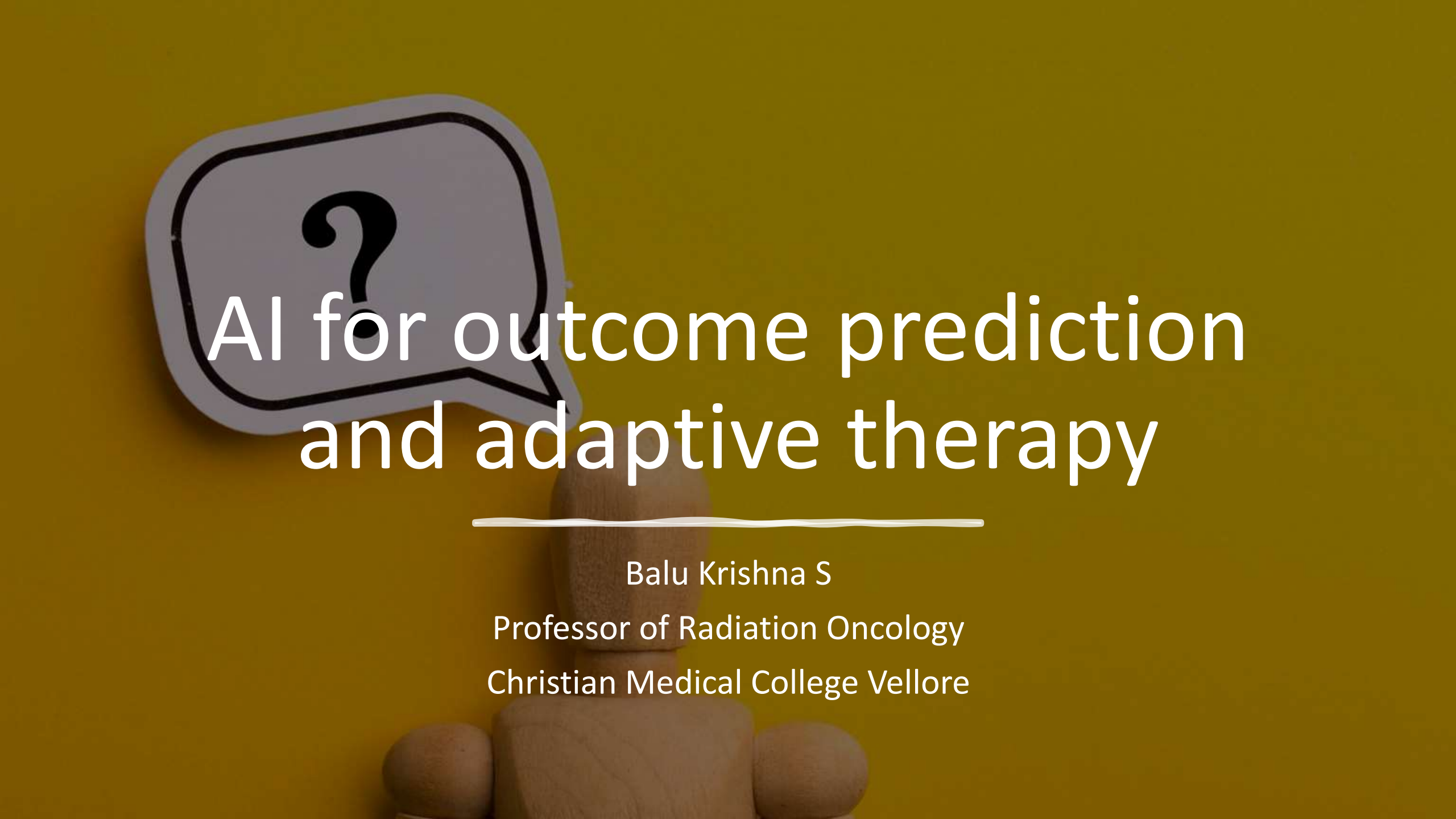


AI for outcome prediction and adaptive therapy

Balu Krishna S

Professor of Radiation Oncology

Christian Medical College Vellore

In the next 20 mins

- Key role of AI in Radiotherapy
- AI in outcome prediction
  - What outcomes do we oncologists want?
  - How do we perform on these predictions?
  - How does AI predict?
  - How do we evaluate the predictions made by AI?
- AI in adaptive radiotherapy
  - Key areas of application
- Where are we with the clinical implementation of AI?
- What is the radiation oncologist's role in AI research/implementation?

A.I. applications in Radiotherapy

Do things more efficiently than humans

Automation

- Patient Scheduling
- Lesion/ organ contouring
- Treatment Plan generation
- Treatment Plan Optimization
- Quality control and Assurance

⇩

- ➢ Saves time
- ➢ Increase reliability
- ➢ Reduce inter-operator variability
- ➢ Optimal use of resources (Personnel and machines)
- ➢ Expert interpretation

Do things that humans cannot do

Inference

- Creating new images (e.g Synthetic CT (sCT) from MRI)
- Classification of disease using multi-modal data
- Predicting disease outcomes, efficacy, toxicity
- Adapting a therapy based on longitudinal/new information

⇩

- ➢ New discoveries
- ➢ New opportunities/new protocols

AI in outcome prediction

How do clinicians predict these outcomes?

Often struggle when decisions depend on more than 5 data points

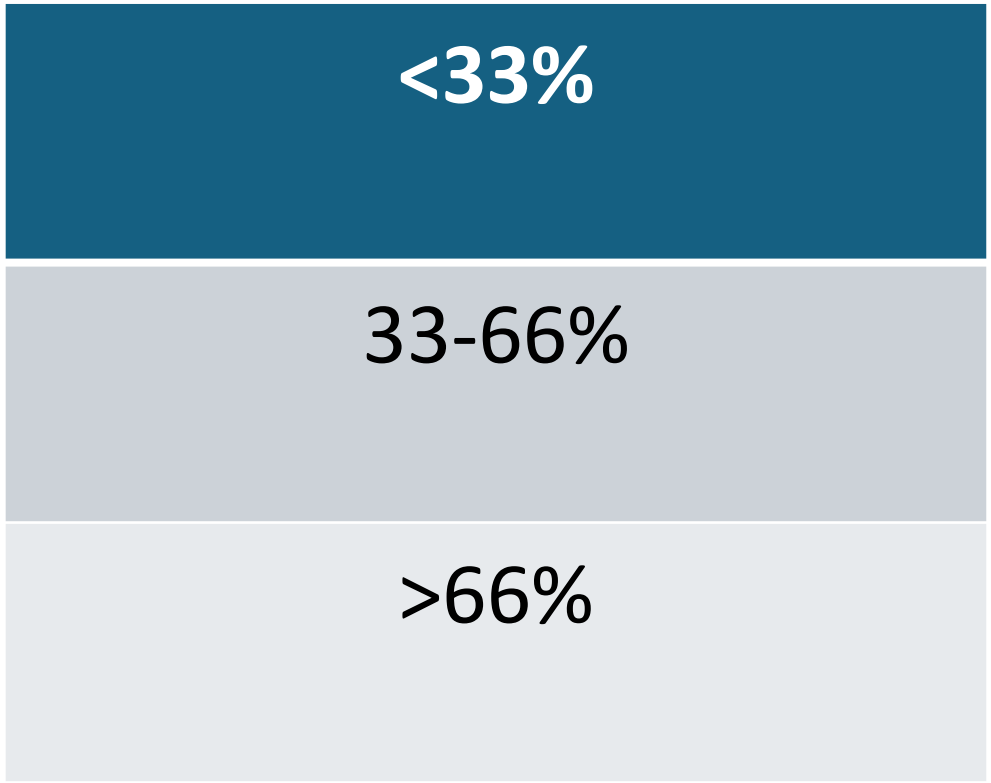
When these data points are non-linearly correlated

doi: 10.3978/j.issn.2224-5820.2015.08.04

Predict the chance of this patient surviving to 5 years without disease

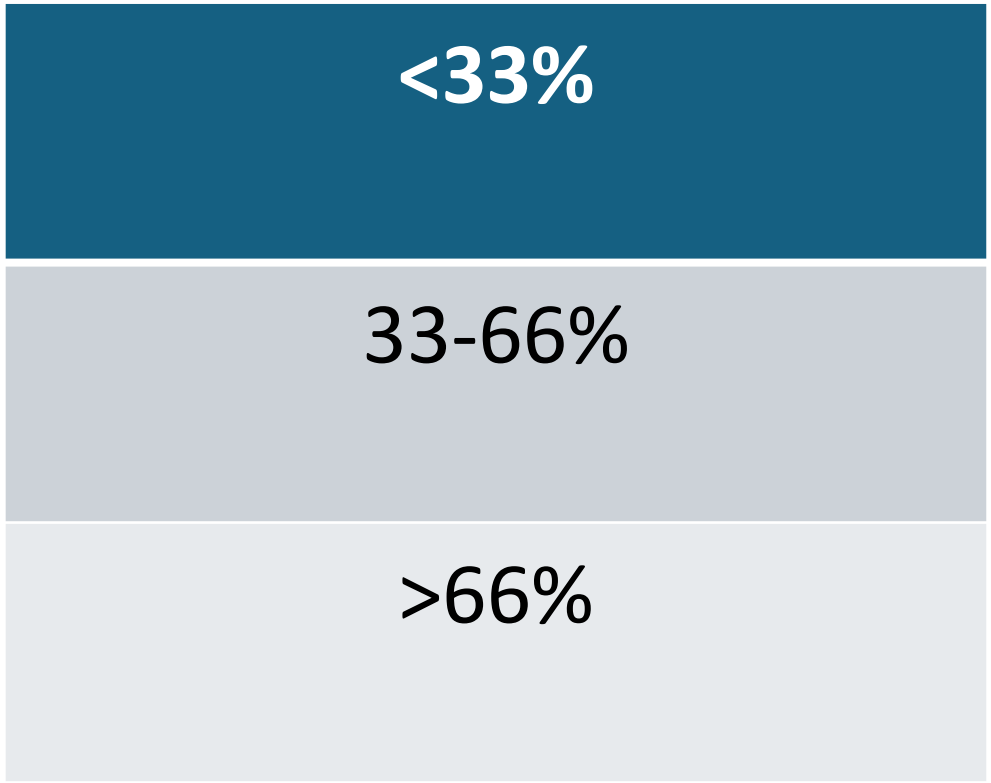
Given

- Vocal cord cancer
- T4 N2



Predict the chance of this patient surviving to 5 years without disease

- 66-year old male
- Weighs 40Kg
- P16 positive
- No social support
- Treat only on government funds
- Remote location
- Only Cobalt-60 available
- Senior Doctor going on leave next two months
- ICU beds are always full in the city



Reality of the predictions

- Doctors' prognostic estimates of their terminally ill patients are **often wrong and usually more optimistic**
- Only **20% of the doctors' predictions were accurate**: 63% were overoptimistic and 17% were overpessimistic
- Most types of **doctors are prone to error**, in most types of patients
- The greater the experience of the doctor the greater the prognostic accuracy, but **a stronger doctor-patient relationship is associated with lower prognostic accuracy**

Review Article

The accuracy of clinicians' predictions of survival in advanced cancer: a review

Stephanie Cheon, Arnav Agarwal, Marko Popovic, Milica Milakovic, Michael Lam, Wayne Fu, Julia DiGiovanni, Henry Lam, Breanne Lechner, Natalie Pulenzas, Ronald Chow, Edward Chow

Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada

Contributions: (I) Conception and design: S Cheon, M Popovic, E Chow; (II) Administrative support: B Lechner, N Pulenzas, R Chow; (III) Provision of study materials or patients: H Lam; (IV) Collection and assembly of data: S Cheon, A Agarwal; (V) Data analysis and interpretation: S Cheon, A Agarwal; (VI) Manuscript writing: S Cheon; (VII) Final approval of manuscript: All authors.

Correspondence to: Dr. Edward Chow, MBBS, MSc, PhD, FRCPC. Department of Radiation Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, Toronto, ON, Canada. Email: Edward.Chow@sunnybrook.ca.

Extent and determinants of error in doctors' prognoses in terminally ill patients: prospective cohort study

Nicholas A Christakis, Elizabeth B Lamont

Abstract

Objective To describe doctors' prognostic accuracy in terminally ill patients and to evaluate the determinants of that accuracy.
Design Prospective cohort study.
Setting Five outpatient hospice programmes in Chicago.
Participants 343 doctors provided survival estimates for 468 terminally ill patients at the time of hospice referral.
Main outcome measures Patients' estimated and actual survival.
Results Median survival was 24 days. Only 20% (92/468) of predictions were accurate (within 33% of actual survival); 63% (295/468) were overoptimistic and 17% (81/468) were overpessimistic. Overall, doctors overestimated survival by a factor of 5.3. Few doctors are more likely to err in certain types of patients; and neglect of the possibility of different determinants of optimistic and pessimistic error. Therefore, we conducted a large, prospective cohort study of terminally ill patients to evaluate the extent and determinants of prognostic error.

Participants and methods

Our cohort consisted of all patients admitted to five outpatient hospice programmes in Chicago during 130 consecutive days in 1996. Participating hospices notified us about patients on admission, and we immediately contacted the referring doctors to administer a four minute telephone survey. Of the 767 patients (referred by 502 doctors), 65 did not meet the entry criteria (they were children, were denied hospice admission, or refused to give consent) and 51 died

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Nicholas A Christakis *associate professor*
Robert Wood Johnson Clinical Scholars Program, University of Chicago Medical Center
Elizabeth B Lamont *fellow*
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What outcomes do oncologists want to predict?

Treatment Response	Effectiveness Dosage Requirements	**Biomarker Discovery**	Identification of Biomarkers
Adverse Reactions	Side Effects Toxicity	**Patient Stratification**	Risk Assessment
Disease Progression	Prognosis Recurrence Risk	**Quality of Life**	Functional Outcomes Symptom Management
Survival Rates	Overall Survival Progression-Free Survival	**Genetic & Genomic Insights**	Genetic Predispositions Pharmacogenomics

Can AI help?

Original Investigation | Health Informatics

May 31, 2022

Prospective Comparison of Medical Oncologists and a Machine Learning Model to Predict 3-Month Mortality in Patients With Metastatic Solid Tumors

Finly J. Zachariah, MD[1]; Lorenzo A. Rossi, PhD[2]; Laura M. Roberts, MS[3]; et al

» Author Affiliations | Article Information

JAMA Netw Open. 2022;5(5):e2214514. doi:10.1001/jamanetworkopen.2022.14514

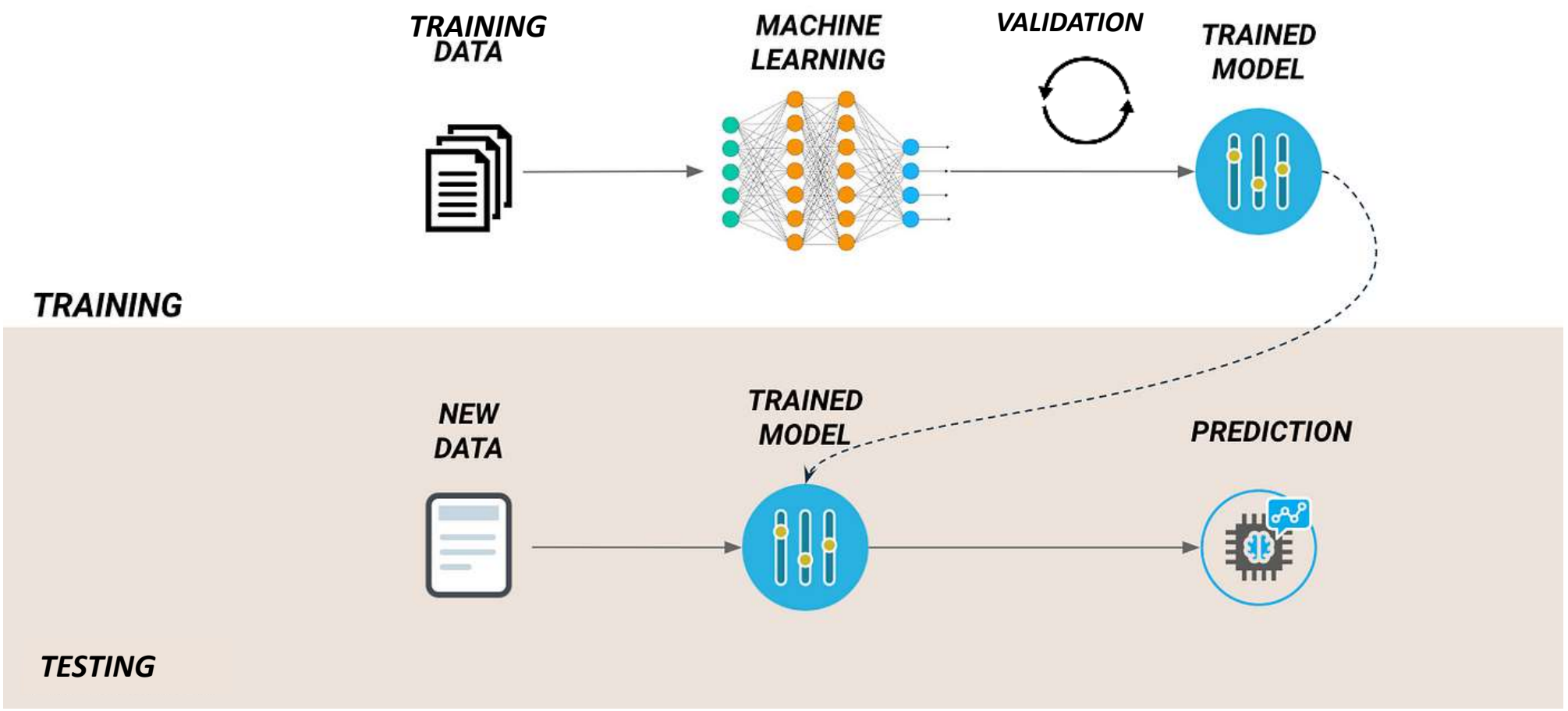
AI model predicted 3-month mortality in 2000+ solid tumours more accurately than 74 oncologists.

Key Points

Question How do oncologists and a machine learning model compare in predicting 3-month mortality for patients with advanced solid tumors?

Findings In this prognostic study, the machine learning model significantly outperformed 74 oncologists in predicting 3-month mortality for 2041 patients with metastatic solid tumors overall and in gastrointestinal and breast cancer subpopulations. Findings were not significant in genitourinary, lung, and rare cancer groups.

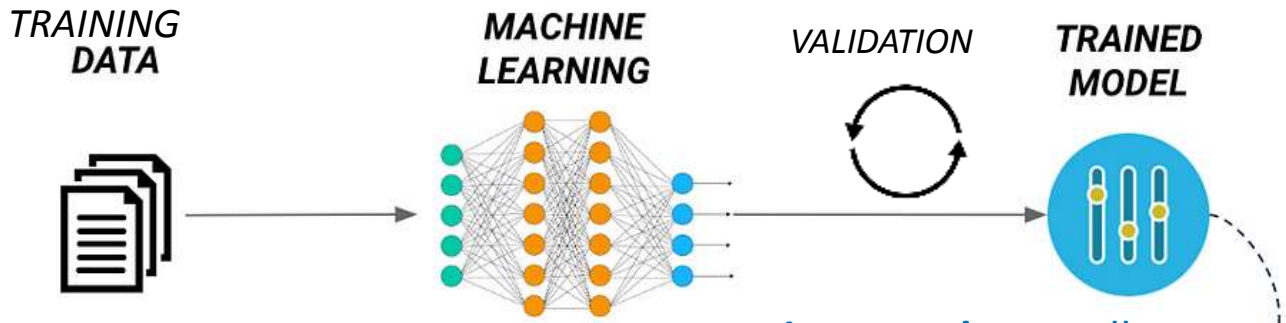
How does AI predict?



learning to recognize patterns and make decisions based on these experiences

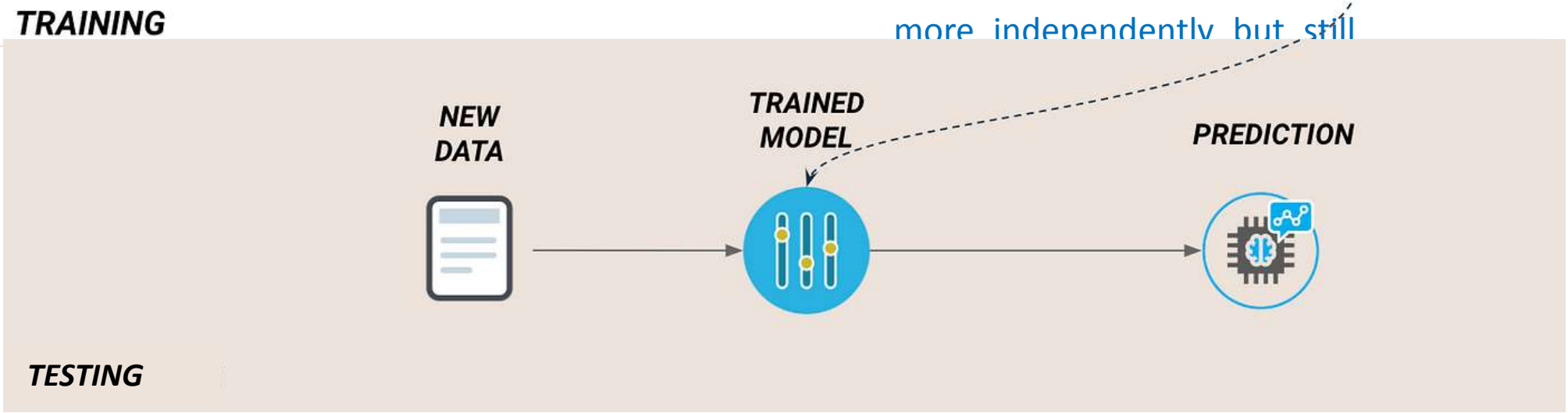
Medical cases

Medical Resident



Medical Training

Practice rounds: Handle cases more independently but still



University Board exam

New, unseen case

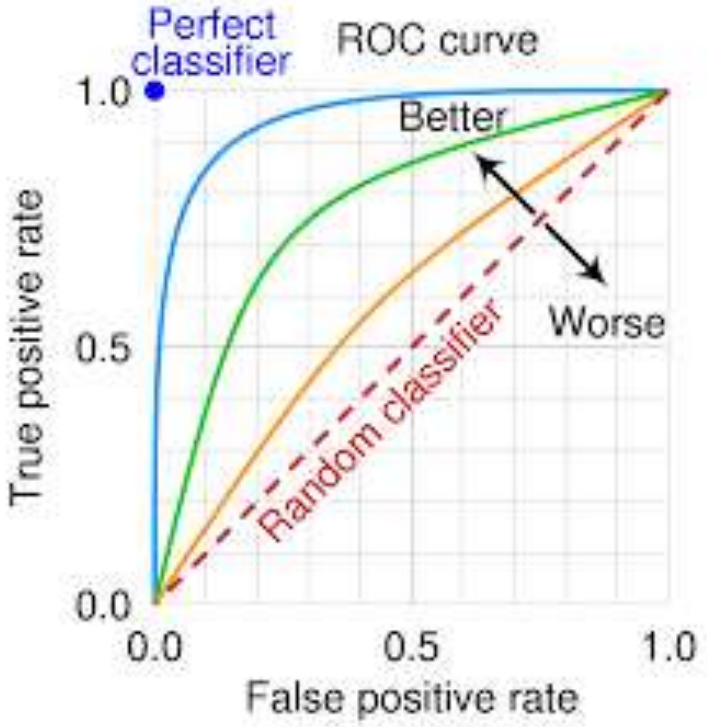
Apply learned knowledge to assess new patient

The exam results determine if the resident has developed a robust, generalizable skill set or if they need further training

Key Parallels

- **Learning from Real Cases**: Just as residents learn from real patient cases, ML models learn from training data.
- **Supervised Practice**: Both residents and ML models go through a phase of supervised practice to refine their skills.
- **Feedback and Refinement**: Continuous feedback helps improve both clinical skills and model performance.
- **Final Assessment:** Both residents and ML models are ultimately tested on new, unseen cases to evaluate their generalization capabilities.
- The process is iterative

How do we evaluate the AL model's prediction?



The **A**rea **U**nder the Receiver Operating **C**urve

AUC is preferred as

Scale-invariant

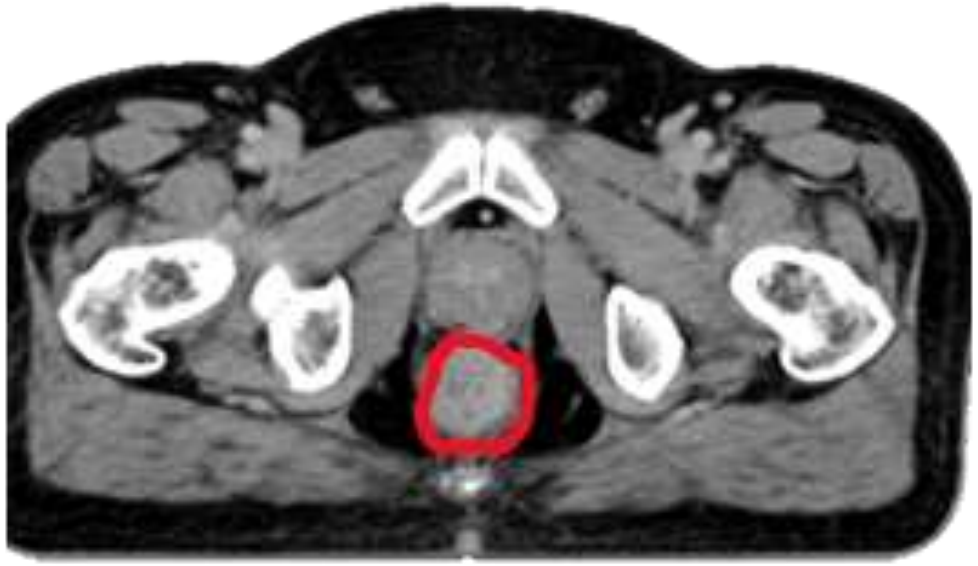
Measures how well predictions are ranked, rather than their absolute values

Classification-threshold-invariant

Measures the quality of the model's predictions regardless of the classification threshold chosen

Few examples of outcome predictions

Predict treatment response



Journal of Gastrointestinal Cancer
https://doi.org/10.1007/s12029-024-01073-z

RESEARCH

Can Pretreatment MRI and Planning CT Radiomics Improve Prediction of Complete Pathological Response in Locally Advanced Rectal Cancer Following Neoadjuvant Treatment?

Jeba Karunya Ramireddy[1] · A. Sathya[1] · Balu Krishna Sasidharan[1] · Amal Joseph Varghese[1] · Arvind Sathyamurthy[1] · Neenu Oliver John[1] · Anuradha Chandramohan[2] · Ashish Singh[3] · Anjana Joel[3] · Rohin Mittal[4] · Dipti Masih[5] · Kripa Varghese[5] · Grace Rebekah[6] · Thomas Samuel Ram[1] · Hannah Mary T. Thomas[1]

Accepted: 19 May 2024

Abstract

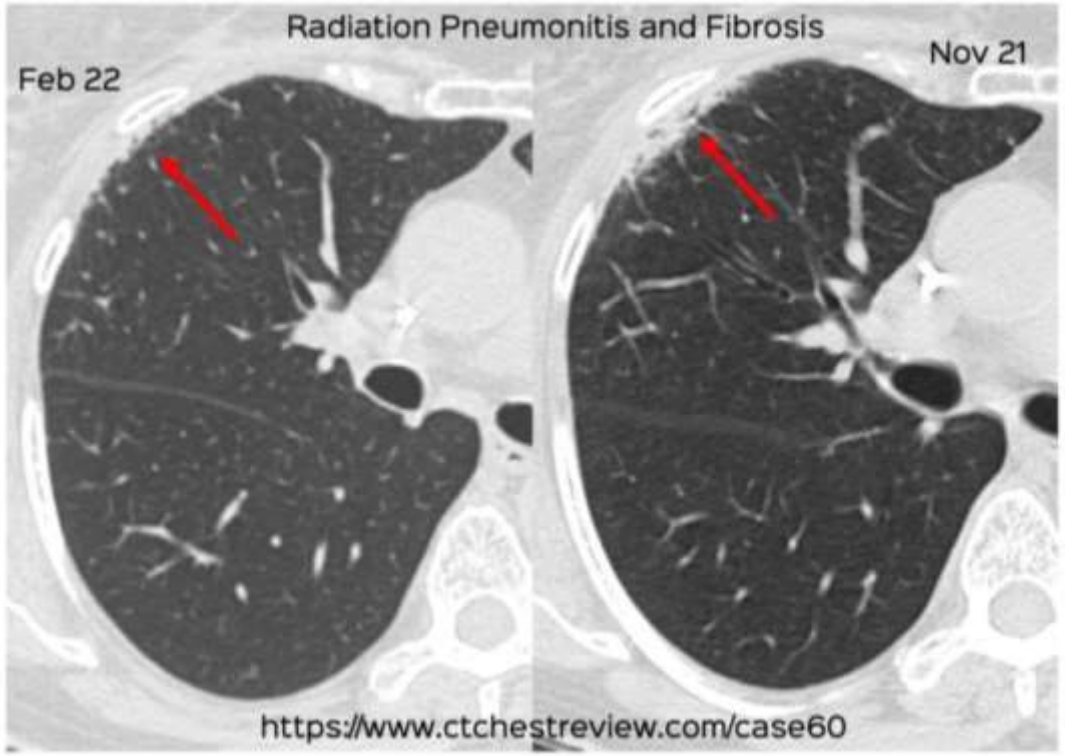
Objective(s) The treatment response to neoadjuvant chemoradiation (nCRT) differs largely in individuals treated for rectal cancer. In this study, we investigated the role of radiomics to predict the pathological response in locally advanced rectal cancers at different treatment time points: (1) before the start of any treatment using baseline T2-weighted MRI (T2W-MR) and (2) at the start of radiation treatment using planning CT.

Methods Patients on nCRT followed by surgery between June 2017 to December 2019 were included in the study. Histopathological tumour response grading (TRG) was used for classification, and gross tumour volume was defined by the radiation oncologists. Following resampling, 100 and 103 pyradiomic features were extracted from T2W-MR and planning CT images, respectively. Synthetic minority oversampling technique (SMOTE) was used to address class imbalance. Four machine learning classifiers built clinical, radiomic, and merged models. Model performances were evaluated on a held-out test dataset following 3-fold cross-validation using area under the receiver operator characteristic curves (AUC) with bootstrap 95% confidence intervals.

Results One hundred and fifty patients were included; 58/150 with TRG 1 were classified as complete responders, and rest were incomplete responders (IR). Clinical models performed better (AUC = 0.68) compared to radiomics models (AUC = 0.62). Overall, the clinical + T2W-MR model showed best performance (AUC = 0.72) in predicting the pathological response prior to therapy. Clinical + Planning CT-merged models could only achieve the highest AUC of 0.66.

Conclusion Merging clinical and baseline T2W-MR radiomics enhances predicting pathological response in rectal cancer. Validation in larger cohorts is warranted, especially for watch and wait strategies.

Predict toxicity



ELSEVIER
Oncology*Biology*Physics
Volume 114, Issue 3, Supplement, 1 November 2022, Pages e118-e119

2261

Can CBCT-Based Delta Radiomics Predict Normal Lung Toxicity during Thoracic Radiation?

N. Jose [1], A.J. Varghese [1], H.M. Thomas [2], A. Irodi [3], J.C. Paul [3], M. Mathew [1], R. Isiah [4], S. John [5], H.F. Godson [1], T.B. Peace [1], S.P. Pavamani [6], D. Devadhas [7], B.K. Sasidharan [4]

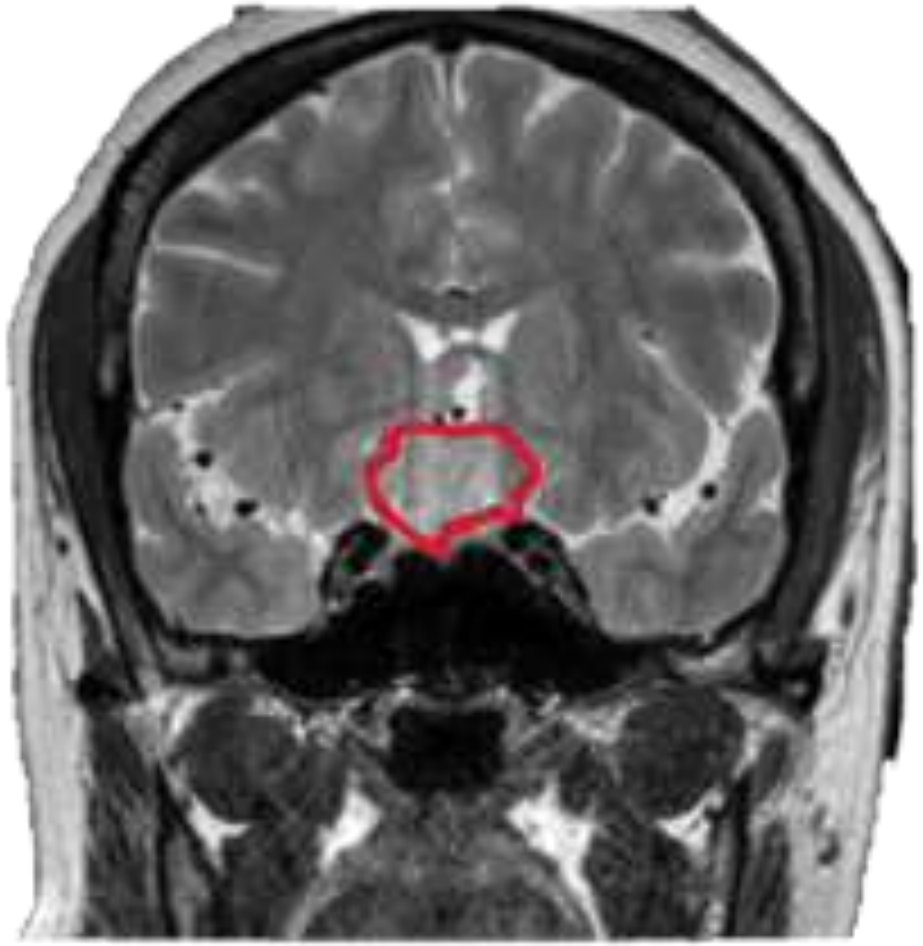
https://doi.org/10.1016/j.ijrobp.2022.07.934

Purpose/Objective(s)

Delta radiomics which refers to longitudinal changes of radiomic features over time has shown the potential to predict treatment response. However, its role in predicting normal lung toxicity has not been studied extensively. This study evaluates the potential for CBCT based delta radiomics in predicting radiotherapy induced lung parenchymal changes during thoracic radiotherapy.

Materials/Methods

Risk Stratification



> Acta Neurochir (Wien). 2024 Feb 20;166(1):91. doi: 10.1007/s00701-024-05977-4.

Is radiomics a useful addition to magnetic resonance imaging in the preoperative classification of PitNETs?

Sathya A [1], Abhijit Goyal-Honavar [2], Ari G Chacko [2], Anitha Jasper [3], Geeta Chacko [4], Devadhas Devakumar [5], Joshua Anand Seelam [3], Balu Krishna Sasidharan [1], Simon P Pavamani [1], Hannah Mary T Thomas [6]

Affiliations + expand

PMID: 38376544 DOI: 10.1007/s00701-024-05977-4

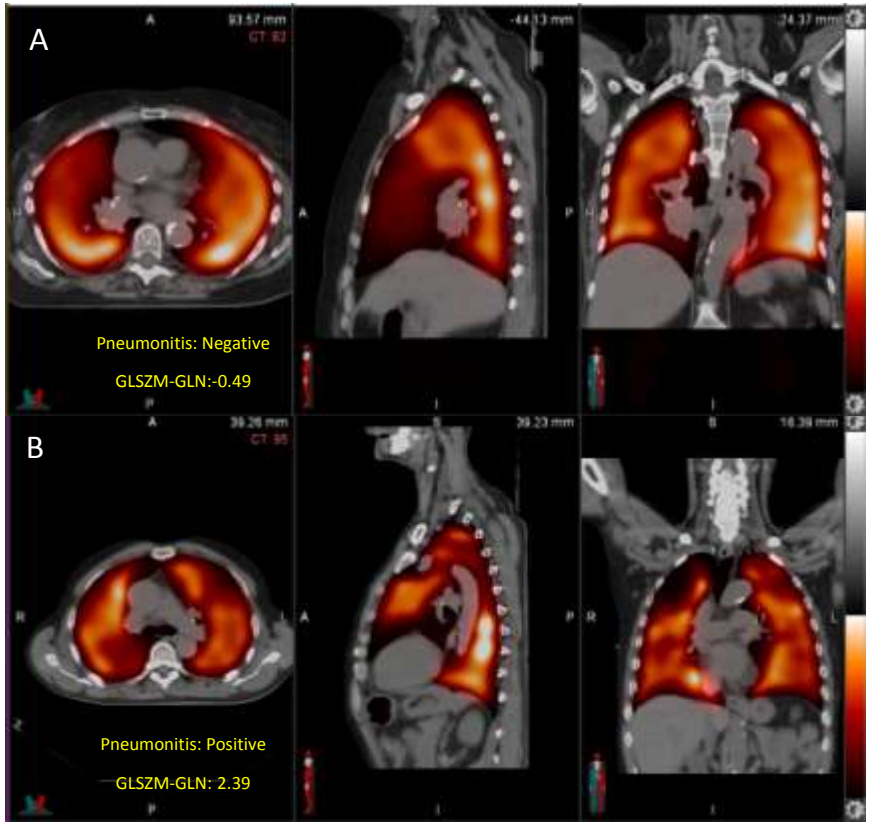
Abstract

Background: The WHO 2021 introduced the term pituitary neuroendocrine tumours (PitNETs) for pituitary adenomas and incorporated transcription factors for subtyping, prompting the need for fresh diagnostic methods. Current biomarkers struggle to distinguish between high- and low-risk non-functioning PitNETs. We explored if radiomics can enhance preoperative decision-making.

Methods: Pre-treatment magnetic resonance (MR) images of patients who underwent surgery between 2015 and 2019 with available WHO 2021 classification were used. The tumours were manually segmented on the T1w, T1-contrast enhanced, and T2w images using 3D Slicer. One hundred Pyradiomic features were extracted from each MR sequence. Models were built to classify (1) somatotroph and gonadotroph PitNETs and (2) high- and low-risk subtypes of non-functioning PitNETs. Feature were selected independently from the MR sequences and multi-sequence (combining data from more than one MR sequence) using Boruta and Pearson correlation. Support vector machine (SVM), logistic regression (LR), random forest (RF), and multi-layer perceptron (MLP) were the classifiers used. Data imbalance was addressed using the Synthetic Minority Oversampling TEchnique (SMOTE). Performance of the models were evaluated using area under the receiver operating curve (AUC), accuracy, sensitivity, and specificity.

Results: A total of 222 PitNET patients (train, n = 149; test, n = 73) were enrolled in this retrospective study. Multi-sequence-based LR model discriminated best between somatotroph and gonadotroph PitNETs, with a test AUC of 0.84, accuracy of 0.74, specificity of 0.81, and sensitivity of 0.70. Multi-sequence-based MLP model perfomed best for the high- and low-risk non-functioning PitNETs, achieving a test AUC of 0.76, accuracy of 0.67, specificity of 0.72, and sensitivity of 0.66.

Risk Stratification



Discover Oncology

Discover

Research

Radiation and immune checkpoint inhibitor-mediated pneumonitis risk stratification in patients with locally advanced non-small cell lung cancer: role of functional lung radiomics?

Hannah M. T. Thomas[1,2] · Daniel S. Hippe[3] · Parisa Forouzannezhad[1] · Balu Krishna Sasidharan[2] · Paul E. Kinahan[4] · Robert S. Miyaoka[4] · Hubert J. Vesselle[4] · Ramesh Rengan[1] · Jing Zeng[1] · Stephen R. Bowen[1,4]

Received: 6 June 2022 / Accepted: 23 August 2022
Published online: 01 September 2022

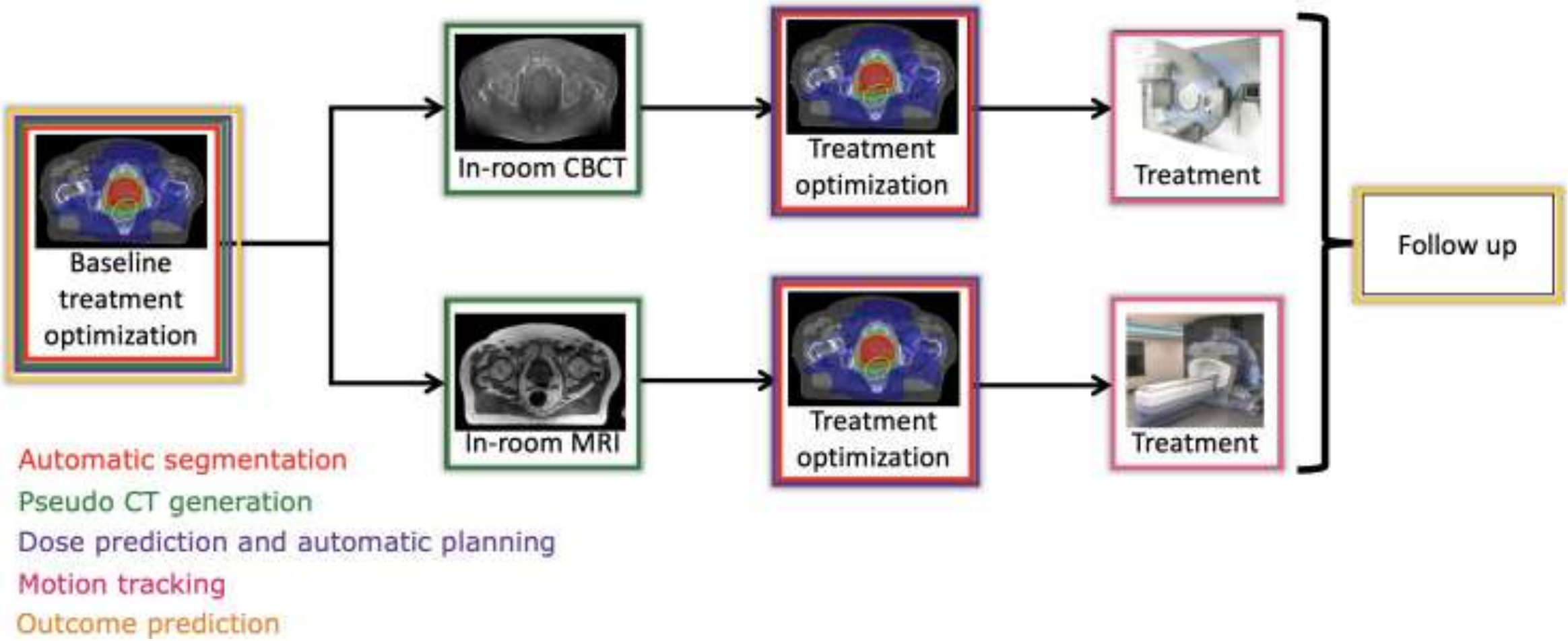
Abstract

Background Patients undergoing chemoradiation and immune checkpoint inhibitor (ICI) therapy for locally advanced non-small cell lung cancer (NSCLC) experience pulmonary toxicity at higher rates than historical reports. Identifying biomarkers beyond conventional clinical factors and radiation dosimetry is especially relevant in the modern cancer immunotherapy era. We investigated the role of novel functional lung radiomics, relative to functional lung dosimetry and clinical characteristics, for pneumonitis risk stratification in locally advanced NSCLC.

Methods Patients with locally advanced NSCLC were prospectively enrolled on the FLARE-RT trial (NCT02773238). All received concurrent chemoradiation using functional lung avoidance planning, while approximately half received consolidation durvalumab ICI. Within tumour-subtracted lung regions, 110 radiomics features (size, shape, intensity, texture) were extracted on pre-treatment [^{99m}Tc]MAA SPECT/CT perfusion images using fixed-bin-width discretization. The performance of functional lung radiomics for pneumonitis (CTCAE v4 grade 2 or higher) risk stratification was benchmarked against previously reported lung dosimetric parameters and clinical risk factors. Multivariate least absolute shrinkage and selection operator Cox models of time-varying pneumonitis risk were constructed, and prediction performance was evaluated using optimism-adjusted concordance index (c-index) with 95% confidence interval reporting throughout.

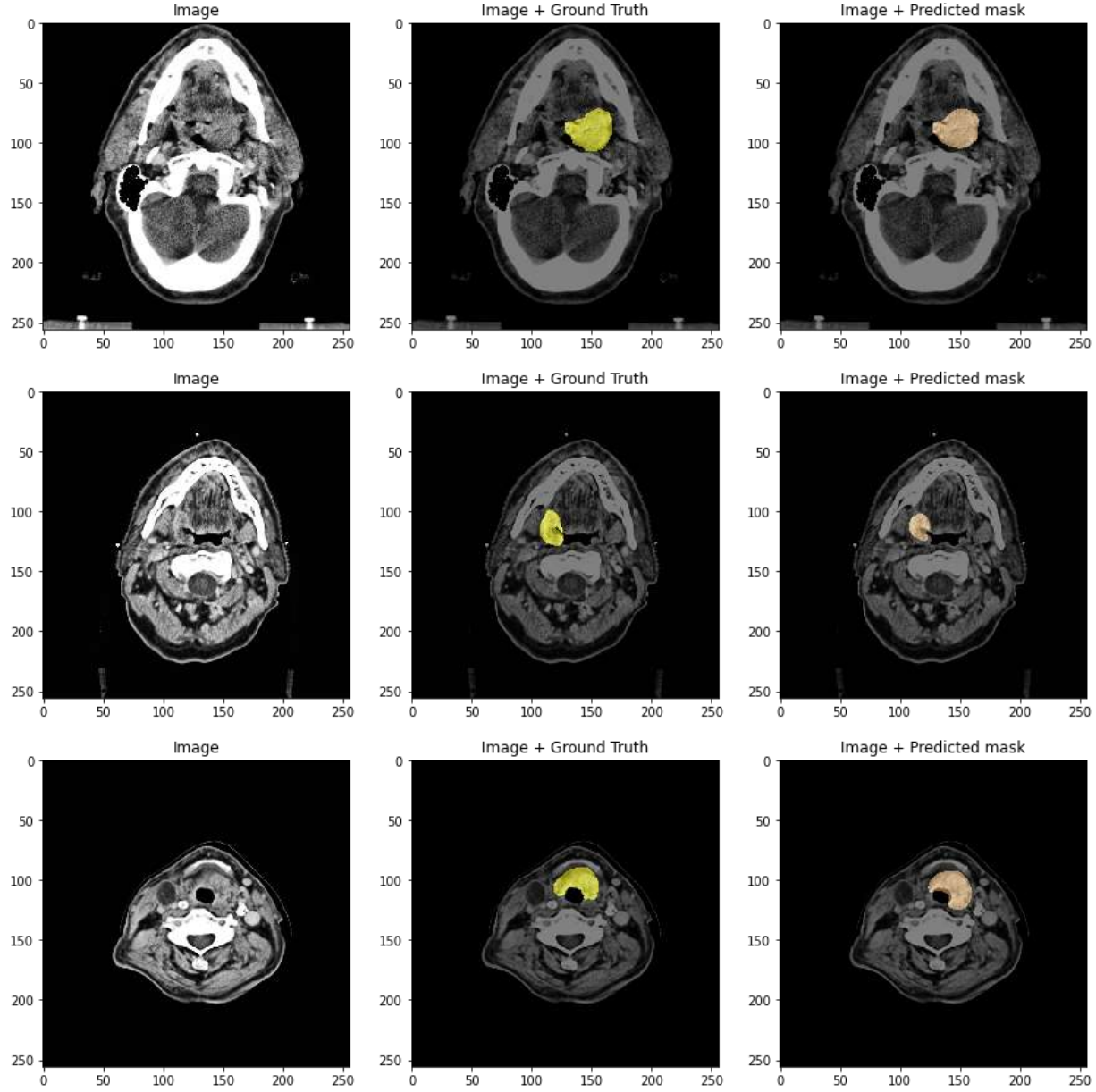
Results Thirty-nine patients were included in the study and pneumonitis occurred in 16/39 (41%) patients. Among clinical characteristics and anatomic/functional lung dosimetry variables, only the presence of baseline chronic obstructive pulmonary disease (COPD) was significantly associated with the development of pneumonitis (HR 4.59 [1.69–12.49]) and served as the primary prediction benchmark model (c-index 0.69 [0.59–0.80]). Discrimination of time-varying pneumonitis risk was numerically higher when combining COPD with perfused lung radiomics size (c-index 0.77 [0.65–0.88]) or shape feature classes (c-index 0.79 [0.66–0.91]) but did not reach statistical significance compared to benchmark models ($p > 0.26$). COPD was associated with perfused lung radiomics size features, including patients with larger lung volumes (AUC 0.75 [0.59–0.91]). Perfused lung radiomic texture features were correlated with lung volume (adj $R^2 = 0.84–1.00$), representing surrogates rather than independent predictors of pneumonitis risk.

AI in Adaptive therapy



Where AI may play a role in adaptive RT

Landry G, Kurz C, Traverso A. The role of artificial intelligence in radiotherapy clinical practice. BJR Open. 2023



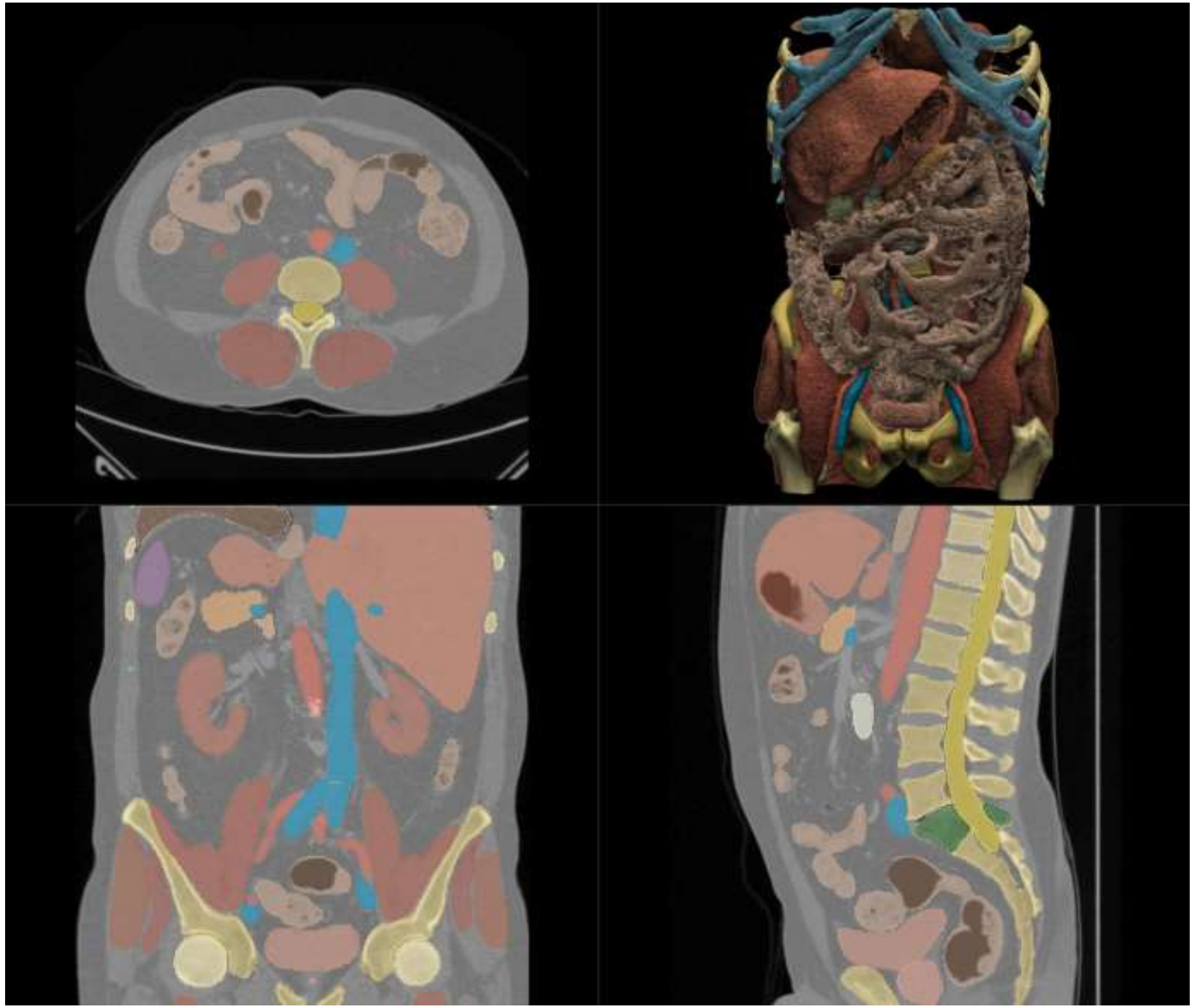
AUTOSEGMENTATION OF TARGETS

CMC-NITK Suratkal Collaboration

Automated Delineation of Head and Neck Cancer primary tumour on CT Images using Deep Convolutional Neural Networks

TotalSegmentator

104 normal organ delineations ,<3 mins



https://github.com/lassoan/SlicerTotalSegmentator#totalsegmentator

Synthetic CT from CBCT

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Article | Open access | Published: 24 April 2023

CBCT-based synthetic CT generated using CycleGAN with HU correction for adaptive radiotherapy of nasopharyngeal carcinoma

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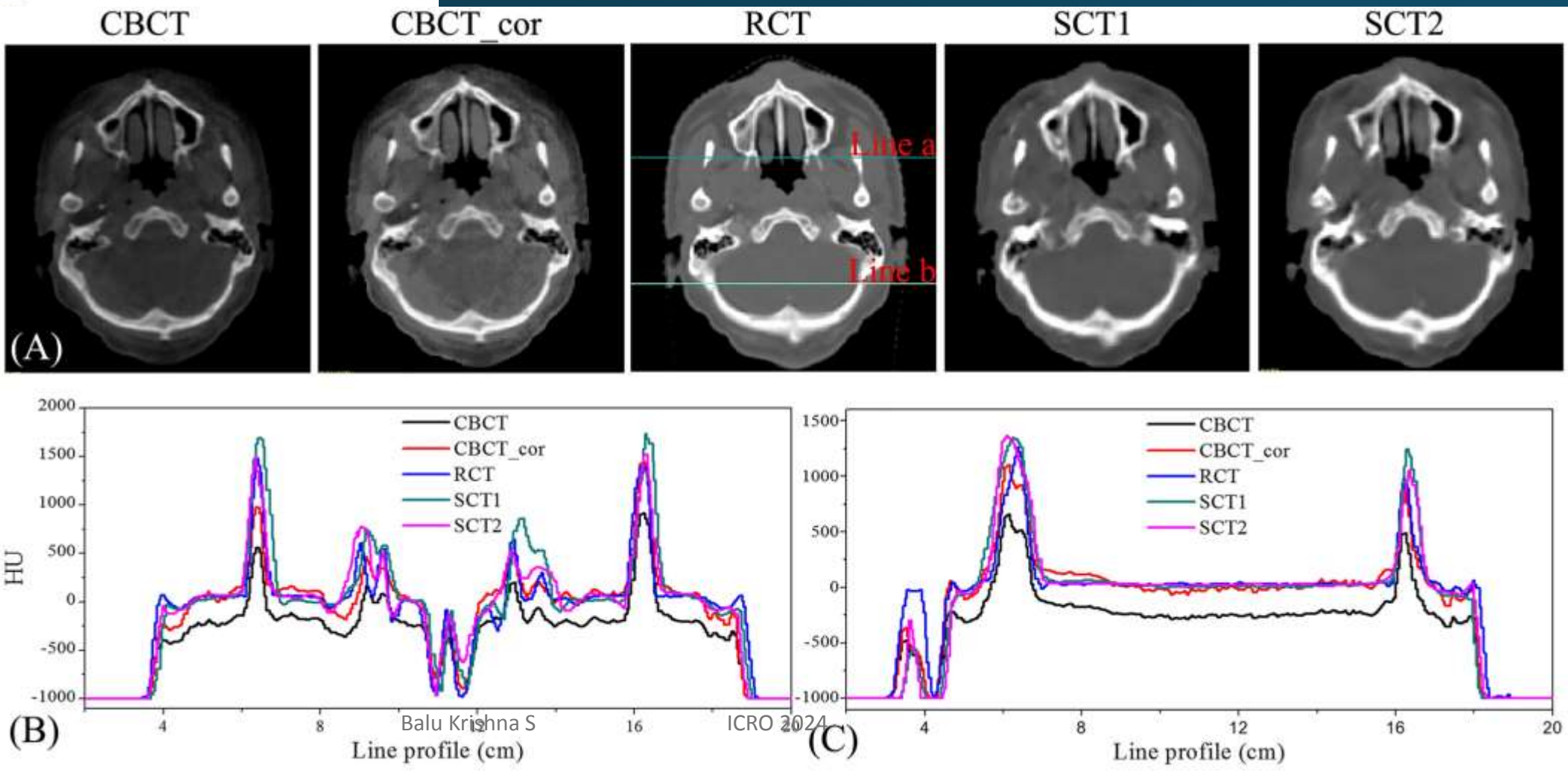
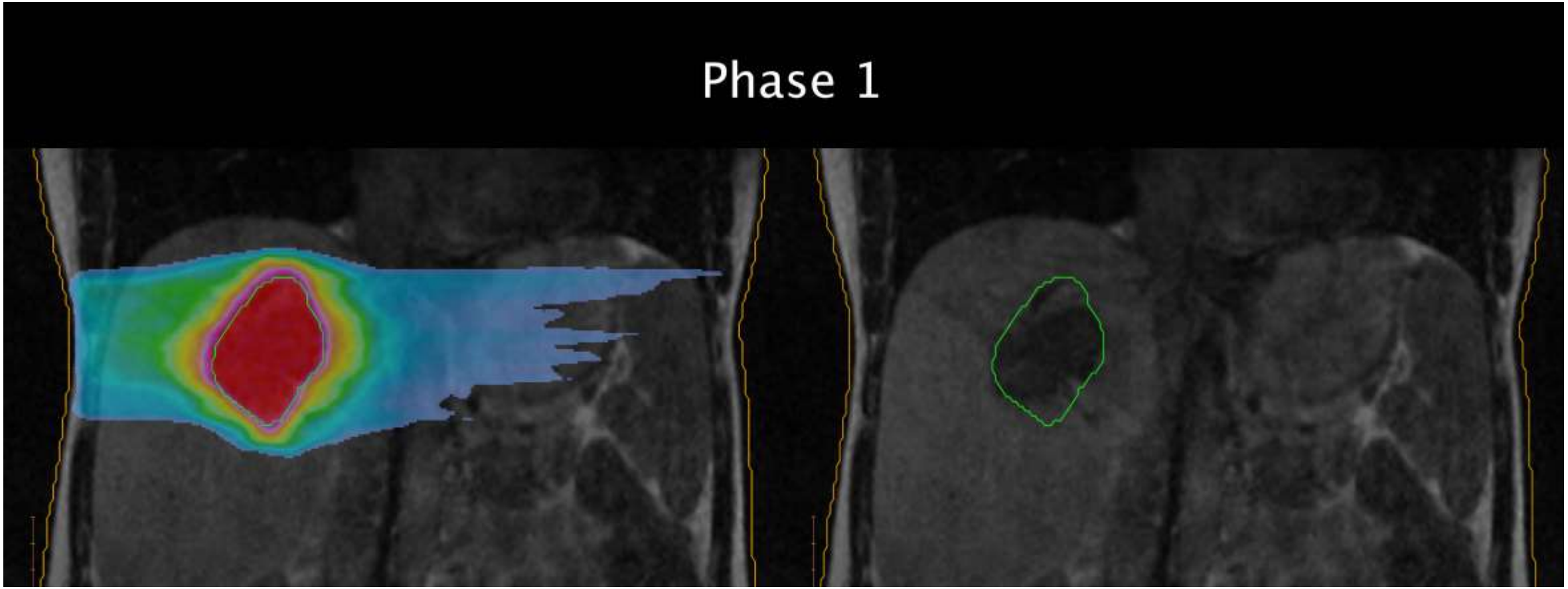
Chen Jihong, Quan Kerun, Chen Kaiqiang, Zha

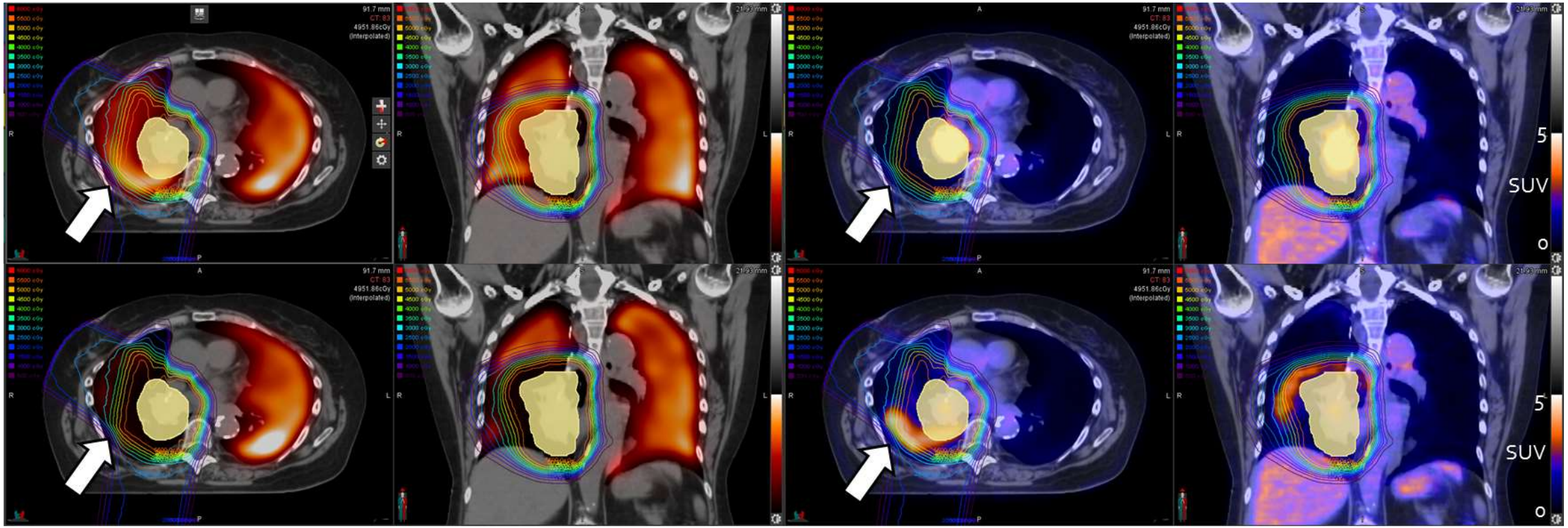


Motion tracking and dose prediction



https://shenglab.dgsom.ucla.edu/pages/interests

Adaptive avoidance and planning



Thomas HMT et al Comparison of regional lung perfusion response on longitudinal MAA SPECT/CT in lung cancer patients treated with and without functional tissue-avoidance radiation therapy. *The British Journal of Radiology*.

Are we close to clinical implementation of AI
in outcome prediction and adaptive therapy?

NOT YET!

1. Generalizability: AI models trained on specific datasets may not perform well across different institutions or patient populations.
2. Ethical concerns: Data privacy, consent, and potential biases in AI algorithms: yet to be addressed.
3. Interpretability and explainability is limited
4. Legal and regulatory are still Unclear - Liability
5. Integration with existing workflows -challenging
6. Validation and clinical trials - not available
7. Skill gaps - Huge

How should we choose a questions for AI based modelling?

Clinically relevant

Impact on healthcare

Not just for the sake of joining the AI bandwagon

Small projects / Burst of ideas / Bad AI

Non-sustainable in the long run

When does prediction matter?

- Dose escalation
- Treatment de-intensification

- Confusion matrix

What is our role as a RadOnc ?

- Find the right question to address
- Model - based on clinical utility
- Create data sets with correct data points
- Automate processes that have high variability
- Collaborate. Learn, Create - Federated learning

As a team, we grow

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