CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD

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UCBL Lyon 1

Dosimetric impact of intra-fraction motion during moderate hypo-fractionated prostate radiotherapy treatment: population-based anisotropic margin for CTV-prostate

F. di Franco[1,2], T. Baudier[1,2], F. Gassa[1], D. Sarrut[1,2], M.C. Biston[1,2]

[1] Léon Bérard Cancer Center, Université de Lyon, Lyon F-69373, France
[2] CREATIS, INSA, Université de Lyon, CNRS UMR5220, Inserm U1044, Lyon F-69622, France

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+

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Located in Lyon, France

León Bérard Cancer Center (CLB)

1700 employees

+11 500 patients/year

37 050 followed patients

2000 patient/year in clinical trials

Our group (~15 persons) is located at CLB

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CREATIS lab

- Medical Imaging research lab
  - ~ 200 persons
  - 4 teams:
    - MYRIAD Modeling & Analysis for Medical Imaging and Diagnosis
    - ULTIM Ultrasound Imaging
    - TOMORADIO Tomographic Imaging and Radiation therapy
    - MAGICS NMR and Optics: from Measure to Biomarker

- Institutions
  - CNRS: French National Centre for Scientific Research
  - Lyon university

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A bit of statistics...

Global Cancer Statistics 2020
19,3 millions new cases
10 millions dead

1 of 6

1 of 5

+ 2,3 millions breast cancer **11,7% of new diagnosis**
11,4% lungs
10% colon
7,3% prostate
5,6% stomach

Cancer treatments

Radiotherapy **Chemotherapy** **Surgery**

2019 Italy: 62% treated by radiotherapy
15% more for 2025

Radiotherapy workflow

The process of radiation therapy will be customized for patients, depending on which form of radiation therapy patients and their physicians choose as their options.

5 steps

1) Initial consultation

2) Simulation

3) Treatment planning

4) Treatment Delivery

5) Post Treatment Follow-up

Prostate cancer (1)

Epidemiology:

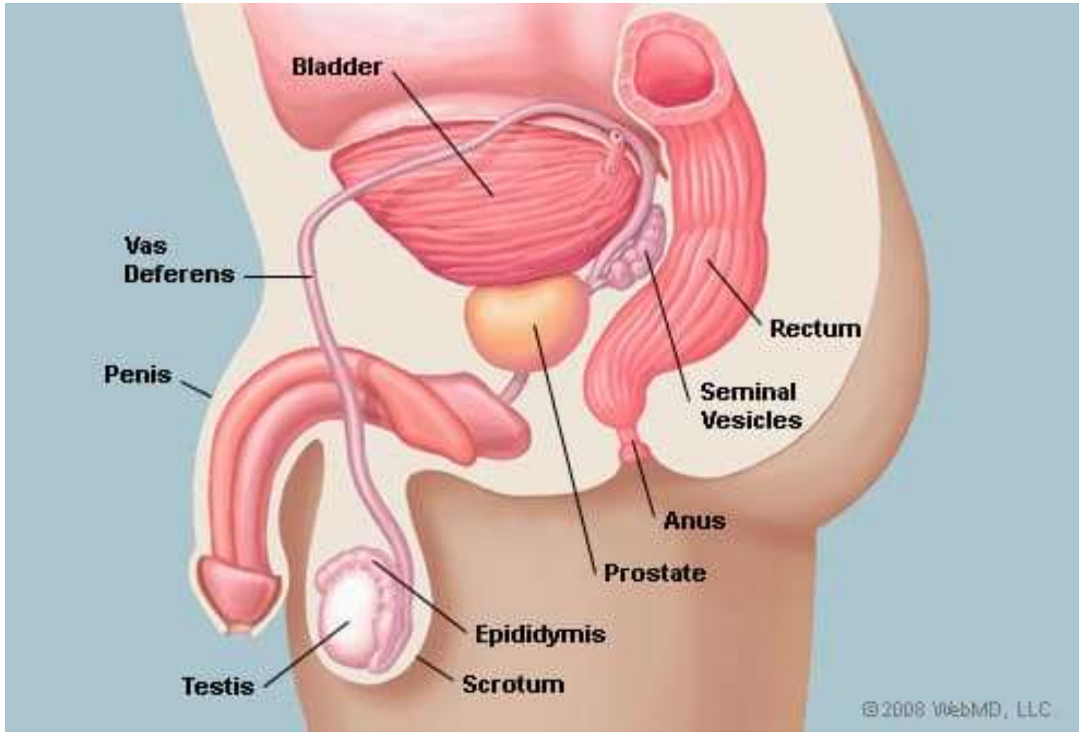
In Italy 1 on 8 men is likely to develop prostate cancer during lifetime
2017: 34.800 new cases
2020: 36.074 new cases (19% of male cancers).

Treatment:

Surgery: prostatectomy
Radiotherapy (also post surgery)
Cryotherapy
Hormone Therapy
Chemotherapy
Immunotherapy

Treatment protocols:

Total dose of 66 Gy (prostatectomy) 74-80 Gy (prostate)
2 Gy per fraction (> 30 fractions) **Conventional radiotherapy**
> 2 Gy per fractions **Hypofractionation**



Prostate cancer (2)

Treatment protocols:

2 Gy per fraction (> 30 fractions) **Conventional radiotherapy**
3 or 5 Gy per fraction **Hypofractionation**

Why more fractions?

PROSTATE: very sensitive to the dose administered for each fraction $\alpha/\beta = 1{,}4$ **LINEAR QUADRATIC MODEL**

Reducing the number of fractions by increasing the dose of each could improve local tumor control

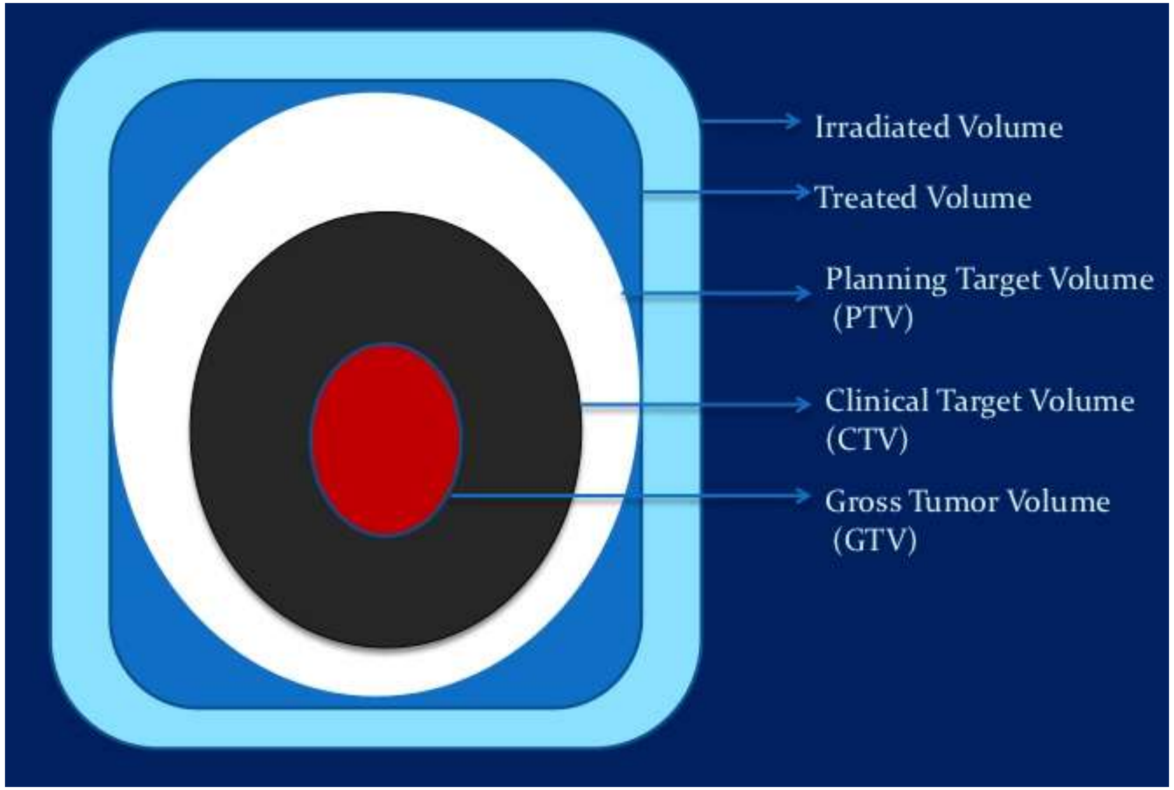
Hypofractionated radiation therapy: effective in treating prostate cancer at high risk of recurrence

Higher dose per fraction = 3 to 5 Gy per fraction → shorter treatments

Need to increase accuracy in dose delivery while reducing treatment margins, which is inconsistent with increased session time.

Treatment margins (1)

International Commission on Radiation Units and Measurements (ICRU)

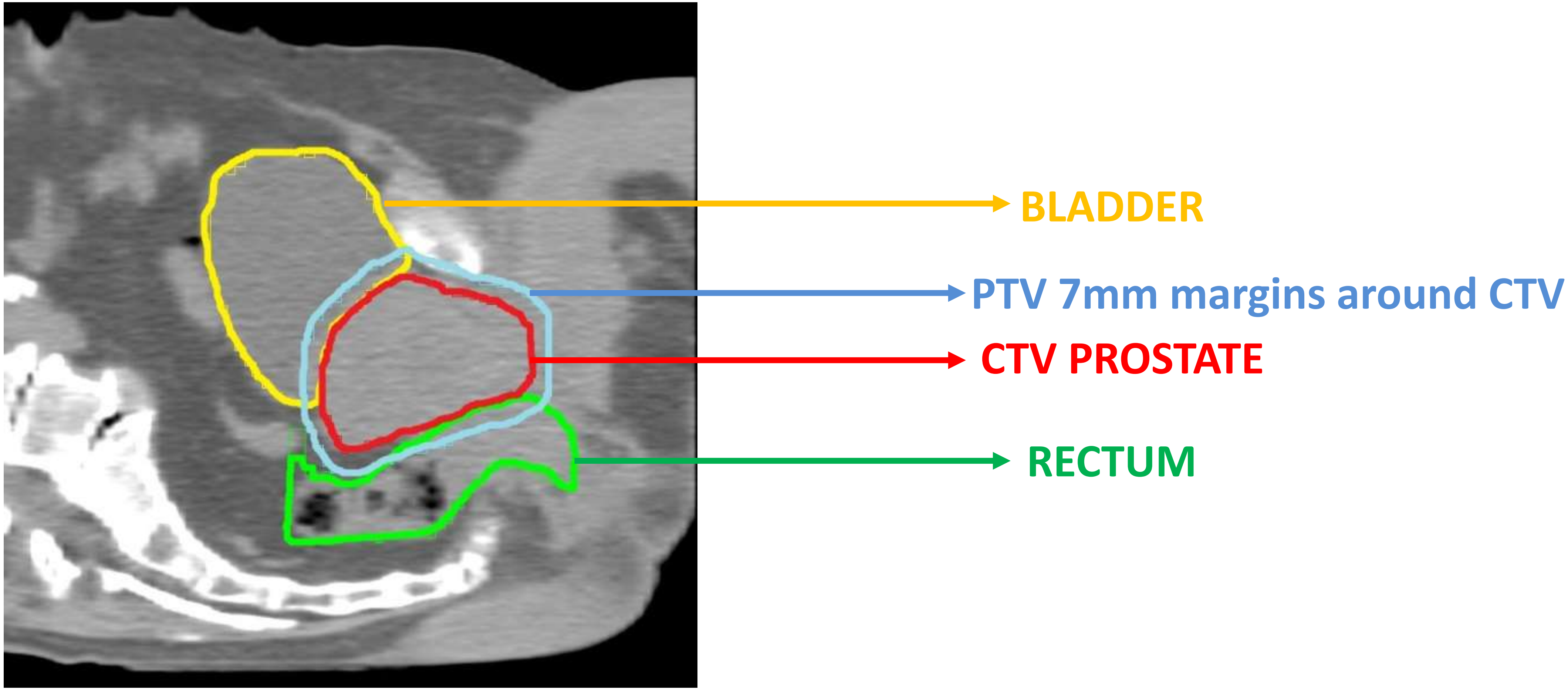


GTV = the gross demonstrable location and extent of tumor. It is what can be seen, palpated or imaged

CTV = contains the GTV, plus a margin for sub-clinical disease spread which therefore cannot be fully imaged

PTV = allows for uncertainties in planning or treatment delivery. It is a geometric concept designed to ensure that the radiotherapy dose is actually delivered to the CTV

Treatment margins (2)



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Prostate movements

Inter-fraction motion = due to patient positioning → target position is not the same position between simulation and delivery days

Intra-fraction motion = due to anatomical movements during the treatment → target position is not the same between the beginning and the end of the session

Patient & session's dependent
Anatomical variations: bladder & rectum
Directions dependent

How to monitor those movements?

How to monitor movements? (1)

Various techniques have been developed to enable real-time online prostate localization and monitoring:

- implanted electromagnetic transponders
- fiducial markers (FMs)
- real-time X-ray imaging
- MRI-linac imaging

Radiofrequency systems - need to implant transponders inside the target volume:

- Calypso (Varian Medical Systems, Palo Alto, CA)
- RayPilot (Micropos Medical AB)

Ultrasound systems - don’t need to implant transponders inside the target volume:

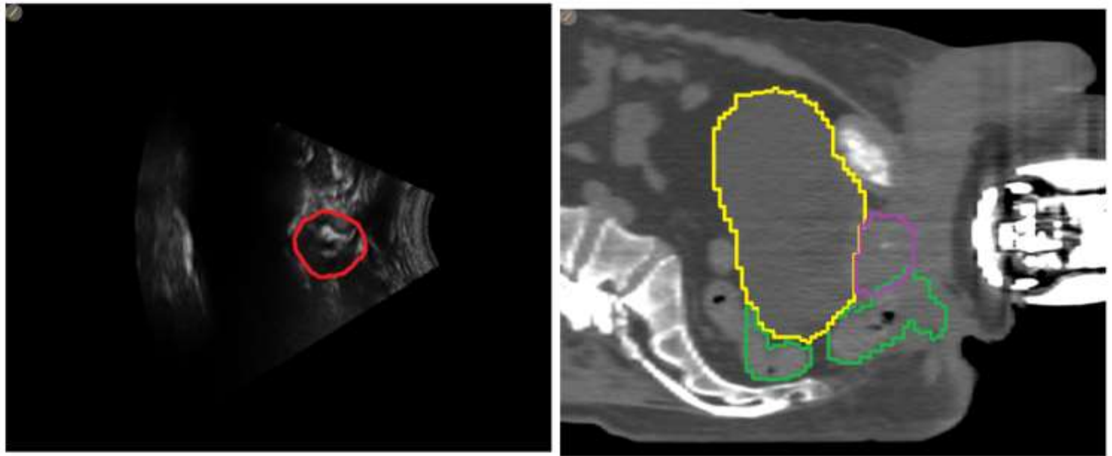
- Clarity (Elekta Inc., Stockholm, Sweden)

How to monitor movements? (2)

Clarity® TPUS

- TransperiNeal (TP) ultrasound (US) probe allowing the pelvic area to be viewed during treatment without interfering with the beam
- Real-time reconstruction of 3D prostate's images
- A reference US image is acquired during the treatment simulation stage, with the patient in the same position as the CT image. During the treatment sessions, a US acquisition is performed and then re-aligned to the reference US image

Elekta



Our objective (1)

2000

THE PROBABILITY OF CORRECT TARGET DOSAGE: DOSE-POPULATION HISTOGRAMS FOR DERIVING TREATMENT MARGINS IN RADIOTHERAPY

MARCEL VAN HERK, PH.D., PETER REMEIJER, PH.D., COEN RASCH, M.D. AND JOOS V. LEBESQUE, M.D., PH.D.

2018

Determination of Intrafraction Prostate Motion During External Beam Radiation Therapy With a Transperineal 4-Dimensional Ultrasound Real-Time Tracking System

Dwi Seno Kuncoro Sihono [1], Michael Ehmann [2], Sigrun Heitmann [2], Sandra von Swietochowski [2], Mario Grimm [2], Judit Boda-Heggemann [2], Frank Lohr [3], Frederik Wenz [2], Hansjörg Wertz [2]

2020

Duration-dependent margins for prostate radiotherapy—a practical motion mitigation strategy

Eric Pei Ping Pang[1,2] · Kellie Knight[2] · Sung Yong Park[1] · Weixiang Lian[1] · Zubin Master[1] · Marilyn Baird[2] · Jason Wei Xiang Chan[1] · Michael Lian Chek Wang[1,3] · Terence Wee Kiat Tan[1,3] · Melvin L. K. Chua[1,3,4] · Eu Tiong Chua[1,3] · Wen Shen Looi[1,3] · Wen Long Nei[1,3] · Jeffrey Kit Loong Tuan[1,3]

According to the literature, large displacements (>1cm) can occur during the treatment session.

Prostatic movements are generally more important in AP and SI directions

Numerous "margin recipes" for the correction of inter-fraction movement have been proposed in the literature but these do not always consider intra-fraction movement.

Our objective (2)

We want to propose

Population-based study

To retrieve

Non-isotropic margins

Using

A real-time intrafraction monitoring device

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Mat & Met (1)

18 patients – **346** sessions

Randomly chosen from a cohort of 46 (MHyF) patients

Re-planning process: 0, 3, 4, 5 and 6 mm CTV-to-PTV margins

Auto-planning optimization algorithm
Monaco TPS v5.59
Elekta

Prostate displacements
3D

Clarity Autoscan for prostate
Elekta

Are the protocol's constraints respected in presence of motion?

Moderate hypo-fractionated radiation treatment: 60 Gy in 20 fractions to the CTV

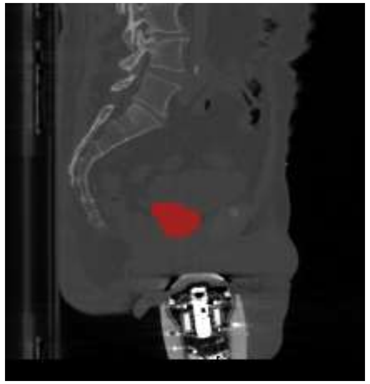
Treatment goal: 100% of the prescribed dose must cover 99% of the CTV-target (prostate)

PROFIT clinical trial

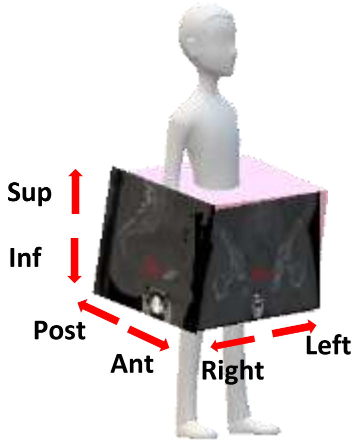
Mat & Met (2)

[1] **Voxel shifting method**: evaluate the robustness of the treatment plan moving the structures with the shifts observed during the treatment process.

CTV Prostate structure
No motion



Displace the CTV in 3D
(LR SI AP directions)



Treatment duration: 200-600s
Structure motion: each 5 s

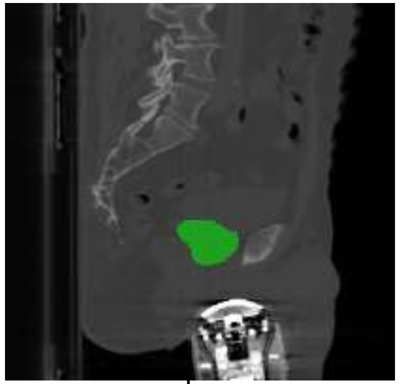
Moved CTV structure

[1] Unkelbach, Jan, et al. "Robust radiotherapy planning." Physics in Medicine & Biology (2018).

Mat & Met (3)

Moved CTV structure

Isodose 60 Gy



Superimpose the two structures to study CTV's coverage

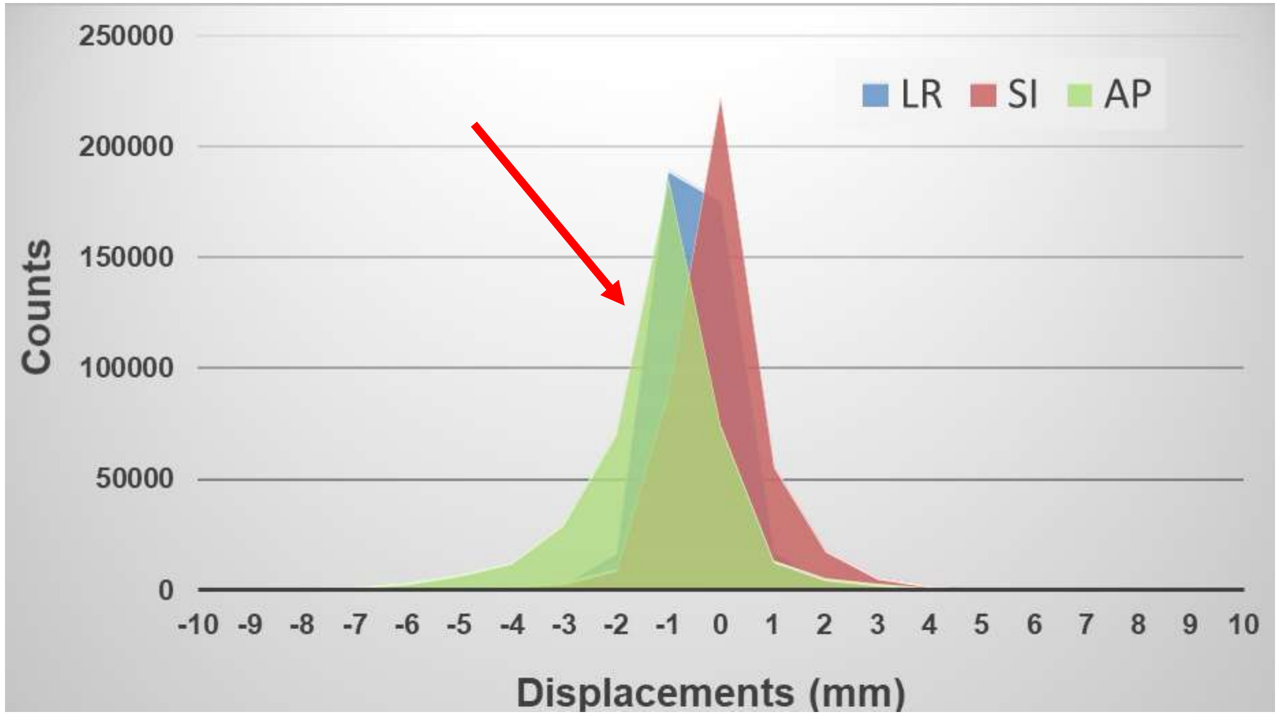
% of CTV outside the ISO 60Gy

Results (1)

Tot # of patient = **46**
Tot # of sessions = **876**

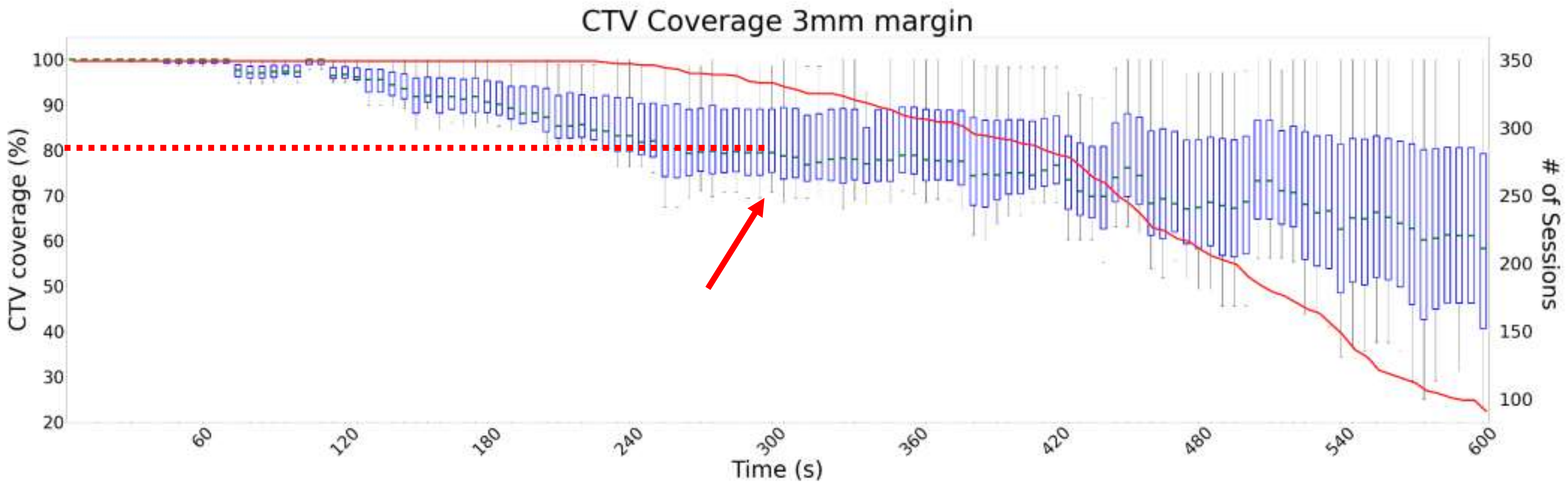
Cumulative intra-fractional prostate displacements

	Mean (mm)		
Time (min)	LR	SI	AP
1	0.0 ± 0.4	0.0 ± 0.7	-0.1 ± 0.6
2	0.0 ± 0.4	0.1 ± 0.7	-0.2 ± 0.6
3	0.0 ± 0.4	0.2 ± 0.7	-0.2 ± 0.6
4	0.0 ± 0.4	0.2 ± 0.7	-0.3 ± 0.6
5	0.0 ± 0.4	0.3 ± 0.7	-0.4 ± 0.6
6	0.0 ± 0.4	0.3 ± 0.7	-0.5 ± 0.7
7	0.0 ± 0.4	0.4 ± 0.8	-0.6 ± 0.7
8	0.0 ± 0.4	0.4 ± 0.8	-0.6 ± 0.7
9	0.0 ± 0.4	0.4 ± 0.8	-0.7 ± 0.7
10	0.0 ± 0.4	0.4 ± 0.8	-0.7 ± 0.7



Greater displacements in INFERIOR and POSTERIOR directions

Results (2)



CTV Coverage 3mm margin
CTV coverage (%)
100
90
80
70
60
50
40
30
20
60
120
180
240
300
360
420
480
540
600
Time (s)
350
300
250
200
150
100
# of Sessions

Results (3)

% of fractions well-covered by ISO100 for different isotropic margins, at different time

Time (min)	0 mm	3 mm	4 mm	5 mm	6 mm
1	97	99	100	100	100
2	93	97	99	99	100
3	83	91	95	98	100
4	76	83	89	96	98
5	70	79	84	91	97
6	71	79	84	92	96
7	69	77	81	91	95
8	60	67	74	81	95
9	58	63	72	81	92
10	58	58	69	78	90

Results (4)

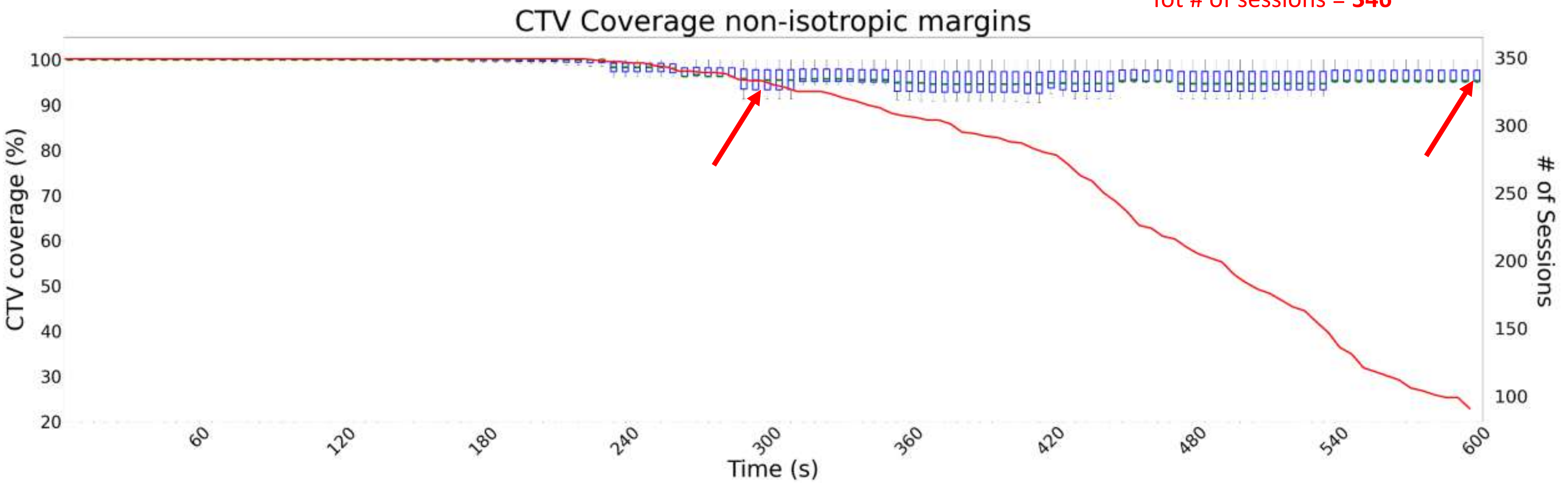
Necessary non-isotropic margins (mm) for meeting 95%/99% coverage criteria

	95% PP - 99% D					
Time (min)	**Left**	**Right**	**Superior**	**Inferior**	**Anterior**	**Posterior**
1	0	0	0	0	0	0
2	0	0	0	0	0	2
3	0	0	0	0	0	3
4	0	0	0	2	2	4
5	0	0	0	3	2	5
6	0	0	2	3	3	5
7	0	0	2	3	3	5
8	0	1	2	3	3	6
9	0	1	3	4	4	7
10	0	1	3	4	4	8

Tot # of patient = **46** Tot # of sessions = **876**

Results (5)

Tot # of patient = **18**
Tot # of sessions = **346**



Constraints on CTV prostate were achieved in 95% of fractions after 5 minutes treatment. We obtain the same mean target coverage as a homogeneous margin of 5 mm but by drastically reducing margins in LR, SI and anterior directions.

Same situation after 10 minutes treatment.

Results (6)

Non Isotropic Margins						
Authors	# of patients	Observation time (min)	Margins LR (mm)	Margins SI (mm)	Margins AP (mm)	Notes
Pang et al. (17)	55	8	1.02	2.41	2.65	Prostate monitoring: Clarity 4D TPUS Margins calculation: Van Herk's formula
		15	1.84	4.29	4.63	
Sihono et al. (8)	38	4	1.25	1.10	1.33	Prostate monitoring: Clarity 4D TPUS Margins calculation: Van Herk's formula
Steiner et al. (23)	17	15	2.3	3.9	6.2	Prostate monitoring: Fiducials Margins calculation: Van Herk's formula
di Franco et al.	46	4	0.6	1.3	2.4	Prostate monitoring: Clarity 4D TPUS Margins calculation: Van Herk's formula
		8	1.2	2.7	5.2	
		10	1.5	3.2	6.2	
Asymmetric Margins						
Pang et al. (13)	60	8	0.8 left 0.8 right	1.7 sup 2.7 inf	1.7 ant 2.9 post	Prostate monitoring: Clarity 4D TPUS Margins calculation: Van Herk's formula 90PP – 95D
di Franco et al.	46	8	0.4 left 0.5 right	0.7 sup 1.5 inf	0.9 ant 3.2 post	Prostate monitoring: Clarity 4D TPUS Margins calculation: Van Herk's formula 90PP – 95D
di Franco et al.	46	8	0 left 1 right	3 sup 3 inf	3 ant 6 post	Prostate monitoring: Clarity 4D TPUS Margins calculation: voxel shifting 95PP – 99D
		10	0 left 1 right	3 sup 4 inf	4 ant 8 post	

Our results are in line with recent literature.

The greatest differences are in AP directions:

- patients' diet
- dosimetric criterion
- treatment protocol

Conclusions

Prostate movements impact dose distribution and target coverage

Prostate shifts are not isotropic: larger shifts in posterior & inferior directions

Increasing treatment time, larger prostate displacements could be observed

Anisotropic and non-symmetric margins would be required to optimally take into account intra-fraction motion especially during hypofractionated treatments

Ongoing studies

- Influence of patient anatomical changes (bladder and rectal filling) on the dose delivered during HF radiotherapy treatments
- Influence of patient anatomical changes (bladder and rectal filling) on prostate displacements
- Exploring the dose delivered to the OARs using asymmetric margins

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Grazie per l’attenzione

Francesca.Di-Franco@creatis.insa-lyon.fr