Motion management for indications beyond the thorax region

Per Poulsen, Danish Centre for Particle Therapy

DANISH CENTRE FOR PARTICLE THERAPY

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Motion management for ~~indications beyond the thorax region~~ liver

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Disclaimer

- Number of liver patients treated to date at DCPT: 0

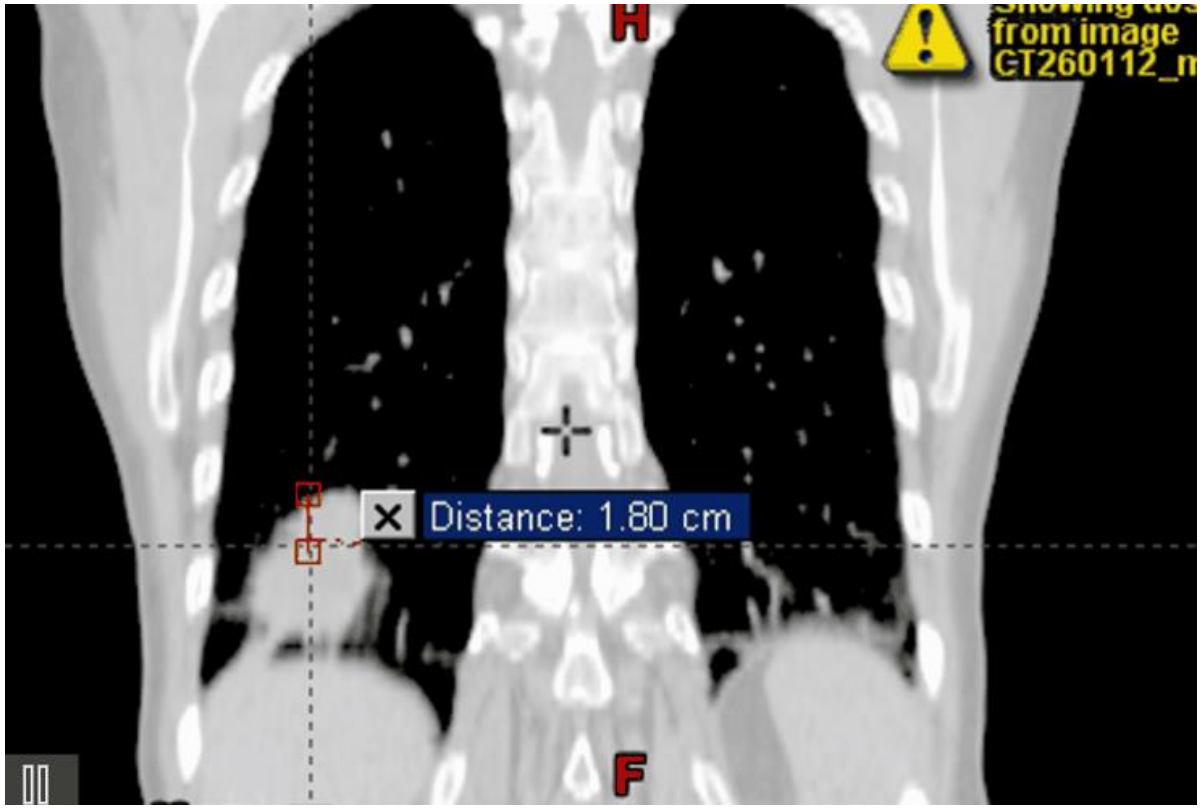
Liver tumor motion

Small motion →

Medium motion →

Large motion →

Liver →



Liver versus thorax region

- Larger motion in general
- Less organ deformation
- More homogeneous tissue with smaller density variations
- Less complicated marker implantation

Agenda

- Proton trial for HCC
- Gating latency, fiducial markers
- Motion monitoring at treatment
- Motion-including dose reconstruction
- Non-uniform dose prescription
- Summary

Hepatocellular carcinoma (HCC)

- ~350 new cases per year in Denmark
- Often cirrhotic liver and severe co-morbidity
- Poor survival rates:
  - <40% after 1 year
  - ~10% after 5 years
- Treatment options:
  - Surgery: Gold standard if possible
  - RF-ablation: Good local control for tumors <3 cm
  - X-ray SBRT: Good local control for tumors <5 cm. RILD is dose-limiting toxicity
  - Proton therapy: Can reduce irradiated normal liver volume and thus risk of RILD*

*Mizumoto IJROBP 2012, Hsieh IJROBP 2019

Danish national phase II study of proton therapy for HCC

- 50 patients not eligible for surgery, RF-ablation or transplantation
  - Tumors <5 cm (currently offered photon SBRT)
  - Tumors <12cm (total diameter of max 3 tumors, currently offered palliative TACE)

- Mean CTV dose:
  - 67.5 Gy(RBE) / 15fx (Peripheral tumors, >2 cm from porta)
  - 58 Gy(RBE) / 15fx (Central tumors, ≤2 cm from porta hepatis)

Danish national phase II study of proton therapy for HCC

- Imaging for planning: 4DCT, 3-4 exhale breath-hold CTs (with IV contrast)
- Will be repeated at day 3, 8 and 15

- Motion management strategy:
  - Exhale respiratory gating
  - Exhale breath-hold (only if breath-hold level is stable)
  - Free breathing (only if motion <1cm or gating not feasible)
    - Abdominal compression may be used

- Imaging at treatment:
  - CBCT for marker-based setup
  - X-ray imaging before or during each field delivery
  - External motion monitoring throughout the fraction

Danish national phase II study of proton therapy for HCC

- Primary endpoint: Death or RILD within 4 months after start of radiotherapy
- Secondary endpoints:
  - Toxicity, local control, survival
  - Normal liver sparing relative to x-ray RT
  - Ability to obtain planned dose when accounting for patient-specific uncertainties

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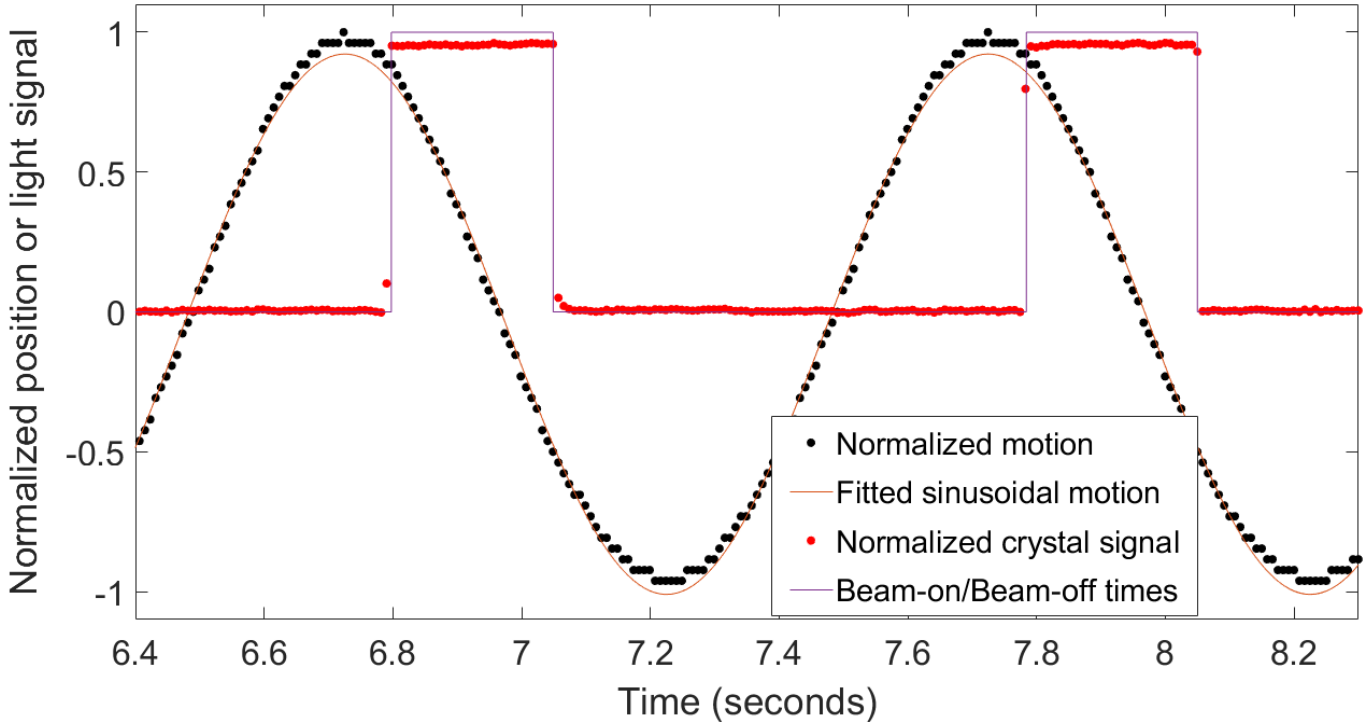
Gating latency measured with scintillating crystal

- Pencil beam hitting a scintillating crystal
- Sinusoidal motion, gating
- Motion and light signal recorded with GoPro camera (120 fps)

Gating latency measured with scintillating crystal



Gating latencies:

- Beam-on latency τ_{on} ~ 270 ms (→ Reduced duty cycle)
- Beam-off latency τ_{off} ~ 104 ms (→ Reduced accuracy)
  - Errors <1mm in >95% of the beam-on time

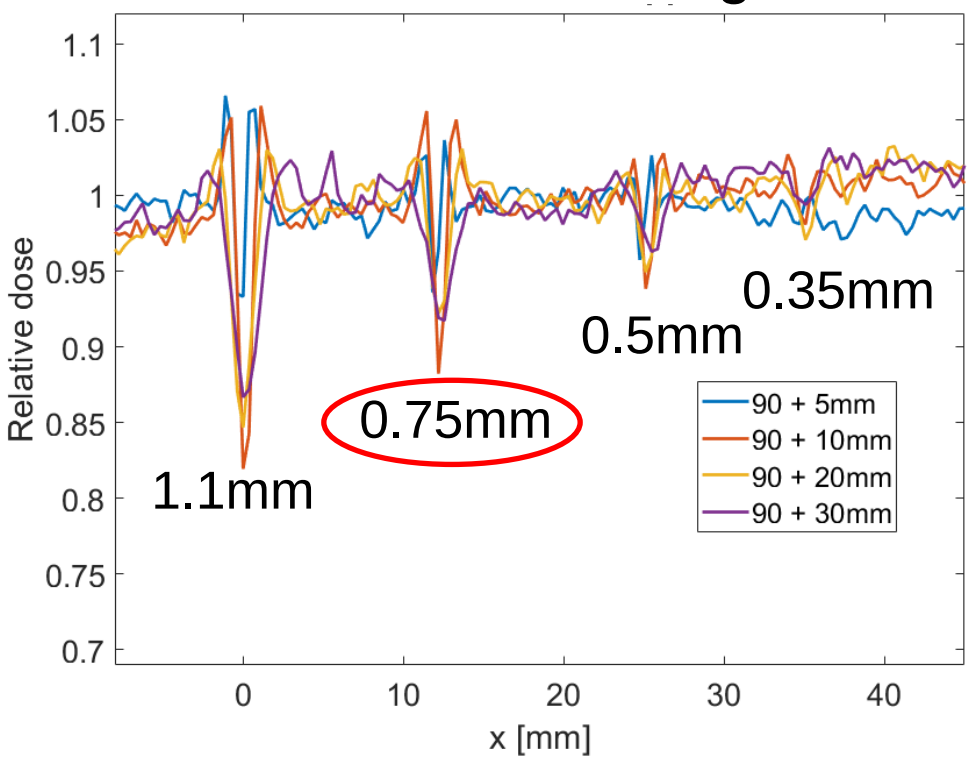
Esben Worm

Fiducial markers

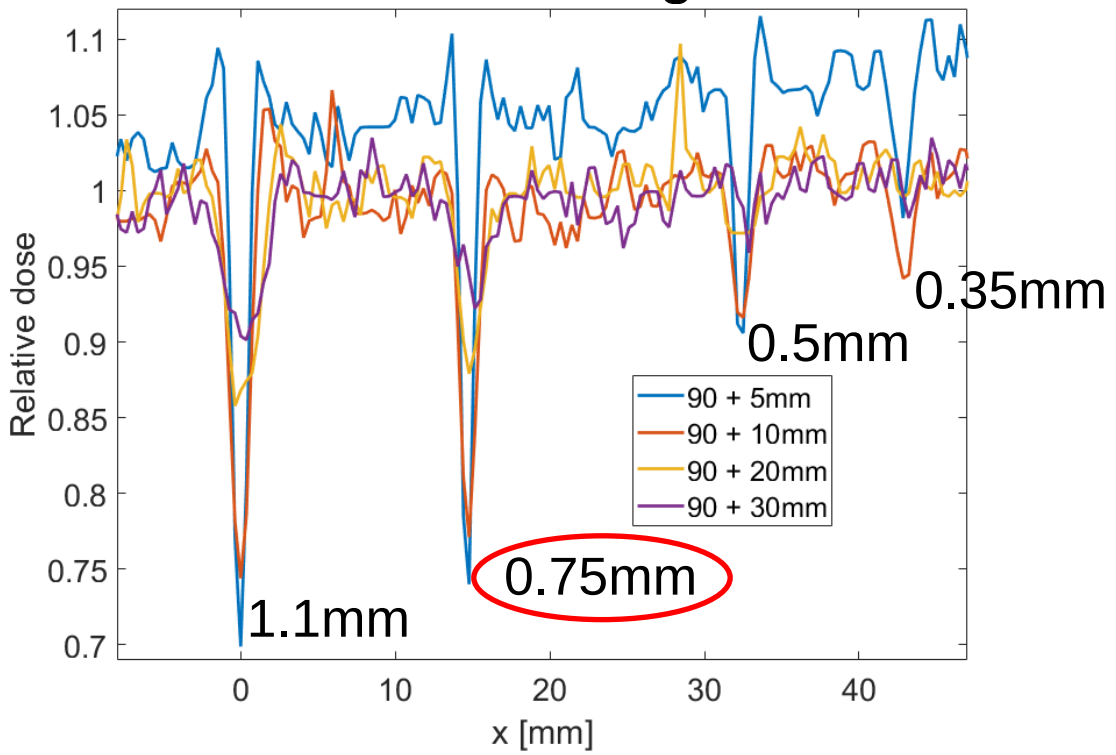
- Transcutaneous implantation
- Marker choice is a compromise between:
  - High visibility in x-ray images (e.g. CBCT projections)
  - Acceptably low perturbation of the proton dose

Fiducial markers: 5 mm Visicoils

Horizontal marker alignment



Vertical marker alignment



<u>0.75mm Visicoil seems to be reasonable compromise</u>

- ~8-10% dose perturbation
- Good x-ray visibility

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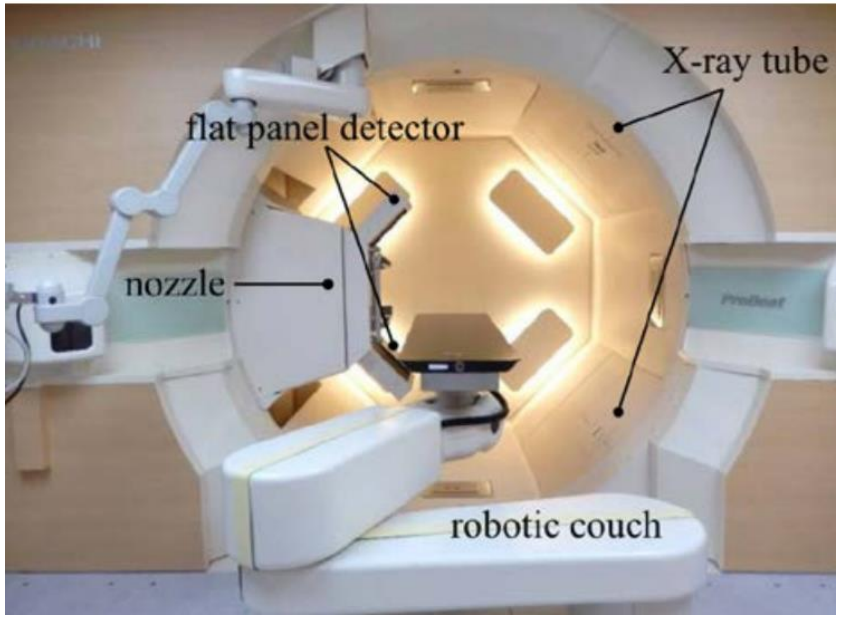
Motion monitoring at treatment: Respiratory signal

- External surrogate
- Gives information on breathing phase and stability

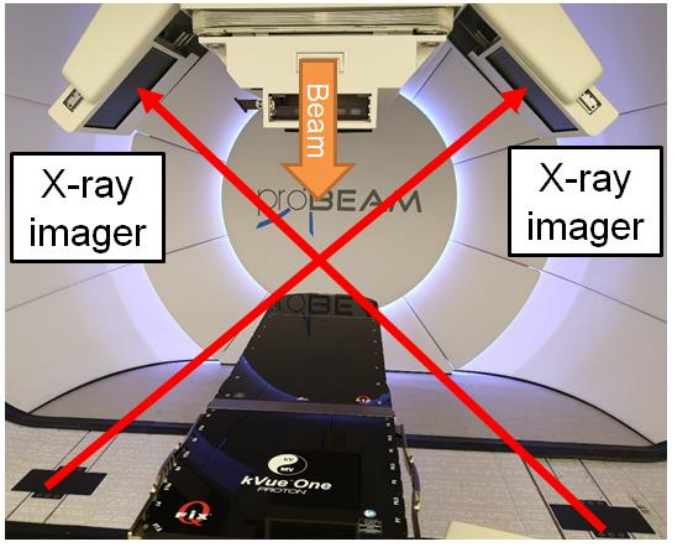
Motion monitoring at treatment: X-ray imaging

- RGPT (Real-time-image gated proton therapy)
  - Hokkaido University
  - Gantry-mounted dual x-ray imagers
  - Intra-treatment fluoroscopy for gating



Yamada, Phys Med 2016

- Varian ProBeam (+other vendors)
  - Gantry-mounted dual x-ray imagers
  - Only used for patient positioning
  - Lacks solutions for fluoroscopy and for imaging during treatment



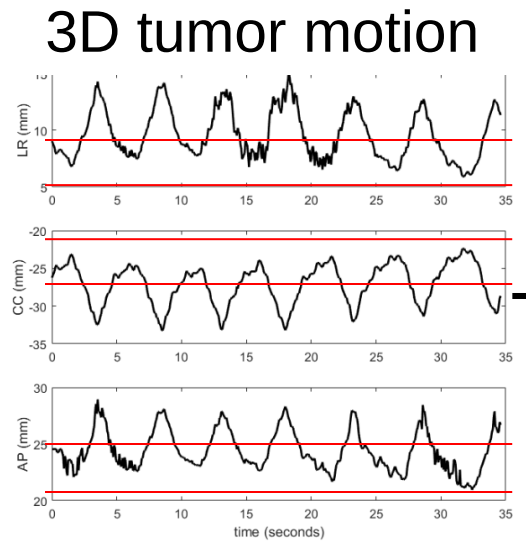
X-ray based motion monitoring at treatment

1. Before treatment: Setup CBCT

CBCT projections (liver)

Maryland Proton Treatment Center

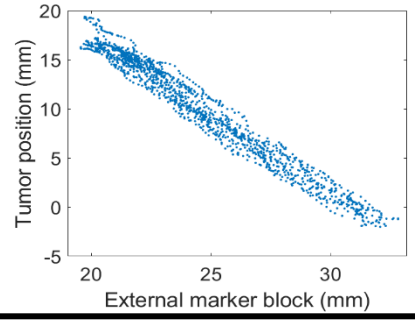
KIM



Auto-calculated couch pos for gating

Respiratory signal

External-internal motion correlation model (ECM)

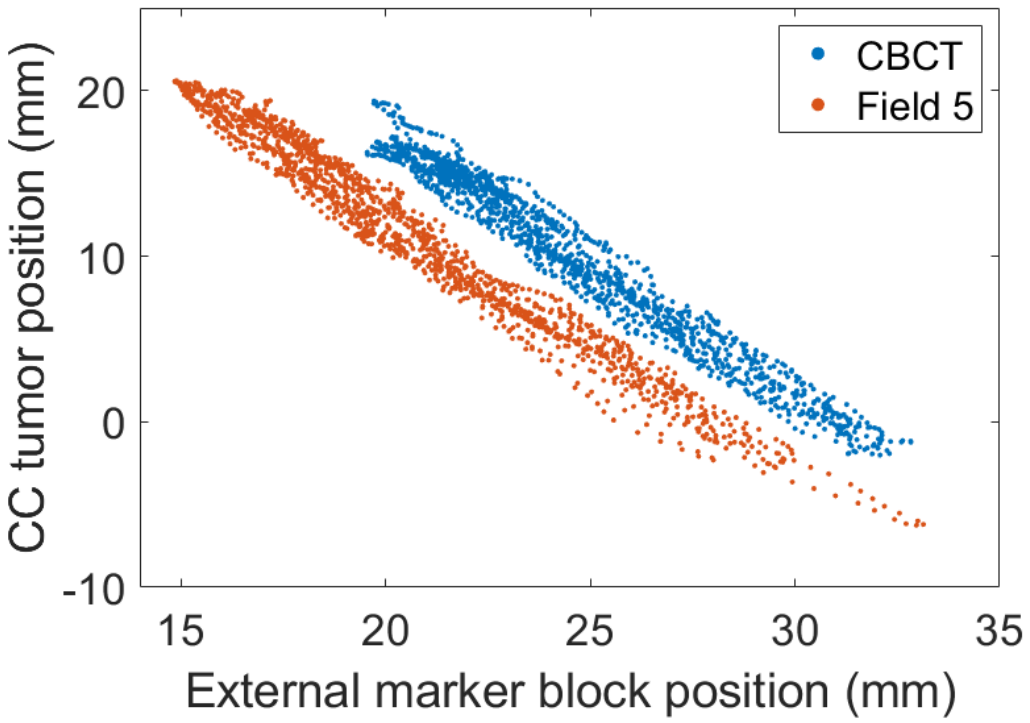


2. During treatment delivery:
   - Continuous respiratory signal → 3D tumor motion estimated from ECM
   - Dual x-ray imaging during the fraction → 3D tumor position → Update ECM

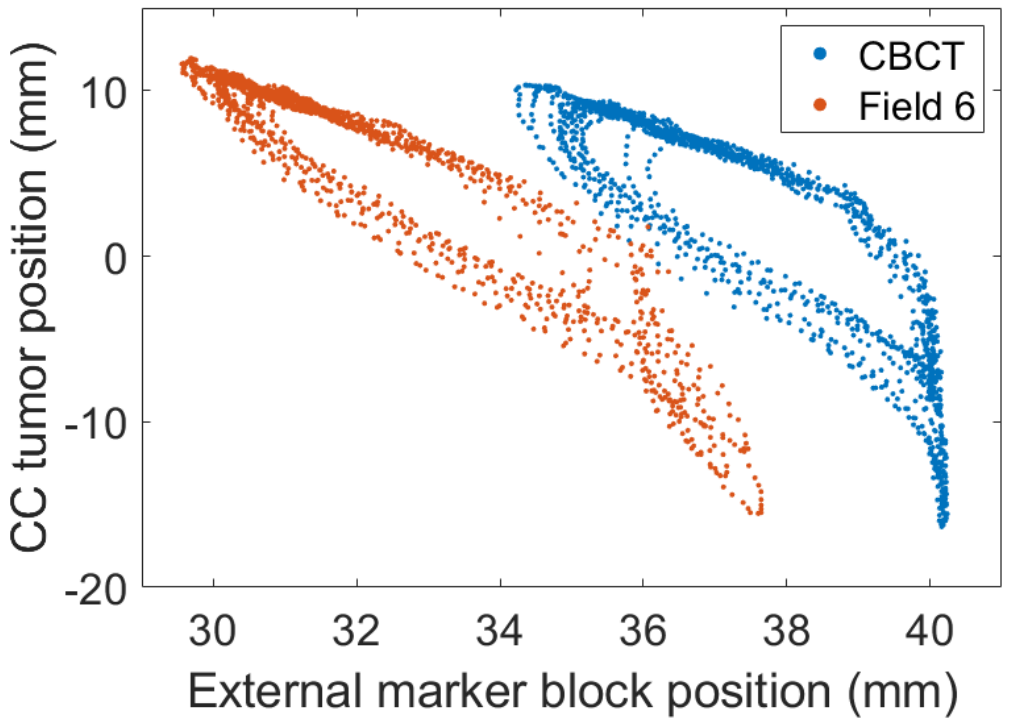
Note: Similar to COSMIK on TrueBeam linac, Bertholet, PMB 2018

Drift of liver tumor ECM during treatment

Patient 1, fx 1



Patient 3, fx 1



From liver Calypso data, unpublished

Intrafaction x-ray imaging for ECM update

Three possibilities:

1. 10-20 x-ray image pairs before each field (The CyberKnife way)

2. 10 seconds dual x-ray fluoroscopy before each field

3. Dual x-ray fluoroscopy during each field

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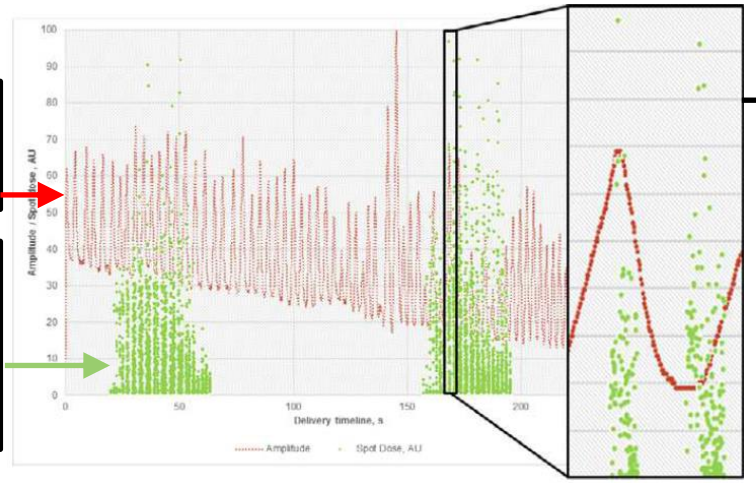
Motion-including dose reconstruction

Method 1: 4DCT dose reconstruction

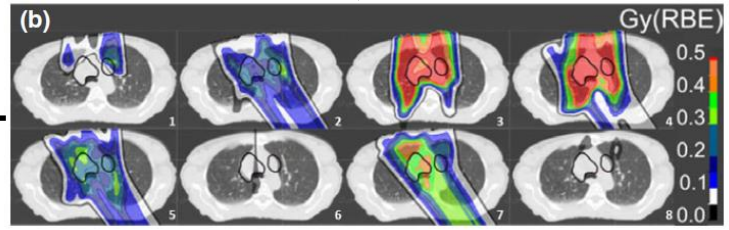
Recorded breathing signal

Spot delivery times in machine log files

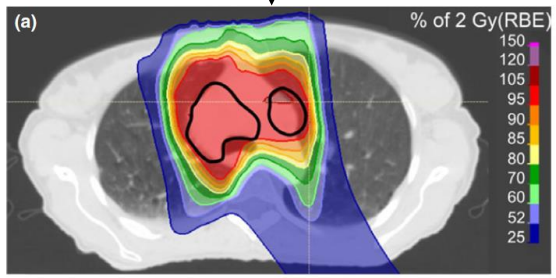


Spots distributed into 4DCT phases

4DCT phase specific doses in TPS



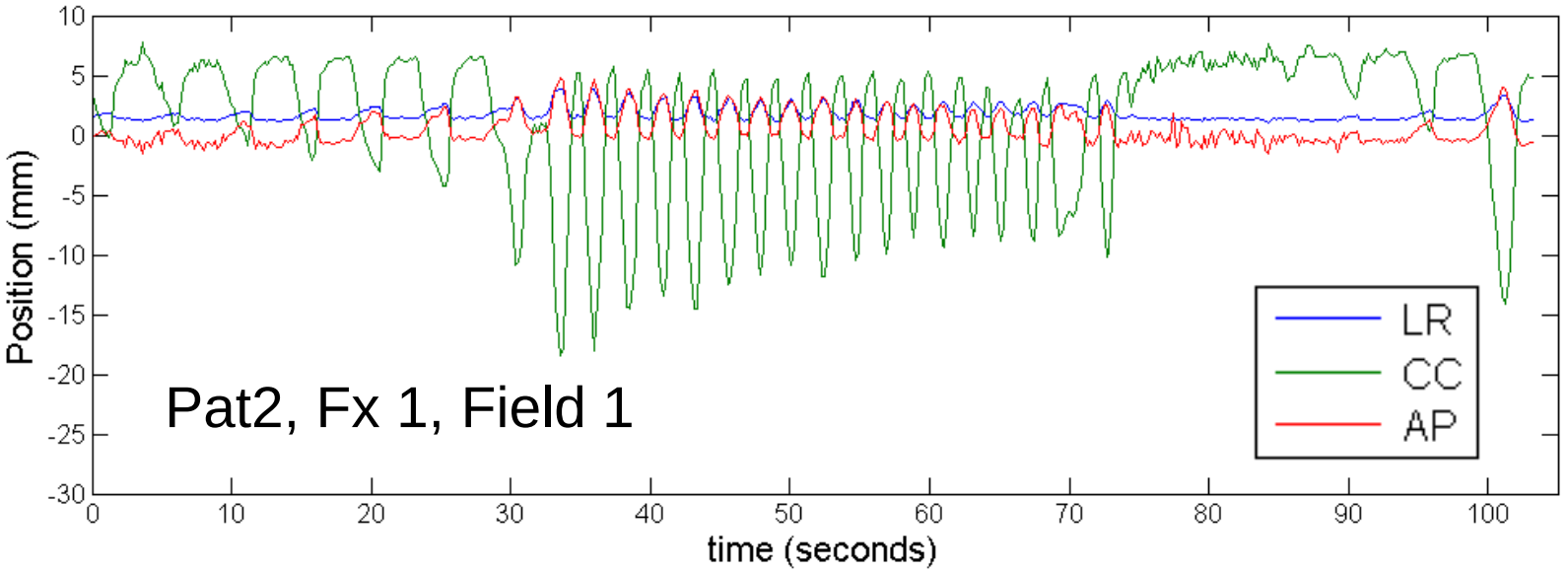
DIR-based dose accumulation



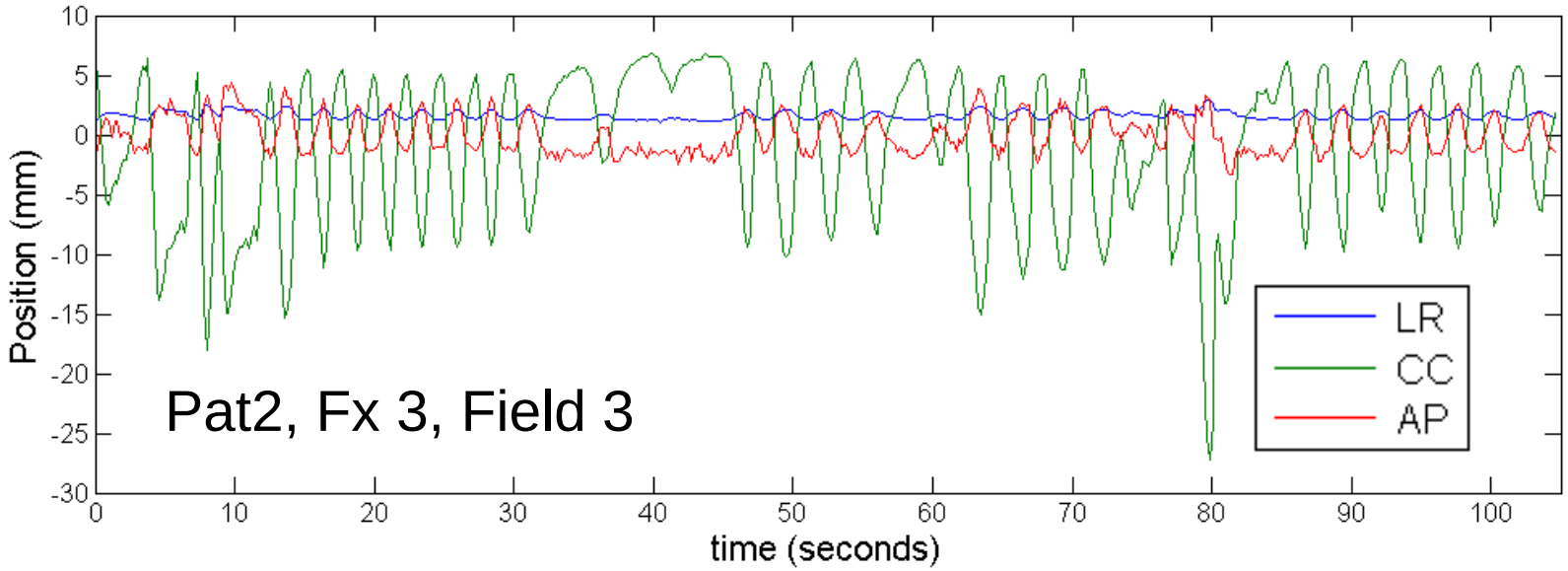
Meijers, Medical Physics 2019

- Basic assumption: 4D anatomy at treatment = 4D anatomy in 4DCT
  - The anatomy at treatment is fully described by the breathing phase

Liver tumor motion during (x-ray) treatments (KIM)



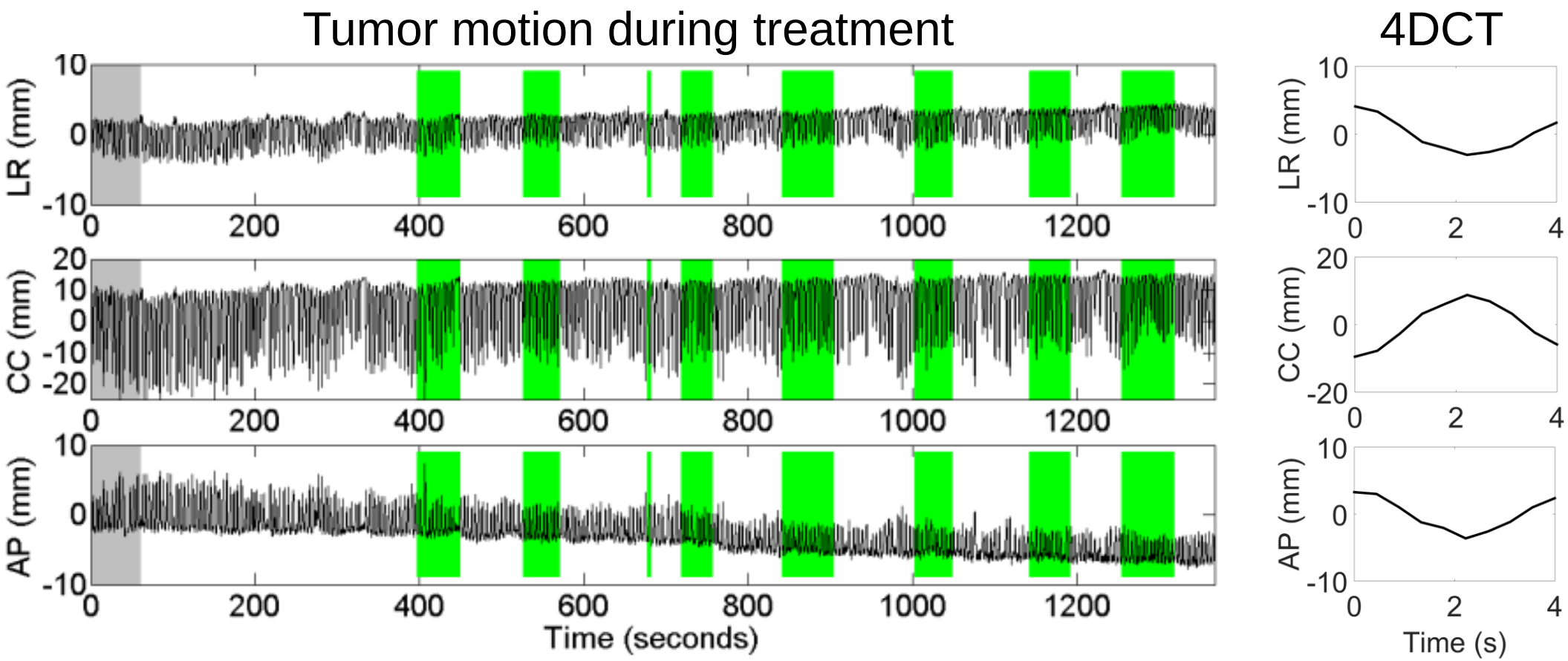
CC motion
4DCT



CC motion
4DCT

Poulsen, Radiother Oncol 2014

Liver tumor motion during (x-ray) treatments (Calypso)



Worm, IJORBP 2018

Motion-including dose reconstruction

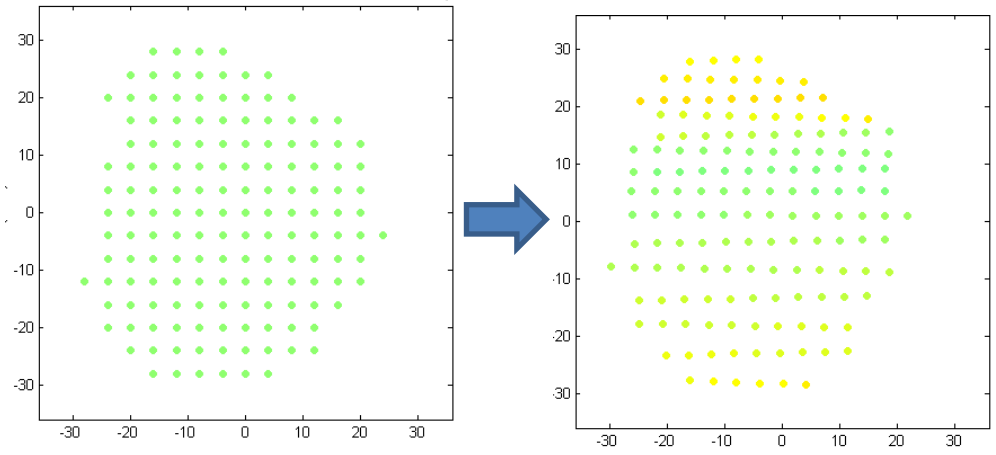
Method 2: Spot-shift dose reconstruction

- Basic assumption: Respiratory deformations can be neglected in the tumor region

1. Manipulate the original treatment plan:

- Replace static spot map with motion spot map
- Emulate depth motion as proton energy shifts (*)

2. Recalculate motion-including plan in TPS

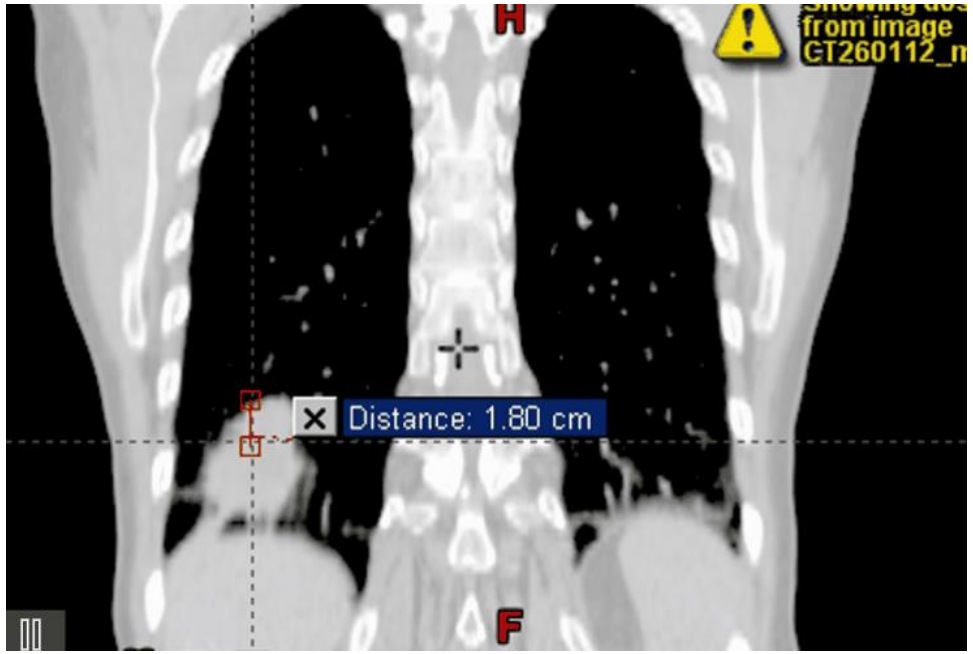


(*)Range[g/cm^2] = 0.00244 E[MeV]$^{1.75}$ (Paganetti 2012)

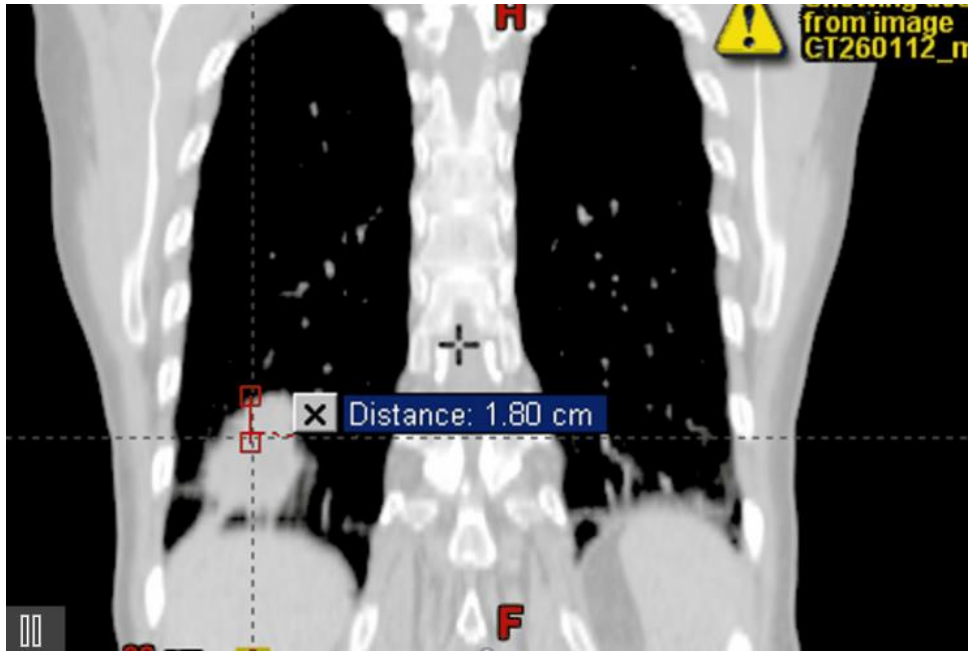
Colvill, PMB 2018

4DCT versus spot-shift dose reconstruction

4DCT

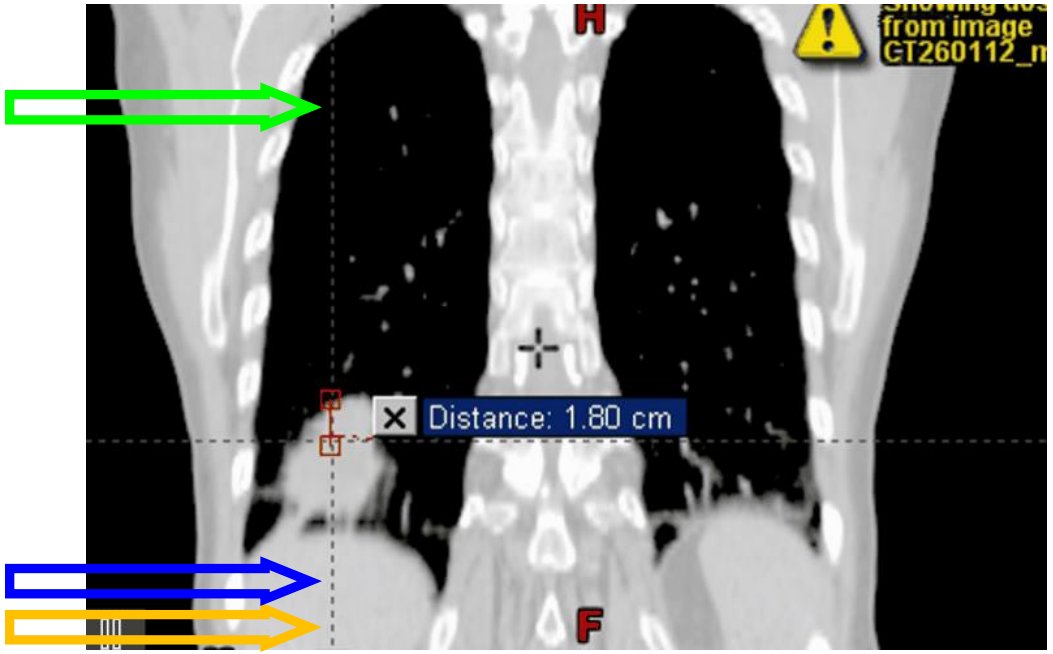


Spot shift

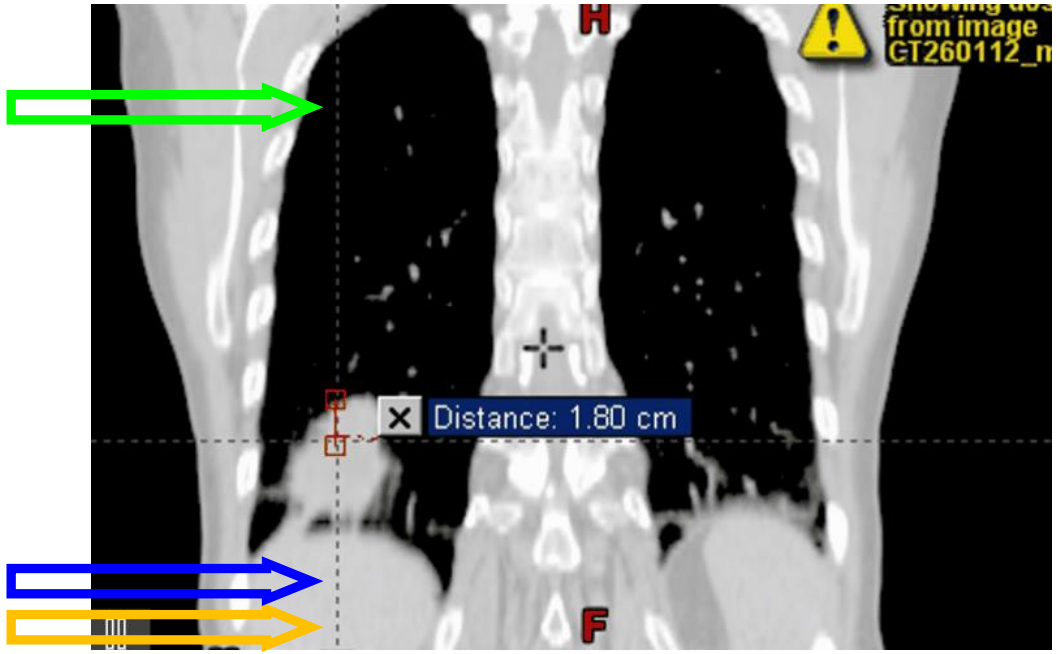


4DCT versus spot-shift dose reconstruction

4DCT: Exhale



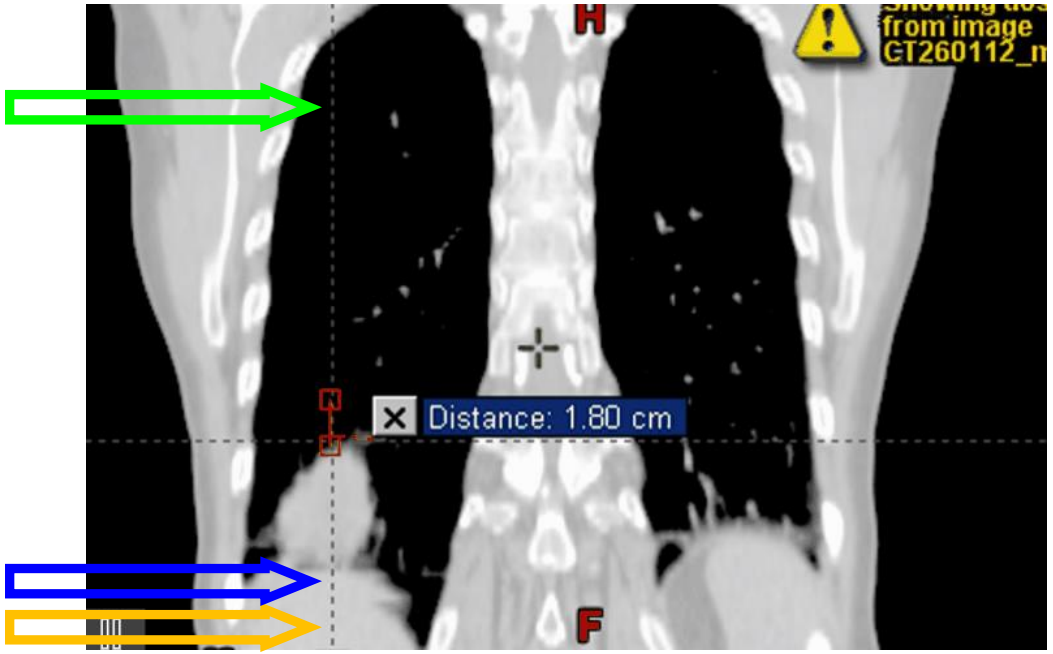
Spot shift: Exhale



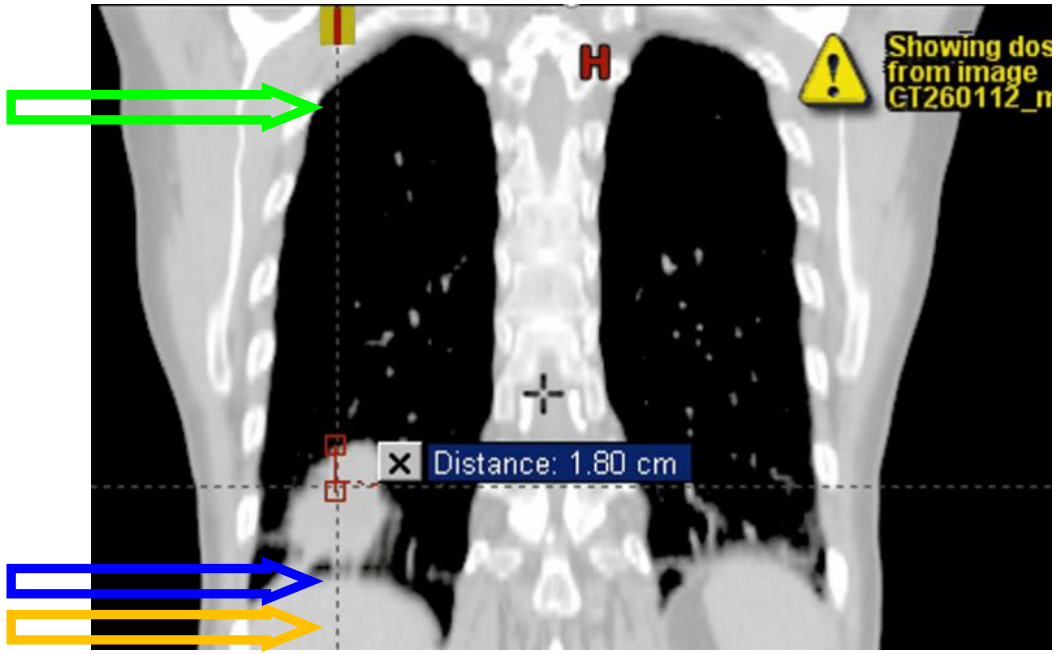
- Exhale phase (reference phase): Identical anatomy

4DCT versus spot-shift dose reconstruction

4DCT: Inhale

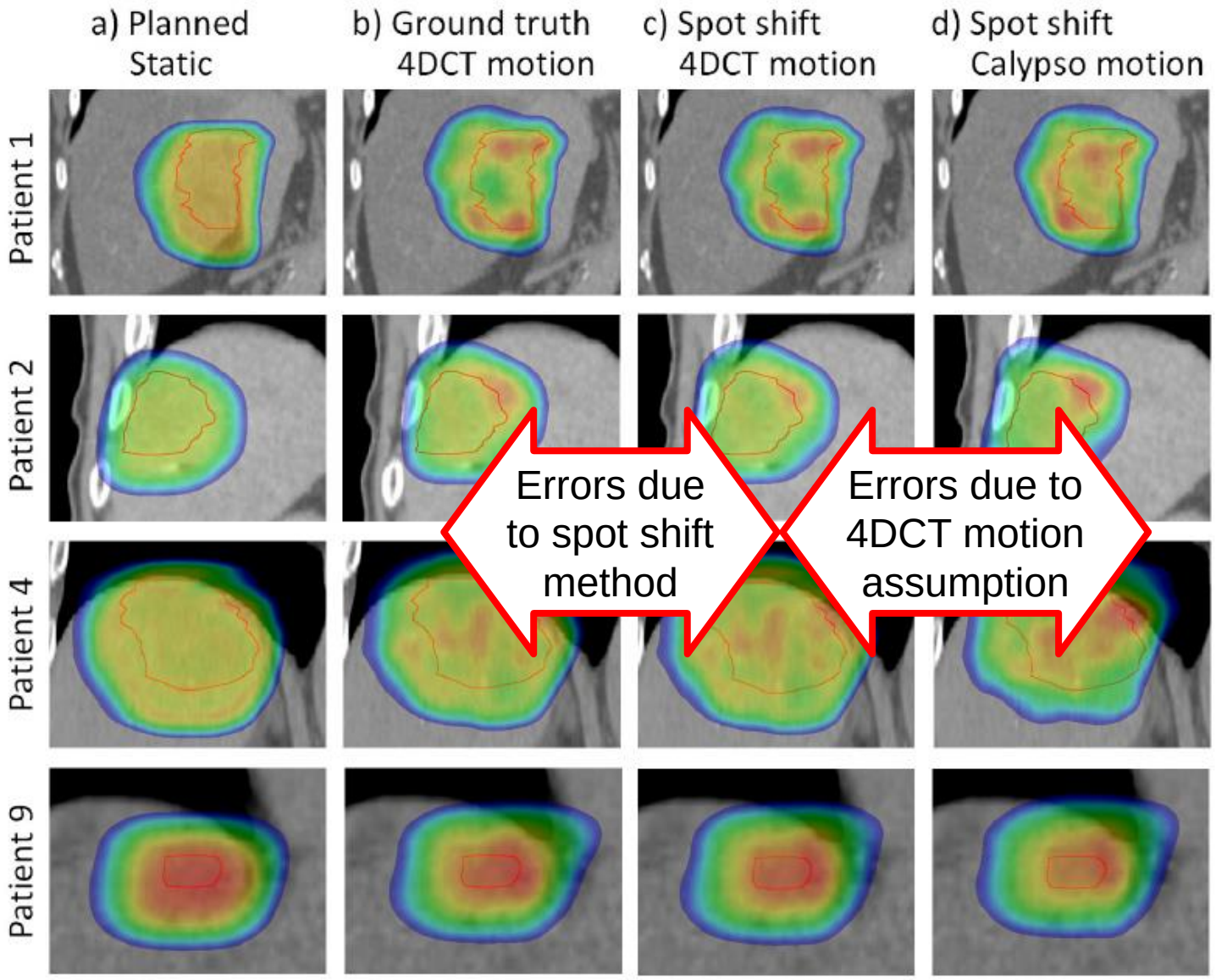


Spot shift: Inhale (=shifted exhale)



- Exhale phase (reference phase): Identical anatomy
- Inhale phase:
  - Identical liver and diaphragm shape if motion is rigid
  - Wrong entrance beam path through rib cage

4DCT versus spot-shift dose reconstruction



Colvill, PMB 2018

Spot shift reconstructed dose in liver:

- Similar to 4DCT dose in tumor
- Less good in low dose regions
- RMSE due to spot shift method: 2.5% (in >70% dose region)
- Can model the actual tumor motion during treatment (Calypso)
- RMSE due to 4DCT motion assumption: 6.3% (>70% dose region)

Motion-including dose reconstruction

Method 2: Spot-shift dose reconstruction

- Main limitation:
  - Only valid for tissue that moves rigidly with the tumor
    - Not good for OARs, not good in thorax

- Main advantage:
  - Accounts for actual tumor motion seen at treatment (incl drift, setup errors, BH)

Motion-including dose reconstruction

Method 3: Dose reconstruction in 4DCT-MRI(*)

- Generate 4DMRI based on internal 2D navigator for image sorting(**)
- Deform static reference 3DCT (from possibly another subject) to 4DMRI
- Accounts for deformations, cycle-to-cycle variations and drift motion
- Used in several studies of motion mitigation strategies (repainting etc)
- Limitation for dose reconstruction:
    - The 4DMRI is not the actual patient anatomy during treatment

(*) Boye, Med Phys 2013. Bernatowicz, IJROBP 2016

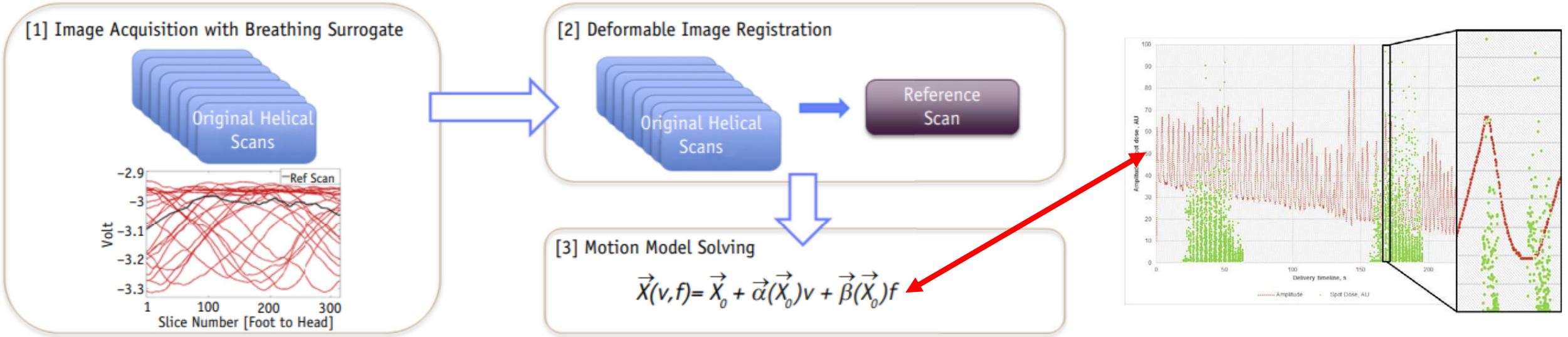
(**) von Siebenthal, PMB 2007

Other 4D motion models

- 5DCT (*)
- 25 free-breathing fast helical CT scans
- DIR to 1st scan

  ⇒ Deformation vector $\vec{X}(v,f)$ for each voxel as function of the amplitude (v) and time derivative (f) of the breathing signal

  ⇒ CT volume as function of v and f



(*)Low, PMB 2013. Dou, IJROBP 2015

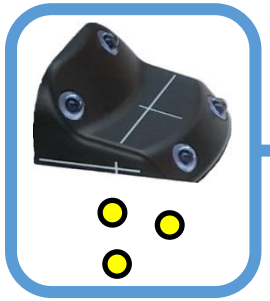
Motion-including dose reconstruction

Method 4: DoseTracker

- Developed for real-time motion-including dose reconstruction for x-ray RT

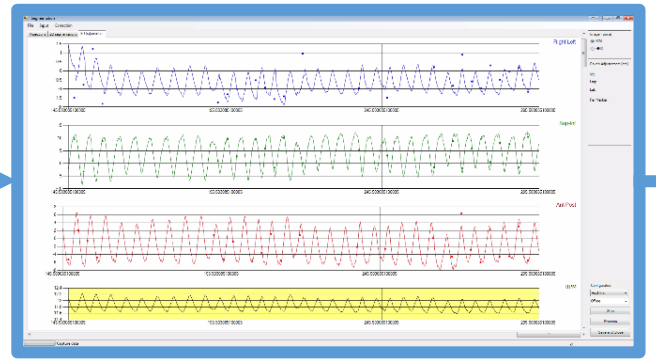
Ravkilde, PMB 2014. Skouboe, Radiother Oncol 2019

DoseTracker with real-time input from COSMIK (liver)



COSMIK

Tumor position



Treatment machine

Treatment machine parameters

DoseTracker (during treatment)

Calculate tumor dose
- Actual
- Planned

Skouboe *et al*, Radiother Oncol 2019

Motion-including dose reconstruction

Method 4: DoseTracker

- Developed for real-time motion-including dose reconstruction for x-ray RT

- Ongoing adaptation to proton therapy:
  - Pencil-beam dose algorithm
  - Real-time ray-tracing through CT matrix

Ravkilde, PMB 2014. Skouboe, Radiother Oncol 2019

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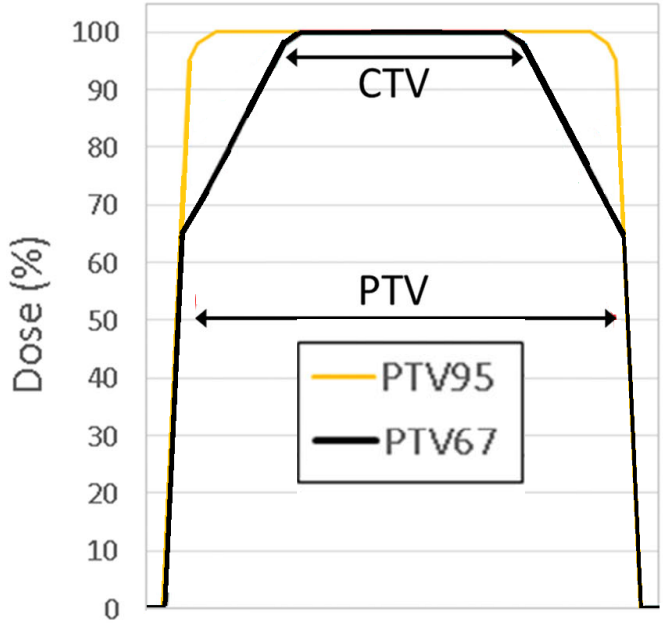
Non-uniform dose prescription

- Often used for x-ray based SBRT
  - Allows higher tumor dose for same toxicity risk

- Could non-uniform dose prescription be feasible for proton SBRT of liver tumors?

Prescribed dose in x-ray SBRT

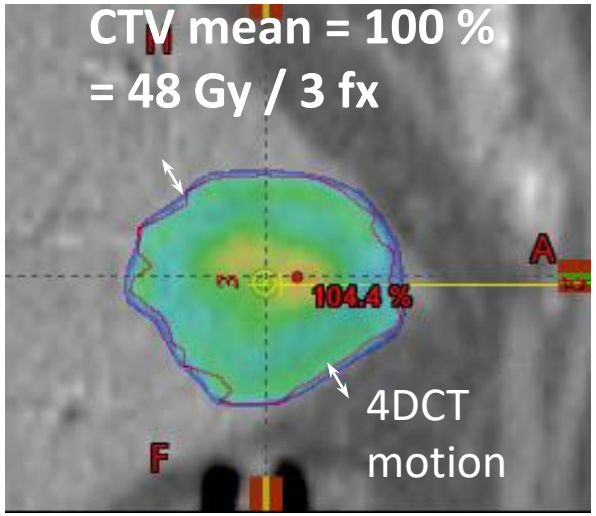


Worm *et al*, PMB 2021

Generation of iso-toxic proton plans

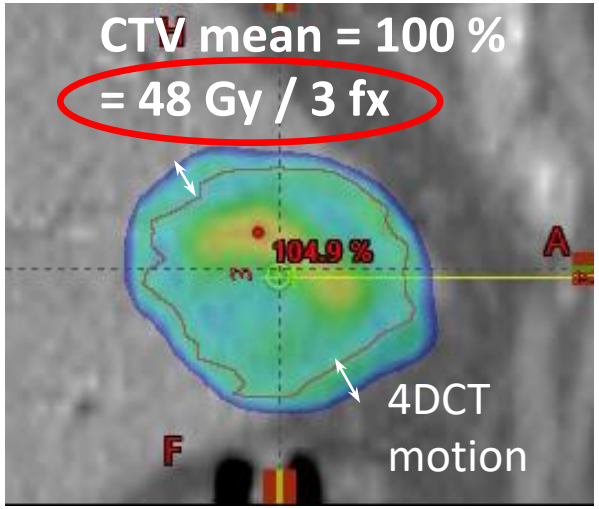
Non-uniform robust plan
- D98 ≥ 95% without motion
- D98 ≥ **67%** with 4DCT motion

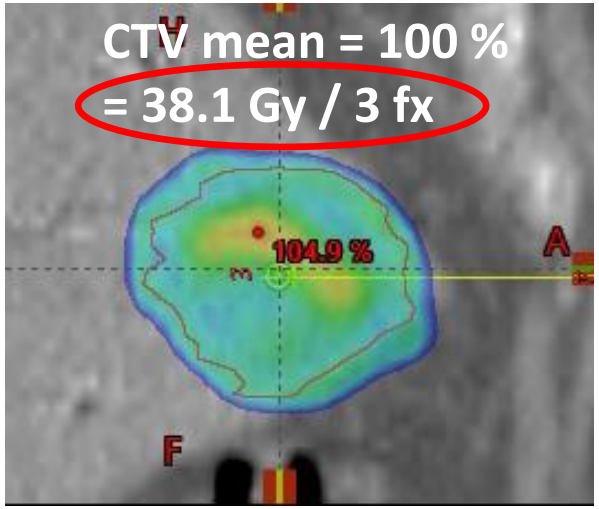
Uniform robust plan
- D98 ≥ 95% without motion
- D98 ≥ **95%** with 4DCT motion



Compare NTCP for RILD*

Iso-toxic* (RILD)





* LKB RILD NTCP model, Dawson IJROBP, 2002

Worm *et al*, PMB 2021

Treatment simulations

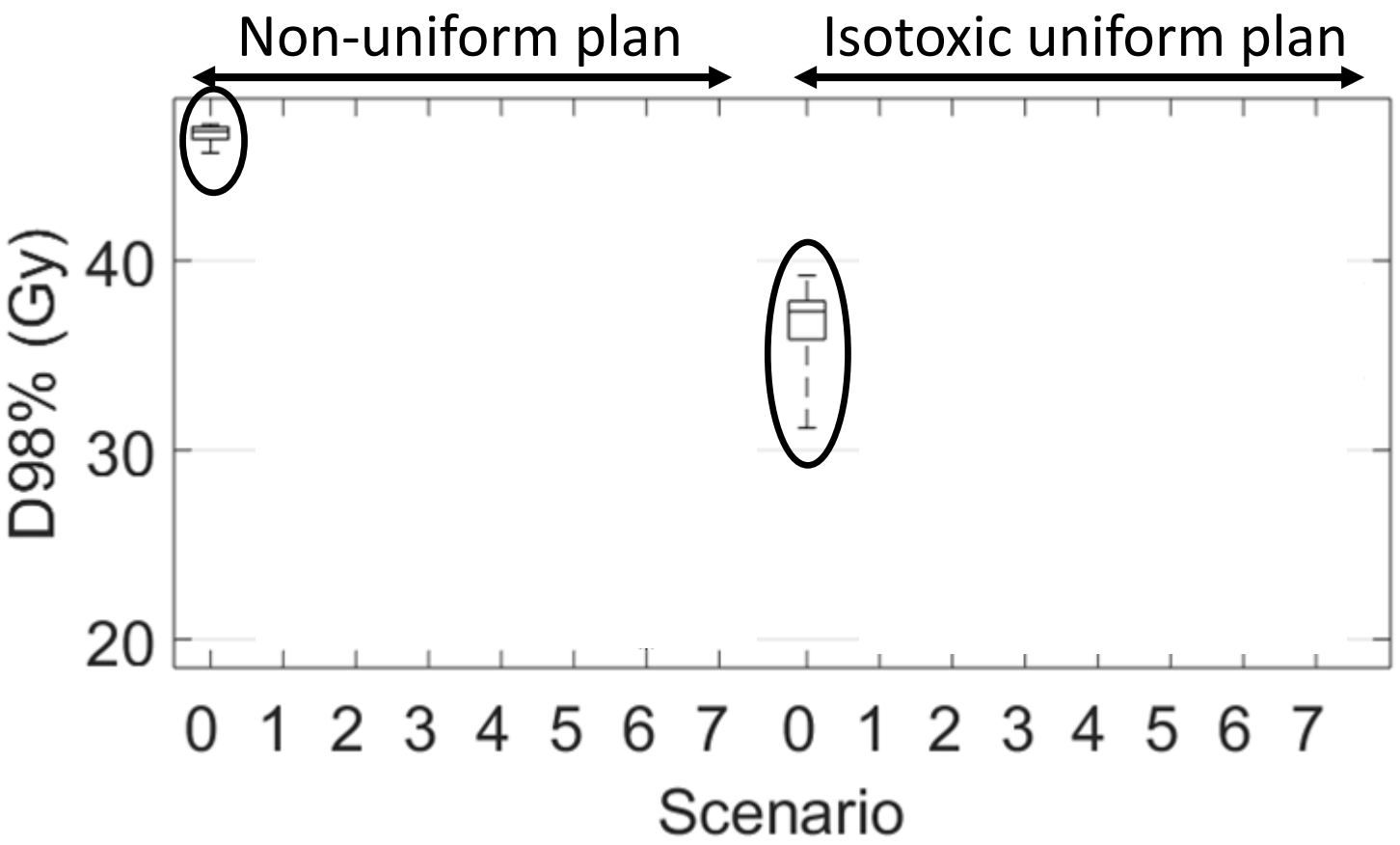
14 liver SBRT patients, 42 fractions simulated

- Non-uniform and uniform plans
- With 4DCT motion and Calypso-measured motion
- With and without breath-sampling repainting (*)
  - Even distribution of repaintings over the breathing cycle
  - Wait time between spots used to extend layer duration to one cycle
  - 1,2,4,8 or 16 interlaced repaintings depending on spot MU
  - Very efficient interplay migration after few fractions
- Dose reconstruction by spot-shift method

(*) Poulsen, IJROBP 2018

Worm *et al*, PMB 2021

CTV D98 for non-uniform and uniform plans



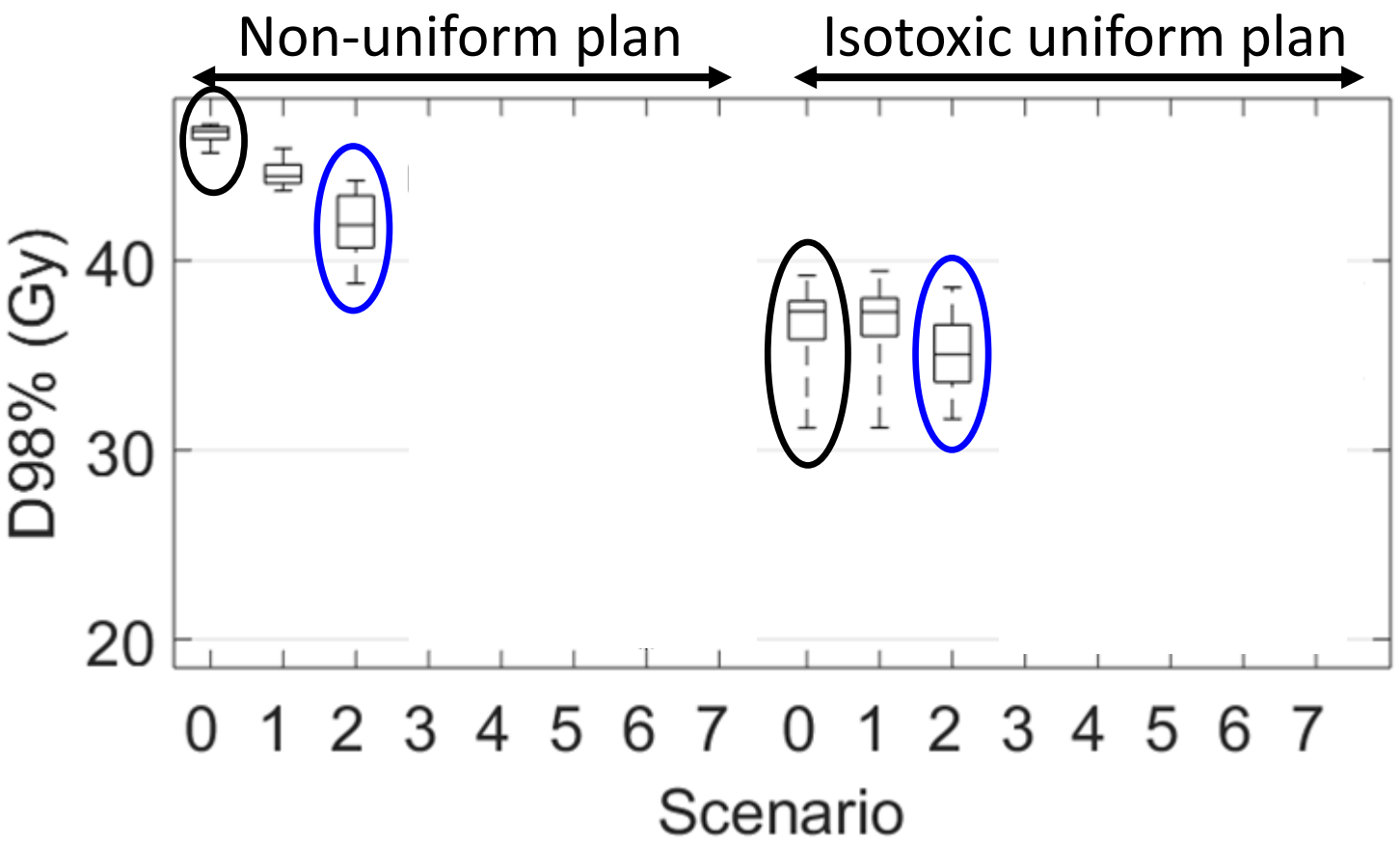
Scenarios:

0. Static
1. 4DDose
2. 4DCT
3. 4DCT repainted
4. Calypso 1 Fx
5. Calypso 3 Fx
6. Calypso 1 Fx, repainted
7. Calypso 3 Fx, repainted

Static:

- Non-uniform plans: Average D98 = 46.6 Gy
- Uniform plans: Average D98 = 36.7 Gy

CTV D98 for non-uniform and uniform plans



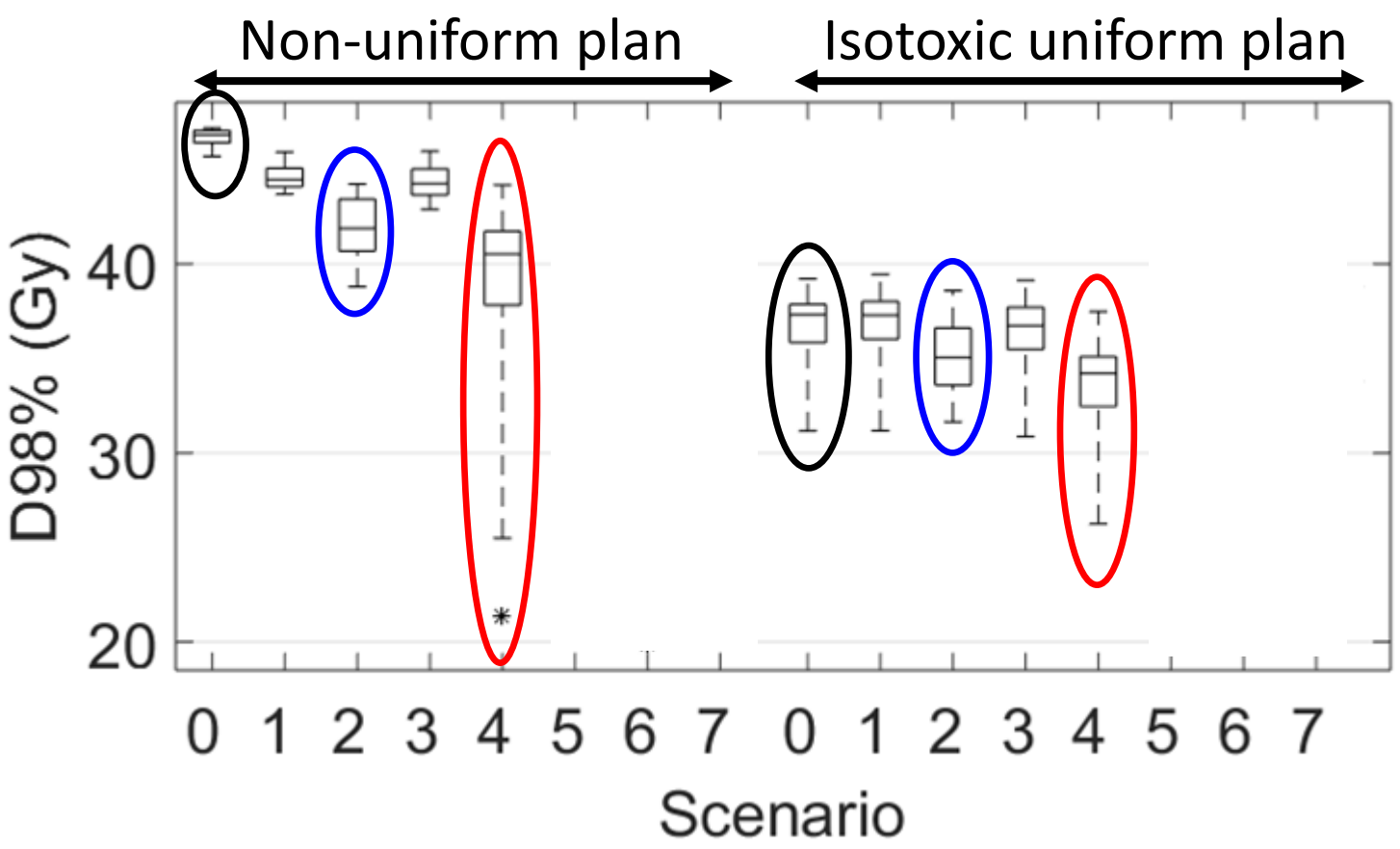
Scenarios:

0. Static
1. 4DDose
2. 4DCT
3. 4DCT repainted
4. Calypso 1 Fx
5. Calypso 3 Fx
6. Calypso 1 Fx, repainted
7. Calypso 3 Fx, repainted

4DCT motion:

- Largest relative drop in D98 for non-uniform plans, but still higher absolute D98

CTV D98 for non-uniform and uniform plans



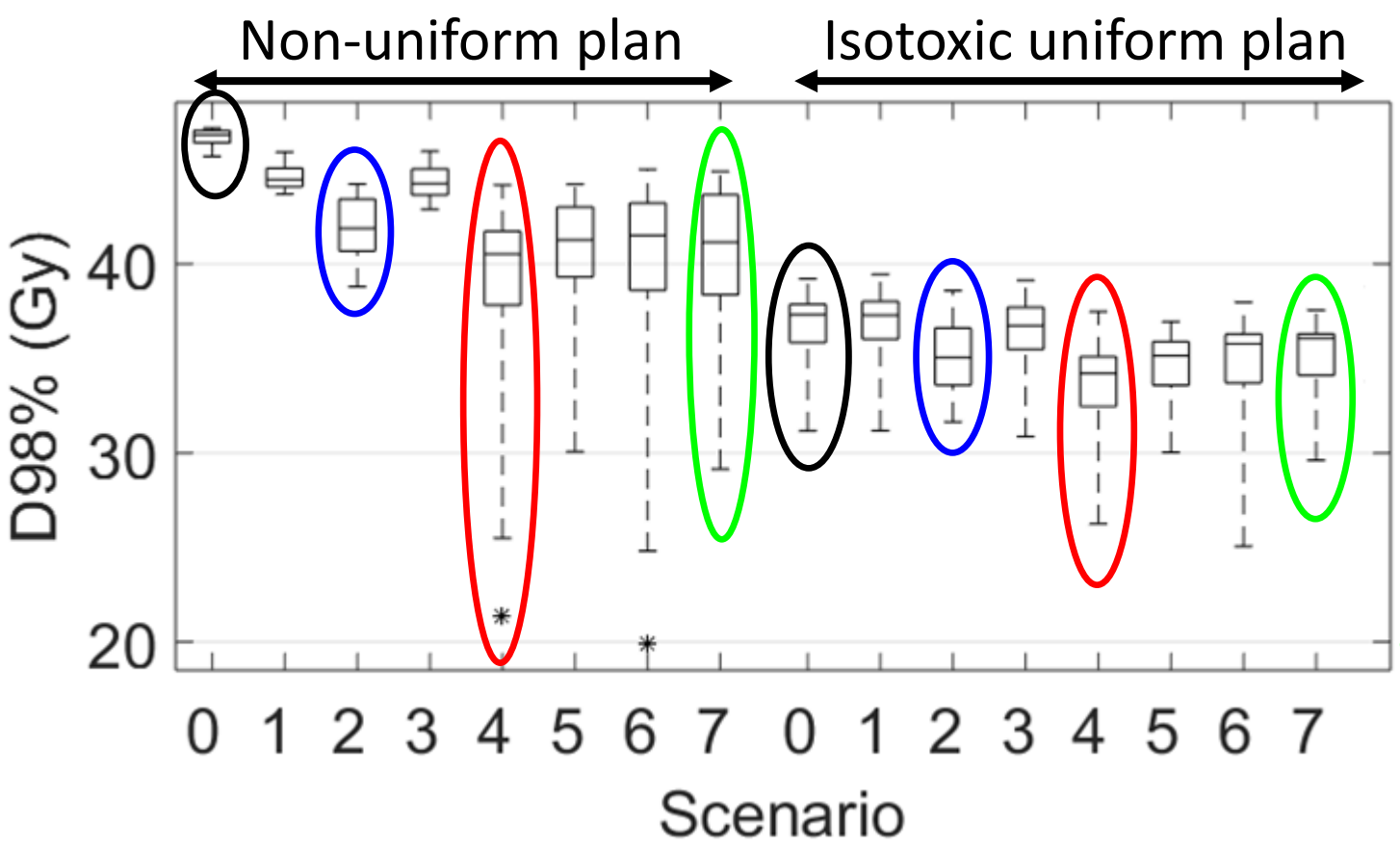
Scenarios:

0. Static
1. 4DDose
2. 4DCT
3. 4DCT repainted
4. Calypso 1 Fx
5. Calypso 3 Fx
6. Calypso 1 Fx, repainted
7. Calypso 3 Fx, repainted

Calypso motion, delivery of 1 fraction:

- Larger drop in D98 than with 4DCT motion and most for non-uniform plans
- Non-uniforms plans have highest D98 for 37 out of 42 fractions

CTV D98 for non-uniform and uniform plans



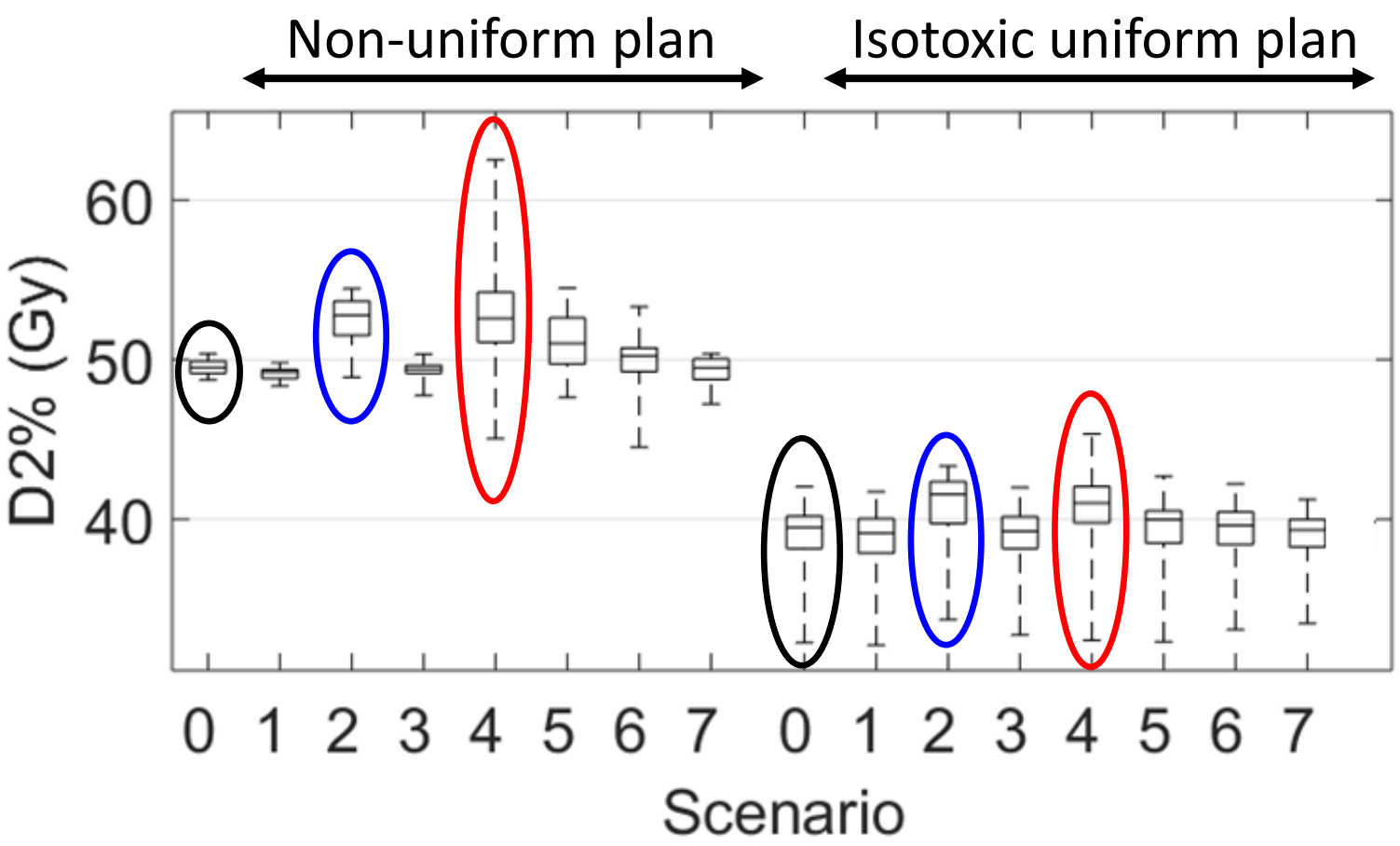
Scenarios:

0. Static
1. 4DDose
2. 4DCT
3. 4DCT repainted
4. Calypso 1 Fx
5. Calypso 3 Fx
6. Calypso 1 Fx, repainted
7. Calypso 3 Fx, repainted

Calypso motion, delivery of 3 fraction with repainting:

- Non-uniforms plans have highest D98 for 13 out of 14 patients
- On average D98 was 15.2 % higher with non-uniform plans

CTV D2 for non-uniform and uniform plans



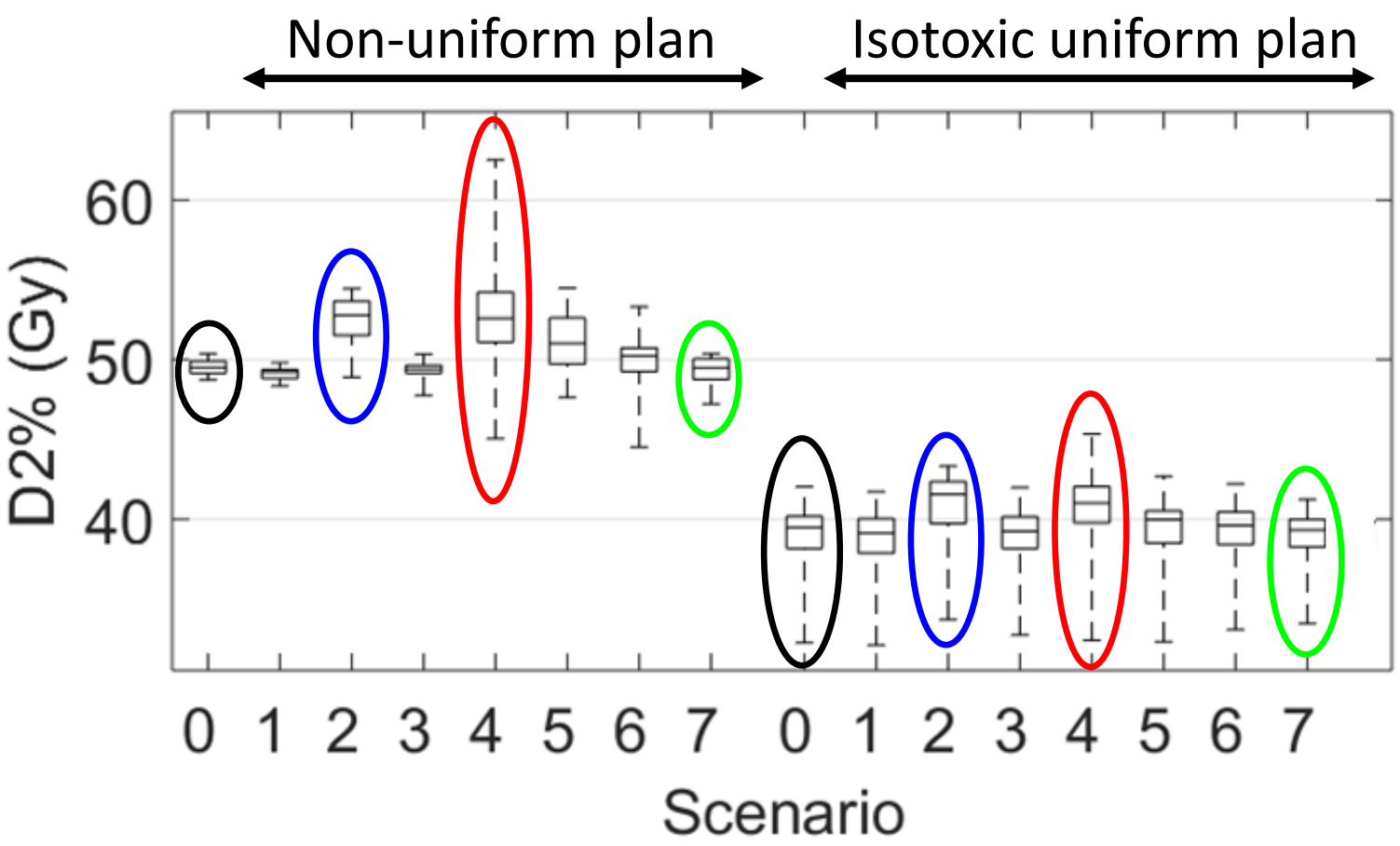
Scenarios:

0. Static
1. 4DDose
2. 4DCT
3. 4DCT repainted
4. Calypso 1 Fx
5. Calypso 3 Fx
6. Calypso 1 Fx, repainted
7. Calypso 3 Fx, repainted

Calypso motion, delivery of 1 fraction:

- Large D2 variations because of interplay effects

CTV D2 for non-uniform and uniform plans



Scenarios:

0. Static
1. 4DDose
2. 4DCT
3. 4DCT repainted
4. Calypso 1 Fx
5. Calypso 3 Fx
6. Calypso 1 Fx, repainted
7. Calypso 3 Fx, repainted

Calypso motion, delivery of 3 fractions with repainting:

- Small D2 variations (effective interplay mitigation)

Summary: Non-uniform dose prescription

- The gain in CTV dose by non-uniform dose prescription clearly outweighed the lower robustness against motion
- Non-uniform dose-prescription may provide a better trade-off between achievable CTV dose and normal tissue dose for proton therapy in the liver

Agenda

- Proton trial for HCC
- Gating latency, fiducial markers
- Motion monitoring at treatment
- Motion-including dose reconstruction
- Non-uniform dose prescription
- Summary

Summary: DCPT plans for PT of HCC

- National HCC protocol almost ready to go
- Non-gated or exhale gated (FB or BH)
- No repainting planned (15 fractions)
- Setup CBCT $\rightarrow$ 60 sec tumor motion trajectory $\rightarrow$ ECM
- ECM + intrafraction x-ray imaging $\rightarrow$ tumor motion during treatment
    - Spot shift dose reconstruction for each fraction
    - Gradual move from offline to online real-time with DoseTracker

Summary: Some discussion points

- Use of fiducial markers in the liver
- How best to monitor liver tumor motion during treatment?
- Motion-including dose reconstruction?
- How to make more realistic and accessible patient models?
- Uniform versus non-uniform dose prescription
- How to convince vendors to develop software and workflows for better use of their built-in x-ray imagers (fluoroscopy, dual-energy CBCT, etc)?

Thank you

- Esben Worm
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