

# Emerging Data-Driven Approaches for Treatment Planning

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Frontiers in AI and Its Applications in Medical Physics

Tom Purdie, PhD, MCCPM  
Princess Margaret Cancer Centre

# Disclosures

Method and System for Automated Planning of Radiation Therapy technology patented in PCT/CA2011/001130

Automated Quality Assurance (QA) and Planning technology patented in WO2014197994 A1

Receive royalties from RaySearch Laboratories for license of technology for Automated Breast Treatment Planning and Machine Learning-based Automated Treatment Planning

Have an equity interest in an AI healthcare startup, licensee of technology for Machine Learning-based for Automated Quality Assurance in Radiation Oncology



# Outline

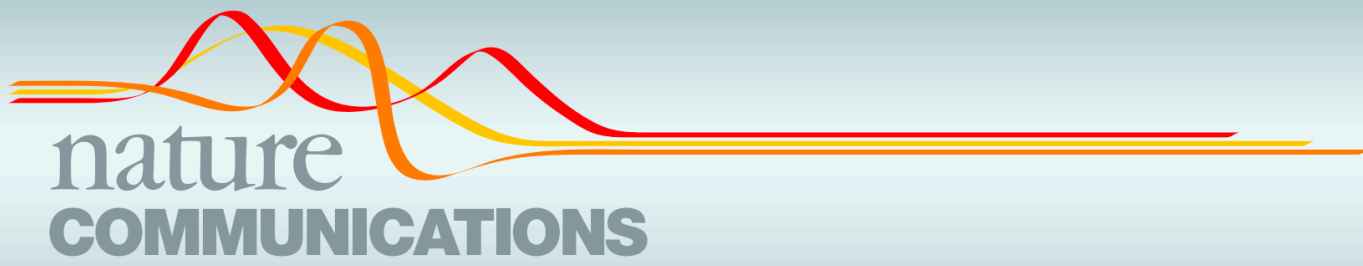
Applications of Artificial Intelligence (AI) and Machine Learning (ML)

Machine Learning Architectures/Methods

- Convolution Neural Networks (CNNs) → U-Net
- Generative Adversarial Networks
- Reinforcement Learning
- Atlas Regression Forest

Open Knowledge Based Planning (KBP) Challenge

# AI to Infer New Knowledge



## ARTICLE

Received 25 Nov 2013 | Accepted 29 Apr 2014 | Published 3 Jun 2014 | Updated 7 Aug 2014

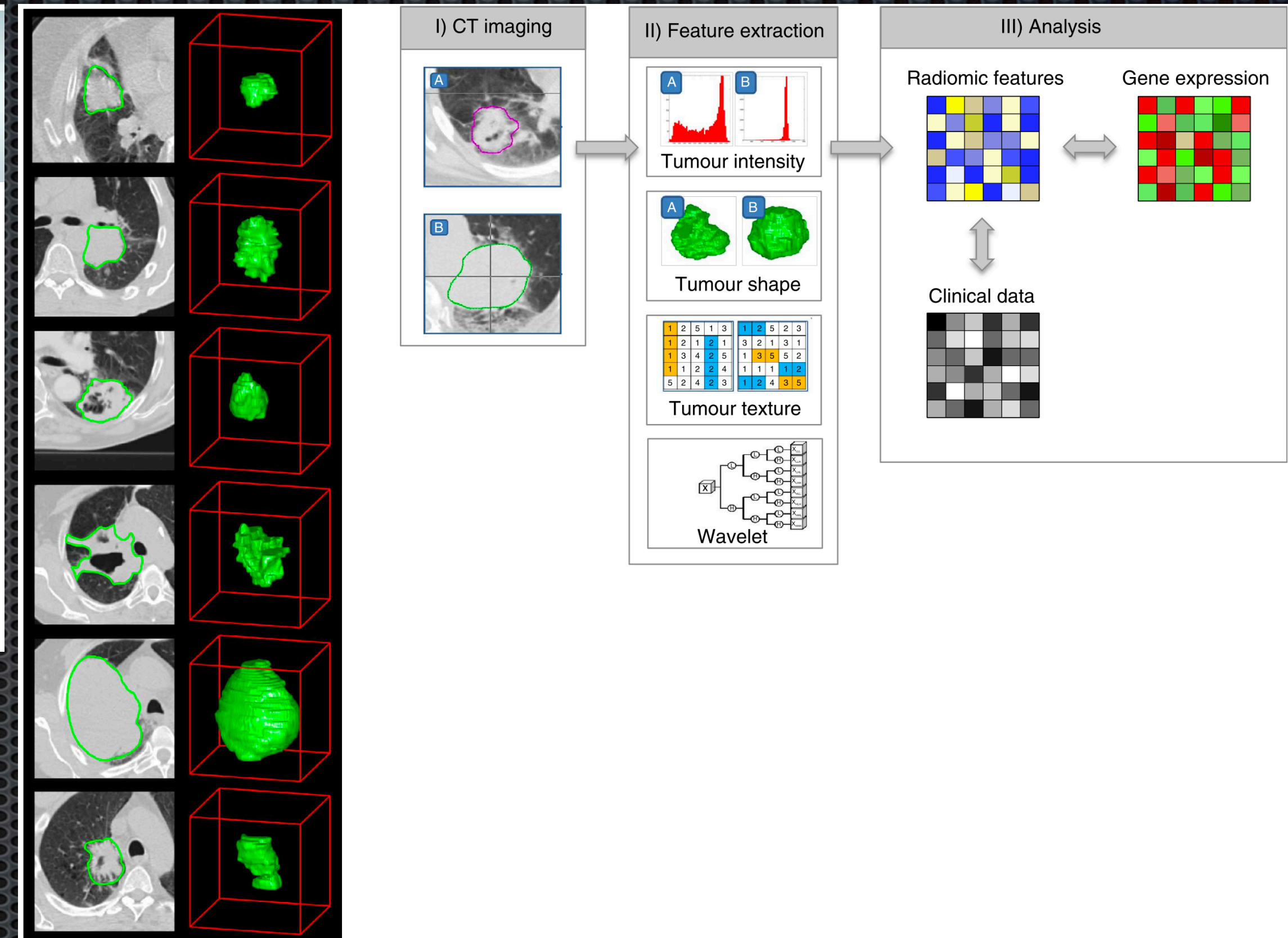
DOI: 10.1038/ncomms5006

OPEN

## Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach

Hugo J.W.L. Aerts<sup>1,2,3,4,\*</sup>, Emmanuel Rios Velazquez<sup>1,2,\*</sup>, Ralph T.H. Leijenaar<sup>1</sup>, Chintan Parmar<sup>1,2</sup>, Patrick Grossmann<sup>2</sup>, Sara Carvalho<sup>1</sup>, Johan Bussink<sup>5</sup>, René Monshouwer<sup>5</sup>, Benjamin Haibe-Kains<sup>6</sup>, Derek Rietveld<sup>7</sup>, Frank Hoebers<sup>1</sup>, Michelle M. Rietbergen<sup>8</sup>, C. René Leemans<sup>8</sup>, Andre Dekker<sup>1</sup>, John Quackenbush<sup>4</sup>, Robert J. Gillies<sup>9</sup> & Philippe Lambin<sup>1</sup>

- AI recognizes complex data in images and can give quantitative metrics
- **Radiomics** → High throughput extraction of quantitative image features (non-human detectable) for biomarker discovery



# AI to Make Predictions → Replicate Human Tasks

## LETTER

doi:10.1038/nature21056

### Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteva<sup>1\*</sup>, Brett Kuprel<sup>1\*</sup>, Roberto A. Novoa<sup>2,3</sup>, Justin Ko<sup>2</sup>, Susan M. Swetter<sup>2,4</sup>, Helen M. Blau<sup>5</sup> & Sebastian Thrun<sup>6</sup>

<sup>1</sup>Department of Electrical Engineering, Stanford University, Stanford, California, USA. <sup>2</sup>Department of Dermatology, Stanford University, Stanford, California, USA. <sup>3</sup>Department of Pathology, Stanford University, Stanford, California, USA. <sup>4</sup>Dermatology Service, Veterans Affairs Palo Alto Health Care System, Palo Alto, California, USA. <sup>5</sup>Baxter Laboratory for Stem Cell Biology, Department of Microbiology and Immunology, Institute for Stem Cell Biology and Regenerative Medicine, Stanford University, Stanford, California, USA. <sup>6</sup>Department of Computer Science, Stanford University, Stanford, California, USA.

\*These authors contributed equally to this work.

2 FEBRUARY 2017 | VOL 542 | NATURE | 115

AI algorithm tested for diagnosing skin lesions representing the most common and deadliest skin cancers with 21 board-certified dermatologists used as control

### Bottom line

AI Algorithm matched the performance of dermatologists

# AI to Create New Processes

## Dose Prediction for Automated Treatment Planning

**Dose Prediction**

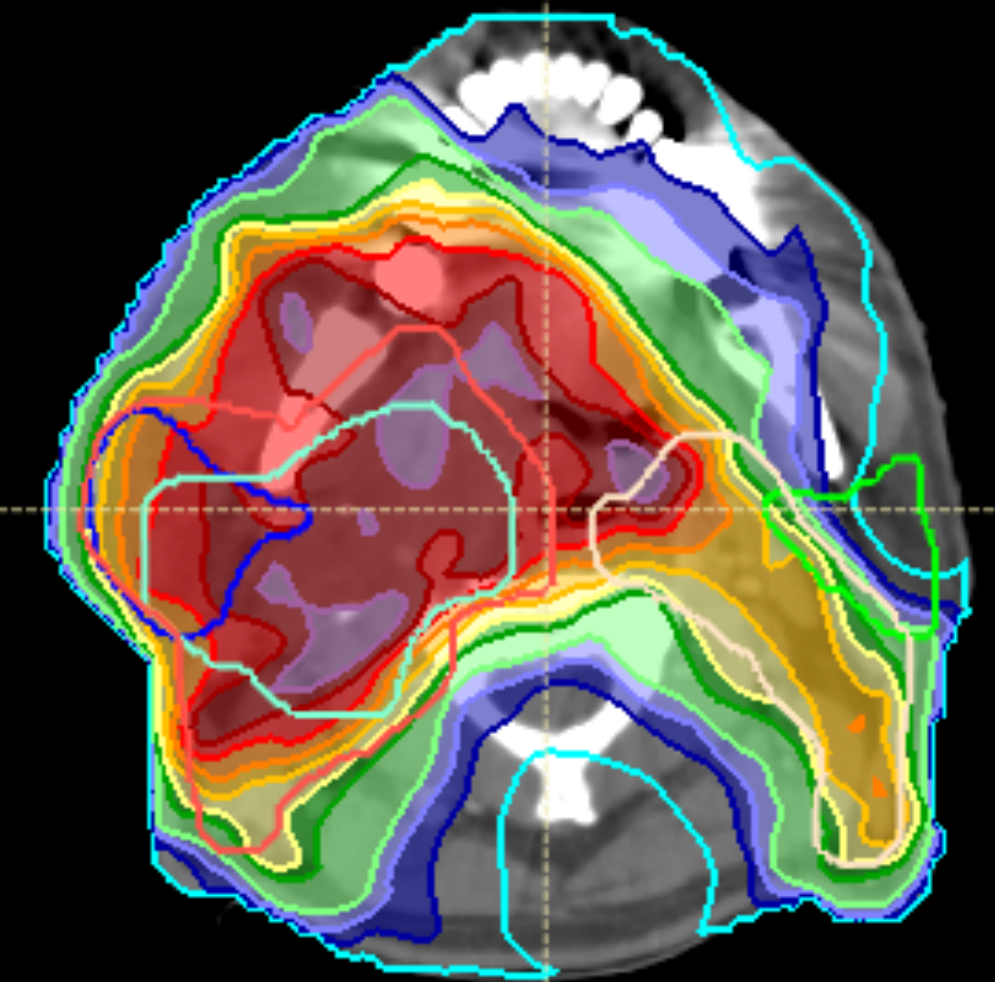
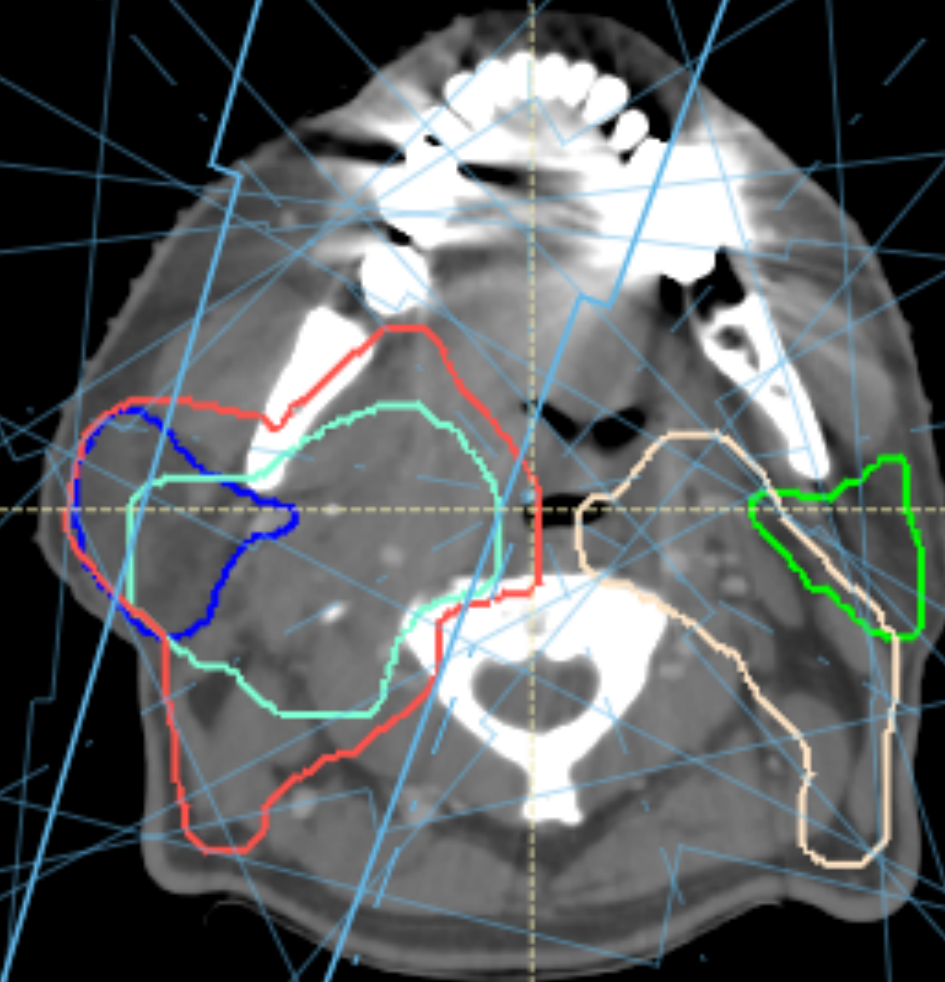
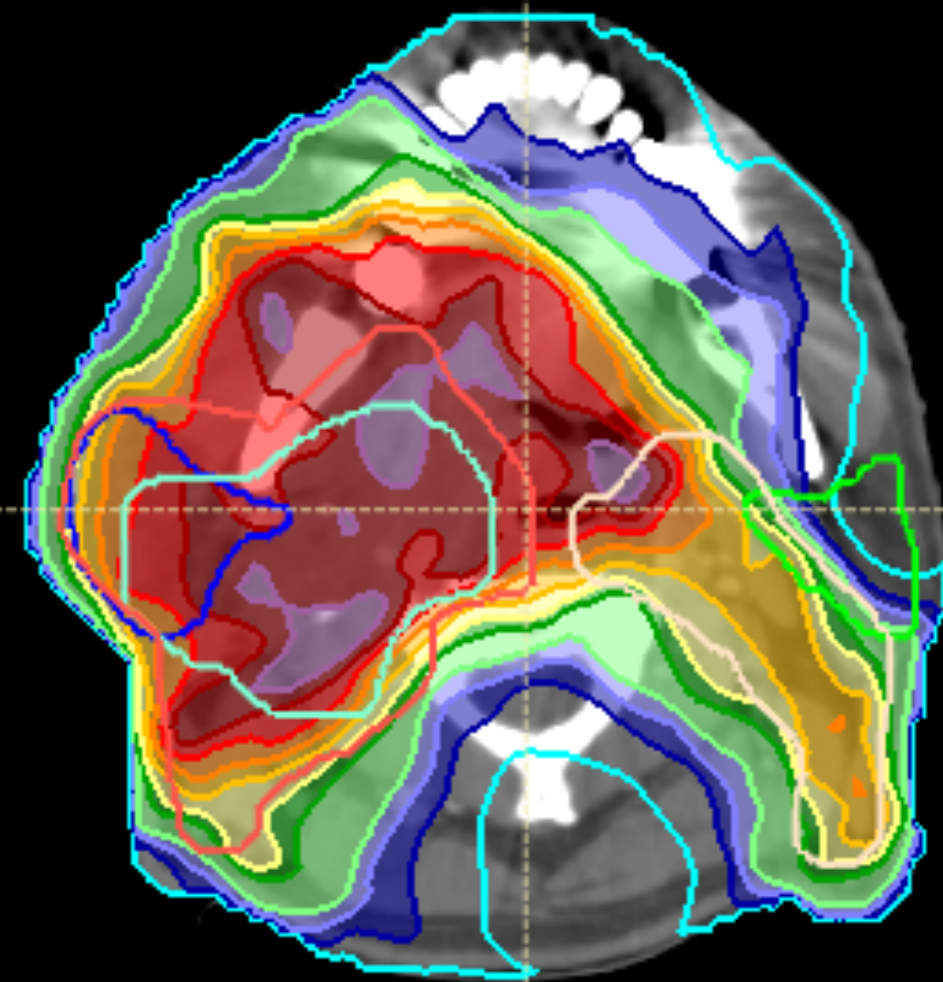
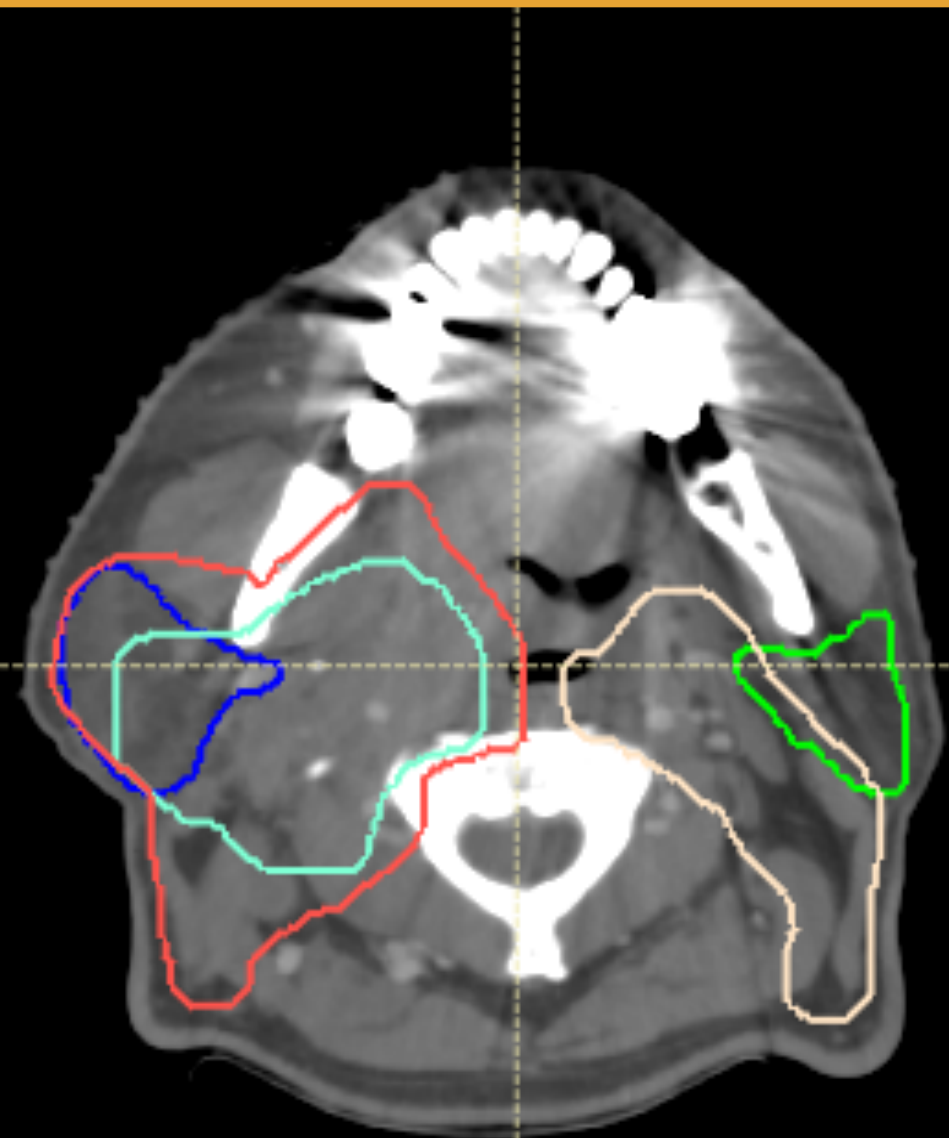
**Optimization**

Image + Contours

Dose

Beams

Final Dose

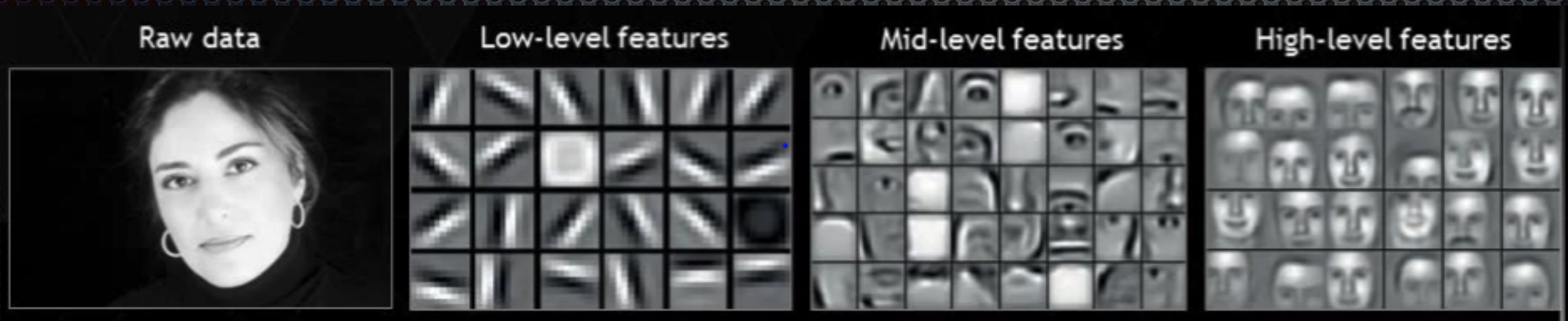


$\Delta$ Dose

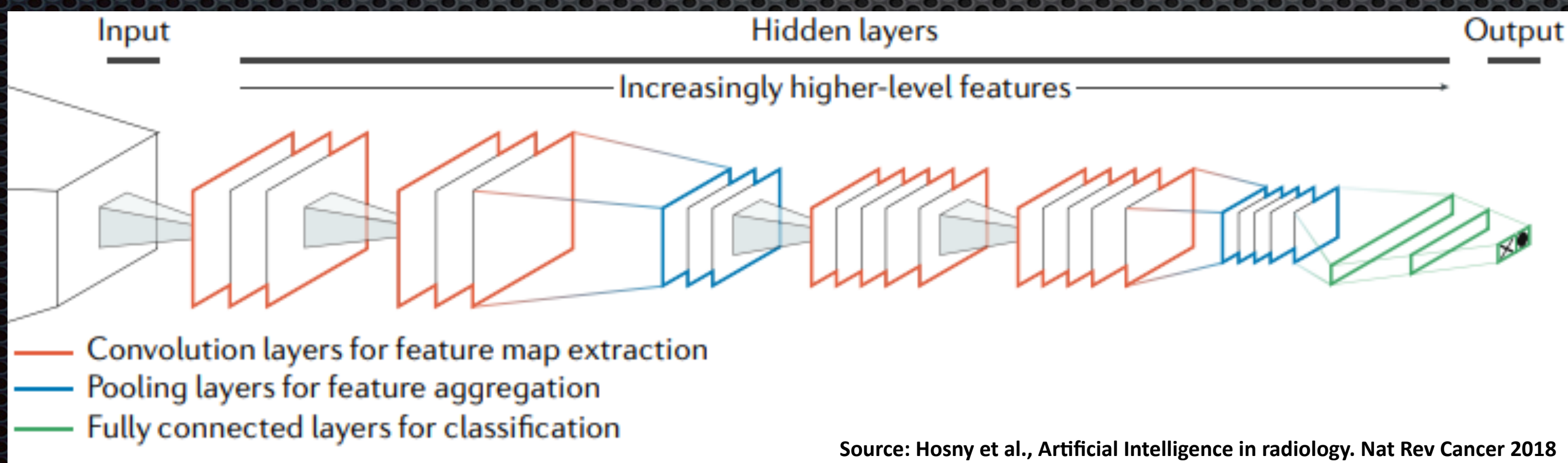
# The “Black Box”

## Convolutional Neural Networks (CNNs)

- Learns from very complex data, like medical images
- Automatically generates relevant features in systematic way



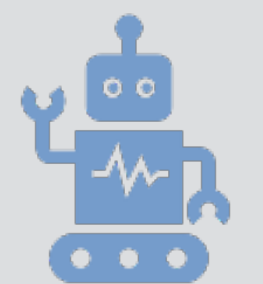
Source: Machine Learning for Humans, Vishal Maini and Samer Sabri. <https://medium.com/machine-learning-for-humans>



Source: Hosny et al., Artificial Intelligence in radiology. Nat Rev Cancer 2018

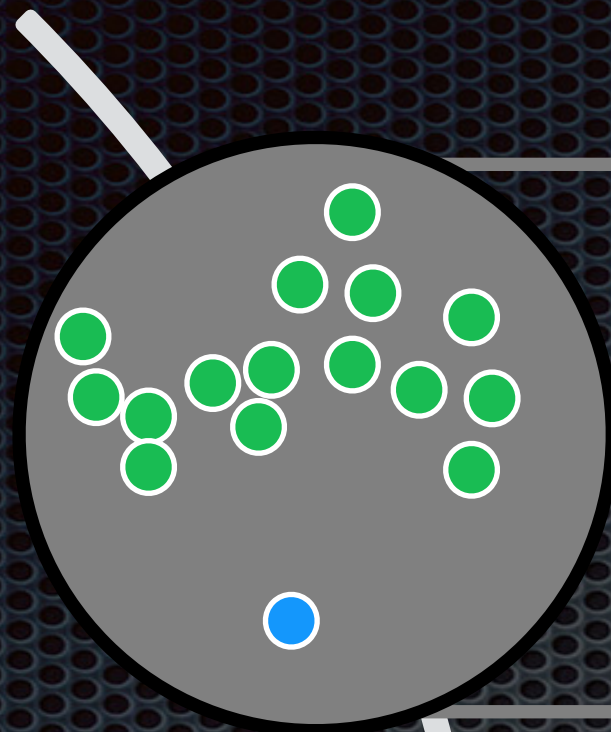
# AI *for* the Clinic → AI *in* the Clinic

 Tension between Accuracy and Interpretability

 Machine Prediction meets Human Judgement

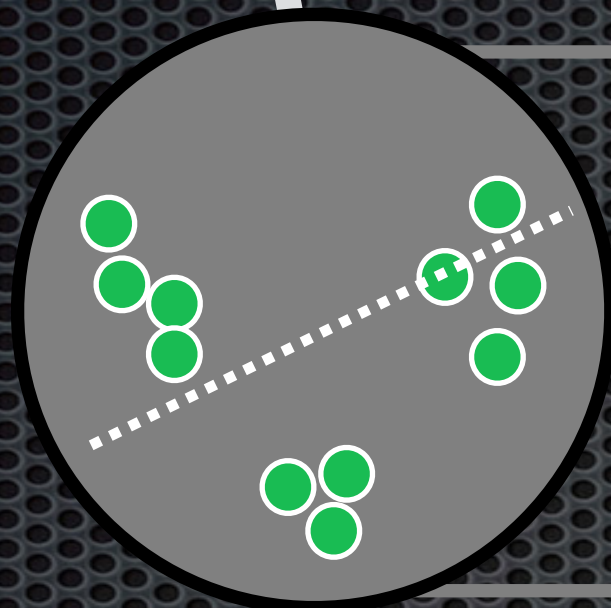
 Workflow Integration

# Potential Sources of Error in Building AI Models



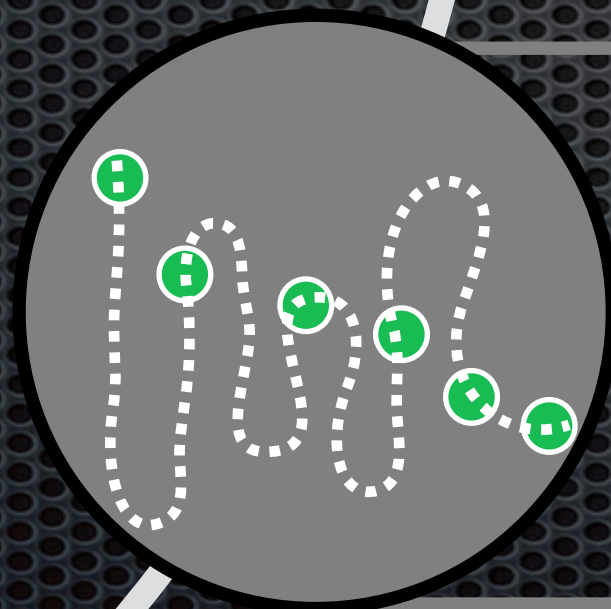
## **Class Imbalance & Outliers**

**Non-standard practice difficult to capture**  
**Potential to confound model**



## **Under-fitting**

**Lots of historical data... not collected for this purpose**  
**Inaccurate assumptions/simplifications of the model**



## **Over-fitting**

**Detect the signal, not the noise!**  
**Less general and lacks inter-institutional applicability**

# U-Net for Image Segmentation

## U-Net: Convolutional Networks for Biomedical Image Segmentation

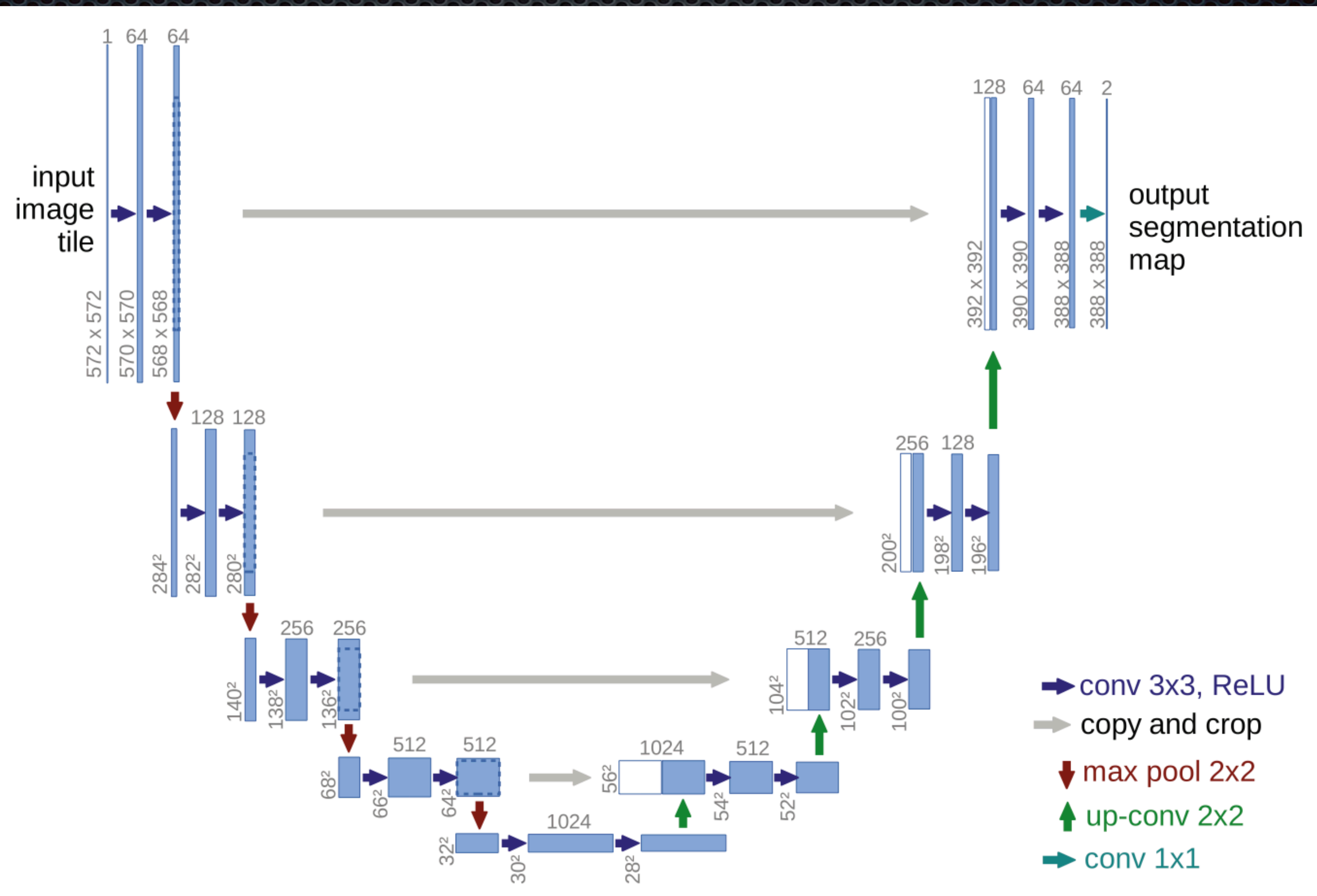
Olaf Ronneberger, Philipp Fischer, and Thomas Brox

Computer Science Department and BIOS Centre for Biological Signalling Studies,  
University of Freiburg, Germany  
[ronneber@informatik.uni-freiburg.de](mailto:ronneber@informatik.uni-freiburg.de)  
<http://lmb.informatik.uni-freiburg.de/>

Nassir Navab · Joachim Hornegger  
William M. Wells · Alejandro F. Frangi (Eds.)

## Medical Image Computing and Computer-Assisted Intervention – MICCAI 2015

18th International Conference  
Munich, Germany, October 5–9, 2015  
Proceedings, Part III



# Dose Prediction: ResNet

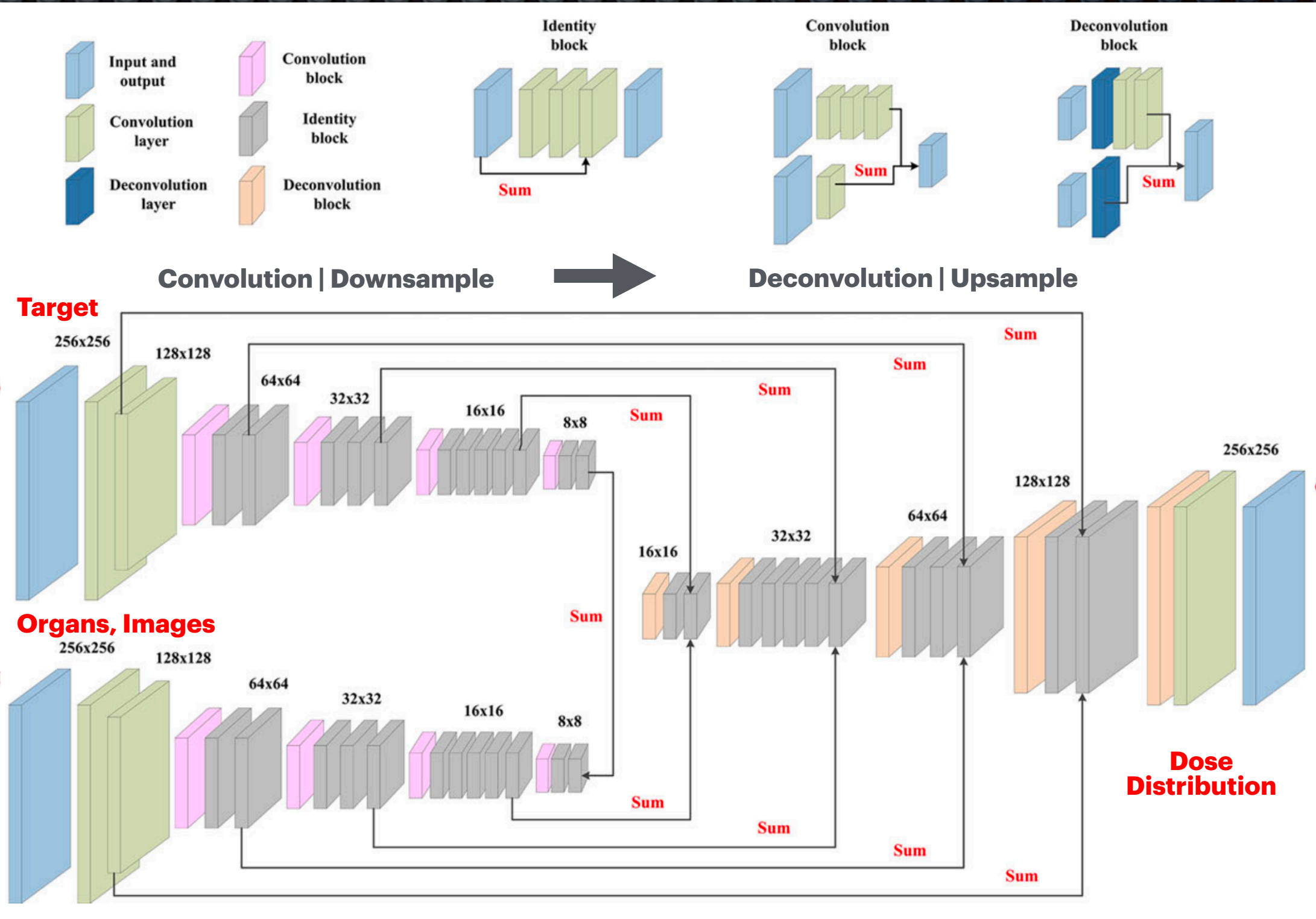
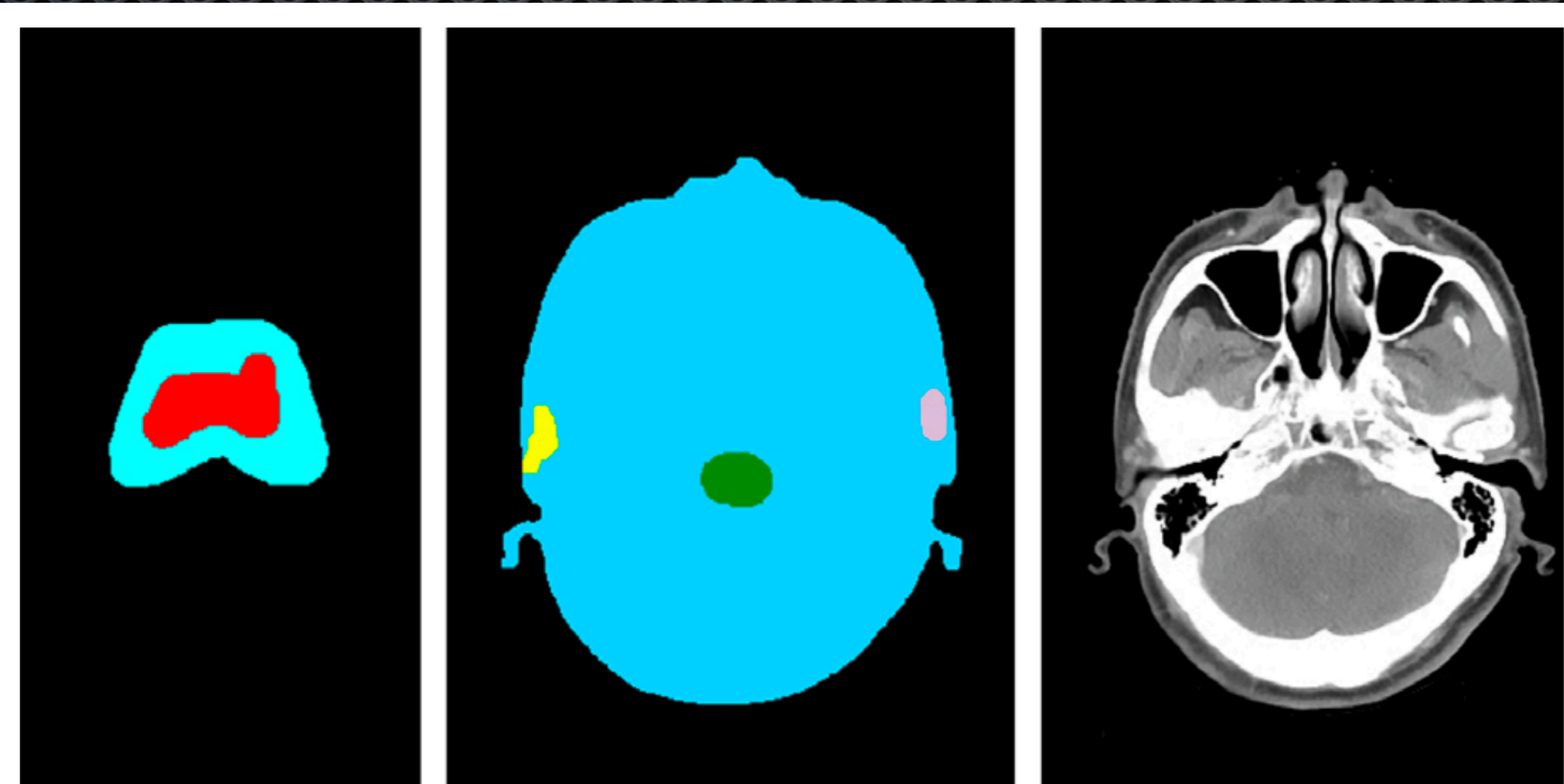
## Automatic treatment planning based on three-dimensional dose distribution predicted from deep learning technique

Jiawei Fan\* and Jiazhou Wang\*  
Department of Radiation Oncology, Fudan University Shanghai Cancer Center, Shanghai 200032, China  
Department of Oncology, Shanghai Medical College Fudan University, Shanghai 200032, China

Zhi Chen\*  
Department of Radiation Oncology, Fudan University Shanghai Cancer Center, Shanghai 200032, China  
Department of Oncology, Shanghai Medical College Fudan University, Shanghai 200032, China  
Department of Medical Physics, Shanghai Proton and Heavy Ion Center, Shanghai 201321, China

Chaosu Hu, Zhen Zhang, and Weigang Hu<sup>a)</sup>  
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(Received 19 July 2018; revised 16 October 2018; accepted for publication 26 October 2018; published 28 November 2018)



# Dose Prediction: DoseNet

Physics in Medicine & Biology



PAPER

## DoseNet: a volumetric dose prediction algorithm using 3D fully-convolutional neural networks

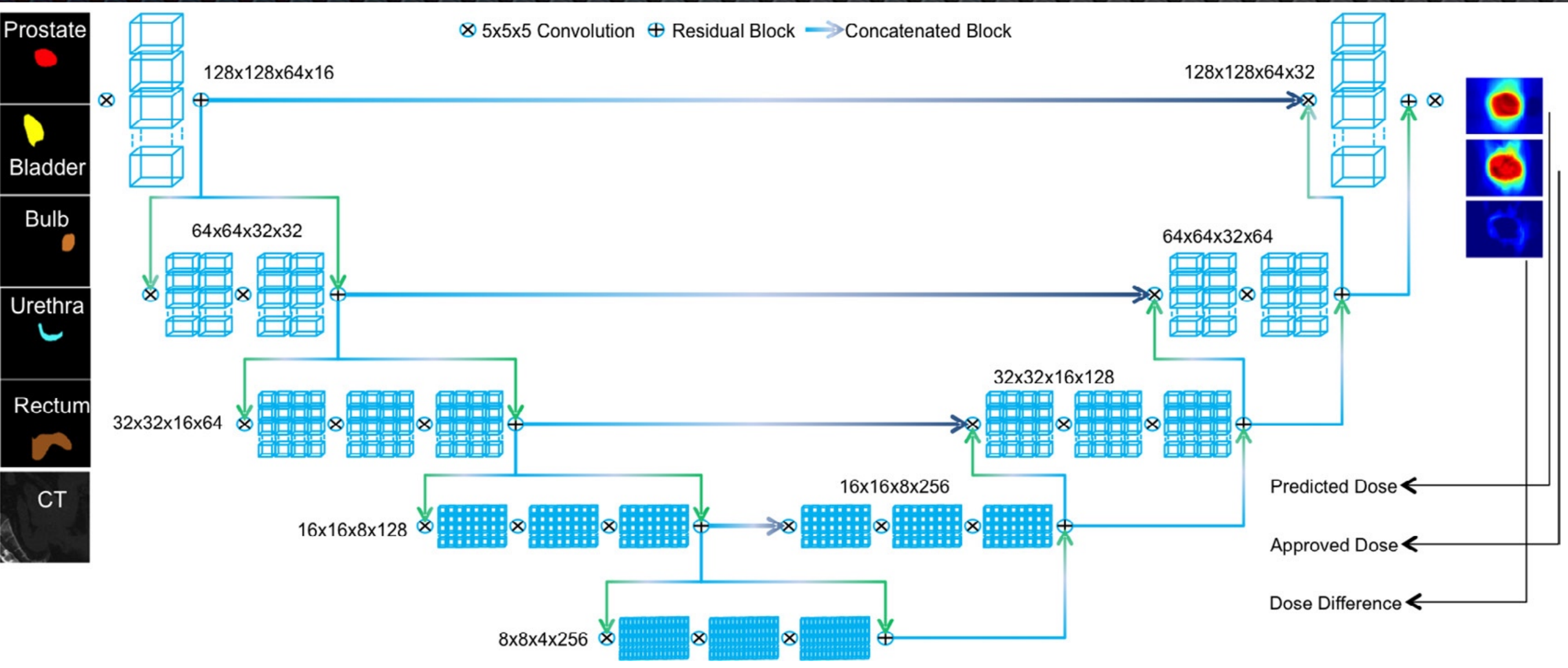
Vasant Kearney<sup>1</sup>, Jason W Chan<sup>1</sup>, Samuel Haaf, Martina Descovich and Timothy D Solberg

Department of Radiation Oncology, University of California, San Francisco, CA 94115, United States of America

<sup>1</sup> These two authors contributed equally.

E-mail: [vasant.kearney@ucsf.edu](mailto:vasant.kearney@ucsf.edu)

**Keywords:** dose prediction, convolutional neural networks, knowledge based planning, radiation oncology, machine learning, automated treatment planning, deep learning



# Dose Prediction



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10 January 2019

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31 January 2019

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18 March 2019

PAPER

## 3D radiotherapy dose prediction on head and neck cancer patients with a hierarchically densely connected U-net deep learning architecture

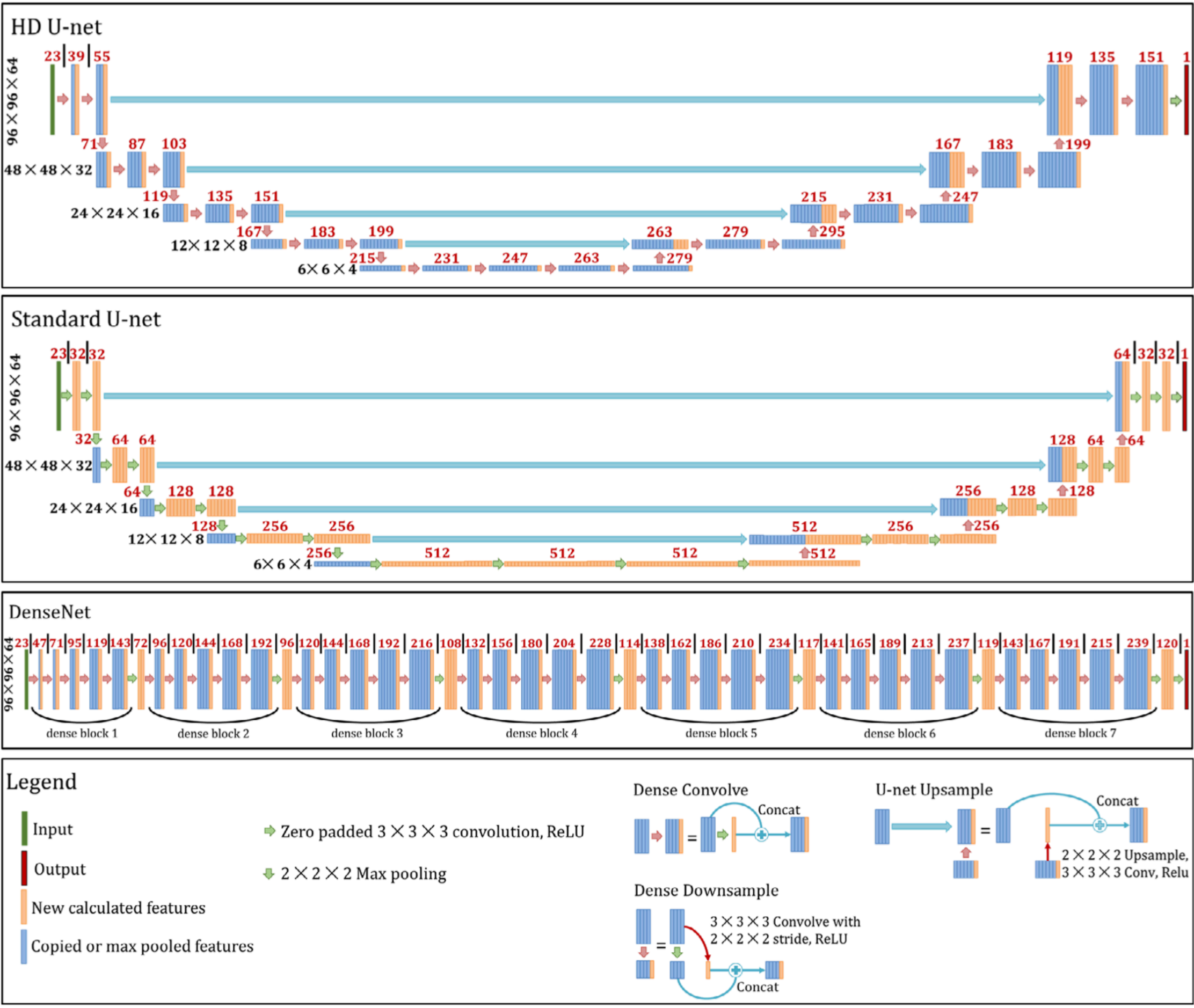
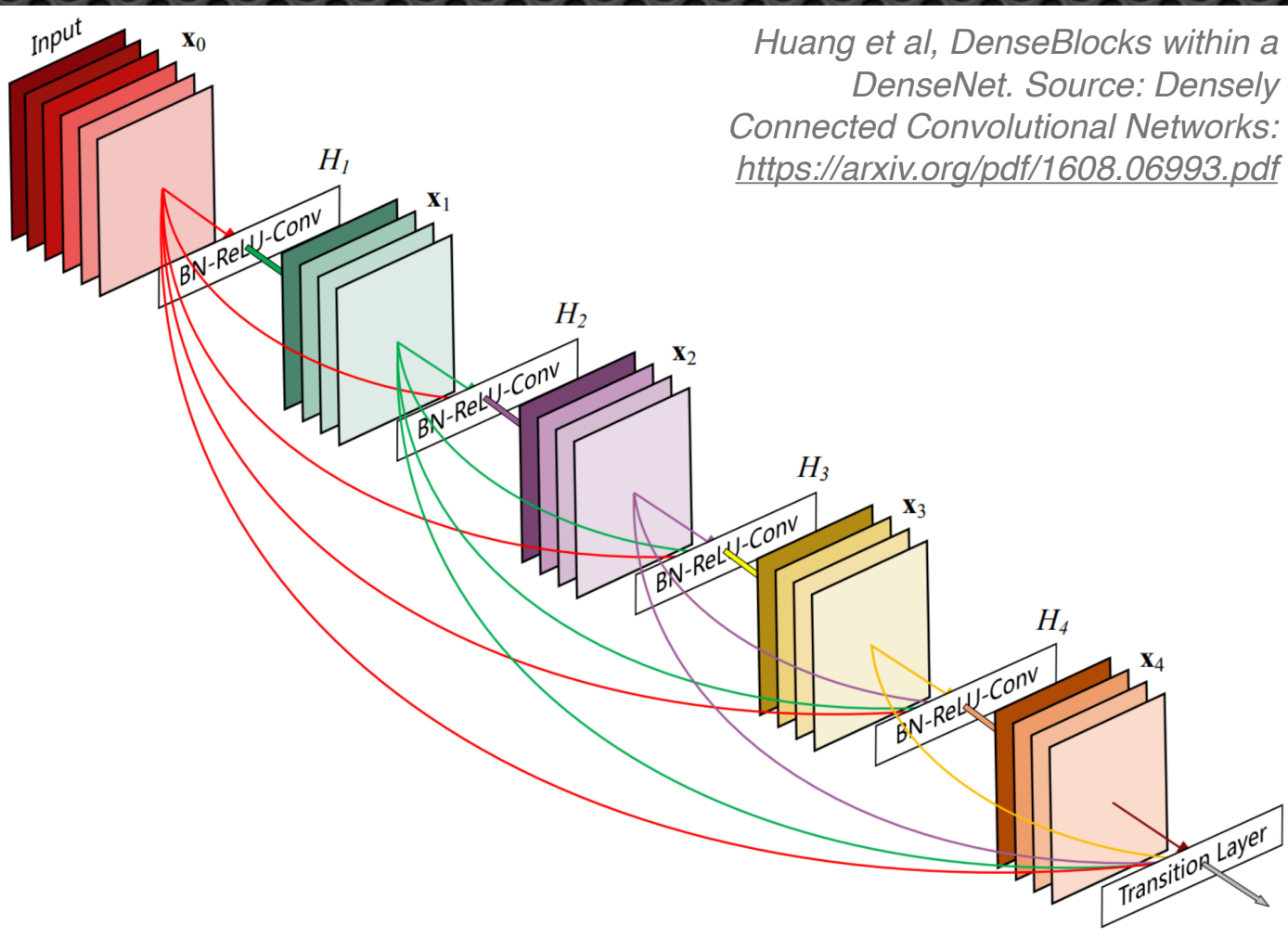
Dan Nguyen<sup>1</sup>, Xun Jia, David Sher, Mu-Han Lin, Zohaib Iqbal, Hui Liu and Steve Jiang

Medical Artificial Intelligence and Automation Laboratory, Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX 75390, United States of America

<sup>1</sup> Author to whom any correspondence should be addressed.

E-mail: [Dan.Nguyen@UTSouthwestern.edu](mailto:Dan.Nguyen@UTSouthwestern.edu)

**Keywords:** radiation therapy, deep learning, artificial intelligence, dose prediction, head and neck cancer, U-net, DenseNet



# U-Net for Dose Prediction:

www.nature.com/scientificreports

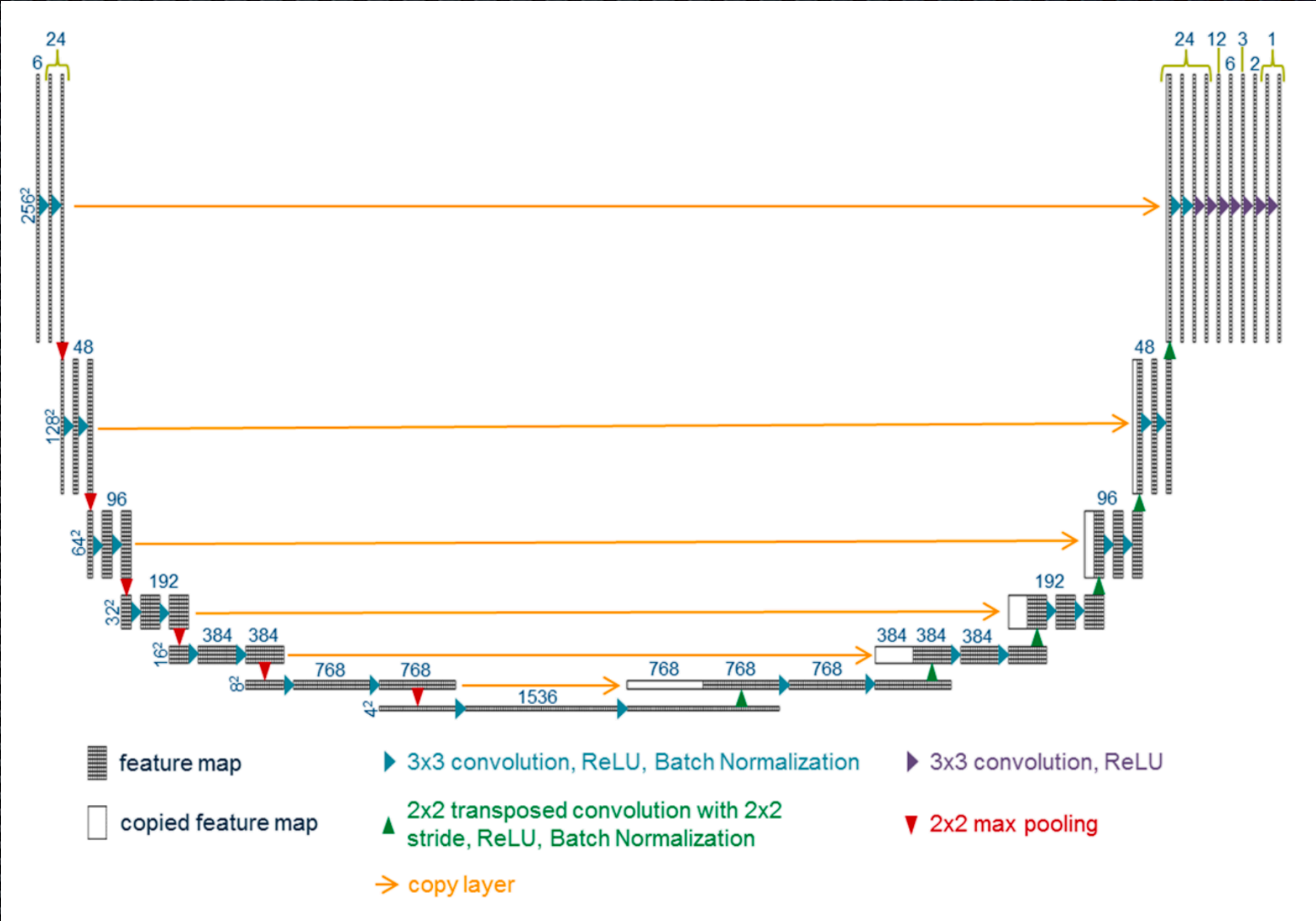
## SCIENTIFIC REPORTS

OPEN

A feasibility study for predicting optimal radiation therapy dose distributions of prostate cancer patients from patient anatomy using deep learning

Dan Nguyen, Troy Long, Xun Jia, Weiguo Lu, Xuejun Gu, Zohaib Iqbal & Steve Jiang

Received: 30 May 2018  
Accepted: 13 November 2018  
Published online: 31 January 2019



# Generative Adversarial Networks (GAN) for Dose Prediction

## Knowledge-based automated planning with three-dimensional generative adversarial networks

Aaron Babier<sup>a)</sup>, and Rafid Mahmood  
*Department of Mechanical and Industrial Engineering, University of Toronto, 5 King's College Road, Toronto, ON, M5S 3G8, Canada*

Andrea L. McNiven  
*Radiation Medicine Program, UHN Princess Margaret Cancer Centre, 610 University of Avenue, Toronto, ON, M5T 2M9, Canada*  
*Department of Radiation Oncology, University of Toronto, 148 - 150 College Street, Toronto, ON, M5S 3S2, Canada*

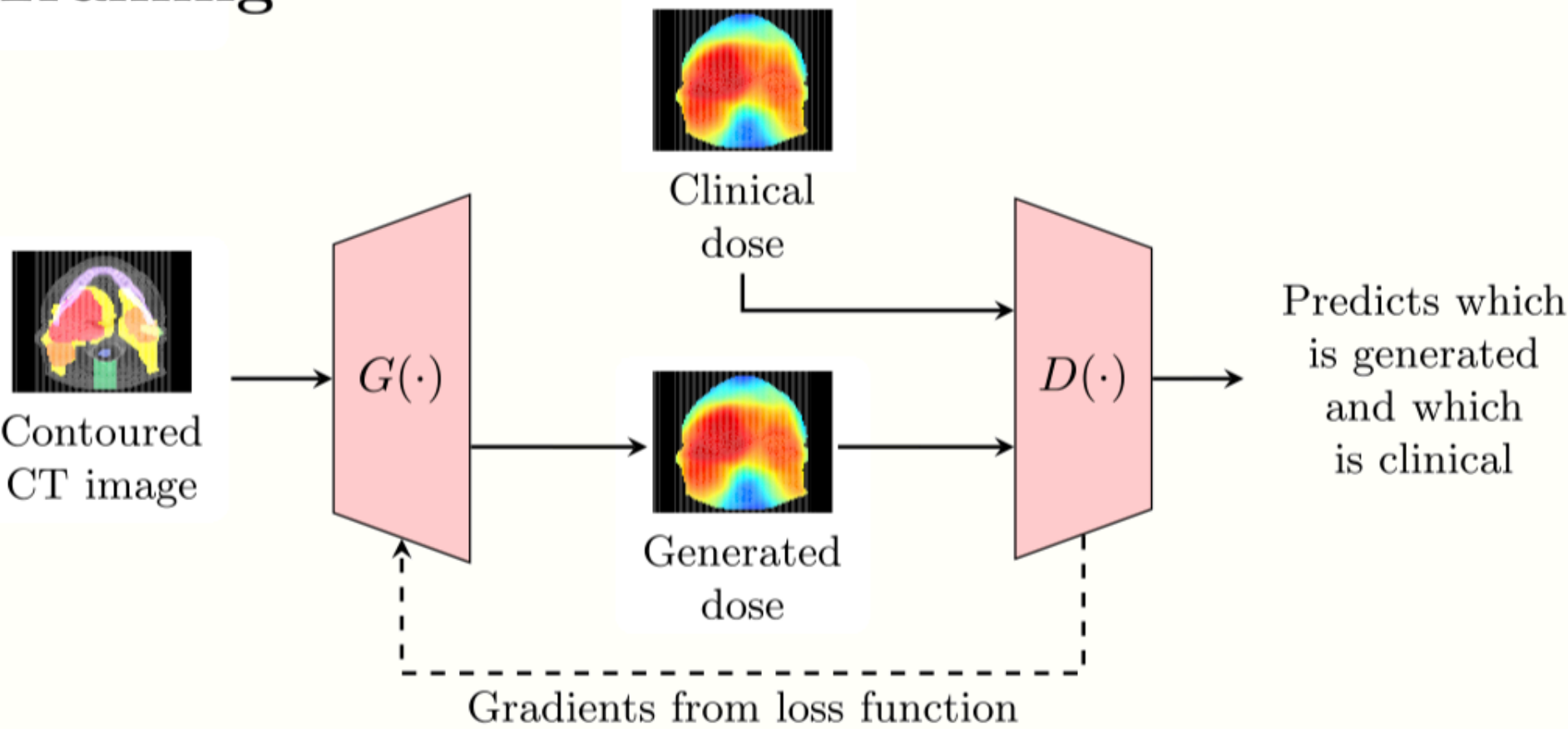
Adam Diamant  
*Schulich School of Business, York University, 111 Ian MacDonald Blvd, North York, ON, M3J 1P3, Canada*

Timothy C.Y. Chan  
*Department of Mechanical and Industrial Engineering, University of Toronto, 5 King's College Road, Toronto, ON, M5S 3G8, Canada*  
*Techna Institute for the Advancement of Technology for Health, 124 - 100 College Street, Toronto, ON, M5G 1P5, Canada*

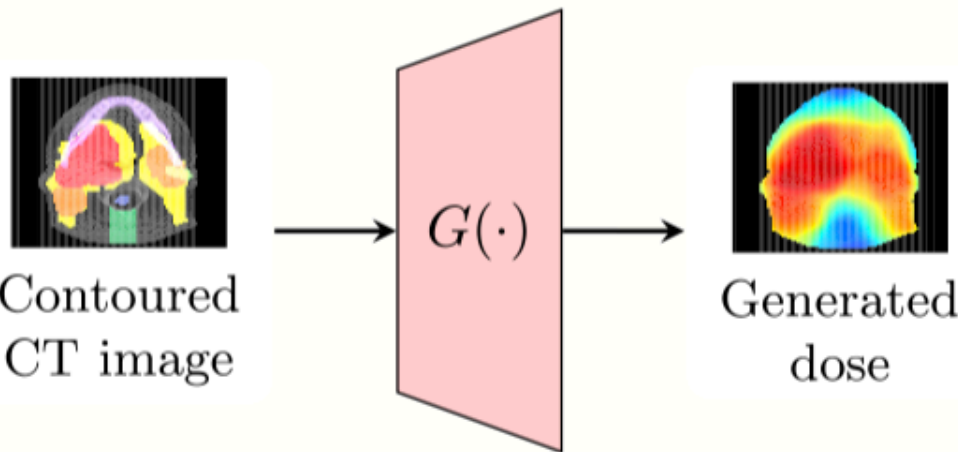
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297 Med. Phys. 47 (2), February 2020 0094-2405/2020/47(2)/297/10 © 2019 American Association of Physicists in Medicine 297

### Training



### Testing



# Mixed Density Networks for Dose Prediction

IOP Publishing

Phys. Med. Biol. 66 (2021) 055003

<https://doi.org/10.1088/1361-6560/abdd8a>

Physics in Medicine & Biology




IPEM

Institute of Physics and Engineering in Medicine

CrossMark

PAPER

Probabilistic dose prediction using mixture density networks for automated radiation therapy treatment planning

Viktor Nilsson<sup>1,2,5,\*</sup>, Hanna Gruselius<sup>1,5</sup>, Tianfang Zhang<sup>1,2</sup>, Geert De Kerf<sup>3</sup> and Michaël Claessens<sup>3,4</sup>

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RaySearch Laboratories, Stockholm, Sweden

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Iridium Cancer Network, Antwerp, Belgium

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Department of Radiation Oncology, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium

5

These authors contributed equally to this work.

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**Keywords:** mixture density network, dose prediction, dose mimicking, knowledge-based planning, deep learning, radiation therapy treatment planning

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12 February 2021

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The figure consists of two parts. The top part is a line graph showing the probability density of radiation doses. The x-axis is labeled 'Dose [cGy]' and ranges from 4000 to 7000. The y-axis is labeled 'Probability density' and has a '0' at the origin. Two curves are plotted: a solid blue line representing the 'Mixture' model and a dotted black line representing 'Protocols'. The 'Protocols' curve has a single sharp peak at approximately 5000 cGy. The 'Mixture' curve is bimodal, with a primary peak at approximately 5000 cGy and a secondary, lower peak at approximately 5600 cGy. The bottom part of the figure shows two axial CT slices of a human pelvis. The slices are overlaid with a color map representing the radiation dose distribution. A legend on the right indicates the scale in '% of 7000 cGy', with a color gradient from blue (0) to red (110). The dose distribution is concentrated in the central pelvic region, with higher percentages (red) in the center and lower percentages (blue) towards the edges.

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AAPM Annual Meeting July 26, 2021

# Deep Learning for Automated Fluence Map Generation



PAPER

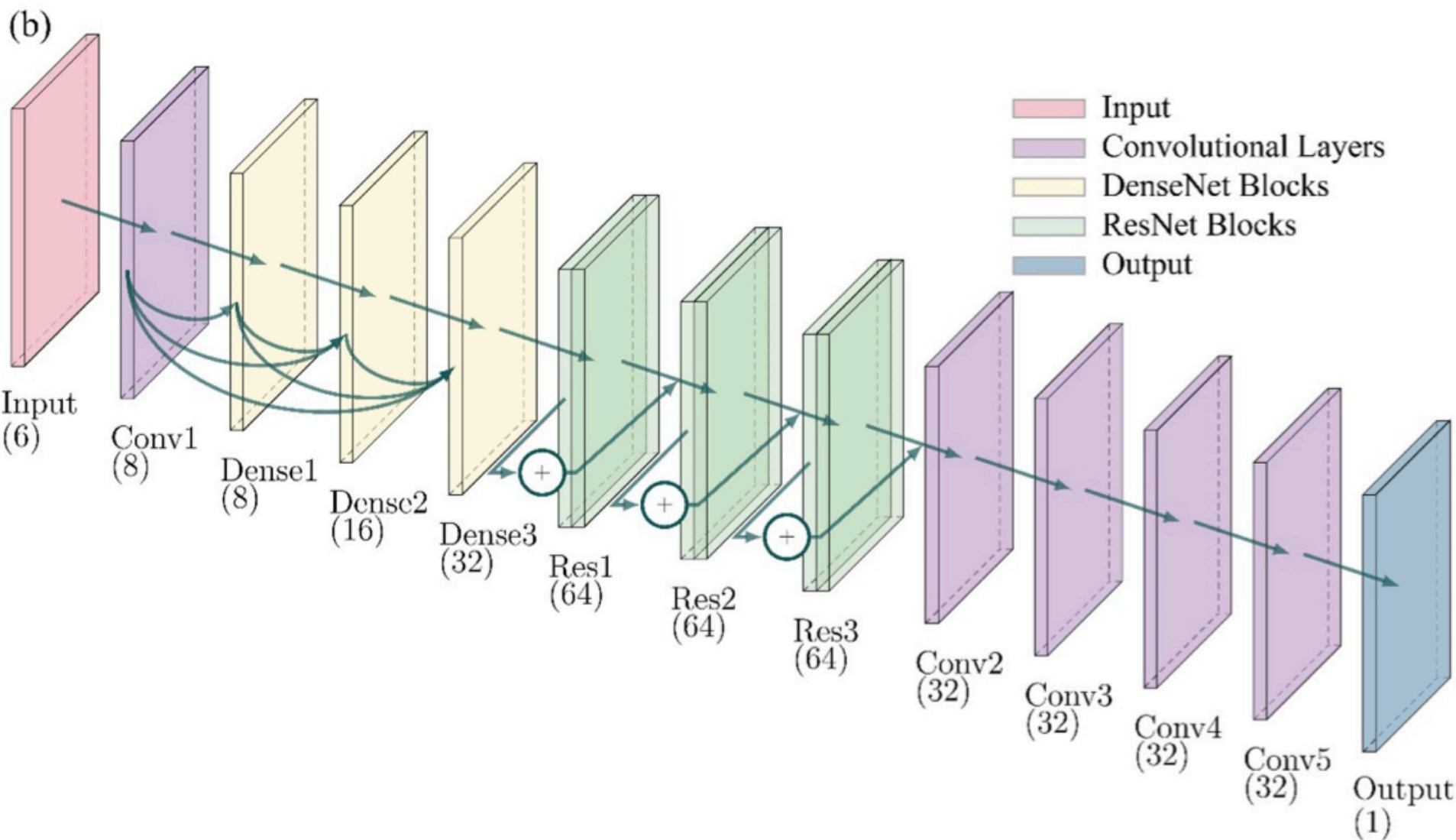
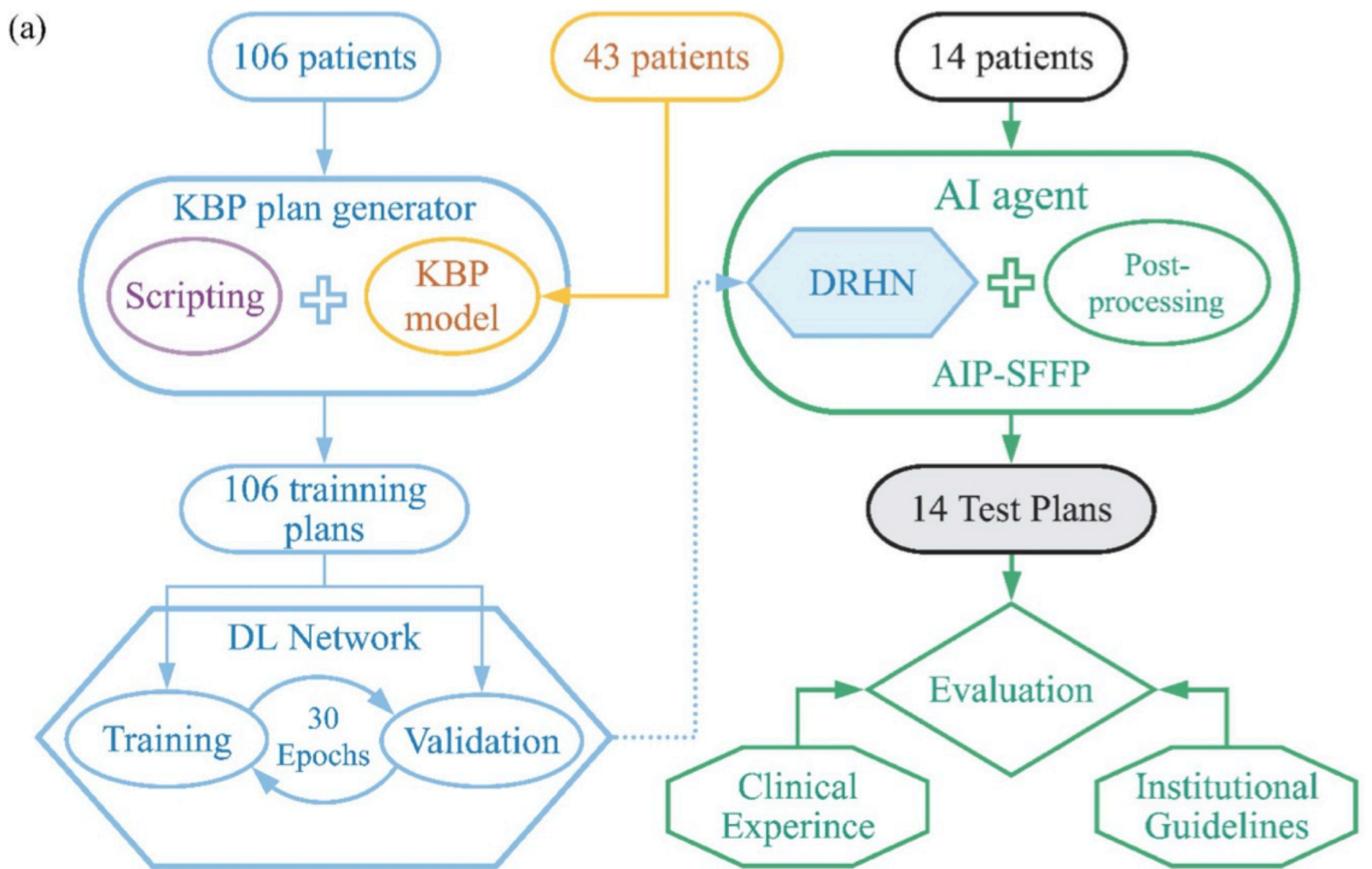
## Automatic IMRT planning via static field fluence prediction (AIP-SFFP): a deep learning algorithm for real-time prostate treatment planning

Xinyi Li<sup>1</sup>, Jiahan Zhang<sup>1</sup>, Yang Sheng<sup>1</sup>, Yushi Chang<sup>1</sup>, Fang-Fang Yin<sup>1</sup>, Yaorong Ge<sup>2</sup>, Q Jackie Wu<sup>1</sup> and Chunhao Wang<sup>1,3</sup>

<sup>1</sup> Department of Radiation Oncology, Duke University Medical Center, Durham, NC, United States of America  
<sup>2</sup> University of North Carolina at Charlotte, Charlotte, NC, United States of America  
<sup>3</sup> Author to whom any correspondence should be addressed.

E-mail: [chunhao.wang@duke.edu](mailto:chunhao.wang@duke.edu)

Keywords: auto-planning, deep learning, prostate, IMRT



# Reinforcement Learning

## Operating a treatment planning system using a deep-reinforcement learning-based virtual treatment planner for prostate cancer intensity-modulated radiation therapy treatment planning

Chenyang Shen<sup>a)</sup>

Medical Artificial Intelligence and Automation (MAIA) Laboratory, Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA  
Innovative Technology Of Radiotherapy Computation and Hardware (iTORCH) Laboratory, Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA

Dan Nguyen and Liyuan Chen

Medical Artificial Intelligence and Automation (MAIA) Laboratory, Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA

Yesenia Gonzalez

Medical Artificial Intelligence and Automation (MAIA) Laboratory, Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA  
Innovative Technology Of Radiotherapy Computation and Hardware (iTORCH) Laboratory, Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA

Rafe McBeth

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Nan Qin

Medical Artificial Intelligence and Automation (MAIA) Laboratory, Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA  
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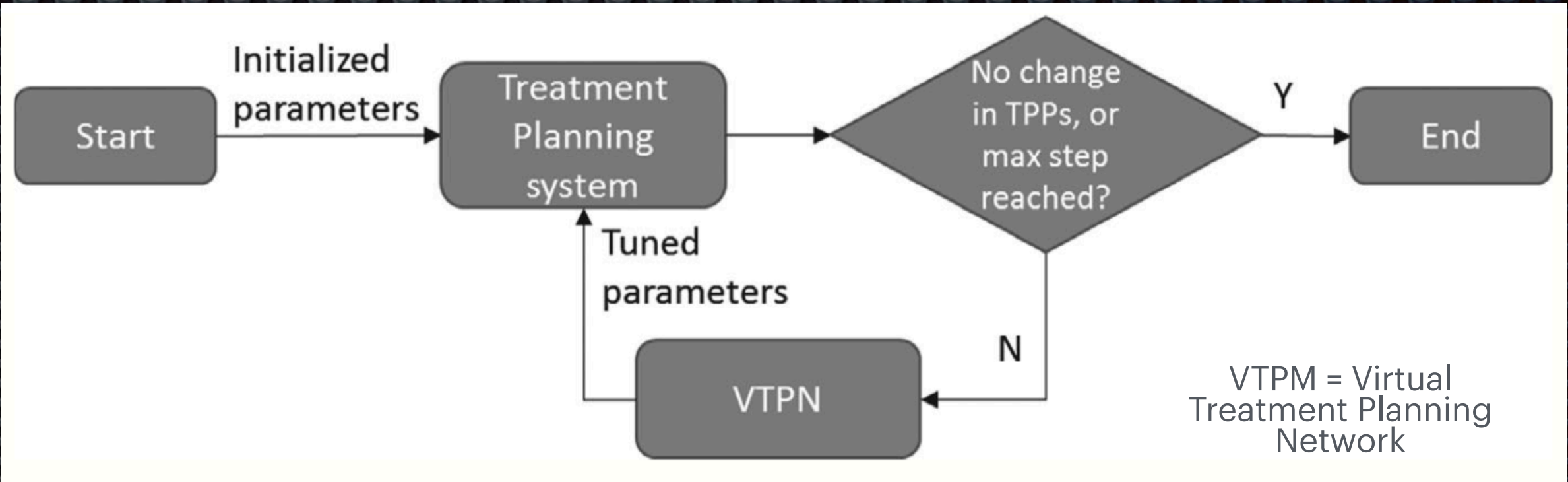
Steve B. Jiang

Medical Artificial Intelligence and Automation (MAIA) Laboratory, Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA

Xun Jia<sup>a)</sup>

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(Received 11 September 2020; revised 21 January 2020; accepted for publication 22 February 2020; published 28 March 2020)

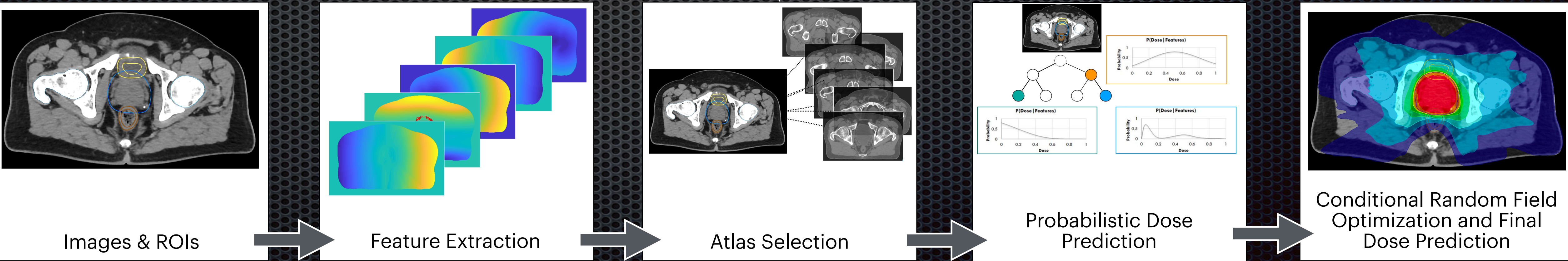


# Atlas Regression Forests

## Training



## Novel Patient



# Input Data Variations on Automated Planning



## PAPER

# Performance stability evaluation of atlas-based machine learning radiation therapy treatment planning in prostate cancer

**Leigh Conroy<sup>1,2,3</sup> , Aly Khalifa<sup>3</sup> , Alejandro Berlin<sup>1,2,4</sup>, Chris McIntosh<sup>3,4,5,6,7</sup> and Thomas G Purdie<sup>1,2,3,4</sup> **

<sup>1</sup> Radiation Medicine Program, Princess Margaret Cancer Centre, Toronto, Canada

<sup>2</sup> Department of Radiation Oncology, University of Toronto, Toronto, Canada

<sup>3</sup> Department of Medical Biophysics, Faculty of Medicine, University of Toronto, Toronto, Canada

<sup>4</sup> Techna Institute, University Health Network, Toronto, Canada

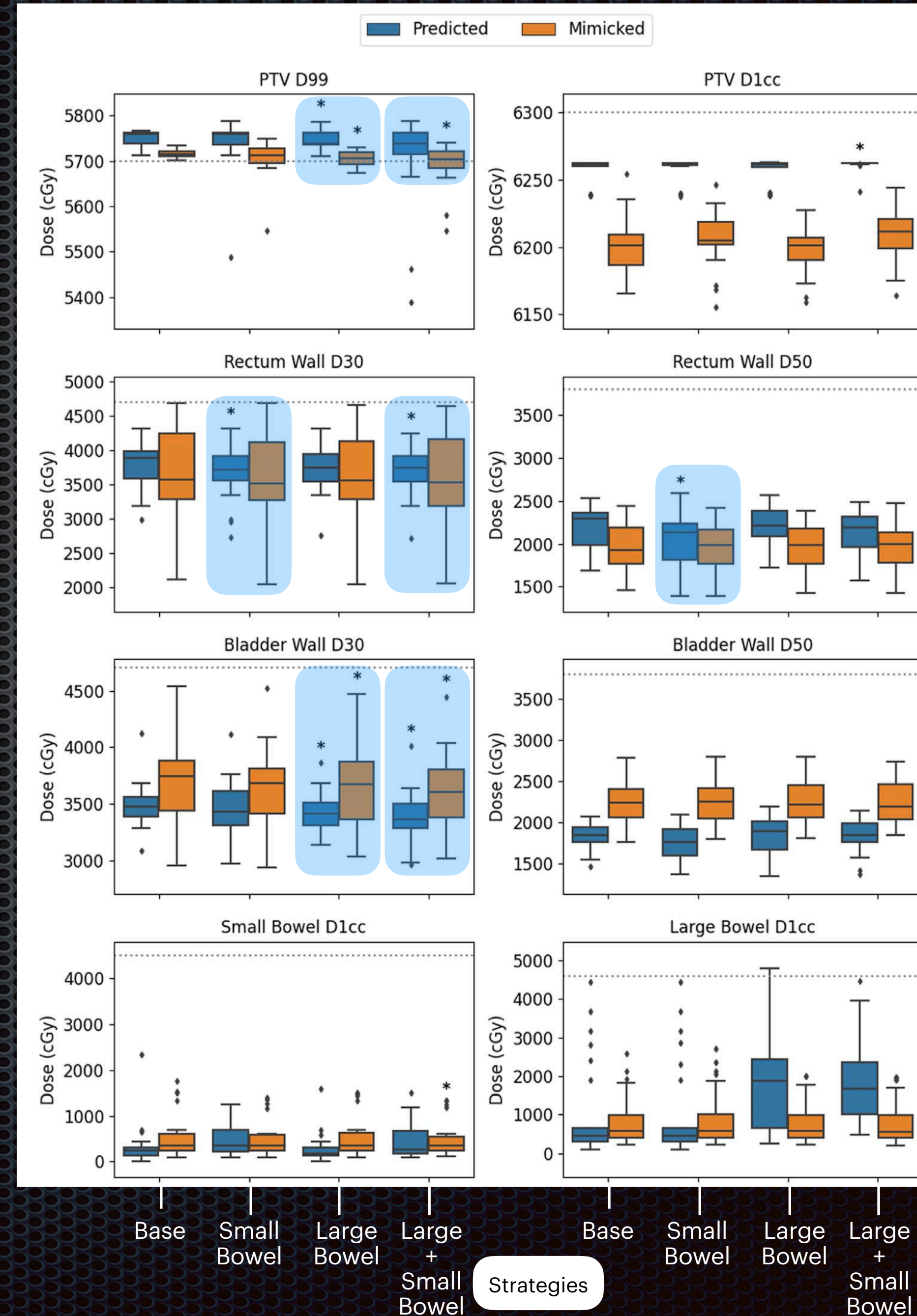
<sup>5</sup> Peter Munk Cardiac Centre, University Health Network, Toronto, Canada

<sup>6</sup> Joint Department of Medical Imaging, University Health Network, Toronto, Canada

<sup>7</sup> Vector Institute, Toronto, Canada

**Keywords:** machine learning, automated treatment planning, atlas-selection, dose prediction, external beam radiotherapy, quality assurance, benchmarking

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Improving Health  
Through Medical Physics

## The Open Knowledge-Based Planning Challenge (OpenKBP)

### An AAPM Grand Challenge

The aim of the OpenKBP Challenge is to advance fair and consistent comparisons of dose prediction methods for knowledge-based planning (KBP). Participants of the challenge will use a large dataset to train, test, and compare their prediction methods, using a set of standardized metrics, with those of other participants.

**TH-F-TRACK 5-3 (Thursday, 7/29/2021) 4:30 PM - 5:30 PM [Eastern Time (GMT-4)]**

An International Validation of Knowledge-Based Planning

**Aaron Babier**

UC San Diego



UNIVERSITY OF  
TORONTO



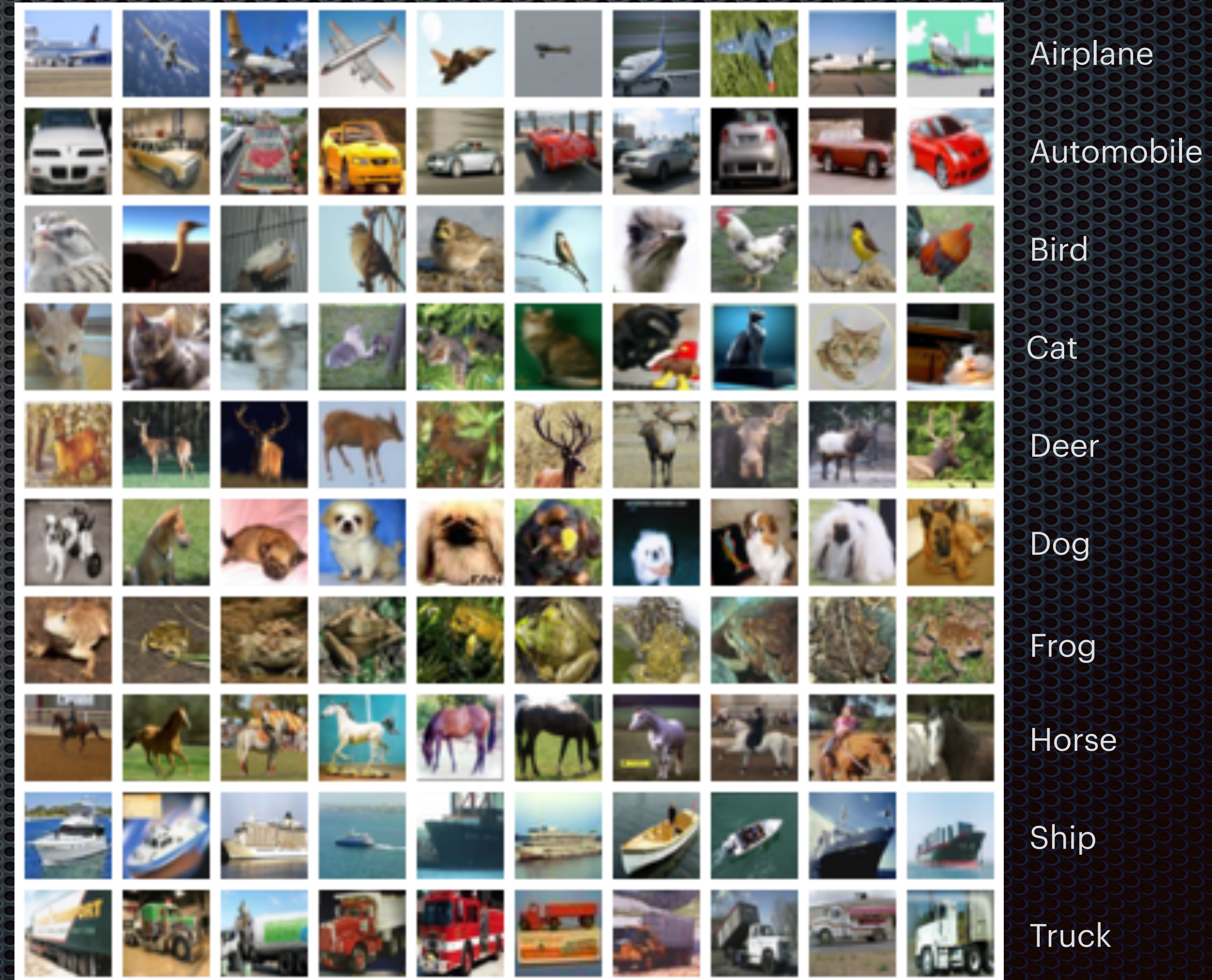
# Open Knowledge-Based Planning (OpenKBP) Challenge

AAPM Grand Challenge 2020 Open Source Dataset

OpenKBP Challenge is the first competition for knowledge-based planning (KBP)

Open source, highly curated datasets (e.g., ImageNet →) are staples of thriving artificial intelligence driven fields

Used public and private data sources and augmented public data with new plans for OpenKBP release



# Open Knowledge-Based Planning (OpenKBP) Challenge

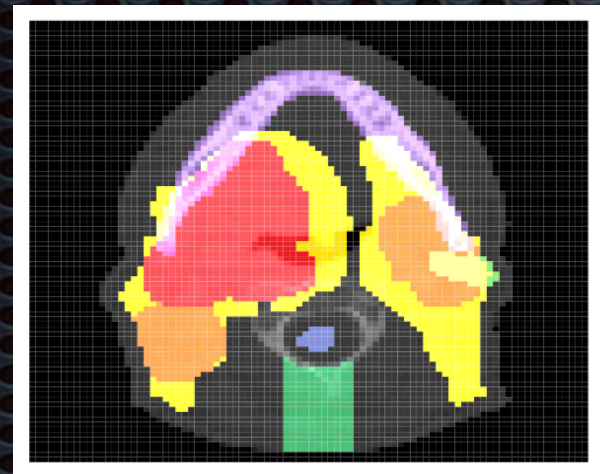
AAPM Grand Challenge 2020 Competition

## Objective

Implement the most accurate KBP dose prediction method on a large open-access dataset

## Evaluation

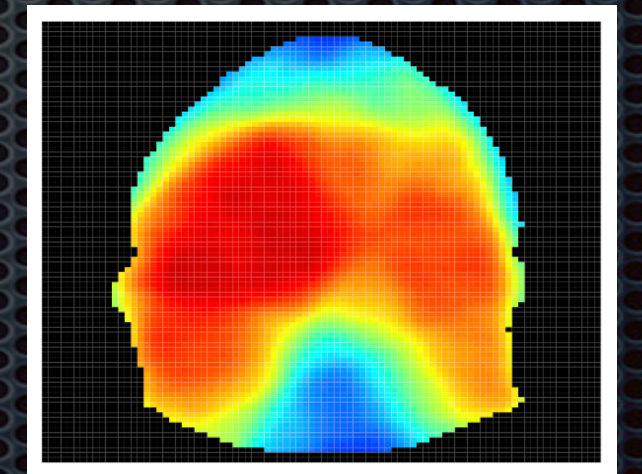
All models are trained on the same data, and evaluated with standard metrics



Planning CT + ROIs



Dose Prediction Method



Predicted Dose

# Open Knowledge-Based Planning (OpenKBP) Challenge

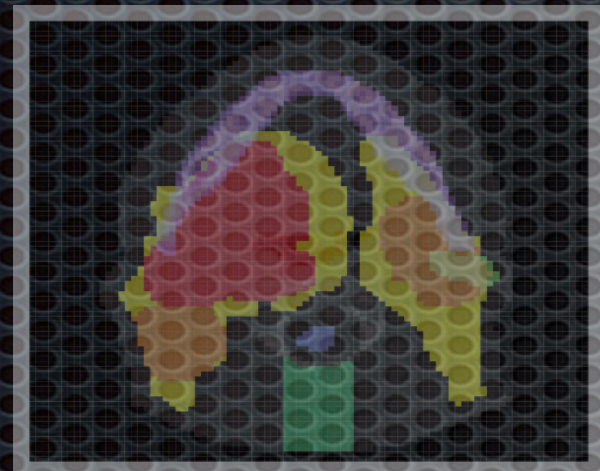
AAPM Grand Challenge 2020 Competition

## Objective

Implement the most accurate KBP dose prediction method on a large open-access dataset

## Evaluation

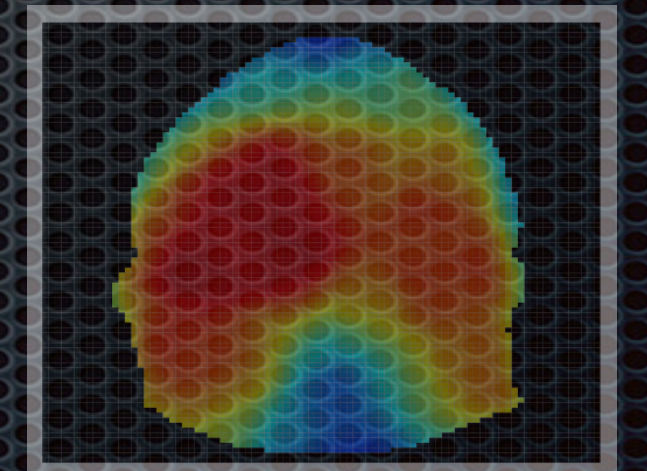
All models are trained on the same data, and evaluated with standard metrics



Planning CT + ROIs



Dose Prediction Method



Predicted Dose

## Validation phase

Each team's best validation submission was displayed on a public leaderboard



## Testing Phase

Each team made one submission to the testing phase  
Winners determined based on the one submission  
Scores were blinded until competition closed

# Challenge Leaderboard Streams

**3D Leaderboard**

**DVH Leaderboard**

**Ranking**

Lowest average error

**Ground Truth**

Plan dose distribution

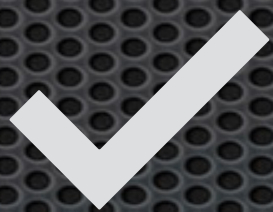
Plan DVH

**Error Measure**

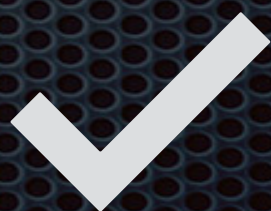
Mean absolute error  
voxel-by-voxel

Mean absolute error at  
dose volume metrics

**3D stream**



**DVH stream**



# Challenge Participants

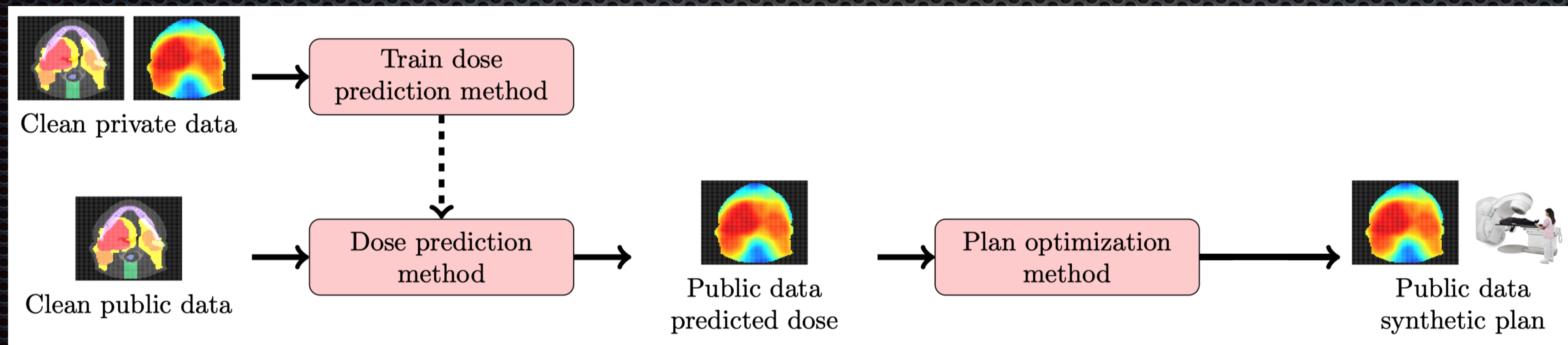
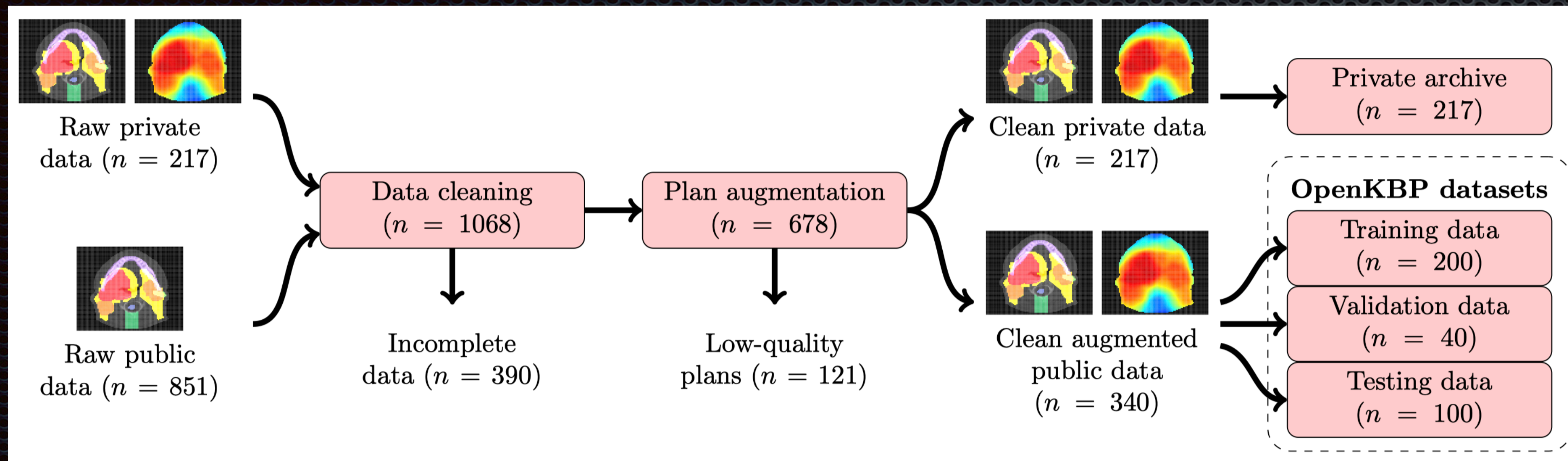
	Registration	Active in Validation	Active in Testing
Total participants	195	73	54
Total teams	129	44	28
Number of submissions	---	1750	28

## New interest to research community

**57%**  
say primary research is Not “Medical Physics”

**62%**  
say NEVER done KBP research before

# Data → Curation | Generation | Augmentation



**TH-F-TRACK 5-3 (Thursday, 7/29/2021) 4:30 PM - 5:30 PM [Eastern Time (GMT-4)]**

An International Validation of Knowledge-Based Planning

**Aaron Babier**

# Summary

Machine Learning → Dose Prediction

Machine Learning Architecture/Methods:

- Convolution Neural Networks → U-Net
- Generative Adversarial Networks
- Atlas Regression Forest
- Reinforcement Learning

Open Knowledge-Based Planning (OpenKBP) Challenge

- Voxel-based dose prediction
- DVH prediction