MATLAB EXPO

Machine learning for cancer research and discovery

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May 10-11, 2023 (Virtual)

National Institutes of Health

Congressionally Directed Medical Research Programs CDMRP Department of Defense

MOFFITT CANCER CENTER

National and Global AI/ML interest

National AI Initiative Act of 2020 (NAIIA)

Became law on January 1, 2021
As part of the "*William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021*", *H.R. 6395, Division E.*

DIVISION E—NATIONAL ARTIFICIAL INTELLIGENCE INITIATIVE ACT OF 2020

SEC. 5001. SHORT TITLE.
This division may be cited as the "National Artificial Intelligence Initiative Act of 2020".

Microsoft
Moffitt Cancer Center
NASA
National Center for Atmospheric Research
National Center for Supercomputing Applications at the University of Illinois at Urbana-Champaign
National Energy Technology Laboratory

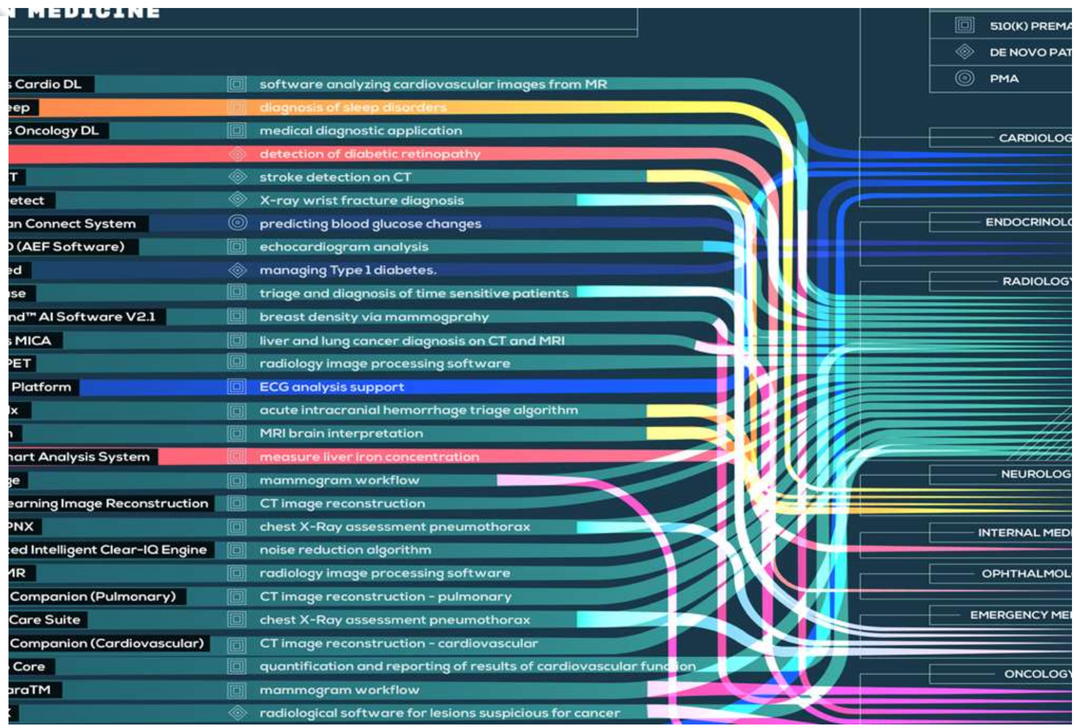
EUROPEAN COMMISSION

Brussels, 21.4.2021
COM(2021) 206 final
2021/0106(COD)

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

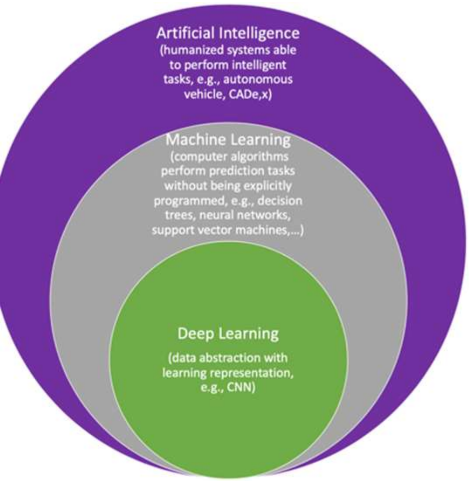
LAYING DOWN HARMONISED RULES ON ARTIFICIAL INTELLIGENCE (ARTIFICIAL INTELLIGENCE ACT) AND AMENDING CERTAIN UNION LEGISLATIVE ACTS

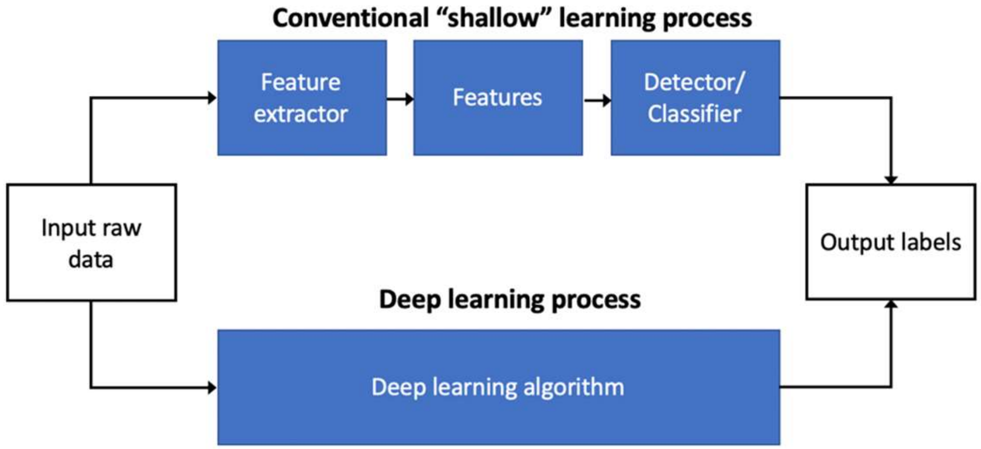


https://www.ai.gov/wp-content/uploads/2023/01/NAIRR-TF-Final-Report-2023.pdf

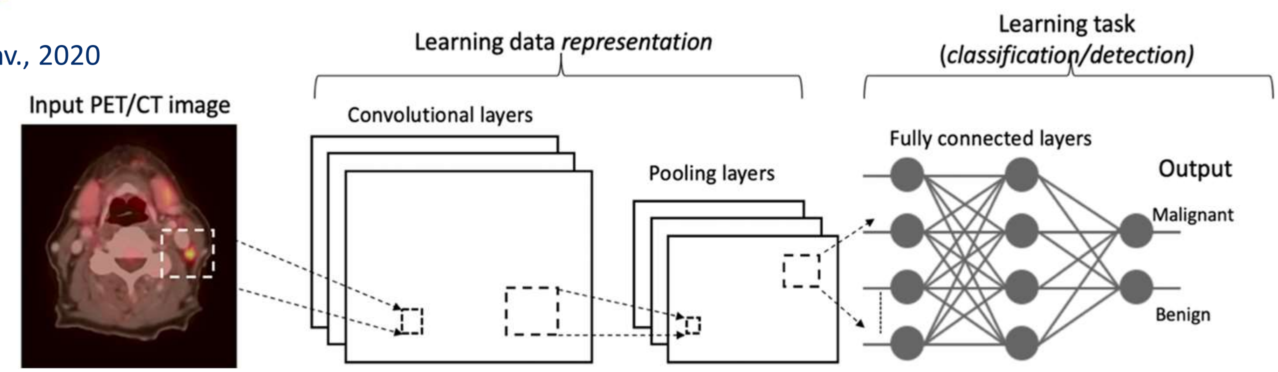
Benjamens, S., Digital medicine, 2020

Deep vs conventional machine learning

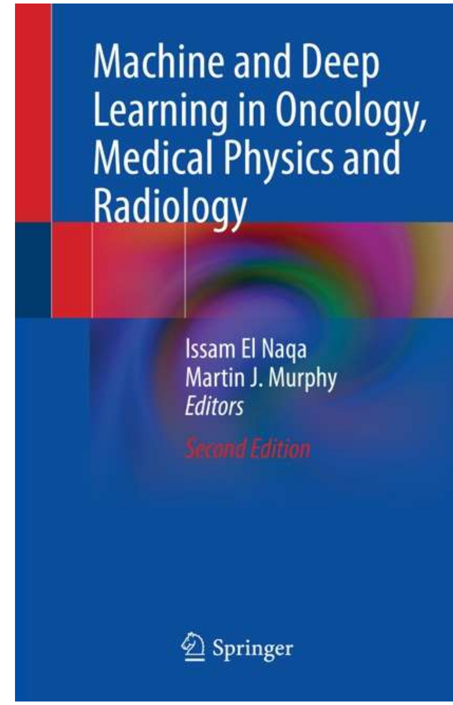




El Naqa, BJR 125th Annv., 2020



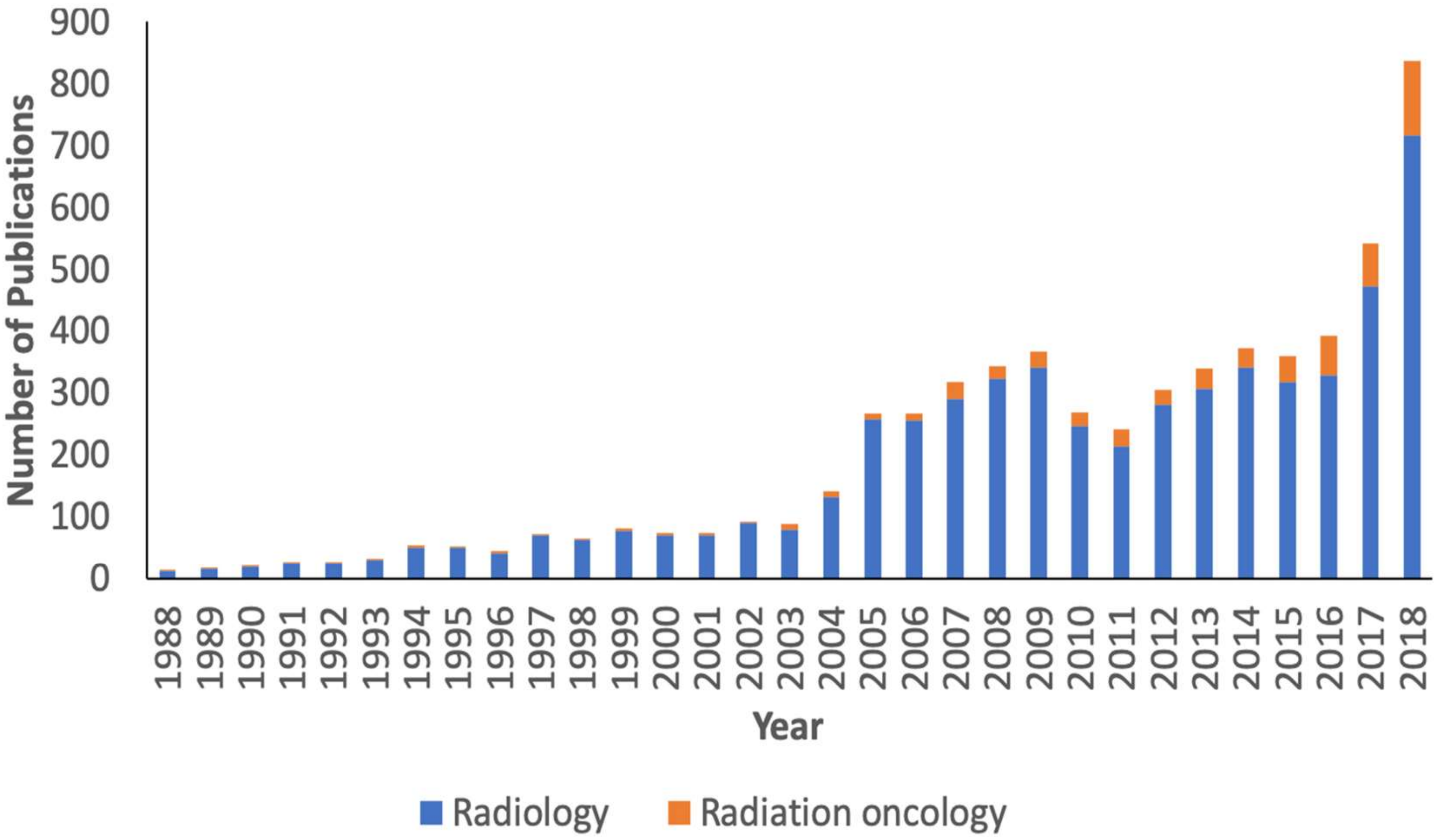
Zaidi and El Naqa, Annu. Rev. Biomed. Eng., 2021



BJR 125TH ANNIVERSARY SPECIAL FEATURE: REVIEW ARTICLE

Artificial Intelligence: reshaping the practice of radiological sciences in the 21st century

[1]ISSAM EL NAQA, PhD, [2]MASOOM A HAIDER, MD, [3]MARYELLEN L GIGER, PhD and [1]RANDALL K TEN HAKEN, PhD



ML at Moffitt

(@ml4onco)

COVER STORY

GUEST EDITORIAL

Moffitt Cancer Center: Why we are building the first machine learning department in oncology

By Issam El Naqa and Dana Rollison

VISION

To transform personalized cancer care and accelerate scientific discovery in cancer research with machine/deep learning

MISSION

To design, develop, and translate state-of-the-art patient-centered machine and deep learning algorithms

VALUE
Patient-centered ML/DL for facilitating cancer care and research

VALUE
Unbiased, generalizable, and *interpretable* ML/DL from blended data

VALUE
Translate ML/DL findings into the clinic to improve cancer care and research

Moffitt.org/MachineLearning

ML Strategic Priorities @ Moffitt

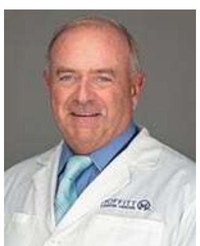
Primary Faculty





Secondary Faculty





Strategic Priority
1. Integration of ML into MCC research and clinical care
1.1 Develop a robust and secure ML infrastructure that also leverages existing MCC resources
1.2 Convert clinical care data into research data including linkage of unstructured data using NLP methods
1.3 Establish ML working group for R&D (Machine Learning League [MLL])
2. Establish translational ML research program in priority areas
2.1 Multimodality radiological and pathological imaging for diagnostic and outcomes
2.2 Information retrieval and annotation with natural language processing (NLP)
2.3 Outcome modeling and decision support by longitudinal integration of pan-omics data and using PROs for retrospective and prospective studies
2.4 Molecular and computational biology and in silico trial designs
3. Establish basic ML research programs in priority areas
3.1 Visual analytics, explainable and interpretable ML/AI
3.2 Automated ML architectures and evolutionary learning
3.3 Physics-based quantum ML, hybrid systems, and stochastic processes
4. Develop team science initiatives
4.1 Program project or center of excellence to address clinical ML role
4.2 Program project or biotechnology resource to address basic science ML role
5. Develop residency/training programs
5.1 PhD/Residency programs in ML for oncology

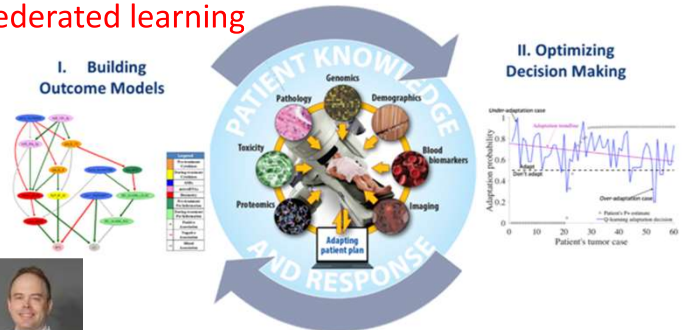
Staff (ML Engineers)


Moffitt.org/MachineLearning

El Naqa Lab / Machine Learning

@ielnaqa

Optimal Decision Making Using Panomics Analytics with Federated learning



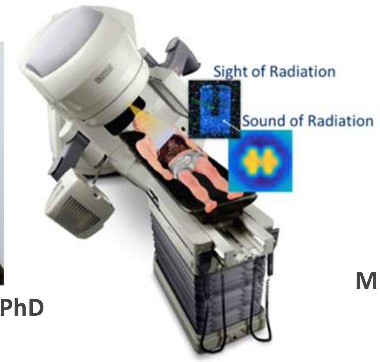
Dipesh Niraula, PhD

Funding resource: NIH/NCI R01 CA233487 + Supplementary

John Mayfield, M.D.

Image-guided radiotherapy (sight & sound)

Glebys Gonzales, PhD



Muhammad Ali, PhD

Ibrahim (Abe) Oraiqat, PhD

Funding resources: NIH/NCI R37 CA22221, R41 CA243722, R01CA266803

Medical Imaging and Data Resource Center (MIDRC) for Rapid Response to COVID-19 Pandemic

Palak Dave, PhD

MIDRC
MEDICAL IMAGING AND DATA RESOURCE CENTER.

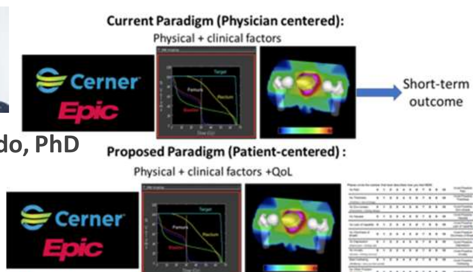
Naveena Gorre, MS

Funding Resource: University of Chicago (Prime: NIH/NIBIB 75N92020D00018/75N92020F0001)

Data Science to Improve Treatment Planning for Advanced Prostate Cancer Patients Treated with Radiotherapy

Funding resources (with Heather Jim) : W81XWH-22-1-0277

Ruwani Fernando, PhD



Denis Dudas, PhD

Undergrad students:

Skylar Kyzer
Yasmin Saeed

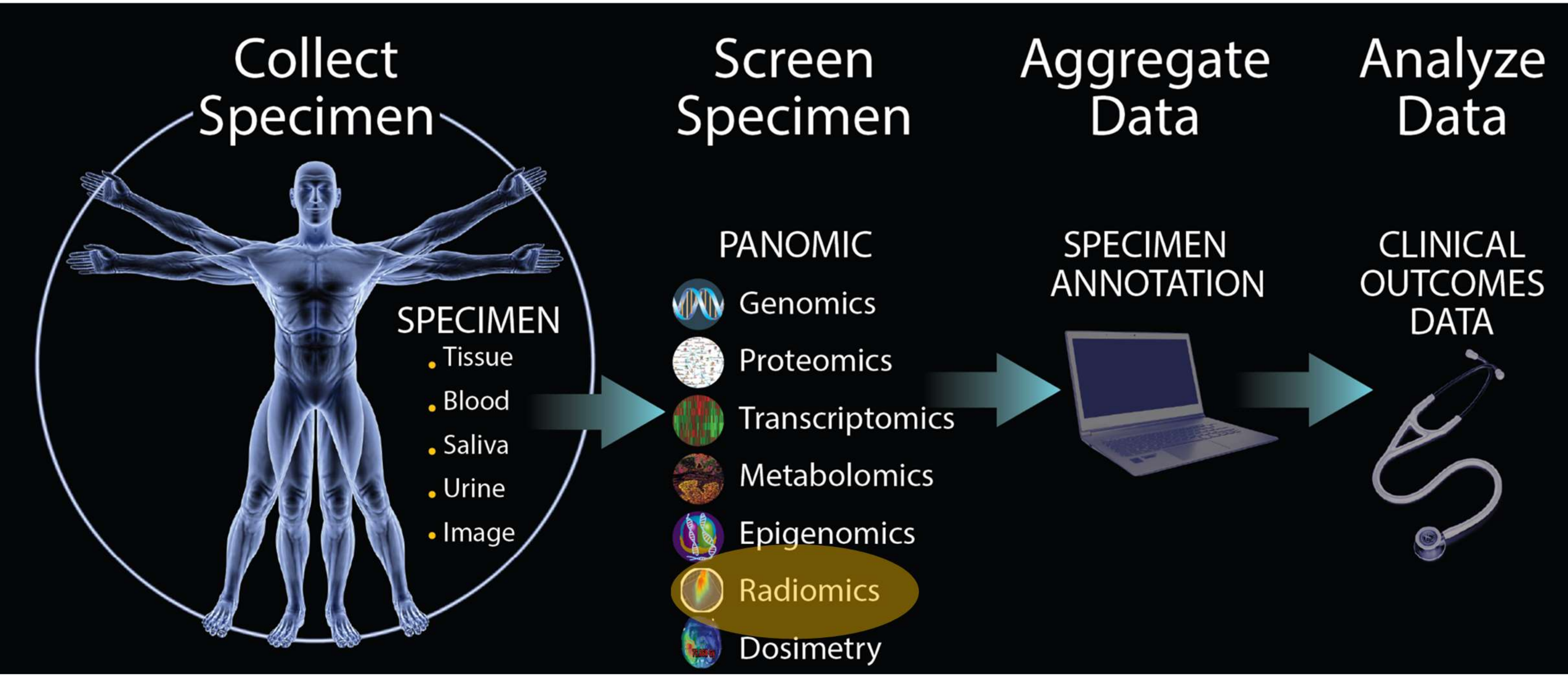
Adaptive radiotherapy with MR-Linac

Funding source: Industrial alliance

Jesutofunmi Fajemisin, MS

http://lab.moffitt.org/elnaqa/research-projects/

The *Pan-Omics* of Oncology



El Naqa et al, PMB, 2017

Modern Radiomics

MEDICAL PHYSICS

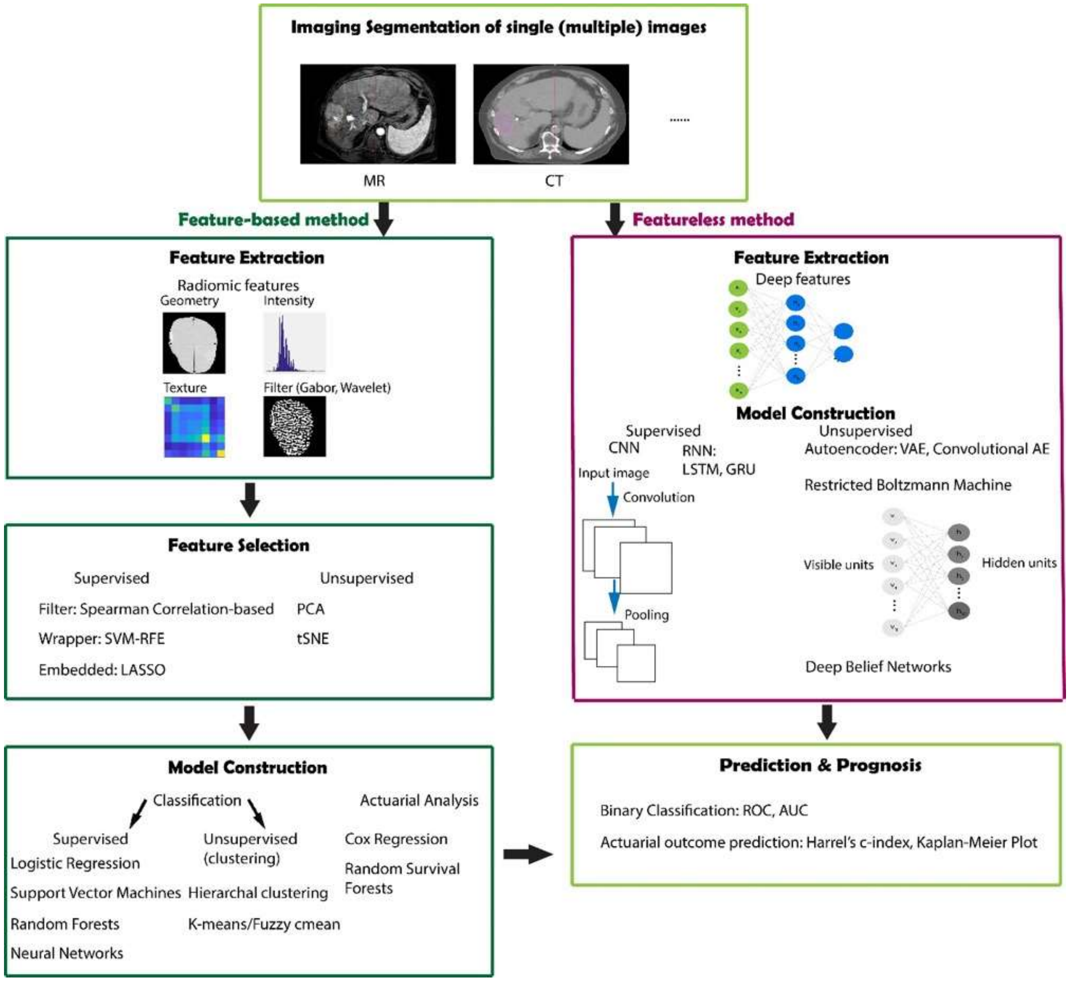
The International Journal of Medical Physics Research and Practice

Special Issue Paper

Machine and deep learning methods for radiomics

Michele Avanzo, Lise Wei, Joseph Stancanello, Martin Vallières, Arvind Rao, Olivier Morin, Sarah A. Mattonen, Issam El Naqa ... See fewer authors

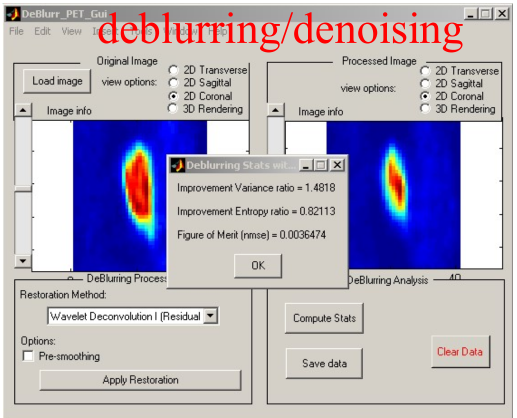
First published: 17 May 2020 | https://doi.org/10.1002/mp.13678 | Citations: 51



Avanzo, Wei, Med Phys, 2020

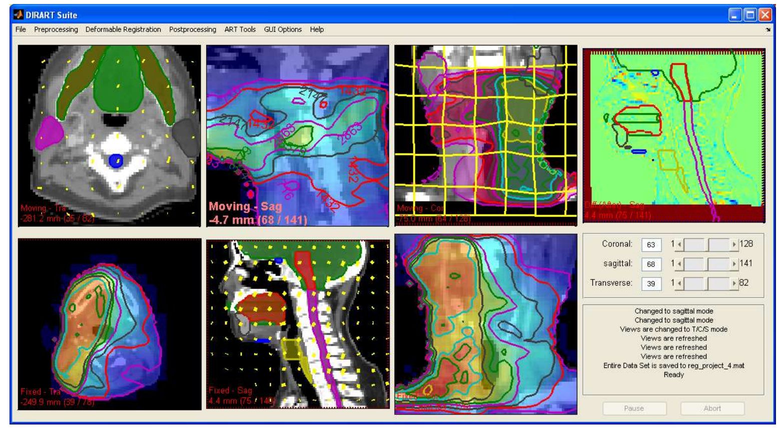
Radiomics Toolkits I: Imaging

Pre-processing: deblurring/denoising



El Naqa et al, Med Phys, 2006

Registration



Yang et al, Med Phys, 2010

Segmentation

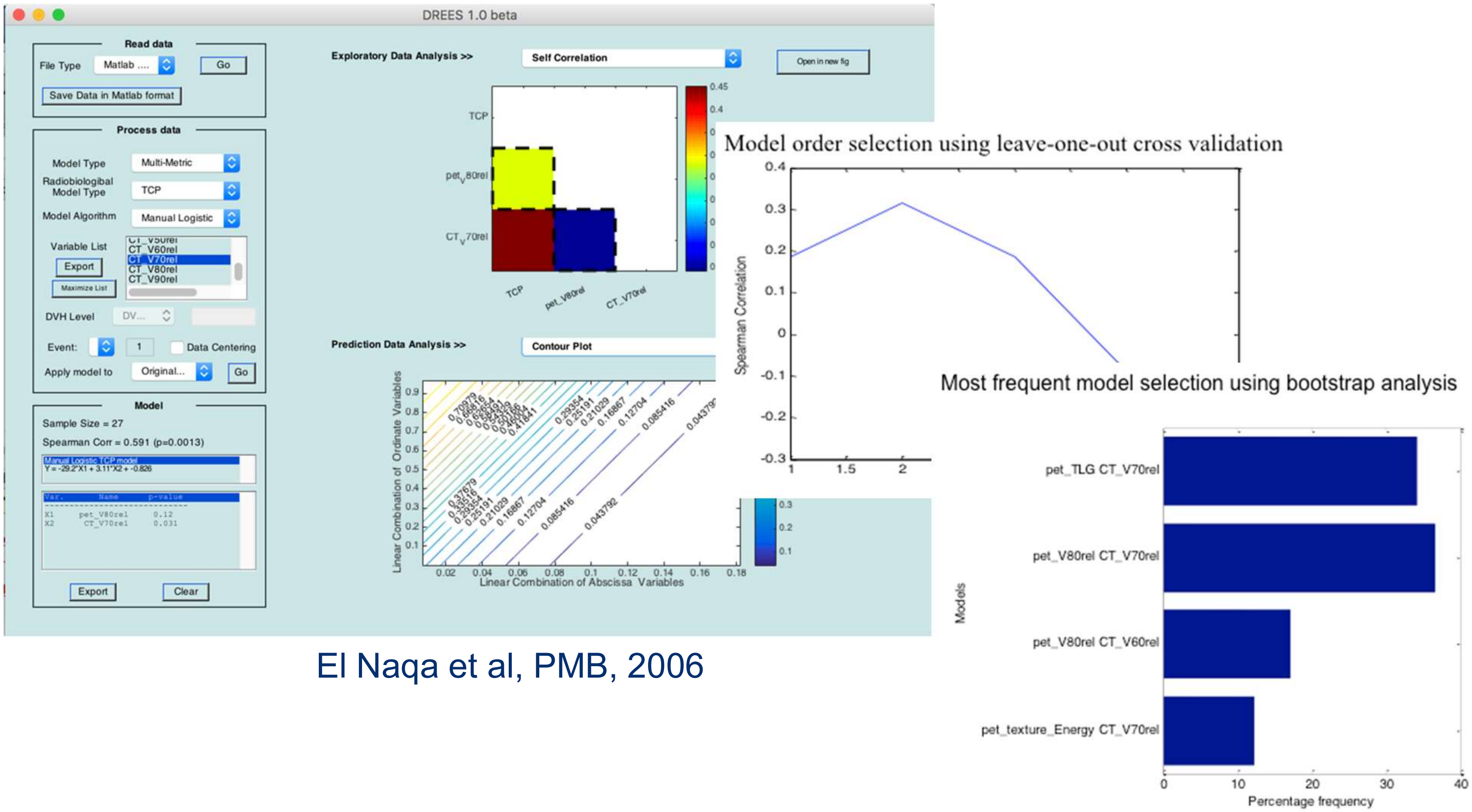
Yang et al., JROI, 2009

Feature Extraction

Piert et al., 2016

https://lab.moffitt.org/elnaqa/software-tools/

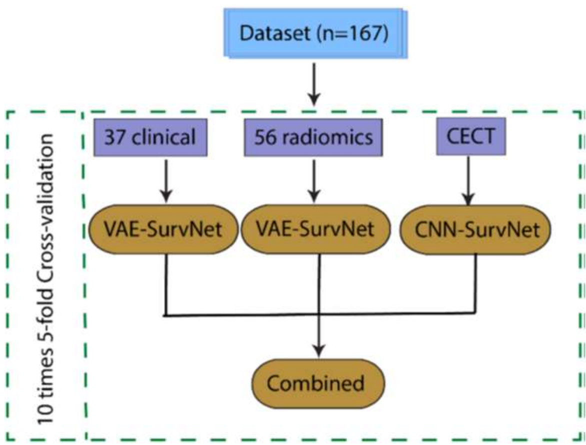
Radiomics Toolkits II: Modeling (DREES)

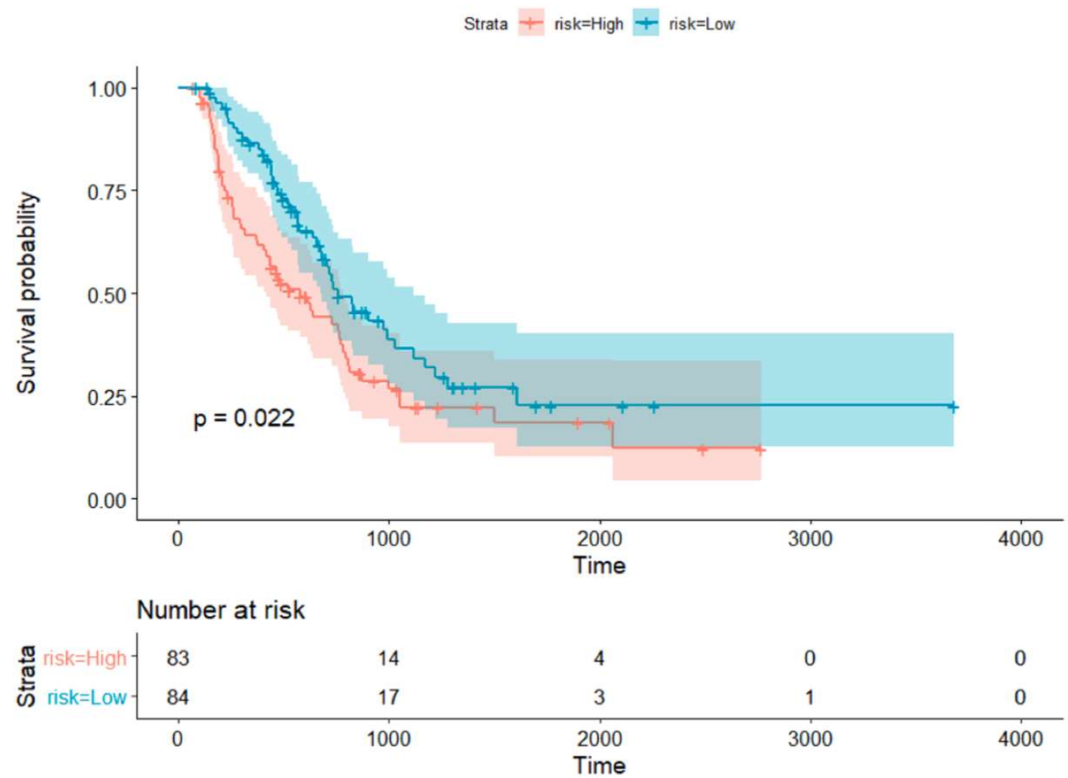


El Naqa et al, PMB, 2006

https://lab.moffitt.org/elnaqa/software-tools/

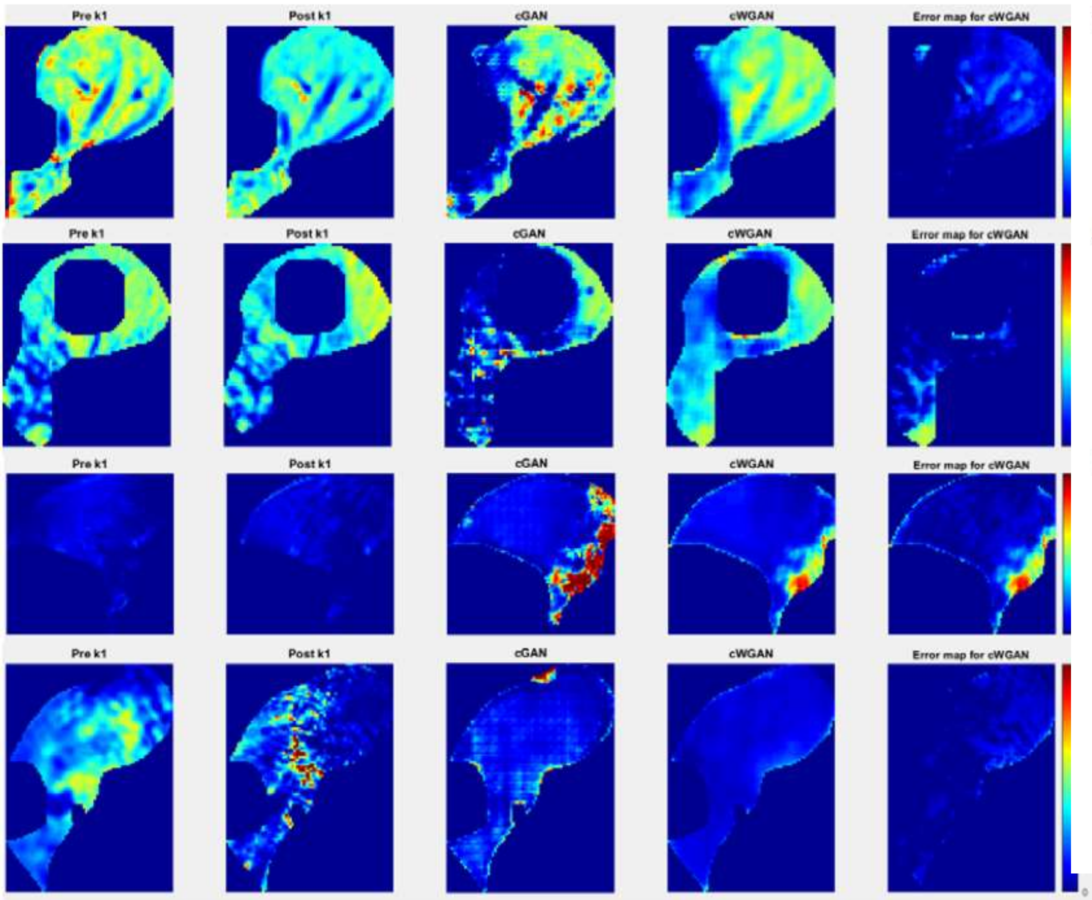
Deep Survival Radiomics model for Liver Cancer

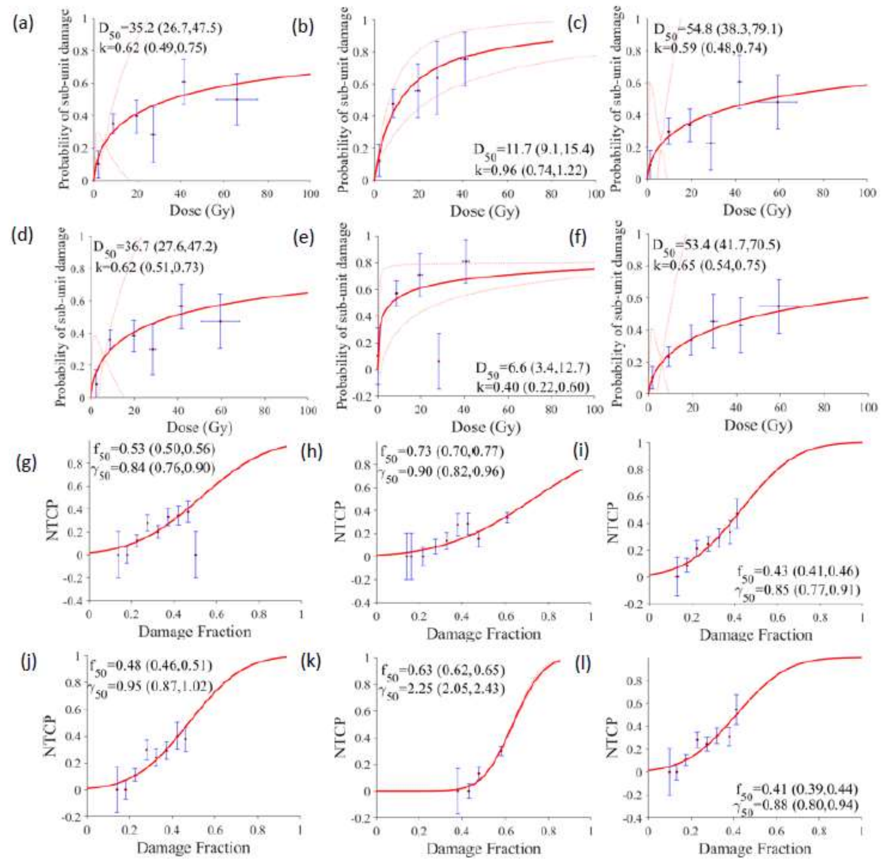




Wei et al, Physica Medica, 2021

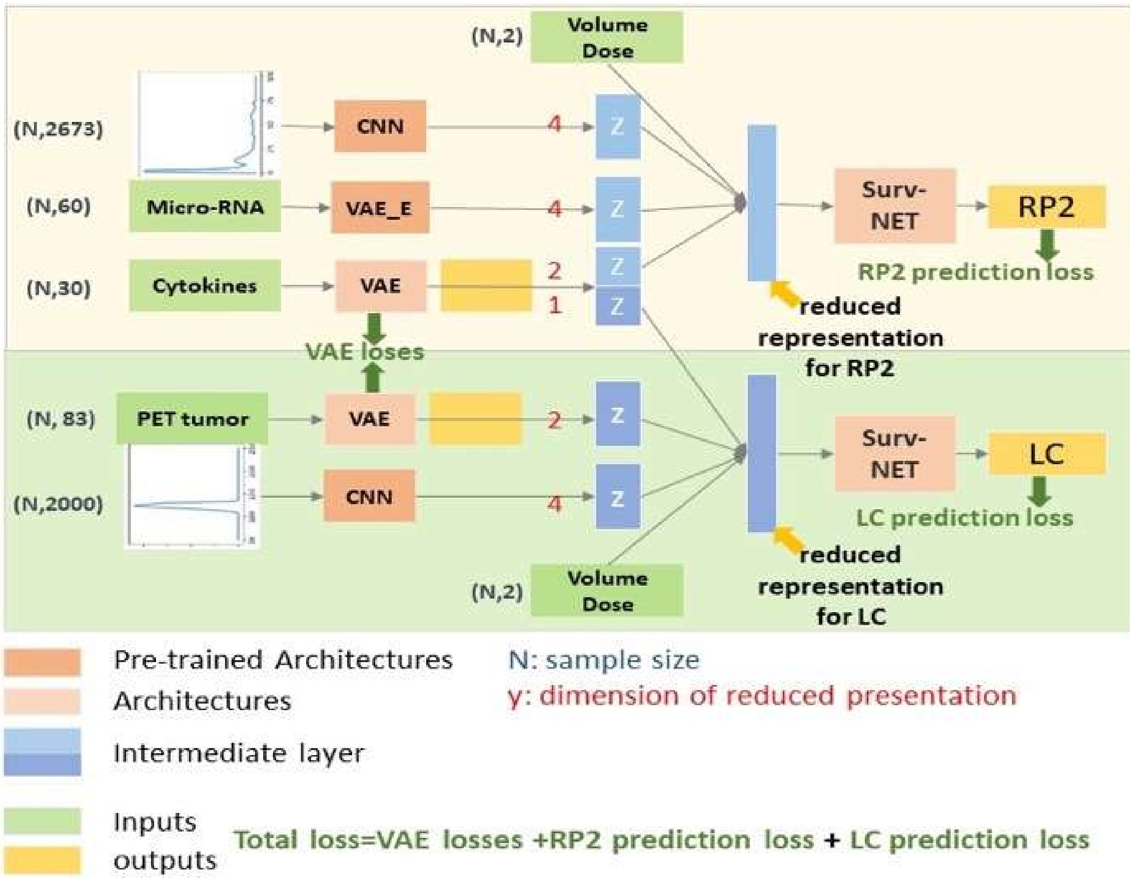
Deep Learning Prediction of post-SBRT Liver Function Changes and NTCP Modeling in HCC based on DGAE-MRI





Wei et al, Med Phys, 2023

Multi-omics response model with deep survival neural networks

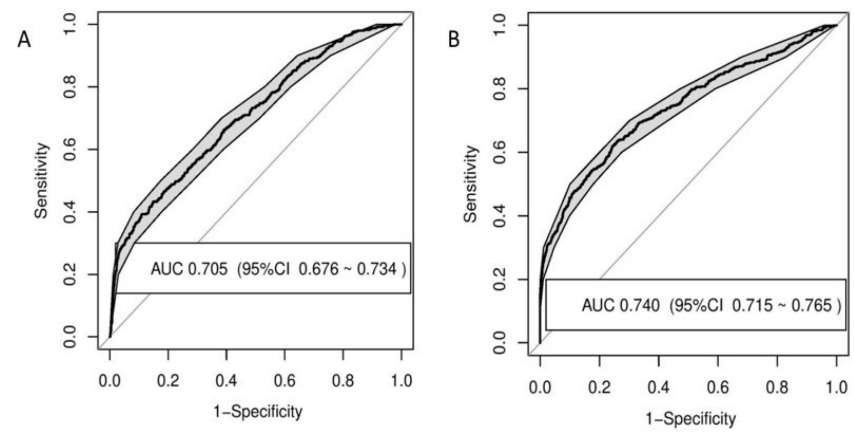


20 times of 5-fold cross validations

C-index (95%CI)	RP2	LC
NN-com	*0.705 (0.676~0.734)*	*0.740 (0.715 ~0.765)*
NN-DVH	0.660 (0.630~0.690)	0.727 (0.700~0.753)
Lyman/log-logistic	0.613 (0.583~0.643)	0.569 (0.545~0.594)

Independent test on 25 newly treated patients

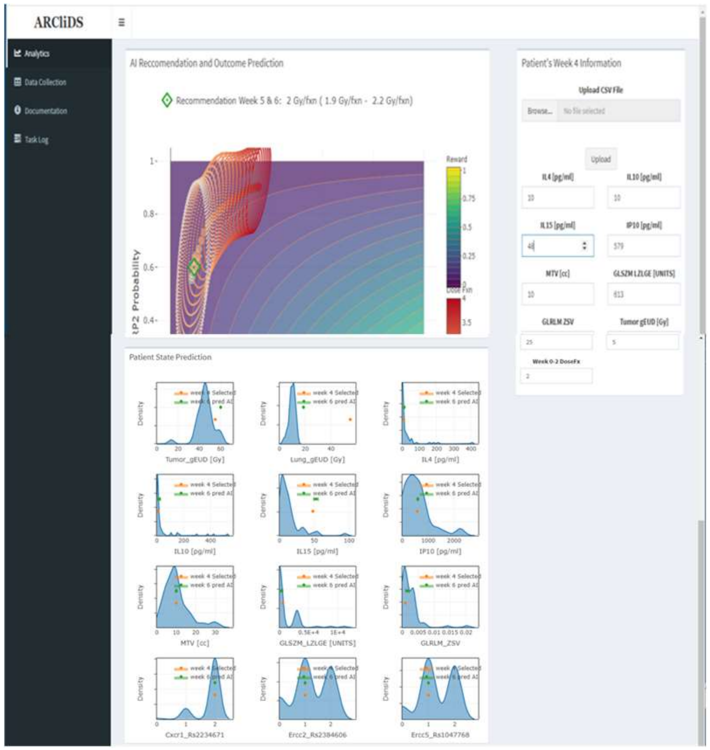
C-index (95%CI)	RP2	LC
NN-composite	0.692	0.721
NN-DVH	0.684	0.706
Lyman/log-logistic	0.588	0.573



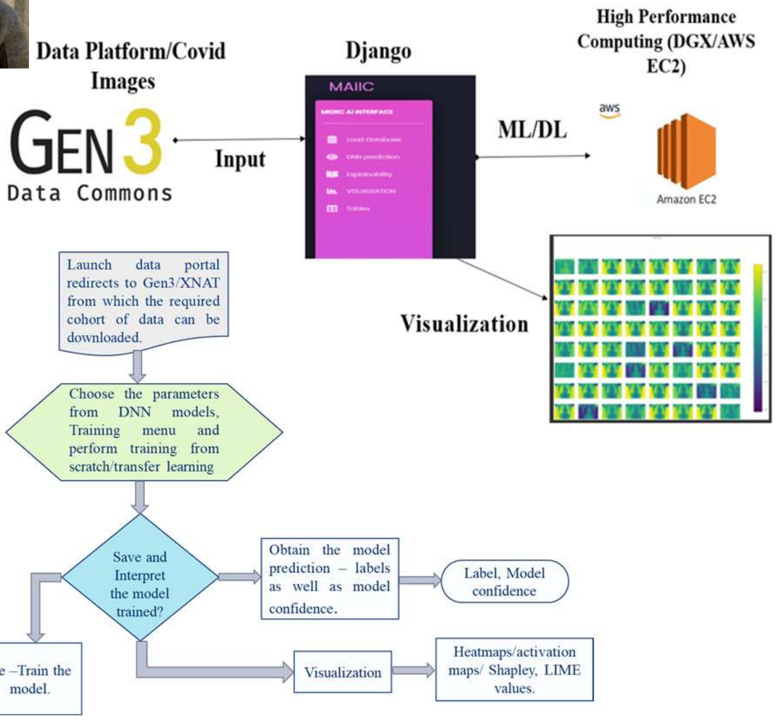
Cui et al, IJROBP, 2021

Software tools (prototypes) for AI Clinical Application

Recommender System for adaptive intervention in radiotherapy (ARCliDS)



Multi-institutional AI Platform for image interpretability (MIDRC)



➢ User Factors in AI implementation

Niraula, Nature Scientific Reports, 2023; Sun CMPB, 2022

Gorre, SPIE, 2023; PMB, 2023

AI/ML is nothing but perfect!

- Google Flu Trends (GFT) (Ginsberg, 2009)
  - GFT called out sick 2013 due to overestimation!
- Predicting pneumonia risk (Caruana, 2015)
  - Patients with pneumonia and asthma to be at a lower risk of death from pneumonia than patients with pneumonia but without asthma!
- Skin cancer risk prediction (Esteva, 2017)
  - Presence of a ruler as a sign of high risk would skew prediction
- Lung disease prediction from xray (Rajpurkar, 2017)
  - Presence of tube can indicate high risk
- Covid-19 infection of AI (Deshpande, 2020; Roberts, 2021, El Naqa, 2021)
  - Unreliable AI models for Covid-19 prediction

⇒Data quality and context matters

COMPUTING

Racial Bias Found in a Major Health Care Risk Algorithm

Black patients lose out on critical care when systems equate health needs with costs

By Starre Vartan on October 24, 2019

Man is to Computer Programmer as Woman is to Homemaker? Debiasing Word Embeddings

Amazon scraps secret AI recruiting tool that showed bias against women

Study finds gender and skin-type bias in commercial artificial-intelligence systems

Examination of facial-analysis software shows error rate of 0.8 percent for light-skinned men, 34.7 percent for dark-skinned women.

External Validation of a Widely Implemented Proprietary Sepsis Prediction Model in Hospitalized Patients

Andrew Wong, MD[1]; Erkin Otles, MEng[2,3]; John P. Donnelly, PhD[4]; et al

EPIC's Sepsis Model Is Not Ready for Prime Time

Aaron J. Calderon, MD, FACP, SFHM, reviewing Wong A et al. JAMA Intern Med 2021 Aug

Despite its widespread use, the proprietary electronic health record system missed sepsis 67% of the time.

Check List for AI/ML in Medical Physics (CLAMP)

- Purpose and justification of AI/ML algorithm selection
- Dataset characteristics (acquisition, size, partitioning [3Ts: training, tuning, testing])
- ML methods
  - Optimization, loss function, augmentation, regularization
  - Performance metrics and evaluations (internal, external)
- Significance of results
  - Interpretation of ML performance
  - Clinical translation and actionability

4712 | MEDICAL PHYSICS AI IN MEDICAL PHYSICS

TABLE 1 Checklist for AI in *Medical Physics* (CLAMP)

Indicate whether each section clearly summarizes or describes:	Checkboxes		
1. Abstract	**Yes**	**No**	**N/A**
a. Purpose, rationale, novelty or significance			
b. AI/ML methods and data type, dataset partitioning into training, validation (tuning), and test sets (include numbers used in training, validation, and test sets)			
c. Main results, including statistical analyses			
2. Introduction			
a. Purpose and justification of using AI/ML algorithm approach			
b. Contribution(s) of AI/ML to medical physics application			
c. Stage of development (e.g., pilot study, mature study)			
3. Materials			
a. Dataset characteristics including sample size and clinical acquisition sites			
b. Device(s) used for data acquisition (e.g., scanner makes), start-end dates of acquisition (or equivalent means with biotechnology generated data), and any data harmonization, augmentation, and enrichment strategies, or pre-processing are clearly described			
c. For imaging data: image or data acquisition modality, acquisition protocol, or parameter ranges are detailed			
d. For patient data: method to obtain the sample, representativeness of the population for the purpose of the study, IRB approval (or equivalent), and relevant patient demographics plus clinical variables such as prevalence(s) of disease(s) or lesion characteristics			
e. For phantom data: Type of phantom and method for generating phantom data			
f. Data composition appropriateness for AI/ML application			
g. Description of the "ground truth," that is, the reference standard, including the annotation process, level of subjectivity, and uncertainty			
h. Data partitioning into training, validation (tuning), and test sets including any criteria to mitigate bias and justification of sample sizes			
i. Final validation using public dataset or study dataset to be shared/made publicly available (desirable but not required).			
4.1 Methods: Machine learning algorithm			
a. Methodology in sufficient detail to allow replication, including model architecture, hyperparameters, inputs, dimensionality of the input (e.g., 2D or 3D images), pre-processing, output type and definition, and discretization/binning, if any.			
b. Training/optimization method including loss function, regularization approach, data imbalance mitigation process (if needed), measures to minimize overfitting and bias, and ablation studies, if any.			
c. AI/ML software code to be shared/made publicly available (desirable but not required).			
4.2 Methods: Performance and statistics			
a. Performance metric(s) including any postprocessing (such as scoring criteria, decision threshold, binning) of the AI/ML output.			
b. Method(s) to estimate the uncertainty (such as 95% confidence intervals) of the performance metric(s).			
c. Significance of the obtained results compared to the null hypothesis (if applicable) or compared to a suitable benchmark metric.			
d. Subgroup analyses for important subgroups (e.g., by age, lesion size).			
e. Demonstrative results for the training, validation (tuning), and test sets.			
5. Discussion			
a. Conclusions as supported by the results.			
b. Limitations of the study.			
c. Discussion/summary of innovation (algorithm or application), significance (clinical or scientific), and/or contributions to the field of medical physics.			

Issam El Naqa[1]
John M. Boone[2]
Stanley H. Benedict[3]
Mitchell M. Goodsitt[4]
Heang-Ping Chan[4]
Karen Drukker[5]
Lubomir Hadjiiski[4]
Dan Ruan[6]
Berkman Sahiner[7]

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Novelty	Please briefly (150 words or less) describe the novelty and/or significance of your study.: N/A If there is anything you wish to tell the editor that is not covered in this submission questionnaire, please enter it here: N/A
Artificial Intelligence and Machine Learning	Is this article on the topic of artificial intelligence or machine learning?: Yes The number of training, validation, and test sets are described in the Abstract. The number of input data and output results, along with the type of data (e.g. MRI images, CT images, etc.) are mentioned in the Abstract.: No The stage of development is described in the manuscript Introduction.: Yes The data, its source, and data composition are described in detail in the Materials section.: No The details of the machine learning algorithm, including pre-processing and training method, are provided in the Methods section. All major results are accompanied by appropriate tests of statistical significance.: No The innovation, significance, and/or contributions to the field of medical physics are discussed in the Discussion section.: Yes
Author ORCID Status	0 of 1 ORCIDs available.
NIH Funding	No funding has been received from NIH
CrossCheck Manuscript	Never Processed / Send File

Manuscript Items

Issam El Naqa[1]
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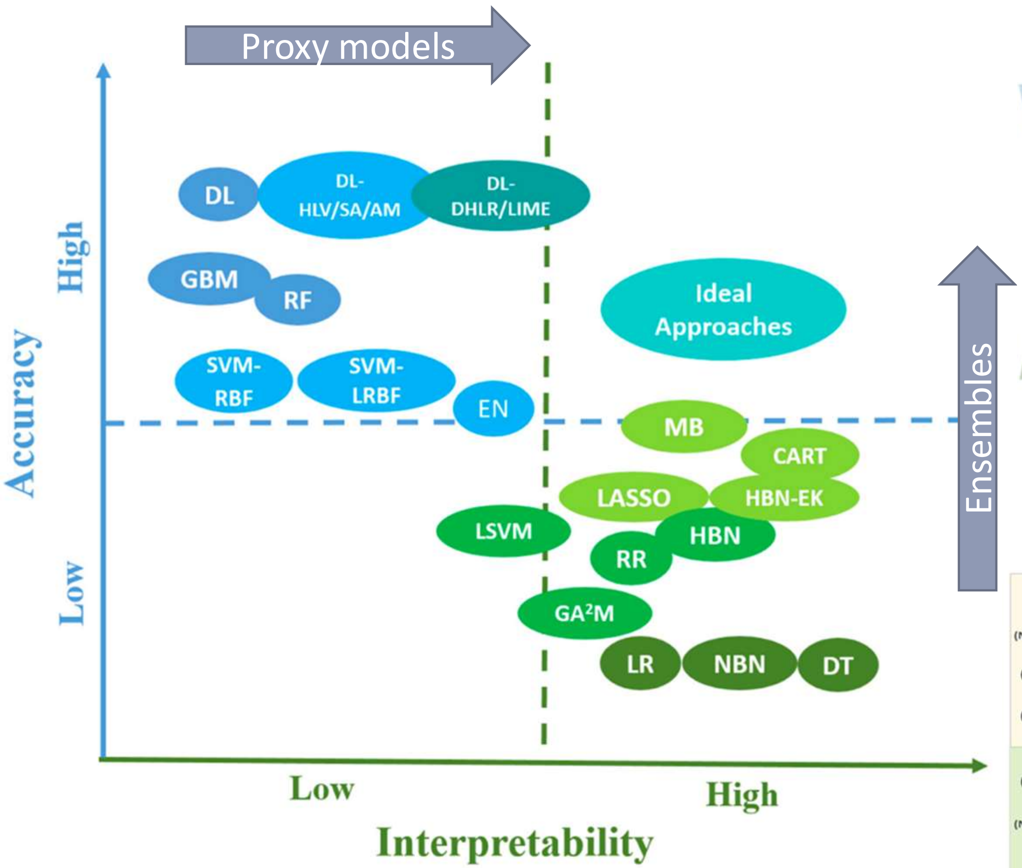
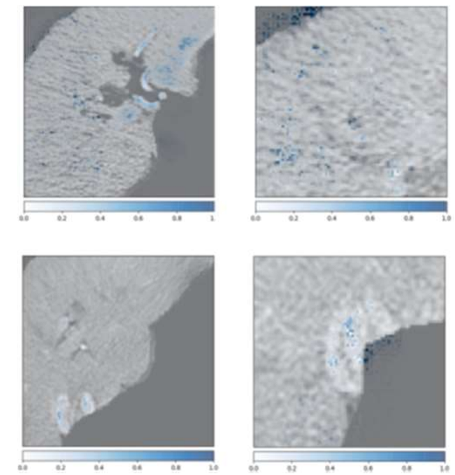
Heang-Ping Chan[4]
Karen Drukker[5]
Lubomir Hadjiiski[4]
Dan Ruan[6]
Berkman Sahiner[7]

ML Accuracy versus interpretability



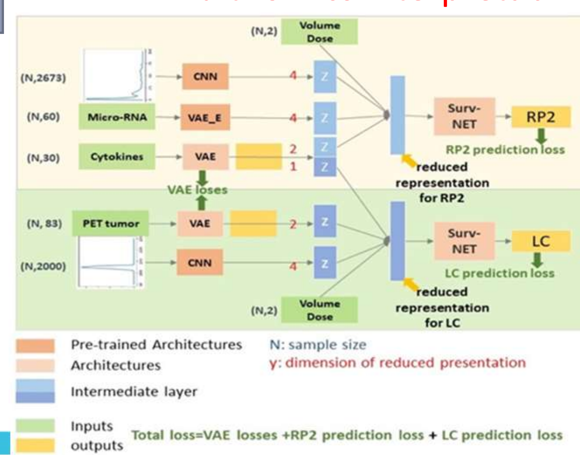
Luo, BJR-O, 2019

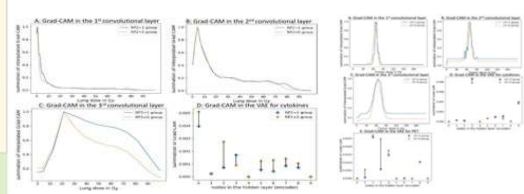
Radiomics Interpretability for Liver Cancer (Grad-CAM)



Wei et al, Physica Medica, 2021

Multi-omics interpretability for Lung Cancer





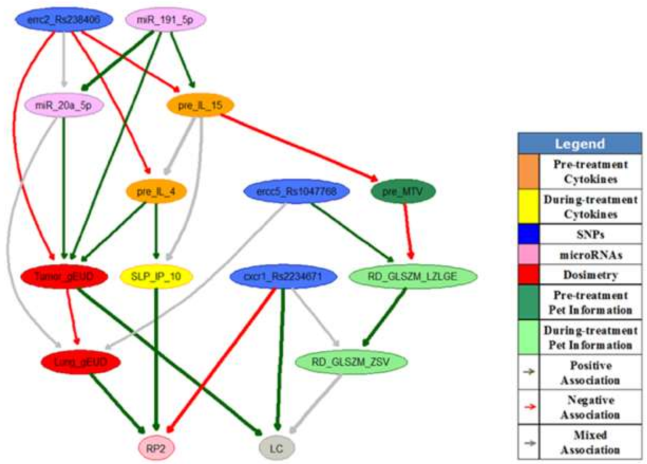
Cui et al, IJROBP, 2021

Intelligence augmentation (IA) instead of AI

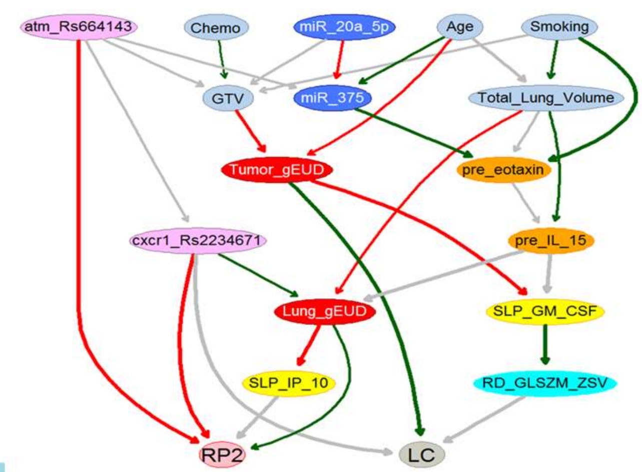
Human in the loop!

Figure 1. A "Fundamental Theorem" of informatics.
(C. Friedman)

Data-driven ML



Human + Data-driven ML

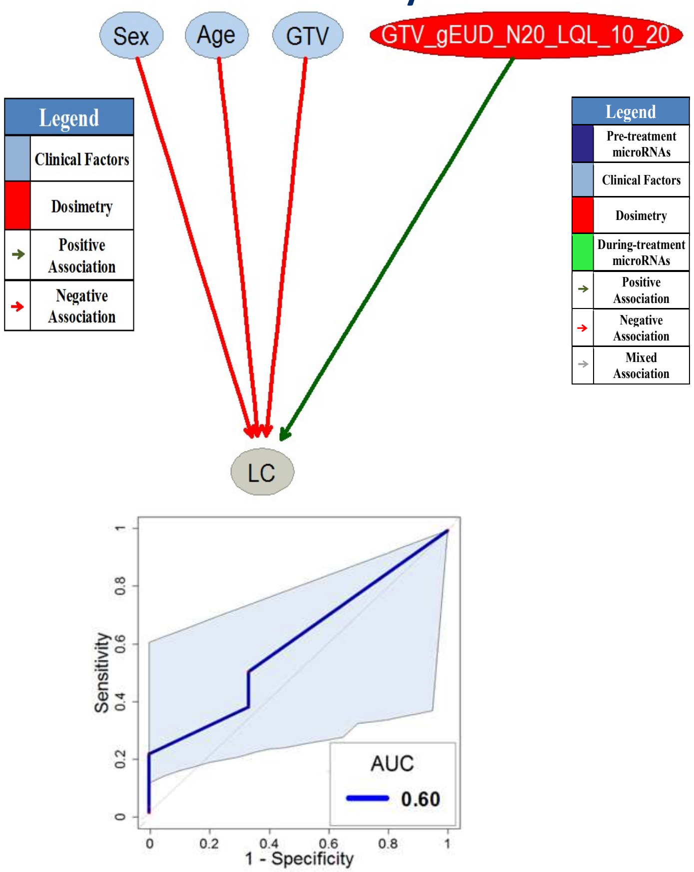


Tighter CIs but similar predictions!

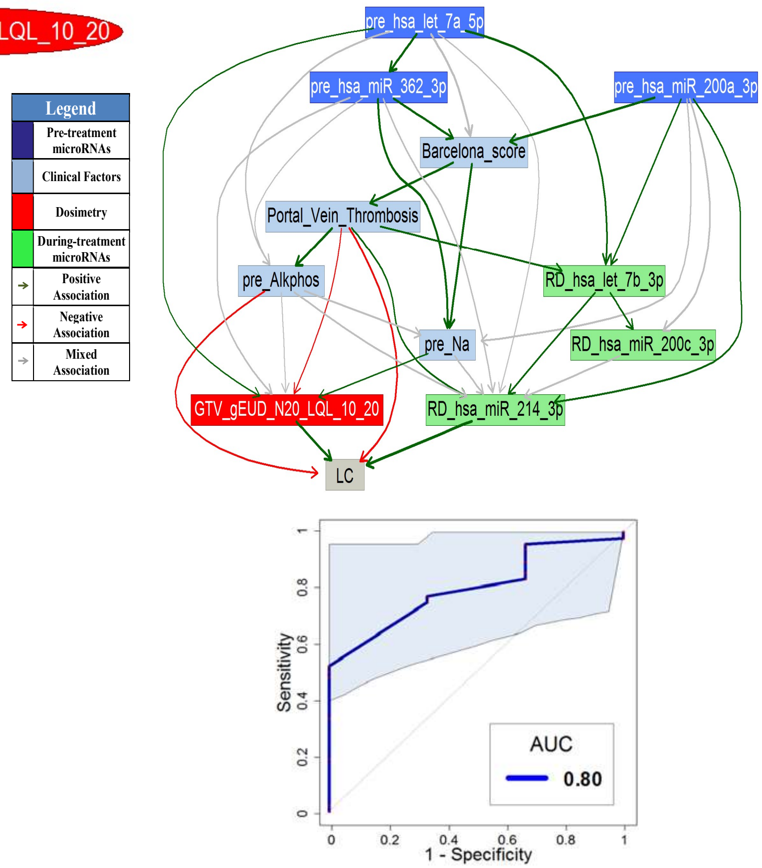
Luo, Physica Medica (Editor Choice), 2021

Human-in-the loop: Predicting Local Control in Liver Cancer

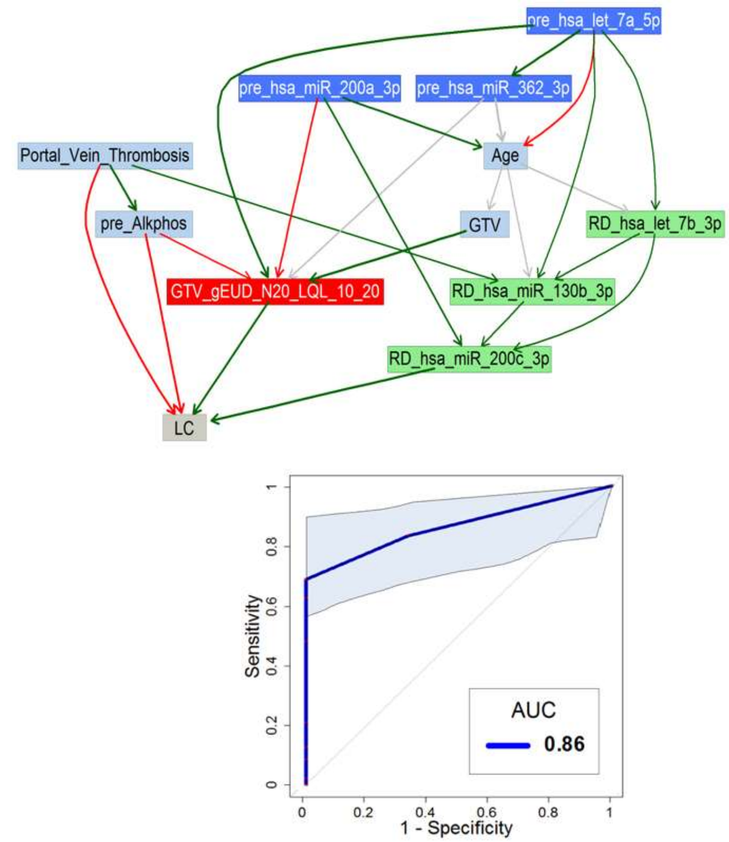
Human only



Machine only



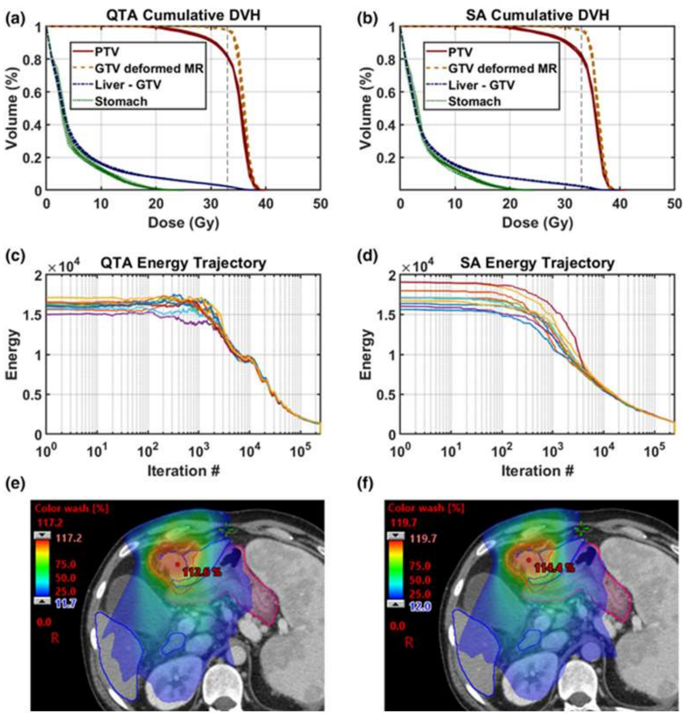
Human + Machine



Luo et al, Front Oncol, 2022

Can Quantum theory help develop more robust AI/ML algorithms?

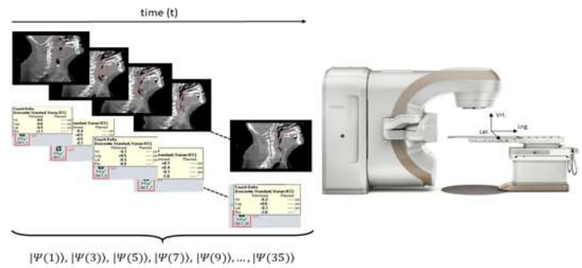
Treatment Planning

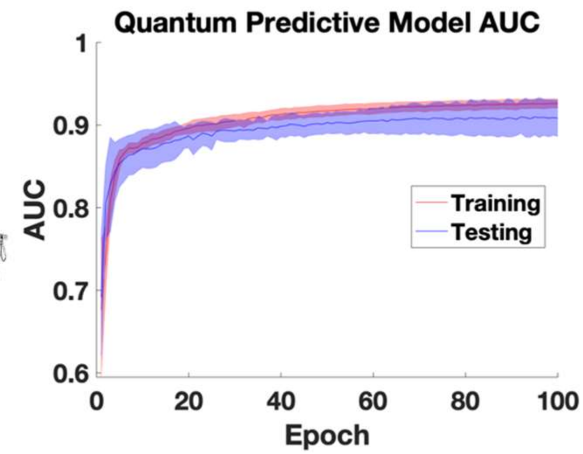


Algorithm	Width Function	Mean Convergence Rate (s)
SA	N/A	1157 ± 154.5
QTA	Hybrid	757.8 ± 162.3
QTA	MOCVD	622.1 ± 103.2
QTA	Sinusoid	526.2 ± 126.1

Pakela, Med Phys, 2020, (Editor's Choice)

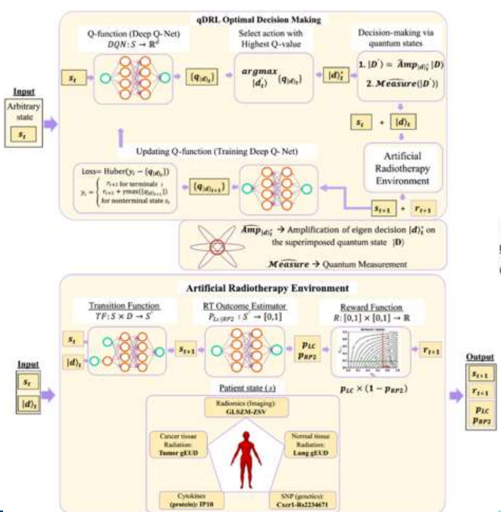
Image-guided radiotherapy

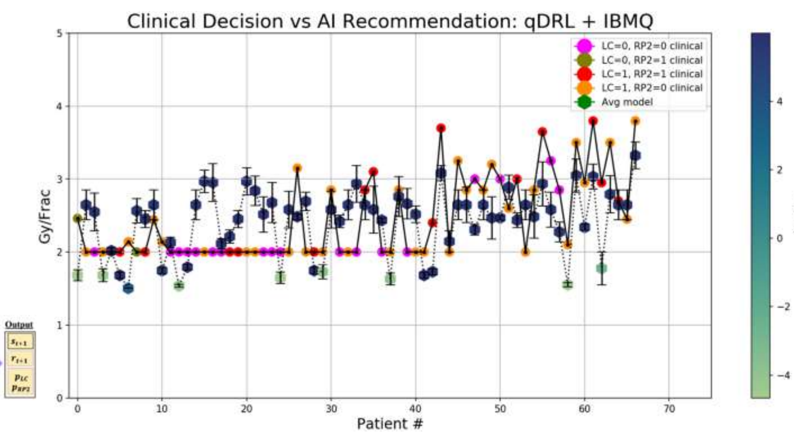




Pakela et al, PMB, 2021

Clinical Decision support





Niraula et al, Nature Sci Rep, 2021

Take home Messages

- Artificial intelligence/machine learning offers new opportunities to develop better understanding of oncology and its diagnosis, prognosis, and treatment regimens
- ML/DL algorithms vary in accuracy and interpretability levels and choice of proper algorithm(s) is an application and data dependent
- Proper development and deployment of AI/ML involves following guidelines (CLAMP) while adhering to ethical AI standards to achieve trustworthiness
- To overcome current barriers in AI/ML for healthcare emerging methods include visualization for interpretability (Grad-CAM) and behavioral science (human-in-the loop), and physics-based (quantum computing) techniques
- Collaboration between stakeholders (data scientists, biologists, physicists, economists, clinical practitioners, regulators & vendors) will allow for safe and beneficial application of AI in biomedicine, radiology and oncology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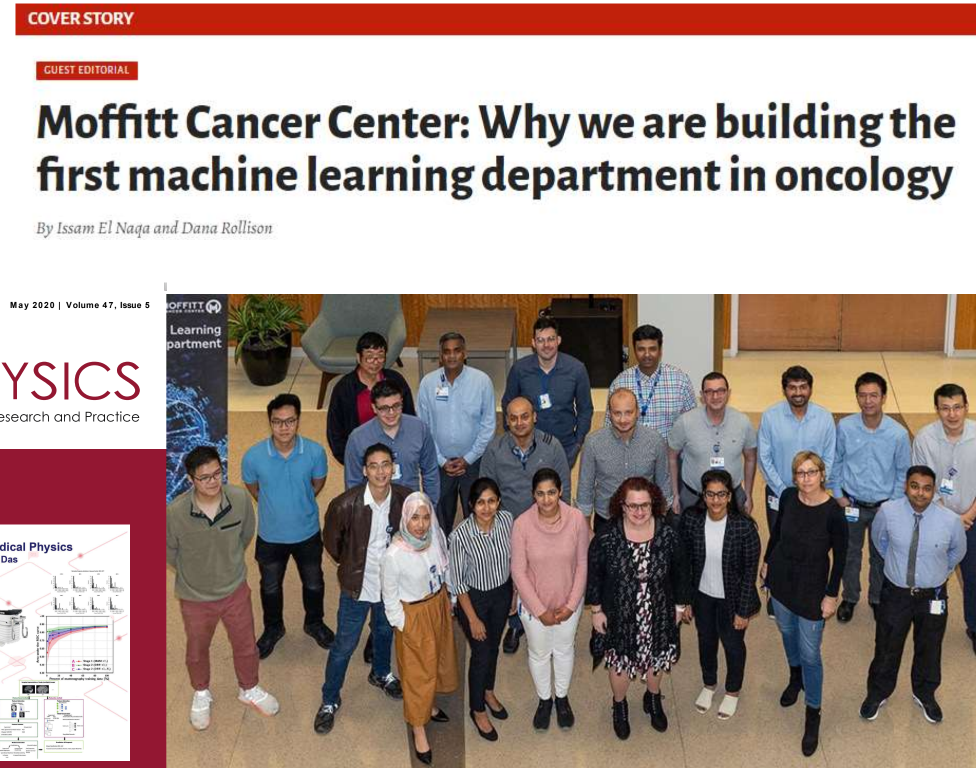
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