Artificial Intelligence in Proton Therapy

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Tuesday, July 14 -7:30am PDT
Virtual Meeting

Learning Objectives

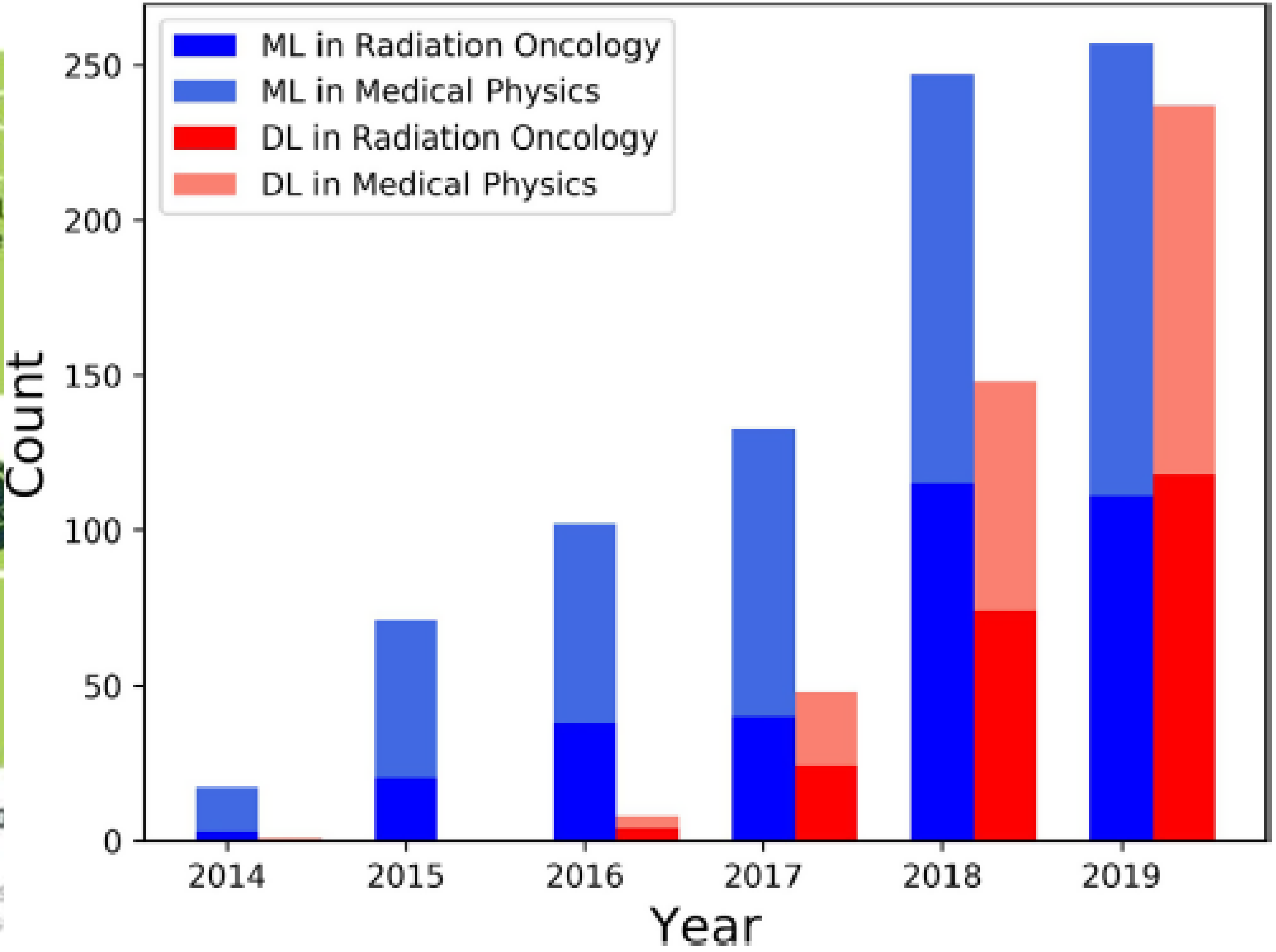
- Review new AI applications in Proton Therapy
- Discuss trends and limitations
- Recommend future strategies

- Not to learn about AI techniques/algorithms

Disclosures

- Research grants: NIH Grant; Sponsored Research Grant from Varian
- Speaker Bureau Honorarium: Varian
- Consortium: Varian FlashForward™

What is AI?



- **AI: a broad concept of "incorporating human intelligence to machines"**
- **ML: enable machines to learn by themselves (using data and algorithms provided by human)**
- **DL: a subset of ML inspired by the information processing pattern of human brain**

Where are AI Applications in Proton Therapy (PT)?

Patient Selection	Simulation	Treatment Planning & QA	Adaptive RT	Outcome Studies
Why PT?	Target delineation	HU-to-SPR Conversion (CT/DECT)	Change Prediction	Survival
Expected improvement?	Auto-segmentation	Dose Calculation	Anatomy changes	Toxicities
Comparison to other treatment modalities?		Auto-Planning	Range changes	Combination Therapies
		2nd MU Calc	Dosimetric changes	Comparative Studies
		Plan Check	On-line planning	Radiomics
		Patient QA	HU-to-SPR Conversion (CBCT)	
			Plan QA	
			Patient QA	

Data

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Machine Learning for 2nd MU Calc

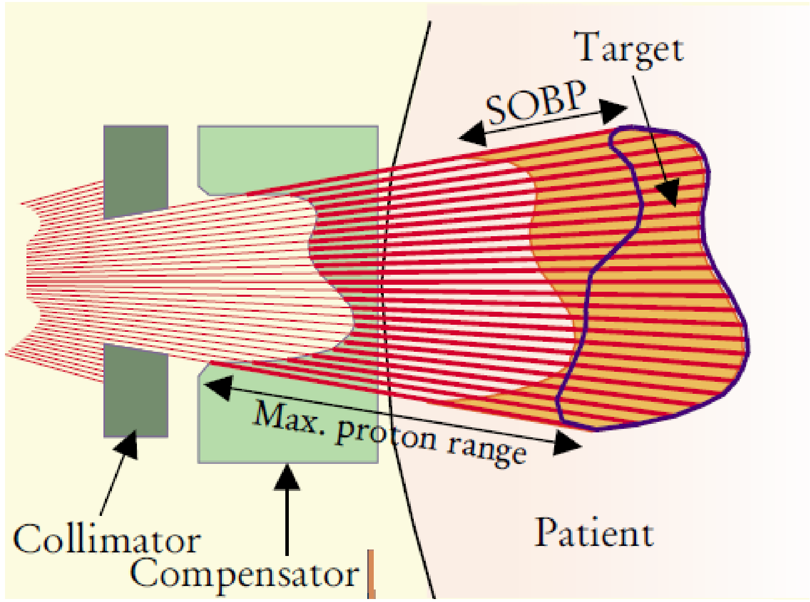
- Rationale: (1) TPS does not generate MUs for PSPT plans; (2) current workflow requires Patient QA measurement to determine MU set per field; (3) improve a semi-empirical model (Kooy 2005)

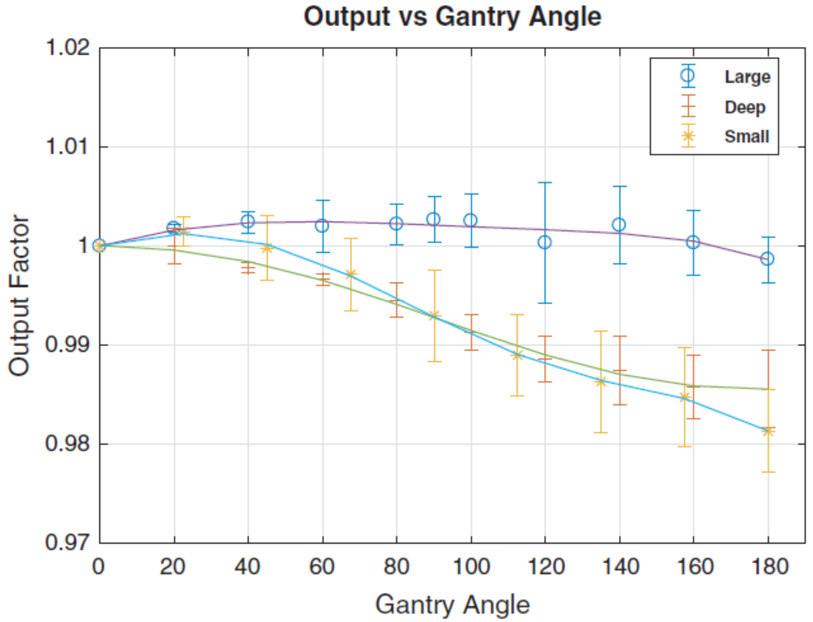
- Sun, B., Lam, D., Yang, D., Grantham, K., Zhang, T., Mutic, S., & Zhao, T. (2018). ***A machine learning approach to the accurate prediction of monitor units for a compact proton machine.*** *Medical physics*, *45*(5), 2243-2251.
- Grewal, H. S., Chacko, M. S., Ahmad, S., & Jin, H. (2020). ***Prediction of the output factor using machine and deep learning approach in uniform scanning proton therapy.*** *Journal of Applied Clinical Medical Physics*.

Machine Learning for 2nd MU Calc

- **Input parameters:**
  - RMW selection (field size; range; modulation range)
  - FSS selection (second scatter; energy absorber etc)
  - Gantry angle dependence (WashU)
  - Field size dependence: aperture block ratio; snout distance

- **Ground truth for training**
  - 1754 QA Measurements (Sun et al)
  - 4231 QA measurements (Grewal et al)

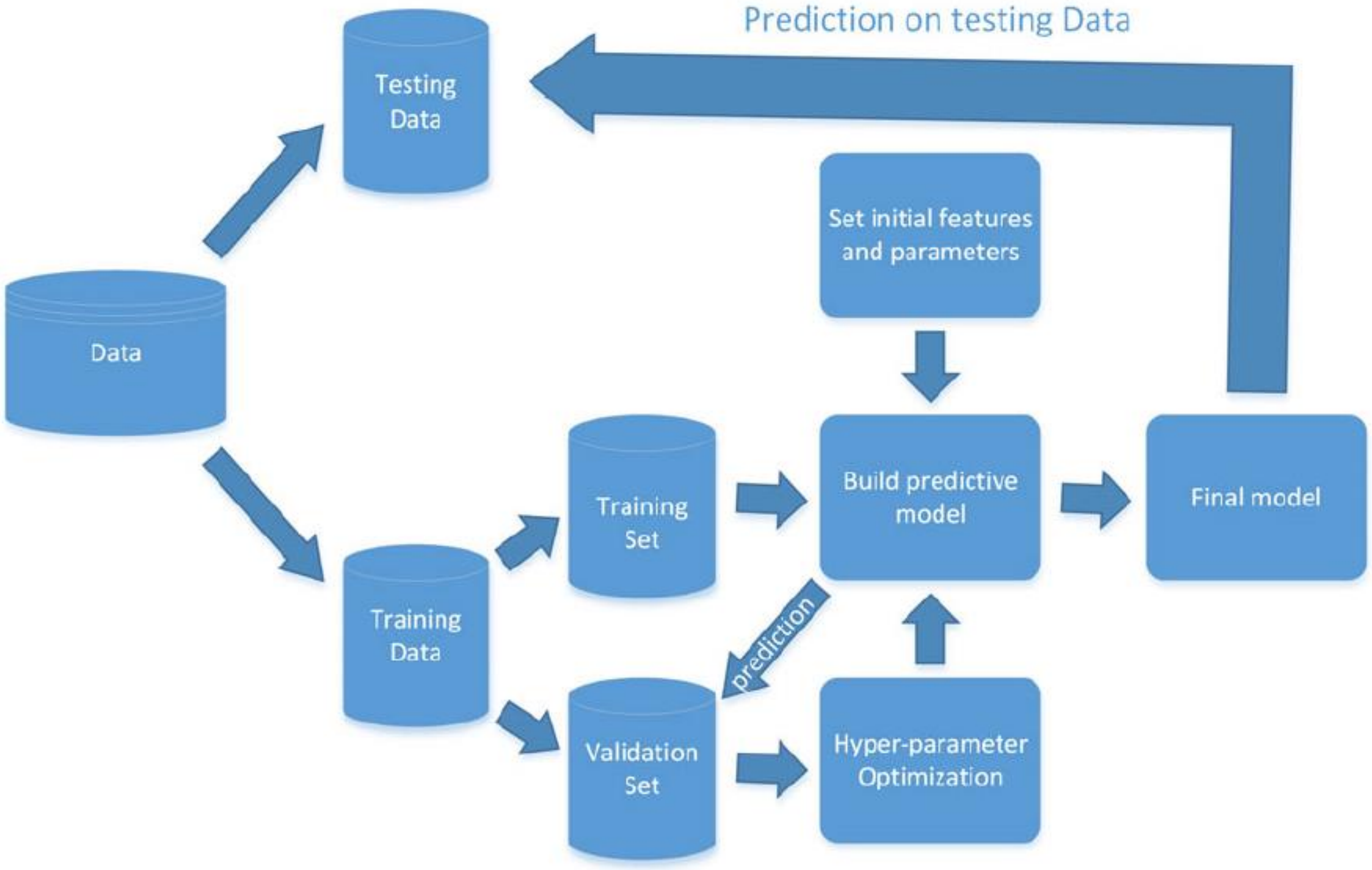




Machine Learning for 2nd MU Calc

- **ML Algorithms (Sun et al.)**
  - Random Forest
  - XGBoost
  - Cubist

- **ML Algorithms (Grewal et al.)**
  - Gaussian process regression (Bayesian non-linear regression)
  - Shallow neural network (fewer (2) hidden layers)



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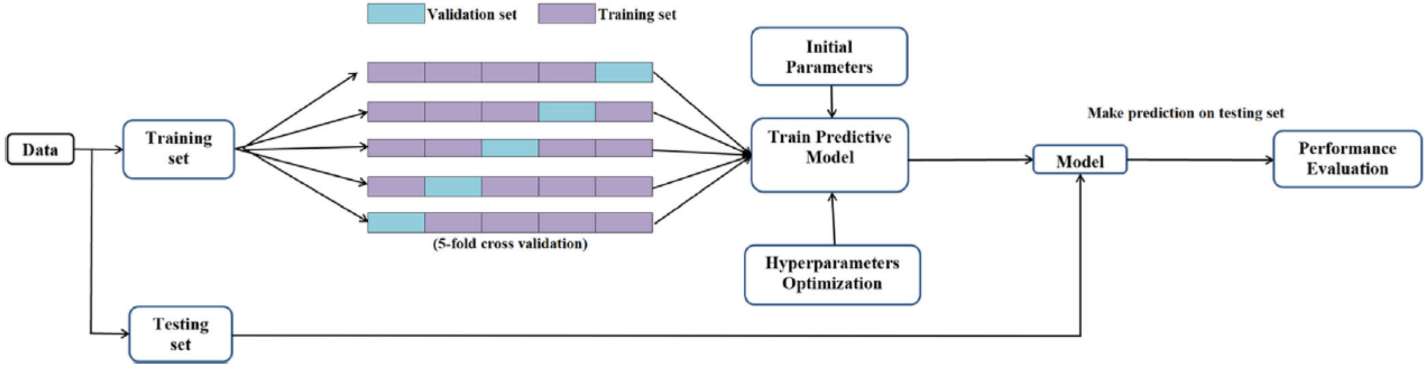
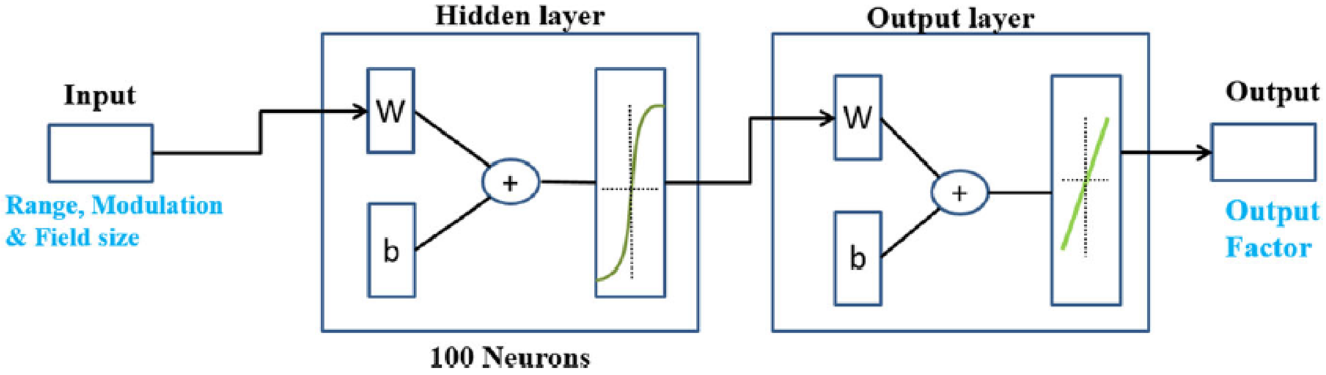
Supervised learning for Gaussian process regression



Shallow neutral network design



Machine Learning for 2nd MU Calc

- **ML Algorithms (Sun et al.)**
  - Random Forest
  - XGBoost
  - Cubist
  - Dr. Kooy's empirical method

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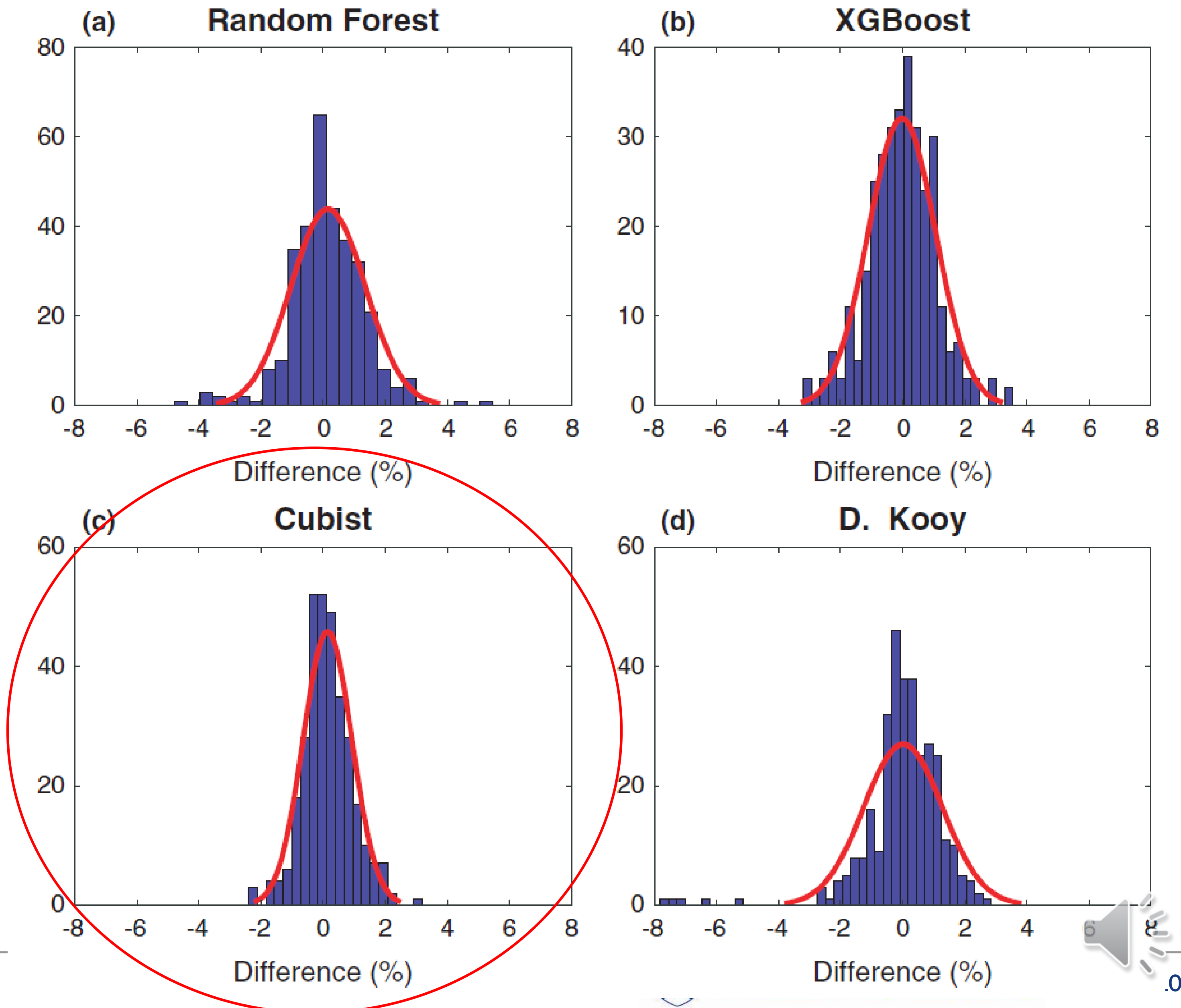

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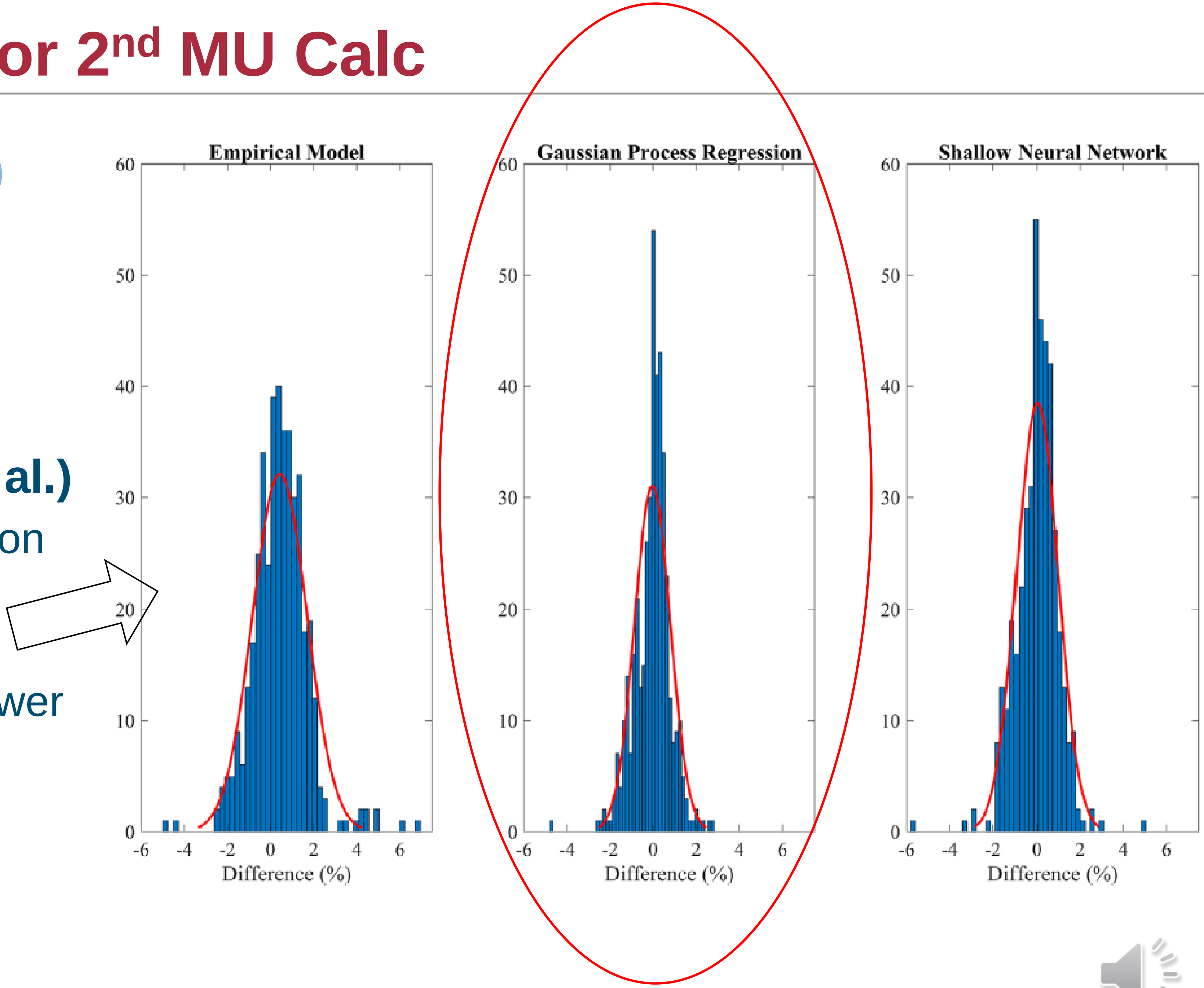
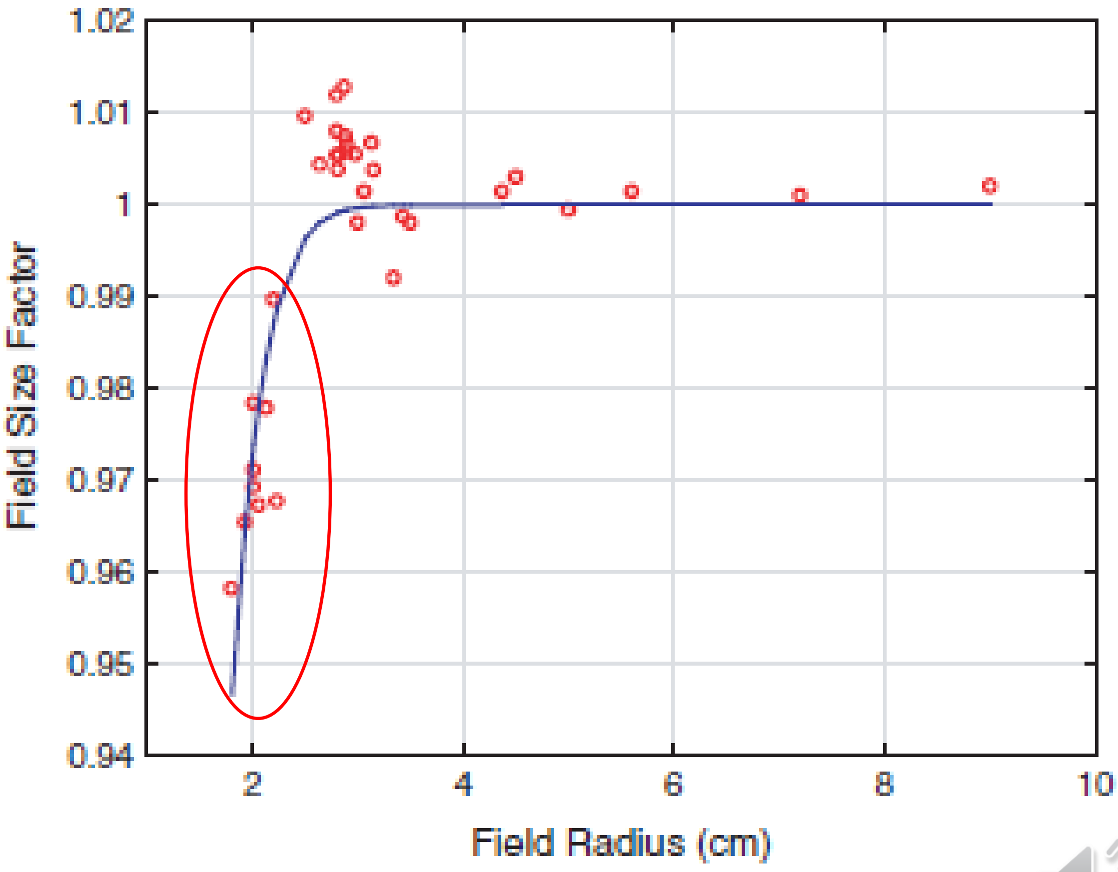


Machine Learning for 2nd MU Calc - Summary

- **An Excellent AI Application for Proton Therapy**
  - Fill in a clinical need
  - Relatively low risk
  - Strong supporting data

- **Limitations**
  - Unknown failure modes
    - Situations of “small field”

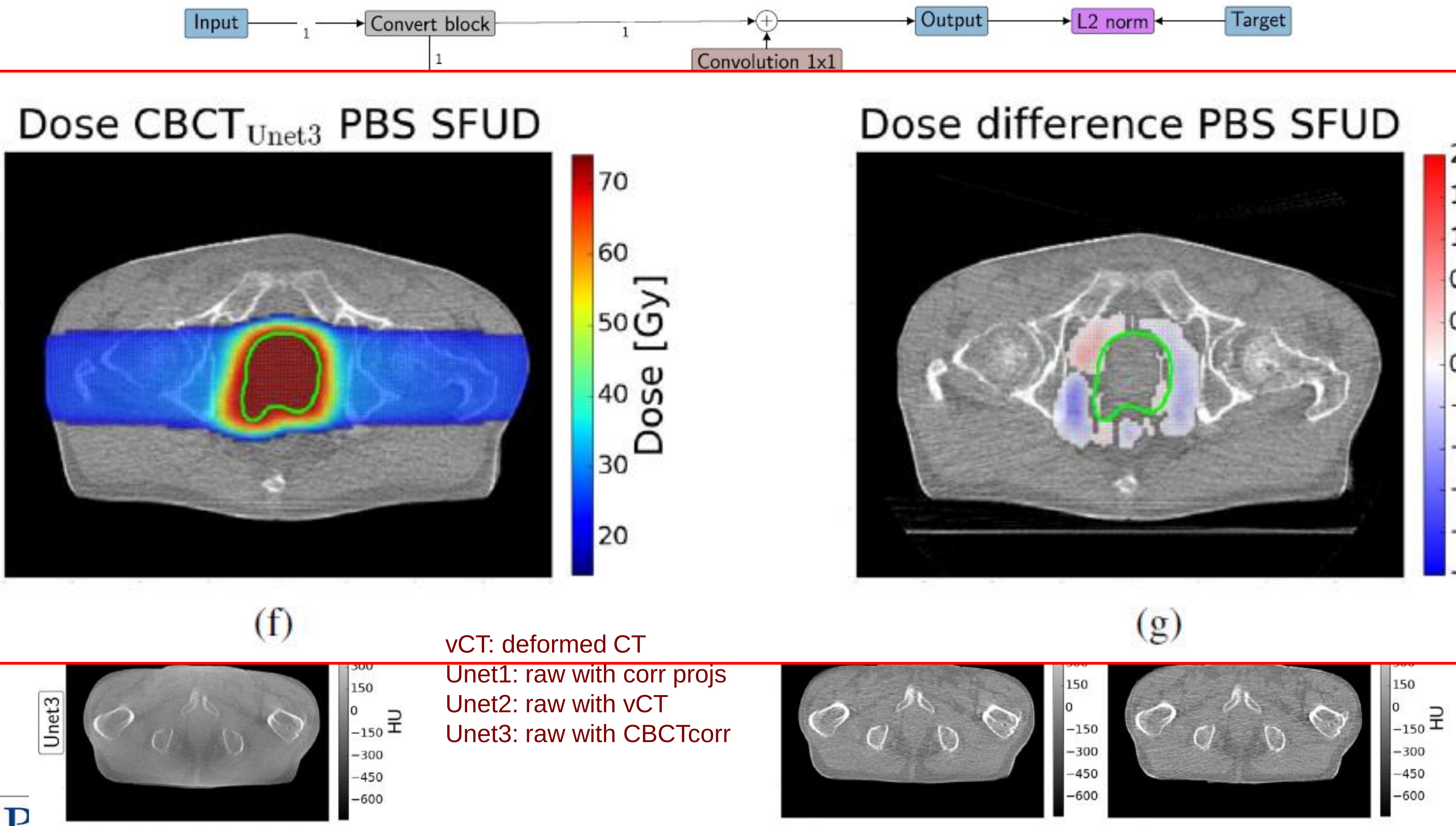


Machine Learning to Convert CBCT HU to Proton SPR

Method	References	Anatomical Site
DIR	Veiga et al (2015); Kurz et al (2015); Landry (2015)	All sites
Projection-based	Park et al. (2015); Kurz et al. (2016);	HN, Pelvis,
Deep Learning (including project-correction)	Hansen et al. (2018); Landry et al. (2019); Nomura et al. (2019) Hamms et al. (2019) Koike et al. (2020) Thummerer et al. (2020) … etc.	All sites

- Arai K *et al* 2017 Feasibility of CBCT-based proton dose calculation using a histogram-matching algorithm in proton beam therapy *Phys. Med.* **33** 68–76
- Chen S, Qin A, Zhou D and Yan D 2018 Technical Note: U-net-generated synthetic CT images for magnetic resonance imaging only prostate intensity-modulated radiation therapy treatment planning *Med. Phys.* **45** 5659–65
- Han X 2017 MR-ba
- Hansen D C, Landr
- Harms J, Lei Y, Wa *hys.* **46** 3998–4009
- Janssens G, Jacqu
- Kida S, Nakamoto neural network *Cureus* **10** e2548
- Kurz C *et al* 2016a
- Kurz C, Dedes G, F in adaptive intensity-modulated photon and proton therapy for h
- Kurz C, Nijhuis R, F
- Landry G *et al* 2015
- Landry G *et al* 2015
- Landry G, Hansen rapy dose calculations *Phys. Med. Biol.* **64**
- Li Y, Zhu J, Liu Z, T for adaptive radiotherapy of nasopharyngeal carcinoma *Phys. M*
- Liang X, Chen L, N cleGAN for adaptive radiation therapy *Phys. Med. Biol.* **64** 1250
- Lim-Reinders S, Ke
- Nagarajappa A K, D
- Nakano H, Mishima ay *Dentomaxillofac. Radiol.* **42** 26397438
- Niu T, Sun M, Star-
- Park Y K, Sharp G C,
- Peroni M, Ciardo D, S *Phys.* **84** e427–e433
- Pileggi G, Speier C MR Acta Oncol. 57 1521–31
- Shi L, Tsui T, Wei J
- Sonke J J, Aznar M and Rasch C 2019 Adaptive radiotherapy for anatomical changes Semin. Radiat. Oncol. 29 245–57
- Spadea M F, Pileggi G, Zaffino P, Salome P, Catana C, Izquierdo-Garcia D, Amato F and Seco J 2019 Deep convolution neural network (DCNN) multi-plane approach to synthetic CT generation from MR images—application in brain proton therapy Int. J. Radiat. Oncol. Biol. Phys. 105 495–503

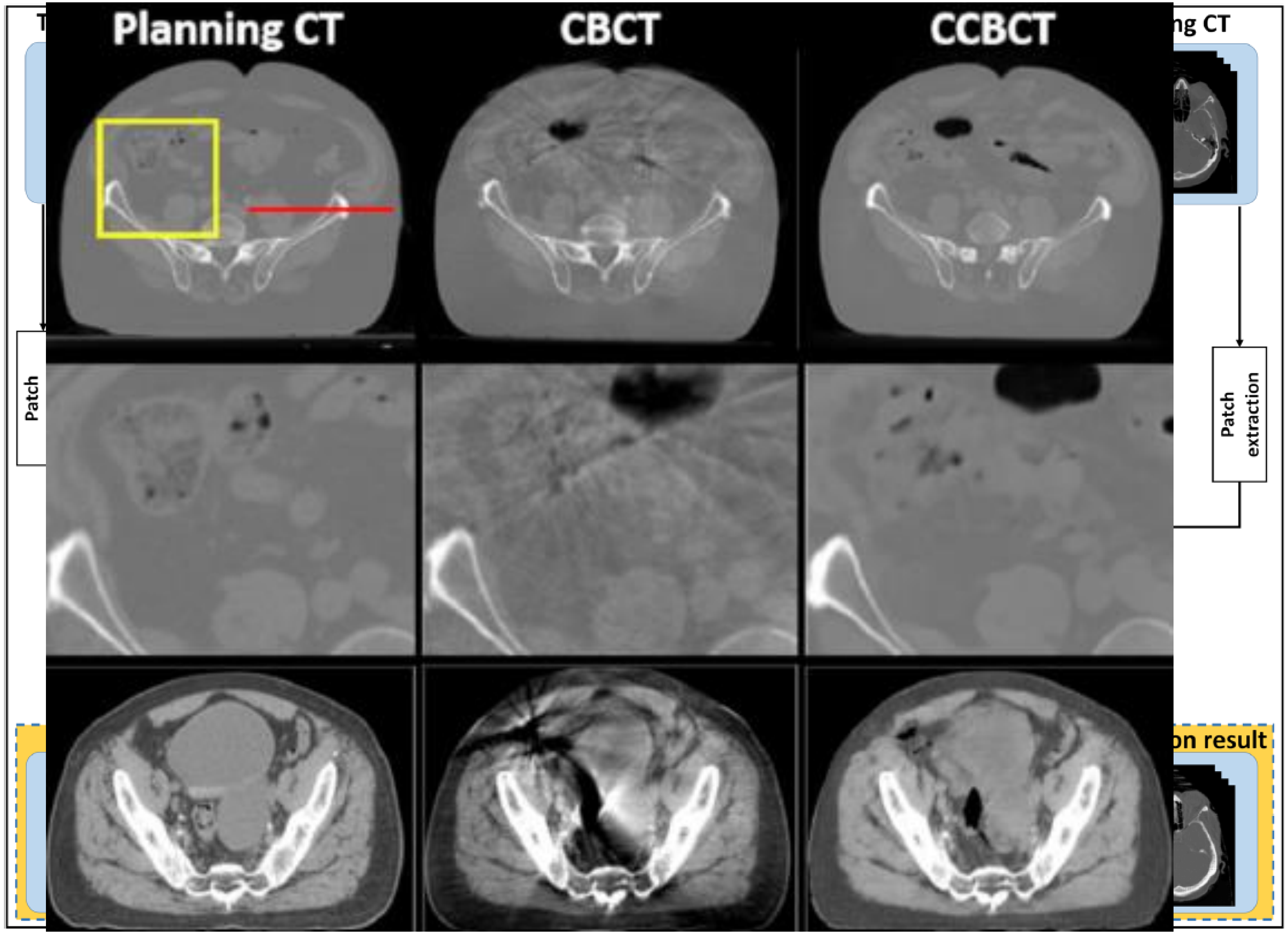
Landry et al. (2018) Unet for CBCT image correction



vCT: deformed CT
Unet1: raw with corr projs
Unet2: raw with vCT
Unet3: raw with CBCTcorr

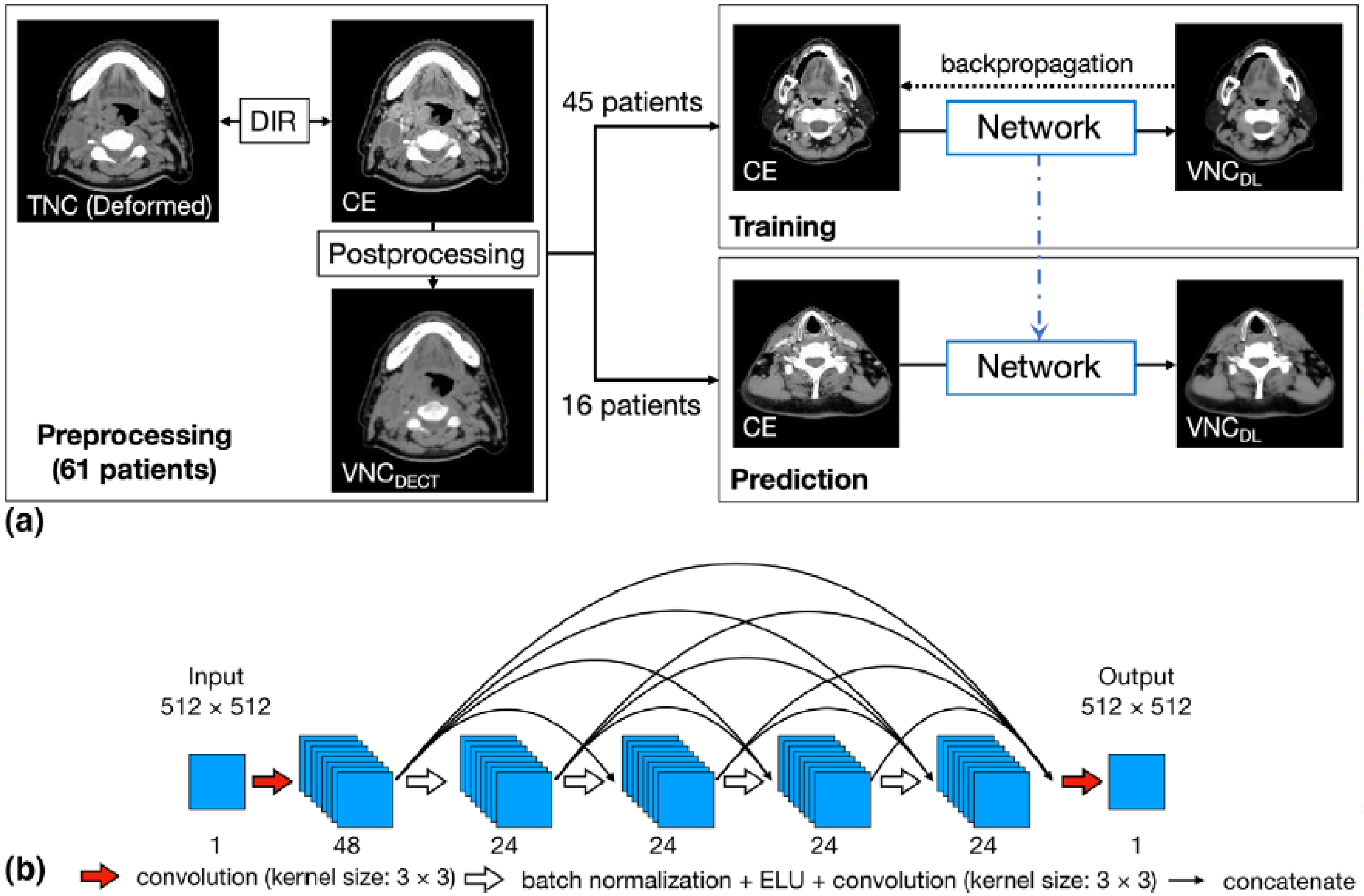
Cycle-consistent adversarial network (cycle-GAN)

- **Harms et al. "Paired cycle-GAN-based image correction for quantitative cone-beam computed tomography." Medical physics 46.9 (2019).**
- **Limitations:**
  - Work only in image domain (no registration)



Create Virtual Non-contrast CT from Contrast CT Scans

- Koike, Yuhei, et al. "Deep learning-based virtual noncontrast CT for volumetric modulated arc therapy planning: Comparison with a dual-energy CT-based approach." Medical physics 47.2 (2020): 371-379. (Osaka University, Japan)

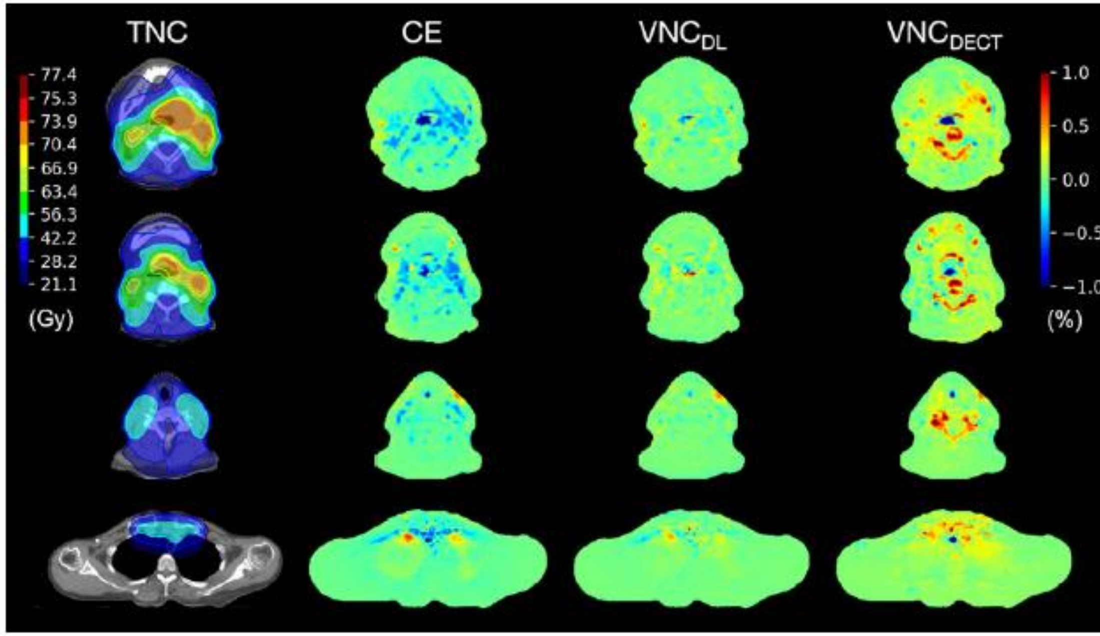


True Non Contrast CT

Contrast CT

Virtual Non Contrast CT

DECT-based Virtual Non Contrast CT

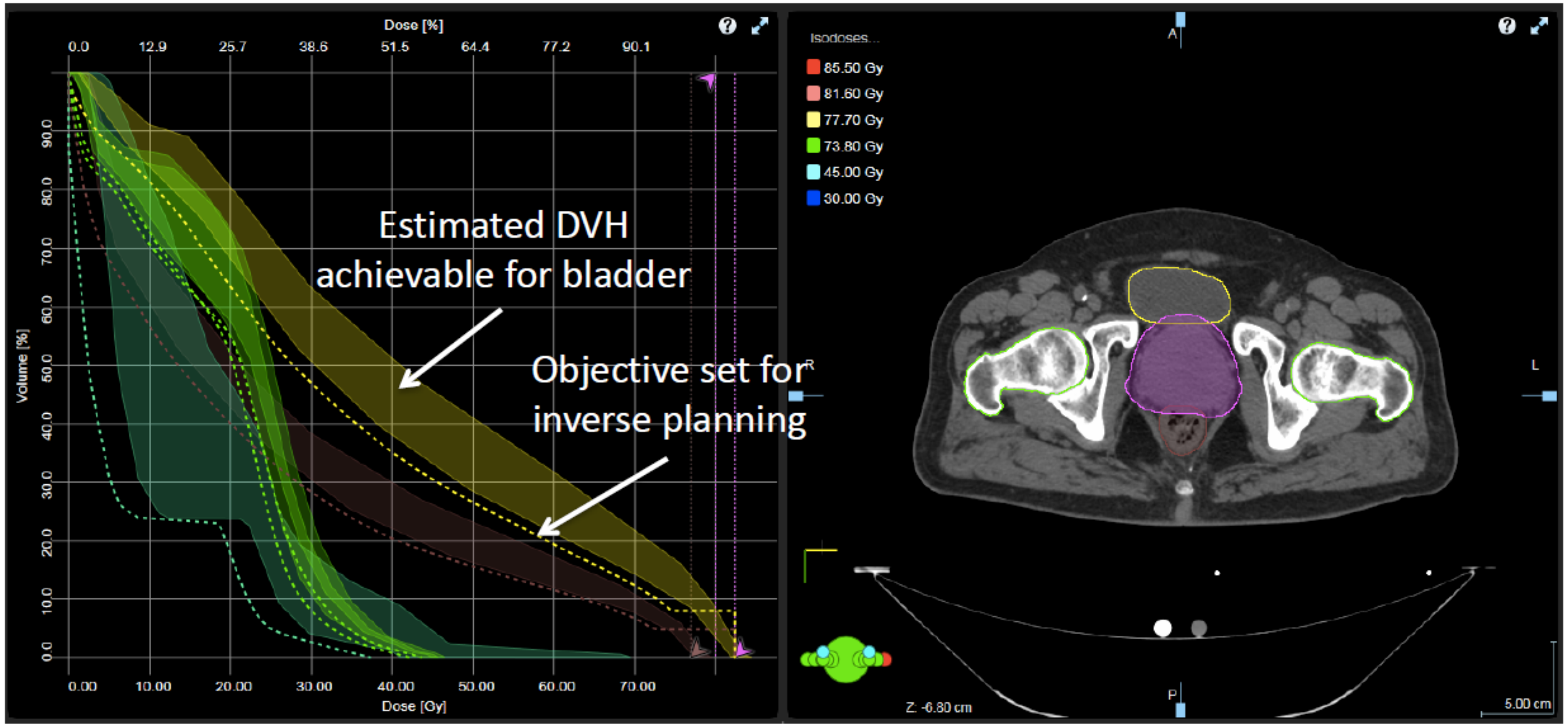


Varian RapidPlan™

- **Varian's solution for knowledge-based planning**

DVH estimation model

Automated objective setting



How to predict OAR DVH?

Each OAR is partitioned into the following sub-volumes:

- **Out-of-field**

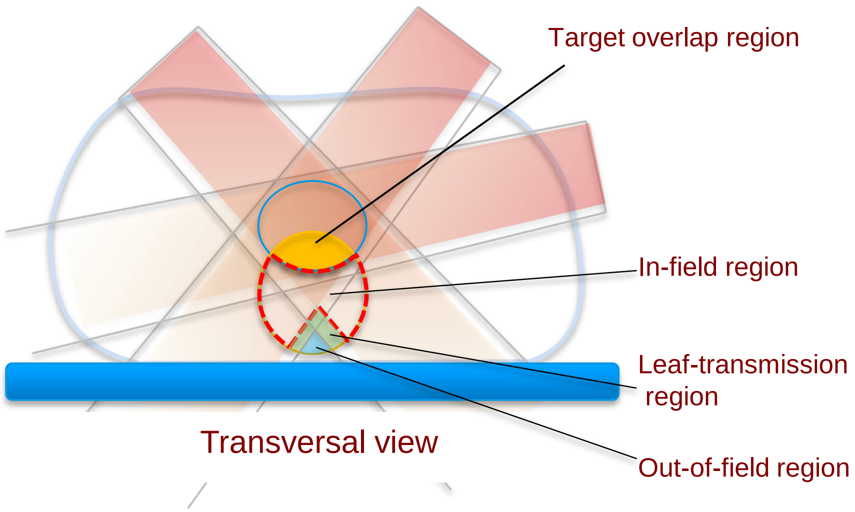
  Only scattered dose

- **In-field**

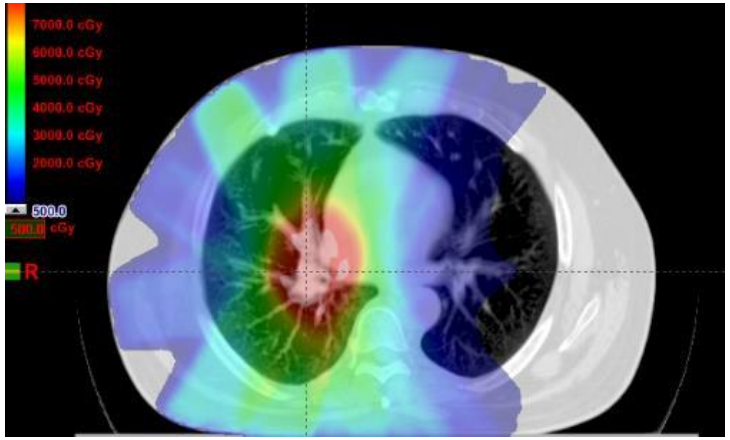
  Dose affected much by the optimization →regression model used

- **Target overlap**

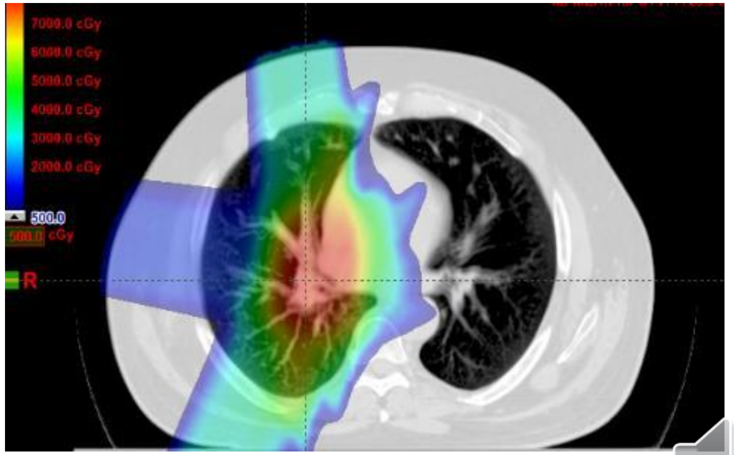
  Dose level comparable to target distribution



X-rays (IMRT)

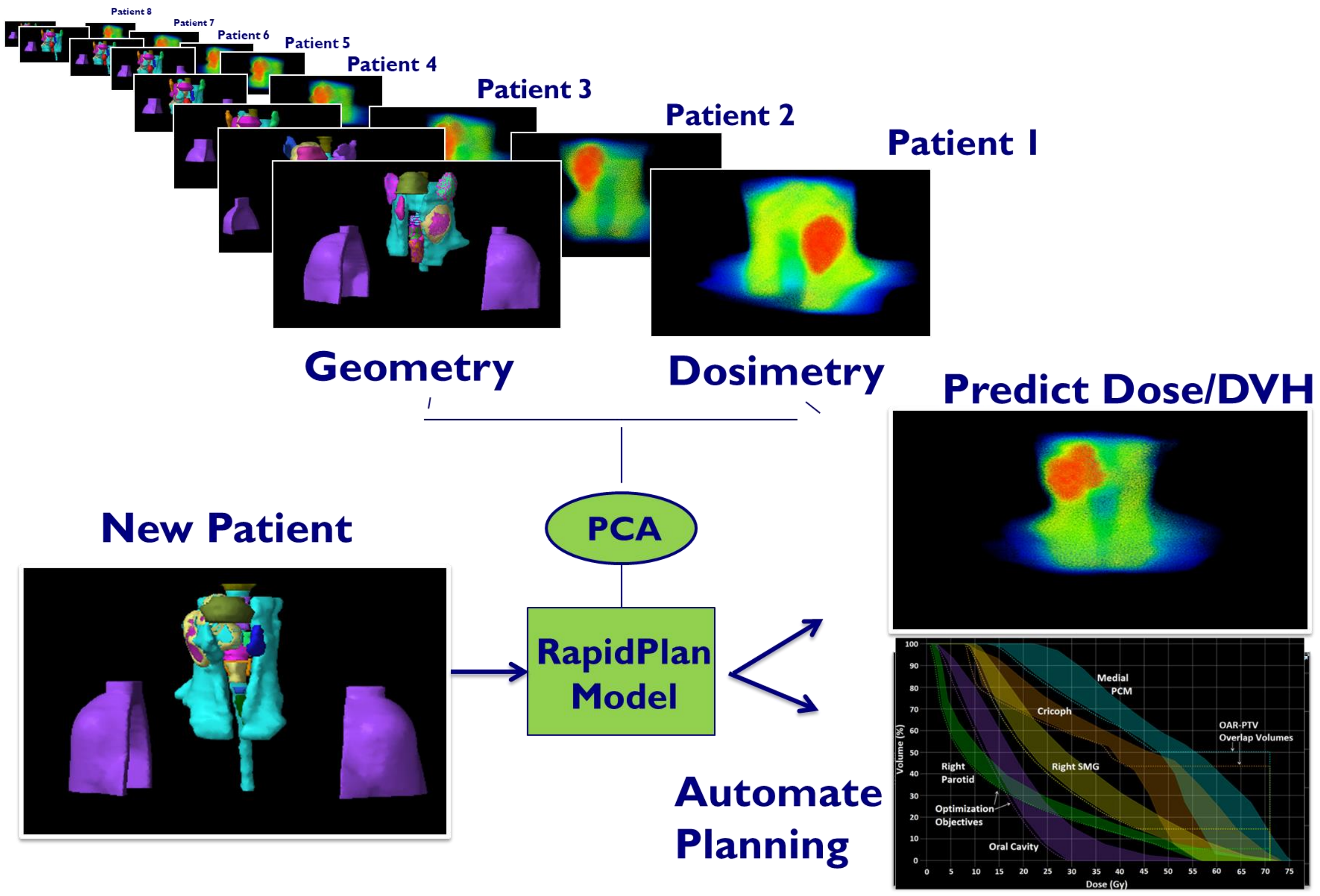


Protons



Knowledge-based Planning for Protons

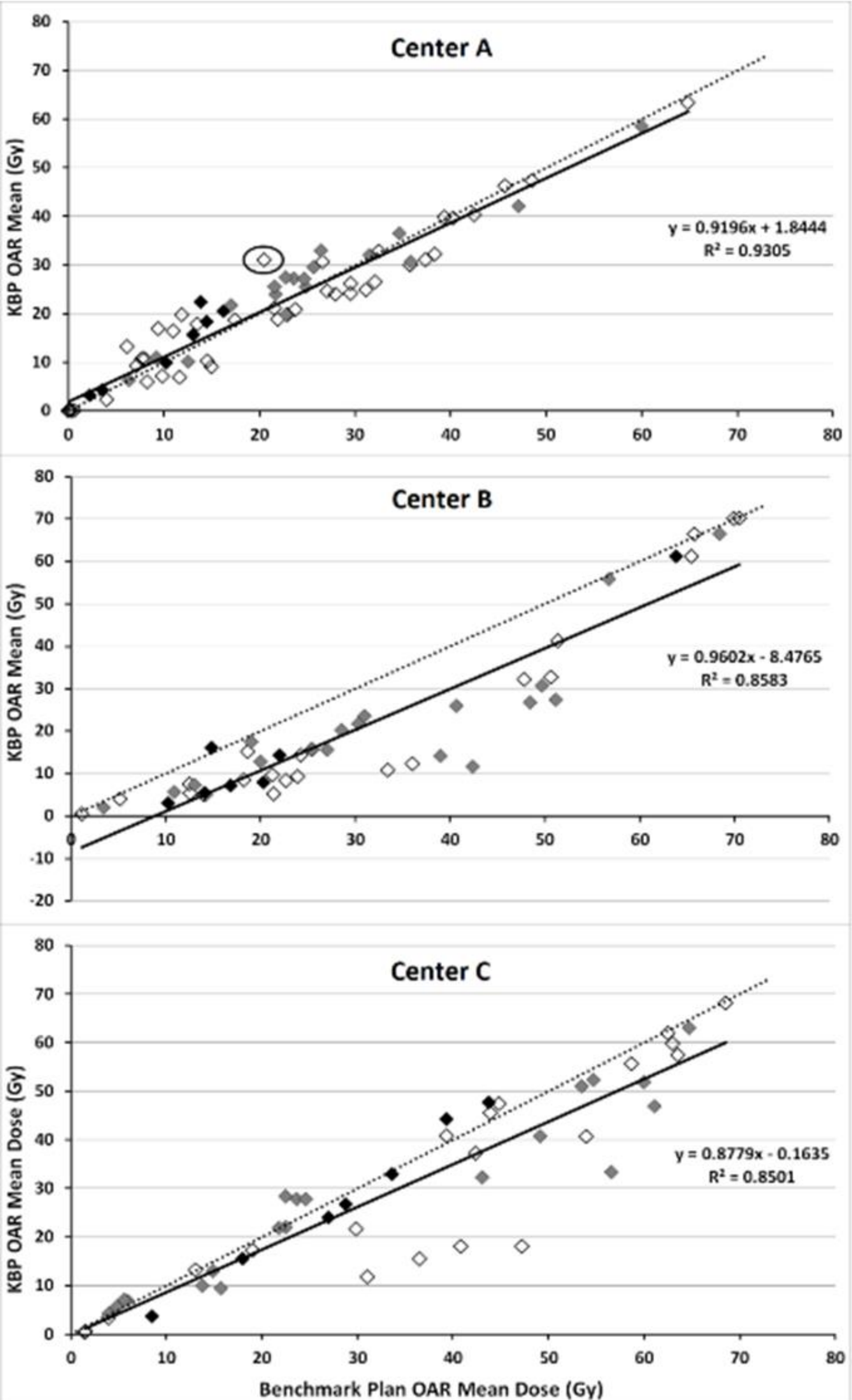
- Out-of-field: lateral of beams, no exiting dose beyond the range
- In-field: anything in the beam path *Different from photons
- Target and OAR overlap: the same as photon plans



AR Delaney et al. Cancers **2018**, 10, 420

Results

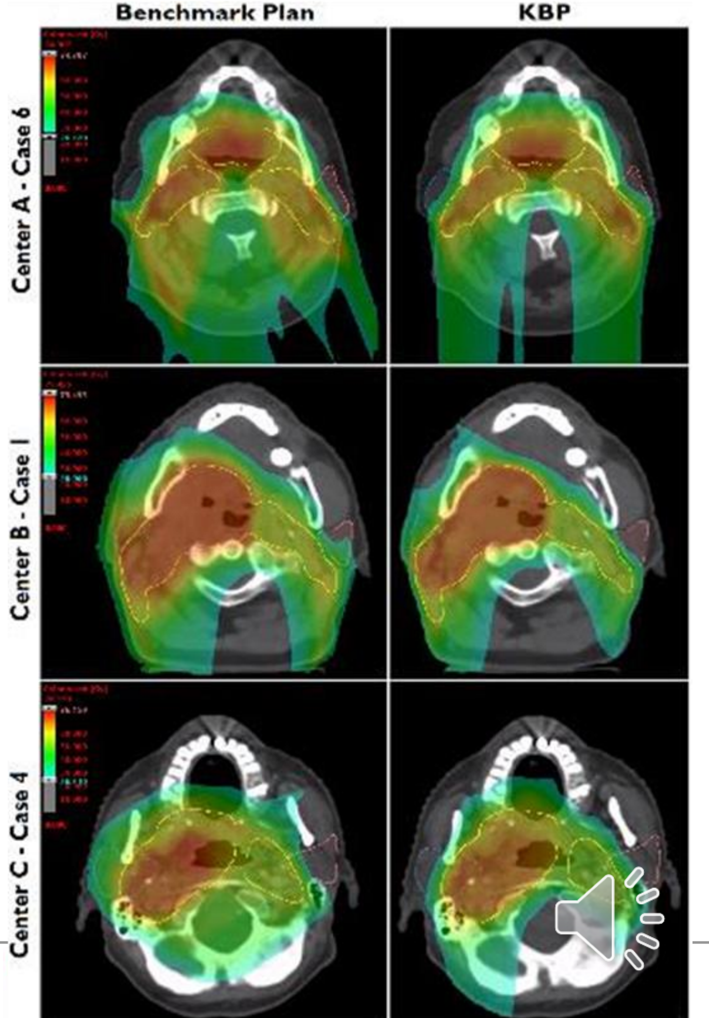
- **VUmc RP model**
  - Cancer Center Amsterdam
  - Library of 50 IMPT plans (VUmc)
  - 21 RP plans, standard “Y” beam arrangement
- **Testing: HNC IMPT, 3 centers, 7plans/center**
  - Own optimized beam arrangements



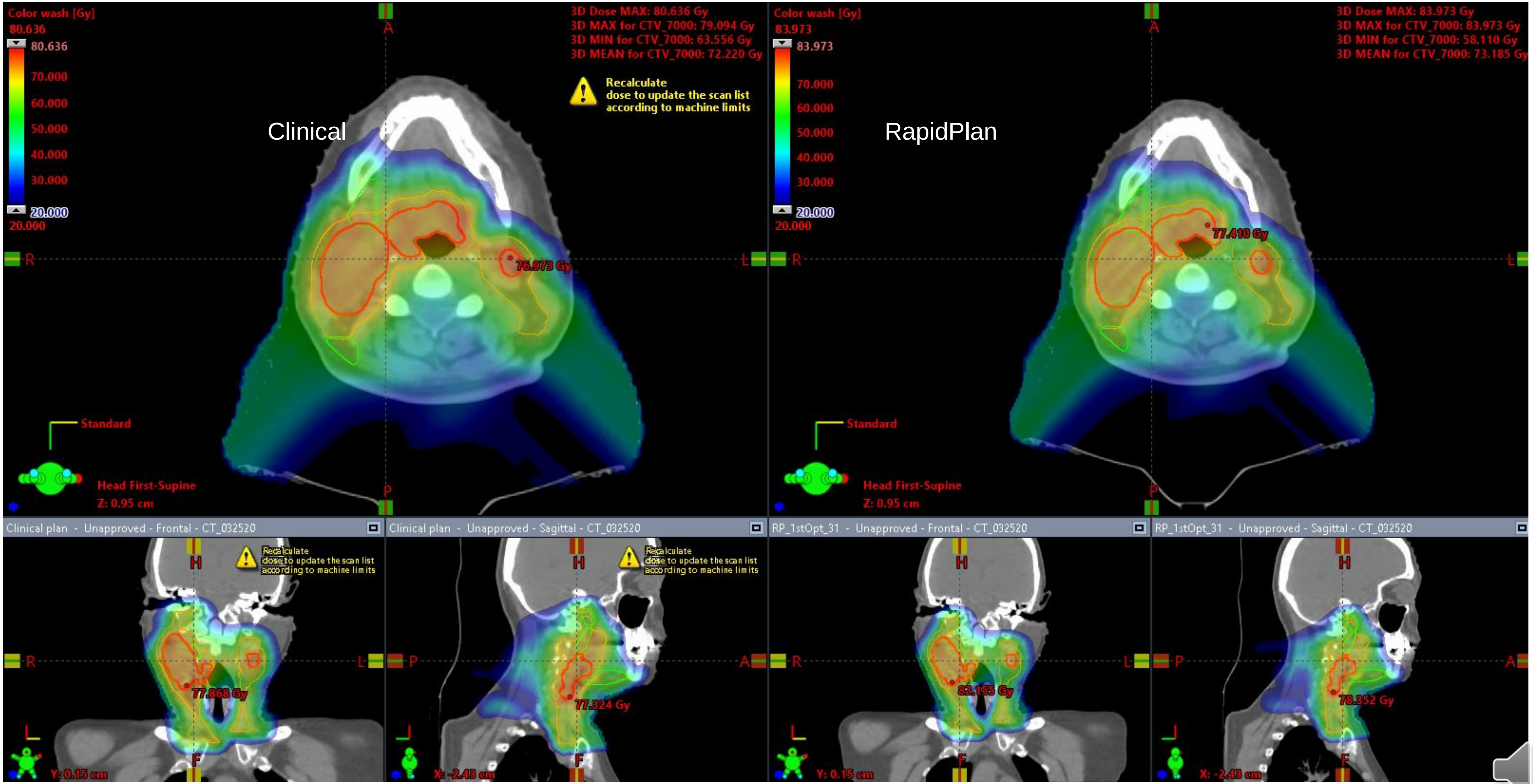
Grey: salivary glands

Black: oral cavity

White: all other parallel OAR

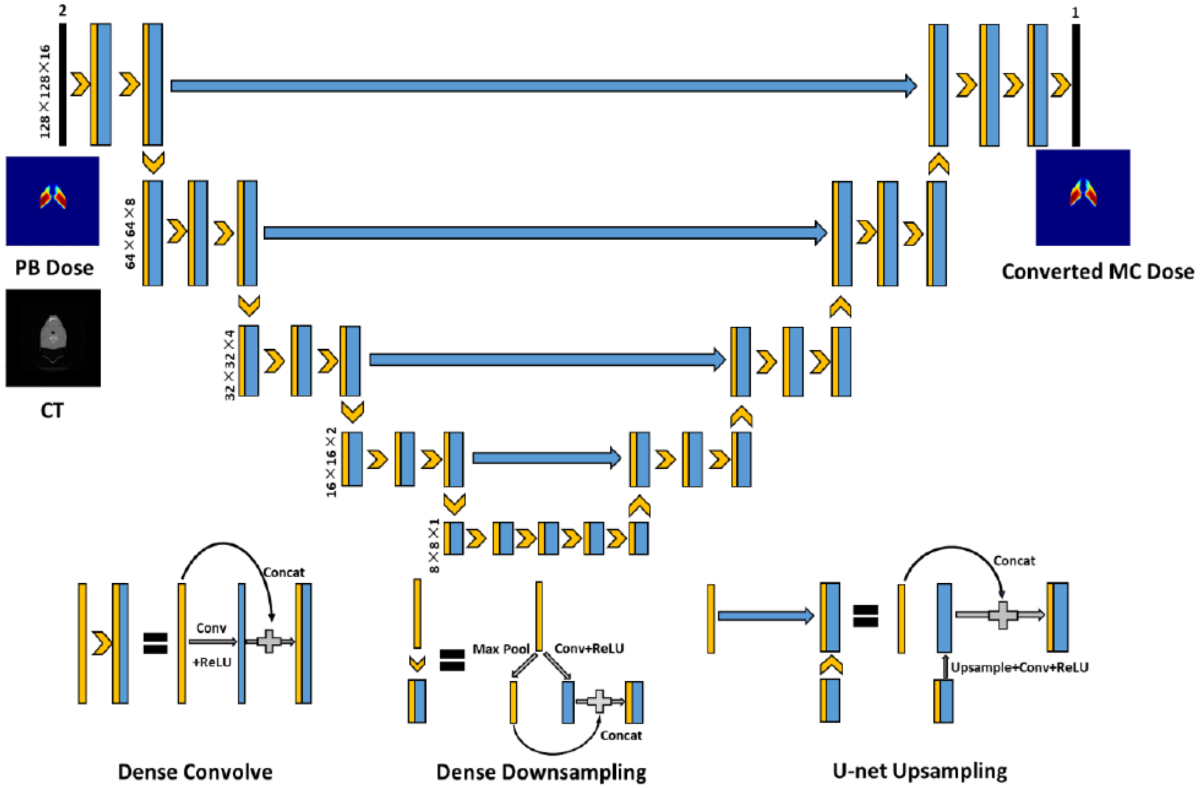


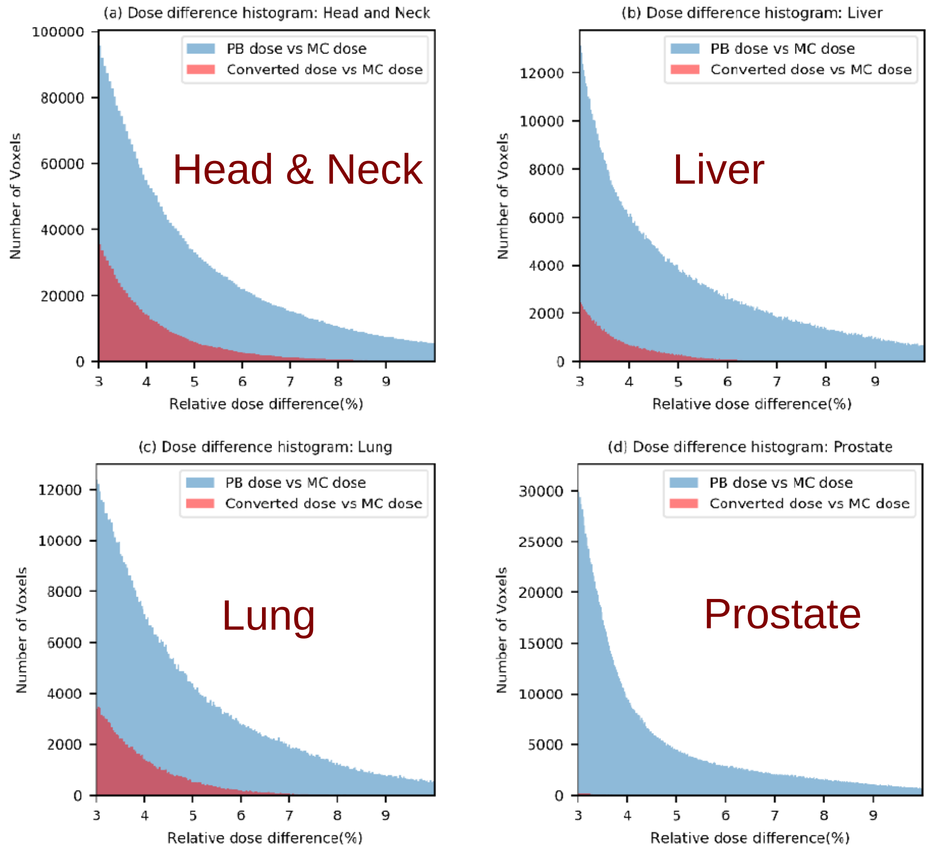
Clinical Plan vs. Varian Proton RapidPlan™



Converting Proton PB Dose Calc to Monte Carlo Dose Calc

- Wu, Chao, et al. "Improving Proton Dose Calculation Accuracy by Using Deep Learning." *arXiv preprint arXiv:2004.02924* (2020).
- Goal: to improve dose calculation accuracy in inhomogeneous geometry
- Method: Hierarchically Densely connected U-net deep learning architecture (Nguyen D, 2019)





Summary - Where is the future of AI in Proton Therapy?

Standardization

Validation

Patient Selection
- Why PT?
- Expected improvement?
- Comparison to other treatment modalities?

Simulation
- Target delineation
- Auto-segmentation

Treatment Planning & QA
- HU-to-SPR Conversion (CT/DECT)
- Dose Calculation
- Auto-Planning
- 2nd MU Calc
- Plan Check
- Patient QA

Adaptive RT
- Change Prediction
- Anatomy changes
- Range changes
- Dosimetric changes
- On-line planning
- HU-to-SPR Conversion (CBCT)
- Plan QA
- Patient QA

Outcome Studies
- Survival
- Toxicities
- Combination Therapies
- Comparative Studies
- Radiomics

Data