



IMAGE GUIDANCE AND REGISTRATION – PARTICULAR CHALLENGES IN CASE OF RE- IRRADIATION

MARTIN F. FAST

ACKNOWLEDGEMENTS / SLIDE CREDITS



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CONFLICTS OF INTEREST

- Financial and technical support from Elekta AB under research agreements
- NKI-AvL is part of the Elekta Atlantic MR-linac Research Consortium



<https://mrrt.elekta.com/>

OUTLINE

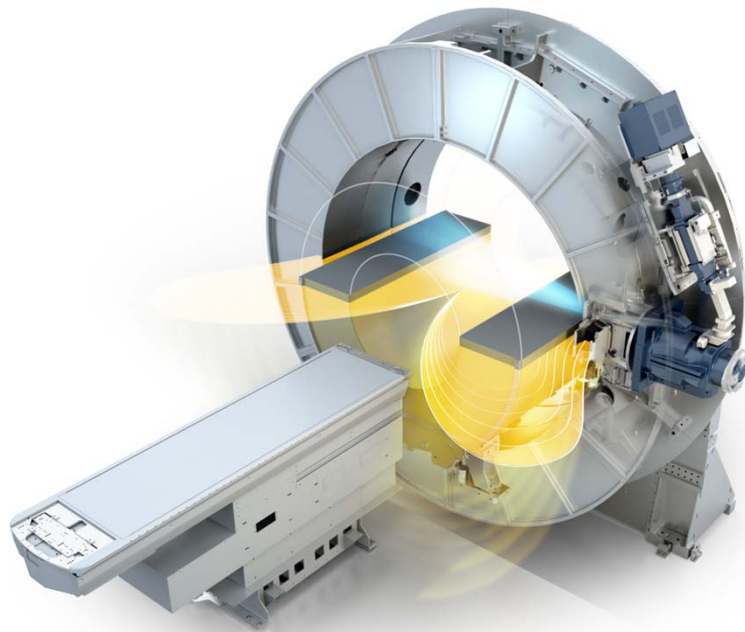
THE FUTURE IS NOW – MRI-GUIDED RADIOTHERAPY

THE WORKING HORSE – CBCT-GUIDED RADIOTHERAPY

DOSE ACCUMULATION – READY FOR CLINICAL USE?

IMAGE REGISTRATION – CHALLENGES AND OPPORTUNITIES

ELEKTA UNITY MR-LINAC



- 1.5 T Philips magnet
- 7 MV linac
- 22x56 cm² treatment field
- Real-time cine-MR imaging
- MLC based on Agility design

Photo courtesy: Elekta AB

ELEKTA UNITY MR-LINAC AT NKI-AVL

INSTALLATION

- May 2016

INITIAL RESEARCH PHASE

- Phantom measurements
- Volunteer imaging
- Patient volunteer imaging

FINAL UPGRADE

- June-August 2018

Elekta Unity

Celebrating CE mark



ELEKTA UNITY MR-LINAC AT NKI-AVL

First patient treated TODAY
(September 6th, 2018)



MR-LINAC AT NKI

Clinical focus

- Prostate cancer
- Rectal cancer
- *Oligometastases (especially liver)*

Technical focus

- EPID dosimetry
- *Practical 4D solutions*
- Quantitative imaging

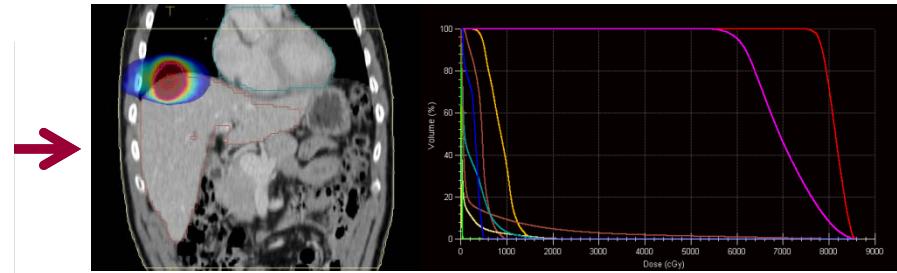
NKI'S LIVER RT WORKFLOW FOR THE MR-LINAC

PRE-TREATMENT IMAGING

4D-CT + 4D-MRI



TREATMENT PLANNING



DAILY IMAGING

4D-MRI

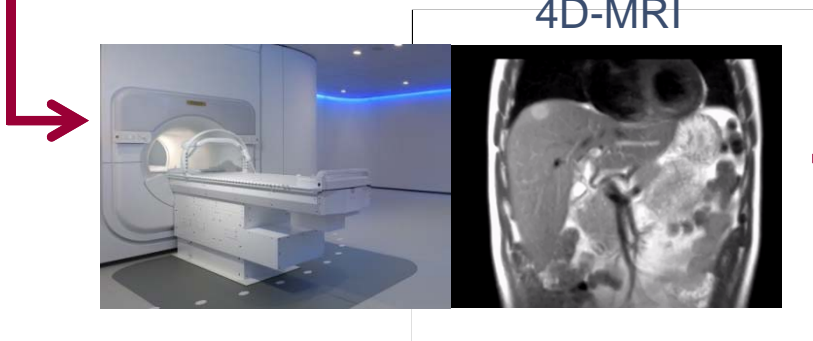
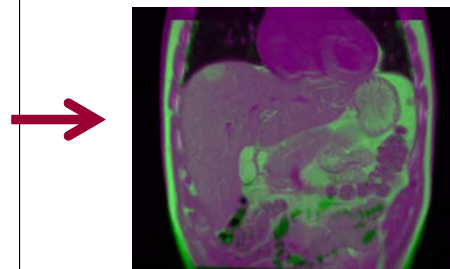
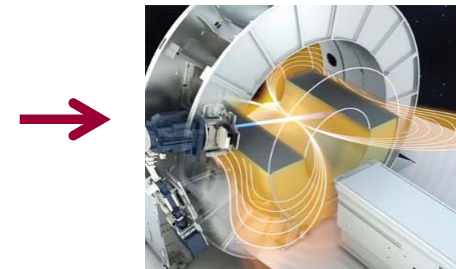


IMAGE REGISTRATION & PLAN ADAPTATION



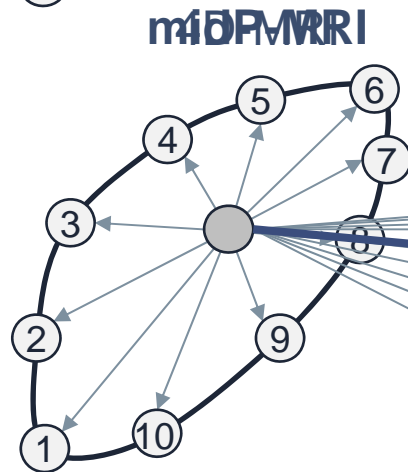
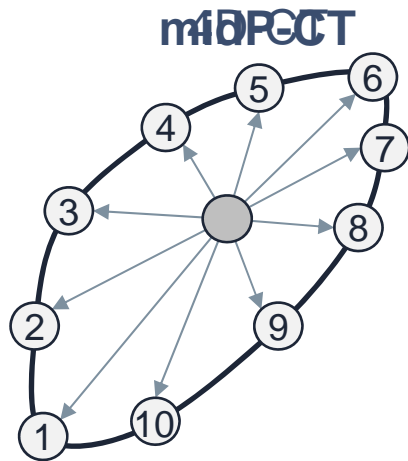
TREATMENT DELIVERY



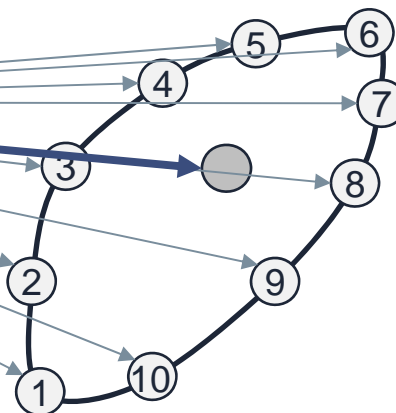
MID-POSITION STRATEGY ON THE MR-LINAC

Simulation

Pre-beam



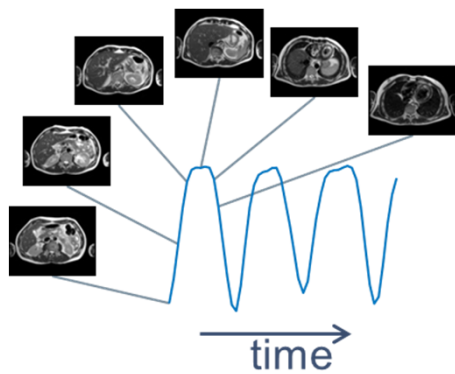
Daily
4D-MRI



**Simple
Dose
Shift**

SELF-GATED 4D-MRI

2D SEQUENCE



DATA ACQUISITION

Data from arbitrary respiratory phases



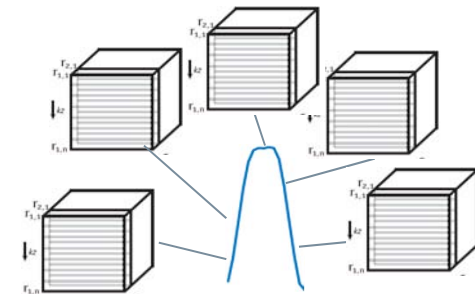
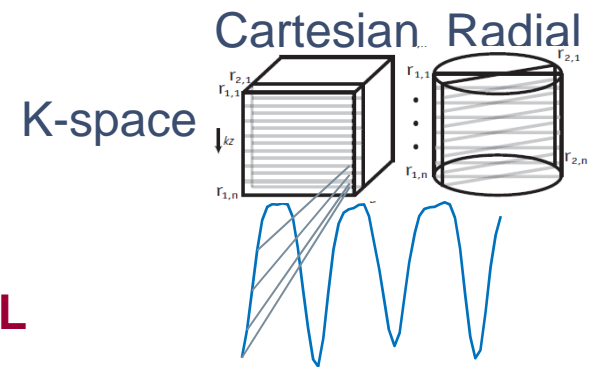
RESPIRATORY SIGNAL



DATA SORTING

To amplitude or phase

3D SEQUENCE

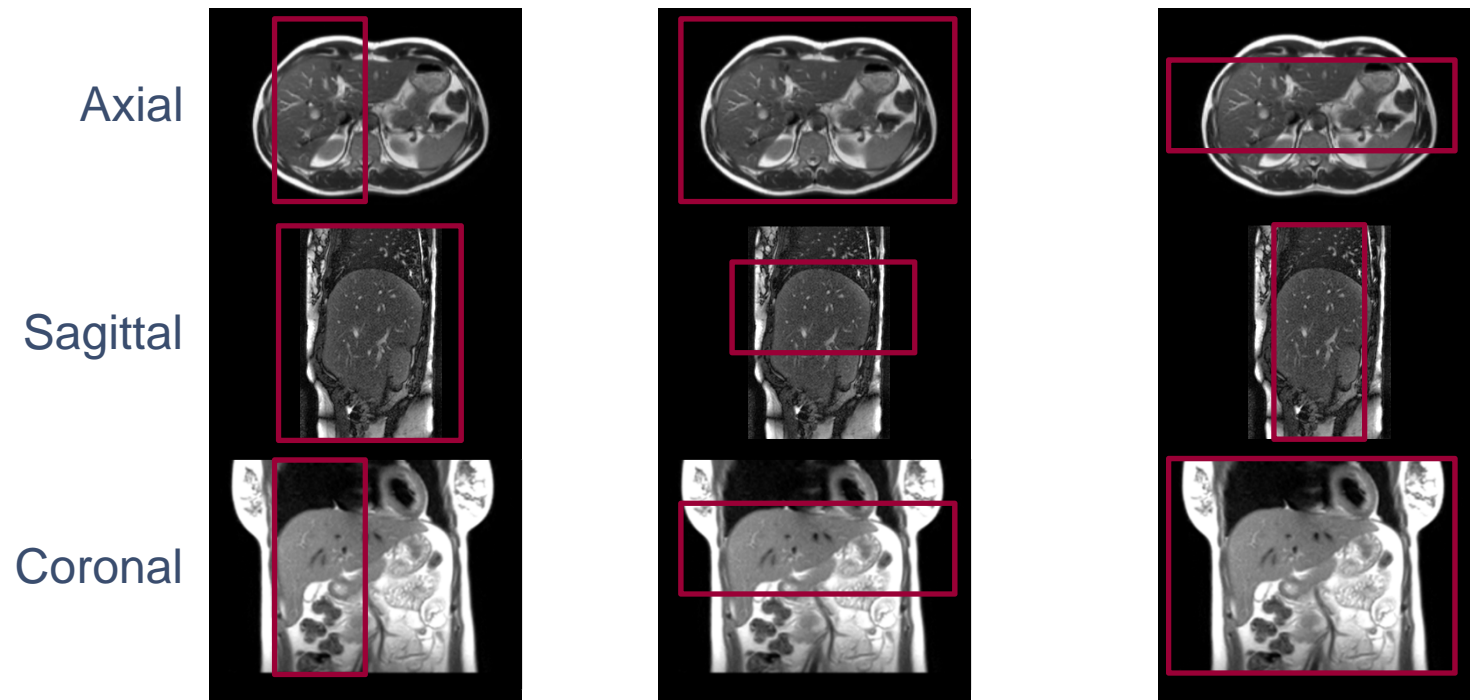


4D-MRI ACQUISITION: 2D VS 3D

Acquisition	2D	3D
SNR (spatial resolution)	-	+
Acquisition / reconstruction time	~minutes (3-15min)	<minute ~hours / dedicated reconstruction server
Pulse sequences	Standard	Tailored
Contrasts	T1 or T2 - weighted	T1-weighted

2D-BASED 4D-MRI

2D Orientation	Sagittal	Axial	Coronal
CC-motion	In-plane	Out-of-plane	In-plane
FOV coverage / acquisition time	-	+	+



FOV: 25 slices of 5mm, Acq time: ~4min

AXIAL/CORONAL 4D-MRI



Contents lists available at [ScienceDirect](#)

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4D-MRI

Retrospective self-sorted 4D-MRI for the liver

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MRI-guidance
Liver
MR-Linac
Self-gating

ABSTRACT

Purpose: Daily MRI-guidance this study was to develop a 4 reconstruction time <5 min.
Materials and Methods: Imi sequence, repeated a variabl the data by computing corr phases and missing data wer unteers. The SsS, image quali assessed as a function of th with liver metastasis on the
Results: SsS was in good ag 0.4 ± 0.6% to 37.1 ± 6.6% for The RMSD of quantified m >10 dynamics.
Conclusion: For 30 dynamics in the validation experiment
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Clinical Investigation

A Self-Sorting Coronal 4D-MRI Method for Daily Image Guidance of Liver Lesions on an MR-LINAC

Tessa van de Lindt, MSc, Jan-Jakob Sonke, PhD, Marlies Nowee, MD, PhD, Edwin Jansen, MD, PhD, Vivian van Pelt, Uulke van der Heide, PhD, and Martin Fast, PhD

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RESULTS: SELF-SORTING SIGNAL ANALYSIS

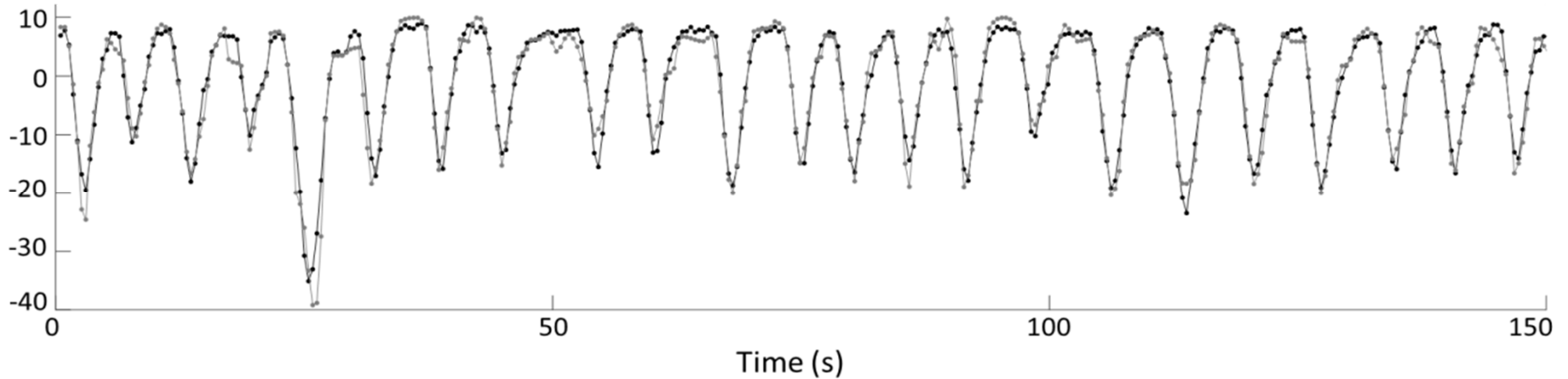
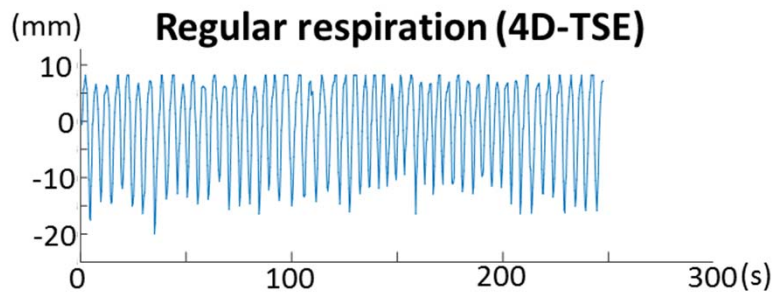


Table1: Image-based self-sorting signal vs navigator signal results

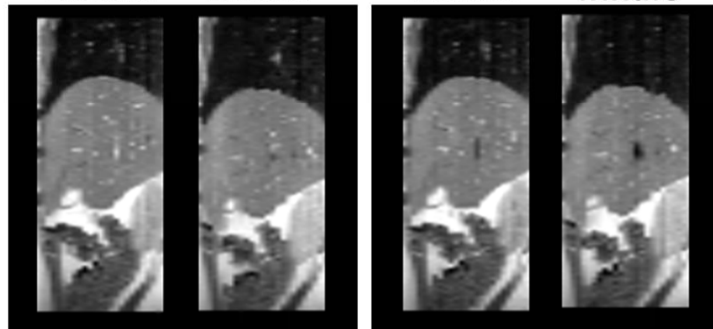
ImS vs NavS

Correlation	0.95 – 0.97	(range)
RMSD (mm)	1.39 – 2.13	(range)
Time difference inhale positons (s)	0.06 ± 0.13	(mean \pm SD)
Bin difference for amplitude-binning	0.41 ± 0.64	(mean \pm SD)
Bin difference for phase-binning	0.23 ± 0.47	(mean \pm SD)

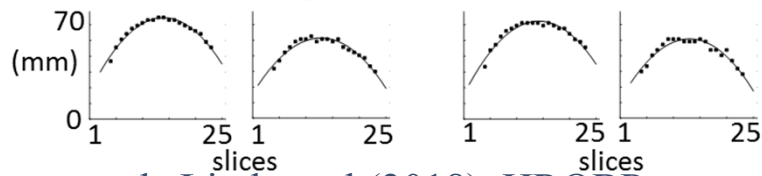
RESULTS: AMPLITUDE VS PHASE SORTING



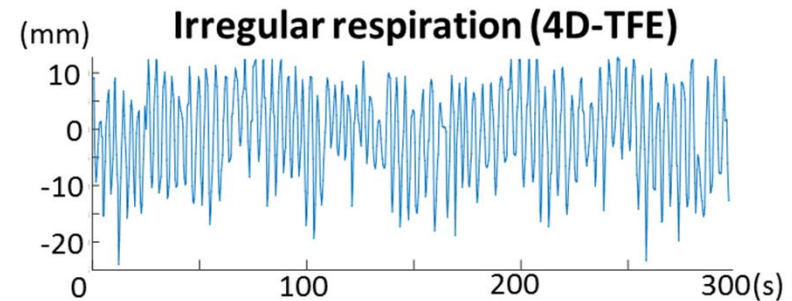
Amplitude **Phase**
Exhale **Inhale** **Exhale** **Inhale**



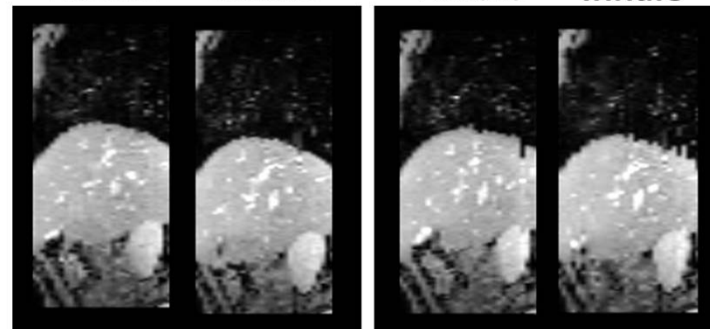
RMSD **RMSD** **RMSD** **RMSD**
1.4mm **1.8mm** **1.8mm** **2.2mm**



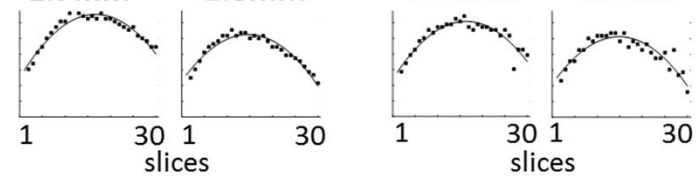
van de Lindt et al (2018), IJROBP



Amplitude **Phase**
Exhale **Inhale** **Exhale** **Inhale**

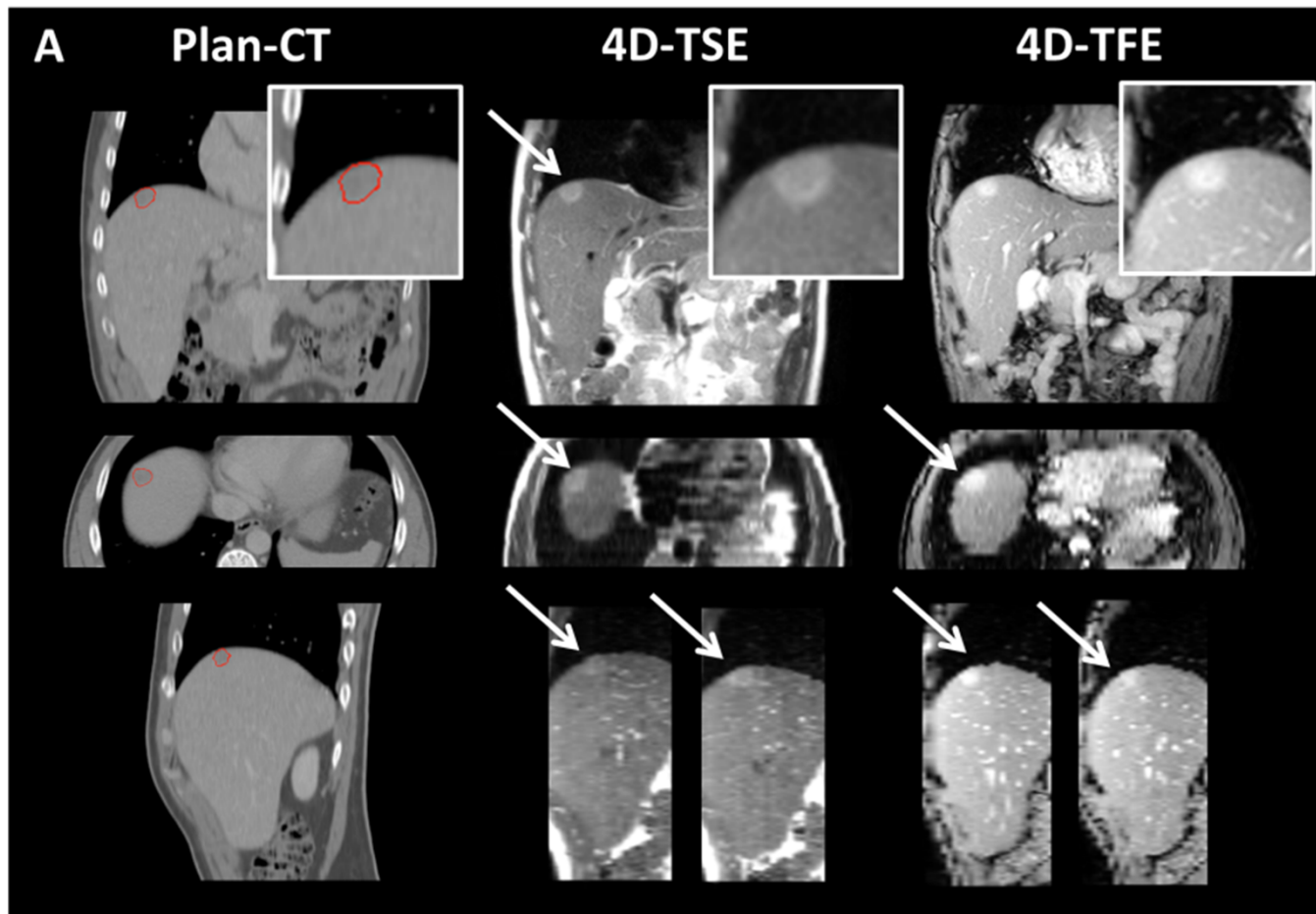


RMSD **RMSD** **RMSD** **RMSD**
1.7mm **1.8mm** **3.9mm** **4.0mm**

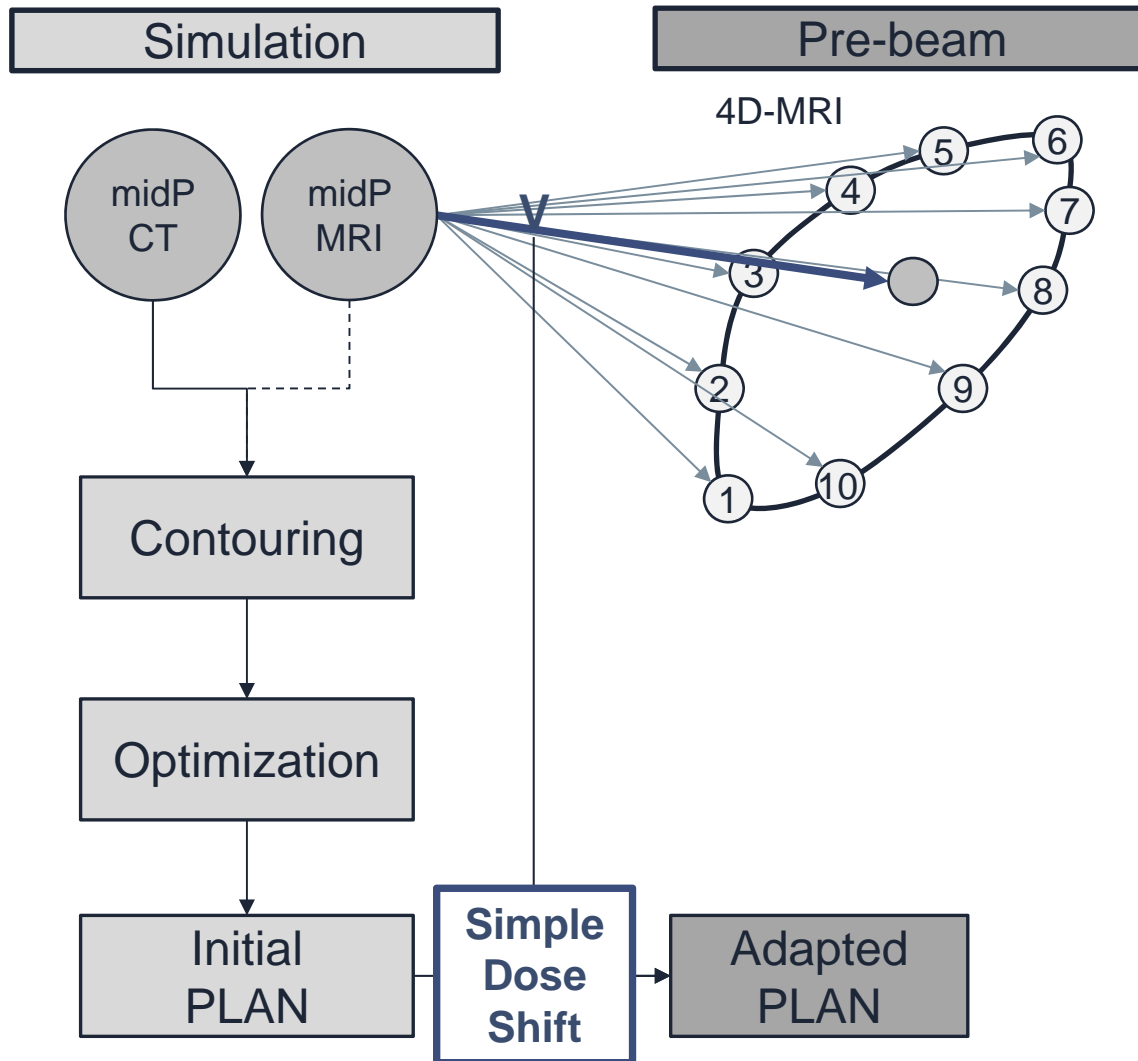


RESULTS: TUMOR VISIBILITY

Lesion: 15mm



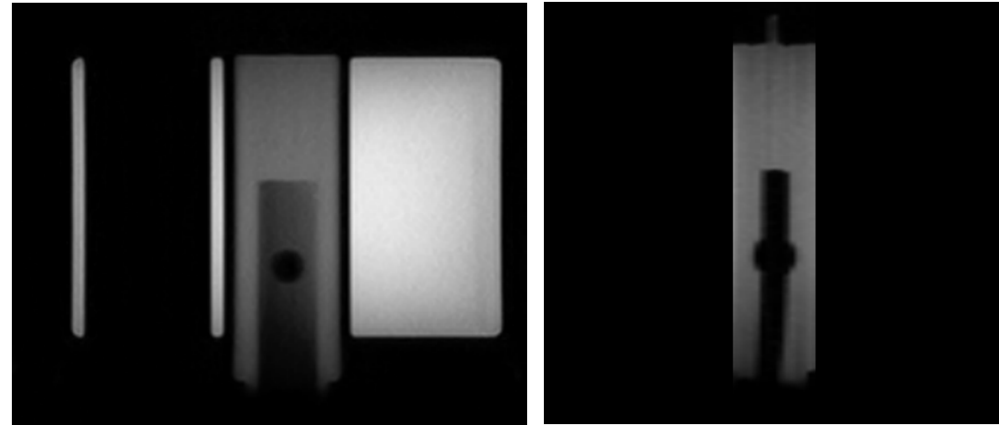
MR-LINAC: DAILY PLAN ADAPTATION IS A MUST



MATERIALS & METHODS: EXPERIMENTAL VALIDATION

4D-MRI¹

- Unity MR-Linac
- Coronal multi-2D TSE



TREATMENT PLANNING

- Monaco v5.19
- 10-beam step-and-shoot IMRT
- 3x20 Gy

PHANTOM MOTION

- Periodic CC motion
 - $A = 15$ mm
 - $T = 4$ s
- CC baseline shifts
 - 0, 5, 10 and 15 mm



¹ TN van de Lindt et al., IJROBP., 2018

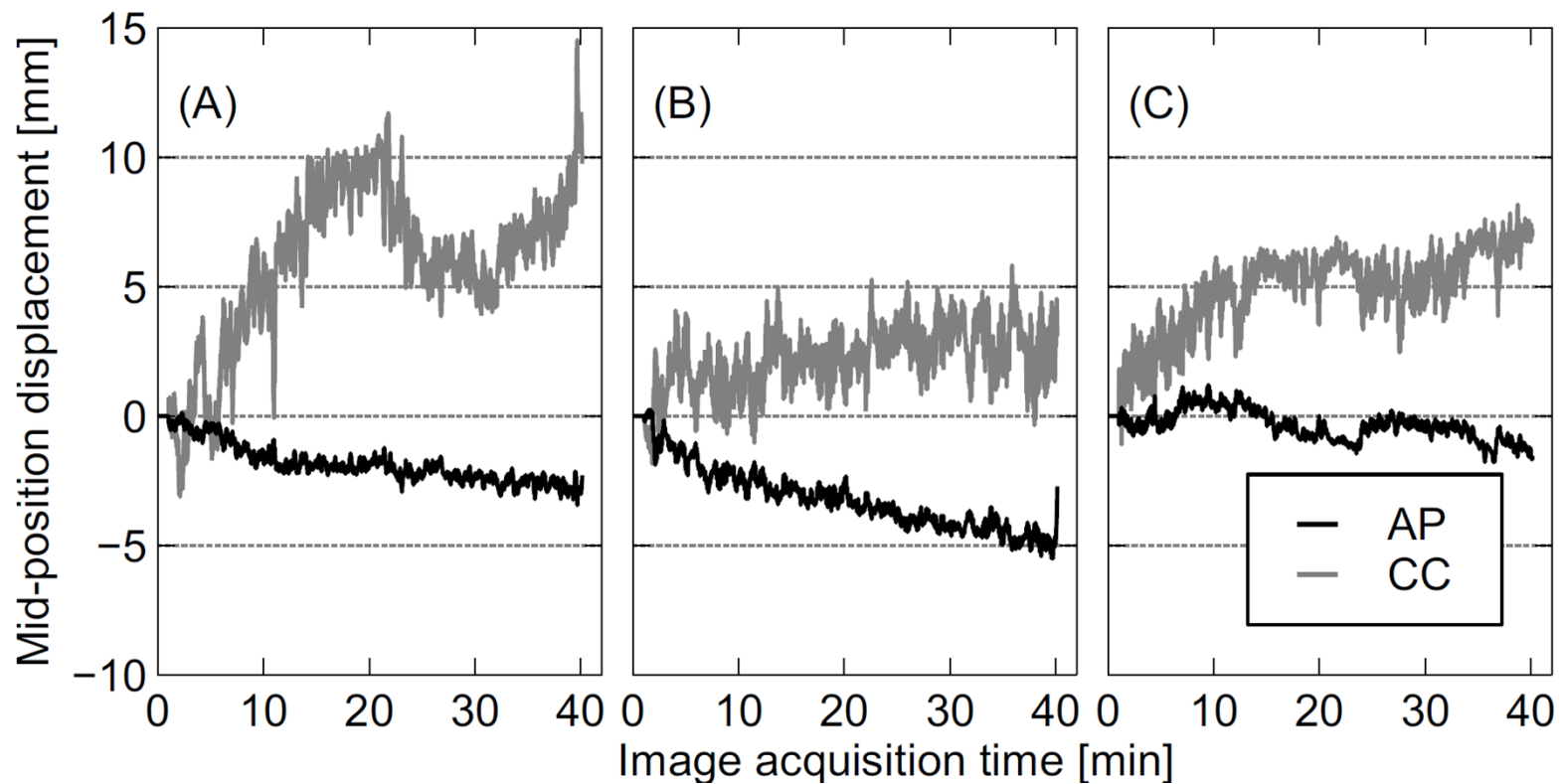
RESULTS

GEOMETRIC AND DOSIMETRIC RESULTS

	EPID		MRI	Film	
Baseline shift (mm)	MidP (mm)	Cine (mm)	4D (mm)	Residual CC-shift (mm)	γ pass rate (%)
5	5.0	5.3	3.8	1.6 – 1.8	86 – 91
10	9.8	10.6	10.0	0.2 – 0.8	97 – 99
15	15.0	15.5	14.3	-0.1 – 0.8	93 – 99
Δ Mean \pm SD	0.1 \pm 0.1	-0.5 \pm 0.1	0.6 \pm 0.6	0.8 \pm 0.8	94 \pm 5

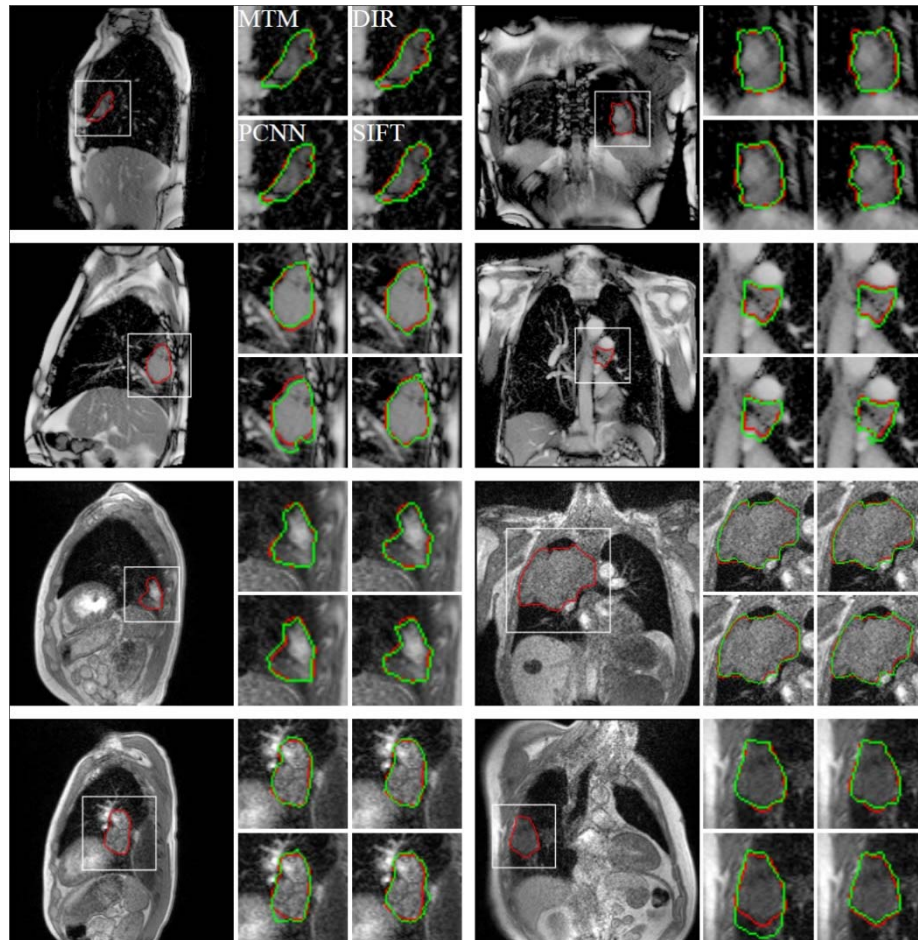
Gamma analysis: 3%/2mm

NEXT FRONTIER: REAL-TIME ADAPTATIONS



Motion variability not captured by 4d imaging

CINE MRI + AUTO-CONTOURING



- 6 patients
- 22 image series: sequence (bSSFE vs GRE) + image orientation
- Dice: 0.92 (median)
- Centroid distance: 1.5 mm (median)
- Multi-template matching (MTM) and deformable image registration (DIR) performed best

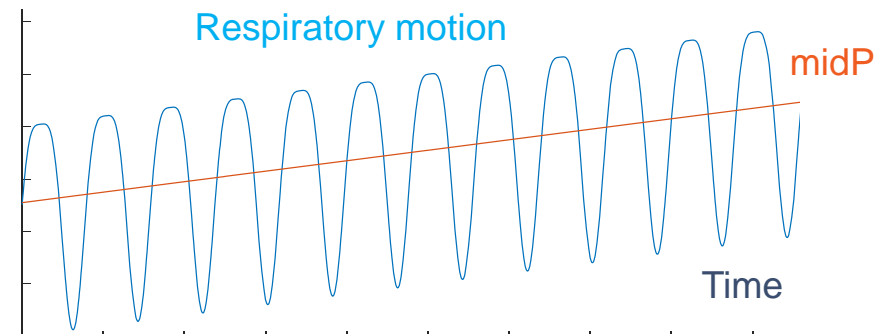
TUMOUR TRAILING

REGULAR MOTION

- High-frequency motion components
- Accounted for in mid-position planning strategy

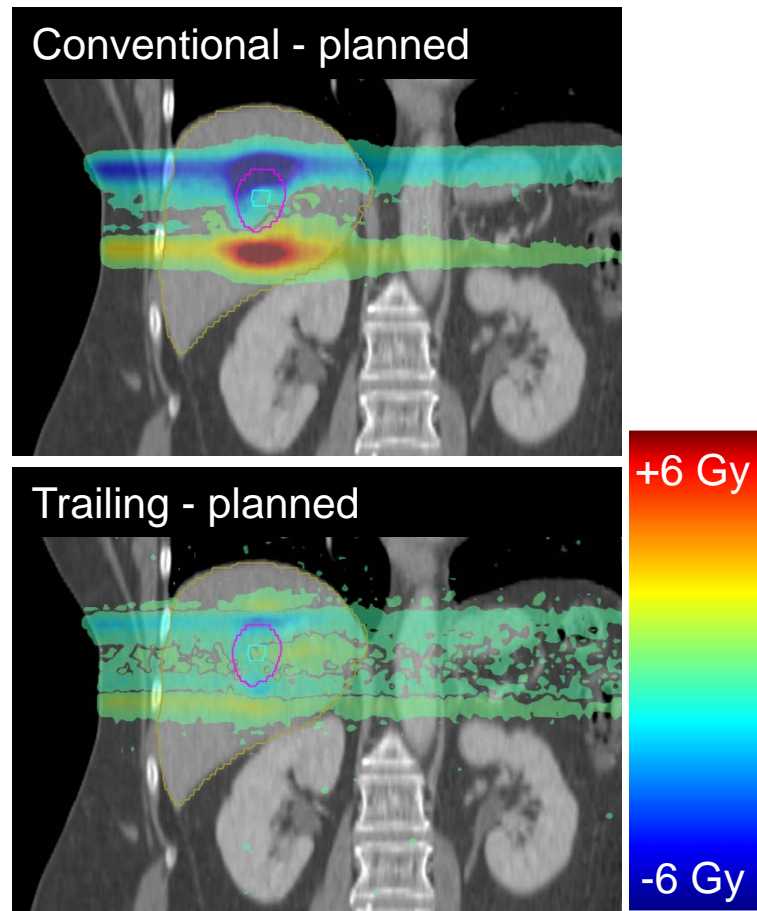
IRREGULAR MOTION

- Low frequency motion components (slow baseline drifts)
- Following mid-position changes during treatment → Tumour trailing[#]



[#]Trofimov et al (2008), Med. Phys. 35 / George et al (2008), Med. Phys. 35

MR-LINAC: FEASIBILITY OF TRAILING



- 3x20 Gy liver SBRT
- Simulated delivery to midP CT (full consideration of interplay)
- Baseline drift: 0.5 mm/min (CC) & 0.25 mm/min (AP)
- *Isocentre-shift*[‡] dose reconstruction
- Trailing vs Conventional vs Planned

[‡]Poulsen et al (2012), Med. Phys. / Fast et al (2018), IJROBP

MR-LINAC: TRAILING PROOF-OF-PRINCIPLE

Motion monitoring

- Sagittal b-FFE cine-MRI
- $1 \times 1 \times 10 \text{ mm}^3$
- 3 Hz

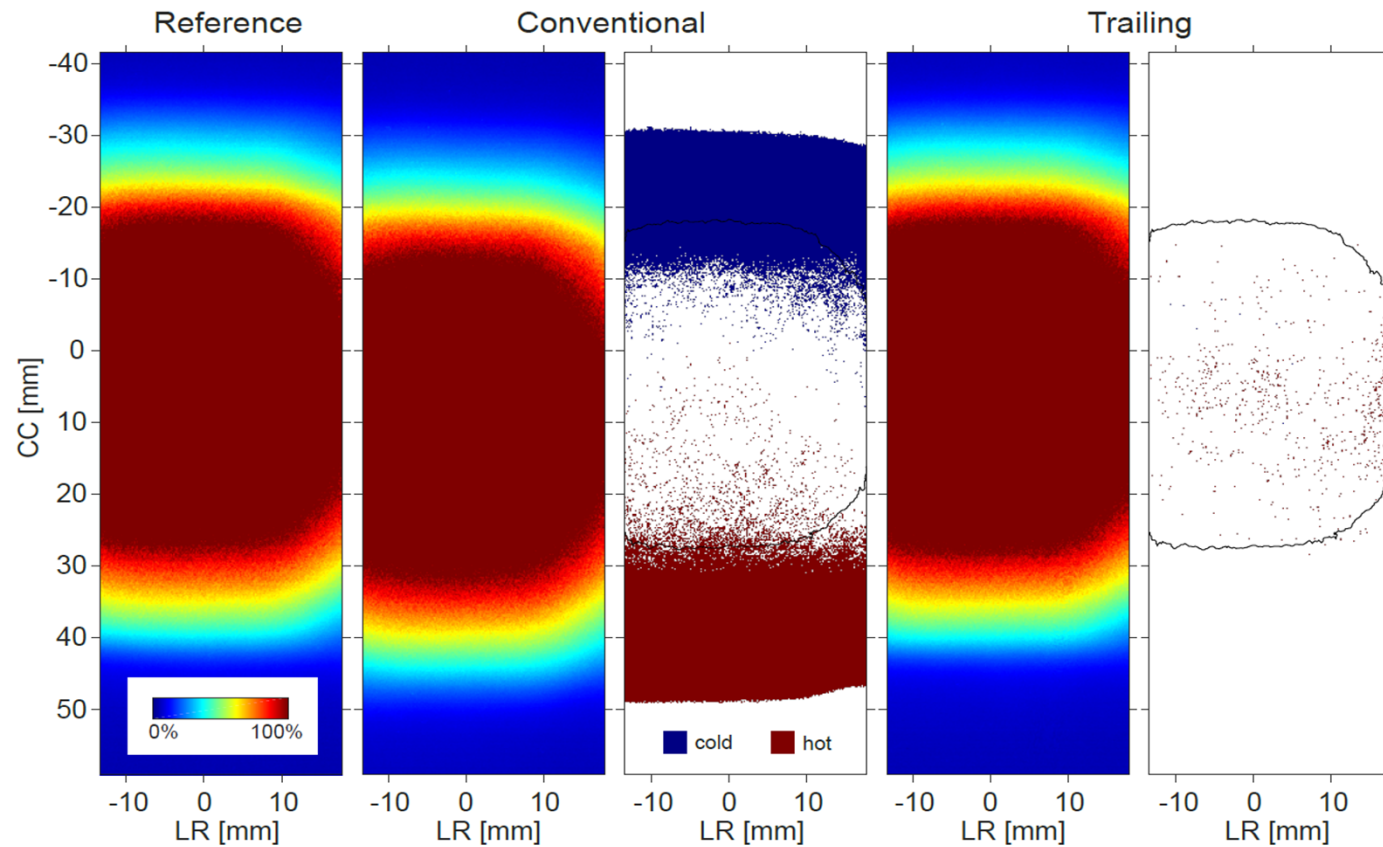
Plan adaptation

- Triggers for motion $\geq 1 \text{ mm}$
- Adapts MLC to target in beam's-eye-view

Trailing

- Starts with initial plan
- Pauses linac when needed
- Transfers adapted plan via iCom interface

RESULTS: DOSE AND GAMMA-DISTRIBUTION



Gamma analysis: 3%/2mm

DynaPlan

Planning Edit View Window Shaping DataIO Plugins

Dose volume histograms

Dvh: (N)TCP EUD Cell Survival (N)TCP curves

Dose (Gy)

Dose volume histogram options

Current dose: [dropdown] Current dose

Inclusive DVH Absolute dose values

Patient Geometry

Planning CT <-> Dose blending

Blend (%) [slider] Show isolines

Slice view scrolling

LR [slider] 256

AP [slider] 256

CC [slider] 89

CT view A/B CT view 3D Debug

CT view (planning / CBCT)

Center (HU) [slider]

Width (HU) [slider]

CT Overlay Slot A

Dose statistics

Show contours... More options...

Vis	Name	Mean	StdDev	Min	Max
<input checked="" type="checkbox"/>	*GTV20	0.0 Gy	0.0 Gy	0.0 Gy	0.0 Gy
<input checked="" type="checkbox"/>	*Lungs	0.0 Gy	0.0 Gy	0.0 Gy	0.0 Gy
<input type="checkbox"/>	*Patient	-	-	-	-

Beam eye views

Beam 0 (200) Beam 1 (240) Beam 2 (280) Beam 3 (320) Beam 4 (0) Beam 5 (40) Beam 6 (80) Beam 7 (120) Beam 8 (160)

Optimization control

Dose influence data

Load Load multiple phases

Tracking listener

Connection

172.16.5.67 1200

Connect Disconnect

Dose reconstruction mode

Ignore position data

Dose reconstruction region

min: 32 max: 134

3D GUI tracking visualization

Show target movement

Show MLC shape

Show multiphase bone

Observer

Connection for position data established
Try connecting to host:
172.16.5.67:1201
Connection for MLC shape data established
Try connecting to host:
172.16.5.67:1202
Connection for control logic established
Received MLC info
Send structure set info

Dose states and fluence processing

Dose state visualization

dose cube A dose cube B

Current dose [dropdown] Current dose [dropdown]

Total Dose [dropdown]

Dose states

Duplicate... Remove... Manage...

Fluence actions

Dose calc PB Dose calc MC

Dose calc PB warped Dose calc MC warped

More actions...

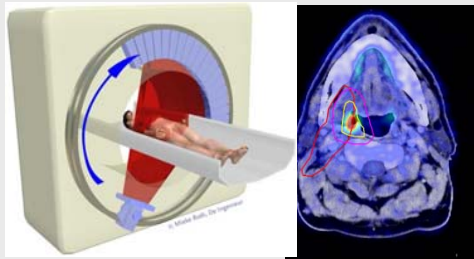
Real-time 4D dose reconstruction for tracked dynamic MLC deliveries

Zoom: [slider] Selection mo

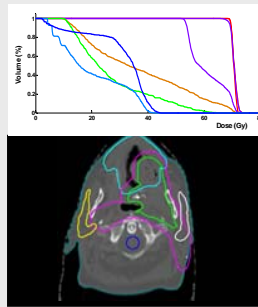
19:03 01/07/2015

The (adaptive) Radiotherapy Process

Pre-treatment imaging



Treatment-planning



Treatment delivery (~30/35 fx)



In-room imaging

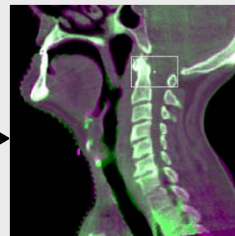
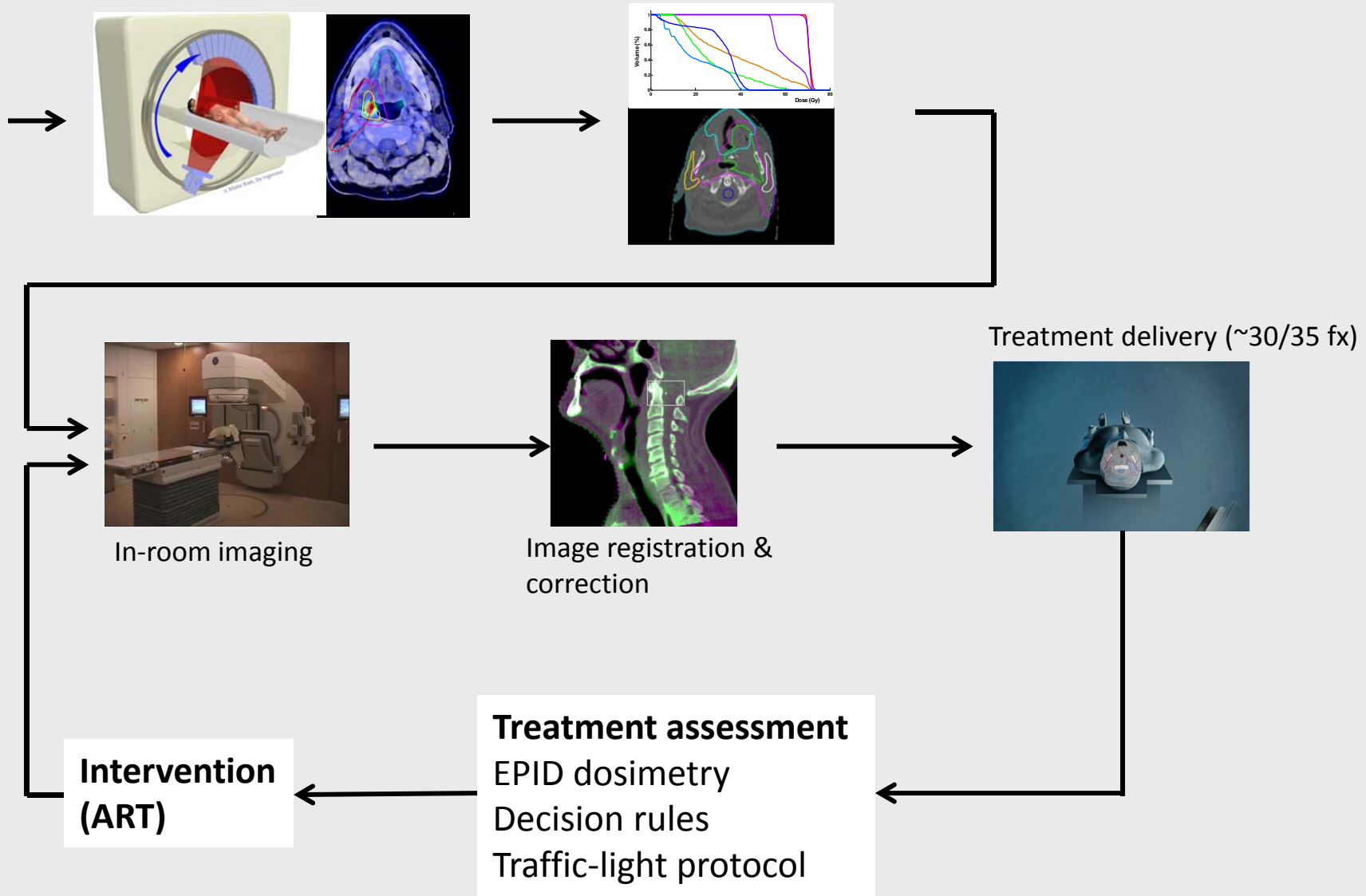


Image registration & correction

**Intervention
(ART)**

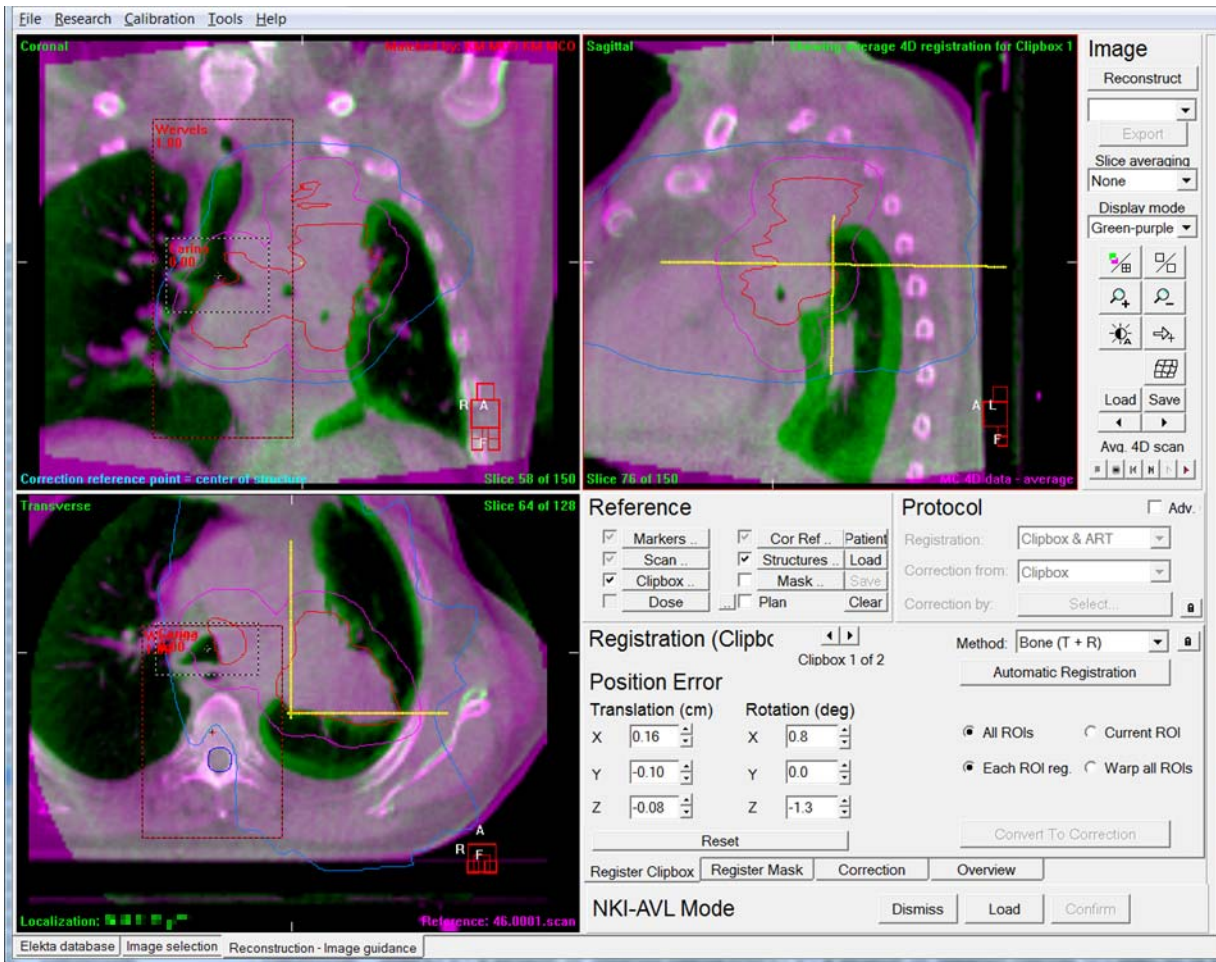
Treatment assessment
EPID dosimetry
Decision rules
Traffic-light protocol



Introduction – current practice

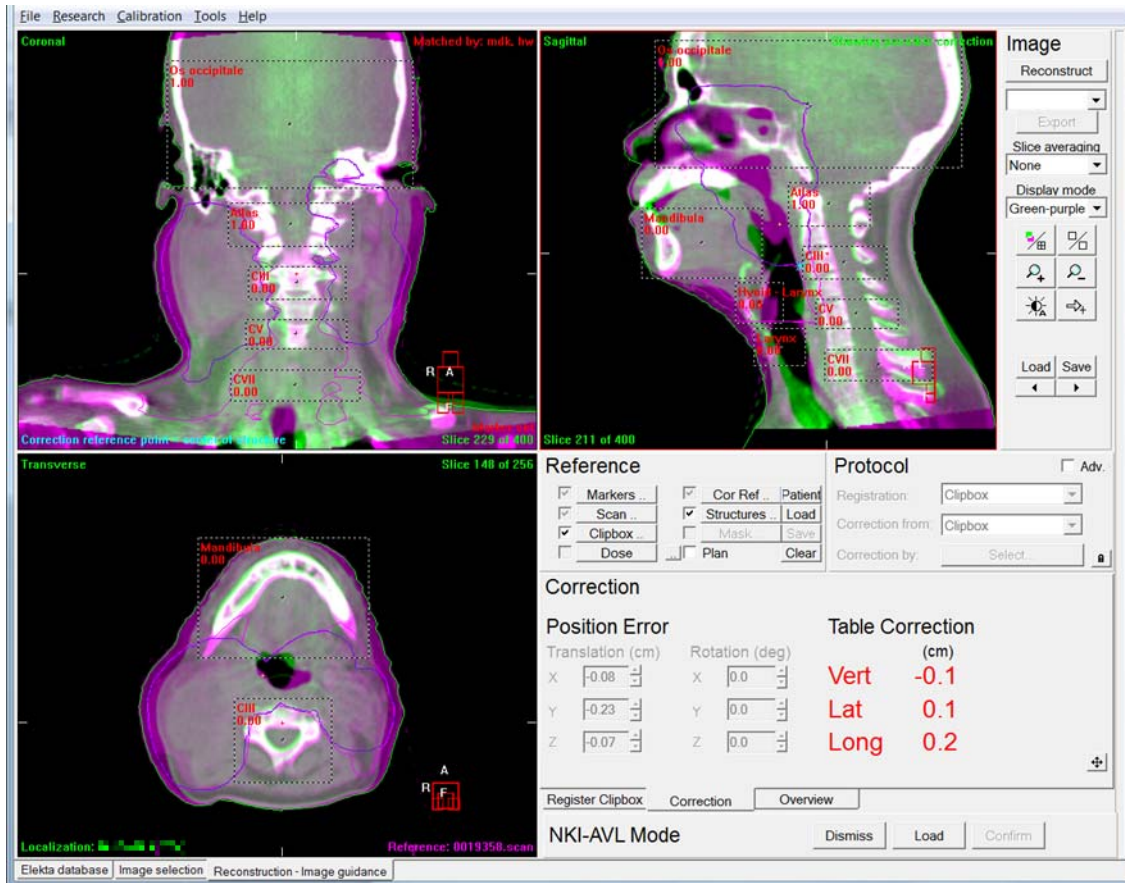
- EPID: *traffic-light* for dose differences with planned
>> but what does it mean in the anatomy?
- IGRT: Decision rules & *traffic-light* protocol
>> we see deformations, what does it mean?
 - Dual registration Lung
 - Multi-clipbox HNC
- Ad hoc assessment: editing the pCT for weightloss/deformations in Pinnacle ...

Example lung



Lung Cancer
60 Gy, 30 fxs
Previously irradiated:
cord dose < 20 Gy
NTD (a/b=2)

Example HNC



- Nasopharynx
- SIB 70 Gy, 35 fxs
- Large PTV
- Many OARs:
N. Opticus, Chiasm,
Brainstem
- mROI with weights
1/0

What these examples show

Mental exercise...

- Isodose lines: is that what we delivered?
- Deformations: how does that change CTV/OAR dose?
- History: Systematic? Random? Trend?
- Timing: How much can we still gain with replanning?
- Upon replanning: what about dose already delivered?

→ We see geometry, we must think dose...

>> HEADACHE!



Alternative: dose accumulation

alternative: dose accumulation

*compute the total delivered dose
in the patient while accounting for
dosimetrical and geometrical discrepancies*



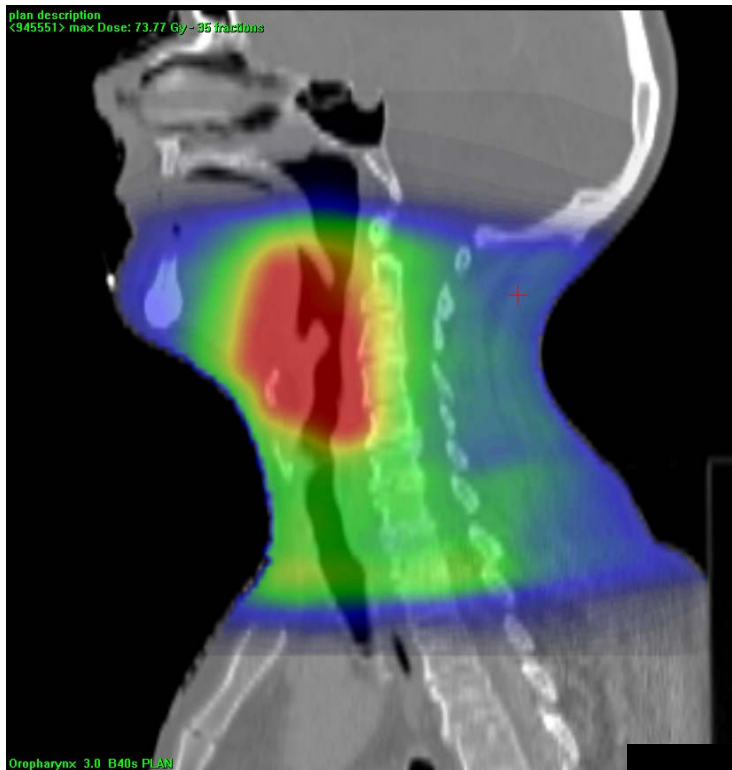
2 important steps:

- Dose distribution delivered is different than planned
- Dose ends up at different location than planned

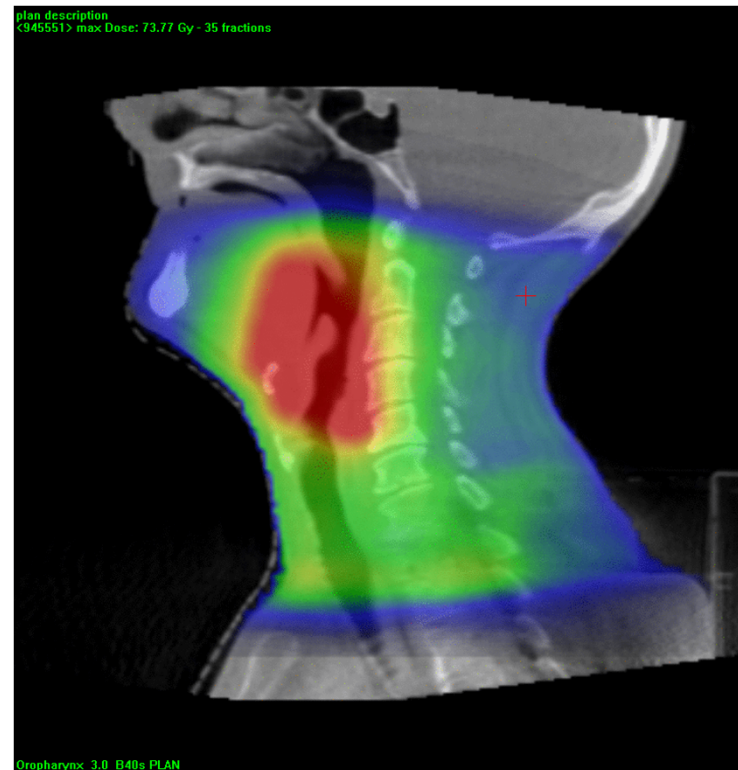


Dose accumulation

Step 1: Dose distribution delivered is different than planned



Planned dose in pCT



planned/recalculated dose in CBCT

Dose accumulation

Step 2: Dose ends up at different location than planned



Deformation & anatomy differences



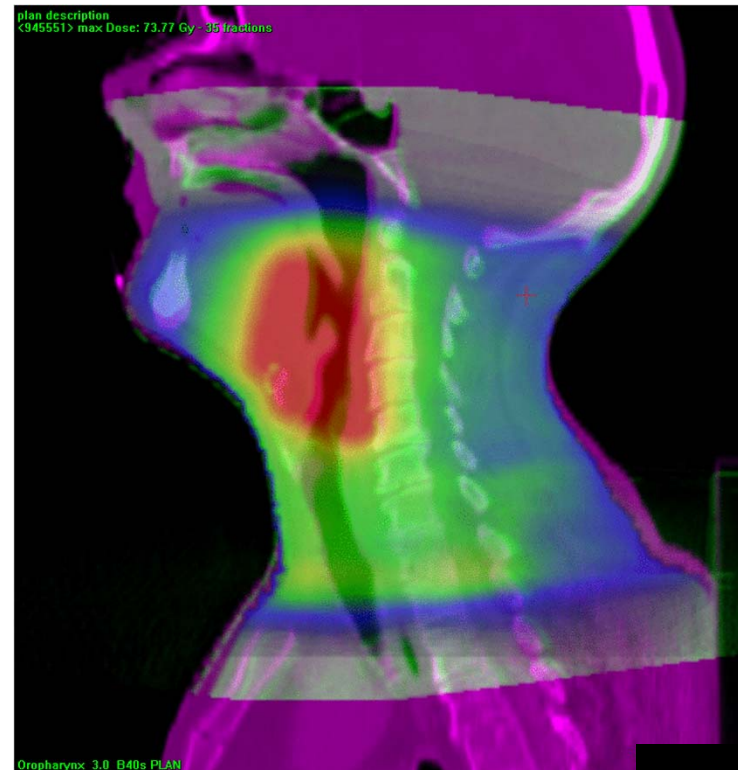
CBCT warping

Dose accumulation

Step 2: Dose ends up at different location than planned



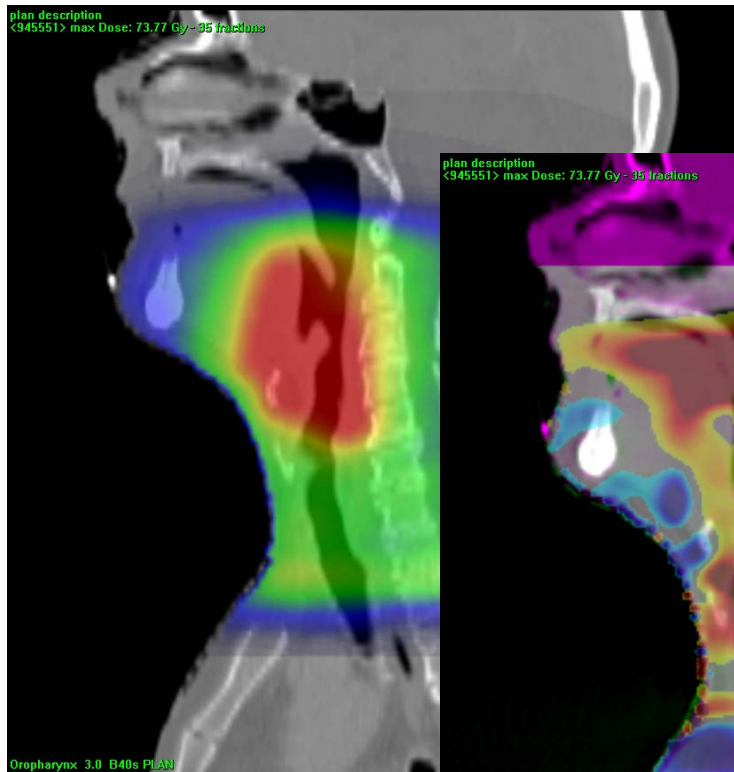
Deformation & anatomy
differences



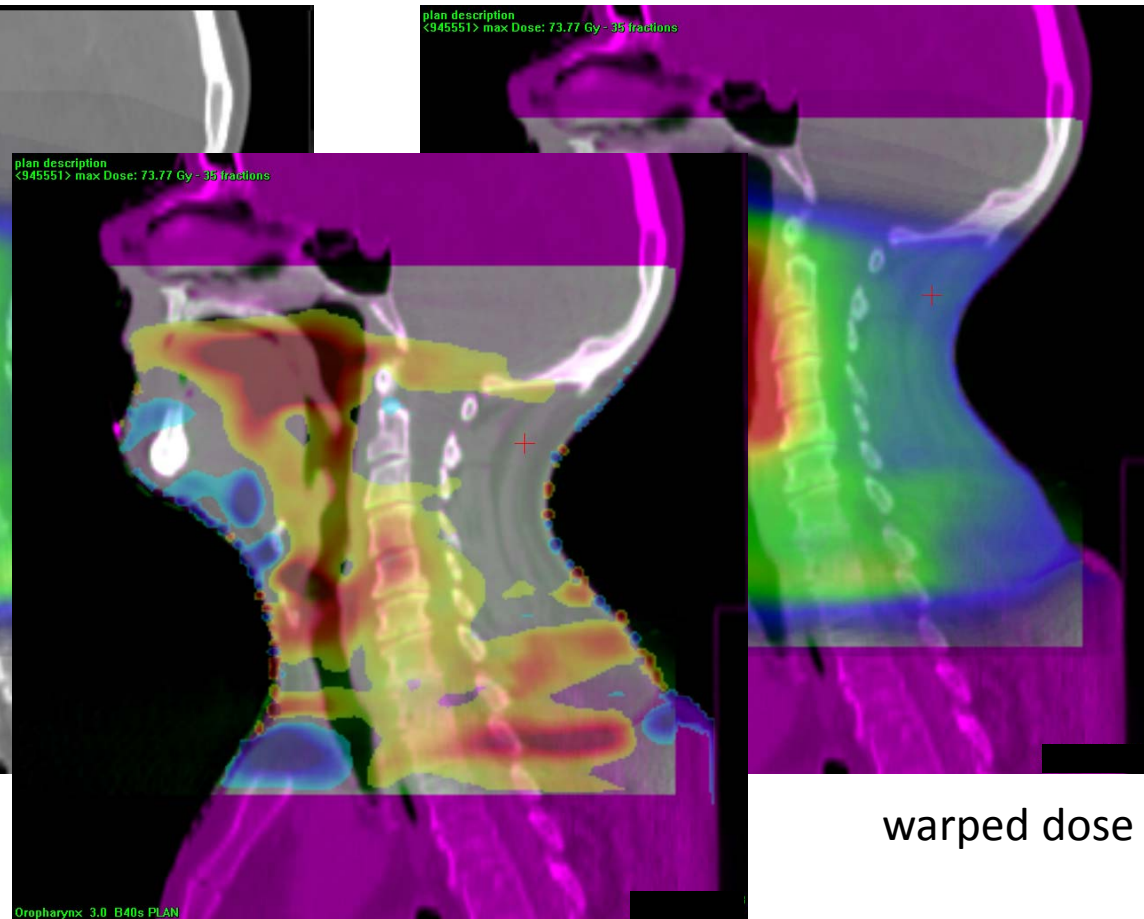
dose warping

Dose accumulation

After dose warping: common reference



planned dose



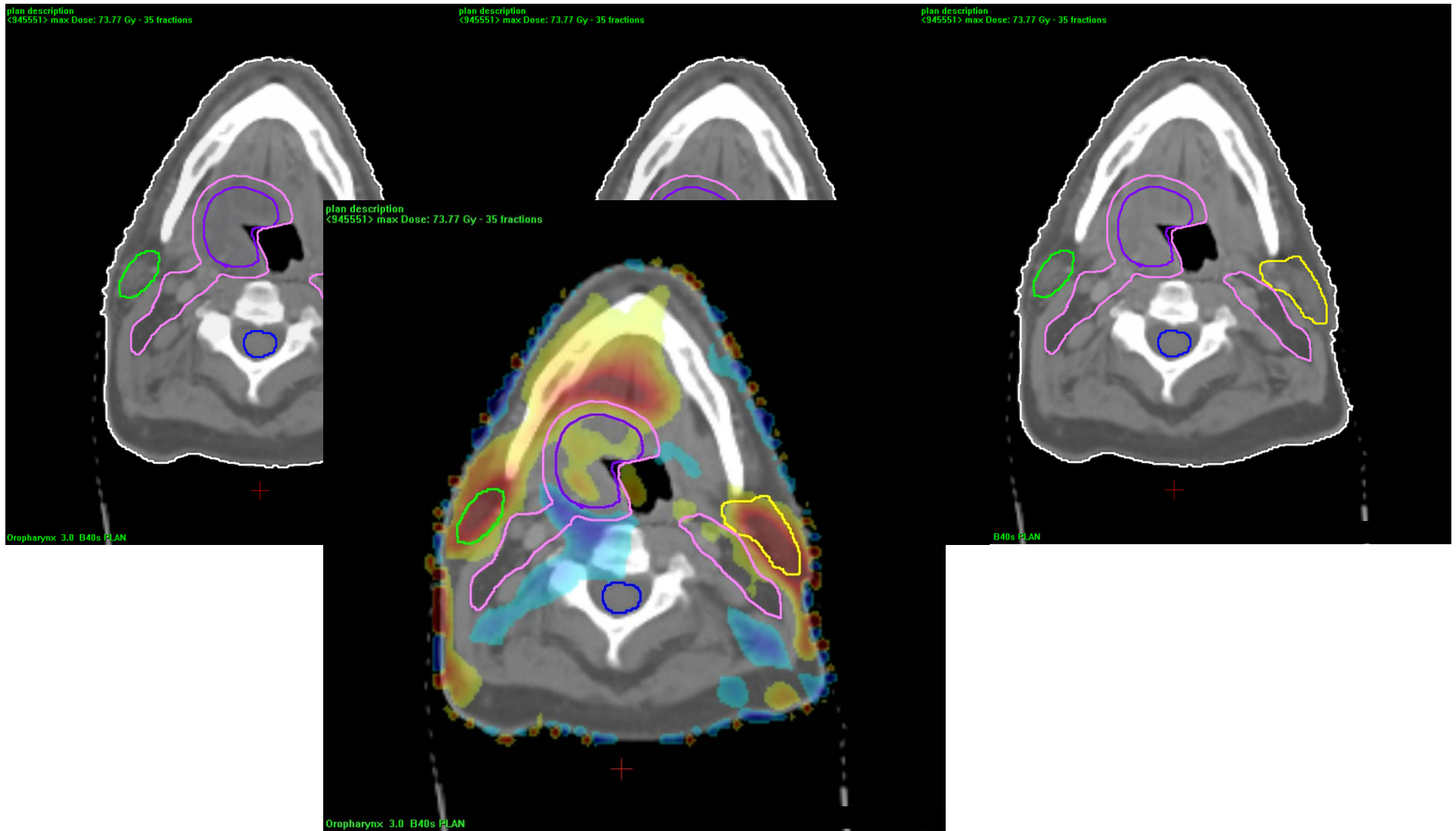
warped dose

Dose accumulation

Planned dose

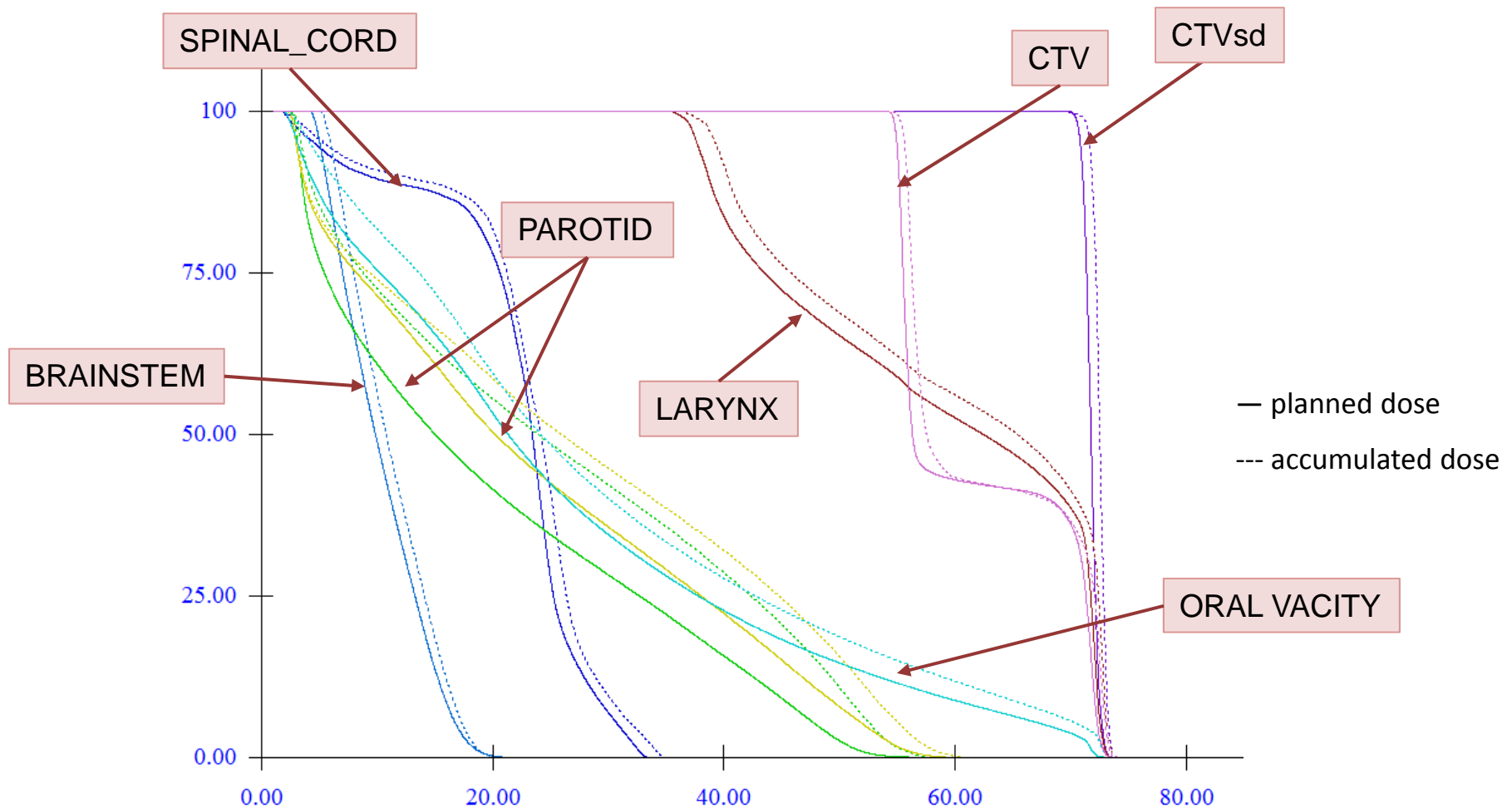
Accumulated dose

Difference dose

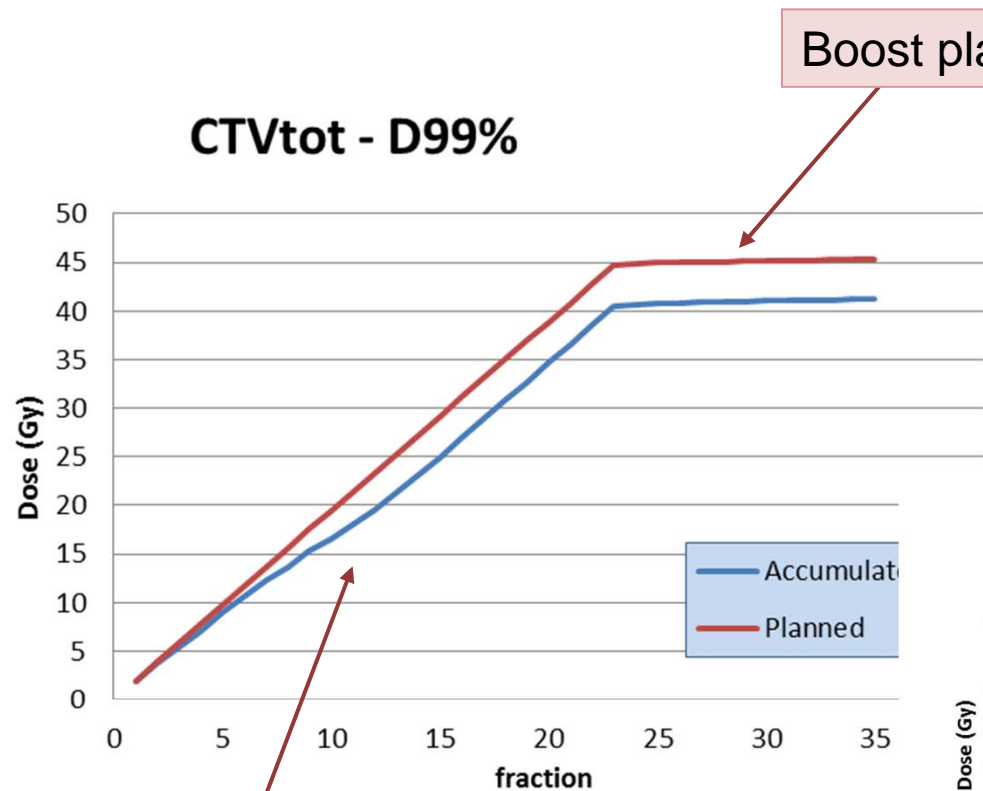


Dose accumulation: DVH differences

DVH: accumulated dose vs planned dose

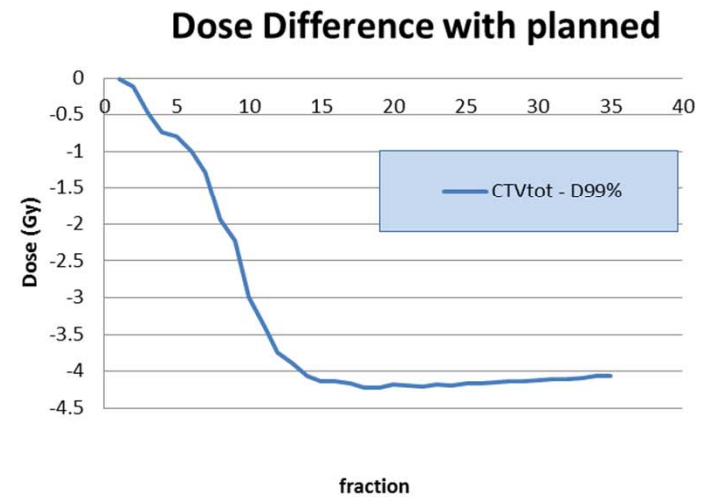


Challenges: prediction of final dose



ART @ fx 14

Boost plan

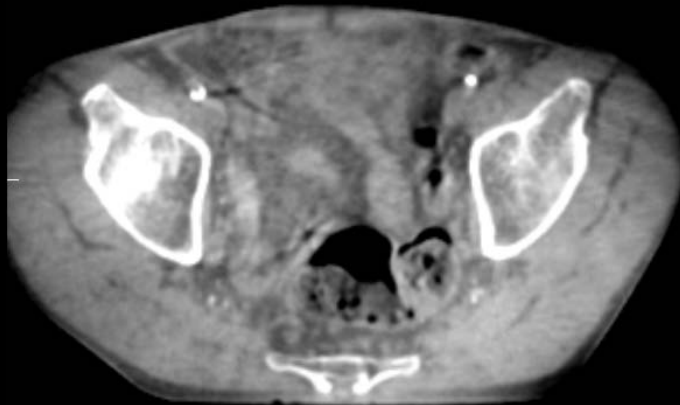


Challenges: DIR with limited Image Quality

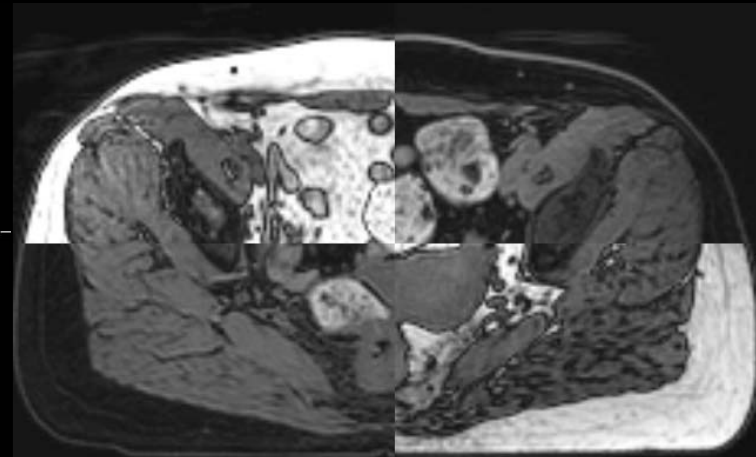
- HNC: OK...
- Lung: WIP...

Example image quality rectum

CBCT



MR



Courtesy Sander Uilkema & Lisa Hartgring

DynaPlan
 Planning Edit View Window Shaping DataIO Plugins

Dose volume histograms

Dvh (NTCP) EUD Cell Survival (NTCP curves)

Dose (Gy)

Dose volume histogram options
 Current dose
 Inclusive DVH
 Absolute dose values

Patient Geometry

Planning CT <-> Dose blending
 blend (%) Show isolines

Slice view scrolling
 LR 256
 AP 256
 CC 58

CT view A/B CT view 3D Debug

3D CT visualization
 Threshold (HU) -230
 Alpha (%)

Dose statistics

Show contours... More options...

Vis	Name	Mean	StdDev	Min	Max
<input type="checkbox"/>	PTV5mm	6.9 Gy	1.3 Gy	1.3 Gy	7.9 Gy
<input type="checkbox"/>	*PTV3mm	6.7 Gy	1.4 Gy	1.3 Gy	7.9 Gy
<input checked="" type="checkbox"/>	PTV1mm	7.0 Gy	1.1 Gy	1.8 Gy	7.9 Gy
<input type="checkbox"/>	PTV	6.8 Gy	1.3 Gy	1.3 Gy	7.9 Gy
<input type="checkbox"/>	PTV_added_...	-	-	-	-
<input type="checkbox"/>	Rectum	3.4 Gy	2.0 Gy	0.1 Gy	7.5 Gy
<input checked="" type="checkbox"/>	CTV	7.1 Gy	0.9 Gy	3.1 Gy	7.9 Gy
<input type="checkbox"/>	*BODY1	0.4 Gy	nan Gy	0.0 Gy	7.9 Gy
<input type="checkbox"/>	Bladder	1.3 Gy	2.0 Gy	0.0 Gy	7.5 Gy

Beam eye view

Beam 0 (1206) Beam 1 (1257) Beam 2 (1309) Beam 3 (19) Beam 4 (151) Beam 5 (1103) Beam 6 (1154)

Speed up: 4x

Beam eye view

(38.58) (190.28)

Beam 0 Fluence view

Optimization control

Dose influence data
 Load Load multiple phases

Dose calculation
 Reconstruct dose for offline tracking
 Calc dose for center beams Test phases

Optimization strategy
 Fluence Optimization

Optimization settings
 Weight Initialization: Memory
 Maximum iterations FO: 25
 Convergence criterion FO: 0.100
 Number of Shapes: 0
 Start Stop Reset

Dose states and fluence processing

Dose state visualization
 dose cube A dose cube B
 Current dose Current dose
 Total Dose

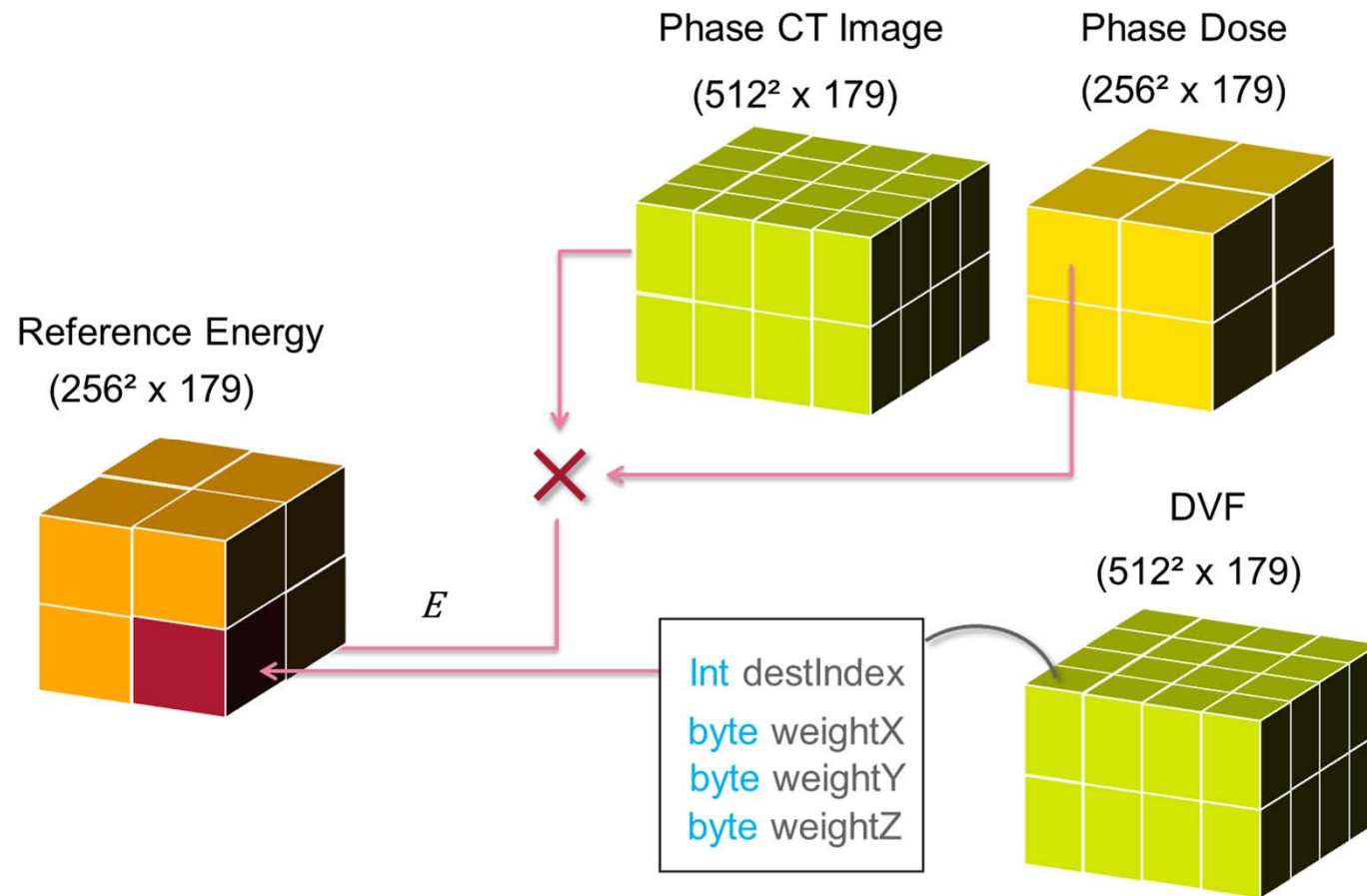
Dose states
 Duplicate... Remove...
 Manage...

Fluence actions
 Dose calc PB Dose calc MC
 Dose calc PB warped Dose calc MC warped
 More actions...

Zoom: Selection mo

19:28
 30/06/2015

DOSE ACCUMULATION: ENERGY-MASS TRANSFER



Li et al. (2014), Med. Phys. / Ziegenhein et al (2018), Sci. Rep.

SUMMARY & OUTLOOK

- MRI-guidance provides excellent soft-tissue contrast
- Novel 4D-MRI radiotherapy solutions are being developed
- Margin reduction / active motion management will provide scope to allow for re-irradiations
- Away with the surrogate reality: start looking at dose in anatomy daily