Intra-fractional motion management

The 1st UPLIFT school on “Advanced Radiotherapy”

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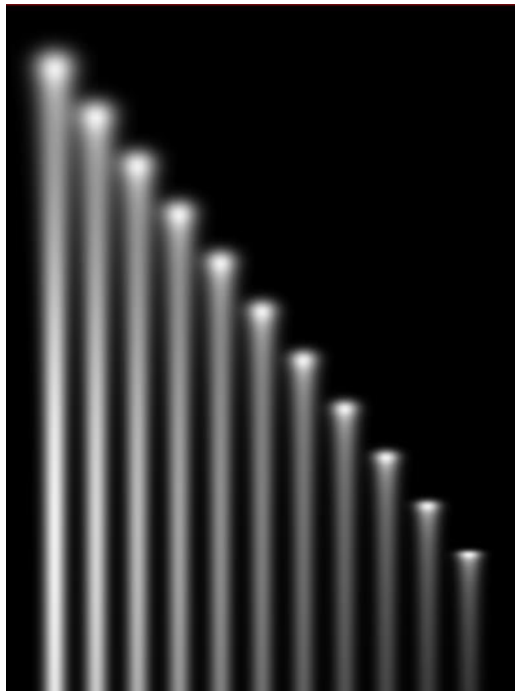
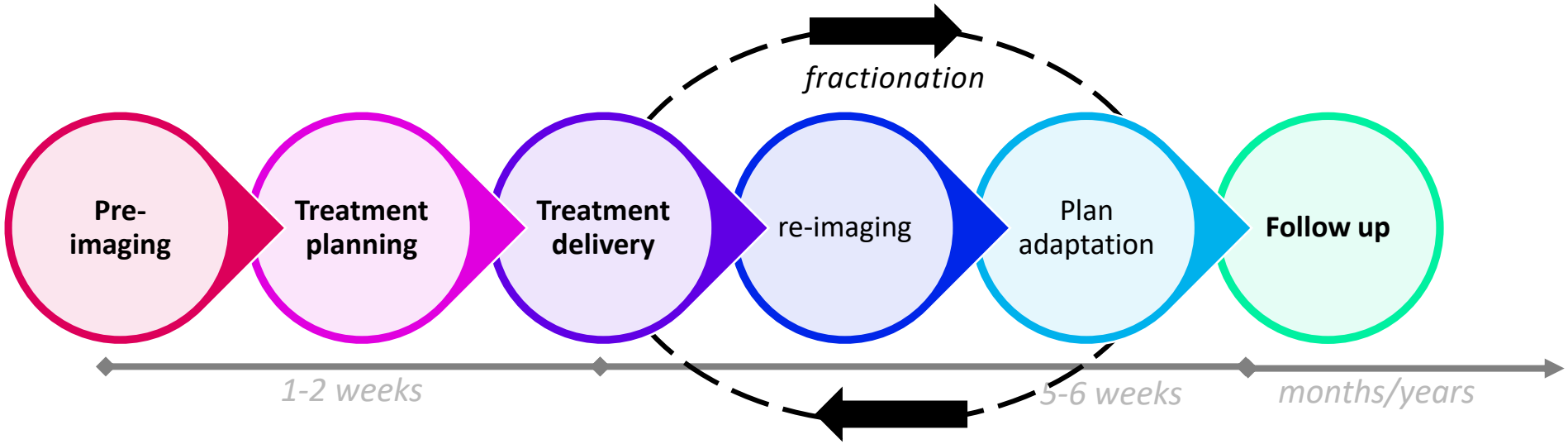
Contents of this presentation



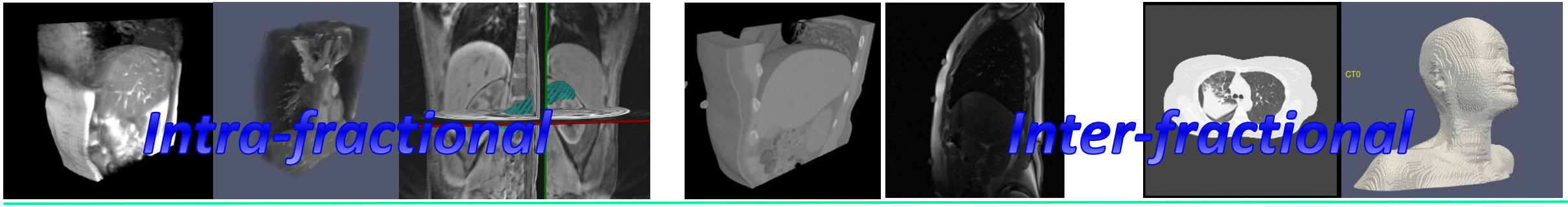
What is 4D treatment? and why?



Intra-fractional: respiration, heart beating (deformable movement)

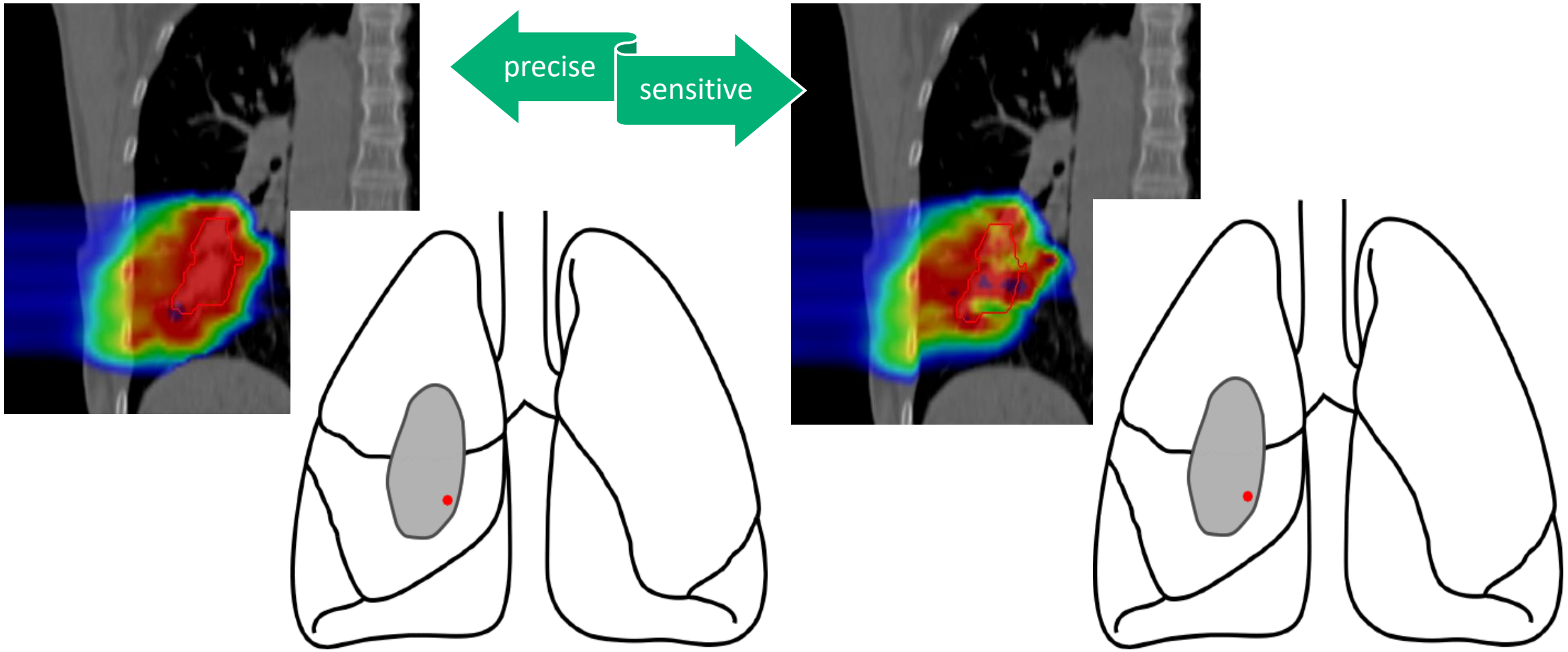
+ digesting movement, muscle relaxation (deformation, drift)

Inter-fractional: anatomy variation (deformable grows, shrinks, shift)

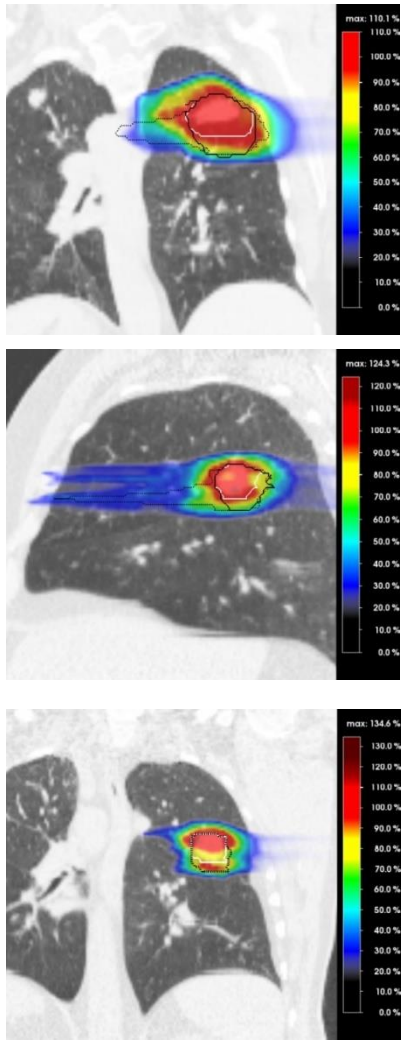


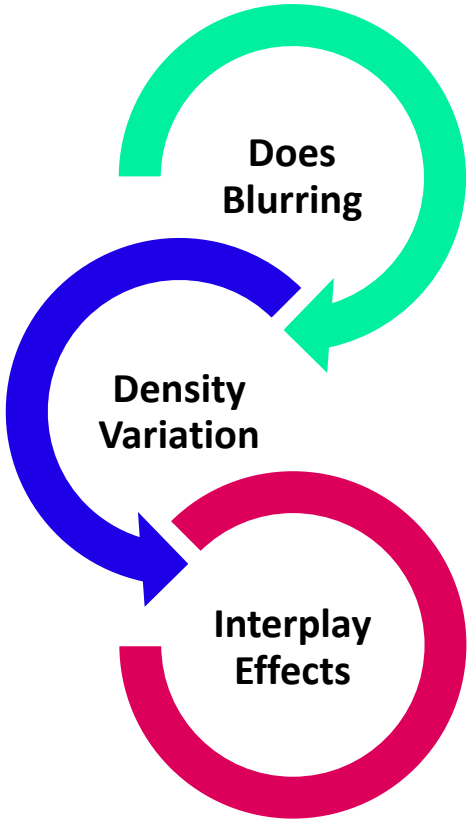
4D -> any geometric difference between the phase of planning and the phase of dose delivery

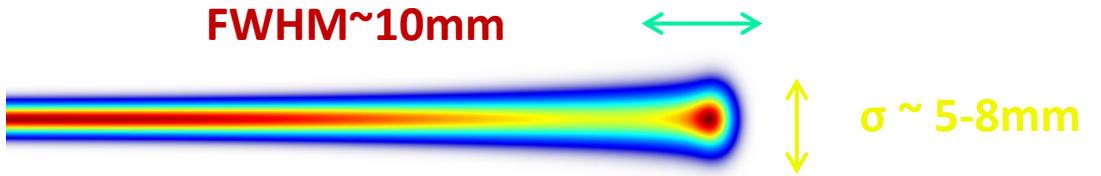
Pencil beam scanned proton is a double-edged sword

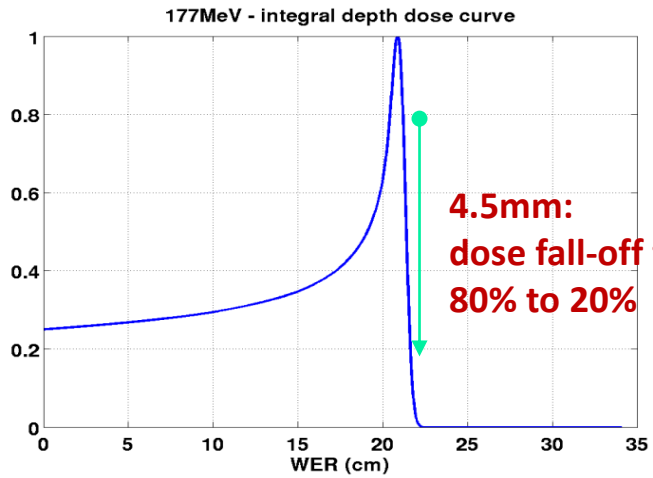


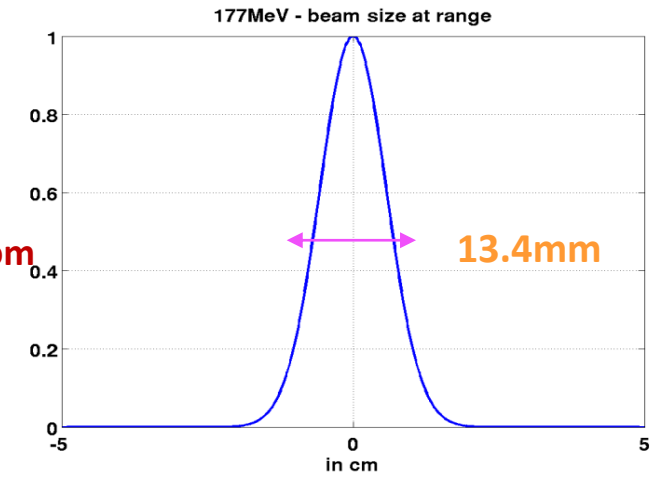
Intra-fractional motion effects







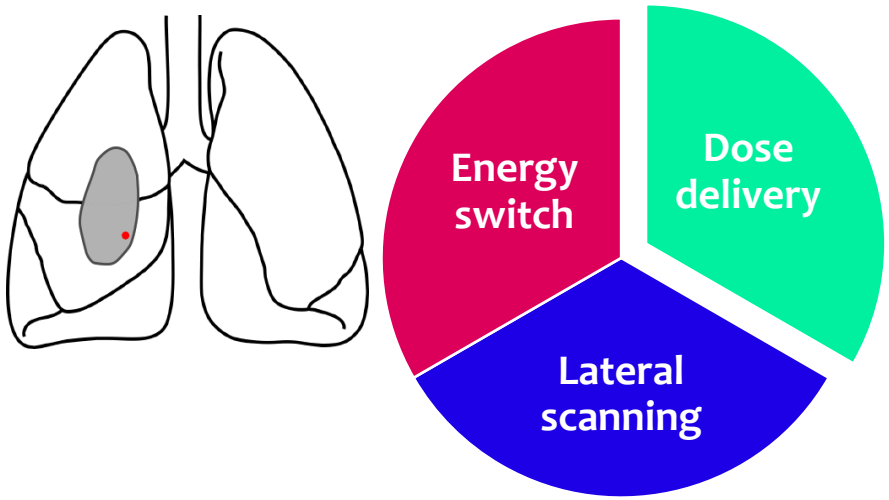


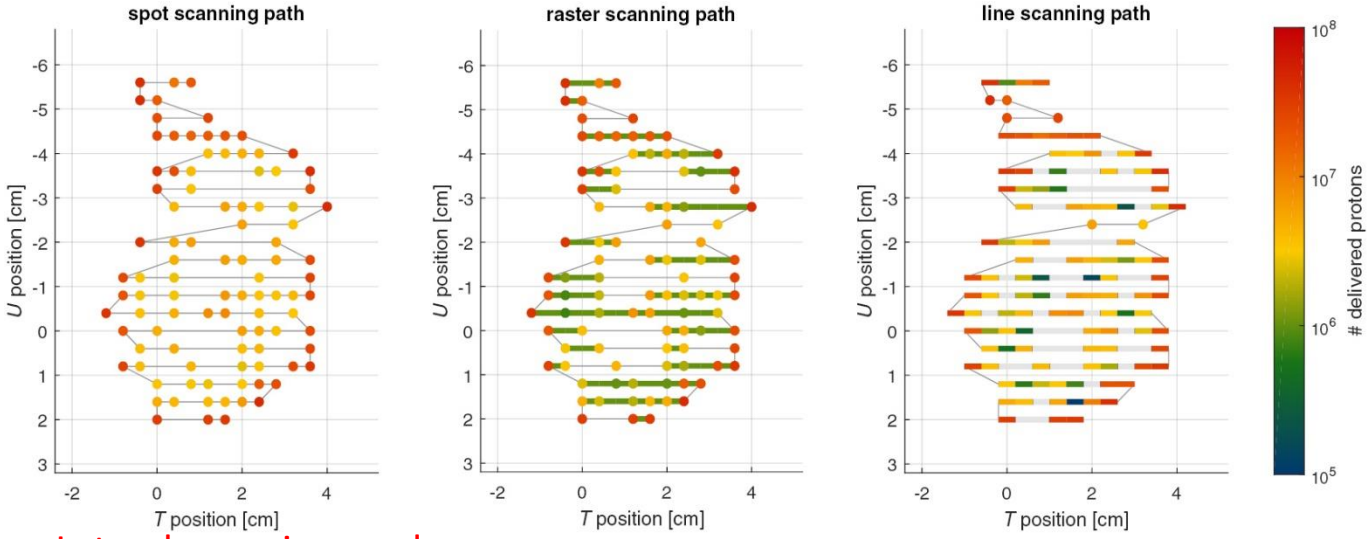


- **lateral dose conformity:** Universal for any external RT target out of planned dose delivery field
- **distal dose conformity:** for particle therapy density variations in the beam path
- **dose homogeneity:** only for scanning delivery Interference target motion and timing of active scanning

Intra-fractional motion effects are significant, requiring individual assessment and combined mitigation strategy

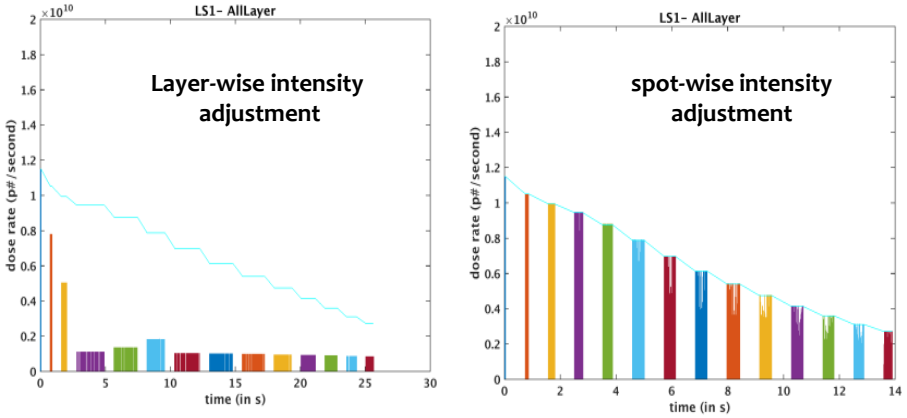
Dynamic beam delivery



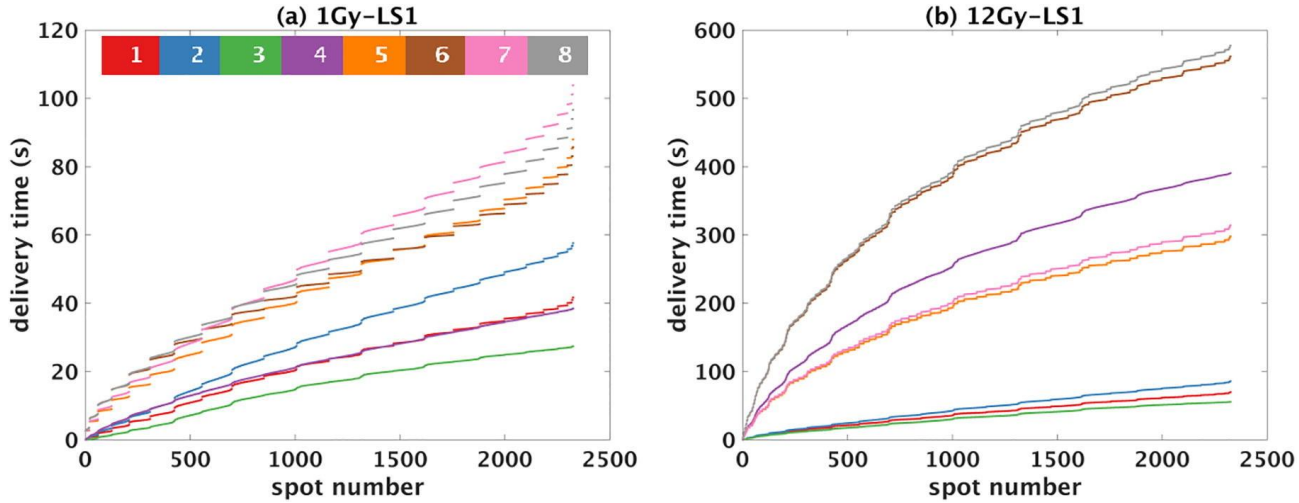


Lateral scanning mode

G Klimpki et al 2018 PMB



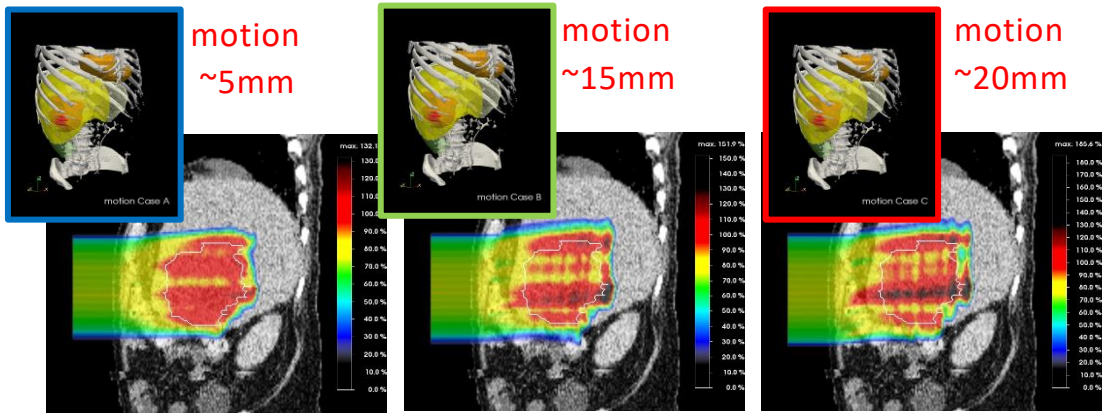
beam current



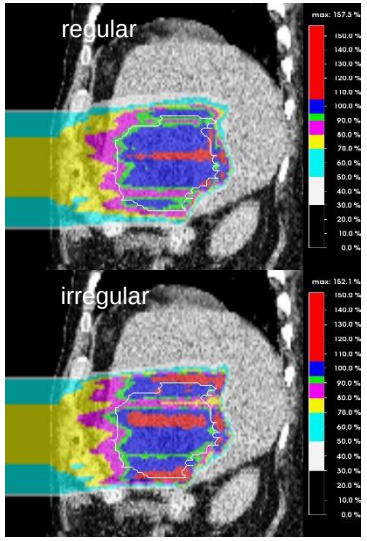
Interplay effects for dynamic dose delivery

- The **interplay effect** are significant, individualized and can be influenced by many 4D parameters
- **4D dose distribution** patterns is very difficult to predict without appropriately modelling the dynamics from both *moving organ* and *PBS-based dose delivery*

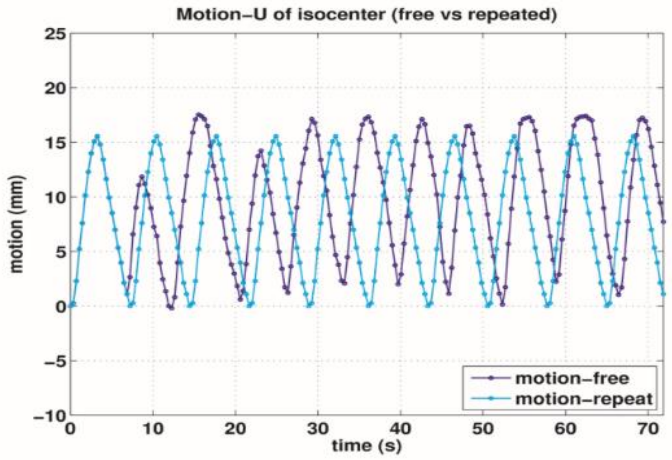
Effects of motion amplitude



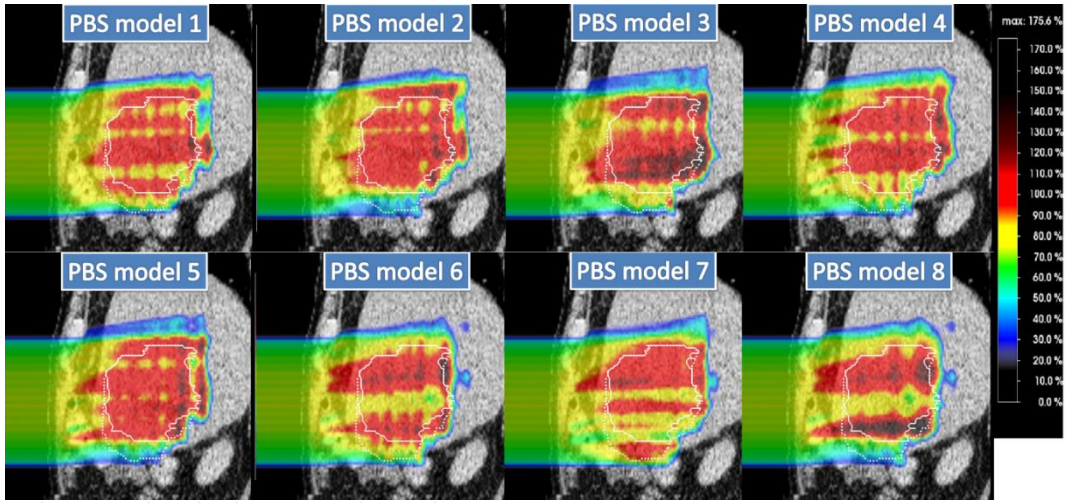
Zhang et al PMB 2017



Effects of motion irregularity

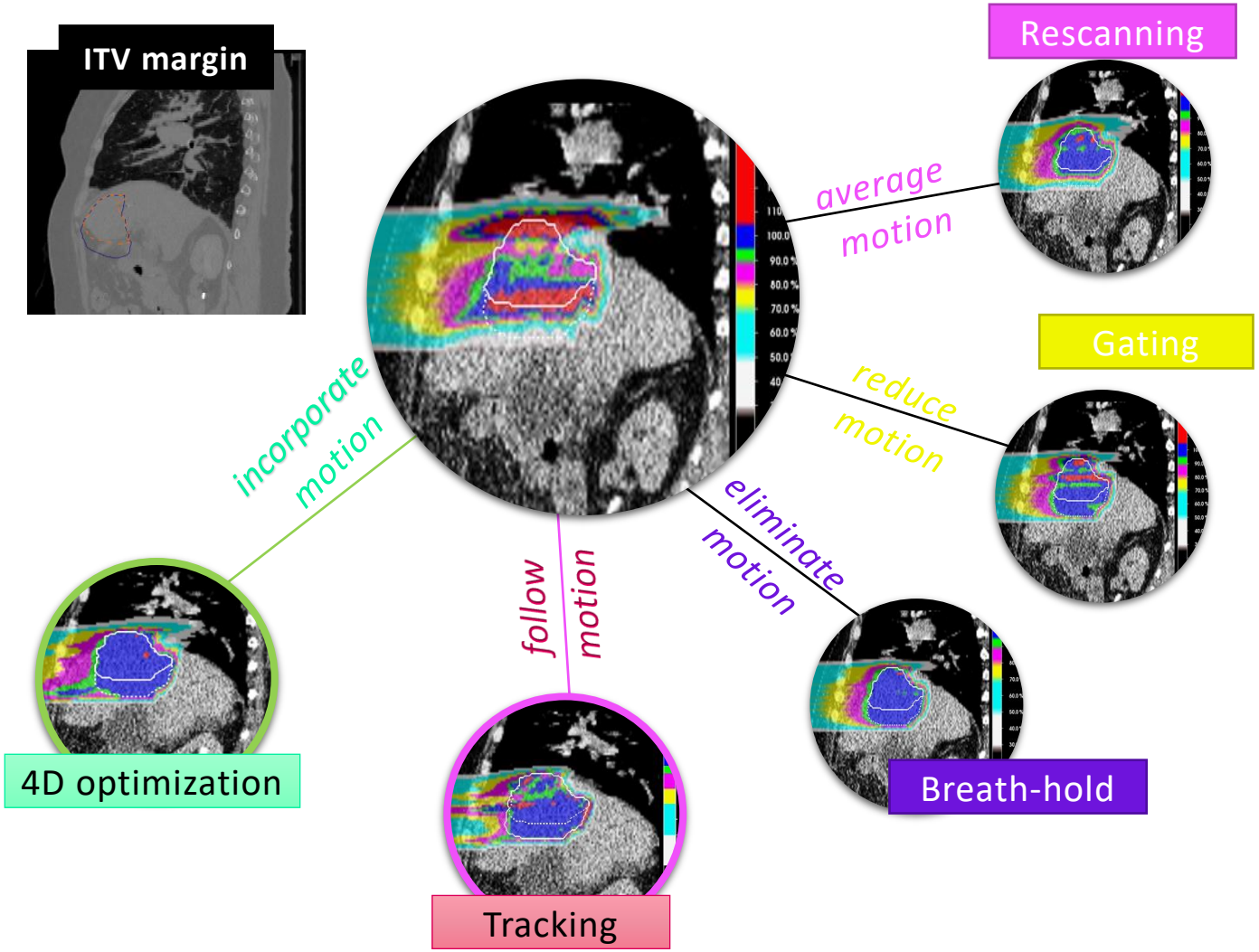


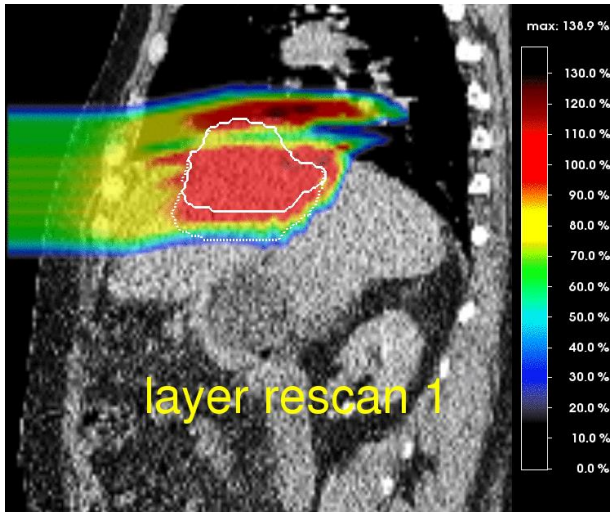
Effects of PBS scanning dynamics

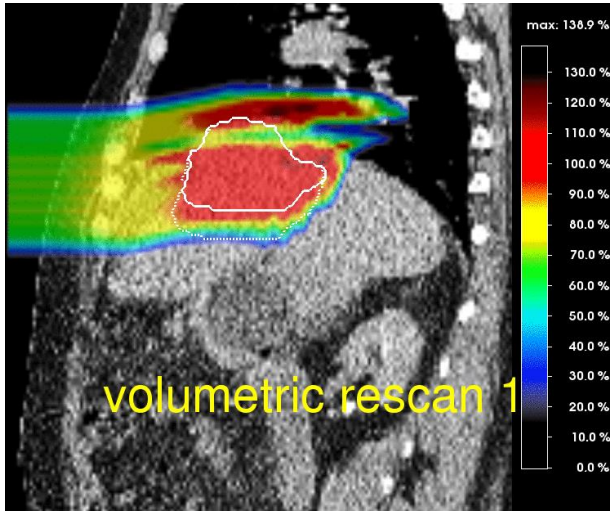


Zhang et al Radiotherapy and Oncology 2016

Intra-fractional motion mitigation







Breath-hold: fast delivery and patient cooperation

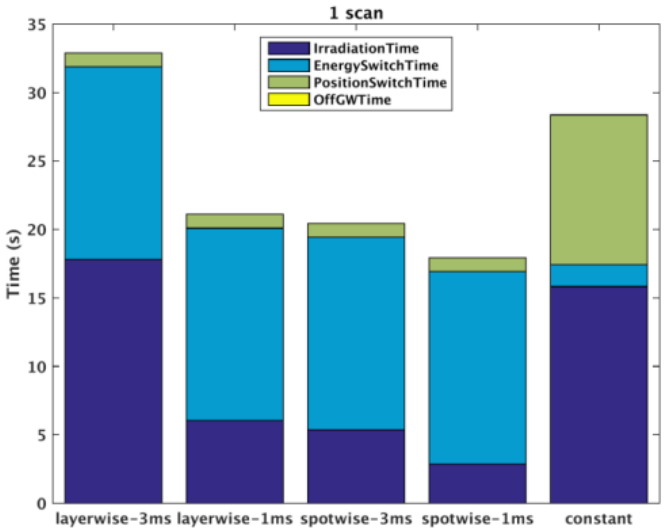
PSI

Technical challenges

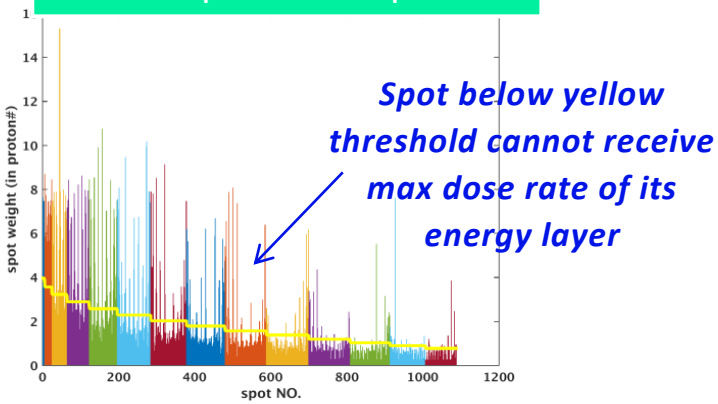
- Max. beam current for Cyclotron
- Energy dependent beamline transmission
- Max. acceptable beam current for beam diagnostic
- Achieve the minimal spot duration

Plan requirements

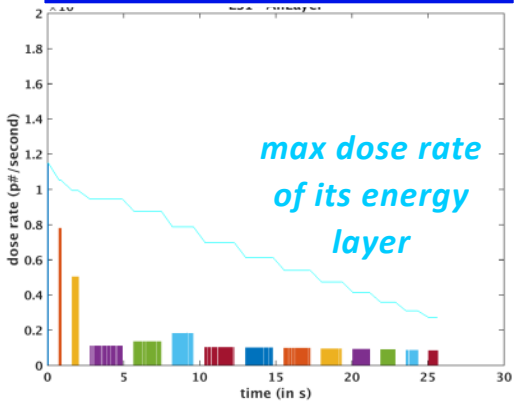
- high spot weight dynamics with each energy layer varies up to 10 times
- More low weight spots due to rescanning
- Capability to irradiate small weight spot



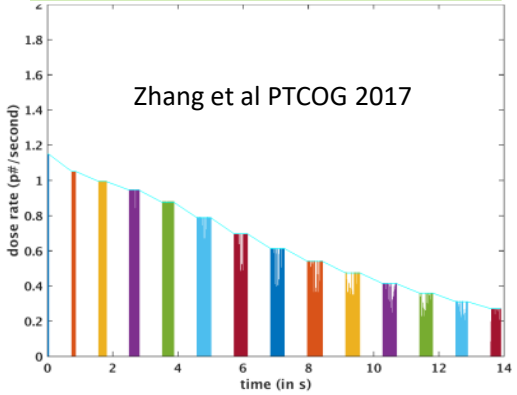
Example clinical plan



layer-wise adjustment

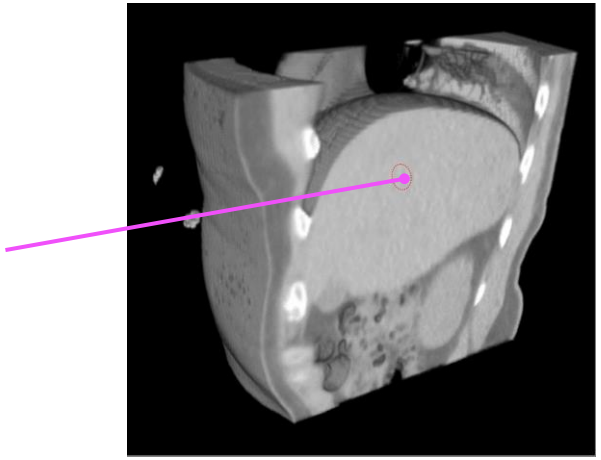


spot-wise adjustment



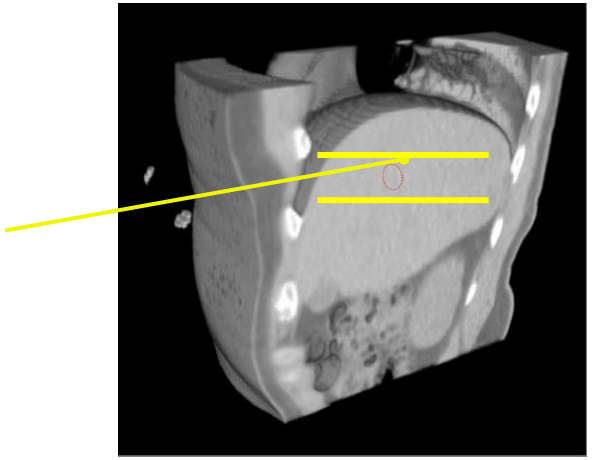
Rescanning-gating: a clinical practical approach

rescanning

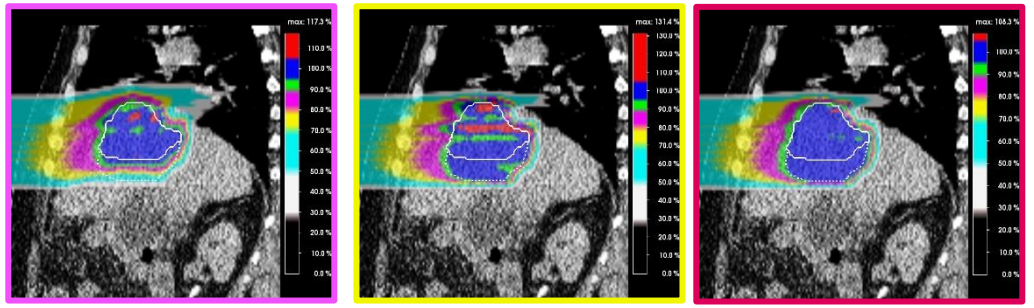


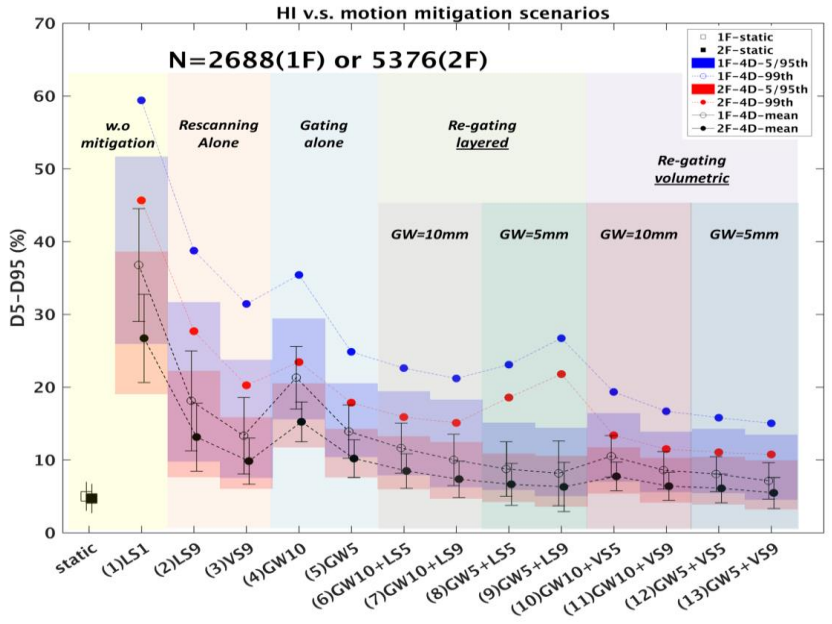
- easy to implement
- prolonged treatment duration
- extended irradiation volume
- appropriate ITV predefined
- scanning dynamic dependent
- need sufficient rescan number
- Statistical averaging is insufficient for **large** motion

gating



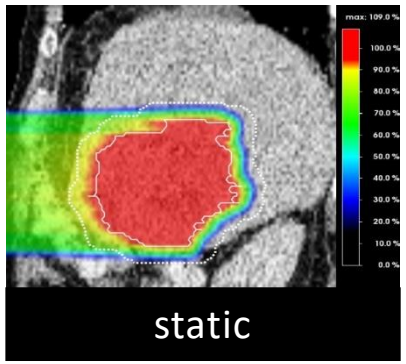
- not difficult to implement
- prolonged treatment duration
- Restricted target volume expansion
- need to tackle the residual motion (wi rescanning)
- need online motion monitoring and correlation
- need to update gating window (baseli shift)

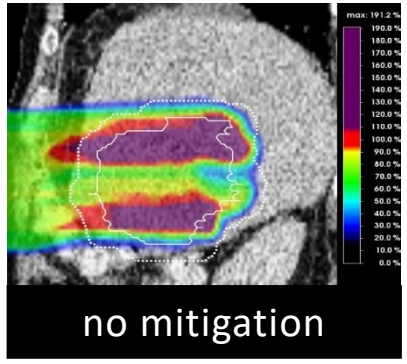


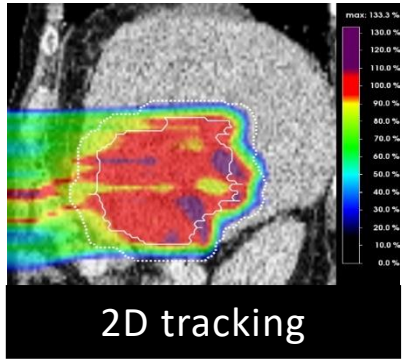


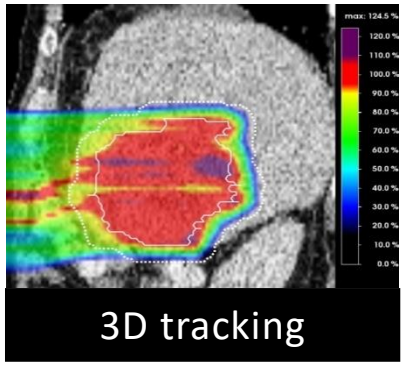
Zhang et al Radiotherapy and Oncology 2018

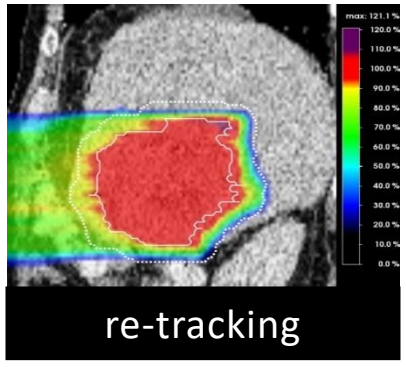
Beam tracking: towards real-time plan adaptation







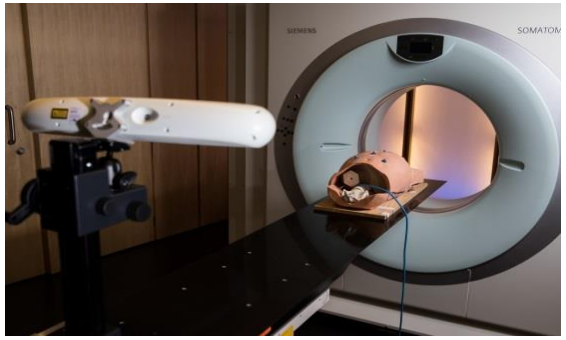


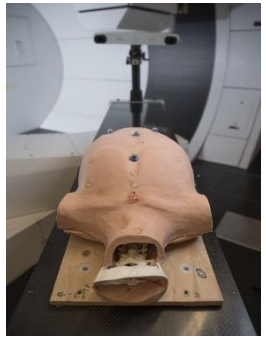


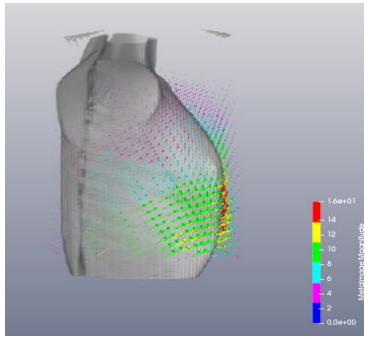
Zhang et al 2014 PMB

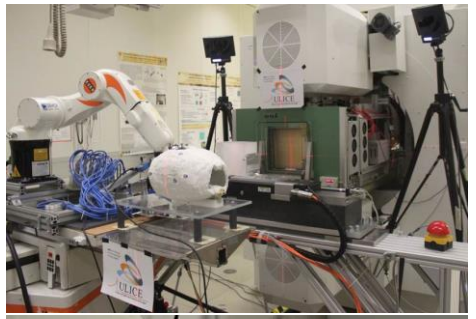
clinical beneficial → **technical feasible** → ***clinical applicable?***

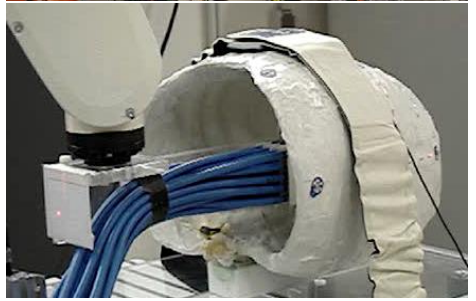
- Real-time motion monitoring without “too much additional” imaging dose
- Low latency (~50ms) measurements with high accuracy (<1mm)
- Fast energy adaptation with good beam quality
- Capable of adapting treatment field according to real-time updates





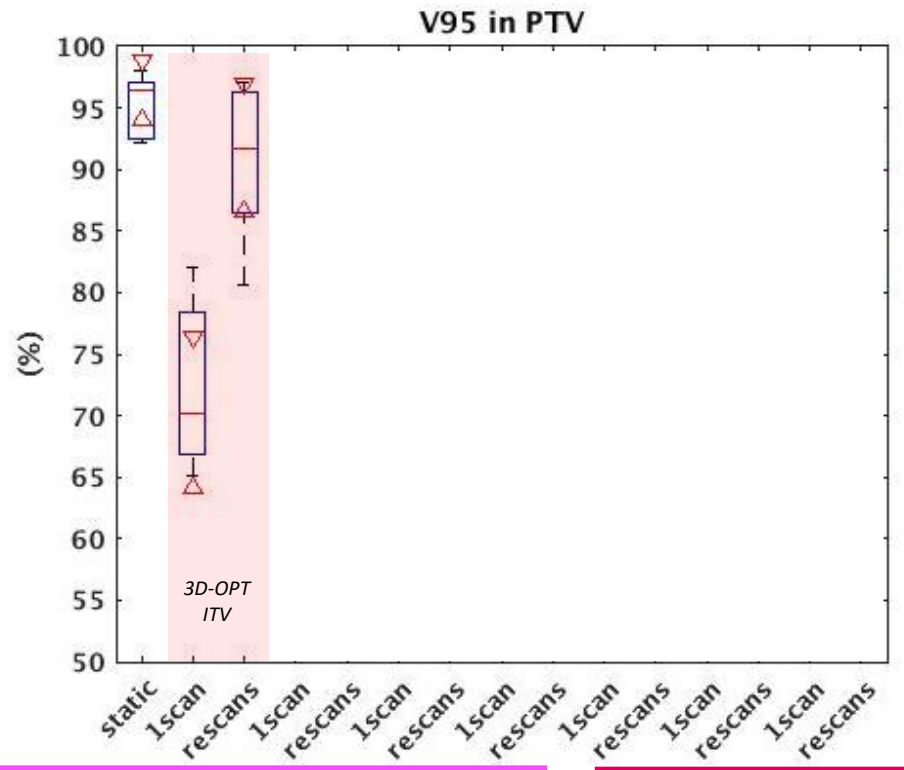


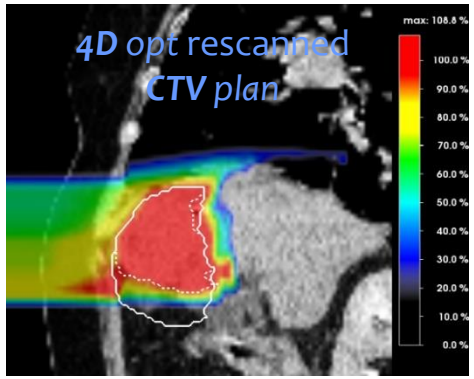


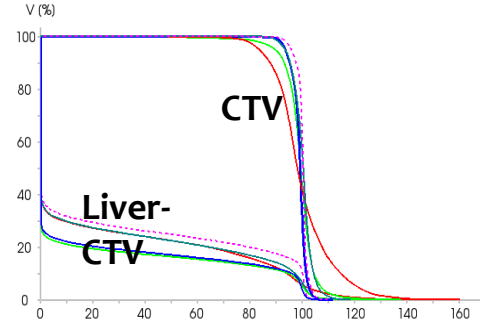


Steidl et al 2012 PMB (project from GSI)

4D optimization: making plan robust by itself







Advantage
No prolonged delivery time
No extended ITV margin

Disadvantage
Sensitive to difference in motion for optimization and for delivery
(if motion used by 4D optimization was not reproducible for validation, optimized dose homogeneity would collapse)

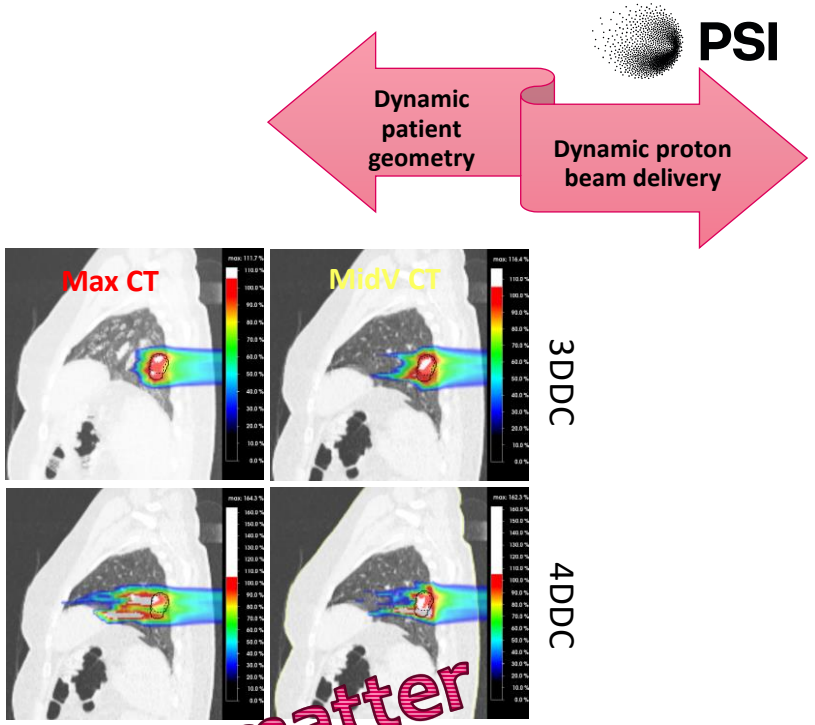
clinical beneficial → ***technical feasible?*** → ***clinical applicable?***

Graeff et al 2014 PMB
Bernatowicz et al 2017 PMB
Zhang et al ESTRO2018, AAPM2018
Engwall et al MP 2018

How to calculate 4D dose perspective ?

PSI

- The interplay effects are significant, individualized and can be influenced by many 4D parameters
- 4D dose is sensitive to all input factors from either machine side or patient side.
- 4D dose distribution is very difficult to predict without appropriately modelling the dynamics from both sides (moving organ and PBS-based dose delivery)
- It can be risky to make any conclusion or decision when only partial parameters are considered



Anything would change delivery timeline is matter

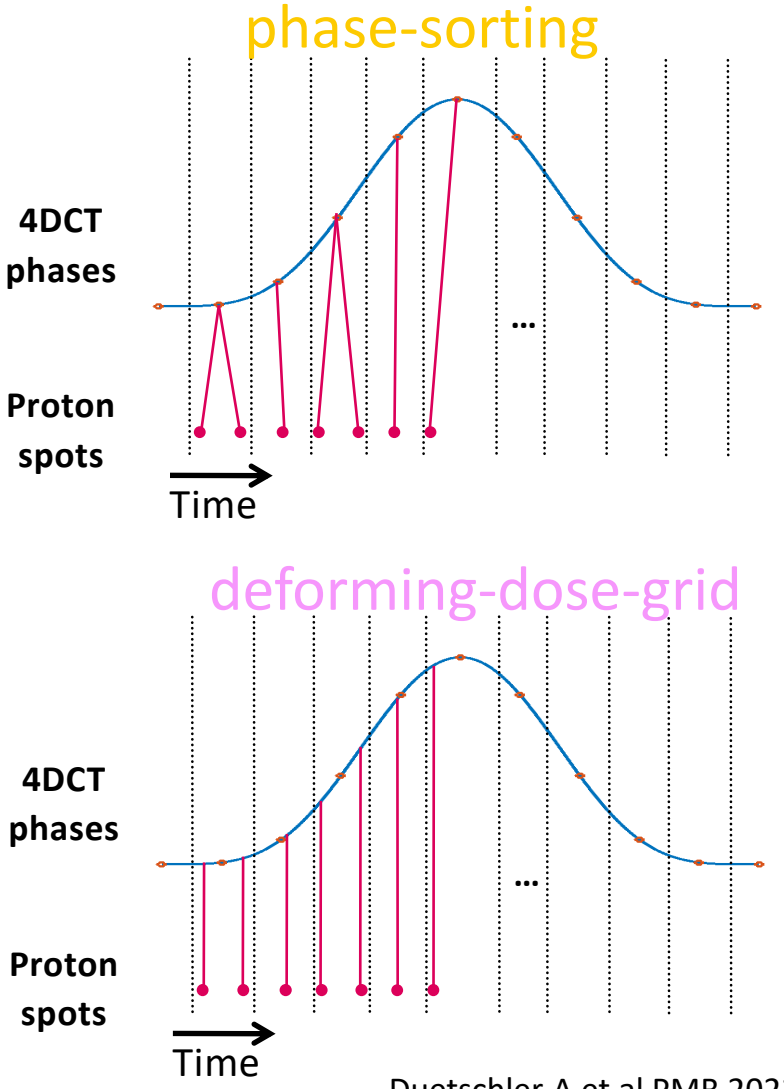
Motion mitigation	
rescanning	Type/path Number min-MU
gating	Gating window Surrogate type Phase or amplitud Duration
Breath hold	Reproducibility
tracking	2D/3D w/wo weight optimization
4D optimization	scenarios

Motion	delivery dynamics	Interactions
amplitude	Lateral scanning mode: • raster or spot-wise	Starting phase for beam delivery
period	Lateral scanning speed	
direction	Energy switching time	Starting phase for multi-field combination
deformation	Dose rate	
Irregularity in period or amplitude	Dose deposition mode: • constant • varied layer-wise • varied spot-wise	Number of field Number of fractionation

Initial 3D plan	
Patient geometry	PBS beam data
Field direction	Field arrangement
Spot distance	Energy layer distance
Scanning path	Scanning direction
Prescribed dose	Fractionation scheme
3D plan density: Max/mean/midV CT	3D plan geometry: CTV/gITV/rITV

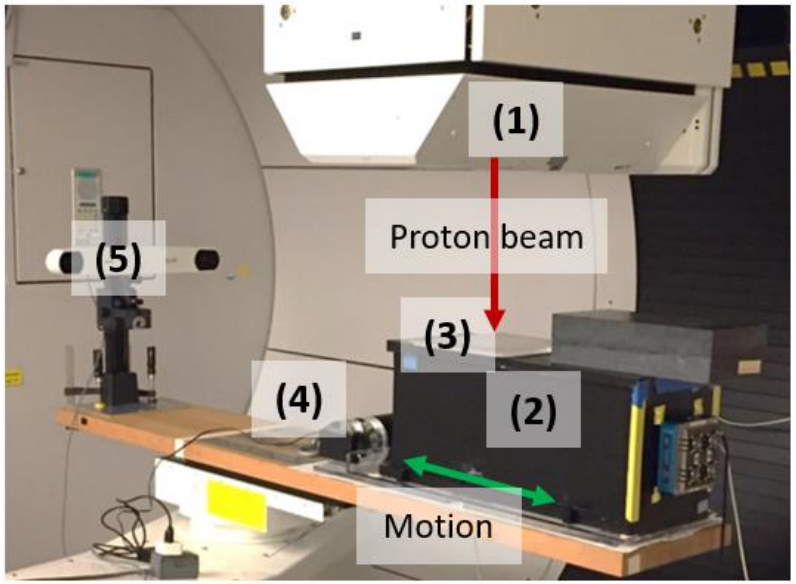
4DDC approach and implementation

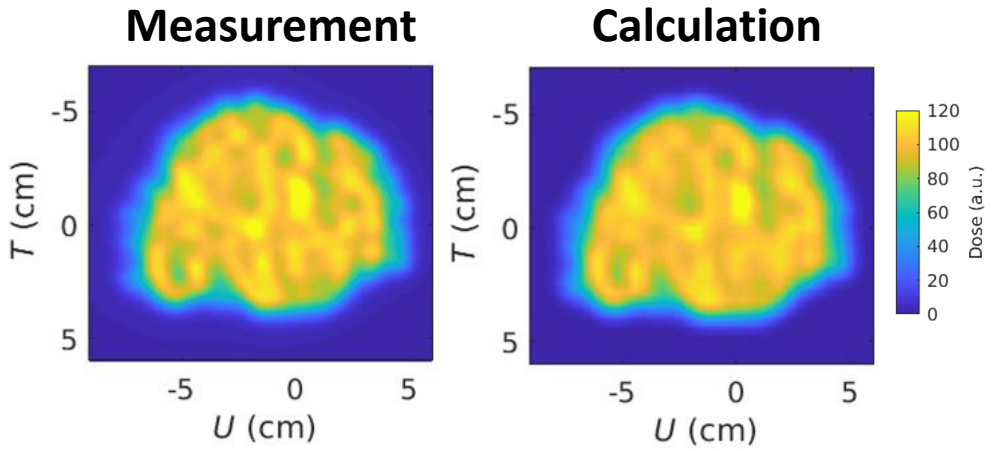
- Always remember 4DDC is based on 3DDC
  - analytical, pencil beam, MC …
- 4DDC is calculating sub-groups of proton beams to their corresponding patient model of the beam delivery time, then summing them up to one defined geometry
  - Density model: CT (CT-like image)
  - Motion model: 4D images + deformable registration
  - Induced density variation model: 4DCT or warped 4DCT
- Calculation/prediction for the dose delivery timeline is essential
- Beam to motion assignment

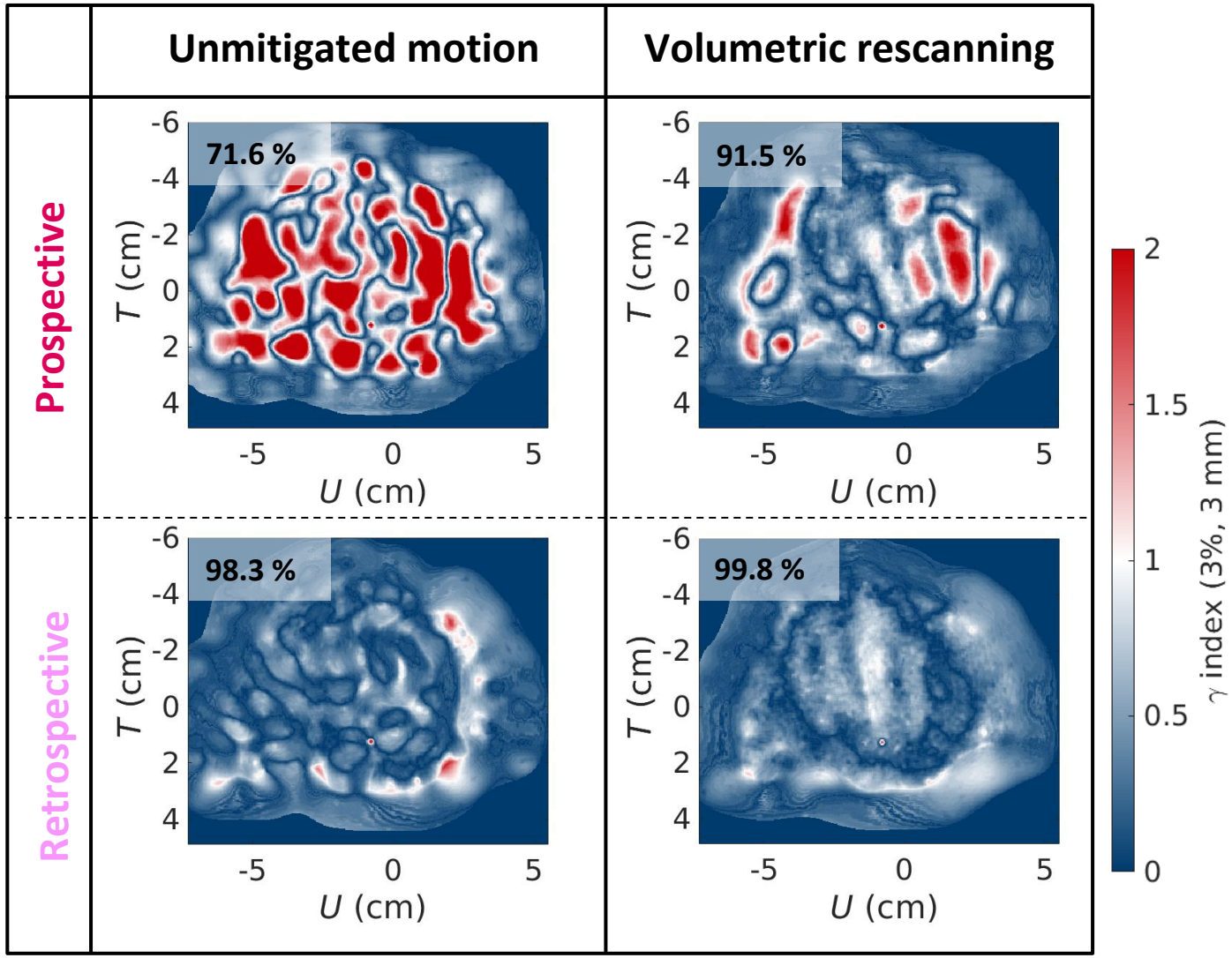


Duetschler A et al PMB 2023 015015

Experimental validation of the 4DDC algorithm







Krieger et al PMB 2018

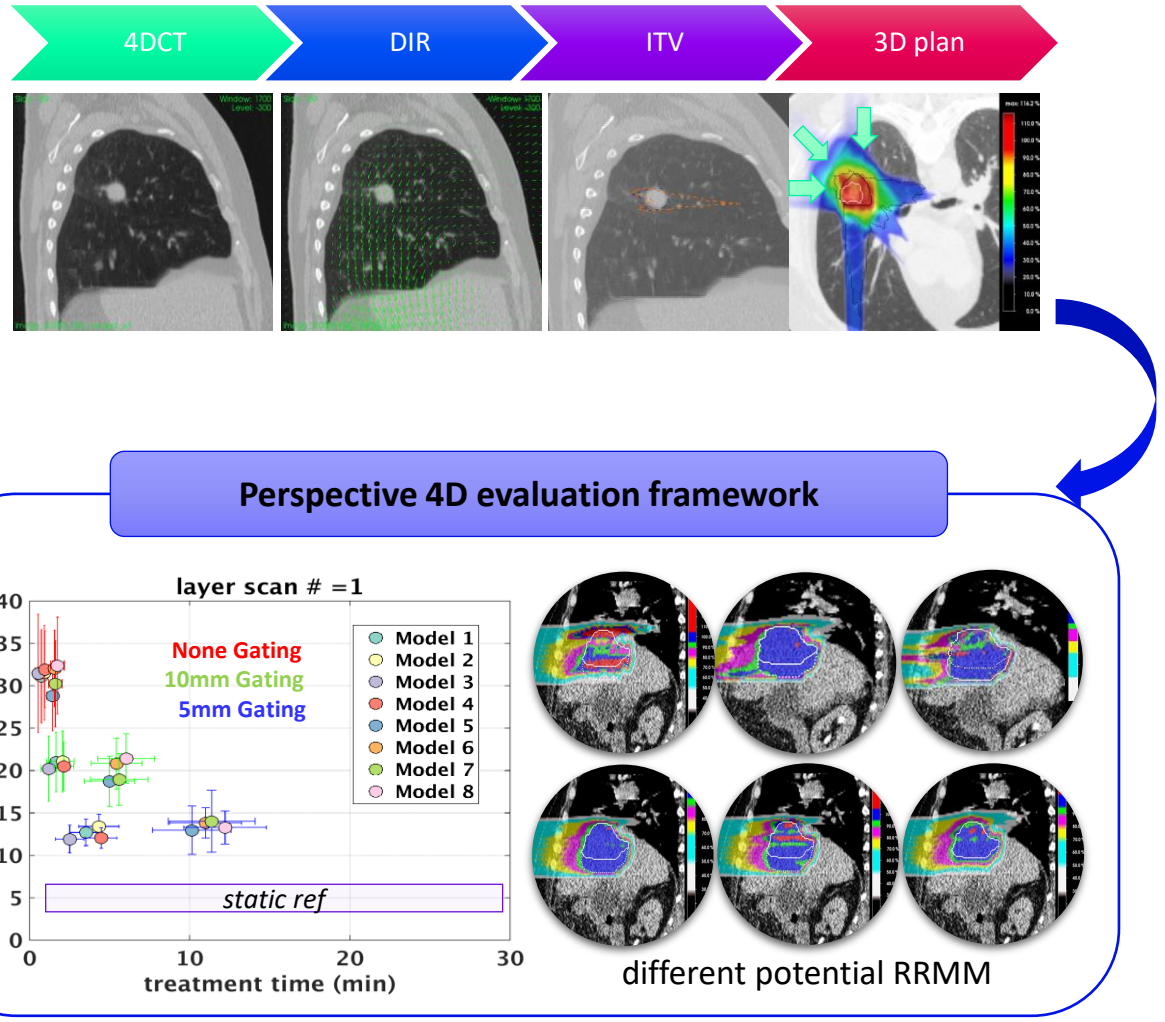
How to use *perspective* 4DDC in clinics?

Patient specific 4D treatment evaluation

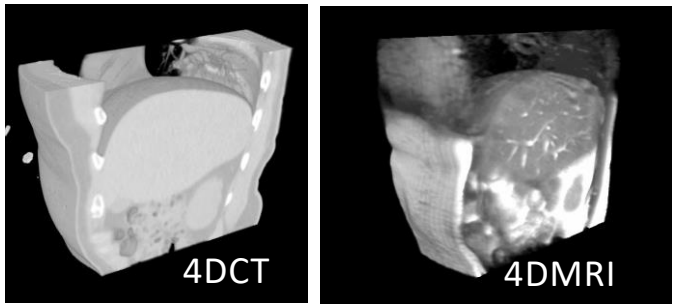
- to quantify interplay effect
- to determine effective motion management strategy
- to estimate potential uncertainty of fractional dose delivery

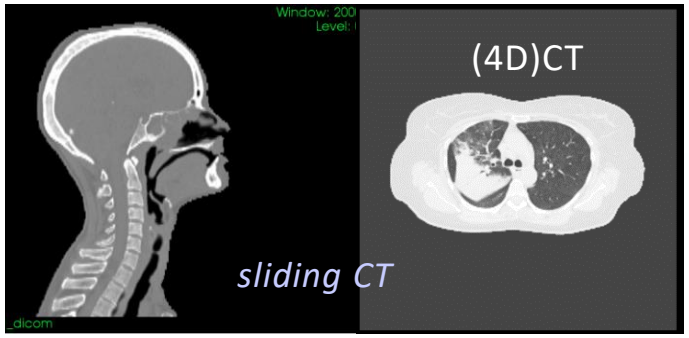
However, it is difficult to achieve due to the high dimension 4D parameters

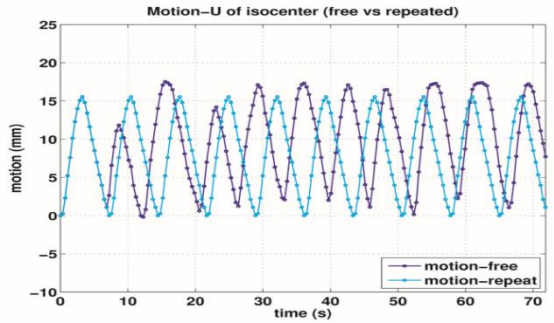
Calculation load will increase exponentially The uncertainty from both machine delivery and patient motion during the dose delivery

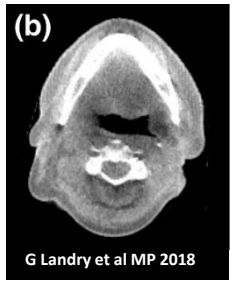


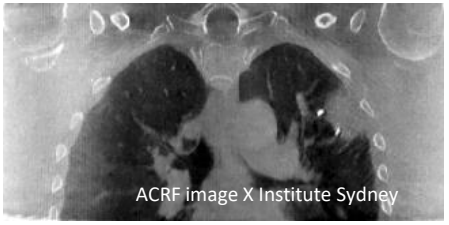
4D image guidance: o*ffline, online* and *real time*

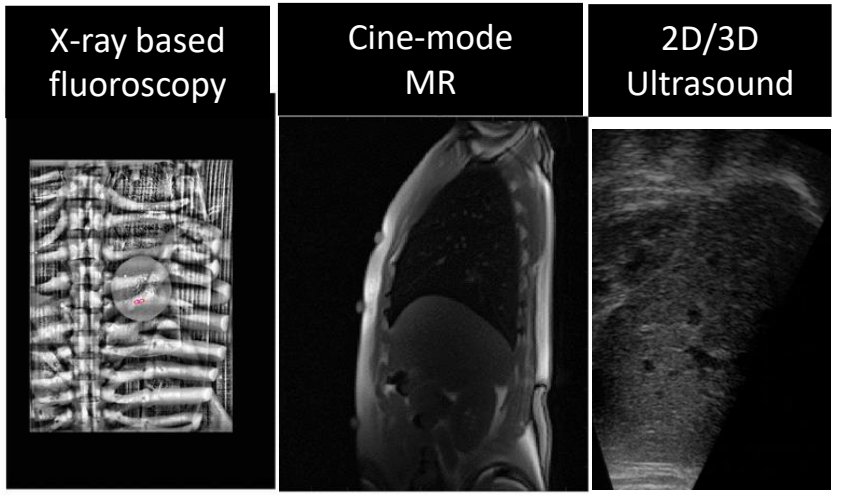








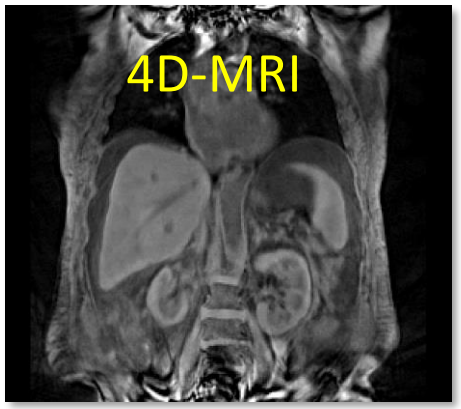


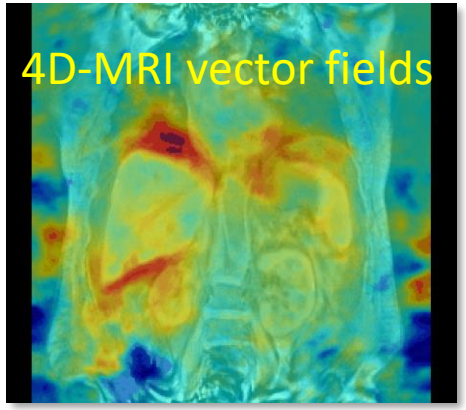


Volumetric	+++	++	-
Precise density	+++	+/-	-
Time resolved	++/+++	++	+++
Real time	-	+	+++
Sufficient VOI	+++	++	+
At treatment position	-	++	+++

Pre-treatment | Before Fx treatment | During treatment

4DMR for 4D planning and evaluation

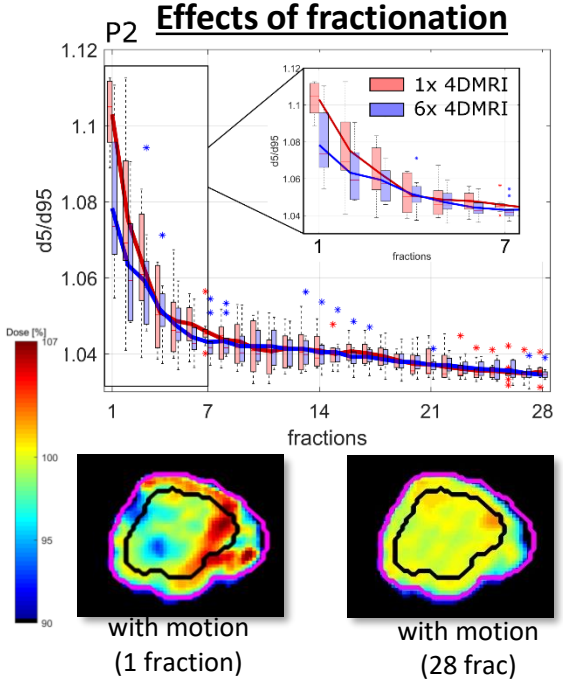




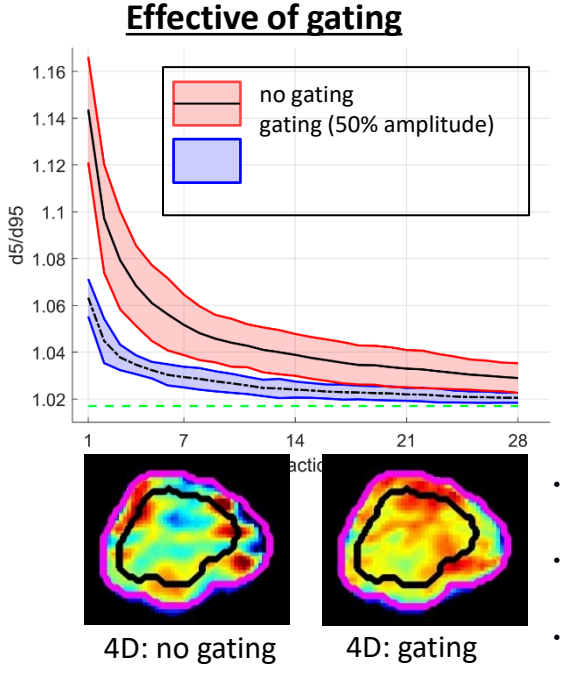
Planning 3D-CT

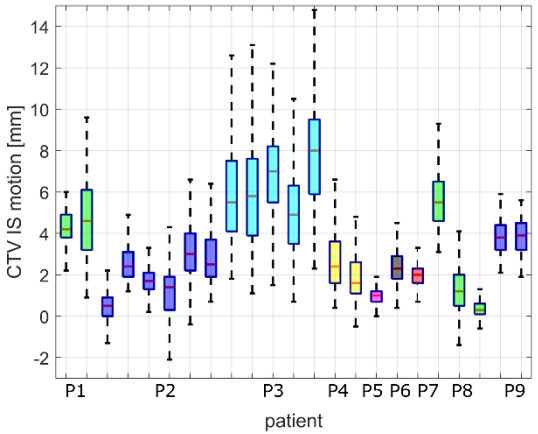
Synthetic 4D-CT

Effects of fractionation

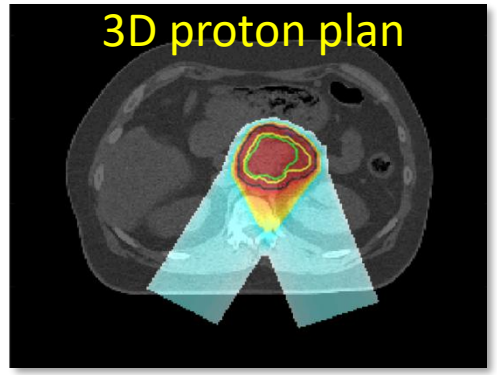


Effective of gating





3D proton plan



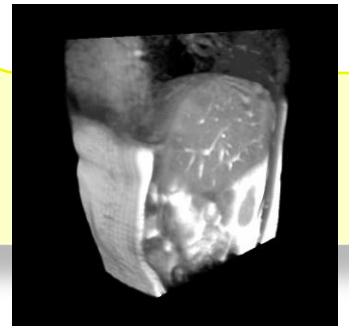
- K. Dolde, P. Naumann, C. David, R. Gnirs, M. Kachelriess, A.J. Lomax, N. Saito, D.C. Weber, A. Pfaffenberger, **Ye Zhang**. 4D dose calculation for PBS proton therapy of pancreatic cancer using repeated 4DMRI dataset. *Physics in Medicine and Biology,* 63(16) (2018) 165005 **(PMB 2018 Highlights collection)**
- K. Dolde, **Ye Zhang**, N. Chaudhri, C. David, M. Kachelriess, A.J. Lomax, P. Naumann, N. Saito, D.C. Weber, A. Pfaffenberger. 4DMRI-based investigation on the interplay effect for pencil beam scanning proton therapy of pancreatic cancer patients. *Radiation Oncology* (2019) vol: 14 (1) pp: 30 (shared first authorship)
- K. Dolde, P. Naumann, A.J. Lomax, N. Saito, D.C. Weber, A. Pfaffenberger, **Ye Zhang**. Comparison the effectiveness and efficiency of various gating approaches for PBS proton therapy of pancreatic cancer using 4DMRI datasets. *Physics in Medicine and Biology* (2019), 64 085011

Motion model: bridging offline and online info

PSI

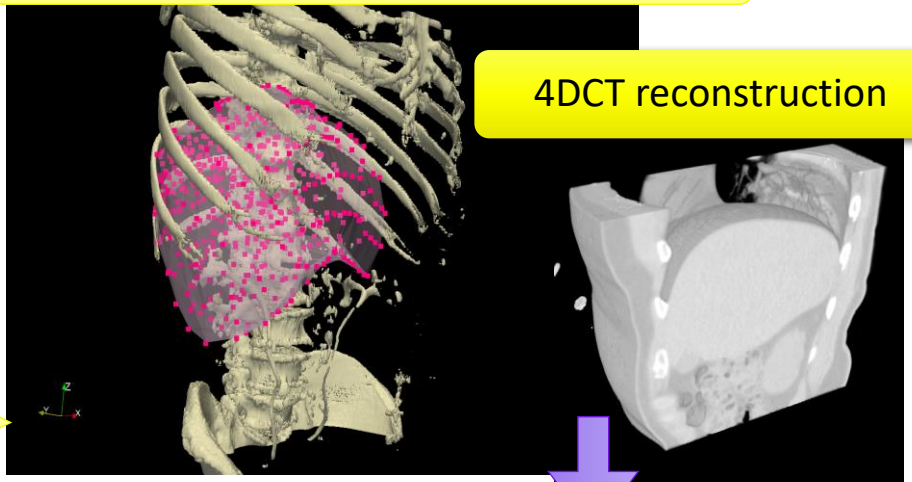
Pre-treatment

Capture example motion
- 4DMRI+ DIR
- Obtaining correlation using PCA

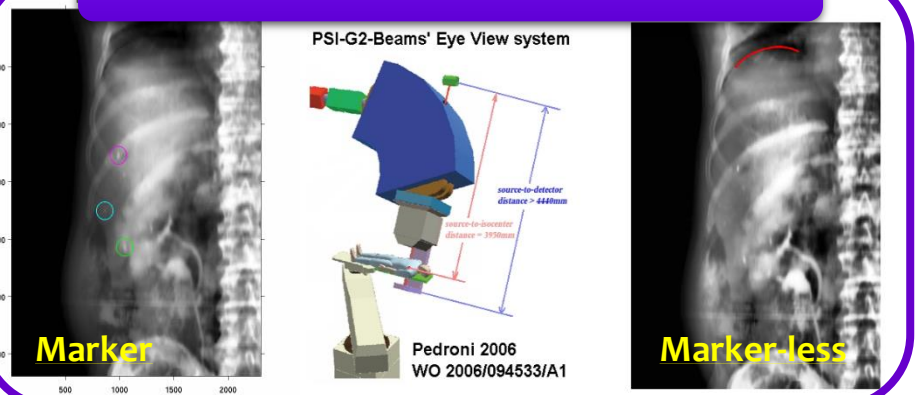


PCA motion model

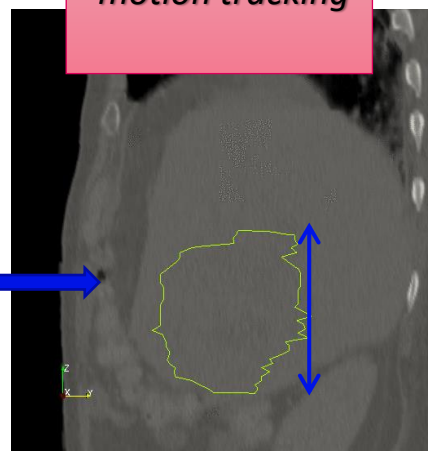
online deformable motion prediction



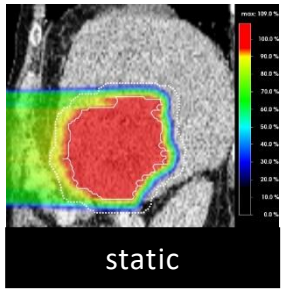
online traced sparse surrogate motion

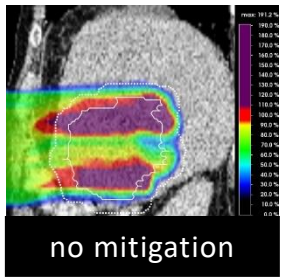


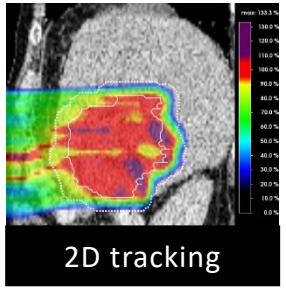
Conventional motion tracking

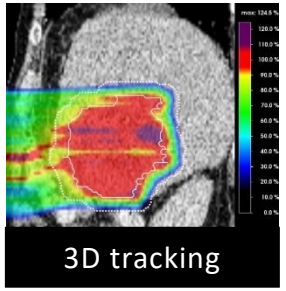


Deformable motion tracking



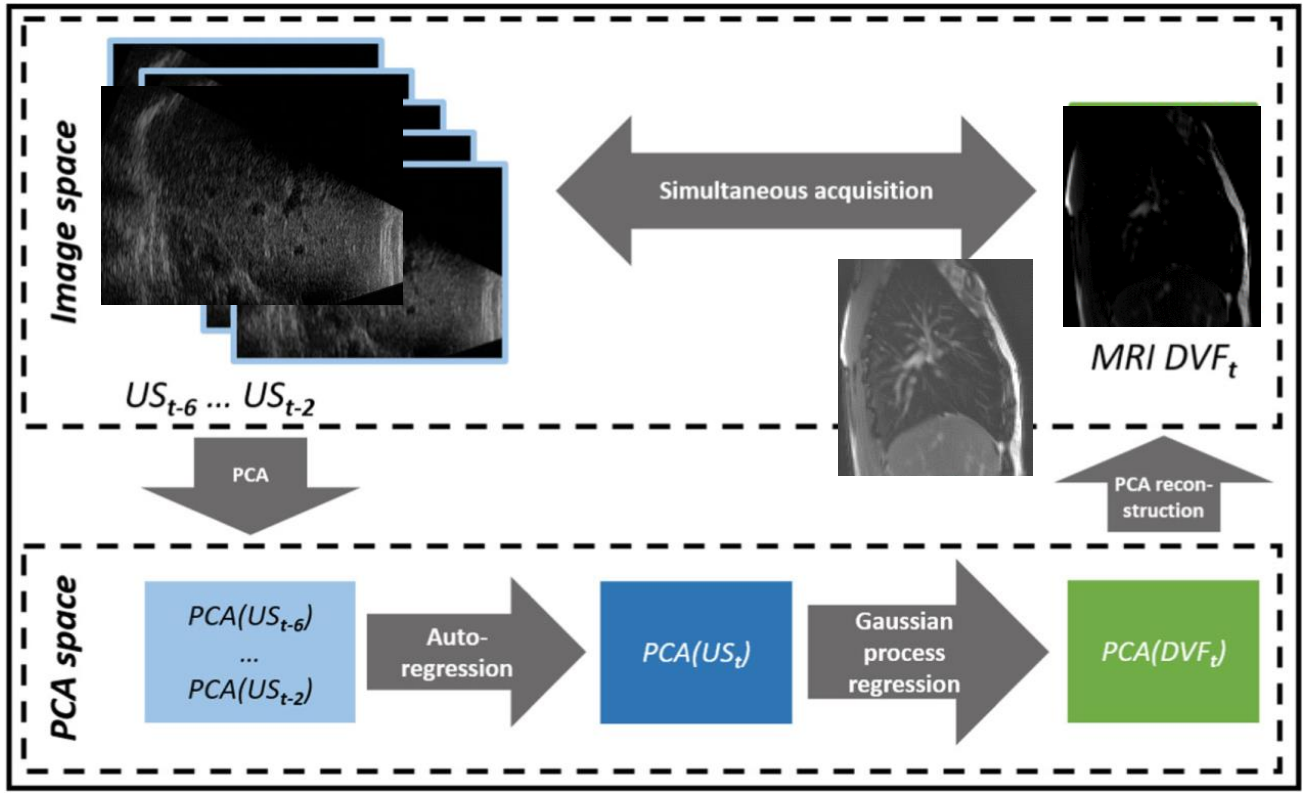


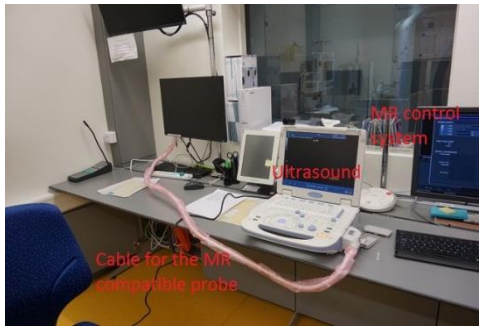


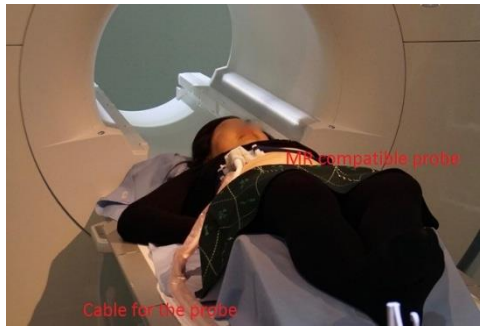


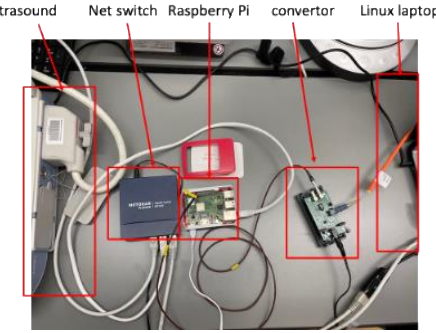
Zhang et al 2013 PMB, 2014 PMB

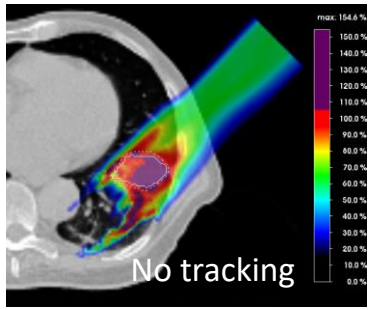
Liver-Ultrasound-guided lung tumour tracking

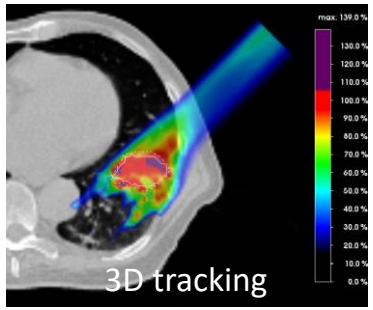


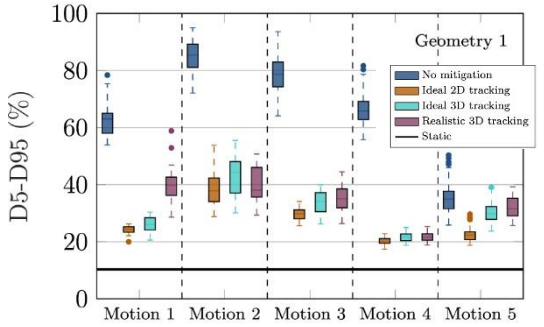


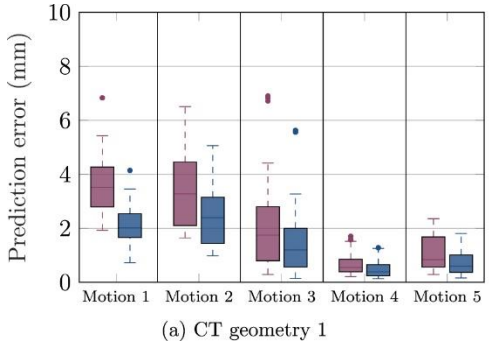








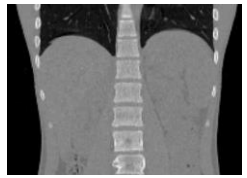




Krieger and Giger, et al, Zhang 2020 PMB, 2021 PMB

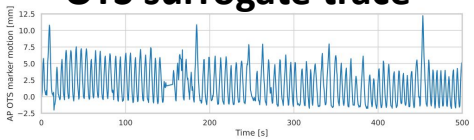
Motion model-guided Log file based 4D dose recon: method

4DCT



planning CT

OTS surrogate trace



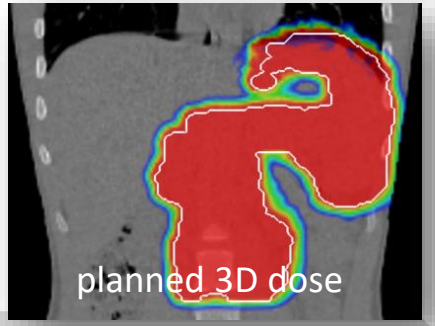
treatment log-file

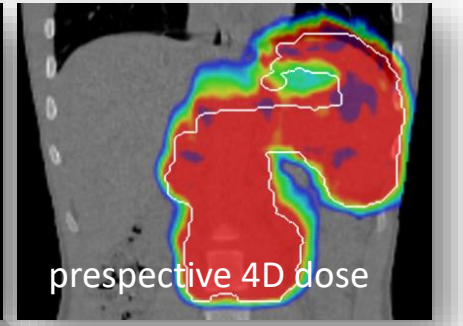
PCA motion-model

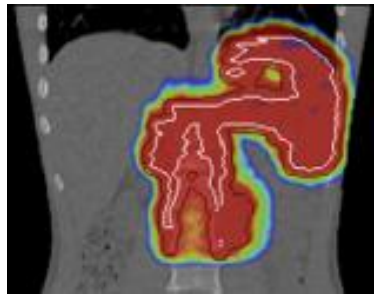
- patient-specific based on 4DCT
- reconstruction from OTS traces

4D dose reconstruction

- based on treatment log-files



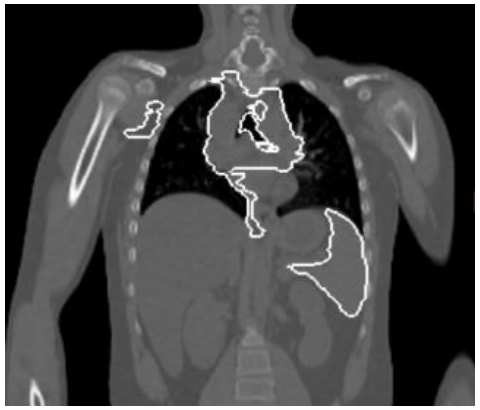




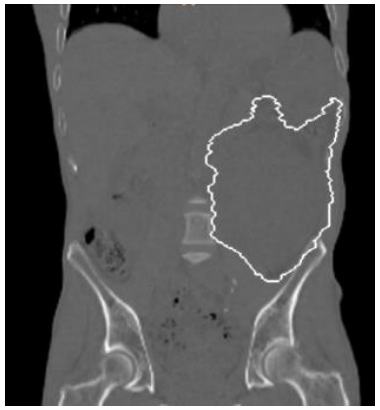
- Alisha Duetschler, Lili Huang, Giovanni Fattori, Gabriel Meier, Sairos Safai, Damien C. Weber, Antony J. Lomax, Ye Zhang. A motion model-guided 4D dose reconstruction for pencil beam scanned proton therapy. Physics in Medicine and Biology, 68 (2023) 115013

Motion model-guided Log file based 4DDR: clinic case

Case A
(Hodgkin's)



Case B
(Hodgkin's)

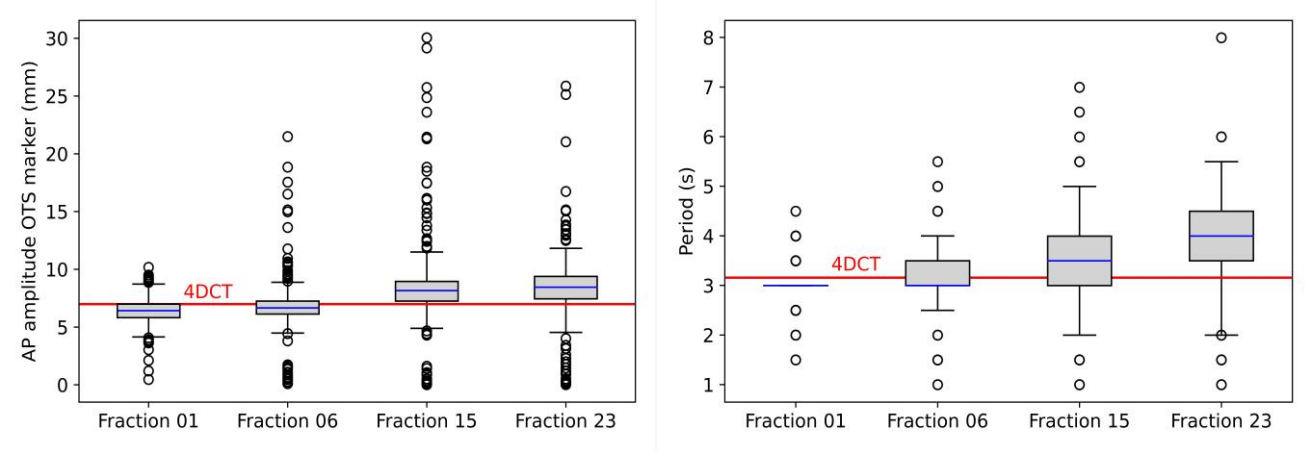


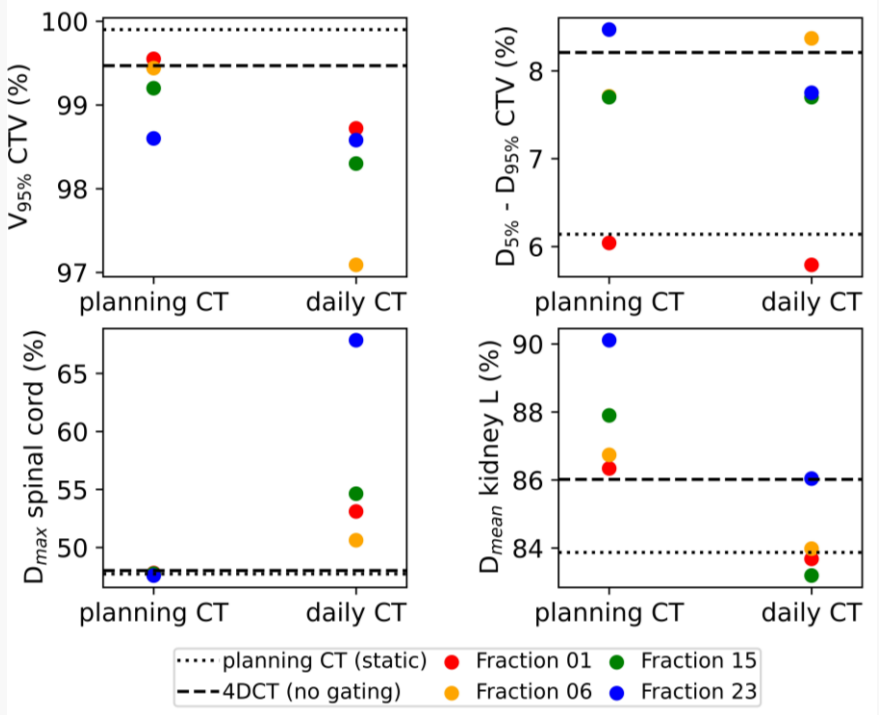
Case C
(malignant neoplasm)

Inter-fractional differences

- up to 2.0% in CTV $V_{95\%}$
- up to 2.9% in $D_{5\%}$-$D_{95\%}$

Intra- and inter-fractional motion variability



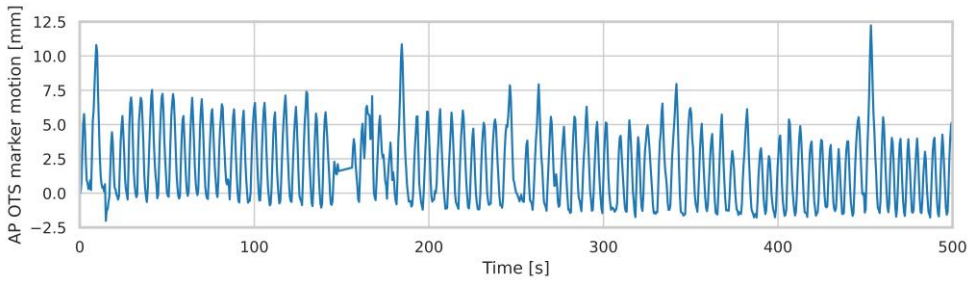


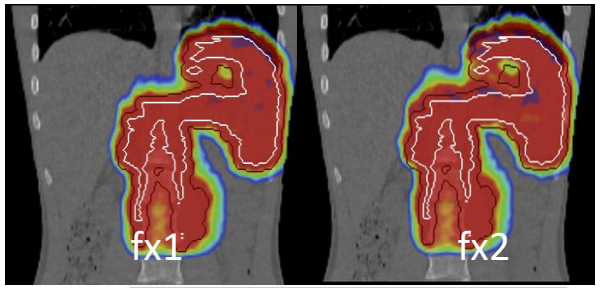
Duetschler A et al PMB 2023

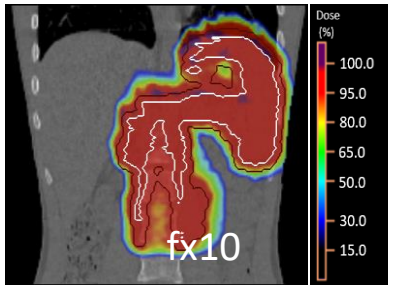
Joint efforts of perspective 4DDC and retrospective 4DDR

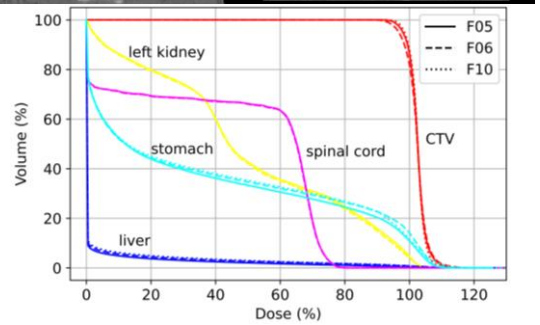
PSI

Retrospective fx 4D dose verification

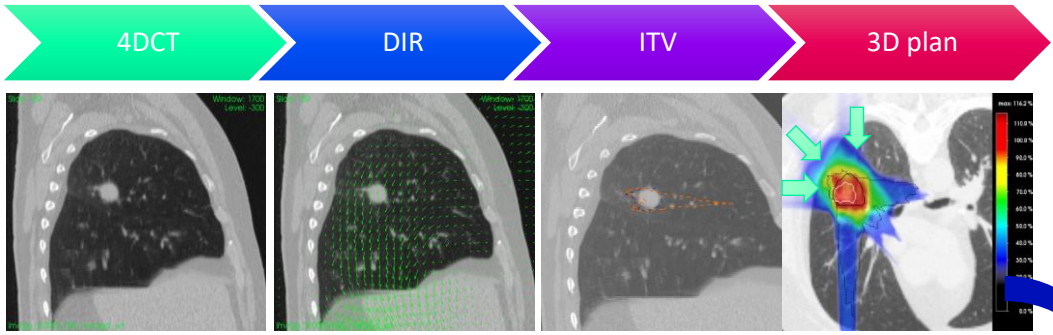


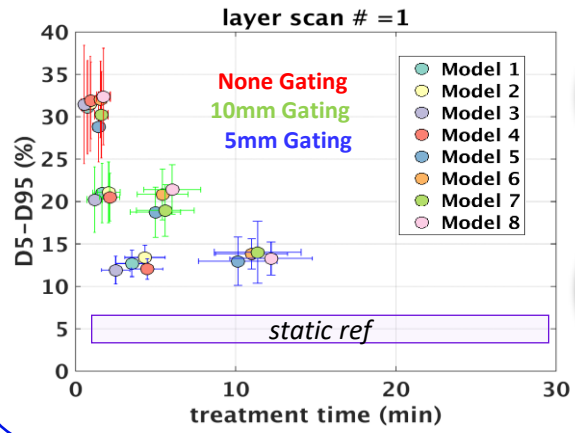


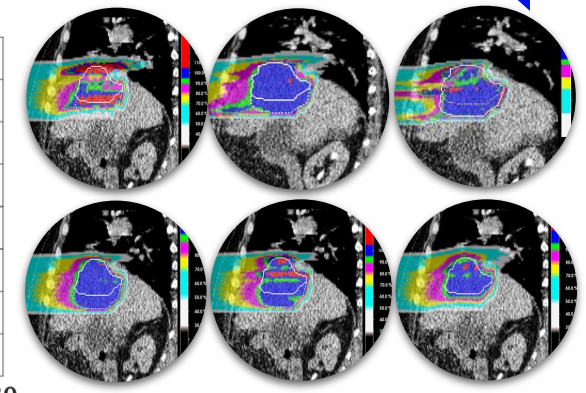




Perspective 4D evaluation framework





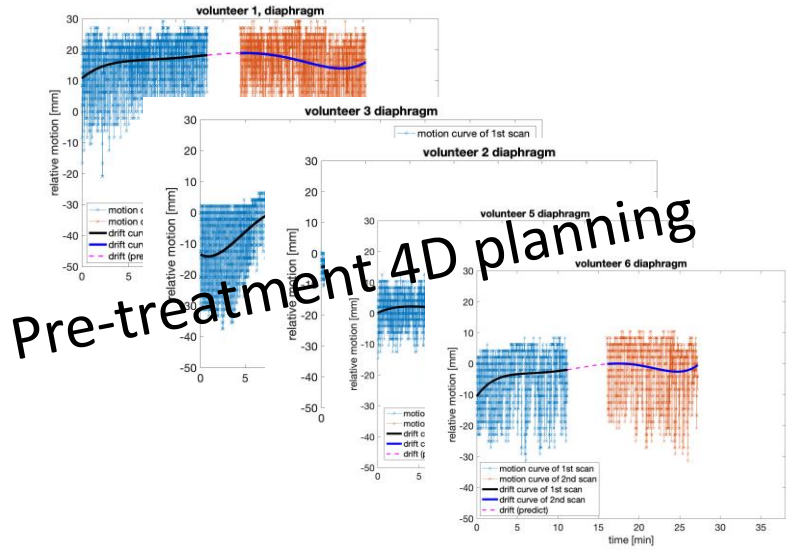


different potential RRMM

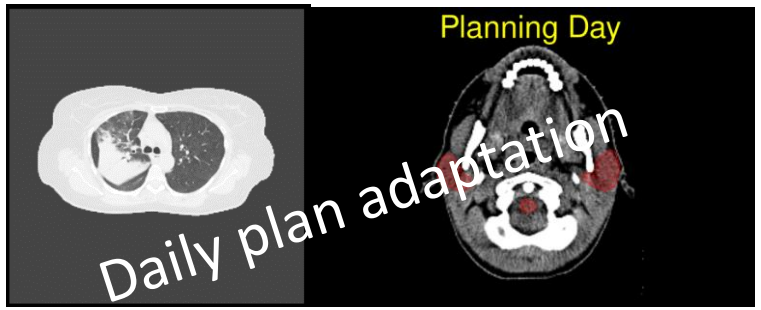
DAPT for 4D treatment – motion variability

PSI

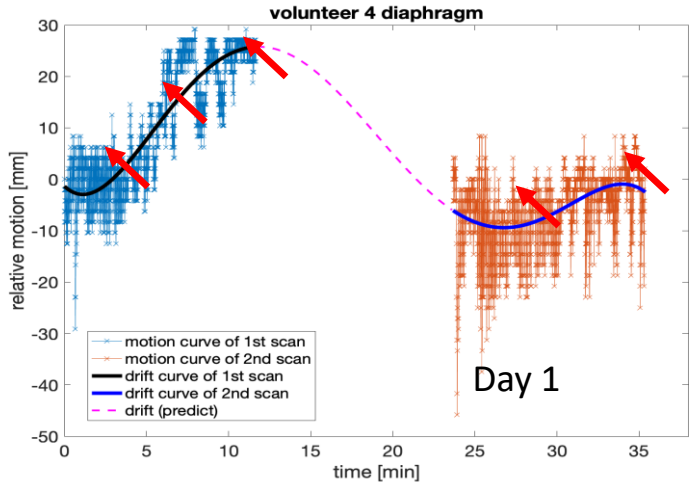
Patient specific motion characteristics

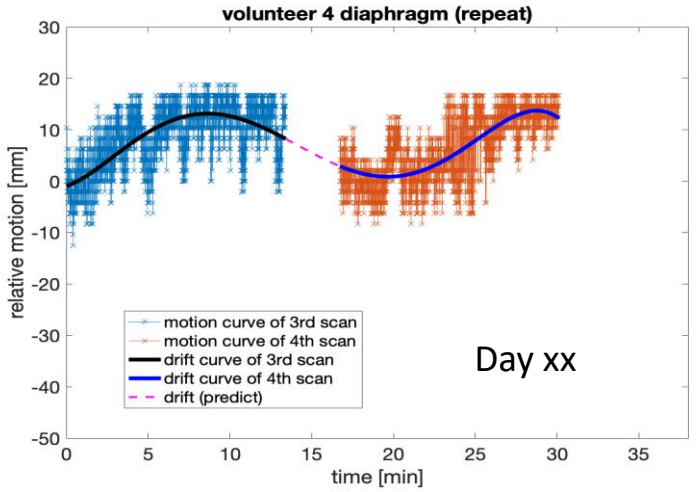


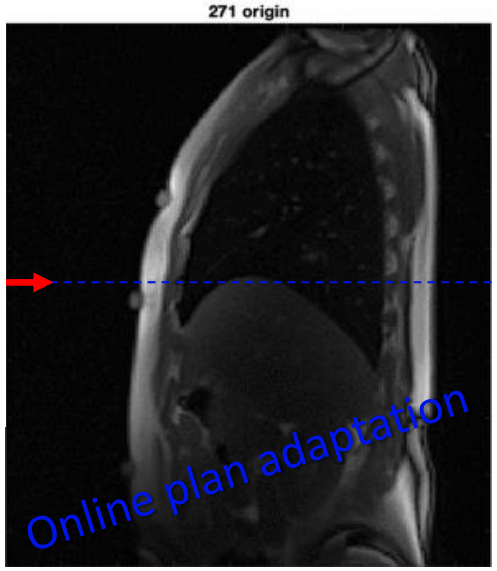
Anatomic variations during full treatment



"variations" of the motion irregularity *inter*-fractionally





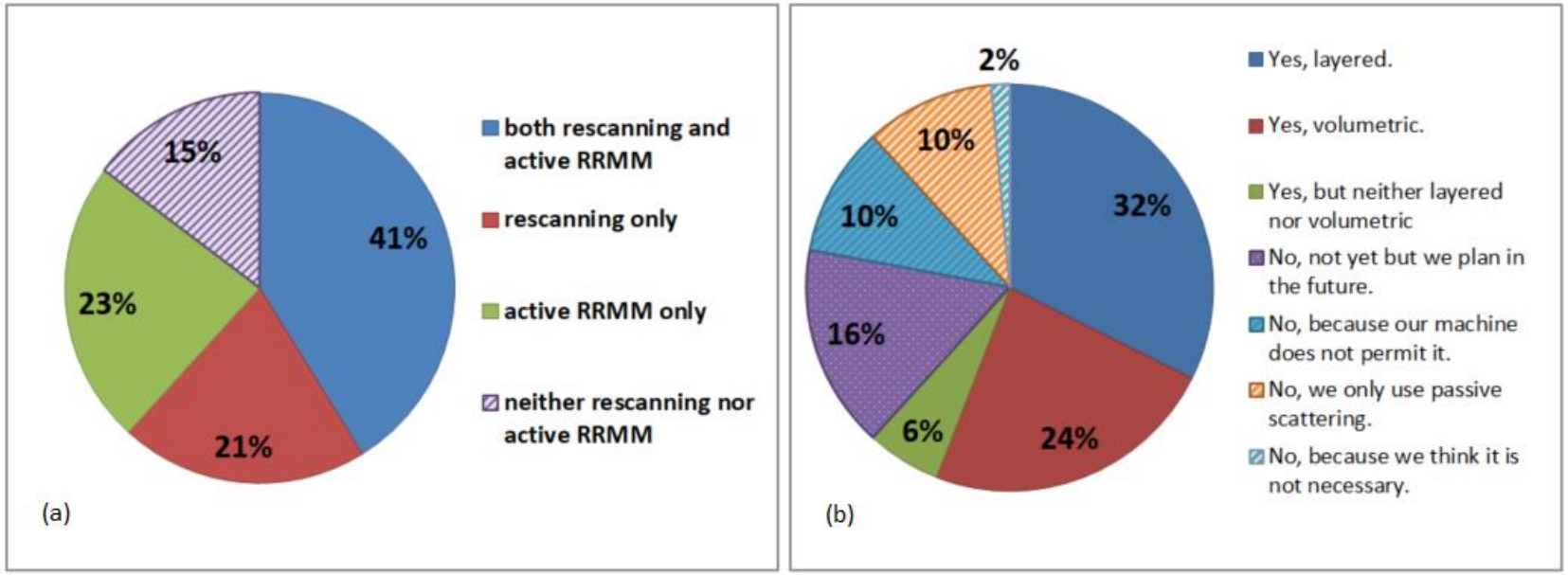


Baseline can drift intra-fractional, which is not reproducible inter-fractionally

EKNZ 2019-01060

Current status of motion mitigation

RRMM implementation globally (N=68)



Status of rescanning application in clinics

Zhang Y, Trnkova P, Toshito T, Heijmen B, Richter C, Aznar M, Albertini F, Bolsi A, Daartz J, Bertholet J, Knopf A. A survey of practice patterns for real-time intrafractional motion management in particle therapy. Physics and Imaging in Radiation Oncology 2023 Apr 11;26:100439

Current status of motion mitigation

Summary of the most important conclusions from 3 round DELHI consensus analysis

VISION AND RECOMMENDATIONS

- Real-time motion management is needed for adaptive treatment of moving targets
- Future real-time motion management should combine strategies according to the individual patient selection criteria

- Dosimetric deteriorations for both target and OARs are considered equally important
- The rescanning parameters should be evaluated and optimized for an individual patient
- The selection criteria of active RRMM should be based on pre-treatment motion characteristics
- The uncertainty of the motion model should be considered in the 4D evaluation
- The pre-treatment 4D plan evaluation should be recorded for multi-centre clinical trial

- 4D dose calculation including uncertainty evaluation, is the top required feature on clinical software in the next 2 years

Zhang Y, Trnkova P, Toshito T, Heijmen B, Richter C, Aznar M, Albertini F, Bolsi A, Daartz J, Bertholet J, Knopf A. A survey of practice patterns for real-time intrafractional motion management in particle therapy. Physics and Imaging in Radiation Oncology 2023 Apr 11;26:100439

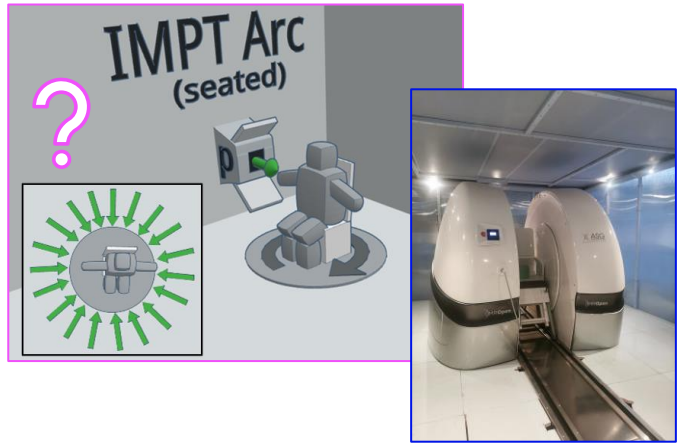
Go beyond/exceed MR guided photon therapy

Current mature solution for MR linear accelerator

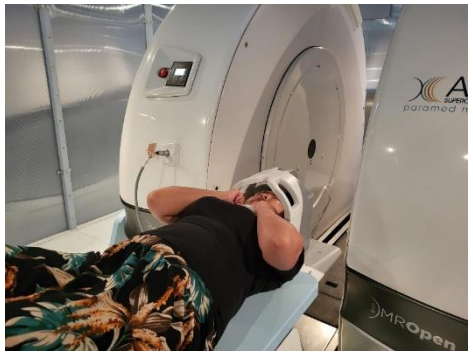
cost^2

complex^2

Potential conceptual designs for MR-guided proton machine



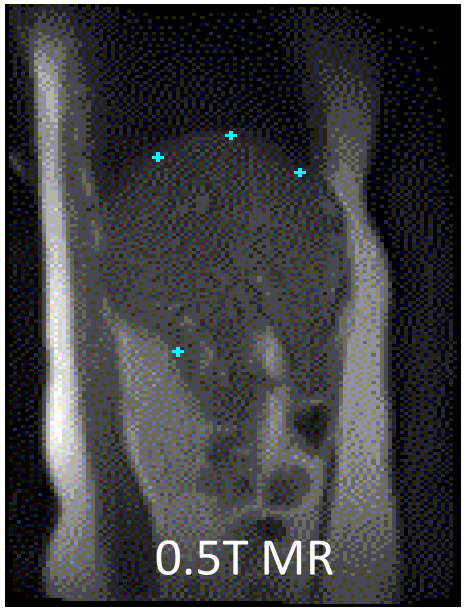
Enable online MR for proton without anti-democratization

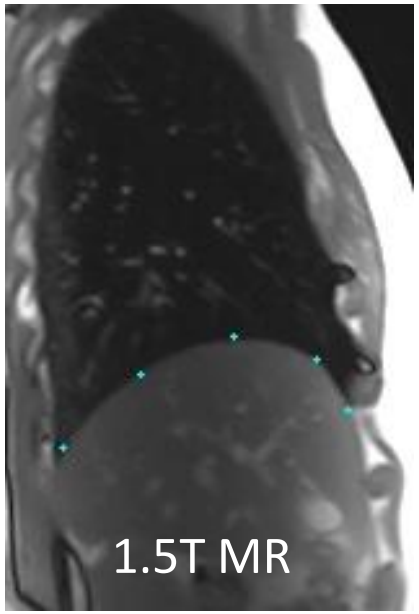


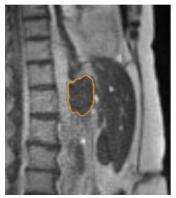
Real-time 4DMRI based online motion tracking

PSI

Real-time 2D motion tracking using transformer-based foundation model



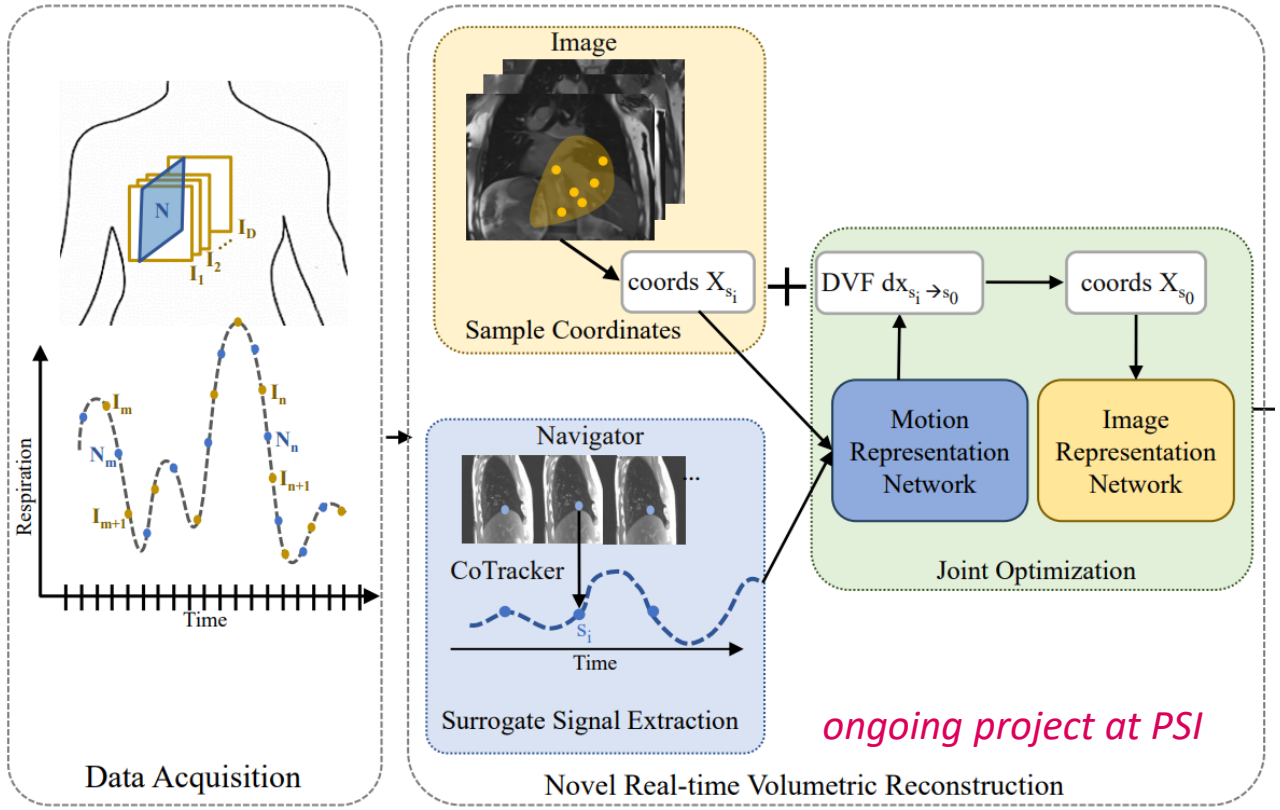




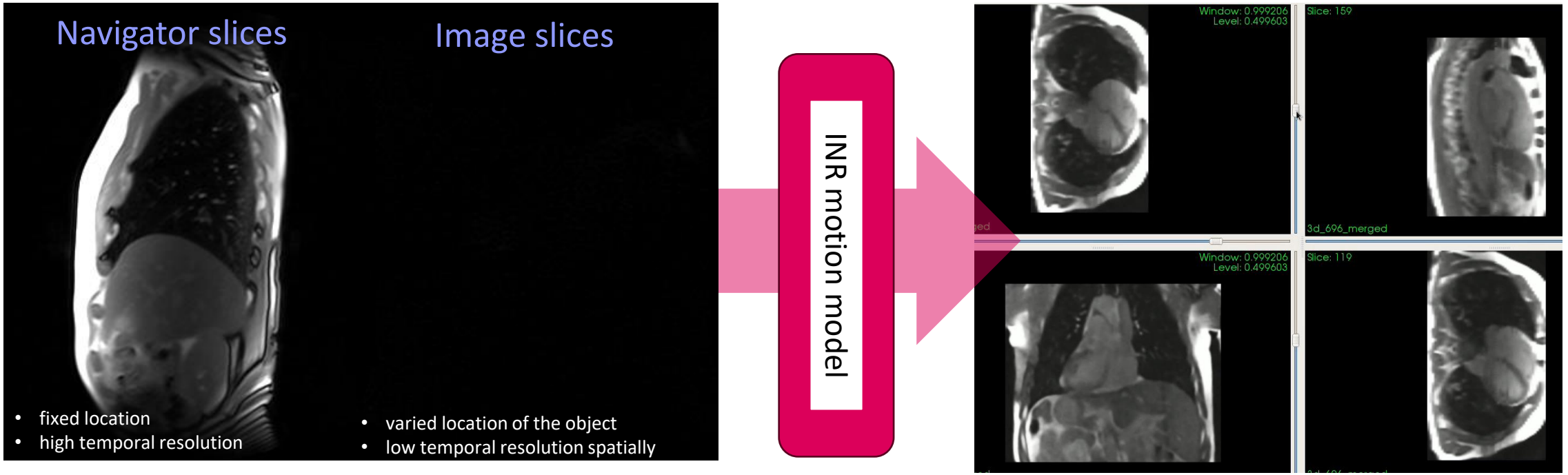
TrackRAD

Real-time tumor tracking for MRI-guided RT

4DMRI reconstruction and concurrent motion tracking using *Implicit Neural Representation*



Real-time 4DMRI for online motion tracking

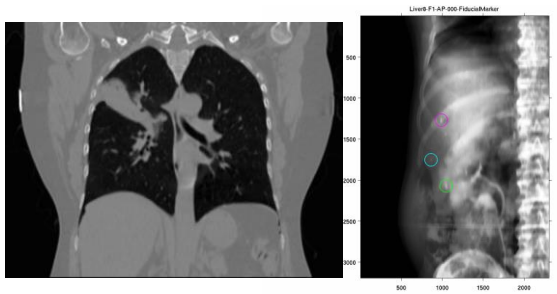


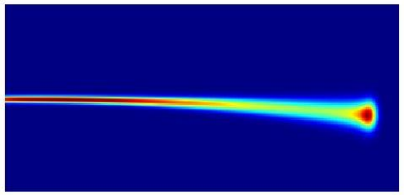
Wu et al. manuscript under preparation

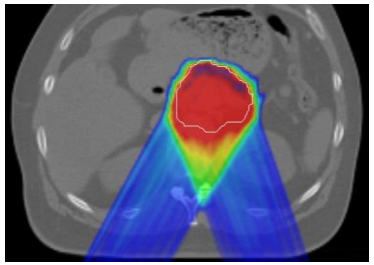
MRgPT: Next-generation 4D treatment and image guidance

PSI

High soft-tissue contrast
No radiation image dose
Real-time imaging

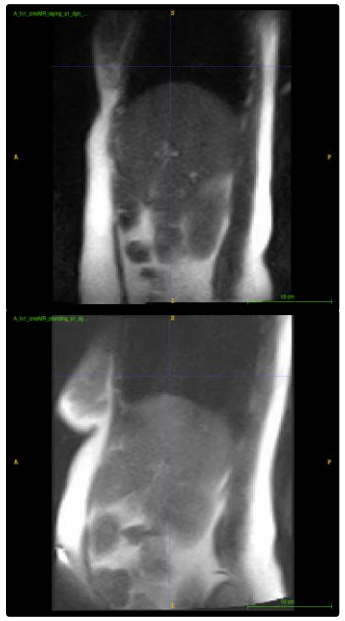






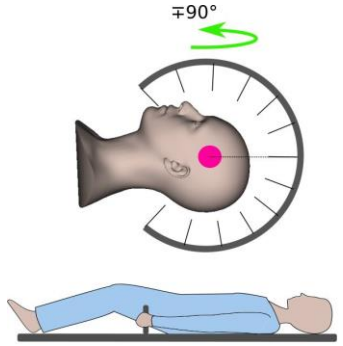
proton dose calculation under magnetic field

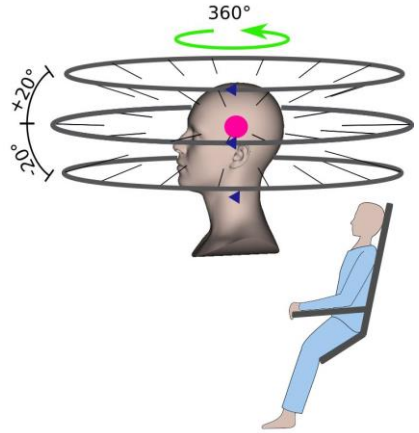
Onboard MR-guided proton therapy **Upright treatment**



MR-guided upright proton therapy

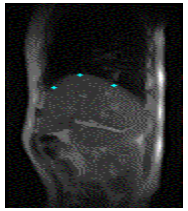
Reduced facility cost
Increase clinical advantage
Possibility for advanced IGRT

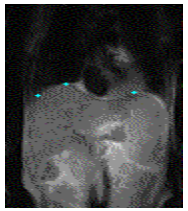


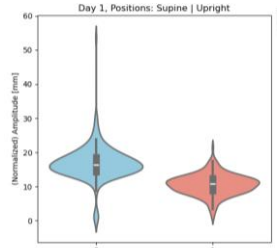


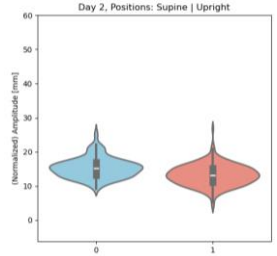
Recumbent

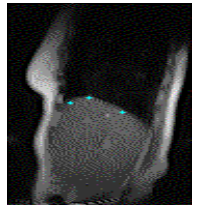
Upright

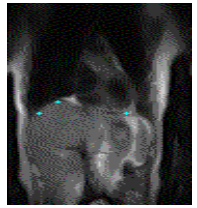






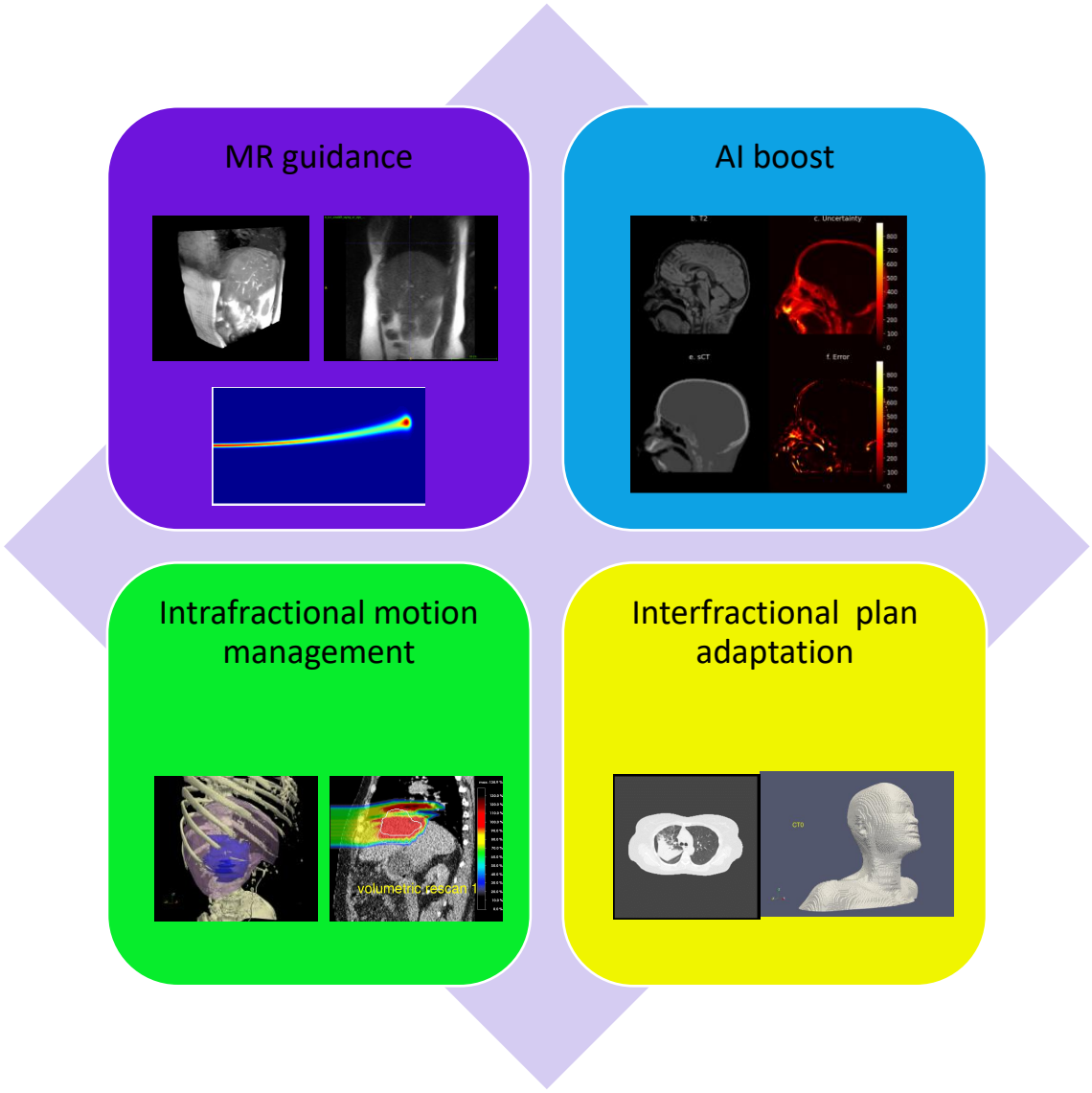






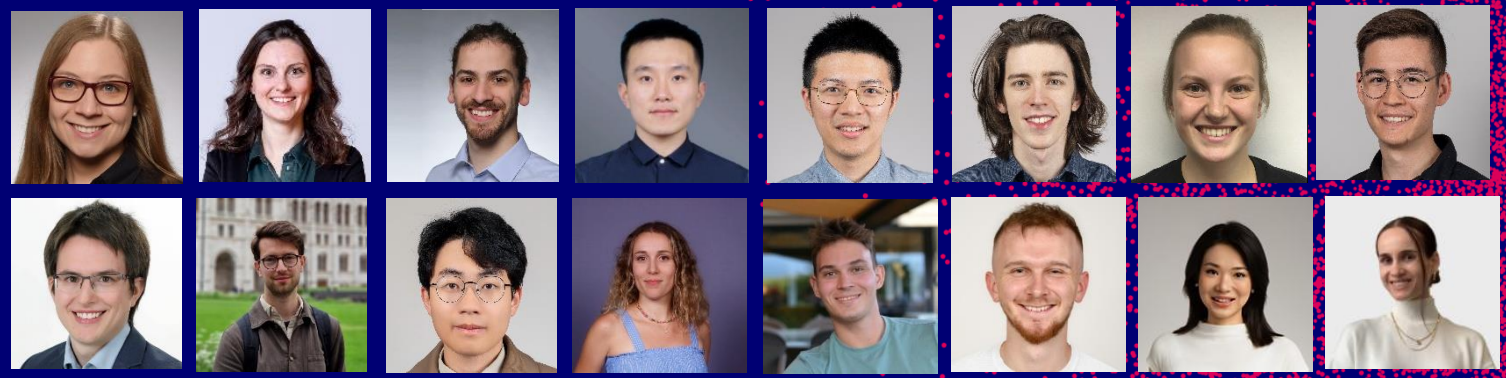
Conclusion and outlooks

- Intra- and inter-fraction motions for PBS proton are significant but can be evaluated prospectively or retrospectively using 4D dose calculation, image guidance, motion model, daily plan adaptation
- Joint impact of intra- and inter-fraction motion effects must be emphasized and mitigated in the next five years
- MR should play a more critical role in further proton therapy, offline, online or in real-time.
- Combining upright treatment with open MR would be a feasible solution for onboard MRgPT
- Advanced image processing techniques based on AI will significantly improve the efficiency of proton therapy workflow for the ultimate goal towards true real-time adaption



PSI

Thank you!



krebsliga

Strategic Focus Area
Personalized Health and Related Technologies

Swiss National Science Foundation

Schweizerische Eidgenossenschaft
Confédération suisse
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