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Elia Lombardo | 30.06.2020

Real-Time Tumor Tracking with MRI Guidance

Advanced Motion Compensation Seminar

Supervisor: Prof. Marco Riboldi

Outline

1. Introduction
2. MRI Guidance Basics
3. Motion Management with MRI Guidance
4. Comparison of State-of-the-Art Technologies
5. Summary and Outlook
6. Literature Search

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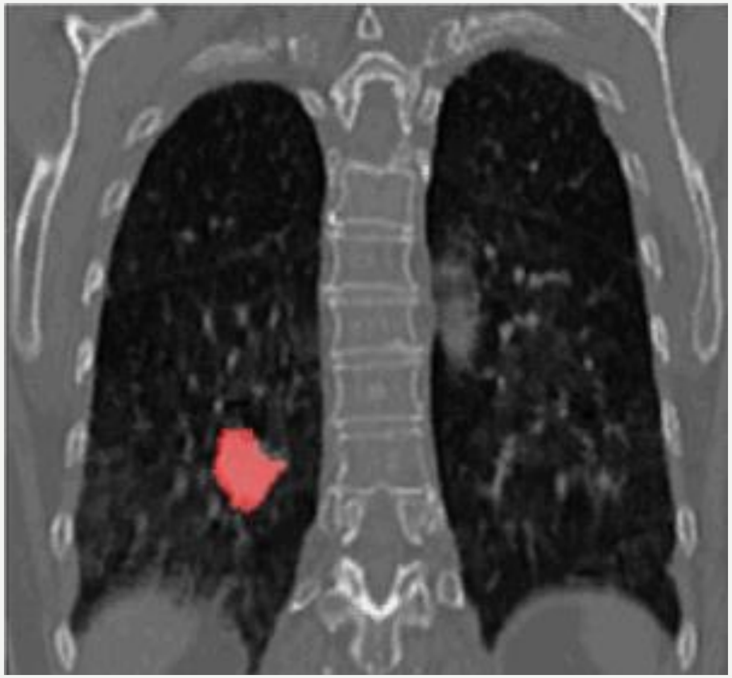
Introduction
Motivation

Challenge

- Intra-fractional motion leads to decreased normal tissue sparing and less conformal tumor dose



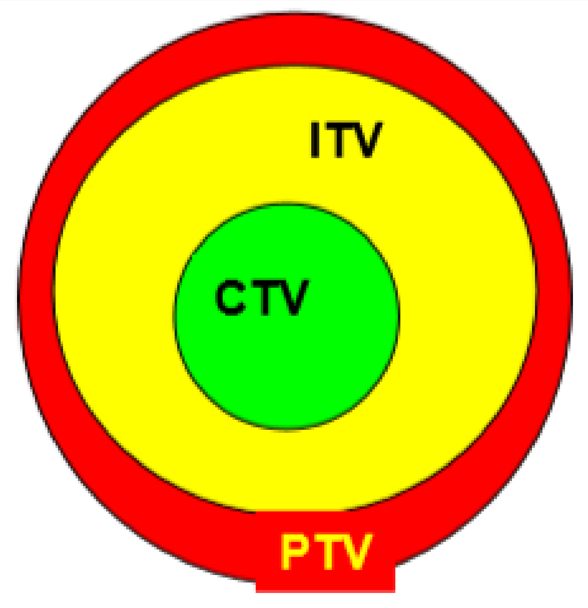
Solutions

- Site dependent: respiratory, skeletal, muscular, cardiac, gastrointestinal system
- Respiratory motion affects all tumor sites in thorax and abdomen → research focus

Introduction
Respiratory Motion Compensation

Delivery strategies to deal with respiratory motion

1. **Margin expansion**: ITV concepts
2. **Robust treatment planning**: incorporate motion probability function in optimization
3. **Respiratory gating**: administer radiation within particular portion of breathing cycle (*Talk by Dinu Purice*)
4. **Breath-hold methods**: generate reproducible state of breathing in which radiation is applied (*Talk by Yuqing Xiong*)
5. **Respiratory-synchronized real-time tumor tracking**: shift dose in space to follow tumor during free breathing (*Francesca Neri, **this talk** and Stefanie Götz*)



Introduction

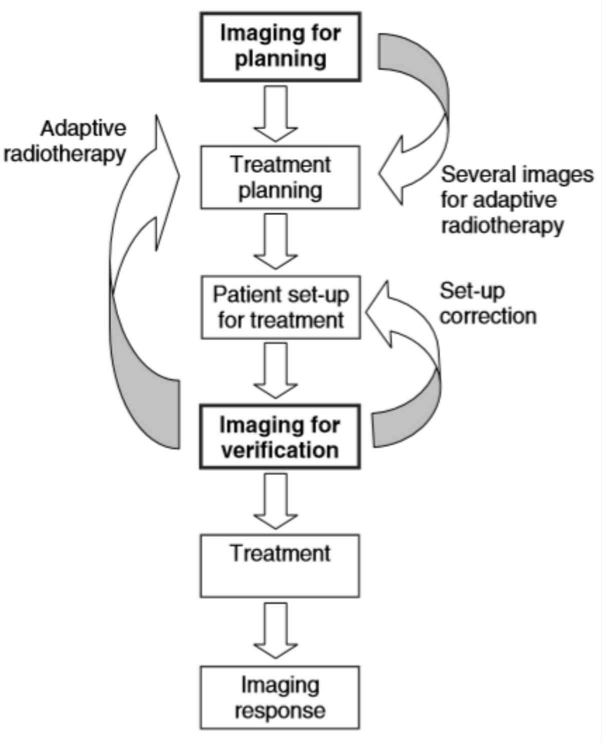
Real-Time Tumor Tracking

Key elements of real-time tumor tracking (Keall et al., 2006):

1. Identify tumor position in real time
2. Anticipate for tumor motion to allow for time-delays
3. Reposition the beam
4. Adapt the dosimetry

Allowing for Image Guided Radiotherapy (IGRT):

- Altering patient position (set-up corrections)
- Adapt treatment plan with respect to anatomical changes that occur during treatment (**ART,** adaptive radiotherapy)



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Monitoring motion using MRI

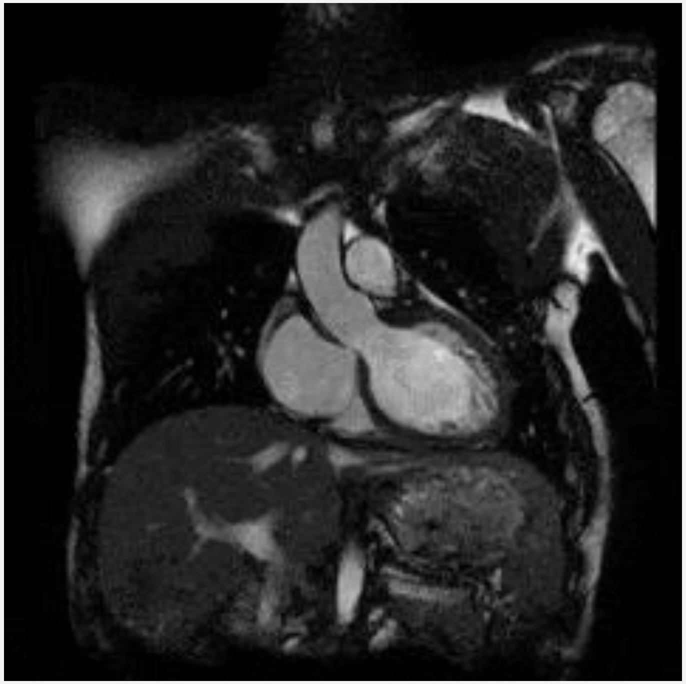
Pros:

- Superb soft tissue contrast

→ Direct visualization of Tumor/OAR

- No radiation dose

→ Frequent (or continuous) verification



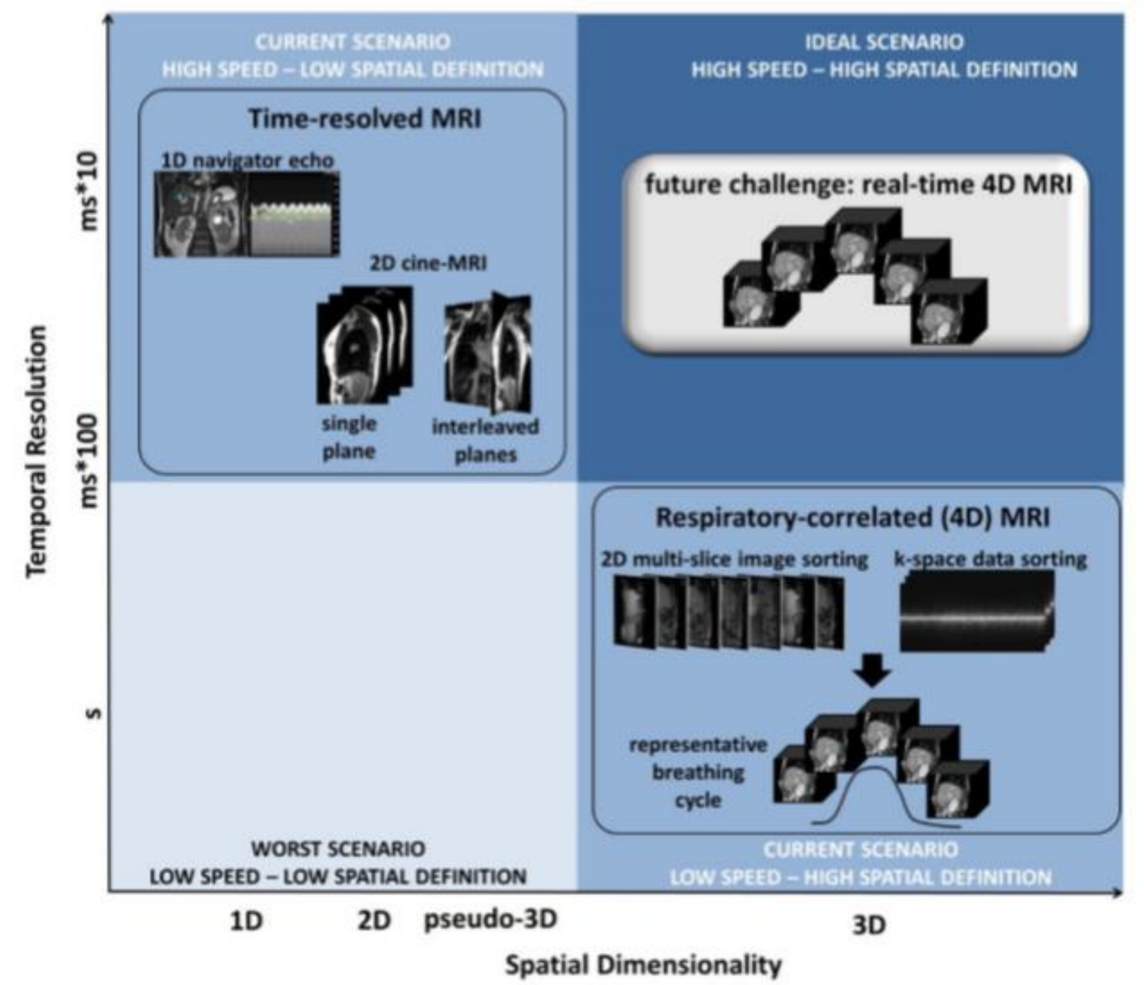
Cons:

- Lack of electron density information

→ Sophisticated dose calculation methods

- Spatial distortions
- Patient suitability

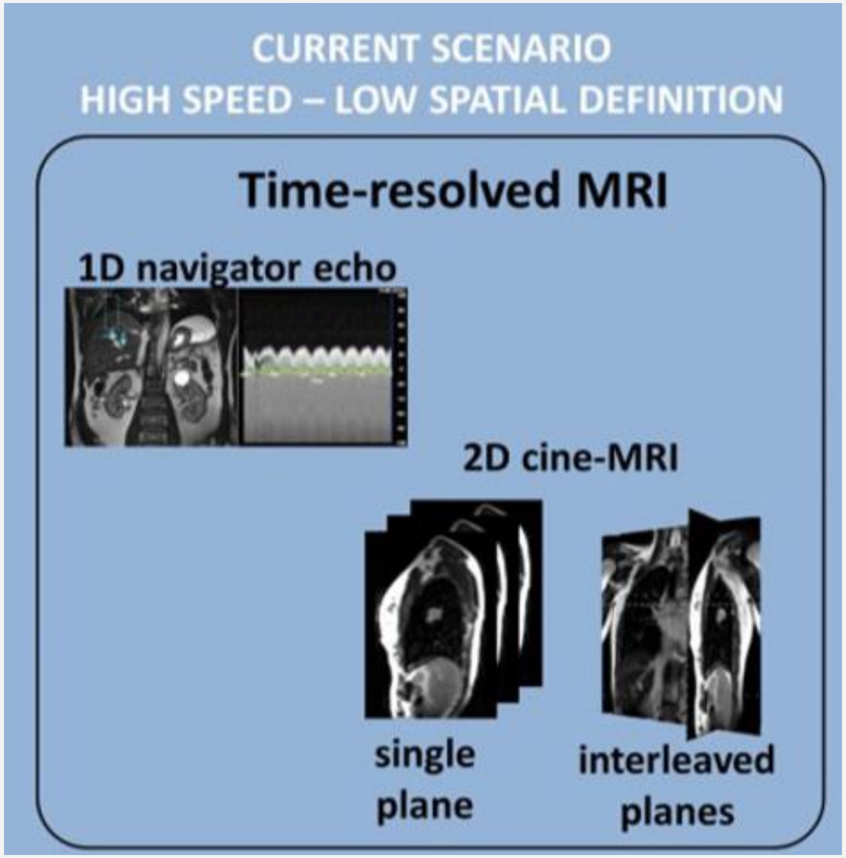
The challenge of real-time 4D-MRI: Temporal vs. Spatial resolution



MRI Guidance Basics

1. Time-resolved MRI

- **1D navigator echo**
  - Serial acquisition of “1D” (1-2 cm wide) image to map position of diaphragm
  - Temporal resolution $\approx 10\ ms$
- **2D cine-MRI**
  - Very fast pulse sequences needed
  - Balanced steady state free precession (bSSFP) or T2-weighted turbo spin echo (TSE)
  - Temporal resolution $\approx 300\ ms$
  - Shorter acquisition $\approx 150\ ms$ using acceleration techniques (k-space sampling, parallel imaging)
  - Pseudo-3D images using interleaved orthogonal planes

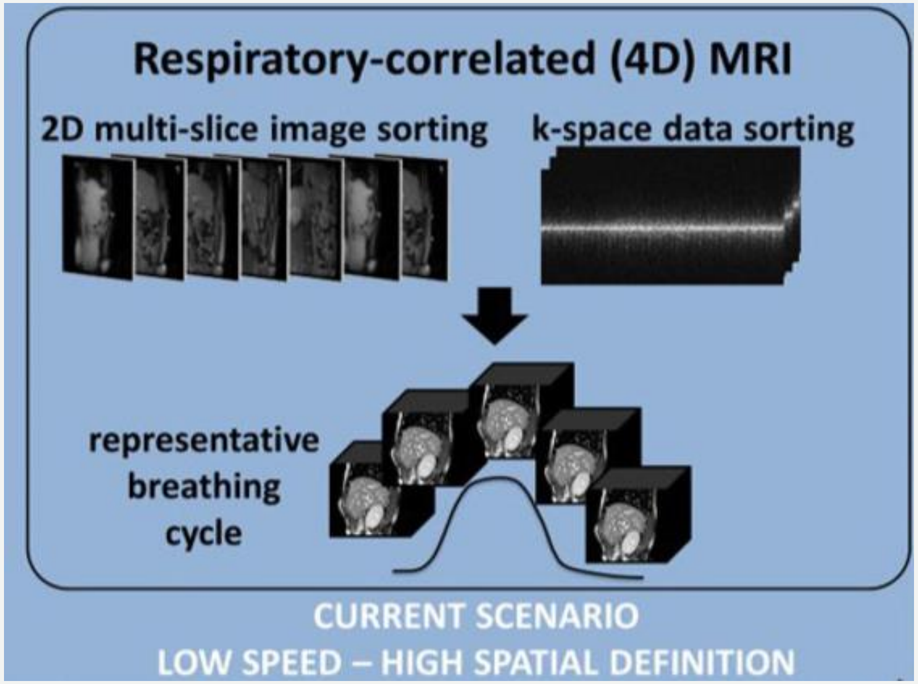


→ Real-time but low-quality images

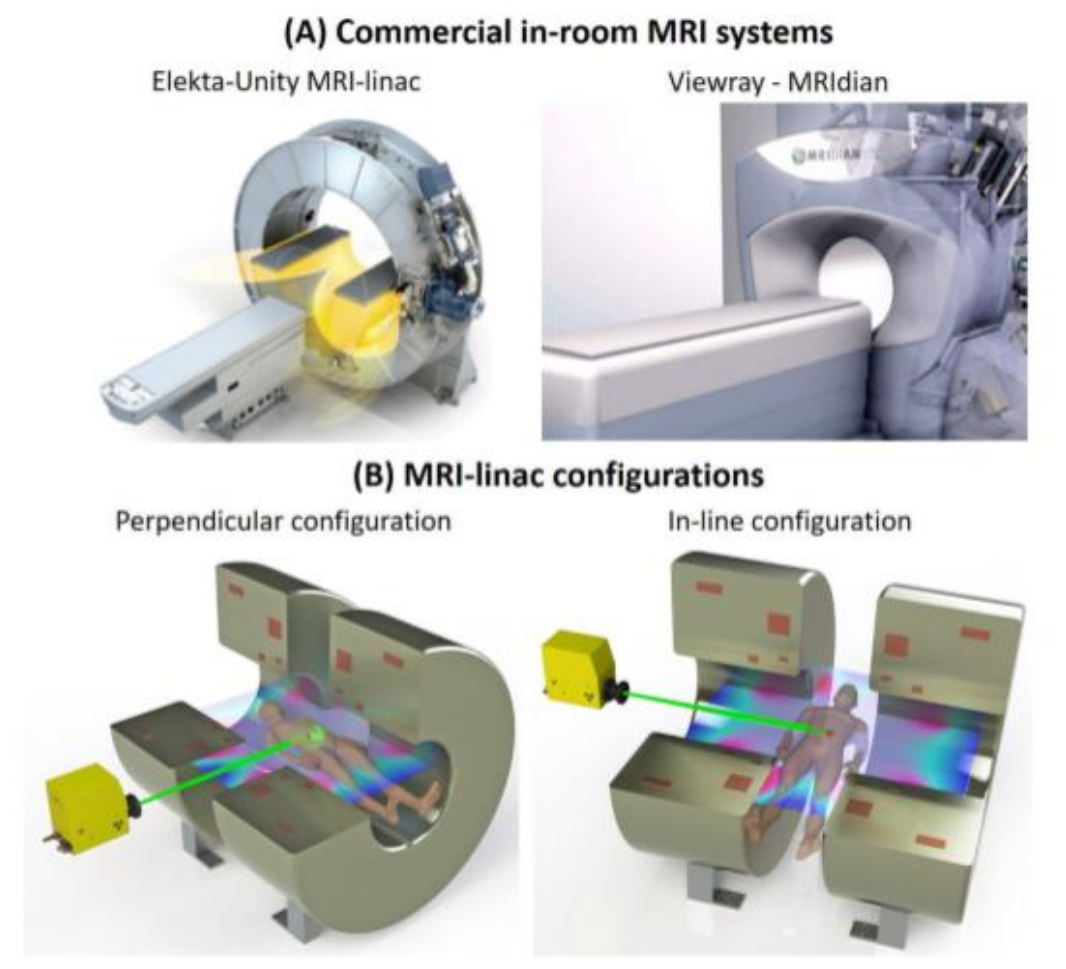
MRI Guidance Basics
2. Respiratory-correlated (4D) MRI

- **Stacked 2D cine-MRI**
  - Sorting in image domain
  - Using navigator sequences or image-derived approaches for sorting
- **K-space data sorting**
  - Sorting in frequency domain
  - Breathing signal for sorting extracted directly via frequent sampling of k-space center

→ Good quality images of entire (*mean*) breathing cycle with combined acquisition and reconstruction time of $\approx 5\ min$

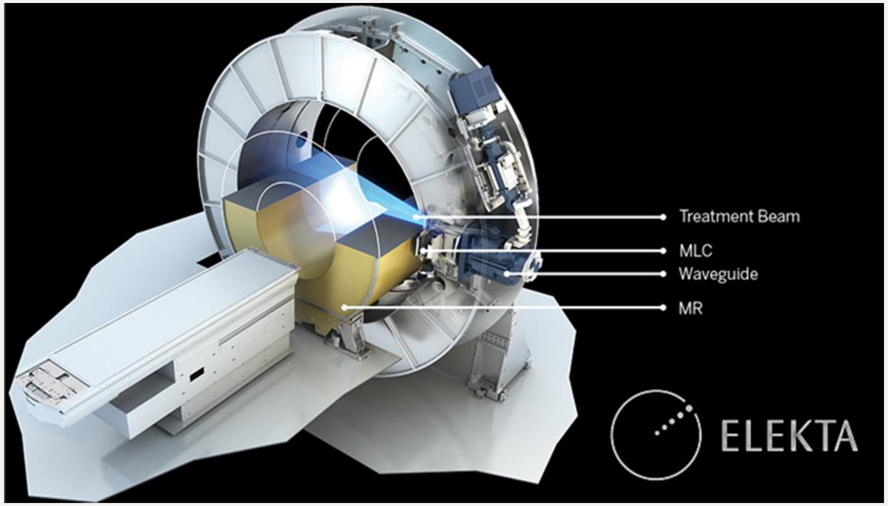


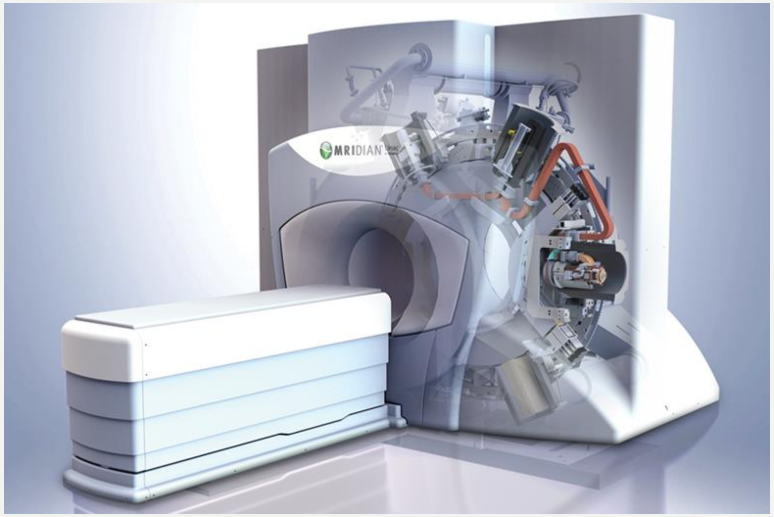
In-room MR-guided radiotherapy systems



MRI Guidance Basics

Commercial MR-Linacs





Elekta - Unity

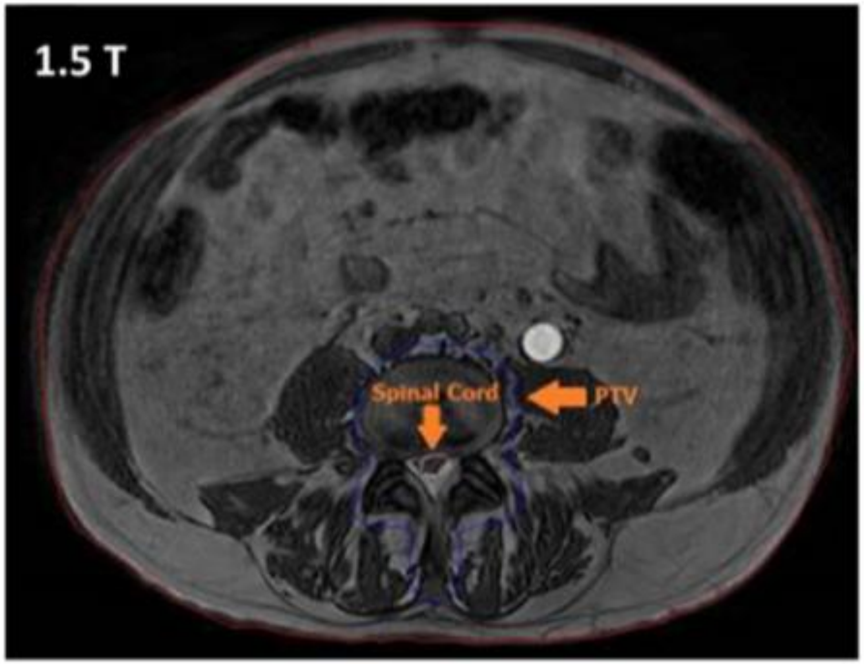
- 7 MV linac
- 1.5 T Philips closed bore magnet
- Perpendicular orientation
- 160 single focused MLC

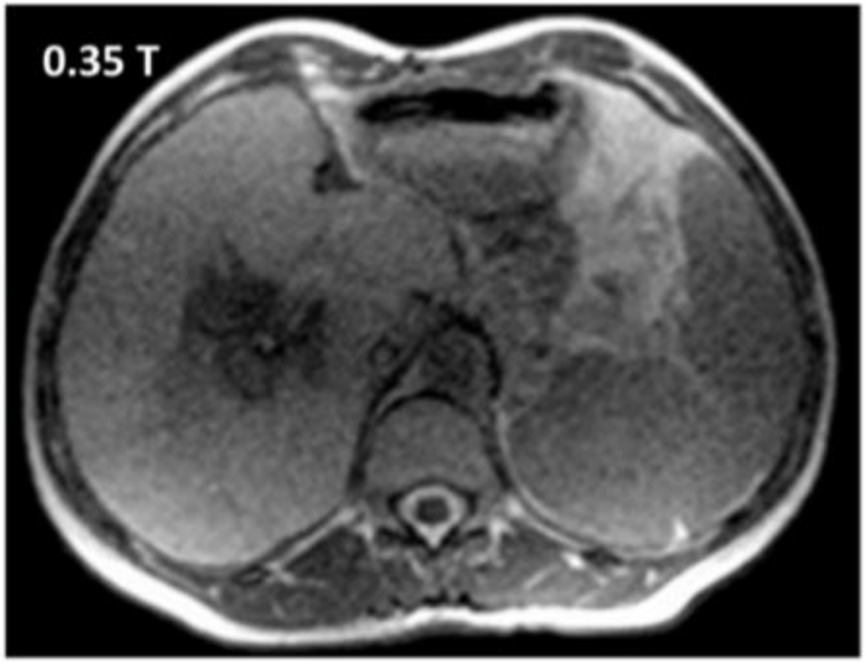
Viewray – MRIdian

- 6 MV linac (originally Cobalt-60)
- 0.35 T split bore magnet
- Perpendicular orientation
- 138 double focused MLC

MRI Guidance Basics

Commercial MR-Linacs





Elekta - Unity

- 1.5 T Philips closed bore magnet
- 3D sequence: TSE
- Voxel sizes down to $1.2 \times 1.2 \times 1.6\ mm^3$

Viewray – MRIdian

- 0.35 T split bore magnet
- 3D sequence: TRUFI
- Voxel sizes down to $1.5 \times 1.5 \times 1.5\ mm^3$

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MRI-guided treatment delivery

- **Inter-fraction motion management**
  - Quantify anatomo-pathological changes *between different fractions*
  - Acquisition of imaging data before each treatment session
  - On-table re-optimization
  - MRI ideal tool for online, dose-free, good quality 3D patient imaging → ART
- **Intra-fraction motion management**
  - Quantify anatomo-pathological changes *between the same fraction*
  - Considered in clinical practice by performing gated beam delivery
  - Standard approaches rely on correlation between internal markers and external surrogates
  - Time-resolved MRI is an ideal tool for real-time anatomy monitoring → real-time ART

→ In both scenarios **geometric and dosimetric adaptation** can be performed

Motion Management

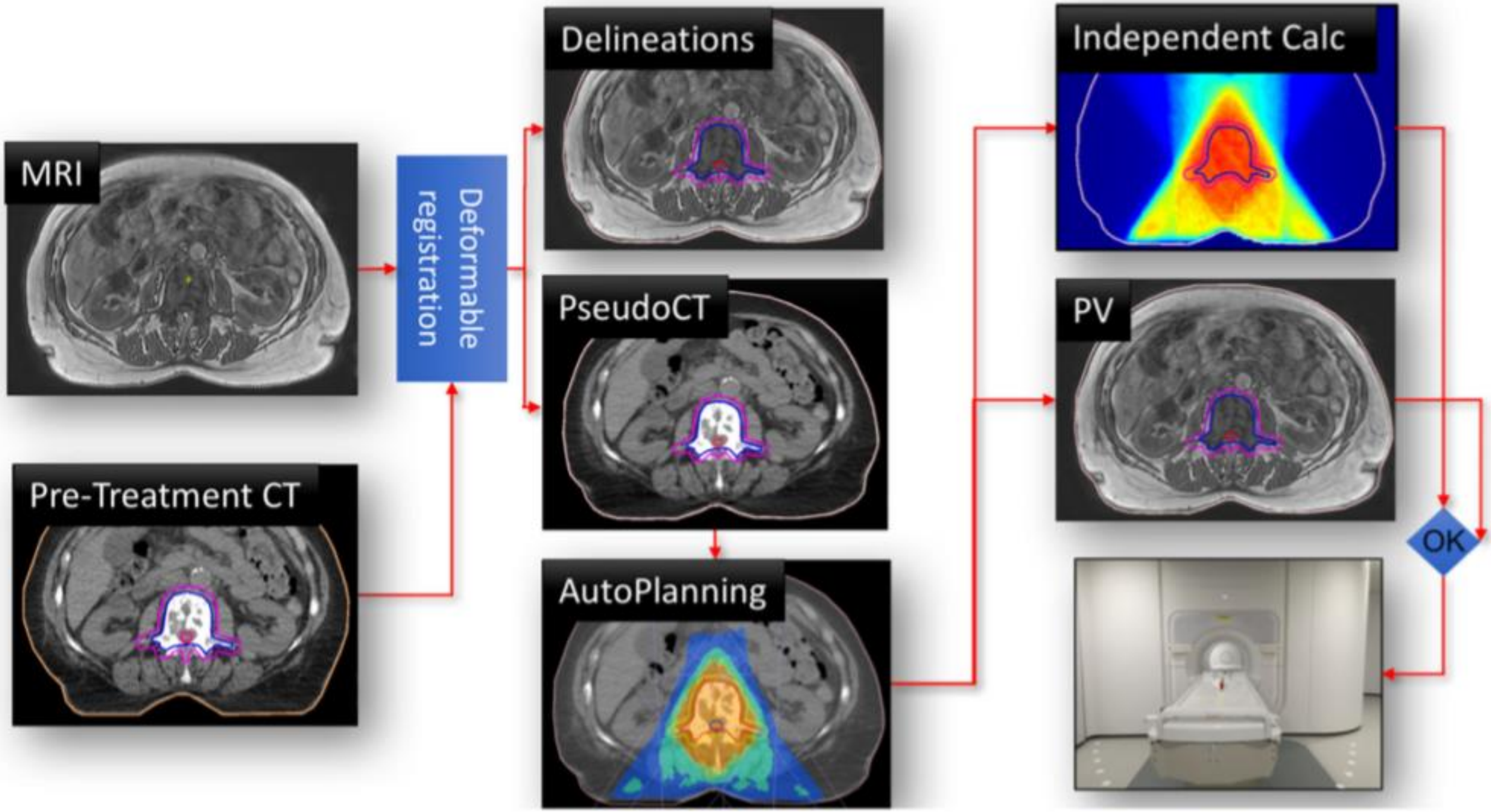
Inter-fractional

Online adaptive MRgRT workflow

- **Patient immobilization** and 3D in-room imaging
- **Patient alignment**
  - Couch shift (constrained by geometry of MR-linac systems)
  - Virtual couch shift (i.e. shift the MLCs)
- **Dose re-calculation** based on daily anatomy → treatment adaptation ?
- For dose calculation, 3D **electron density map needed** → obtained via pseudo-CT generation
  - Current clinical practice uses deformable image registration (DIR) based on planning CT as moving image and treatment MRI as fixed image
- **Updated contours** obtained from same DIR used for pseudo-CT generation, followed by manual adaptation by expert → time consuming → deep learning based auto-segmentation
- Fast Monte-Carlo dose engines used for **re-planning** → 5-10 min in clinics!

Motion Management

Inter-fractional



Motion Management

Intra-fractional

Real-time ART remains a *challange* !

Current strategies for intra-fractional motion management

1. Gated beam delivery
2. Tumor trailing
3. Dose accumulation

→ Real-time tumor tracking needed → 2D+t cine MRI

Motion Management
Intra-fractional

1. Gated beam delivery

- Current clinical practice
- If deliniated tumor moves outside of user-defined gating area → stop beam
- Breath-hold techniques used to enhance beam on time
- Disadvantage: prolonged treatment times

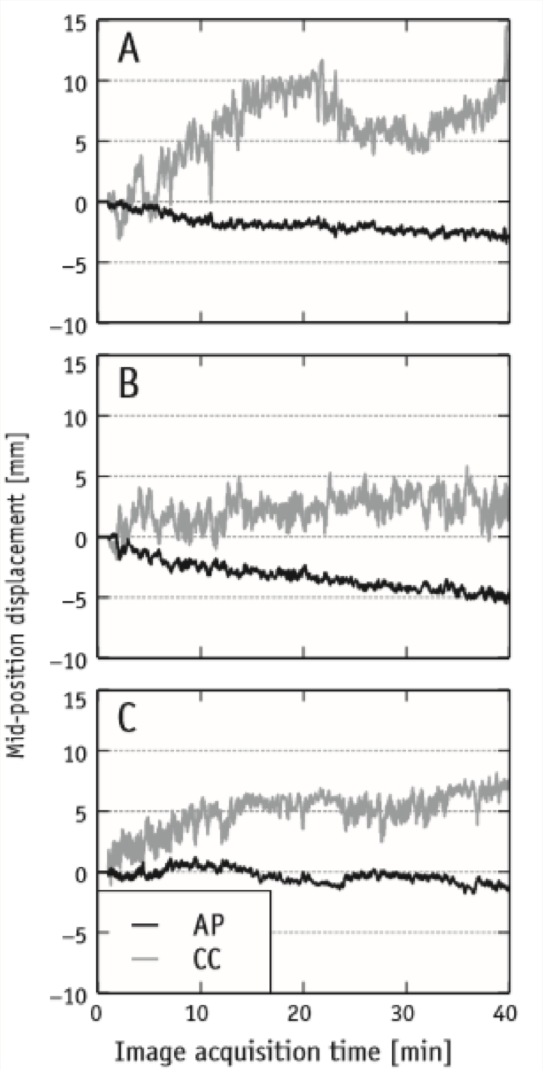
→ *Talk by Dinu Purice*

Motion Management
Intra-fractional

2. Tumor trailing

- Currently at research level only !
- ‚Continuously' adjust beam aperture according to last available time-averaged position of target
- Accounts for baseline drifts (up to 1 cm !)
- MR-linac ideally suited as it provides real-time monitoring

→ can be used to update time-averaged target position



Motion Management
Intra-fractional

Tumor trailing for liver SBRT on MR-Linac (Fast et al, 2018)

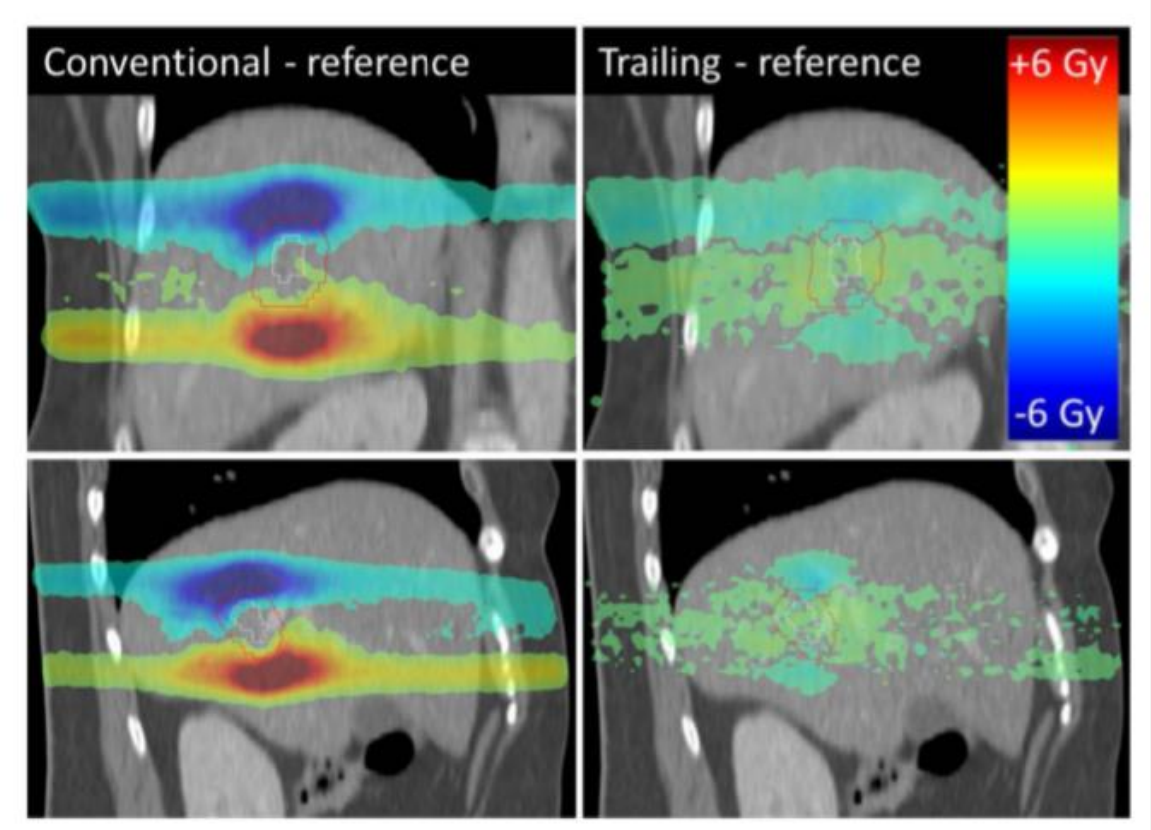
- 17 retrospective patients with oligometastatic liver disease
- Previously treated with conventional linac
- Treatment was re-planned for Elekta-Unity MR-linac
  - 3 x 20 Gy, 11-beam IMRT
  - Treatment was ‚delivered' using in-house treatment emulator
  - Different motion scenarios were modeled
  - Delivered dose is calculated using isocenter-shift methodology
  - Effect of 1.5 T field considered in all calculations
- Tumor trailing was also experimentally validated with motion phantom
  - Continuous periodic motion: $15\ mm$ peak-to-peak amplitude SI
  - Continuous linear drift: $0.5\ mm/min$ SI and $-0.25\ mm/min$ AP
  - Dedicated film insert in coronal plane

Motion Management

Intra-fractional

Tumor trailing for liver SBRT on MR-Linac (Fast et al, 2018)

- Treatment was ‚delivered' and dose calculated

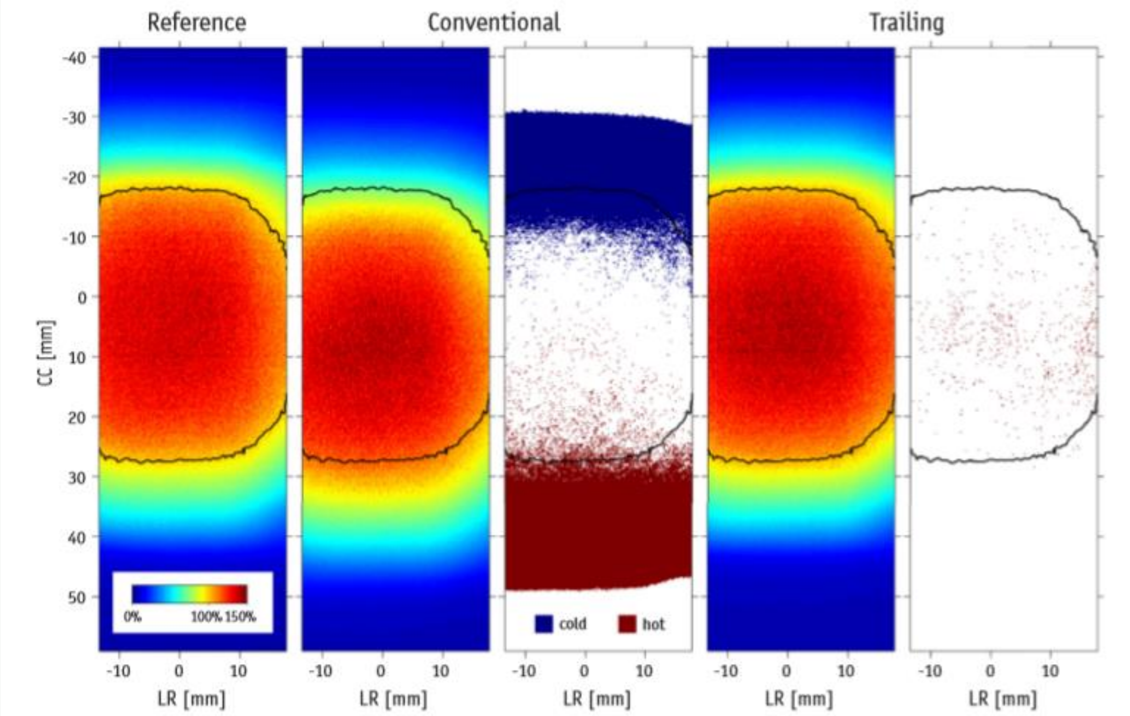


→ Assuming predominately **cranial** baseline **motion trailing prevented hot spot** creation

Motion Management
Intra-fractional

Tumor trailing for liver SBRT on MR-Linac (Fast et al, 2018)

- Tumor trailing was experimentally validated with motion phantom



Conventional vs. Trailing 3%/2mm **gamma** pass **rates:** $49 \pm 3\%$ & $98 \pm 3\%$

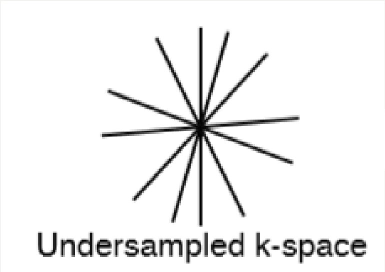
Motion Management

Intra-fractional

Beyond tumor trailing – Towards real-time ART

- Estimated motion could be used to adapt beam to current anatomy
- Problems
  - Motion must be quickly estimated
  - Acquisition, estimation and dose dose delivery < $200\ ms$ (Keall et al., 2006)
  - Biggest source of latency in MR-linac feedback chain: MR acquisition

→ Current research focuses on decreasing acquisition times
  - Parallel imaging used but acceleration factors limited by image quality
  - Compressed sensing cannot be used due ‚large‘ reconstruction times
  - Deep learning (DL) based reconstruction of undersampled k-space (Terpstra et al., 2020)



Motion Management

Intra-fractional

DL based image reconstruction and motion estimation (Terpstra et al, 2020)

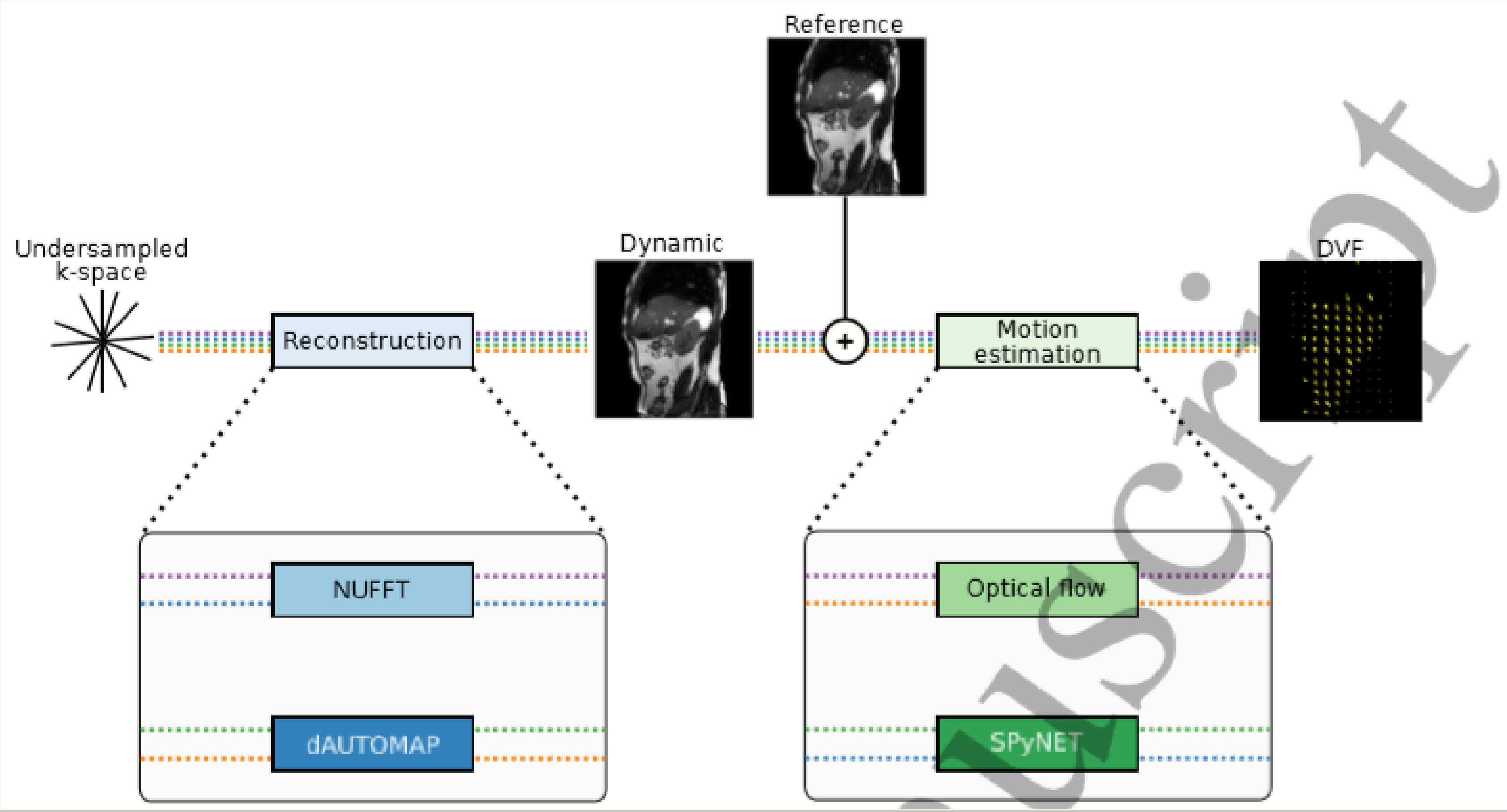
- 2D cine MRI acquired at 1.5 T from 135 patients
- Tumors in abdomen, liver, kidneys and pancreas
- Undersampled radial golden angle acquisition were restrospectively simulated
- Deformation vectors fields (DVFs) were obtained via combinations of conventional and DL methods for reconstruction and motion estimation
- 4 approaches in total:

Motion Management

Intra-fractional

DL based image reconstruction and motion estimation (Terpstra et al, 2020)

- 4 approaches in total:



Motion Management

Intra-fractional

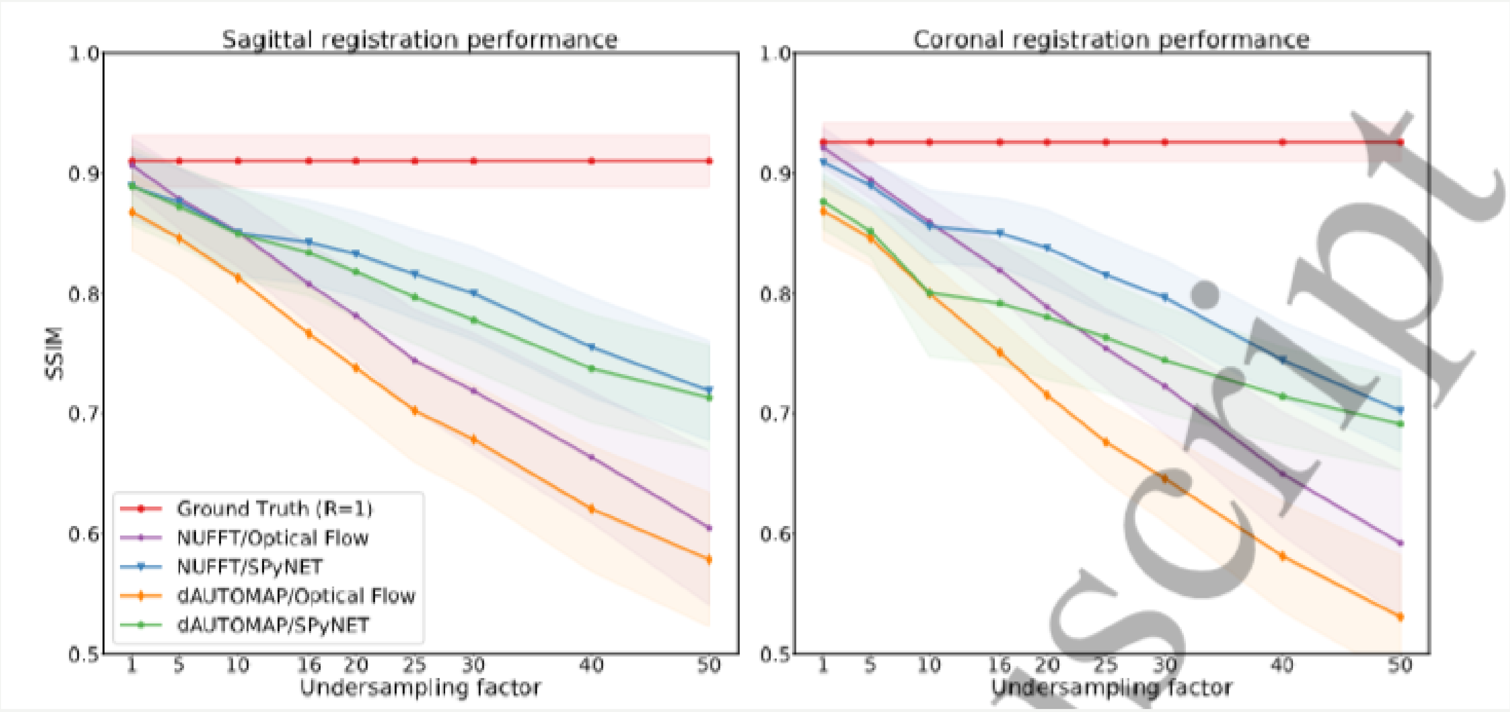
DL based image reconstruction and motion estimation (Terpstra et al, 2020)

- 4 approaches in total
- Evaluation of approaches based on following criteria:
  - Correctness of DVFs
  - Time

Motion Management
Intra-fractional

DL based image reconstruction and motion estimation (Terpstra et al, 2020)

- Results



→ Fully conventional methods more accurate at low undersampling

→ Conventional reconstruction + DL estimation best at high undersampling

Motion Management

Intra-fractional

DL based image reconstruction and motion estimation (Terpstra et al, 2020)

- NUFFT/SPyNET best approach
- Root-mean squared displacement < $1\ mm$ compared to ground truth DVF
- Acquisition, reconstruction and motion estimate $\approx 60\ ms$

→ Ample time to adapt beam to motion (not investigated)

→ Could enable real-time tumor tacking to account for intra-fraction motion

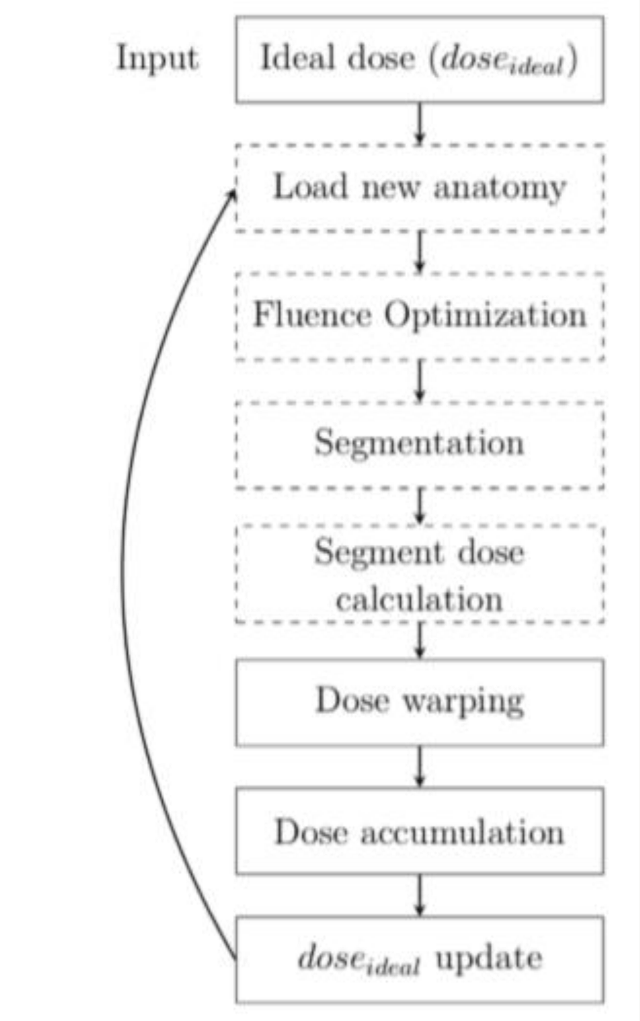
- Major limitation: High-quality ground-truth DVFs needed to train SPyNET

Motion Management
Intra-fractional

3. Dose accumulation

- Currently at research level only !
- Gating and trailing focus on geometric adaptation
- Why not directly adapting the final dose?

→ Dose accumulation
  - Monitor motion continuosly
  - Keep track of already delivered dose
  - Use already delivered dose to optimize remaining dose to be delivered

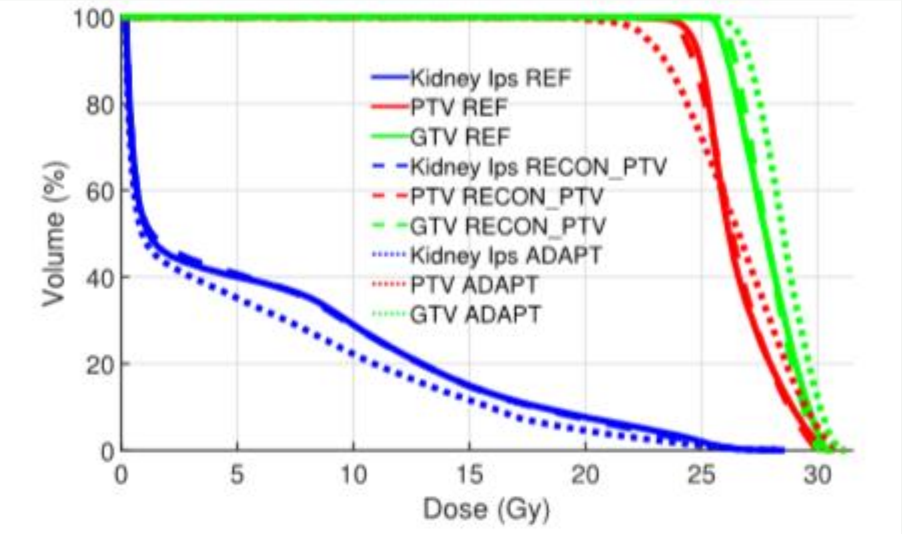


Motion Management

Intra-fractional

Fast online intra-fraction replanning with MR-linac (Kontaxis et al, 2017)

- Treatment was simulated for 2 previously treated patients and 1 healthy volunteer
- Fast online adaptive treatment compared with conventional plan based on $3\ mm$ planning target volume (PTV)
- Adaptive treamtent lead to
  - Higher dose to GTV
  - Increased sparing of healthy tissue
- Mean treatment delivery time:
  - Static: $16.7\ min$
  - Adaptive: $18.5\ min$
  - Most time consuming: dose calculation
- However, workflow *was not* optimized in terms of time



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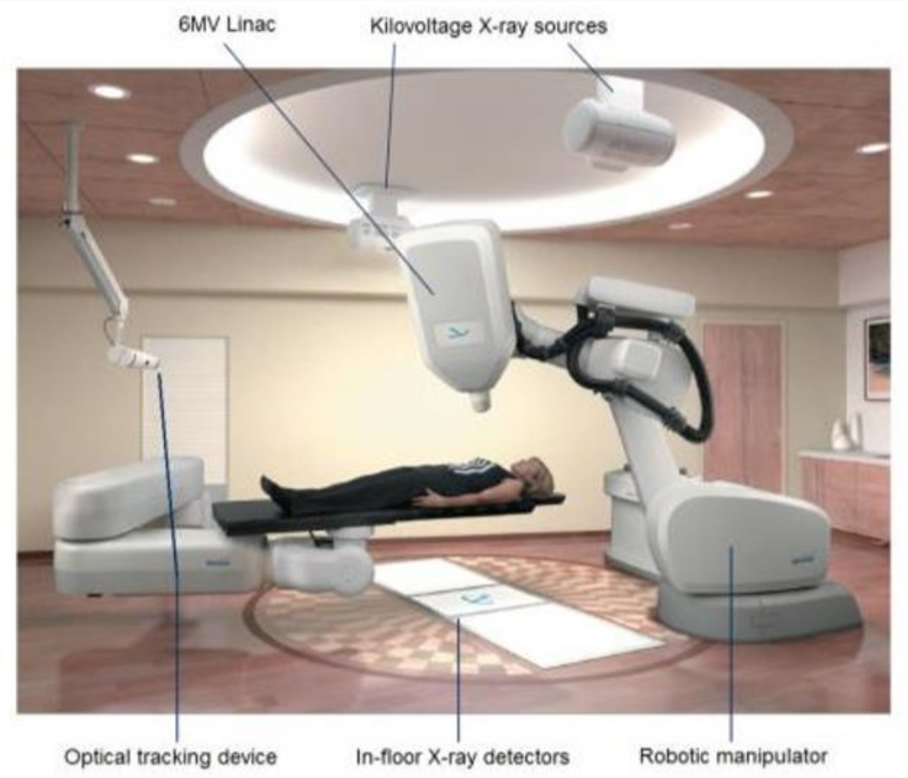
Comparison

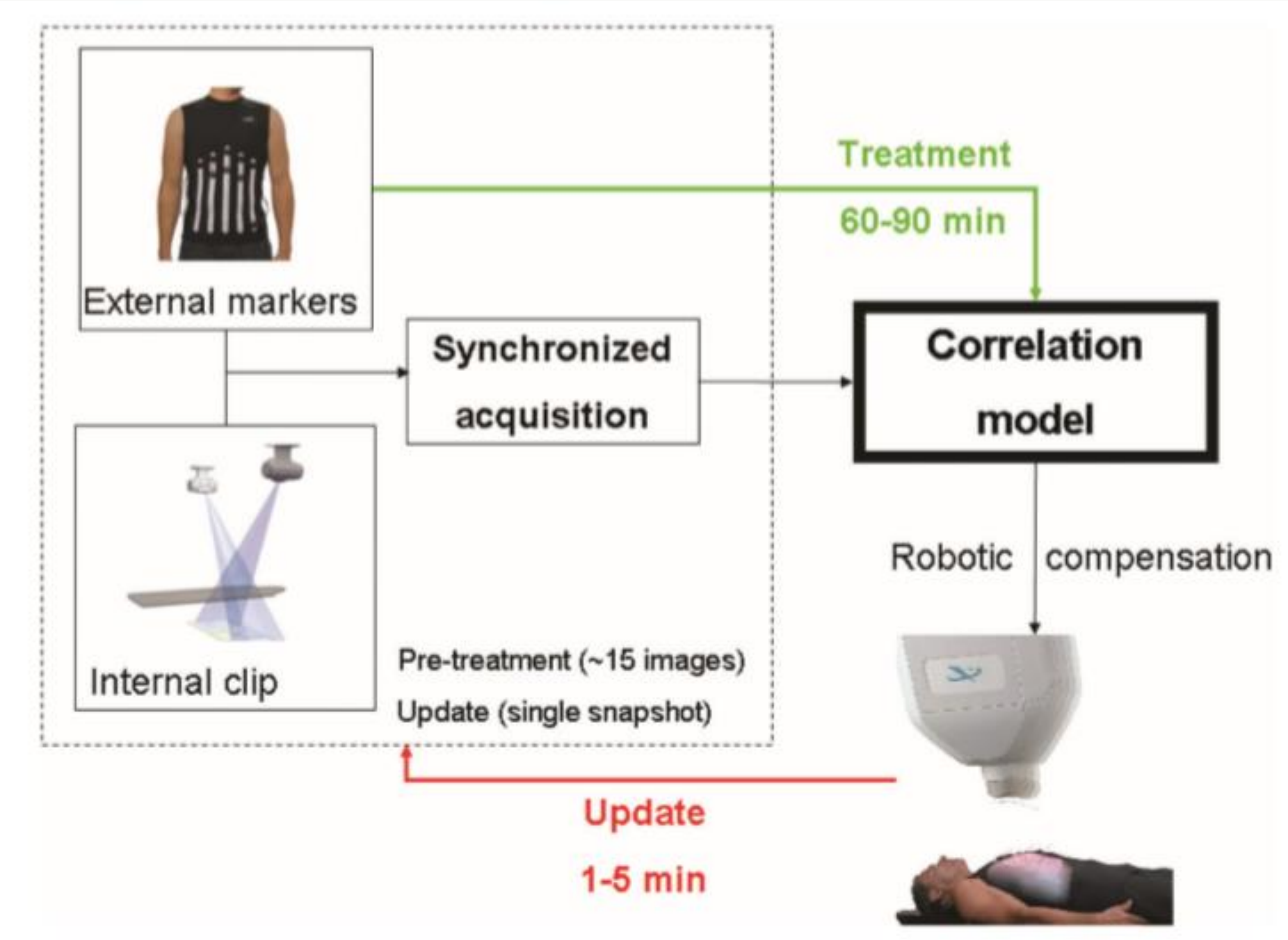
Cyberknife

The Cyberknife Robotic Radiosurgery System (Kilby et al, 2010)

- Originally developed as frameless alternative to intra-cranial stereotactic radiosurgery systems
- Since 2010, applicable to any site in the body where radiosurgery is indicated (h&n, lung, prostate, etc.)
- Robotic manipulator with 6 MV linac → high precision beams
- X-ray image guidance system
- Stereo camera system → continuous optical marker tracking
- Motion management strategies implemented → real-time tumor tracking with continuous irradiation (site dependent solutions)



Cyberknife Synchrony respiratory tracking (Kilby et al, 2010)



- Episodic X-rays combined with continuos optical imaging ($\approx$ 30 Hz)
- External/internal polynomial correlation model
- Correlation model built at beginning of session and updated during treatment
- Predictor model used to account for communication and linac inertia latencies
- Robotic arm is moved dynamically → 100% duty cycle

Comparison
Cyberknife & MR-Linac


- Low soft tissue contrast with additional dose

- Implantation of markers is invasive

+ Static targeting accuracy: $< 0.95\ mm$

- Long treatment times $\approx 60\ min$

+ Real-time ART: clinical since 2010

+ Real-time tumor tracking, motion prediction and beam adjustement implemented

+ Superb soft tissue contrast with no dose

- Corrections needed for magnetic field

+ Static targeting accuracy: $1.0\ \pm 0.1\ mm$

+ Treatment times comparable with conventional LINACs (best case)

- Real-time ART: still at research level

- Real-time 4D MRI remains a challange

Caveat: clinically seen, almost no competition !

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Summary & Outlook

Summary

- MRgRT offers effective real-time tumor and anatomy tracking

→ Inter- & intra-fractional motion management

→ Better treatment customization

→ Increased dose to tumor while sparing healthy tissue

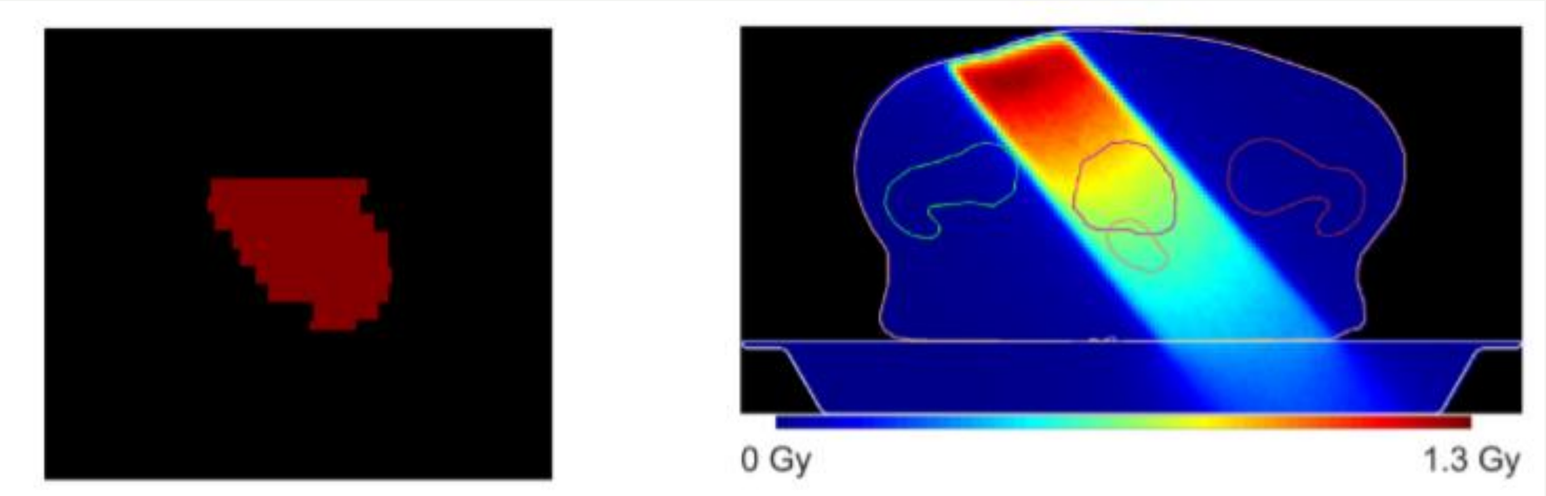
Outlook

- Intra-fractional changes still tackled with gated delivery
- Main limitations to real-time ART
  - Time resolution of 4DMRI
  - Fast dose calculations

Outlook
Fast dose calculations

DeepDose: Fast dose calculation engine using deep learning (Kontaxis et al, 2020)

- Proof-of-concept application of DeepDose network
- Convolutional neural network used to predict dose
- Task: derive dose distribution of individual MLC shapes on given anatomy
- Result: Full plan in 1 min compared with GPU-MC in 3 min
- Future aim: integrate DeeDose in their online adaptive workflow



Literature Search

Research Engines:

- Pubmed
- Google scholar
- Google
- References in papers

Inclusion/Exclusion Criteria:

- Keywords: MRI guidance, MRgRT, image guided RT, MR linac, intrafraction replanning, adaptive radiotherapy, real-time tumor tracking, deep learning for motion estimation, cyberknife review
- Low impact factor according to JCR
- Focus on recent papers

Manufacturer Pages:

- ViewRay
- Elekta

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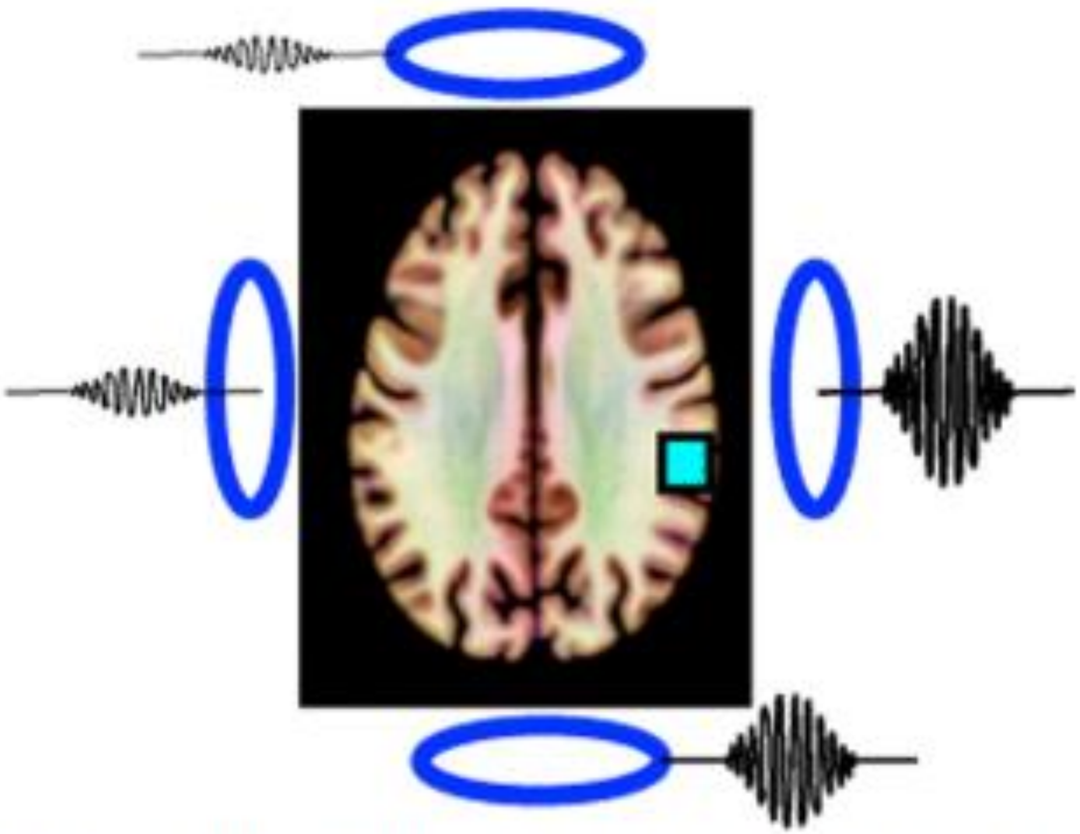
Thank you for your attention !

Additional Slides

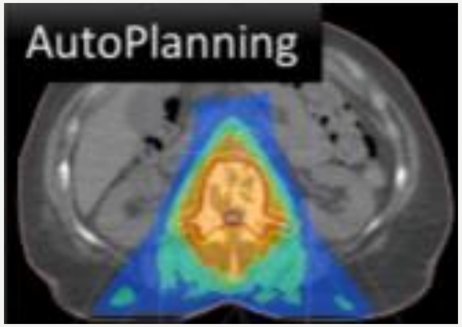
Parallel Imaging



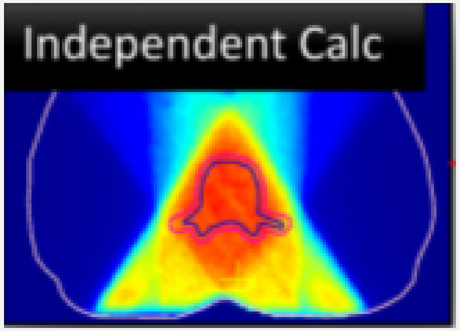
Principle underlying parallel imaging: use coil sensitivity information to assist in spatial localization

Sources: http://mriquestions.com/what-is-pi.html

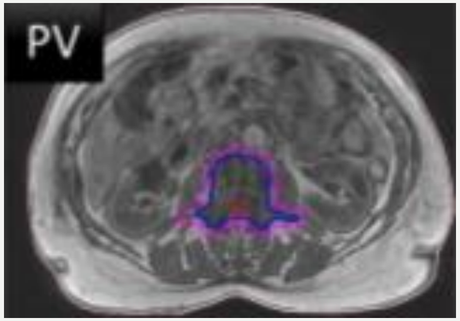
Inter-fractional motion management with Elekta-Unity at UMC, Utrecht, 2017



- **Autoplanning:**
  - IMRT plan for MRI-Linac, including 1.5 T field is generated using research version of Monaco TPS (Elekta AB, Sweden)
  - Independet re-calculation of this plan done with OnCentra (Elekta, AB) for quality assurance

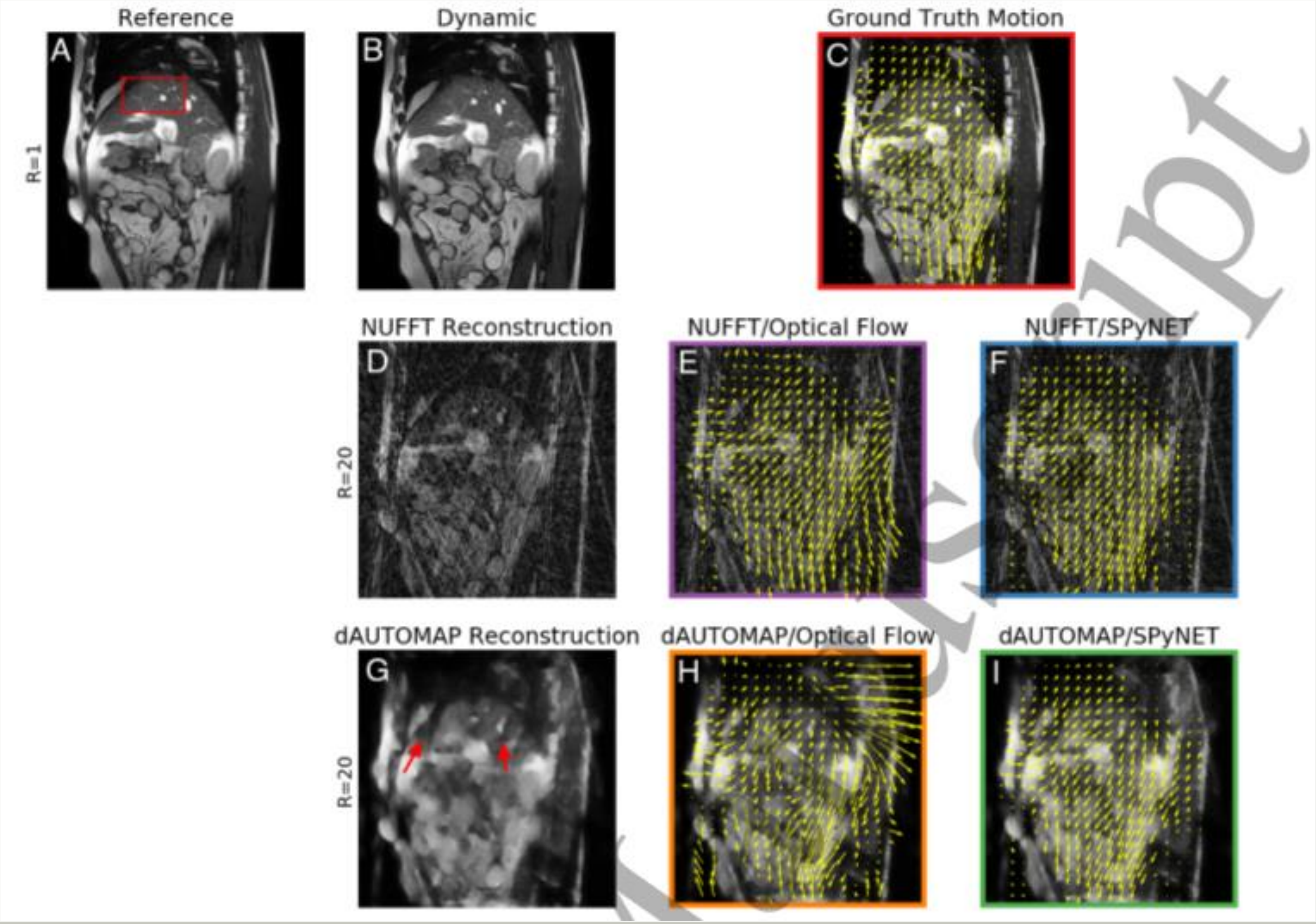


- **Position Verification (PV):**
  - To check patient stability after the contour and planning steps another 3D MRI scan is done
  - Contours are overlaid and visually checked for alignment before the radiation oncologist approves proceeding



DL based image reconstruction and motion estimation (Terpstra et al, 2020)

- Results



Sources: [17]

Fast online intra-fraction replanning with MR-linac (Kontaxis et al, 2017)

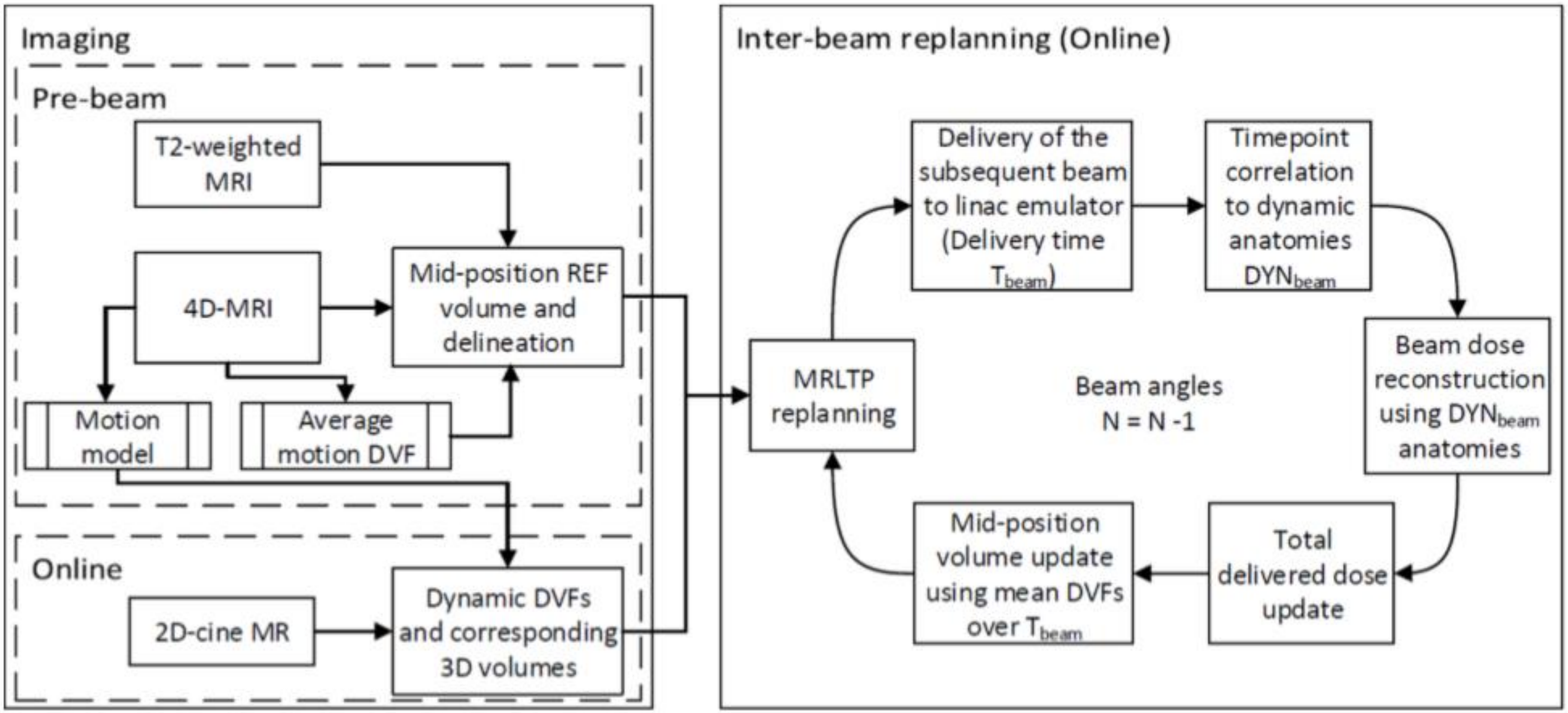
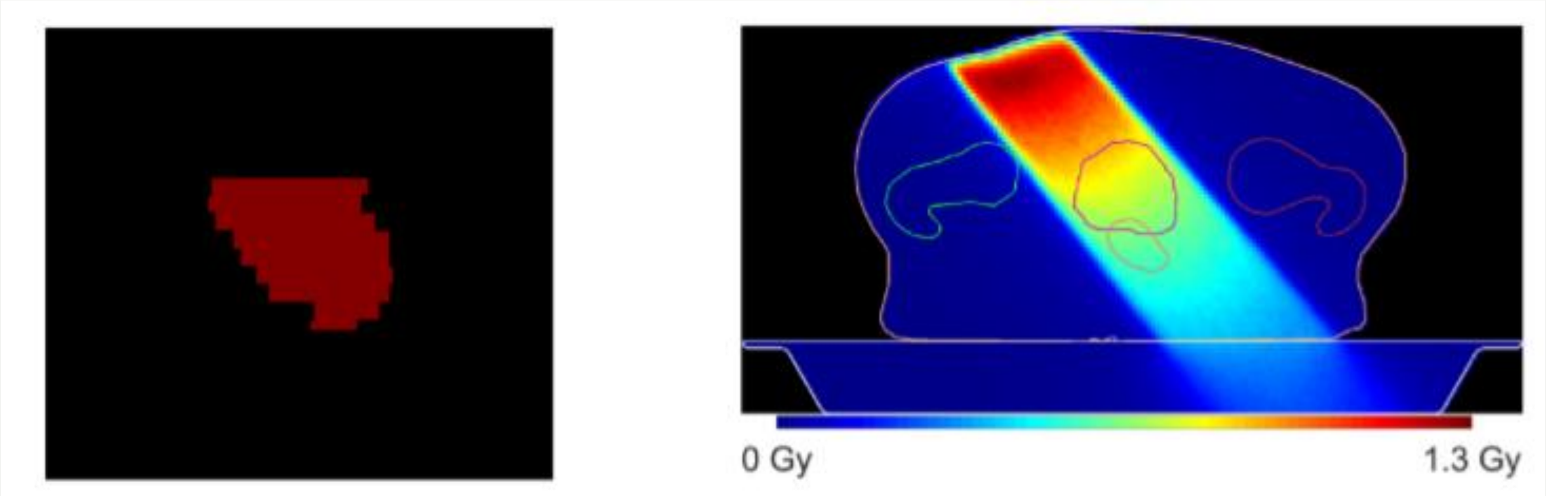


Figure 1. Treatment pipeline consisting of simulated pre-beam and online phases.

DeepDose: Fast dose calculation engine using deep learning (Kontaxis et al, 2020)

- Proof-of-concept application of DeepDose network
- 101 prostate patients previously treated with fixed-beam IMRT
- Convolutional neural network used to predict dose
  - U-net architecture
  - 80 patients for training, 10 for validation, 11 for testing
- Task: derive dose distribution of individual MLC shapes on given anatomy

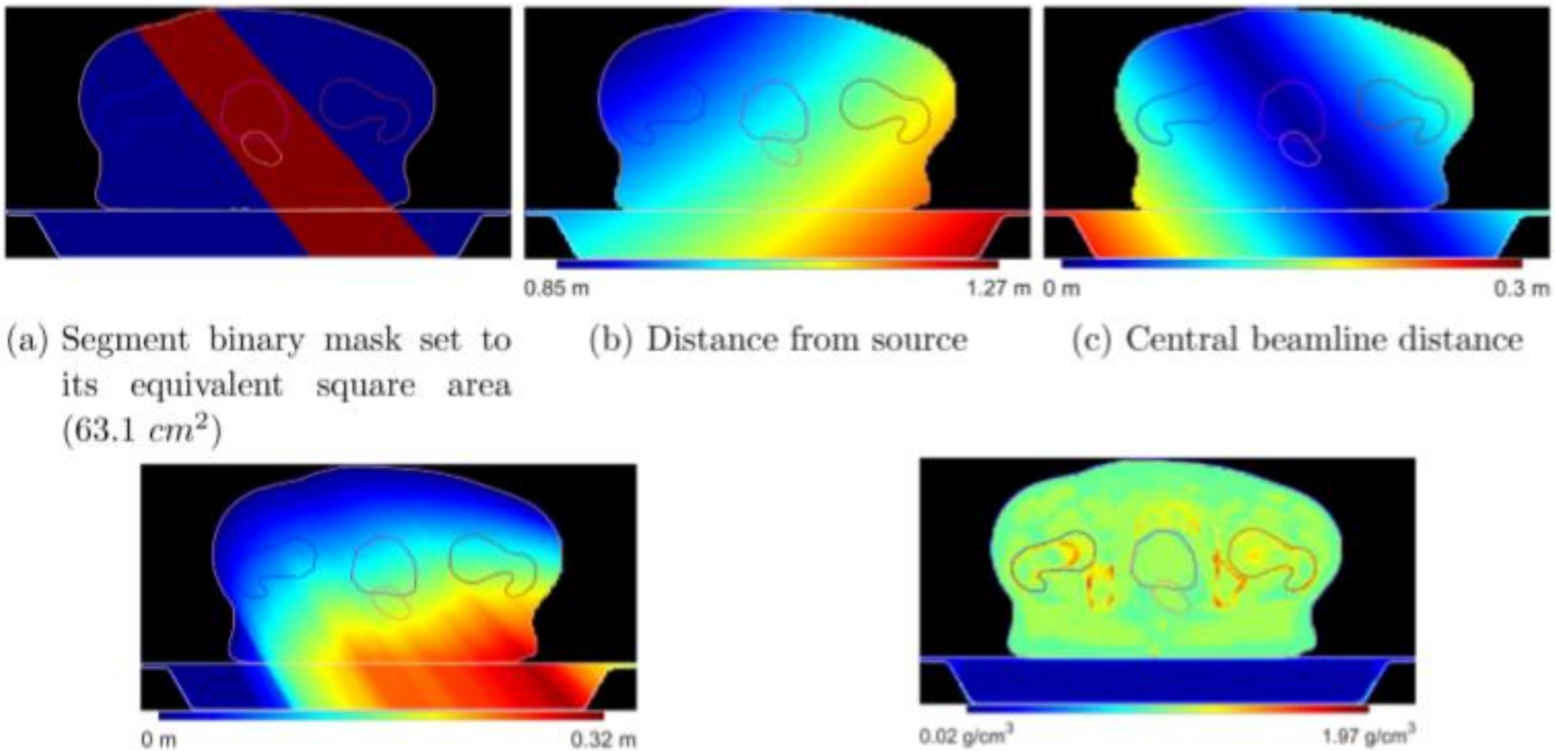


Additional Slides

Fast dose calculations

DeepDose: Fast dose calculation engine using deep learning (Kontaxis et al, 2020)

- MLC shape was encoded as 5 different 3D volumes
- Input of network (*batch , width, height, depth, channels*): $16 \times 192 \times 128 \times 80 \times 5$



(a) Segment binary mask set to its equivalent square area ($63.1\ cm^2$)
(b) Distance from source
(c) Central beamline distance
(d) Radiological depth
(e) Volume density

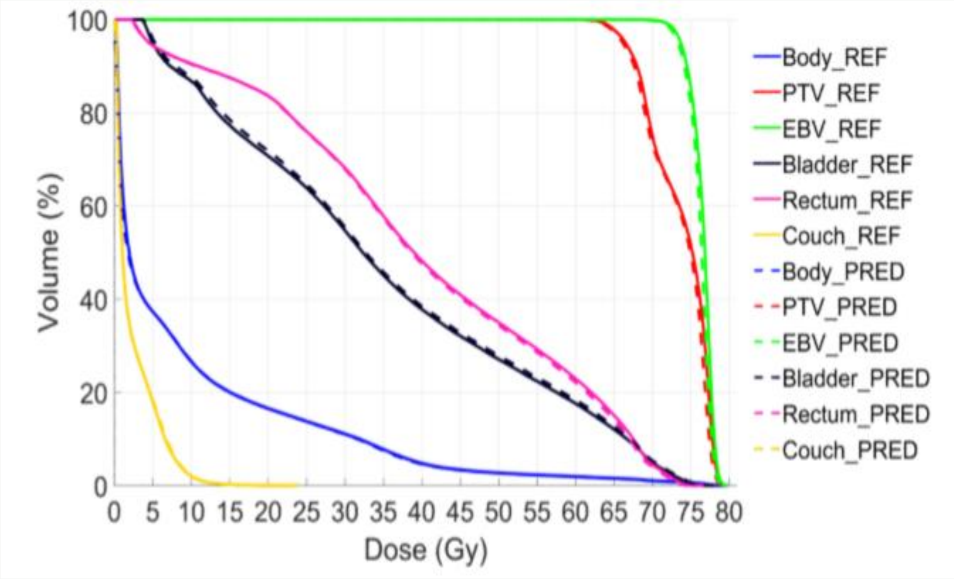
Sources: [23]

Additional Slides

Fast dose calculations

DeepDose: Fast dose calculation engine using deep learning (Kontaxis et al, 2020)

- Results
  - Stopped training when validation loss was stable
  - Used trained network to infer dose per segment for testing patients
  - Individual segment doses summed to obtain total predicted plan dose
  - Comparison of predicted dose with Monte Carlo (MC) calculation



- Good agreement
- $99.9\ \pm 0.3\ \%$ gamma pass rates ($3\% \ / \ 3\ mm$)
- Fast inference in $0.6\ sec$ for whole patient volume per segment
- Full plan in $1\ min$ compared with GPU-MC in $3\ min$

→ Future aim: integrate DeeDose in their online adaptive workflow

Additional Slides

U-Net Architecture (Kontaxis et al, 2020)

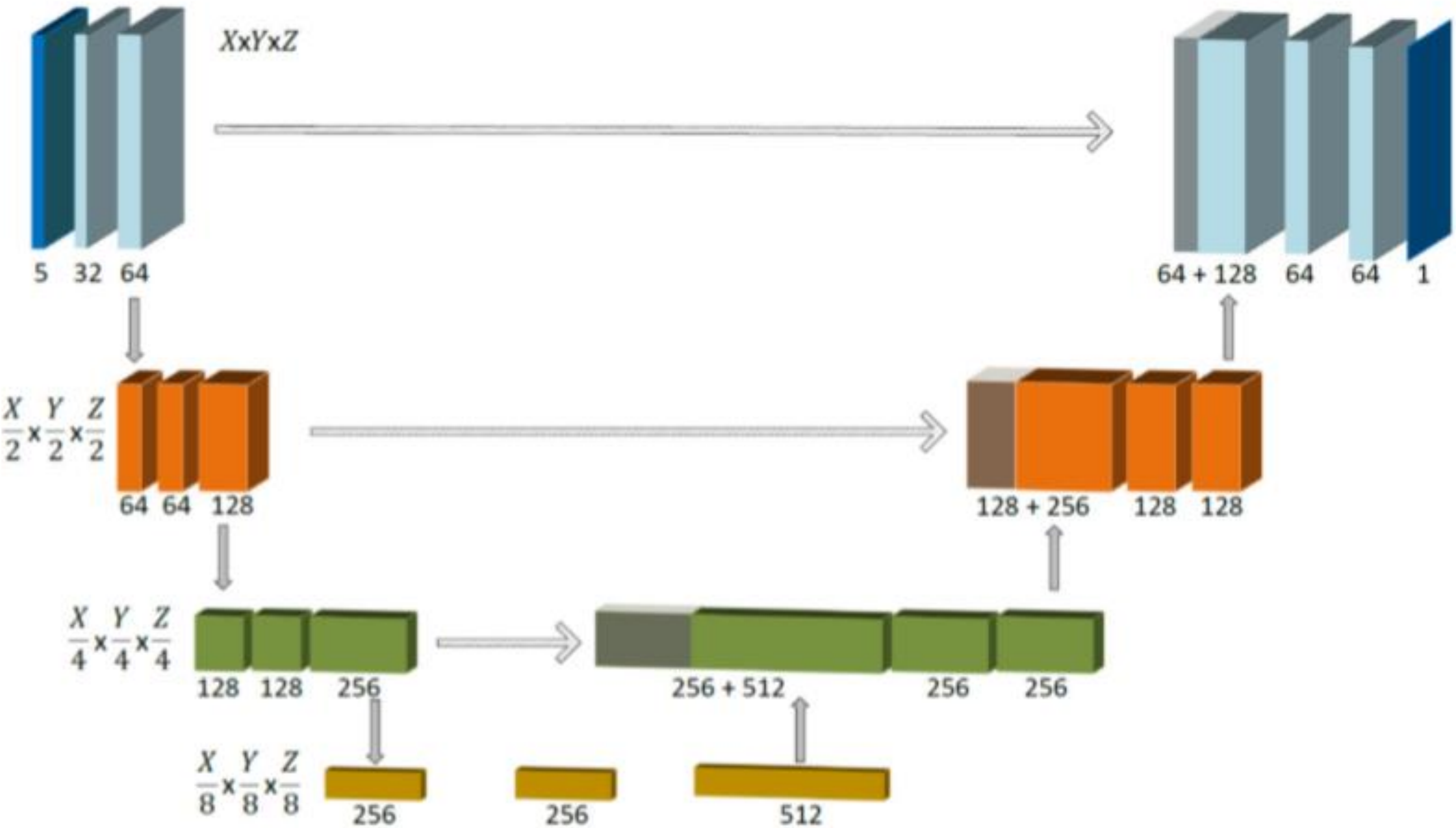


Figure 1. 3D U-Net

Sources: [23]