Radiotherapy Research at the Cutting Edge: What's Next?

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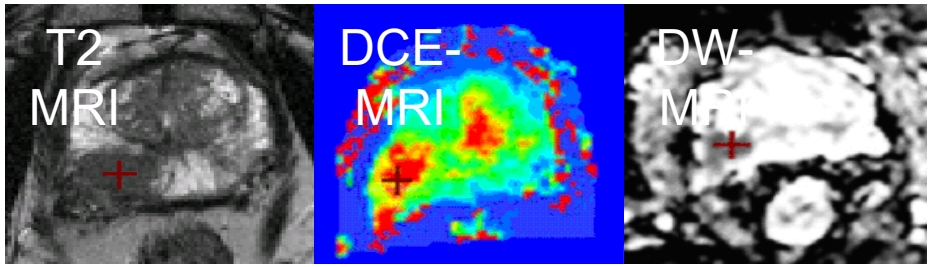
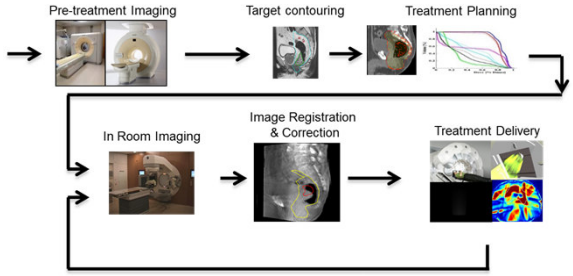
Trends in radiotherapy

- More precise
- More personalized
- More efficient





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Trends in radiotherapy

- More precise

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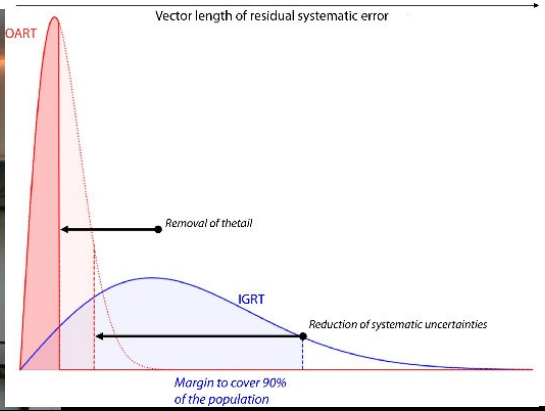
High precision radiotherapy

- Very high precision achieved with gating on MR-linac systems
- Delivery uncertainties become very small
- Outliers are avoided



Janssen et al. Int J Radiat Oncol Biol Phys, 122(3):554-557, 01 Jul 2025

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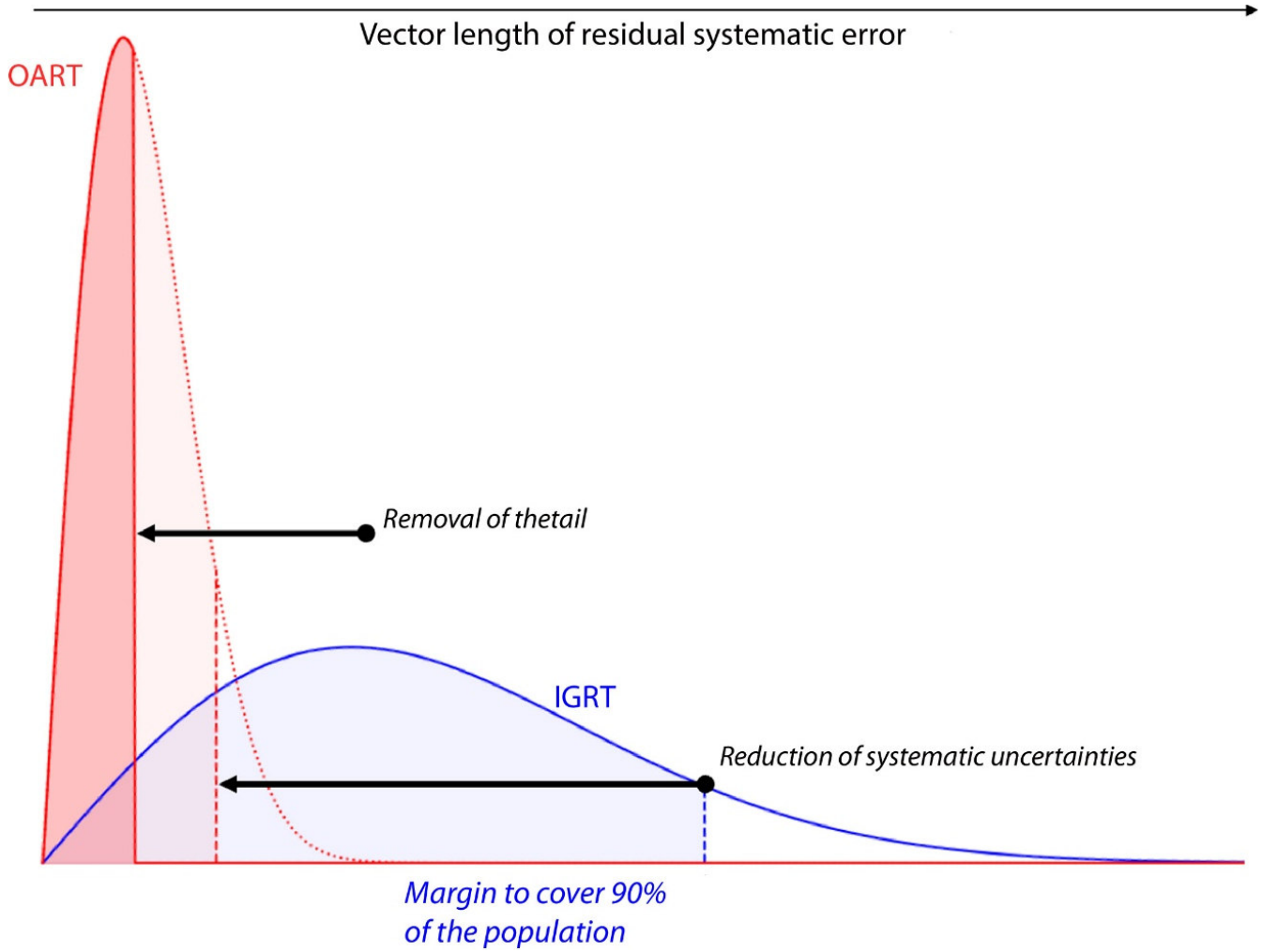
High precision

- Outliers are avoided
- **Do we really need PTV margins?**



Janssen et al. Int J Radiat Oncol Biol Phys, 122(3):554-557, 01 Jul 2025

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DESTINATION trials - Dose escalation to the MRI-visible GTV

ICR The Institute of Cancer Research

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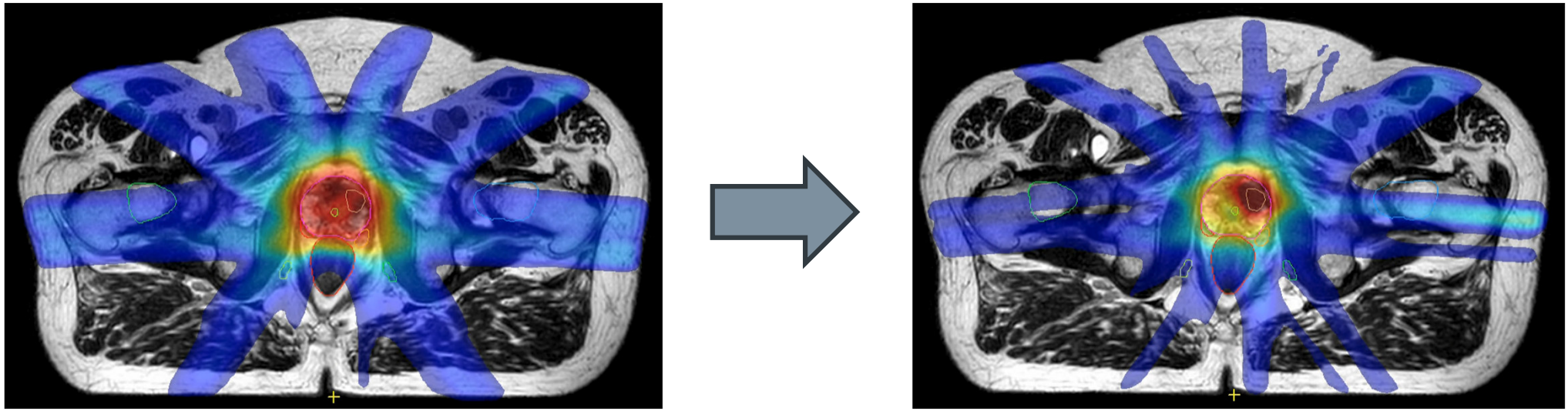
Sunnybrook HEALTH SCIENCES CENTRE



Reducing dose to the urethra, bladder and neurovascular tissue by:

- Dose de-escalation to the prostate
- No PTV margin

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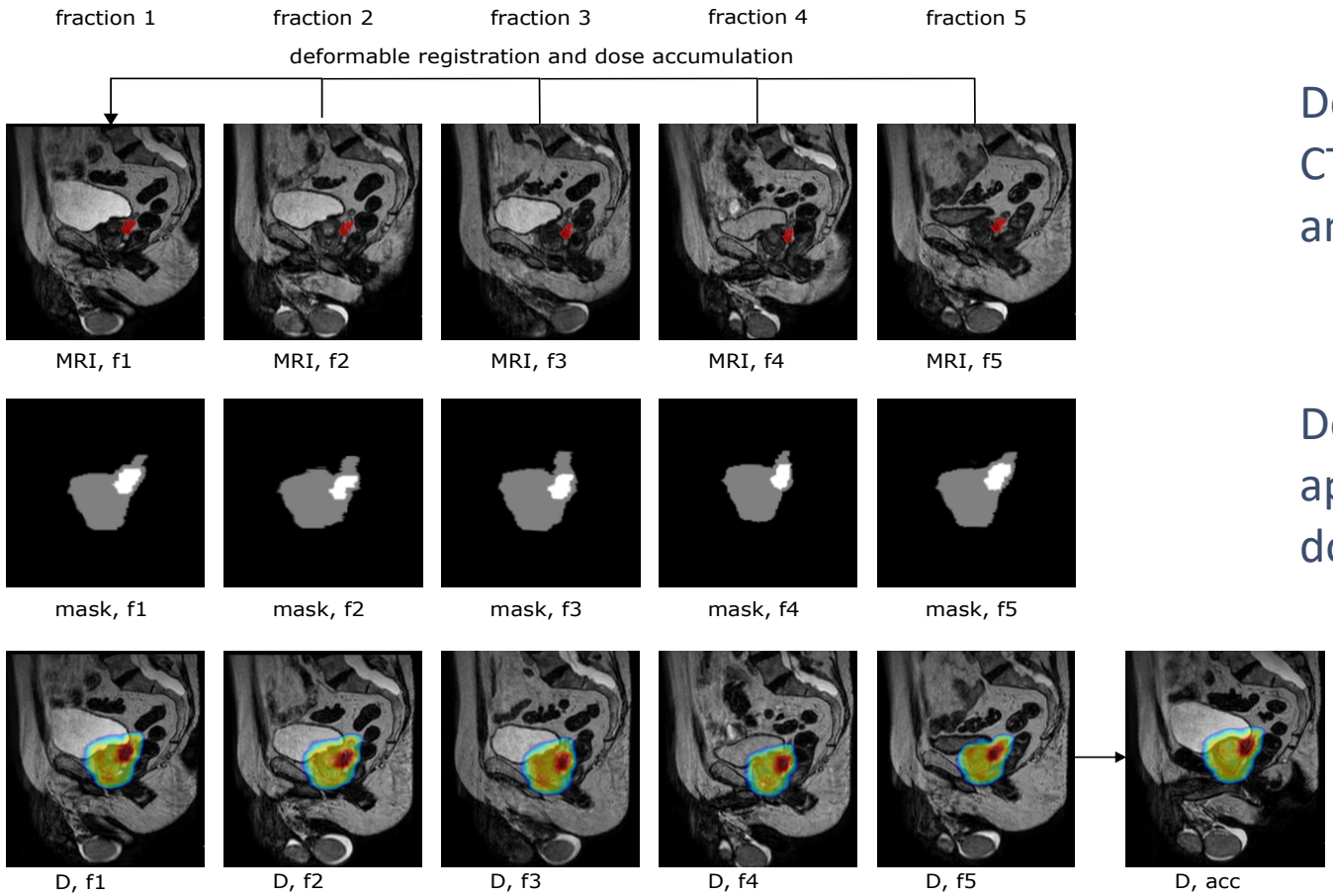
Dose accumulation pipeline



Deformable registration of the CTV of fraction 2-5 to match the anatomy of the CTV of fraction 1

Deformation vector fields were applied to their corresponding dose distribution

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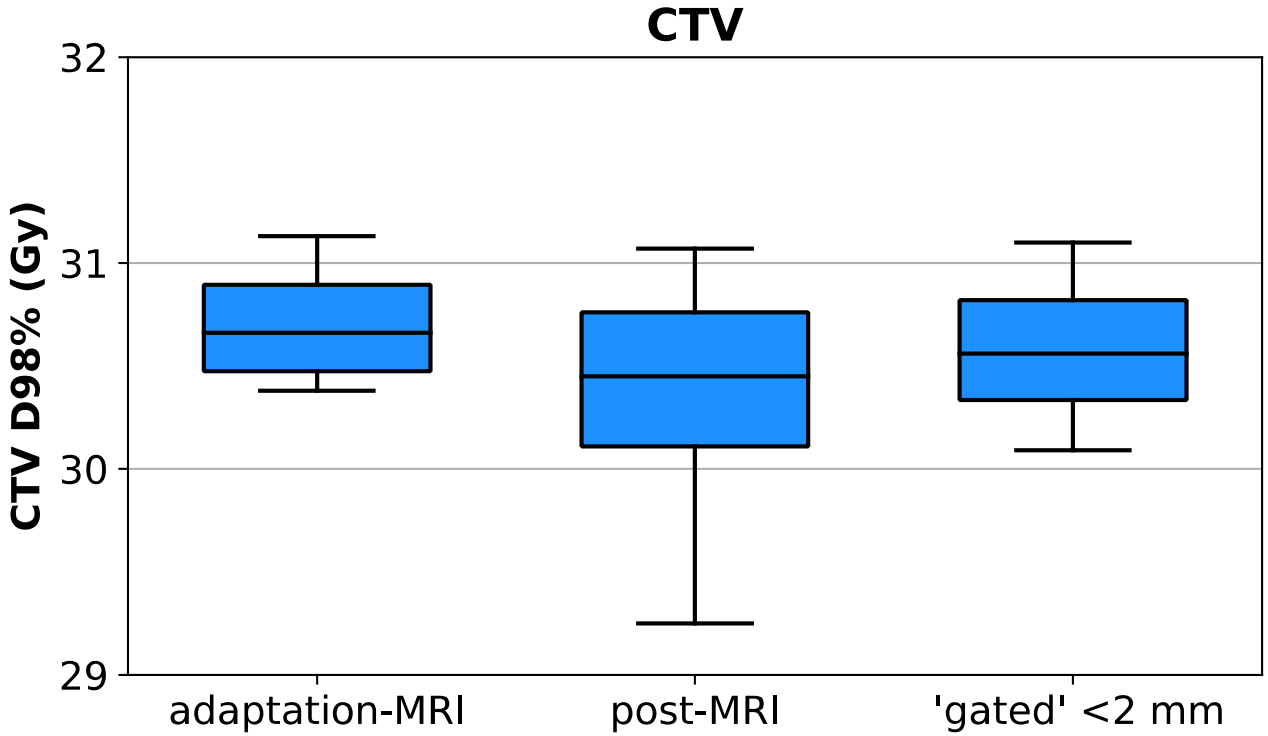
Dose coverage of the CTV without PTV margin

In 90% of all fractions:

D98% to the CTV on the post-MRI was > 29 Gy

In 90% of fractions with motion < 2 mm:

D98% to the CTV on the post-MRI was > 30 Gy



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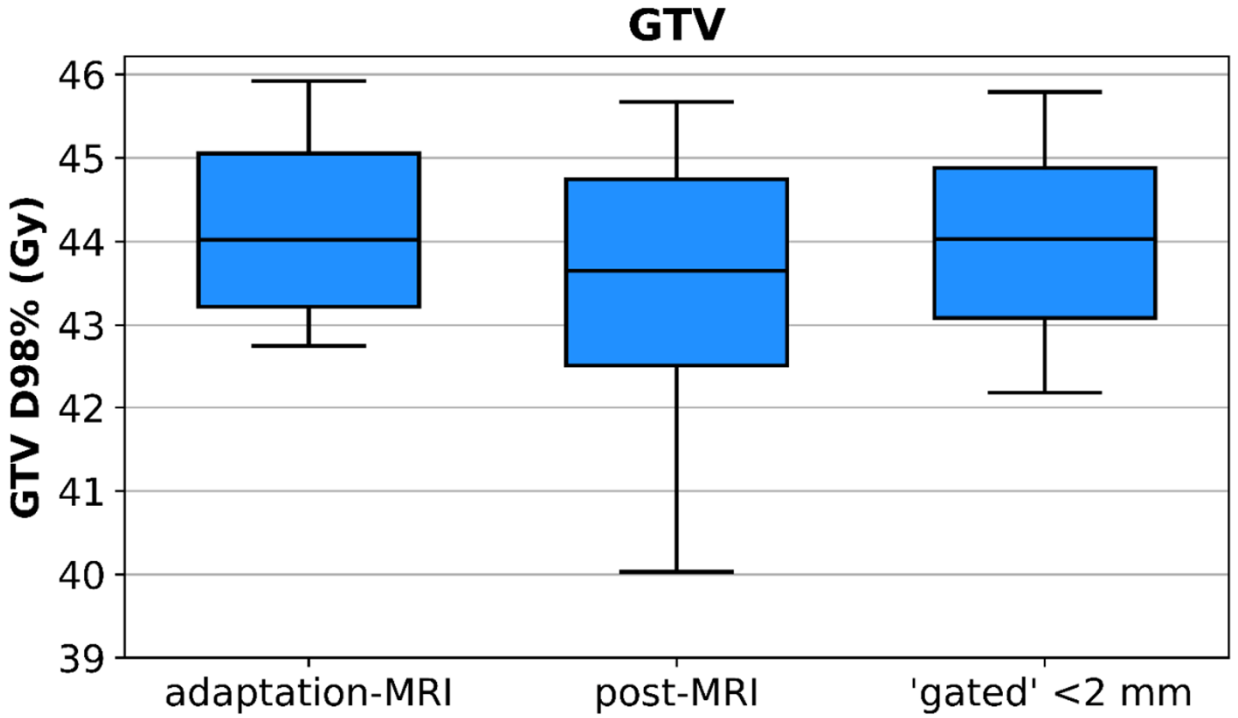
Dose coverage of the GTV without PTV margin

In 90% of all fractions:

D98% to the GTV on the post MRI was > 40 Gy

In 90% of fractions with motion < 2 mm:

D98% to the GTV on the post MRI was > 42 Gy



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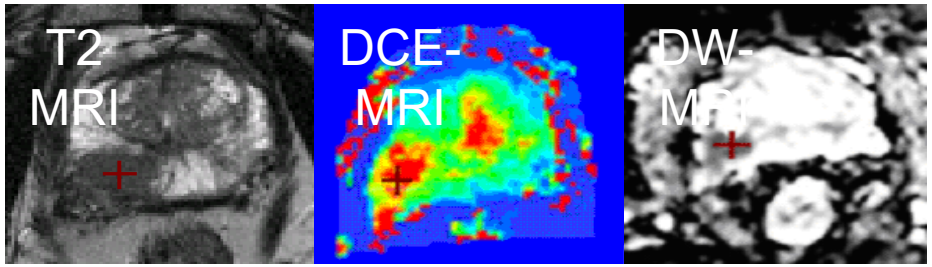
Trends in radiotherapy

- More personalized



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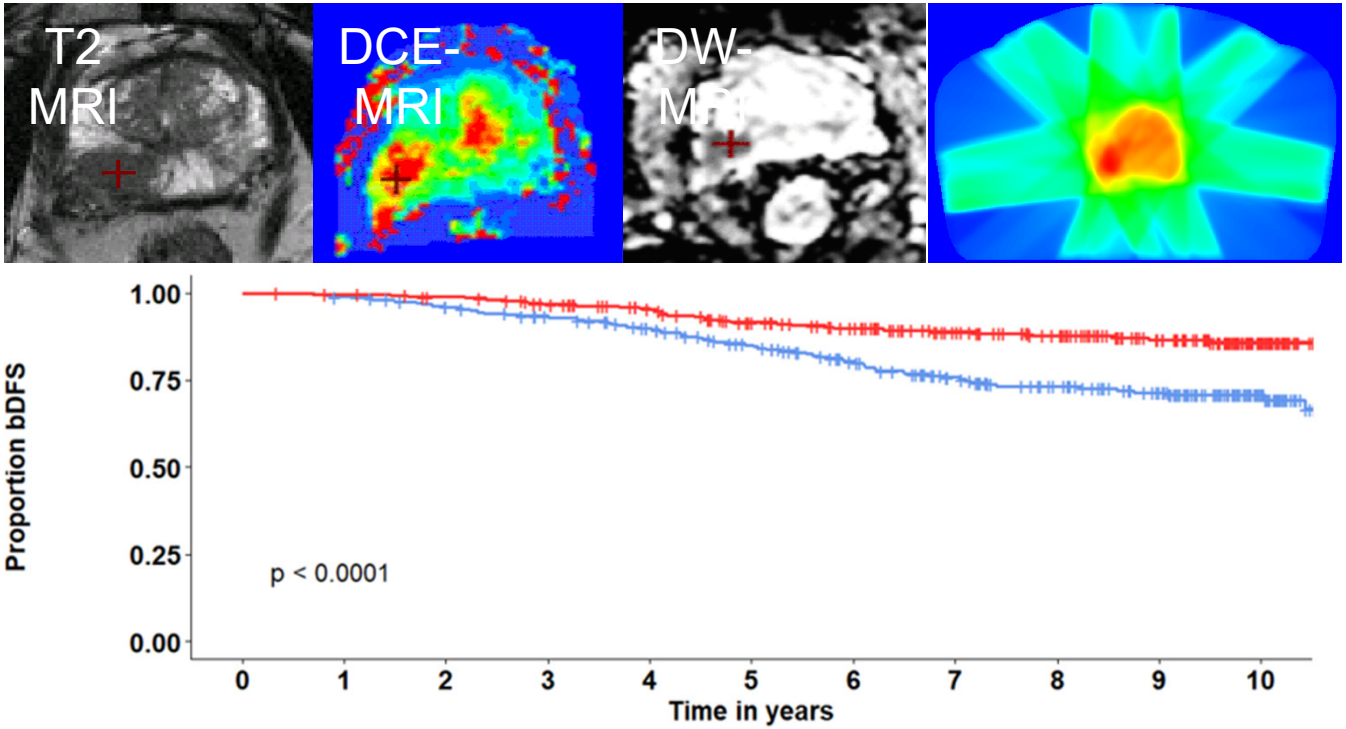
Personalized radiotherapy

FLAME trial:

Focal boosting of the GTV inside the prostate results in 15% improvement in bDFS



Menne Guricová J Clin Oncol, 43(28):3065-3069,

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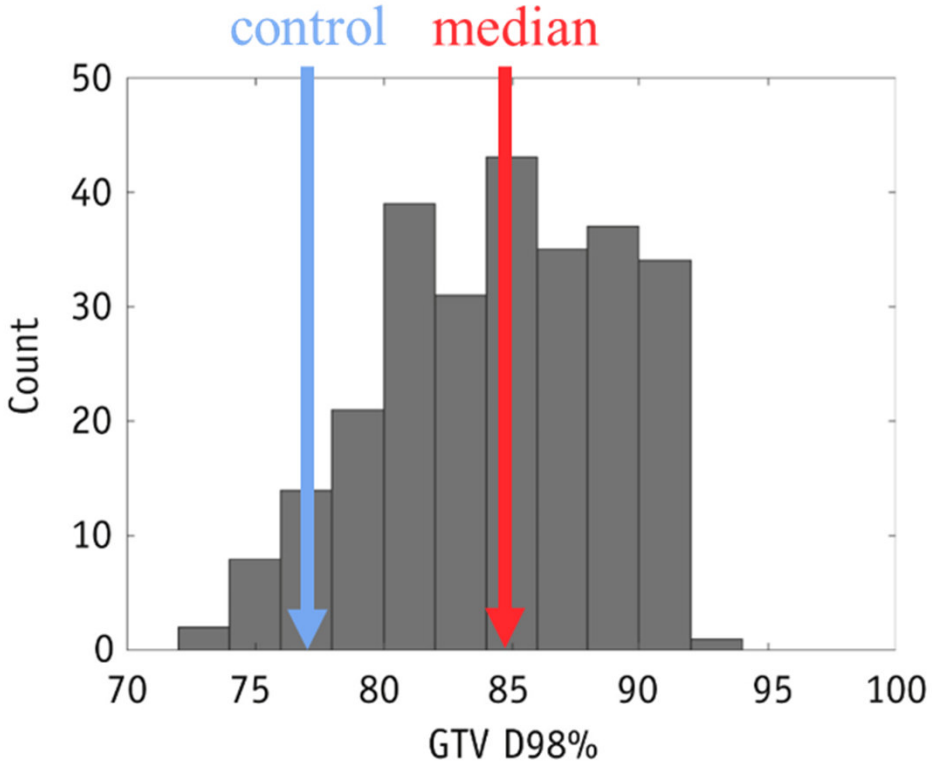
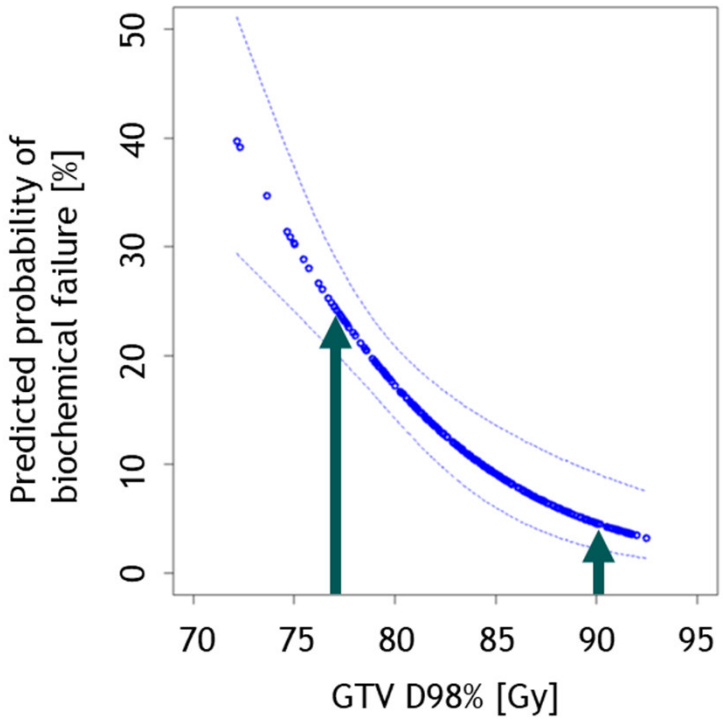
Reduce boost dose if required to spare organs at risk



Van Schie et al. Int J Radiat Oncol Biol Phys, 108(4):1055-1062



Menne Guricová J Clin Oncol, 43(28):3065-3069,

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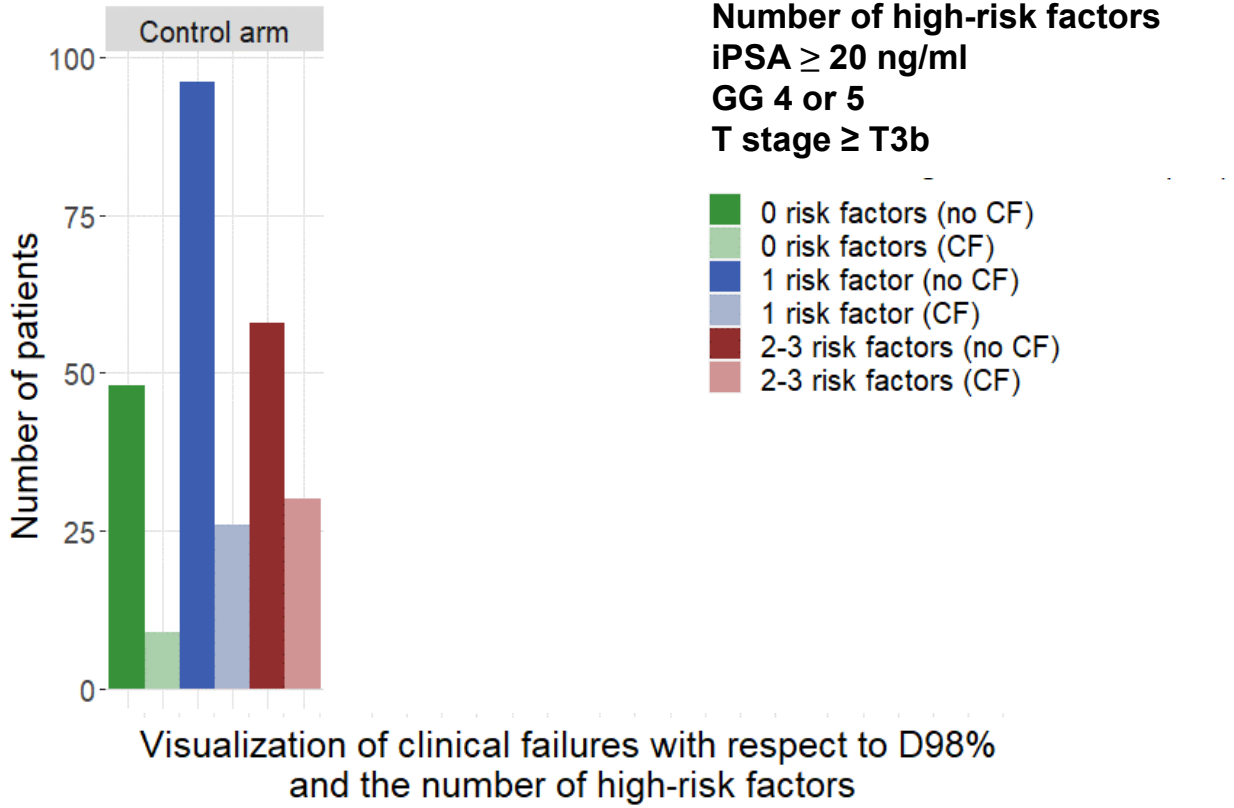
Patients with ≤T3a disease and Grade-group 1 disease show low failure rates at standard dose



Menne Guricová, Int J Radiat Oncol Biol Phys. 2024 Jan 1;118(1):66-73.

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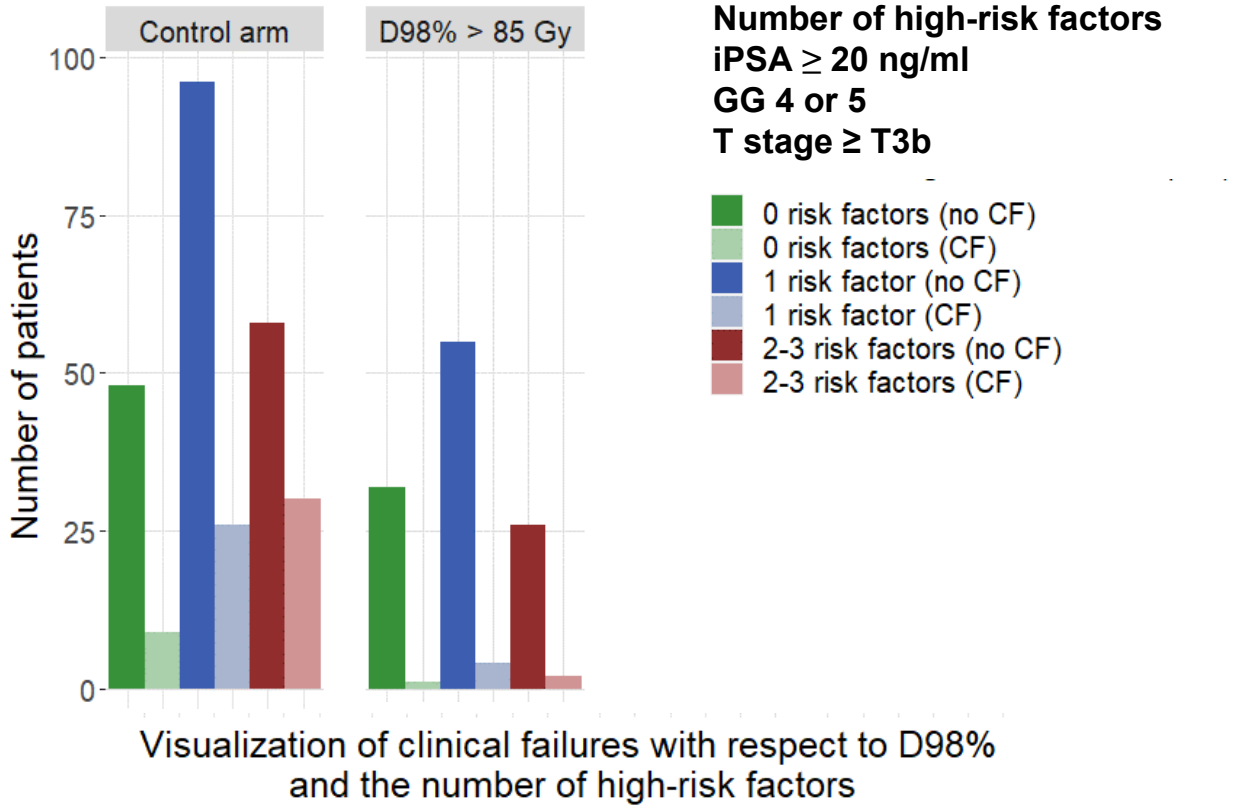
Boosting is beneficial in patients with more risk factors



Visualization of clinical failures with respect to D98% and the number of high-risk factors

Menne Guricová, Int J Radiat Oncol Biol Phys. 2024 Jan 1;118(1):66-73.

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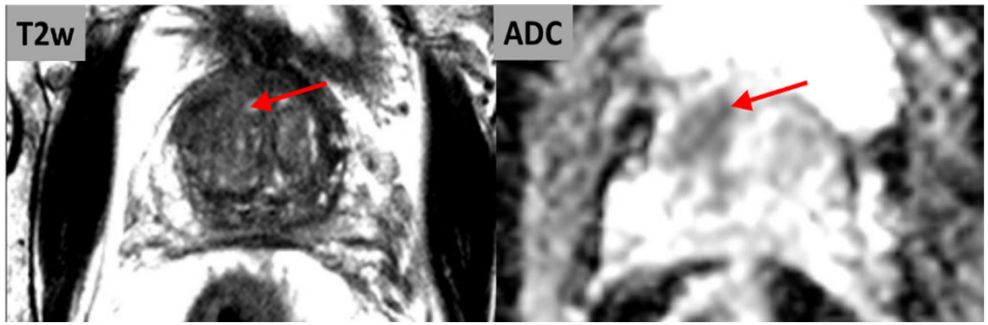
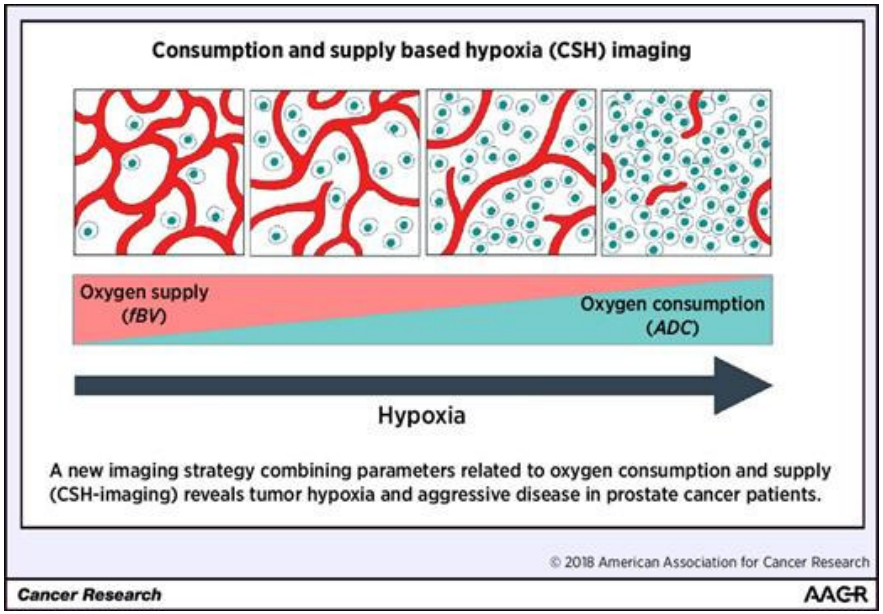
Can we use imaging to identify high-risk tumors?





Hypoxia is an important prognostic factor in cancer

It is a result of an imbalance between oxygen consumption and supply

Diffusion can be used to assess cell density (consumption)

Perfusion fraction can be used to assess blood perfusion (supply)

Hompland et al. Cancer Res. 2018 Aug 15;78(16):4774-4785

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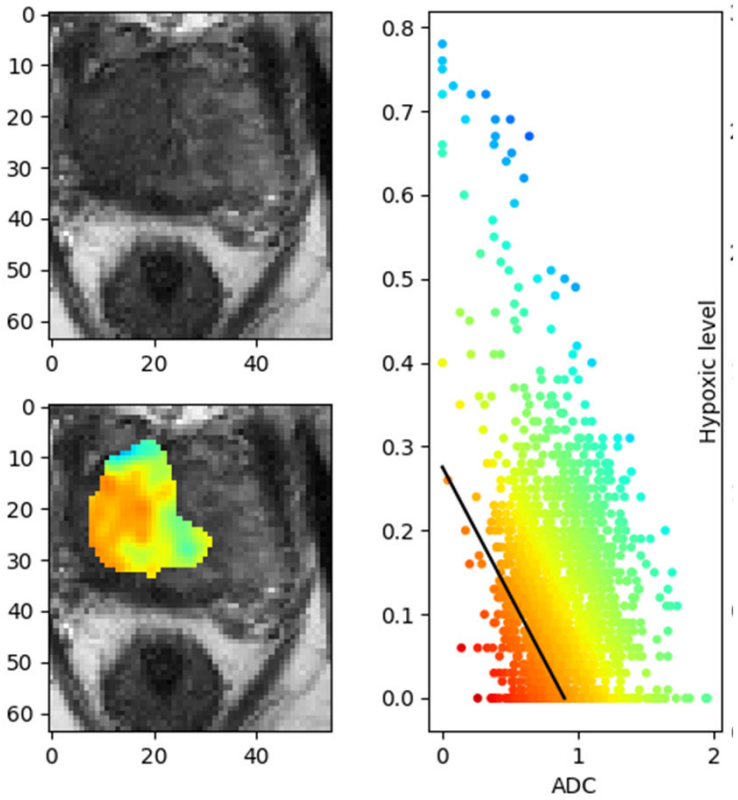
Apply the same model to the FLAME cohort



Hypoxia Score (HS): distance from the line

$$\frac{\mathrm{fBV}}{\mathrm{fBV}_0} + \frac{\mathrm{ADC}}{\mathrm{ADC}_0} = 1$$

Hypoxia Fraction (HF): relative number of voxels below the line

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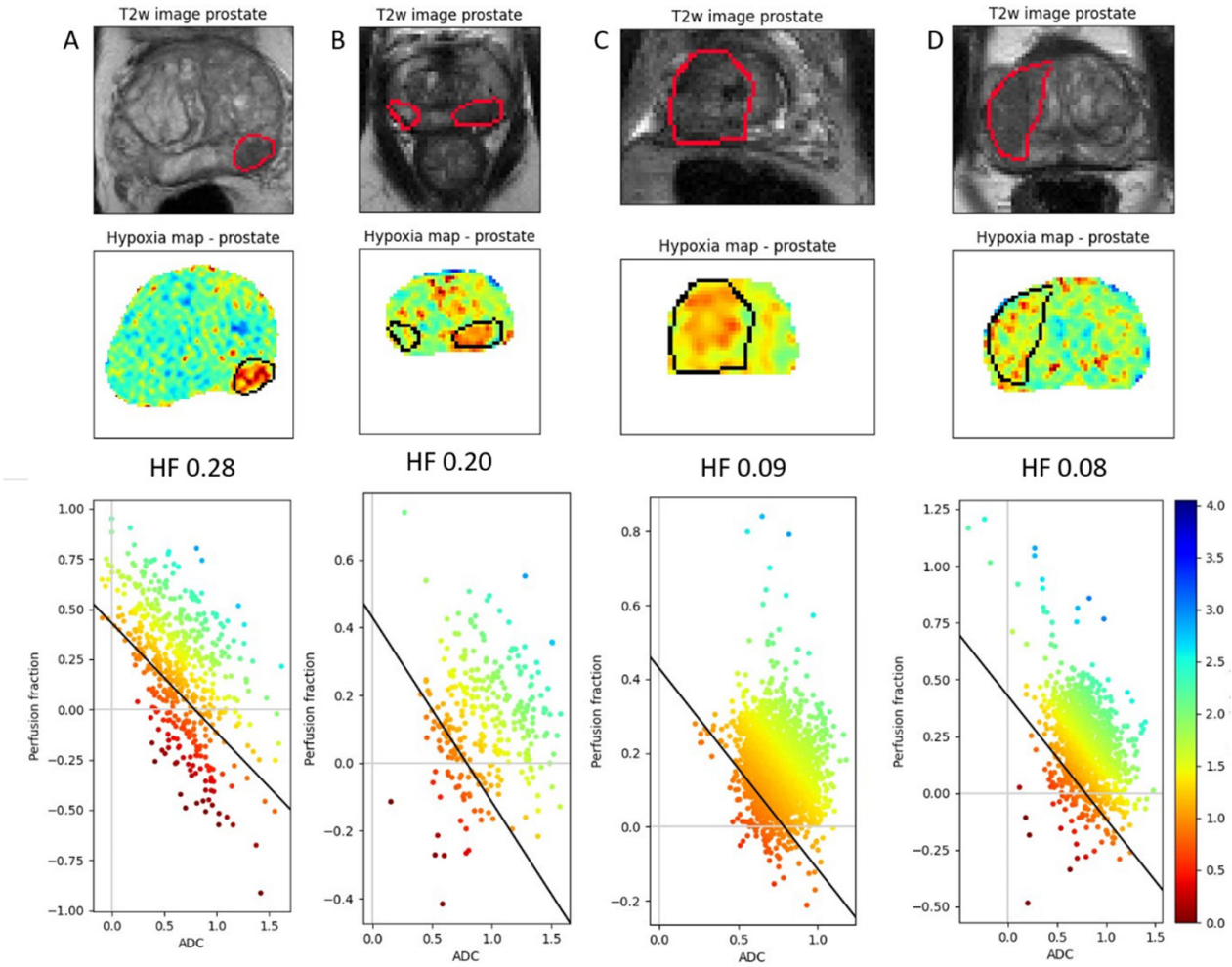
Apply the same model to the FLAME cohort



273 patients non-hypoxic
(hypoxic fraction < 0.26)

96 patients hypoxic
(hypoxic fraction > 0.26)

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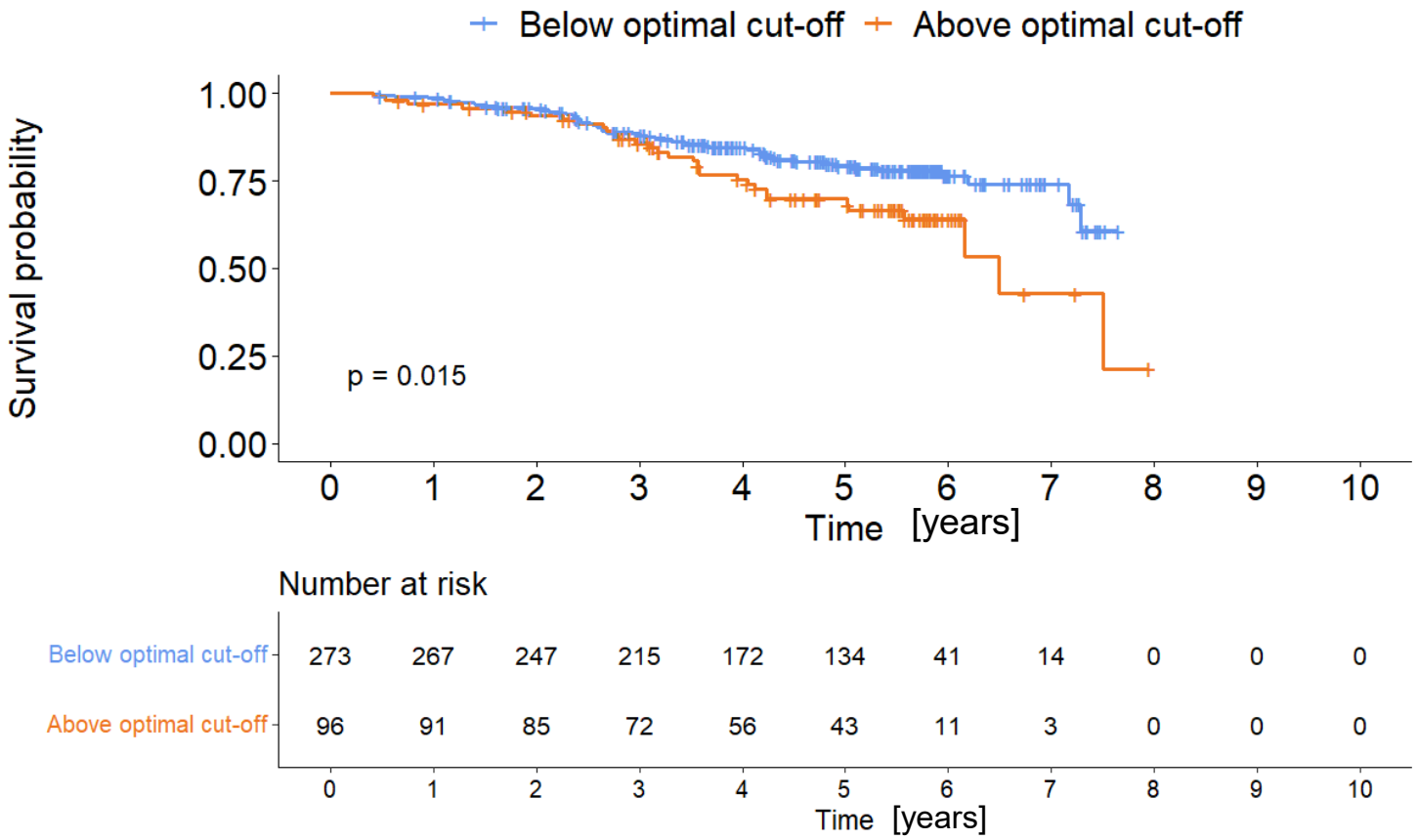
Biochemical failure-free survival is lower in patients with a larger hypoxic fraction



Hypoxic fraction cut-off 0.26

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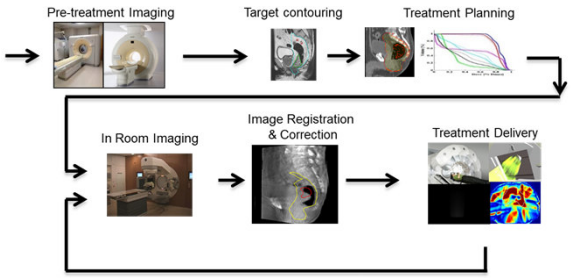
Trends in radiotherapy

- More efficient



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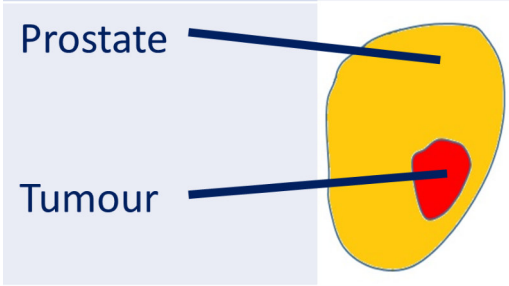
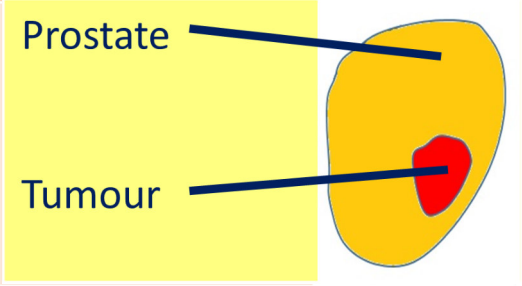
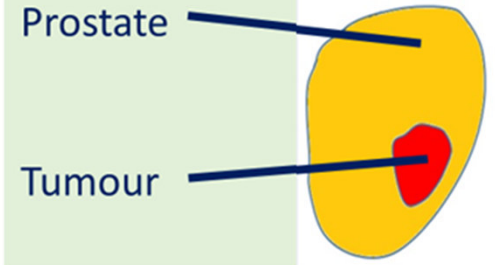
From standard to ultra-hypofractionation

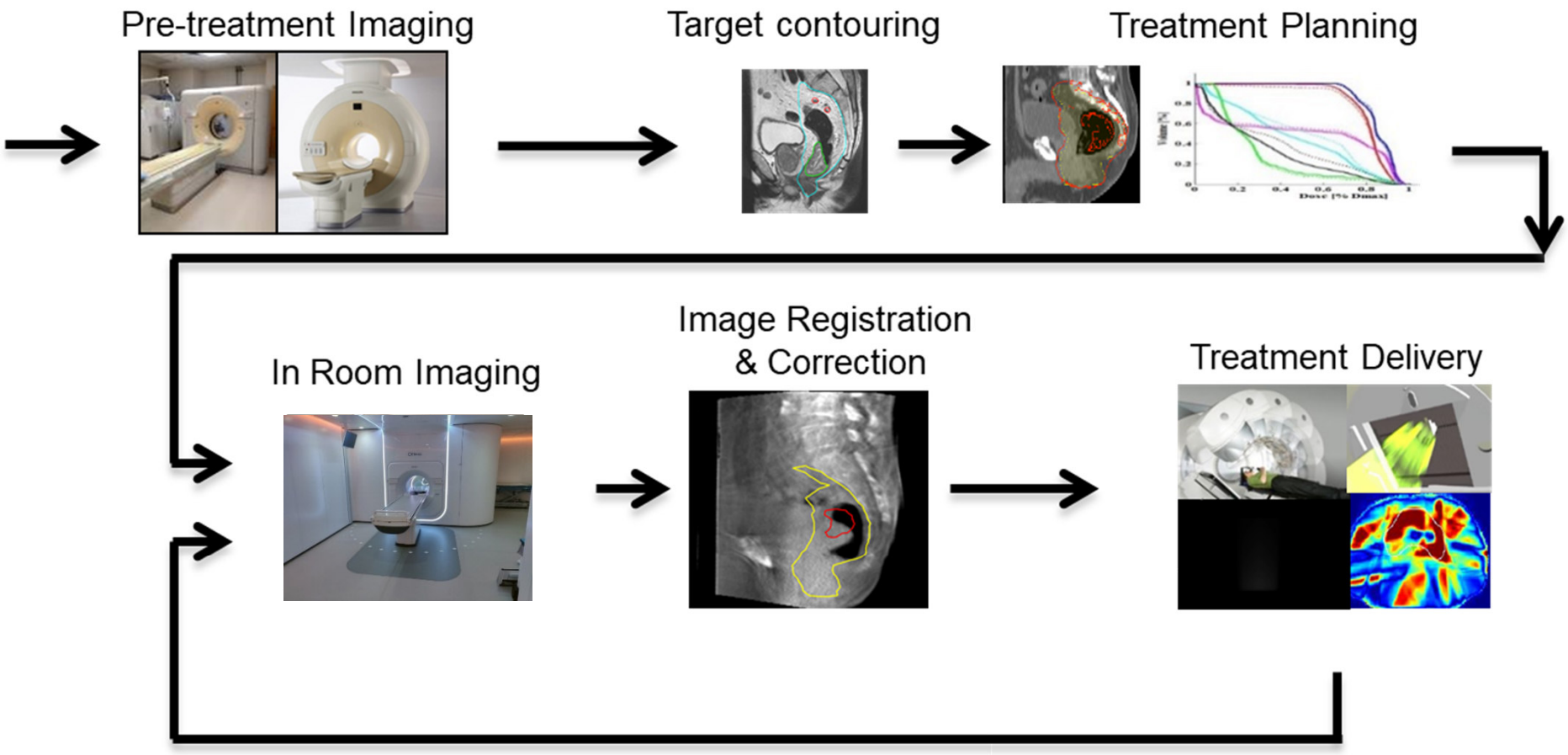
High risk

FLAME (NCT01168479; phase III)	hypo-FLAME 2.0 (NCT04045717; phase II)
OTT = 7 weeks	OTT = 15 days
35 fractions, 5x/week	5 fractions, 2x/week
Whole-gland irradiation ± focal tumour boost	Whole-gland irradiation + focal tumour boost
	

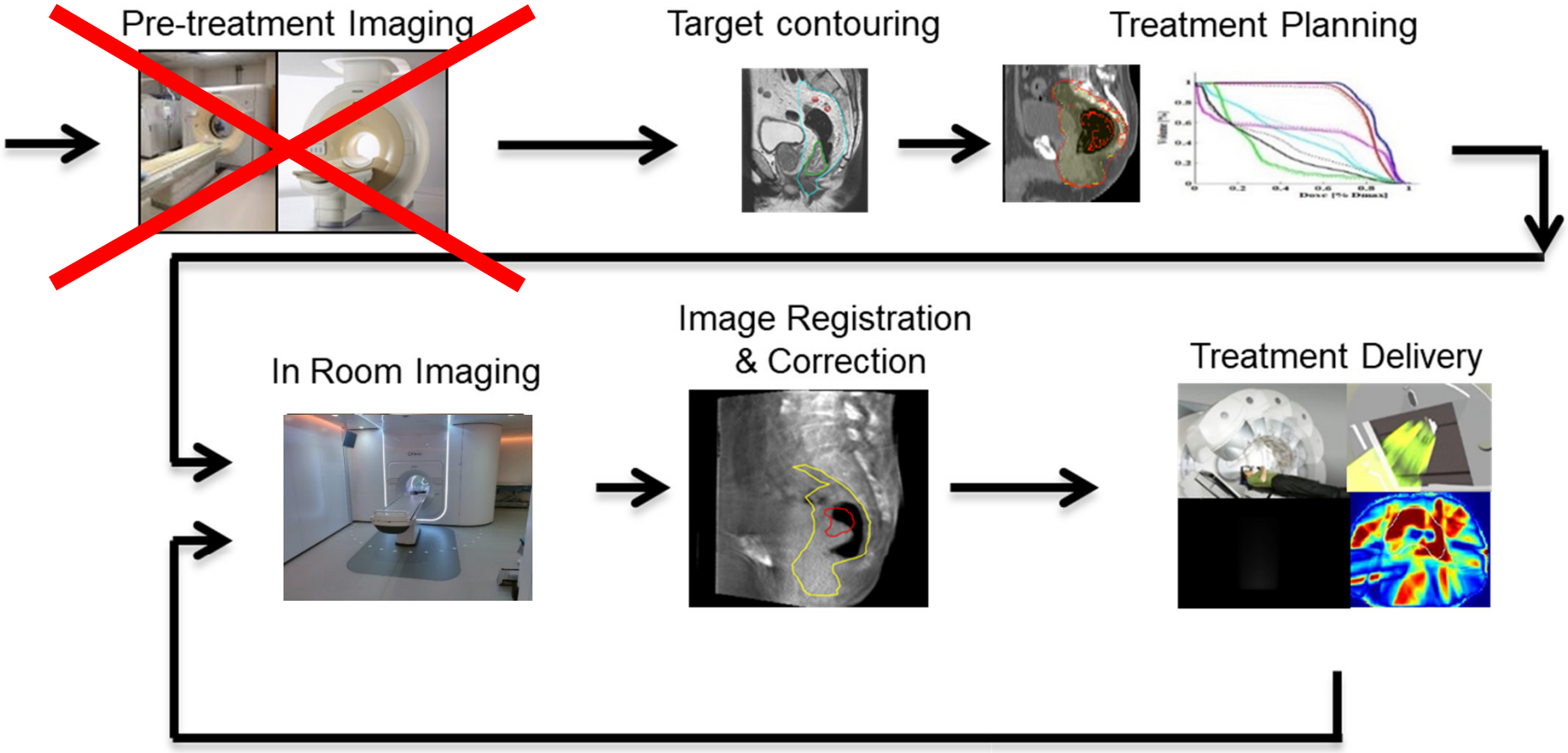
Favorable intermediate risk

Destination (NCT05709496; technical feasibility)
OTT = 7 days
2 fractions, 1x/week
Dose de-escalation to whole gland + focal boost


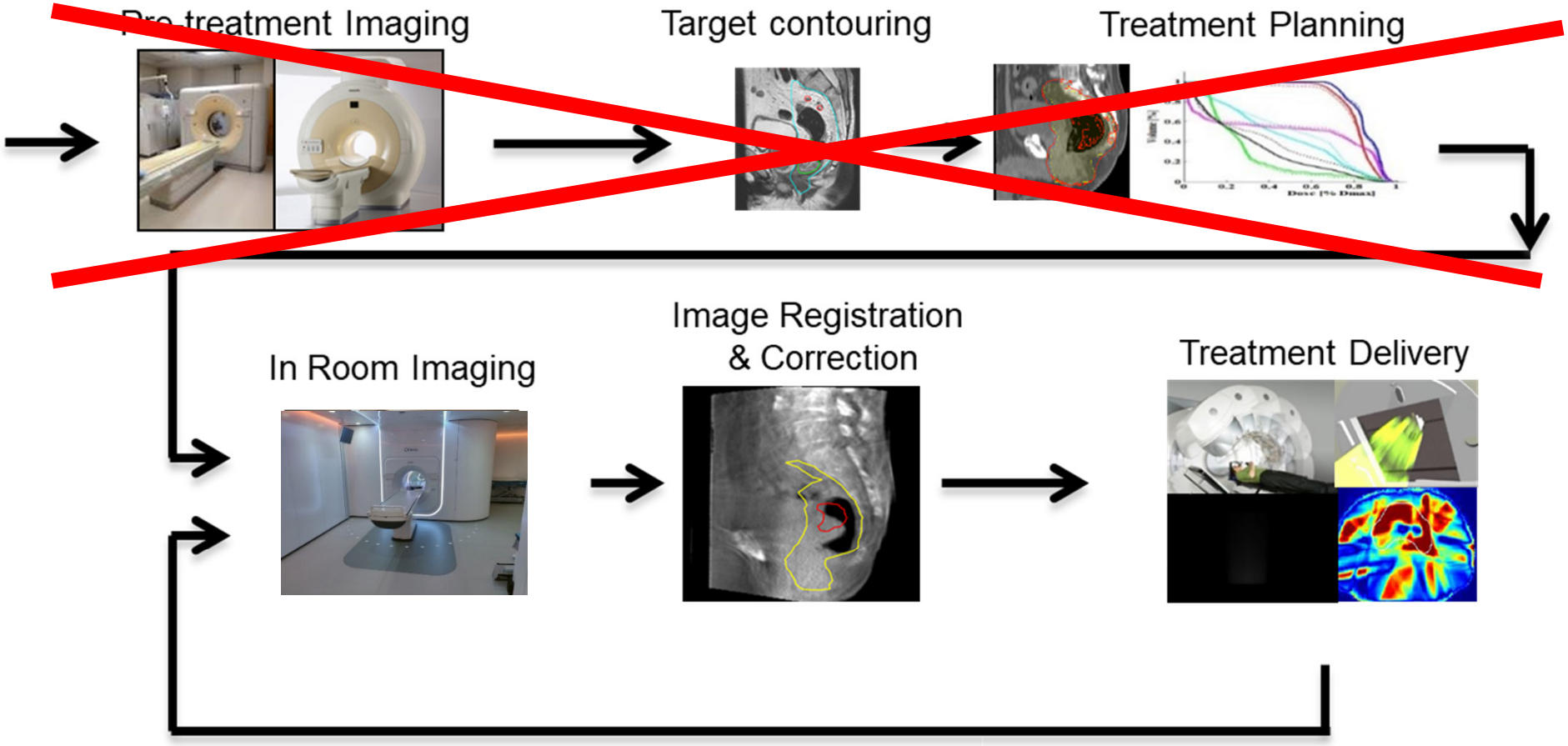
Standard workflow in radiotherapy



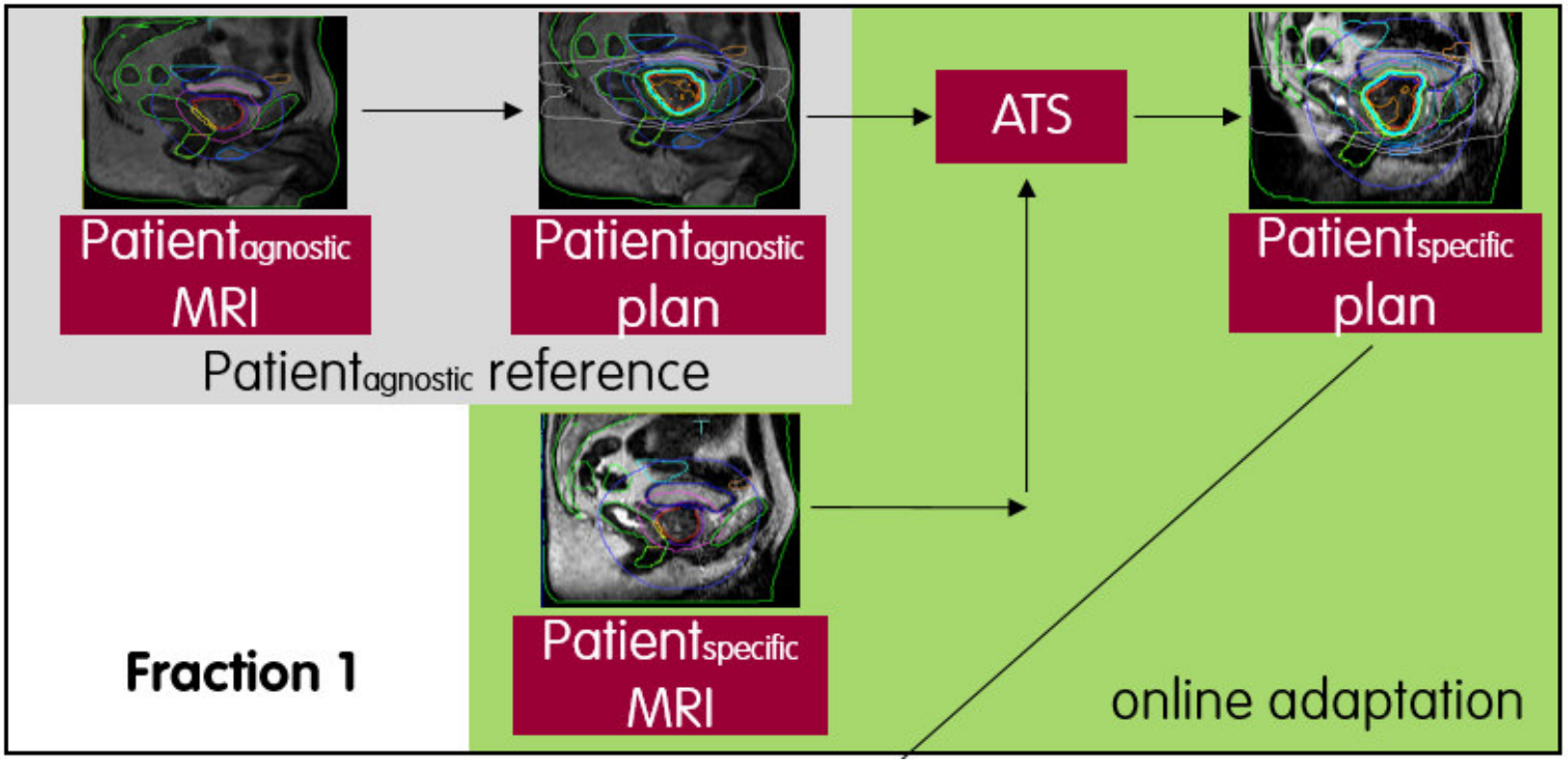
Remove the dedicated RT imaging



Remove the entire preparation phase



Use a generic patient as reference for on-line adaptation during fraction 1



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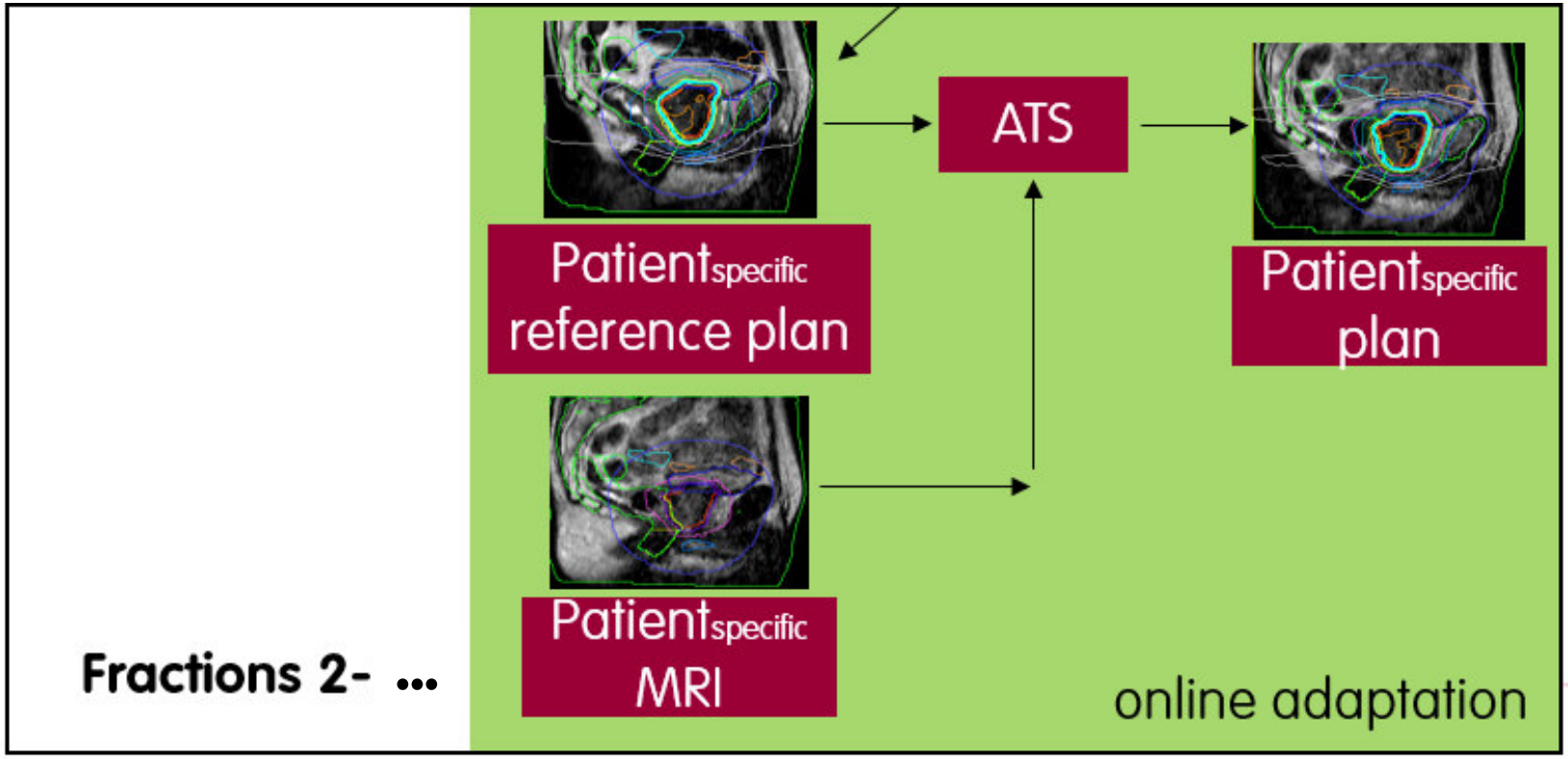
Use plan of fraction 1 as reference for later fractions



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Abolish preparation phase
at the cost of a minor increase in fraction 1

	Image matching	Contouring	TPO	Total
Fraction 1	0.4 min	6.7 min (3.4 – 10.4)	5.4 min (3.2 – 9.8)	12.5 min (10.5 – 16.3)
Fraction 2	0.4 min	4.2 min (1.3 – 10.7)	4.7 min (2.8 – 6.2)	9.3 min (5 - 15.5)

Evaluating the on-line adaptation steps in 10 patients.

Patients were treated previously using the standard workflow

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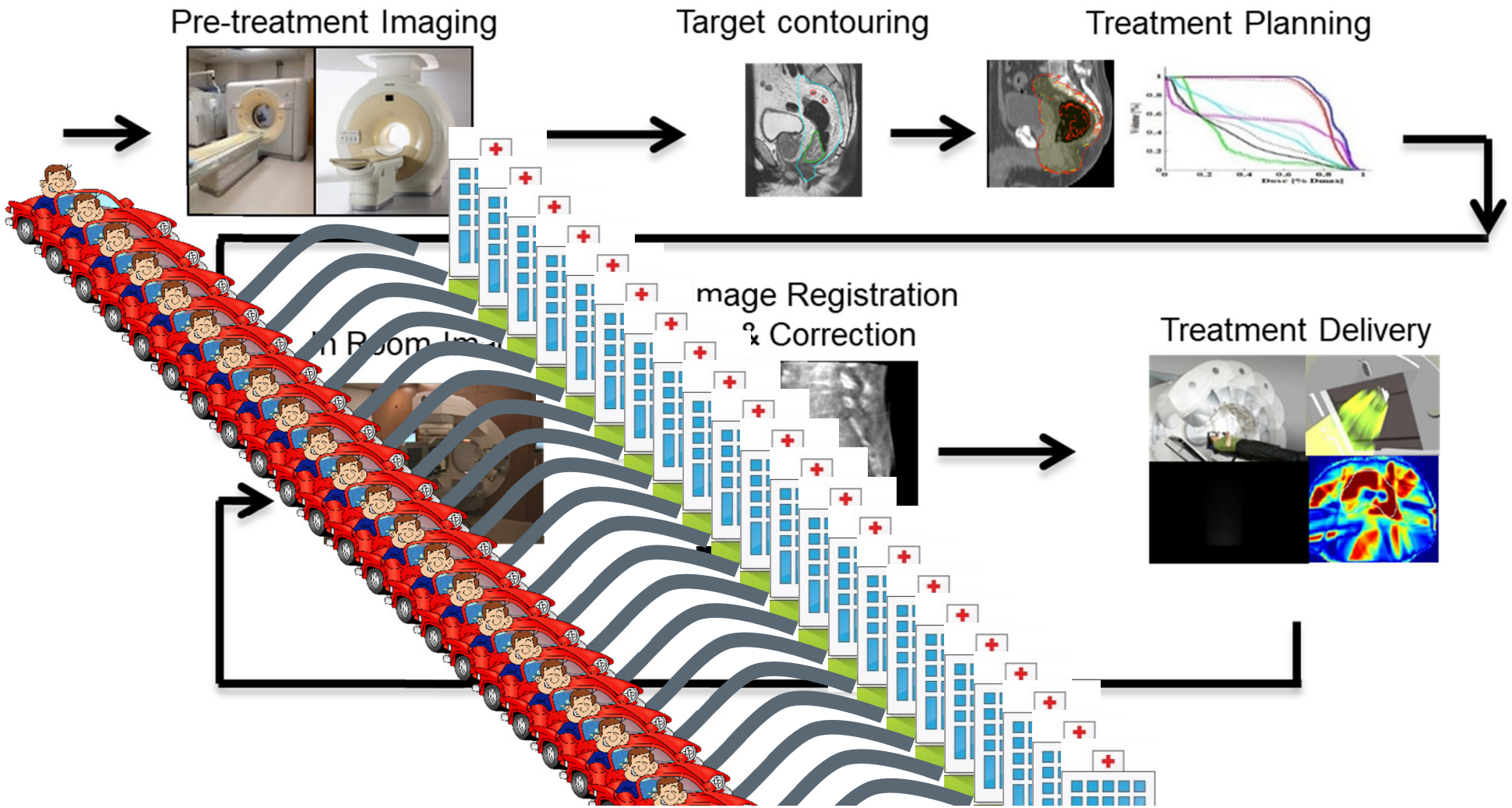
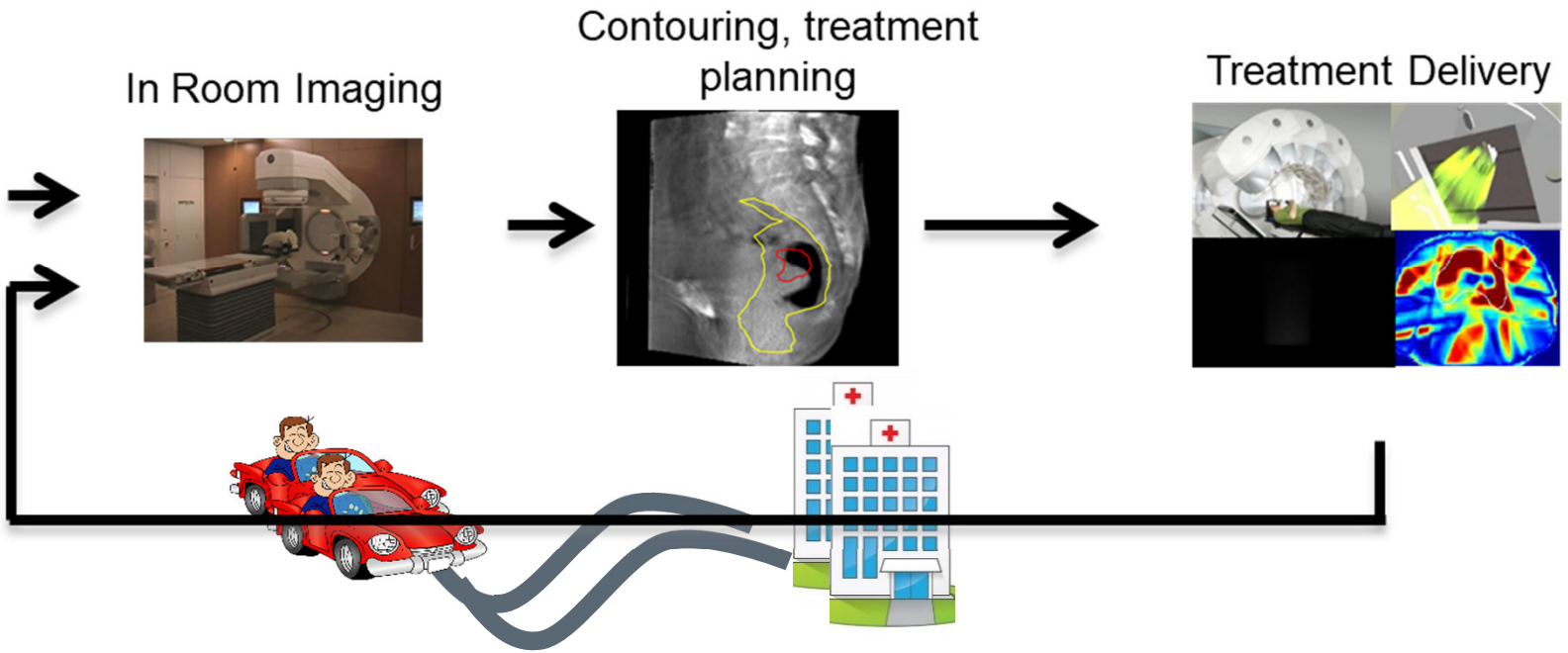
Conventional radiotherapy of prostate cancer



2 fractions, direct to treatment



Cutting edge radiotherapy

Increased precision of MRI-guided on-line adaptive radiotherapy results in extremely high precision of delivery

- The vision of 0 mm PTV margins becomes a realistic prospect

Using non-invasive biomarkers, such as quantitative MRI, patient selection for more or less dose escalation becomes feasible

- Decide on focal boosting of prostate cancer based on MRI-based hypoxia signature

Ultra-hypofractionation and Direct-to-treat workflows improve cost-efficiency and patient comfort

- Prostate radiotherapy may need only 2 visits to the radiotherapy department

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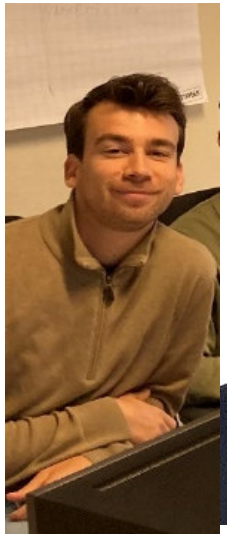
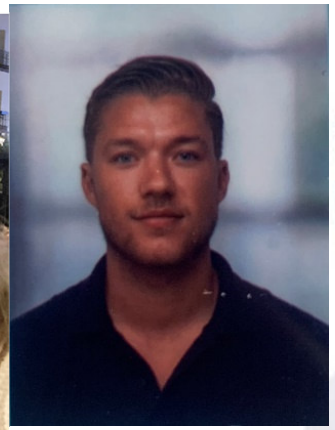
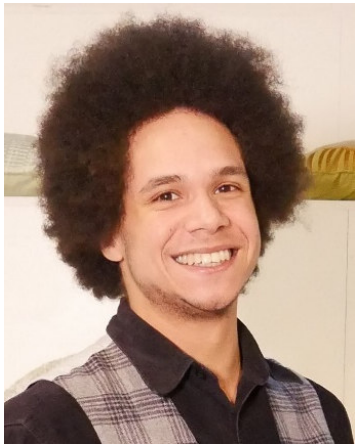
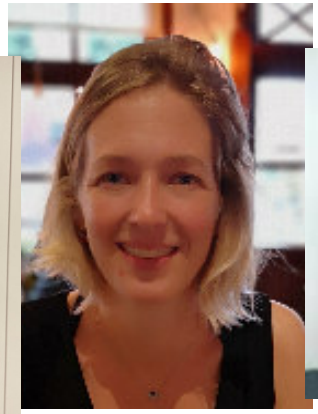
Interdisciplinary collaboration









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