Lung - AI planning approaches

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Acknowledgments

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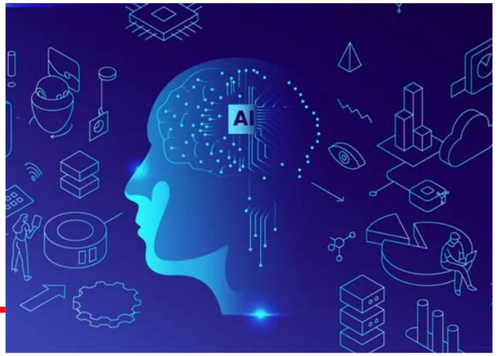
Definitions
(disclosure in the use of AI term)



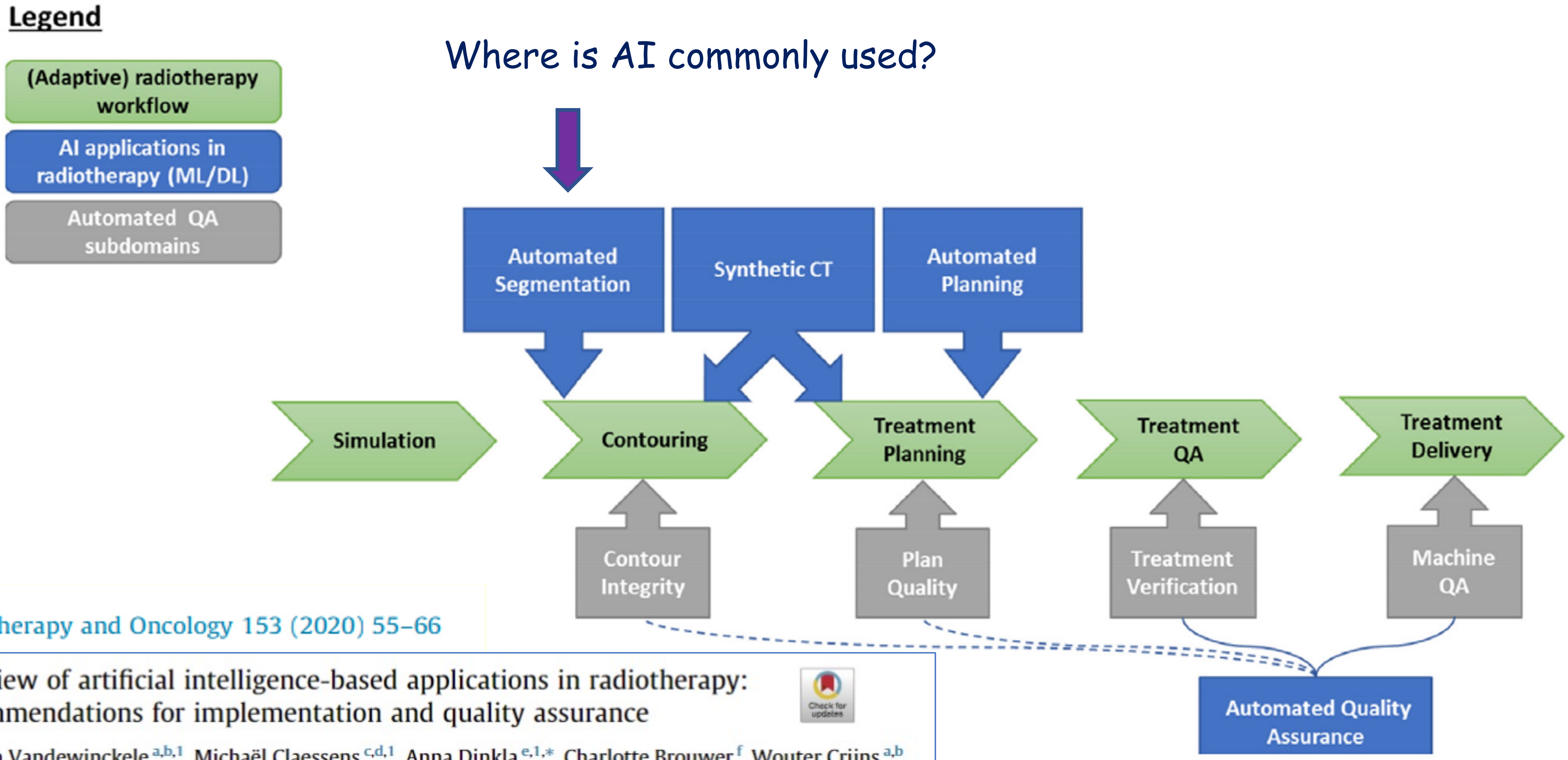
Artificial Intelligence (AI) is here used as **umbrella term** encompassing a wide range of computer science technologies aiming at giving machines the ability to perform tasks requiring human intelligence such as problem solving, decision taking and image recognition.

These are often accomplished by adoption of sophisticated machine learning (ML) algorithms to mimic human learning capability (**Meskó and Görög 2020)**, but also simpler approaches such as iterative learning.

The same work hypothesis as in the review *Applications of artificial intelligence in stereotactic body radiation therapy* (Mancosu et al, PMB, 2022)

so this includes the use of automatic planning such as Knowledge Based Planning (i.e. Rapidplan)

Following the patient journey



Radiotherapy and Oncology 153 (2020) 55–66

Overview of artificial intelligence-based applications in radiotherapy: Recommendations for implementation and quality assurance

Liesbeth Vandewinckele [a,b,1], Michaël Claessens [c,d,1], Anna Dinkla [e,1,*], Charlotte Brouwer [f], Wouter Crijns [a,b], Dirk Verellen [c,d], Wouter van Elmpt [g]

AI in target and OAR segmentation

Atlas contouring in lung cancer

Clinical evaluation of atlas and deep learning based automatic contouring for lung cancer

Tim Lustberg [a,*], Johan van Soest [a], Mark Gooding [b], Devis Peressutti [b], Paul Aljabar [b], Judith van der Stoep [a], Wouter van Elmpt [a], Andre Dekker [a]

[a] Department of Radiation Oncology (MAASTRO), GROW School for Oncology and Developmental Biology, Maastricht University Medical Centre+, The Netherlands; [b] Mirada Medical Ltd., Oxford, United Kingdom

Automatic contouring as a tool:

- to reduce contouring time
- and improve consistency
- In particular for SABR: large number of OARs

20 CT scans of NSCLC pts

Lung, esophagus, spinal cord, heart, mediastinum

20 min	manual contouring
8 min	atlas contouring
10 min	deep learning contouring

Conclusion

Automatic contouring software as a starting point for clinical contours of OARs in lung radiation therapy allows for a significant time gain when contouring lungs, spinal cord, heart and mediastinum. DLC shows promising results with regard to the creation of institution-based models and to automatically generate high quality contours, providing a greater time saving compared to existing solutions. In addition, clinicians are able to assess if a software generated contour will potentially save time or not.

AI in target and OAR segmentation

frontiers in Oncology

ORIGINAL RESEARCH
published: 07 June 2021
doi: 10.3389/fonc.2021.626499

Training and Validation of Deep Learning-Based Auto-Segmentation Models for Lung Stereotactic Ablative Radiotherapy Using Retrospective Radiotherapy Planning Contours

Performance of a commercial pre-treatment deep learning based on self segmentation software (Lymbus)

Comparison among two centers

200 CT scans
OARs and GTV
Test on 50 + 50 CT scans

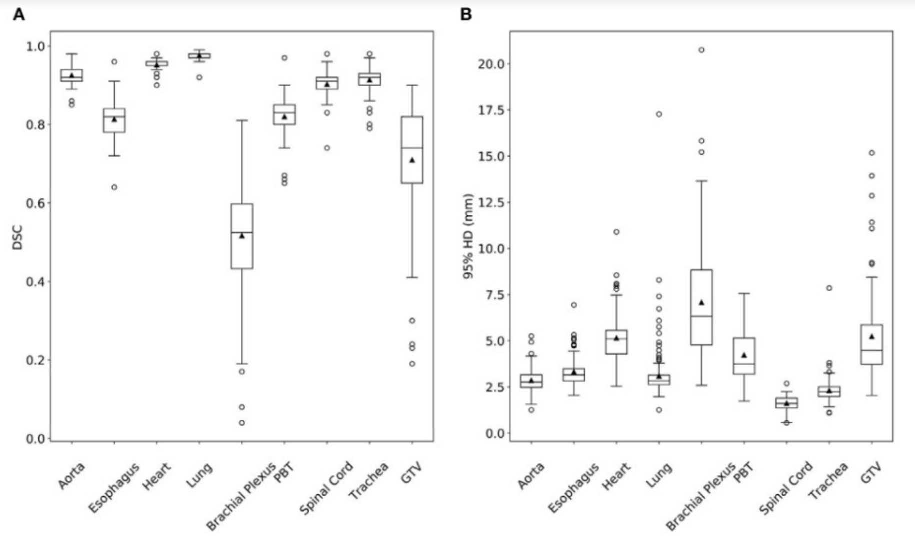


FIGURE 1 | Dice Similarity Coefficient (DSC, **A**) and 95% Hausdorff distance (HD, **B**) box plots from comparing deep learning-based auto-segmented contours to clinical contours for lung stereotactic ablative radiotherapy planning structures. (PBT, proximal bronchial tree; GTV, gross tumor volume).

Deep learning contours for structures with more variations, due to anatomic or disease factors, perform less accurately

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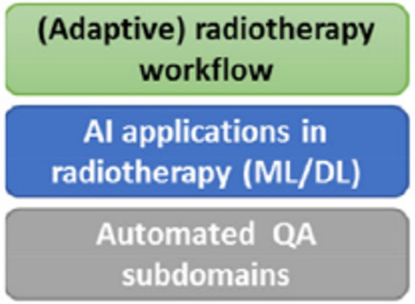
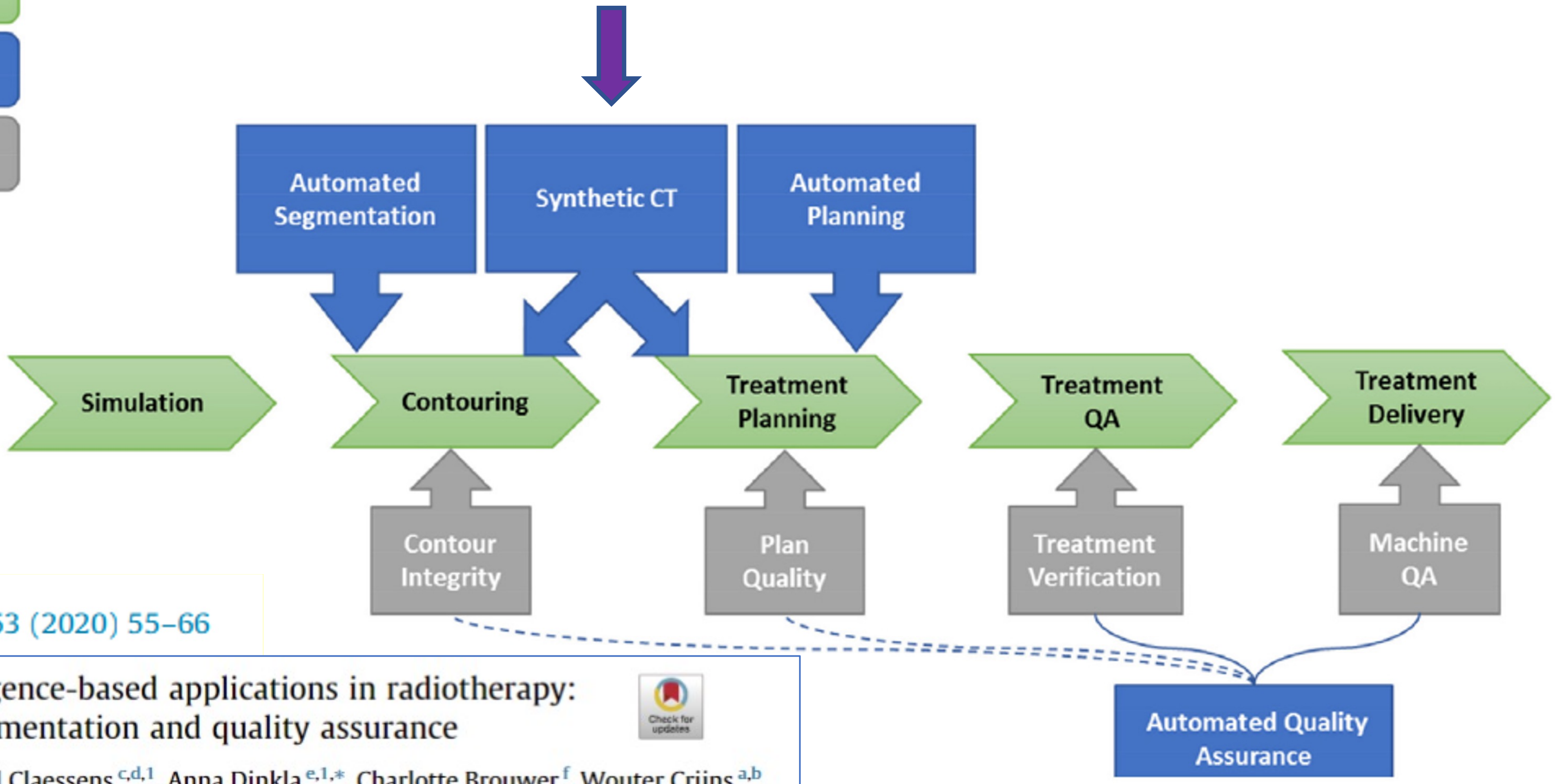
Following the patient journey

Legend



Where is AI commonly used?



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Overview of artificial intelligence-based applications in radiotherapy: Recommendations for implementation and quality assurance

Liesbeth Vandewinckele [a,b,1], Michaël Claessens [c,d,1], Anna Dinkla [e,1,*], Charlotte Brouwer [f], Wouter Crijns [a,b], Dirk Verellen [c,d], Wouter van Elmpt [g]

Radiotherapy and Oncology 176 (2022) 31–38

Contents lists available at ScienceDirect

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journal homepage: www.thegreenjournal.com

Original Article

A deep learning approach to generate synthetic CT in low field MR-guided radiotherapy for lung cases

Jacopo Lenkowicz [a], Claudio Votta [a,b,*], Matteo Nardini [a], Flaviovincenzo Quaranta [b], Francesco Catucci [b], Luca Boldrini [a], Marica Vagni [a], Sebastiano Menna [b], Lorenzo Placidi [a], Angela Romano [a], Giuditta Chiloiro [a], Maria Antonietta Gambacorta [a], Gian Carlo Mattiucci [b,c], Luca Indovina [a], Vincenzo Valentini [a,c], Davide Cusumano [a,b]

[a] Fondazione Policlinico Universitario "Agostino Gemelli" IRCCS, Rome; [b] Mater Olbia Hospital, Olbia (SS); and [c] Università Cattolica del Sacro Cuore, Rome, Italy

Aim:

To generate a synthetic CT (sCT) of the lung using the deep learning architecture cGAN trained on low-field MR (0.35T) images of 32 patients. The sCT was validated on two cohorts of 10 patients each, one in-house and the another coming from a different hospital.

Novelty:

Generating sCT of the lung is particularly challenging due to the heterogeneity of electron density. They are the first to produce a sCT by training a cGAN that has high image fidelity and reasonable dose planning performance. Moreover, they proved stability of the generated sCT across different MR machines.

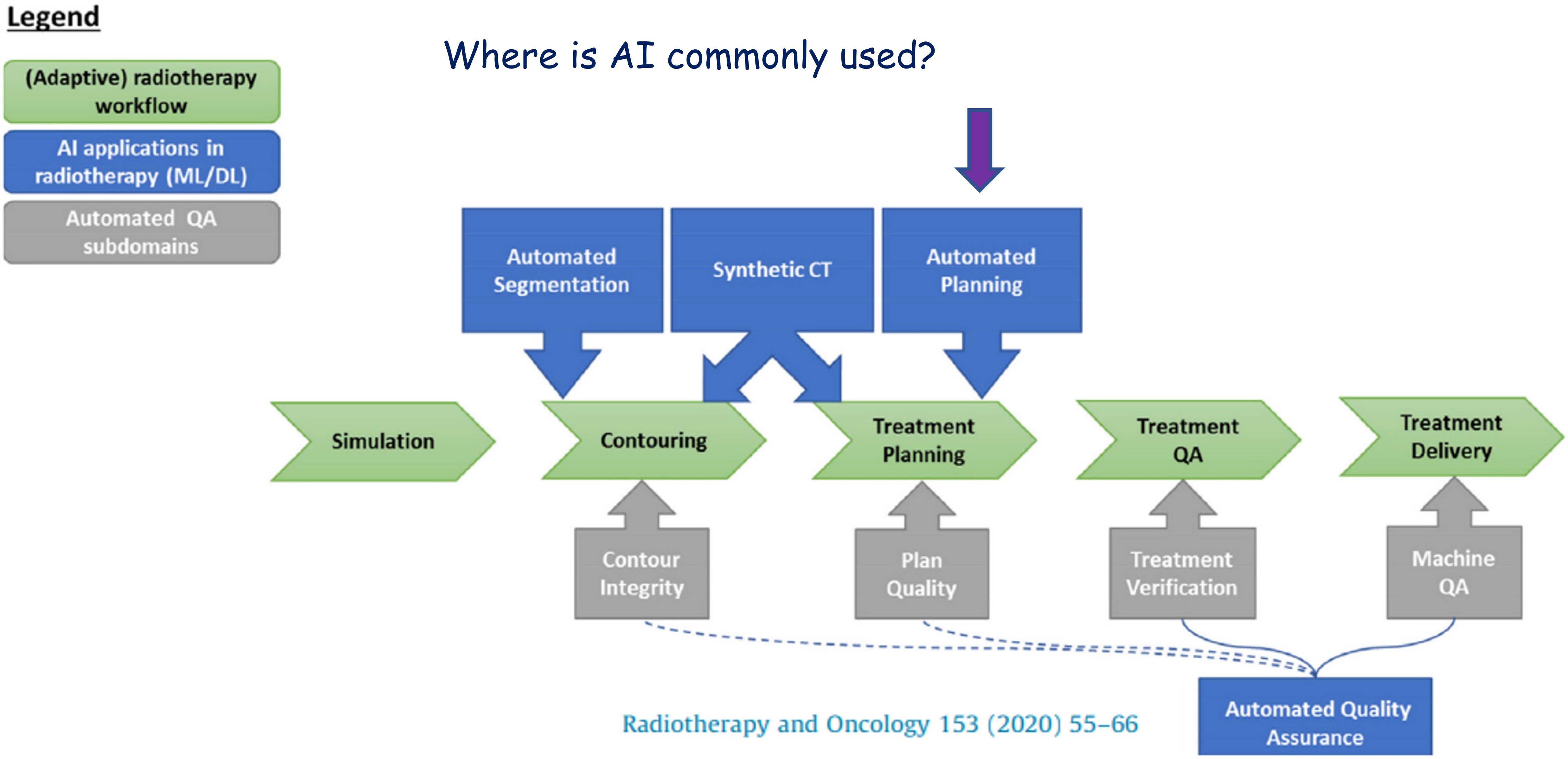
Results:

Image accuracy was evaluated by computing MAE and ME of the HU maps which resulted in very low scores thus demonstrating **good image quality**. Dose distribution comparison was performed by gamma passing rates and target DVH comparisons. A passing rate of 95% for a 2%/2 mm criterion was found. However, **up to 20% difference in dose was found for PTV V95% criteria**. The latter decreased to 11% by comparing CT versus hybrid sCT, a sCT with GTV density override which is typically used in MR-linac workflows.

Discussion:

- Images were taken in deep-hold inspiration which should help to the stability of the structures producing better quality training images.
- The relatively high difference in dose comparison makes this particular sCT suitable for palliative cases.
- To be able to apply this to curative cases e.g. high doses per fraction, the authors propose two things should be done: obtain a larger training cohort and use a more complex neural network with perhaps novel image pre-processing or data augmentation techniques.

Following the patient journey



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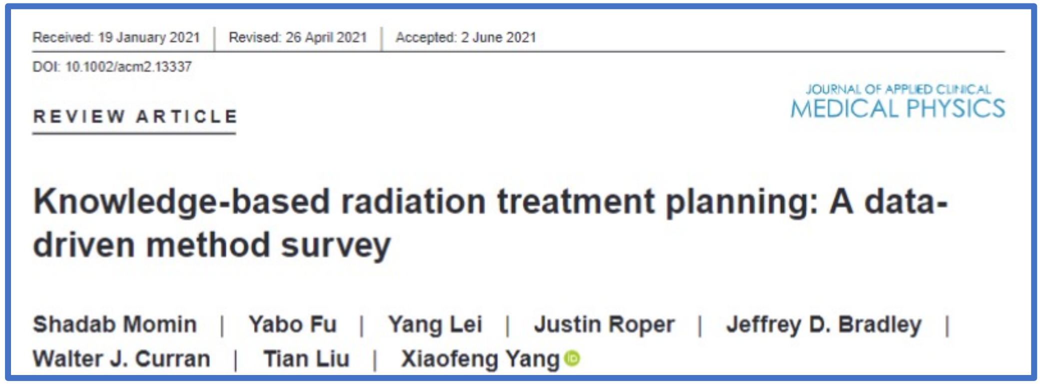
AI in treatment planning

Classified in two categories:

1) Traditional KBP methods: studies that require geometric or anatomical features to either find the best-matched case(s) from a repository of prior treatment plans or to build dose prediction models.



Received: 19 January 2021 | Revised: 26 April 2021 | Accepted: 2 June 2021

DOI: 10.1002/acm2.13337

REVIEW ARTICLE

JOURNAL OF APPLIED CLINICAL MEDICAL PHYSICS

Knowledge-based radiation treatment planning: A data-driven method survey

Shadab Momin | Yabo Fu | Yang Lei | Justin Roper | Jeffrey D. Bradley | Walter J. Curran | Tian Liu | Xiaofeng Yang

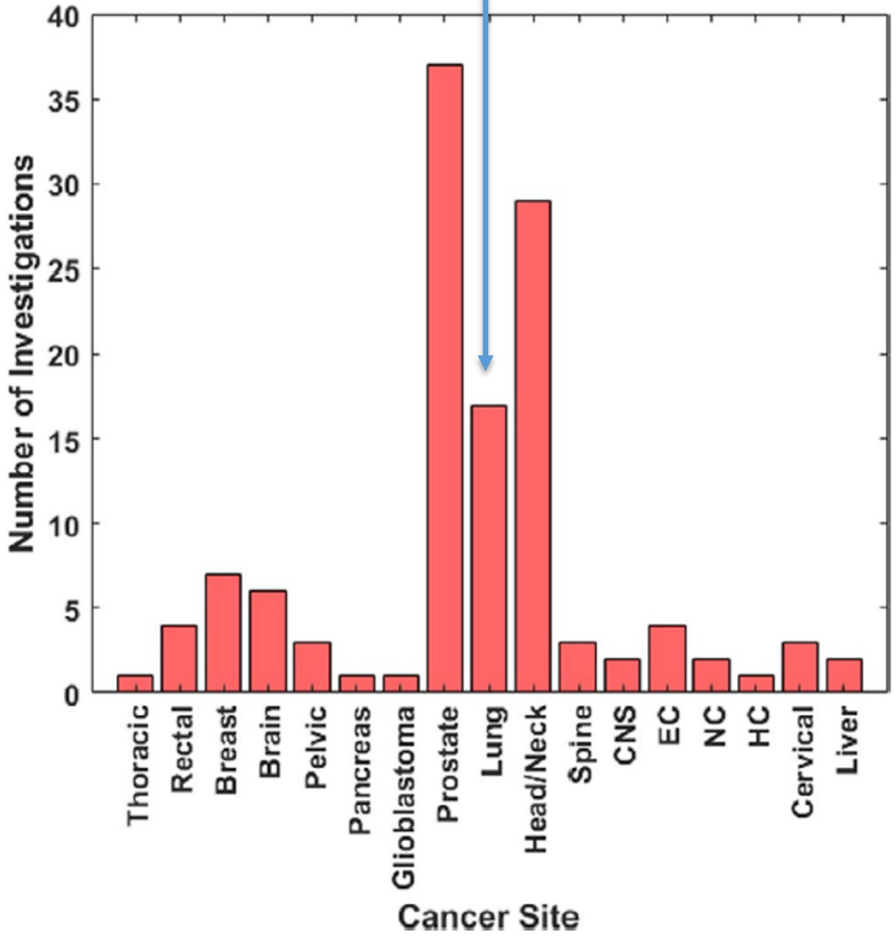


FIGURE 2 The total number of traditional KBP investigations on dose prediction for various cancer sites. EC, Esophageal cancer; NC, Nasopharyngeal carcinoma; HC, Hepatocellular Cancer

AI in treatment planning

Classified in two categories:

2) Deep learning (DL) methods—according to their techniques of utilizing previous knowledge.

- Most studies for lung have been based on traditional automatic methods

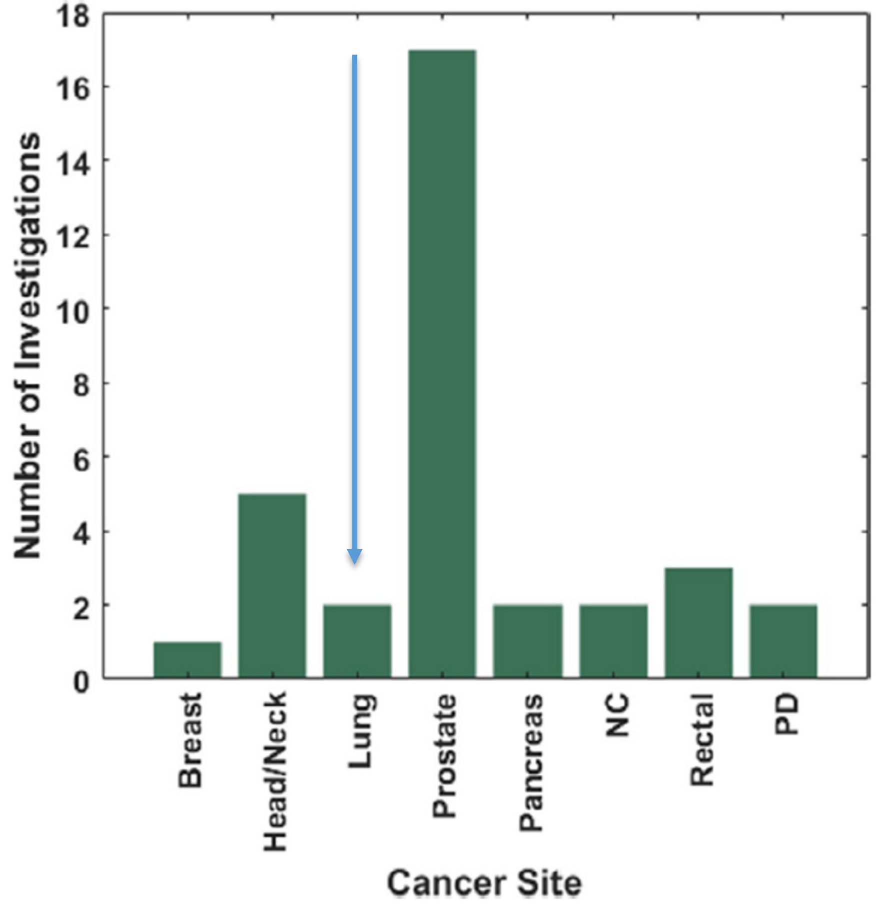


FIGURE 5 The total number of DL-based dose prediction investigations for various cancer sites. NC, Nasopharyngeal Cancer; PD, Personalized Dosimetry

AI in treatment planning: examples

JOURNAL OF APPLIED CLINICAL MEDICAL PHYSICS, VOLUME 17, NUMBER 6, 2016

Development and evaluation of a clinical model for lung cancer patients using stereotactic body radiotherapy (SBRT) within a knowledge-based algorithm for treatment planning

Karen Chin Snyder,[a] Jinkoo Kim, Anne Reding, Corey Fraser, James Gordon, Munther Ajlouni, Benjamin Movsas, and Indrin J. Chetty

- evaluation of the model performance & applicability to different planning techniques, tumor location, beam arrangements

- data set: 105 SBRT plans (several tumour locations, beam arrangements, IMRT and VMAT)
- model validation: 25 pts

- KBP, based on Rapidplan, can generate lung SBRT plans comparable to the clinical ones (but some trade-offs between the spinal cord and the heart)

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UNIVERSITAS CATHOLICA SACRI CORDIS JESU MEDIOLANI

AI in treatment planning: examples

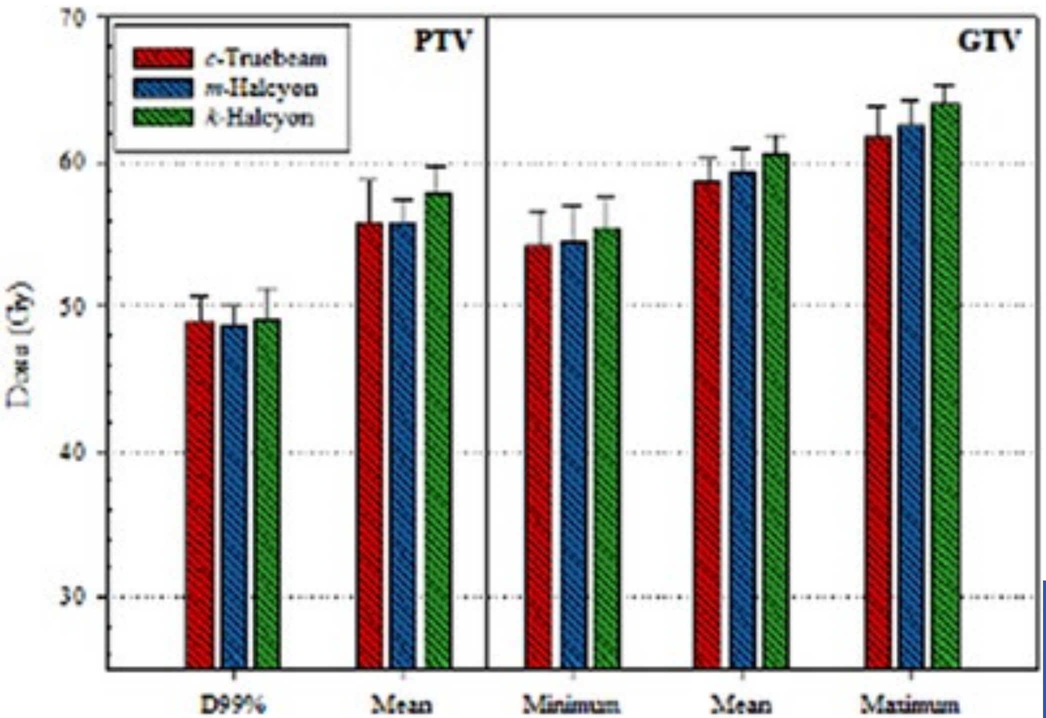
> J Appl Clin Med Phys. 2021 Nov;22(11):54-63. doi: 10.1002/acm2.13427. Epub 2021 Sep 25.

Fast generation of lung SBRT plans with a knowledge-based planning model on ring-mounted Halcyon Linac

Justin Visak [1], Aaron Webster [1], Mark E Bernard [1], Mahesh Kudrimoti [1], Marcus E Randall [1], Ronald C McGarry [1], Damodar Pokhrel [1]

- Automatic planning as an essential tool for fast adaptive re-planning.

- treatment planning feasibility of SBRT for **centrally located lung tumors** on Halcyon Linac via a previously validated KBP model



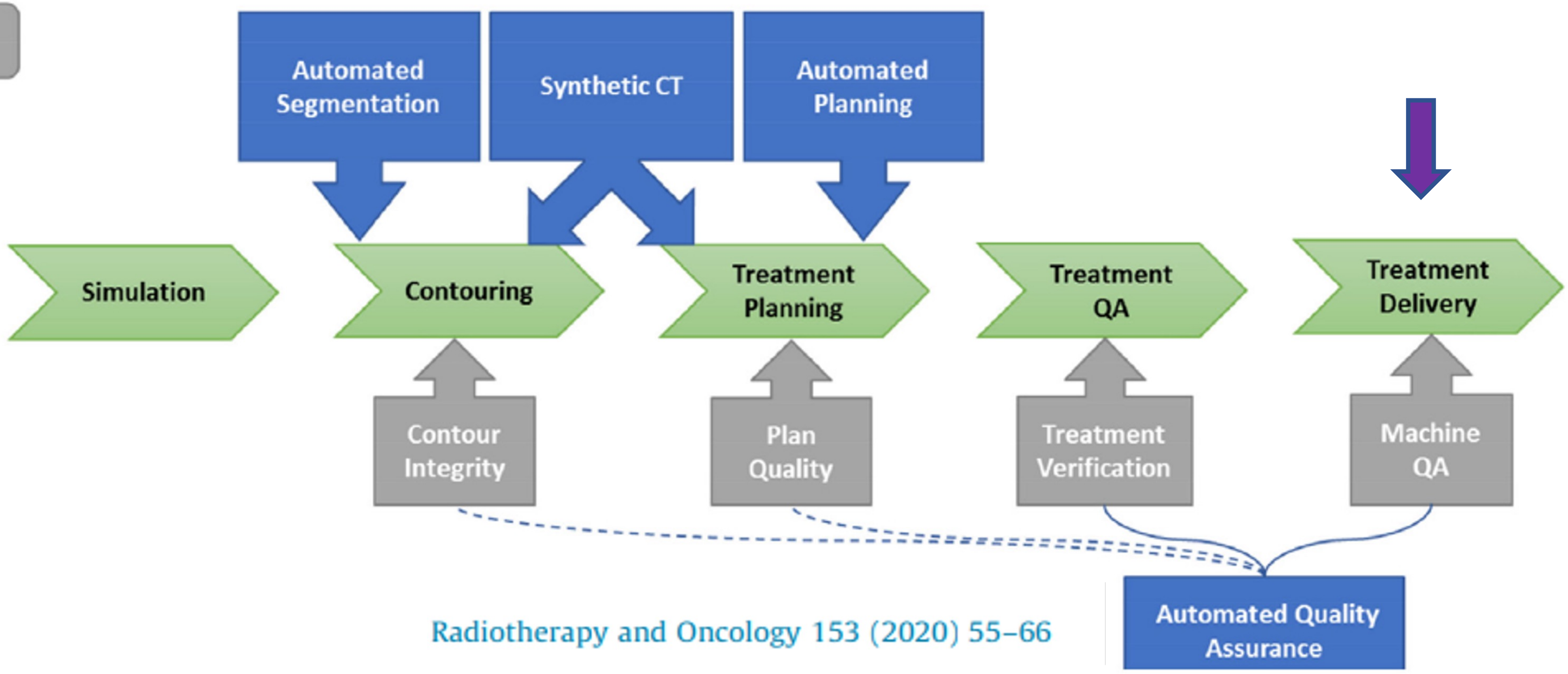
This study reports on the plausibility of generating lung SBRT plans for centrally located early-stage NSCLC patients on ring-mounted Halcyon Linac using a previously trained and validated Truebeam KBP model. It has been demonstrated that the KBP model can be used to generate high-quality lung SBRT plans on the Halcyon Linac that are dosimetrically equivalent or better quality when compared to manually generated Halcyon and SBRT-dedicated Truebeam plans. This lung SBRT

Following the patient journey

Legend

- (Adaptive) radiotherapy workflow
- AI applications in radiotherapy (ML/DL)
- Automated QA subdomains

Where is AI commonly used?



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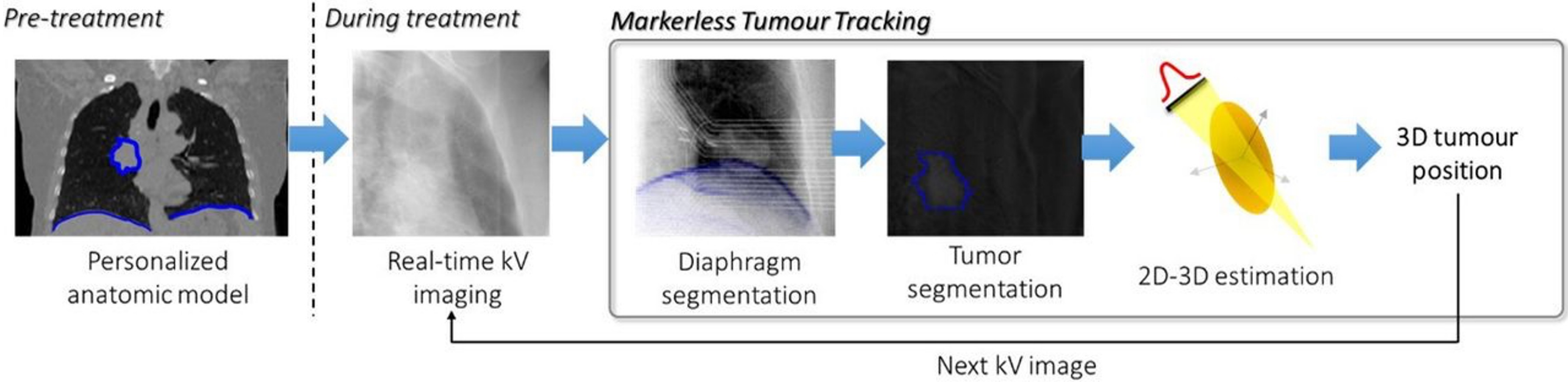
AI in delivery: tumour position tracking (MAGIK)



4D-CT to build **model** of patient anatomy

The anatomic model is used to segment the tumour in the intrafraction kV images

The 3D tumour position is estimated from the 2D position → using a **statistical model**

BMJ Open
MArkerless image Guidance using Intrafraction Kilovoltage x-ray imaging (MAGIK): study protocol for a phase I interventional study for lung cancer radiotherapy

Marco Mueller,[1] Jeremy Booth,[2] Adam Briggs,[2] Dasantha Jayamanne,[2] Vanessa Panettieri,[3] Sashendra Senthi,[3] Chun-Chien Shieh,[1,4] Paul Keall[1]

DOI: 10.1136/bmjopen-2021-057135

AI in delivery: tumour changes

To predict anatomical changes of lung tumour and esophagus during definitive radiotherapy, potential tumour shrinkage, improve therapeutic ratio

The sw analyzes the spatial-temporal distribution using a data-set of 60 pts

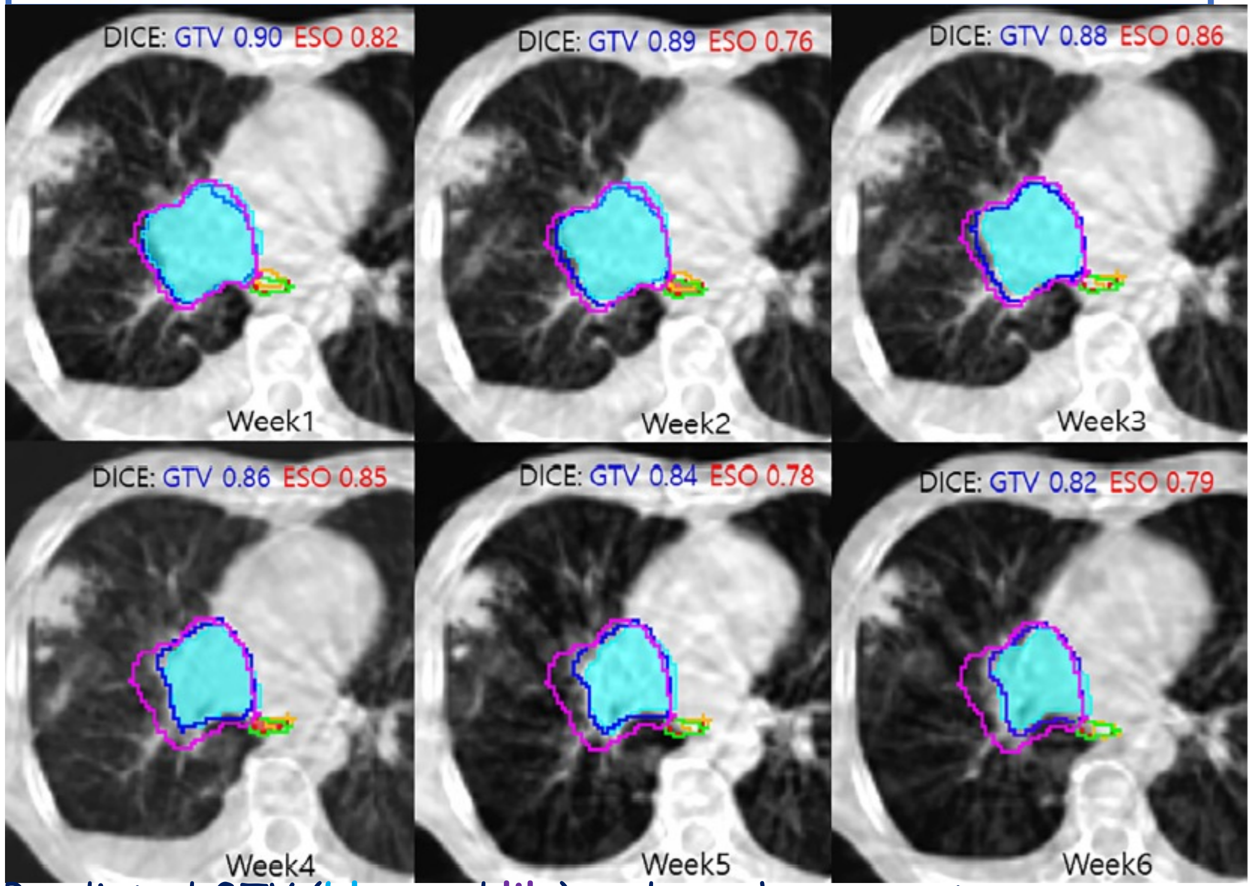
Seq2Seq (software)

It starts with the primary tumor and esophagus observed on the planning CT to predict their geometric evolution during radiotherapy, on a weekly basis

then, it updates the predictions with new info (snapshots) acquired via weekly CBCTs.

Deep learning driven predictive treatment planning for adaptive radiotherapy of lung cancer

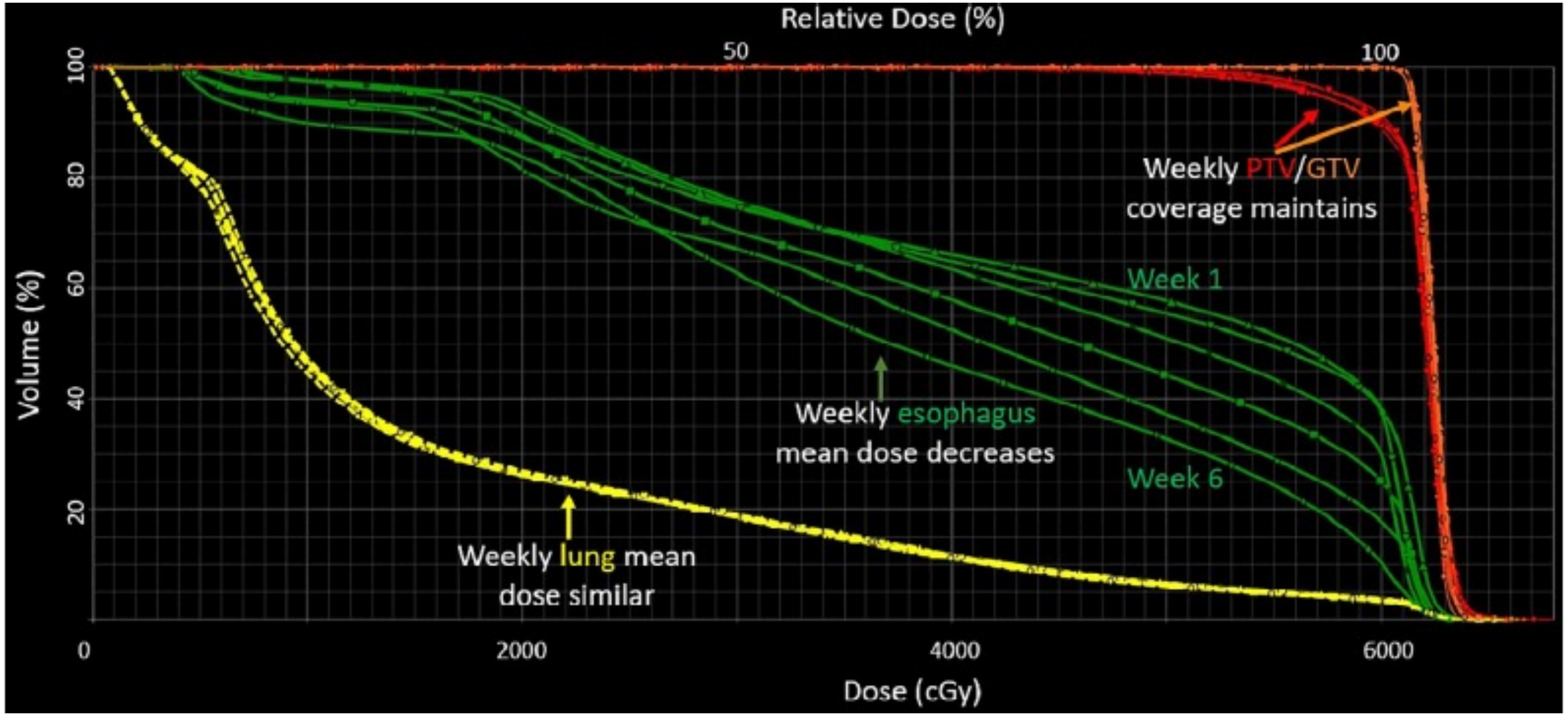
Donghoon Lee[a], Yu-chi Hu[a], Licheng Kuo[a], Sadegh Alam[a], Ellen Yorke[a], Anyi Li[a], Andreas Rimner[b], Pengpeng Zhang[a,*]



Predicted GTV (blue and lila) and esophagus contours (green) from planning to week 6

…weekly predictive plans

- ok 60 Gy prescription dose to the PTVs
- reduced mean dose to esophagus due to tumour shrinkrage (reduced NTCP esophagitis)

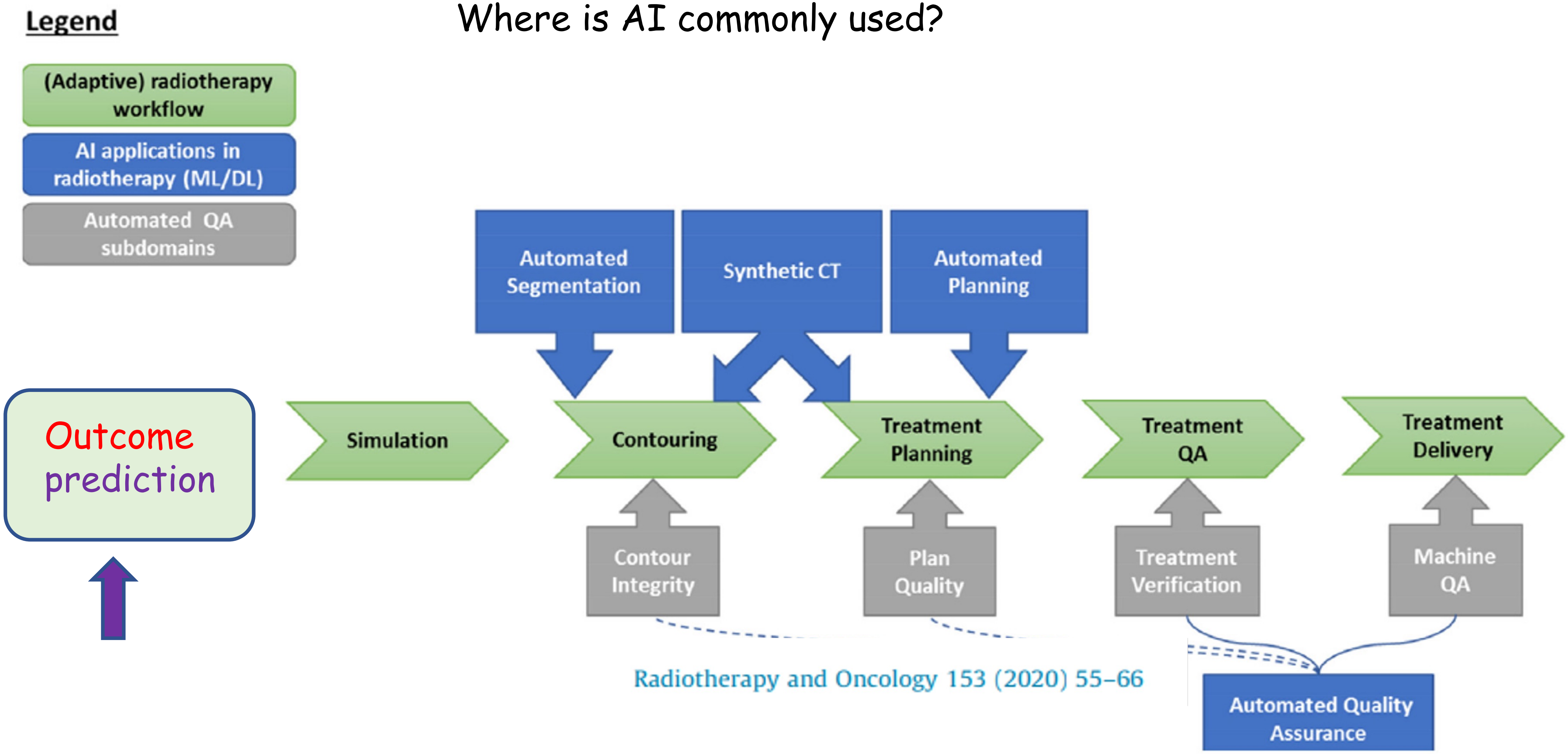


DVHs of predictive plans from week 1 to week 6

…improved efficiency and effectiveness in the whole process…

Following the patient journey: new avenues

Where is AI commonly used?



Radiotherapy and Oncology 153 (2020) 55–66

AI for outcome prediction using doses and images

Received: 16 September 2020 | Revised: 20 July 2021 | Accepted: 2 August 2021
DOI: 10.1002/mp.15178

RESEARCH ARTICLE

MEDICAL PHYSICS

Combining computed tomography and biologically effective dose in radiomics and deep learning improves prediction of tumor response to robotic lung stereotactic body radiation therapy

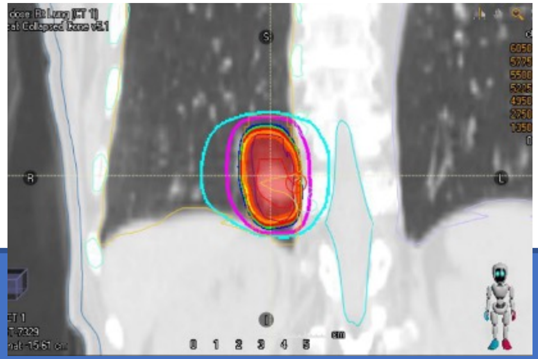
Michele Avanzo[1] | Vito Gagliardi[1] | Joseph Stancanello[2] | Oliver Blanck[3] | Giovanni Pirrone[1] | Issam El Naqa[4] | Alberto Revelant[5] | Giovanna Sartor[1]

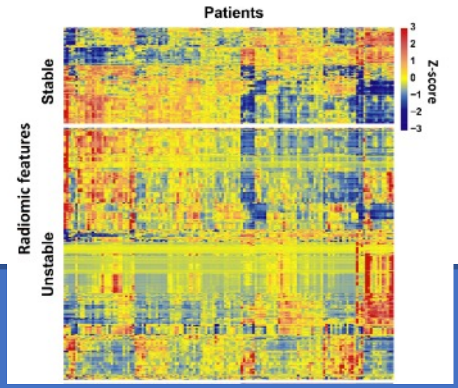
Aim: to improve the performance of ML models in predicting response to NSCLC treated with SBRT

How: integrating image features from CT planning with BED features

Conclusions: including BED features improves response prediction of ML models for NSCLC SBRT pts, regardless the use of CT features

AI&SBRT





segmentation Plan Delivery Outcome prediction

Hybrid approach
AI plus human supervision before the next part

+ harmonization
+ speed up the process

Human responsibility

Only proof of concept

Human supervision after

+ High potentiality

Responsibility?

Need of a new legislation

Many retrospective studies

Need for prospective studies

Now ML; DL should be fully explored

Need to QA each step of the process

Mancosu et al. PBM 2022

Main Findings

1. **AI in target and OARs segmentation**:
   - Fully automated segmentation with no human supervision is not currently feasible
   - Hybrid approach with auto-segmented volumes reviewed by an experienced clinician could speed up the SBRT contouring process
   - Necessity of guidelines and benchmark studies for contours harmonization (Kawata *et al*, Cha *et al,* Ibragimov *et al,* Dong *et al,* Cui *et al*)
2. **AI in SBRT planning**:
   - Fully automated SBRT planning guided by AI is still not available
   - The prediction of dose distribution from a high-quality plan looks promising (Skarpman Munter J and Sjölund, Campbell *et al*, Kearney *et al*, Wang *et al*, Momin *et al*)
   - AI automation could help in planning harmonization, as the quality of the treatment plan still depends on the planner's experience
3. **AI during the SBRT delivery**:
   - AI applications in SBRT delivery are in an early stage of exploration
   - Most of the studies were retrospective, with few AI-based approaches applied in clinical practice (Liang *et al*, Liu *et al*, Valdes *et al*)
   - An effective integration with the radiation units and related control systems are necessary to use AI tools in practice
4. **AI for outcome prediction after SBRT**:
   - Prospective studies aiming at validating radiomic findings are required
   - Machine learning algorithms have the potential to predict tumour control from radiomic features (Lafata *et al*, Dissaux *et al*, Yu *et al*, Wei *et al*)
   - The potential of deep learning has still to be fully explored and is of high interest

Mancosu et al. PBM 2022

Applying Artificial Neural Networks to Develop a Decision Support Tool for Tis–4N0M0 Non–Small-Cell Lung Cancer Treated With Stereotactic Body Radiotherapy

Artificial neural network to predict treatment outcomes for NSCLC patients receiving SBRT

Retrospective, 692 pts with Tis-T4N0M0 NSCLC treated between 2005-2019, plus 100 pts for external validation

Two neural networks for prediction of overall survival and cancer prediction 5 ys after SBRT

Neural networks could select low risk cancer progression groups, suggesting that 48% of the patients with peripheral Tis-T4N0M0 NSCLC can be at low risk for cancer progression

Use: about half of the patients with Tis.T4N0M0 NSCLC recommended to undergo SBRT with the same dose prescription could be informed beforehand of the prediction of a low cancer progression rate on the basis of the group into which they were cathegorized.

Where could AI be especially useful for lung RT and lung planning?

Care path/ automation of the care path

Autosegmentation

many structures to draw, ex for the bronchus case: aorta, brachial plexus (left and right),oesophagus, heart, intermediate bronchus, main bronchus (left and right), pulmonary artery, stomach, thoracic wall (left and right), trachea, vena cava inferior and vena cava superior

Prediction, especially in SBRT

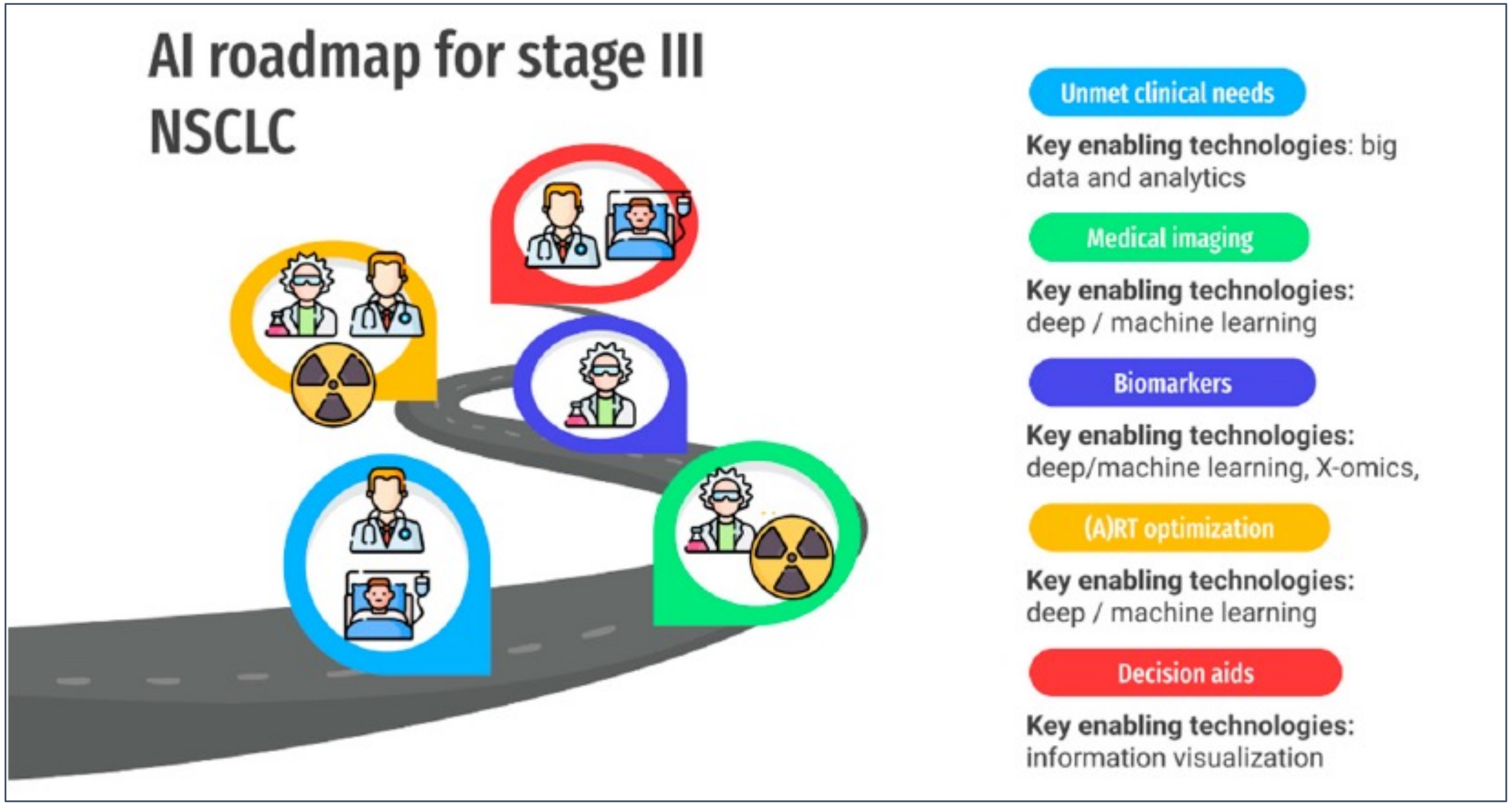
In the "systems" dedicated to SBRT

Adaptive and tumortracking

Issues for the RT community

Limits in the adoption of existing tools

- Technological — e.g. autosegmentation
  Model performance
  several manual adjustments are required
  (Yang JZ, AAPM 2017)
- Legal (hospital, industry) — Intellectual property, data transfer, data sharing agreement
- Implementation in the clinic — Commissioning
  QA procedures
  Reproducibility tests
  Medical Device Regulation requirements



cancers

MDPI

Review

Artificial Intelligence Applications to Improve the Treatment of Locally Advanced Non-Small Cell Lung Cancers

Tumor Heterogeneity Research and Innovation in Biologically Based Radiation Therapy From the National Cancer Institute Radiation Research Program Portfolio

Jeffrey C. Buchsbaum, PhD, MD, AM[1]; Michael G. Espey, PhD[1]; Ceferino Obcemea, PhD[1]; Jacek Capala, PhD[1]; Mansoor Ahmed, PhD[1]; Pataje G. Prasanna, PhD[1]; Bhadrasain Vikram, PhD[1]; Julie A. Hong, MS[1]; Beverly Teicher, PhD[1]; Molykutty J. Aryankalayil, PhD[1]; Michelle A. Bylicky, PhD[1]; and C. Norman Coleman, MD[1]

Buchsbaun, JCO, 2022

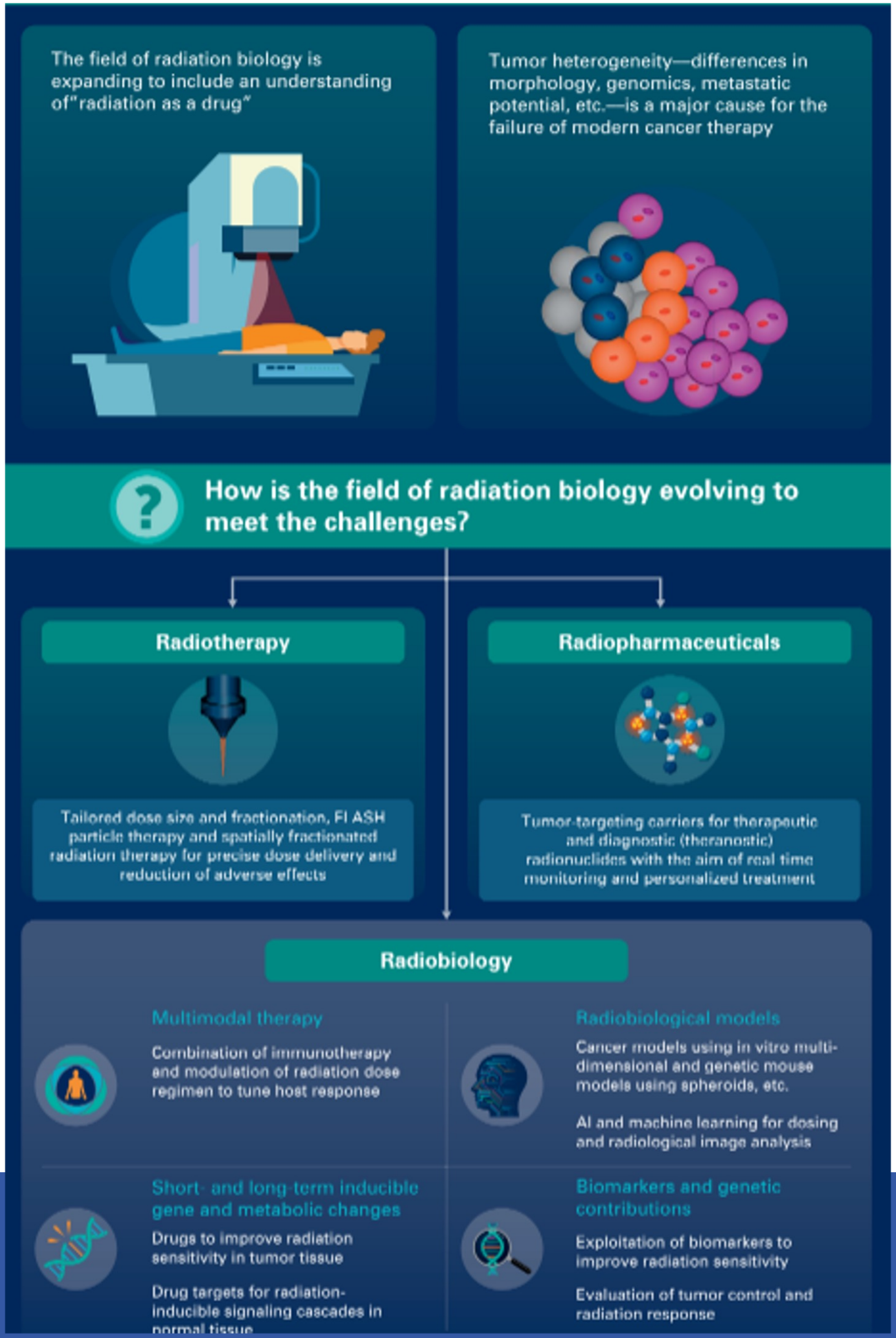
…how radiobiology and clinical care are innovating and evolving to address heterogeneity

One key concept:

radiation in its different forms as different drugs

…that in many cases can have very precise spatial and temporal control thereby potentially producing a specified biological effect.

This approach includes using imaging and molecular biomarkers to enable assessment and determine the appropriate treatment parameters using radiation plus other systemic therapies.



Future approaches in radiation biology must include

adaptation and plasticity data

as well as

longitudinal multiscale measurements and prediction

Addressing tumor heterogeneity: present state and future directions

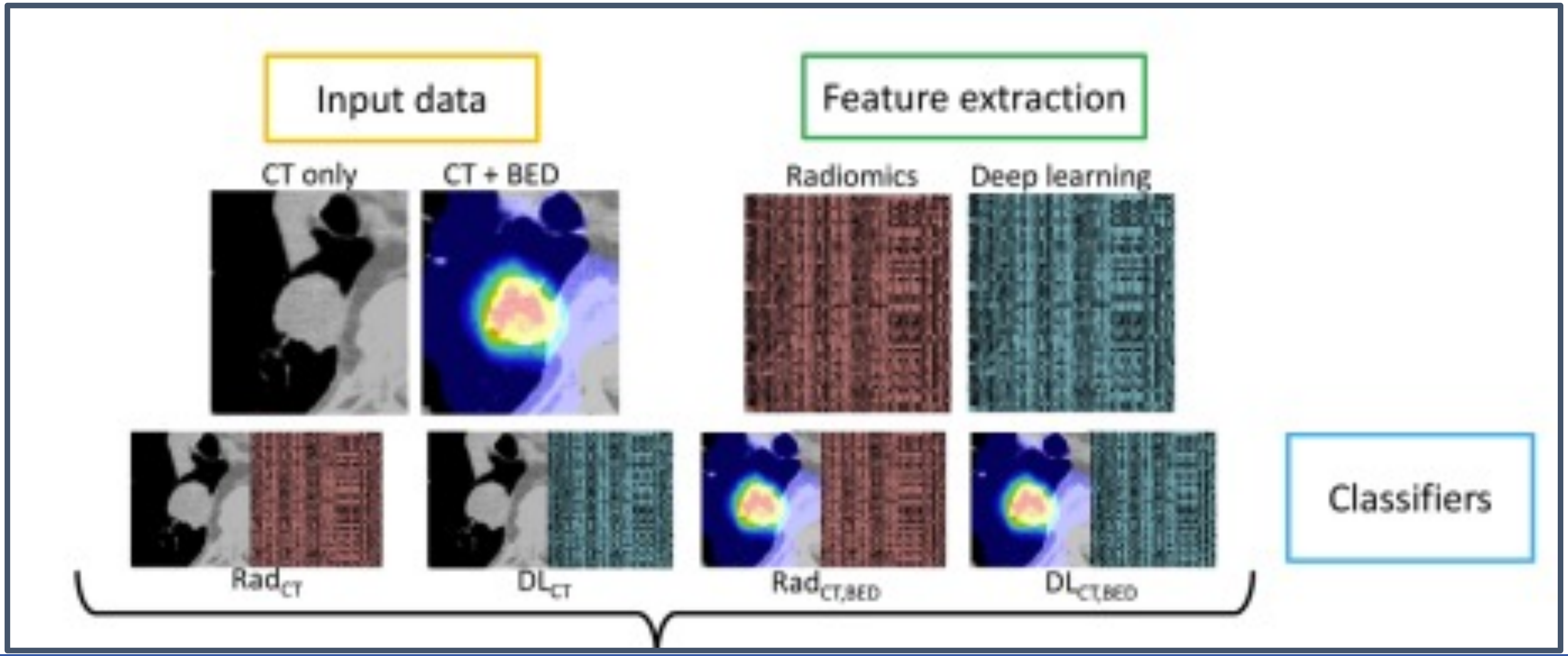
TABLE 1. Selected Hot Research Topics Regarding Radiation Oncology Targeting and Heterogeneity

Topic	Research Questions	Comments and References (PMIDs)
Physics-technology	Does ultrafast dose delivery increase the therapeutic ratio? Does it spare tumor?	1. No normal tissue sparing was seen at 10 Gy/s (33520724). 2. Possible sparing of normal tissue at higher dose rates (32222332). 3. Beam parameters need to be studied (32853355, 33548337). 4. Planning may be complex (33924627). 5. Tumor cells may not be spared at doses over 40 Gy/s (25031268, 29172684).
Oligometastases	Can cure be achieved for some patients with metastatic disease via the use of radiation therapy?	1. Data supporting that these patients exist (30521067). 2. Patients may significantly benefit if oligometastatic lesions are treated with radiation in addition to chemotherapy in some cases (28973074).
Radiopharmaceuticals (RPT)	What is the optimal combination of RPT with other therapeutic modalities, including immunotherapy and external RT (both need proper RPT dosimetry)? Is there an advantage to using combinations of radionuclides with different ranges of emitted radiation, and high- and low-molecular-weight targeting agents, to match the size of the tumor and target distribution, and to take advantage of different clearance routes (renal and hepatic)?	1. Overview and need for dosimetry (33610302, 33277396). 2. Alpha emitter support currently (34378064). 3. Two and possibly fewer time points needed for dosimetry (30761545, 33443063). 4. Combination therapy has promise (34625828)
Radiation biology	Because radiation induces targets, do match trials necessarily need to be matched to the on-treatment context more precisely?	1. Radiation target induction creates a new opportunity (32554542). 2. The type of radiation affects the genetic expression pattern significantly (28599420). 3. Senescence and radiation side effects are likely intertwined, making new discoveries in this space potentially able to decrease late normal tissue side effects (29776716).
Combined modality therapy	Would earlier integration with radiation benefit drug design, given these drugs need to be able to work well with radiation?	1. Involvement of radiation early in drug design may open up new success (34348172). 2. Proposed standards to improve the current standards have recently been published by the NCI preclinical U01 consortium (34454045).
Immuno-oncology	How can we select dose and fractionation to optimize immuno-oncology (the abscopal effect)? Sequencing? What are the best biomarkers of a clinical abscopal response? How do we study and prevent side effects, in particular chronic side effects, from immuno-oncology that is or is not combined with radiation?	1. Data show that Trex1 regulates induced tumor immunogenicity (28598415). 2. Fraction sizes and methods to best induce and maintain an abscopal effect are variable and under investigation (33827904).
Normal tissue heterogeneity	What biomarkers should be used, and how should they be used, to properly measure heterogeneity of radiation response and predict clinical outcome?	1. Genetic risk prediction (33398198). 2. Immune response (28630051). 3. MicroRNA (34364390). 4. Liquid biopsies (33049623). 5. ctDNA (31711920). 6. Cell-free DNA (33828112). 7. DNA profiling (28899864). 8. Novel approaches to concurrently and continuously [illegible]
AI/ML	How to best use AI and ML to enhance clinical research and care?	Focus on many recent articles and recent [illegible] workshops and meetings

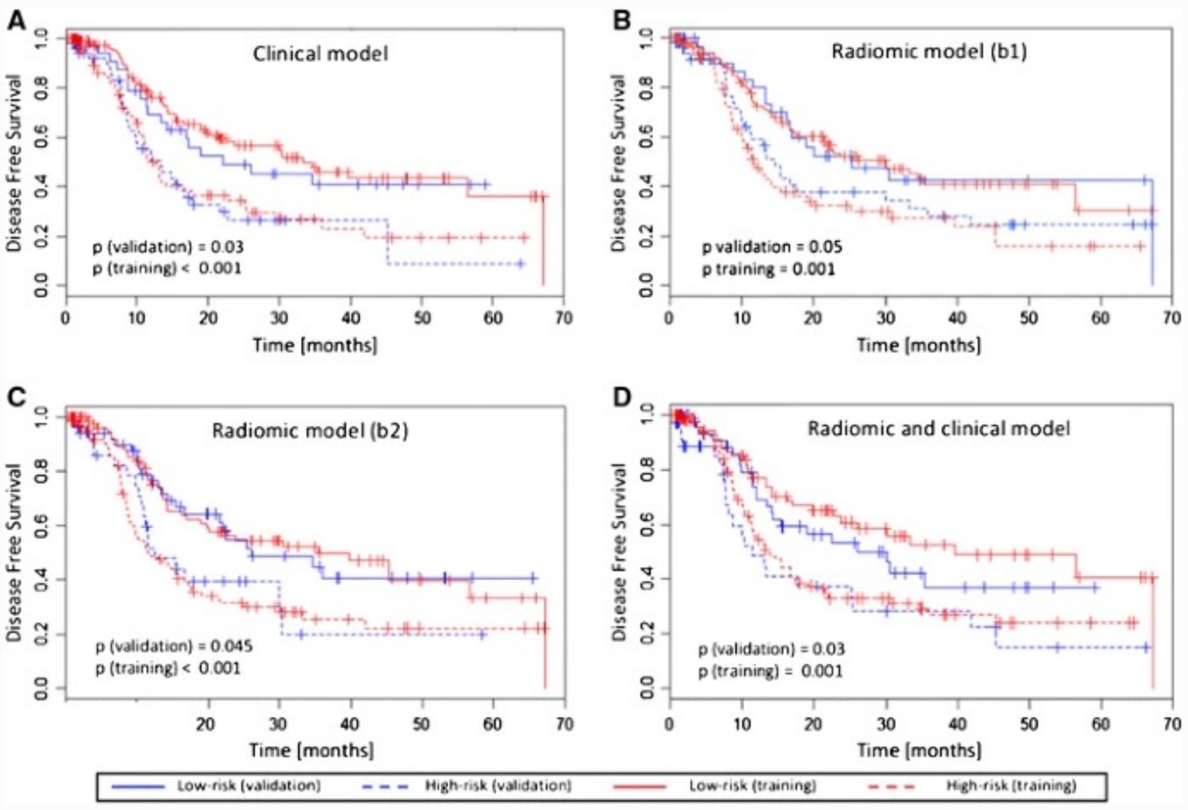
Major points of the talk

- Terminology
- AI application areas
- Needs and potential development
- Issues in lung RT - AI

- 76 pts early stage NSCLC, SBRT,
- GTV on CT, CTV on CT + PET/CT, + 3 mm PTV
- Cyberknife, 45Gy, 3 fractions
- Tumour response on follow-up CT, sometimes PET/CT



AI for outcome prediction using images



Disease-free survival prediction results for the PET+CT data. Kaplan-Meier curves for the DFS resulting from the Cox regression models built using clinical variables (**a**), the radiomic signature (**b** and **c**), and their combination (**d**) for the training and validation groups within the PET+CT dataset

2018 Feb;45(2):207-217.

Prediction of disease-free survival by the PET/CT radiomic signature in non-small cell lung cancer patients undergoing surgery

Margarita Kirienko[1], Luca Cozzi[2], Lidija Antunovic[3], Lisa Lozza[4], Antonella Fogliata[1], Emanuele Voulaz[5], Alexia Rossi[1,6], Arturo Chiti[1,3], Martina Sollini[7]

Extraction of radiomics features from PET/CT for outcome prediction (DFS) in NSCLC:

- 295 patients treated with surgery
- The main finding of the study was that image-derived parameters outperformed common clinical predictors, including TNM staging.

PET dataset (*n* = 259)	Univariate *p* value	Cox regression *p* value			
Parameter		Clinical model (a)	Radiomic models (b)		Radiomic and clinical model (c)
			b1	b2	
AUC (95%CI) for the validation cohort		0.61 (0.50–0.73)	0.62 (0.52–0.70)	0.68 (0.58–0.74)	0.65 (0.50–0.72)