Clinical Experience with Knowledge-Based Planning

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- **Speaker Agreement with Varian Medical Systems**
- **License Agreement with Varian Medical Systems**

Learning Objectives

1. Highlight the motivation for knowledge-based planning
2. Describe the clinical indication for KBP
3. Emphasize the importance of proper KBP model training and validation

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Motivation

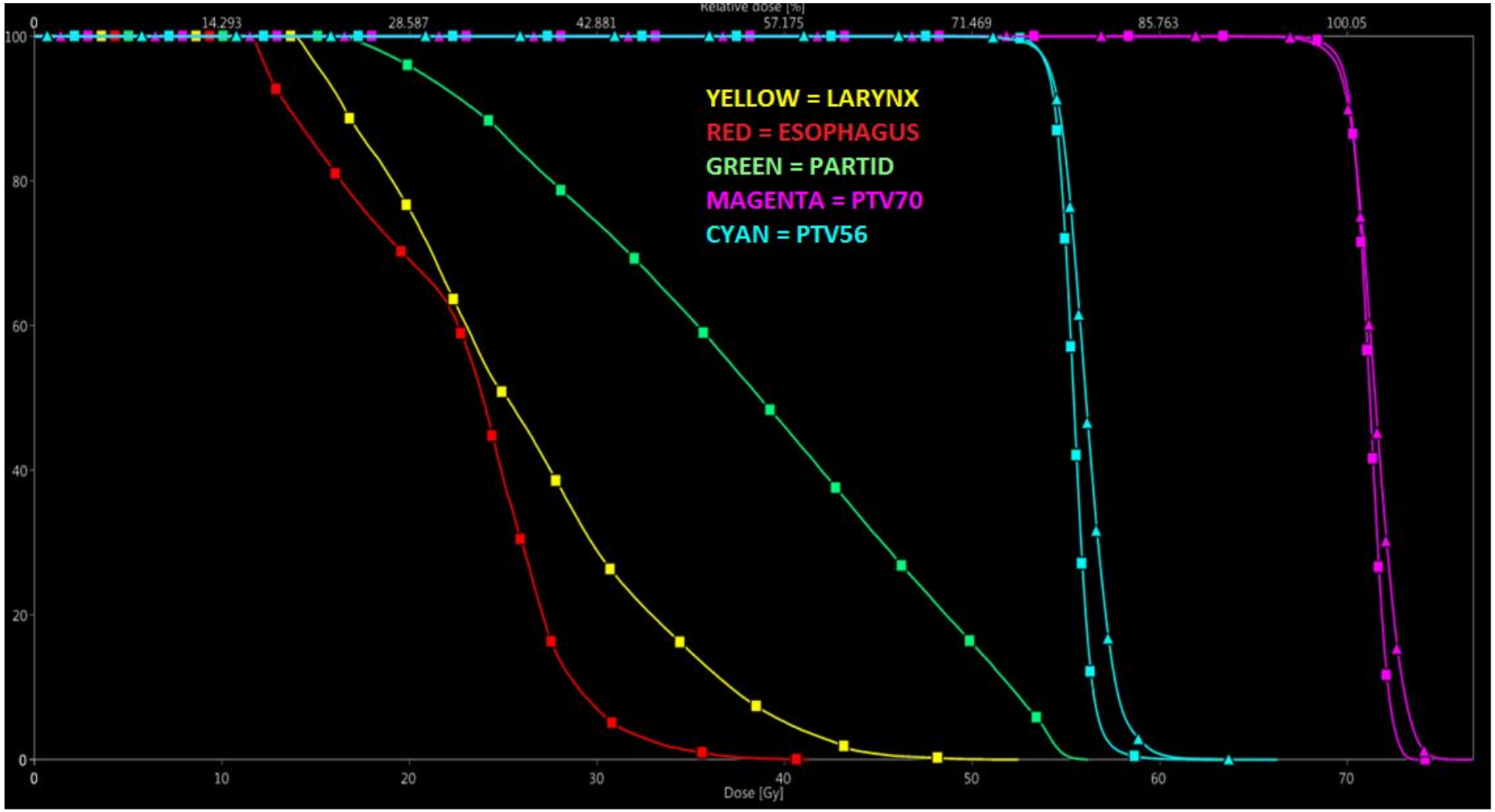
- **Why Knowledge-Based Planning?**
  - Leverage prior clinical and planning experience
  - Minimize repetition
  - Decision support (clinical sanity check)
  - Improve quality, efficiency, and automation

Motivation

Do IMRT planning goals guarantee optimal plans?

		Bilateral Neck Treatment	Ipsilateral Neck Treatment
H&N	**PTV**	95% of PTV > 95% of Rx; Max dose < 110% of Rx	95% of PTV > 95% of Rx; Max dose < 110% of Rx
	Spinal Cord	Max dose 40 Gy	Max dose 40 Gy
	Spinal Cord + Margin	Max dose 52 Gy; < 1% (or 1 cc) exceeds 50 Gy	Max dose 52 Gy; < 1% (or 1 cc) exceeds 50 Gy
	Optic Nerves, Optic Chiasm	Max dose 54 Gy	Max dose 54 Gy
	Brainstem	Max dose 54 Gy; < 1% exceeds 60 Gy	Max dose 54 Gy; < 1% exceeds 60 Gy
	Brain	Max dose 60 Gy; < 1% exceeds 65 Gy	Max dose 60 Gy; < 1% exceeds 65 Gy
	Retina	Max dose 50 Gy; < 5% exceeds 45 Gy	Max dose 50 Gy; < 5% exceeds 45 Gy
	Larynx	As low as possible; mean dose < 45 Gy	As low as possible; mean Dose <25 Gy
	Upper Esophagus	As low as possible; mean dose < 45 Gy	As low as possible; mean dose < 25 Gy
	Parotid	As low as possible; mean dose $\leq$ 26 Gy	As low as possible; mean dose $\leq$ 10 Gy (contralateral)
	Pharyngeal Constrictors	As low as possible; V60 < 60 Gy	As low as possible; V60 < 45 Gy
	Submandibular	As low as possible; mean dose < 39 Gy	As low as possible; mean dose < 24 Gy (contralateral)
	Oral Cavity	As low as possible; mean dose < 35 Gy	As low as possible; mean dose < 20 Gy
	Mandible	Max 70 Gy; < 5% exceeds PTV Rx	Max 70 Gy; < 5% exceeds PTV Rx
	Unspecified Tissue	Less than PTV Rx; < 5% exceeds PTV Rx	Less than PTV Rx; < 5% exceeds PTV Rx

Motivation


Relative dose [%]
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42.881
57.175
71.469
85.763
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YELLOW = LARYNX
RED = ESOPHAGUS
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MAGENTA = PTV70
CYAN = PTV56
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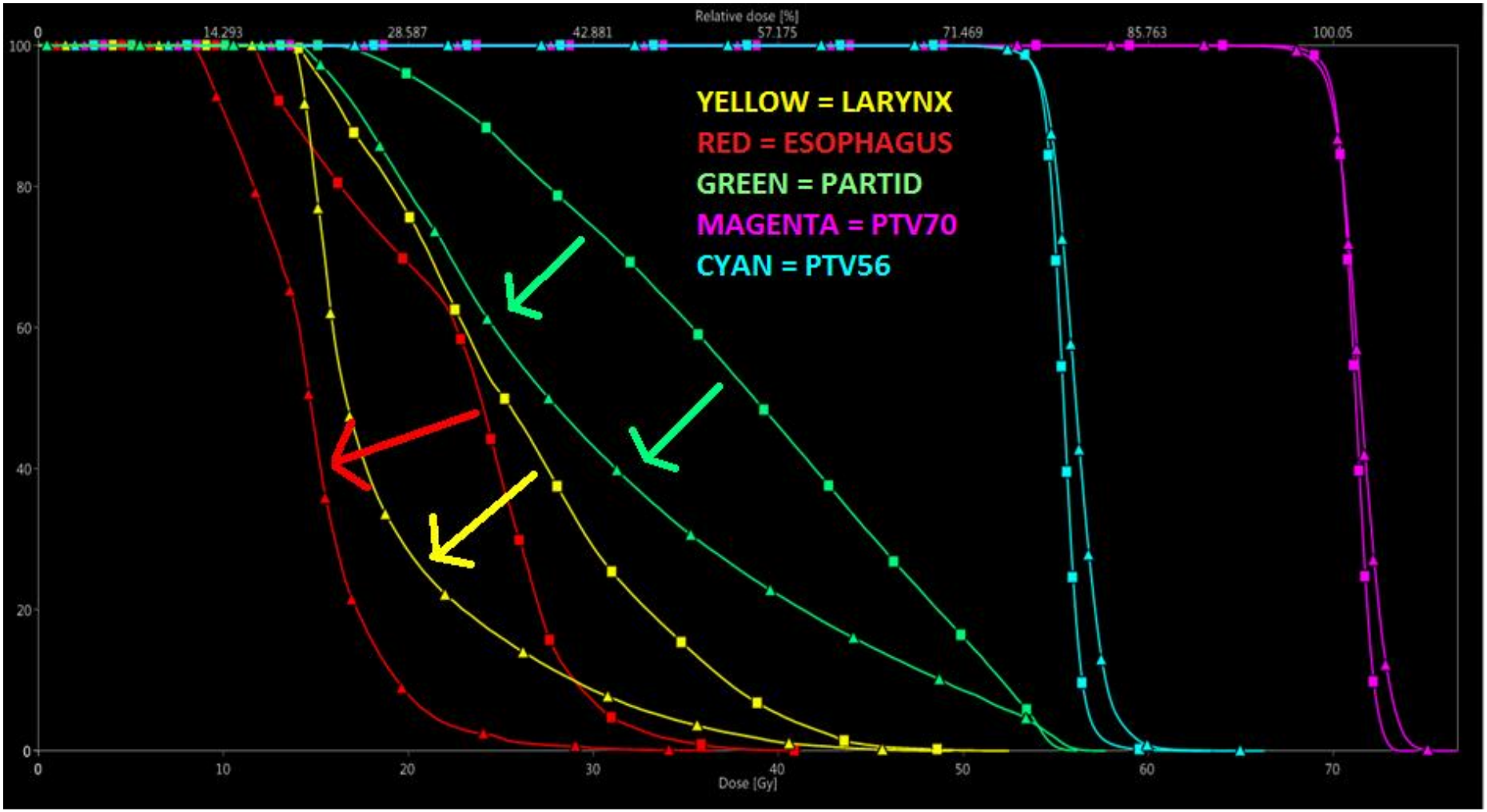
Dose [Gy]

Motivation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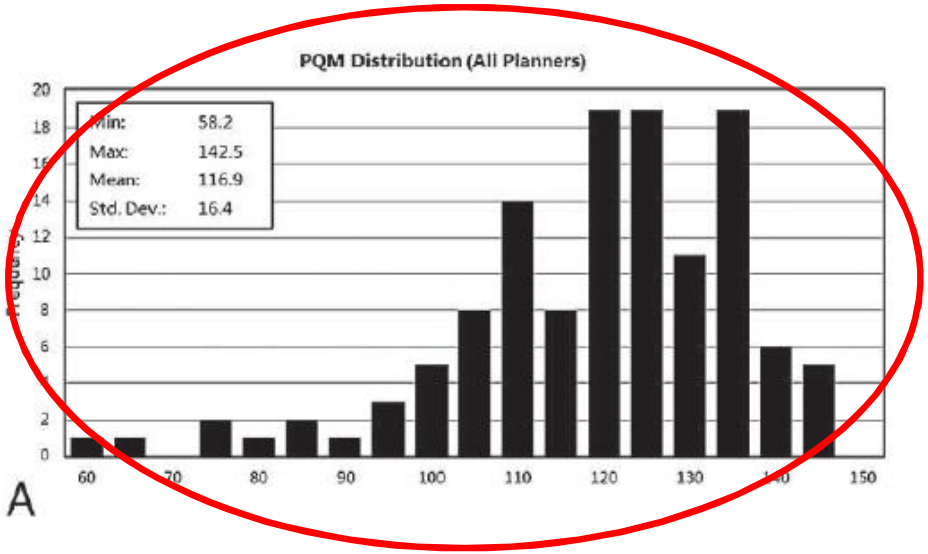
Motivation

Practical Radiation Oncology
Volume 2, Issue 4, October–December 2012, Pages 296–305

Variation in external beam treatment plan quality: An inter-institutional study of planners and planning systems

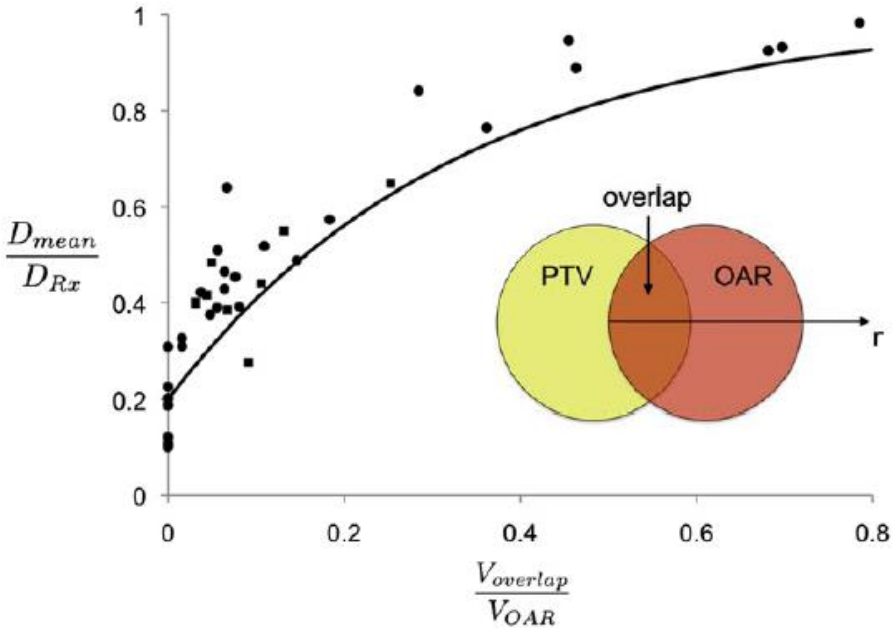
Benjamin E. Nelms PhD[a,b,*], Greg Robinson CMD[c], Jay Markham CMD[c], Kyle Velasco CMD[c], Steve Boyd CMD[c], Sharath Narayan CMD[c], James Wheeler MD, PhD[d], Mark L. Sobczak MD[e]



Conclusions

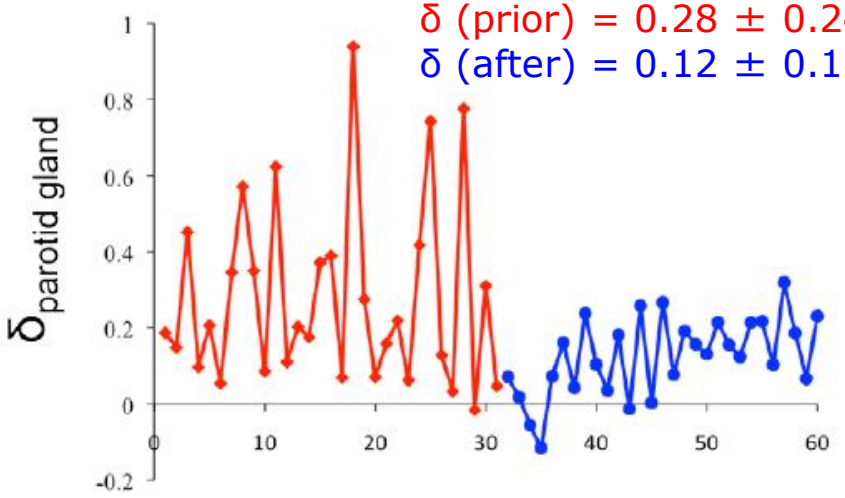
There is a large inter-planner variation in plan quality as defined by a quantitative PQM score that measures the ability of the planner to meet very specific plan objectives. Plan quality was not statistically different between different TPS or delivery techniques and was not correlated to metrics of plan complexity. Certification and education demographics, experience, and confidence level of the planner were not good predictors of plan quality.

Motivation

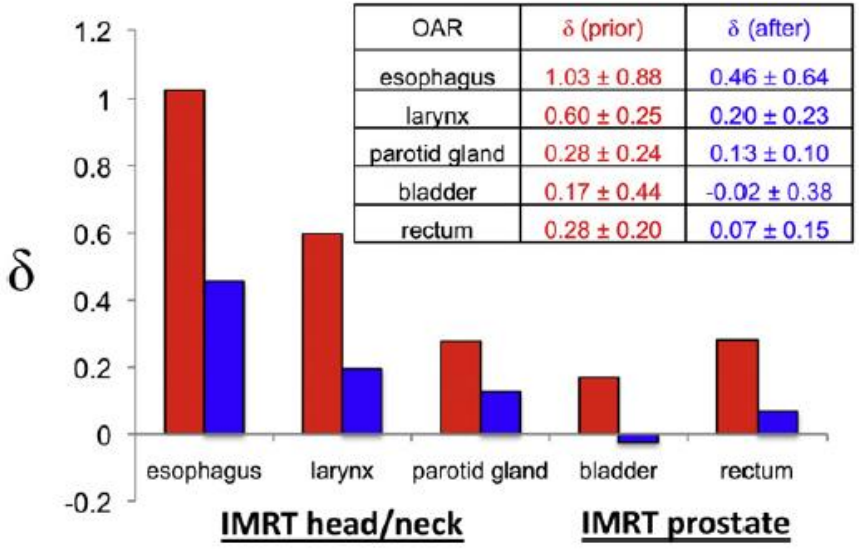


Moore, K.L. *et al.* Experience-based quality control of clinical intensity-modulated radiotherapy planning, Int J Radiat Oncol Biol Phys. 81(2):545-551 (2011)

δ (prior) = 0.28 ± 0.24
δ (after) = 0.12 ± 0.13

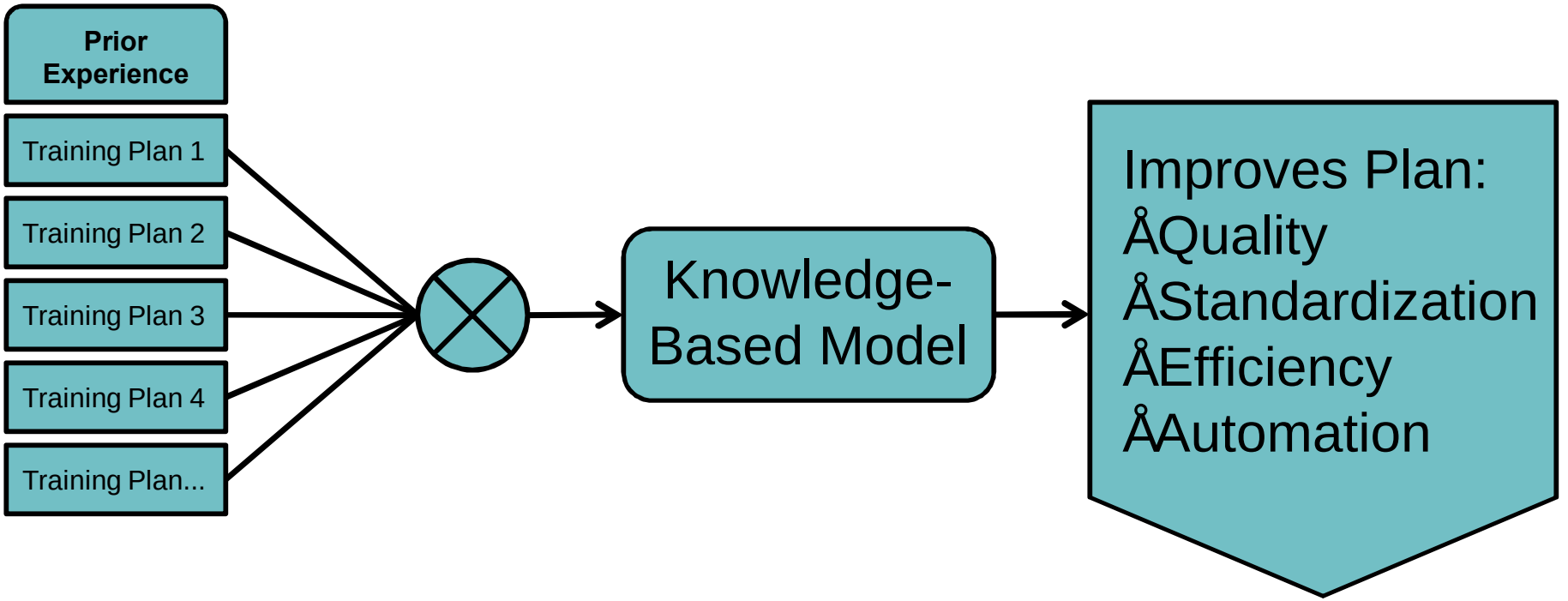


OAR	δ (prior)	δ (after)
esophagus	1.03 ± 0.88	0.46 ± 0.64
larynx	0.60 ± 0.25	0.20 ± 0.23
parotid gland	0.28 ± 0.24	0.13 ± 0.10
bladder	0.17 ± 0.44	-0.02 ± 0.38
rectum	0.28 ± 0.20	0.07 ± 0.15



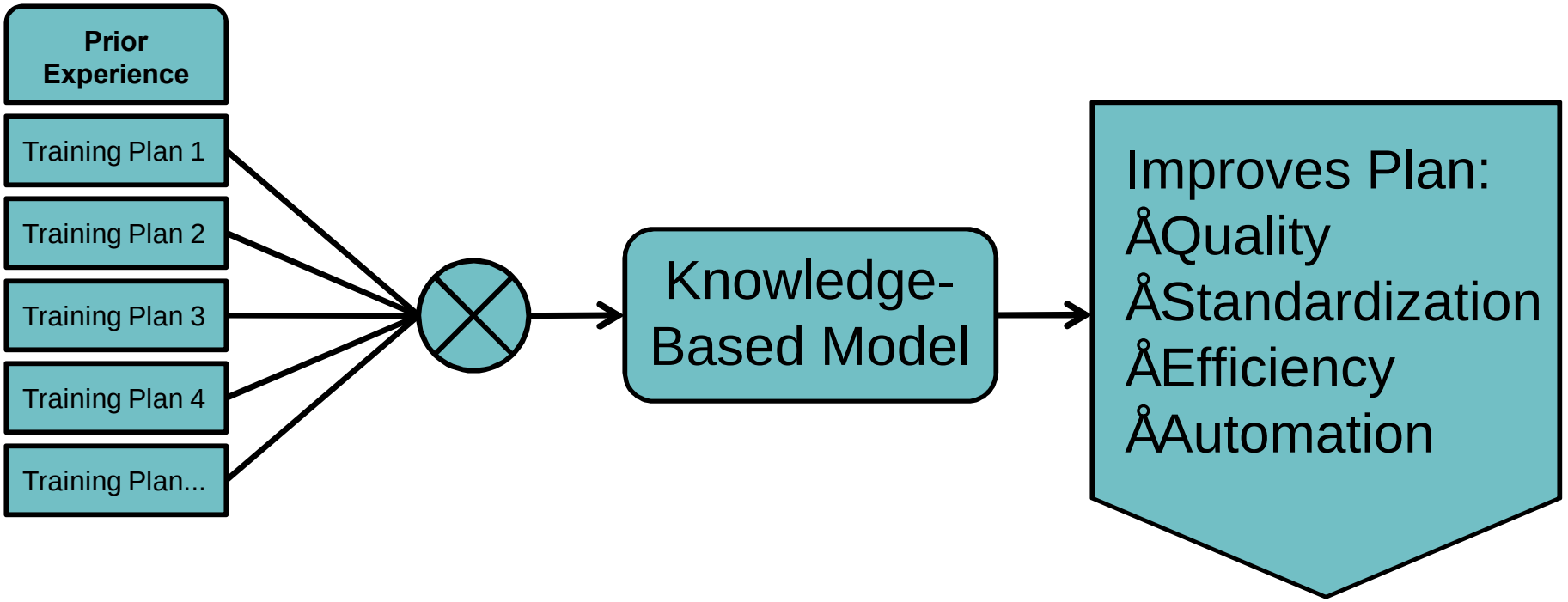
In general…

- Significance of Knowledge-Based Planning



In general…

- **Significance of Knowledge-Based Planning**



Does KBP deliver these claims?

Question 1

In an inter-intuitional study it has been shown that the large inter-planner variation in plan quality

0% a. depends on the planner's experience

0% b. is a direct result of the TPS

0% c. is independent of planner's experience

0% d. depends on planner's certification level

0% e. is a direct result of the technique used

Question 1

In an inter-intuitional study it has been shown that the large inter-planner variation in plan quality

1. a. depends on the planner's experience
2. b. is a direct result of the TPS
3. c. is independent of planner's experience
4. d. depends on planner's certification level
5. e. is a direct result of the technique used

Answer: c. is independent of planner's experience

Reference: B. Nelms, et.al., Variaion in external beam treatment plan quality: An inter-institutional study of planners and planning systems, Practical Radiation Oncology, Volume 2, Issue 4, 2012.

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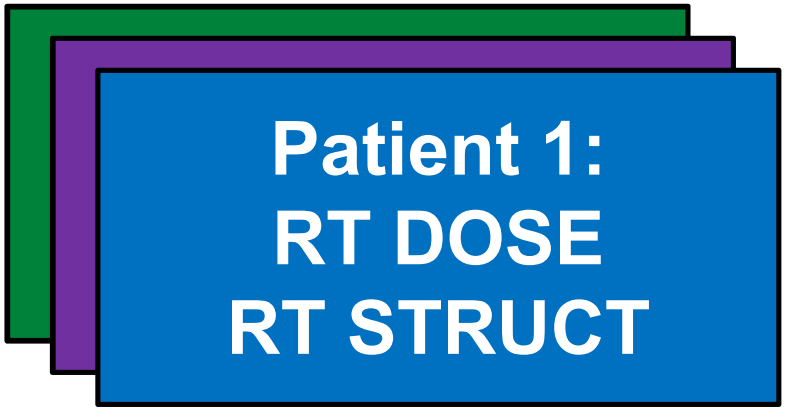
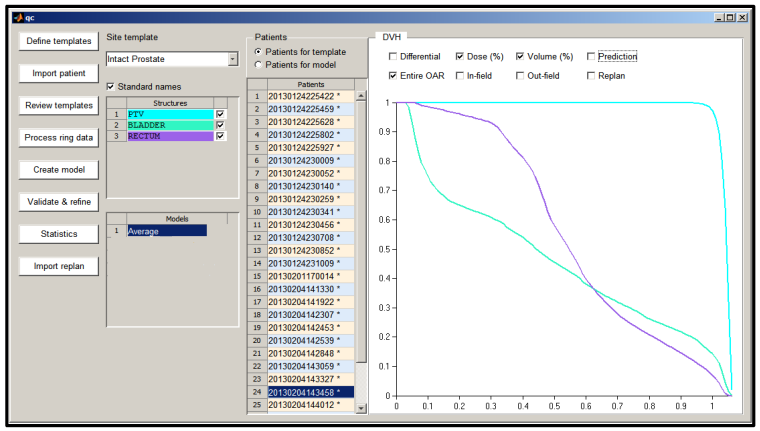
Outside Clinic Study

- RT datasets for 20 clinically treated prostate IMRT plans from an outside institution transferred to Wash U pDVH DICOM tool





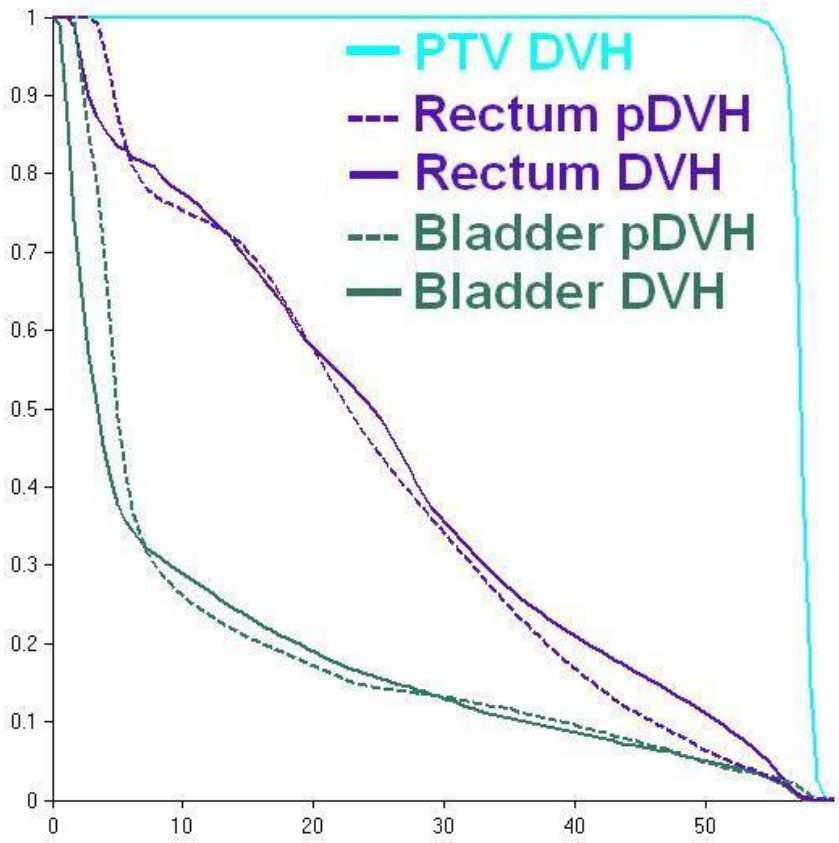
Export DICOM RT files from outside institution TPS

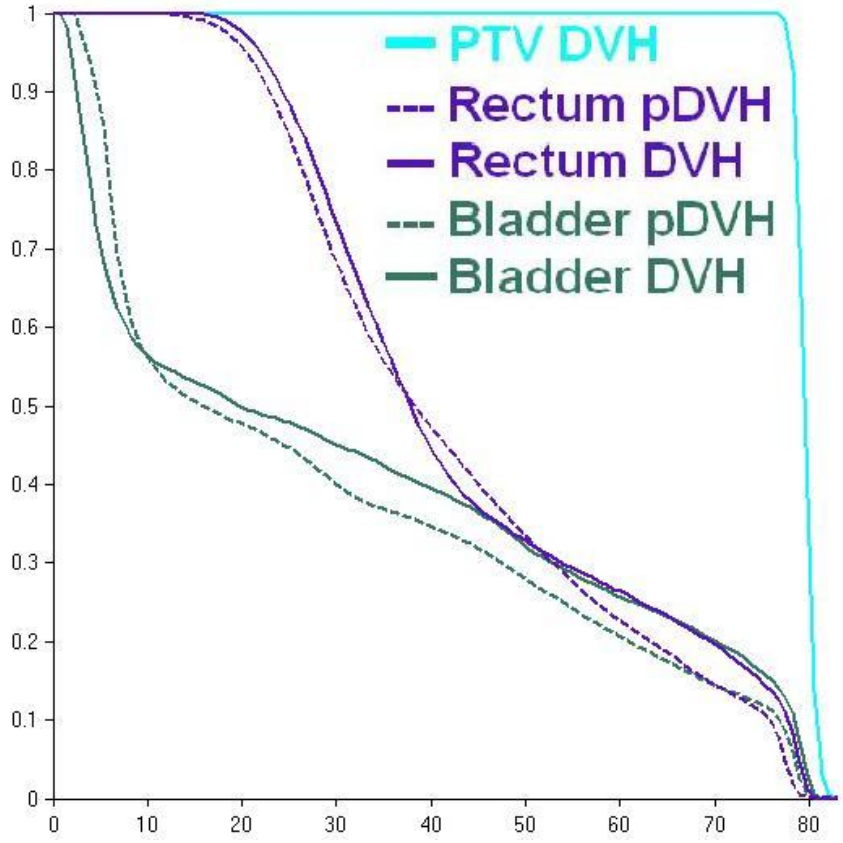
Import files into Wash U pDVH DICOM Tool

Appenzoller L.M., et. al. Predictive DVH models developed at a large institution impact clinically relevant DVH parameters in IMRT plans at an unrelated radiotherapy facility, Oral presentation AAPM 2013.

Outside Clinic Study

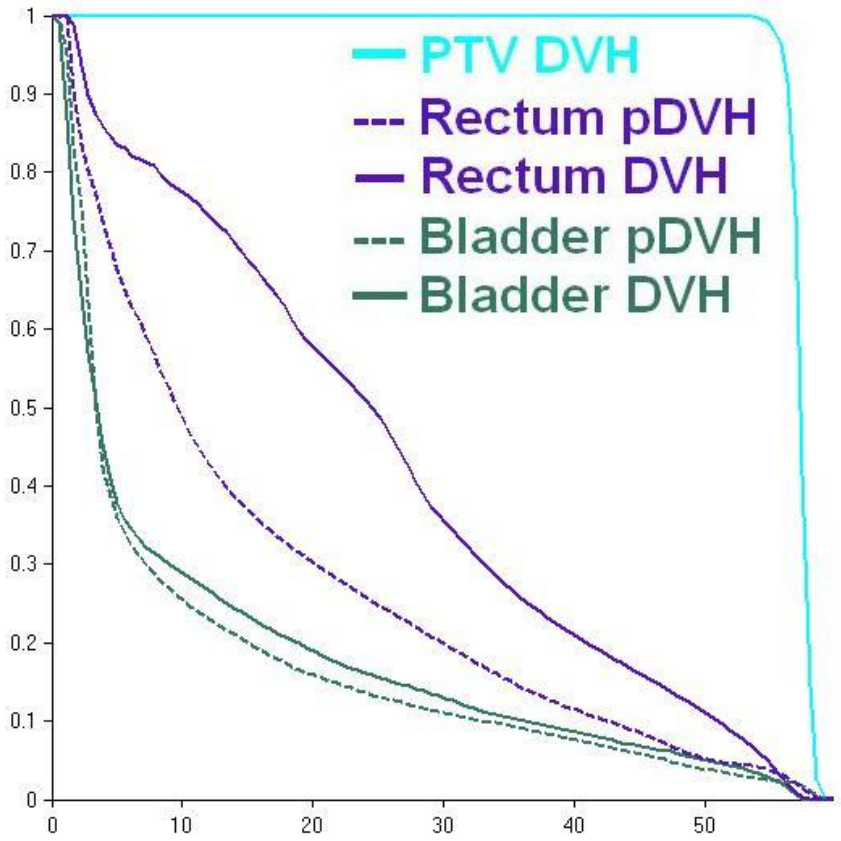
- Clinic specific pDVH model created using institution's own data
  - Similar plan quality demonstrated for all patients
  - No indication for improvement of clinically treated plans

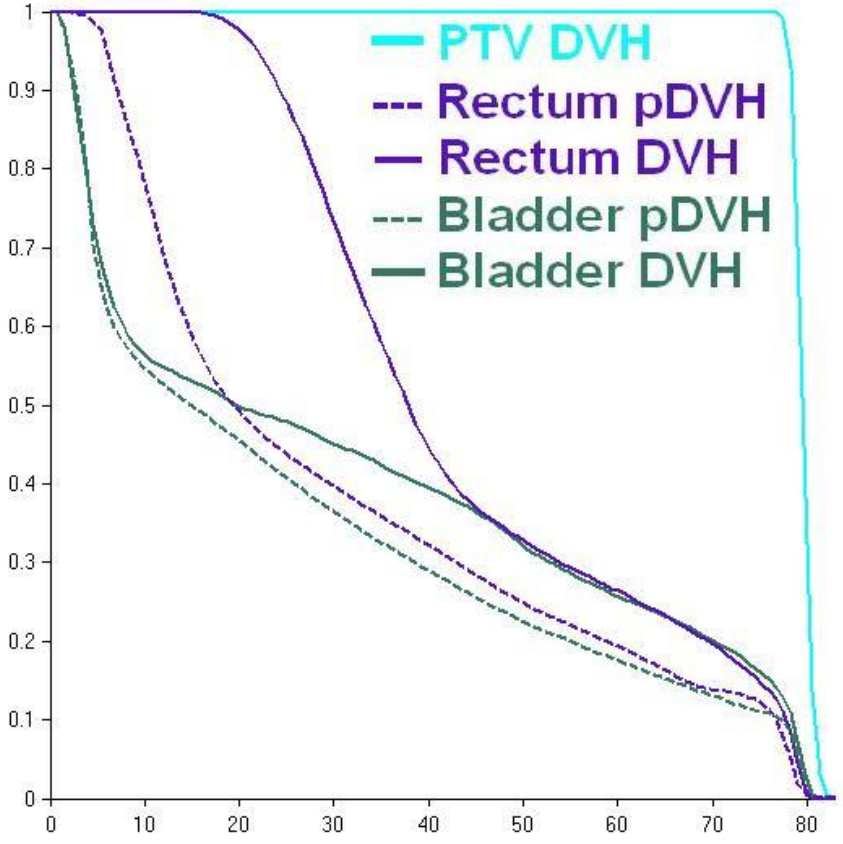




Outside Clinic Study

- **Comparison against validated Wash U prostate model showed large improvements possible for rectum DVHs and small improvements for bladder DVHs for all patients**

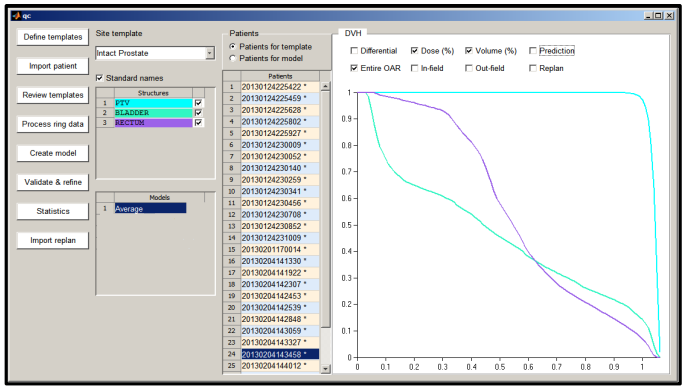




Outside Clinic Study

- Five worst patients identified by sum of residuals between clinical DVH and predicted DVH
- Quantify improvements in clinical rectum and bladder DVHs with knowledge of pDVHs by replanning five worst patients

Replan five patients using optimization objectives exported from pDVH tool

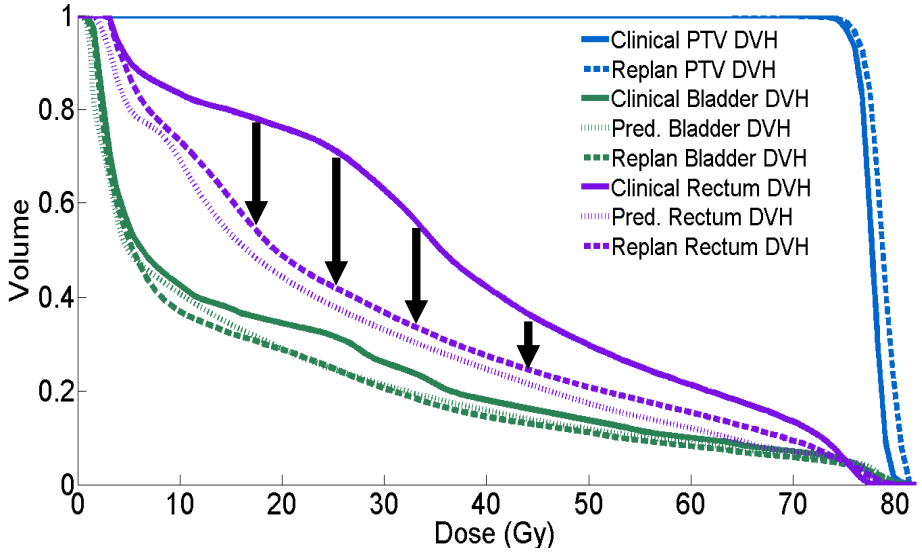


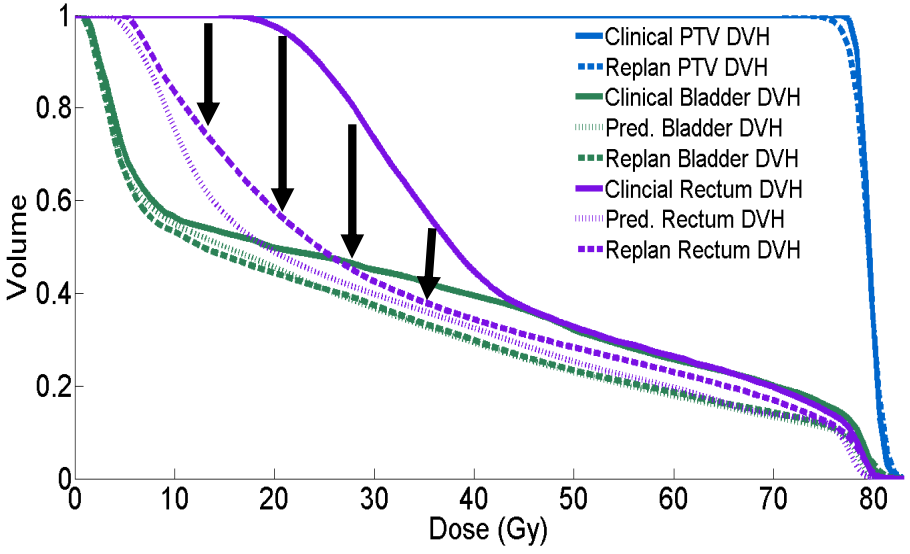
Import replan dose matrix into DICOM tool and compare to original DVHs and pDVHs

Outside Clinic Study

- **All five patients replanned showed similar results…**

Average Reduction in V65 and V40 for Rectum and Bladder				
Organ	**V65(orig)-V65(replan)**	**dV65**	**V40(orig)-V40(replan)**	**dV40**
Rectum	4.8%±2.3%	0.9%±1.1%	17.9%±10.3%	0.7%±1.4%
Bladder	3.4%±2.1%	0.4%±0.5%	6.0%±2.8%	0.6%±0.9%





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Institutional Plan Quality Study

Objective: To assess the impact of DVH prediction (pDVH) models and a standardized planning technique on post-operative endometrial IMRT treatment plan quality.

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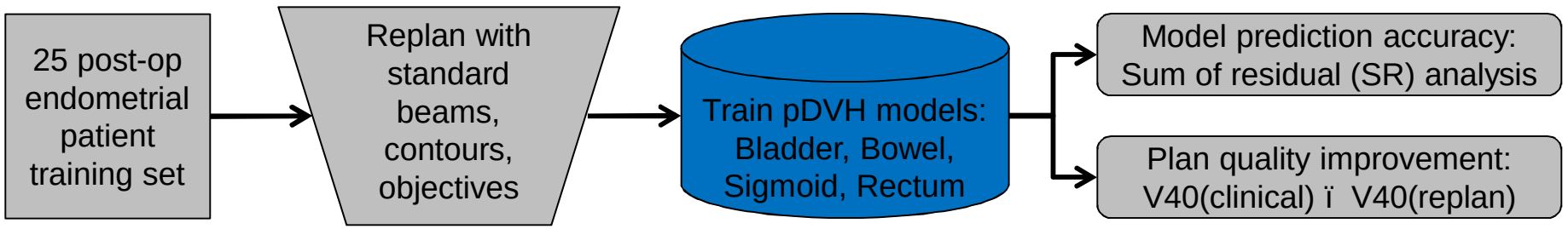

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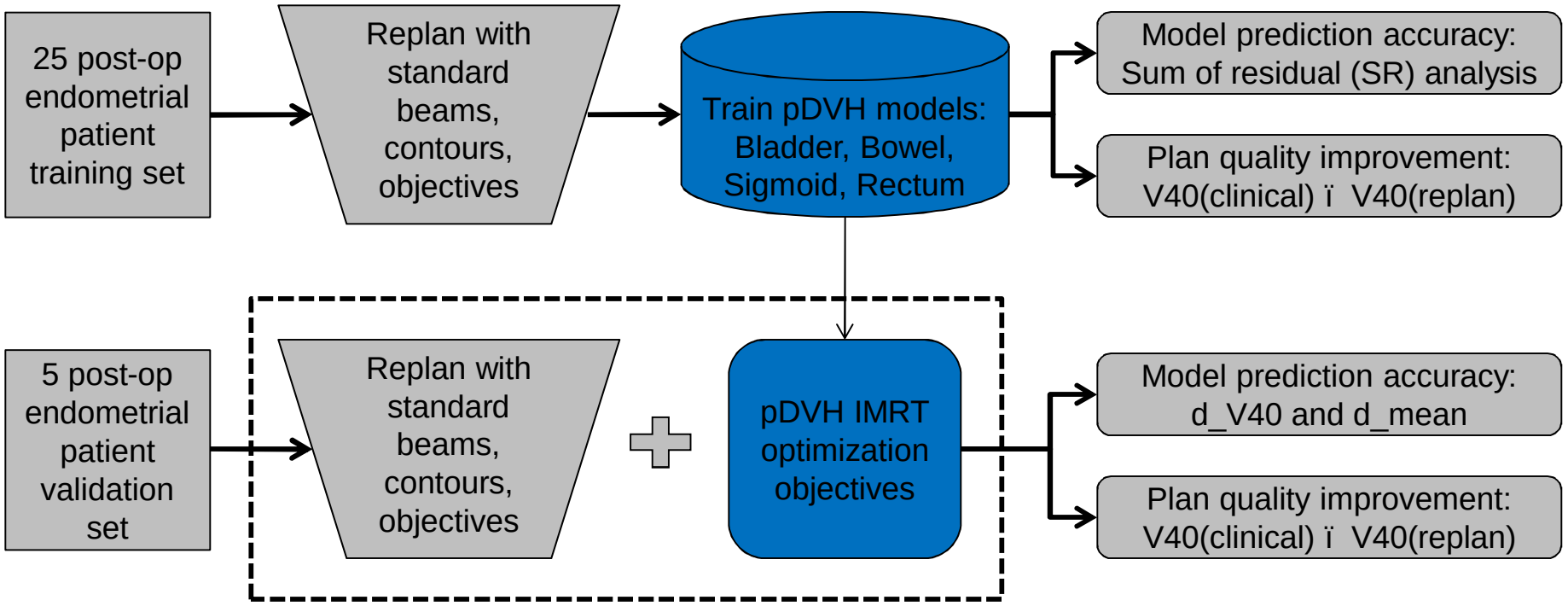

Olsen et al, "Impact of DVH prediction models and a standardized planning technique on post-op endometrial IMRT plan quality." ESTRO 2014.

Results

- The impact of using pDVH models and a standard planning technique is demonstrated by plan quality improvement in the 5 patient validation cohort as seen by a reduction in V40 and mean dose for all OARs compared with the original clinical plan

OAR	25 Patient Training Cohort		
	SR	V40(orig)-V40(replan) (%)	Mean(orig)-Mean(replan) (Gy)
Bladder	0.006 ± 0.045	8.8 ± 7.9	2.5 ± 1.7
Bowel	0.017 ± 0.023	2.7 ± 2.4	2.4 ± 1.6
Rectum	-0.007 ± 0.048	8.3 ± 8.8	3.2 ± 2.4
Sigmoid	-0.012 ± 0.056	12.3 ± 13.9	3.5 ± 2.8

OAR	5 Patient Validation Cohort			
	V40(orig)-V40(replan) (%)	Mean(orig)-Mean(replan) (Gy)	d_V40 (%)	d_mean (Gy)
Bladder	9.8 ± 5.1	2.3 ± 1.5	0.6 ± 5.2	0.5 ± 0.9
Bowel	2.1 ± 2.1	0.5 ± 0.6	1.7 ± 1.4	0.5 ± 1.4
Rectum	9.3 ± 5.9	2.7 ± 3.4	1.8 ± 3.3	0.6 ± 1.1
Sigmoid	9.1 ± 14.8	1.8 ± 2.3	1.3 ± 5.4	0.4 ± 1.5

Plan Quality Study Results

- The impact of using pDVH models and a standard planning technique is demonstrated by plan quality improvement in the 5 patient validation cohort as seen by a reduction in V40 and mean dose for all OARs compared with the original clinical plan

Ongoing prospective clinical trial at Wash U to assess impact on plan quality and efficiency.

OAR	V40(orig)-V40(replan) (%)	Mean(orig)-Mean(replan) (Gy)	d_V40 (%)	d_mean (Gy)
Bladder	9.8 ± 5.1	2.3 ± 1.5	0.6 ± 5.2	0.5 ± 0.9
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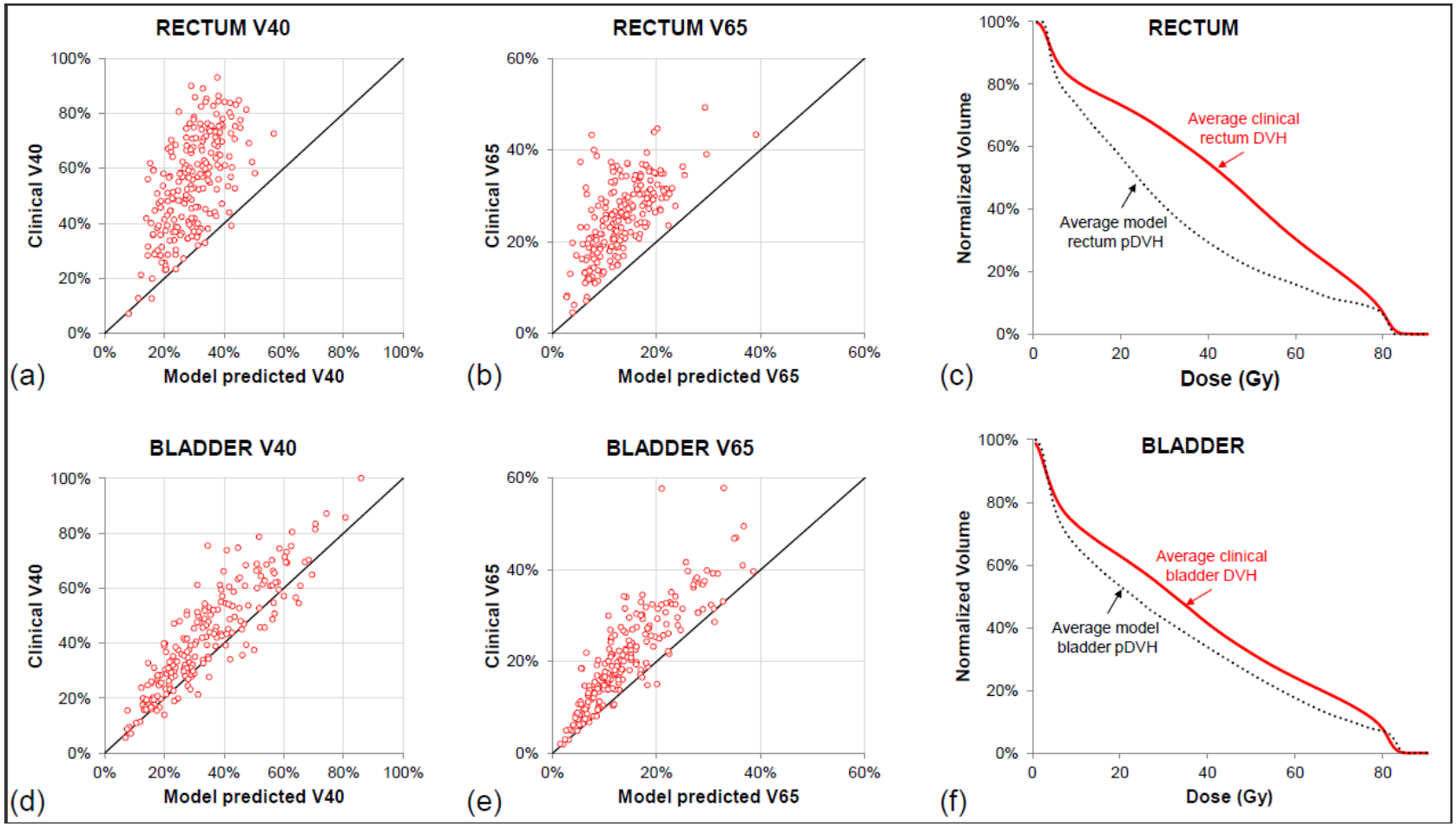
Rectum	9.3 ± 5.9	2.7 ± 3.4	1.8 ± 3.3	0.6 ± 1.1
Sigmoid	9.1 ± 14.8	1.8 ± 2.3	1.3 ± 5.4	0.4 ± 1.5

Multi-Institutional Study

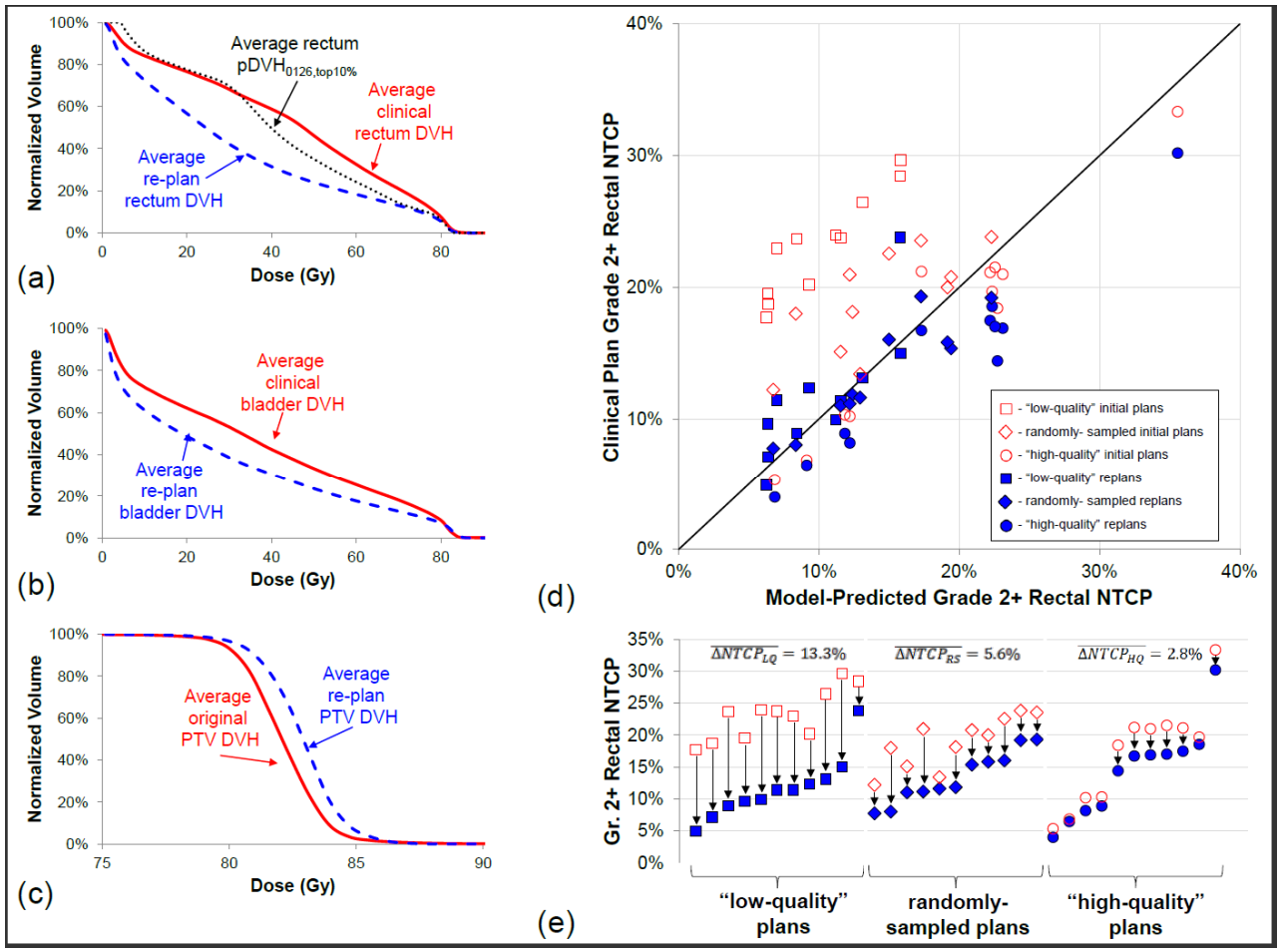
- Secondary analysis of RTOG 0126



K.L. Moore et al, "Quantifying unnecessary normal tissue complication risks due to suboptimal planning: a secondary study on RTOG0126 ." IJROBP, 2015.

Multi-Institutional Study Results

- **Results suggest decreased risk based on NTCP models**



K.L. Moore et al, "Quantifying unnecessary normal tissue complication risks due to suboptimal planning: a secondary study on RTOG0126 ." IJROBP, 2015.

What Have We Learned?

- Treatment plan quality variability is a problem.
  - At Washington University in St. Louis
  - At independent clinics
  - At many of the academic and independent clinics that enrolled patients on RTOG 0126
- Does KBP/auto-planning address these issues?
  - Improves ability to systematically achieve high quality plan
  - Improves efficiency of treatment plan generation
  - Necessary to benchmark models against other institutions

Question 2

Several published studies have demonstrated that knowledge-based planning modelsé

0% a. are helpful QC for structure delineation

0% b. can aid in plan quality improvement

0% c. should never by used by a rad onc

0% d. should only be used by a physicist

0% e. are IMRT optimization algorithms

Question 2

Several published studies have demonstrated that knowledge-based planning models

a. are helpful QC for structure delineation
b. can aid in plan quality improvement
a. should never by used by a rad onc
b. should only be used by a physicist
c. are IMRT optimization algorithms

Answer: b. can aid in plan quality improvement

Reference: L.M. Appenzoller, et. al., ñPredictive DVH models developed at a large institution impact clinical relevant DVH parameters in IMRT plans at an unrelated radiotherapy facilityò, Med. Phys. 40, 386 (2013).

Learning Objectives

1. Highlight the motivation for knowledge-based planning
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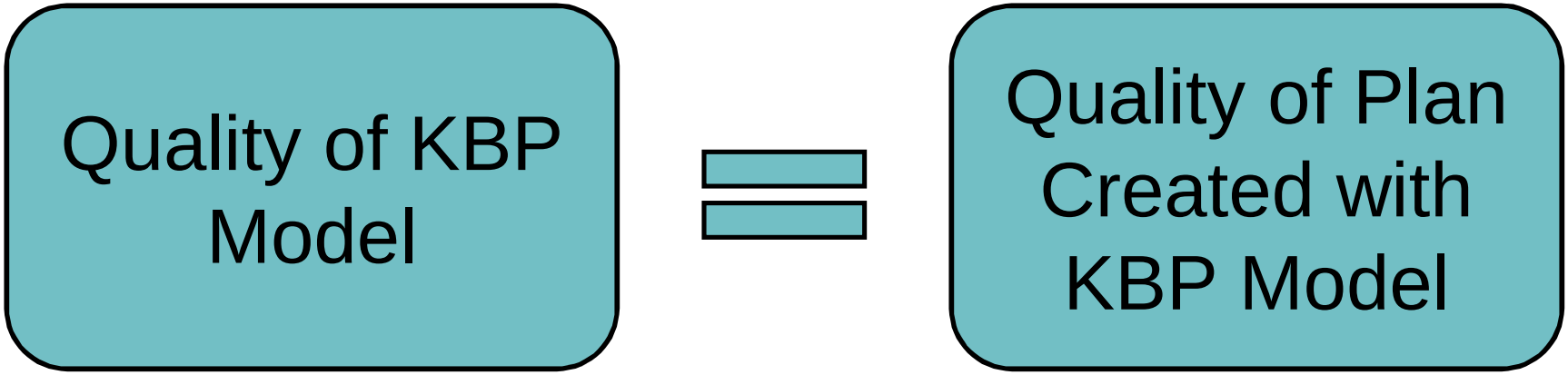
Model Training and Validation

- Importance of systematic KBP model training and validation process:



Training and Validation Process

- Patient selection
- Model training and evaluation
- Model validation
- Clinical use of model

Training and Validation Process

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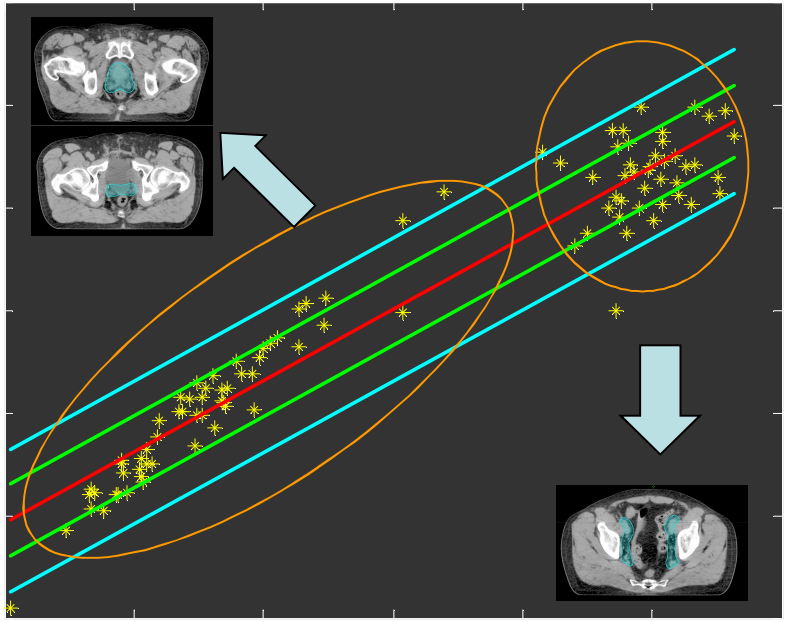
Patient Selection: Geometry

- PTV / OAR Geometry
  - Similar target shape
  - Similar target location
  - Similar relative position of OARs to PTV
- CCMB ex.



Courtesy of J. Alpuche

Patient Selection: Guidelines

- Similar Clinical Objectives
  - Same PTV coverage/OAR sparing criteria
- Similar Clinical Trade-Offs
  - Importance of PTV coverage / OAR sparing
- PTV prescription dose can vary
  - Estimated DVHs will be scaled as a percentage of Rx dose

		Bilateral Neck Treatment	Ipsilateral Neck Treatment
H&N	**PTV**	95% of PTV > 95% of Rx; Max dose < 110% of Rx	95% of PTV > 95% of Rx; Max dose < 110% of Rx
	Spinal Cord	Max dose 40 Gy	Max dose 40 Gy
	Spinal Cord + Margin	Max dose 52 Gy; < 1% (or 1 cc) exceeds 50 Gy	Max dose 52 Gy; < 1% (or 1 cc) exceeds 50 Gy
	Optic Nerves, Optic Chiasm	Max dose 54 Gy	Max dose 54 Gy
	Brainstem	Max dose 54 Gy; < 1% exceeds 60 Gy	Max dose 54 Gy; < 1% exceeds 60 Gy
	Brain	Max dose 60 Gy; < 1% exceeds 65 Gy	Max dose 60 Gy; < 1% exceeds 65 Gy
	Retina	Max dose 50 Gy; < 5% exceeds 45 Gy	Max dose 50 Gy; < 5% exceeds 45 Gy
	Larynx	As low as possible; mean dose < 45 Gy	As low as possible; mean Dose <25 Gy
	Upper Esophagus	As low as possible; mean dose < 45 Gy	As low as possible; mean dose < 25 Gy
	Parotid	As low as possible; mean dose ≤ 26 Gy	As low as possible; mean dose ≤ 10 Gy (contralateral)
	Pharyngeal Constrictors	As low as possible; V60 < 60 Gy	As low as possible; V60 < 45 Gy
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	Unspecified Tissue	Less than PTV Rx; < 5% exceeds PTV Rx	Less than PTV Rx; < 5% exceeds PTV Rx

Patient Selection: Patient Numbers

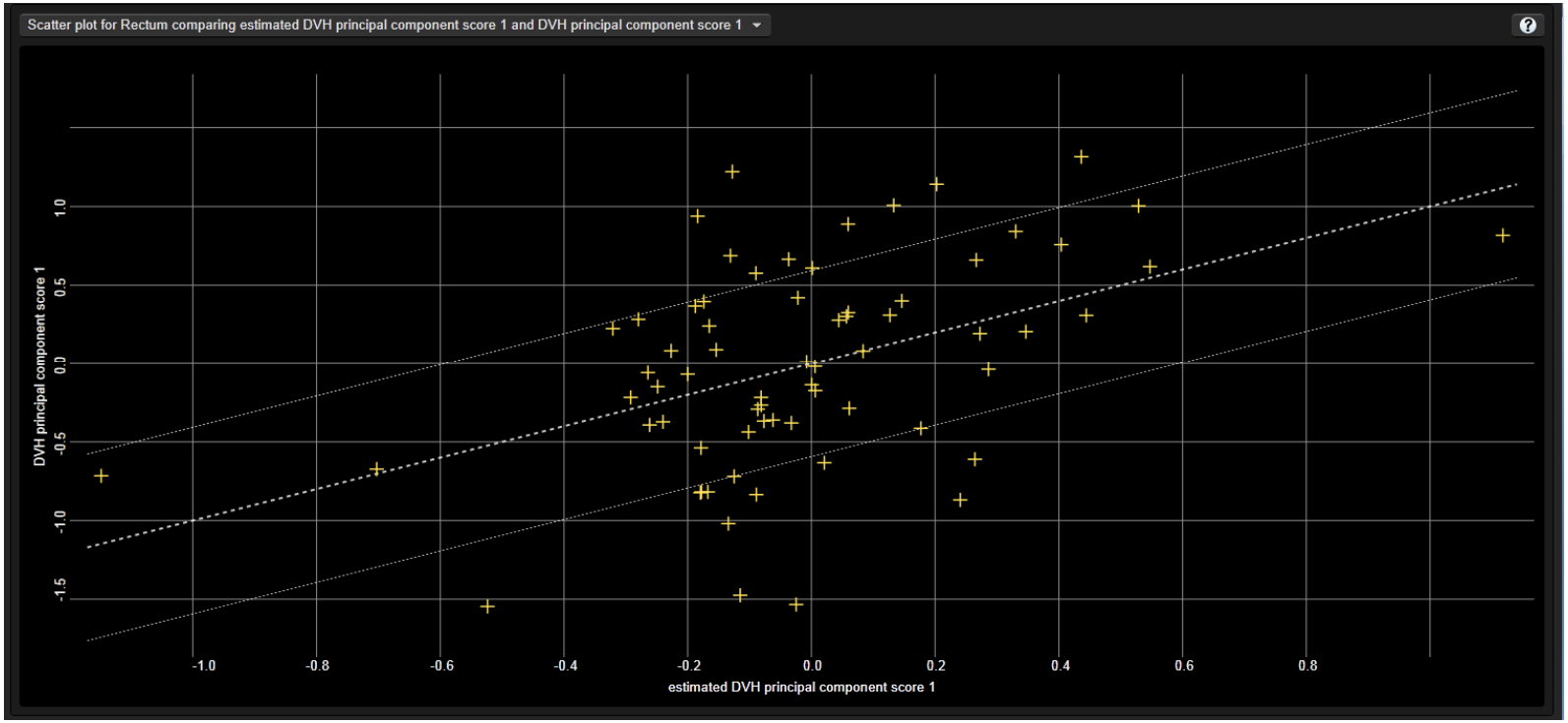
- Number of training patients increases as the model complexity increases.
- Model validation process is used to ensure the number of training patients is sufficient

Patient Selection: Plan Quality

- Training set plan quality
  - Output of KBP model directly correlated to input
  - Statistical noise present in KBP training set can impact model behavior
- QA of training set
  - Clinically approved, safe treatment
  - Consider iterative process in model training to obtain adequate model

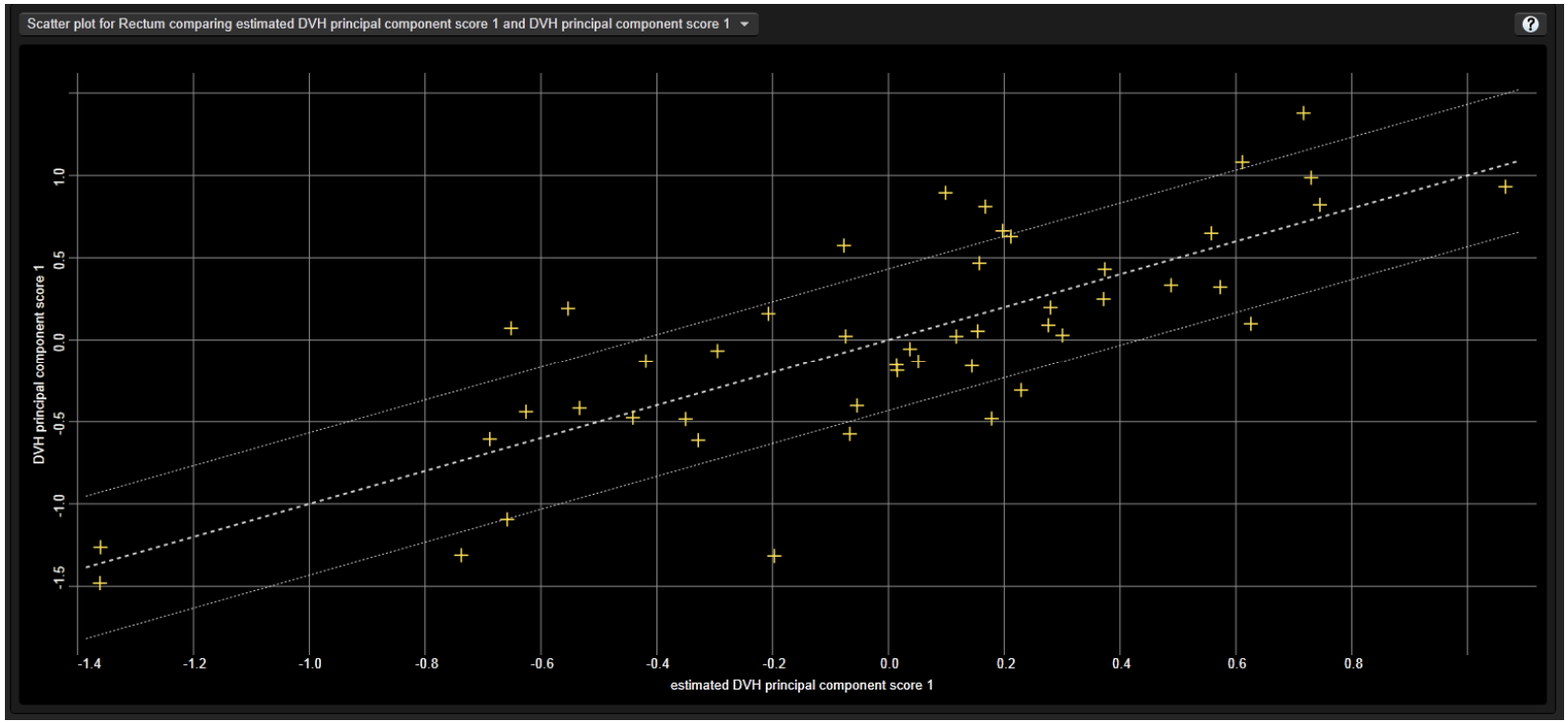
Plan Quality Considerations

- Ex. Prostate and Node model: OAR = Rectum
  - Poor correlation between actual and estimated DVH principal components for model trained with 70 mixed quality treatment plans



Plan Quality Considerations

- Ex. Prostate and Node model: OAR = Rectum
  - Good correlation between actual and estimated DVH principal components for model trained with 48 good quality treatment plans



Training and Validation Process

- Patient selection
- Model training and evaluation
- Model validation
- Clinical use of model

Model Training and Evaluation

- Review the model statistical results
- Review the clinical vs. estimated DVHs
- Review model outliers
  - Geometric and dosimetric

Note: Will discuss model evaluation and validation in context of Varian RapidPlan™. Specific steps will differ depending on algorithm and implementation of KBP software.

Review Model Statistics

- Assess model over-fitting
- Assess predictive ability of the model

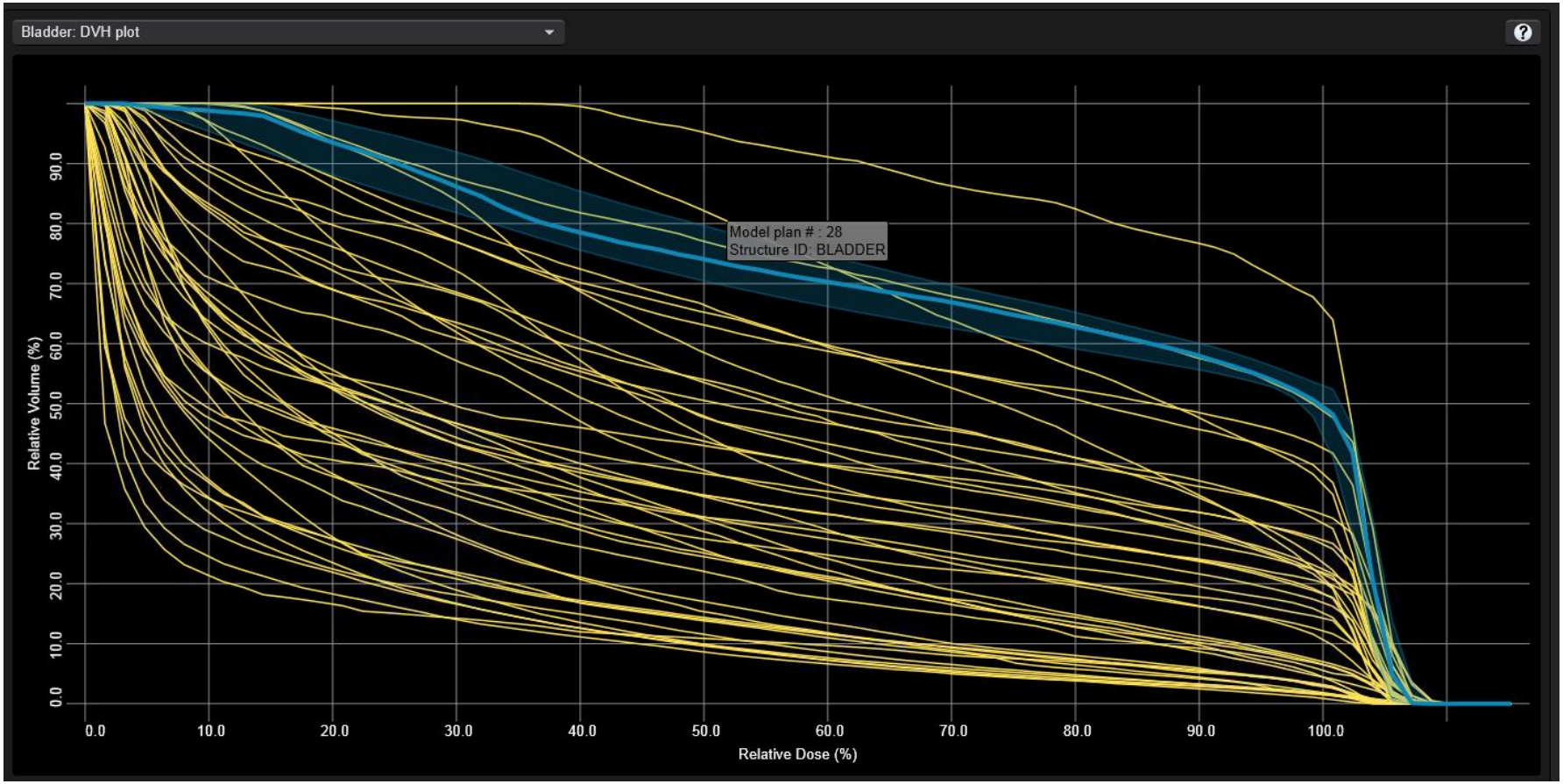
```
Estimation model statistics for structure Rectum:
  Model goodness of fit
    DVH's principal components average fit 0.998977 out of 1.0
    GED's principal components average fit 0.999374 out of 1.0
    Regression model parameters' coefficient of determination 0.772767 out of 1.0
    Regression model's parameters average chi square 1.14286
    Whole estimation model's fit 0.771493 out of 1.0
    Whole estimation model's average MSE 17.4678
  Model goodness of estimation
    Mean squared error between original and estimate 0.00237184
    Statistics outside boundaries:
      Proportion of histogram bins outside boundaries 40.4178
      Mean of absolute deviation of bins outside boundaries -0.00248895
      Mean squared error of bins outside boundaries 0.000618992
      Standard deviation of the error of bins outside boundaries 0.0132559
      Mean of the error of bins outside boundaries 0.0118805

Model was successfully trained with 41 out of 41 plans.

Model training done
```

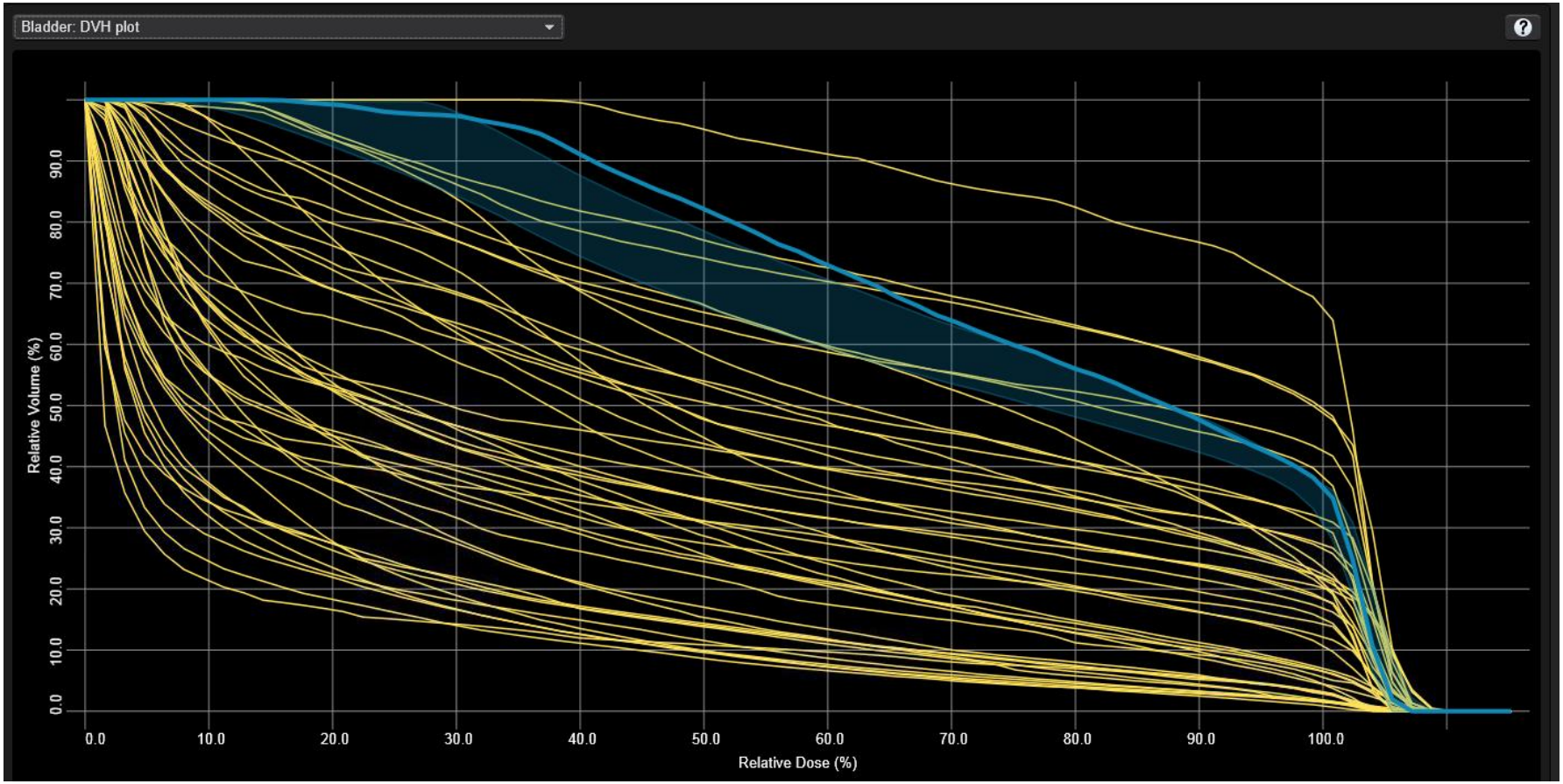
Review Clinical vs. Estimated DVHs

- Model properly identifies variation in training set DVHs



Review Clinical vs. Estimated DVHs

- Clinical DVH > estimate → Outlier
  - Clinically relevant parameter



Identify and Remove Outliers

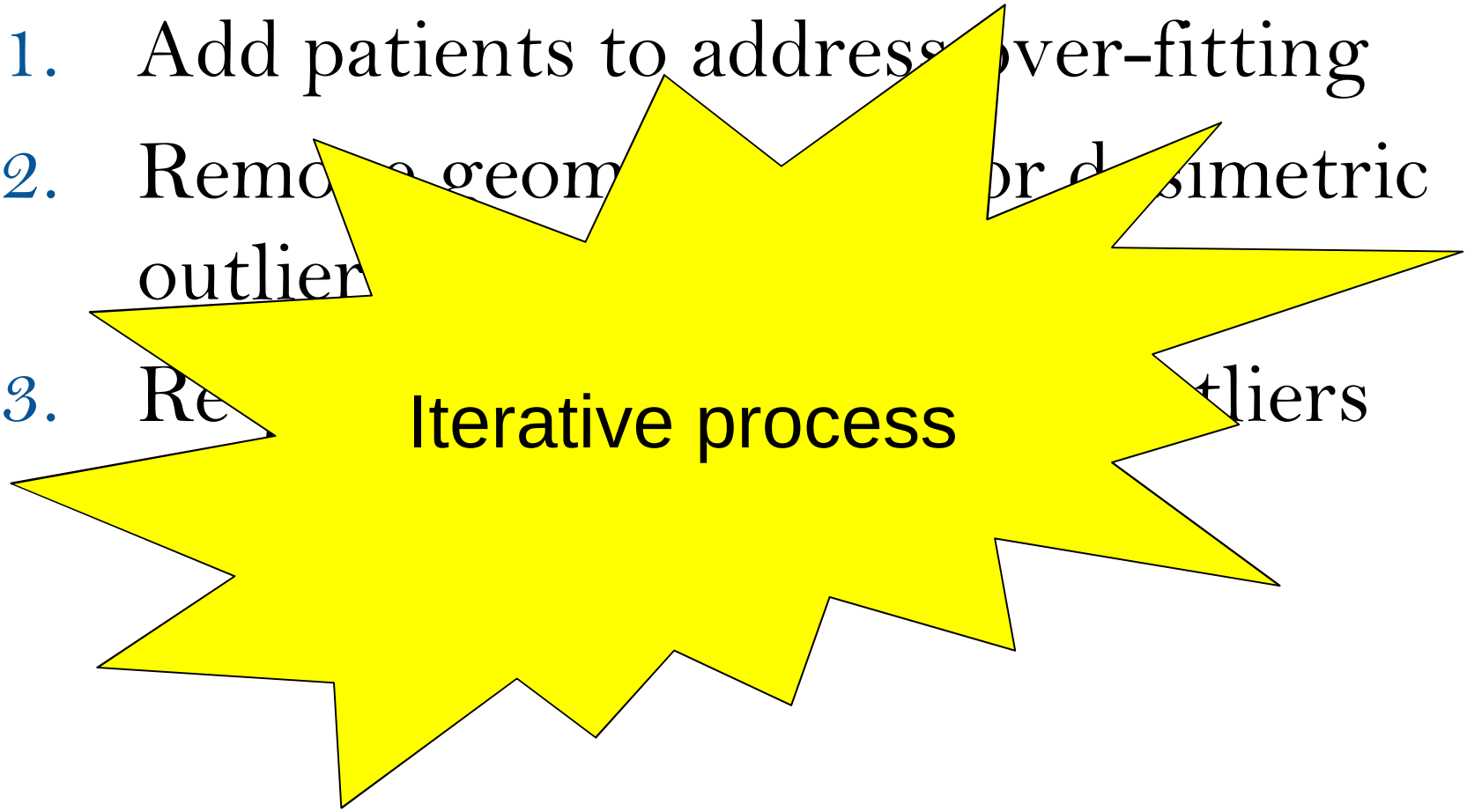
- Dosimetric outlier
  - Clinical DVH substantially differs from estimated DVH based on a clinically significant parameter
- Geometric outlier
  - PTV volume/shape substantially differs from the majority of the training set
  - Structure volume/shape substantially differs from the majority of the training set
  - Positional relationship between structure and PTV substantially differs from the majority of the training set

Steps to Improve Model Quality

1. Add patients to address over-fitting
2. Remove geometric outliers or add similar patients
3. Remove or re-plan dosimetric outliers

Steps to Improve Model Quality

1. Add patients to address over-fitting
2. Remo[illegible] geom[illegible] or d[illegible]simetric outlier[illegible]
3. Re[illegible]tliers



Question 3

In statistical modeling, an outlier is defined as..

0% a. a data point explained by the statistical model

0% b. a data analysis technique

0% c. a data point distant from other observations

0% d. an application that takes input and generates output

0% e. a method of understanding messages in the data

Question 3

In statistical modeling, an outlier is defined as..

a. a data point explained by the statistical model
b. a data analysis technique
c. a data point distant from other observations
d. an application that takes input and generates output
e. a method of understanding messages in the data

Answer: c. a data point distant from other observations

Reference: Boris Iglewicz and David Hoaglin (1993), ñVolume 16: How to Detect and Handle Outliersò, The ASQC Basic References in Quality Control: Statistical Techniques, Edward F. Mykytka, Ph.D., Editor.

Training and Validation Process

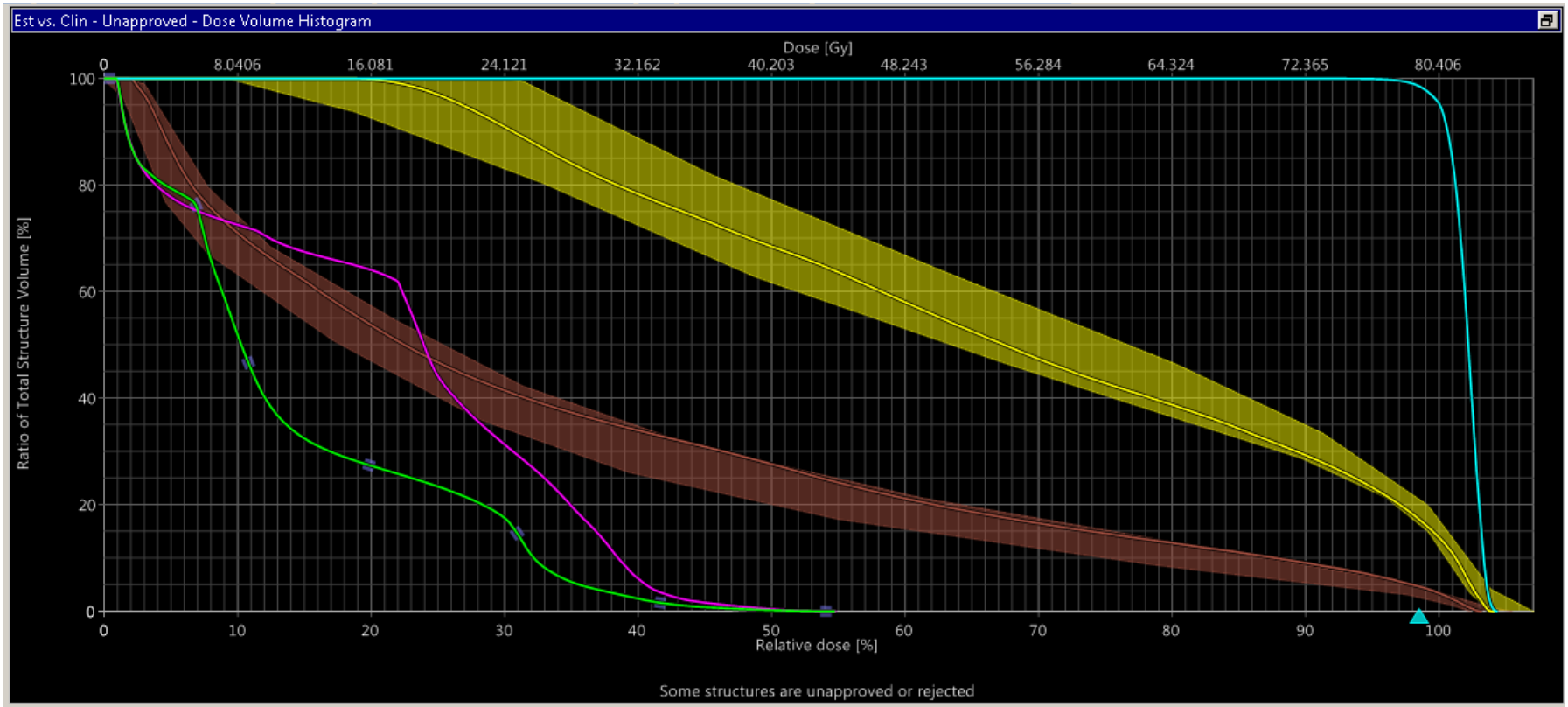
- Patient selection
- Model training and evaluation
- Model validation
- Clinical use of model

Validation Patients

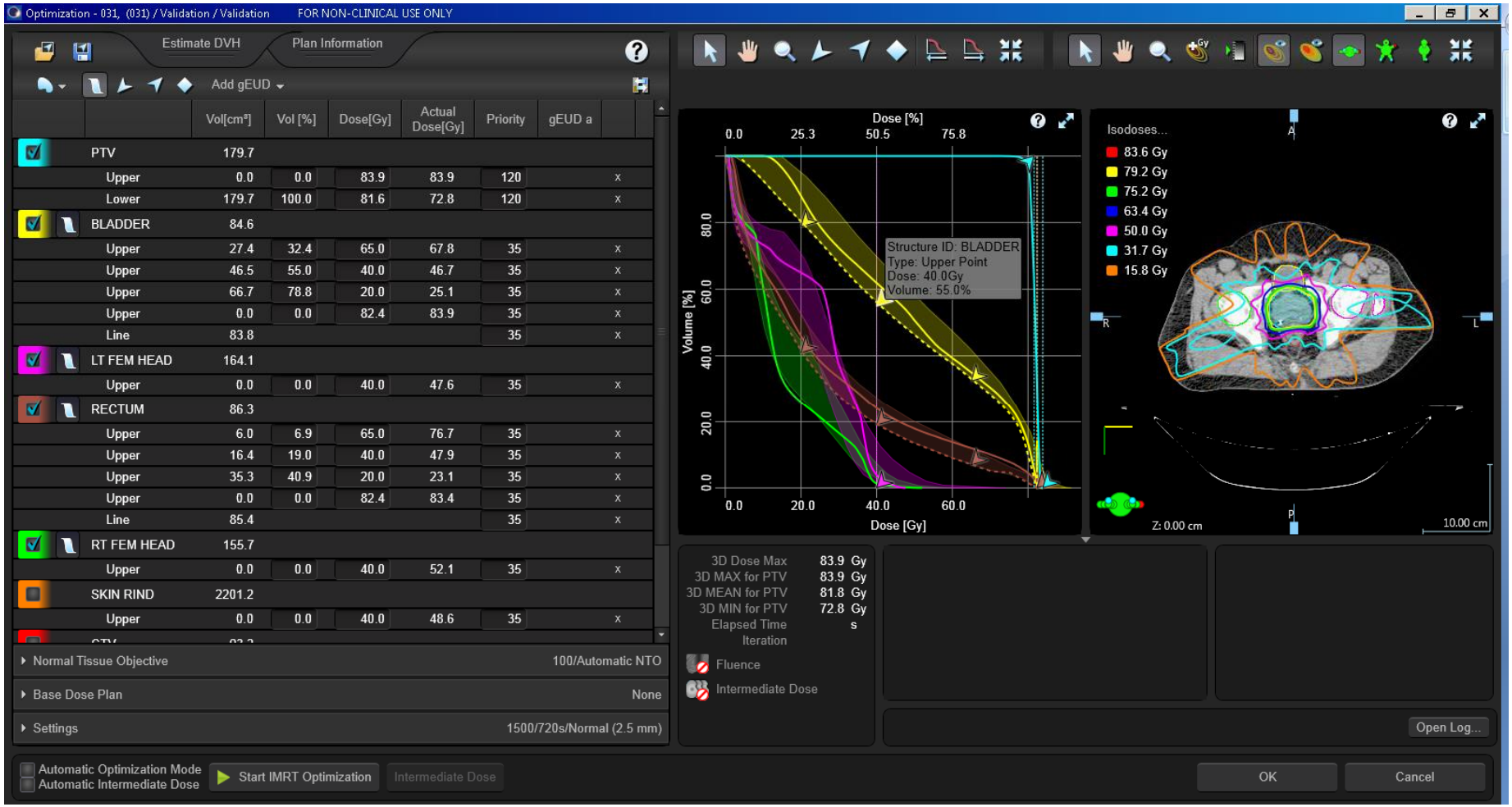
- Independent from patients used to train model
- Represent the range of patient geometries, plan geometries, and plan prescriptions for which the model will be clinically used
- Good plan quality
  - PTV coverage
  - OAR sparing

Clinical vs. Estimated DVHs

- Review that clinically approved plan is within DVH estimation range
- If it is not, it is possible that plan can be improved

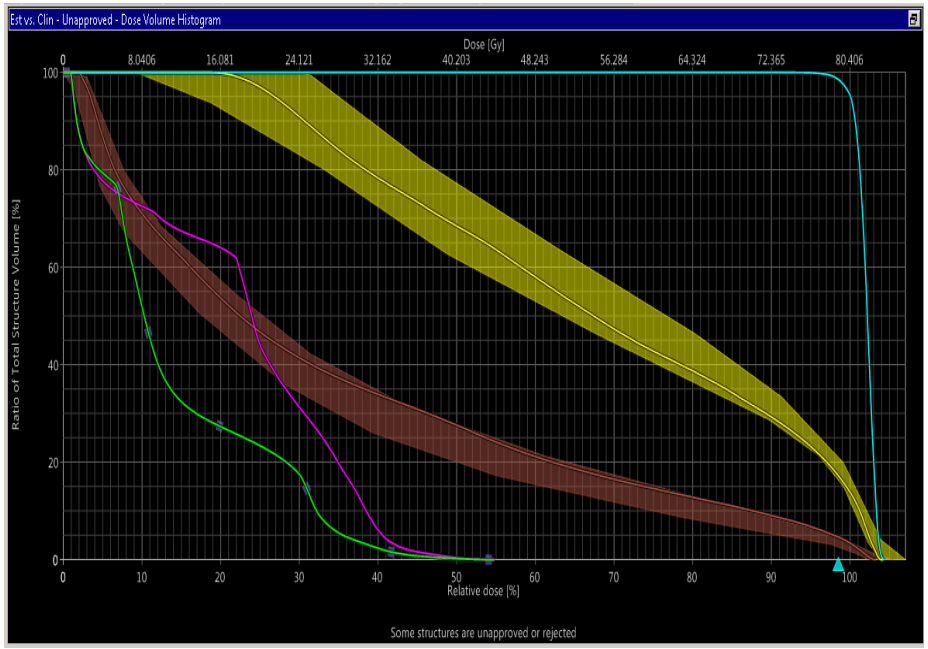


Create Validation Plan w/ Model



Objective Selection

- IMRT objective selection
  - Ensures clinically acceptable plan that achieves model estimate
  - Based on prior clinical experience
  - Priorities and objectives tuned during model validation



Model Structures and Objectives

Add Objectives to Structure...

Target	ID		Vol [%]	Dose	Priority	gEU
Yes	PTV	(PTV)				
	Upper		0.0	105.0 %	120	
	Lower		100.0	103.0 %	120	
	Bladder	(15900)				
	Upper		0.0	104.0 %	35	
	Upper (fixed dose, generated vol.)		Generated	80.0 %	35	
	Upper (fixed dose, generated vol.)		Generated	50.0 %	35	
	Upper (fixed dose, generated vol.)		Generated	25.0 %	35	
	Line		Generated	Generated	35	
	Femur_L	(24475)				
	Upper		0.0	50.0 %	35	
	Femur_R	(24474)				

Normal Tissue Objective

Assess Clinical Acceptability

- Review validation plans as per normal institution clinical standards
  - Isodose distribution
  - Clinical guidelines (scorecard)
    - PTV coverage
    - Hotspots
    - Population-based OAR DVH cut-points
  - Plan technical integrity

Training and Validation Process

- Patient selection
- Model training and evaluation
- Model validation
- Clinical use of model

Clinical Use of Model

- Do not venture far from your validation set
- Consider automation/standardized protocols
  - Beam arrangement
  - Contouring guidelines
  - Plan quality reports (scorecards)
- Develop guidelines for clinical use
  - When should I use the model?
  - When should I plan manually?

Final Thoughts

- Proper model training and validation is necessary for the clinical use of knowledge-based planning models
  - Possibility for systematic errors
- KBP is an exciting advancement, with potential for future development
  - Potential to improve quality, efficiency, and standardization
  - Does not replace human/clinician judgment

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Questions?

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