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ICCR 2024
XXth International Conference on the use of Computers in Radiation therapy

AI for motion management

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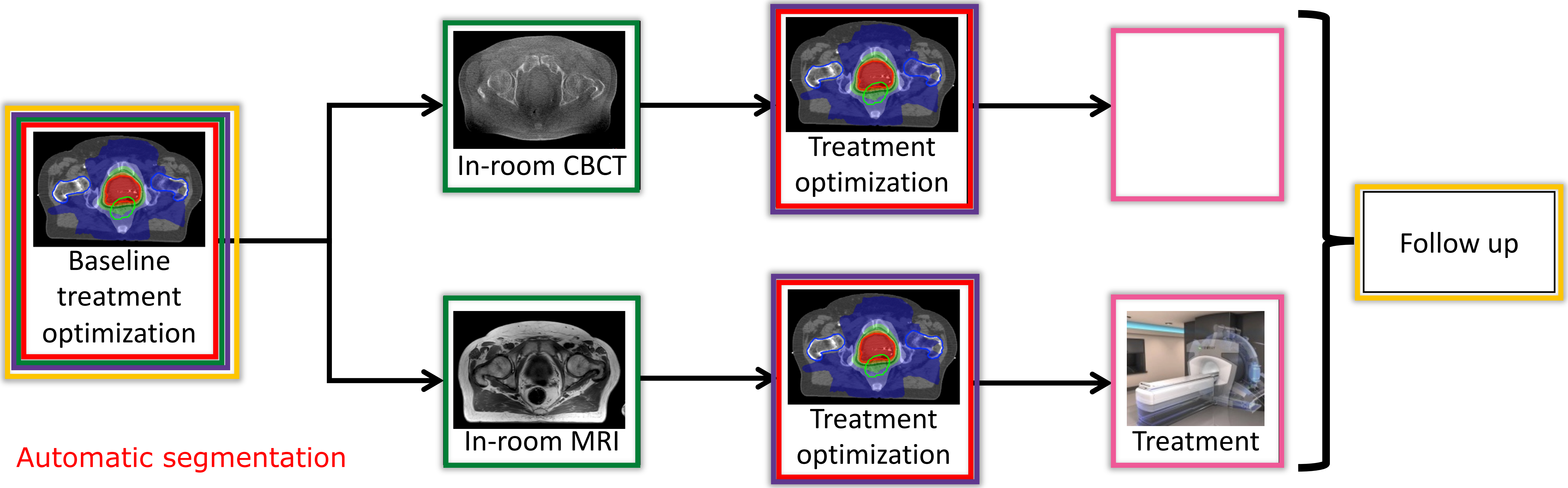
ICCR 2024
July 9th, 2024 – Lyon

Radiotherapy workflow
Where can AI help?



Automatic segmentation

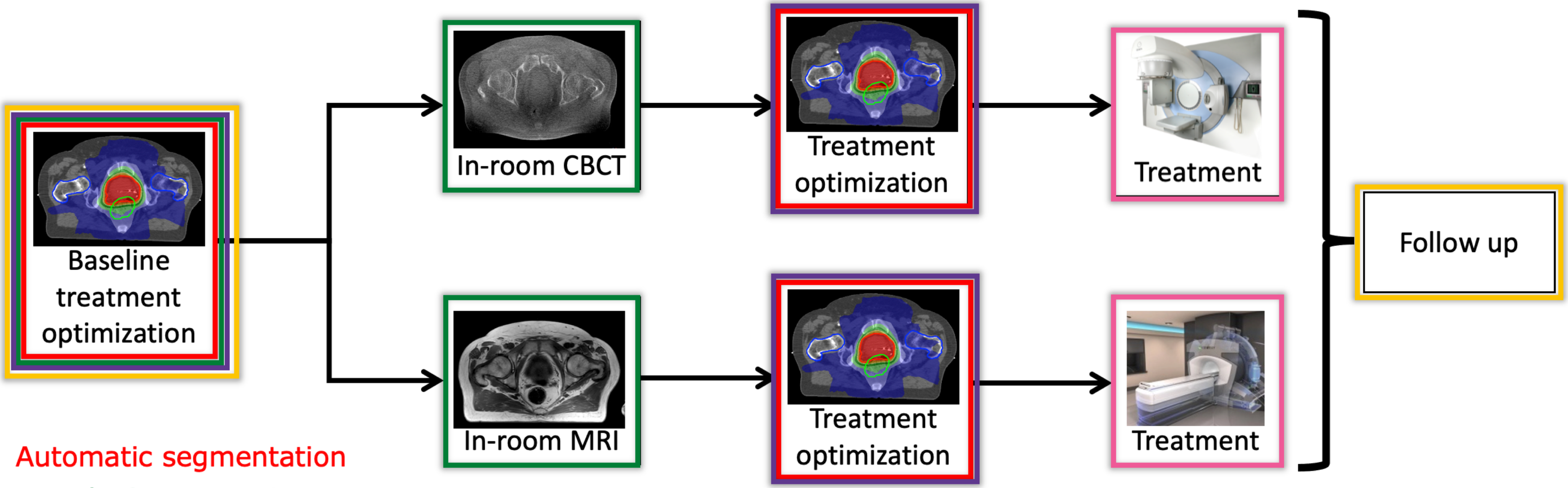
Pseudo CT generation

Dose prediction and automatic planning

Motion tracking

Outcome prediction

Radiotherapy workflow
Where can AI help?



Automatic segmentation

Pseudo CT generation

Dose prediction and automatic planning

Motion tracking

Outcome prediction

AI in RT

Models

- In the vast majority of applications, the U-net is used
- Trained in a supervised fashion
  - We have labels (for example clinical segmentation masks, dose distributions, CT scan)
- In motion tracking applications, we will see more heterogeneous models
  - R-CNN, mask R-CNN, faster R-CNN, Retina Net
  - LSTM
- Often limited labels, cannot train U-net
  - unsupervised training is possible

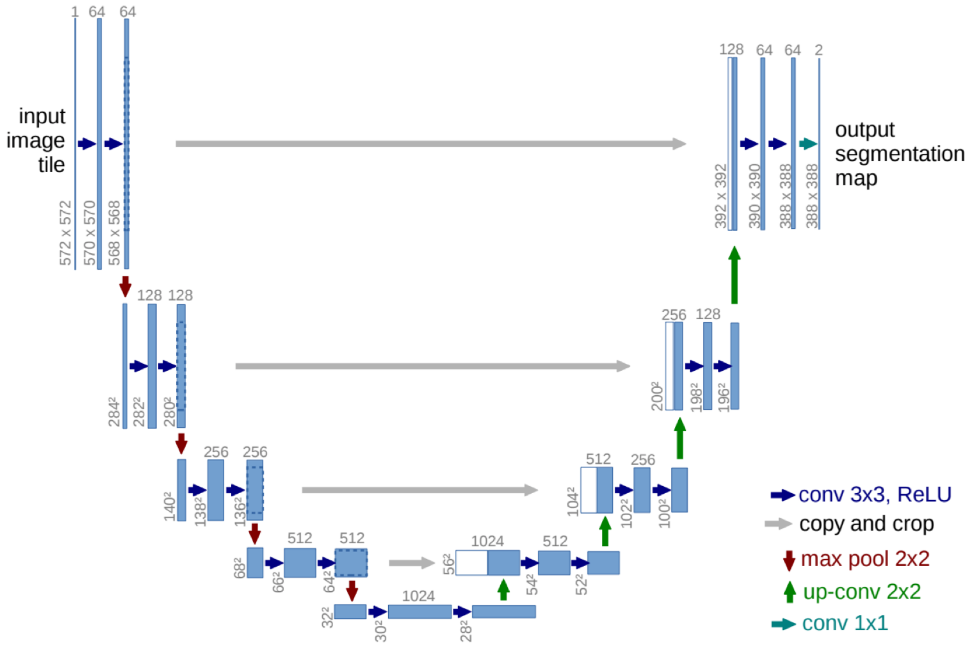


Fig. 1. U-net architecture (example for 32x32 pixels in the lowest resolution). Each blue box corresponds to a multi-channel feature map. The number of channels is denoted on top of the box. The x-y-size is provided at the lower left edge of the box. White boxes represent copied feature maps. The arrows denote the different operations.

https://arxiv.org/pdf/1505.04597.pdf

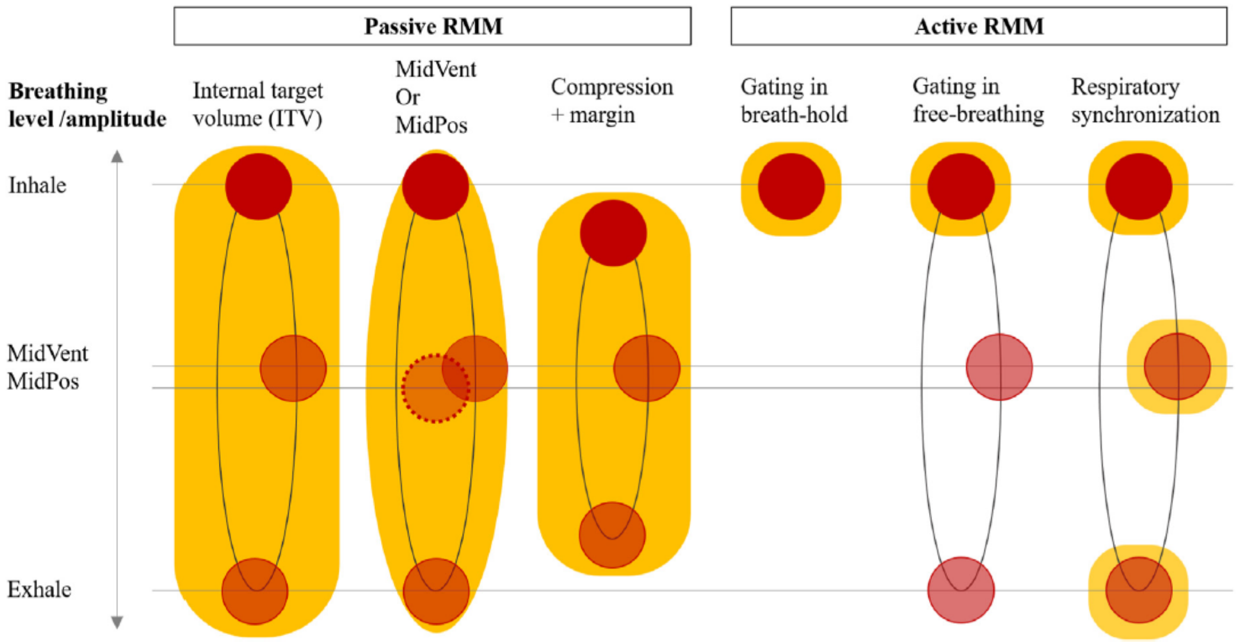
Treatment of moving tumors
Motion management

- Lung tumors are the 1st cause of cancer deaths in men, 2nd in women in Germany (Robert Koch Institute)

- Stereotactic body radiotherapy (SBRT) and hypofractionation has brought long term control in the range of 80-90%

  Timmerman et al. JAMA Oncol 2018
  Ball et al., Lancet Oncol 2019

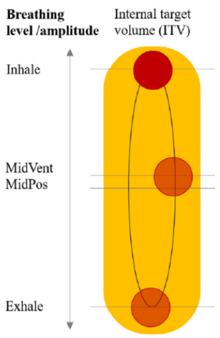
- Successful radiation delivery requires respiratory motion management strategies
  - Also applies to liver, pancreas and other lesions in the abdomen

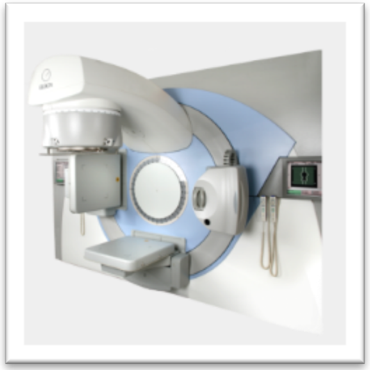


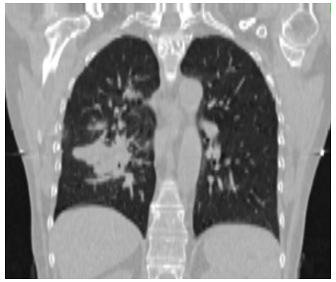
Dhont et al. Clin Oncol 2020

SBRT of moving tumors
Options at the clinic

Conventional linac and ITV



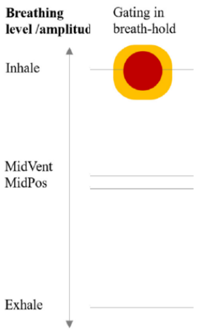


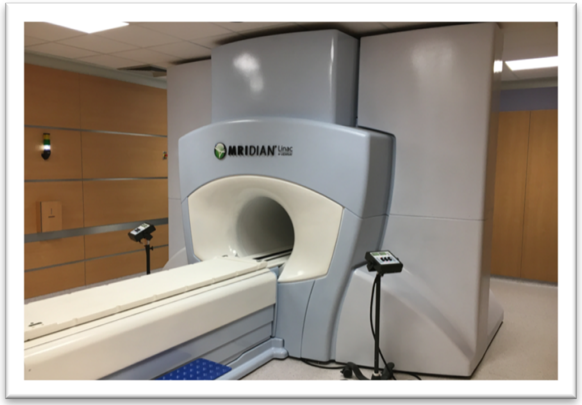


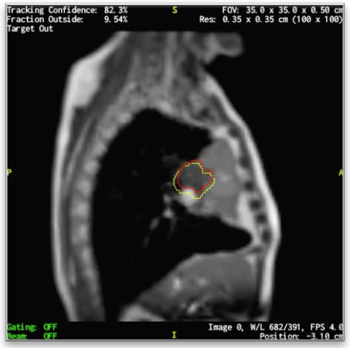
4DCT scan for
ITV determination

- Typically peripheral stage 1-2 tumors
- Pros: relatively simple workflow and limited treatment times
- Cons: larger irradiated volume for larger motion

MR linac and gating



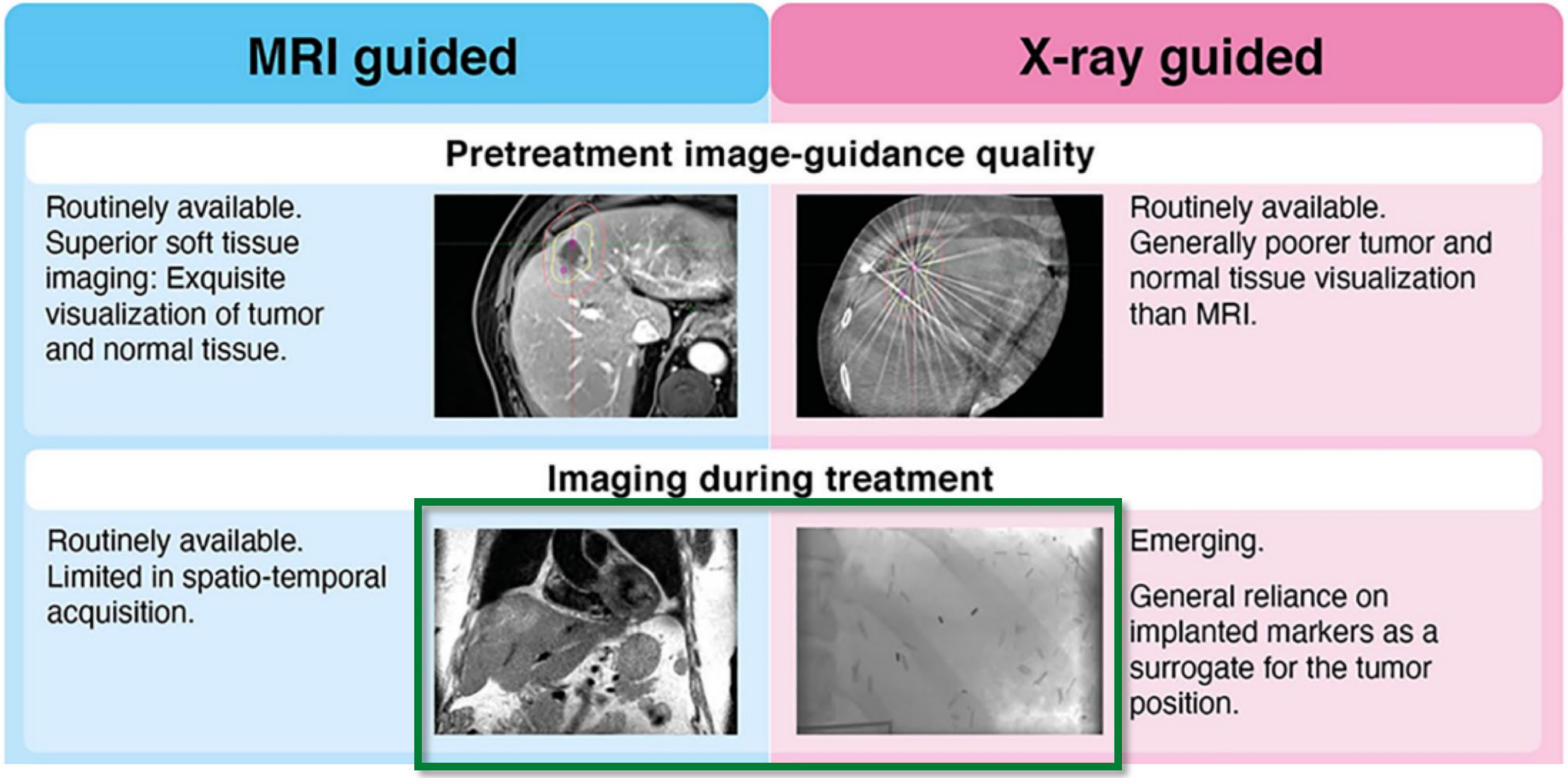




8Hz 2D cine-MRI for target tracking

- Typically central stage 1-2 tumors
- Pros: limited irradiation volume
- Cons: limited throughput, median treatment time 50 minutes, limited availability of technology (5 in Germany), high investment

Background
Image-guided adaptive RT



Timescales

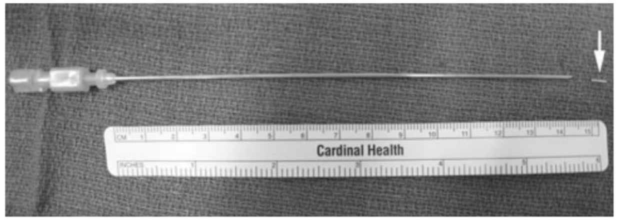
- Pretreatment
  - Minutes
  - Inter-fractional changes
  - Online adaptive RT
- During treatment
  - Second(s) or less
  - Intra-fractional changes
  - Real-time adaptive RT

Adapted from Keall et al. (2022) *ICRU Report 97*

Motion management
X-ray tumor tracking

- Relies on 2D x-ray images, ideally stereoscopic

- Usually requires marker implantation
  - Patient discomfort
  - Risk of infection
  - Risk of marker migration



Fiducial marker implantation apparatus

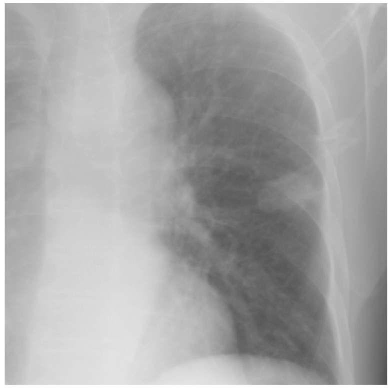
Baghat et al. Cardiovasc Intervent Radiol 2010

- Markerless tracking is challenging
  - Low contrast
  - Shadowing by ribs, mediastinum or diaphragm

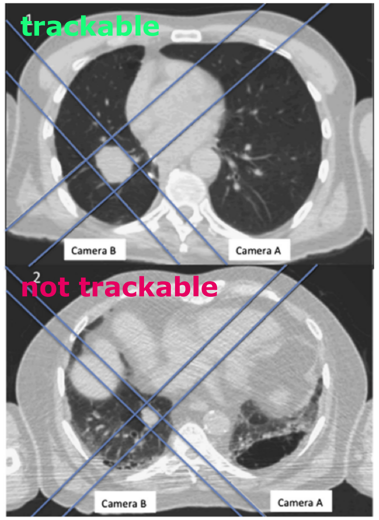
- Typically based on template matching or correlation to surface

- For CyberKnife markerless tracking 66% of selected patient deemed eligible

Bahig et al. Int J Radiat Oncol Biol Phys 2013



LMU lung cancer patient during CBCT acquisition



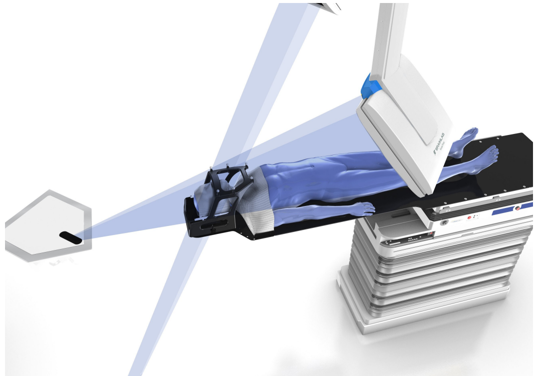
Bahig et al. Int J Radiat Oncol Biol Phys 2013

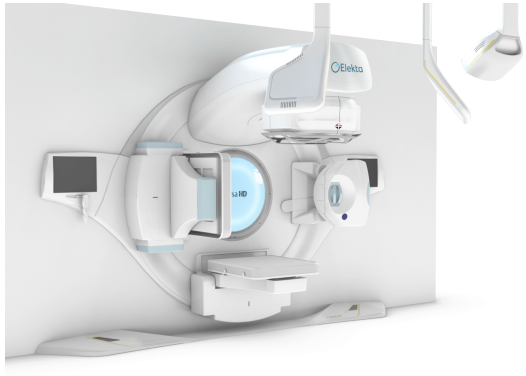
X-ray tracking
Exactrac Dynamic

- Stereoscopic x-rays
- Surface imaging with structured light
- Thermal camera integrated for improved surface definition
- Submillimeter positioning accuracy

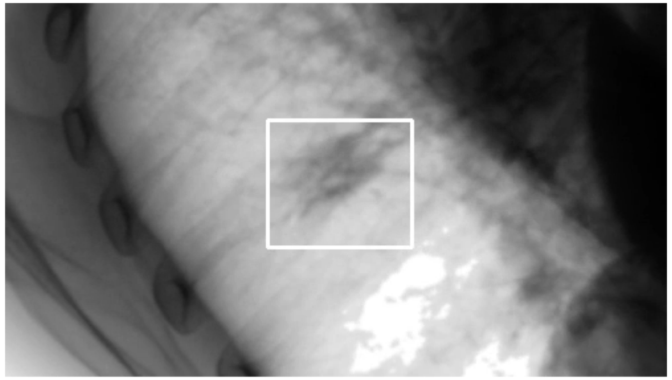
Mendes, …, **Landry**, Freislederer JACMP 2022

- Current use for stereotactic brain radiosurgery and deep inspiration breath hold for breast cancer
- Application to lung cancer is in development
  - Markerless tumor tracking approach
  - For gated breath hold





https://www.brainlab.com/radiosurgery-products/exactrac/



https://www.brainlab.com/radiosurgery-products/lung/

Motion management with AI
Overview

- AI allows shifting calculation time from online to the training phase
- Models are often very fast
  - 10 to few 100 ms
- In RT we often have prior knowledge
  - Diagnostic or RT planning images
  - Allows patient-specific training strategies
- Challenges
  - Tumors are very heterogeneous
  - Need models which limit false positives
  - Object detection networks are good for this

X-ray tracking studies

Study	Imaging modality	Method	Site
Tong et al. 2009 [50]	X-ray	ML	Lung
Terunuma et al. 2018 [51]	Synthetic X-ray	Encoder-decoder CNN	Lung
Edmunds et al. 2019 [52]	X-ray	Mask R-CNN	Diaphragm
Hirai et al. 2019 [53]	X-ray	DNN	Liver and lung
Mori et al. 2019 [54]	X-ray	ML	Chest
Zhao et al. 2019 [37]	Synthetic X-ray	Faster R-CNN	Pancreas
Zhao et al. 2019 [36]	Synthetic X-ray	Faster R-CNN	Prostate
Roggen et al. 2020 [35]	X-ray	Faster R-CNN	Vertebrae
Sakata et al. 2020 [55]	X-ray	ML	Lung
Takahashi et al. 2020 [56]	X-ray	FCN	Lung

MR linac studies

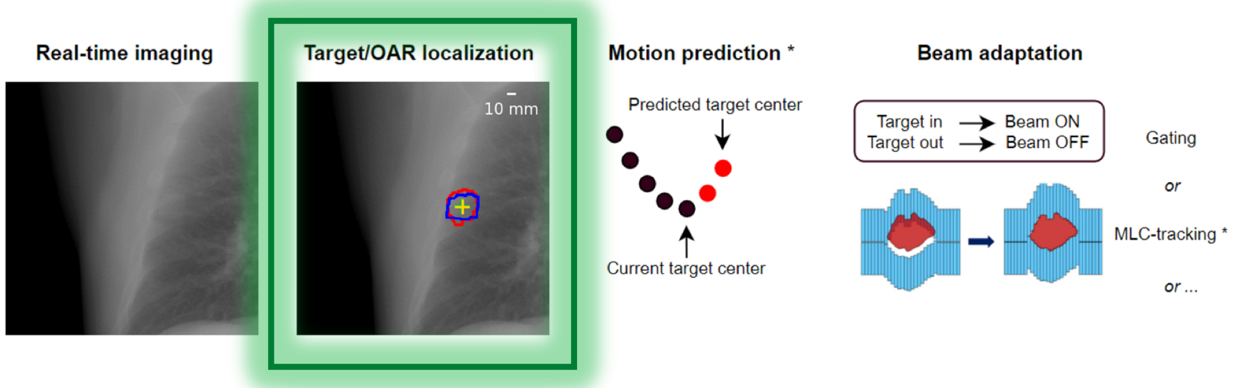
Study	Imaging modality	Method	Site
Cervino et al. 2011 [59]	cine MRI	ML	Lung
Yun et al. 2015 [60,61]	cine MRI	PCNN	Lung
Bourque et al 2017 [62]	cine MRI	ML	Lung
Fast et al. 2017 [63]	cine MRI	PCNN	Lung
Friedrich et al. 2021 [64]	cine MRI	U-net	Liver

Mylonas et al. J Med Imaging Radiat Oncol 2021

Some definitions

Lombardo,..., **Landry**, ..., Placidi Radiother Oncol 2024

Methods for x-ray target localization

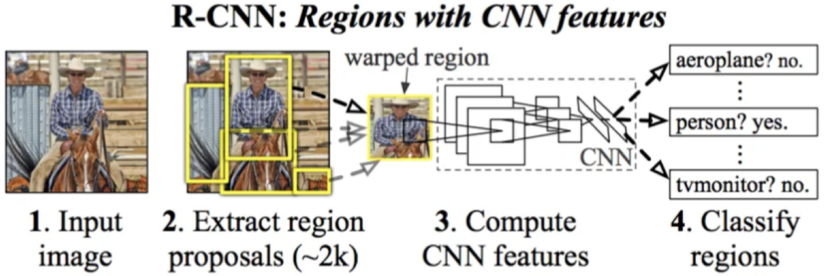


Object detection networks
R-CNN and Retina Net

- Object detection networks
  - Region and CNN: R-CNN
  - Mask R-CNN
  - Faster R-CNN

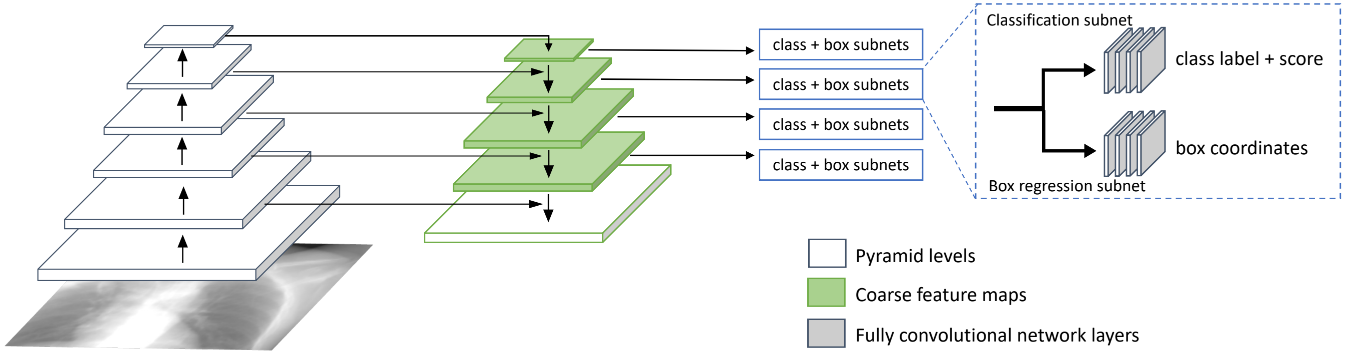
- Retina net is a good example
  - Feature pyramid network
  - Class subnet
  - Box subnet
  - Fast enough

- Outputs a bounding box and a confidence score
- Can also classify the object



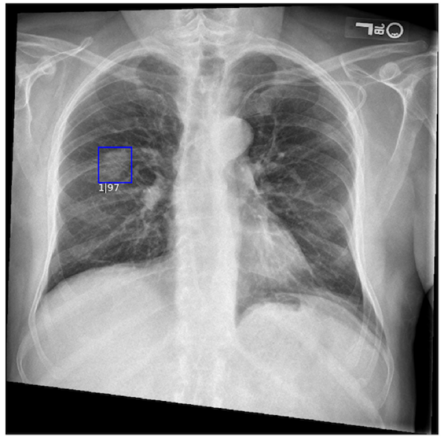
https://towardsdatascience.com/r-cnn-fast-r-cnn-faster-r-cnn-yolo-object-detection-algorithms-36d53571365e

Retina Net



Feature Pyramid Network

LIDC-IDRI-0075



Example output

Object detection networks
X-ray tracking: pancreas

- Pancreas tumor tracking
- Uses Faster R-CNN
- Patient specific training on simulated DRRs from planning CT
  - PTV projection is the ground truth
  - Various projection angles
- Use deformations of planning CT to generate multiple training images

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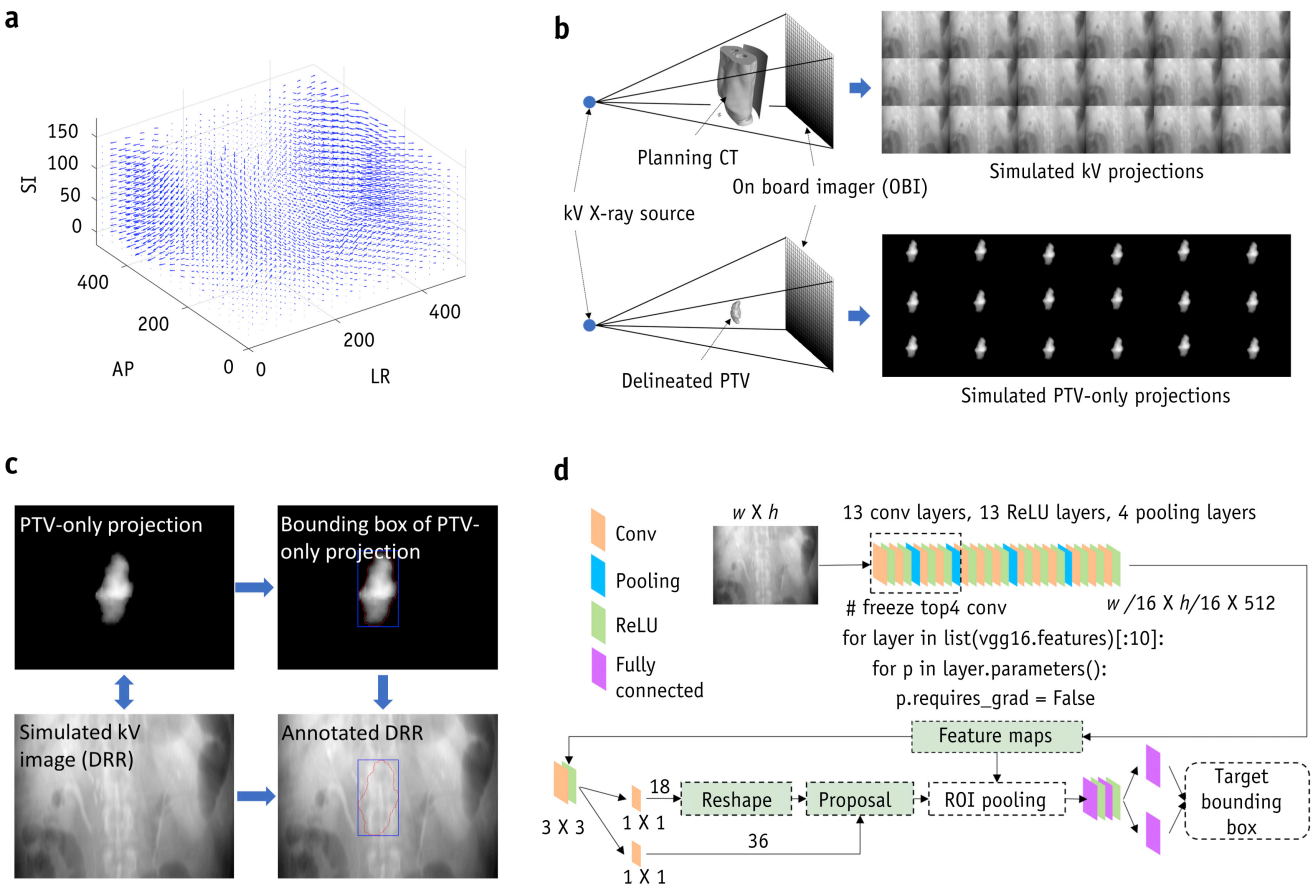
Physics Contribution

Markerless Pancreatic Tumor Target Localization Enabled By Deep Learning

Wei Zhao, PhD,* Liyue Shen, MS,* Bin Han, PhD,* Yong Yang, PhD,* Kai Cheng, PhD,* Diego A.S. Toesca, MD,* Albert C. Koong, MD, PhD,† Daniel T. Chang, MD,* and Lei Xing, PhD*

*Department of Radiation Oncology, Stanford University, Stanford, California; and †Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas



Object detection networks
X-ray tracking: pancreas

- Pancreas tumor tracking
- Uses Faster R-CNN
- Patient specific training on simulated DRRs from planning CT
  - PTV projection is the ground truth
  - Various projection angles
- Use deformations of planning CT to generate multiple training images
- **Potential issue: test images also sampled from the same planning CT**

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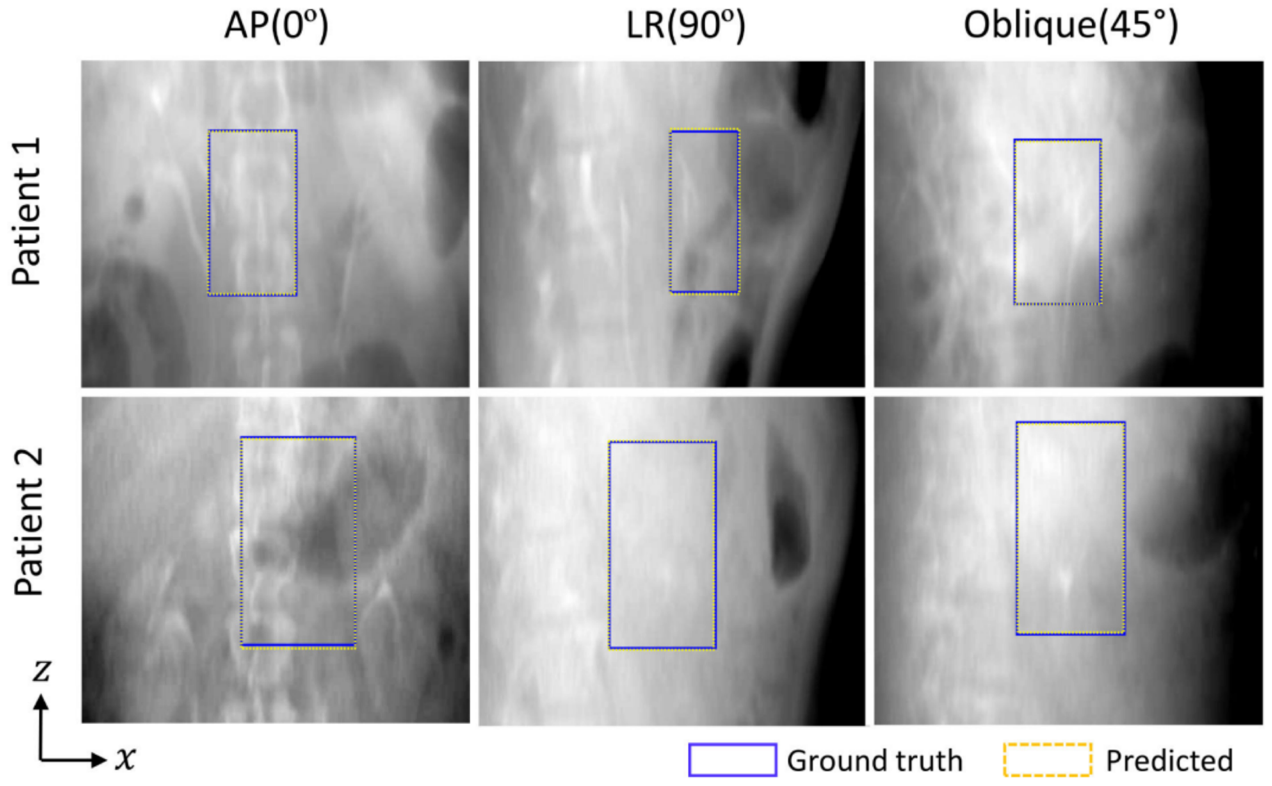
*Department of Radiation Oncology, Stanford University, Stanford, California; and †Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas

Example results: very good agreement



Classical machine learning
X-ray tracking: lung

- Here classical machine learning was used for tracking lung tumors
- Steroscopic x-ray imaging setup similar to the Exactrac

Physics in Medicine & Biology
IPEM Institute of Physics and Engineering in Medicine

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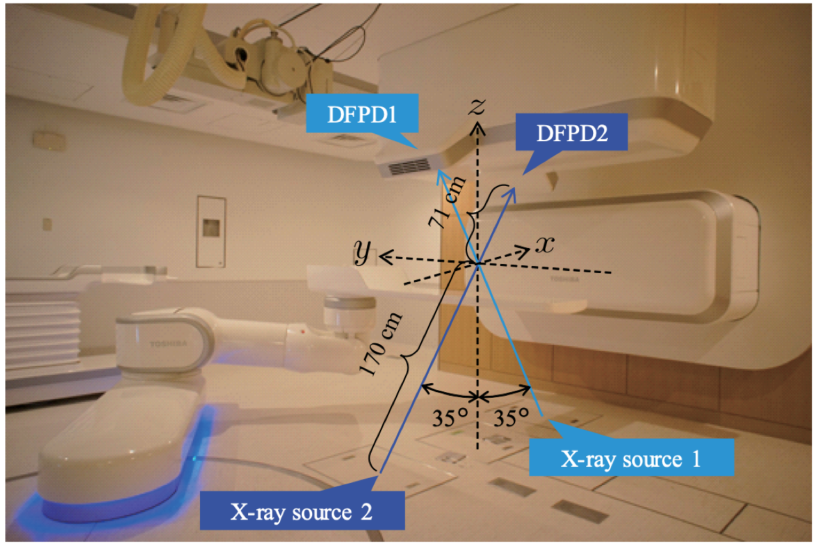
PAPER

A machine learning-based real-time tumor tracking system for fluoroscopic gating of lung radiotherapy

Yukinobu Sakata[1], Ryusuke Hirai[1], Kyoka Kobuna[1], Akiyuki Tanizawa[1] and Shinichiro Mori[2]

[1] Corporate Research and Development Center, Toshiba Corporation, Kanagawa, Japan
[2] Research Center for Charged Particle Therapy, National Institute of Radiological Sciences, Chiba, Japan

Fluoroscopic tracking set up in Chiba, Japan



Classical machine learning
X-ray tracking: lung

- Here classical machine learning was used for tracking lung tumors

- Steroscopic x-ray imaging setup similar to the Exactrac
- Classical ML: random forest approach to classify patches as tumor or non-tumor
  - Convert patches to features before random forest
  - Aggregate positions in likelihood map
  - Only provides a center position

- Good data separation
  - Training: 4DCT
  - Testing: real x-ray images
  - Challenge: manual labelling of ground truth

Physics in Medicine & Biology

IPEM Institute of Physics and Engineering in Medicine

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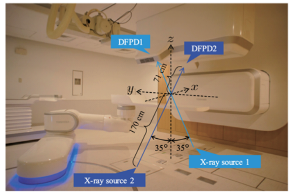

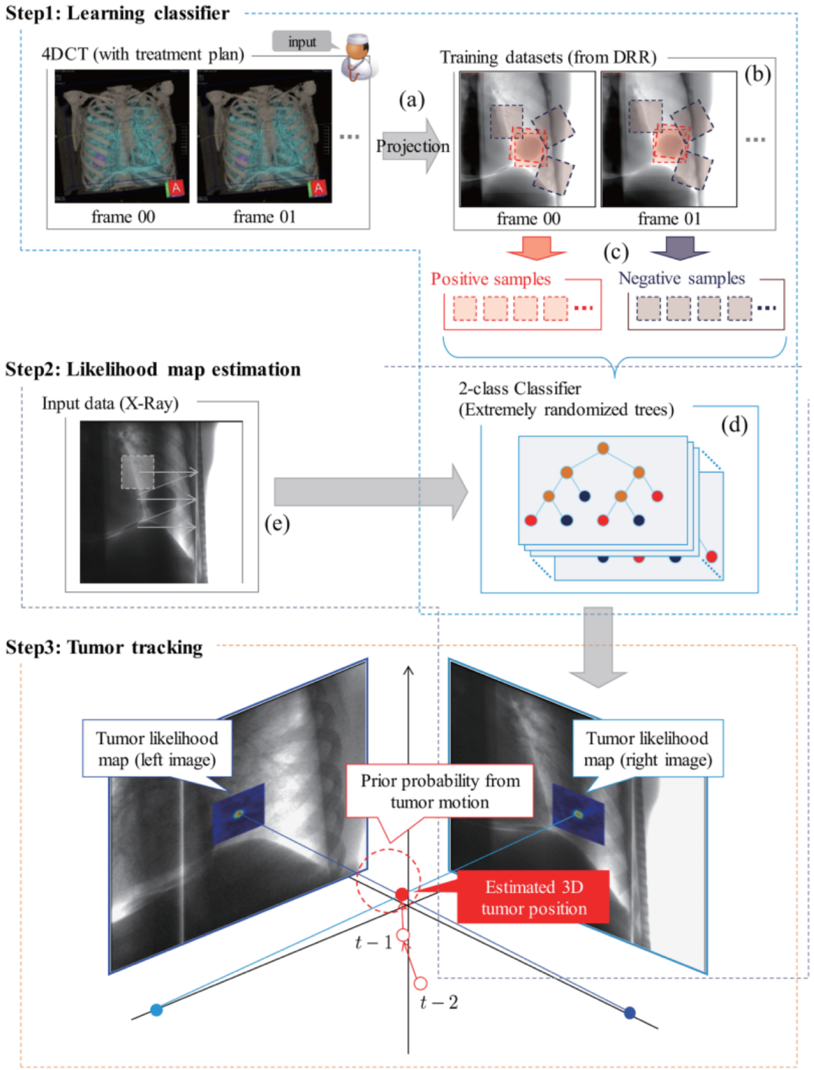

$$g(\mathbf{u}) = \tan^{-1}\frac{I_v}{I_u},\ I_u = \frac{\partial I(\mathbf{u})}{\partial u},\ I_v = \frac{\partial I(\mathbf{u})}{\partial v}$$

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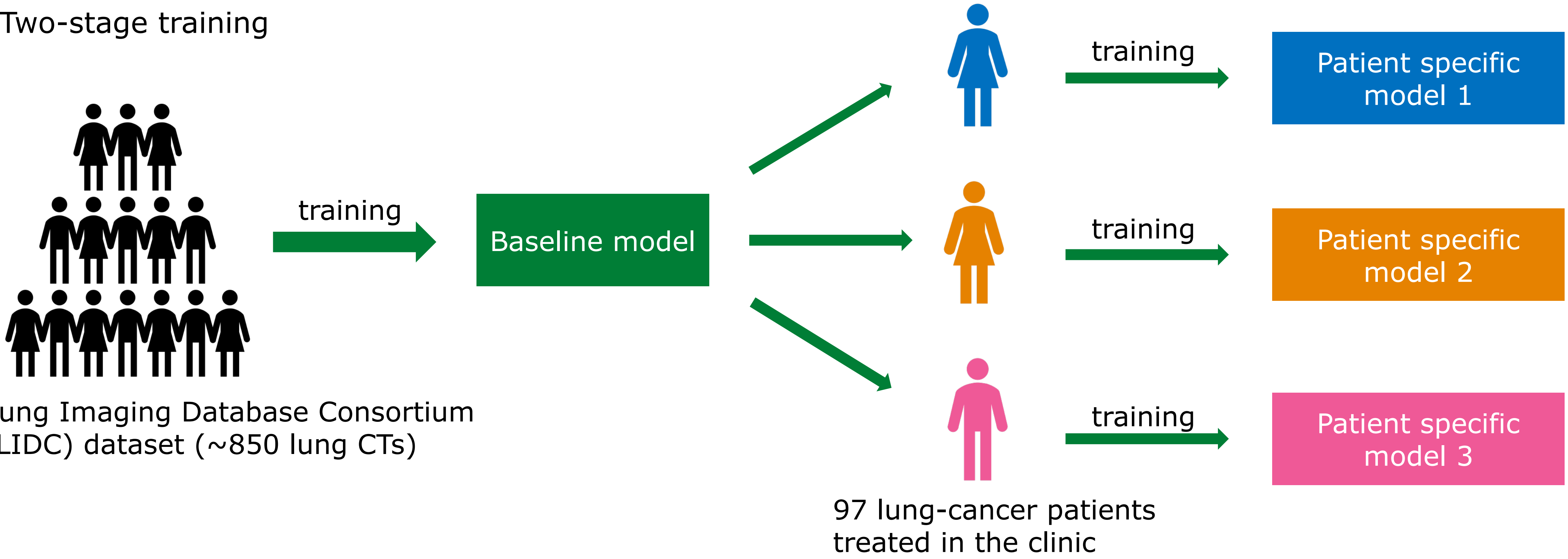
AI for markerless tumor tracking
Patient specific approach

- Two-stage training

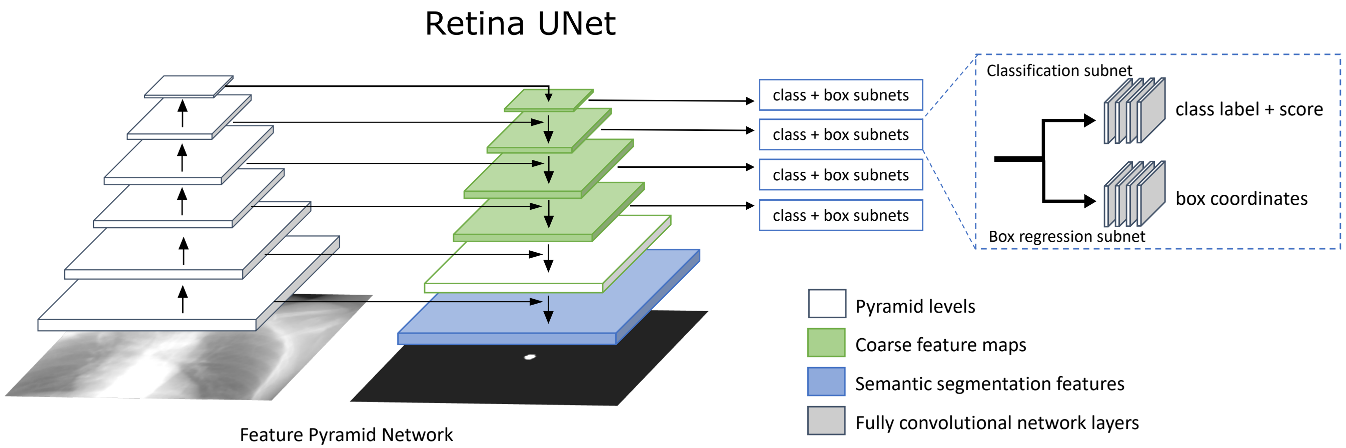


Object detection with AI
Retina U-net

Extra high-res levels for semantic segmentation

→ Another loss for segmentation:

Seg loss = Cross entropy loss + Soft dice loss



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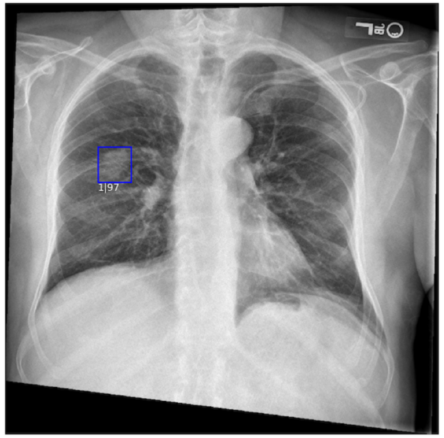
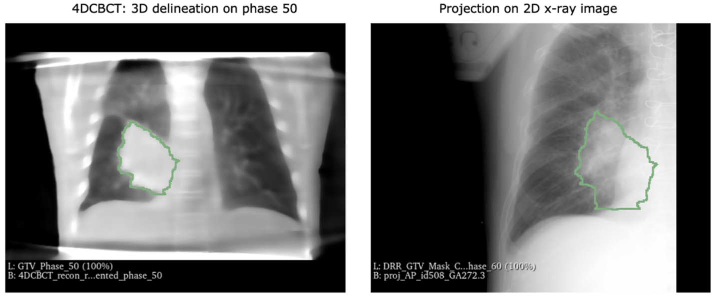
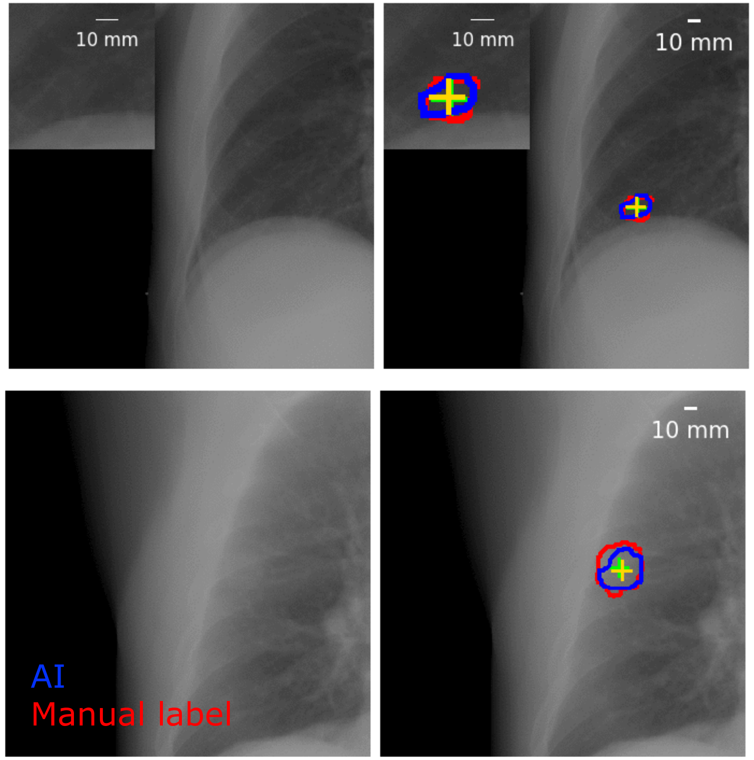




4DCBCT ground truth generation

Validation using 4D labelled CBCT projections



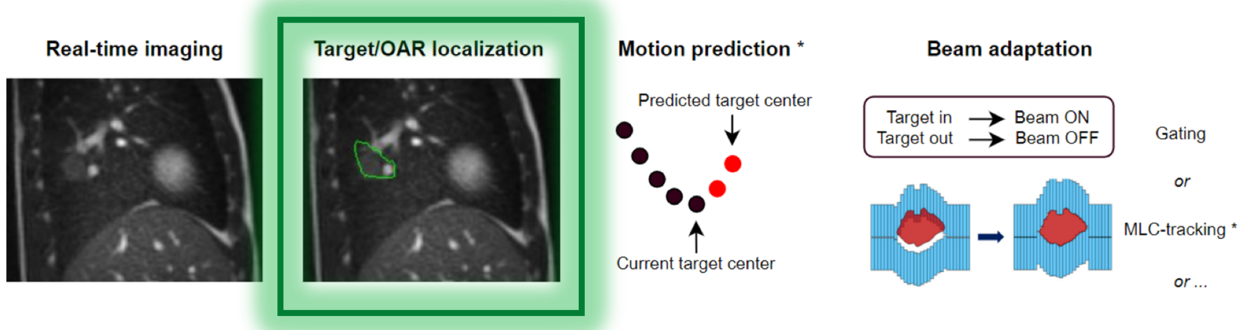
L. Huang

- Localization error 2.5mm
- DSC > 0.8
- Runtime 70 ms per frame

Huang, ..., **Landry,** Riboldi Med Phys 2023

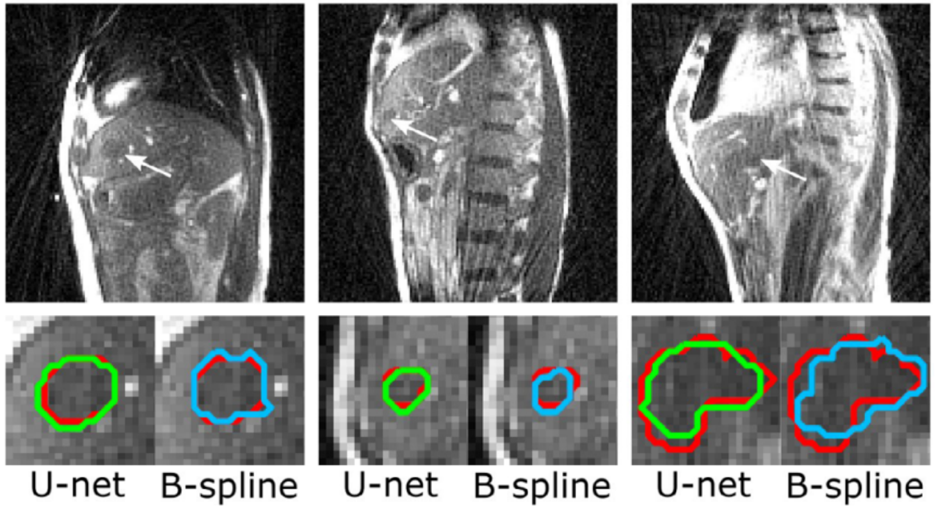
Huang, ..., **Landry** oral at AAPM 2024

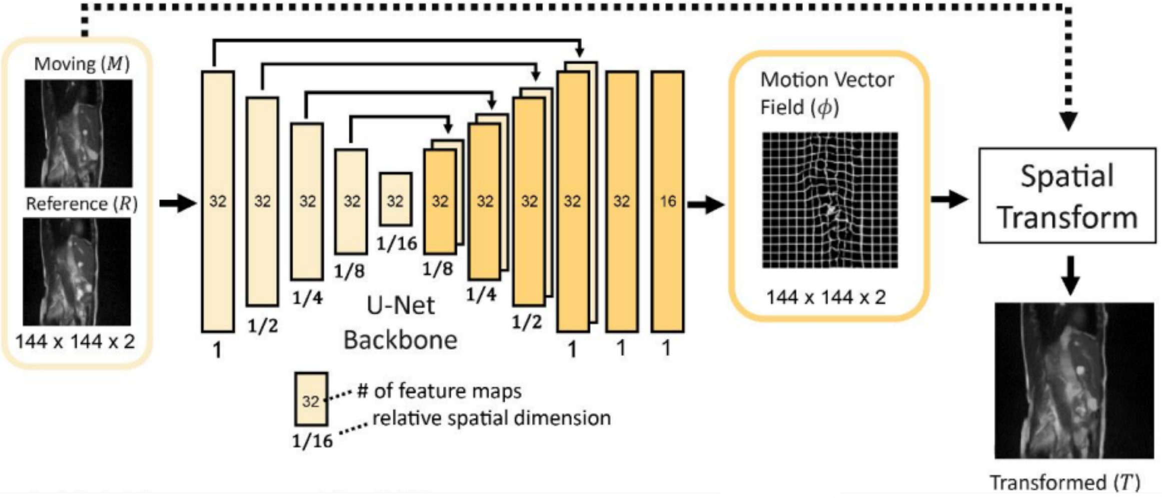
Methods for MR linac target localization



MR linac tracking
Seminal AI efforts

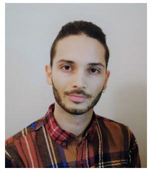
- Friedrich et al. (2021) *Med Phys*
  - U-net auto-segmentation model outperformed B-spline on under-sampled radial cine MRI
  - Manual labels on 150 frames (2 patients)
  - Patient-specific training strategy on 10 manually labeled frames
- Hunt et al. (2022) *IJROBP*
  - U-net DIR model outperformed conventional spline and Demons
  - Cine MRI from vendor (8 Hz)
  - About 600k frames without labels (21 patients)

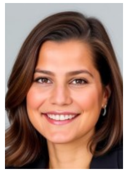




MR linac tracking
Transformers

- Tranformer-based DIR (Transmorph)
  - About 1.4M unlabeled (219 patients) and 8k labeled frames (35 patients)
  - Patient-specific training on 8 labeled frames significantly improved performance compared to unsupervised and supervised training
  - Transformer DIR model outperformed U-net auto-segmentation and B-spline DIR


E. Lombardo


L. Velezmoro

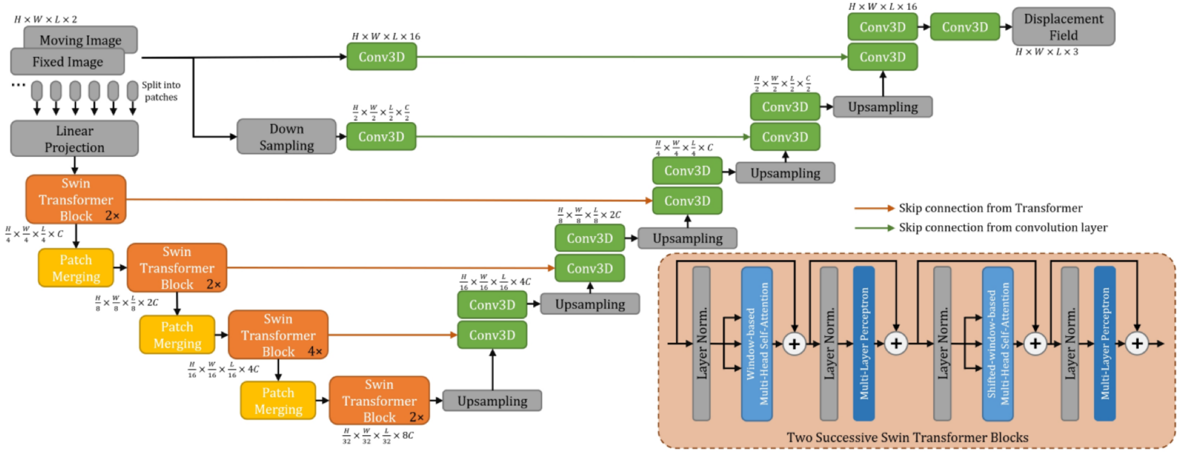
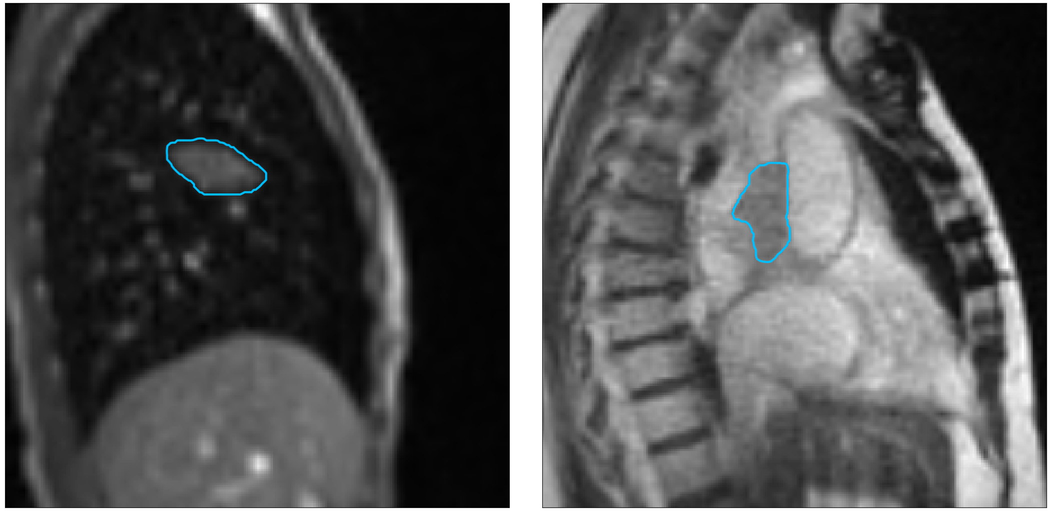
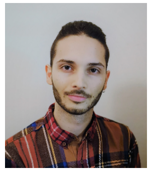
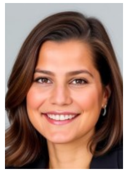


Fig. 1: The architecture of the proposed TransMorph registration network.



Lombardo, Velezmoro …, **Landry** under review
Lombardo, Velezmoro …, **Landry** oral at ESTRO 2024


E. Lombardo


L. Velezmoro

MR linac tracking
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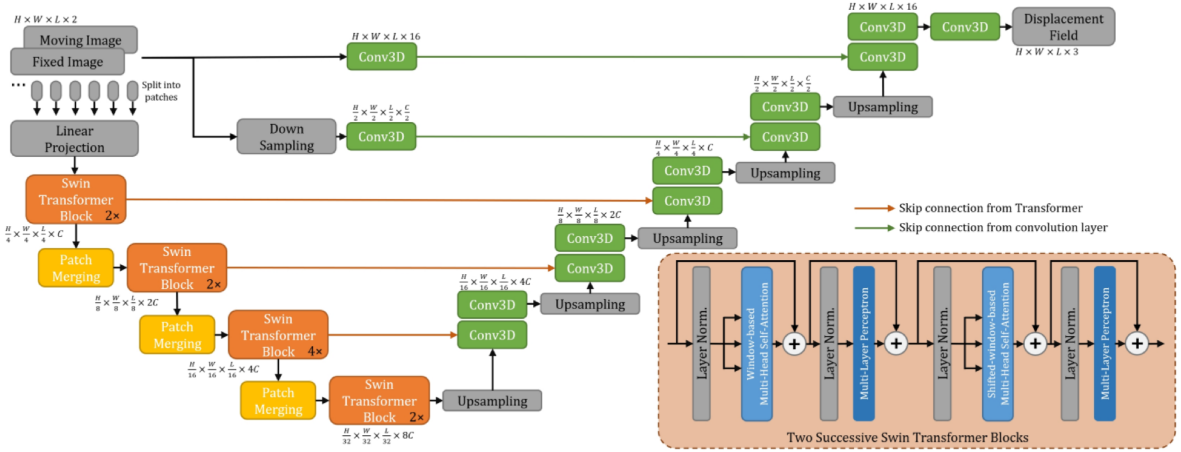
  - Patient-specific training on 8 labeled frames significantly improved performance compared to unsupervised and supervised training
  - Transformer DIR model outperformed U-net auto-segmentation and B-spline DIR
- Disadvantage
  - Patient-specific labelling and training costs additional time
    - 3 minutes labelling
    - 4 minutes training



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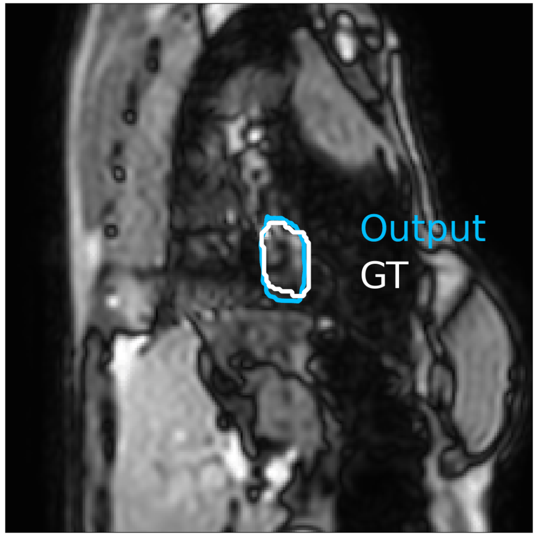


- Transfer learning to 1.5 cine-MRI from Unity MR-linac
- Collaboration with Sichuan Cancer Hospital, Chengdu, China


Dr. Y. Wang

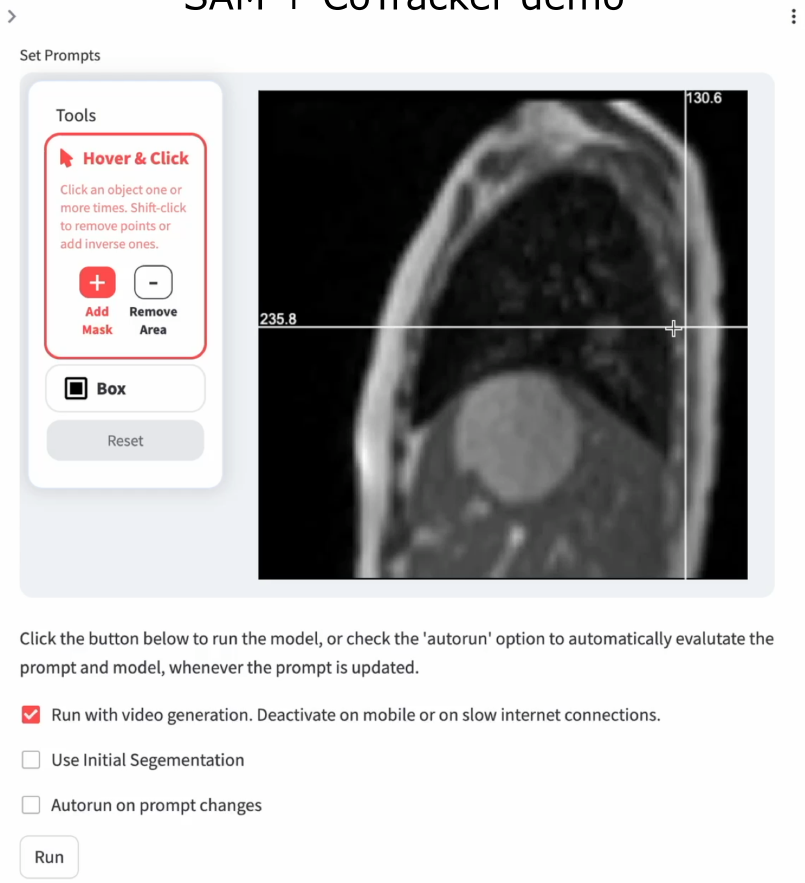
MR linac tracking
Foundation models

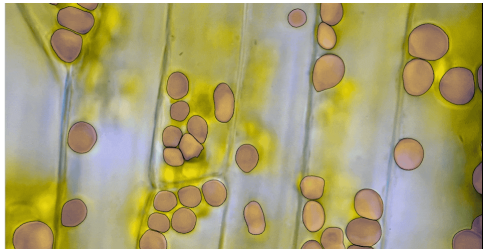
T. Blöcker

- Foundation models may eliminate the need for training (baseline or PS)
  - Large transformers from industry leaders
  - Pre-trained on very large databases

  - *Segment Anything Model (SAM)* and *CoTracker* from Meta AI

SAM + CoTracker demo

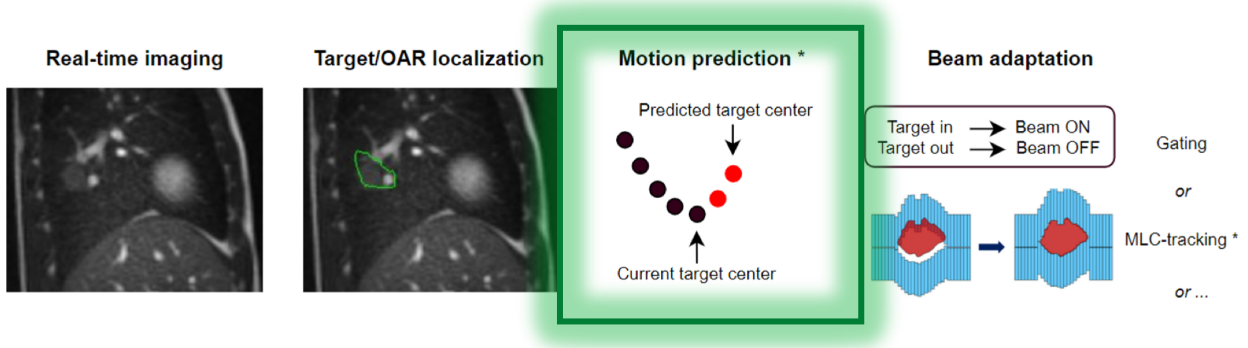


https://www.louisbouchard.ai/meta-sam/

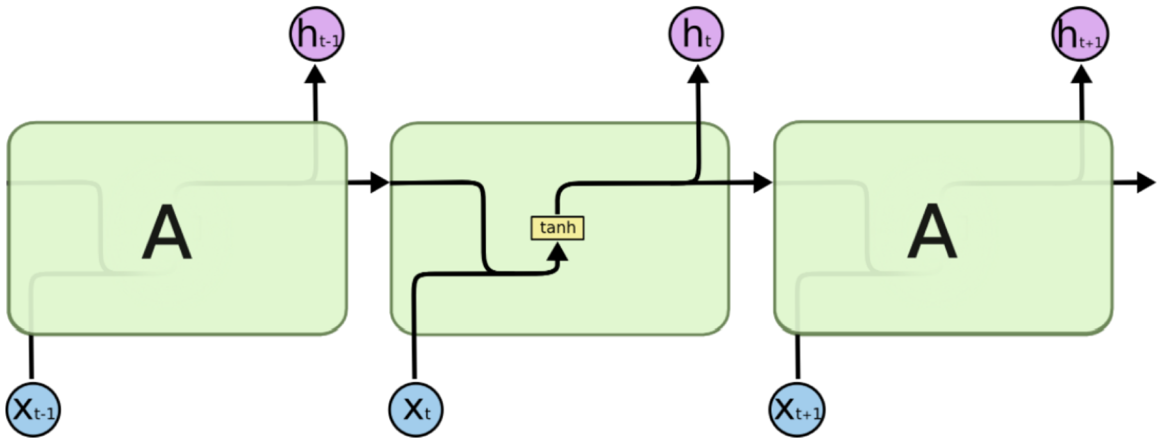
https://co-tracker.github.io/

Methods for motion prediction

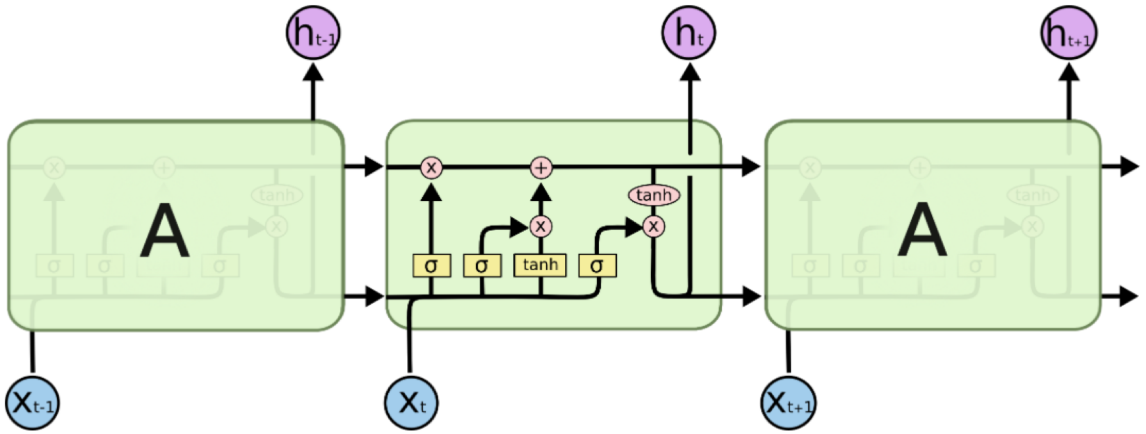


Motion tracking
Long short term memory networks

- Recurrent neural networks (RNNs) are often used for time series
- A particularly relevant approach are long short term memory networks
  - LSTM
- Architecture designed to allow learning long-term dependencies in the input data



The repeating module in a standard RNN contains a single layer.



The repeating module in an LSTM contains four interacting layers.

https://colah.github.io/posts/2015-08-Understanding-LSTMs/

LSTM in radiotherapy
0.35 T MR linac forecasting with LSTM

Gemelli
Fondazione Policlinico Universitario A. Gemelli
Università Cattolica del Sacro Cuore

Physics in Medicine & Biology

DFG Deutsche Forschungsgemeinschaft

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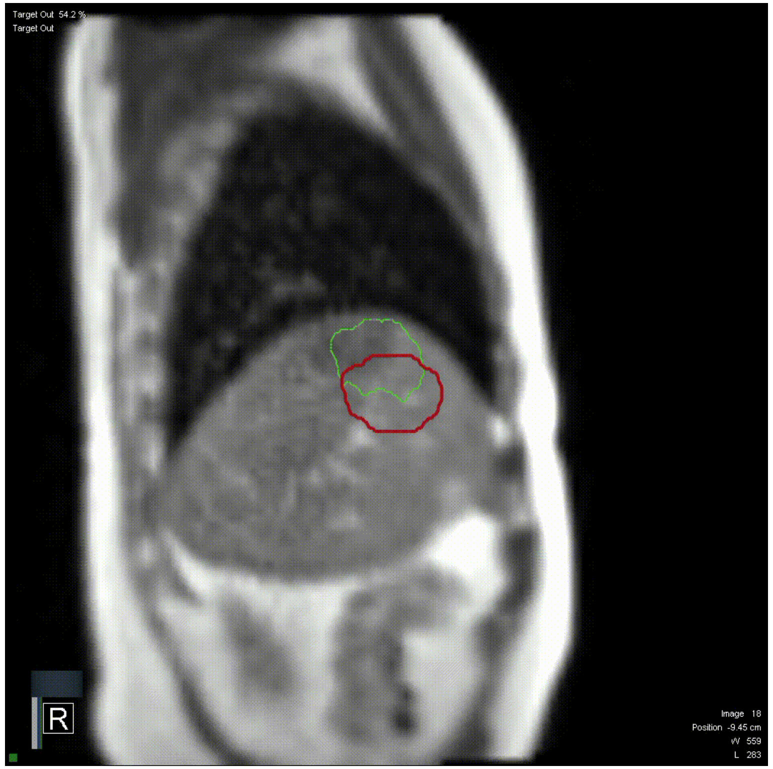
Offline and online LSTM networks for respiratory motion prediction in MR-guided radiotherapy

Elia Lombardo[1], Moritz Rabe[1], Yuqing Xiong[1], Lukas Nierer[1], Davide Cusumano[2], Lorenzo Placidi[3], Luca Boldrini[3], Stefanie Corradini[1], Maximilian Niyazi[1], Claus Belka[1], Marco Riboldi[4], Christopher Kurz[1] and Guillaume Landry[1] – Hide full author list

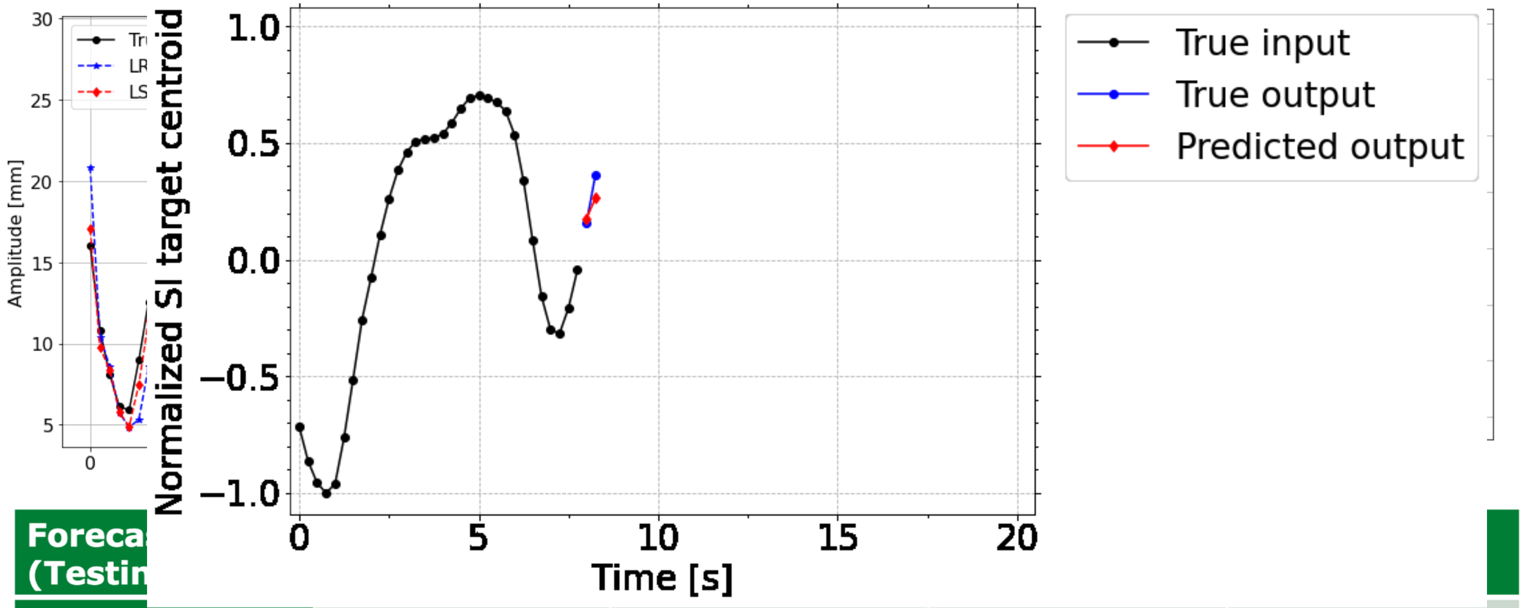
Accepted Manuscript online 24 March 2022 • © 2022 The Author(s). Published by IOP Publishing Ltd.

E. Lombardo

2D motion forecasting in cine-MRI



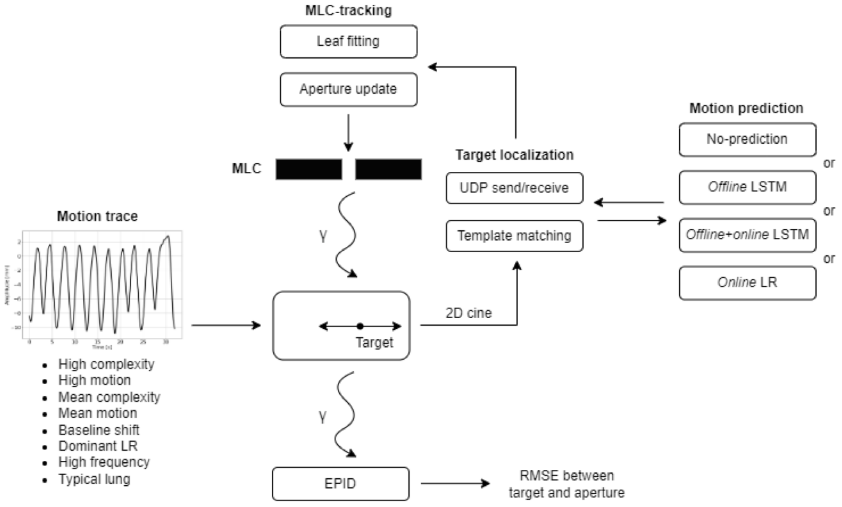
4Hz cine MRI, latency approx. 250 ms



Foreca (Testin				
250	0.47 (0.12)	**0.42 (0.13)**	0.57 (0.14)	0.53 (0.17)
500	1.14 (0.29)	**1.00 (0.31)**	1.52 (0.34)	1.22 (0.30)
750	2.02 (0.48)	**1.77 (0.54)**	2.76 (0.61)	2.02 (0.48)

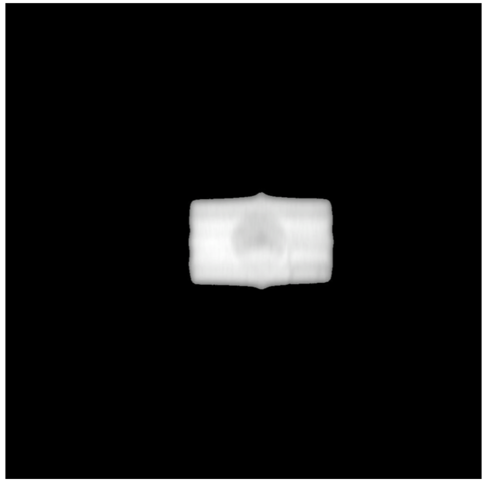
LSTM in radiotherapy
Experimental validation with MLC tracking

experimental setup

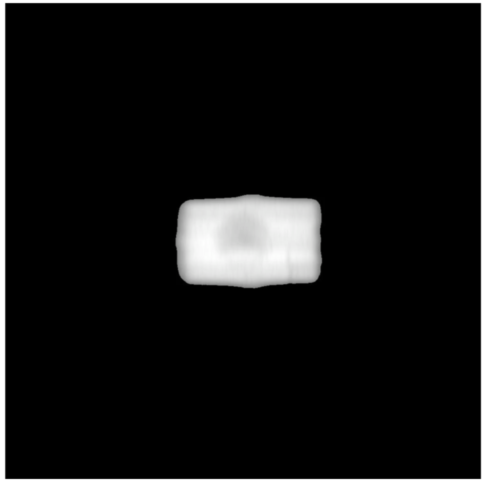


Tracking validation with EPID

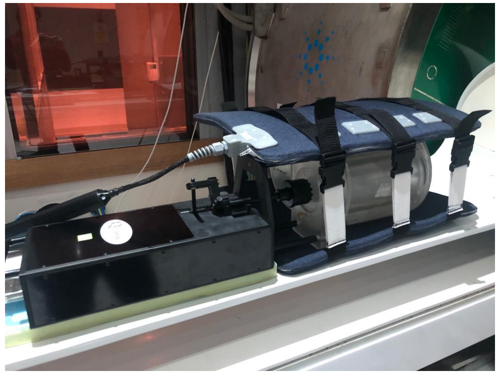
390 ms latency



LSTM



E. Lombardo @
Australian MR linac



phantom

RMSE relative to no prediction (*lower better*)

Motion trace	*Offline* LSTM	*Offline+online* LSTM	*Online* LR
High complexity	0.65; 0.64	**0.58; 0.61**	0.78; 0.87
High motion	0.73; 0.79	**0.63; 0.64**	0.78; 0.88
Mean complexity	0.72; 0.73	**0.61; 0.62**	0.86; 0.72
Mean motion	0.83; 0.71	**0.59; 0.61**	0.71; 0.66

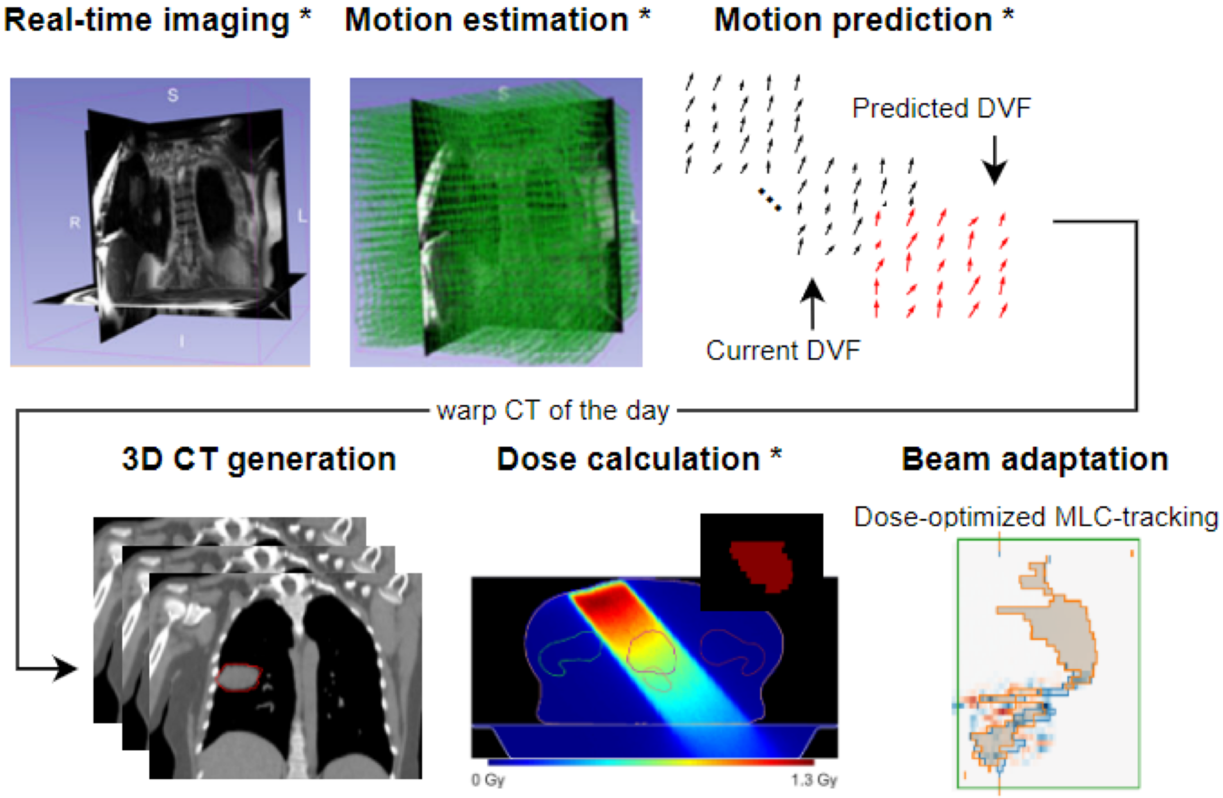
Lombardo,..., **Landry**, Keall *Med Phys* 2023

Motion management and dose

What we hope to achieve

- AI may bring speed increase for real time dose reconstruction
  1. Motion tracking
  2. 3D+t imaging
  3. Dose reconstruction*
  4. Dose accumulation

See talk from **Fan Xiao, Wednesday at 11h00, Auditorium Lumière "**LSTM-based proton dose calculation**"*

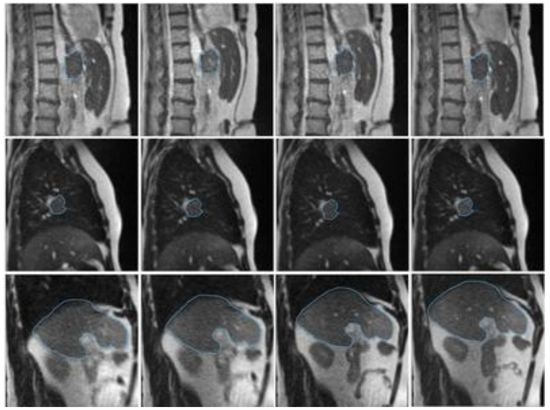


Lombardo,..., **Landry**, ..., Placidi Radiother Oncol 2024

Conclusion

- For target localization on x-rays, object detection models have been mostly used
  - Bounding box prediction
- For MR linac target localization, networks that predict deformations or correspondence between points have been used
- In both cases, some prior knowledge is needed
  - Unlike in OAR segmentation, models do not segment or find the lesion from scratch
- Motion prediction is important for latency and can be done with long-short-term memory networks

TrackRad2025 Challenge



- *Large public 2D-cine MRI dataset*
- *5 participating centers (0.35 T and 1.5 T)*
- *Labelled and unlabelled data*
- ***Expected March 2025!***

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Save the date!
October 14th 2024

- One-day event at the beautiful St Vinzenz Haus in the Munich city center

- Distinguished international speakers
  - *Anna Kirby*
  - *Luca Boldrini*
  - *Jan Jakob Sonke*
  - *Lorenzo Placidi*
  - *Jennifer Dhont*
  - *Lorenzo Placidi*
  - *Niklas Wahl*
  - *Many more!*

St Vinzenz Haus

Xchange 2024 website

- Contact:
  - Guillaume Landry
  - Stefanie Corradini

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Acknowledgements

- **LMU Munich**
  - Christopher Kurz
  - Marco Riboldi
  - Elia Lombardo
  - Lili Huang
  - Laura Velezmoro
  - Claus Belka
  - Stefanie Corradini
  - Michael Reiner
- **Gemelli/Mater Olbia**
  - Luca Boldrini
  - Davide Cusumano
  - Lorenzo Placidi

- **Image X Sydney**
  - Paul Keall
  - Paul Liu
  - David Waddington
  - James Grover
- **Amsterdam UMC**
  - Miguel Palacios
  - Suresh Senan

Conflicts of interest

Research agreements with Brainlab, Elekta and previously ViewRay

Funding

DFG Deutsche Forschungsgemeinscha

Wilhelm Sander-Stiftung fördert medizinische Forschung

Deutsche Krebshilfe HELFEN. FORSCHEN. INFORMIEREN.

Bundesministerium für Bildung und Forschung

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