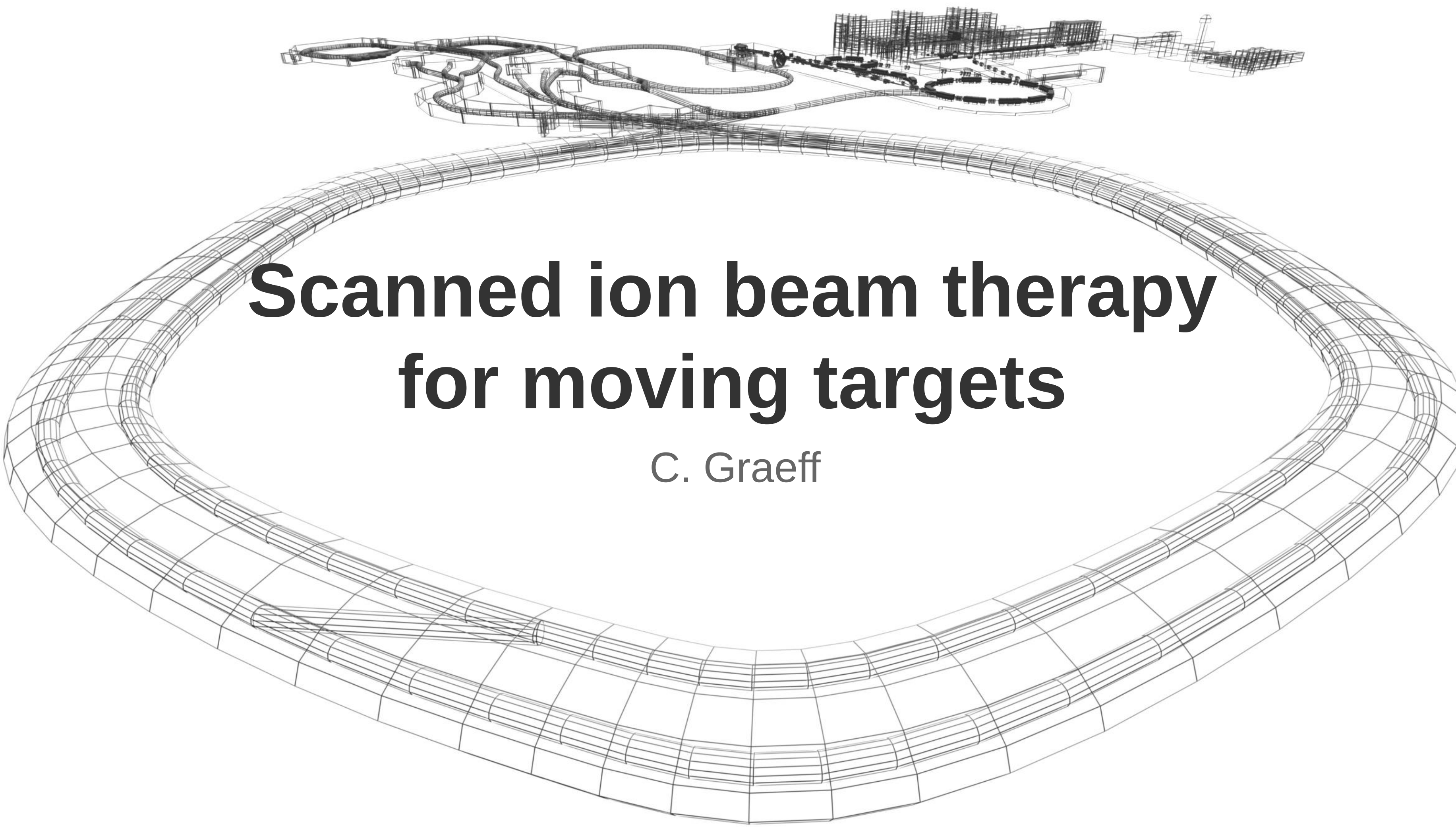
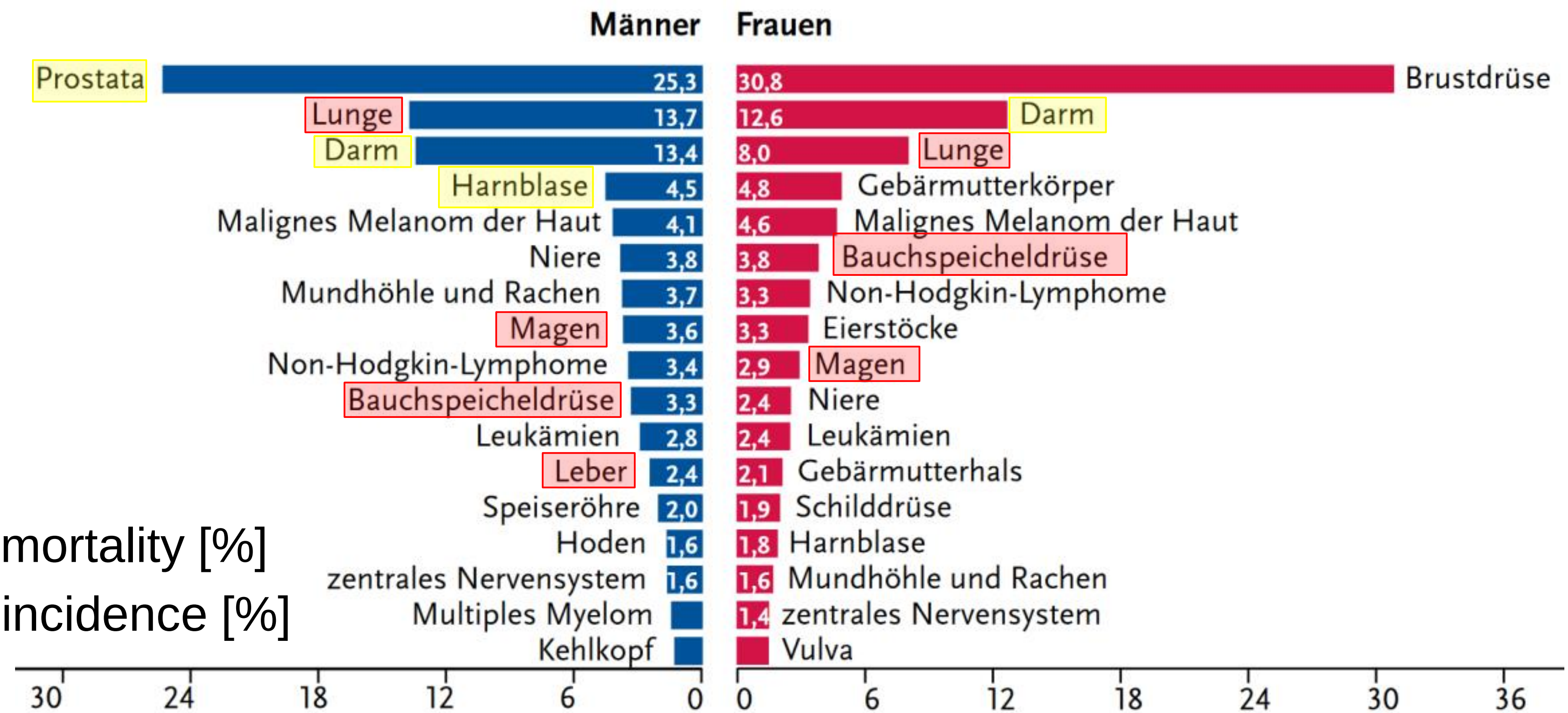
GSI Helmholtzzentrum für Schwerionenforschung GmbH



Scanned ion beam therapy for moving targets

C. Graeff

Cancer incidence and mortality



mortality [%]

incidence [%]

- Cancer of moving organs is common and in many cases has a bad prognosis

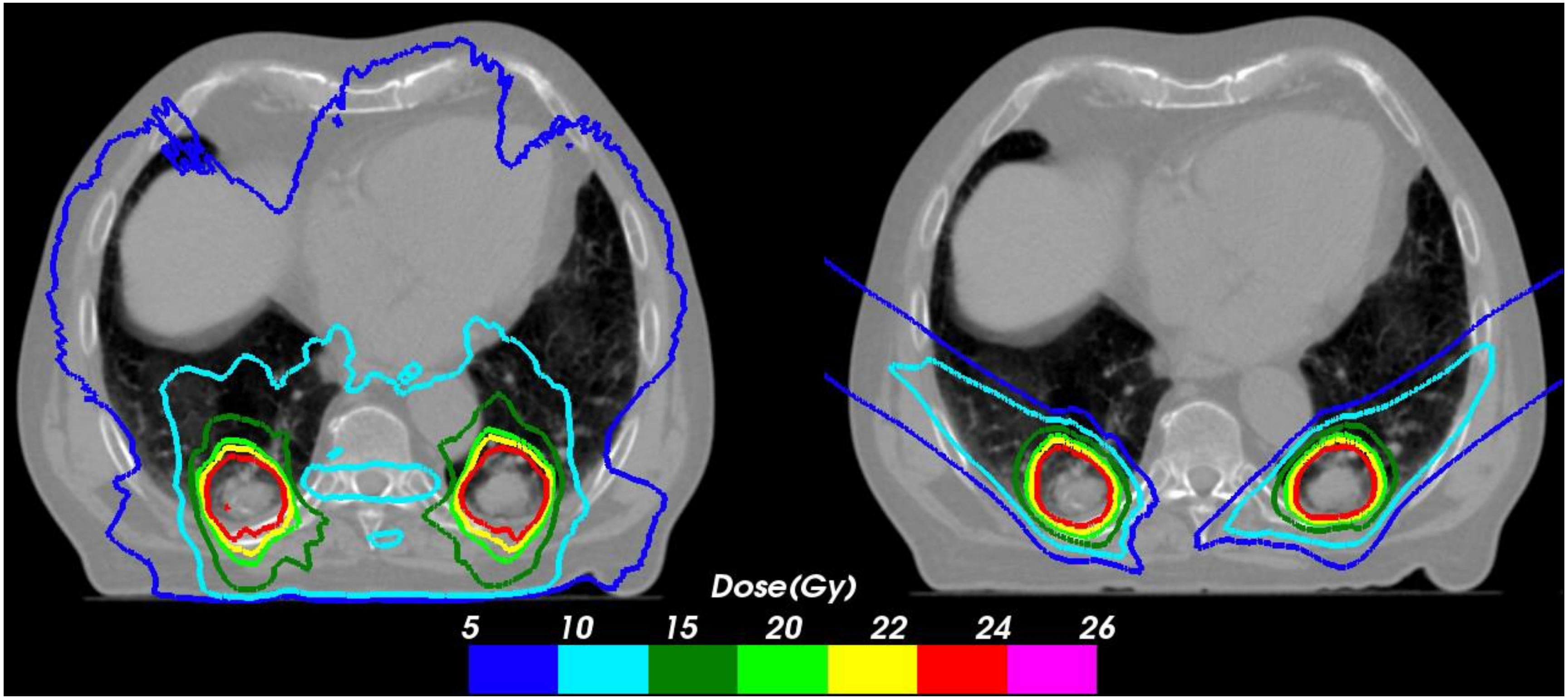
intrafractional motion

interfractional motion

Robert Koch Institute 2015
Data from 2011

Rationale for 4D-treatment with ions

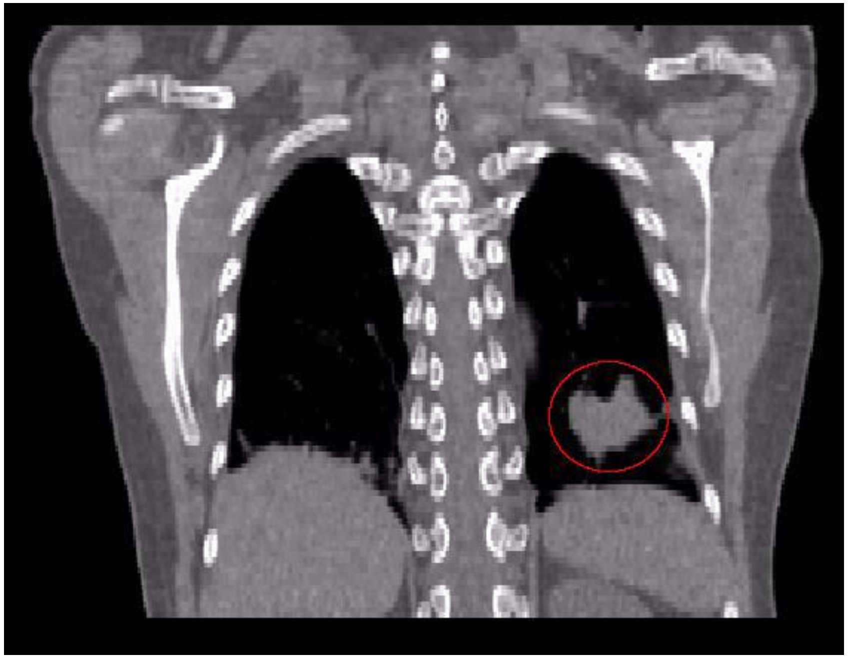
- Same as in 3D - ions more conformal than photons

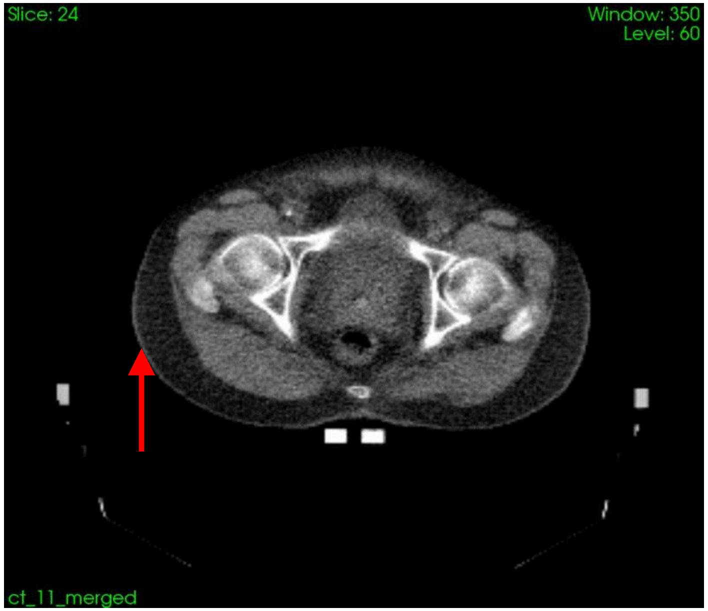


VMAT
(3D dose)

4 field SFUD carbon
Range ITV + rescanning

Types of motion

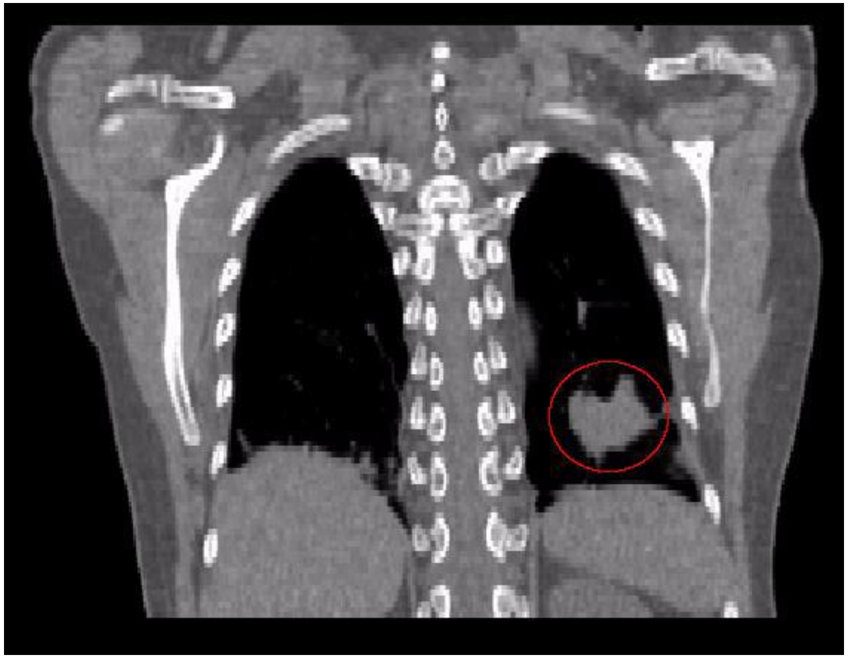


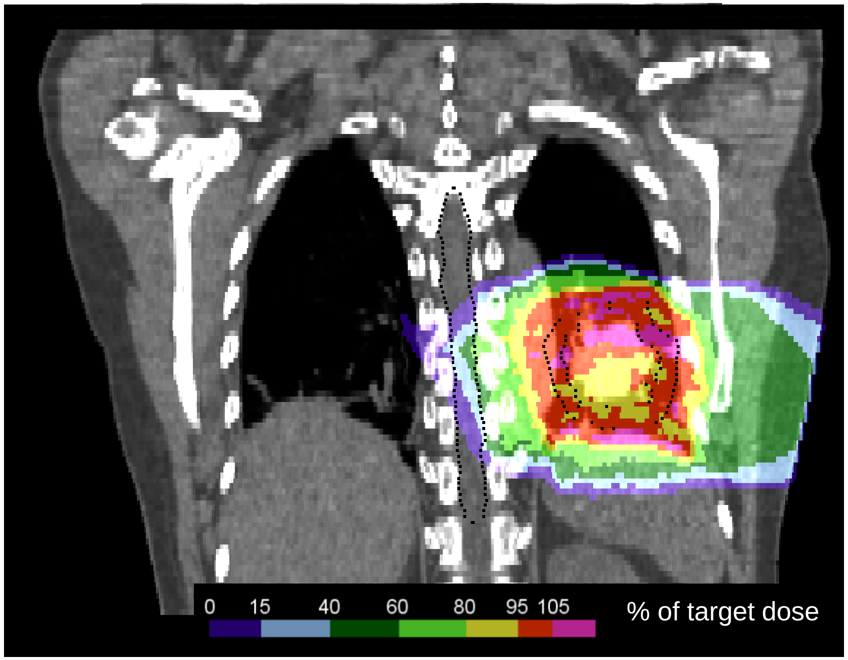


Courtesy A. Rucinski

- Intrafractional motion
  - respiration, heartbeat
  - peristalsis
- Interfractional motion: Peristalsis, anatomy, positioning

The problem: irradiating moving targets

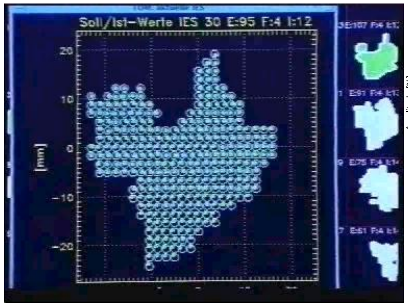


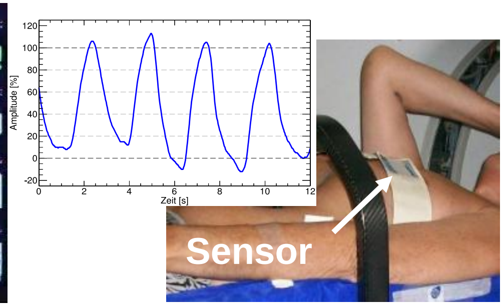


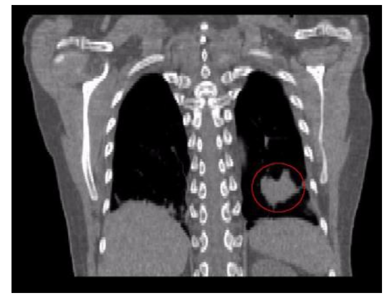
Courtesy M. Söhn, LMU

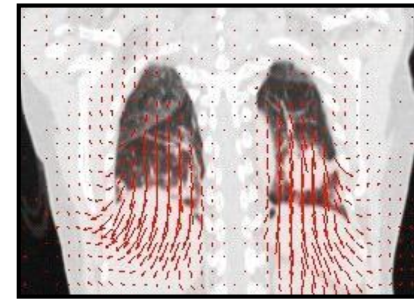
- **Motion**: Target miss
- **Range changes**: variable position of Bragg peaks
- **Interplay**: Interference between target and scanning motion

4D-dose calculation / treatment simulation









beam delivery sequence

motion monitoring

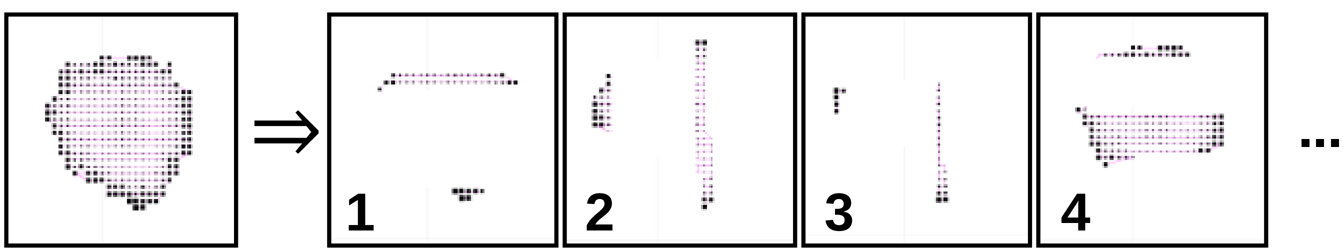
4D-CT → deformable registration

temporal correlation

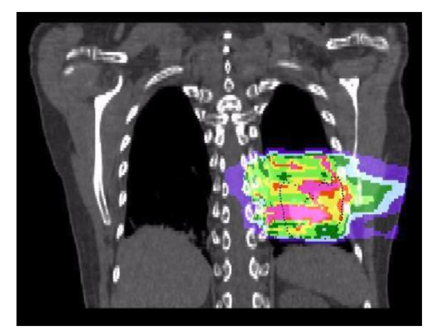
3D plan

4D plan

4D dose calculation



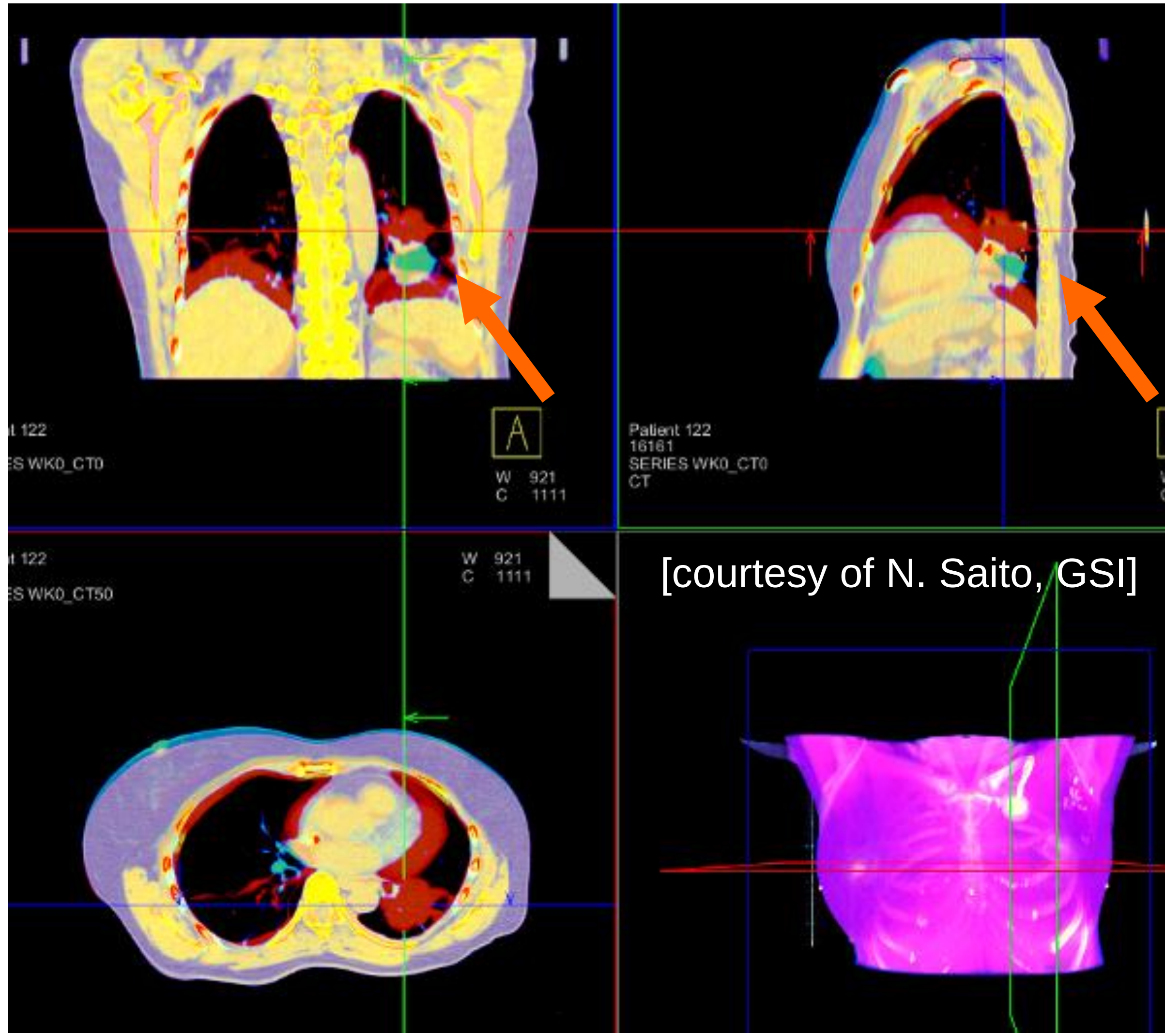
motion phases



4D CT + Transformation Maps

- (non-rigid) image registration
- Determines geometric movement of each CT voxel
- Allows motion estimation and dose summation

4D CT



[courtesy of N. Saito, GSI]

4D CT + Transformation Maps

- (non-rigid) image registration
- Determines geometric movement of each CT voxel
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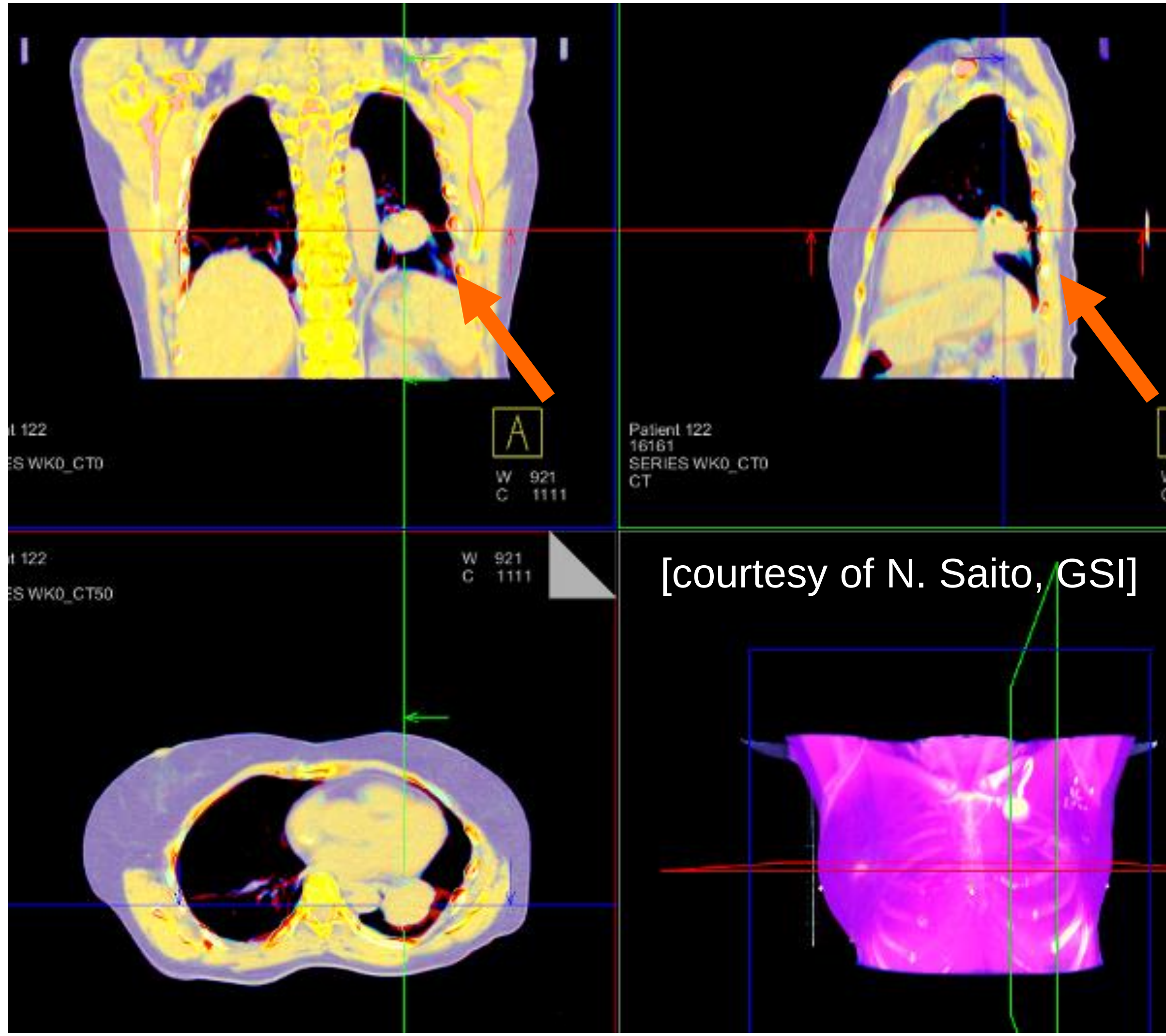
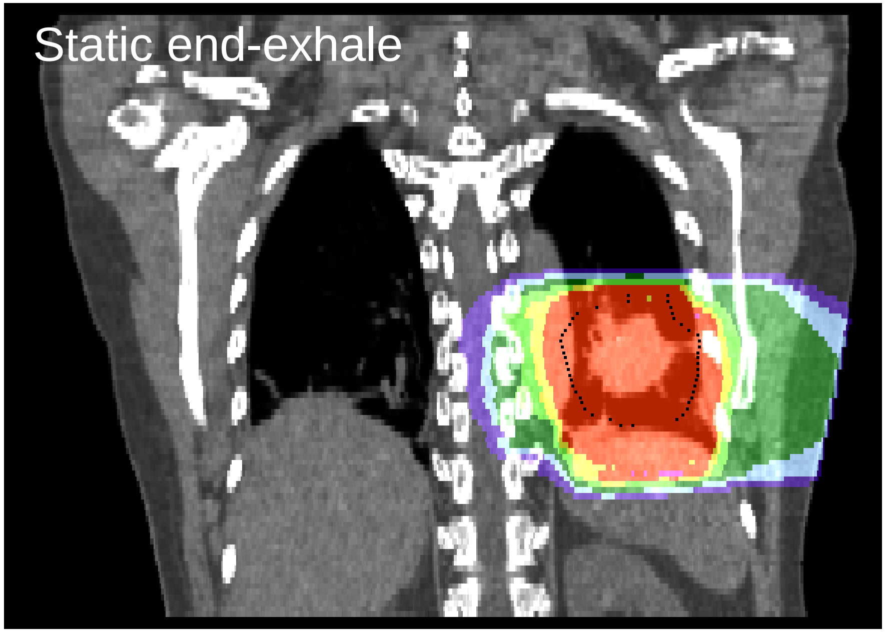
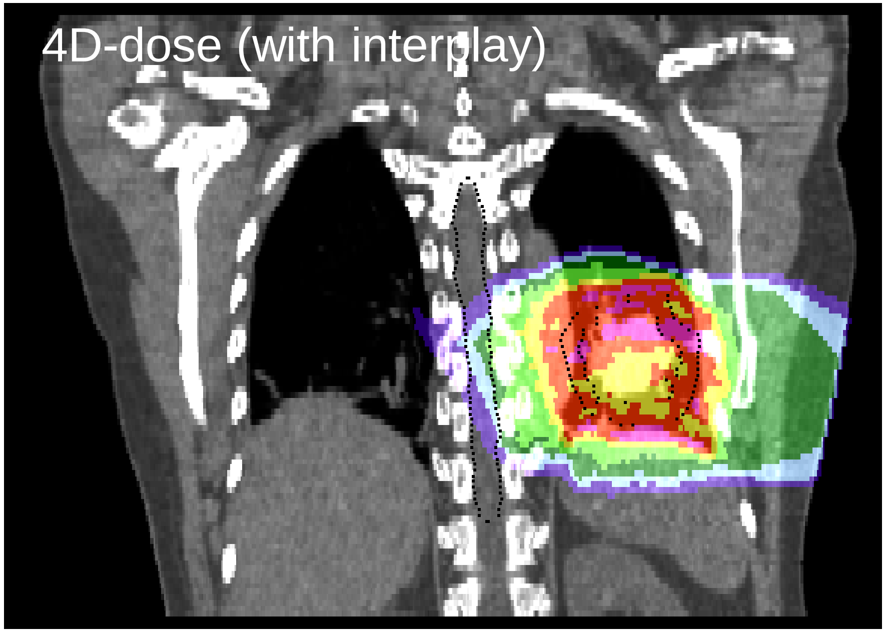
4D CT



Static vs. dynamic dose calculation



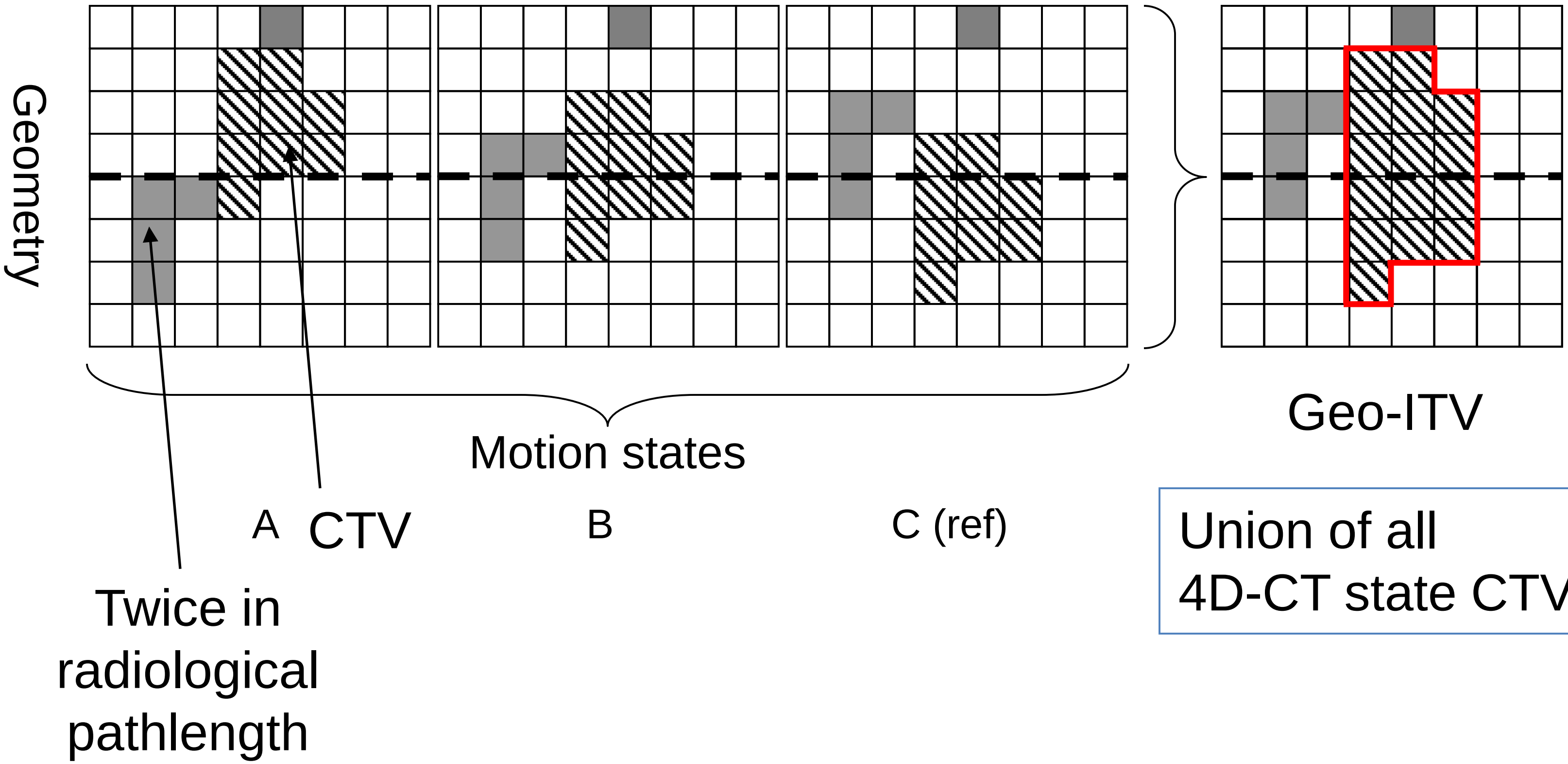


- 4D-dose calculation not available in (most) commercial TPS
- Interplay calculcation not available in any commercial TPS
  - You don't know how worse it can get
  - You also don't know if you're mitigation actually helps...

Motion mitigation strategies

- Motion minimization / control
  - abdominal compression, ABC
- Gating, with or without breathhold
- Rescanning
  - slice-by-slice, volumetric, phase-controlled, iso-weighted,...
- Range-considering ITVs
- Tracking
- 4D-optimization
- Combinations of all of the above
- ...

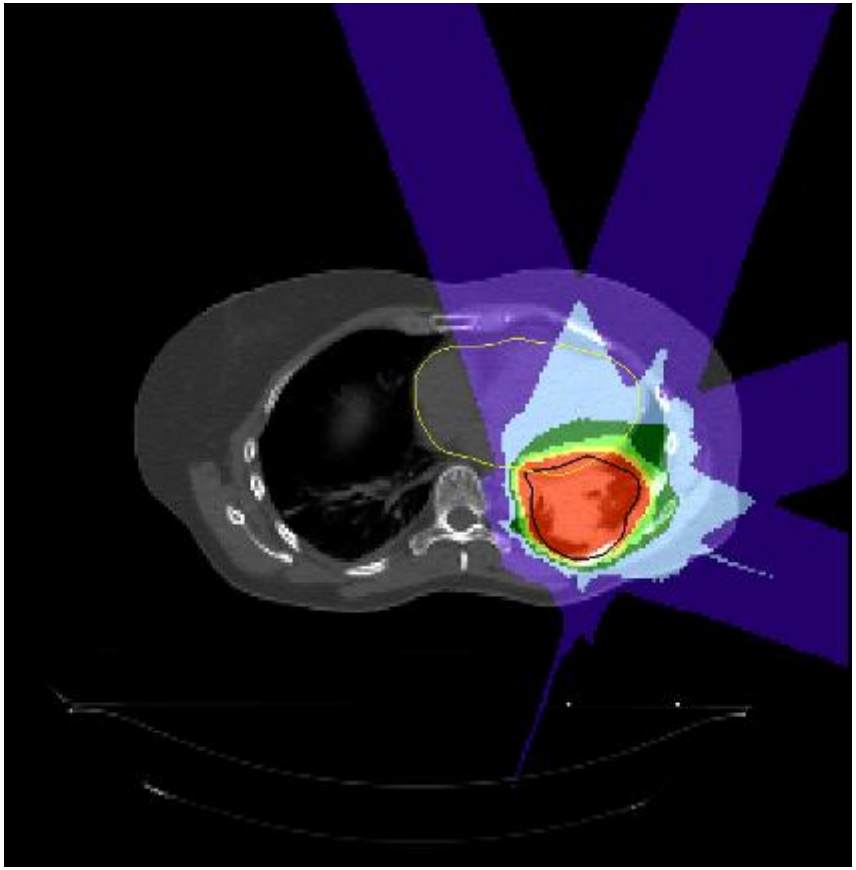
The Geometric ITV



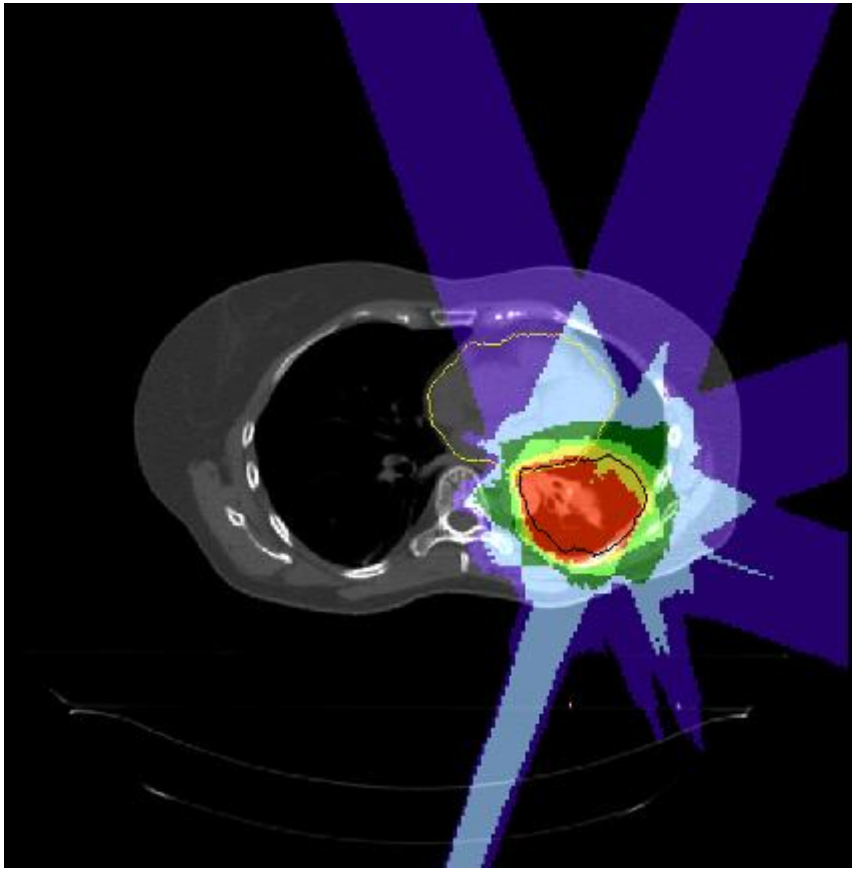
Union of all
4D-CT state CTVs

[Rietzel & Bert, Med Phys, 2010]

Simulated Static Dose: Geometric ITV



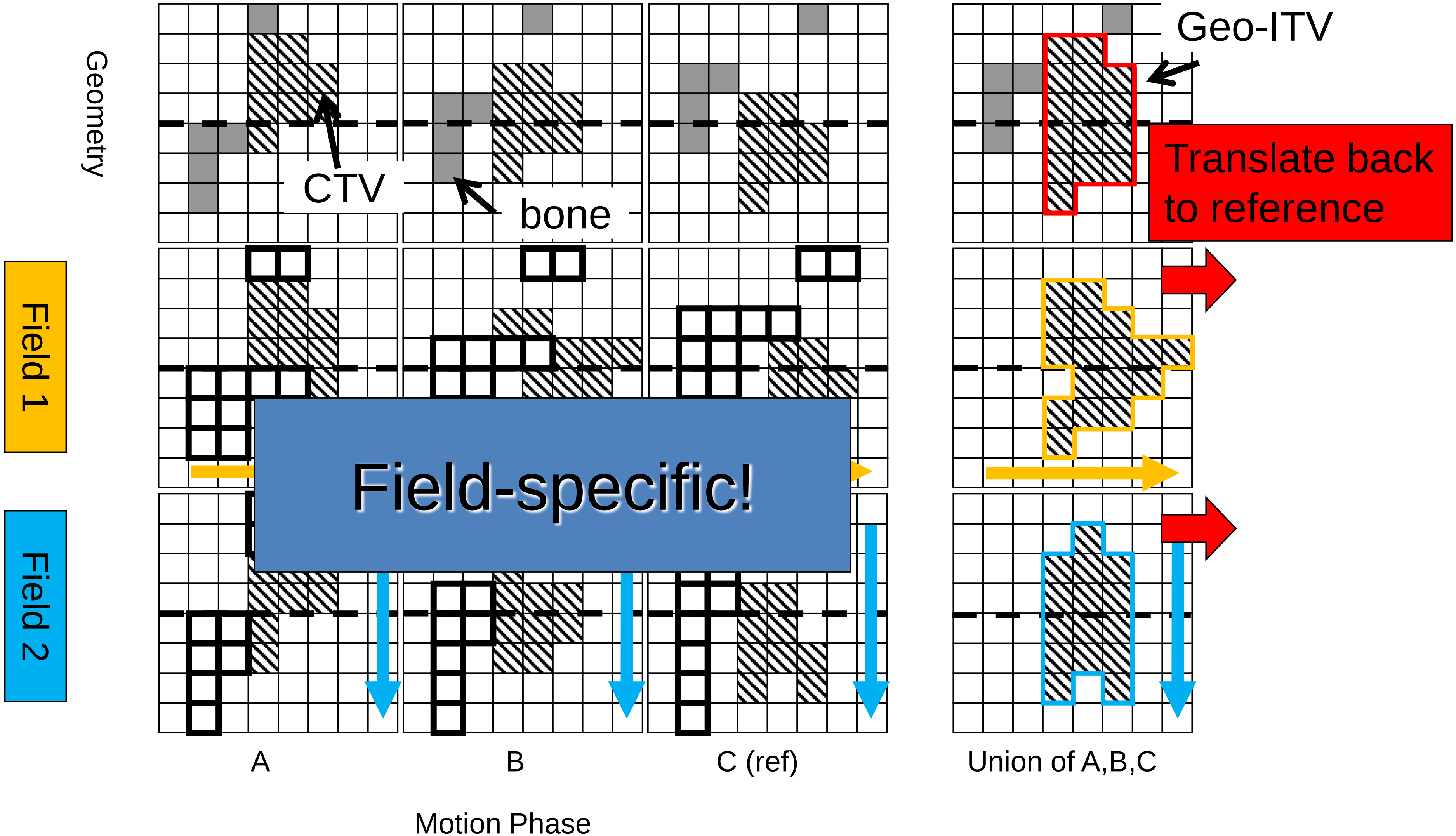
End-Exhale (Ref)



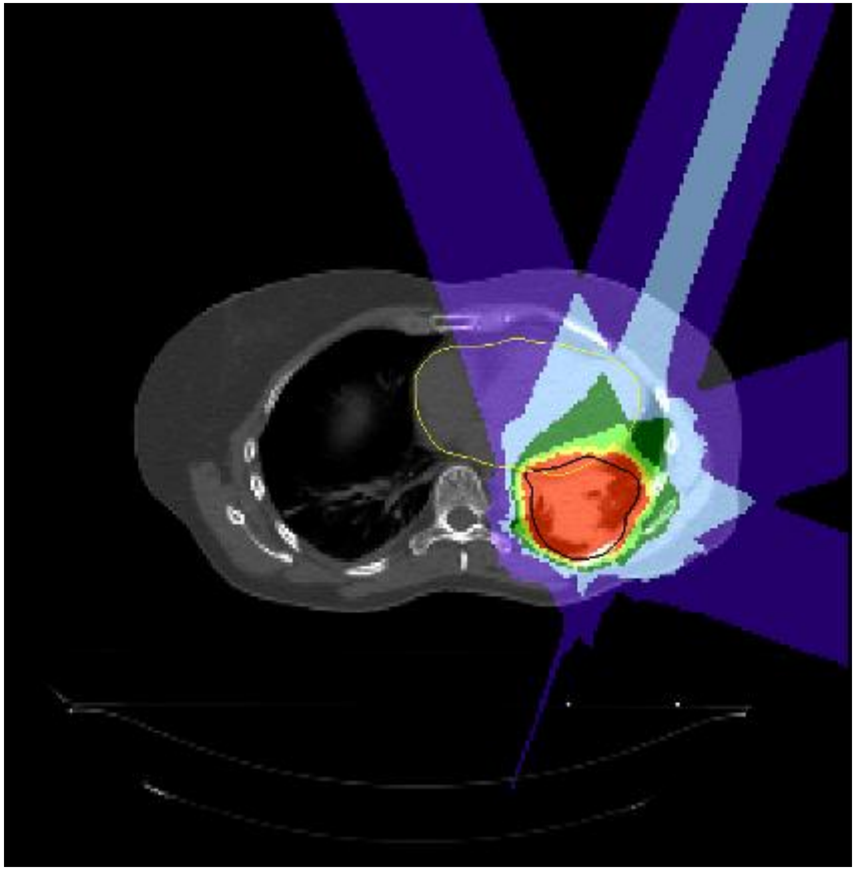
End-Inhale

25 mm motion

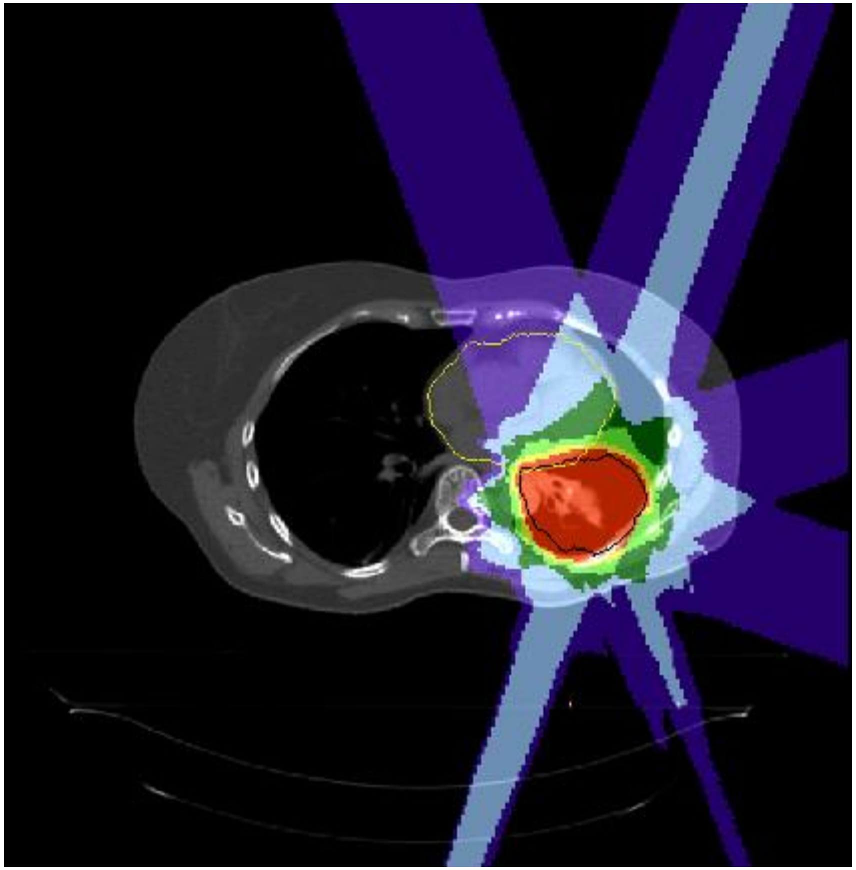
The Range-ITV



Simulated Static Dose: Range-ITV



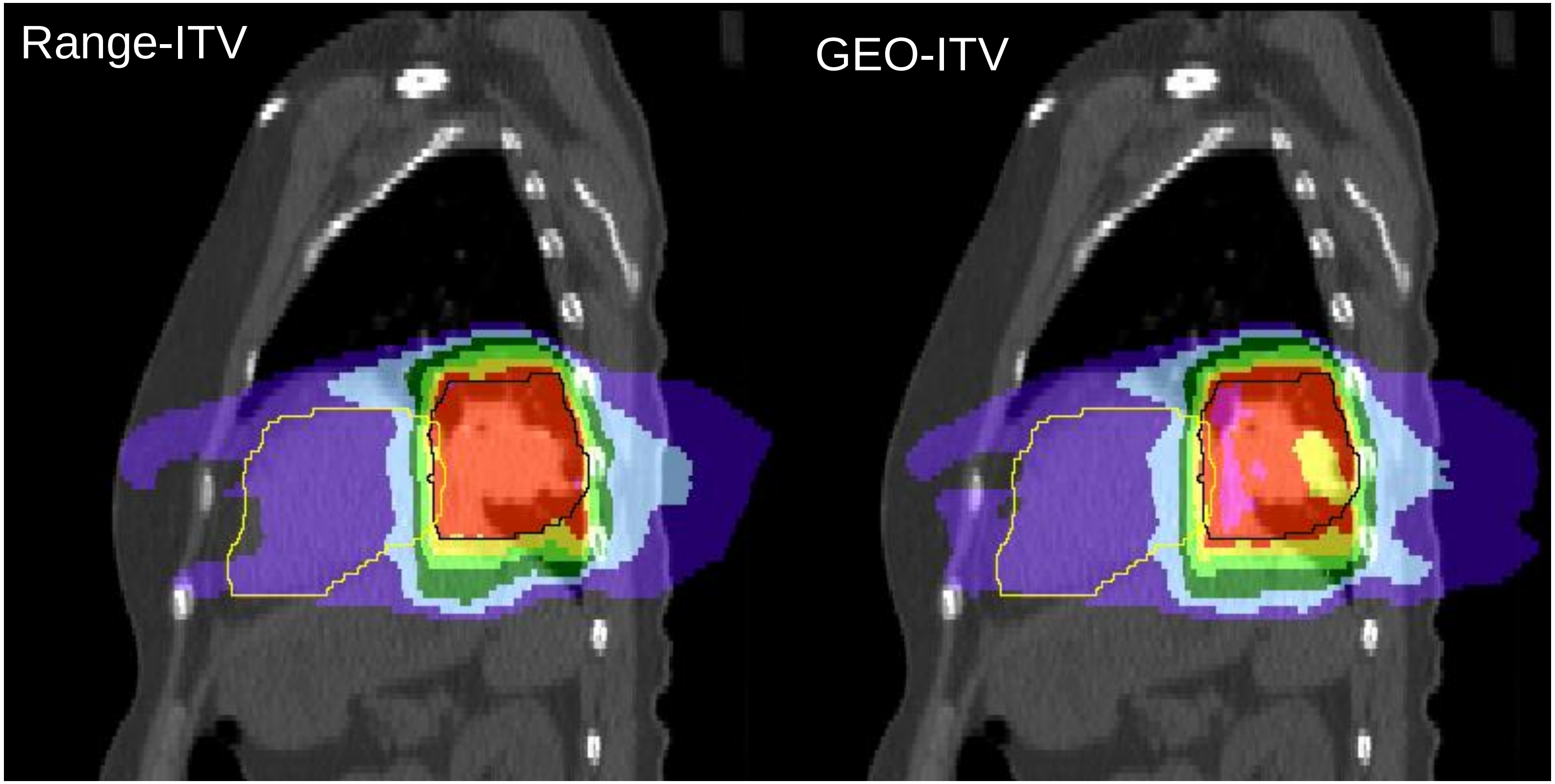
End-Exhale (Ref)



End-Inhale

Simulated 4D-Dose

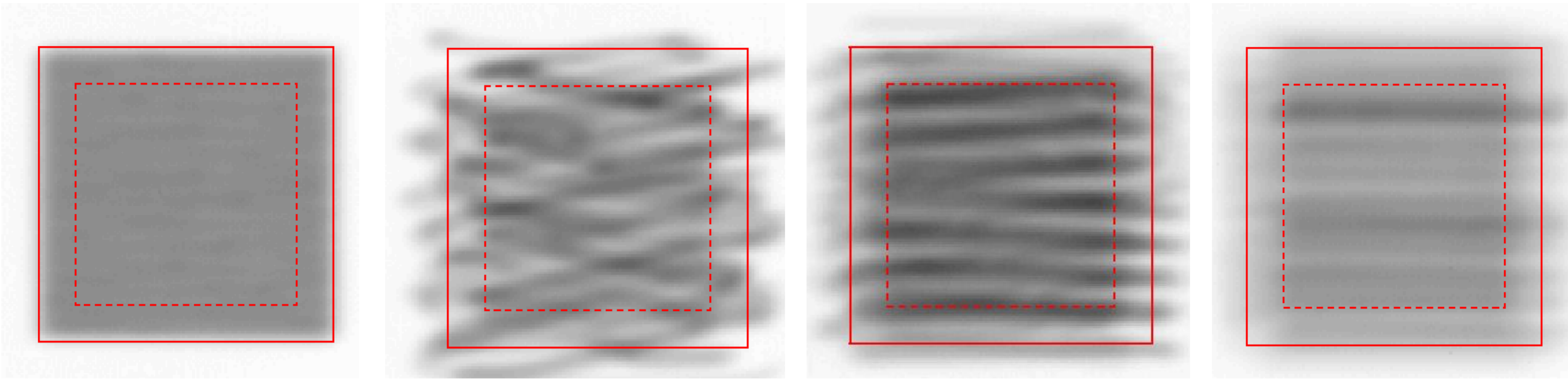
V95	99.3%	V95	91.1%
D5-D95	6.0%	D5-D95	17.0%



- Field-specific range changes are necessary

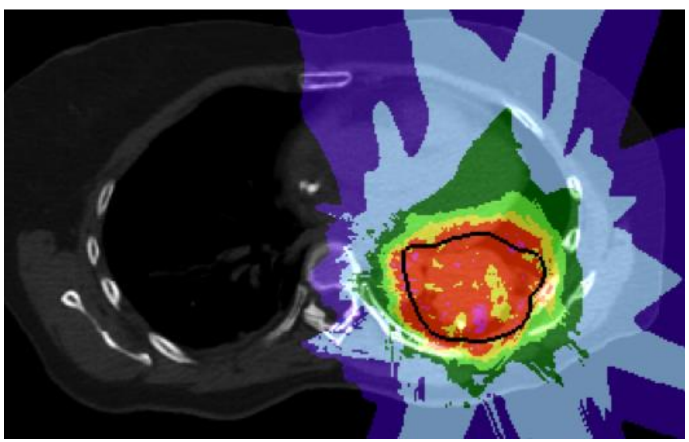
Rescanning

S. Grözinger, PhD thesis, 2004

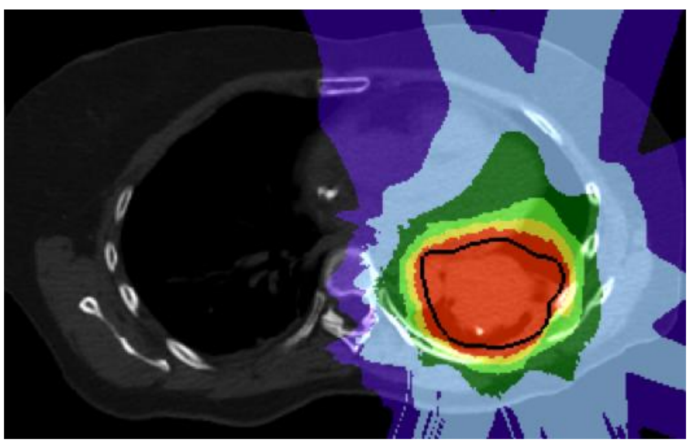


Static | 1 scan | 2 scans | 10 scans

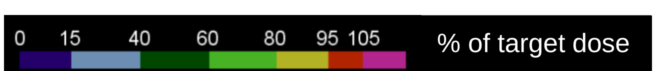
D. Müssig, PhD thesis, 2013



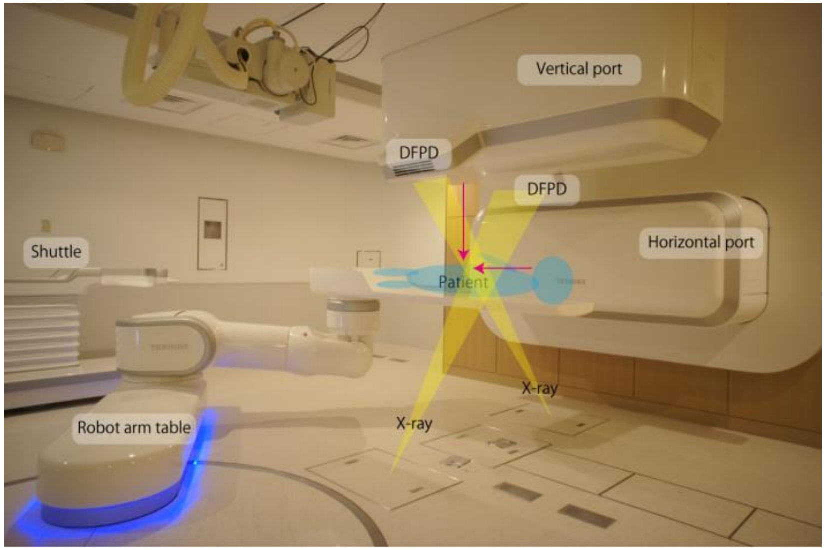
Interplay

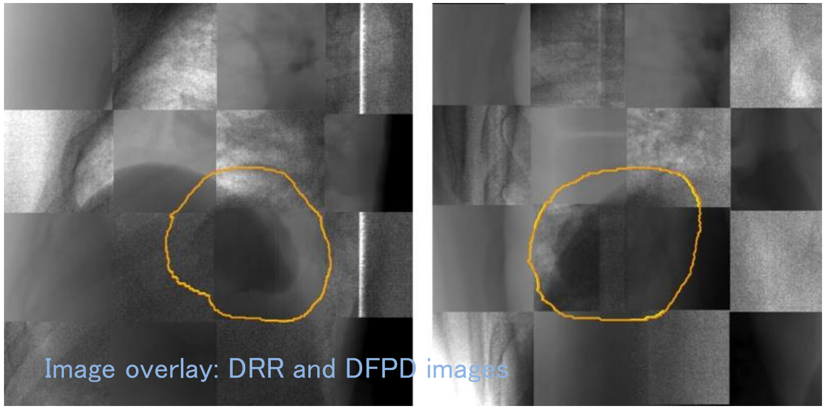


9 x Slice-by-slice rescanning
Phase-controlled rescanning



Gating at NIRS

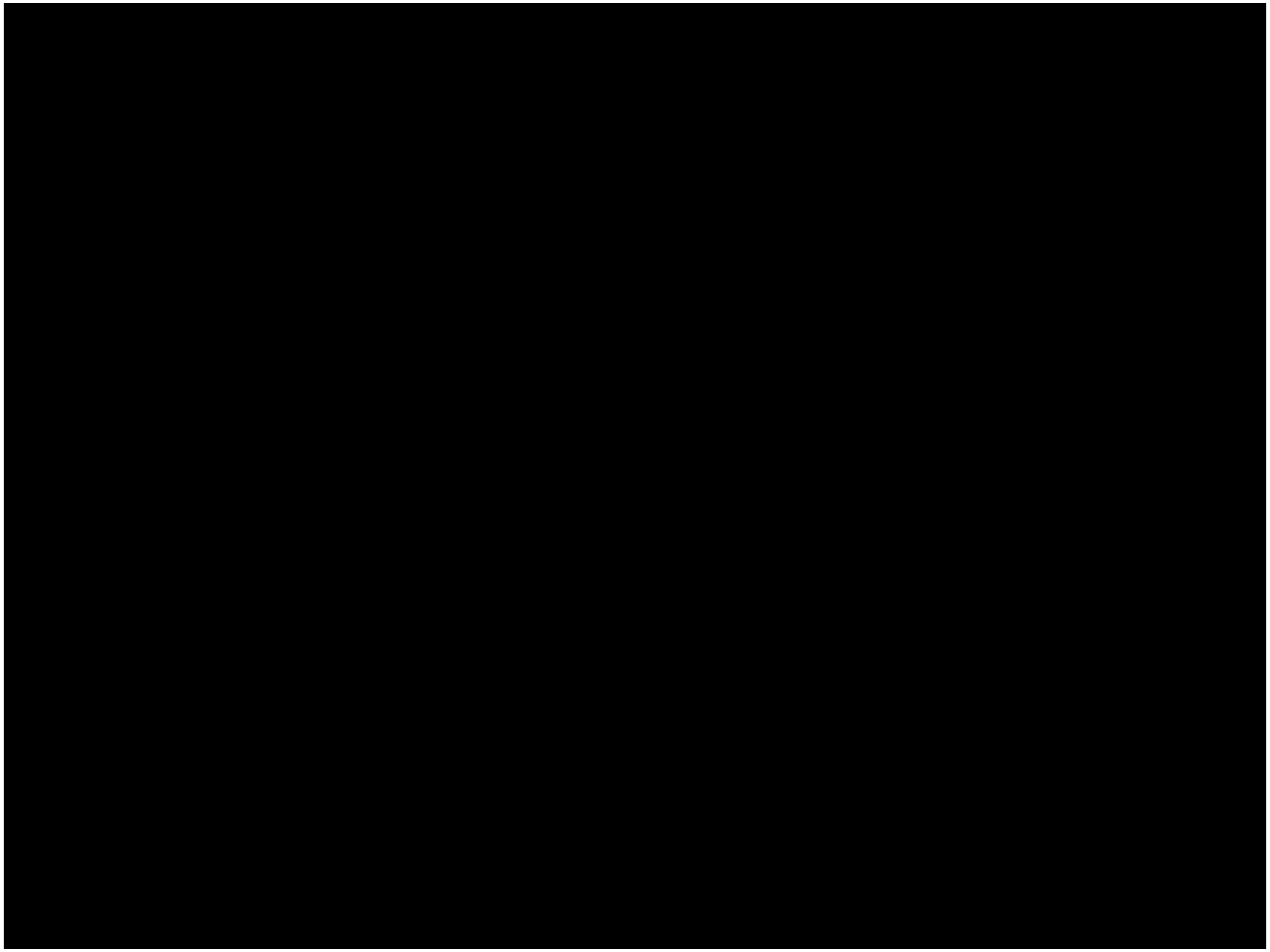




- Amplitude-based gating to counter irregular respiration
- Real time fiducial-free tumor tracking using fluoroscopy
  - liver 20-80mA/4ms, lung 20-40mA/4ms
  - variable rate during treatment: 1-30fps
  - X-ray acquisition to beam on gate < 50ms
  - Accuracy < 0.4±0.1mm

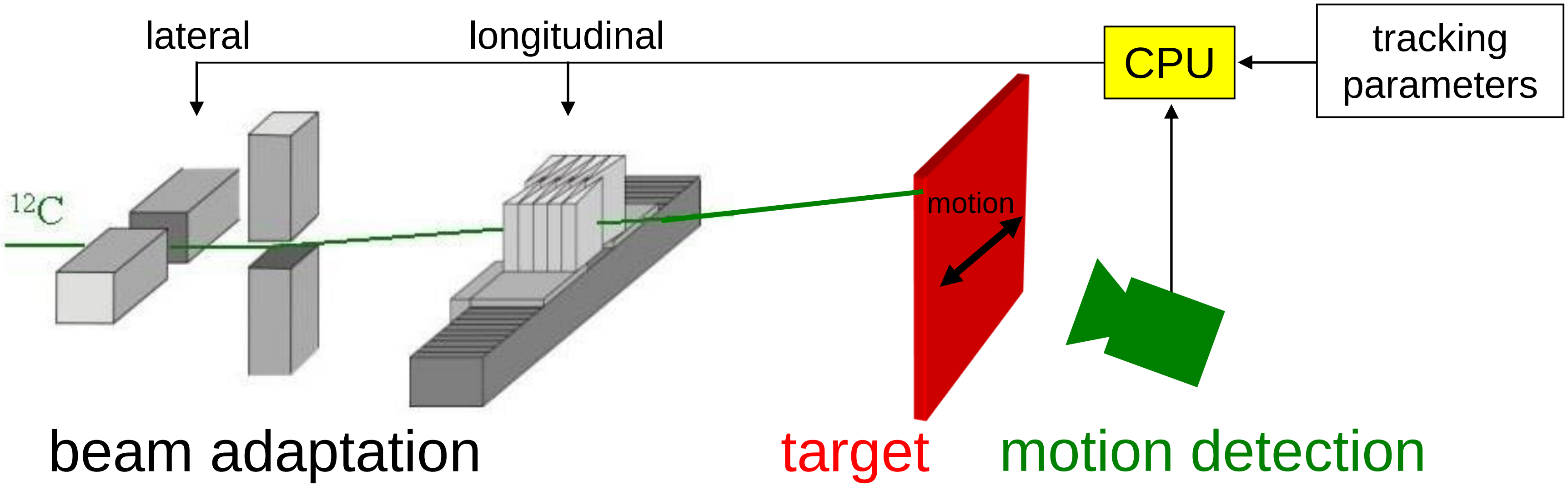
National Institute of Radiological Sciences
Research Center of Charged Particle Therapy

Gating at NIRS

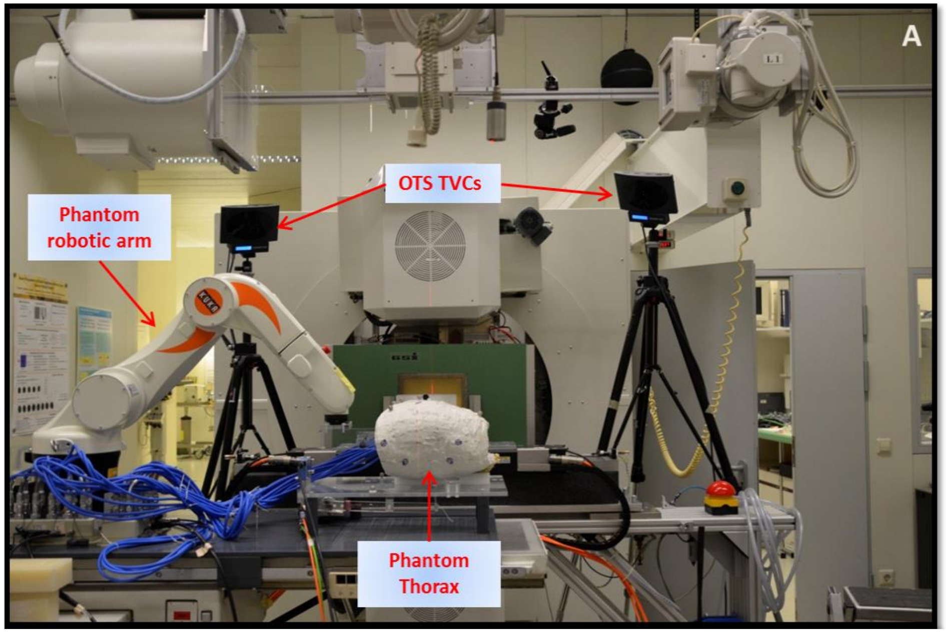


Beam Tracking

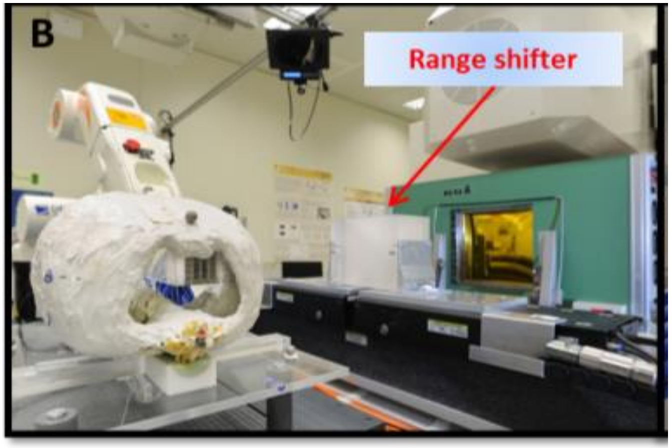
- Tremendous advantage over photons:
  Easy, fast beam deflection



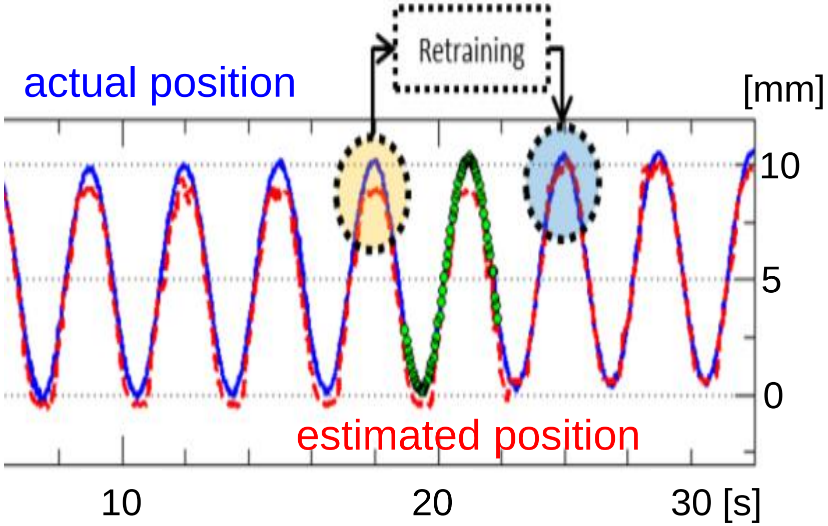
Beam tracking at Cave M



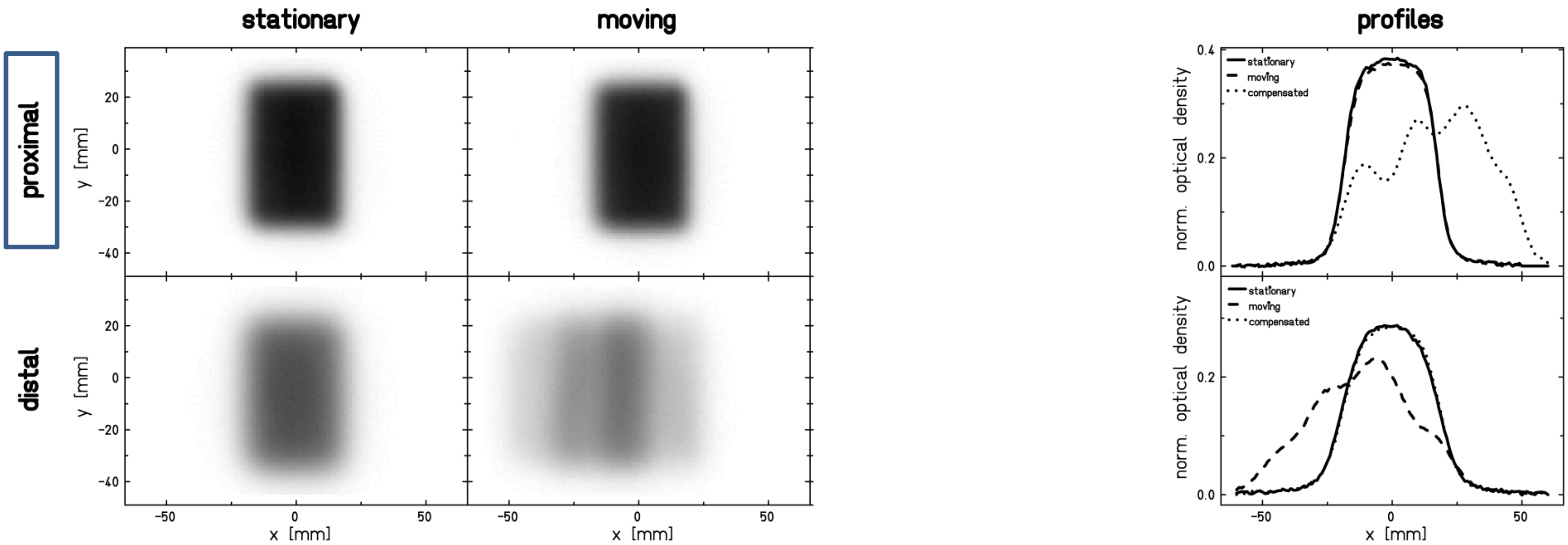
- 3D target motion (10 mm)
- breathing phantom
- optical monitoring plus model prediction
- ➢ dose error reduced from 24% to 3%

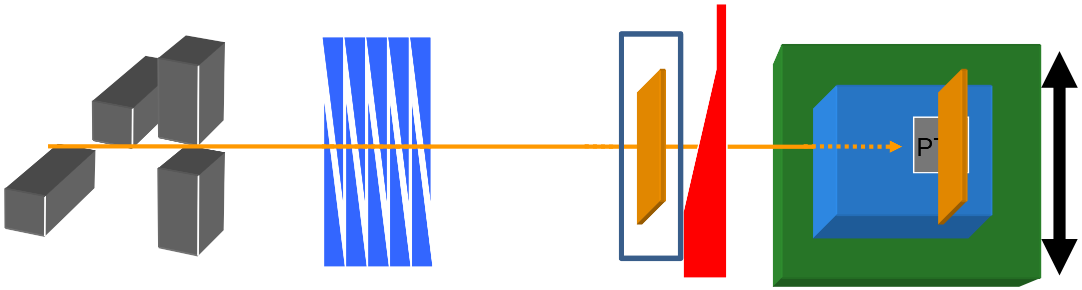


- full 3D beam tracking



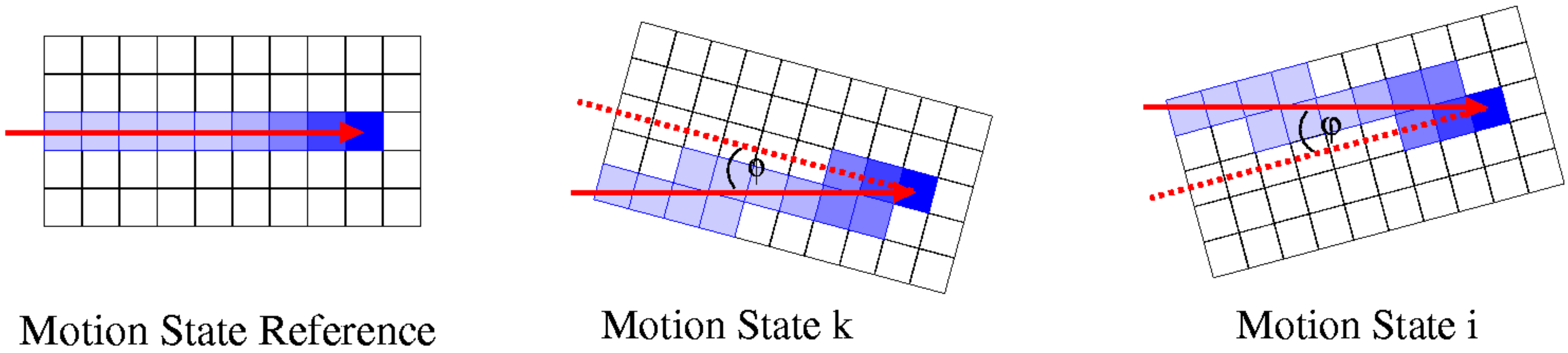
Tracking issues I: inverse interplay





Tracking issues II: complex motion

- Beam tracking compensates translation only
- Preplanned entry channel doses may be wrong!



Conformal 4D-optimization

Voxels

beam spots

motion phases

- 3D Optimization cost function

$$E(\vec{N}) = \sum_{i=1}^{v} \left[D_{pre}^{i} - D_{act}^{i}(\vec{N})\right]^2 = \sum_{i=1}^{v} \left[D_{pre}^{i} - RBE(\vec{N}_k) \sum_{j=1}^{r} c_{ij} N_j\right]^2$$

- Full 4D Optimization cost function

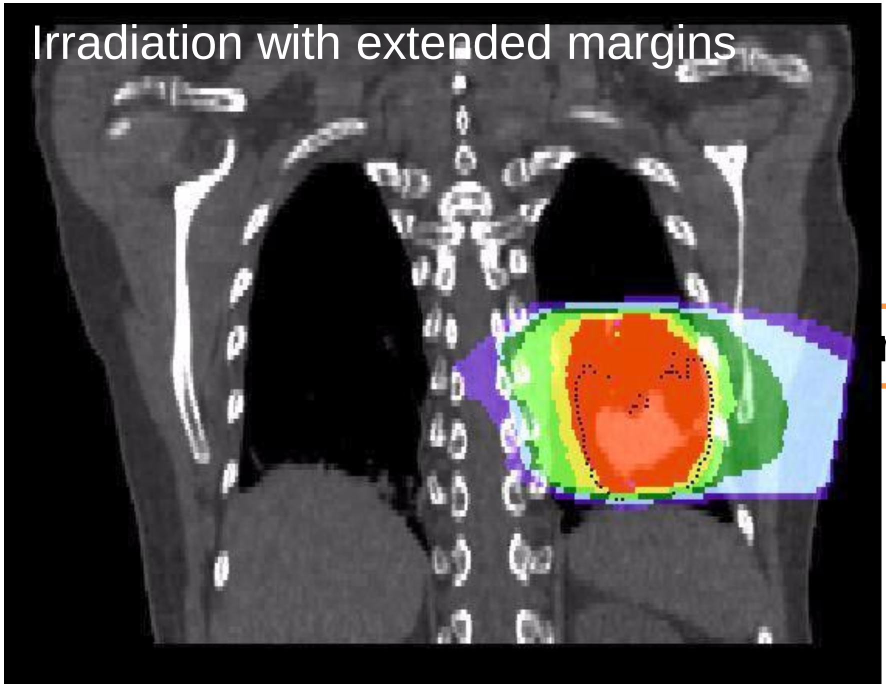
$$E(\vec{N}) = \sum_{k=1}^{m} \sum_{i=1}^{v} \left[D_{pre}^{i} - D_{act}^{ik}(\vec{N}_k)\right]^2 = \sum_{k=1}^{m} \sum_{i=1}^{v} \left[D_{pre}^{i} - RBE(\vec{N}_k) \sum_{j=1}^{r} c_{ijk} N_{jk}\right]^2$$

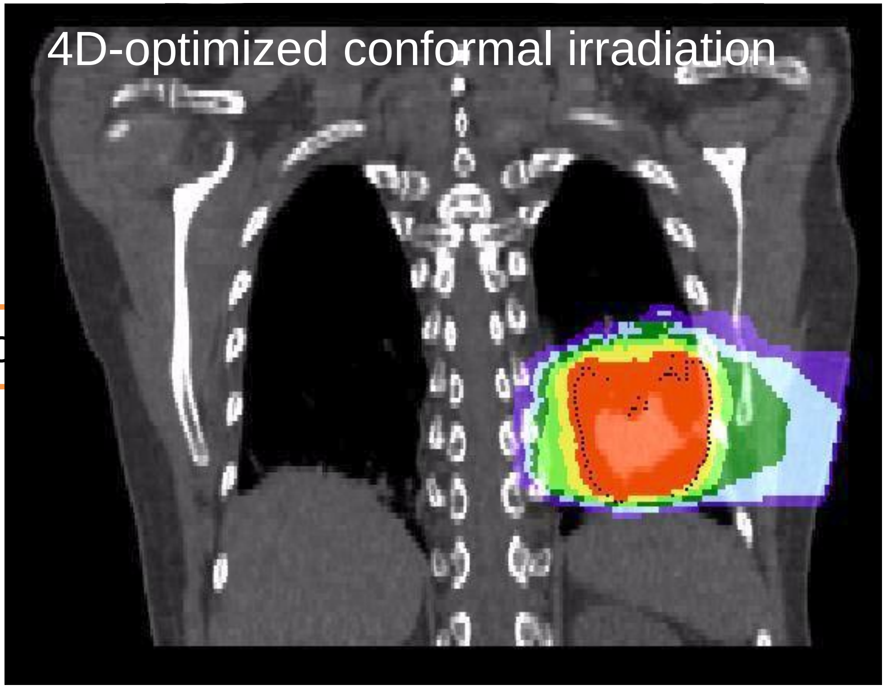
- Different strategies possible to control gradients, reduce problem size, ...

- (OAR terms omitted)

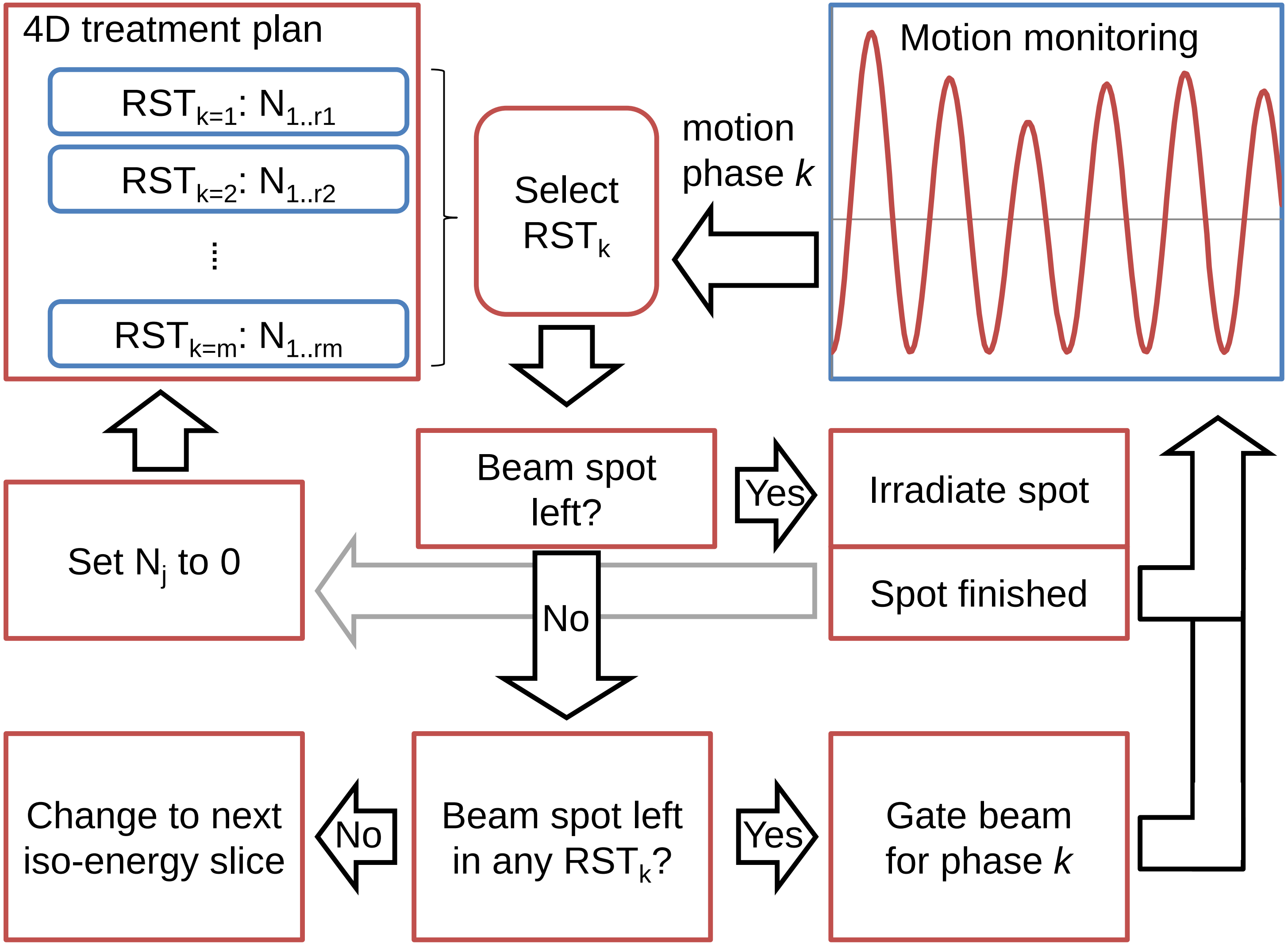
Motion-synchronized delivery

- Conformal 4D-optimization results in a plan library
- Delivery of all plans has to be synchronized to motion



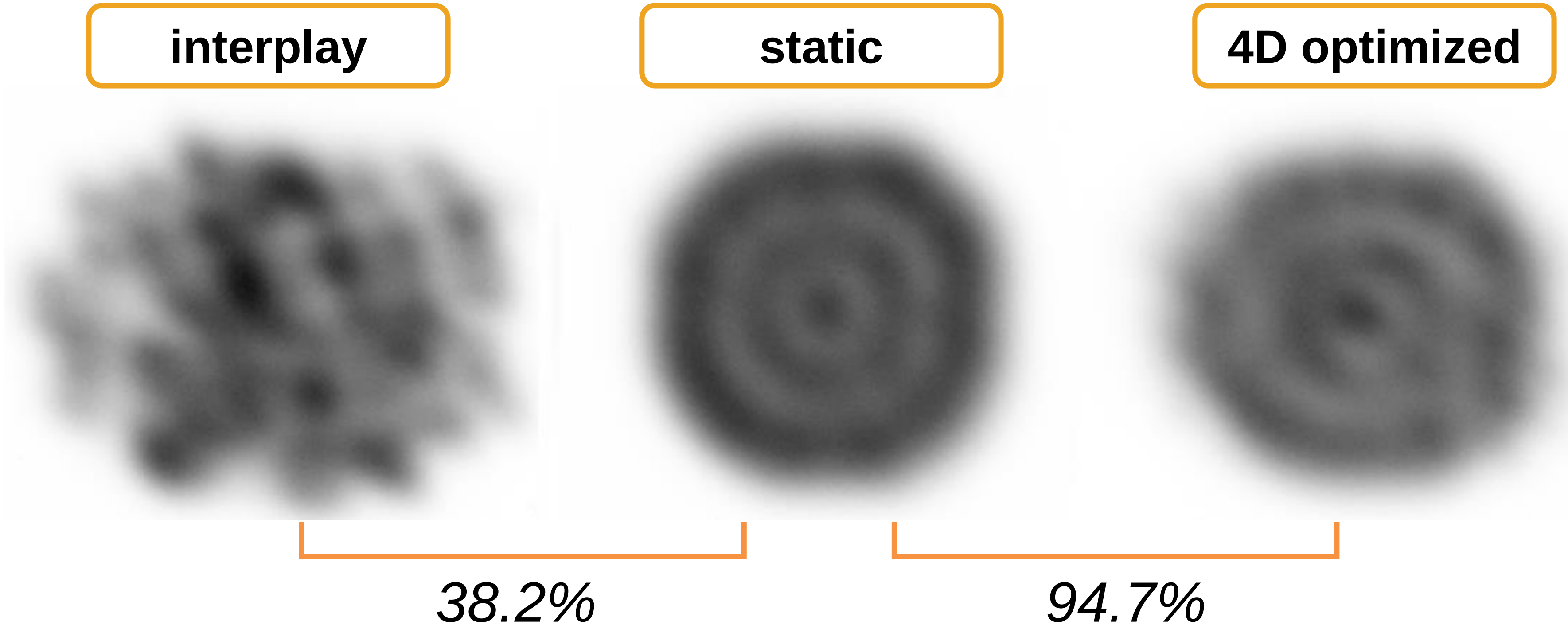


Delivery: The 4D dose delivery system



Graeff at al. Green Journal 2013

Feasibility of 4D-TCS: Film experiment



- Target: 30 mm circle, 20 mm left-right-amplitude
- Comparison: Gamma coefficient (3 mm, 3%)
- Residual motion within the states

Graeff at al. Green Journal 2013

Summary

- Scanned ion beam therapy for moving targets is complex - Clinical transition is only starting
- 4D effects have to be considered – evaluation of 3D doses is not sufficient

- Open questions
  - Identify patients for different mitigation strategies
  - Variability of motion needs to be studied and compensated
  - 3D / 4D Imaging for setup is essential
  - Robust optimization
  - Motion monitoring: position and range?

Requirements for synchronized delivery

- Dose delivery system has to
  - store a set of treatment plans instead of a single one
  - detect motion phases
  - dynamically switch sequence of beam spots to be irradiated
  - gate beam if motion phase is finished
    - gating on flat-top is necessary,
      i.e. fast recovery of irradiation
  - intensity control and flexible flattop duration is extremely helpful for fast & efficient delivery

Robustness:4D-controlled rescanning

- Optimize target coverage **in each motion phase**

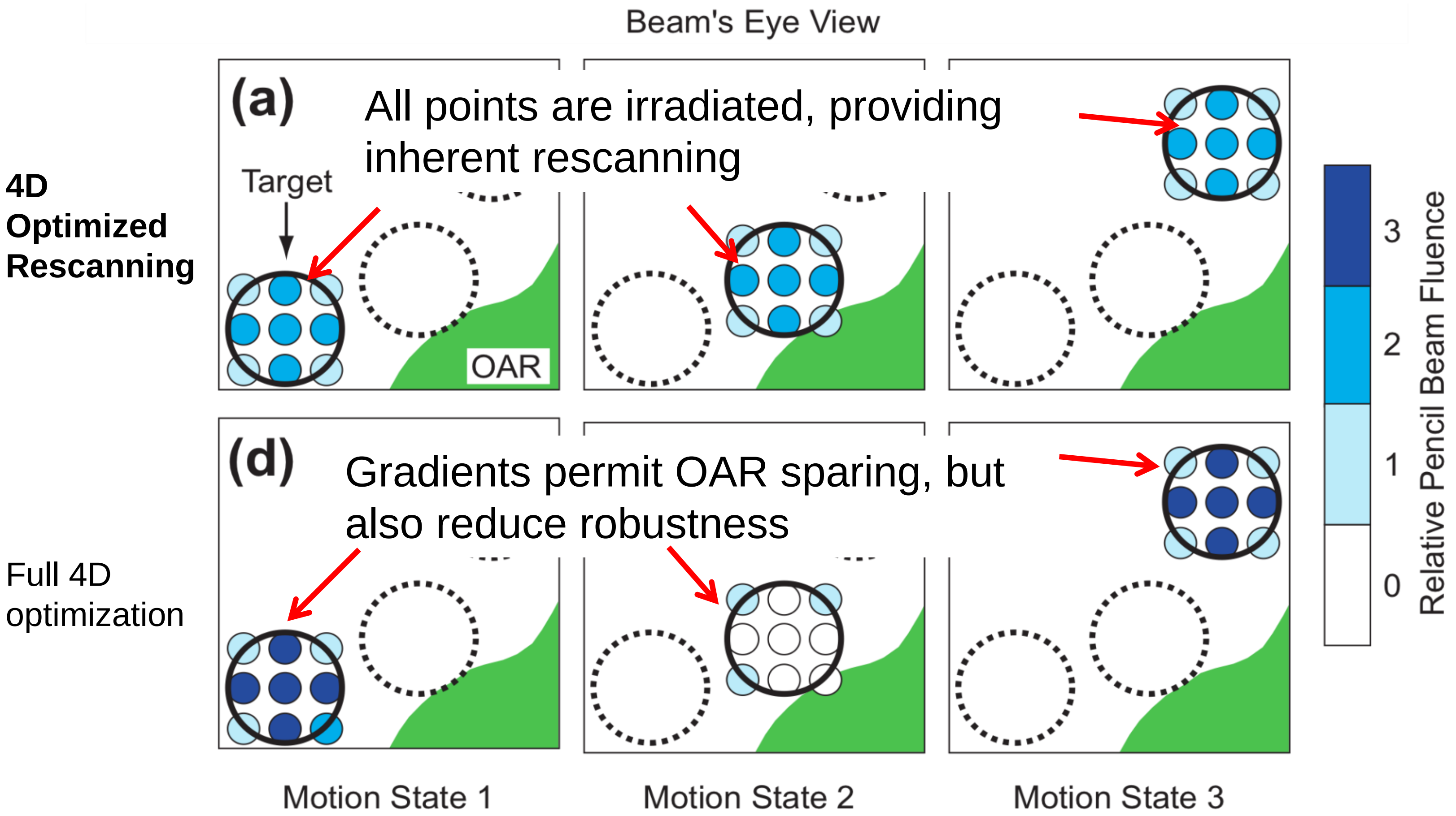


image courtesy of John Eley

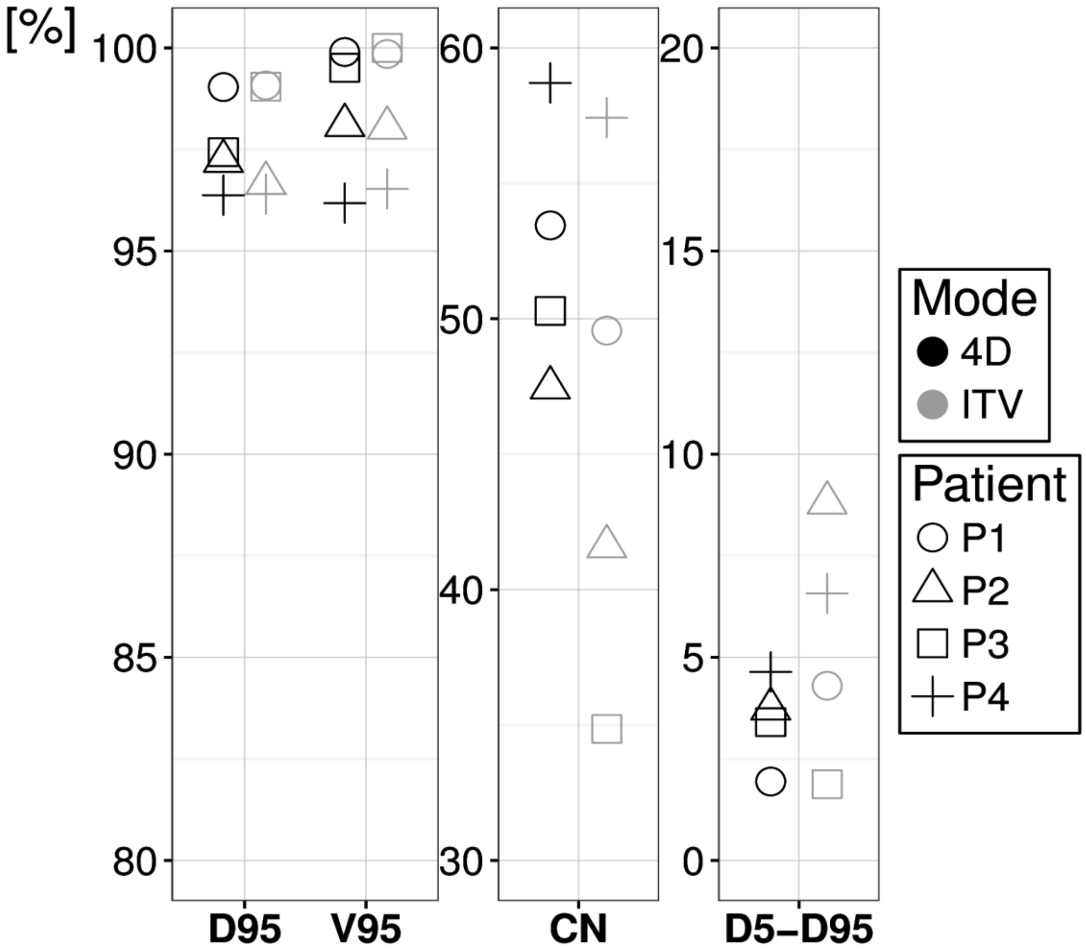
A patient simulation study

- 6 weekly 4D-CTs for each patient
- Planning on first CT, simulation on all subsequent CTs
- Margins needed to achieve V95 > 95% in cumulative dose

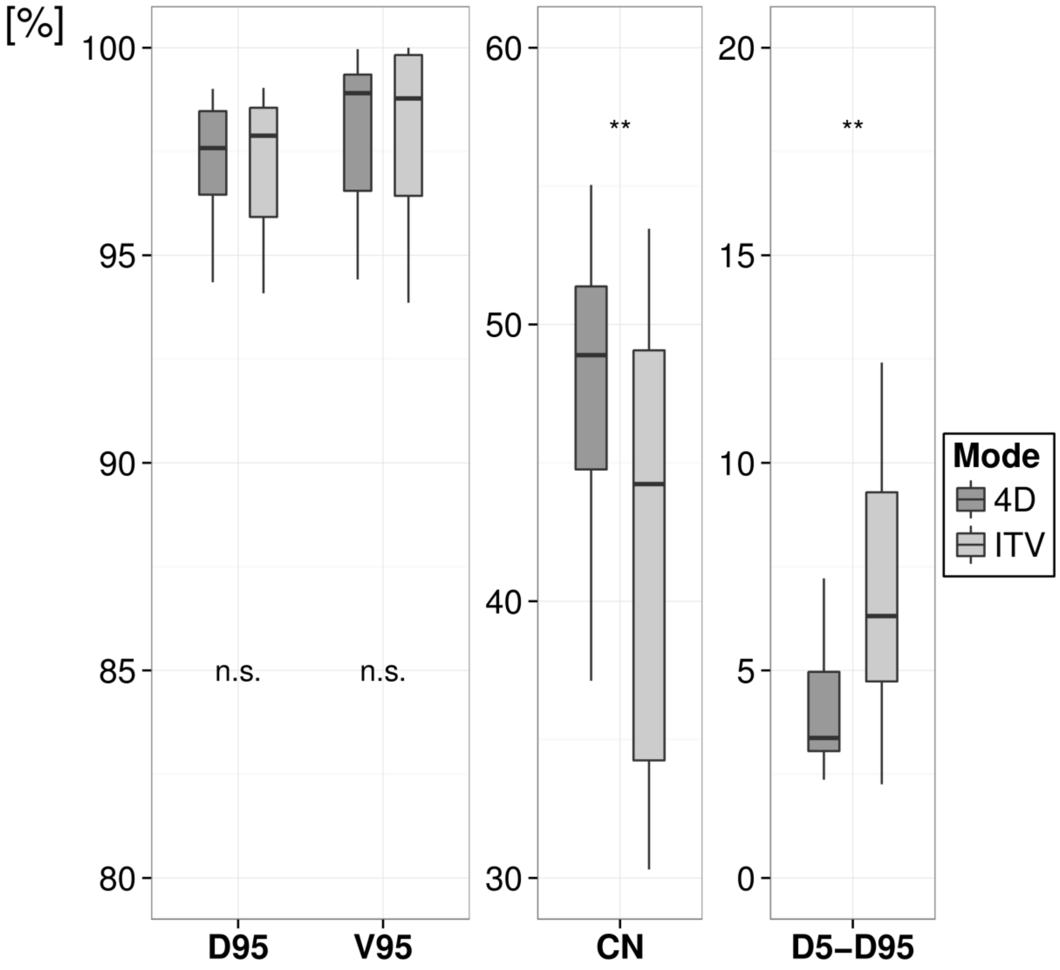
	Fraction 4DCTs (weeks 2 - 6)		
Patient	CTV Amplitude (min - max) [mm]	abs ΔRange: week n - week 1 (median, range) [mm H2O]	Necessary Margins V95>95% [mm + mm,%]
P1	2.8 - 3.9	2.2 (1.3 – 5.9)	3 + 2
P2	6.6 - 15.9	4.3 (1.3 – 6.3)	7 + 2
P3	2.1 - 5.4	1.6 (0.8 – 3.0)	3
P4	20.6 - 27.5	6.9 (4.4 – 11.2)	7 + 2

- Same margins necessary for ITV coverage

Cumulative dose results



Individual fractions

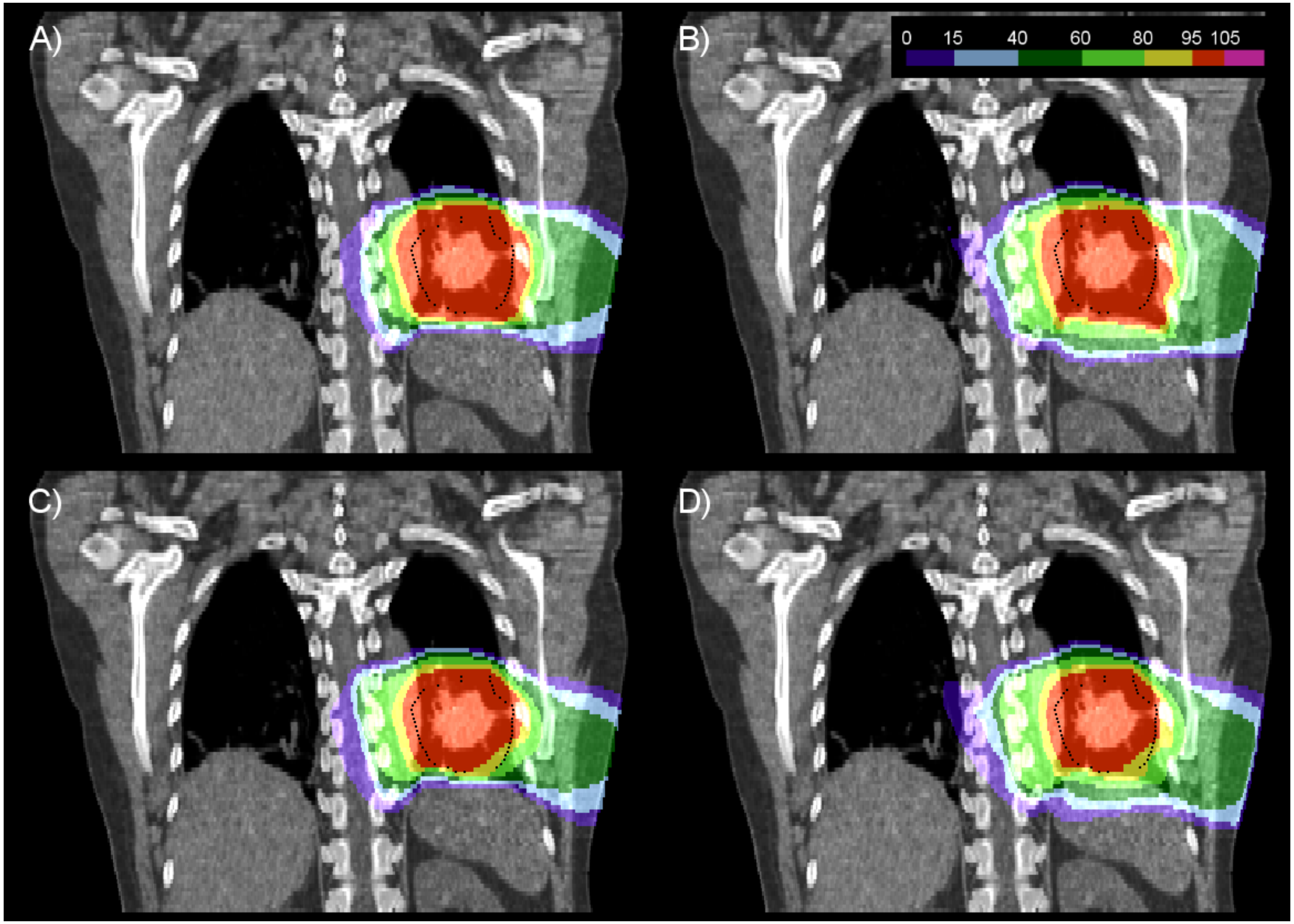


- paired t-test, **: $p < 0.001$

Comparison of ITV and 4D-opt

planned
4D-dose

cumulative
4D-dose



4D-opt

ITV