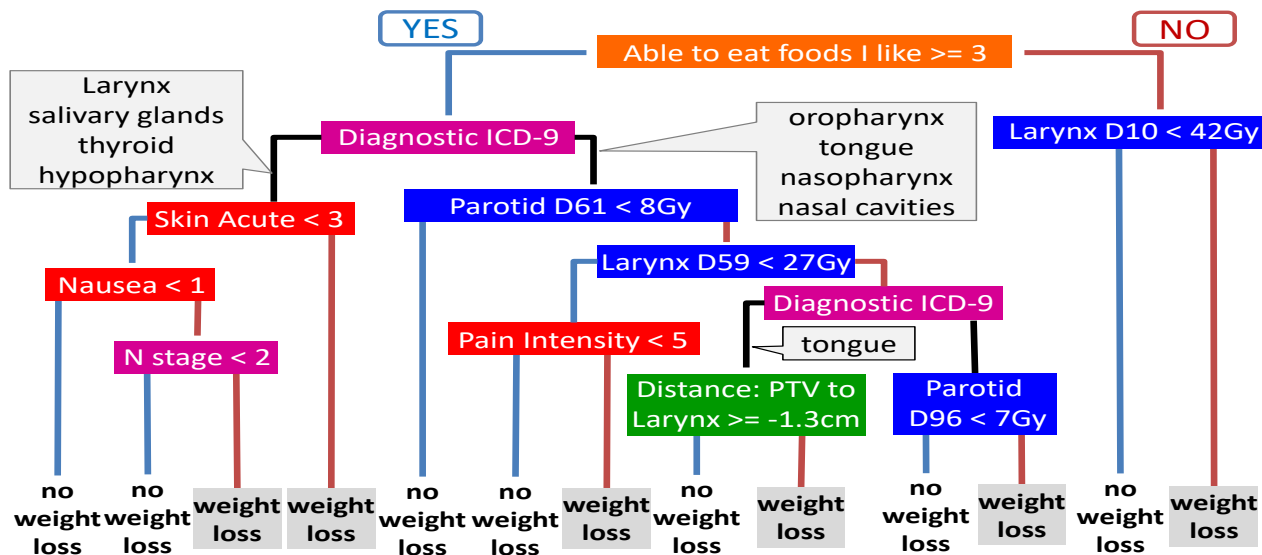
AUC	0.773
Sensitivity	0.766
PPV	0.426
NPV	0.901

# Results: Weight loss prediction during RT

- Predictors: **Endpoint: > 5kg loss at 3 months post RT**

- (1: QOL) patient reported oral intake
- (2: Diagnosis and staging) ICD-9, N stage
- (3: Dosimetry) dose to larynx, parotid
- (4: Toxicity) skin toxicity, nausea, pain
- (5: Geometry) minimum distance b/w PTV, larynx

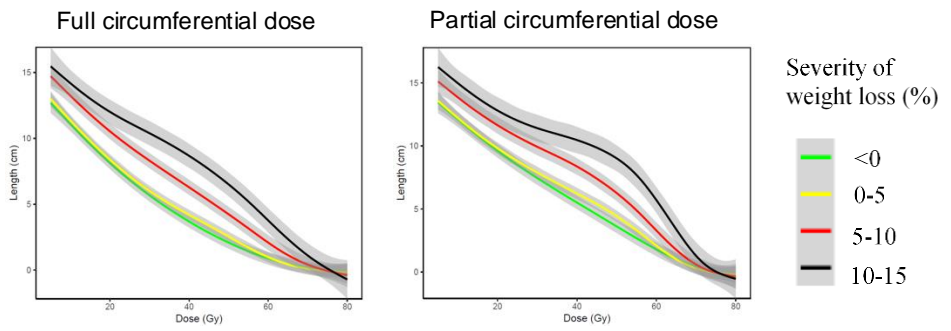
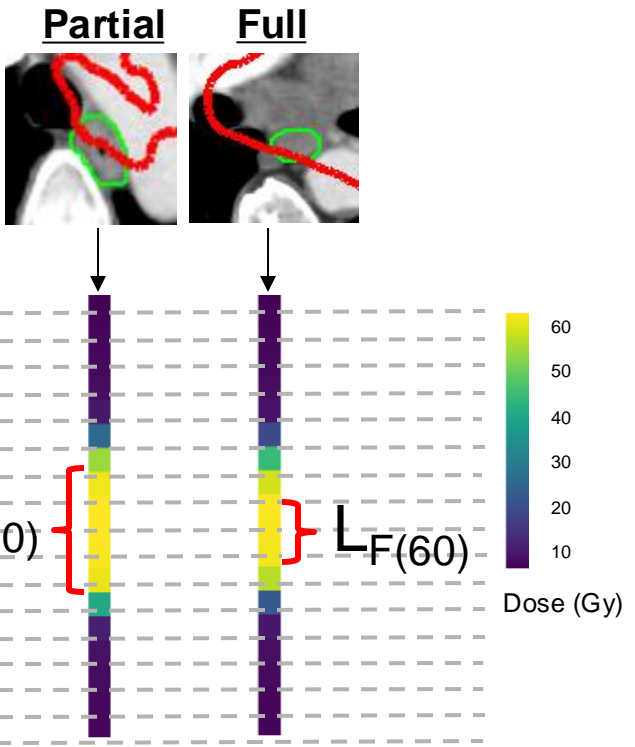
Sierra Zhi Cheng MD MS  
Minoru Nakatsagawa PhD



## Prediction result

AUC	0.821
Sensitivity	0.977
PPV	0.462
NPV	0.986

# Length of circumferential esophageal dose vs weight loss P. Han et al.



**Table 2. Weight loss prediction using Ridge**

Variable	importance*
Pre-treatment albumin	100
$L_F(65)$	85
Marital status	53
$L_F(60)$	45
$L_P(65)$	42
ECOG performance status	36
$L_F(55)$	35
Chemotherapy (full dose vs. none)	32
$L_P(60)$	31
Race	24

# Our Xerostomia Story

**an example of possibilities for data-driven outcome-based planning**



# Toxicity Prevalence

(P. Lakshminarayanan)

## Prevalence

Select criteria:

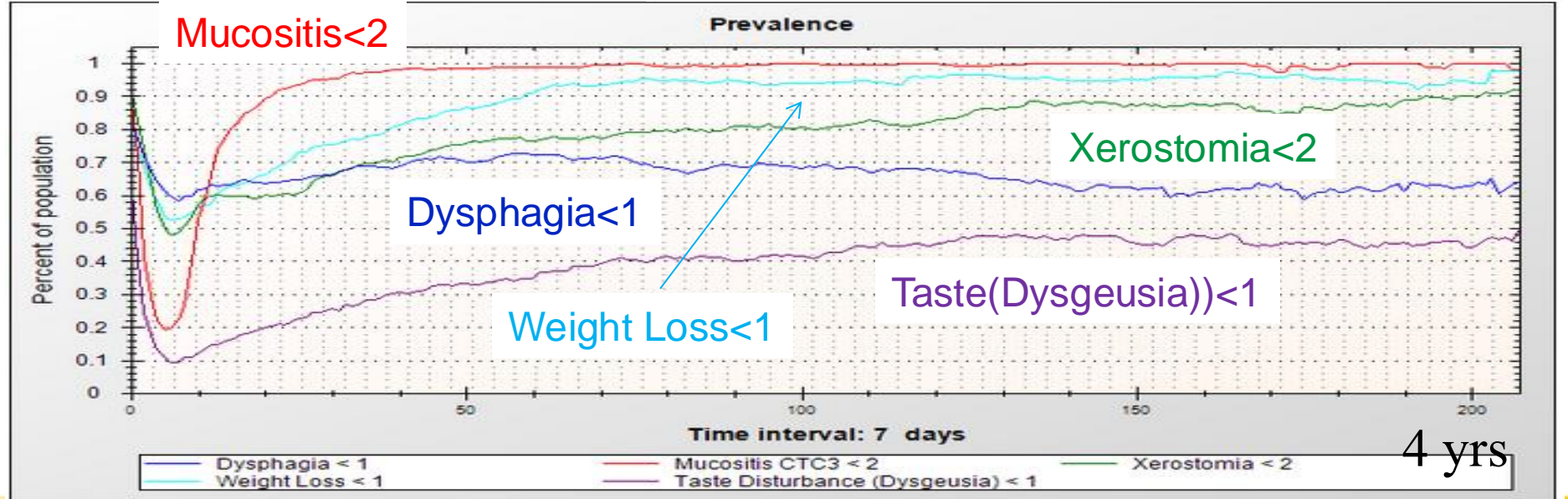
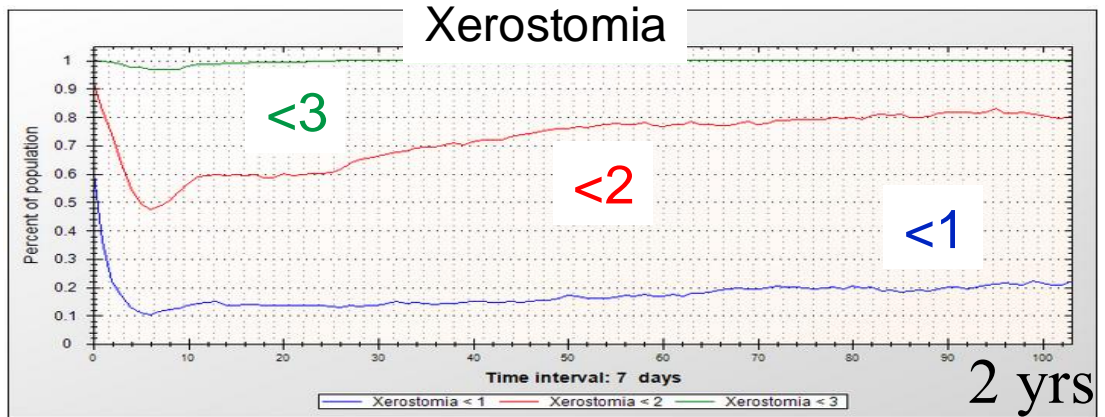
Xerostomia < 3

Select trends to view:

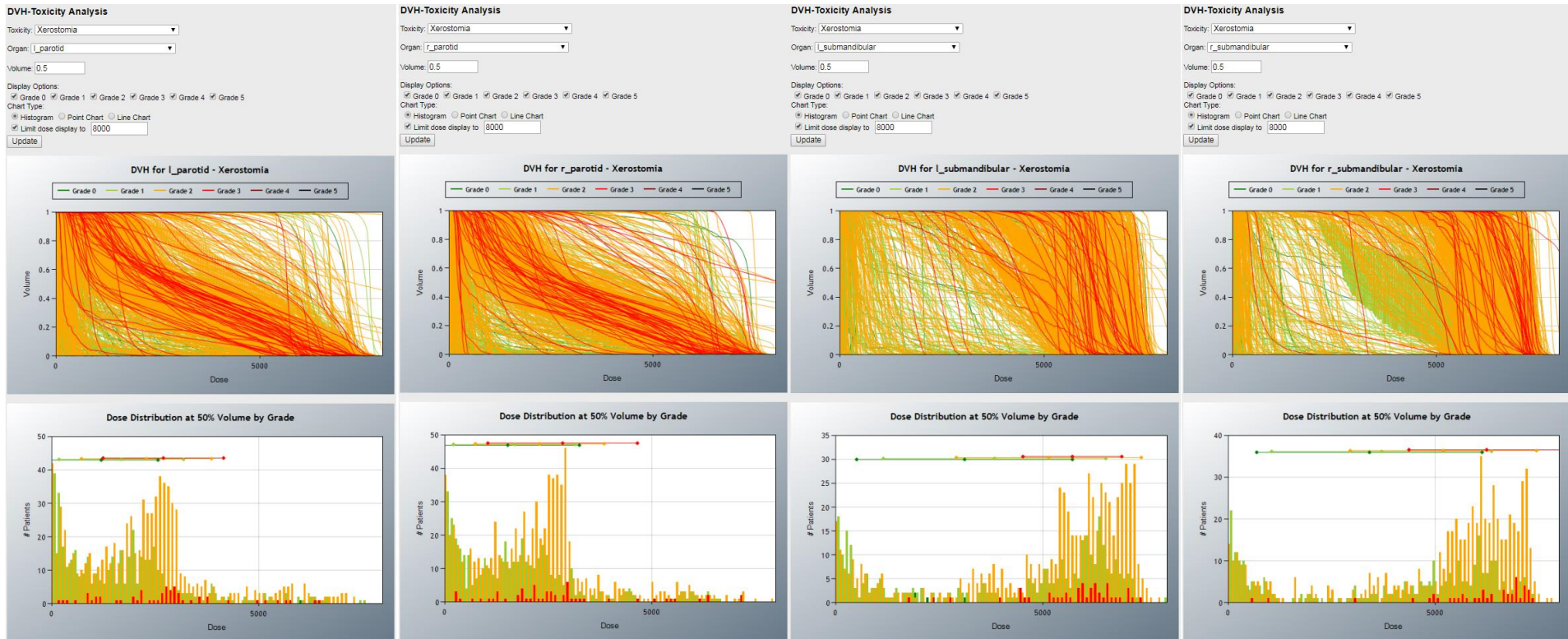
Xerostomia < 1   
 Xerostomia < 2   
 Xerostomia < 3

Time Interval: 7 days

Timespan: 2 years

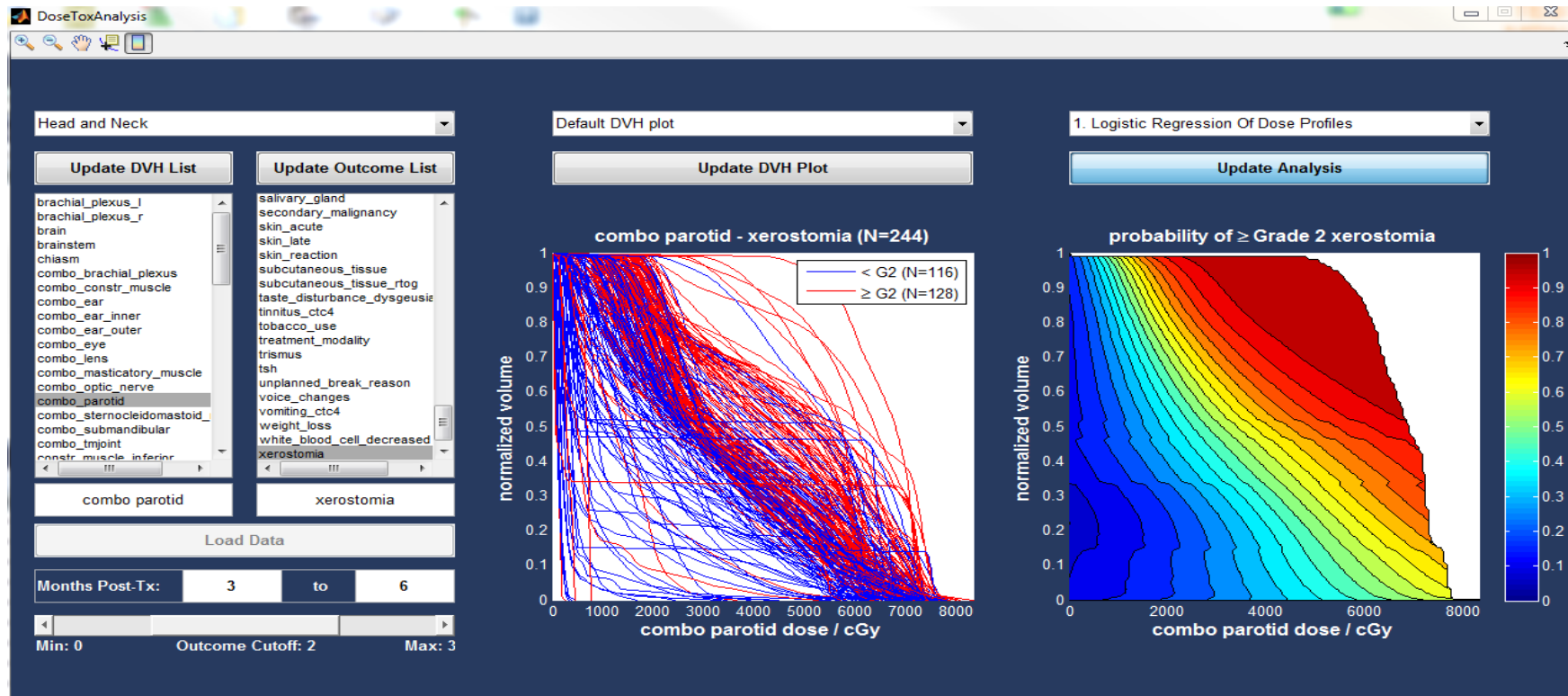


# Raw DVH data for salivary glands

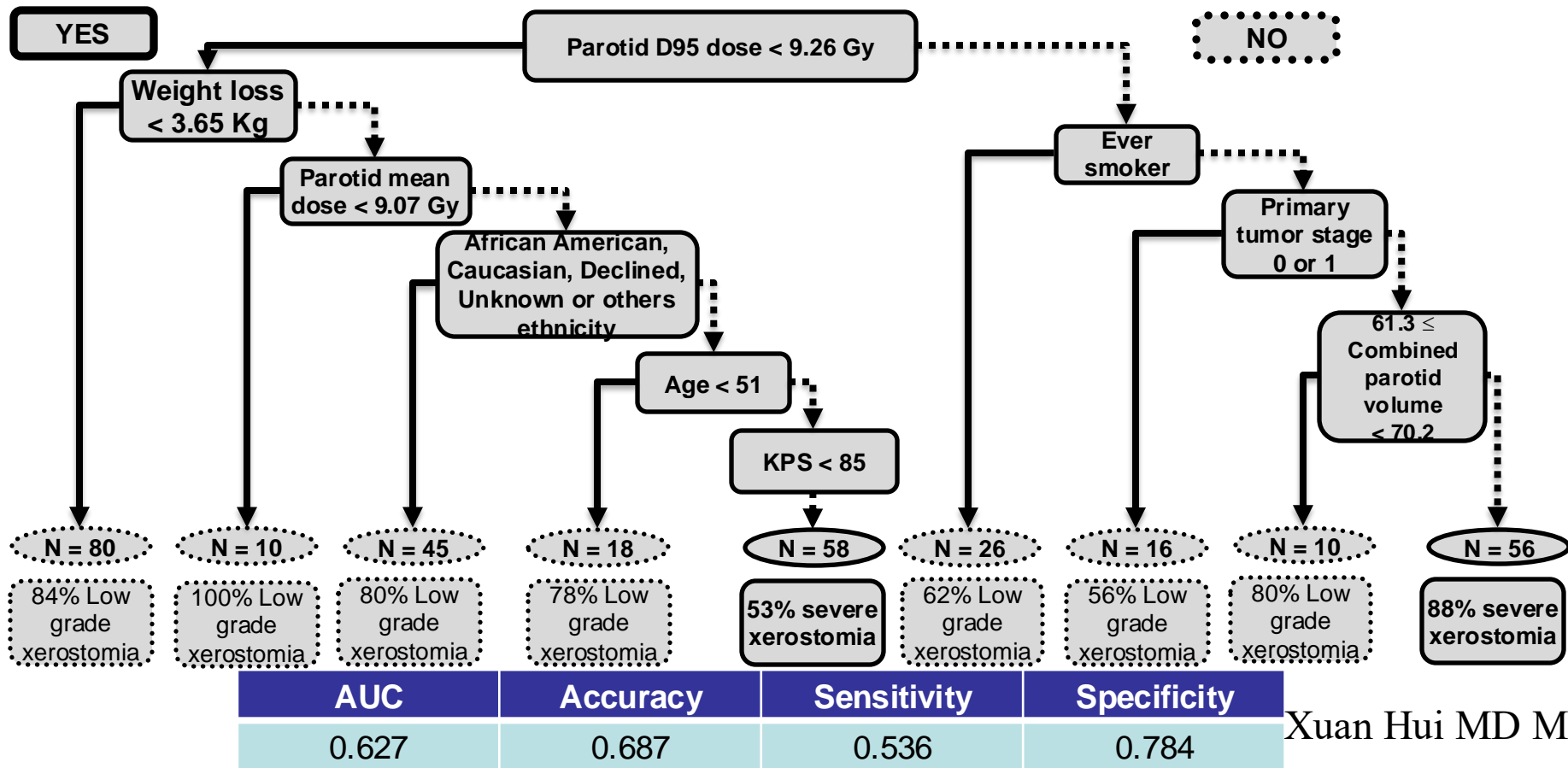


# Toxicity and Dose Volume Histogram

(Scott Robertson et al...)

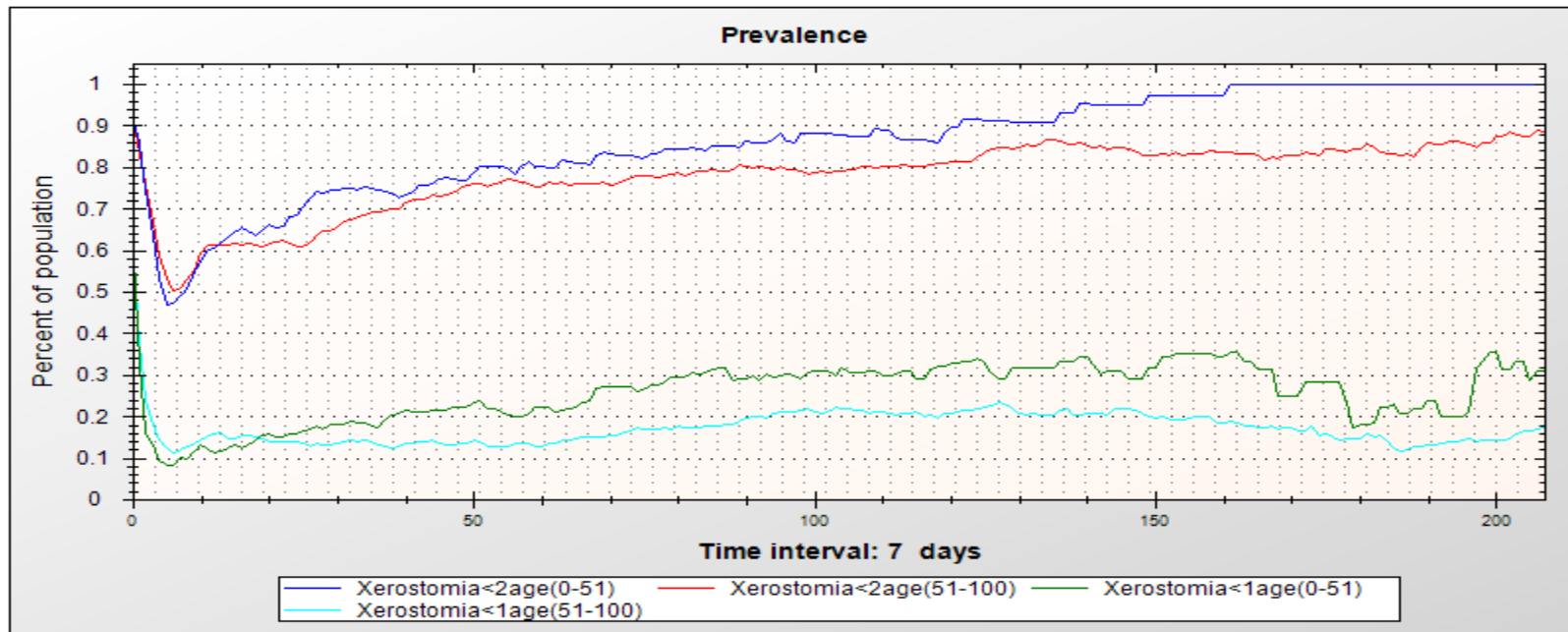


# Xerostomia Prediction (3-6 Months post RT)





# Xerostomia prevalence separated by age = 51



## Xerostomia<2age(0-51) :

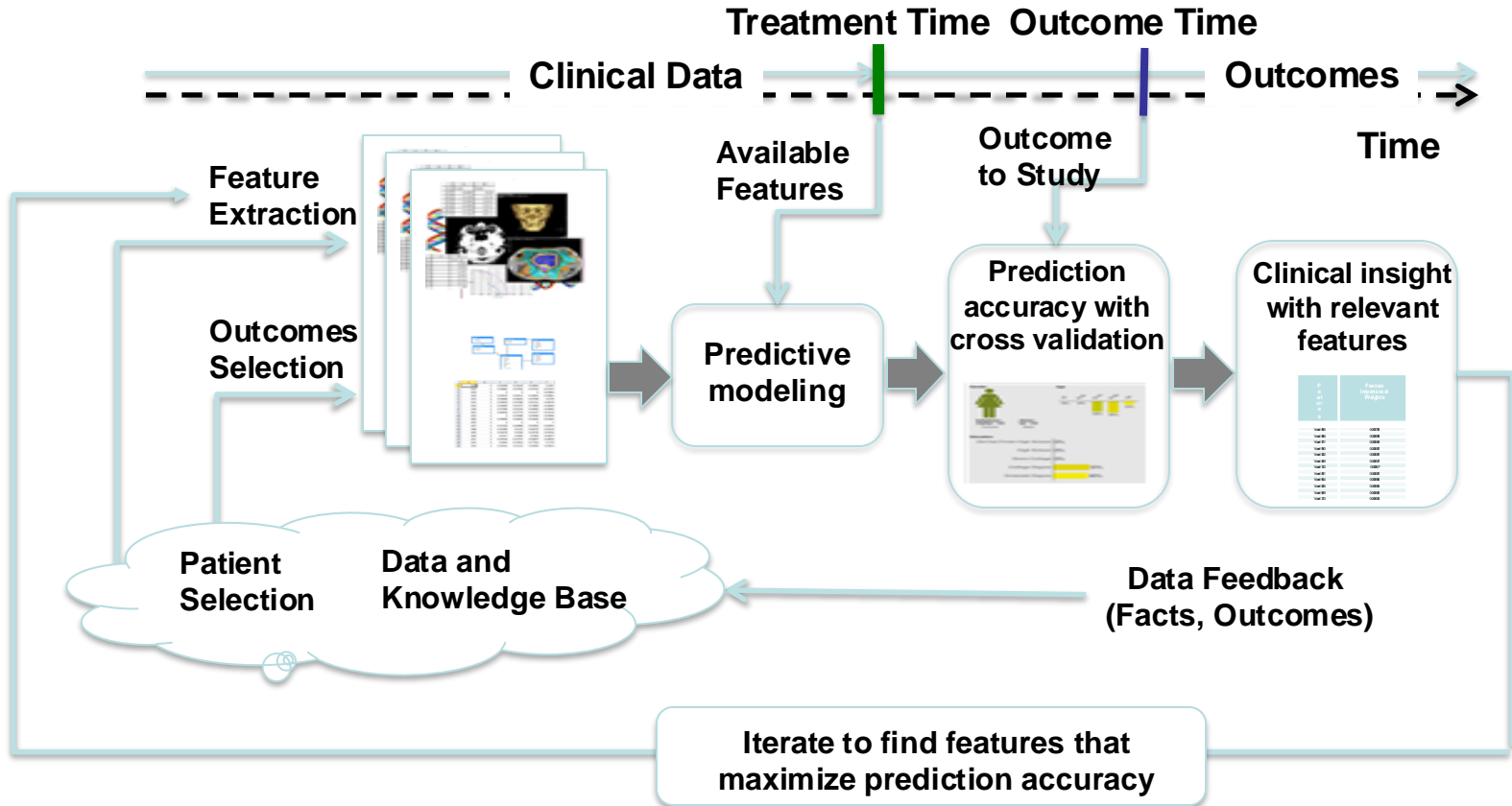
Initial size: 175  
25% lost follow up at time: 26  
50% lost follow up at time: 74

## Xerostomia<2age(51-100) :

Initial size: 654  
25% lost follow up at time: 27  
50% lost follow up at time: 64

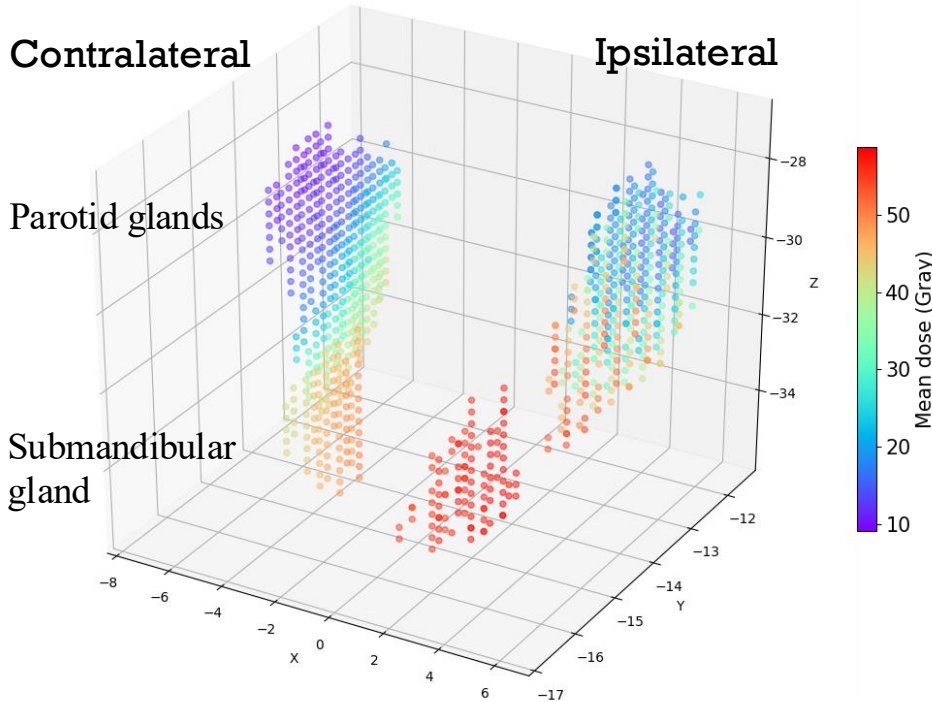


# Learning health system – Hypothesis Derivation

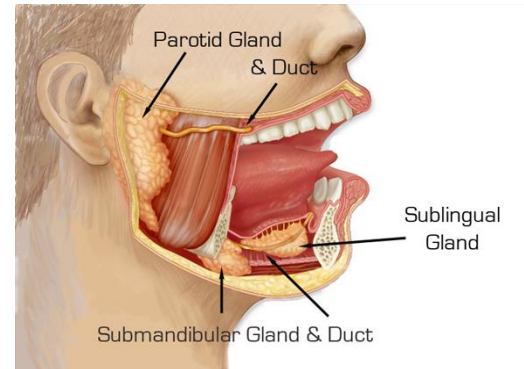
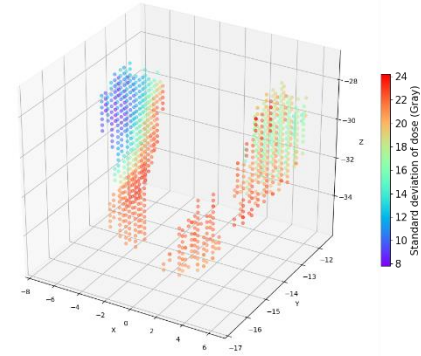


# Radiation dose transformed to standard atlas

## Average dose to each voxel

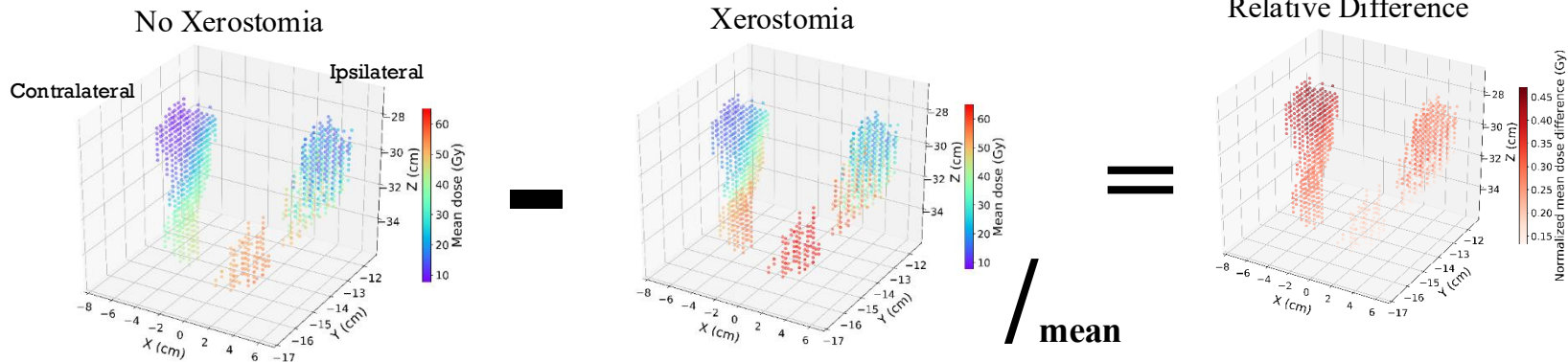


## Standard Deviation of Dose

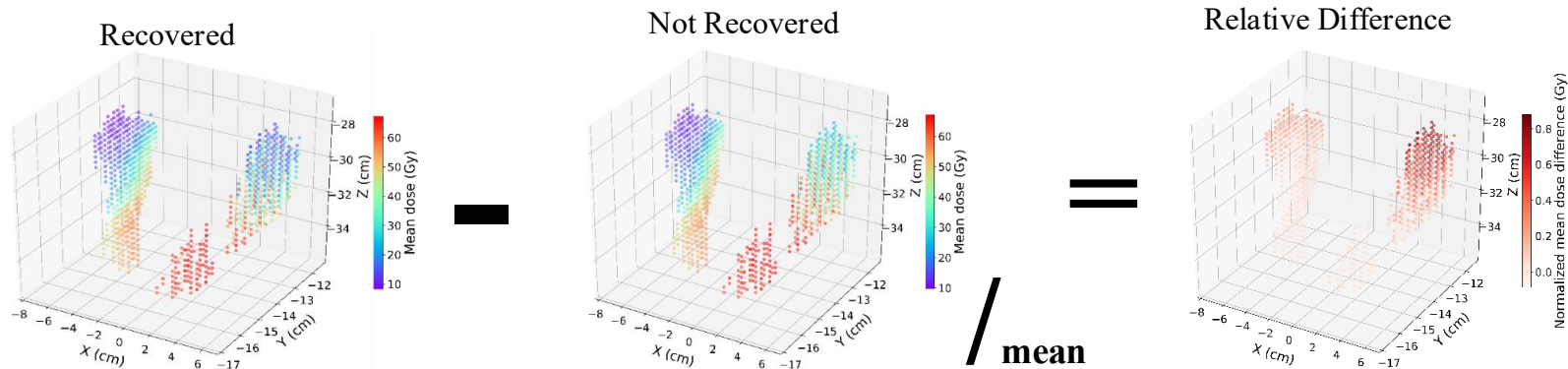


# Mean voxel doses and normalized difference

## Acute Xerostomia



## Recovery



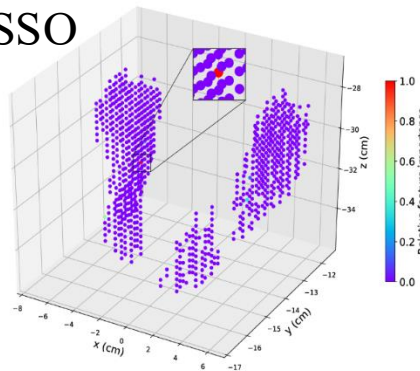
# Voxel importance pattern comparisons by machine learning

## Acute Xerostomia (Injury)



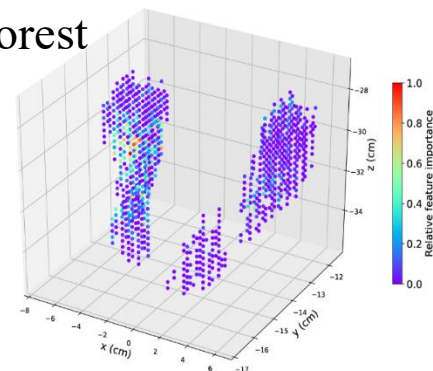
\*\*\* **Ridge** is most appropriate to handle correlated dose variable

### LASSO



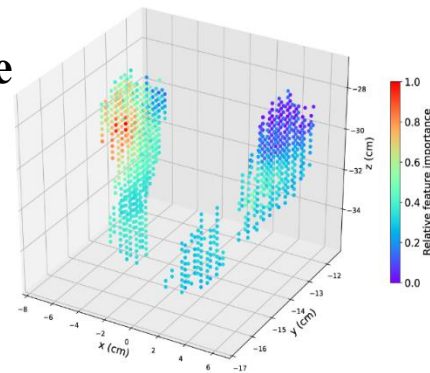
(a) Voxel importance pattern from lasso logistic regression

### Random Forest



(b) Voxel importance pattern from random forest

### Ridge

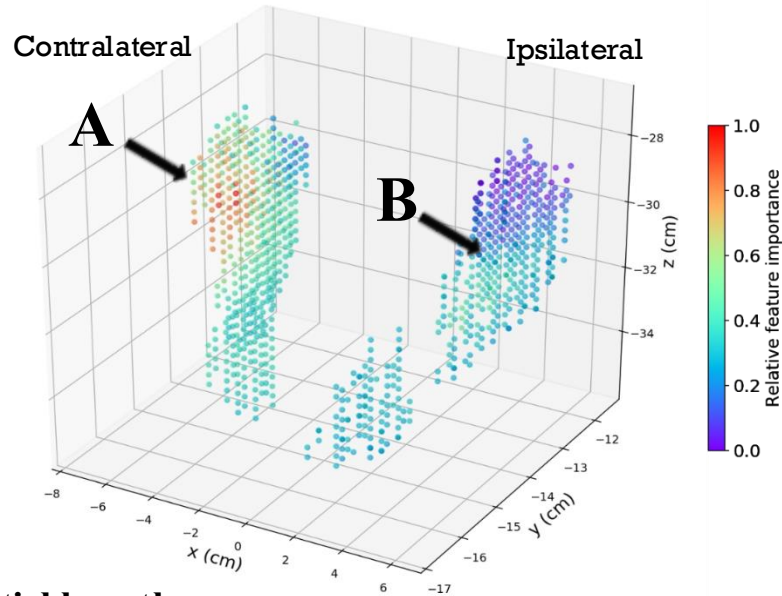


(c) Voxel importance pattern from ridge logistic regression

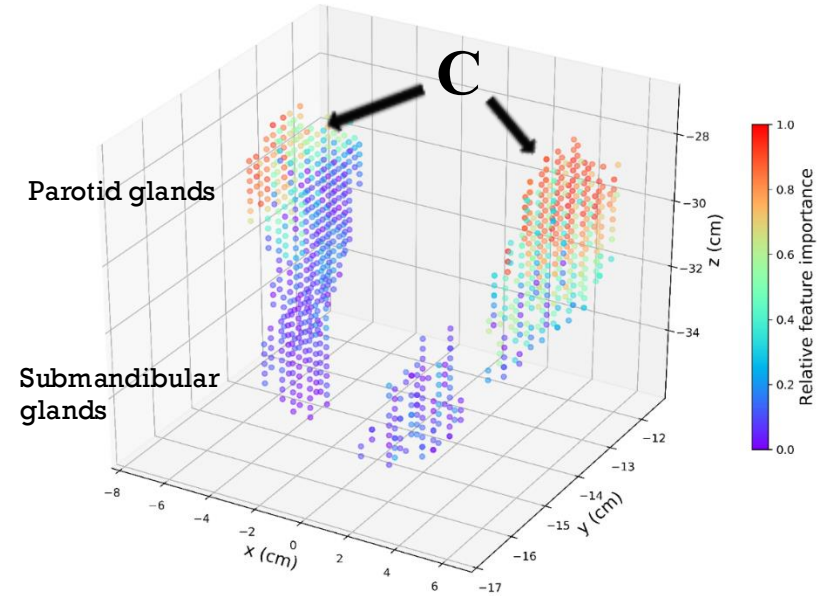
Models	Data set (dimension: 427*961)
	AUC (10-fold cross-validation) Out-of-sample score
<b>Ridge logistic regression</b>	<b>0.70 ±0.04</b>
Lasso logistic regression	0.67±0.04
Random forest	0.69±0.06

# Voxels importance from Ridge logistic regression

## Acute Xerostomia (Injury)



## Recovery

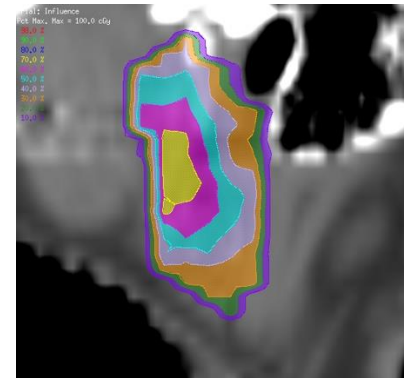
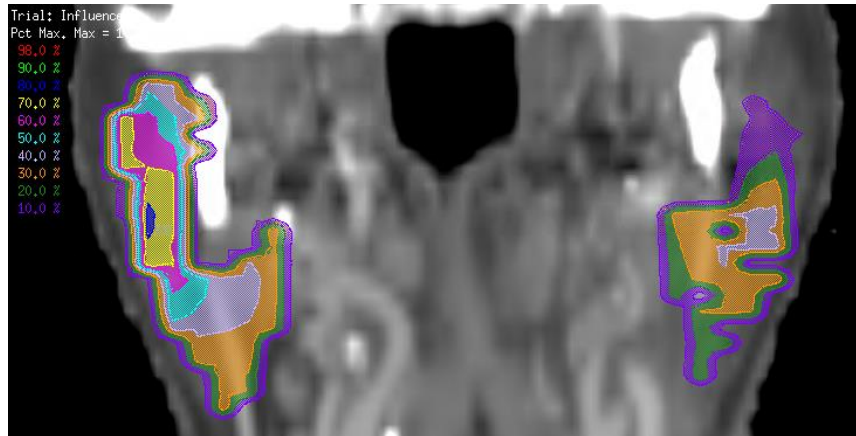
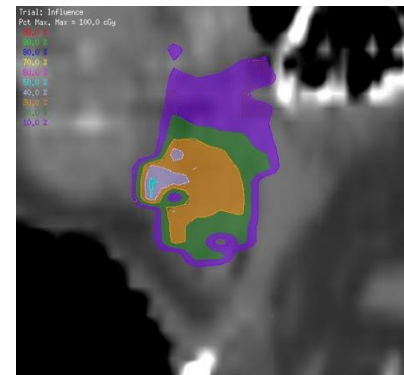
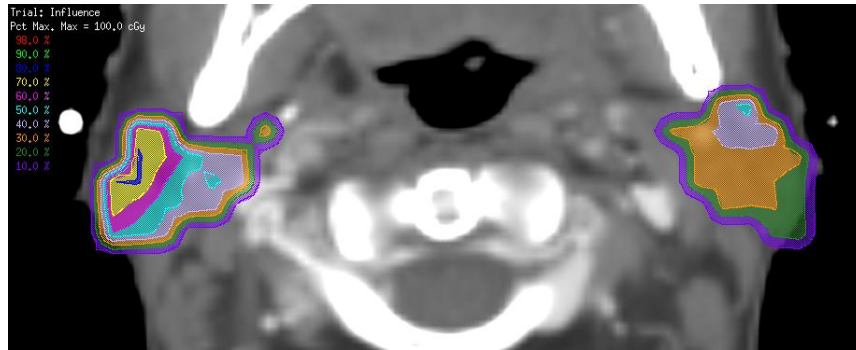


## Potential hypotheses

- The superior portion of the contralateral parotid is the last region to be able to spare (lowest mean dose). If a high dose, there is likely high dose everywhere else, increasing xerostomia.
- Ductal region of ipsilateral parotid has high influence, where the superior portion has very low importance suggesting possible occlusion of duct or serial component of organ function related to injury.
- The superior (lower dose) portions of both parotids influence recovery whereas the higher dose regions have little influence. This suggests a lower dose threshold for preserving the ability to recover salivary function if injured.

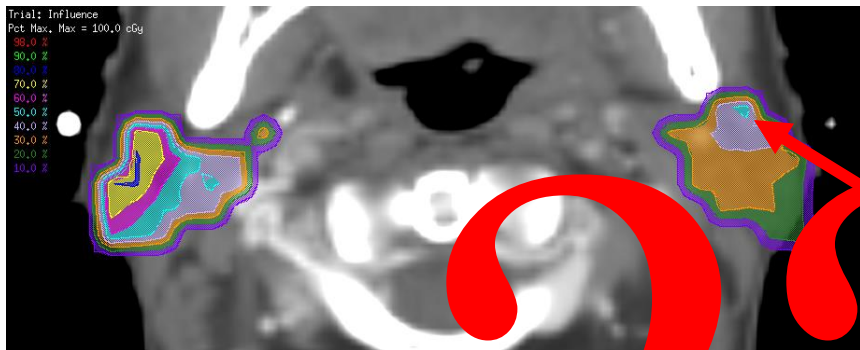


# Influence on CT for Injury



December 3, 2024

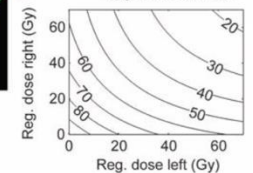
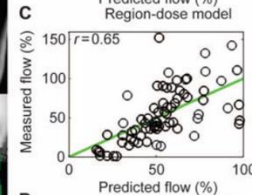
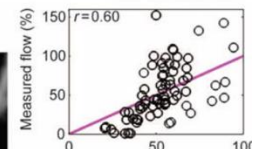
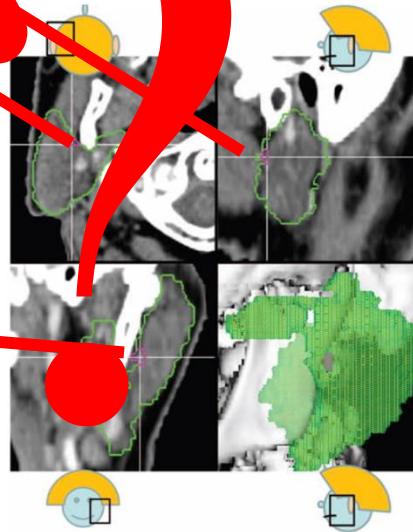
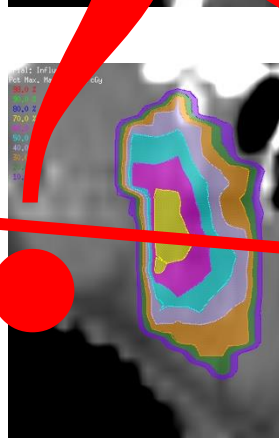
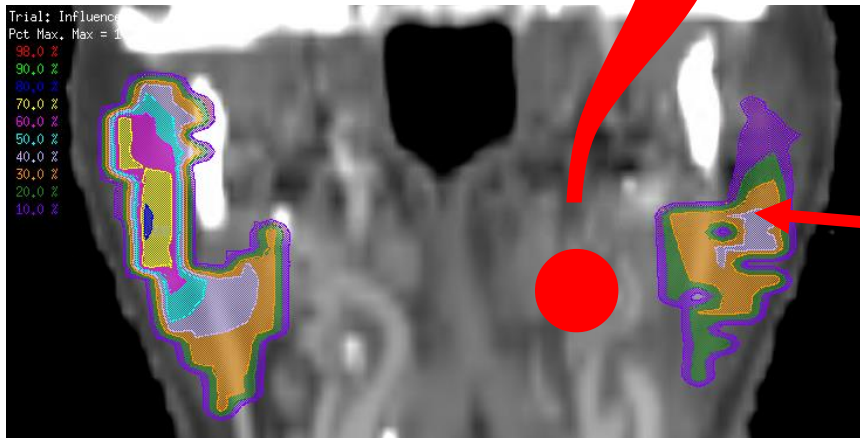
# Influence on CT for Injury



Sci Transl Med. 2015 Sep 16;7(305):305ra147. doi: 10.1126/scitranslmed.aac4441

Sparing the region of the salivary gland containing stem cells preserves saliva production after radiotherapy for head and neck cancer.

van Luijk P<sup>1</sup>, Pringle S<sup>2</sup>, Deasy JO<sup>3</sup>, Moiseenko VV<sup>4</sup>, Faber LP<sup>5</sup>, Hovan A<sup>5</sup>, Baagstra M<sup>6</sup>, van der Laan HP<sup>6</sup>, Kierkels RG<sup>6</sup>, van der Schaaf A<sup>6</sup>, Wilkes MJ<sup>6</sup>, Schreijers JM<sup>7</sup>, Brandenburg S<sup>8</sup>, Langendijk JA<sup>9</sup>, Wu J<sup>9</sup>, Coenen RF<sup>9</sup>

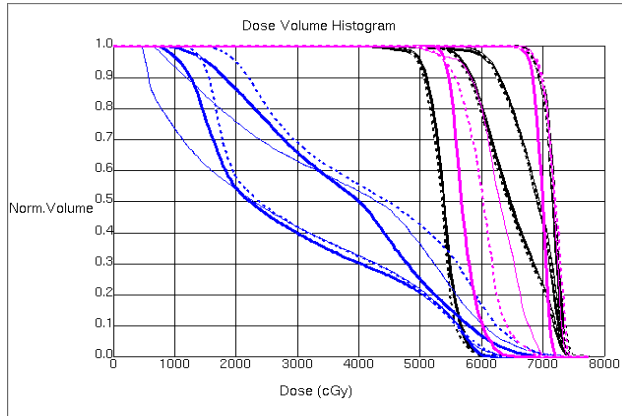


December 3, 2024



# IMRT plans driven by predictions

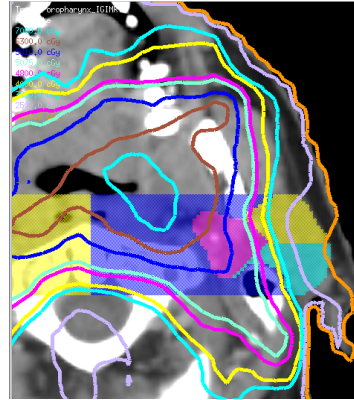
(McNutt, Lee, Sheikh, Quon)



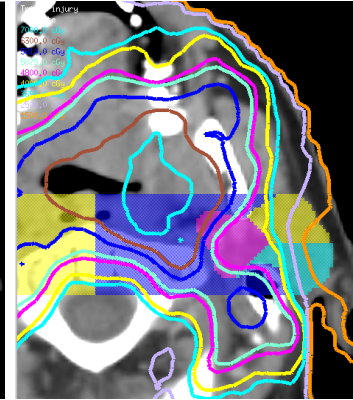
Original – dashed  
 Injury – thick  
 Recovery – thin

Targets – black  
 Parotids – blue  
 Submandibulars – pink

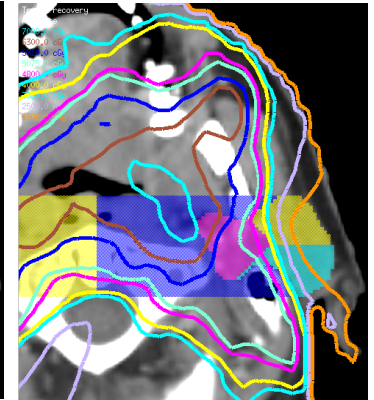
Original



Injury Weighted



Recovery Weighted



	Injury Percentile	Recovery Percentile
Original	81.8	13.5
Injury Wt	64.3	18.1
Recovery Wt	69.7	32.0

# How to stay safe and maintain quality?

- Data is not always the highest quality – must make sure methods/models don't assume it is
- Data does not contain all knowledge. Existing knowledge is often absent
  - If all patients in database meet a dose goal, then there is no knowledge outside of that goal contained in the data.
  - Be wary of situations where you may be outside of the available data bounds
- Data gets old
  - How to keep models current?
  - Do we want to be treated the way patients were treated 2 decades ago?
  - The Rx anomaly may be using an old Rx that has been superseded.



# Acknowledgments

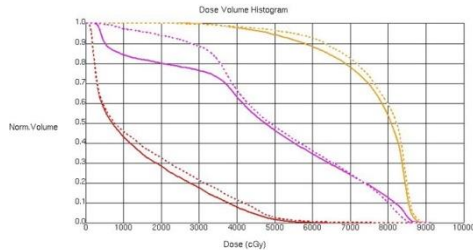
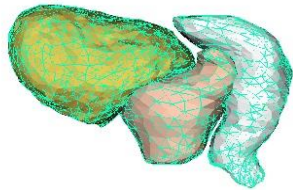
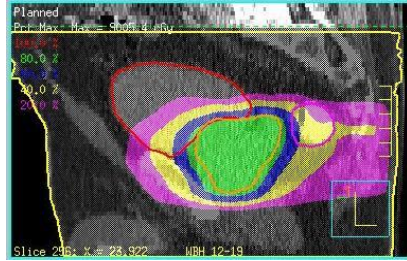
- **JHU-RO**
  - Sierra Cheng MD
  - Michael Bowers BS
  - Joseph Moore PhD
  - Scott Robertson PhD
  - Pranav Lakshminarayanan
  - Xuan Hui MD
  - John Wong PhD
  - Theodore DeWeese MD
- GI Team
  - Joseph Herman MD
  - Amy Hacker-Prietz PA
- H&N Team
  - Harry Quon MD
  - Ana Keiss MD
- **Toronto-Sunnybrook**
  - William Song PhD
  - Patrick Kwok
- **JHU - CS**
  - Russ Taylor PhD
  - Misha Kazhdan PhD
  - Fumbeya Murango BS
- **Philips PROS**
  - Karl Bzdusek BS
- **Toshiba**
  - Minoru Nakatsugawa PhD
  - Bobby Davey PhD
  - Rachel-Louise Kockava
  - John Haller
- **Elekta**
  - Bob Hubbell
- **University of Washington**
  - Kim Evans MS
  - Mark Philips PhD
  - Kristi Hendrickson PhD

# Deformable dose accumulation

Secondary dataset with  
primary IMRT beam  
arrangement



## Primary dataset



Model-based segmentation

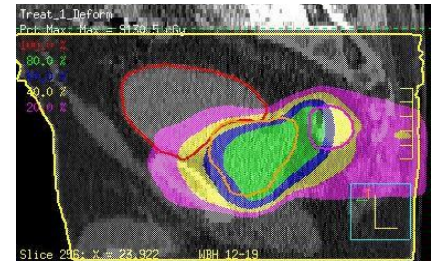
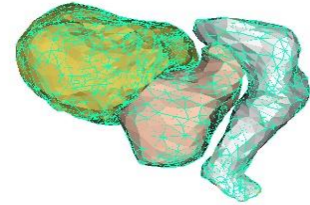
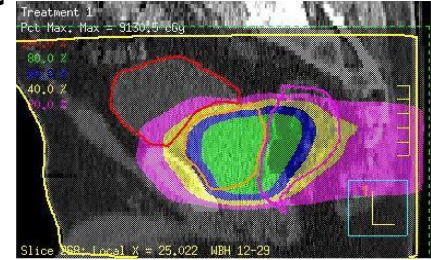


Deformable registration



Dose warping

Secondary dose deformed  
back to primary plan

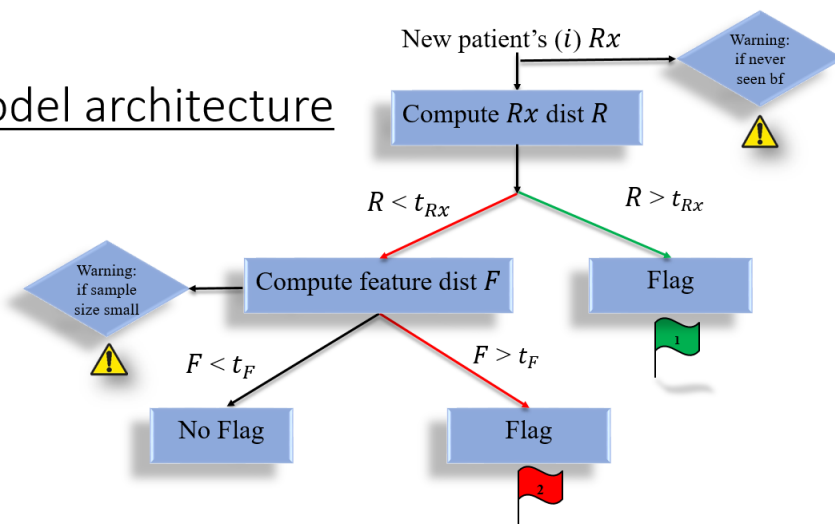


# Radiation Prescription Anomalies

A novel data-driven algorithm to predict anomalous prescription based on patient's feature set

Qiongge Li, R. Voong, R. Hales, J. Wright, T. McNutt (Submitted)

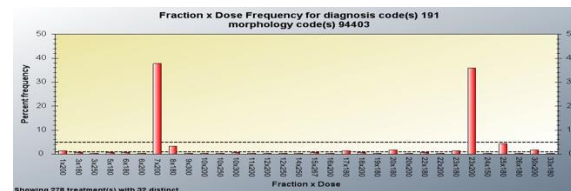
## Model architecture



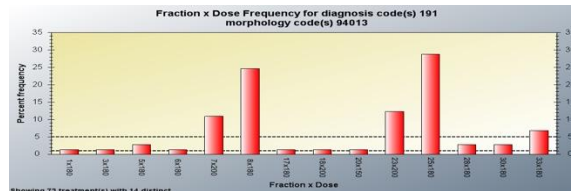
Automated Cross-Referencing of Radiation Prescriptions to Diagnosis: A Proposed Mechanism to Improve Patient Safety

A. Sharabi, T. McNutt, and T. DeWeese; *The Johns Hopkins University School of Medicine, Baltimore, MD*

191 Brain  
AND  
Pathology of  
Glioblastoma



191 Brain  
AND  
Pathology of  
Anaplastic  
Astrocytoma



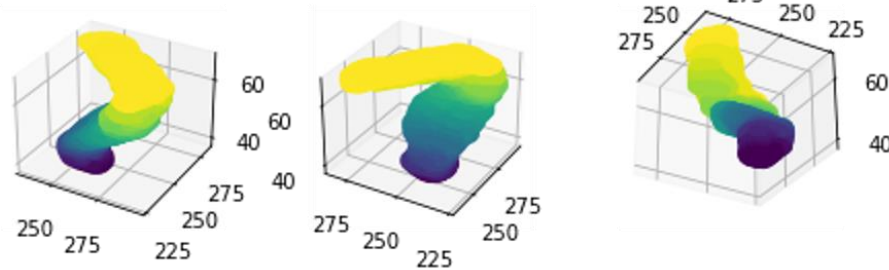
ID	ICD	Diagnosis	Morphology	Site	Age	Sex	Rx	Dose	Count	Rate
191	191.00	Glioblastoma, NOS	94403	Brain	65-74	M	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	75-84	M	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	85-94	M	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	0-4	M	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	5-14	M	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	15-24	M	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	25-34	M	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	35-44	M	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	45-54	M	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	55-64	M	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	65-74	M	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	75-84	M	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	85-94	M	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	0-4	F	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	5-14	F	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	15-24	F	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	25-34	F	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	35-44	F	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	45-54	F	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	55-64	F	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	65-74	F	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	75-84	F	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	85-94	F	RT	1.0000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	0-4	M	RT	0.5000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	5-14	M	RT	0.5000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	15-24	M	RT	0.5000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	25-34	M	RT	0.5000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	35-44	M	RT	0.5000	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	45-54	M	RT	0.5000	1	100%
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191	191.00	Glioblastoma, NOS	94403	Brain	45-54	F	RT	0.5000	1	100%
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191	191.00	Glioblastoma, NOS	94403	Brain	55-64	M	RT	0.2500	1	100%
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191	191.00	Glioblastoma, NOS	94403	Brain	0-4	F	RT	0.2500	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	5-14	F	RT	0.2500	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	15-24	F	RT	0.2500	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	25-34	F	RT	0.2500	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	35-44	F	RT	0.2500	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	45-54	F	RT	0.2500	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	55-64	F	RT	0.2500	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	65-74	F	RT	0.2500	1	100%
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191	191.00	Glioblastoma, NOS	94403	Brain	85-94	F	RT	0.2500	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	0-4	M	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	5-14	M	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	15-24	M	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	25-34	M	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	35-44	M	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	45-54	M	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	55-64	M	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	65-74	M	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	75-84	M	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	85-94	M	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	0-4	F	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	5-14	F	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	15-24	F	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	25-34	F	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	35-44	F	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	45-54	F	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	55-64	F	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	65-74	F	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	75-84	F	RT	0.1250	1	100%
191	191.00	Glioblastoma, NOS	94403	Brain	85-94	F	RT	0.1250	1	100%

# Contour Anomalies

## Anomaly types:

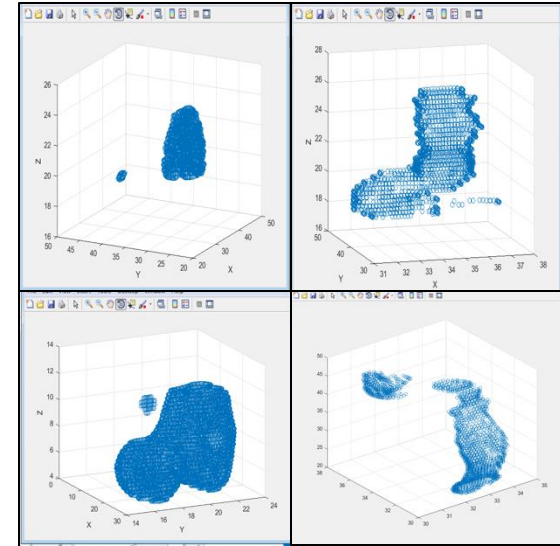
- Discontinuities
- Size/extent inconsistency
- Shape inconsistency
- Anatomic relationships

e.g. Rectum contoured into Sigmoid Colon



Kevin Gorman et. al.

December 3, 2024



RADIATION ONCOLOGY PHYSICS

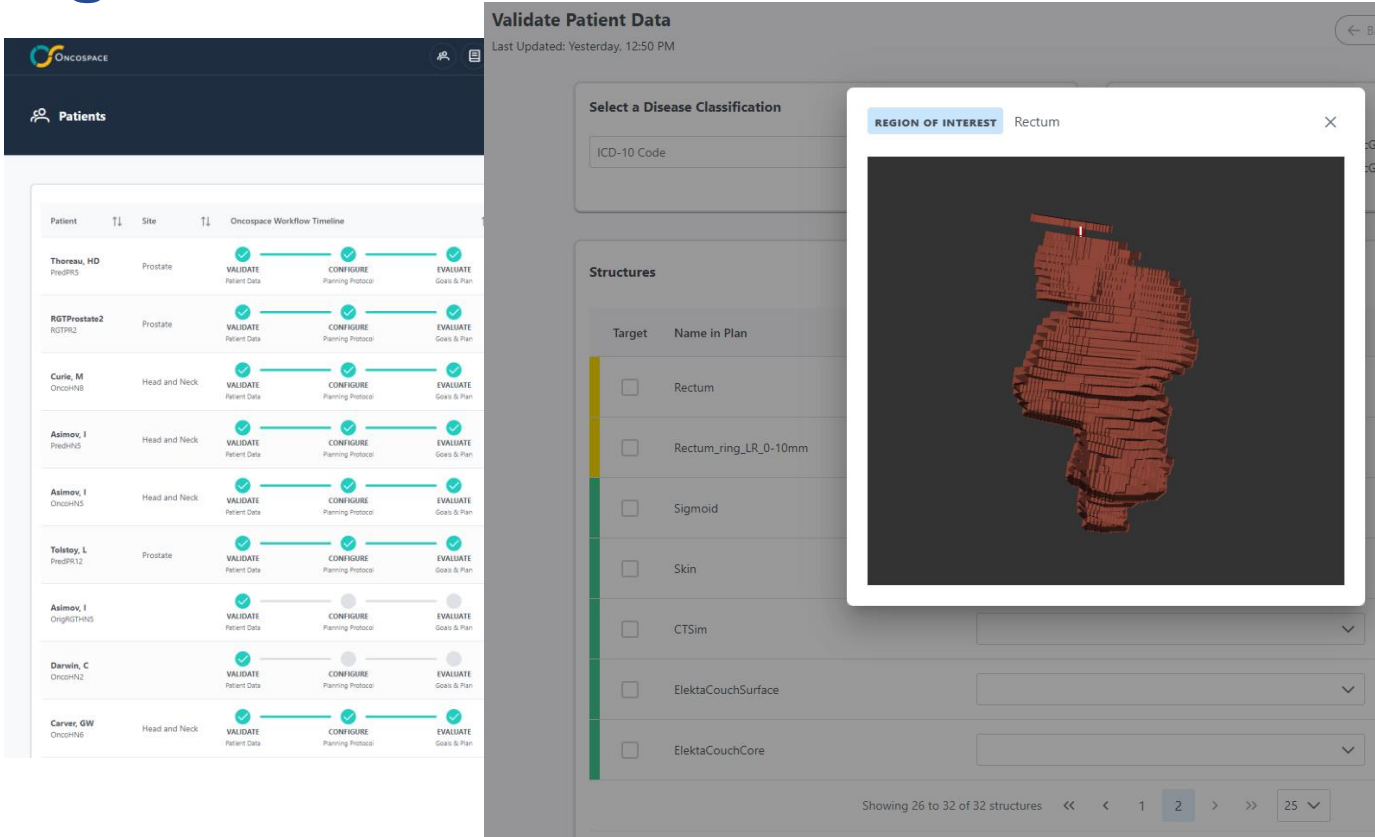
WILEY

Data integrity systems for organ contours in radiation therapy planning

Veeraj P. Shah<sup>1</sup> | Pranav Lakshminarayanan<sup>2</sup> | Joseph Moore<sup>3</sup> | Phuoc T. Tran<sup>1,3</sup> | Harry Quon<sup>1</sup> | Curtiland Deville<sup>1</sup> | Todd R. McNutt<sup>1</sup>

# Putting it together...

- Send contours to system
- Map ROI names (auto)
- Evaluate contour integrity
  - Discontinuity
  - Unexpected volume
  - Unexpected shape
- Select Tx protocol



The screenshot displays the OncoSpace interface. On the left, a table lists patients and their workflow progress through 'VALIDATE Patient Data', 'CONFIGURE Planning Protocol', and 'EVALUATE Goals & Plan'. On the right, the 'Validate Patient Data' window is active, showing a 'Select a Disease Classification' section with an 'ICD-10 Code' field and a 'Structures' list. A 'REGION OF INTEREST' window is overlaid on the 3D model, highlighting the 'Rectum' structure.

Patient	Site	OncoSpace Workflow Timeline
Thoreau, HD PiedPR13	Prostate	VALIDATE Patient Data ✓   CONFIGURE Planning Protocol ✓   EVALUATE Goals & Plan ✓
RGTProstate2 RSTPR2	Prostate	VALIDATE Patient Data ✓   CONFIGURE Planning Protocol ✓   EVALUATE Goals & Plan ✓
Curie, M OrcoHN8	Head and Neck	VALIDATE Patient Data ✓   CONFIGURE Planning Protocol ✓   EVALUATE Goals & Plan ✓
Asimov, I PiedHN3	Head and Neck	VALIDATE Patient Data ✓   CONFIGURE Planning Protocol ✓   EVALUATE Goals & Plan ✓
Asimov, I OrcoHN5	Head and Neck	VALIDATE Patient Data ✓   CONFIGURE Planning Protocol ✓   EVALUATE Goals & Plan ✓
Telstoy, L PiedPR12	Prostate	VALIDATE Patient Data ✓   CONFIGURE Planning Protocol ✓   EVALUATE Goals & Plan ✓
Asimov, I OrcoHN5	Head and Neck	VALIDATE Patient Data ✓   CONFIGURE Planning Protocol ⚪   EVALUATE Goals & Plan ⚪
Darwin, C OrcoHN2	Head and Neck	VALIDATE Patient Data ✓   CONFIGURE Planning Protocol ⚪   EVALUATE Goals & Plan ⚪
Carver, GW OrcoHN6	Head and Neck	VALIDATE Patient Data ✓   CONFIGURE Planning Protocol ✓   EVALUATE Goals & Plan ✓

**Validate Patient Data**  
Last Updated: Yesterday, 12:50 PM

Select a Disease Classification  
ICD-10 Code

**Structures**

Target	Name in Plan
<input type="checkbox"/>	Rectum
<input type="checkbox"/>	Rectum_ring_LR_0-10mm
<input type="checkbox"/>	Sigmoid
<input type="checkbox"/>	Skin
<input type="checkbox"/>	CTSim
<input type="checkbox"/>	ElektaCouchSurface
<input type="checkbox"/>	ElektaCouchCore

REGION OF INTEREST Rectum

Showing 26 to 32 of 32 structures



# Causality

(Shpitser)

## Semi-Parametric Causal Sufficient Dimension Reduction Of High Dimensional Treatments

Razieh Nabj, T. McNutt, I. Shpitser • Published 2017 • Mathematics • arXiv: Methodology

Cause-effect relationships are typically evaluated by comparing the outcome responses to binary treatment values, representing cases and controls. However, in certain applications, treatments of interest are continuous and high dimensional. For example, understanding the causal relationship between severity of radiation therapy, represented by a high dimensional vector of radiation exposure values at different parts of the body, and post-treatment side effects is a problem of clinical interest... [Expand](#)

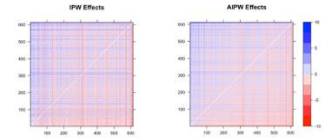


Fig. 4: Heatmaps to illustrate the causal effect of radiation on weight loss, where effects are computed by estimating  $\beta$  via (a) IPW estimator, and (b) APW estimator. Heatmaps are antidiagonally symmetric with opposite color tones.

- Notion of Dimension Reduction with consideration of Causal Inference
  - DVH point is dimension reduction
  - Principle Components...
- Can we blend with anatomical/physiological understanding?
- Does it work with the inherently controlled treatment?
- Spawned interest with van Herk and Christie Hospital – Manchester, UK

# Decision Support Efforts

- Weight loss prediction
  - Head and neck (PEG Tube ?)
  - Thoracic with Image features
- Alcorn BMETS example
- Challenges
  - Clinical decisions that impact trajectory of care