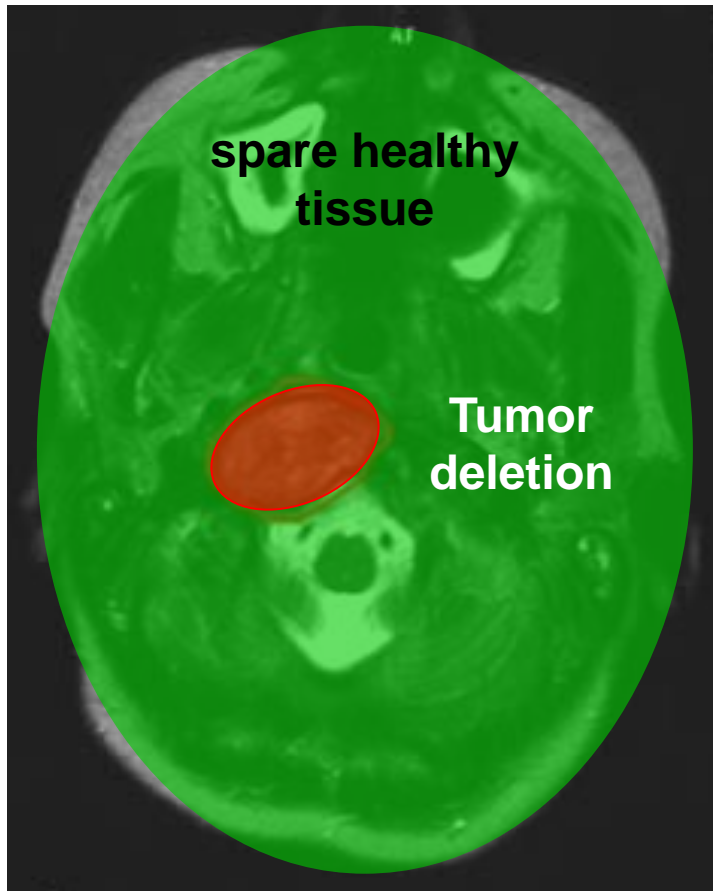
A detailed wireframe 3D model of a particle accelerator. The model shows a large, roughly circular ring structure in the foreground, with a complex network of smaller, interconnected structures and pipes extending from it towards the background. The entire model is rendered in a black wireframe style, highlighting the geometric complexity of the facility.

4D-optimization and motion-synchronized delivery

C. Graeff

Aim of radiotherapy



- Treat tumors - spare surrounding healthy tissue
- Conformal treatment

WHEN YOU SEE A CLAIM THAT A COMMON DRUG OR VITAMIN "KILLS CANCER CELLS IN A PETRI DISH,"

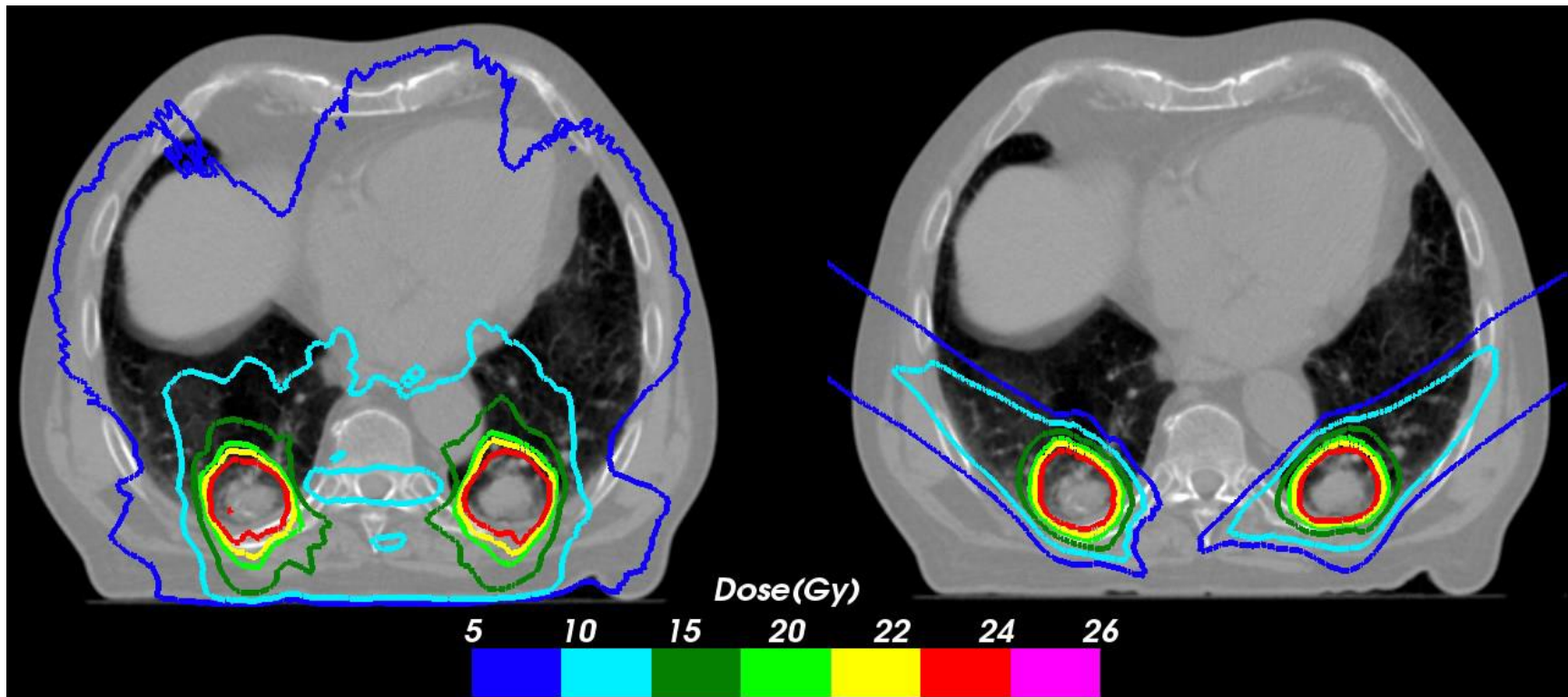
KEEP IN MIND:



SO DOES A HANDGUN.

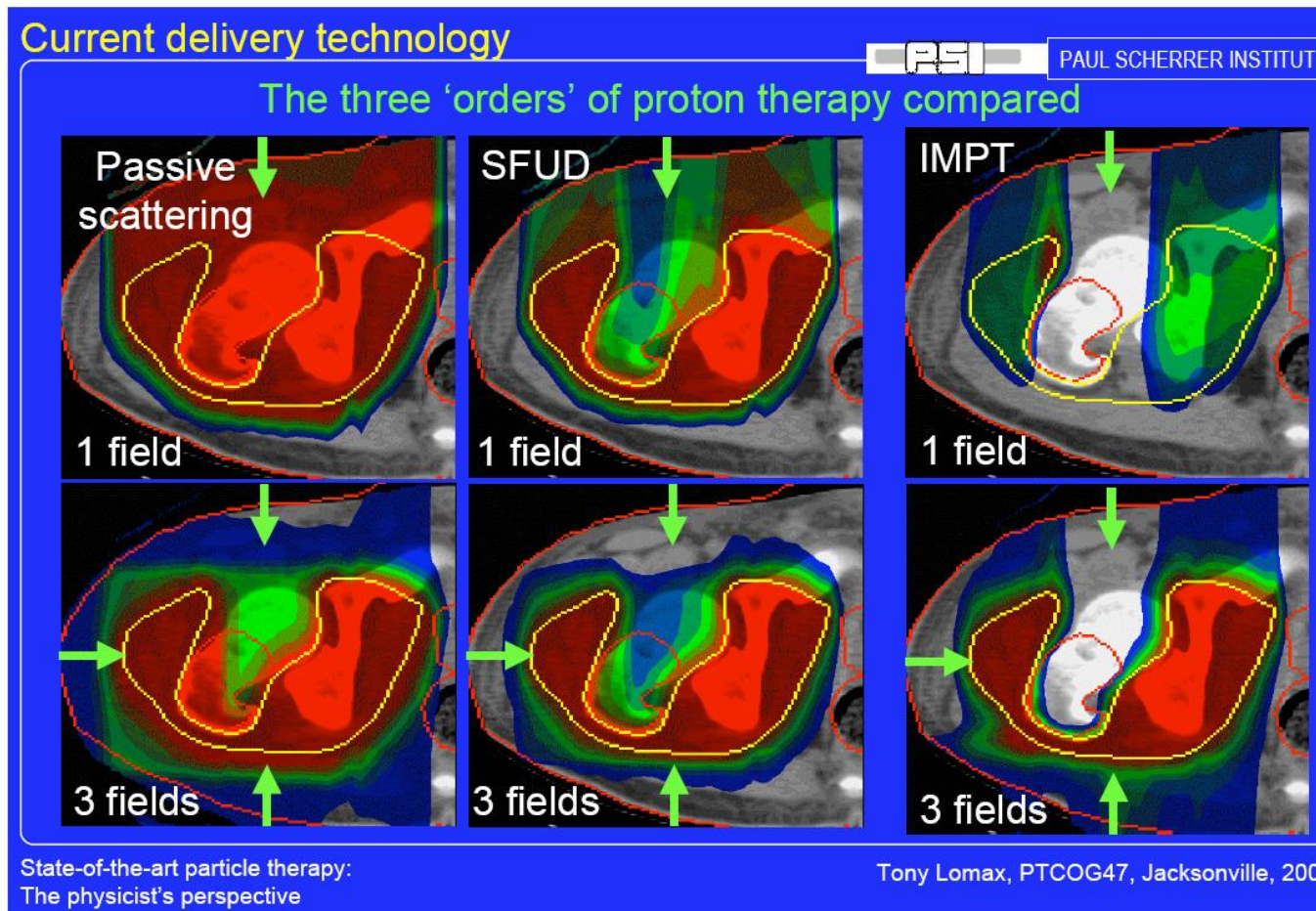
Rationale for 4D-treatment with ions

- Ions more conformal than photons

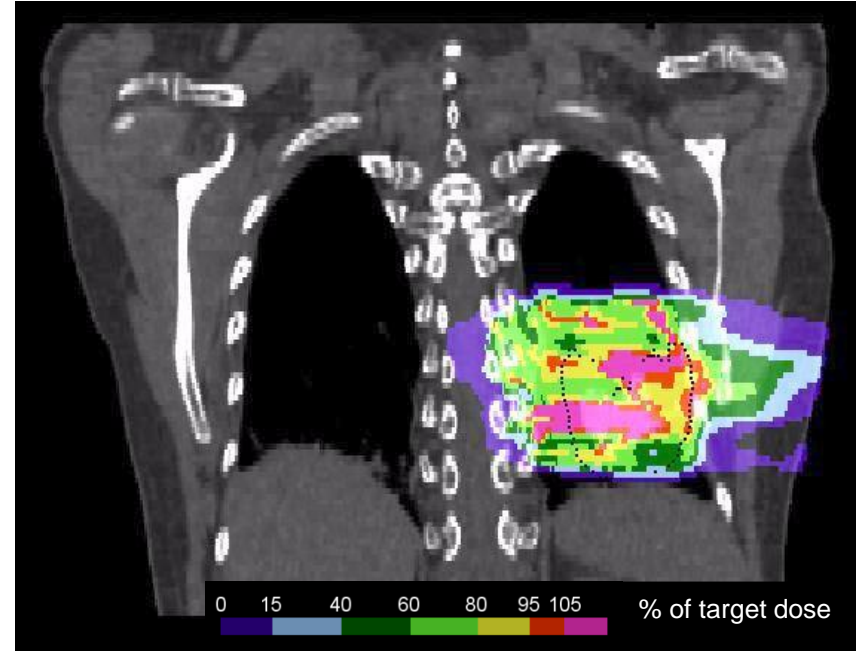
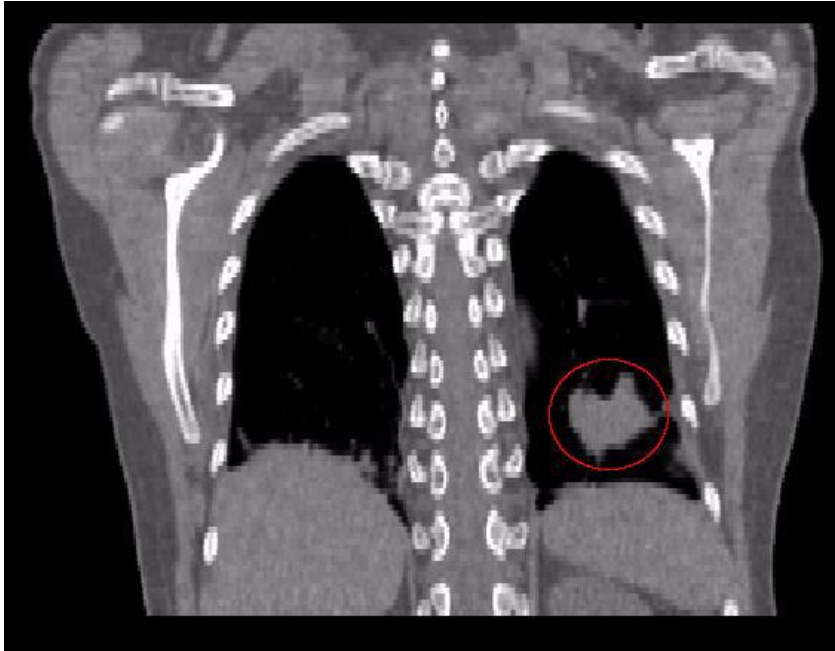


Rationale for 4D-treatment with ions

- Active delivery more conformal than passive



Motion and scanned delivery

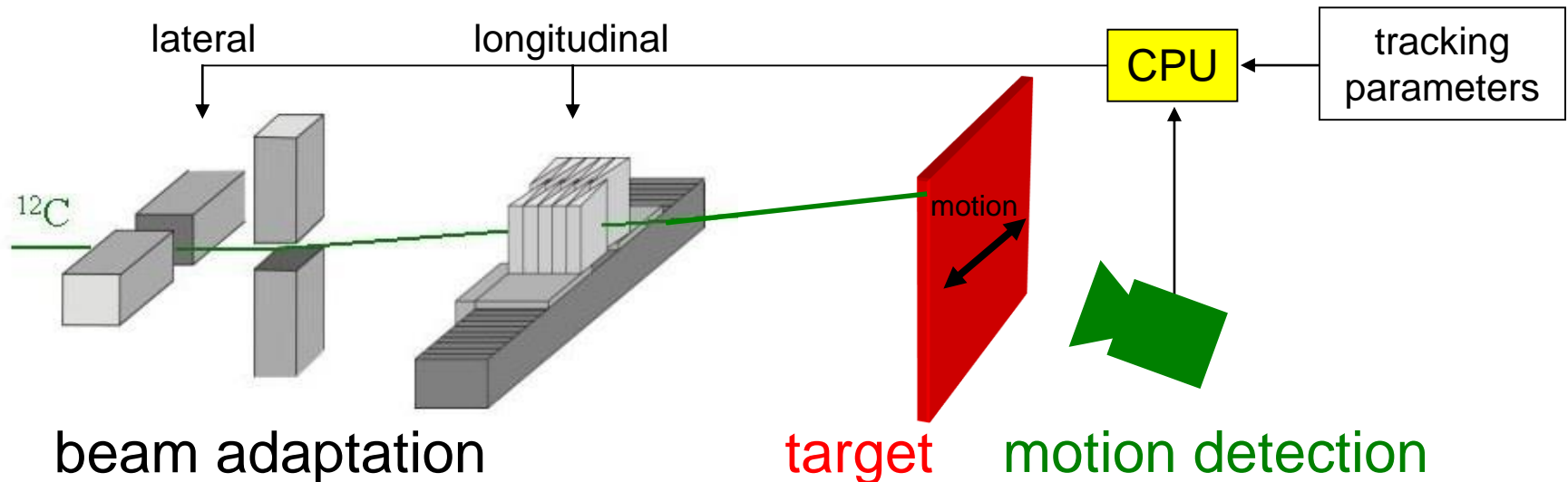


Courtesy M. Söhn, LMU

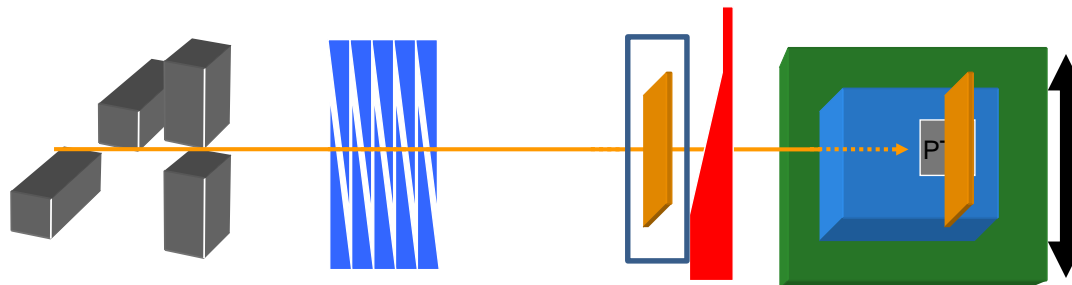
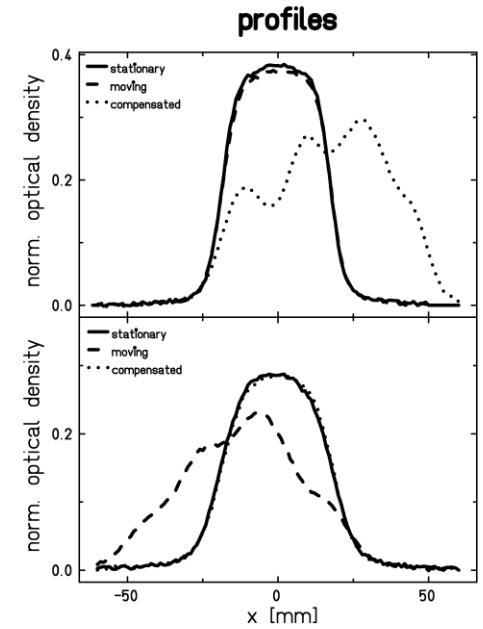
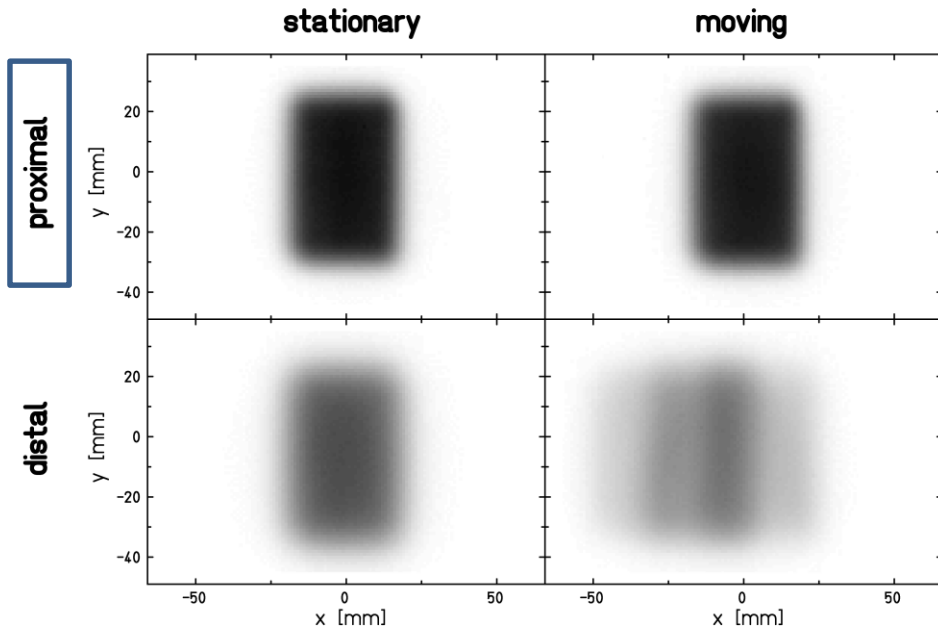
- **Motion:** Target miss
- **Range changes:** variable position of Bragg peaks
- **Interplay:** Interference between target and scanning motion

Beam Tracking

- Tremendous advantage over photons:
Easy, fast beam deflection

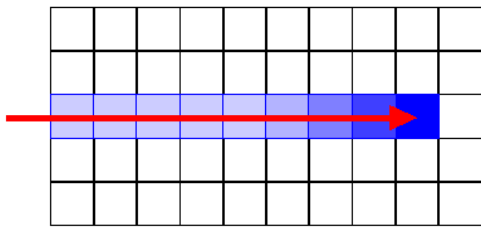


Tracking issues I: inverse interplay

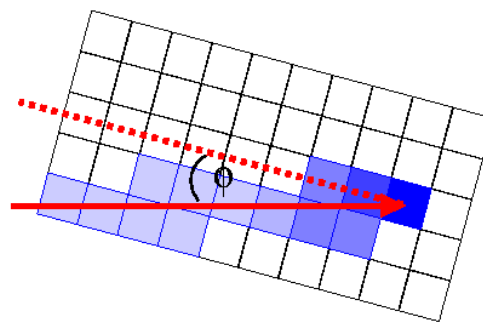


Tracking issues II: complex motion

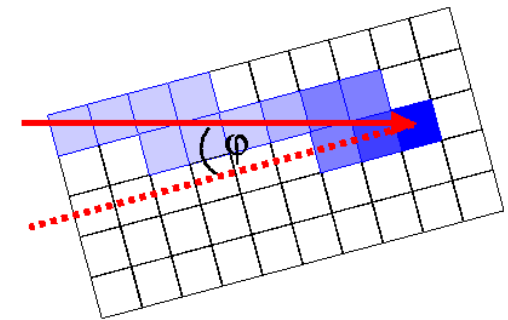
- Beam tracking compensates translation only
- Preplanned entry channel doses may be wrong!



Motion State Reference



Motion State k



Motion State i

Conformal 4D-optimization

- 3D Optimization cost function

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

Voxels

beam spots

- Full 4D Optimization cost function

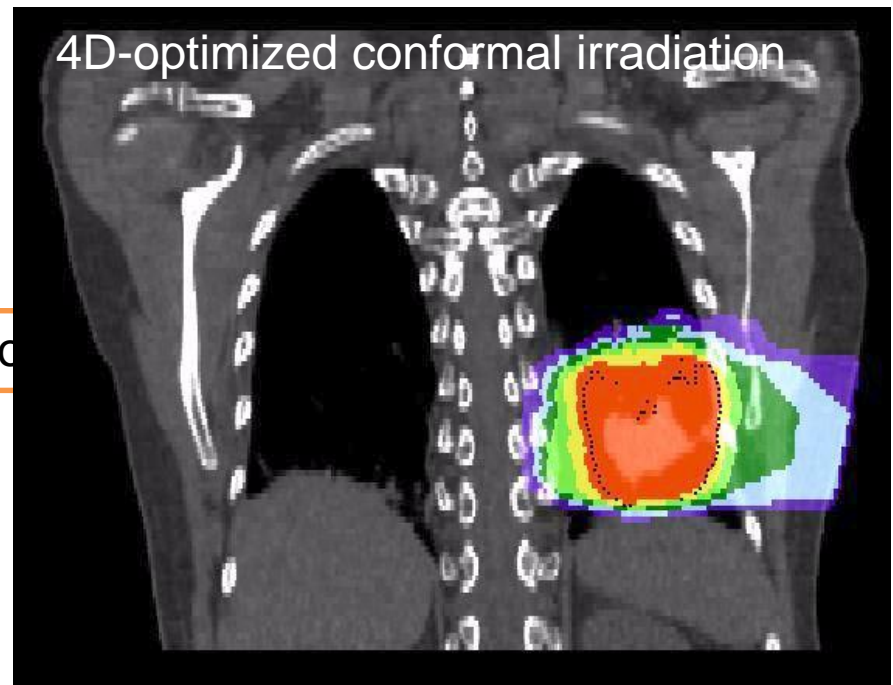
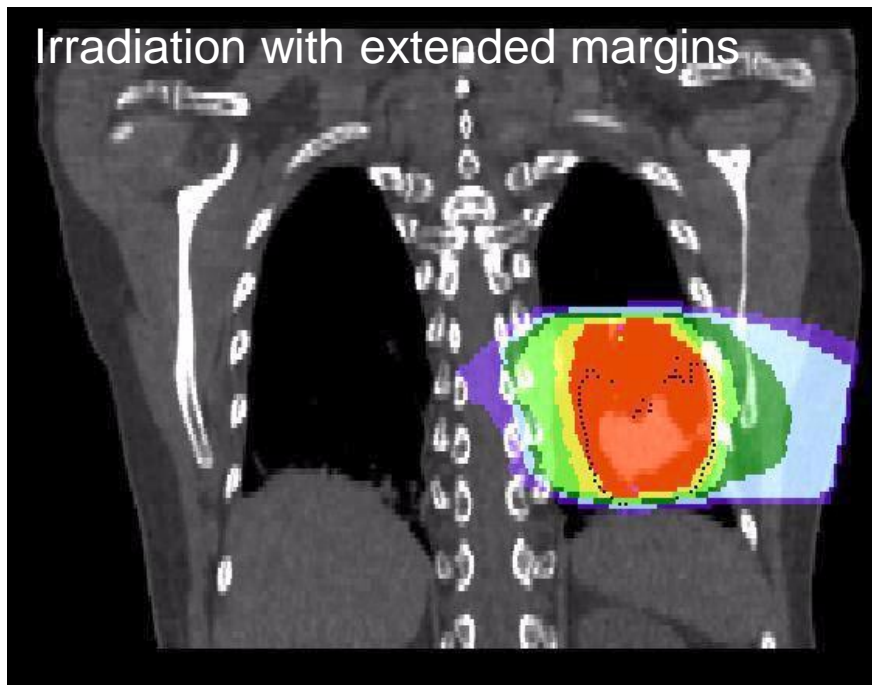
$$E(\vec{N}) = \sum_{k=1}^m \sum_{i=1}^v [D_{pre}^i - D_{act}^{ik}(\vec{N}_k)]^2 = \sum_{k=1}^m \sum_{i=1}^v \left[D_{pre}^i - RBE(\vec{N}_k) \sum_{j=1}^r c_{ijk} N_{jk} \right]^2$$

motion phases

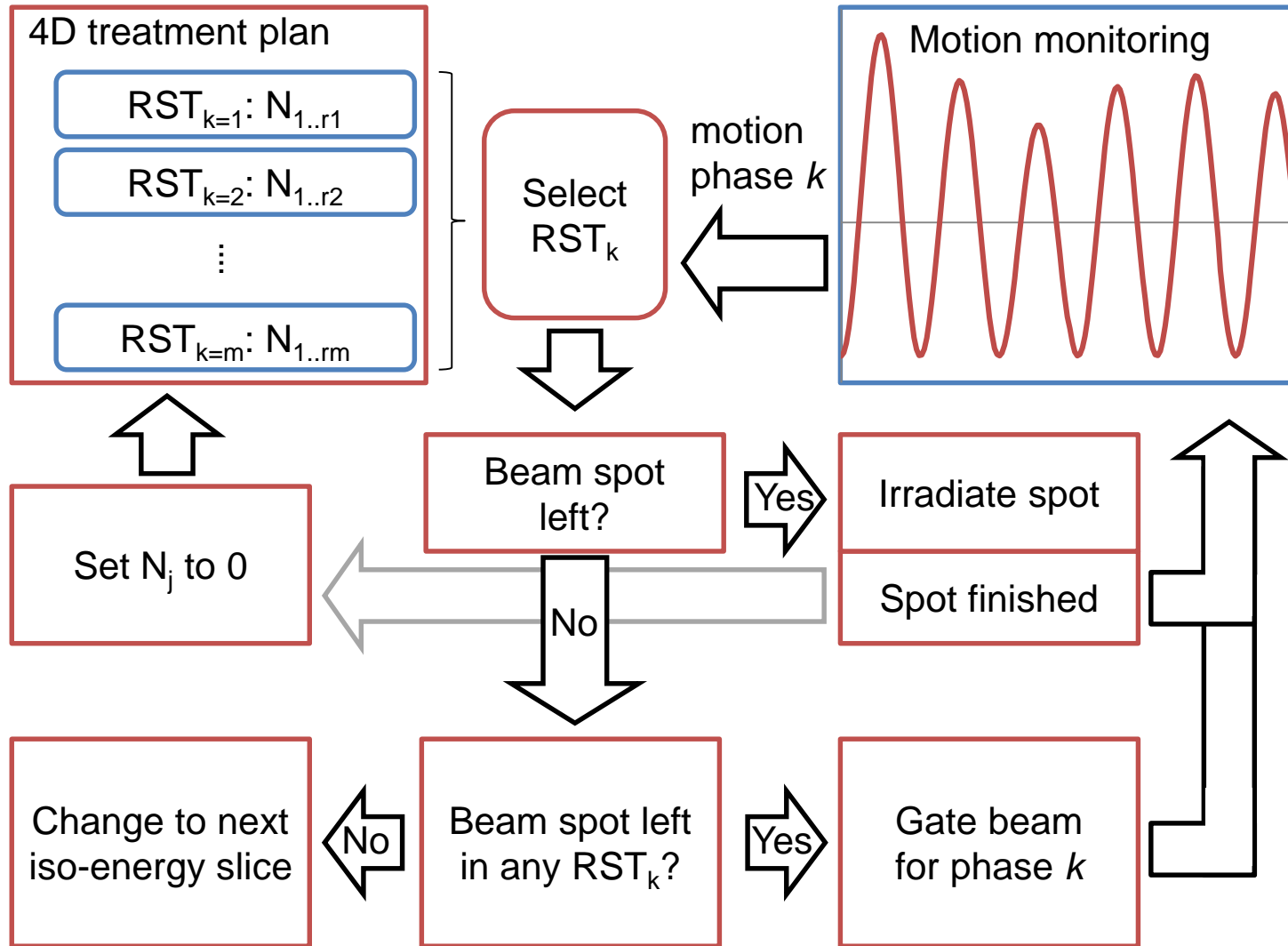
- Different strategies possible to control gradients, reduce problem size, ...
- (OAR terms omitted)

Motion-synchronized delivery

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

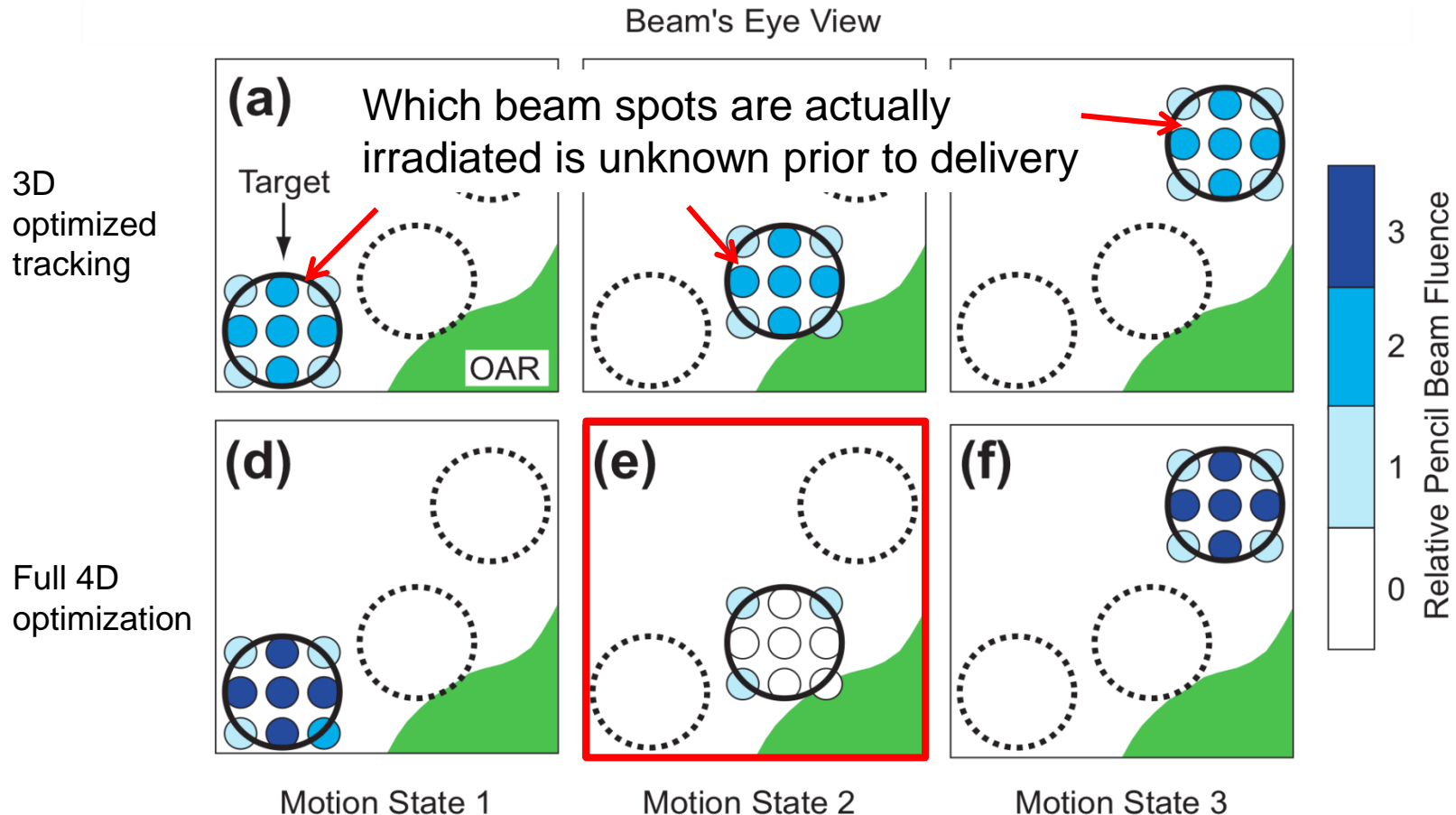


Delivery: The 4D therapy control system

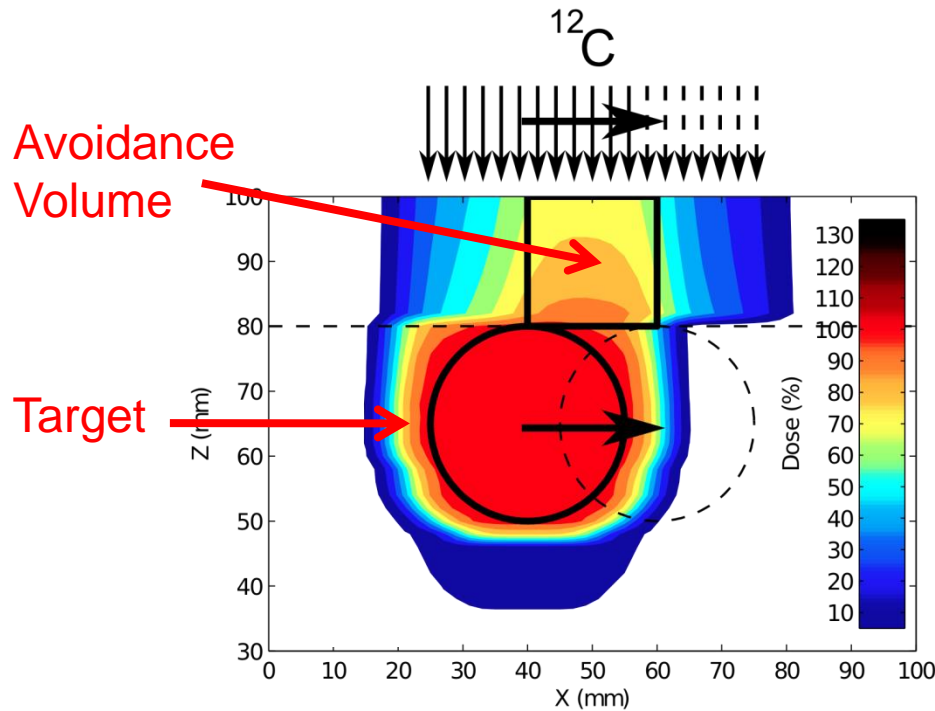


Potential exploitation of differential motion

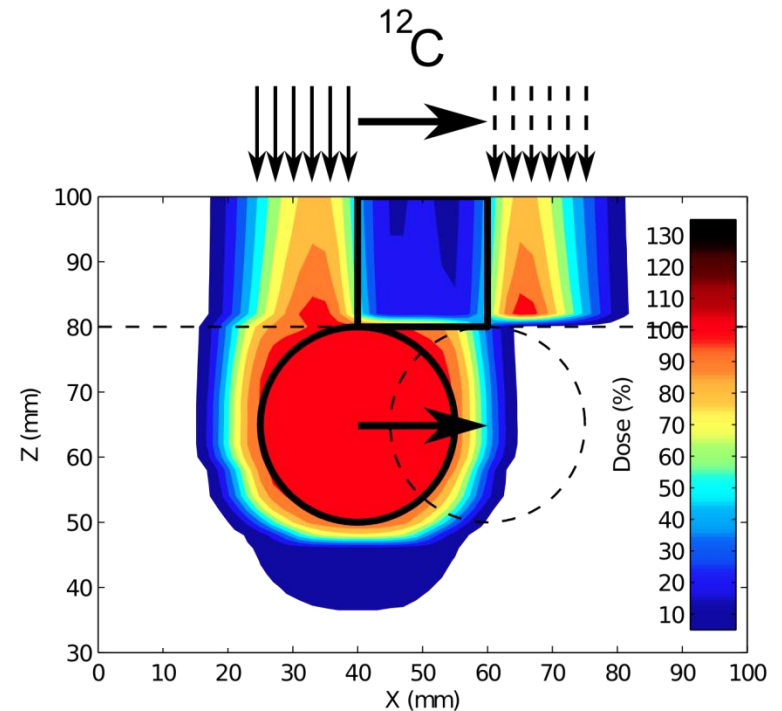
- Reduce fluence when target is closest to organ at risk (OAR)



Simulation - Moving Target in Water Phantom



3D Opt. Tracking



Full 4D Optimization

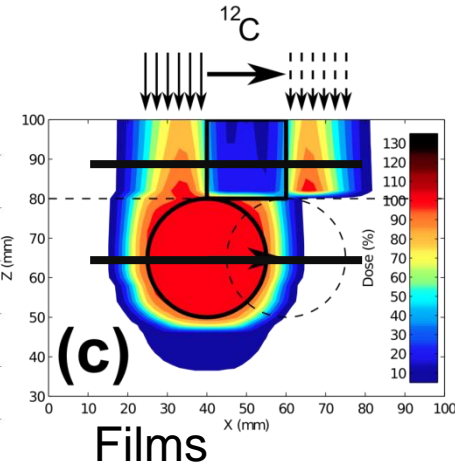
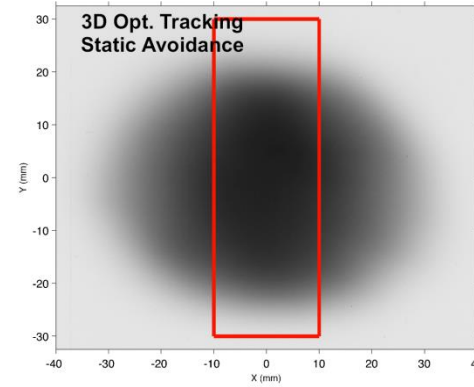
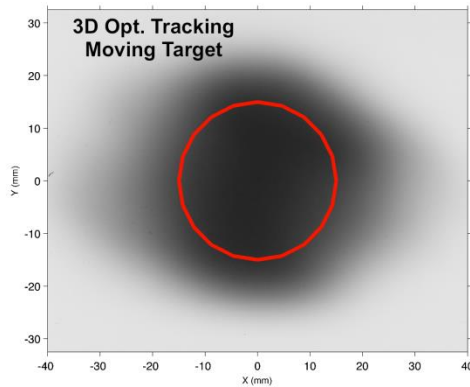
Experimental reproduction

Film Measurements

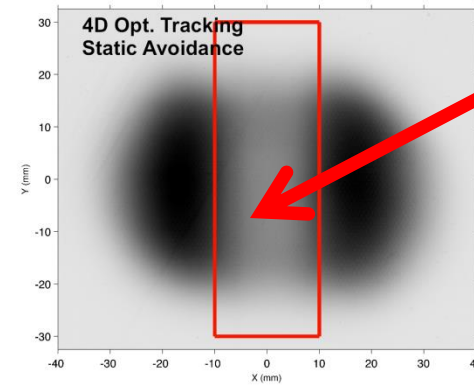
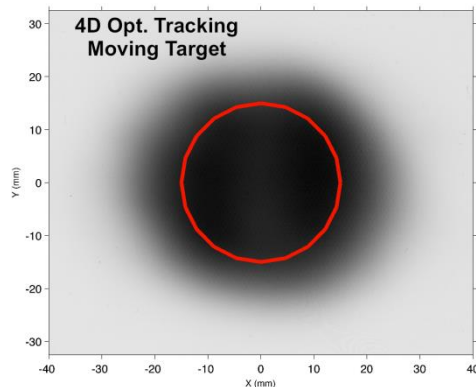
Moving Target

Avoidance Volume

3D Optimized Tracking



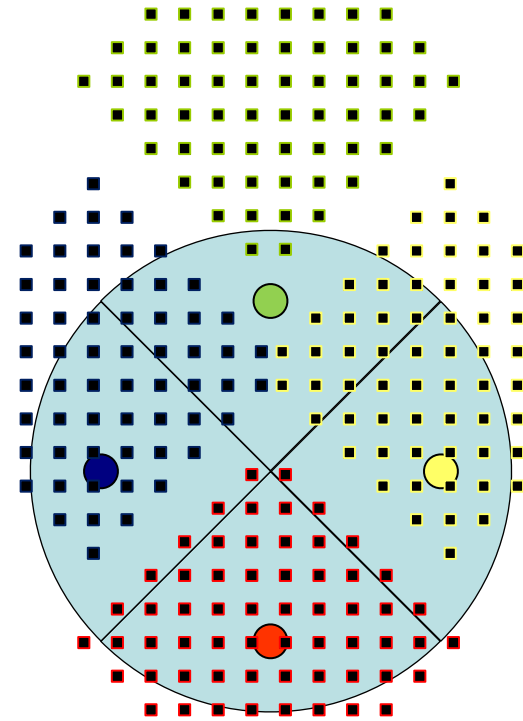
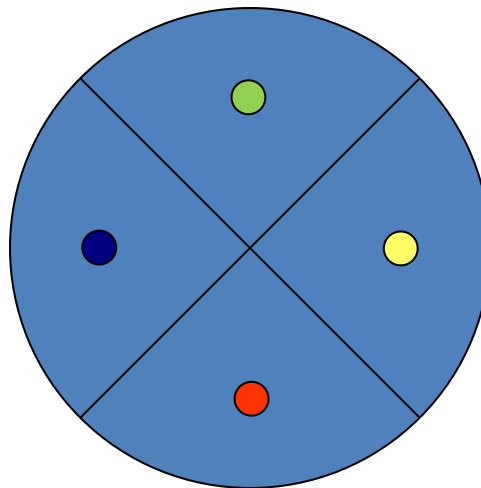
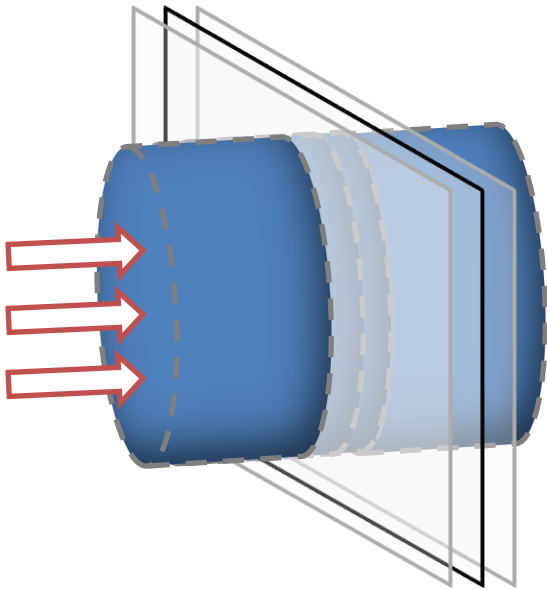
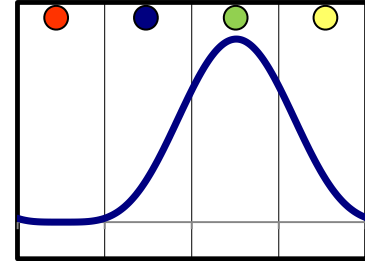
Full 4D Optimization



Sparing of avoidance volume using 4D optimization

4D-sectors: Definition of subsections

- Divide target in slices perpendicular to beam
- Divide slices in sectors for each motion state
- Transform sectors to motion states
- Create RST for each motion state



Feasibility of 4D-TCS: Film experiment

interplay

static

4D optimized



38.2%

94.7%

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

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

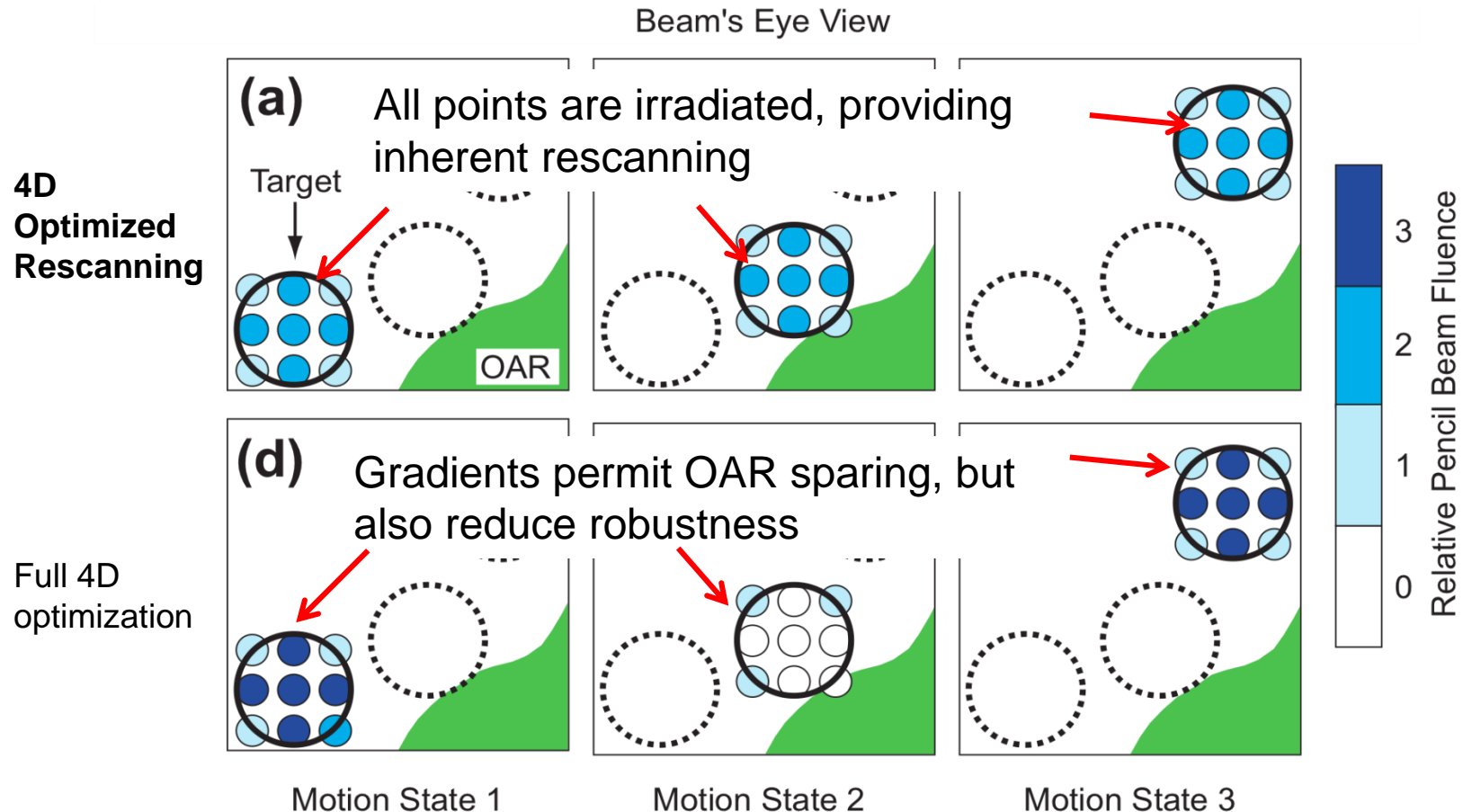


image courtesy of John Eley

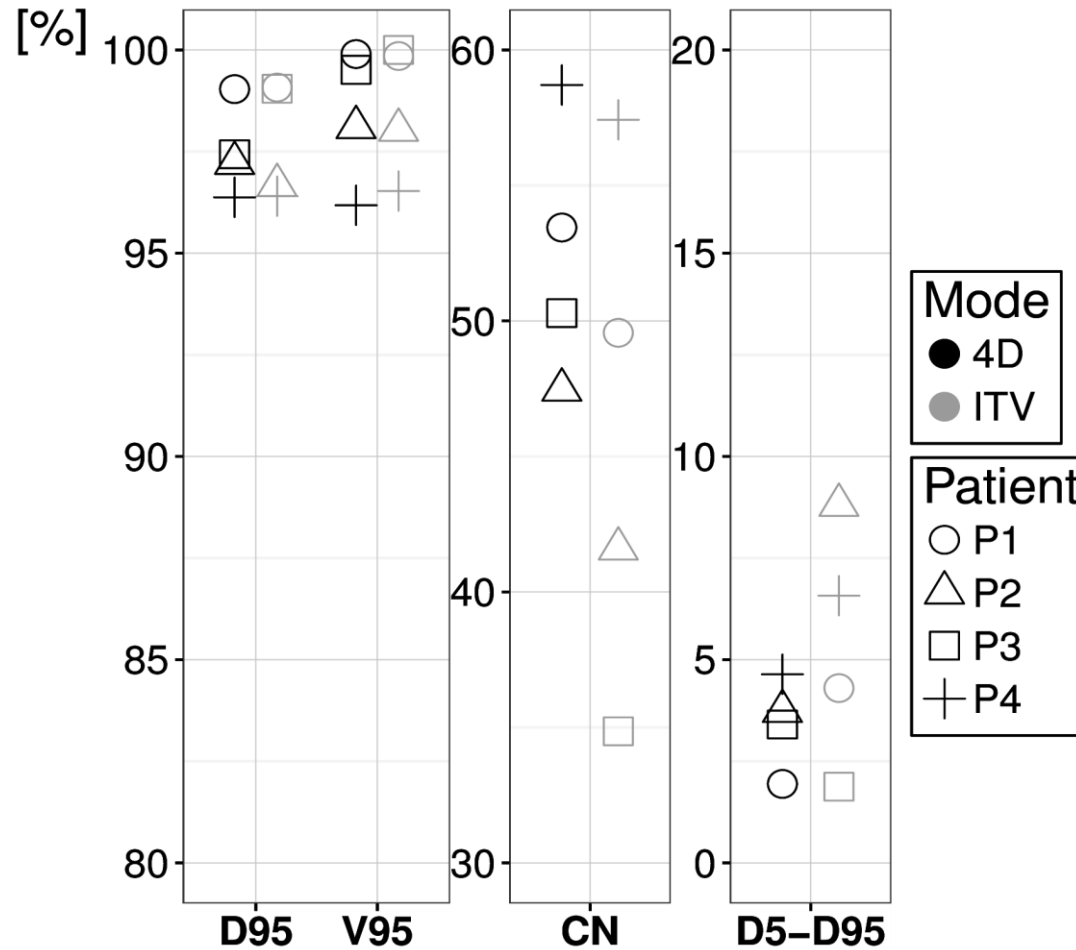
A patient simulation study

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

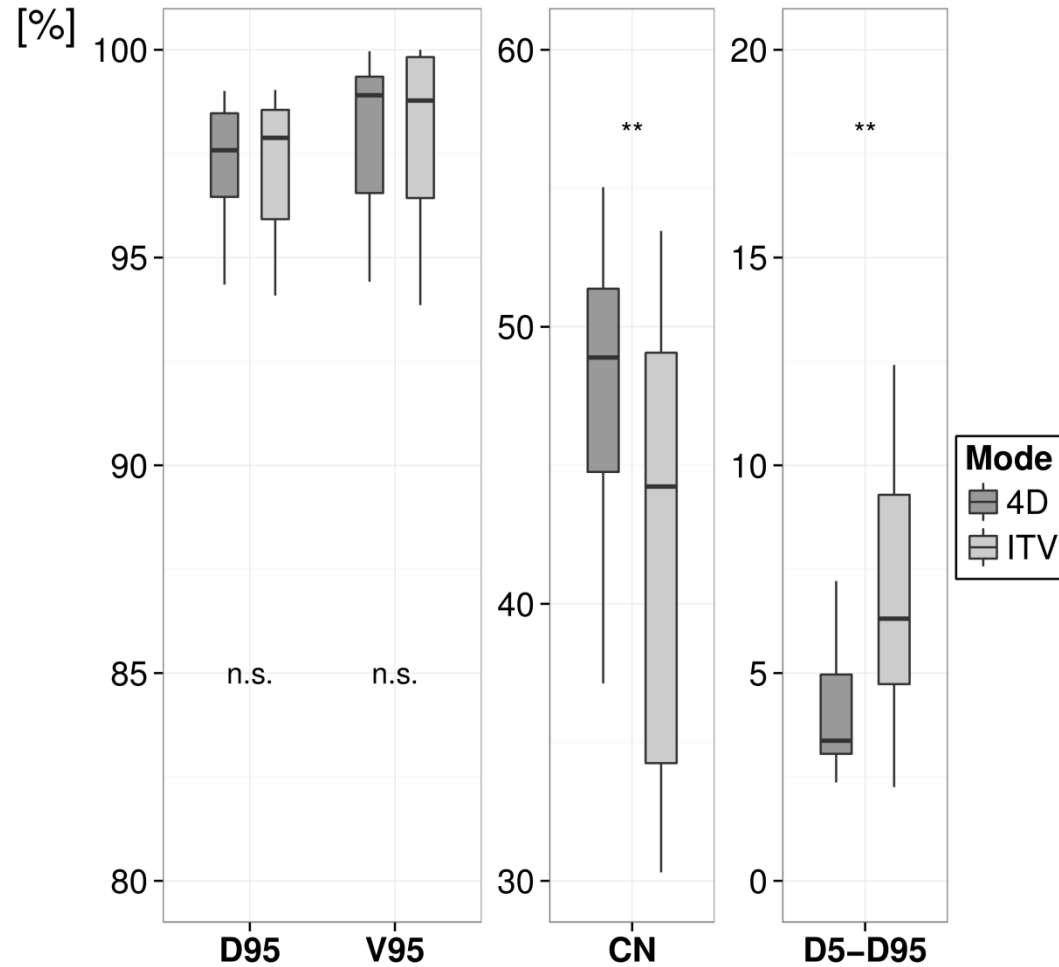
Patient	Fraction 4DCTs (weeks 2 - 6)		Necessary Margins $V_{95} > 95\%$ [mm + mm, %]
	CTV Amplitude (min - max) [mm]	abs Δ Range: week n - week 1 (median, range) [mm H ₂ O]	
P1	2.8 - 3.9	2.2 (1.3 – 5.9)	3 + 2
P2	6.6 - 15.9	4.3 (1.3 – 6.3)	7 + 2
P3	2.1 - 5.4	1.6 (0.8 – 3.0)	3
P4	20.6 - 27.5	6.9 (4.4 –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

- Same margins necessary for ITV coverage

Cumulative dose results



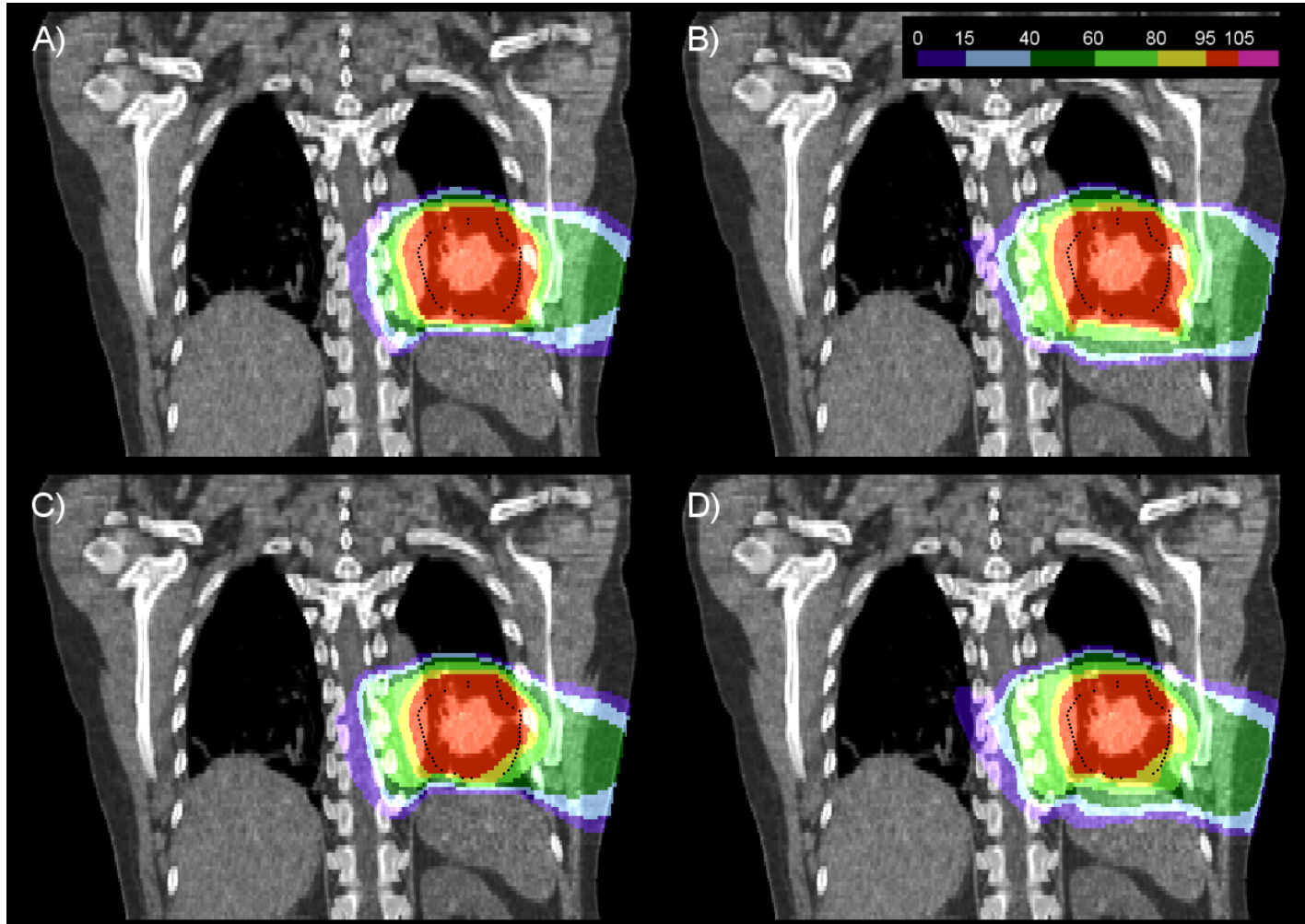
Individual fractions



■ paired t-test, **: p < 0.001

Comparison of ITV and 4D-opt

planned
4D-dose

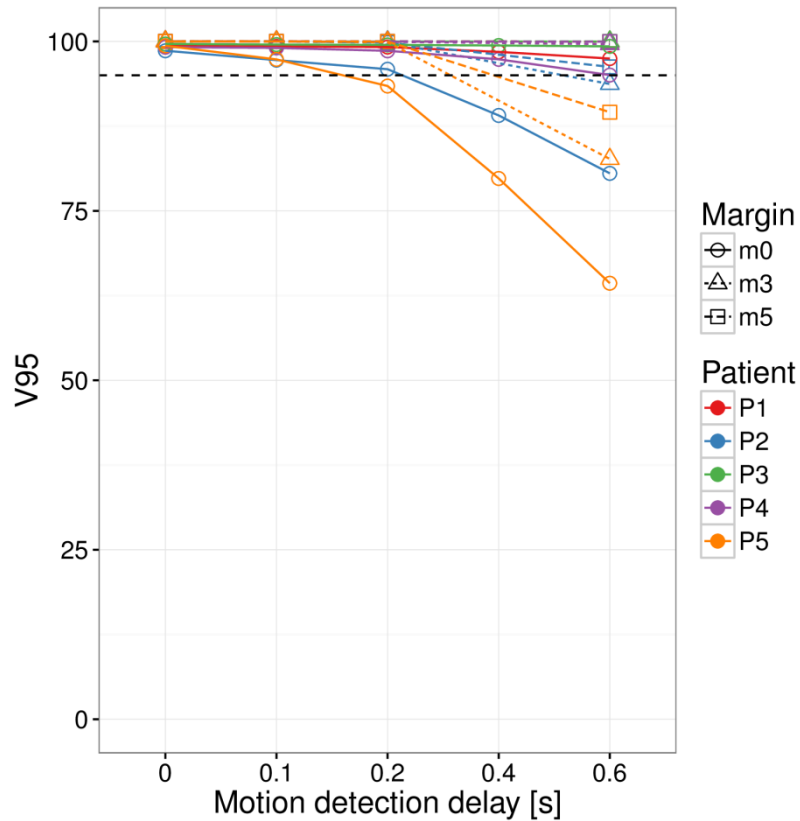


4D-opt

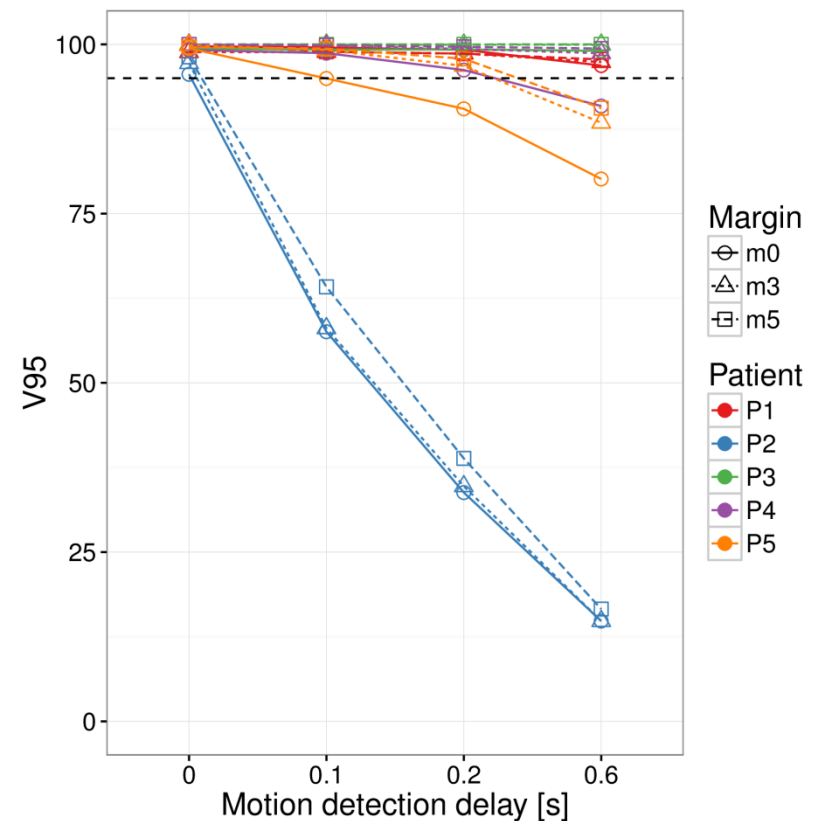
ITV

Robustness: Desynchronization

- Artificial delay induced between motion detection and irradiation



4D-rescanning



4D-sectors

- Gradients between phases are highly relevant!

Outlook

- Renovation of GSI Cave M dose delivery system until 2019 – based on the CNAO DDS
 1. Increased scan speed:
detectors, algorithms,
(intensity control, multi-energy extraction)
 2. Motion integration:
motion detection, 4D-dose reconstruction
 3. Synchronized dose delivery:
within ITN „Optimization of Medical Accelerators“
 - Fully functional, clinically valid system – patient trials??

