Image Guidance in radiotherapy

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Outline

CartCasLab

✓ *Image guidance and Motion modeling*

- Methods to detect and compensate inter-fractional uncertainties
- Basics on rigid point/image registration
- 2D-3D and 3D-3D image registration
- Integration of IR tracking technologies with in-room imaging (CNAO solution)
- Deformable image registration
- Methods to detect and compensate intra-fractional uncertainties (breathing motion)
- Respiratory correlated imaging for treatment planning: 4D-CT and related issues
- Respiratory correlated dose delivery: gating, tracking
- Internal-external correlation (local models)
- Global models (CT-of-the-day)

High-precision radiotherapy: A "*computer assisted surgery*" paradigm

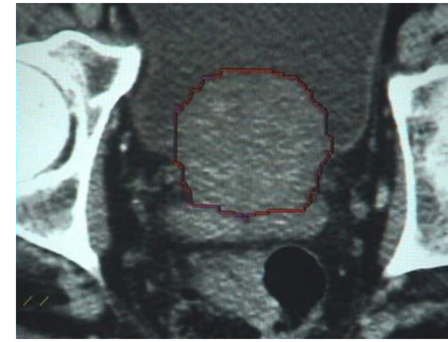
✓ *Planning stage*:

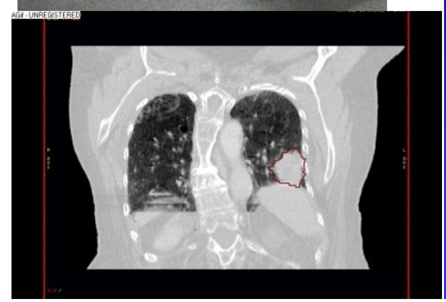
- X-ray volumetric imaging (3D/4D-CT)
- Functional imaging (PET , fMRI)
- Contouring (semi-automatic)
- Definition of treatment physical and geometry parameters
- Dose distribution simulation / optimization / evaluation

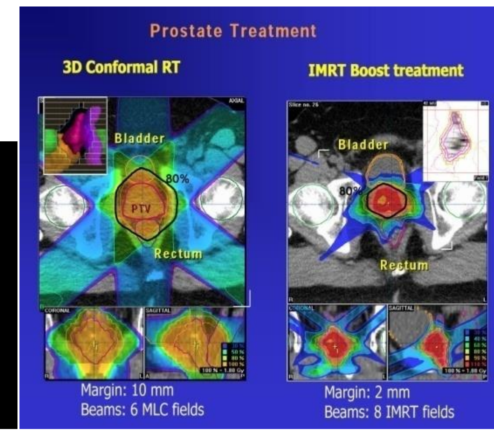
Uncertainties

✓ *Delivery/treatment stage*:

- Fully automatic (medical robotics)
- Patient set-up
- Geometry verification (Image Guidance)
- Compensation of inter-fractional patient deviations
- Dose delivery with compensation of intra-fractional patient deviations

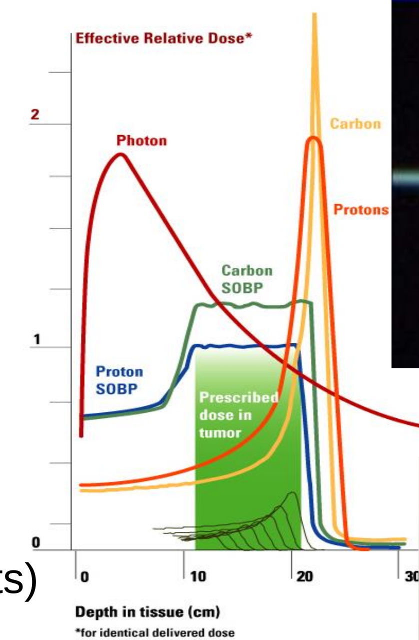


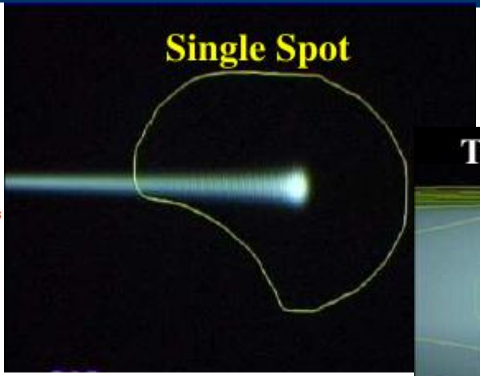


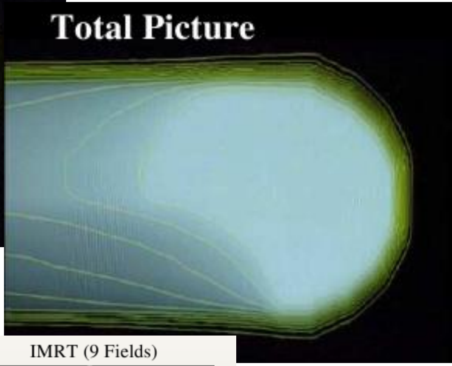


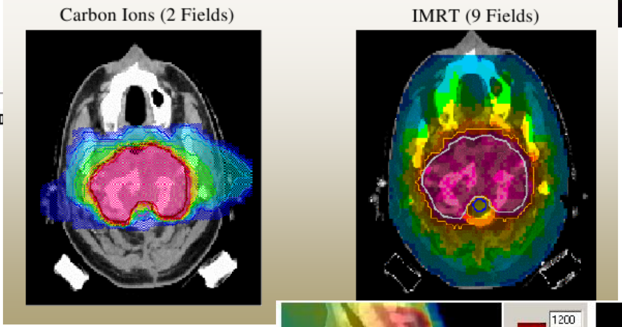
High-precision radiotherapy: Particle therapy

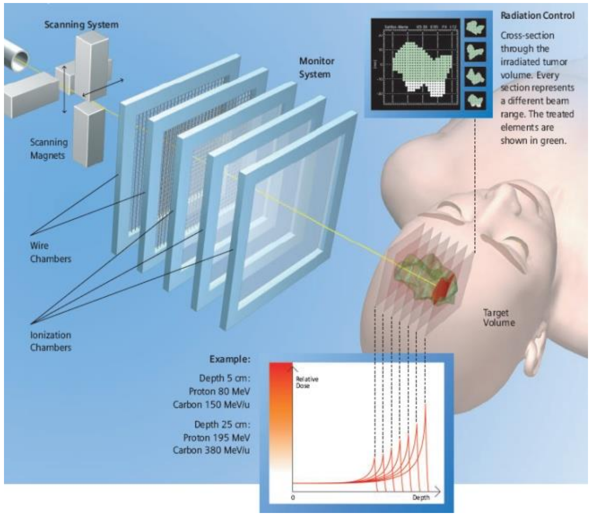
- ✓ Proton and heavy ions
- ✓ Higher biological effectiveness
- ✓ Higher geometrical selectivity
- ✓ Spot scanning delivery techniques for “*dose–sculpting*”
- ✓ Cyclotron (proton) or Synchrotron needed
- ✓ Very sensitive to uncertainties (range variations, interplay effects)

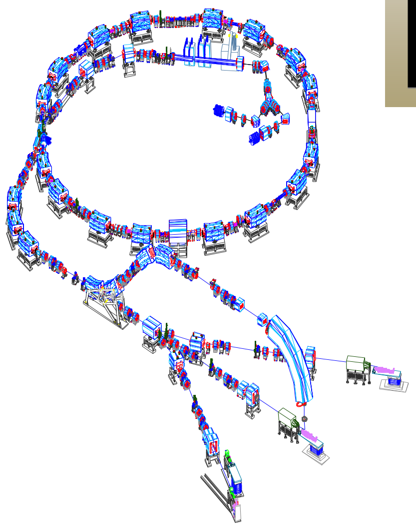


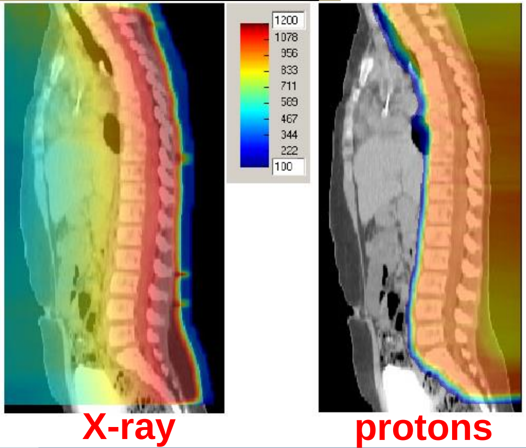




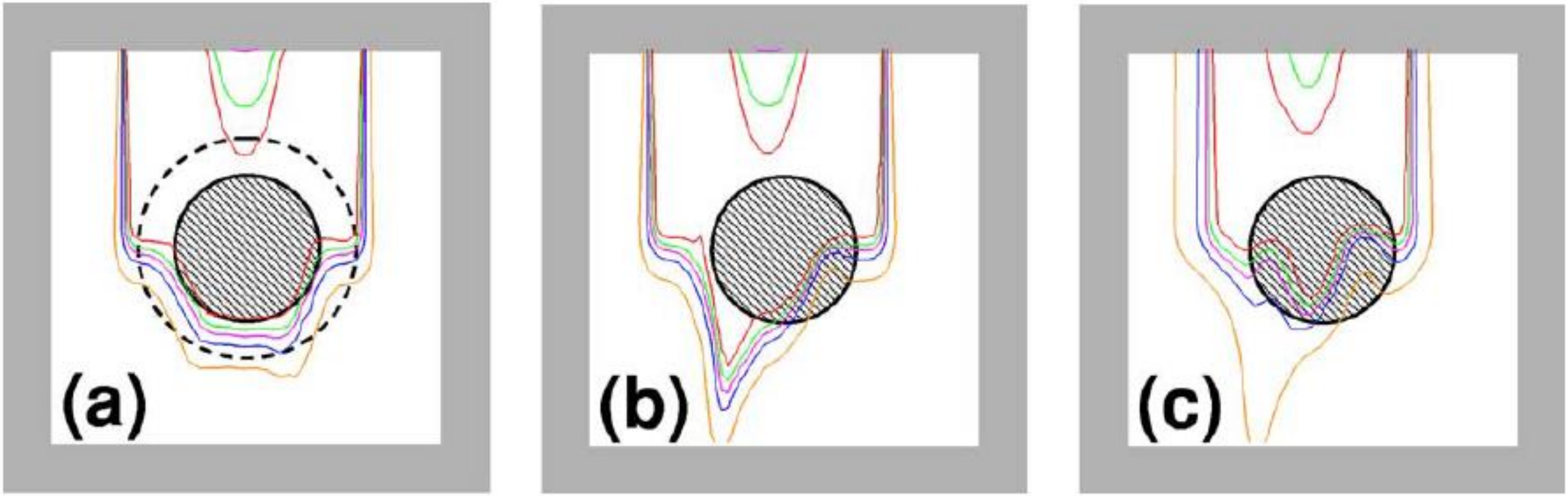








Range uncertainties frustrate geometrical selectivity of particles



ideal case

5 mm systematic error

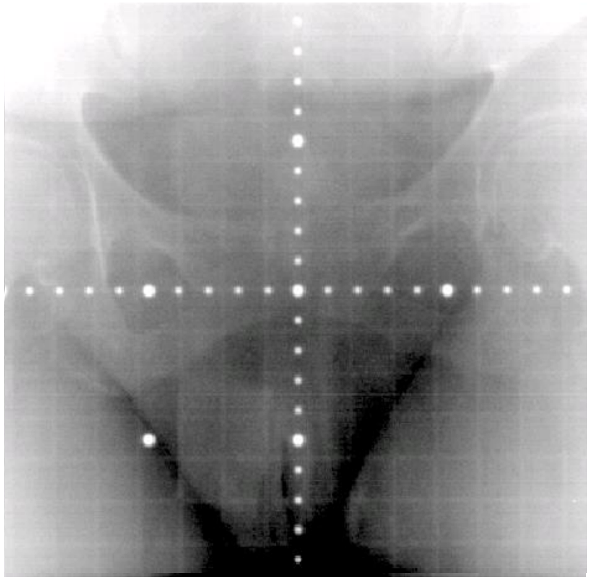
5 mm systematic error
+ 10 mm random

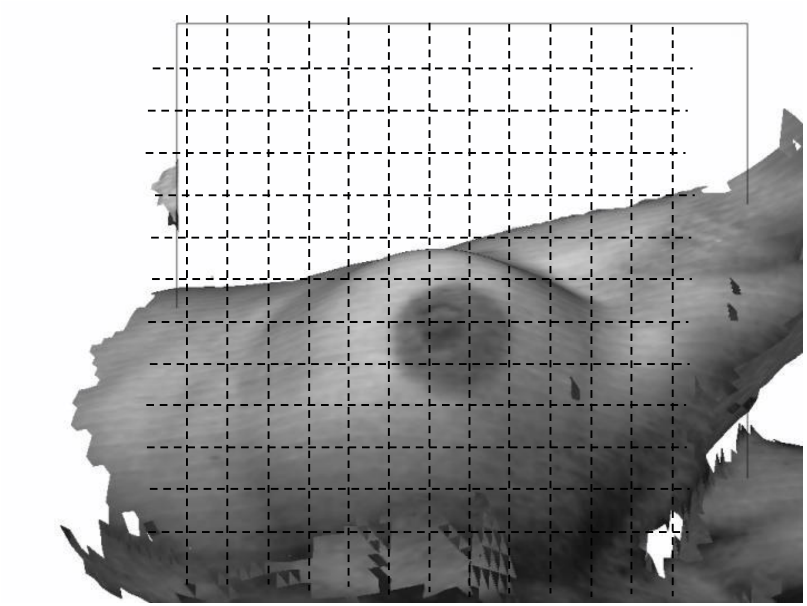
SETUP ERROR

SETUP ERROR
+
BREATHING

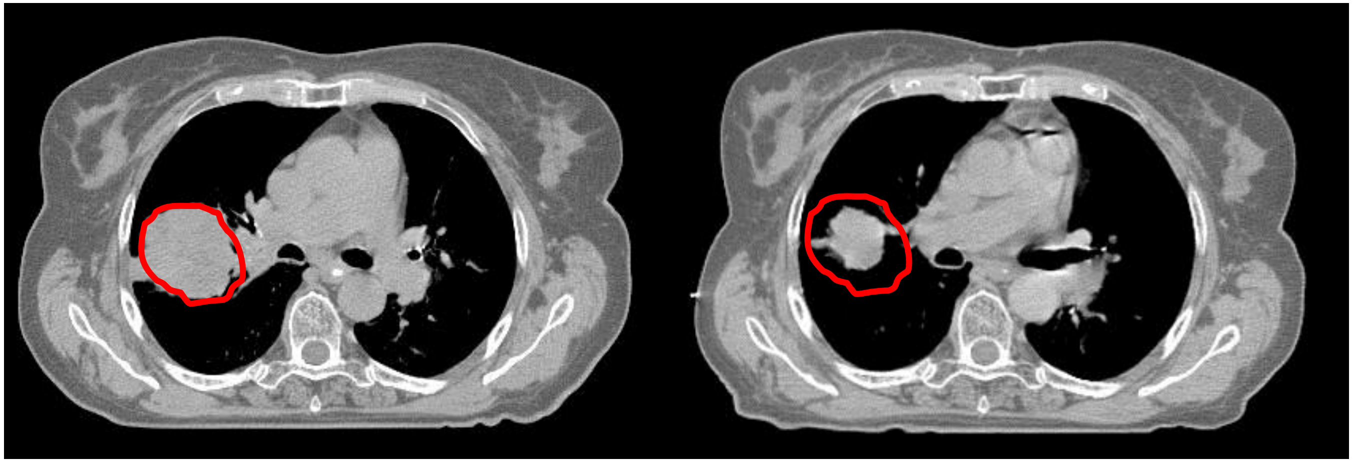
High-precision radiotherapy: Uncertainties
Patient inter-fractional uncertainties

- ✓ Set-up errors
  - Manageable with a rigid approach



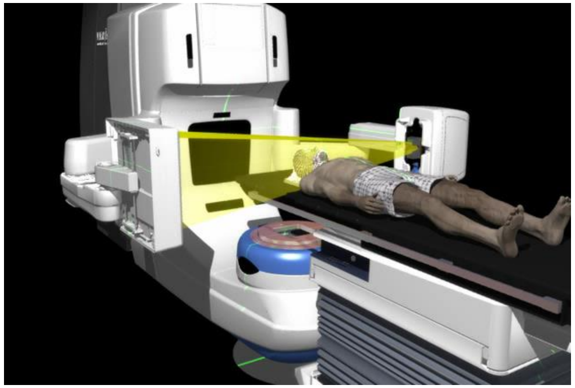


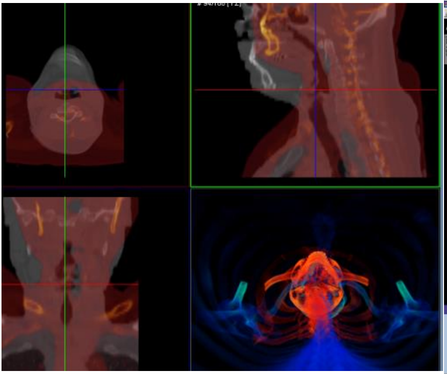
- ✓ Tumor displacements and shrinkage
  - Manageable with a rigid+deformable approach

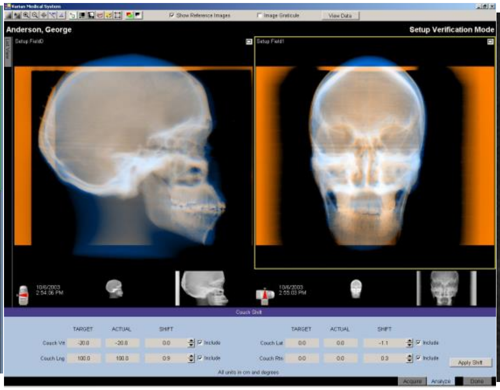


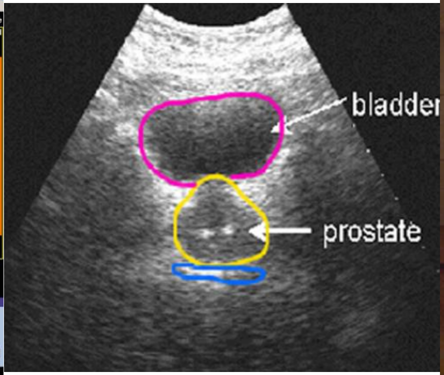
Inter-fractional uncertainties management
Technologies & methods: many different approaches

- ✓ New generation of therapy units equipped with on-board / in-room imaging devices for inter-fractional uncertainties detection and compensation
- ✓ Methods based on rigid and deformable image registration
- ✓ Double X-ray (KV, MV) projection (2D-3D registration)
- ✓ X-ray volumetric imaging (Cone-beam CT)
- ✓ US, MRI unconventional imaging with multimodal registration
- ✓ Voxel-based rigid, affine, deformable registration







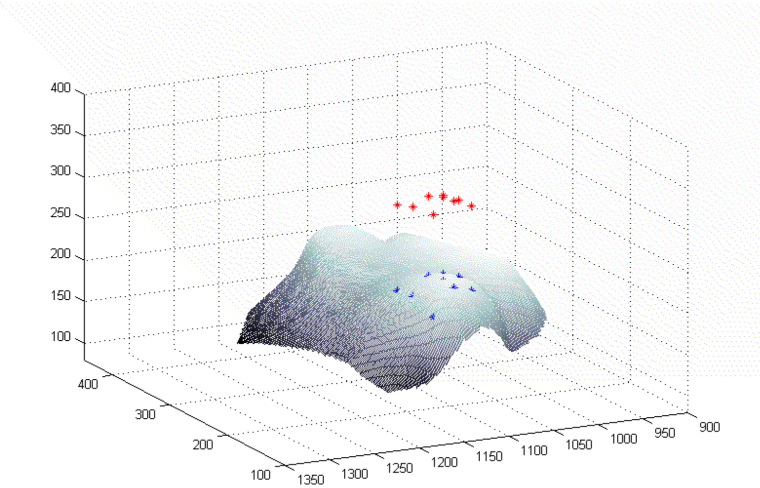


Inter-fractional uncertainties management
Technologies & methods: IR optical tracking

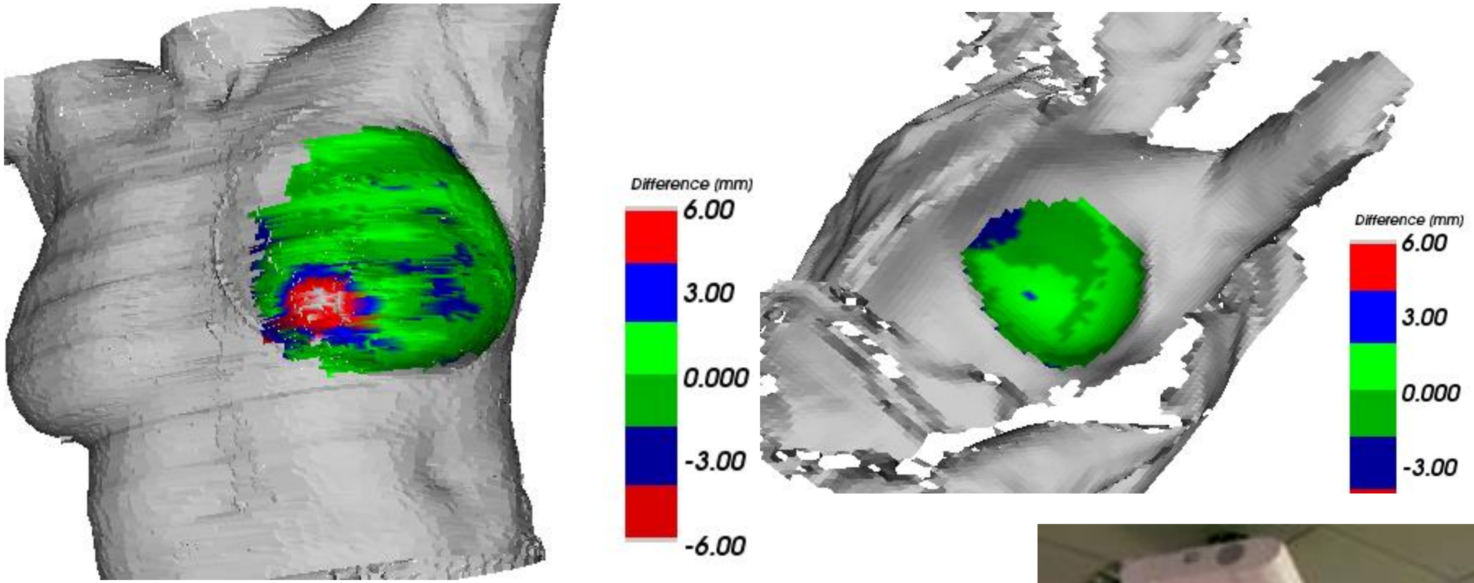
- ✓ Powerful techniques to capture motion in 3D and "*real-time*" (50-100 Hz sampling rate)
- ✓ State of the art of computer assisted surgery for "*navigation*" (intrinsically accurate, FLE<1mm)
- ✓ Applied in radiotherapy for set-up error compensation and breathing motion detection
- ✓ Continuous monitoring during irradiation

Baroni et al *Med Biol Eng Comput,* 1998;
Baroni et al. *Radiother Oncol*. 2000;
Baroni et al *CAS,* 2000;
Baroni et al *IJROB*P, 2004;
Baroni et al *IJROB*P, 2006;

Ribodi et al. *Med Phys,* 2006;
Baroni et al. *J Radiat Res,* 2007
Riboldi et al. *Med Phys,* 2007



Surface matching



- Structured light projection
- Fast (20 Hz) feature detection and stereoscopic reconstruction
- Non corresponding points registration (optimized ICP) with CT model
- Some concerns in registration error minimization

Gierga et al. *IJROBP,* 2008;
Riboldi et al. *Med Phys,* 2009
Schaerer et al, *PMB*, 2012

Image (Optical) guidance framework

Elements :

- ✓ Reference dataset (surface fiducials, TP derived images)
- ✓ Moving dataset (data acquired in-room)
- ✓ Similarity measure (variable/property to minimize/maximize)
- ✓ Ancillary elements: correspondence search, interpolation, …

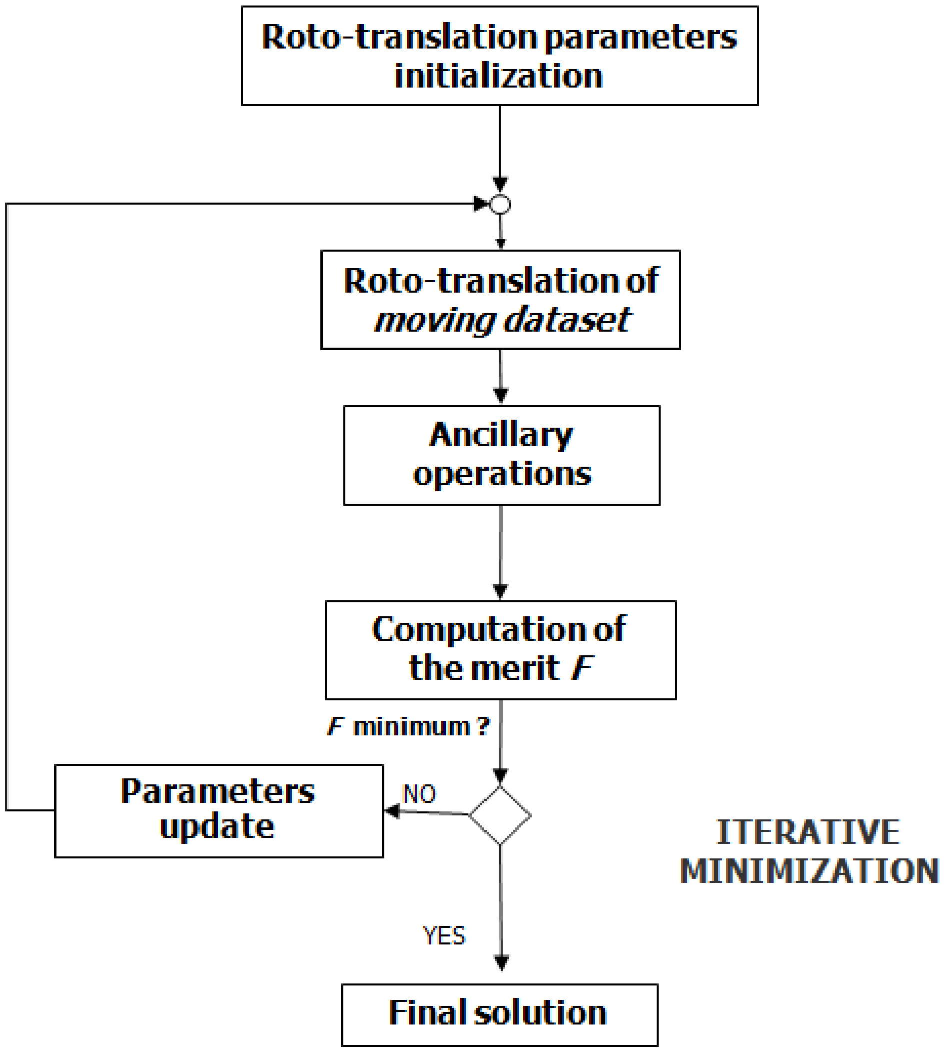
Methods:

- ✓ *Point-based* registration with correspondence (fiducials)
- ✓ *Point-based* registration without correspondence (surface patches)
- ✓ *Image-based* registration working on intensity levels (X-ray projections)

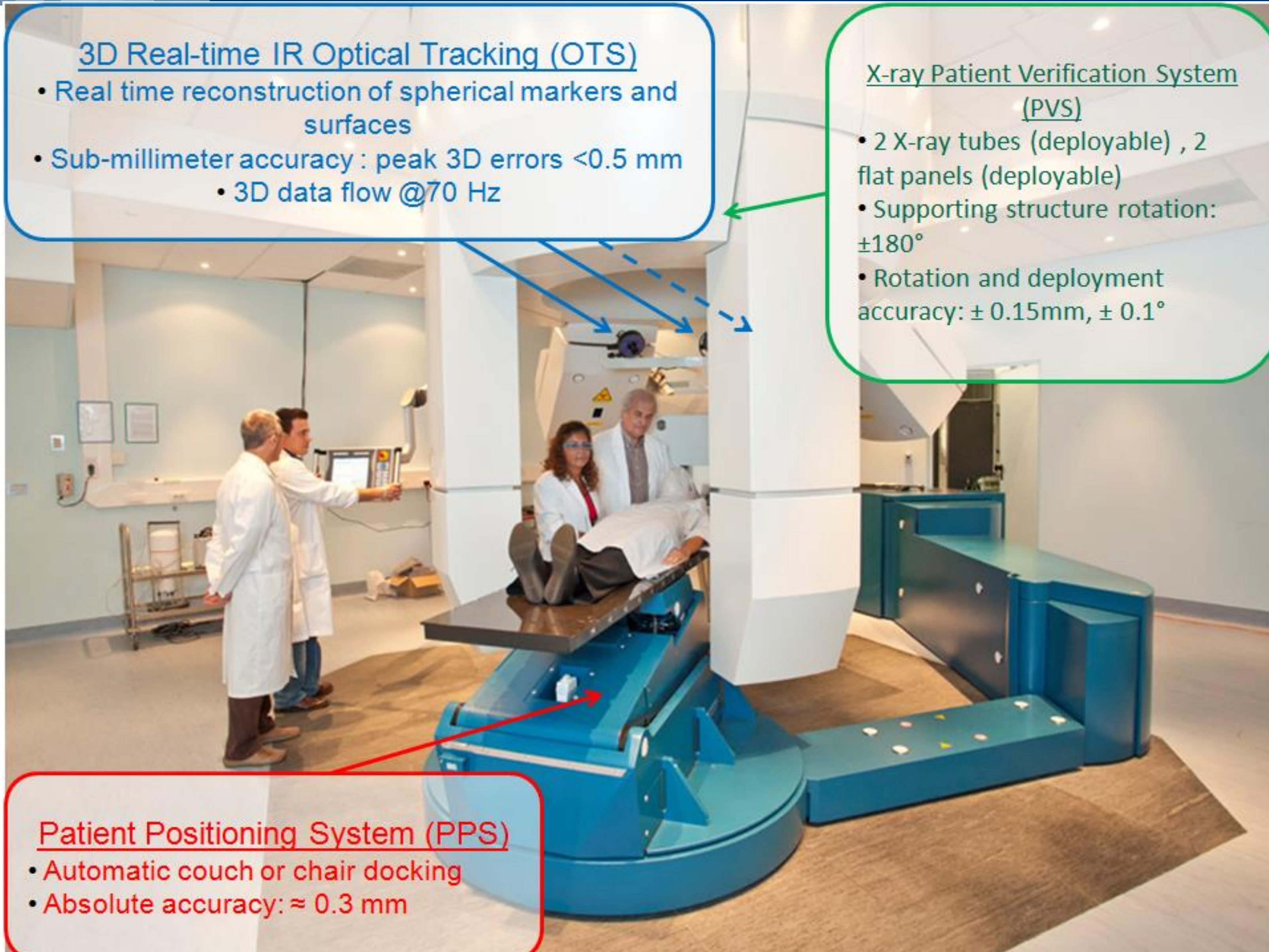
Output:

- ✓ Parameters of a rigid transformation (requires accurate 6 d.o.f. patient positioning systems)

Image (Optical) guidance algorithm



Inter-fractional uncertainties management: Image guidance @ CNAO



3D Real-time IR Optical Tracking (OTS)

- Real time reconstruction of spherical markers and surfaces
- Sub-millimeter accuracy : peak 3D errors <0.5 mm
- 3D data flow @70 Hz

X-ray Patient Verification System (PVS)

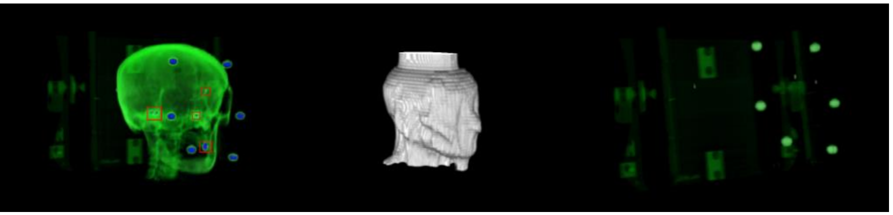
- 2 X-ray tubes (deployable) , 2 flat panels (deployable)
- Supporting structure rotation: ±180°
- Rotation and deployment accuracy: ± 0.15mm, ± 0.1°

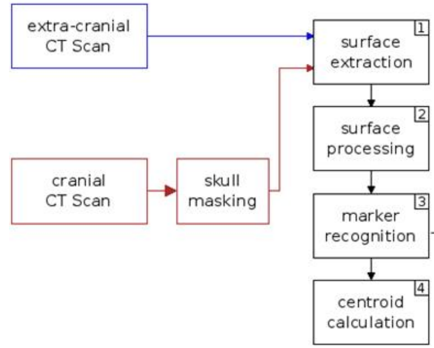
Patient Positioning System (PPS)

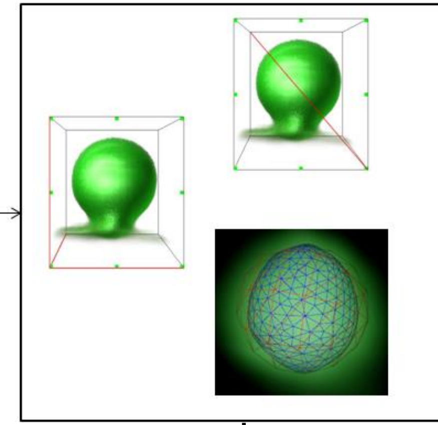
- Automatic couch or chair docking
- Absolute accuracy: ≈ 0.3 mm

Inter-fractional uncertainties management
Optical tracking in particle therapy: the CNAO case

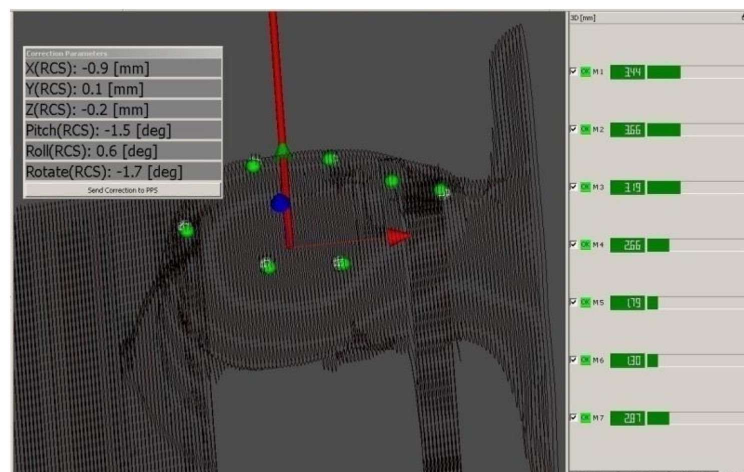
- In CNAO, IR-point-based optical tracking is used for preliminary patient position correction and continuous monitoring





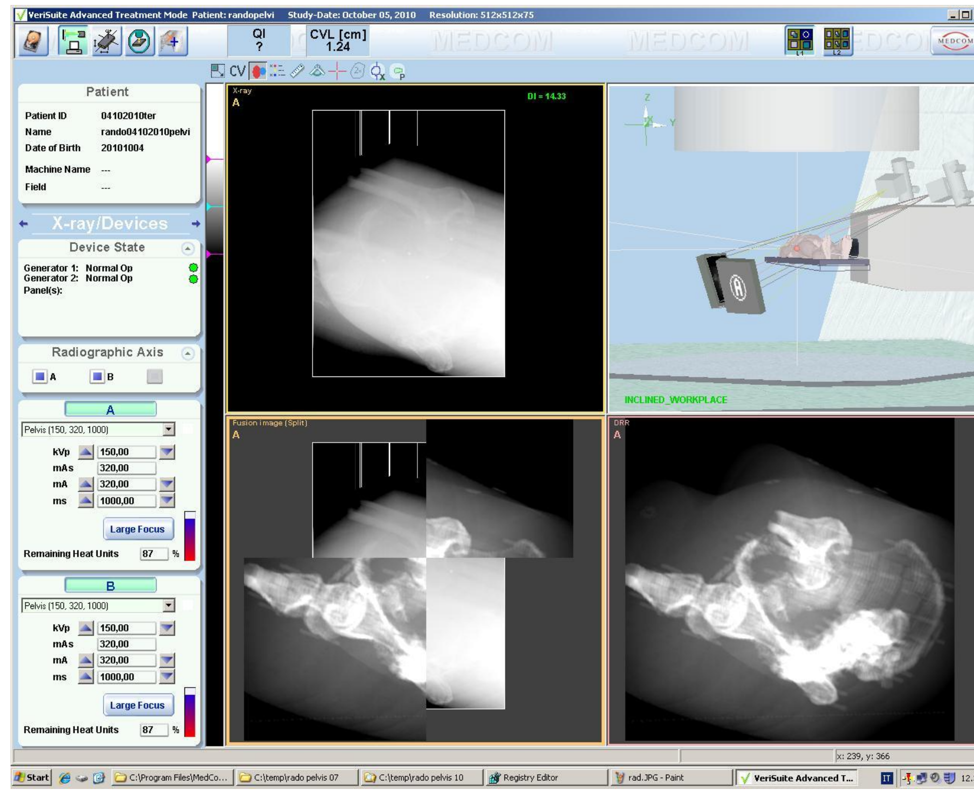


- Reference marker localization (reference dataset) is obtained from CT with an automatic segmentation algorithm (accuracy <0.2 mm) (Fattori et al., IEEE Trans Biomed Eng, 2012)
- Real-time estimation of roto-translation parameters is performed at patient set-up through optimized implementation of Newton-Raphson optimization process minimizing corresponding marker distances (Pella et al., TCRT, 2014)



Inter-fractional uncertainties management
2D-3D image registration @ CNAO

- ✓ 2D-3D rigid image registration is applied for patient positioning refinement based on bony anatomy



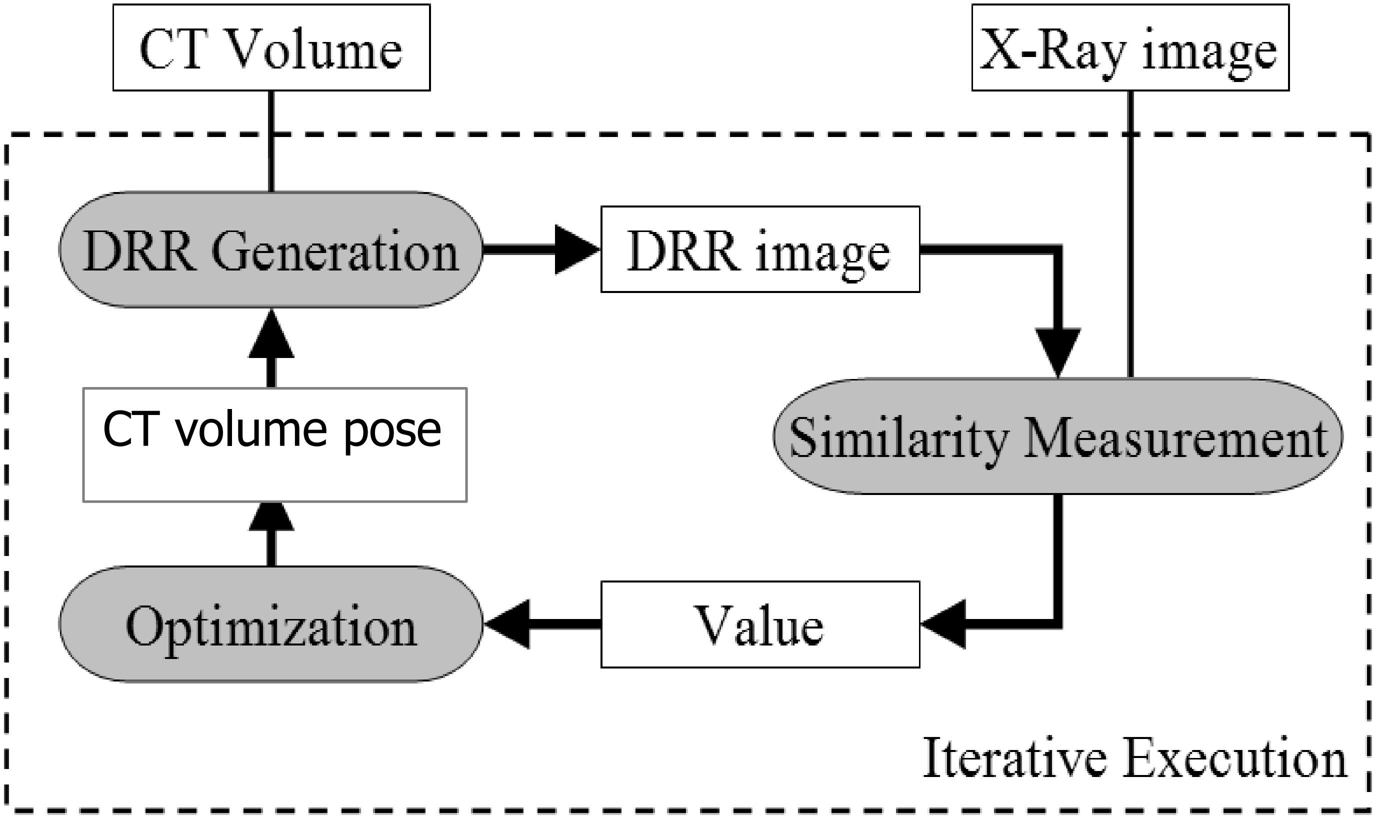
✓ Input *(physical space)*

- CT slice stack for treatment planning
  - voxel size
  - gray-level 3D matrix to be converted to HU units/attenuation data

- in-room image I_{fluoro} intrinsic geometry
  - physical parameters of X-ray beam (energy-current-intensity)
  - pixel physical dimensions
  - detector size and resolution (pixel number)
  - SID (source to imager (detector) distance)

- X-ray projection geometry (known w.r.t. isocentric reference)
  - isocenter position (3D vector from CT voxel [1,1,1] (origin) to projection center)
  - isocentric projection angle
  - SAD (source to axis distance)

✓ Algorithm

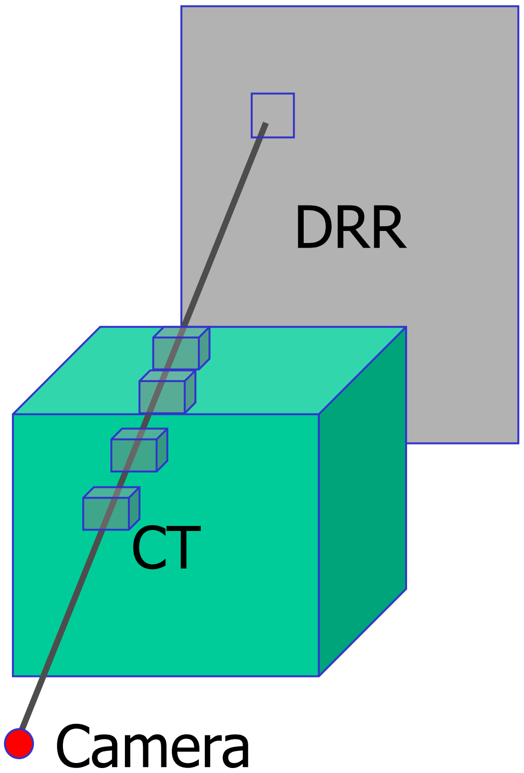

CT Volume
X-Ray image
DRR Generation
DRR image
CT volume pose
Similarity Measurement
Optimization
Value
Iterative Execution

Inter-fractional uncertainties management
2D-3D image registration

✓ Digital Reconstructed Radiography (DRR) generation

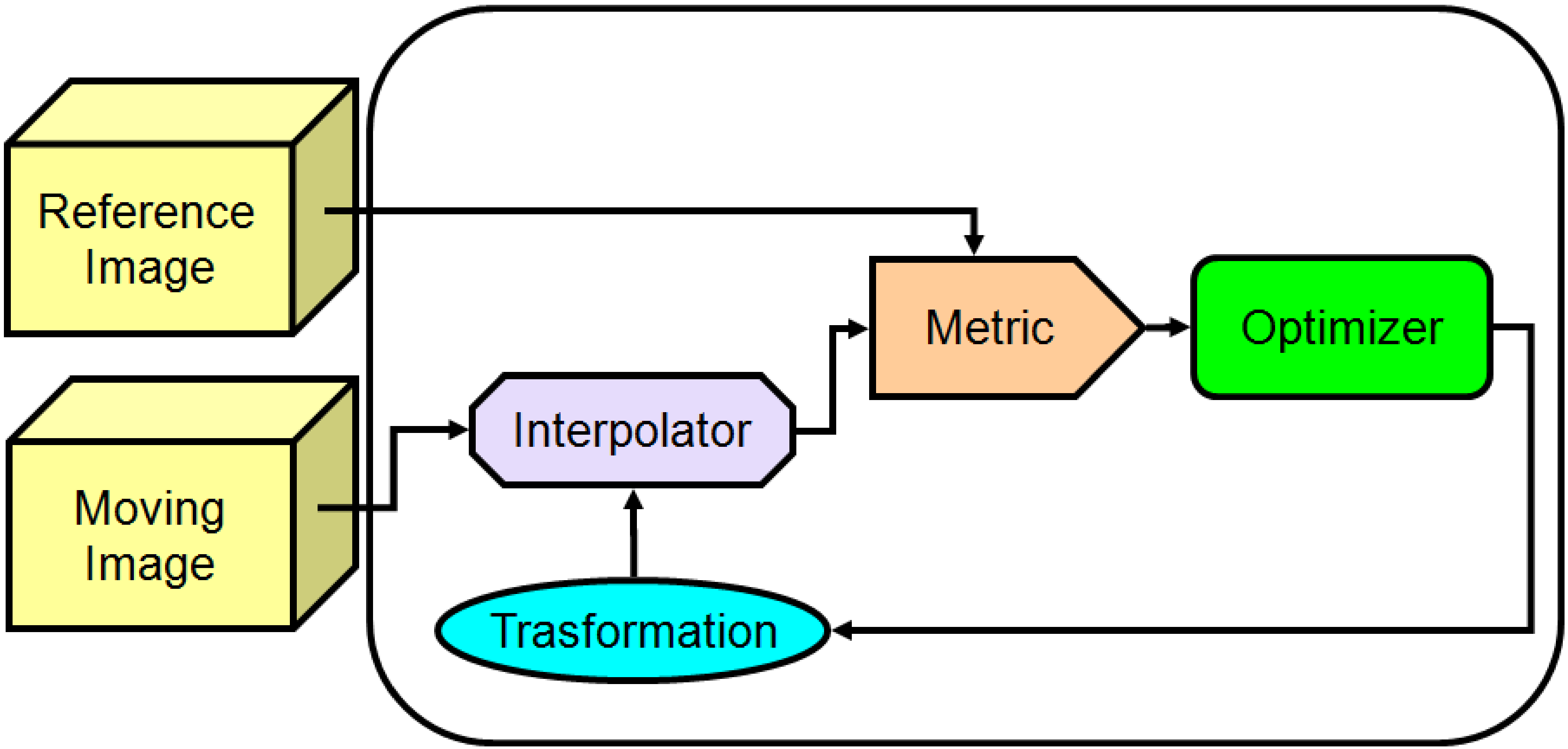
✓ Ray tracing/casting methods

- For each pixel:
  - define ray from pixel to source
  - find intersection with voxels
  - accumulate beam attenuation (Beer's law)
  - light-up pixel as a function of impinging intensity



- quality (artifacts, partial volume effects)
- computational load
- many optimization to increase speed
  - parallel processing
  - GPU-based

✓ Similarity measure and optimization



✓ Similarity measure

Monomodal registration:

MSE (mean squared error) $MSE(A,B) = \frac{1}{N}\sum_{i,j,k}\left[A_{ijk} - B_{ijk}\right]^2$

CC (correlation coefficient) $CC(A,B) = \frac{\sum_{i,j,k}\left(A_{i,j,k} \cdot B_{i,j,k}\right)}{\sqrt{\sum_{i,j,k} A_{i,j,k}^2 \cdot \sum_{i,j,k} B_{i,j,k}^2}}$

…

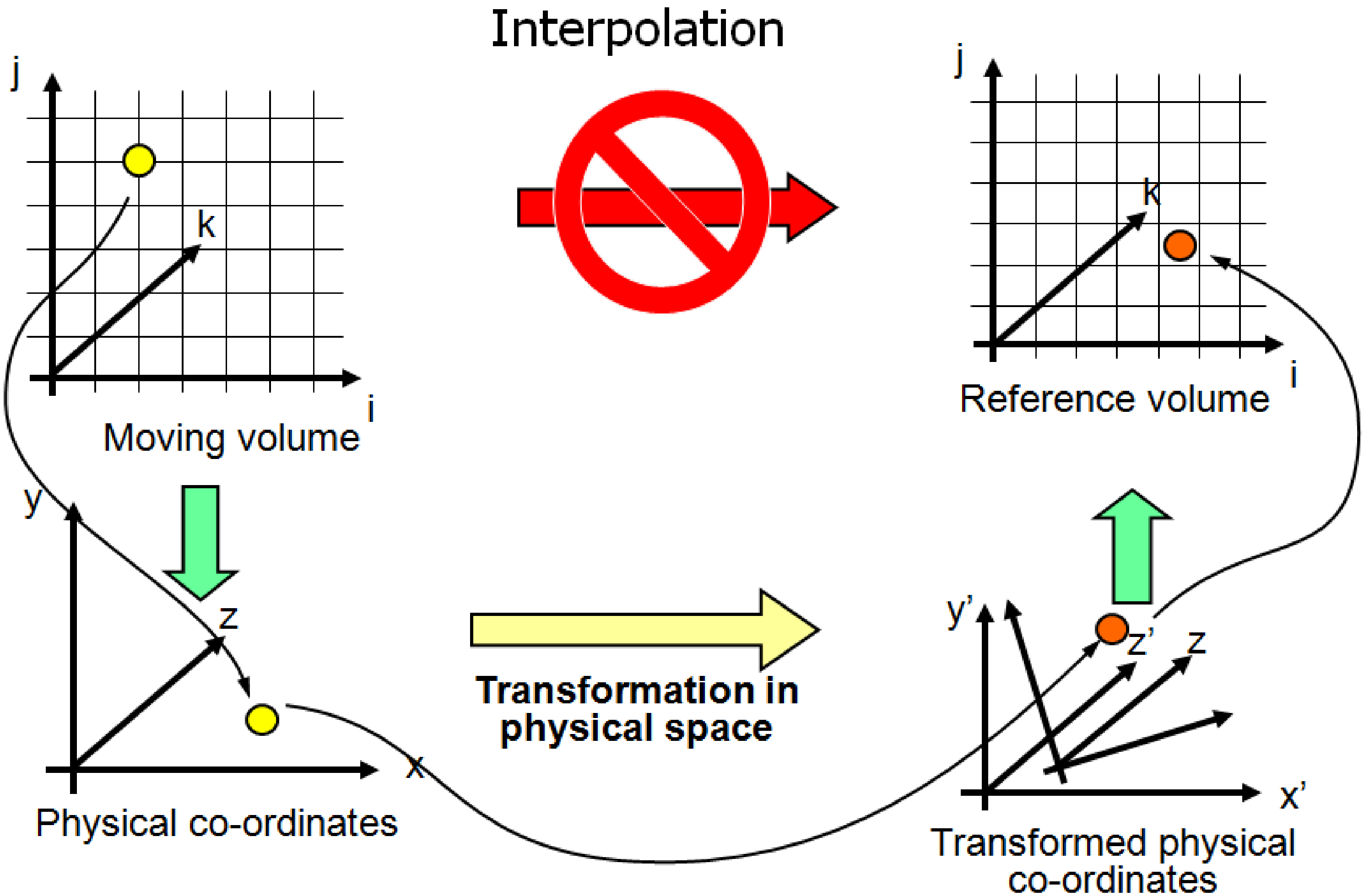
Comparable gray-level intensities

Multimodal registration:

NMI (normalized mutual information) $NMI(A,B) = \frac{H(A,A) + H(B,B)}{H(A,B)}$

where H(..,..) is the Shannon entropy of the joint histogram of the two images

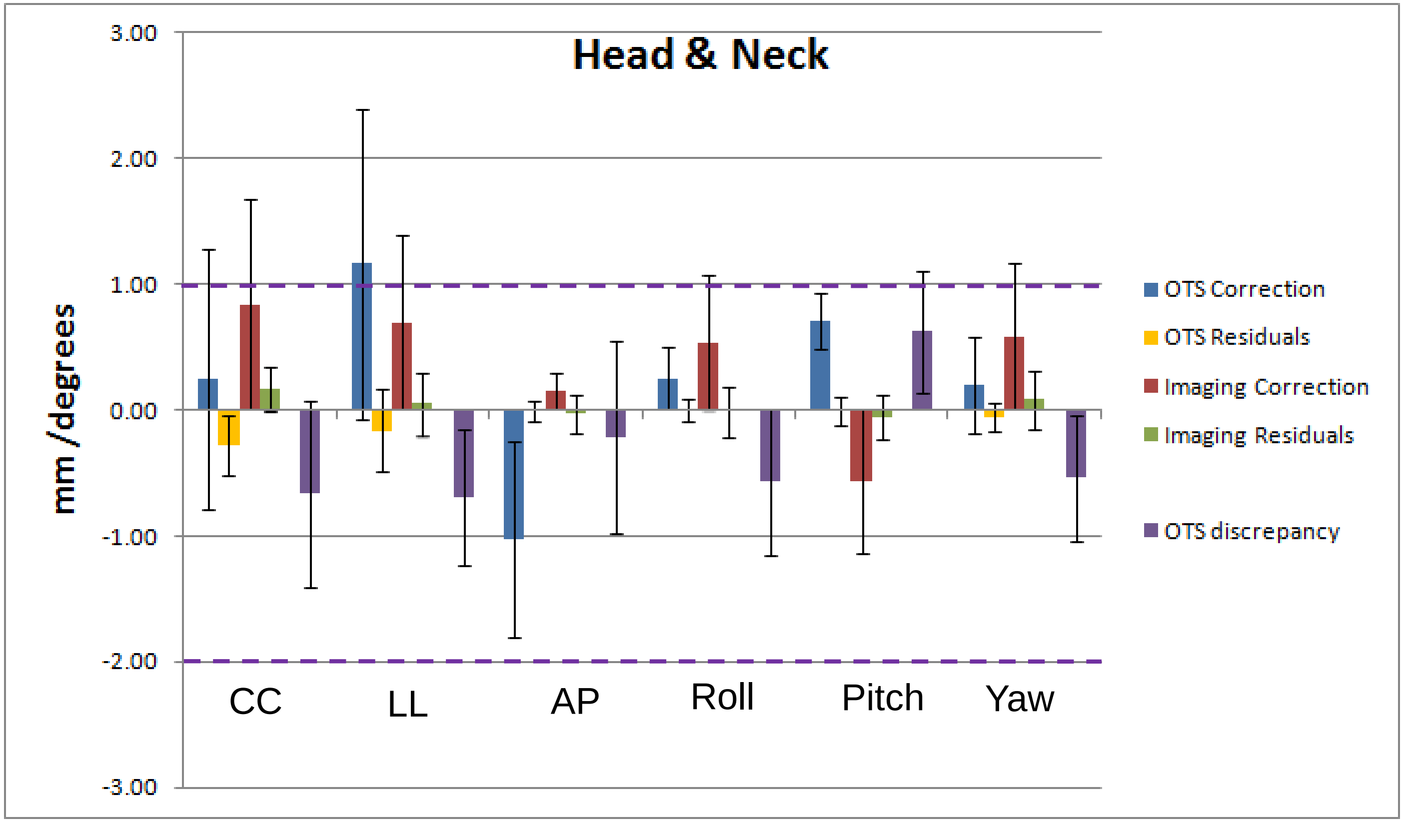
✓ Similarity measure and optimization



- 2D-3D registration wrap-up
  - Input:
    - treatment planning CT slice stack
    - in-room X-ray images I_{fluoro}
    - intrinsic and estrinsic parameters of X-ray projection geometry
    - initial guess of patient (CT volume) position and orientation $\mathbf{p}_i$ w.r.t. isocentric reference system
  - Iterative procedure:
    1. For each $\mathbf{p}_i$ virtual X-ray (DRRs) are generated, I_{DRR}
    2. Disparity assessment between I_{DRR} and I_{fluoro} with interpolation
    3. Parameters update $\mathbf{p}_i+1=\mathbf{p}_i+\mathbf{d}$ for disparity minimization
  - At least two projections needed (typically L-L and A-P) in order to cope with the motion along the projection direction (scale factor)

Combination of optical and image-based set-up correction on CNAO patients

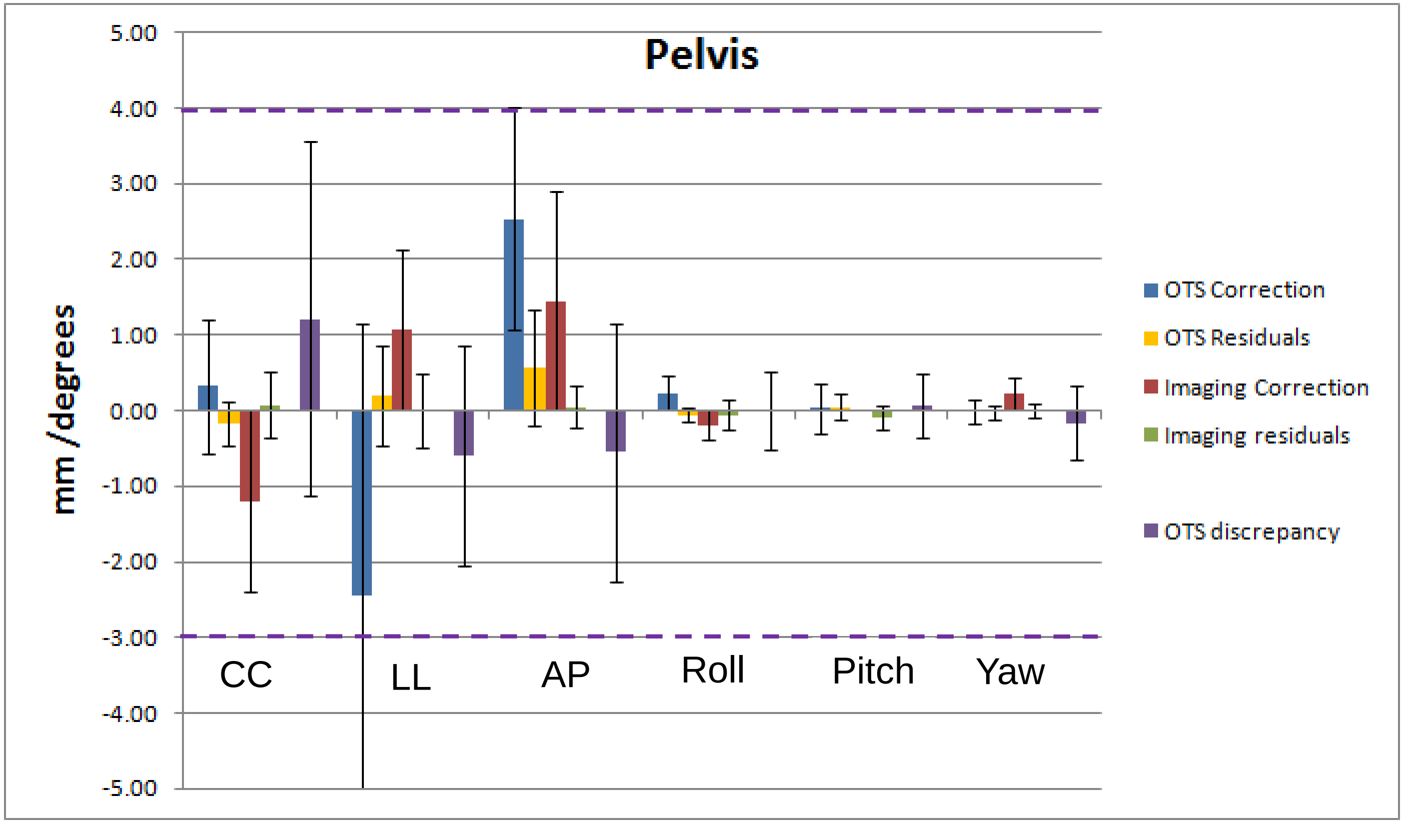
99 fractions



Desplanques et al., *J Radiat Res.*, *2013*

Combination of optical and image-based set-up correction on CNAO patients

72 fractions

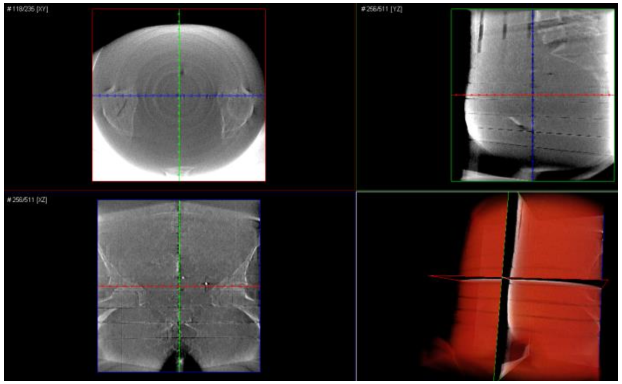


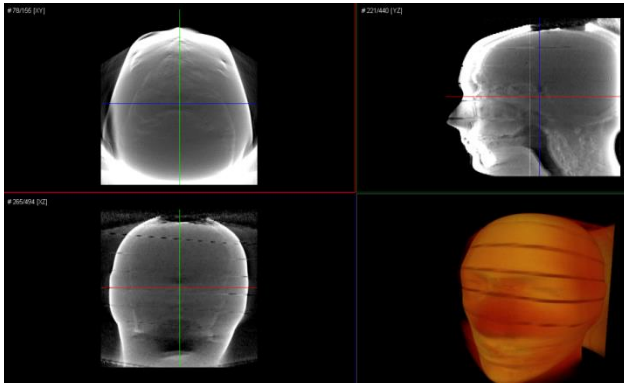
Desplanques et al., *J Radiat Res.*, *2013*

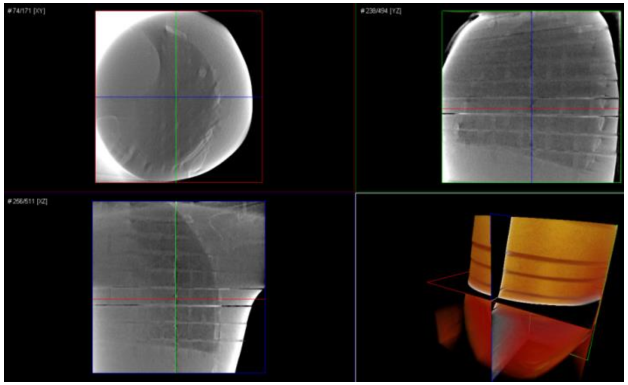
Inter-fractional uncertainties management
3D-3D image registration

- ✓ 3D-3D image rigid registration is an extension of 2D-3D registration
- ✓ Input:
  - treatment planning CT slice stack
  - in-room volumetric imaging (CBCT)

- ✓ At CNAO (Room #2)
  - ✓ 440 projections over 220° ROM
  - ✓ acquisiton time <40 sec
  - ✓ Recostruction time (GPU parallelized FDK) < 60 sec (depends on desired resolution)
  - ✓ 256x256x2.5 mm voxel dimension
  - ✓ 3D-3D registration time <60 sec



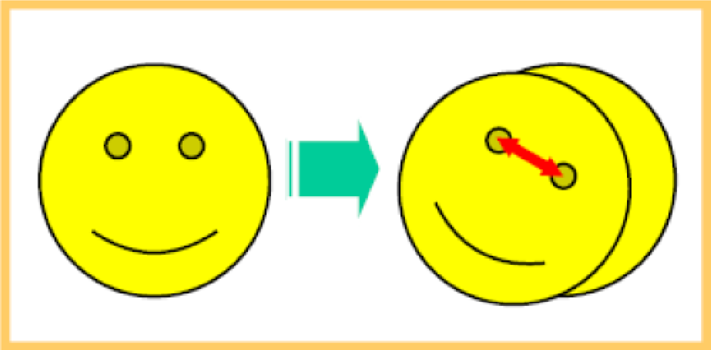




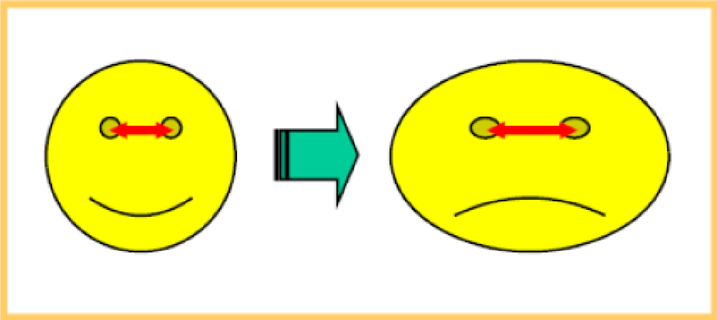
Inter-fractional uncertainties management
Deformable image registration

Rigid
- preserves straightness of lines
- preserves point distance
- transformations: rotation, translation, zoom, skew
- hp: intra-patient, rigid anatomy

KO: PATIENT ≠ RIGID BODY



Non-Rigid/Deformable (DIR)
- tissue deformation (due to organ motion)
- inter-patient
- atlas
- intra-patient but different time series (to evaluate organ motion)



Long time scale: weight loss, tumor reduction
Short time scale: respiration

Inter-fractional uncertainties management
Deformable image registration

Rigid Registration

$$T = \left(\begin{array}{ccc|c} & R(\Omega, \Phi, K) & & \begin{matrix} X \\ Y \\ Z \end{matrix} \\ \hline 0 & 0 & 0 & 1 \end{array} \right)$$

6 parameters
(3 translations + 3 rotations)

T = T(Ω, Φ, K, X, Y, Z)

order of the operations matters

$$\begin{pmatrix} 1 & 0 & 0 & X \\ 0 & 1 & 0 & Y \\ 0 & 0 & 1 & Z \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos(\Omega) & \sin(\Omega) & 0 \\ 0 & -\sin(\Omega) & \cos(\Omega) & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} \cos(\Phi) & 0 & \sin(\Phi) & 0 \\ 0 & 1 & 0 & 0 \\ -\sin(\Phi) & 0 & \cos(\Phi) & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} \cos(K) & \sin(K) & 0 & 0 \\ -\sin(K) & \cos(K) & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

Translation   Rotation around x   Rotation around y   Rotation around z

Affine Registration

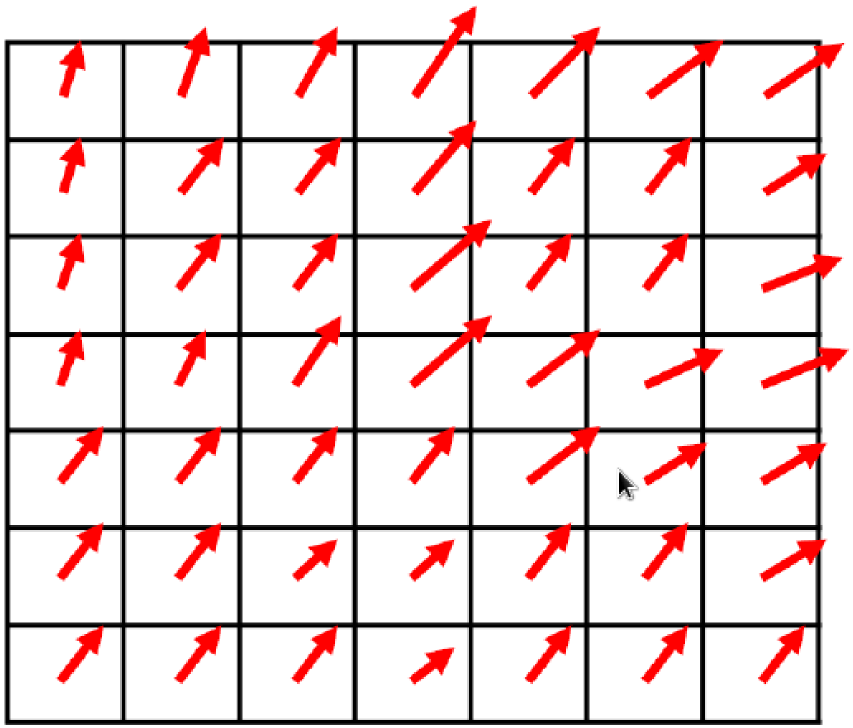
12 parameters
(3 translations + 3 rotations +3 scaling +3 shearing)

Deformable Image Registration (DIR)

T = T(Ω, Φ, K, X, Y, Z, M)

M: deformation model

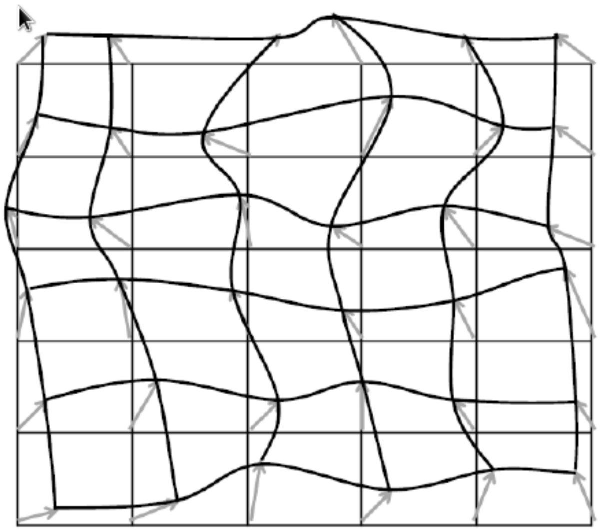
Representation of the deformation: **Vector Field (VF)** → displacement vector



How to compute VF?

- Free-Form Deformation (FFD) - based on B-splines

Free-Form Deformation

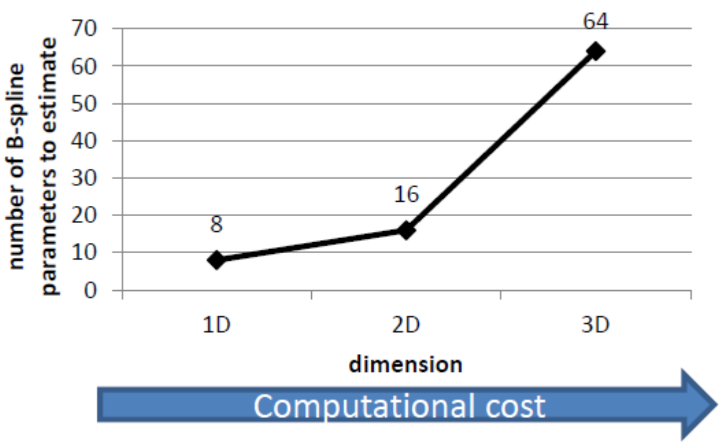


Model transformation elements:

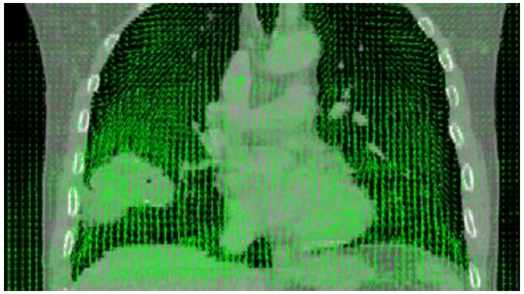
1. Grid of volumetric cells with control points
2. Approximating function (i.e. B-spline)

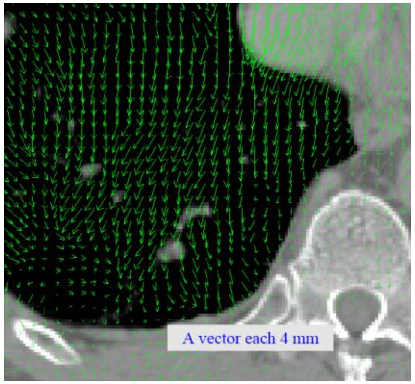
Define the deformation by computing the VF in each control point and interpolating the deformation far from the control points with a B-spline.

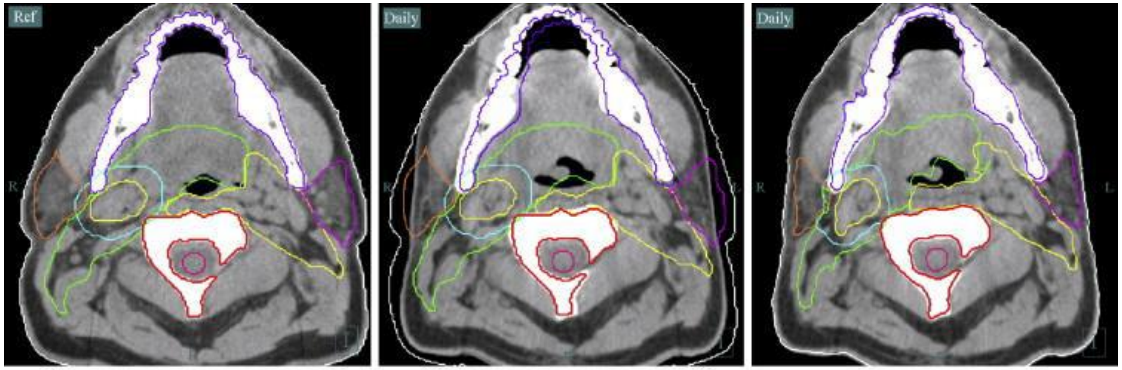
B-splines : 3° order



- Deformable image registration for image guidance: a powerful tool to be used with caution
    - Provides a representation of non-rigid deviation between reference (CT) and moving (CT/CBCT) volumes
    - Supports clinical decisions for re-planning but integration in adaptive clinical workflow is not trivial
    - Paves the way for on-line dose recalculation by means of contour propagation
    - Requires registration quality assessment (ill-posed problem with several approximation and local minima) by means of manually or automatically detected anatomical landmarks







Reference Planning CT | Bone Rigidly Aligned Daily CT | Deformed Contours to Match with the Daily CT

Inter-fractional uncertainties management

- ✓ Integration between optical tracking registration and image-based 2D-3D (or 3D-3D) registration is THE strategy to ensure swift management of inter-fractional uncertainties (Baroni et al., *J Radiat Res*, 2007; Tagaste et al, *IJROBP*, 2012)
- ✓ The role of IR-tracking may be enhanced to provide a preliminary patient adjustments that optimizes and speeds-up image-based registration (Desplanques et al., *2013*)
- ✓ Flexibility and reliability of IR-systems maybe enhanced by integrating point-based and surface based detection/registration capabilities
- ✓ Rigid registration (point-based, image-based) is the currently applied strategy for inter-fractional uncertainties management
- ✓ Deformable image registration is a powerful technique with huge potentials in adaptive treatment strategies, but caution is required

- ✓ The role of IR-tracking to patient immobility verification, management of intra-fractional uncertainties and time-resolved / motion correlated dose delivery is invaluable

Motion monitoring technology:

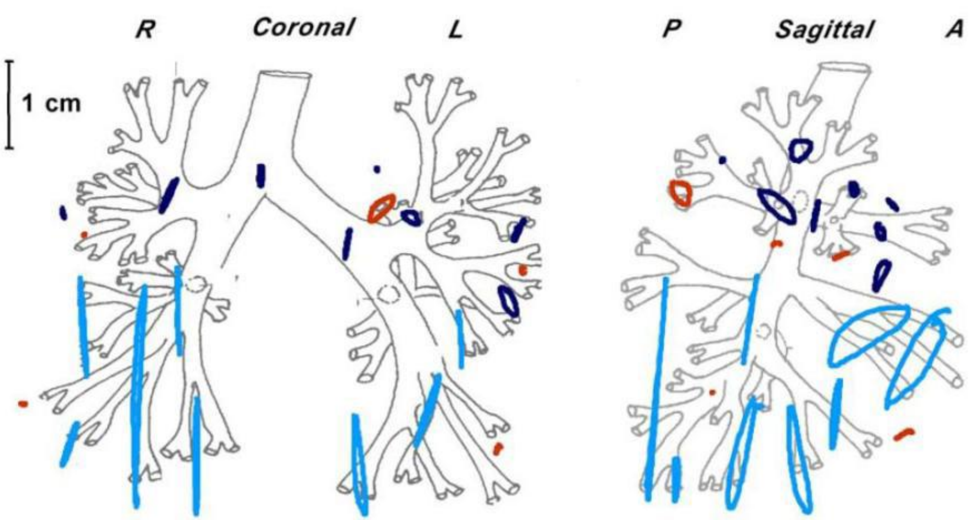
- ✓ Motion monitoring in 4DCT: sufficient as ground-truth ?
- ✓ How to improve ?

Local and global motion modeling beyond tumor tracking

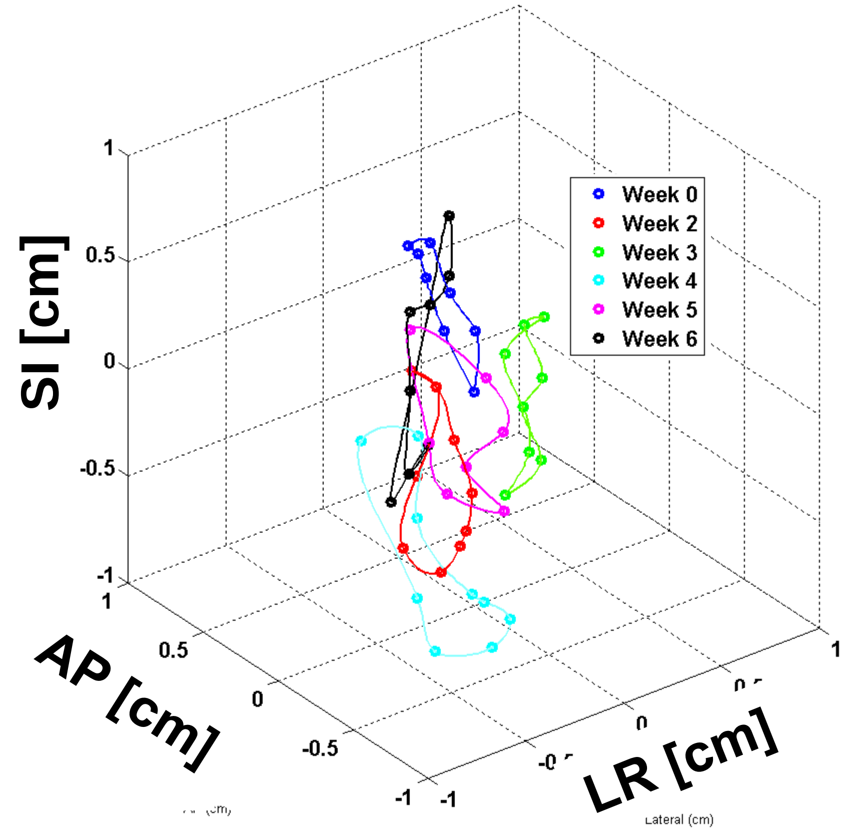
- ✓ In-out correlation models (local)
- ✓ Global motion models for adaptive strategies

Respiratory motion uncertainties

- Main motion component in **superior-inferior** (SI) direction
- Variability in motion trajectory (**hysteresis loop**)
- Inter/intra-fraction changes in respiratory parameters (**baseline**, **amplitude** and **frequency**)



Intra-fractional

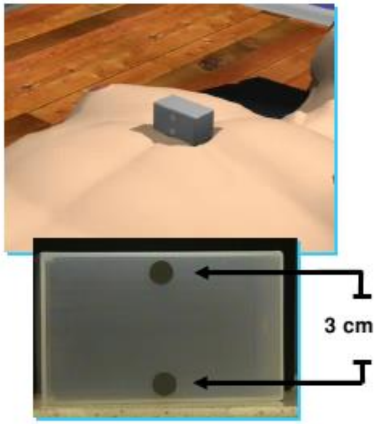


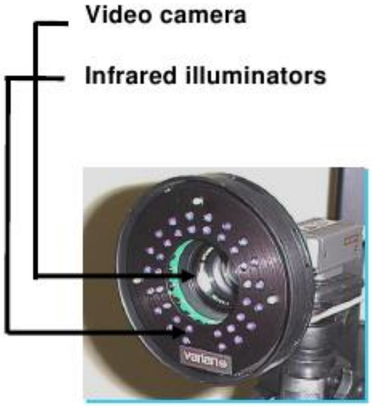
Inter-fractional

4D CT in clinical practice

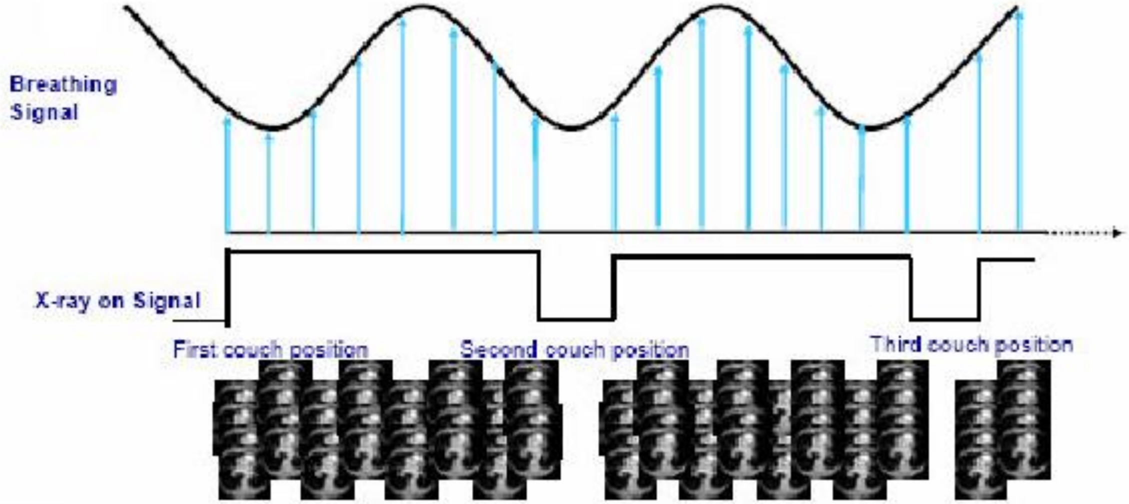
Different technologies for motion monitoring:

- **Infrared markers (Varian RPM)** ⟶
- **Elastic belt**
- **Spirometry**

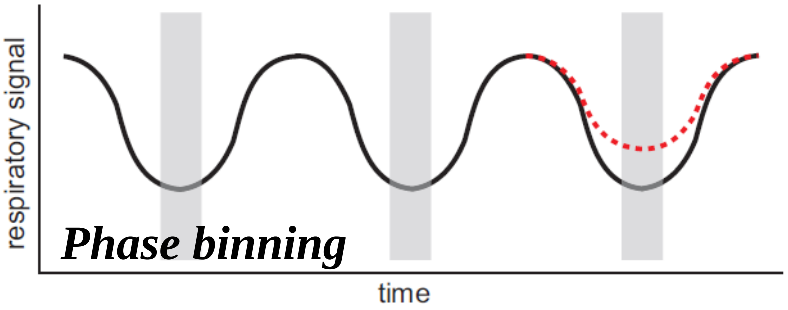


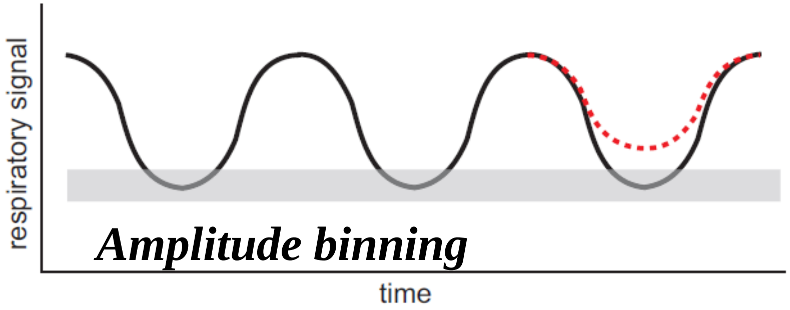


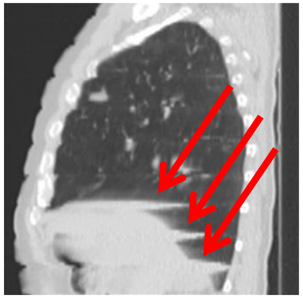
Retrospective image sorting



4D CT artifacts

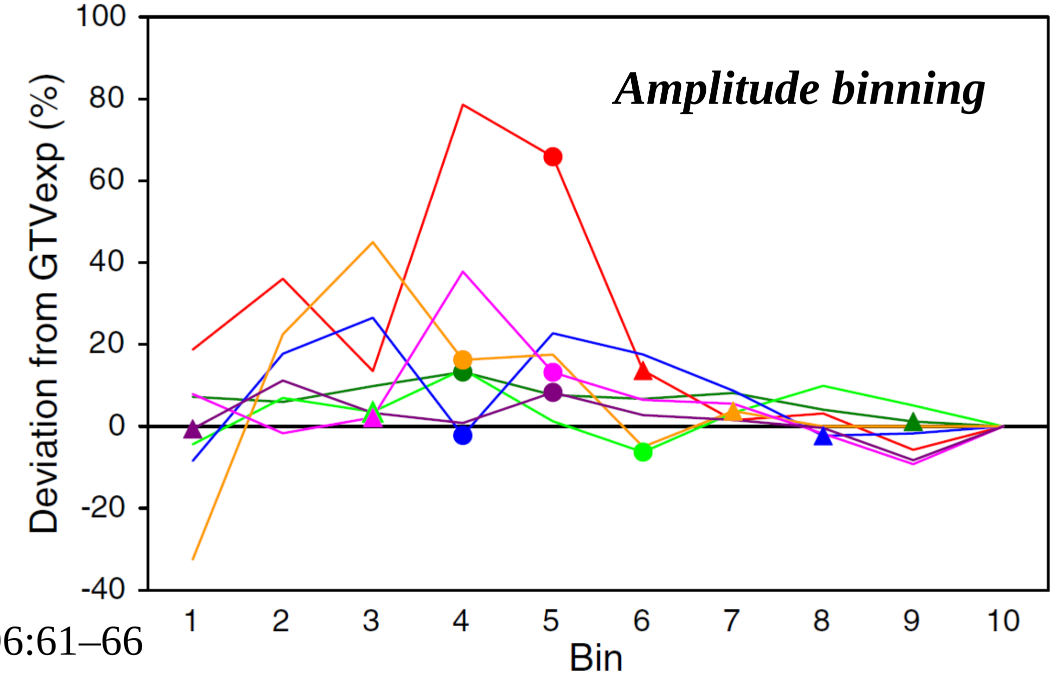






Hugo GD and Rosu M, Z. Med. Phys. 2012;22:258–271

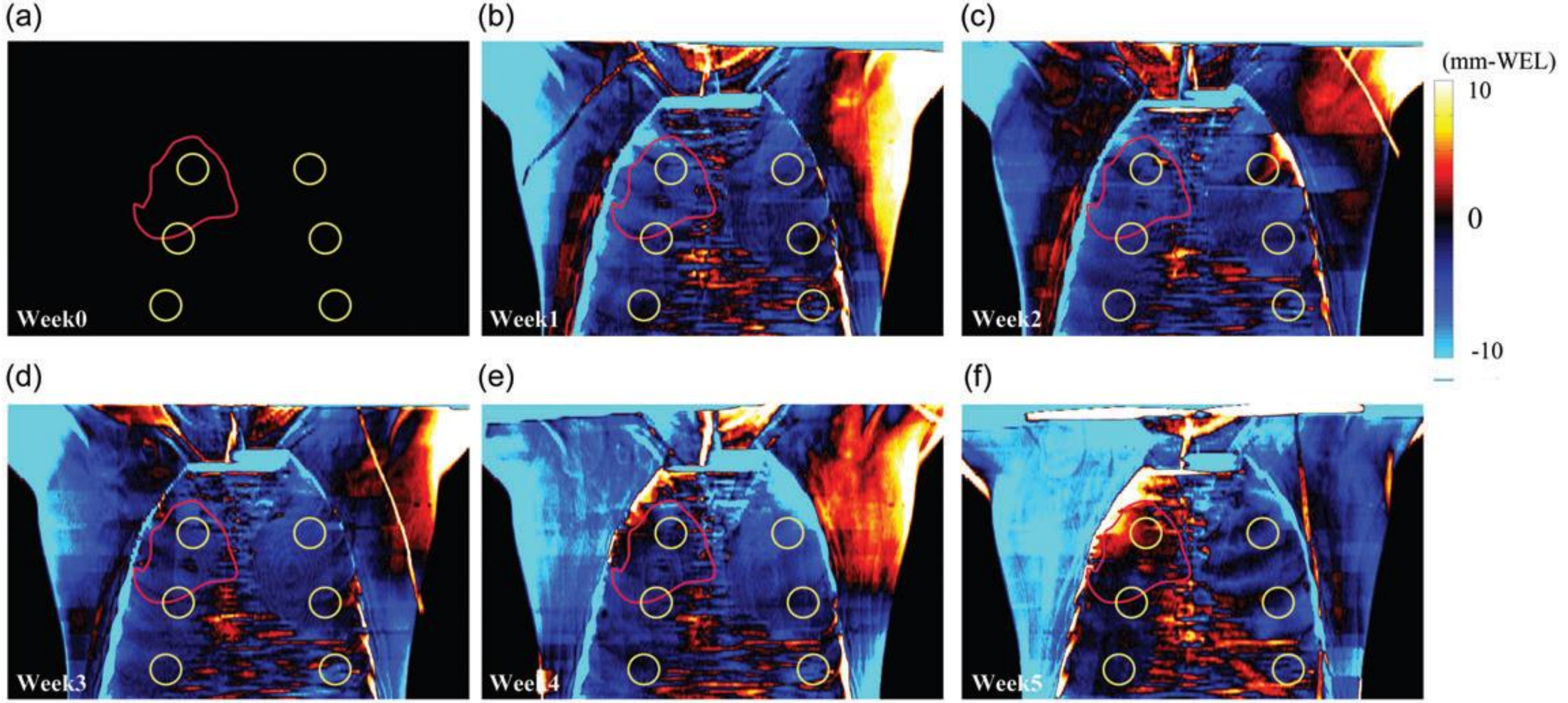
- **GTV size variations significantly correlated to tumor motion** in the cranio-caudal direction for both **amplitude- and phase-binned 4D-CT scans**



Persson GF *et al*, Radiother. Oncol. 2010;96:61–66

4D CT reliability: particle therapy

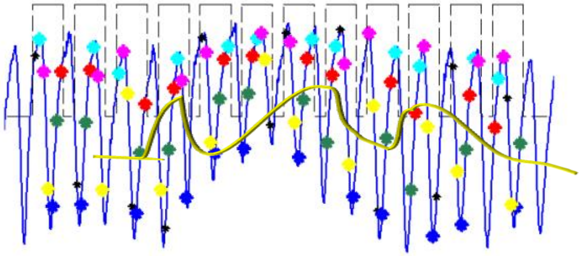
- **Chest wall WEL changes** up to **-1.0 cm** (intra-fraction) and **-2.5 cm** (inter-fraction):
- **Patient setup** (arm position)
- **Breathing inconsistencies** (inter-fraction)



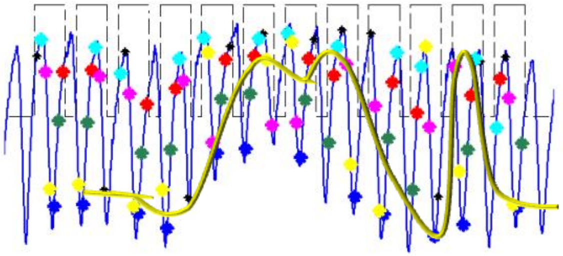
Mori S *et al*, J. Radiat. Res. 2014;55:309–319

Robust 4DCT resorting – multiple markers

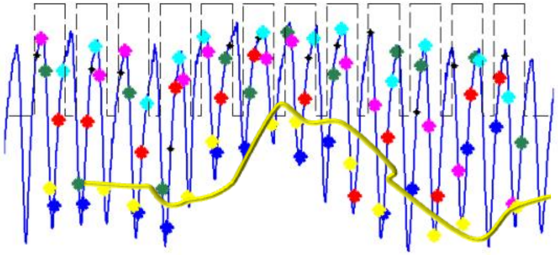
RPM phase

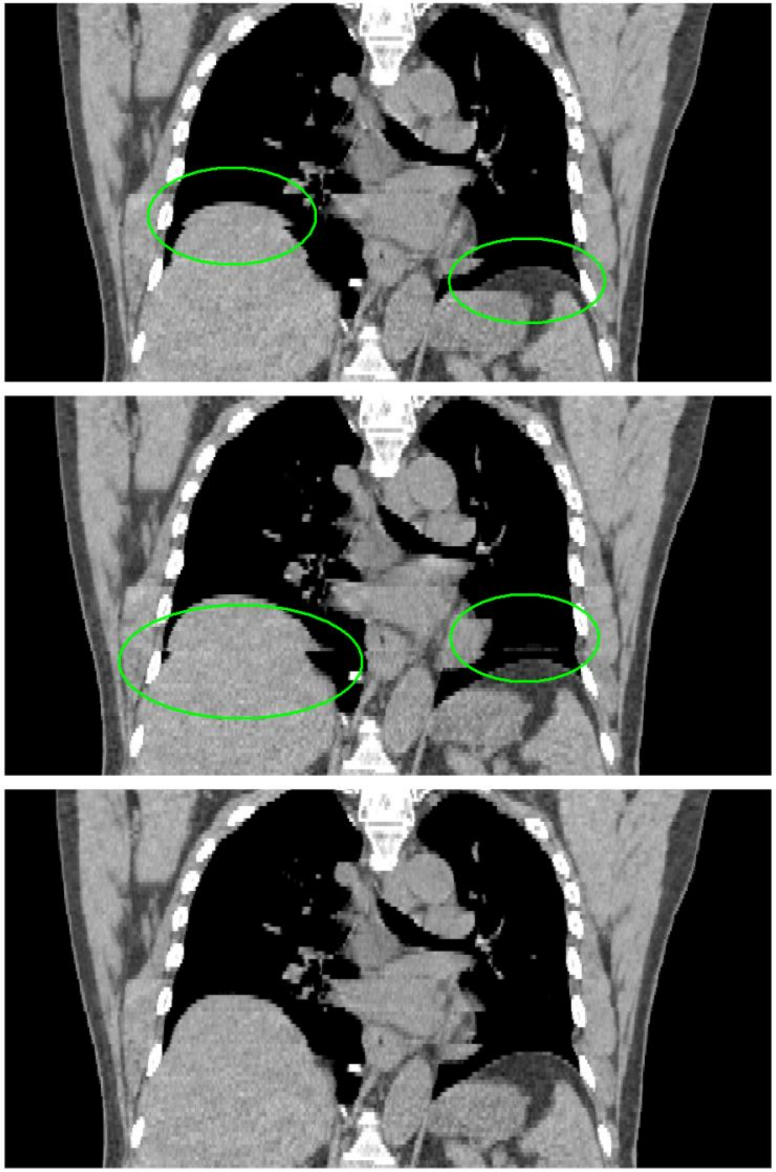


RPM amplitude



Multiple markers





(Gianoli et al, Med Phys 2011)

4DCT quality

"Conventional/commercial" 4DCT:

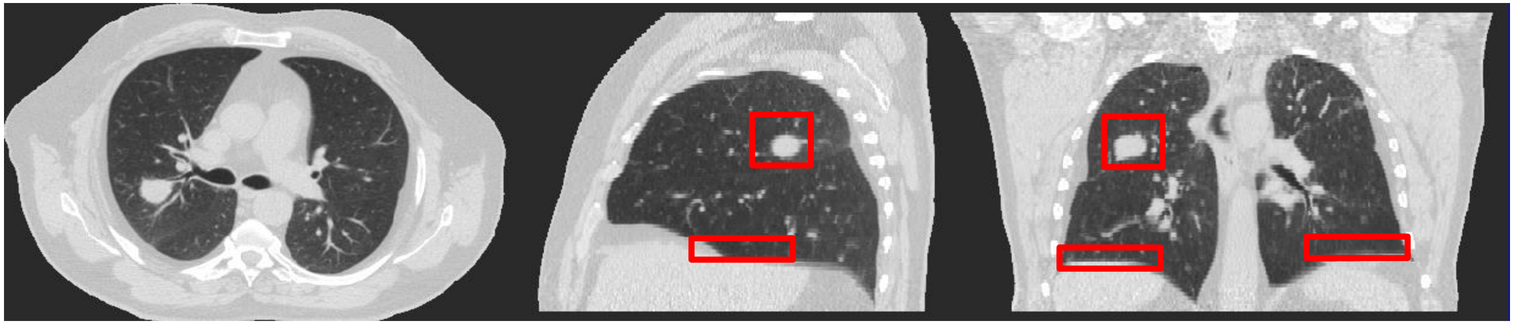
- ✓ relies on a single-dimension breathing signal
- ✓ performs a relatively low temporal resolution in clinical use
- ✓ is prone to motion artifacts resulting in deformation of critical structures

Nevertheless:

- ✓ feeds time-resolved treatment planning and delivery strategies
- ✓ feeds many motion models based on deformable image registration
- ✓ represents the ground truth for motion models assessment

Then ?:

- ✓ Increase the complexity of motion monitoring during CT scanning
- ✓ Adopt more robust imaging modalities for motion description (4D MRI)



Motion compensation in dose delivery

1) ABDOMINAL COMPRESSION

- Reduction of diaphragmatic excursion
- Effective for lower lobe tumors
- Minor or negative effects for upper/middle lobe tumors *[Bouilhol 2012]*

2) BREATH-HOLD

- Dose delivery during breathing interruption at a predefined phase

3) RESPIRATORY GATING

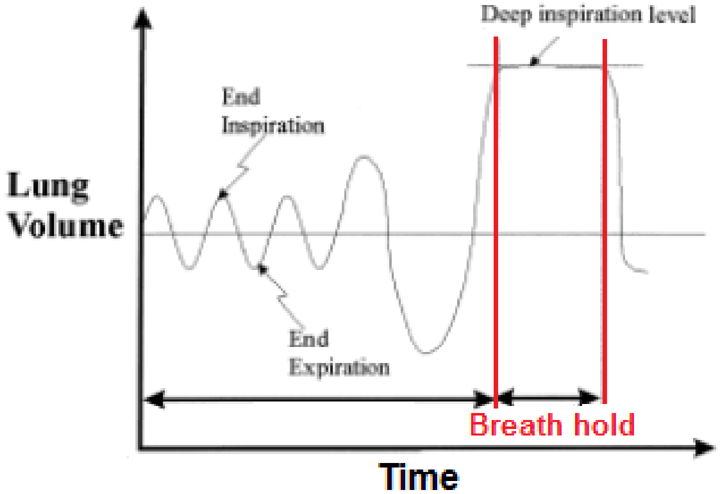
- Dose delivery during a specific window of the breathing cycle

4) TUMOR TRACKING

- Dynamic beam repositioning to follow tumor motion

DEEP INSPIRATION BREATH-HOLD (DIBH)

- Decrease of lung density
- Greater sparing of healthy pulmonary tissues



LIMITATIONS

- Patient compliance and active participation
- Low reproducibility of target position between repeated maneuvers

  - Training session

  - Audio-visual guidance

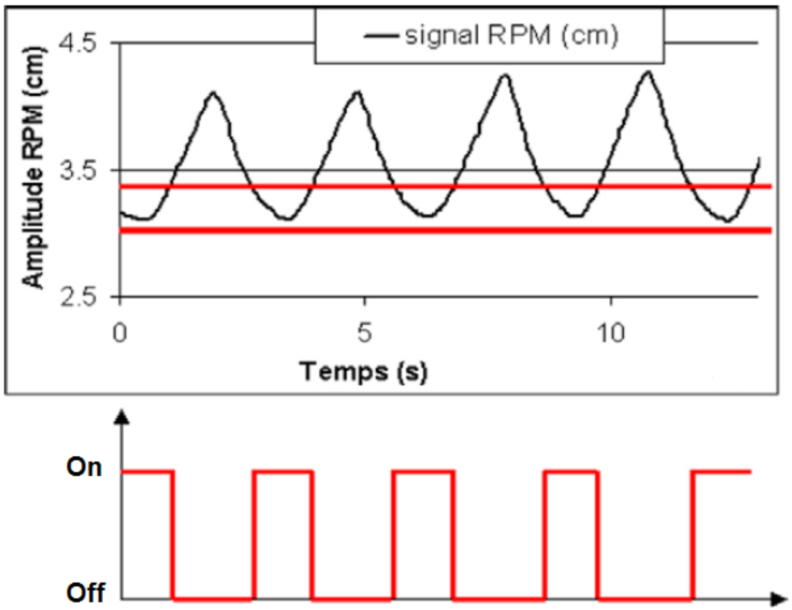
  - Active Breathing Control (ABC): occlusion valve to stop patient air flow at the desired level

Respiratory gating

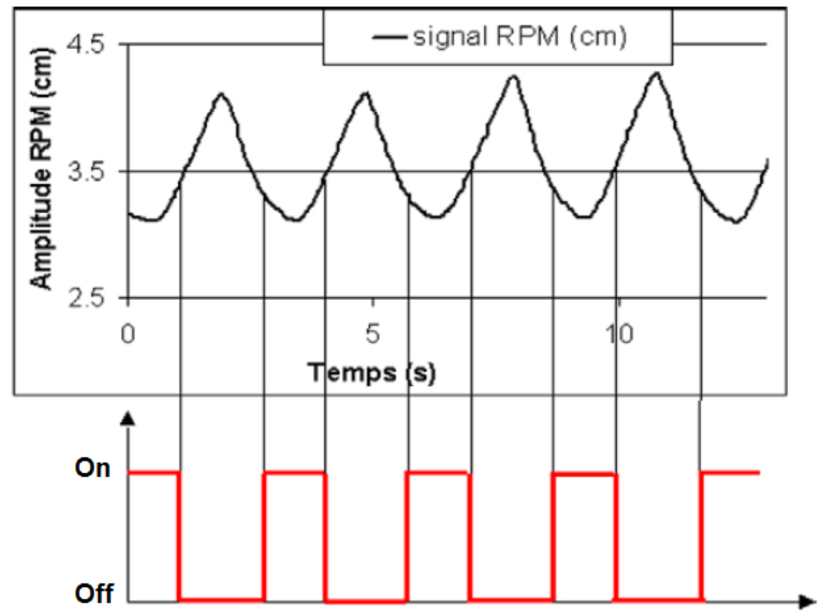
END-EXHALE GATING LEVEL

- Most reproducible/stable respiratory state *[Seppenwoolde 2002]*

1) Amplitude-based gating

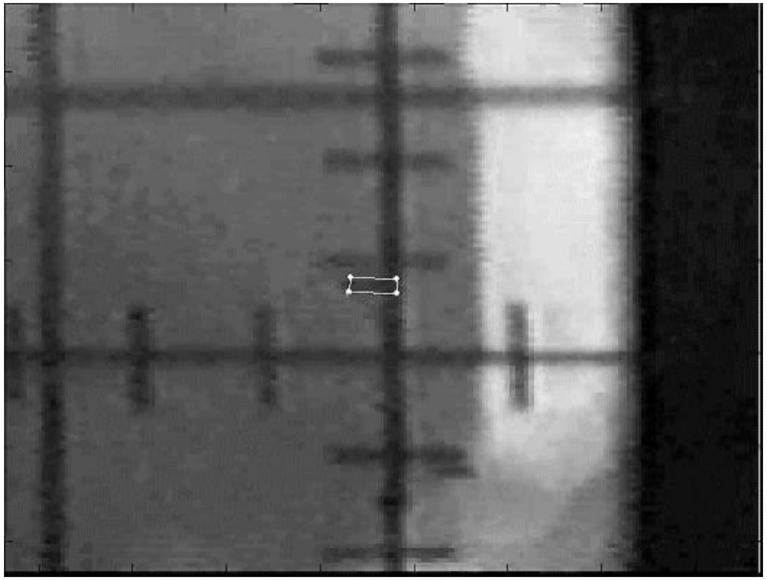


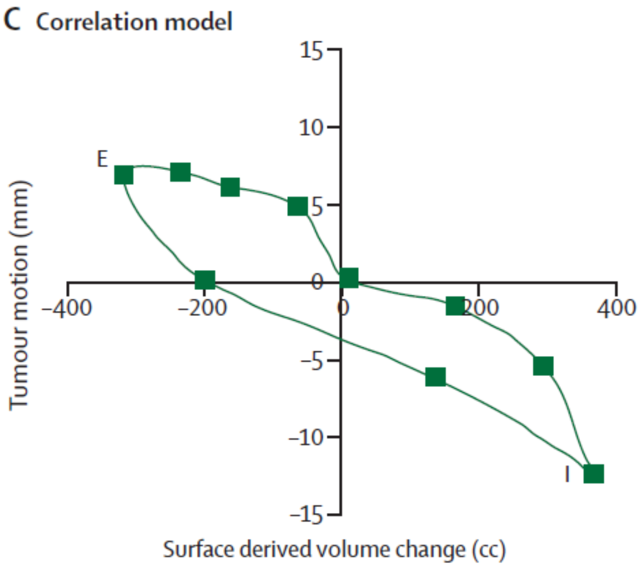
2) Phase-based gating



Tumor tracking

- ✓ Direct tumor imaging
  - ✓ Marker-based methods
    - ✓ X-ray [Shirato et al. *Cancer 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]

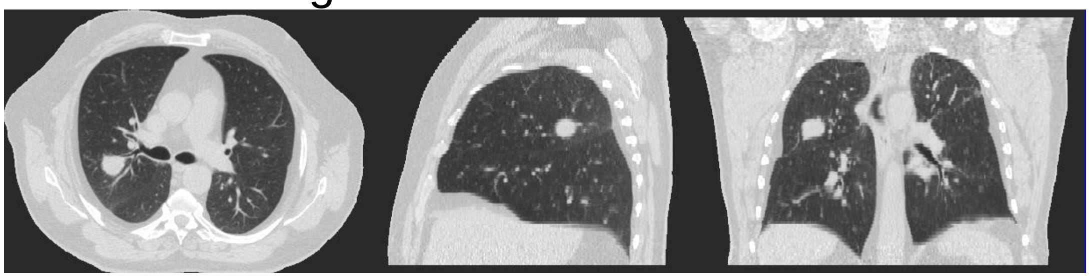


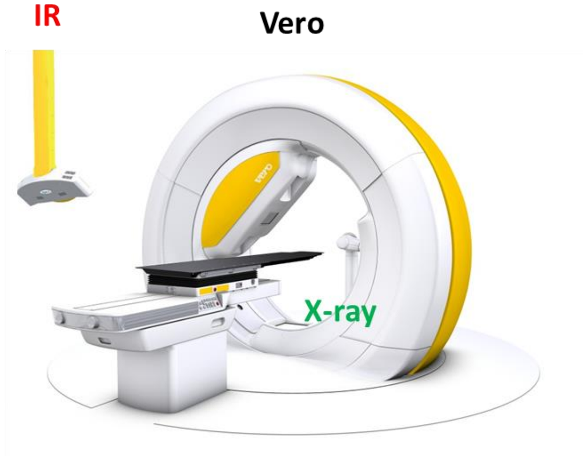


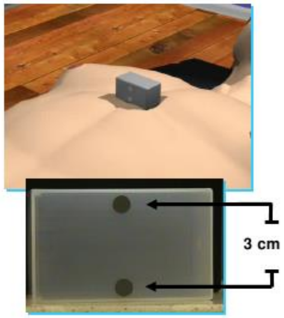
Respiratory correlated / compensated treatment planning and delivery: X-ray radiotherapy

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

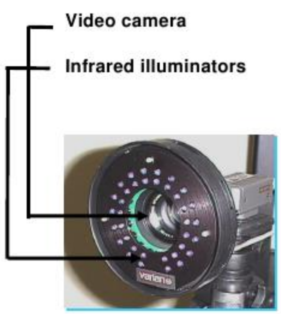
- ✓ time resolved imaging for treatment planning (X-ray and particle)
- ✓ breath-hold irradiation
- ✓ respiratory gating
- ✓ tumor tracking

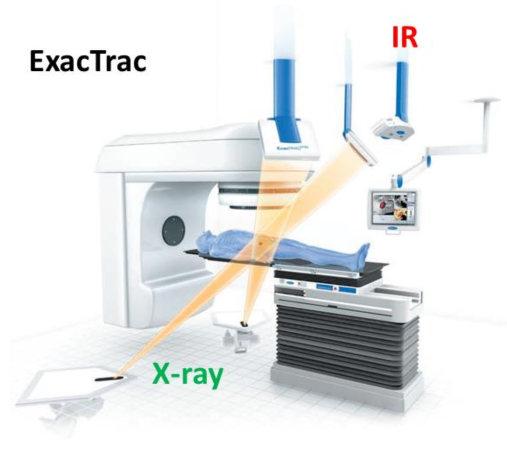




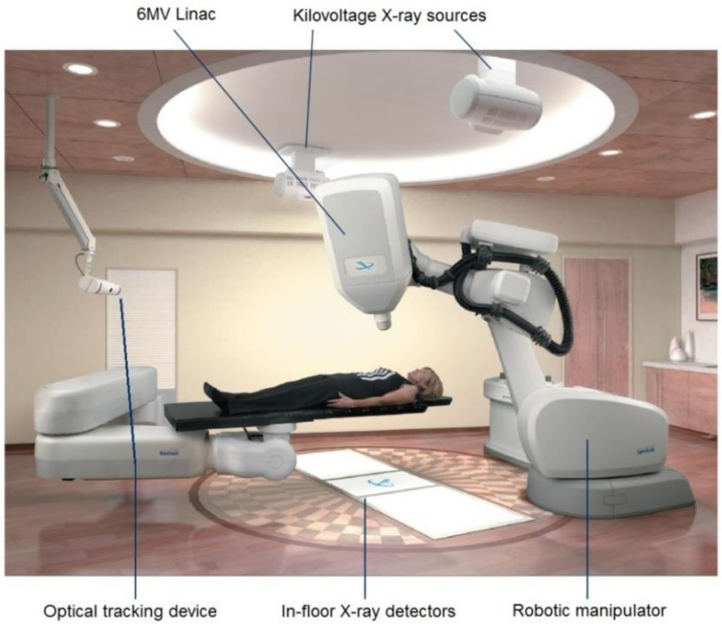


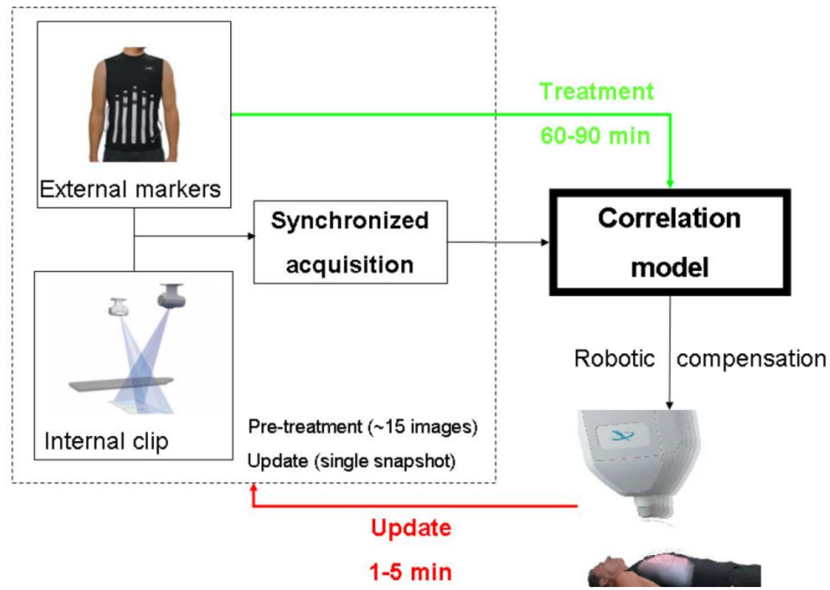
Lightweight reflective marker, distance-calibrated

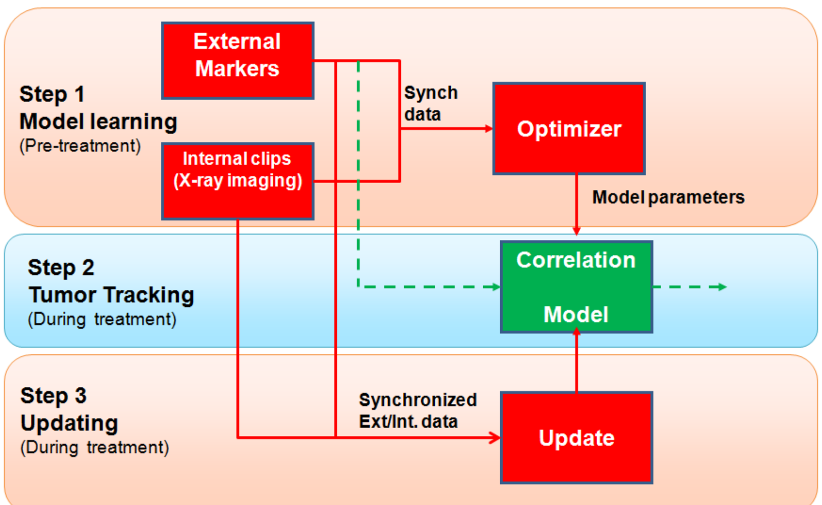


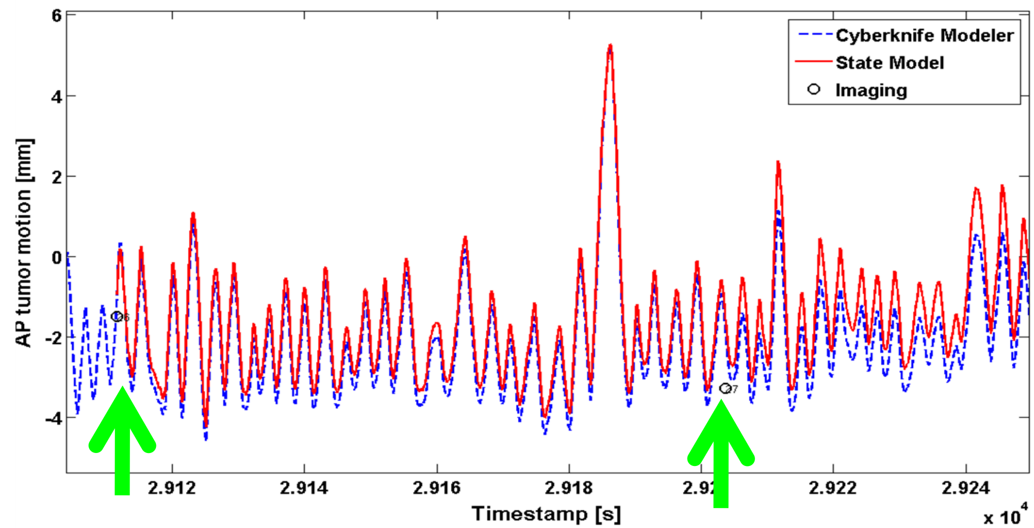


Tumor tracking based on external/internal correlation: the Cyberknife-Synchrony case



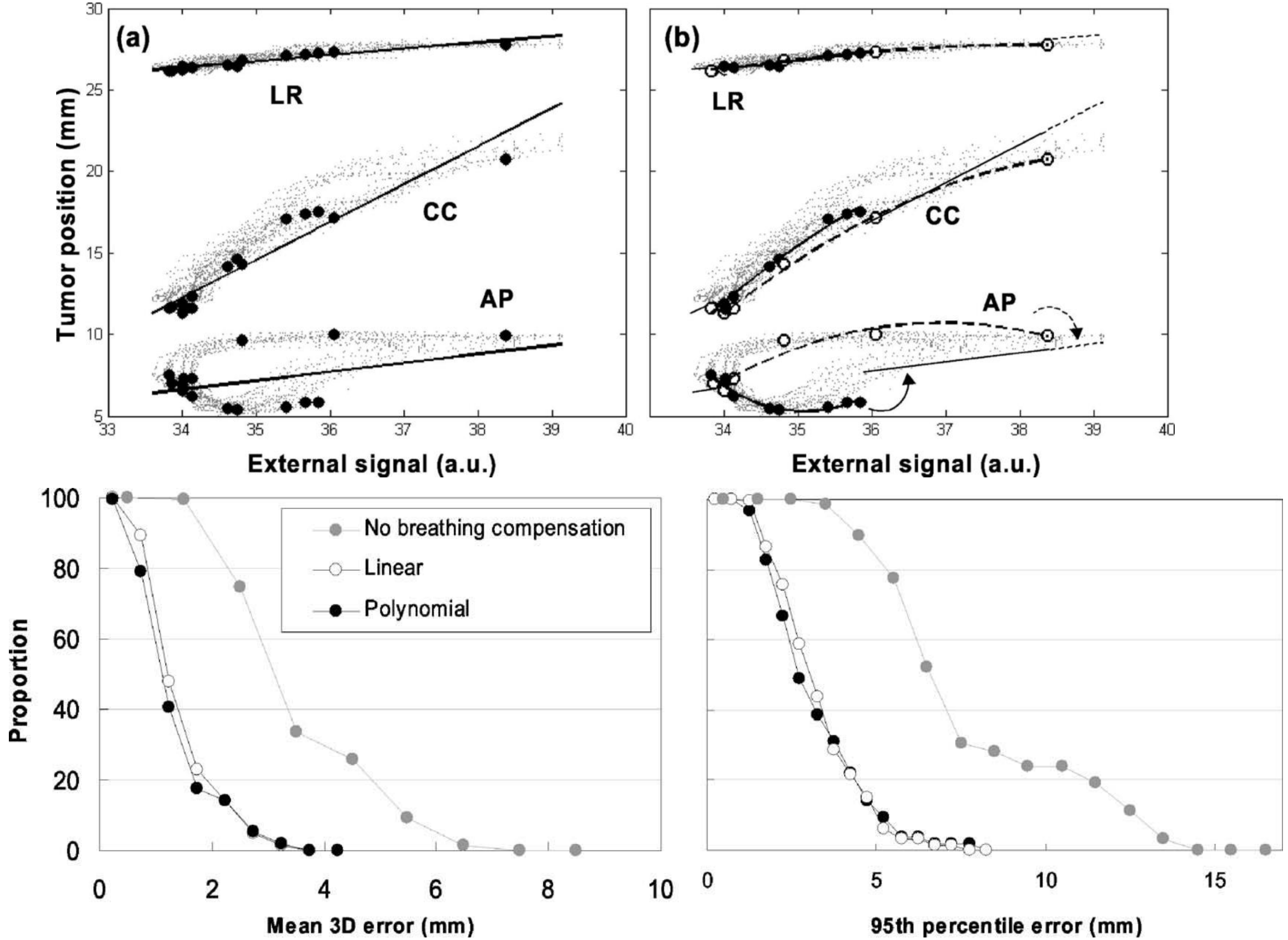






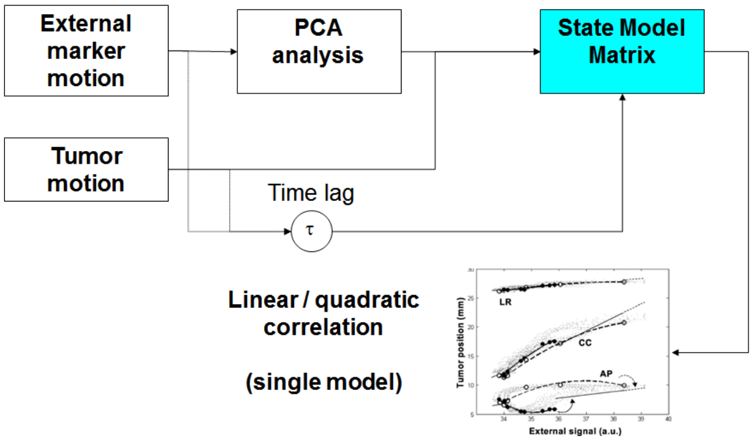
Competitive models for internal/external correlation

✓ Linear + polynomial (Seppenwoolde *et al.*, Med Phys, 2007)

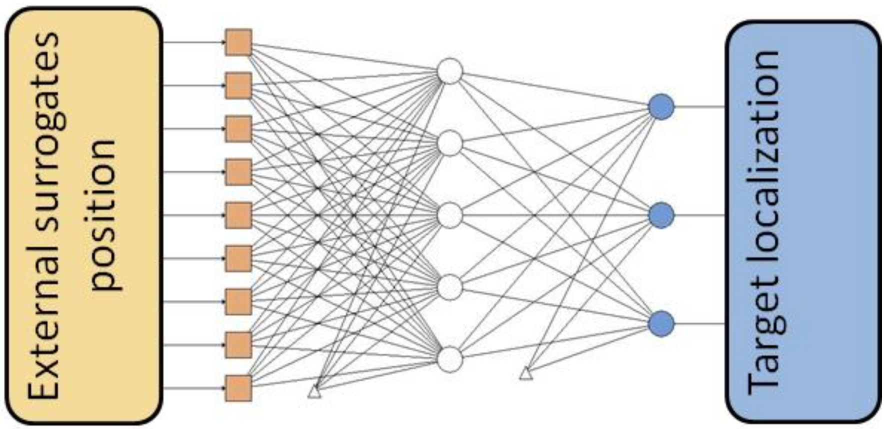


Accuracy of external/internal correlation
Competing models

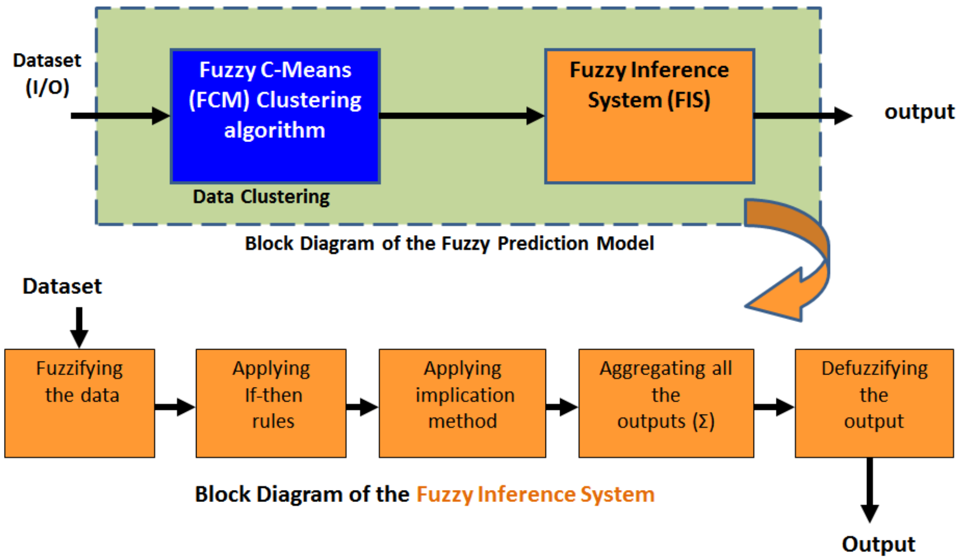
State Model



ANN

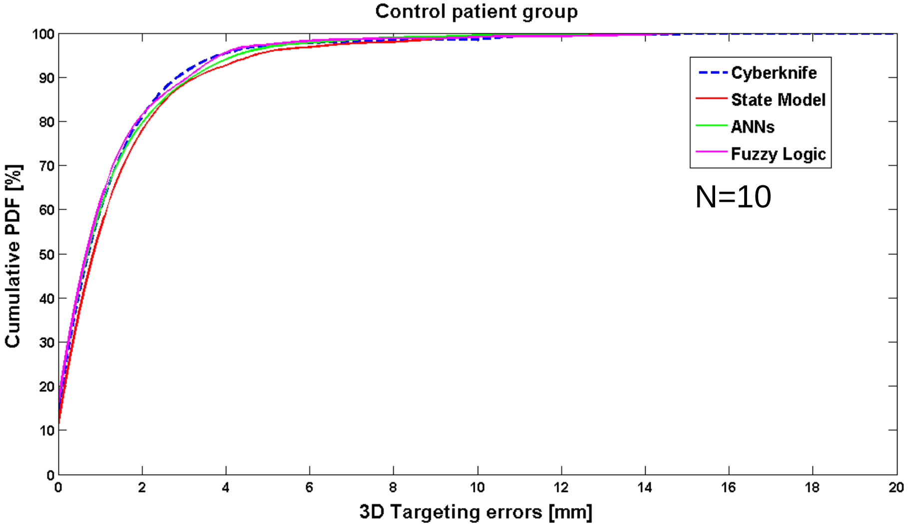


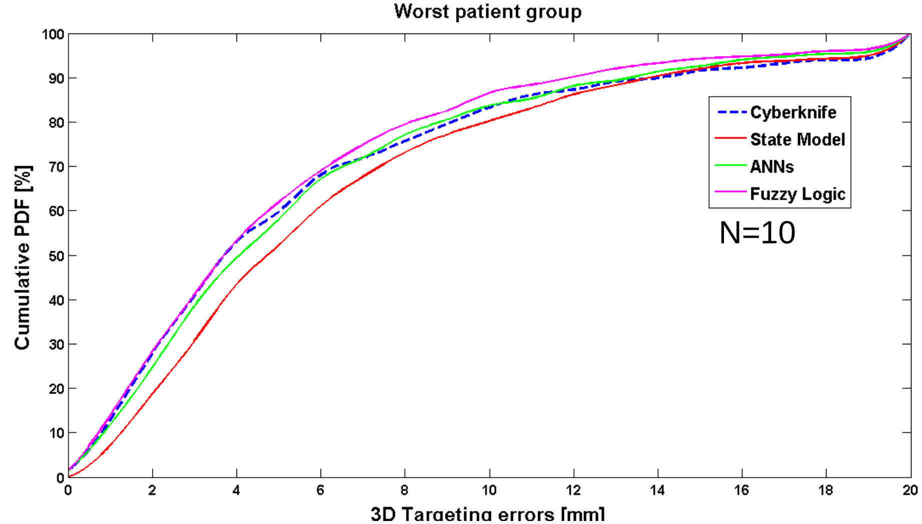
Fuzzy Logic

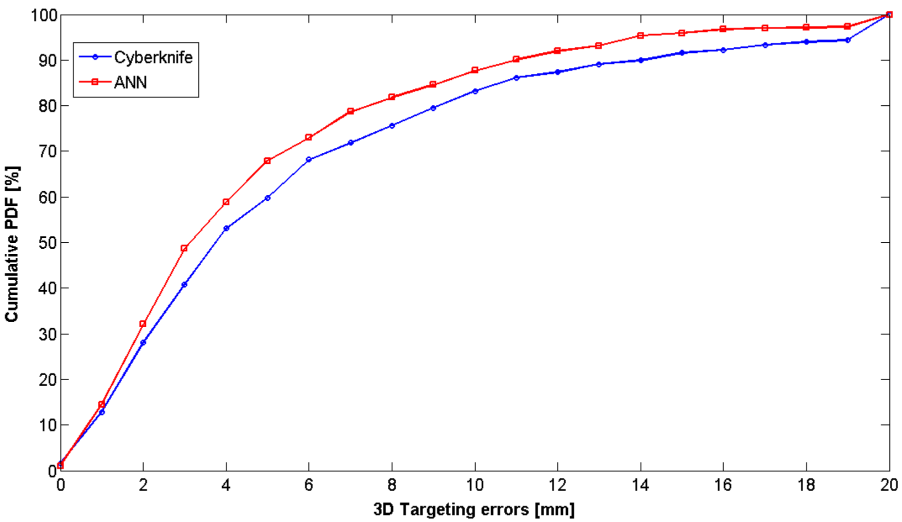


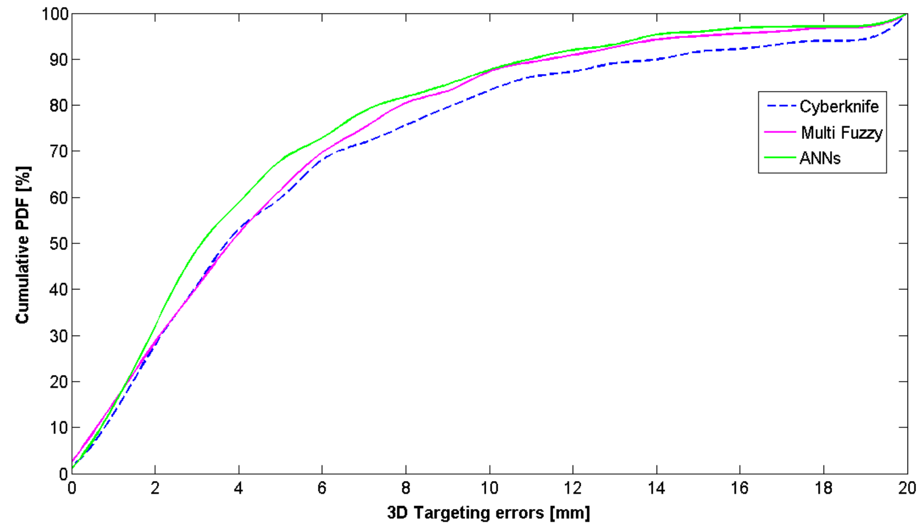
Competitive models for internal/external correlation

- Regular vs. irregular breathers
- Correlation model optimization improves performance (Torshabi *et al*, TCRT, 2010)

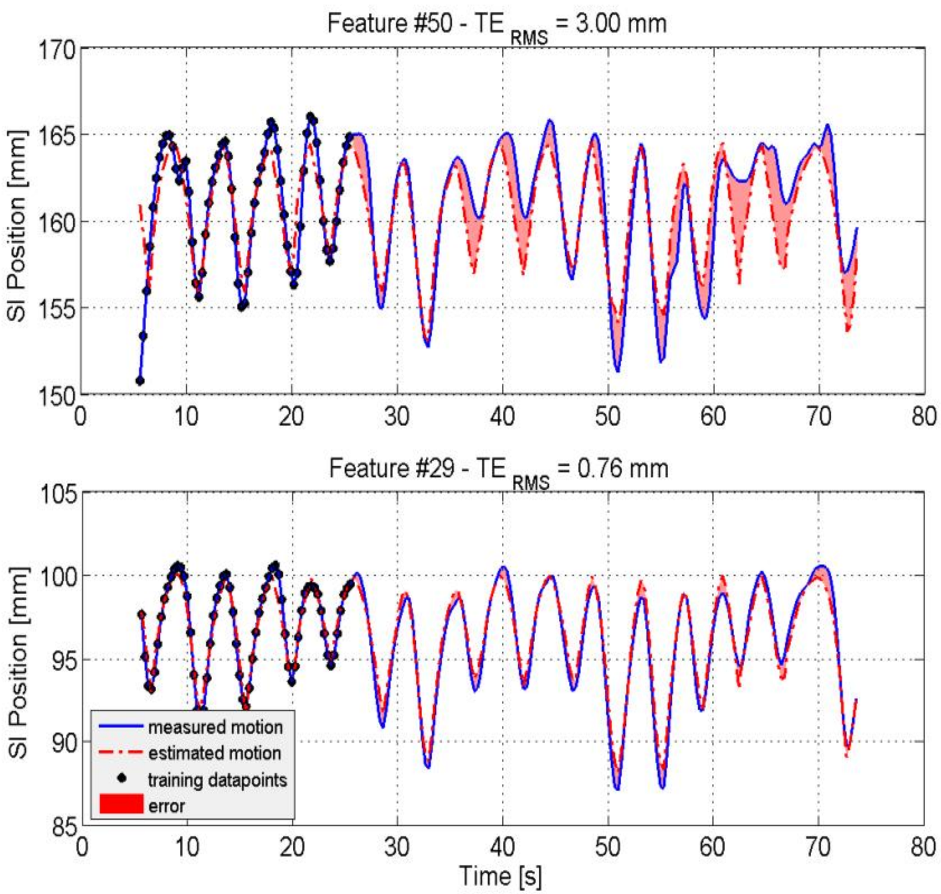


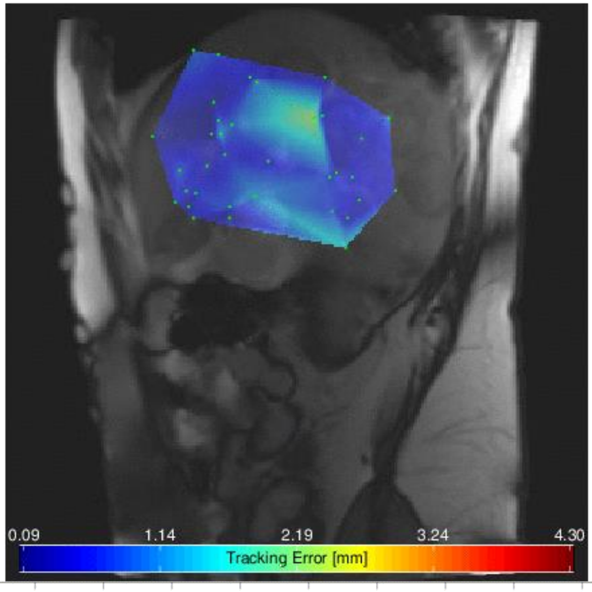


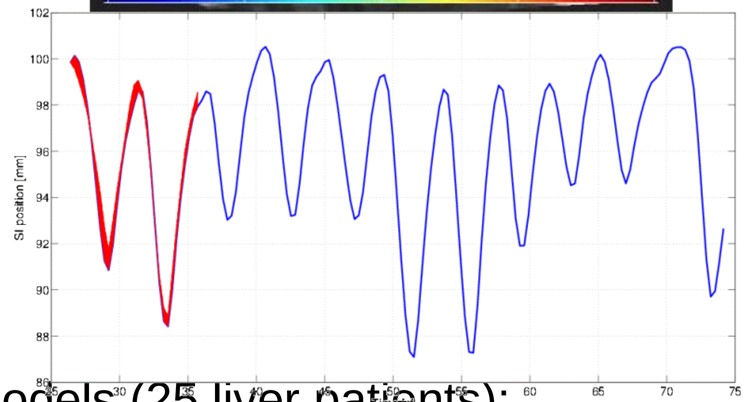




Role of 4D-MRI and automatic feature extraction







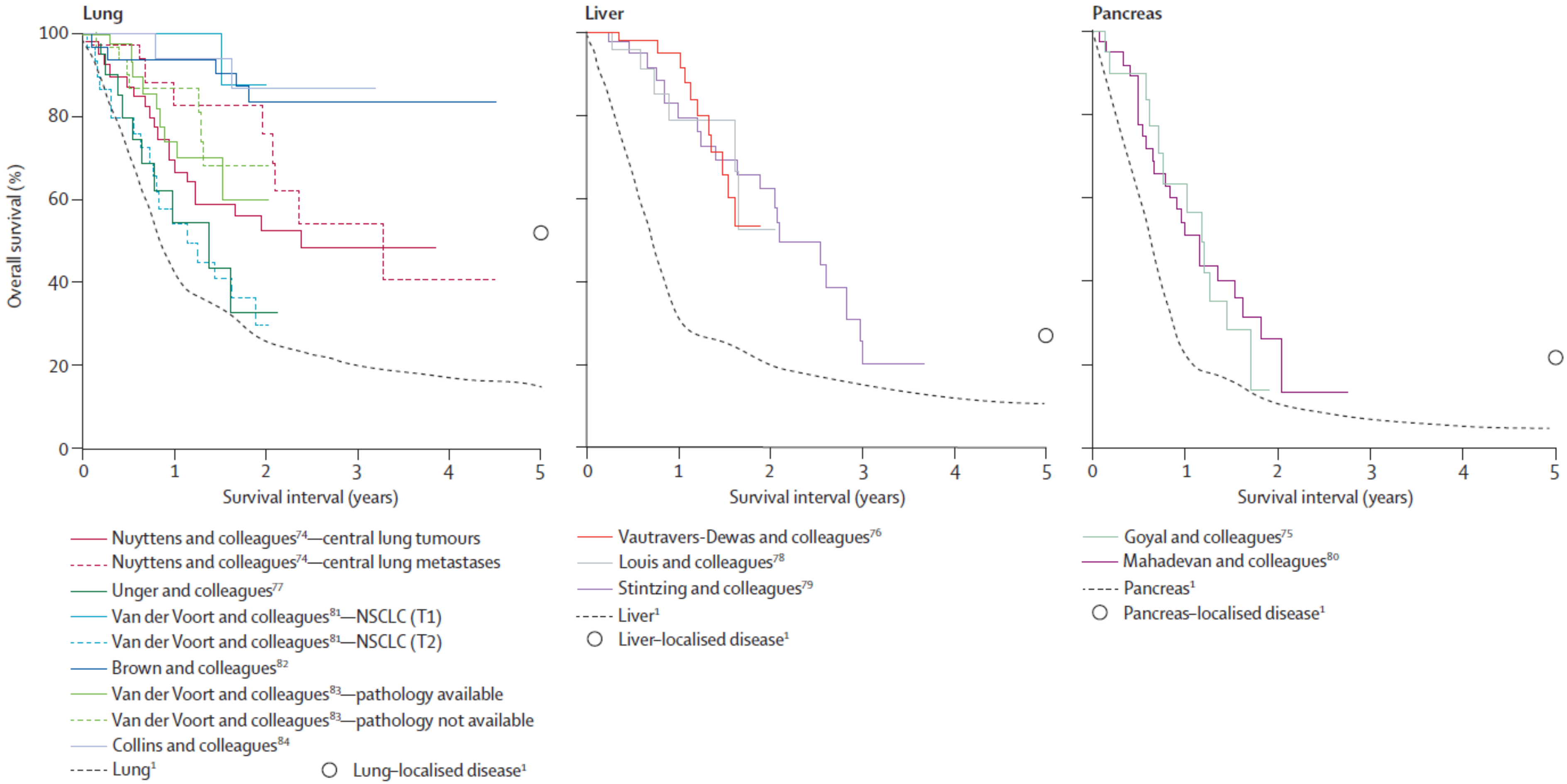
Maximal tracking effectiveness of correlation models (25 liver patients):

- ✓ internal-external **phase-shift within ±10°**
- ✓ **average marker correlation** with the internal motion **> 70 %**

(Paganelli *et al*, IJROBP, 2015)

Tumor tracking clinical results

✓ Clear significance ? (Riboldi *et al*, Lancet Oncol, 2012)



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

1. **Experimental validation** with scanned beams

   → **local** correlation models (**target position**)

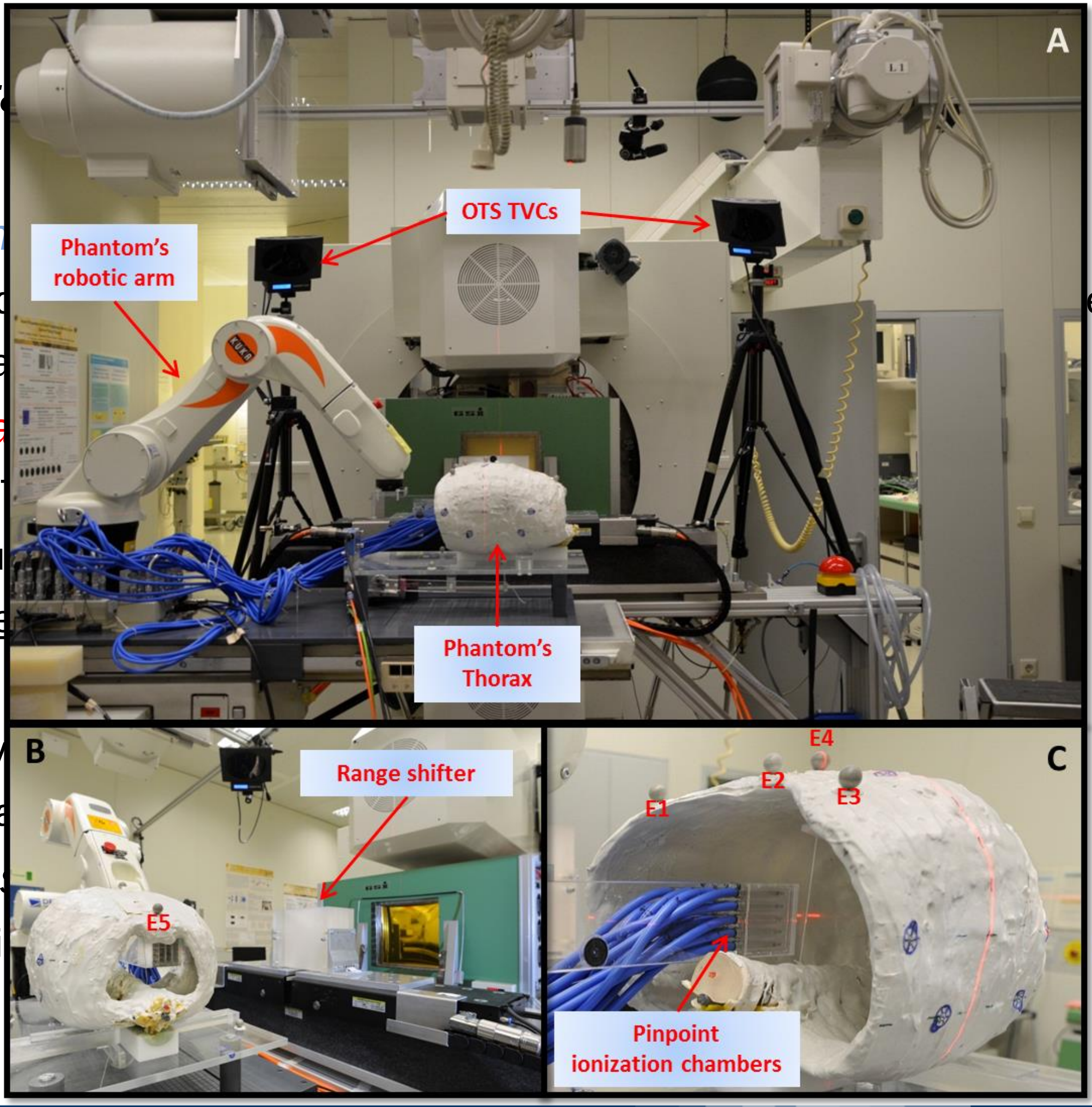
2. **Global 4D modeling**

   → **4D CT** prediction for range variation estimation

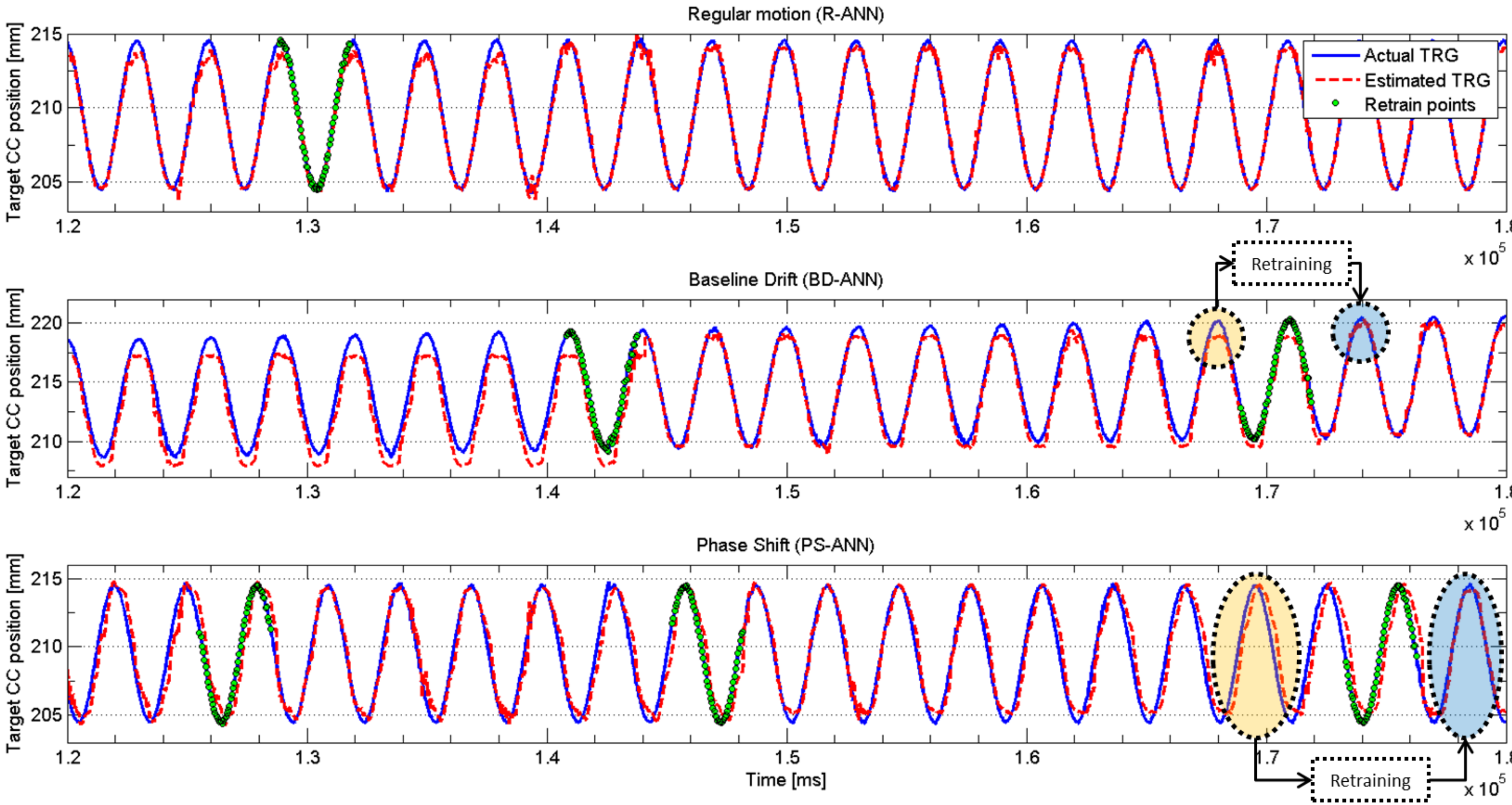
Tumor tracking in particle therapy – proof of principle @GSI

Experiment

- *Robotic ph*
  - ✓ Reproc ependent)
  - ✓ Regula
- *Optical Tra*
  - ✓ SMAR
  - ✓ Measu
  - ✓ Include
- *Treatment*
  - ✓ Receiv
  - ✓ Modula
- *Dose mea*
  - ✓ 20 ioni



Performance of correlation models

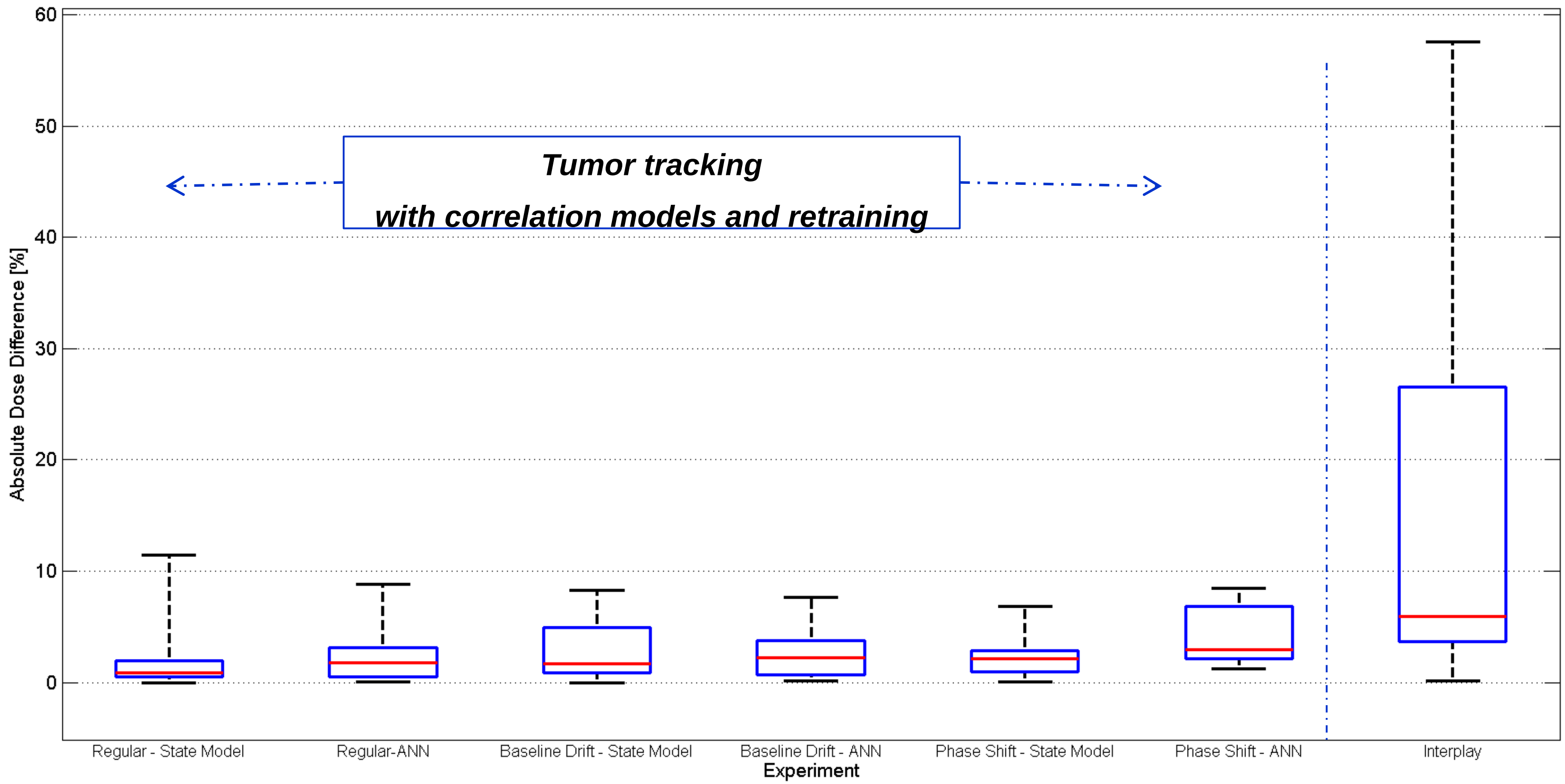


Overall dosimetric results

Dose differences w.r.t. static irradiation

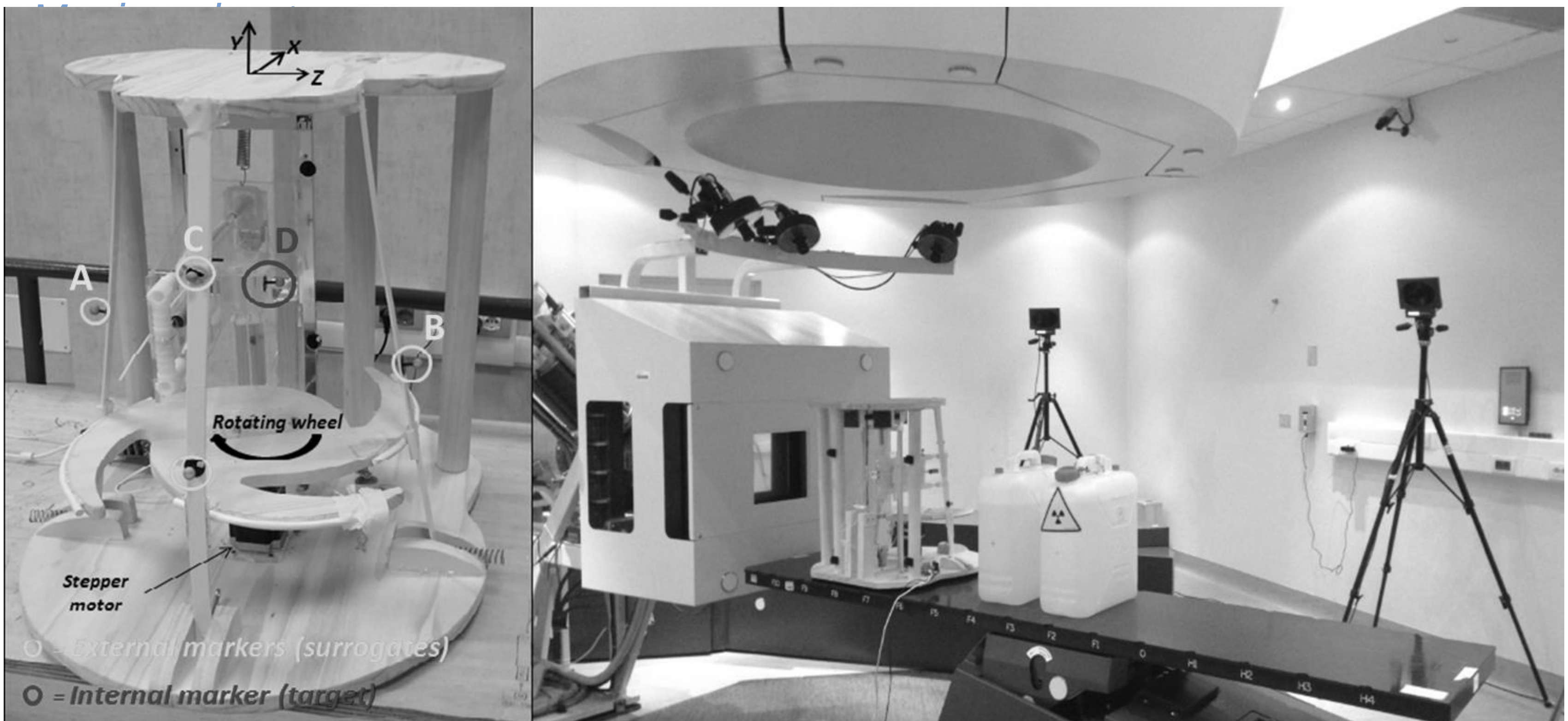
- ✓ Static irradiation = beam fixed, static target
  → Measurement of nominal delivered dose
- ✓ '*Interplay*' = beam fixed, taget moving
  -

(Seregni *et al*, PMB, 2013)



Tumor tracking in particle therapy – proof of principle @GSI

Experimental set-up (CNAO, June 2013)

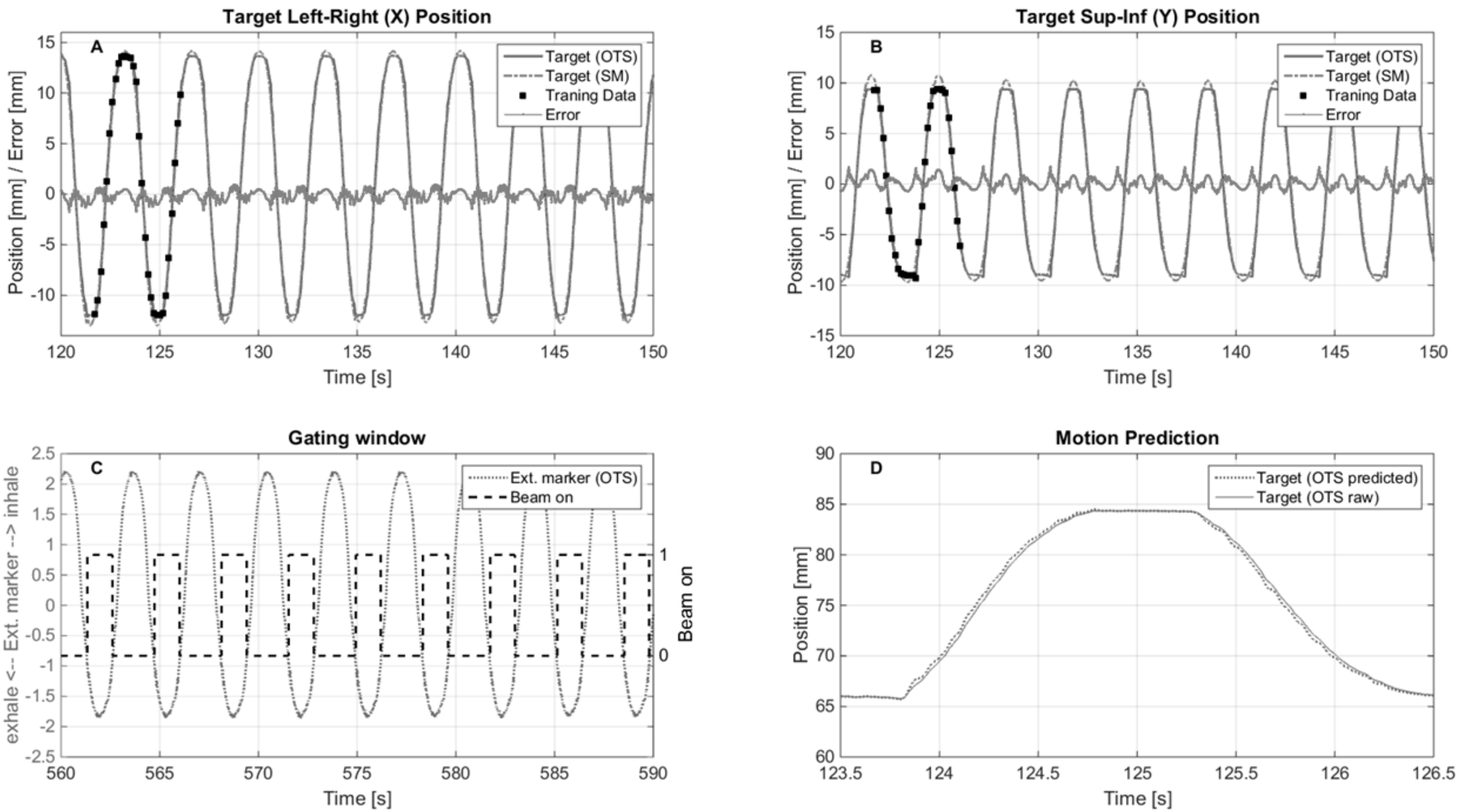


- ✓ OTS – DDS interface based on Xilinx FPGA

- *Dose measurement*
  - ✓ Gafchromic films (EBT3 and Mephisto software for dose assessment)
  - ✓ Measurement area 60x60 mm^2

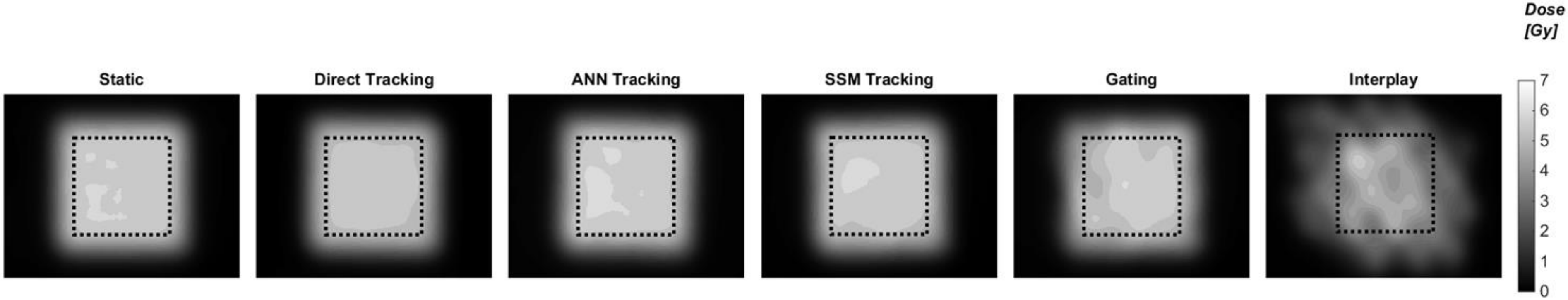
Performance of correlation models (for tracking and gating)

- ✓ Estimated tracking traces (ANN and SSM)
- ✓ 20.6 msec motion prediction for communication delay compensation



Overall dosimetric results

Dose differences w.r.t. static irradiation



	Experiment	Static	Direct Tracking	ANN Tracking	SSM Tracking	Gating	Uncompensated (interplay)
Dose (nominal 6 Gy)	Min : Max	4.70 : 5.95	4.68 : 5.48	4.78 : 6.03	4.38 : 5.98	4.15 : 6.08	1.89 : 5.51
	Median	5.49	5.48	5.57	5.52	5.62	4.08
Inhomogeneity index	ΔIC	--	-0.10	0	+0.10	+0.20	+1.65
Conformity index	ΔCI	--	-0.01	0	0	-0.13	-0.93

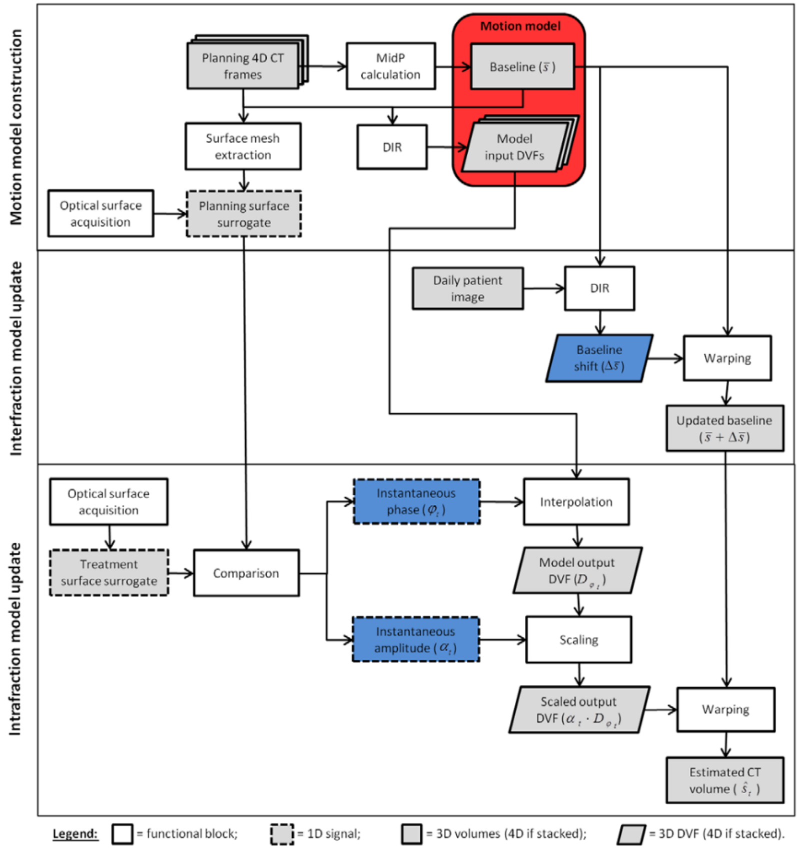
(Fattori *et al*, NIMA-D, *2016*)

Motion modeling beyond tumor tracking

- ✓ Global motion models for adaptive strategies
- ✓ Estimation of anatomical changes due to breathing irregularities

Global modelling: 4DCT-of-the-“day”

- ✓ *4D Motion Modeling* was introduced[1,2,3] to predict CT volumes corresponding to arbitrary respiratory phases
- ✓ Respiratory surrogates are used to estimate CT volumes by means deformable image registration



[1]Vandemeulebroucke *et al.*, *Med Image Comput Comput Assist Interv*, 2009

[2]Fassi *et al.*, *Int J Radiat Oncol Biol Phys*, 2014

[3]Fassi *et al.*, *PMB*, 2015

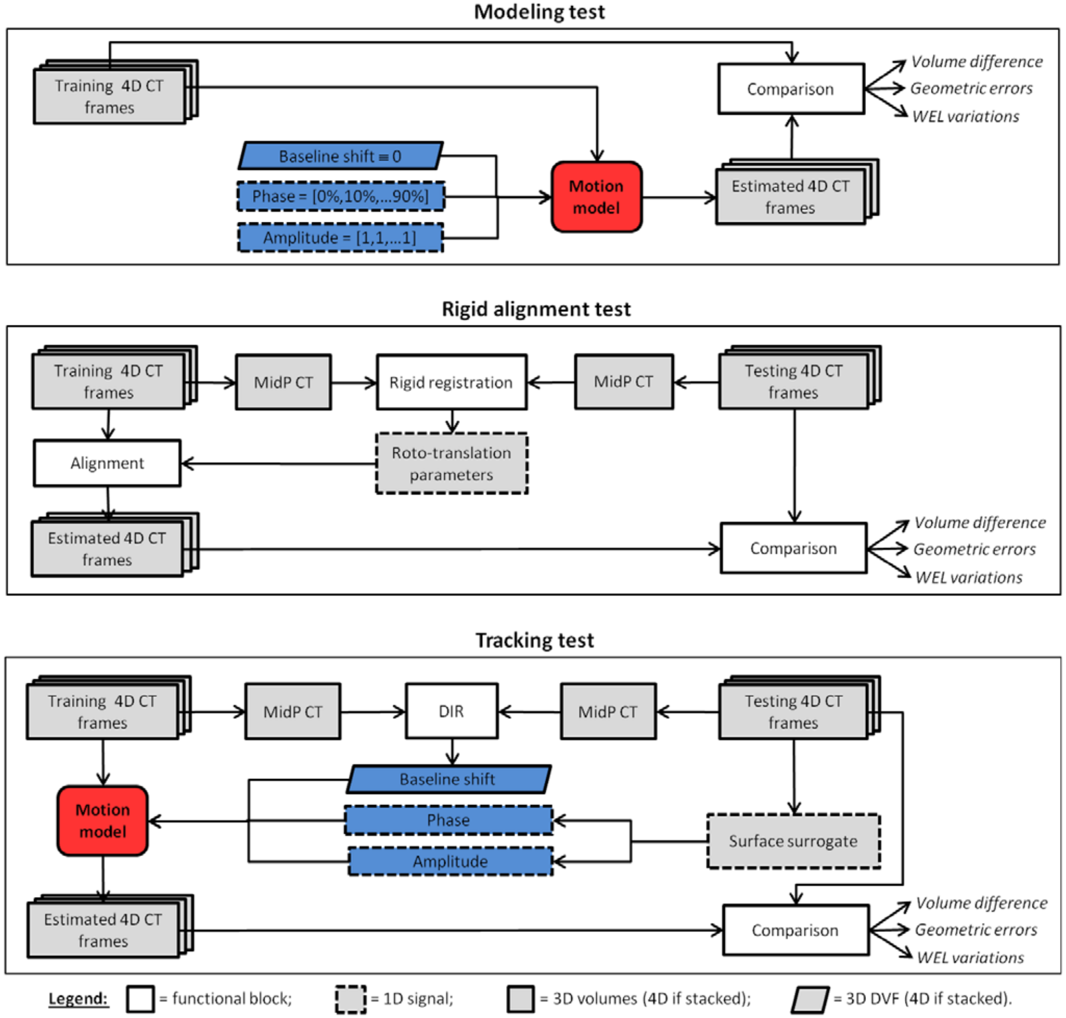
Global modelling: 4DCT-of-the-“day”

- ✓ 7 patients database with repeated 4D CT (1day-18 days time interval)
- ✓ Outcomes: HU differences, COM differences, WEL variations

Model testing (reference)

Worst case (rigid registration)

Surrogate driven warping (DIR model)



(Fassi *et al.*, *PMB*, 2015)

Global modelling: 4DCT-of-the-“day”

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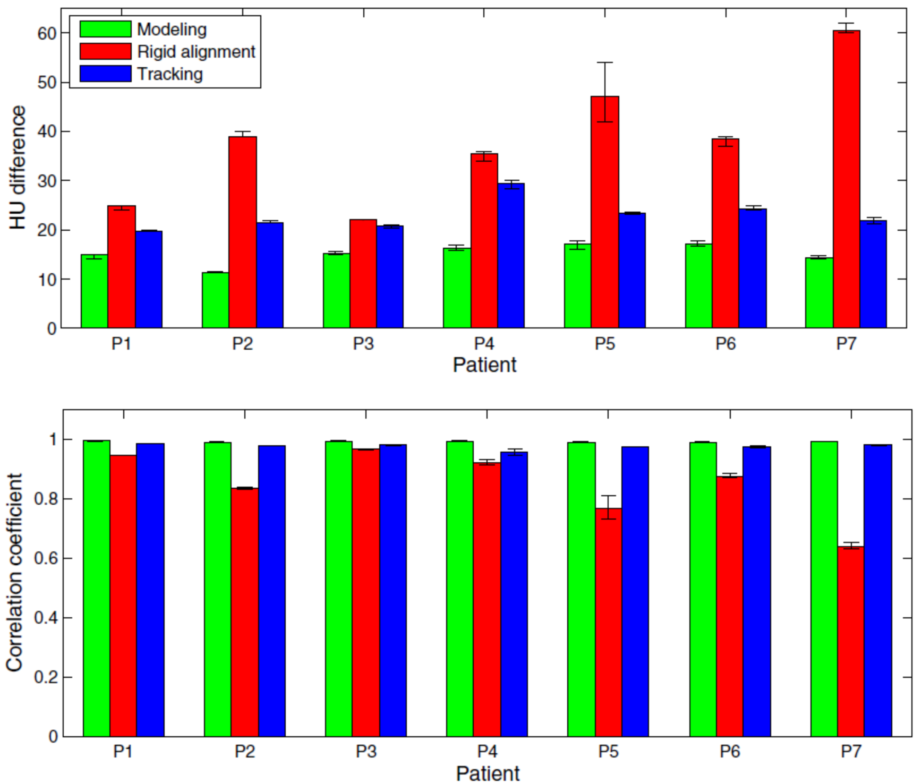
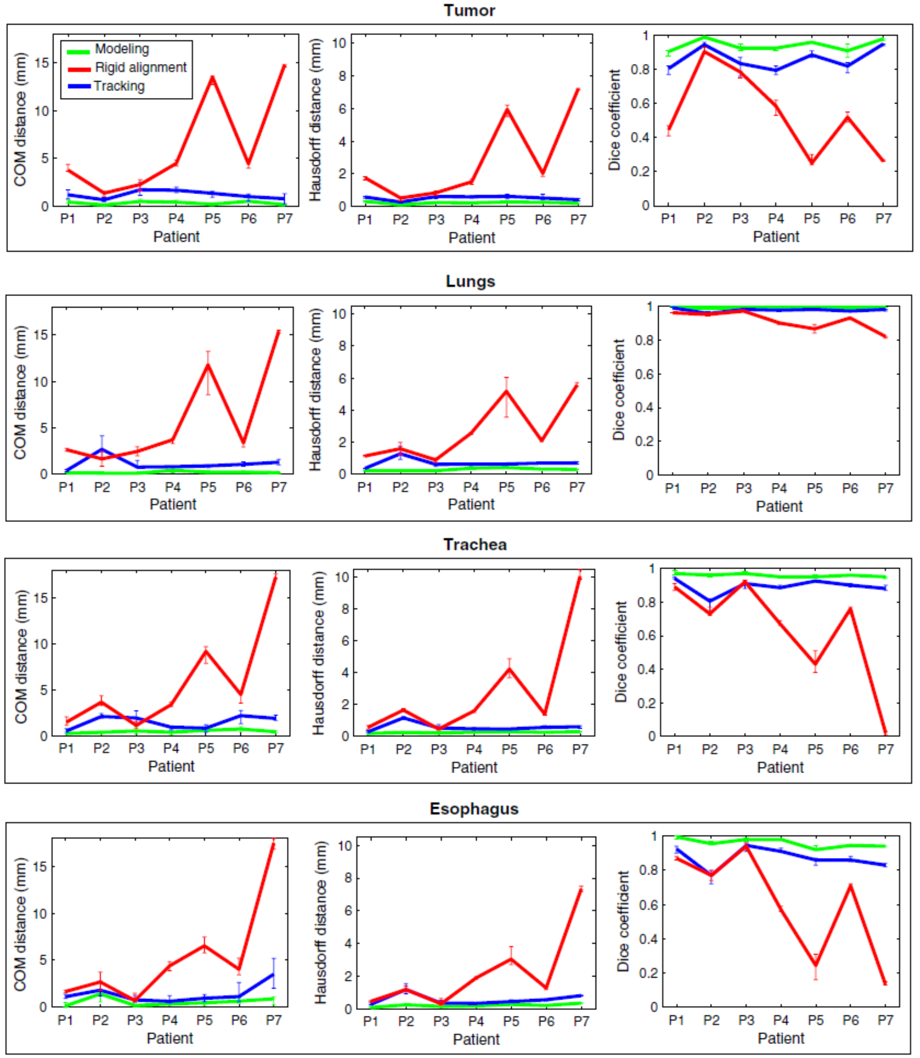


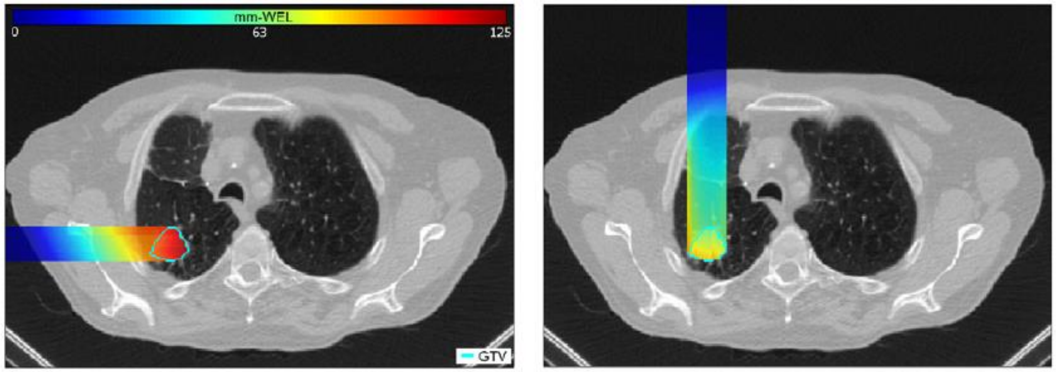


(Fassi *et al.*, *PMB*, 2015)

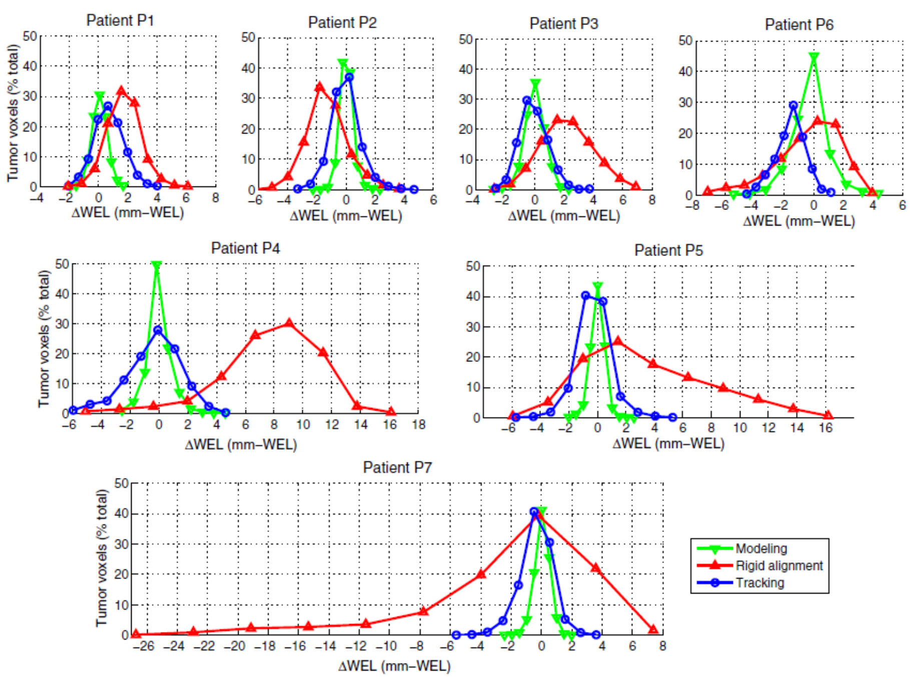
Global modelling: 4DCT-of-the-“day”

✓ WEL variations in GTV voxels and computational cost for ROI

Ipsi-lateral beam WEL (mm-WEL) | Antero-posterior beam WEL (mm-WEL)



according to Jaekel *et al.*, *Med Phys*, 2001



Fassi *et al.*, *PMB*, 2015

	Absolute ΔWEL (mm-WEL)					
	Ipsi-lateral beam			Antero-posterior beam		
Patient	Modeling	Tracking	Rigid	Modeling	Tracking	Rigid
P1	0.42 ± 0.06	1.00 ± 0.23	1.73 ± 0.15	0.61 ± 0.24	0.95 ± 0.60	1.04 ± 0.25
P2	0.30 ± 0.05	0.67 ± 0.10	1.67 ± 0.39	0.65 ± 0.22	1.30 ± 0.53	2.71 ± 0.32
P3	0.49 ± 0.15	0.72 ± 0.22	2.33 ± 0.10	0.72 ± 0.28	1.03 ± 0.60	2.65 ± 0.39
P4	0.56 ± 0.42	1.36 ± 0.92	7.95 ± 0.56	0.74 ± 0.53	1.40 ± 0.32	4.49 ± 0.43
P5	0.38 ± 0.10	0.85 ± 0.16	4.31 ± 0.42	0.81 ± 0.39	1.64 ± 1.03	3.90 ± 0.63
P6	0.70 ± 0.67	1.55 ± 0.72	1.86 ± 0.64	0.80 ± 0.80	1.89 ± 0.83	2.43 ± 0.59
P7	0.37 ± 0.03	0.79 ± 0.14	3.90 ± 0.11	0.31 ± 0.06	0.48 ± 0.13	9.39 ± 0.42
Median ± IQR	0.41 ± 0.20	0.90 ± 0.43	2.33 ± 2.21	0.70 ± 0.45	1.33 ± 0.81	3.03 ± 1.94

	Computational time (s)	
Patient	Ipsi-lateral beam	Antero-posterior beam
P1	0.46 ± 0.03	0.48 ± 0.03
P2	0.64 ± 0.05	0.75 ± 0.05
P3	0.39 ± 0.02	0.60 ± 0.04
P4	0.38 ± 0.02	0.34 ± 0.02
P5	0.40 ± 0.04	0.46 ± 0.04
P6	0.17 ± 0.01	0.15 ± 0.02
P7	0.56 ± 0.04	0.48 ± 0.02
Median ± IQR	0.42 ± 0.18	0.48 ± 0.22

Wrap-up

- ✓ Tumor tracking is a reality in X-ray radiotherapy and relies on external-internal correlation based on the integration between intermittent X-ray imaging and optical tracking technologies
- ✓ The feasibility of the same strategy has been demonstrated technically in active scanning particle therapy (of course alternative approaches exist)
- ✓ On-line global motion modeling driven by external surrogates may represent a way to enrich tumor position estimation with information on range uncertainties due to variable breathing patterns
- ✓ Artifacts-free and reliable 4DCT imaging and deformable image deformation methods are needed
- ✓ Particle therapy of mobile targets is a reality on the “safe path” (gating, rescanning)
- ✓ Need to assess the clinical advantages vs. technical effort of the “tracking path”

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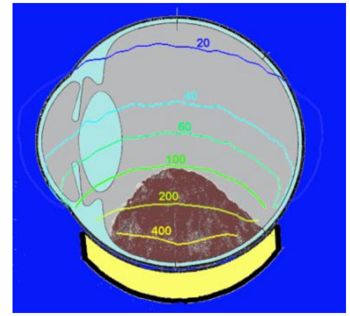
CNAO radio-oncologists

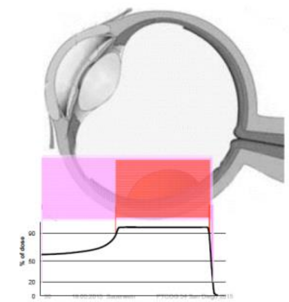
CNAO therapists

Treatment of intraocular tumors

Ophtalmic tumours

- ENUCLEATION (before 1980s)
- RADIATION THERAPY (1980- present)
  - Brachytherapy



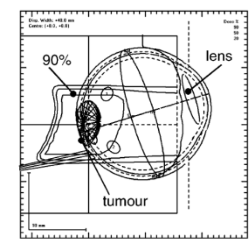


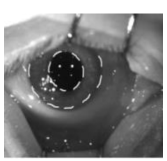
[Kacperek, Appl. Radiat. Isot., 2009]

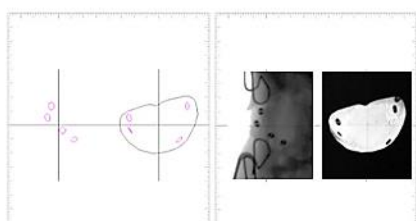
- **Proton Therapy** **14 dedicated beam line in operation worldwide**
  Over 20,000 treated patients

Radiopaque fiducials markers implantation → Treatment simulation → Treatment Plan

In-room orthogonal X-ray imaging system







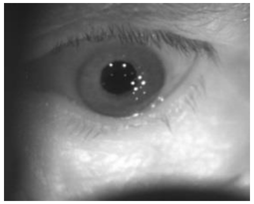
Active patient fixation of a red diode

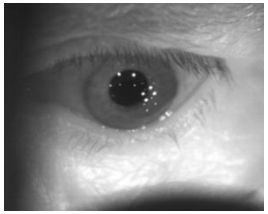
Dose delivery ← Setup verification ← Treatment Setup

Method

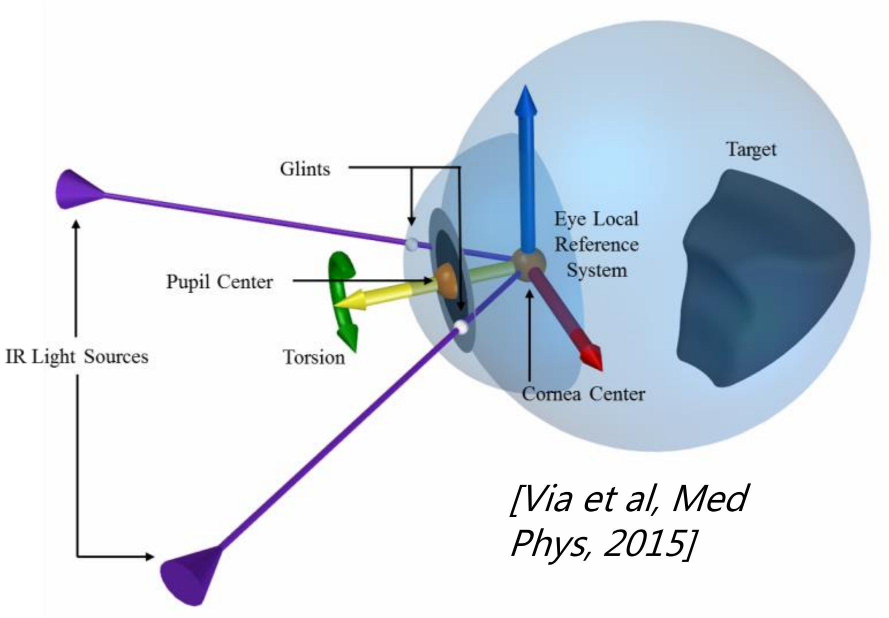
3D infrared video-oculography

- Acquisition of the ocular region by two calibrated cameras
- Eye infrared illumination by multiple non coaxial collimated light sources
- Automatic recognition of the 3D position of cornea and pupil centers (CC,CP)





[Fassi et al, App Opt, 2012]



[Via et al, Med Phys, 2015]

Planning phase (X-ray)
- ETS eye monitoring during planning image acquisition
- Local target coordinates definition

Hypothesis
- Invariance of local tumor coordinates from planning to treatment

Treatment
- 3D target localization

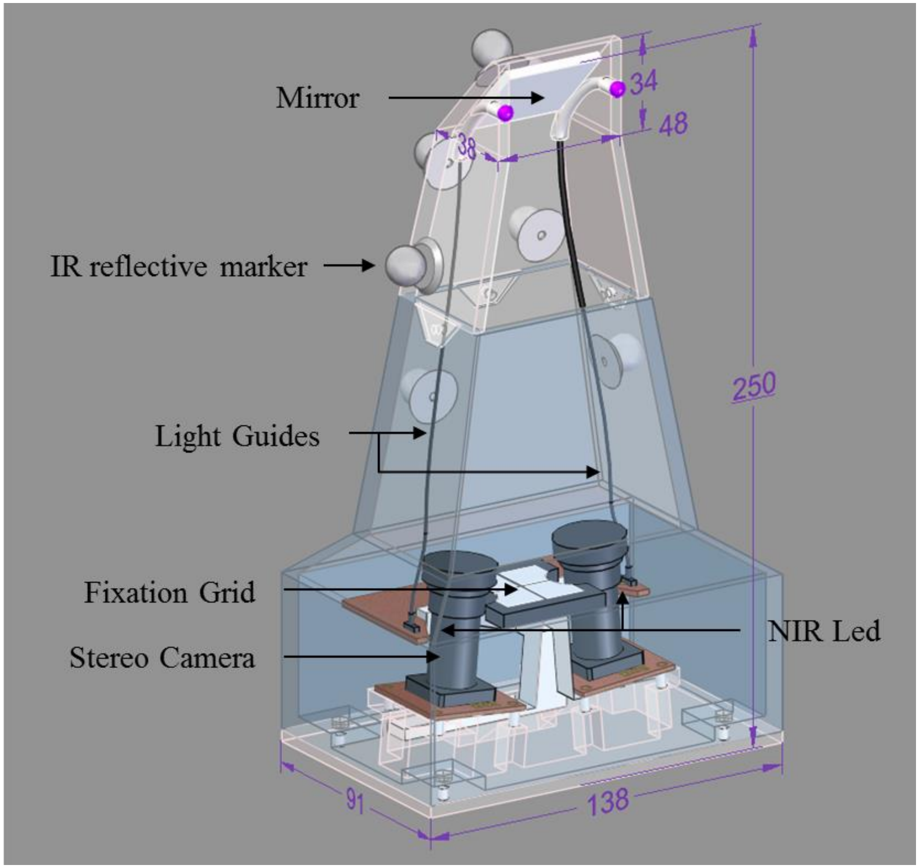
Method

Device development

Requirements
- CT compatibility
- Clinically suited design

Mirror configuration
- Removal of electronic components from the CT FOV
- Miniaturization

Components
- IDS UI-1241-LE-NIR camera.
- Präzisions Glas & Optik: SEA-NIR Front surface Mirror.
- OSRAM LED SFH486 IR Led.
- ABS for device casing.



[Via et al, Med Phys, 2015]

ETS was tested on patients affected with intraocular tumours undergoing proton therapy treatments at Paul Scherrer Institut (PSI) in Villigen, Switzerland

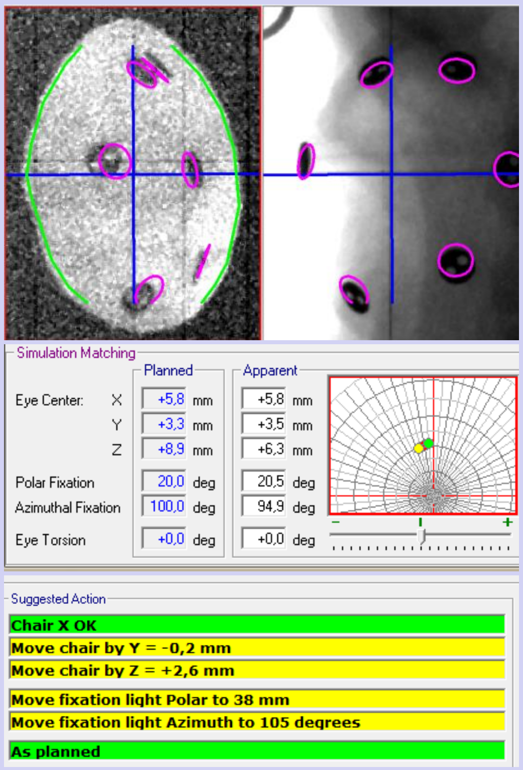
[Via et al, PTCOG 55, 2016]

Purpose

Set-up phase

EyePlan TPS

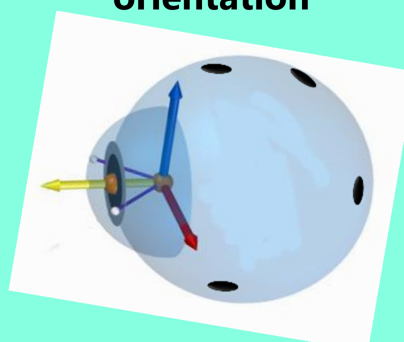
Eye center and fixation diode



***Evaluate dosimetric impact of set-up uncertainties**

ETS

CP CC estimate **Eye position and orientation**



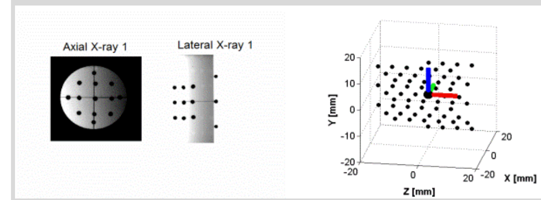
real-time information on:

- Eye Center and fixation diode
- Clip 3D position
- Set-up corrections

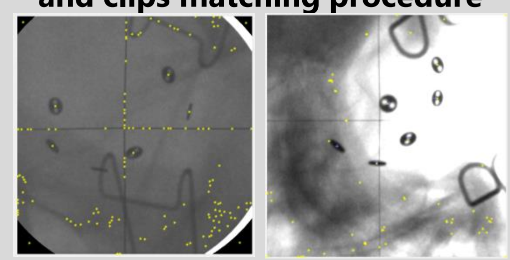
***Real-time eye motion monitoring during dose delivery**

X-ray

of known geometry



Semi-automatic image processing and clips matching procedure



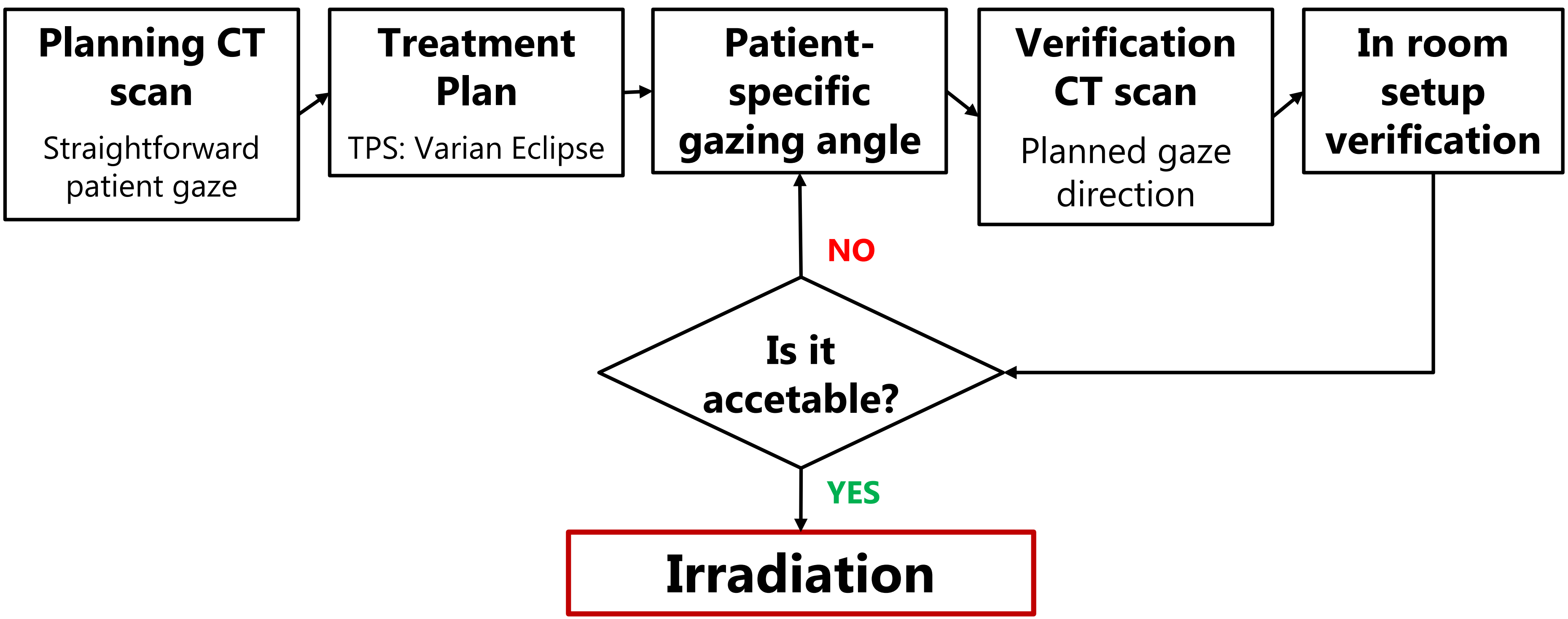
Direct 3D estimate of clip position

Clinical activities @ CNAO

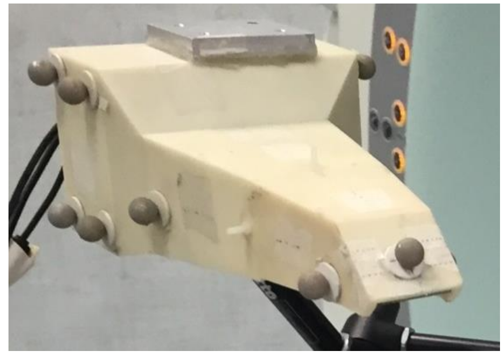
The ETS was used as a gaze stabilization and eye motion monitoring device during CT scans and irradiation

N.B: Non-dedicated beam line

- Active scanning
- Non orthogonal in-room imaging system



The ETS fixation poit is geometrically calibrated with respect to radioopaque markers attached to the device outer case



CT

- Direct localization of fiducials on scans

Treatment Room

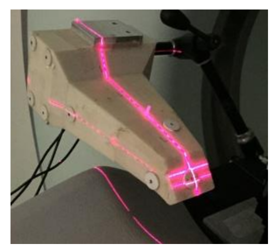
- Optical Tracking System (OTS)

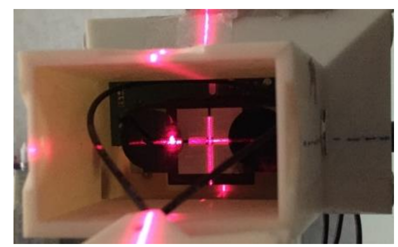
Planning CT scan

Straightforward patient gaze

The ETS fixation point must be aligned to the CT gantry isocenter

Geometrical requirement for treatment planning

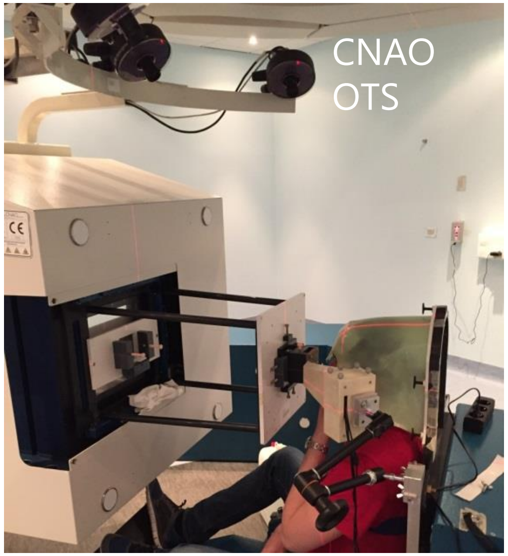




Electronic level verification

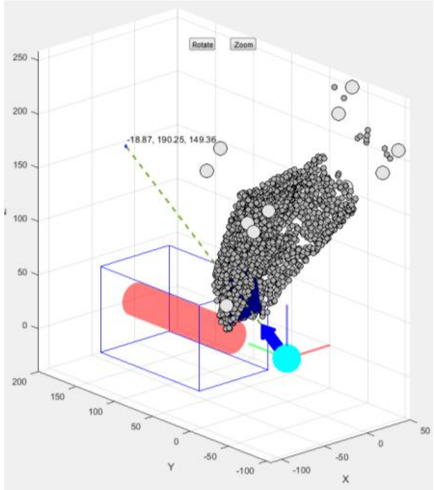
	X(L-L) [mm]	Z (C-C) [mm]
Positioning accuracy	-0.45 [0.68]	-1.62 [1.54]

Clinical activities @ CNAO



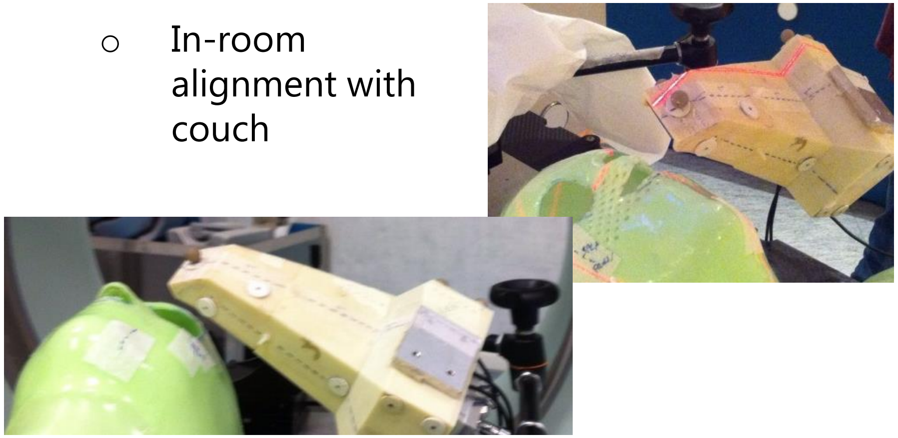
Patient-specific gazing angle

- ETS pre-alignment according to treatment plan prescriptions and monitoring of device position with in-room CNAO OTS
- MATLAB simulation platform of device setup



Verification CT

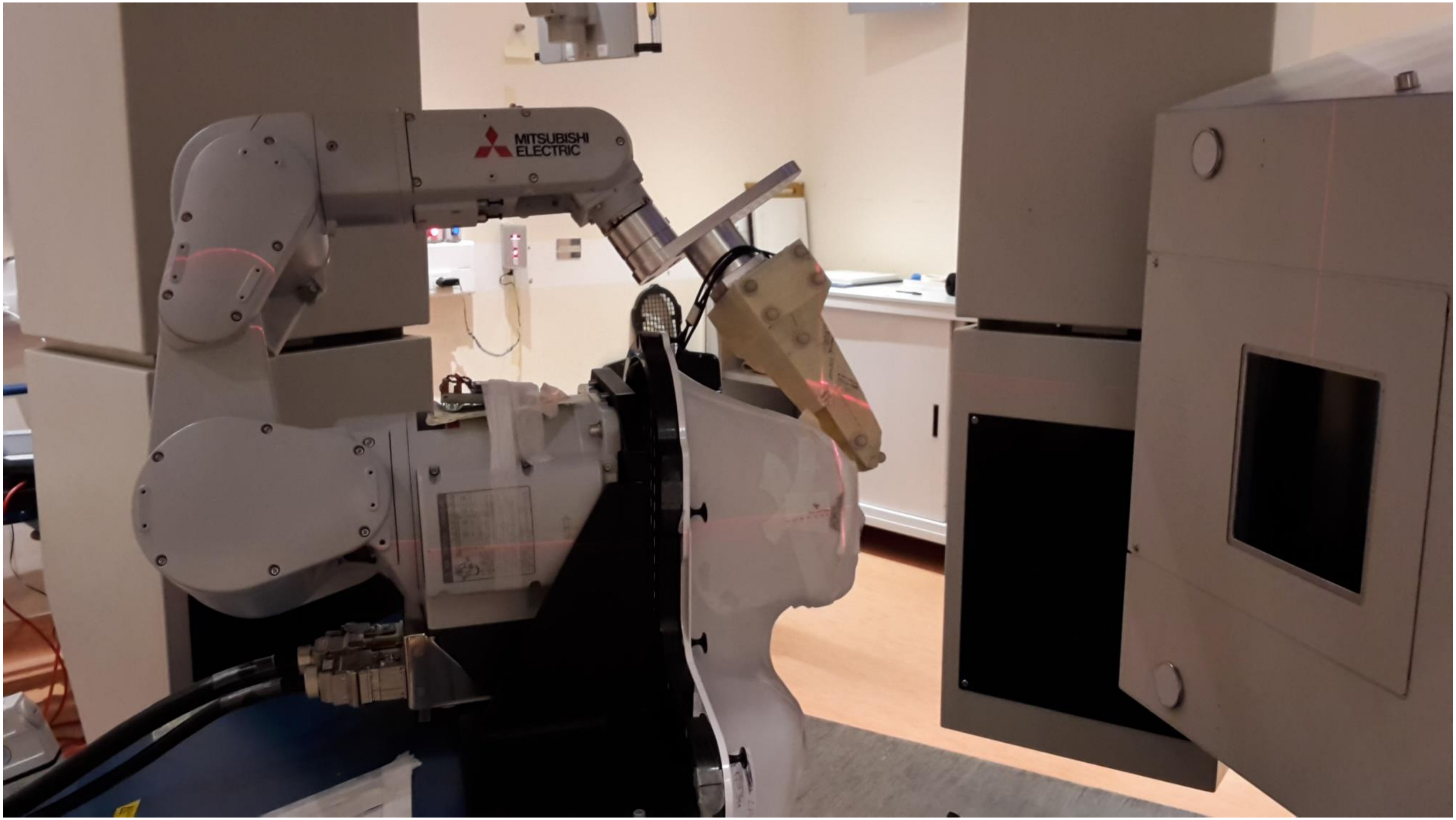
- In-room alignment with couch



Treatment

- In-room alignment with treatment chair
- Manual / robotic

Clinical activities @ CNAO



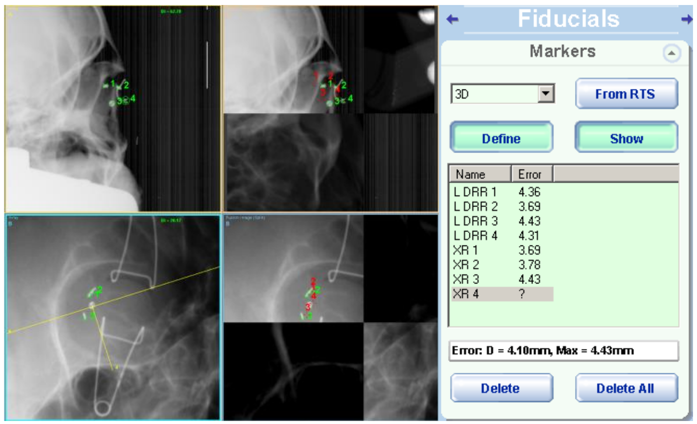
Clinical activities @ CNAO

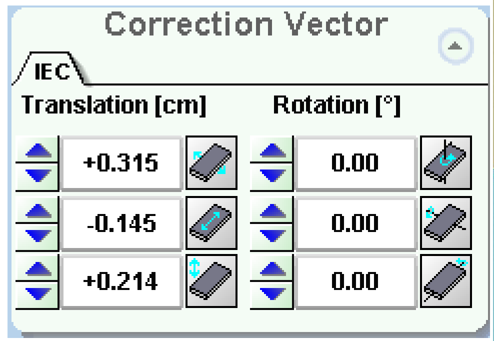
Irradiation

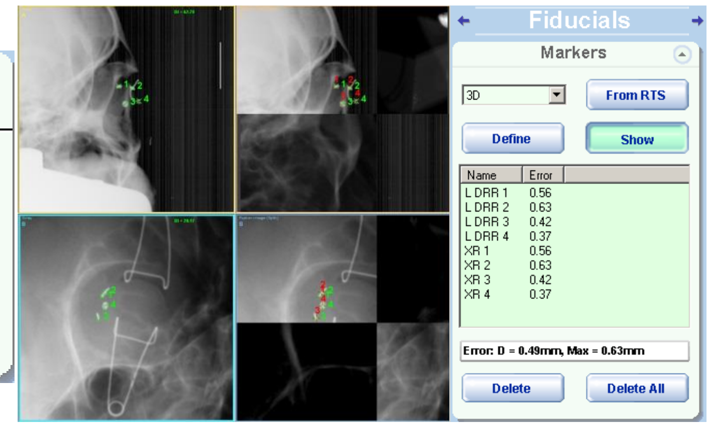
X-ray imaging

Point-based registration on clips

Residuals ≤1mm







Dose delivery