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Hadrontherapy in 4D

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Presentation outline

Challenge of 4D therapy (respiratory correlated irradiation)

- ✓ X-ray radiotherapy inheritage
- ✓ Status and perspectives in particle therapy

4D treatment planning

- ✓ 4D imaging and motion modelling

4D dose delivery in particle therapy

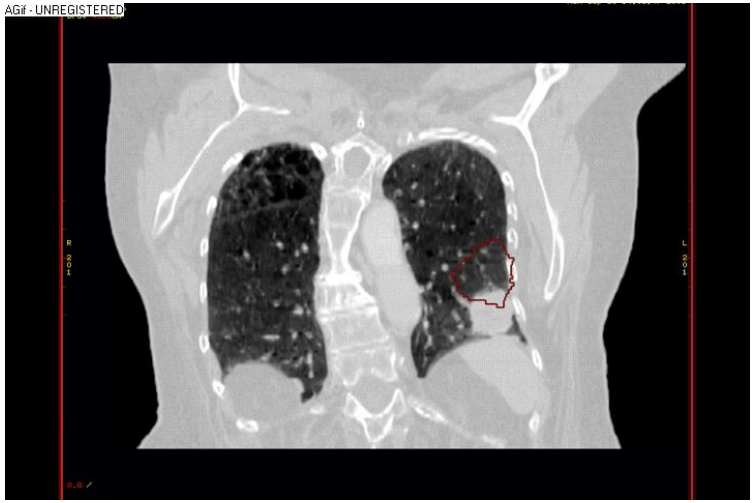
- ✓ Experimental studies (local models)
- ✓ Prediction of daily anatomical changes (global models)

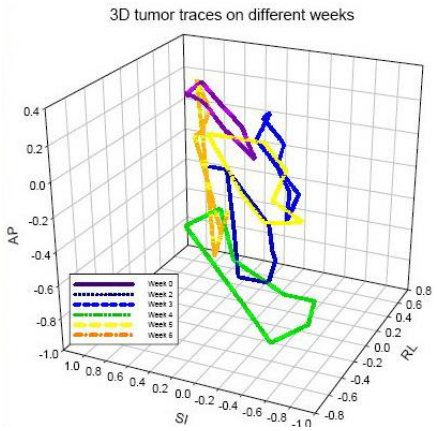
4D treatment verification

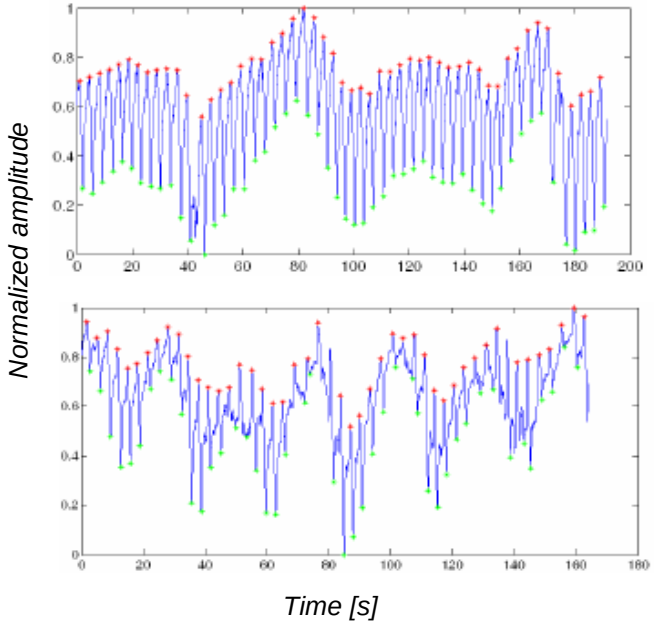
- ✓ Motion compensated in-vivo PET-based dosimetry
- ✓ 4D transmission imaging

Respiratory correlated (4D) therapy

- ✓ **Challenge**: actively targeting a movable and deformable volume featuring variable kinematics and deformation patterns
  - ✓ Combination of inter- and intra-fractional deviations
  - ✓ Tasks (on-the-fly):
    1. **Target localization**
    2. **Treatment geometry adaptation** (beam direction, conformation)

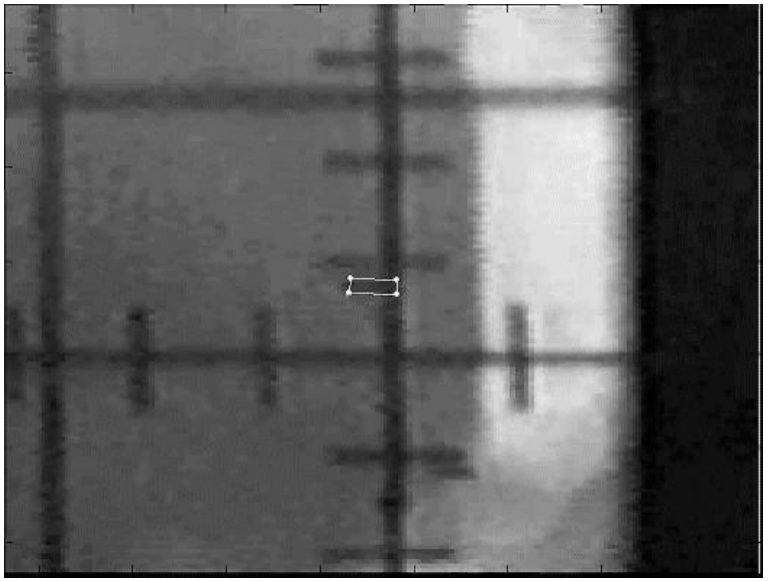


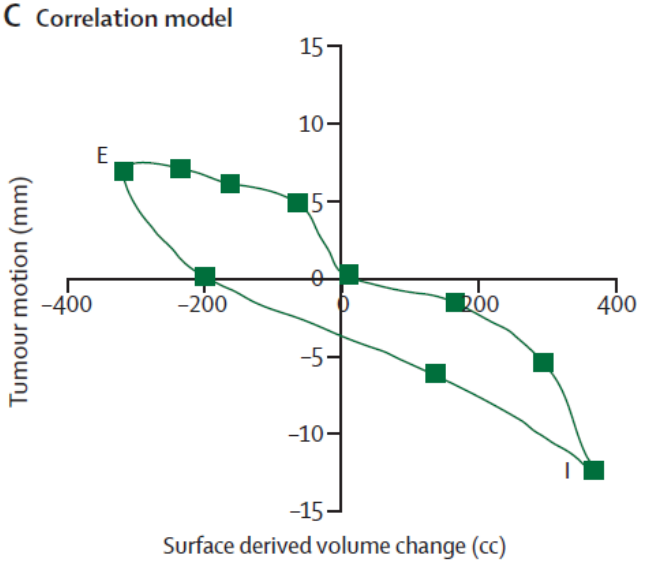




Motion detection strategies
The X-ray radiotherapy heritage

- ✓ Direct tumor imaging
  - ✓ Marker-based methods
    - ✓ X-ray [Shirato et al. C*ancer Sci* 2012;103:1–6]
    - ✓ EM (Calypso^{TM}) [Balter et al. *IJROBP* 2005;61:933–37]
  - ✓ Markerless
    - ✓ Ultrasound [Schlosser et al *Med Phys* 2010;37:6357–67]
    - ✓ Real-time X-ray image registration [Gendrin et al *Radiother Oncol* 2012; 102:274–80**]**
    - ✓ MRI [Fallone et al *Med Phys 2009;*36:2084–88]
- ✓ Indirect tumor localization
  - ✓ Correlation with surrogates
    - ✓ Spirometric measurements [Hughes et al *Radiother Oncol 2009;* 91: 336–41]
    - ✓ Surface fiducials [Baroni et al., *Radiother Oncol 2000;*54:21–27]

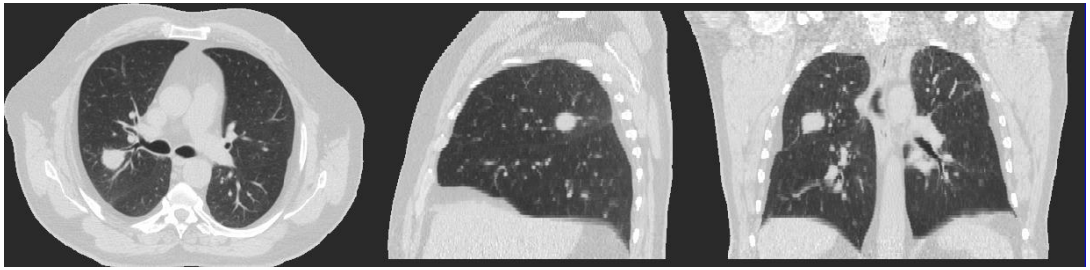


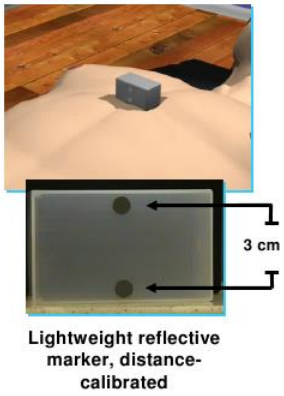


Respiratory correlated / compensated treatment planning and delivery: X-ray radiotherapy

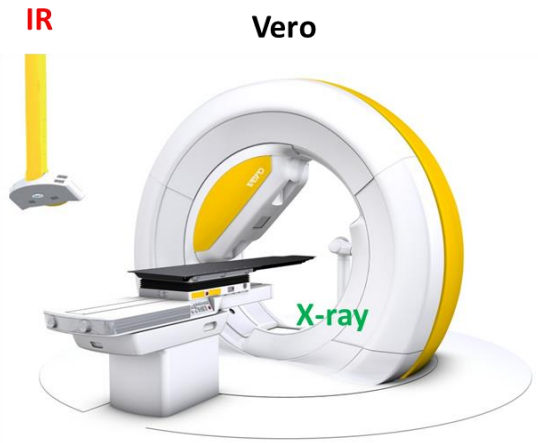
(External) surrogates optical tracking and position correlation with inner anatomy is state of the art in photon therapy for:

- time resolved imaging for treatment planning
- breath-hold irradiation (motion suppression)
- respiratory gating (motion correlation, intermittent irradiation)
- tumor tracking (motion correlation, continous irradiation)

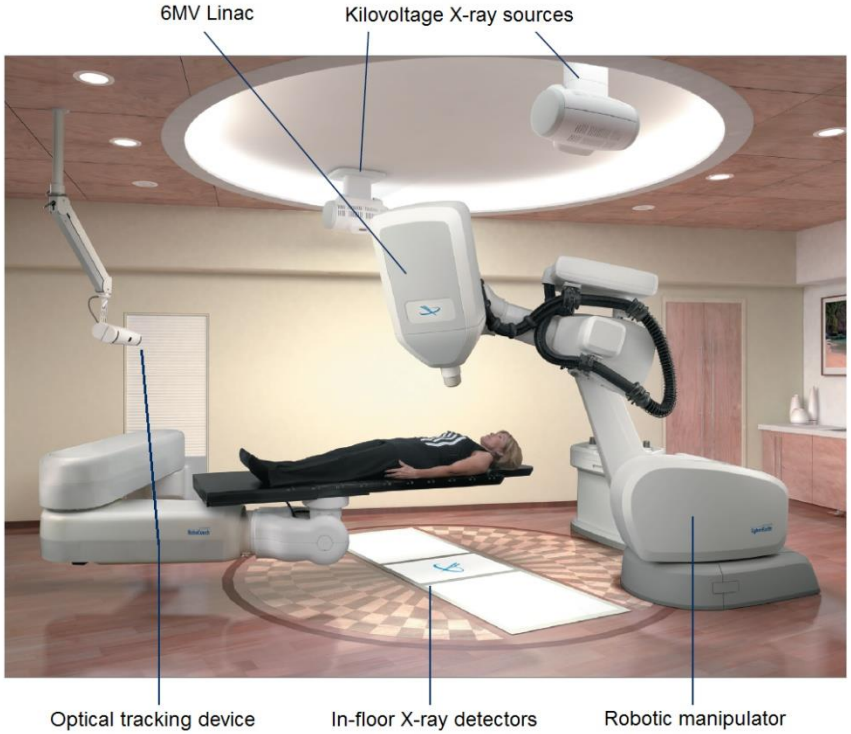


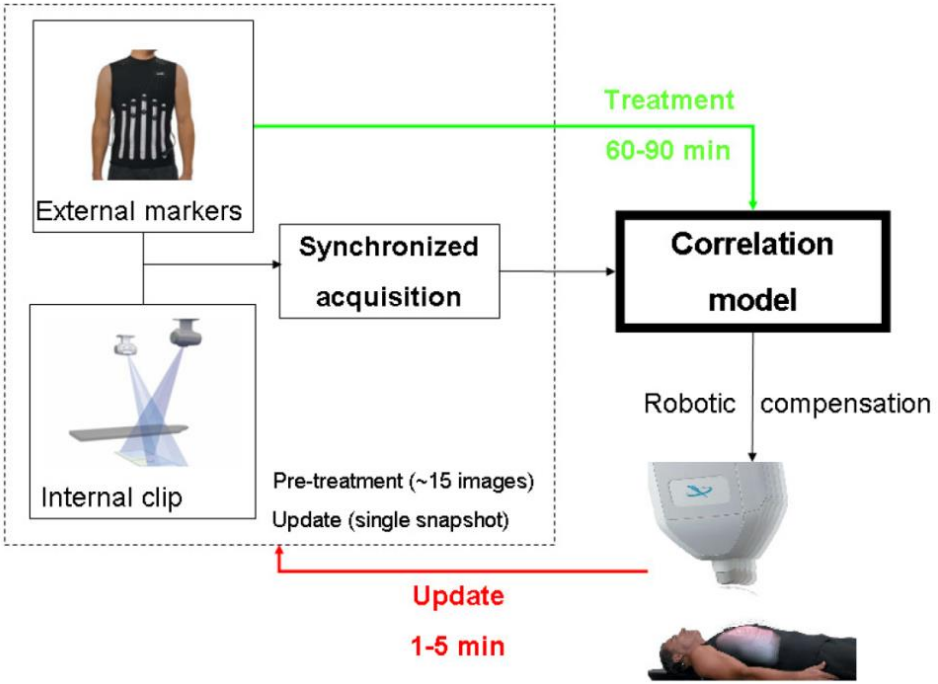


CyberKnife

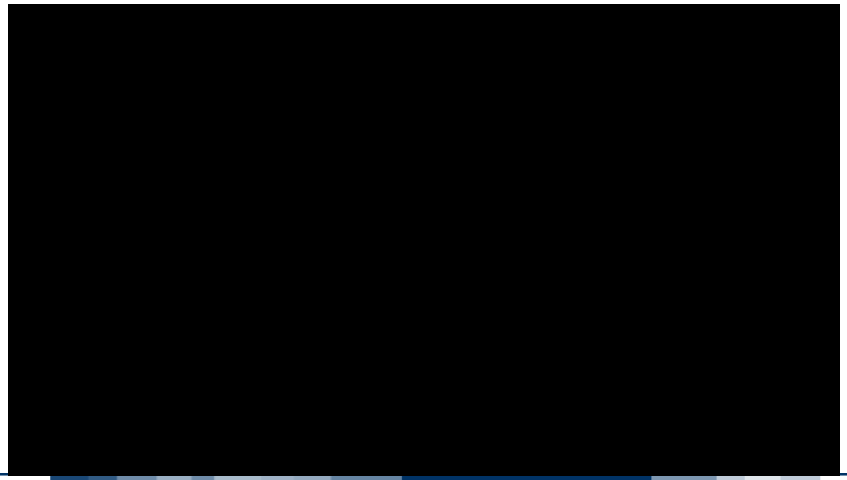


Tumor tracking based on correlation models: the Cyberknife-Synchrony case





- Tumour tracking accuracy better than 1.5 mm *[Kilby 2010]*
- Correlation errors > 5 mm with breathing irregularities *[Torshabi 2010]*



Clinical effectiveness of tumor tracking
(Cyberknife -Synchrony treatments)

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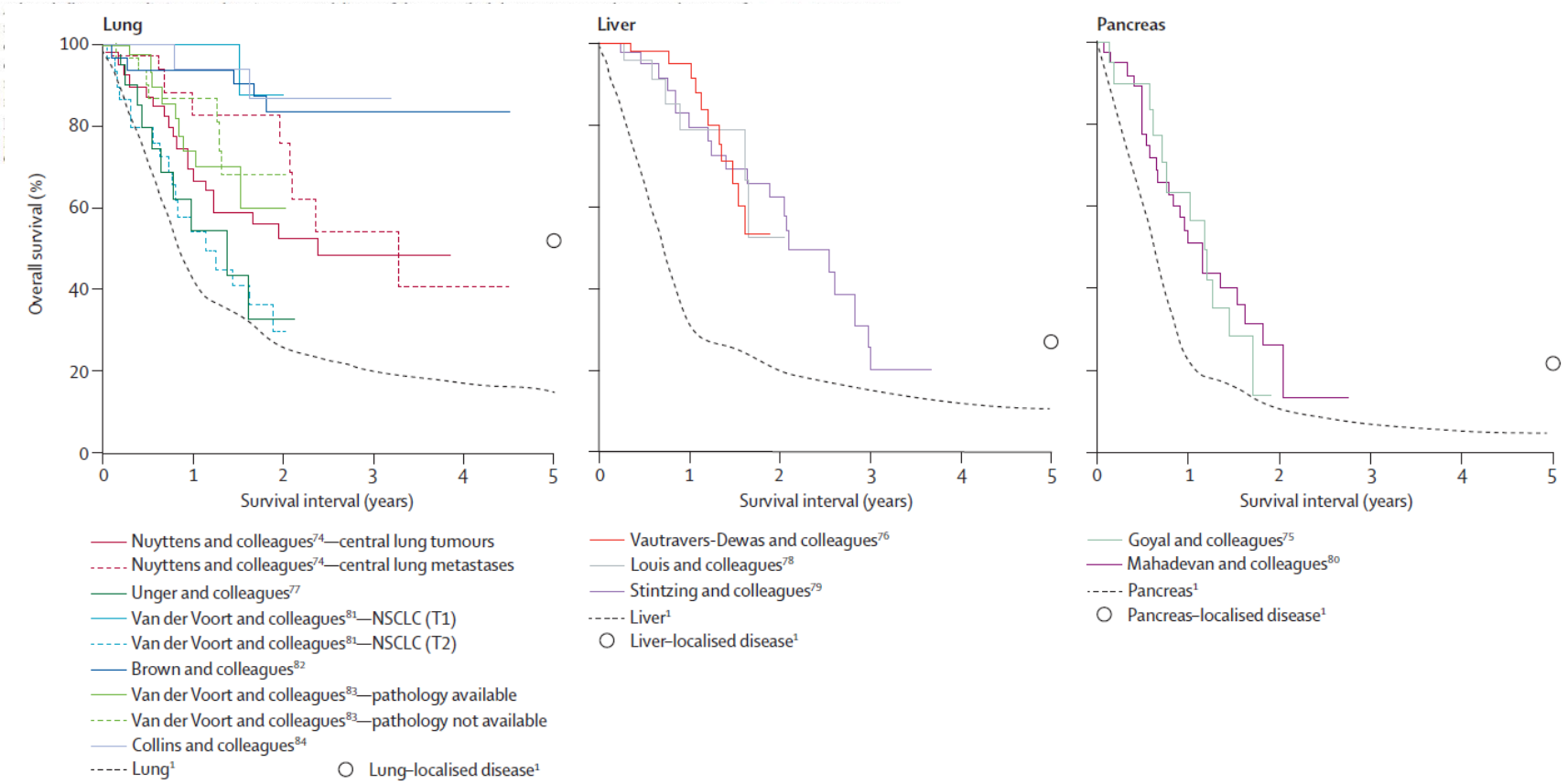
(Riboldi et al, Lancet Oncol 2012)

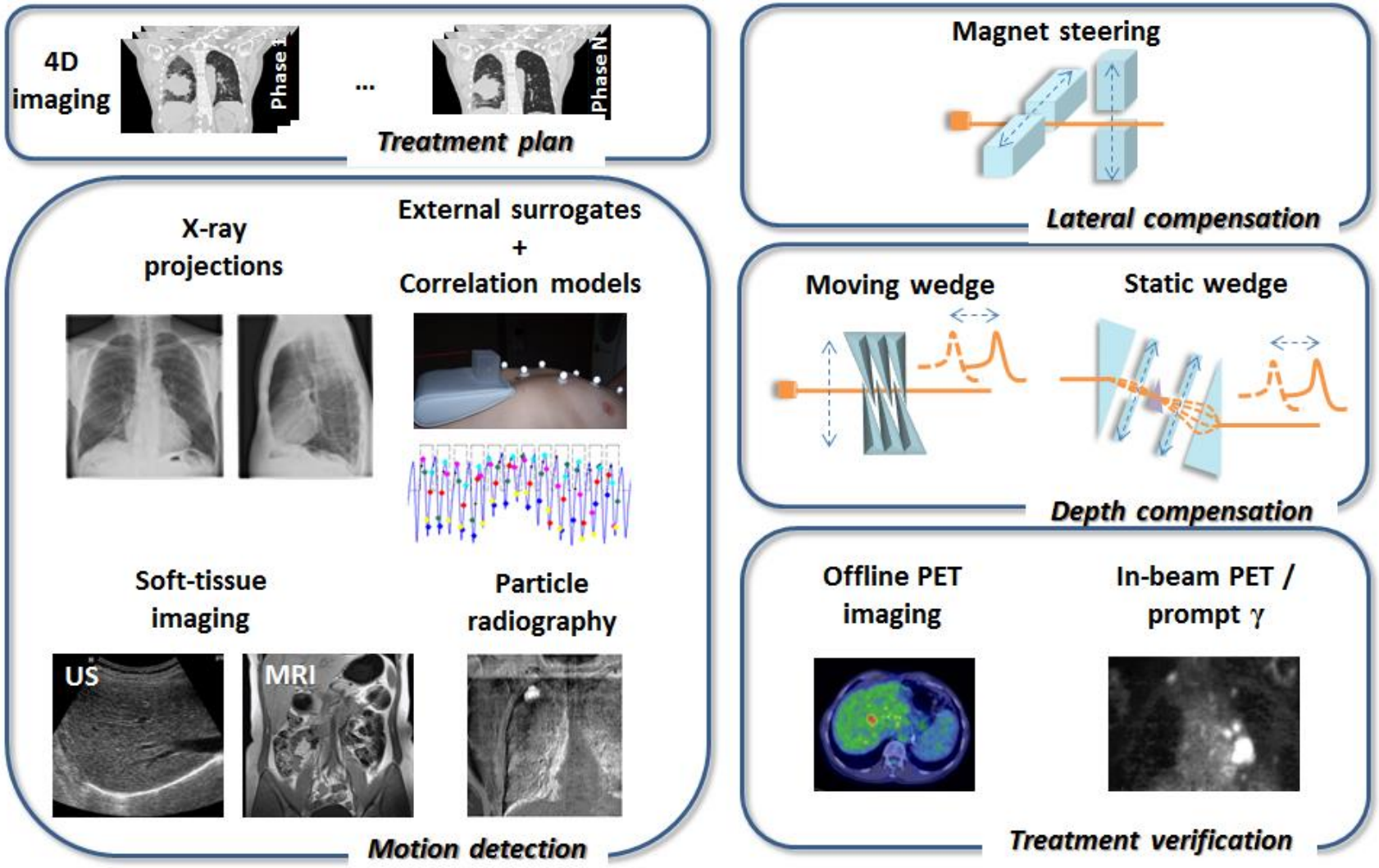
Review

Real-time tumour tracking in particle therapy: technological developments and future perspectives

Marco Riboldi, Roberto Orecchia, Guido Baroni



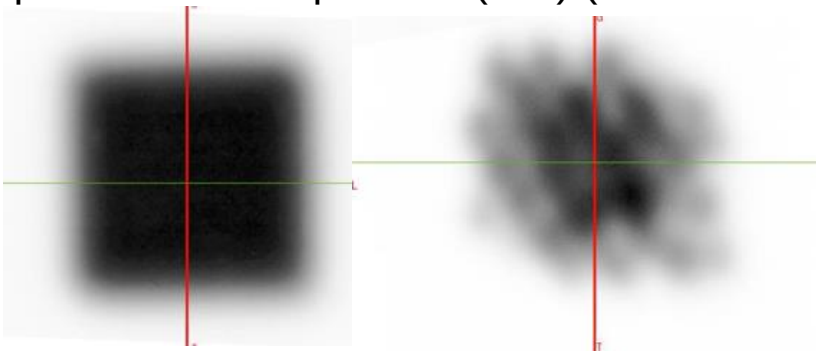
From 4D X-ray to 4D hadrontherapy



4D hadrontherapy

Current status

- ✓ Respiratory gating applied clinically with passive scattering (ext-int correlation)
- ✓ First cases with ion-beam active scanning reported for HCC patients (HIT) (ext-int correlation)
- ✓ No tumor tracking attempted clinically

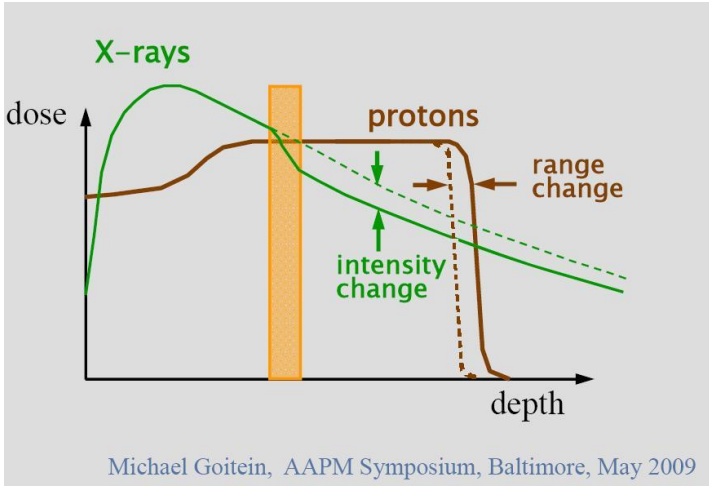


Greatest caution motivated by

- ✓ 4D CT artefacts (uncertainties)
- ✓ Interplay effects (active scanning)
- ✓ Range uncertainties

What is needed

- ✓ Robust artefacts-free treatment planning
- ✓ Accurate tumor localization (local models)
- ✓ Estimation of daily global anatomical changes

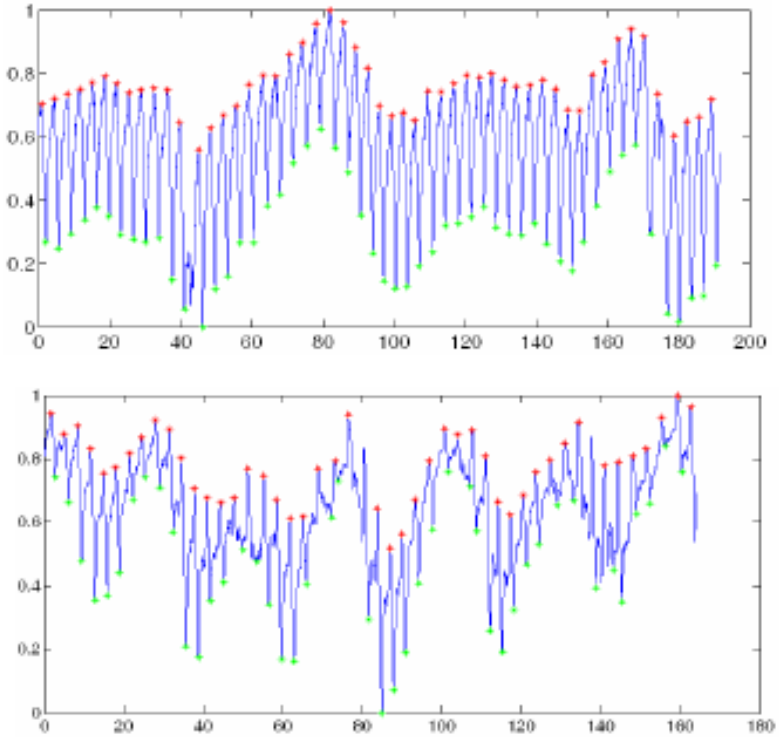


Treatment planning: 4D CT artefacts

Motion monitoring in 4D CT based on **mono-dimensional signal**:

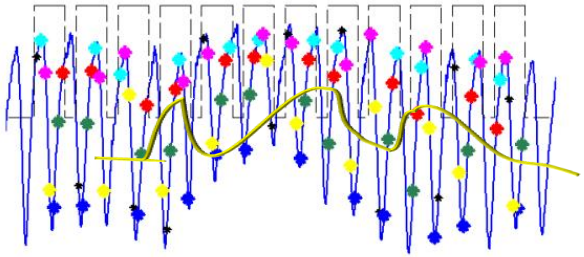
- **uncertainties in breathing phase detection**

→ **Additional contribution to motion artifacts** (besides irregularities)

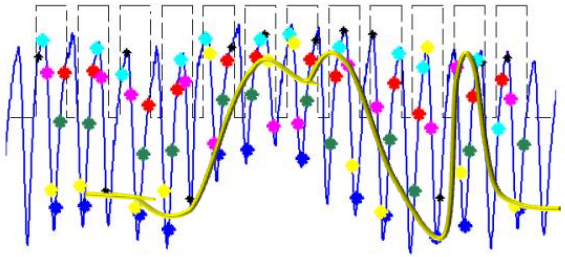


4D CT – multiple markers and data mining techniques

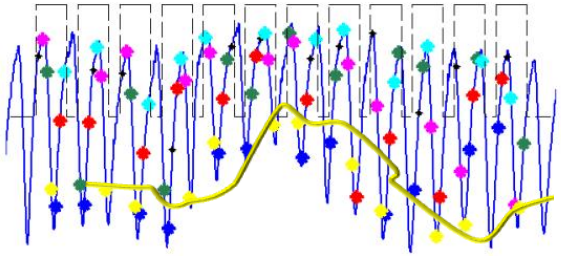
RPM phase

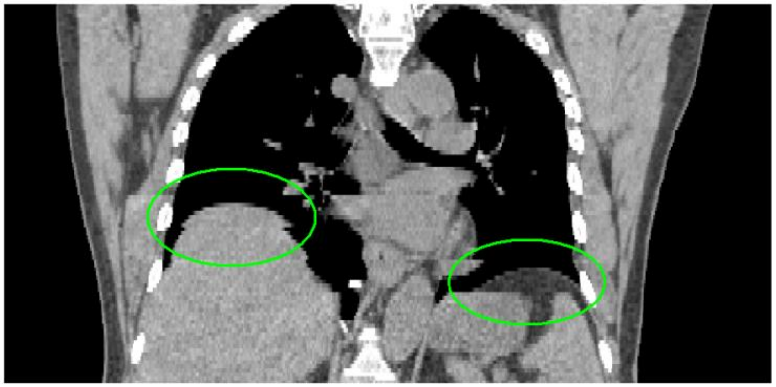


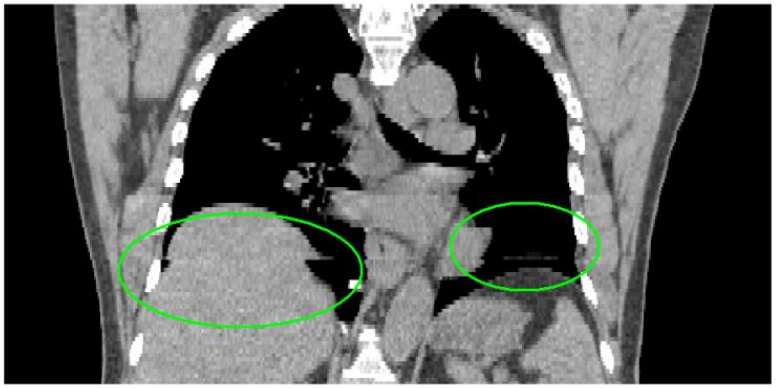
RPM amplitude



Multiple markers



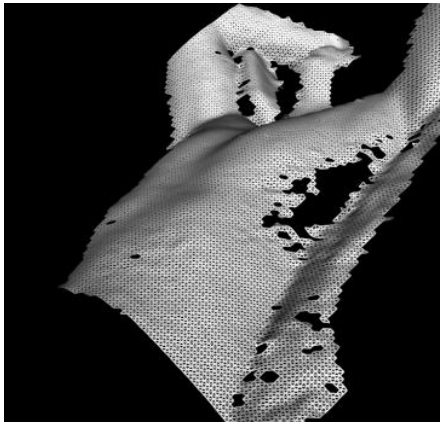


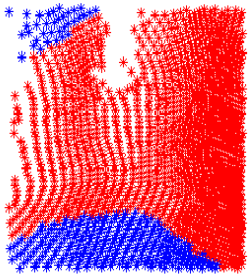


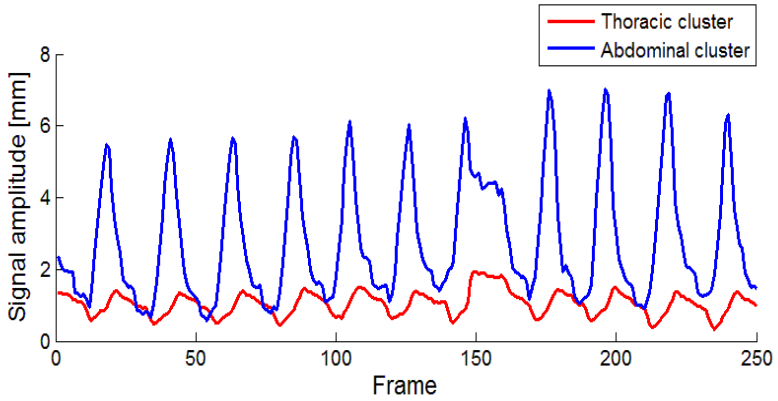
(Gianoli et al, Med Phys 2011)

4D CT based on surface optical tracking: enrich information on rib cage kinematics

- Extract the 3D trajectory of non-correspondent surface points acquired with optical systems (deformable mesh registration) (*Amberg 2007*; *Schaerer 2012*)
- Synthesis of a multi-regional respiratory motion model for robust image sorting and/or for respiratory correlated delivery







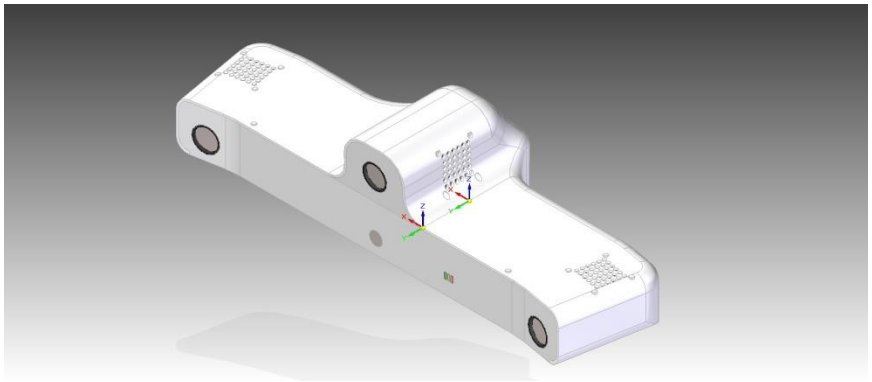
Correlation with diaphragm motion (US) (median ± quartile)(5 subjects)

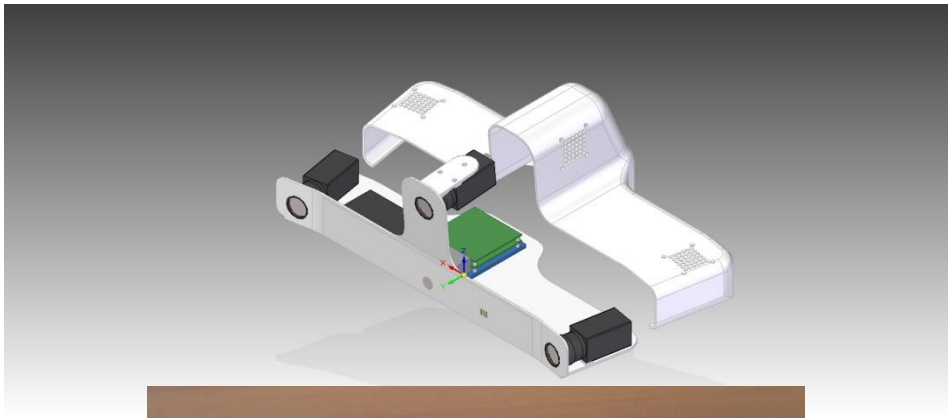
- Principal Component Analysis (PCA)
- K-means clustering
- Self-Organizing Maps (SOM)

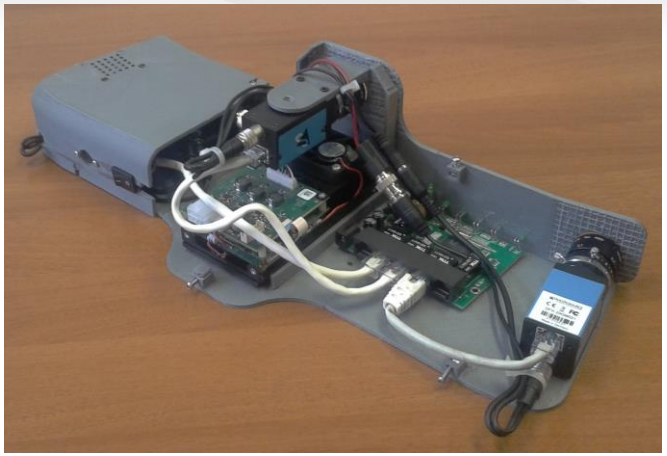
	PCA	K-means	SOM
Pearson correlation coefficient*	0.90 ± 0.17	0.93 ± 0.06	0.91 ± 0.38
Root-mean-square error*	0.15 ± 0.10	0.11 ± 0.06	0.20 ± 0.12

4D CT based on optical measurements: combining points and surface detection

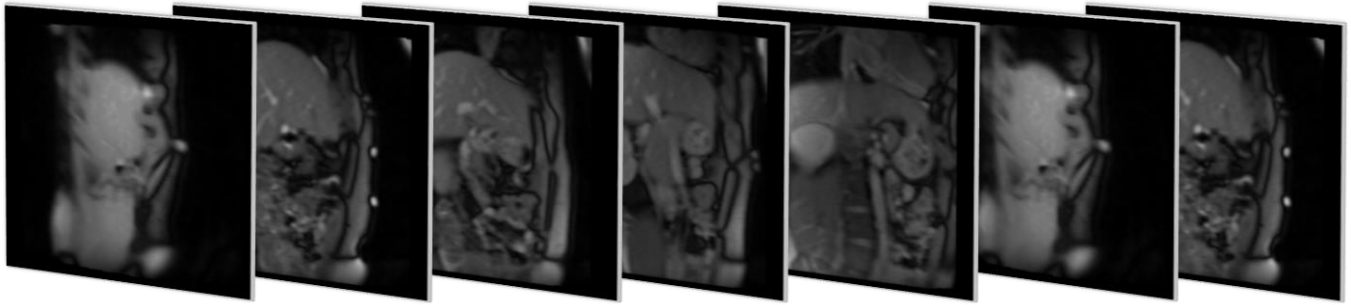
- Novel system under development/testing combining real-time point-based with surface based acquisitions with high spatial and temporal resolution for redundant external surrogates acquisition. Applications in:
- - robust 4D CT (@CNAO early 2014)
- - combined/selectable point/surface patient set-up verification /respiratory gating / tumor tracking





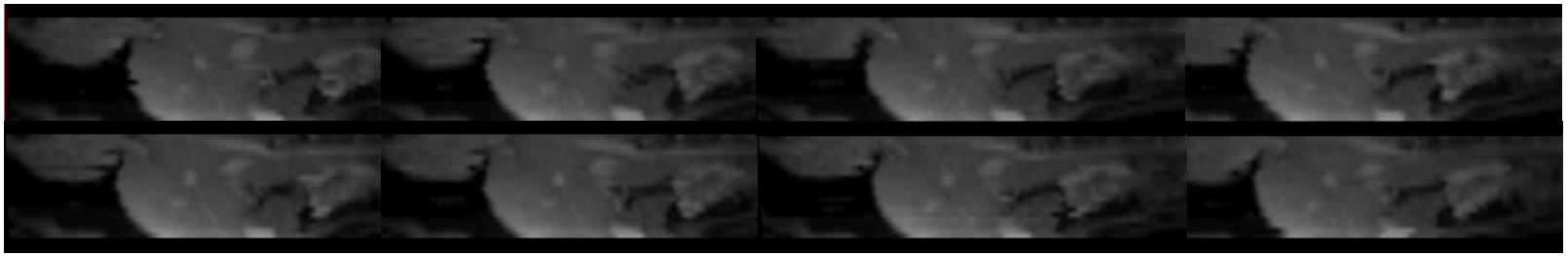


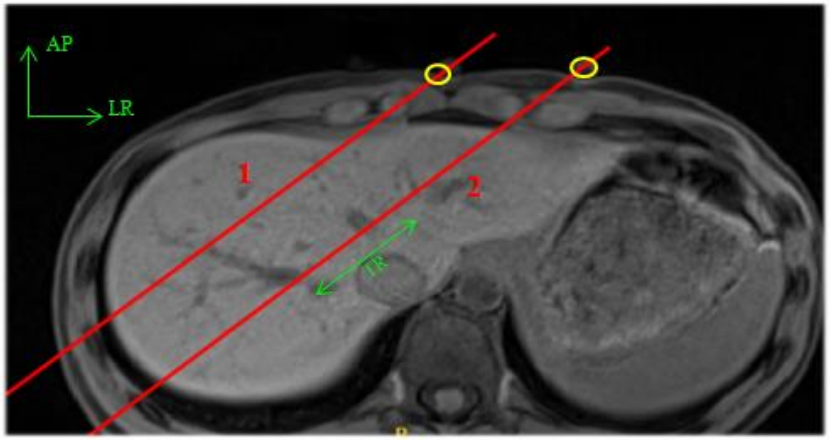
Surrogate-less 4D MRI
Point-based motion modelling/model verification

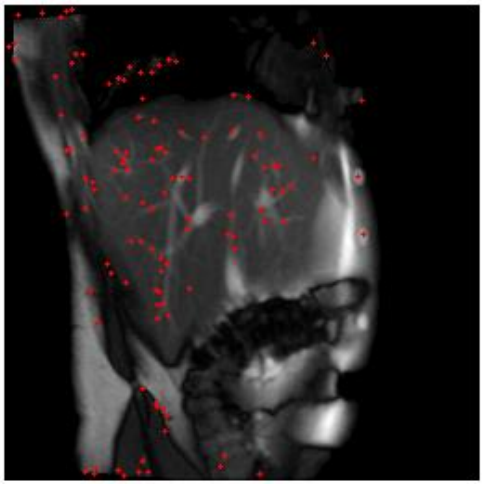


(…)

Internal surrogate: MI







4D hadrontherapy

Application of correlation models for **real-time tumor tracking** in particle therapy:

1. **Experimental validation** with scanned beams in clinical like scenarios:

   → *local correlation models*: acccurate target positioning and beam tracking against interplay effects

2. Development of **global 4D models**

   → *daily 4D CT* estimation to reduce beam range uncertainties

Correlation models in particle therapy

Experimenta

- *Robotic ph*
  - ✓ Reproc
  - ✓ Regula
- *Optical Tra*
  - ✓ SMART
  - ✓ Measu
  - ✓ Include
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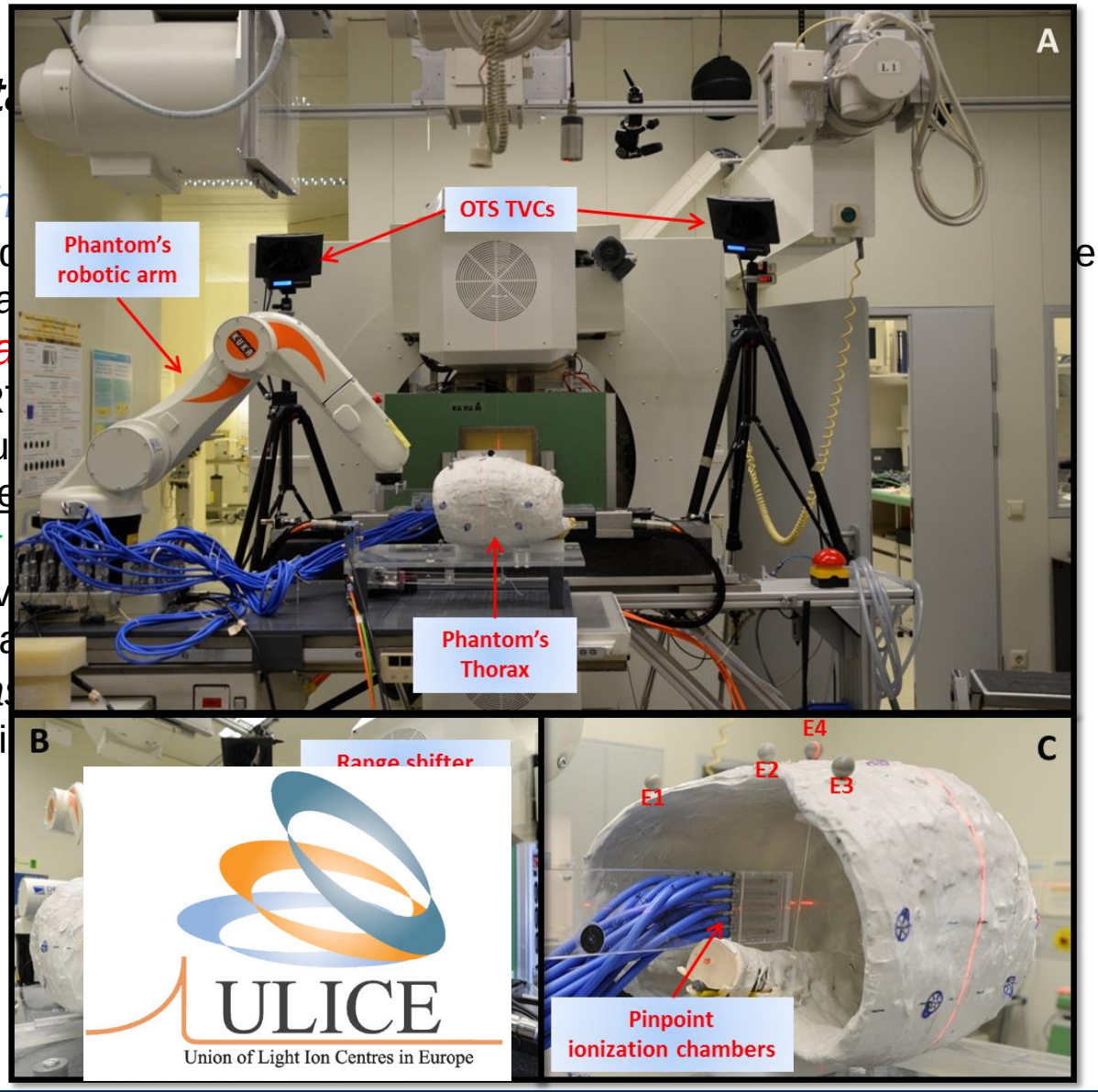
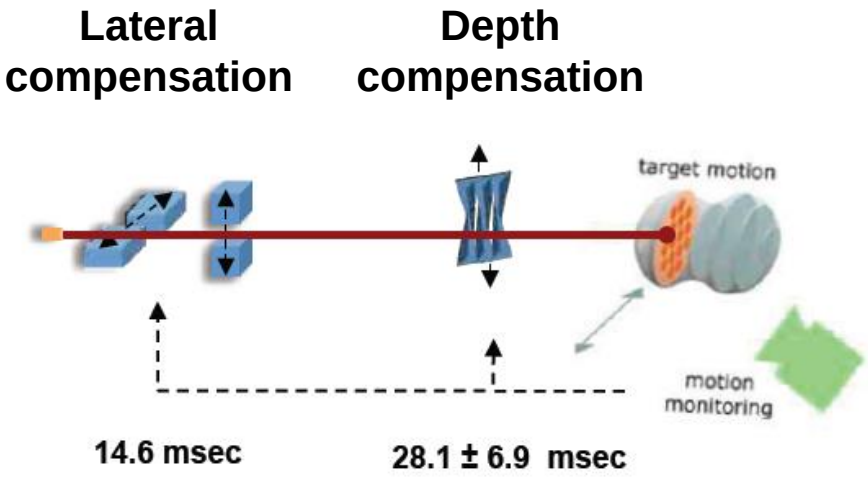
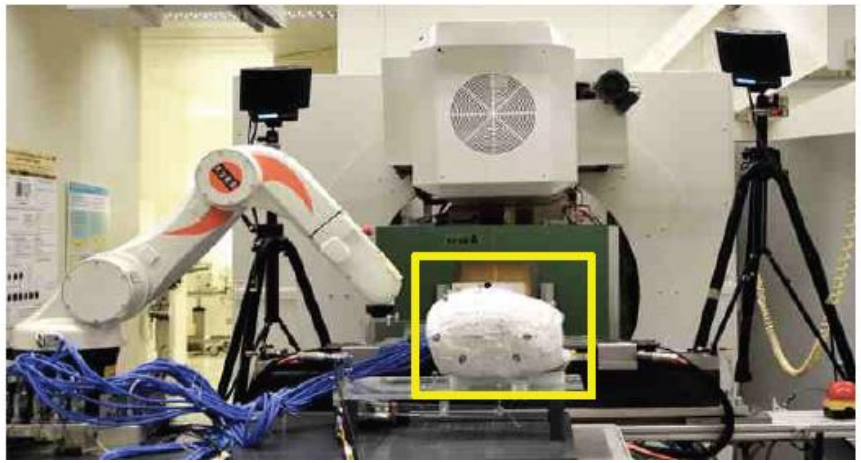


Latency compensation

Commissioning of OTS / TCS integration:

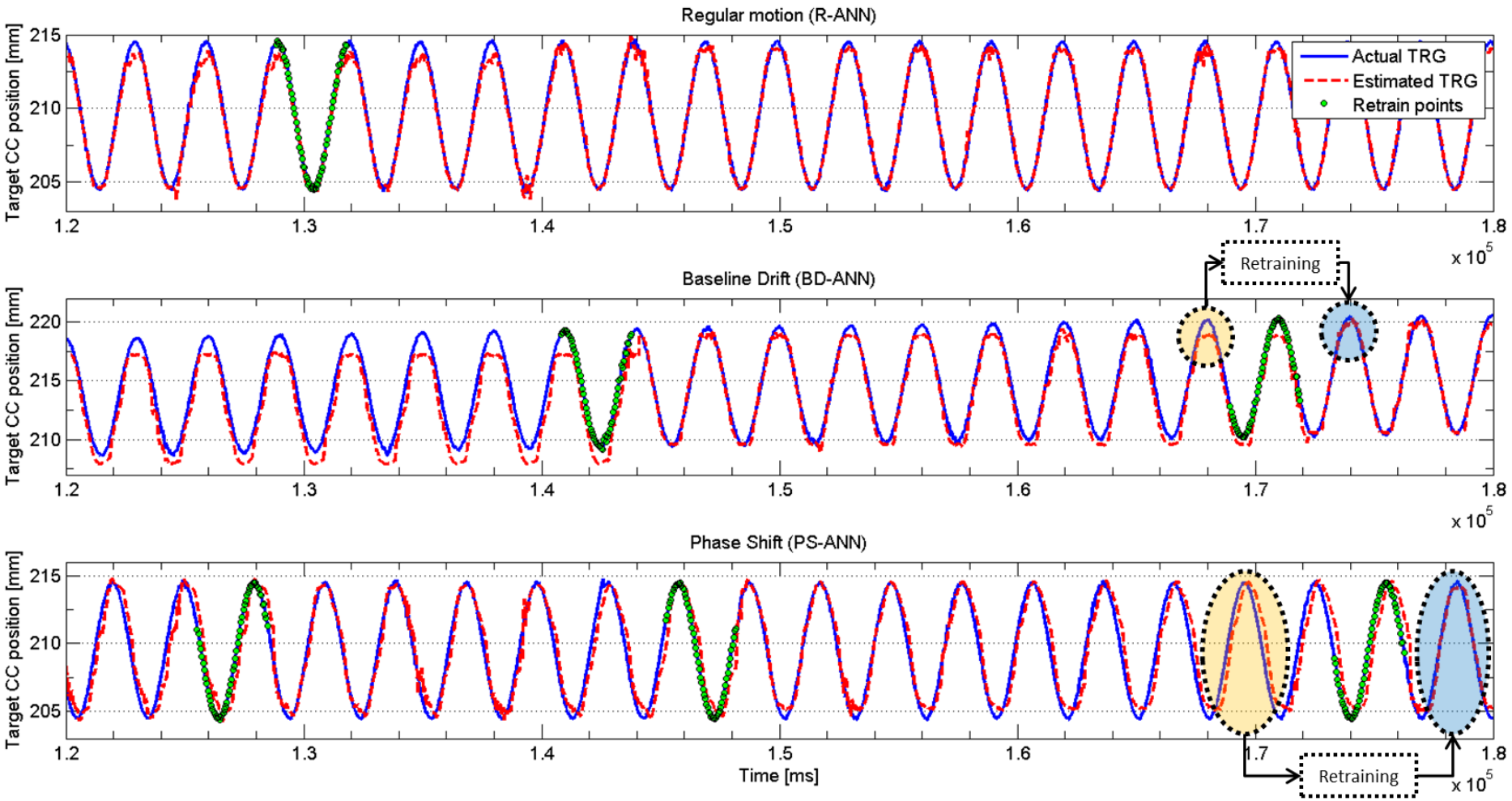
- **Lateral** compensation (magnet steering in BEV)
- **Depth** compensation (dynamic wedge for energy adaptation)





(Fattori et al, TCRT, in press)

Accuracy of correlation models



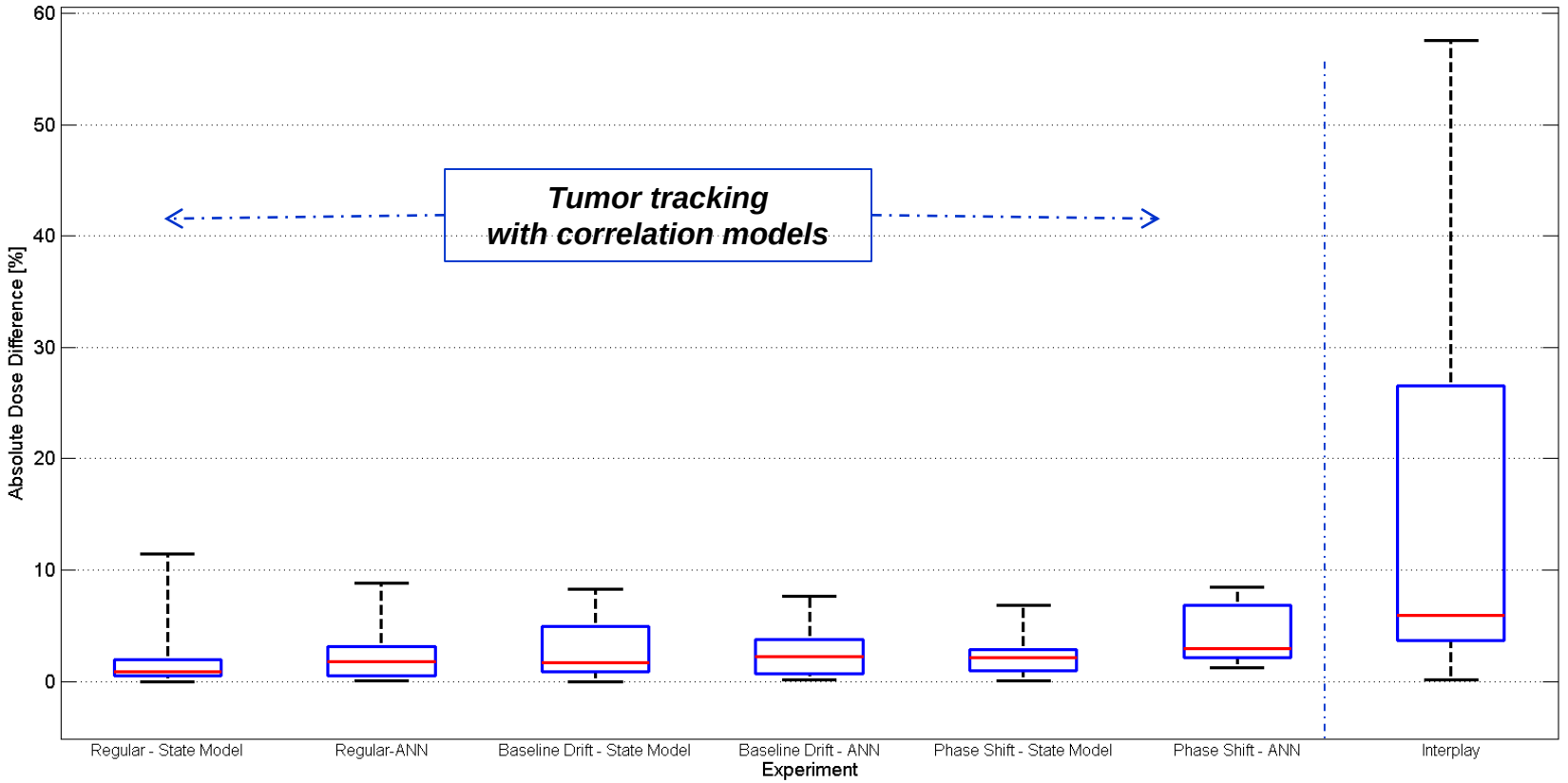
Phase shift	3	2.975	10, 5, 5	0, 0, 0

Dosimetric results

Dose different wrt static irradiation

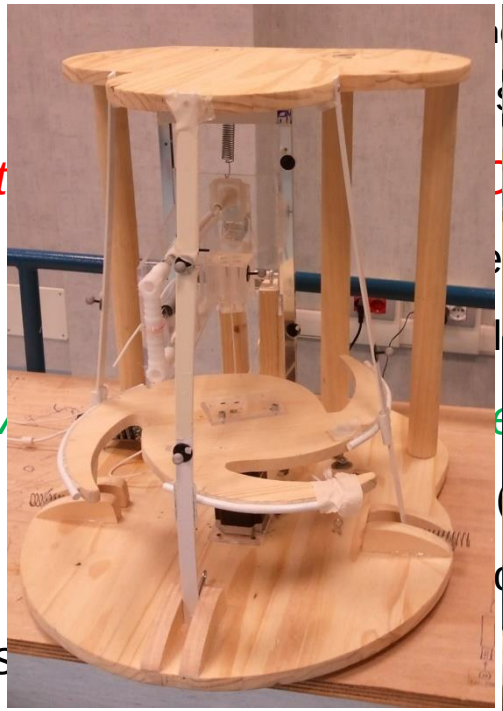
- Static irradiation = beam fixed, static target
  → Measurement of nominal delivered dose
- '*Interplay*' = beam fixed, taget moving
  → Measurement of «motion blurred» dose

(Seregni et al, PMB, 2013)



Experimental set-up (CNAO, December 2012)

- *Robotic phantom*
  - ✓ Custom moving phantom featuring correlated external and internal motion along an
  - ✓
- *Opt*
  - ✓)Hz)
  - ✓
- *CNA*
  - ✓
  - ✓ viation
- *Dos*
  - ✓ Films scanned with proton pencil beam (single square film, 60 mm side)



Dosimetric results (films)

Acq 1 — Static irradiation

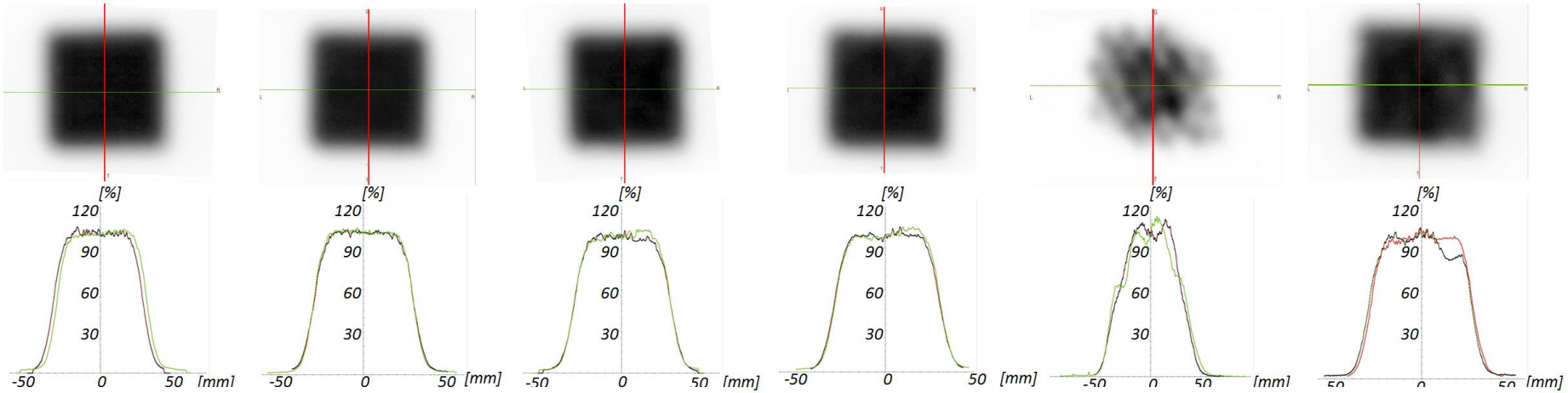
Acq 2 — OTS direct tracking

Acq 3 — ANN prediction

Acq 4 — State space model prediction

Acq 5 — Interplay

Acq 6 — Gating



Average flatness (omogeneity, [%])

Acq 1	Acq 2	Acq 3	Acq 4	Acq 5	Acq 6
4	5.7	6.6	6.1	24	9.5

Average penumbra (principal axes, [mm])

Acq 1	Acq 2	Acq 3	Acq 4	Acq 5*	Acq 6
9.2	9	9	9.2	19	9.1

** Field size: 6.3 and 6.9 mm (principal directions) respectively*

From local to global 4D models

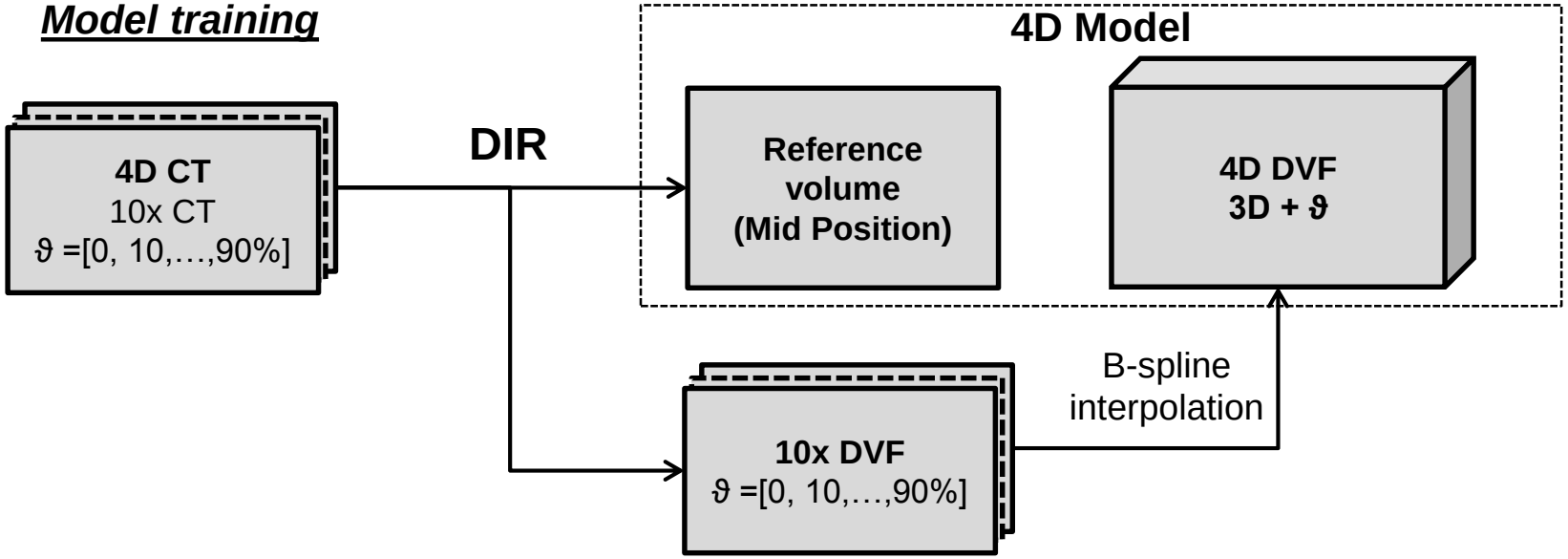
- **Local** correlation models (**target**) experimentally assessed
- Need to evaluate **WEL variations (dosimetric changes) outside the target**

Global 4D model

adapt treatment planning 4D CT to the time of irradiation

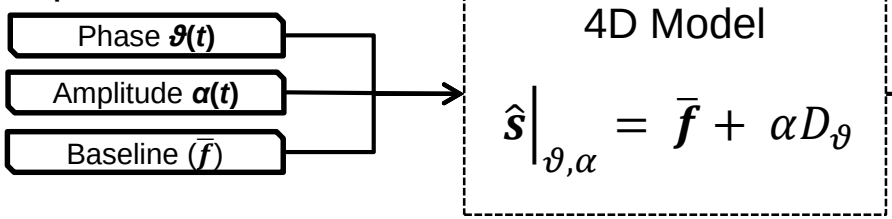
Global 4D model: general framework

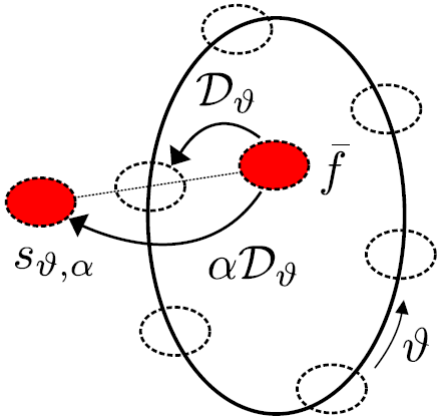
Model training



Model estimate (current fraction)

Respiratory motion parameters





(Vandemeulebroucke et al. 2009; Fassi et al. 2013)

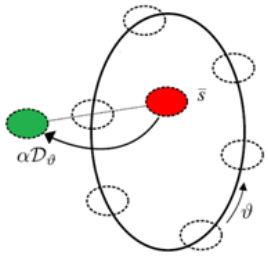
CBCT studies

TREATMENT PLANNING

4D CT image acquisition

Estimation of a patient-specific **breathing motion model**

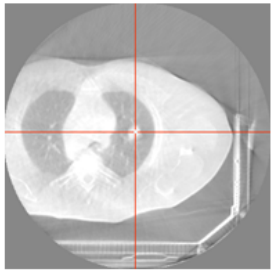
- baseline ($\underline{s}$)
- amplitude (α)
- phase (ϑ)



PATIENT SETUP

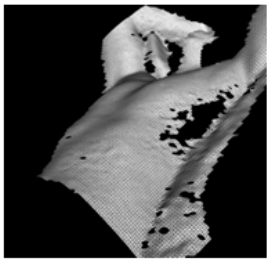
In-room **3D CBCT** image acquisition

Estimation of daily tumor **baseline**



DOSE DELIVERY

Dynamic acquisition of thoraco-abdominal **surface displacement** with optical systems



Estimation of a **breathing surrogate**

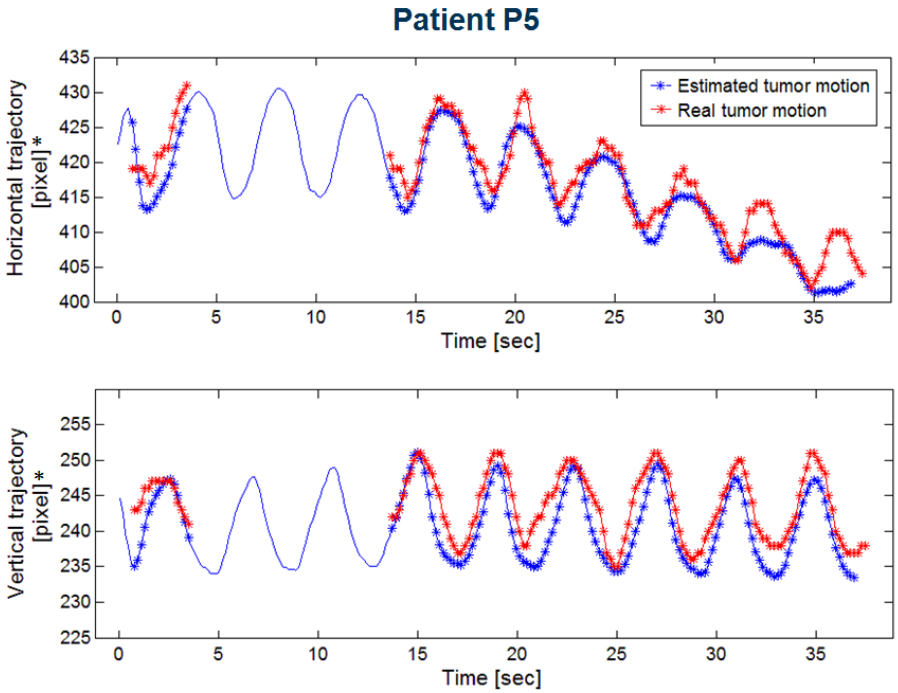
Extraction of respiratory **amplitude** and **phase** parameters

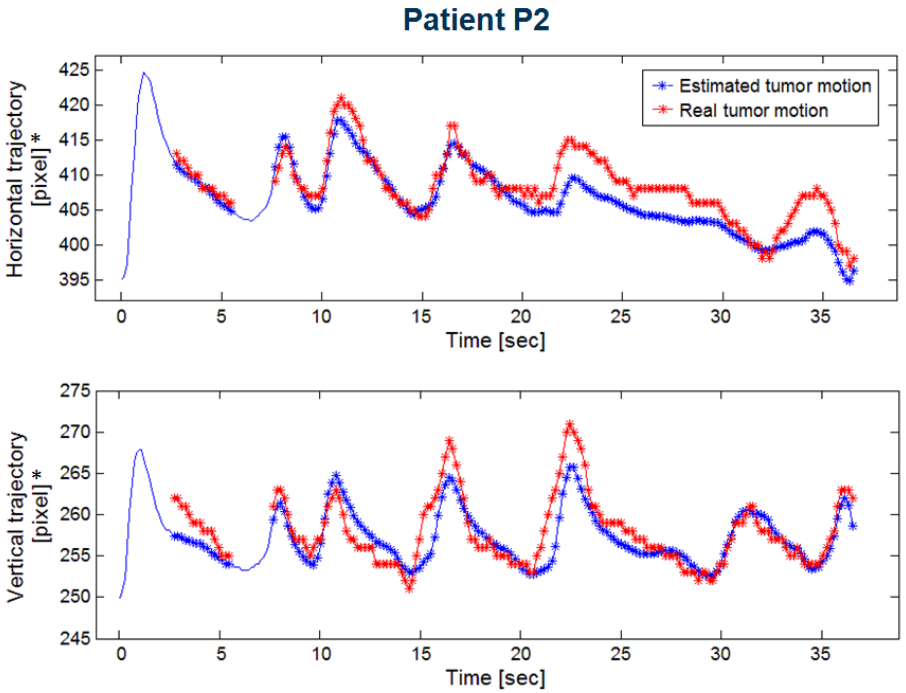
Update of the 4D CT motion model

Tumor motion tracking

(Fassi et al, IJROBP, in press)

CBCT study: sample traces



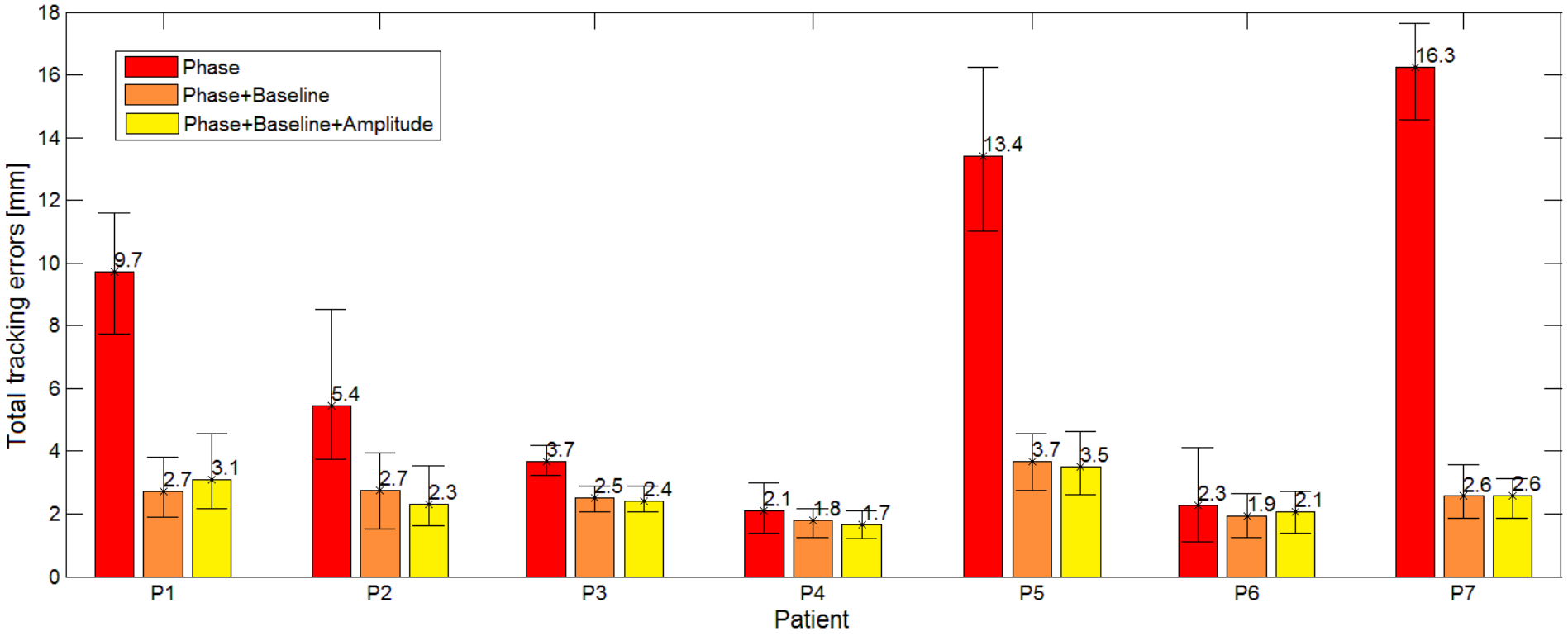


* Pixel spacing of CBCT projections = 0.8 mm/pixel

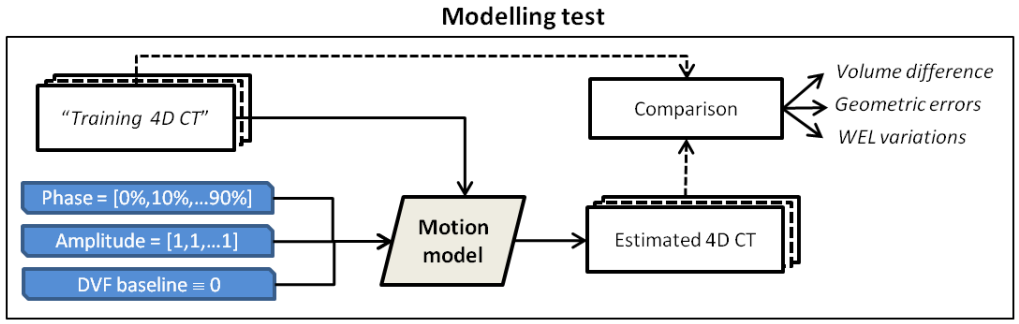
CBCT study: overall results

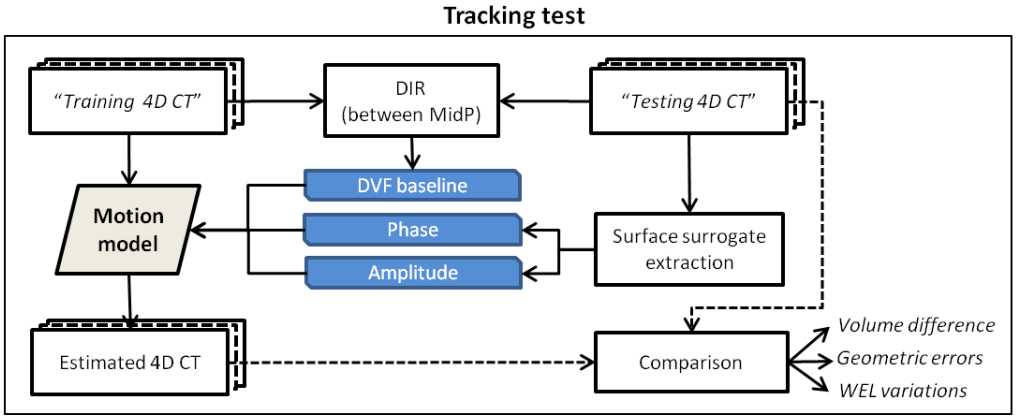
Total tracking error:

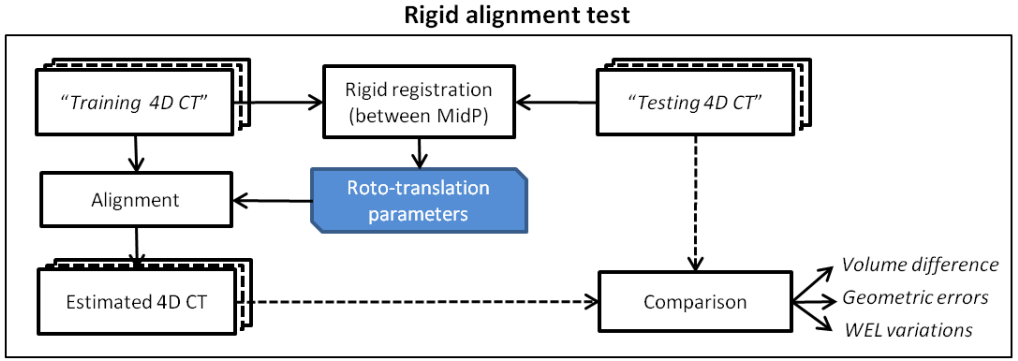
→ RMS error of tumor tracking in the CBCT projection plane



Global 4D model: can we predict a daily 4D CT?







Modeling test

→ intrinsic model errors DIR

Tracking test

→ tracking accuracy evaluation

Rigid alignment Test

→ for comparison

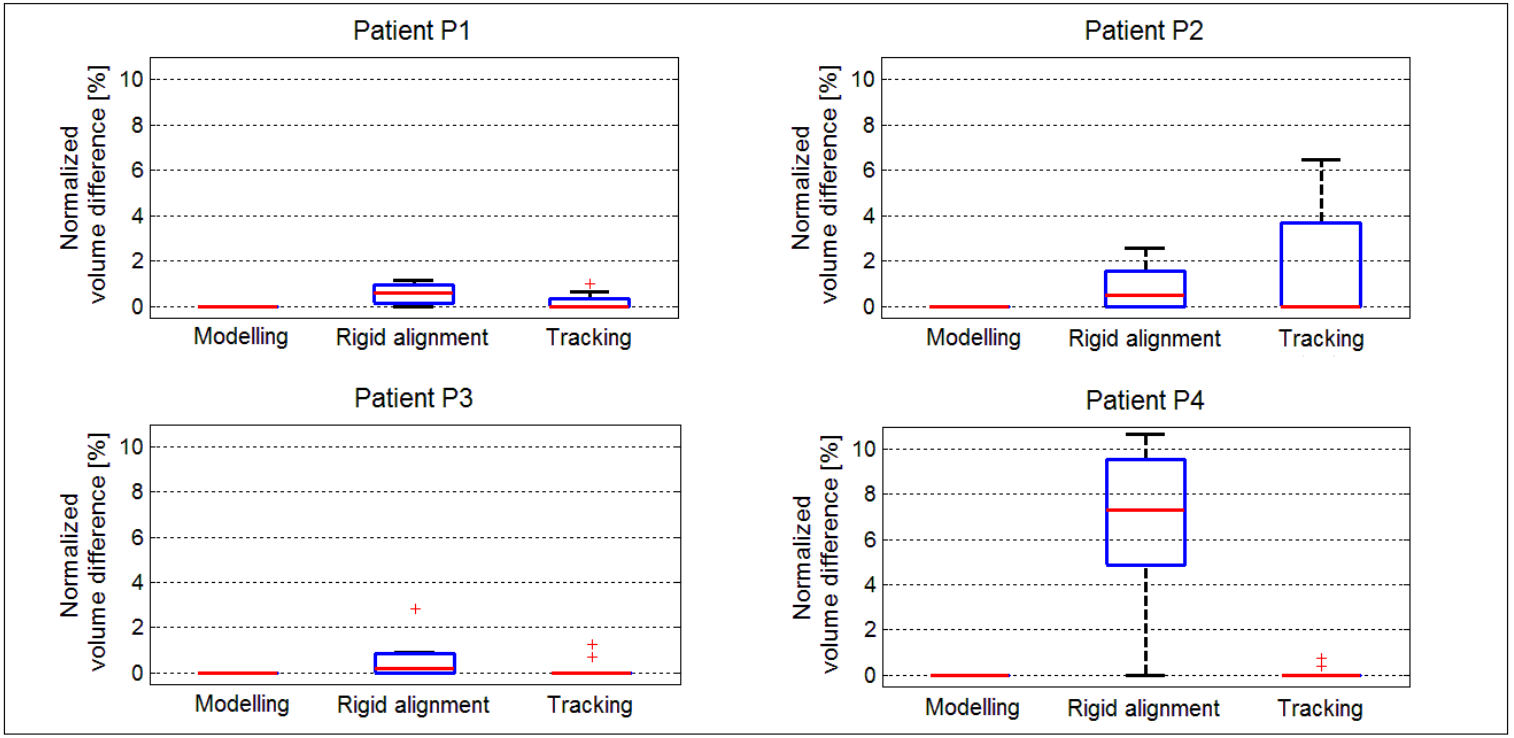
Global 4D model: geometric results

Patient	Experiment	COM distance [mm] GTV	COM distance [mm] Lungs	COM distance [mm] Trachea	COM distance [mm] Esophagus	Hausdorff distance [mm] GTV	Hausdorff distance [mm] Lungs	Hausdorff distance [mm] Trachea	Hausdorff distance [mm] Esophagus	Dice Coefficient GTV	Dice Coefficient Lungs	Dice Coefficient Trachea	Dice Coefficient Esophagus
P1	*Modeling*	0.40	0.42	0.36	0.50	0.31	0.49	0.31	0.21	0.90	0.99	0.94	0.97
	Rigid	4.70	3.66	3.36	4.39	1.61	2.56	1.55	1.89	0.57	0.89	0.67	0.57
	Tracking	**1.58**	**0.78**	**1.01**	**0.84**	**0.63**	**0.64**	**0.51**	**0.34**	**0.80**	**0.97**	**0.88**	**0.91**
P2	*Modeling*	0.51	0.15	0.46	0.21	0.27	0.28	0.24	0.15	0.92	0.99	0.97	0.98
	Rigid	2.30	2.49	1.28	1.07	0.84	0.90	0.48	0.41	0.78	0.97	0.94	0.92
	Tracking	**1.82**	**1.05**	**1.98**	**0.96**	**0.64**	**0.62**	**0.58**	**0.40**	**0.82**	**0.98**	**0.90**	**0.93**
P3	*Modeling*	0.13	0.14	0.34	1.19	0.12	0.22	0.23	0.24	0.99	0.99	0.96	0.96
	Rigid	1.28	1.68	3.73	2.63	0.51	1.62	1.66	1.23	0.91	0.95	0.73	0.76
	Tracking	**0.87**	**2.78**	**2.19**	**2.09**	**0.38**	**1.32**	**1.12**	**1.23**	**0.93**	**0.96**	**0.79**	**0.76**
P4	*Modeling*	0.52	0.15	0.45	0.36	0.32	0.21	0.20	0.11	0.90	0.99	0.97	0.99
	Rigid	3.93	2.63	1.57	1.75	1.75	1.15	0.58	0.47	0.45	0.69	0.89	0.87
	Tracking	**1.26**	**0.41**	**0.65**	**1.17**	**0.56**	**0.36**	**0.31**	**0.33**	**0.80**	**0.99**	**0.94**	**0.92**

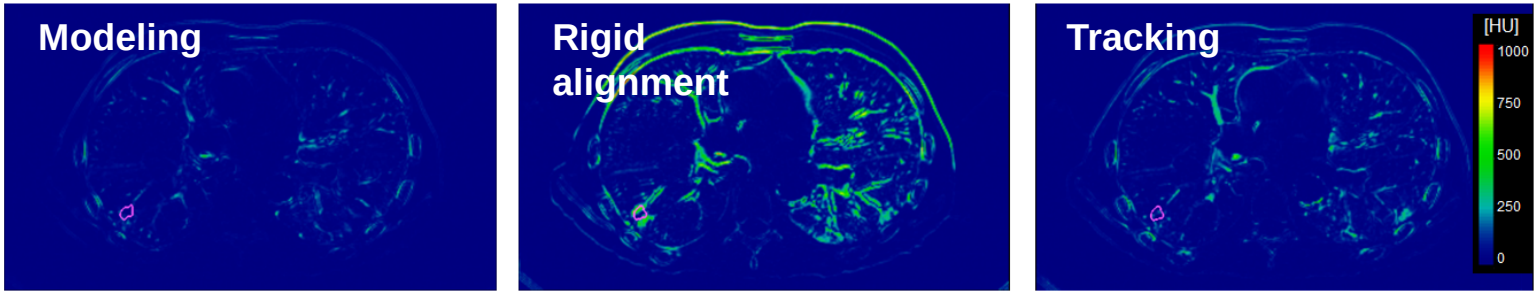
- ✓ Tracking Test:
  - ➢ Localization error (COM) = 1,4 mm (GTV), 1,3 ÷ 1,5 mm (OARs)
  - ➢ Contour surface distance (Haussdorf) = 0,55 mm (GTV), 0,57 ÷ 0,53 mm (OARs)
  - ➢ Volume overlap (Dice) = 0,83 (GTV), 0,87 ÷ 0,93 (OARs)

Global 4D model: HU difference

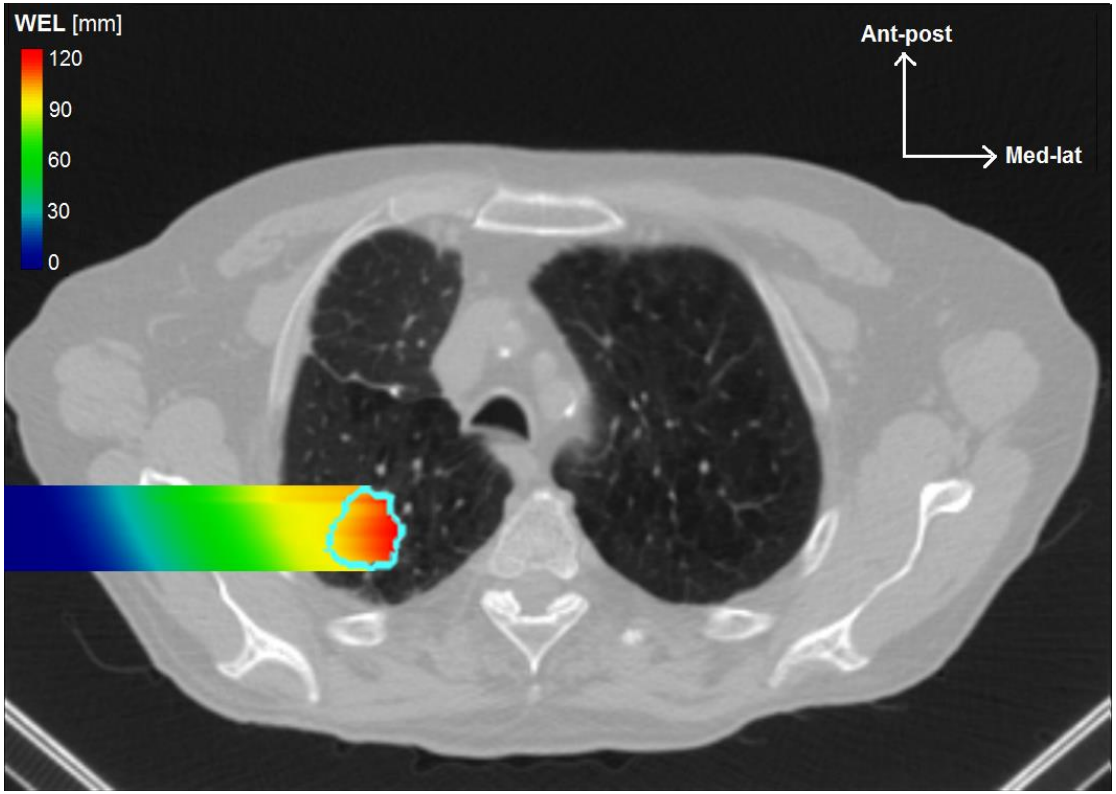
A) Motion state identification error



B) HU difference



Global 4D model: WEL results

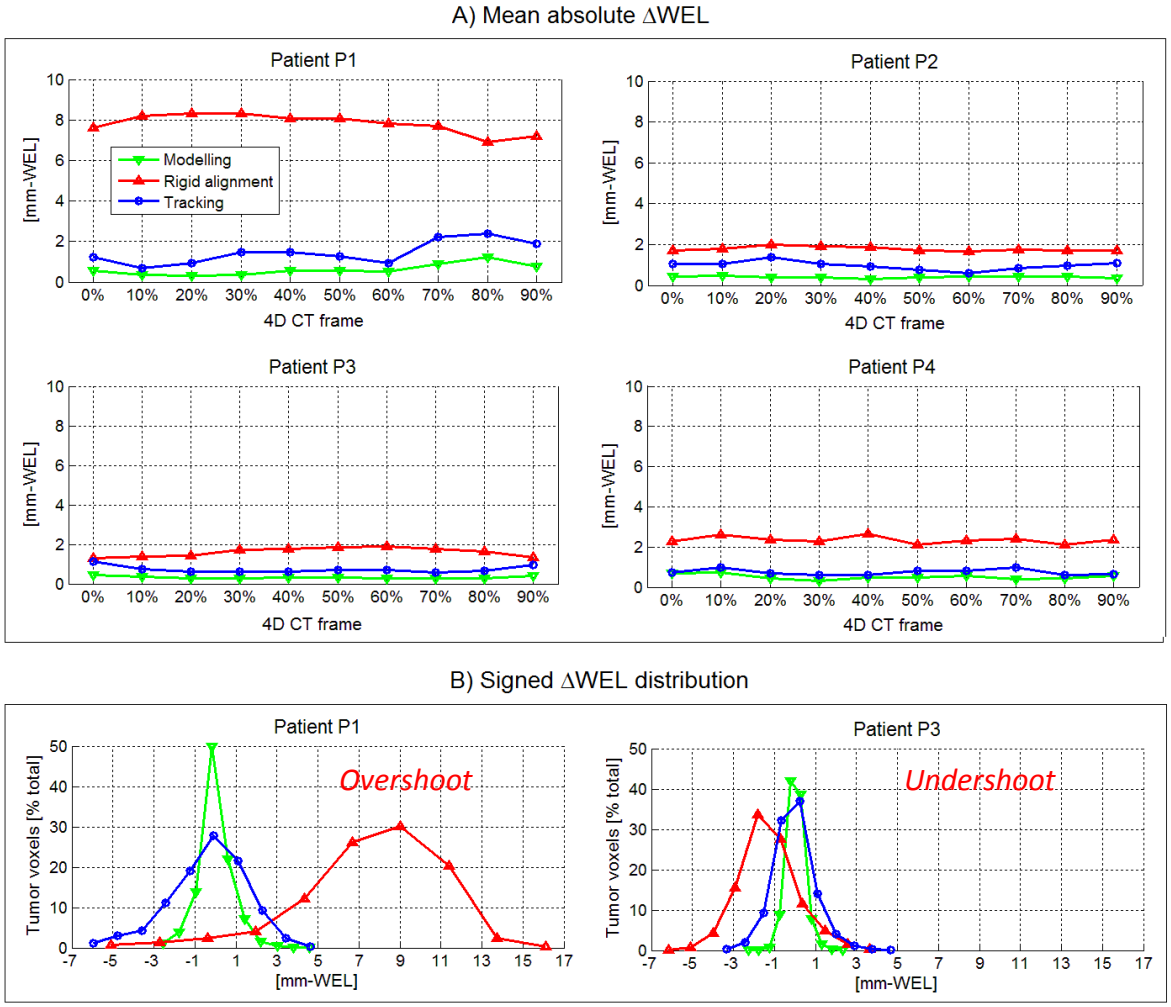


Quantification of range variations

↓

ΔWEL calculation

Global 4D model: WEL results



- ✓ Rigid alignment Test

| ΔWEL | = 1,6 ÷ 7,8 mm

mean(ΔWEL (GTV)) ≠ 0 mm

→ Systematic *variations*

- ✓ Tracking Test:

| ΔWEL | = 0,7 ÷ 1,4 mm

mean(ΔWEL (GTV)) ≈ 0 mm

→ NO *systematic variations*

Discussion: time resolved delivery with particles

1. **Local correlation models** validated experimentally in scanned particle therapy
    - **RMS tracking error** < 1.5 mm
    - **few % dosimetric deviation** wrt static irradiation
2. **Global 4D models** can predict anatomy changes (preliminary)
    - **Results are patient dependent**
    - **Systematic WEL variations** can be **compensated**

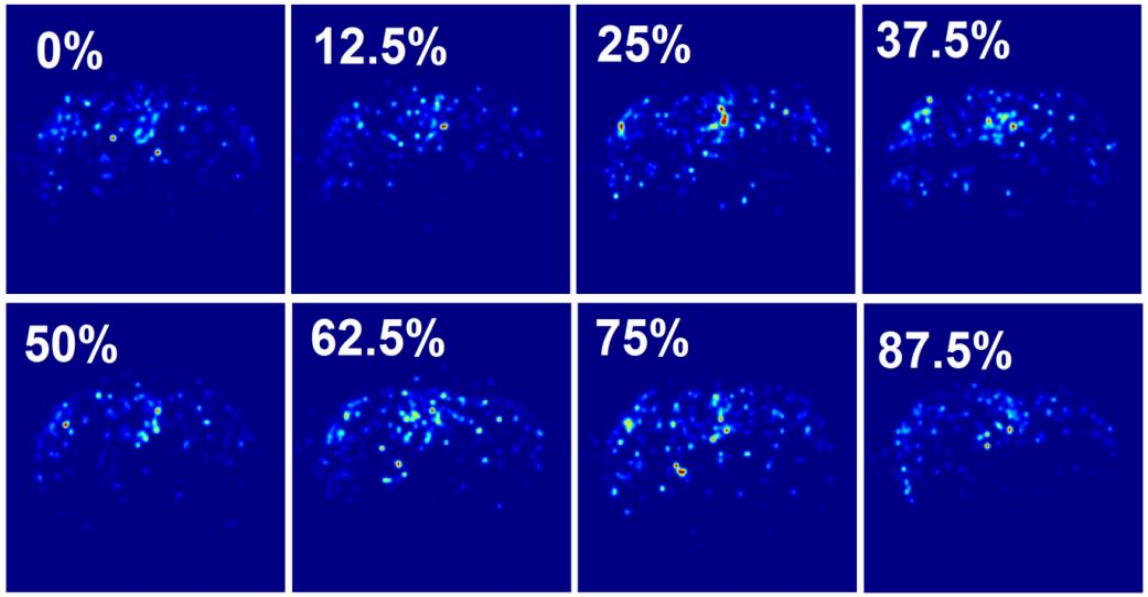
4D treatment verification

Motion compensated PET imaging

- ✓ Off-line PET-based treatment verification for moving target

  - reduced count statistics due to time delay before acquisition

  - reduced count statistics due to 4D acquisition

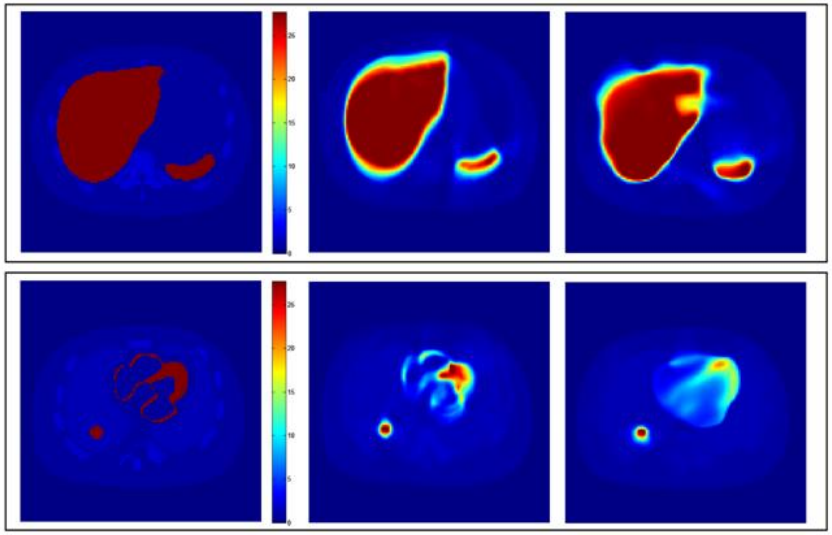


illegible 4D PET images from commercial scanners

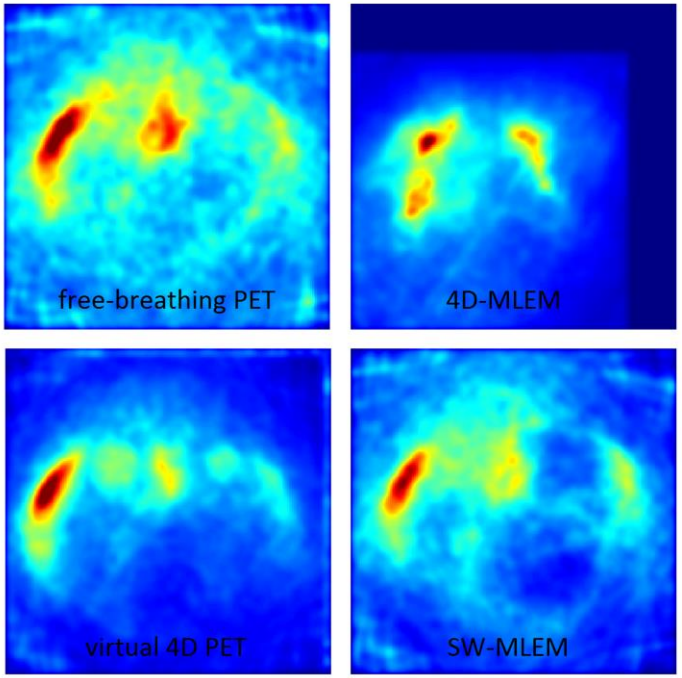
4D treatment verification

Motion compensated PET imaging: alternative strategies

- ✓ 4D MLEM (motion compensation through DIR in image domain)
- ✓ "4D Virtual PET" (Gianoli et al, TCRT, in press)
- ✓ Pre-reconstruction sinogram warping (anticipated motion compensation in sinogram domain)

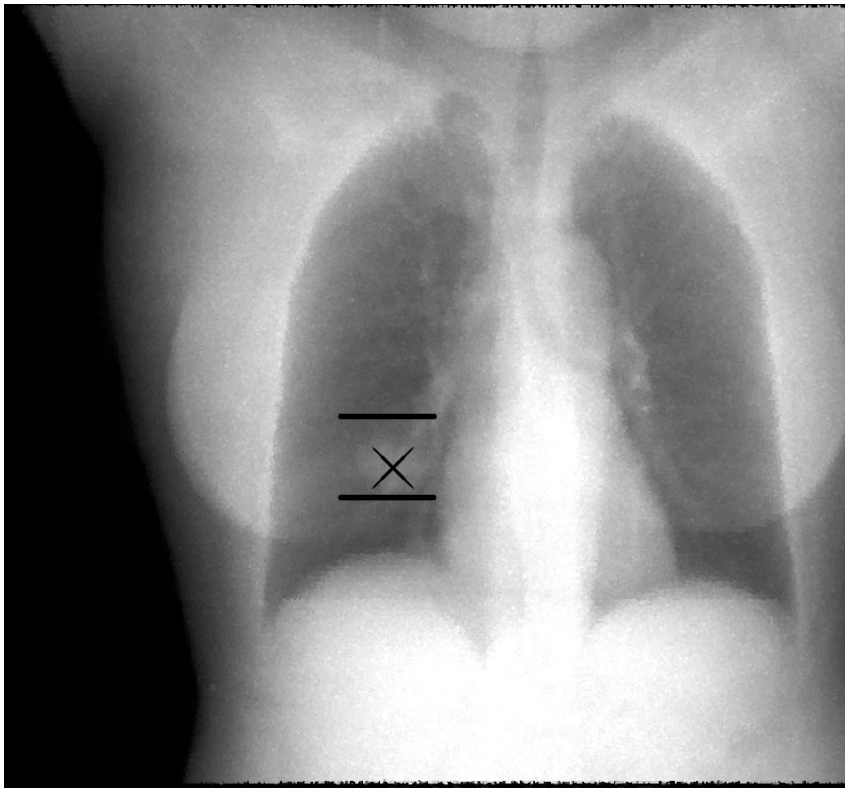


Ideal PET image (NCAT phantom) | SW-MLEM | 4D-MLEM

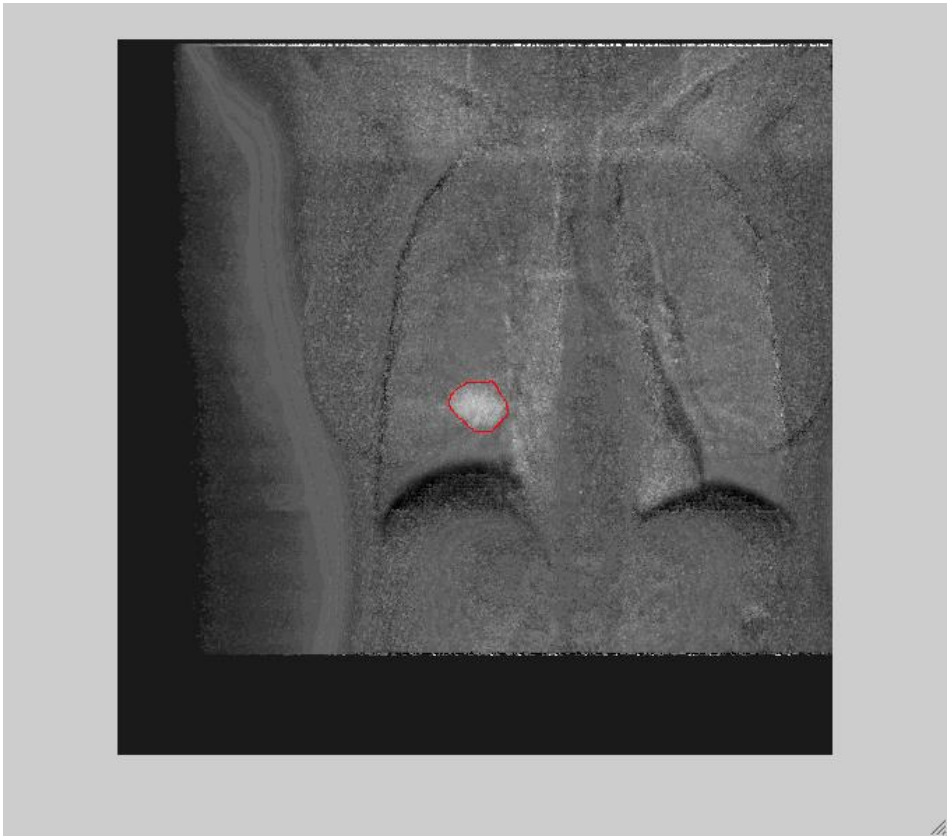


4D Protonradiography

- ✓ Simulated 4D transmission imaging (image contrast through lung masking for lesion detection)



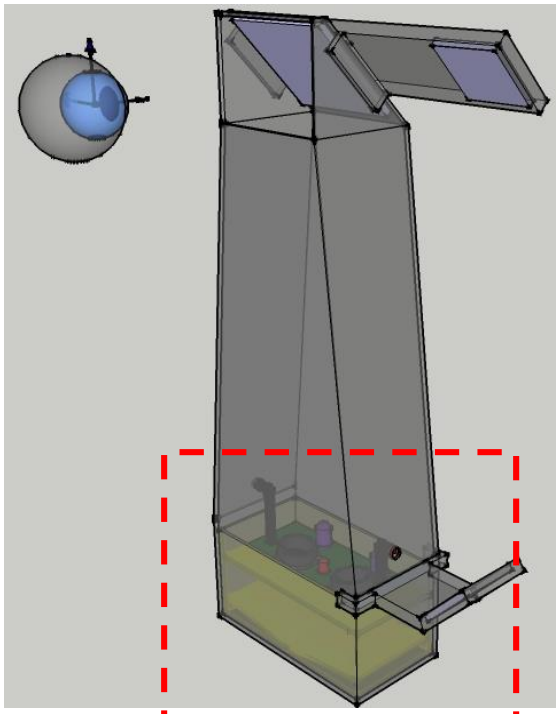
(courtesy of J. Seco)

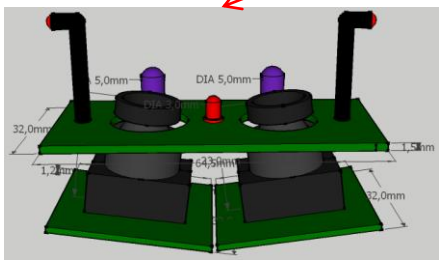


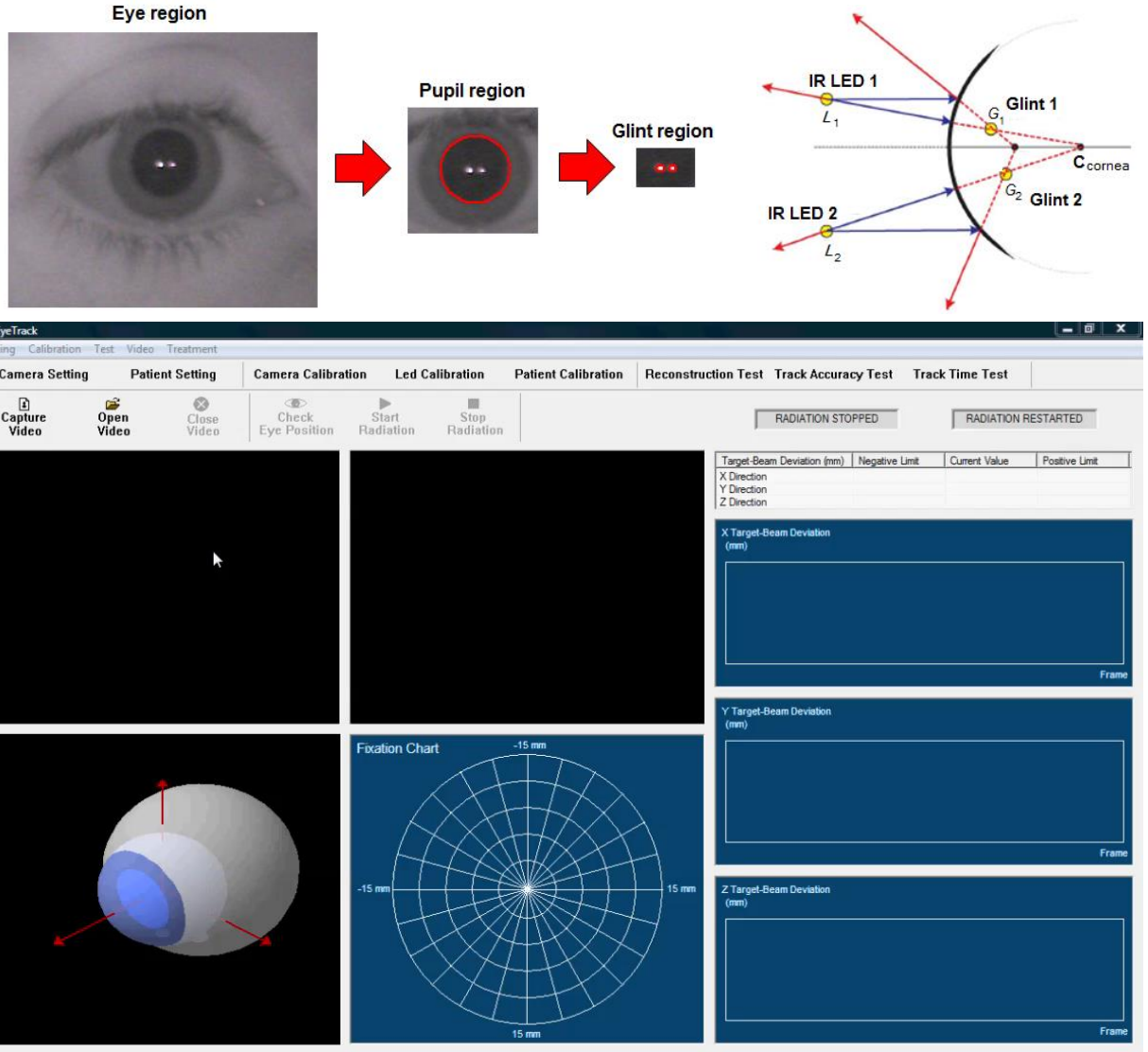
(courtesy of MF Spadea)

4D eye motion monitoring (under development)

- ✓ Infra-red eye tracking technique for real-time 3D clipless eye motion monitoring (Fassi et al. JBO, 2012)







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Thank you

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