Physicist's perspective on 4D proton therapy

Delft 2021

Protons stop in tissue

But where?

And at what time?

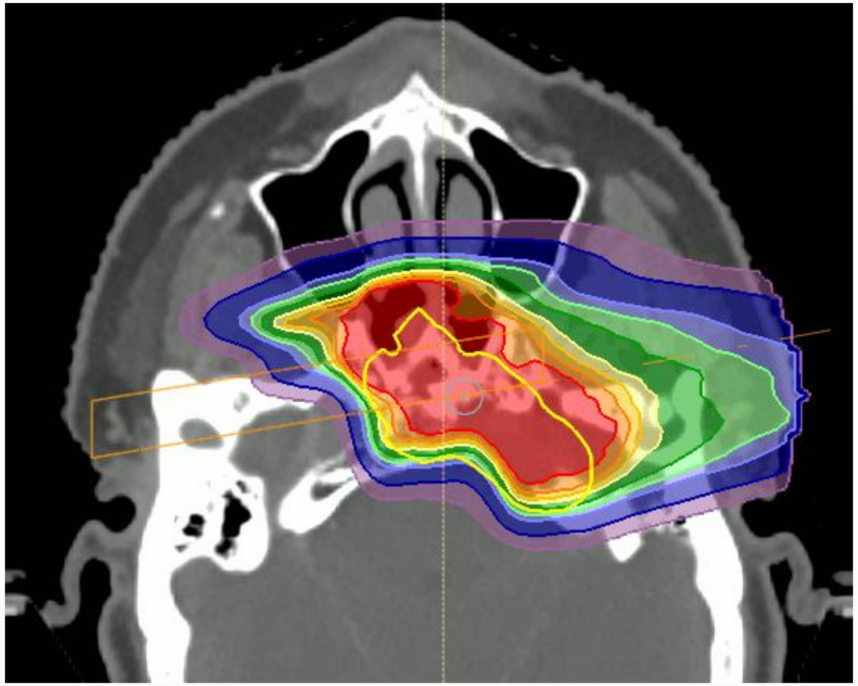
It’s All About Physics (But Where)

electron density

$$S = -\frac{dE}{dx} = \frac{4\pi}{m_e c^2} \cdot \frac{nz^2}{\beta^2} \cdot \left(\frac{e^2}{4\pi\varepsilon_0}\right)^2 \cdot$$

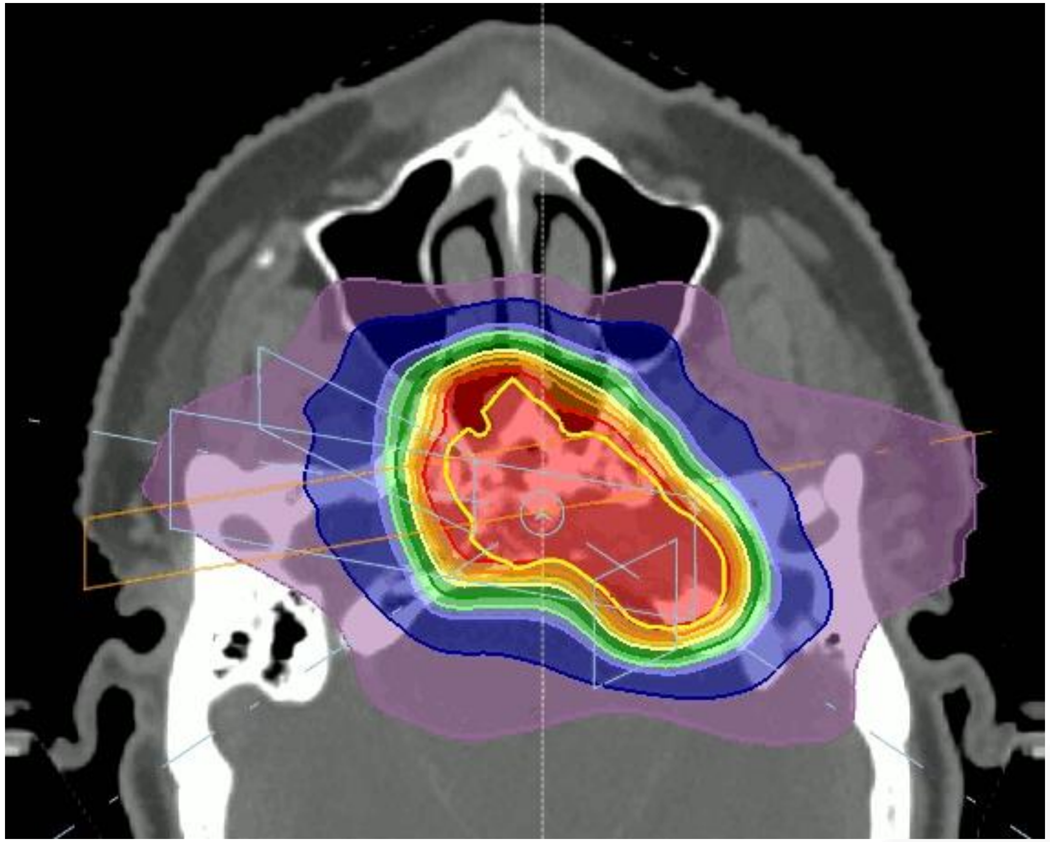
v/c of protons

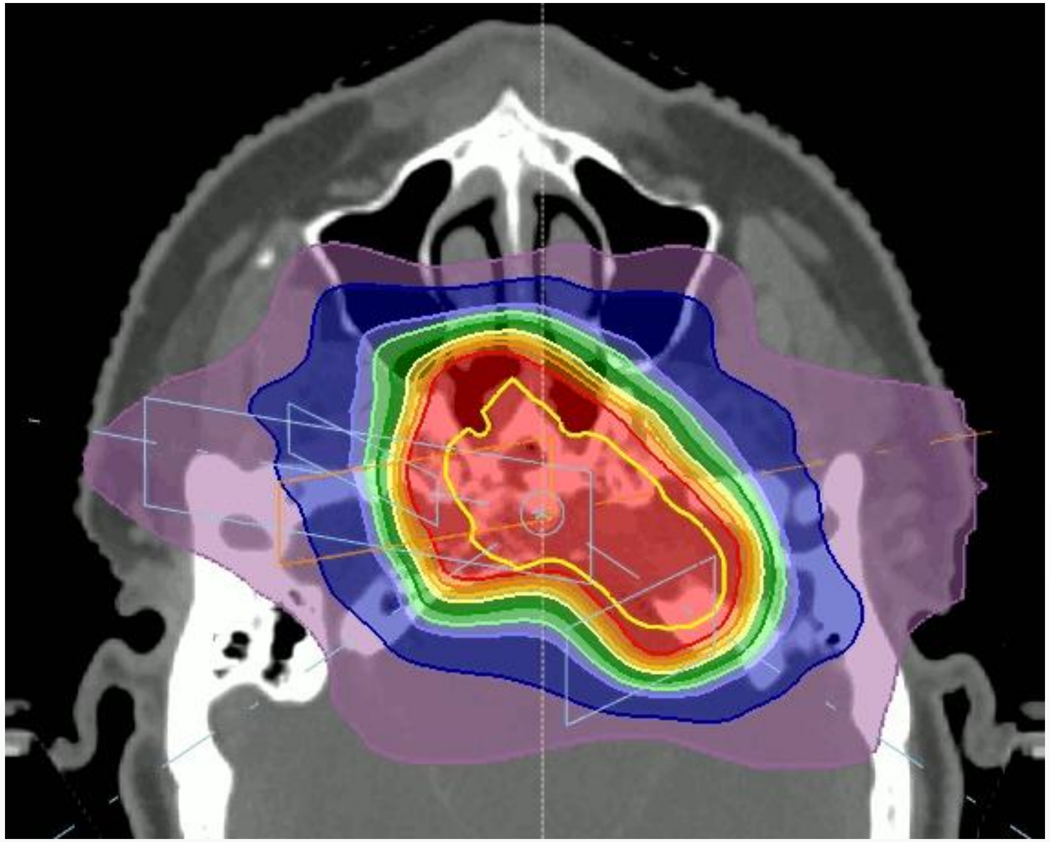
energy loss



Non-robust

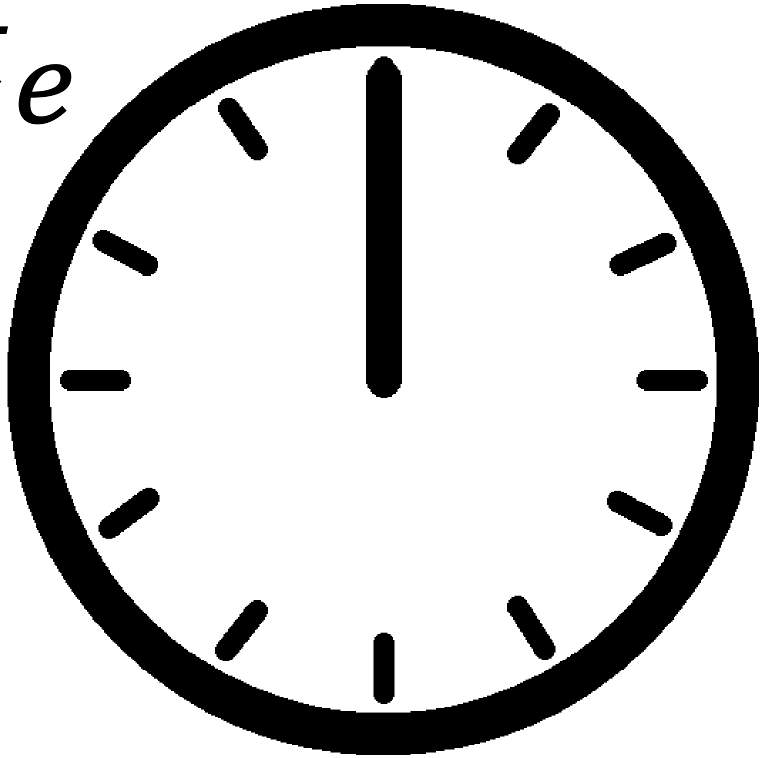
Robust





What About Time?

$$T_x(t) = \int_{t=0}^{t=t_e}$$

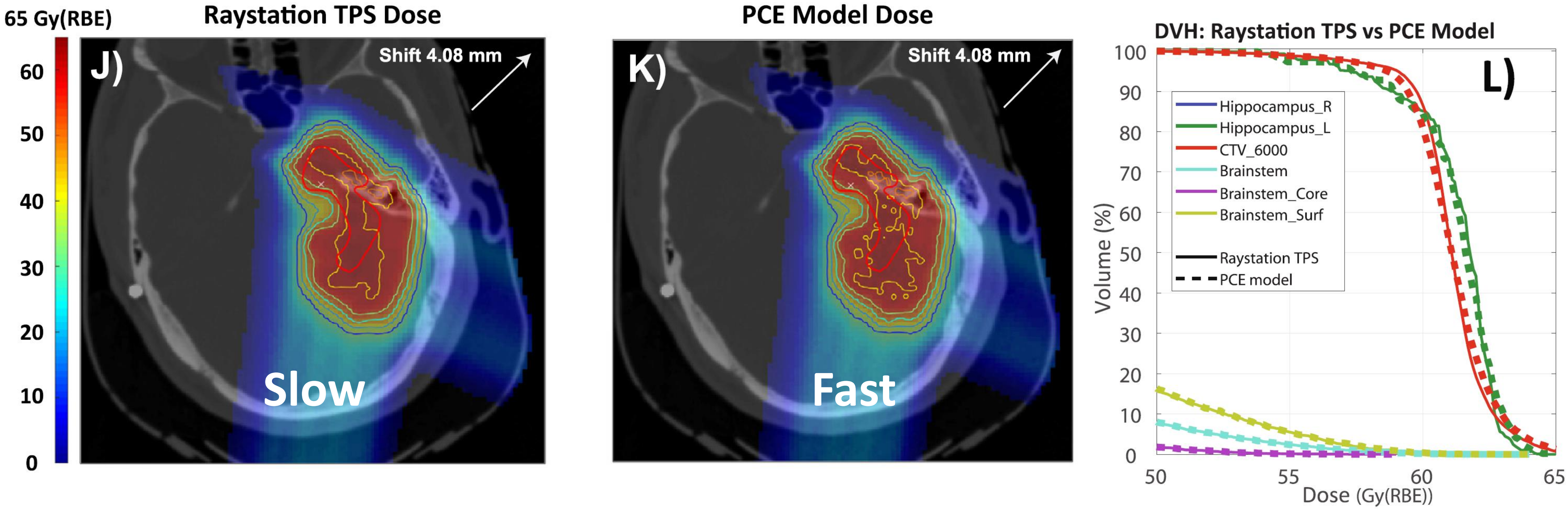


$$dt = \langle T_x \rangle$$

Zoltan Perko

Jesús Rojo-Santiago

Fast Uncertainty Analysis



Rojo-Santiago J, Habraken SJM, Lathouwers D, Méndez Romero A, Perkó Z, Hoogeman MS. Accurate assessment of a Dutch practical robustness evaluation protocol in clinical PT with pencil beam scanning for neurological tumors. Radiother Oncol. 2021 Aug 2;163:121-127.

Expected Dose for Population is Adequate

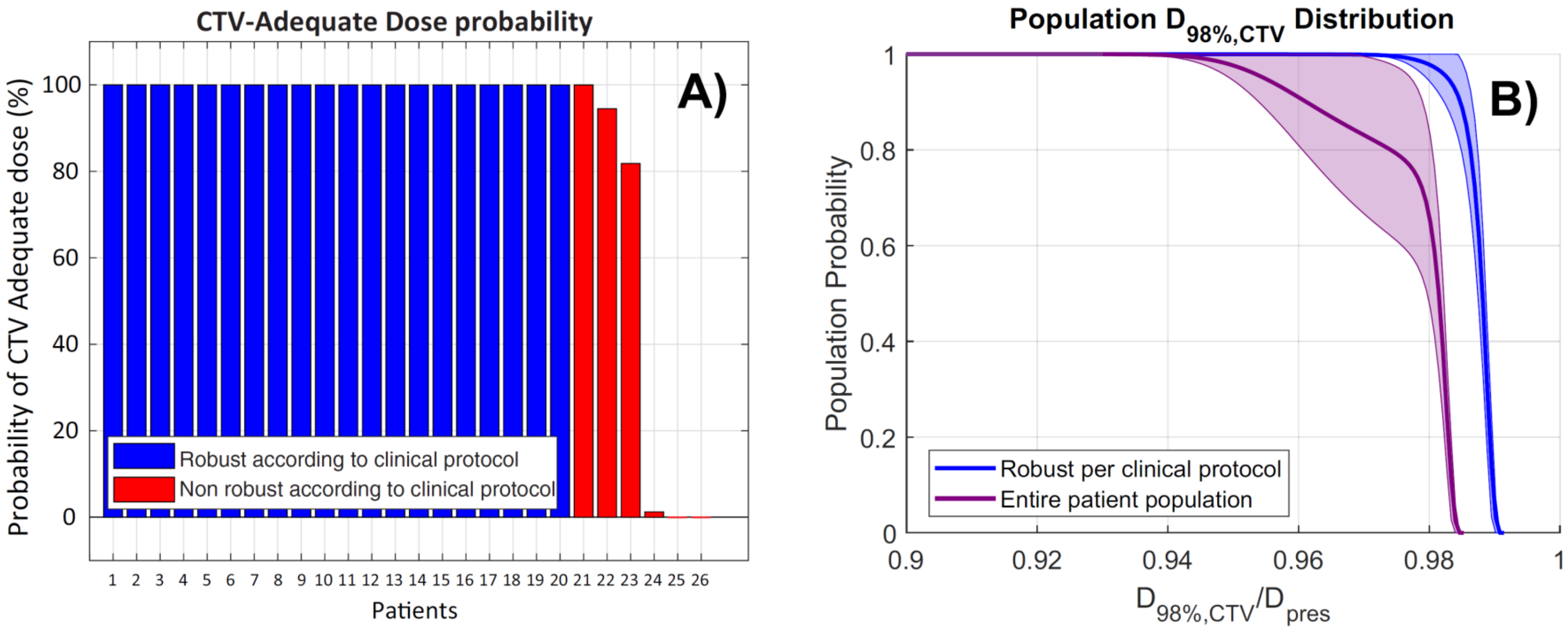
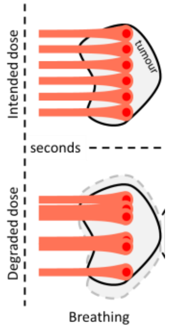
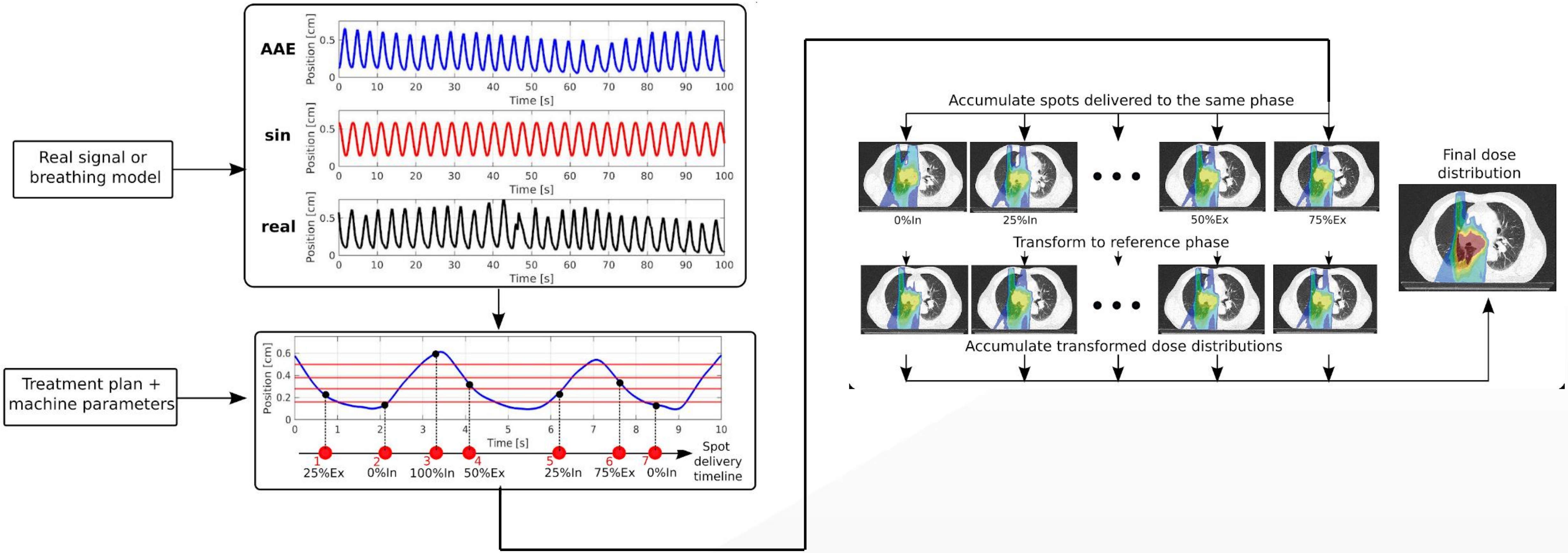


Fig. 3. PCE-based robustness evaluation results. (A) PCE probability of adequate target dose to clinically robust (red) and non-robust (blue) plans. (B) PCE population D

Rojo-Santiago J, Habraken SJM, Lathouwers D, Méndez Romero A, Perkó Z, Hoogeman MS. Accurate assessment of a Dutch practical robustness evaluation protocol in clinical PT with pencil beam scanning for neurological tumors. Radiother Oncol. 2021 Aug 2;163:121-127.

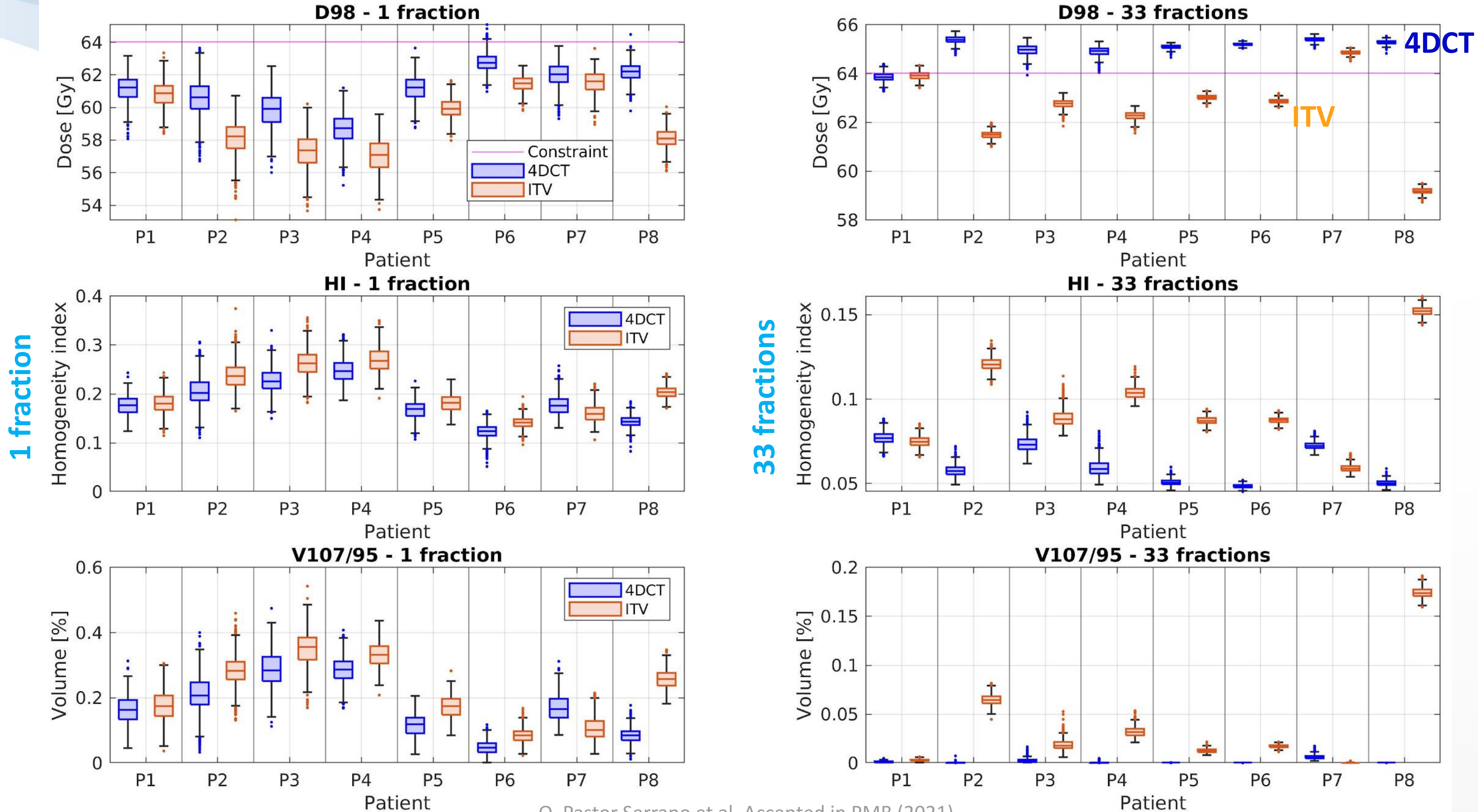


Oscar Pastor Serrano



O. Pastor Serrano et al. accepted PMB (2021) and Pastor-Serrano, O., Lathouwers, D., & Perkó, Z. (2021). A semi-supervised autoencoder framework for joint generation and classification of breathing. Computer Methods and Programs in Biomedicine, 209, 106312

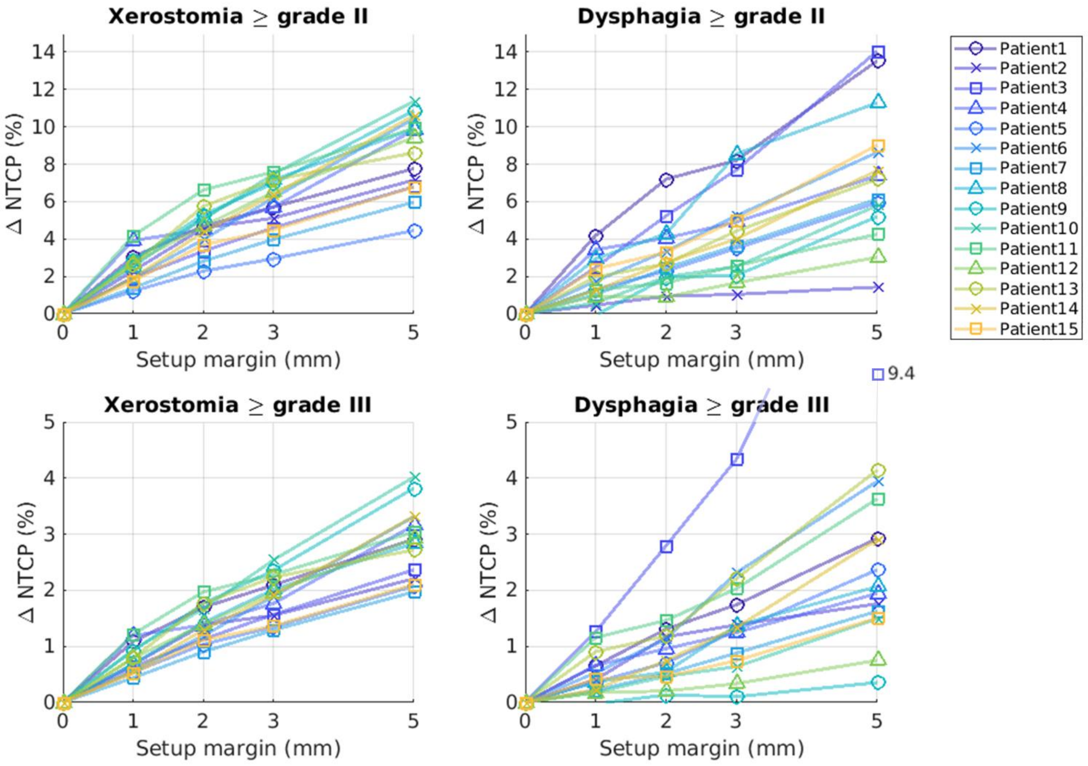
HollandPTC Proton Therapy Centre · TU Delft · Erasmus MC · LUMC Leiden University Medical Center



O. Pastor Serrano et al. Accepted in PMB (2021)

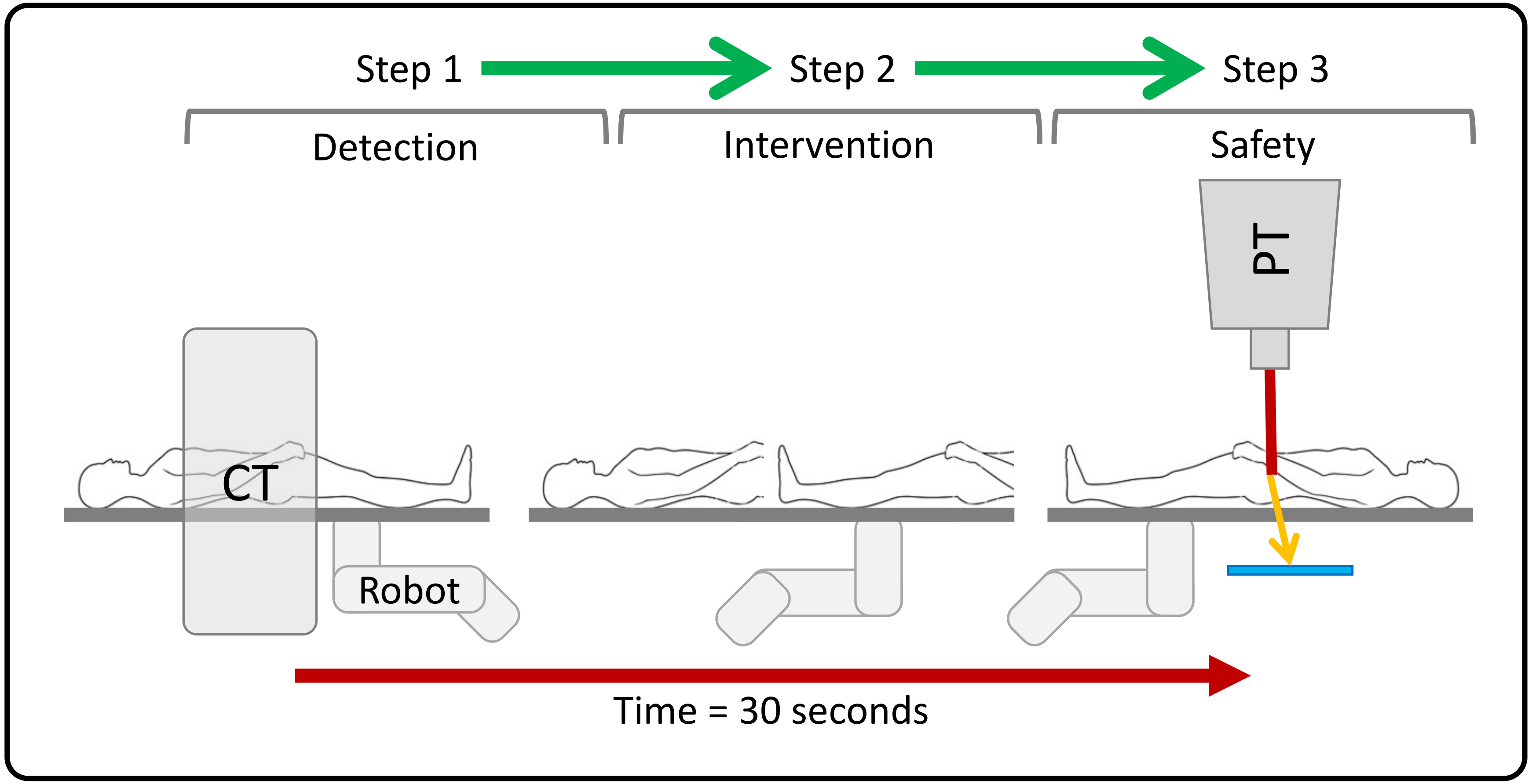
Michelle Oud

NTCP Increases With Increasing SR



M. Oud et al.; van de Water S, van Dam I, Schaart DR, Al-Mamgani A, Heijmen BJ, Hoogeman MS. The price of robustness; impact of worst-case optimization on organ-at-risk dose and complication probability in intensity-modulated proton therapy for oropharyngeal cancer patients. Radiother Oncol. 2016 Jul;120(1):56-62.

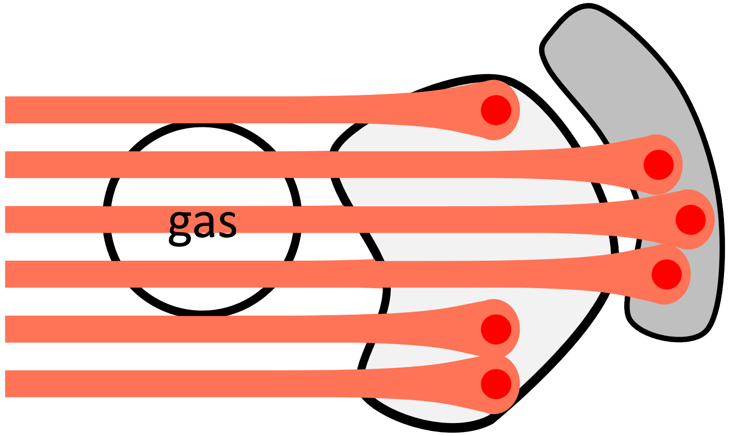
Online Adaptive Proton Therapy

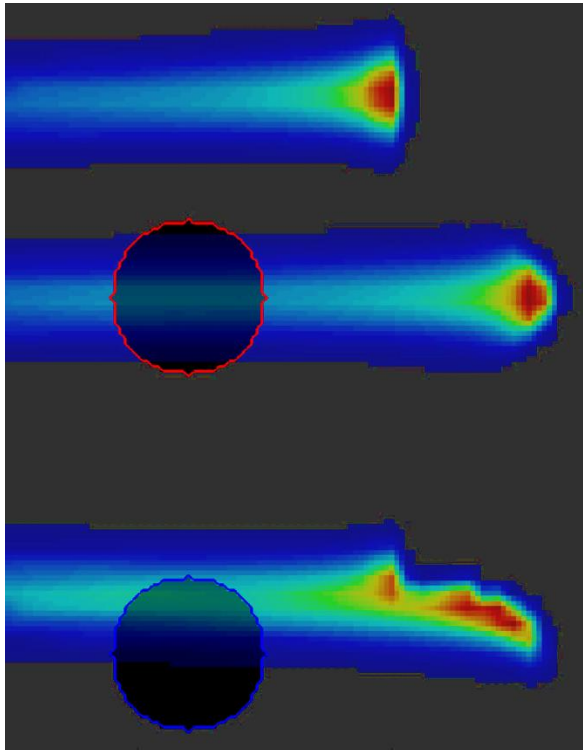


Phys Med Biol. 2018 Jul 2;63(13):135017. Phys Med Biol. 2017 Jun 7;62(11):4254-4272.

Dose Restoration to Account for Density Changes


Thyrza Jagt





Jagt et al. Phys Med Biol. 2017 Jun 7;62(11):4254-4272.

Straightforward Spot Weight Optimization

Voxel-wise minimization of the difference between the actual dose and the planned dose

structure weight

$$s(\boldsymbol{f}) = \left(A\boldsymbol{f} - \boldsymbol{d}^{int}\right)^T W\left(A\boldsymbol{f} - \boldsymbol{d}^{int}\right) + \kappa S$$

planned dose

smoothing term

spot weights

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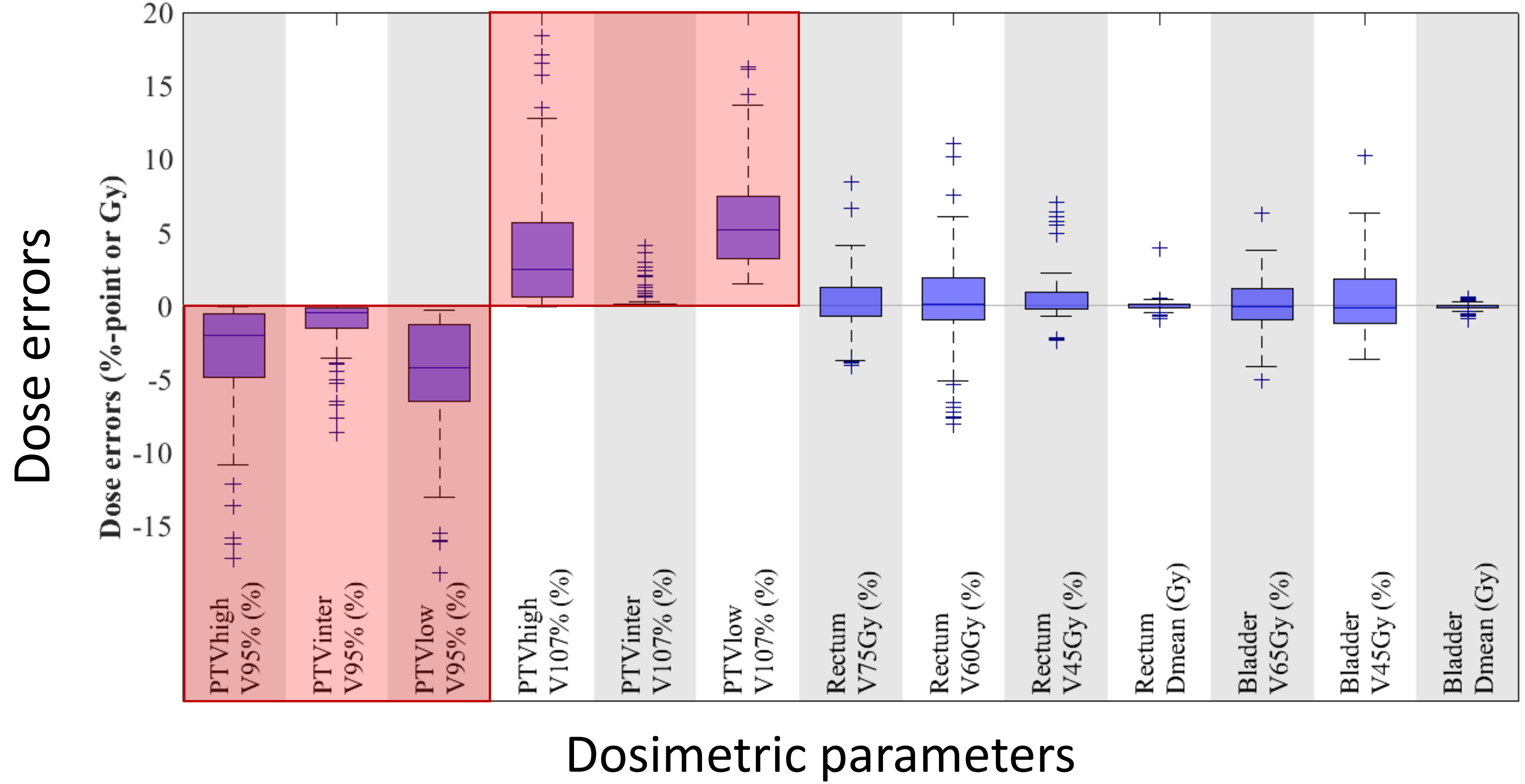
If we do nothing ...

Daily dose – Planned dose



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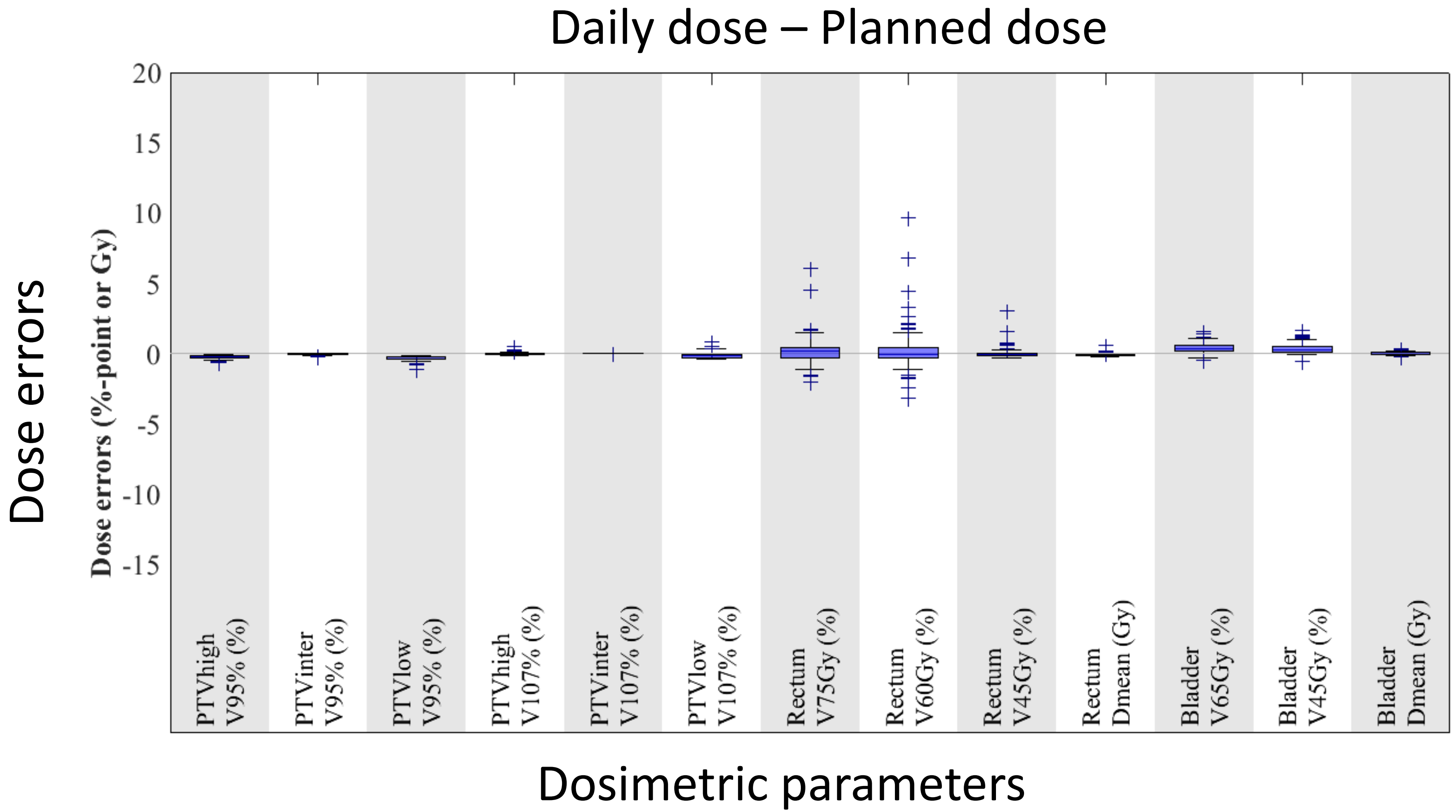
Jagt et al. Phys Med Biol. 2017 Jun 7;62(11):4254-4272.

Or restore the dose ... in 8 seconds



Jagt et al. Phys Med Biol. 2017 Jun 7;62(11):4254-4272.

Pros and Cons of Dose Restoration

Restoration is performed on planning contours (no re-contouring needed)

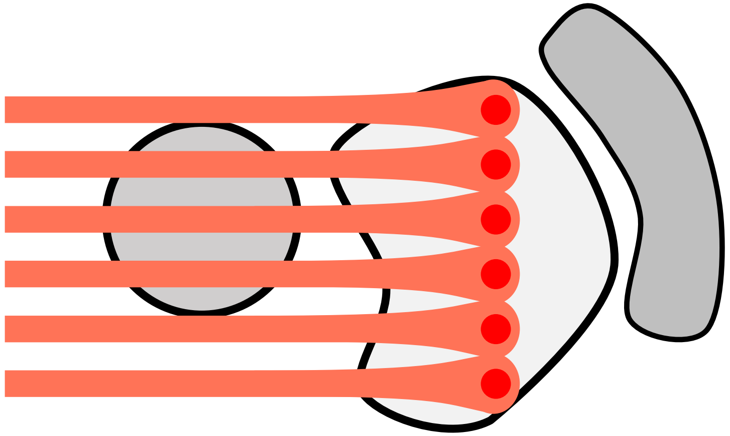
Does not account for changes in shape of target volumes and organs at risk

Restoration still uses an internal margin for organ motion

Illustratie: Fiep Westendorp uit Otje

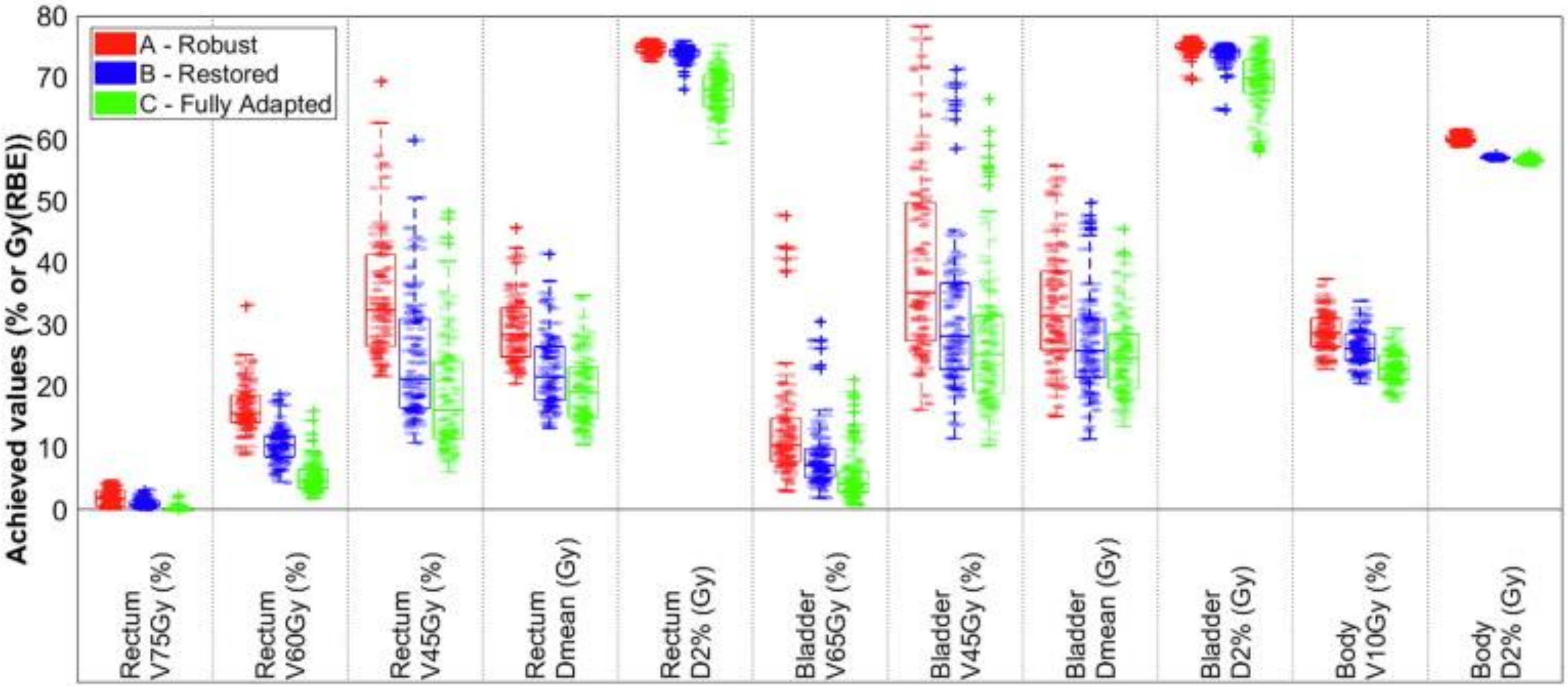
RPM Online-Adaptive Method

Prior plan (input)	Spot-location restoration	Addition of new spots	RPM Spot weight optimization	RPM output (1-2x)
	7.3 seconds	0.6 minutes	1.1 minutes	



Compared To Robust Optimization

100% success rate



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Jagt TZ, et al. Online-adaptive versus robust IMPT for prostate cancer: How much can we gain? Radiother Oncol. 2020 Aug 7;151:228-233. doi: 10.1016/j.radonc.2020.07.054.

Online Adaptive For Pancreatic Ca.

Alba Magallon Barro

Online strategies to adapt treatment plans

Unrestricted automated re-planning

93% success rate

Time-restricted automated re-planning

90% success rate

Impact of using uncorrected CT-based auto-contours

OAR constraints violations were restored in

56-64% success rate

Replanning resulted in better OAR sparing

84-95% success rate

Magallon-Baro A, Milder MTW, Granton PV, Nuyttens JJ, Hoogeman MS. Comparison of Daily Online Plan Adaptation Strategies for a Cohort of Pancreatic Cancer Patients Treated with SBRT. Int J Radiat Oncol Biol Phys. 2021 Sep 1;111(1):208-219.

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Food For Thought

If fully automated, can we just switch on online adaptive radiotherapy if this gives better results for a fraction of the patients?

What is the gain or value that we need to add to execute automated online adaptive workflows?

What will be the role of the human observer?

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Image from Wikipedia

Plan Library


Michelle Oud

Online re-planning puts a high demand on the clinical workflow

Alternatively, you could use a pre-treatment established plan library from which pick the winner of the day

Plan library consists of treatment plans with increasing set-robustness (1, 2, 3, 4, or 5 mm)

Can a plan library reduce NTCP while maintaining adequate target coverage?

=> Tested in-silico including various sources of uncertainty

Target Coverage

Adherence to clinical target constraints

0 mm – 4.0%

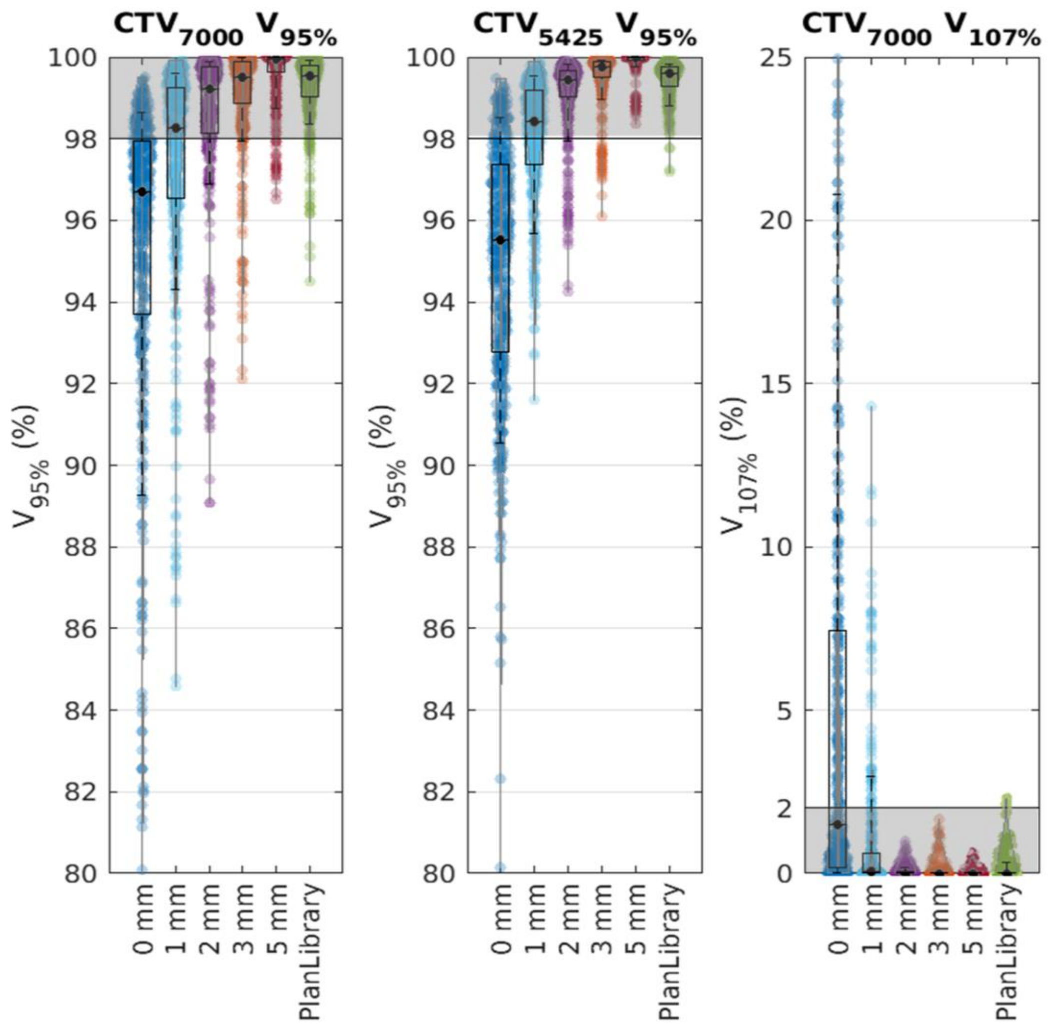
1 mm – 41.3%

2 mm – 69.6%

3 mm – 82.1%

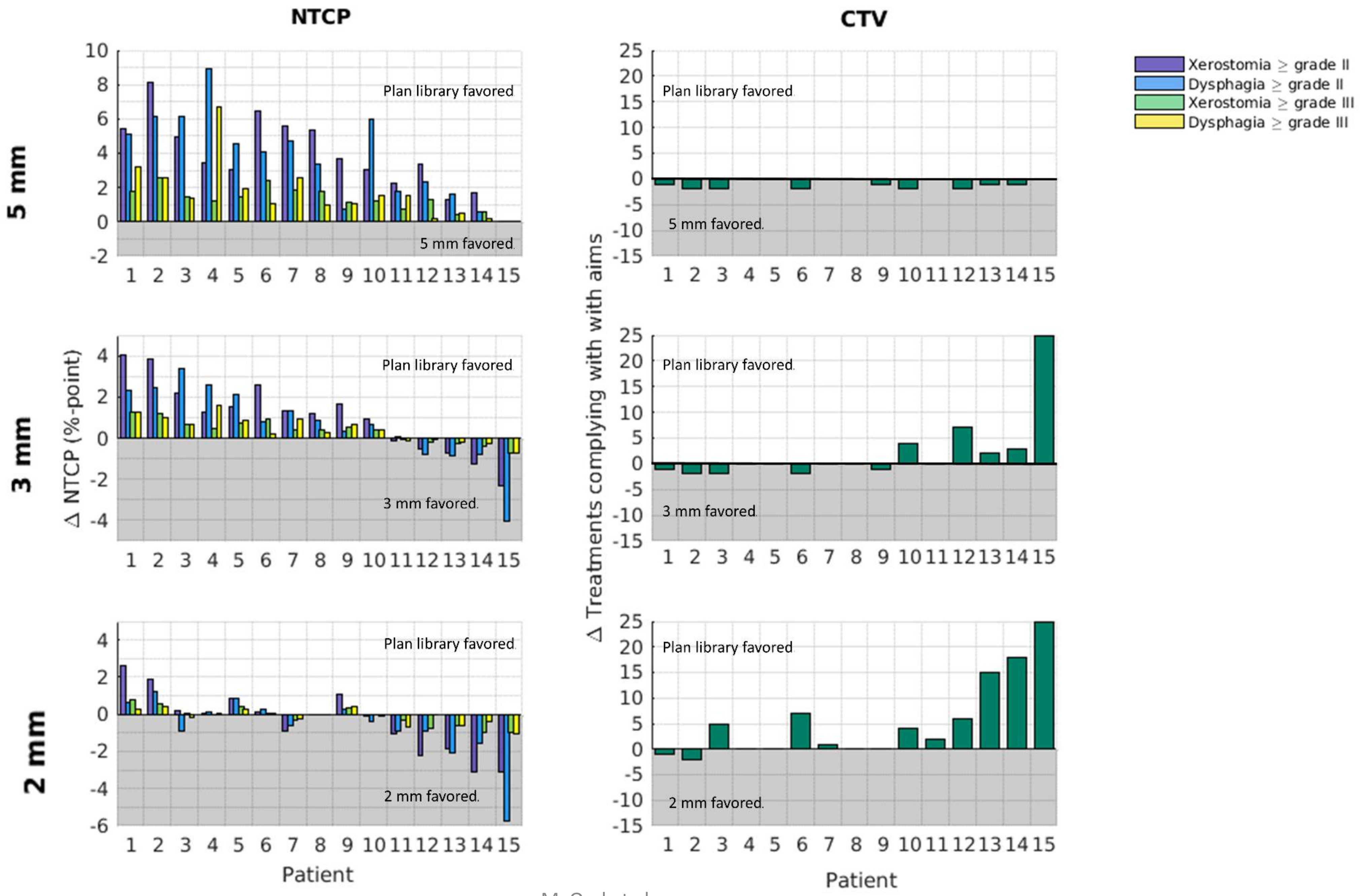
5 mm – 94.7%

Plan library – 91.7%



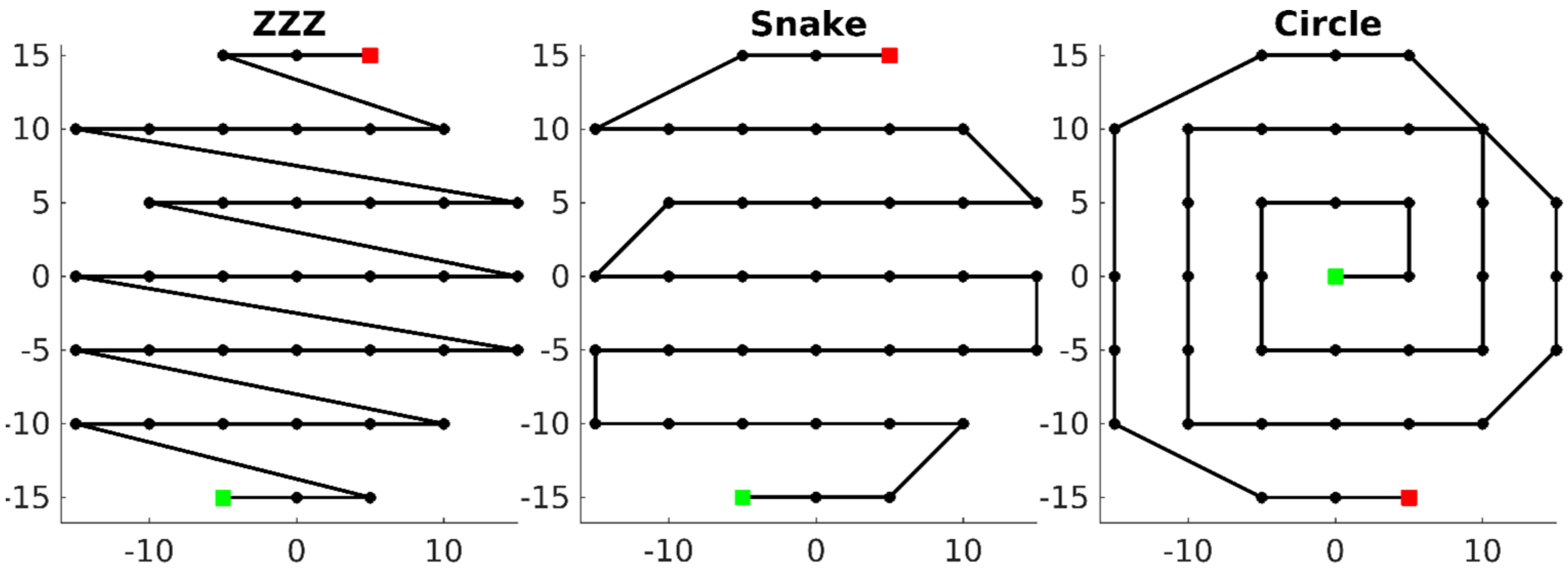
M. Oud et al.

NTCP & Coverage



M. Oud et al.

Which Scan Pattern Is The FLASHiest?



Rodrigo Jose
Santo

TÉCNICO LISBOA

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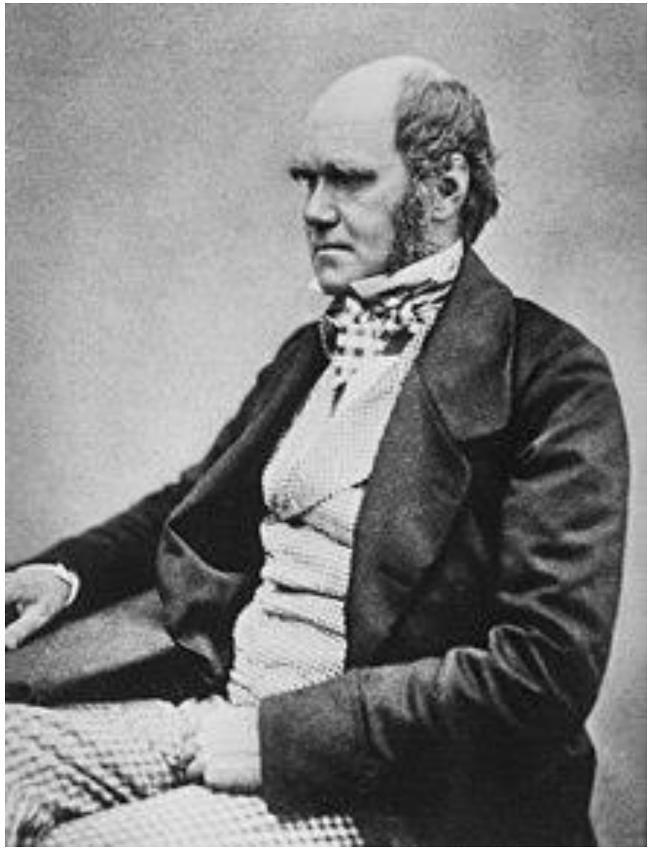
Genetic Algorithm

A genetic algorithm is a search optimization inspired by Charles Darwin's theory of natural evolution

It uses natural selection where the fittest individuals (scan patterns) are selected for reproduction in order to produce offspring of the next generation

Fitness is defined by FLASH coverage

FLASH coverage should increase with evolving generations



Wikipedia

Fitness Function

Directly optimize FLASH coverage

Percentage of tissue outside target volume

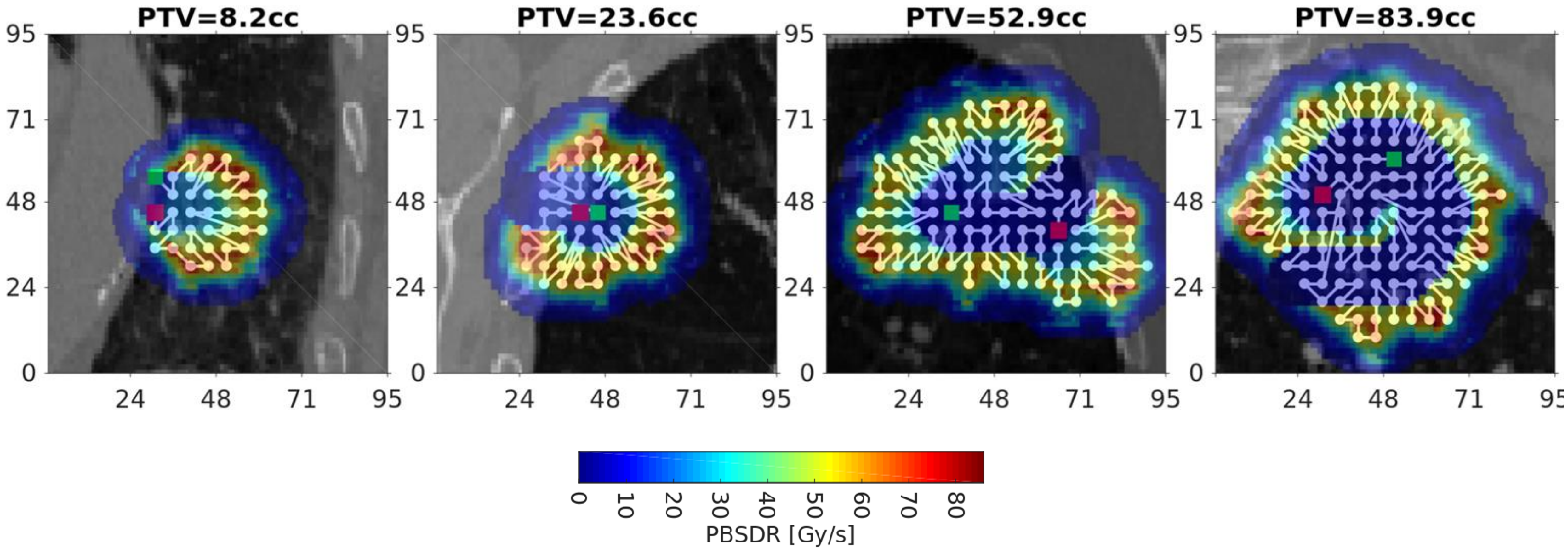
Having a dose higher than dose threshold (8 Gy)

Also has a dose rate higher than dose rate threshold (40 Gy/s)

Only scan pattern is optimized

No dose optimization is performed → no trade-off → only gains

FLASH Optimized Patterns



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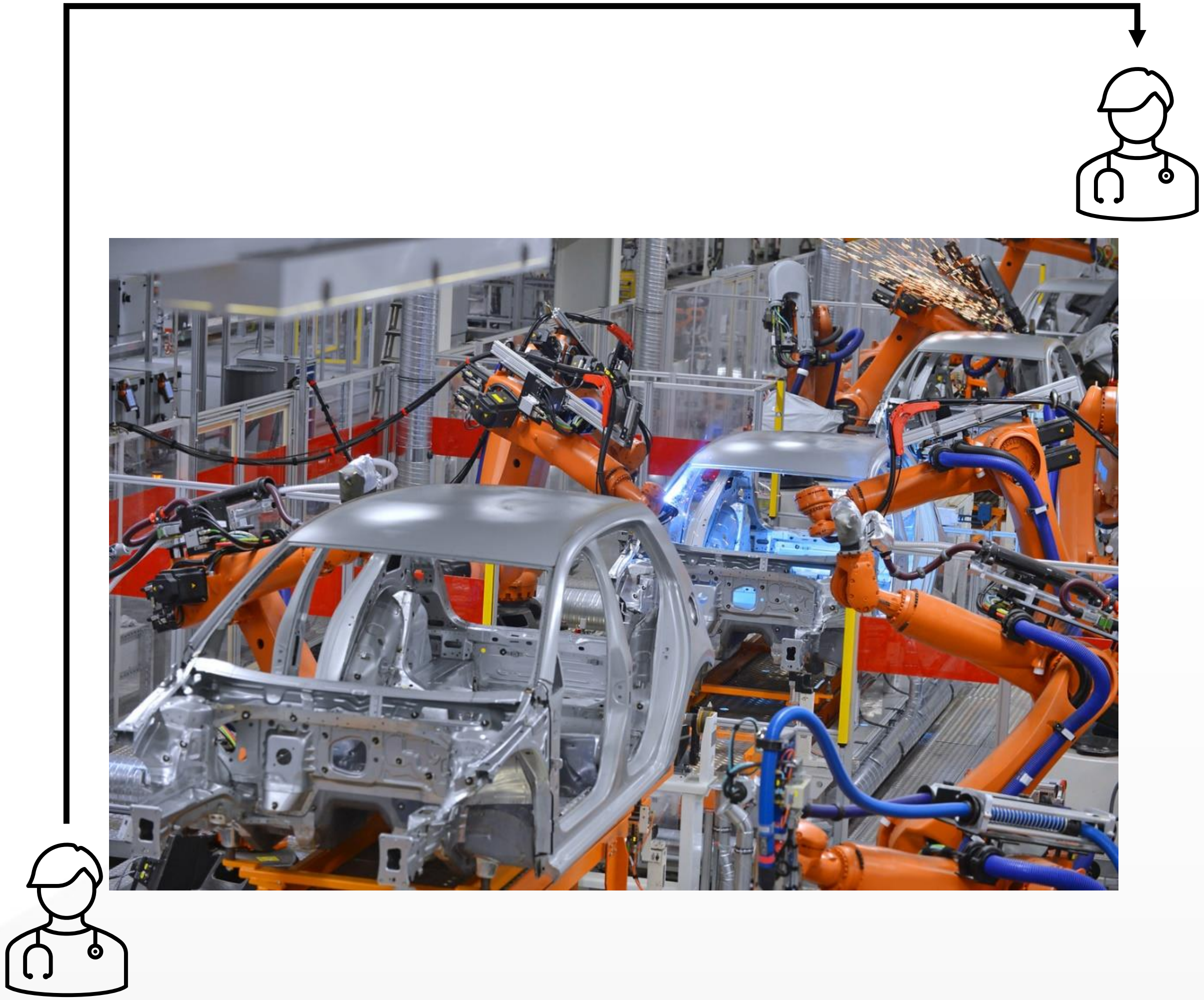
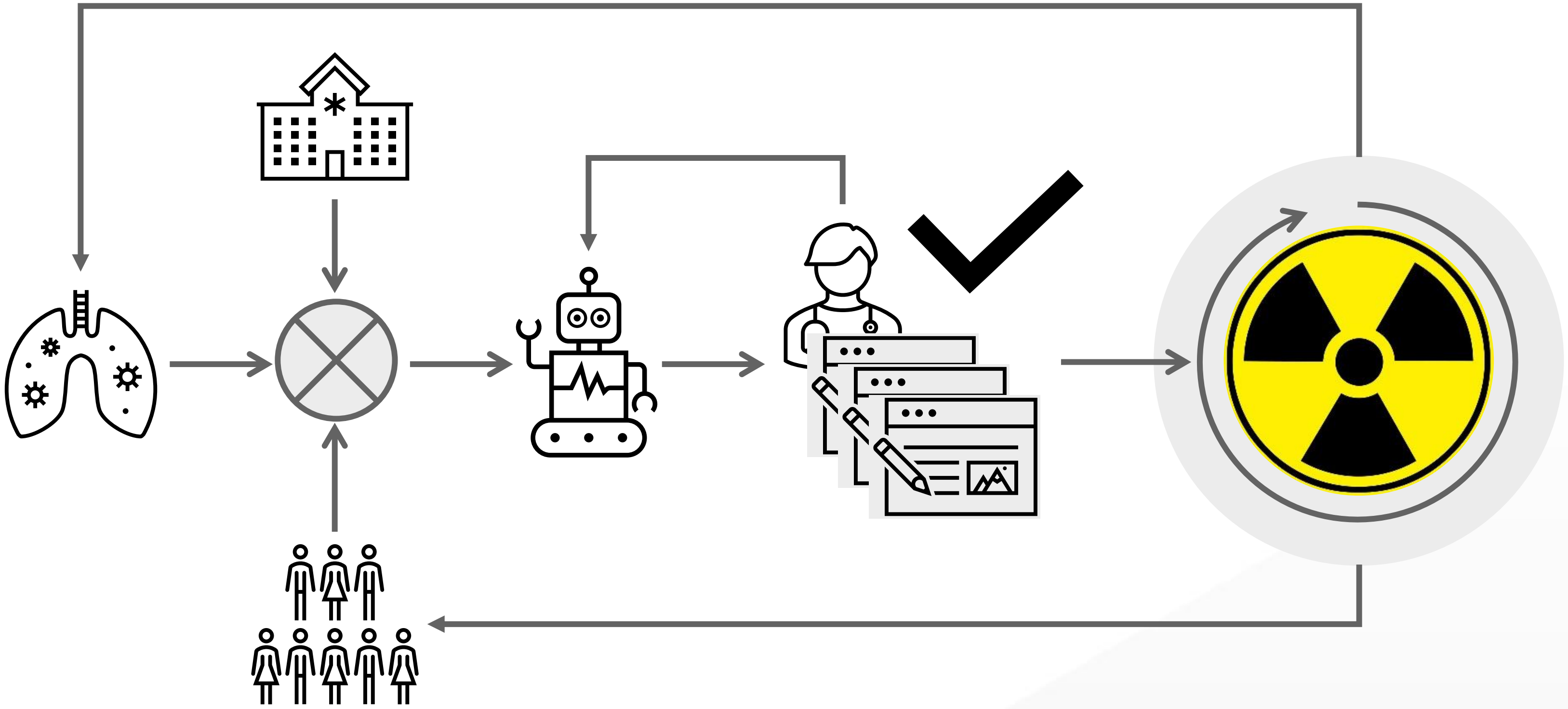
0:10

Time Inversion



Where Do We Want To Go?



Improve decision making

Increase personalization

Have a closed loop automated system

Dramatically shorten overall preparation time

Conclusions

In conventional radiotherapy we try to get rid of time

In online adaptive radiotherapy we try to follow the time

In FLASH we need to be on time

And from a workflow perspective we need to deliver the right information at the right time

Acknowledgements

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Alba Magallon Baro

Michelle Oud

Marta Gizynska

Steven Habraken

… and many others