‘Modern’ dose distributions: what should we not forget?

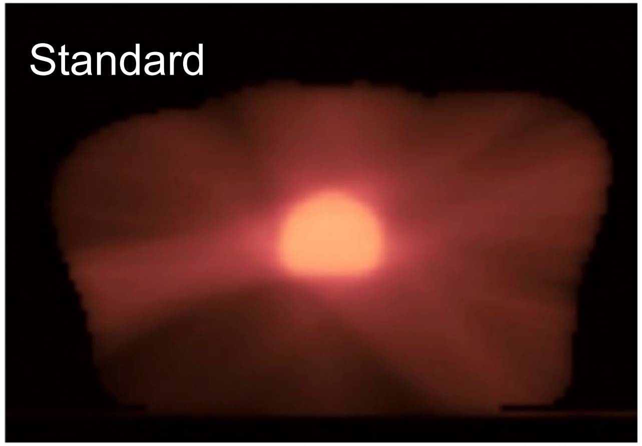
Uulke van der Heide

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

Using CT to delineate the target volume

Example: prostate cancer

Standard: homogeneous dose to
entire prostate

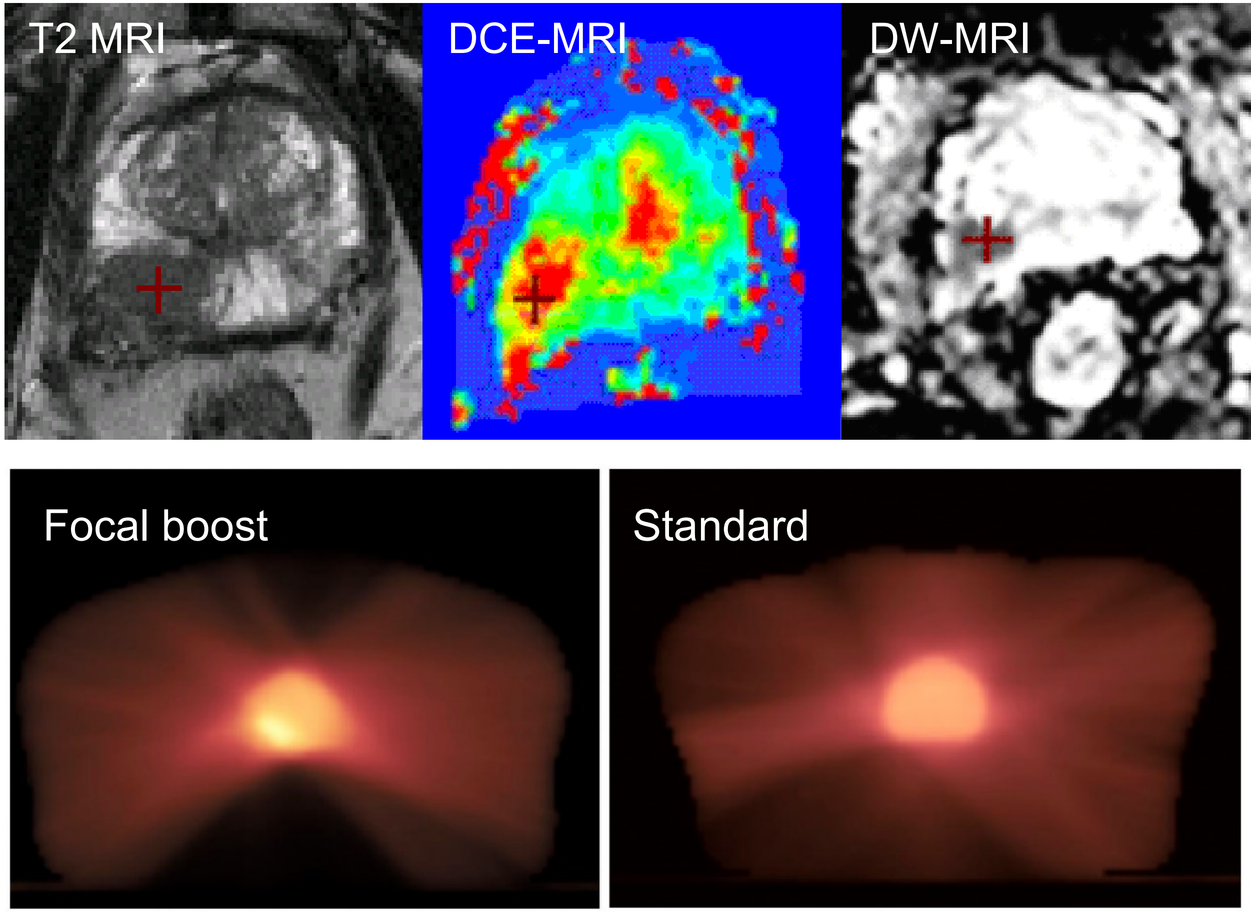


Using multi-parametric imaging to differentiate dose inside the target volume

Example: prostate cancer

Standard: homogeneous dose to entire prostate

New: escalate dose at location of highest tumor burden



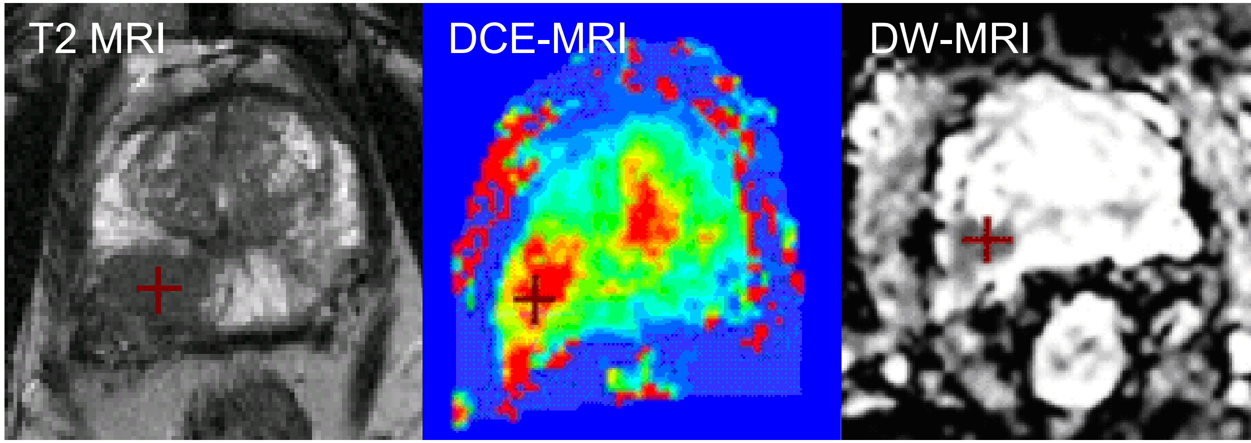
Using multi-parametric imaging to differentiate dose inside the target volume

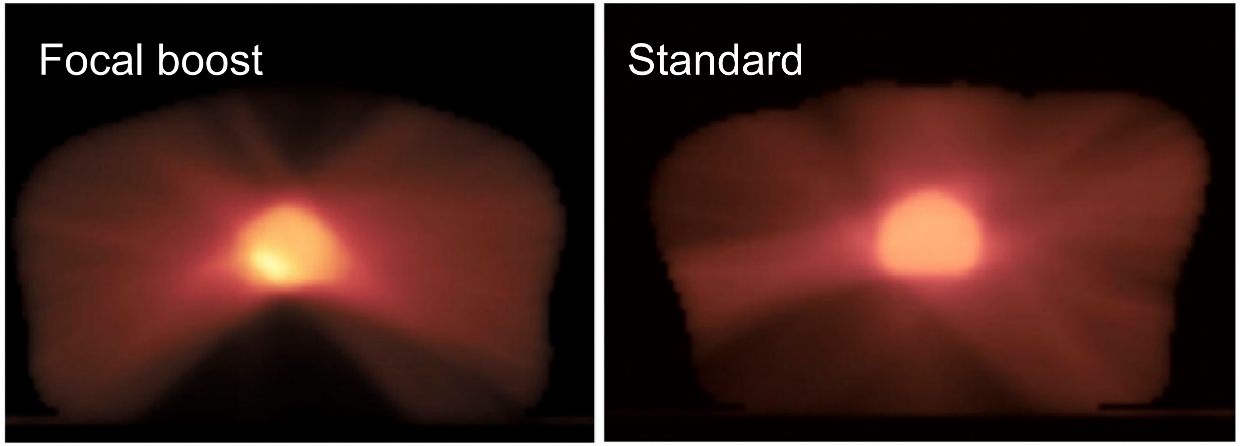
Example: prostate cancer

Standard: homogeneous dose to entire prostate

New: escalate dose at location of highest tumor burden

What about uncertainties?

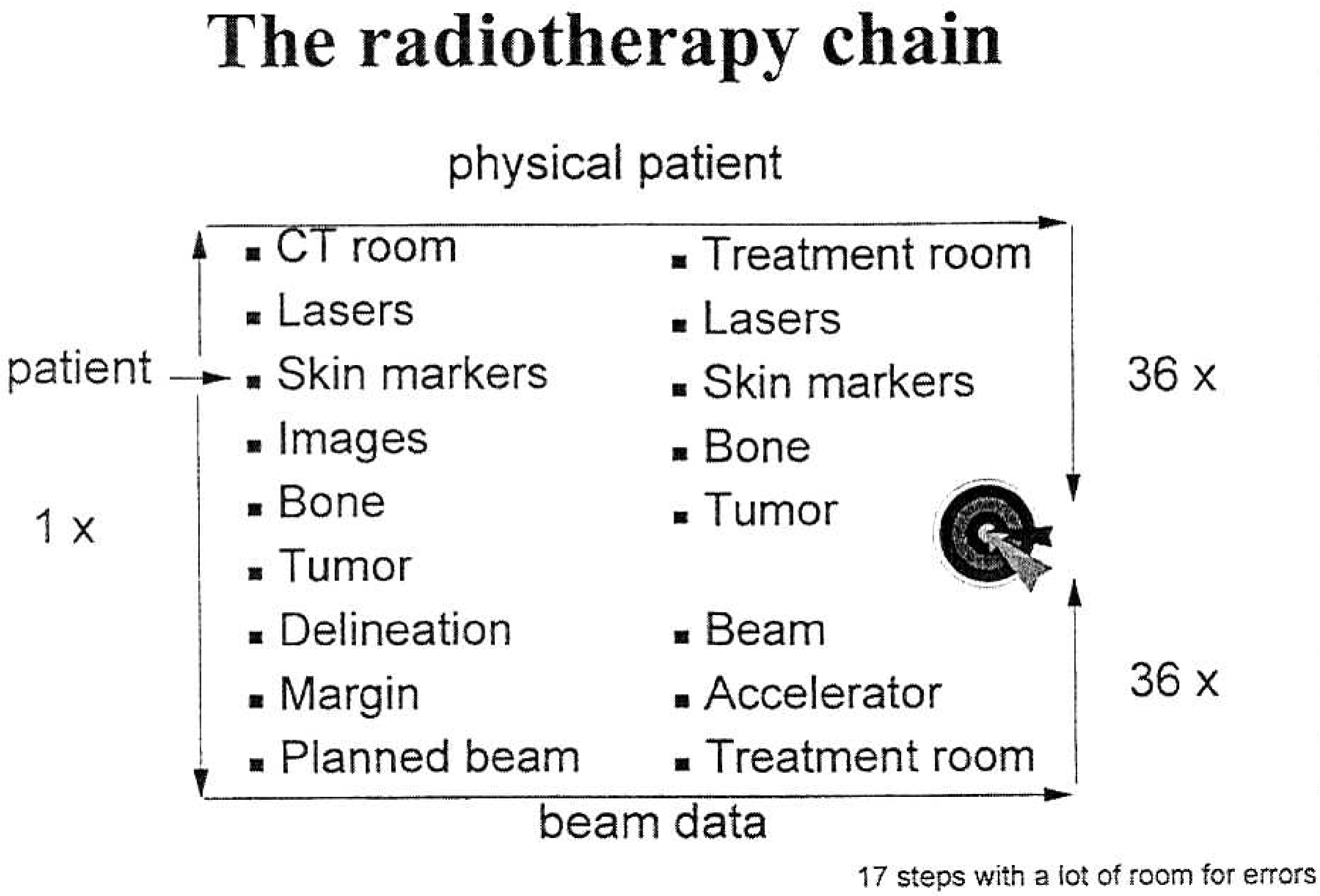




Uncertainties to consider

PTV margins are intended to guarantee that x% of patients receive a minimum dose of ≥ y% of the prescribed dose

- Usually 90% of patients, at least 95% of the dose



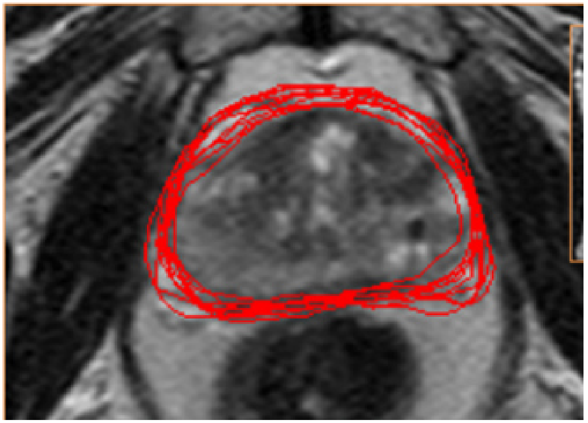
Courtesy Marcel van Herk

NETHERLANDS CANCER INSTITUTE ANTONI VAN LEEUWENHOEK

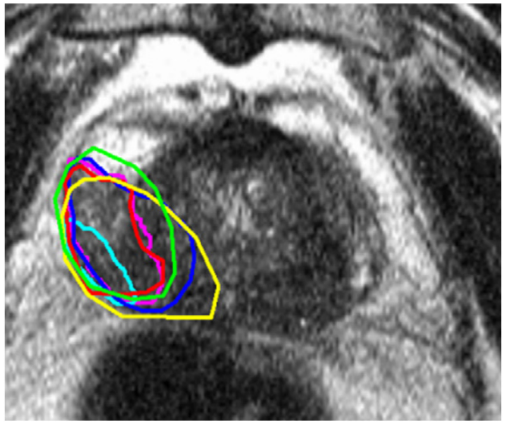
Uncertainties to consider: target definition

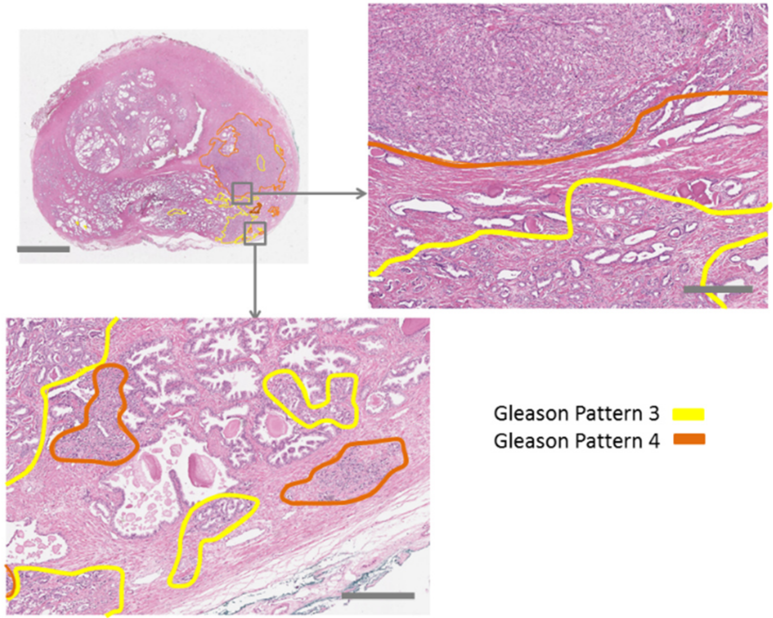
Delineation uncertainties

- Prostate
- Tumor



Nyholm et al. 2013; Radiat Oncol.

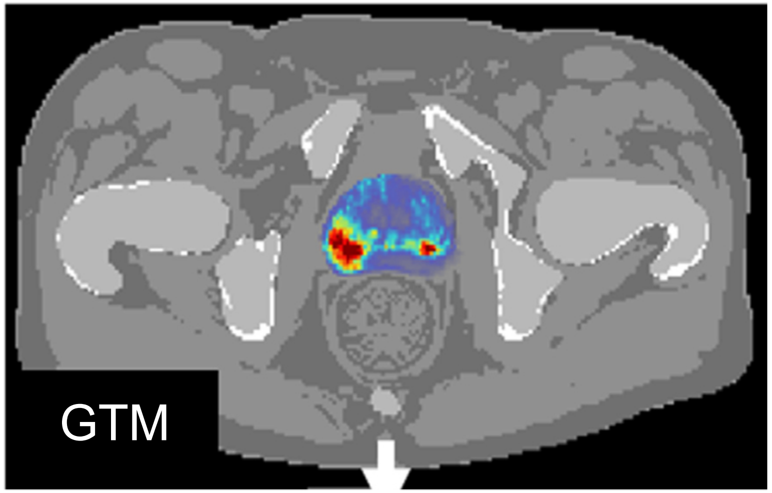




Steenbergen et al. 2015; Radiat Oncol.

NETHERLANDS CANCER INSTITUTE ANTONI VAN LEEUWENHOEK

Towards a probabilistic definition of target volumes

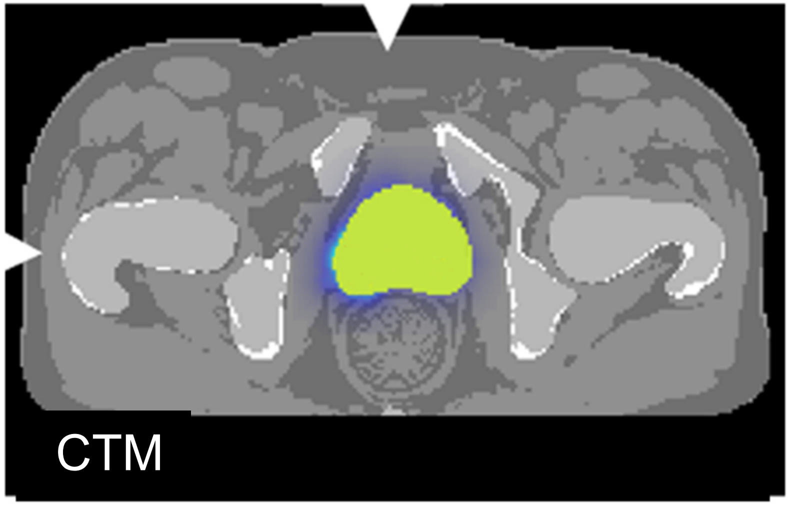


Express uncertainty in the target definition by probabilities

'Gross Tumor Volume' becomes 'Gross Tumor Map'

NETHERLANDS CANCER INSTITUTE ANTONI VAN LEEUWENHOEK

Towards a probabilistic definition of target volumes



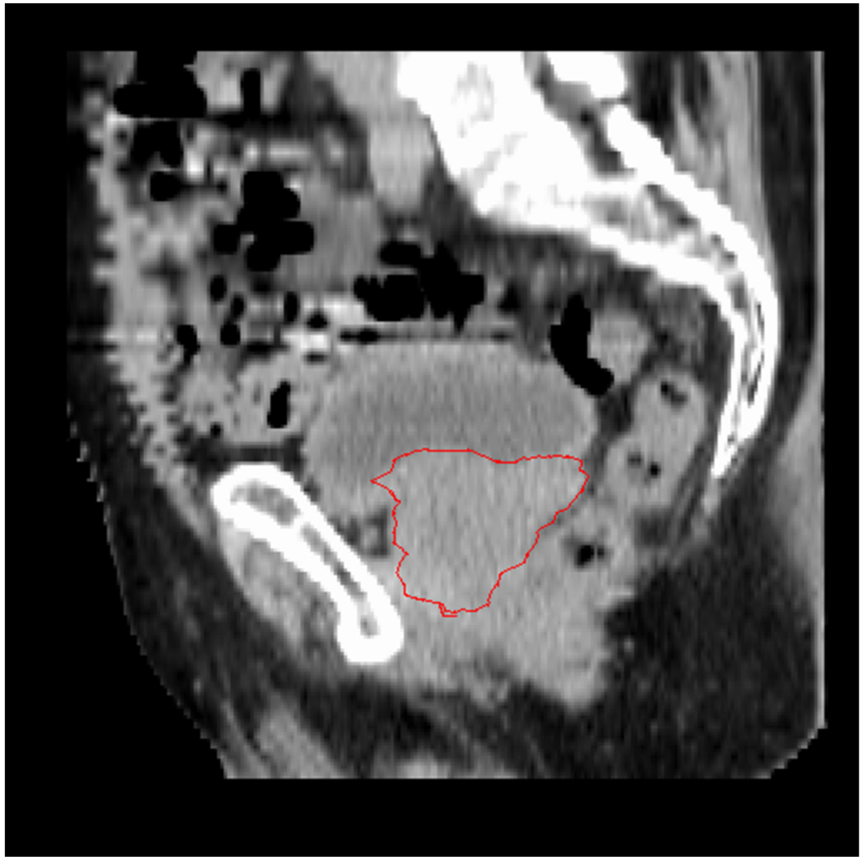
Express uncertainty in the target definition by probabilities
Include likelihood of extra-capsular disease

‘Clinical Tumor Volume’ becomes ‘Clinical Tumor Map’

Uncertainties to consider: positioning uncertainties

Organ motion

- Inter-fraction motion

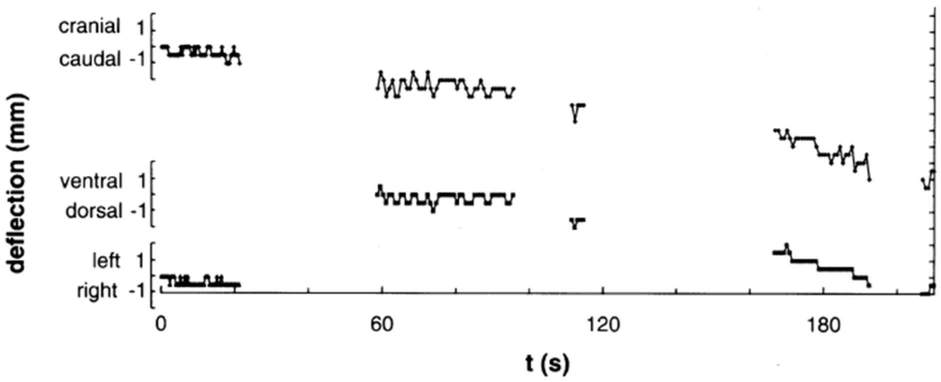


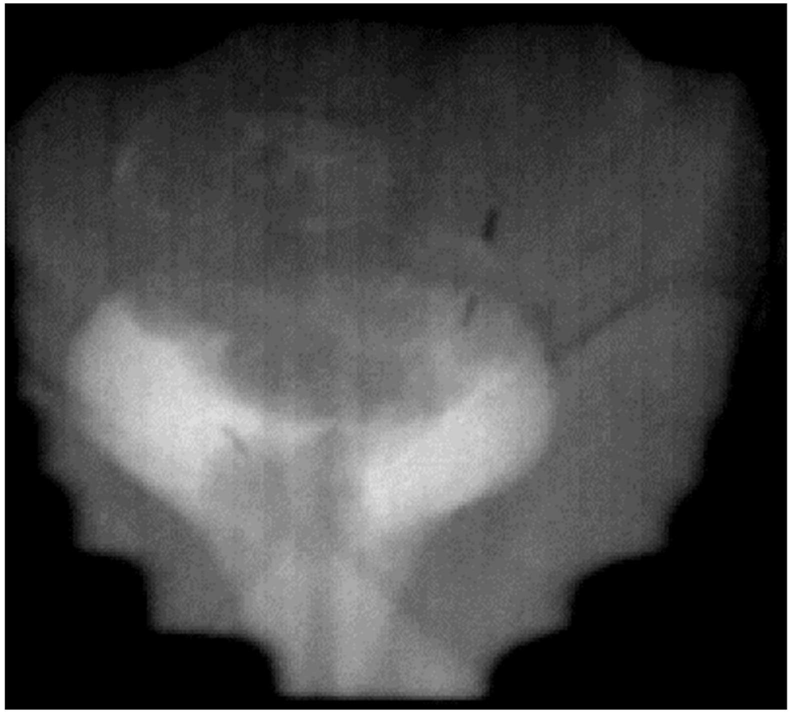
Courtesy Marcel van Herk

Uncertainties to consider: positioning uncertainties

Organ motion

- Inter-fraction motion
- Intra-fraction motion

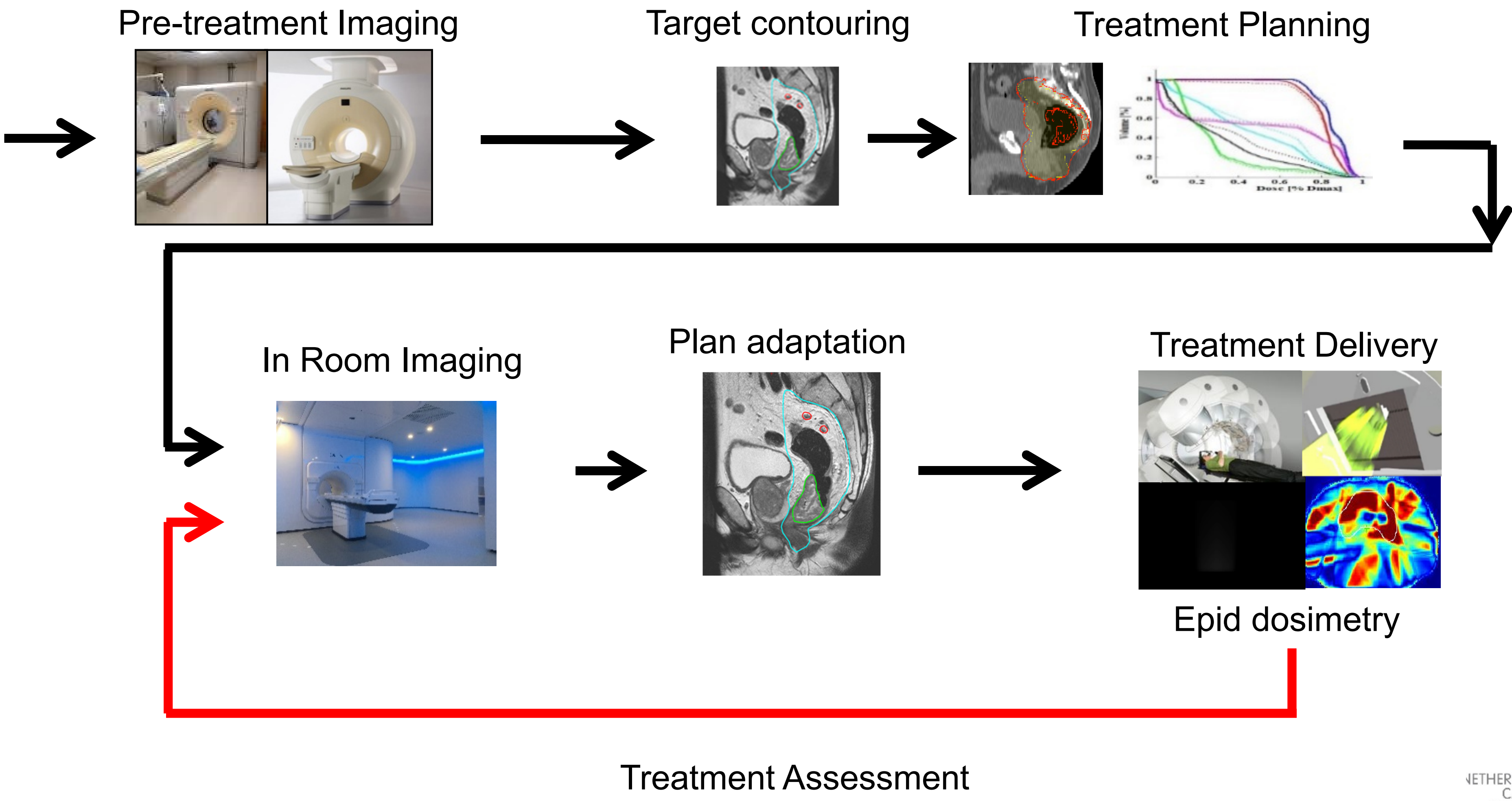




Nederveen et al. Int J Radiat Oncol Biol Phys. 2002 May 1;53(1):206-14

NETHERLANDS CANCER INSTITUTE ANTONI VAN LEEUWENHOEK

Adapt each fraction to the changing shape of the target



NETHERLANDS CANCER INSTITUTE ANTONI VAN LEEUWENHOEK

MRI-guided radiotherapy

ATP: “Adapt to Position”

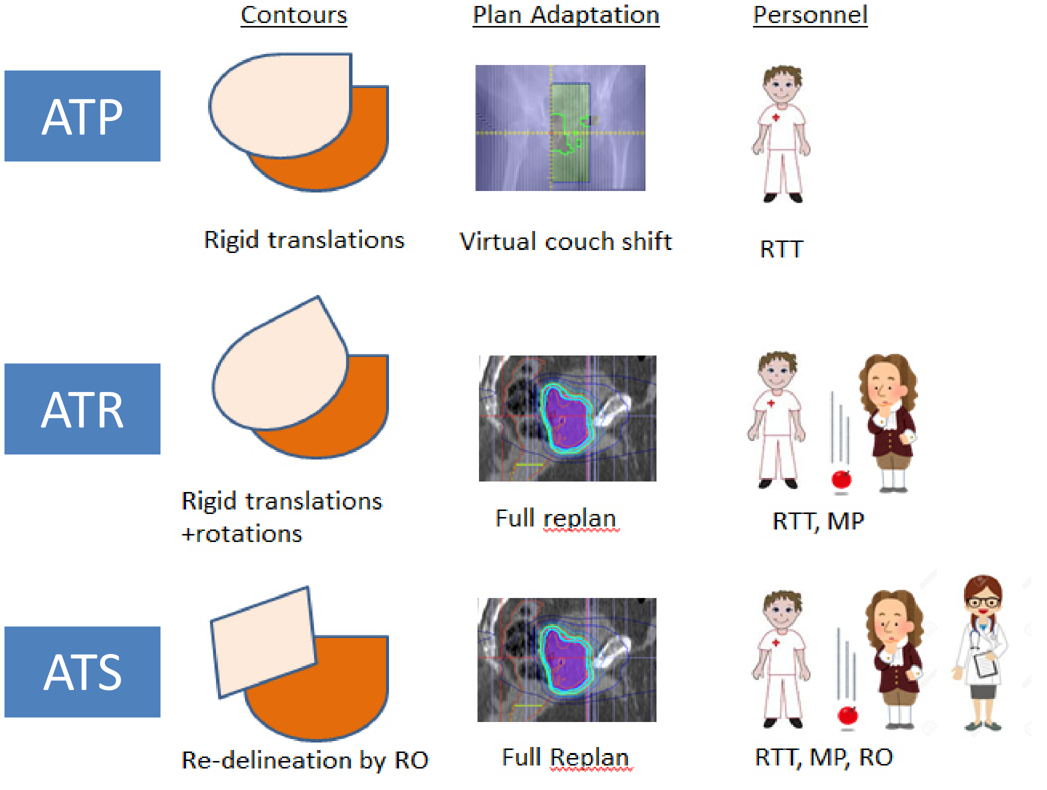
(virtual) couch shift

ATR: “Adapt to Rotation”

Shift and rotate targets rigidly and replan; no re-contouring

ATS: “Adapt to Shape”

Full adaptation



ICRU report 97: MRI-Guided Radiation Therapy Using MRI-Linear Accelerators

NETHERLANDS CANCER INSTITUTE ANTONI VAN LEEUWENHOEK

Uncertainties in on-line adaptive radiotherapy

	ATP	ATR	
Simulation/treatment planning			
Match uncertainty planning CT and planning MRI	S	S	
Contouring uncertainty	S	S	
On-line treatment			
Match uncertainty planning CT and adaptation MRI	R	R	
Contouring uncertainty	-	-	
Geometrical uncertainties of the linac	S/R	S/R	
Intra-fraction motion	R	R	

Uncertainties in on-line adaptive radiotherapy

	ATP	ATR	ATS
Simulation/treatment planning			
Match uncertainty planning CT and planning MRI	S	S	-
Contouring uncertainty	S	S	-
On-line treatment			
Match uncertainty planning CT and adaptation MRI	R	R	-
Contouring uncertainty	-	-	R
Geometrical uncertainties of the linac	S/R	S/R	S/R
Intra-fraction motion	R	R	R

Systematic errors may become random in an on-line adaptive workflow

Assumptions in the 'van Herk recipe' $m_{PTV} = 2.5\,\Sigma + 0.7\,\sigma$

The dose gradient is described with σ_p =3.2 mm

90% of patients receives a minimum dose of ≥ 95% of the prescribed dose

Van Herk, Remeijer; Int. J. Radiat. Oncol. Biol. Phys., Vol. 47, No. 4, pp. 1121–1135, 2000

Assumptions in the 'van Herk recipe' $m_{PTV} = 2.5\,\Sigma + 0.7\,\sigma$

The dose gradient is described with σ_p =3.2 mm

90% of patients receives a minimum dose of ≥ 95% of the prescribed dose

10% of patients must not receive the prescribed dose

Van Herk, Remeijer; Int. J. Radiat. Oncol. Biol. Phys., Vol. 47, No. 4, pp. 1121–1135, 2000

NETHERLANDS CANCER INSTITUTE ANTONI VAN LEEUWENHOEK

Assumptions in the 'van Herk recipe' $m_{PTV} = 2.5\,\Sigma + 0.7\,\sigma$

The dose gradient is described with $\sigma_p = 3.2$ mm

90% of patients receives a minimum dose of ≥ 95% of the prescribed dose

10% of patients must not receive the prescribed dose
(but not a whole lot less)

Van Herk, Remeijer; Int. J. Radiat. Oncol. Biol. Phys., Vol. 47, No. 4, pp. 1121–1135, 2000

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

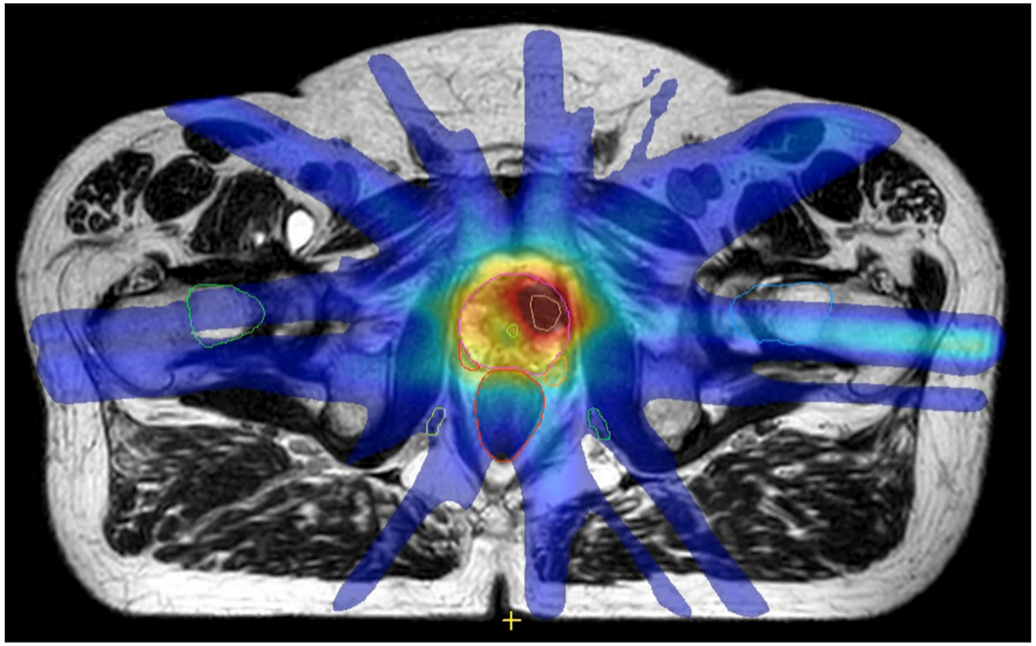
Destination

Low-intermediate risk prostate cancer

5 fractions

GTV: isotoxic boost up to 45 Gy

CTV (prostate): 30 Gy



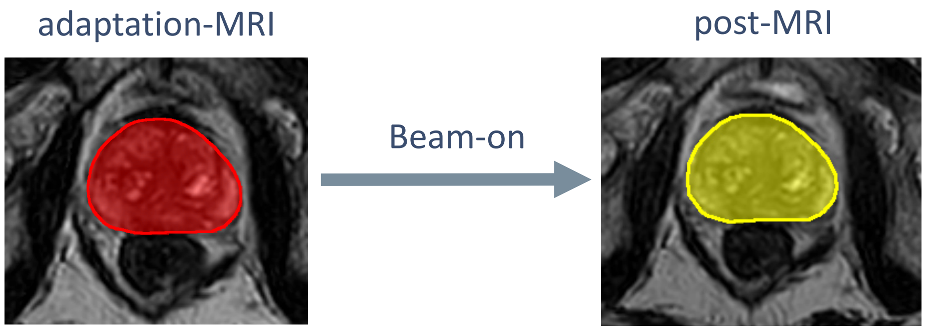
Planning study

23 patients with intermediate risk prostate cancer treated on Elekta Unity 1.5T

T2w MRIs available for adaptation and post-treatment in 5 fractions

GTV: 45 Gy, CTV 30 Gy

PTV = 0 mm



Time interval between adaptation- and post-MRI mean 18 min [14-27]

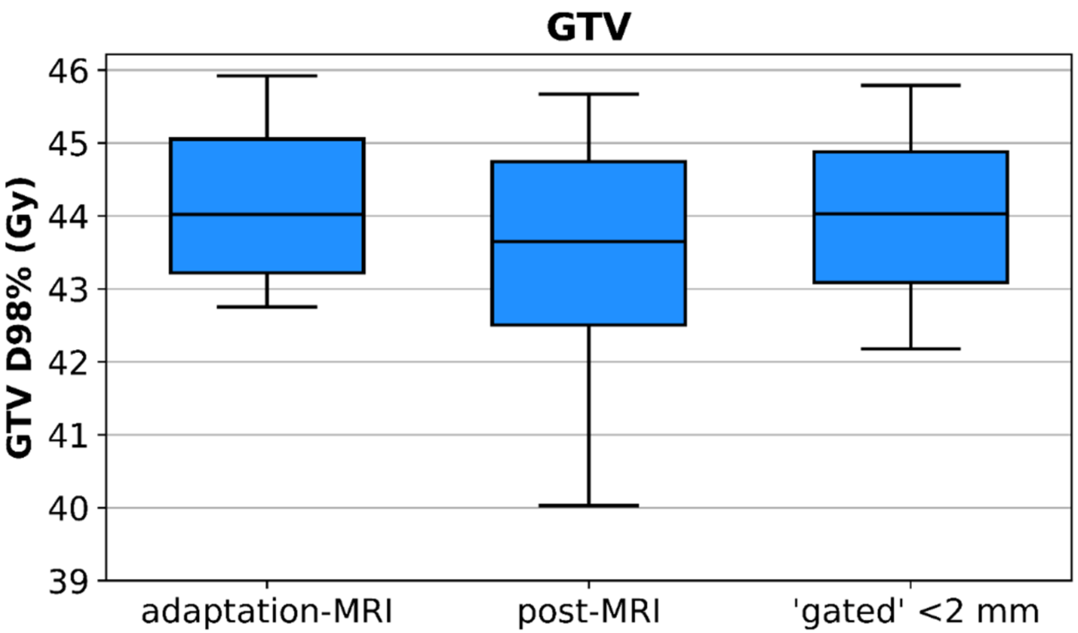
NETHERLANDS CANCER INSTITUTE ANTONI VAN LEEUWENHOEK

Dose coverage of the GTV

D98% > 40 Gy in 90% of fractions

When correcting intra-fraction motion > 2 mm: D98% > 42 Gy in 90% of fractions

Analysis per fraction, renormalized to 5 fractions



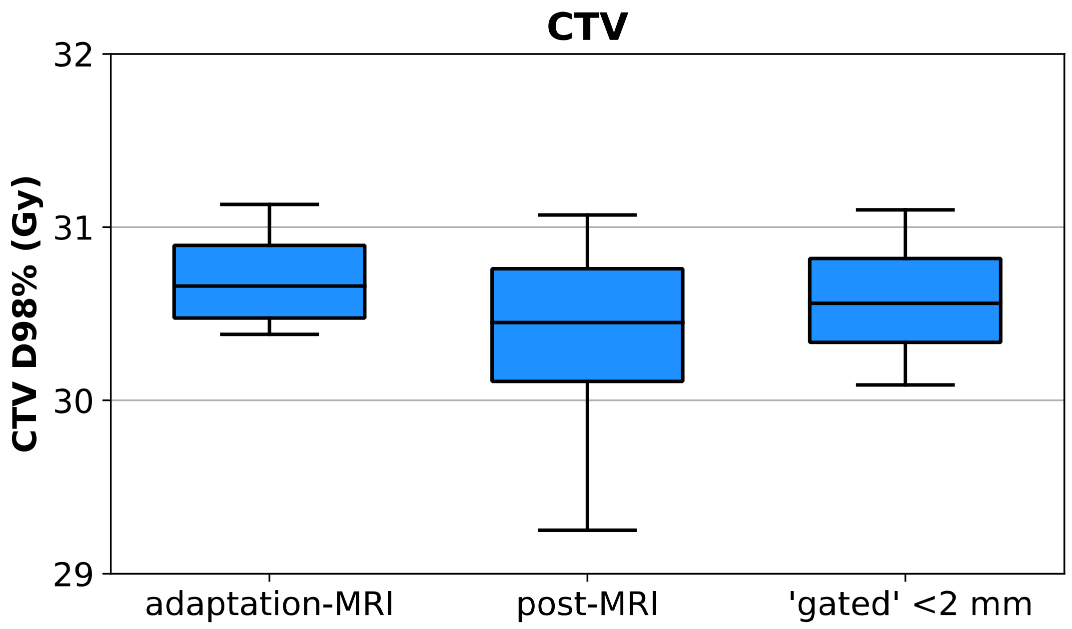
NETHERLANDS CANCER INSTITUTE ANTONI VAN LEEUWENHOEK

Dose coverage of the CTV

D98% > 29 Gy in 90% of fractions

When correcting intra-fraction motion > 2 mm: D98% > 30 Gy in 90% of fractions

Analysis per fraction, renormalized to 5 fractions



NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

Assumptions in the 'van Herk recipe' $m_{PTV} = 2.5\,\Sigma + 0.7\,\sigma$

The dose gradient is described with σ_p =3.2 mm

90% of patients receives minimally the prescribed dose

Tumor cells are homogeneously distributed in the target volume

Van Herk, Remeijer; Int. J. Radiat. Oncol. Biol. Phys., Vol. 47, No. 4, pp. 1121–1135, 2000

Can we estimate the tumor load in the CTV?

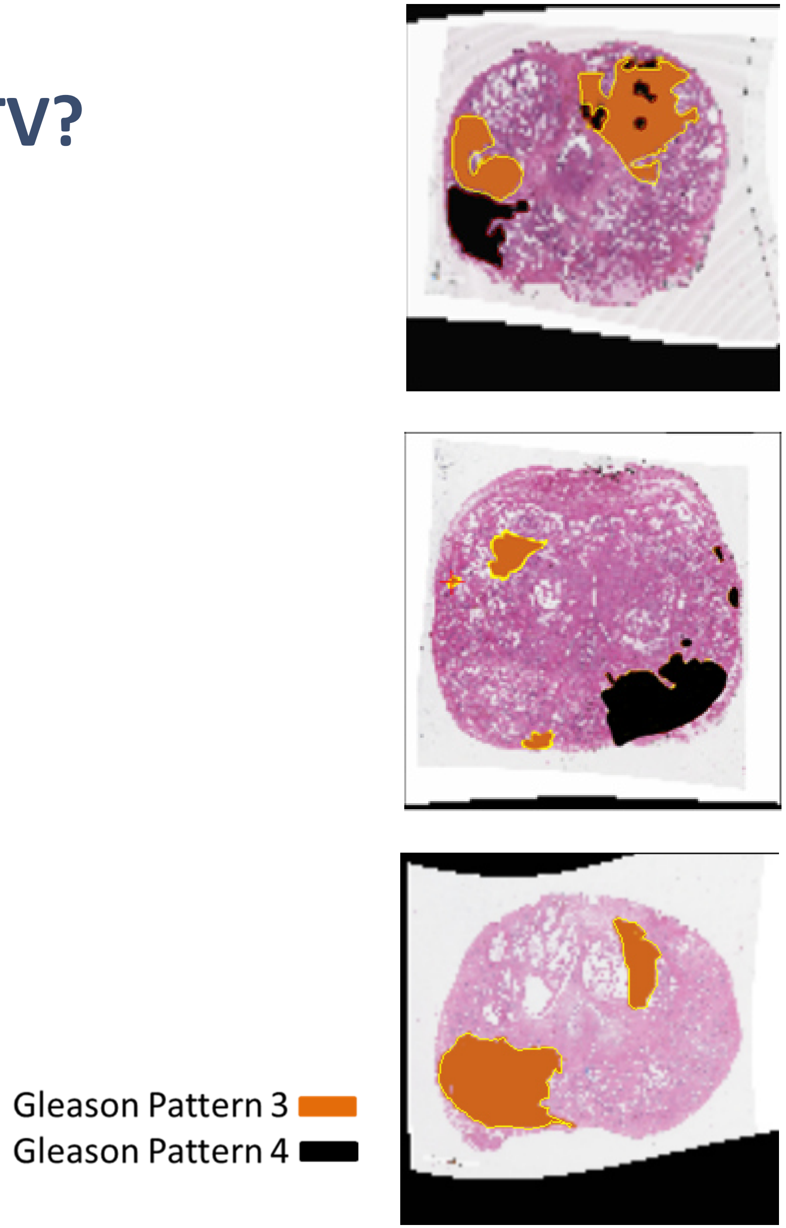
61 prostatectomy specimen

84% of patients had multifocal disease (median 3 foci)

32% of foci smaller than 5 mm diameter

Contribution of small foci to total tumor load 2%

Hollmann et al. Radiother Oncol. 2015 Apr;115(1):96-100



Implications for PTV margins

For CTV the inhomogeneous distribution of tumor cells is not considered in the classical margin recipes

There is a high probability that the underdosed volume contains no cancer at all

The dose doesn't fall to zero

Modern dose distributions: what we shouldn't forget

To express uncertainty, a probabilistic target definition is desirable

With on-line adaptive radiotherapy, positioning errors are substantially reduced

With ultra-hypofractionation, (almost) all errors become systematic

The tumor cells are not homogeneously distributed inside the CTV. This has profound implications for the required PTV margin

Acknowledgements

NKI

Thijs Dassen
Ben Neijndorff
Peter de Ruiter
Thyrza Jagt
Tomas Janssen
Floris Pos

KWF

Elekta

Royal Marsden Hospital/ICR

Alison Tree

Sunnybrook

Danny Vesprini

Elekta

John Christodouleas

University of Wisconsin

Robert Jeraj
Peter Ferjančič