Applications of Deep Learning in Diagnostic Image Analysis

The National Academies of Sciences, Engineering, and Medicine
National Cancer Policy Forum
Workshop on Digital Health
July 13-14th, 2020

Sanjay Aneja, MD

Assistant Professor

Department of Therapeutic Radiology

Yale School of Medicine

Yale | The Aneja Lab

CORE CENTER FOR OUTCOMES RESEARCH AND EVALUATION

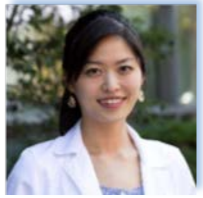
Yale CANCER CENTER
A Comprehensive Cancer Center Designated by the National Cancer Institute

Aneja Lab

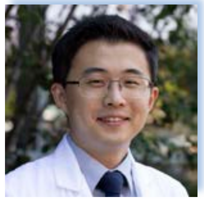
PI
Sanjay Aneja, MD

GRAD STUDENT
Yongfeng Hui

UNDERGRADUATE
Justin Du



RESIDENT
Sarah Gao, MD



RESIDENT
Daniel Yang, MD

RESIDENT
Benjamin Greenberger, MD

ASST. PROFESSOR
Daniel Pinkham, PhD

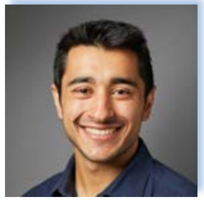
POSTDOC
Sachin Umrao, PhD

MEDICAL STUDENT
Aidan Gilson, BS

MEDICAL STUDENT
Enoch Chang, BS

MEDICAL STUDENT
Rachel Choi, BS

UNDERGRADUATE
Gabriel Saruhashi



MEDICAL STUDENT
Guneet Janda, BS

- CLINICIANS
- DATA SCIENTISTS
- COMPUTER SCIENTISTS
- MATHEMATICIANS
- ENGINEERS

RESEARCH AREAS

1. Machine learning algorithm development
2. Data science theory
3. Clinical applications of existing machine learning techniques

Pathway for Model Development

GOOD CLINICAL QUESTION → **FIND & COLLECT APPROPRIATE DATA** → **COMPARE MODEL CANDIDATES & GOLD STANDARD** → **EXTERNAL VALIDATION** → **SURVEILLANCE & VULNERABILITY STUDIES**

Imaging Biomarkers
Lymph Node Classification

Multi-Institutional Validation of Deep Learning for Pretreatment Identification of Extranodal Extension in Head and Neck Squamous Cell Carcinoma

Benjamin H. Kann, MD[1]; Daniel F. Hicks, MD[2]; Sam Payabvash, MD[3]; Amit Mahajan, MD[3]; Justin Du, BS[4]; Vishal Gupta, MD[2]; Henry S. Park, MD, MPH[4]; James B. Yu, MD[4]; Wendell G. Yarbrough, MD, MMHC[5]; Barbara A. Burtness, MD[6]; Zain A. Husain, MD[7]; and Sanjay Aneja, MD[4]

SCIENTIFIC REPORTS

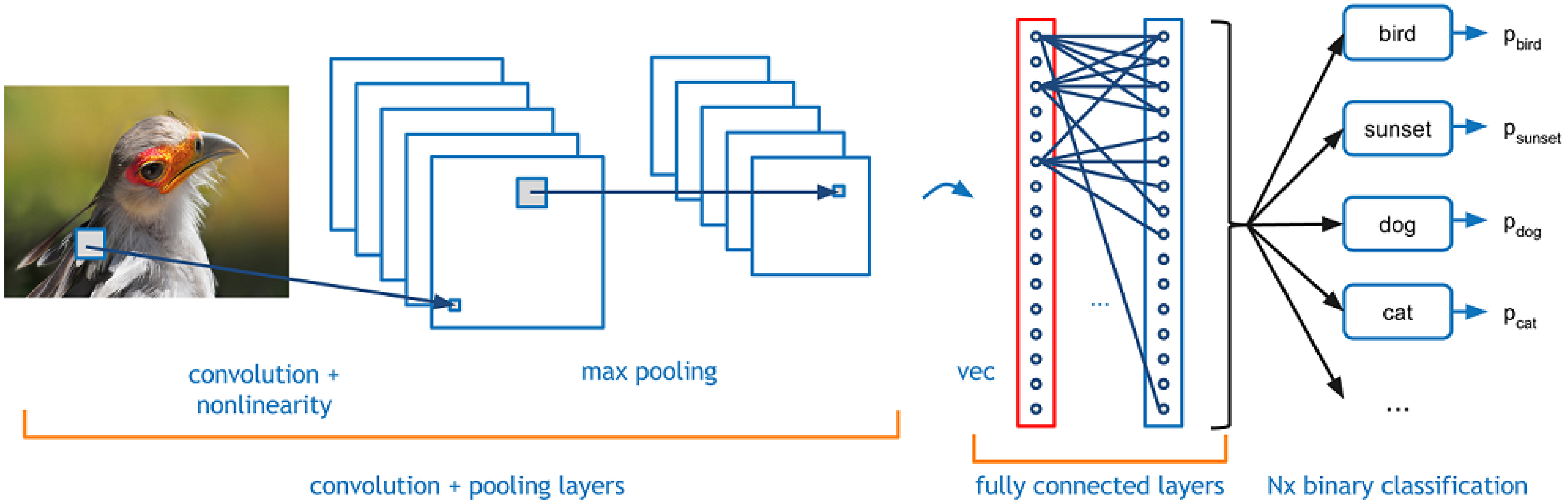
OPEN

Received: 25 May 2018
Accepted: 7 September 2018
Published online: 19 September 2018

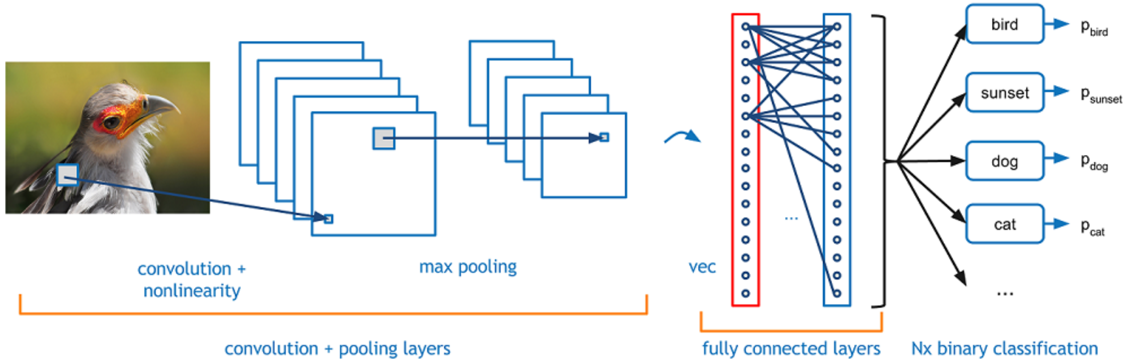
Pretreatment Identification of Head and Neck Cancer Nodal Metastasis and Extranodal Extension Using Deep Learning Neural Networks

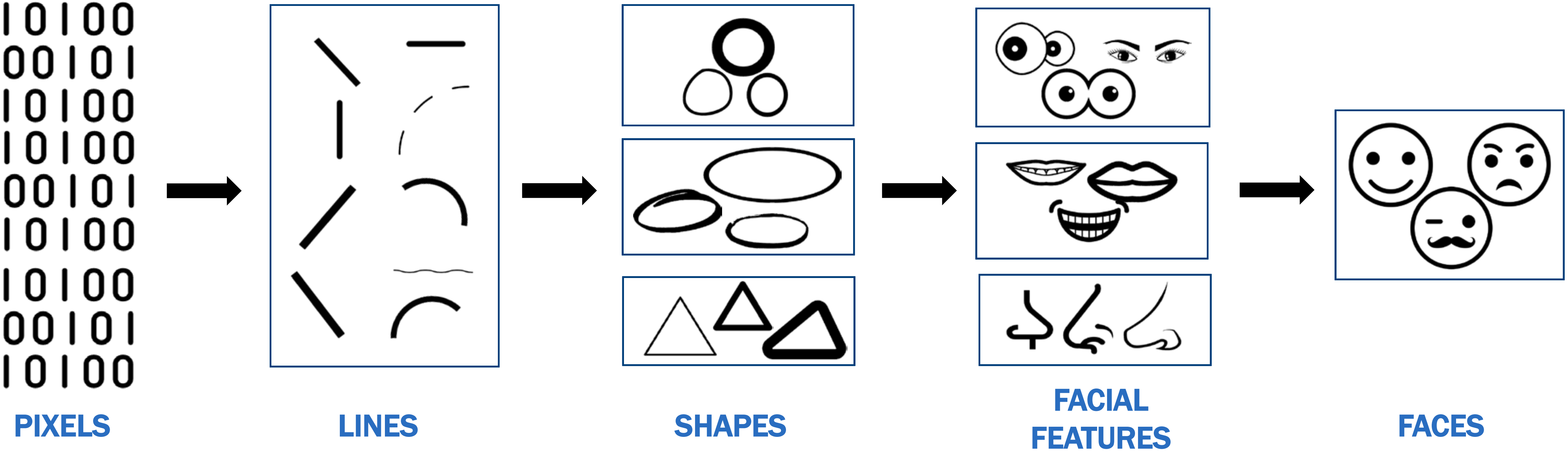
Benjamin H. Kann[1], Sanjay Aneja[1], Gokoulakrichenane V. Loganadane[1], Jacqueline R. Kelly[1], Stephen M. Smith[2], Roy H. Decker[1], James B. Yu[1], Henry S. Park[1], Wendell G. Yarbrough[3], Ajay Malhotra[4], Barbara A. Burtness[5] & Zain A. Husain[1]

Convolutional Neural Networks

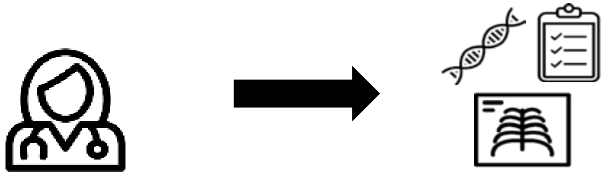


Convolutional Neural Networks





Imaging Biomarkers
Lymph Node Classification

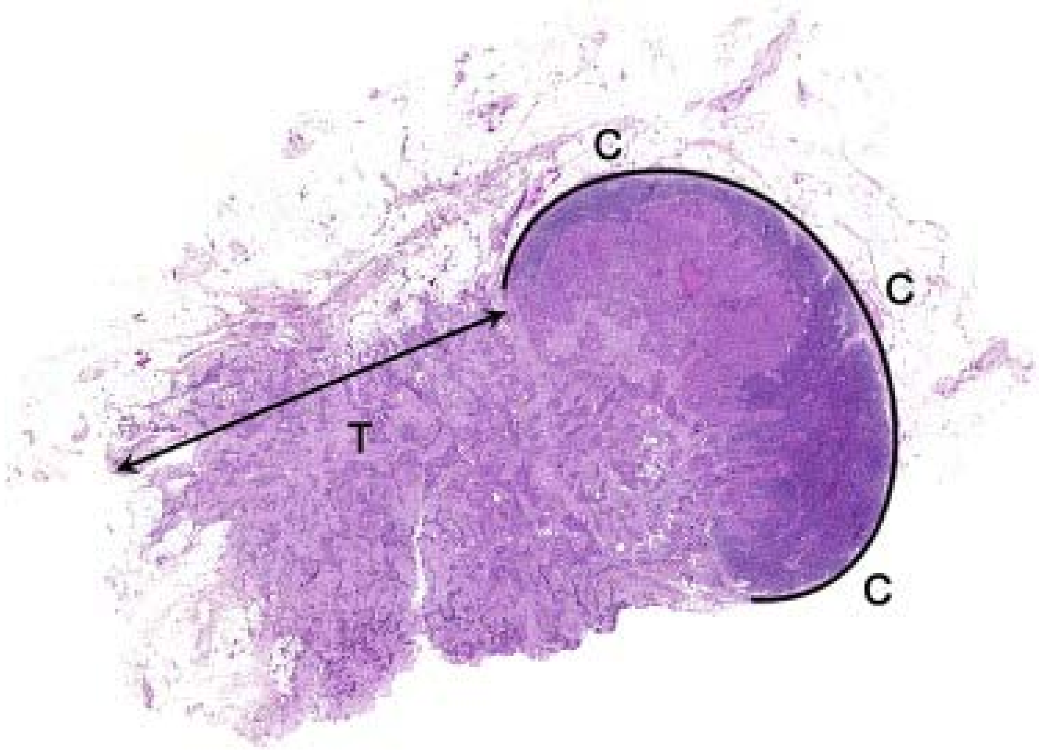


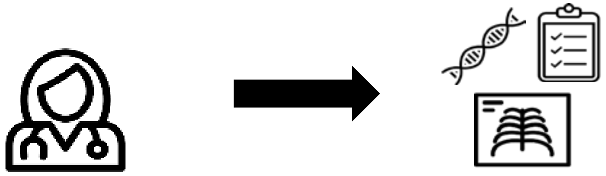
GOOD CLINICAL QUESTION

FIND & COLLECT APPROPRIATE DATA

CLINICAL PROBLEM

- Presence of cancer within LNs affects prognosis
- Identification of cancer within LN is difficult to complete non-invasively
- The presence of extranodal extension (ENE) of cancer in LN is often requires adjuvant treatment escalation
- Preoperative identification of patients with ENE may reduce need for surgical interventions





GOOD CLINICAL QUESTION

FIND & COLLECT APPROPRIATE DATA

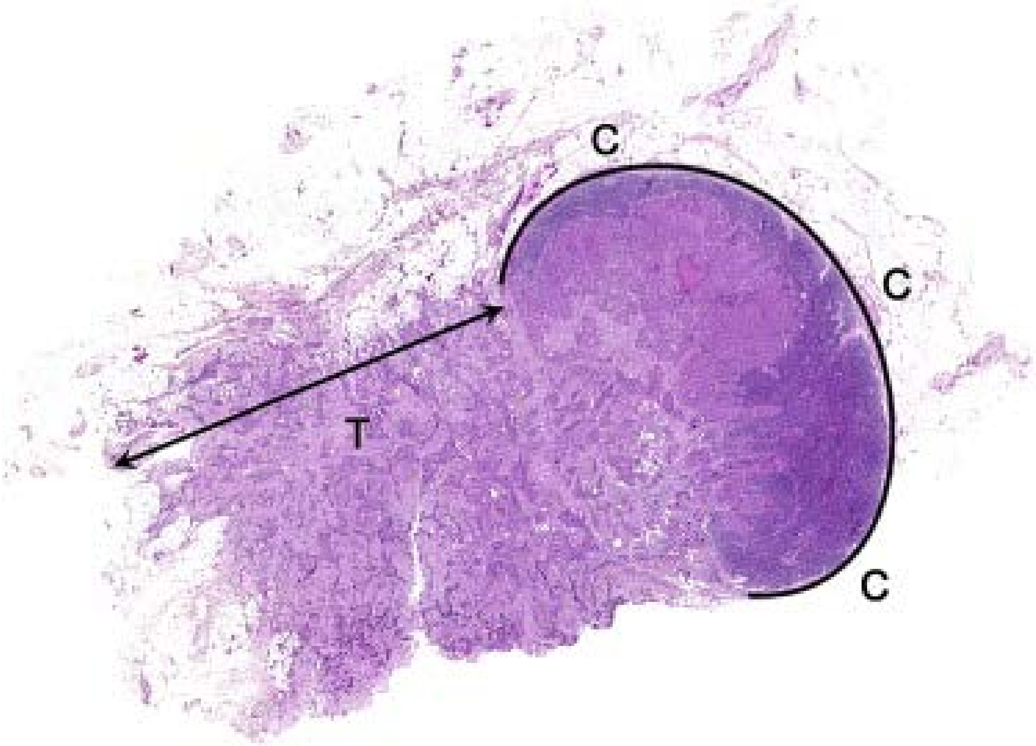
Imaging Biomarkers
Lymph Node Classification

HYPOTHESIS

- **Machine learning analysis of pre-operative diagnostic images could effectively classify LN in head and neck cancer patients**

1. Identification of positive LN on preoperative CT imaging

2. Identification of ENE within LN on preoperative CT imaging



Imaging Biomarkers
Lymph Node Classification

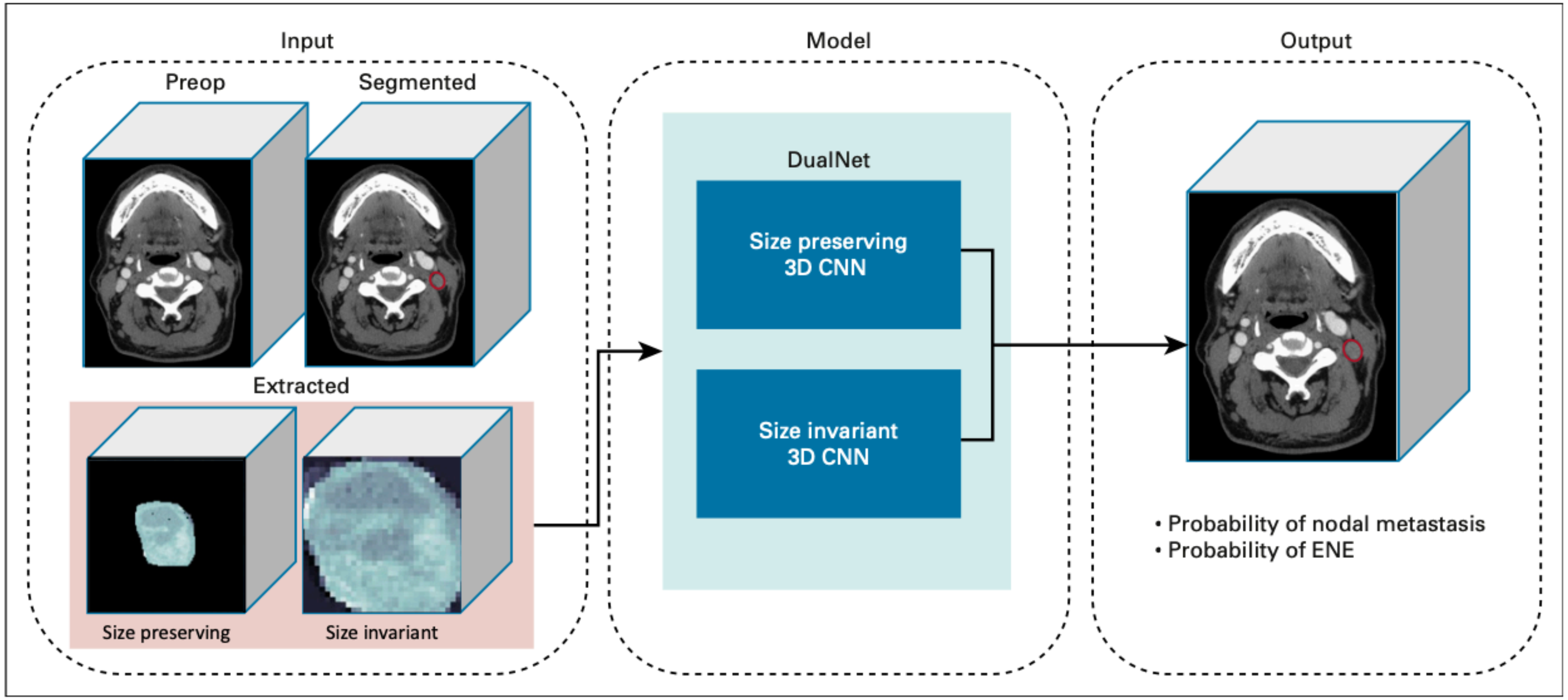
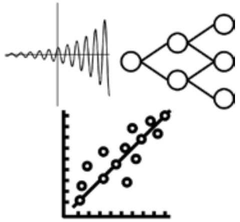
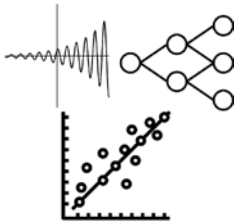


FIG 1. Deep learning algorithm framework. For each patient computed tomography scan, the algorithm uses 3-dimensional (3D) segmented lymph node region-of-interest inputs with two representations: a size-preserving input, and a size-invariant input. These inputs are fed into the DualNet 3D convolutional neural network (CNN), which outputs a probability of nodal metastasis and extranodal extension (ENE) for each input lymph node.

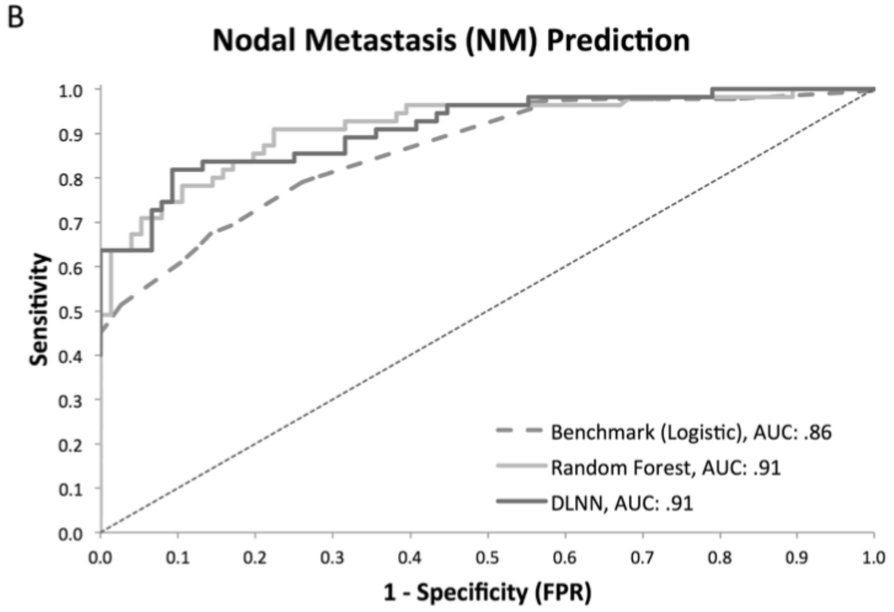


COMPARE MODEL CANDIDATES & GOLD STANDARD

Imaging Biomarkers
Lymph Node Classification



COMPARE MODEL CANDIDATES
& GOLD STANDARD



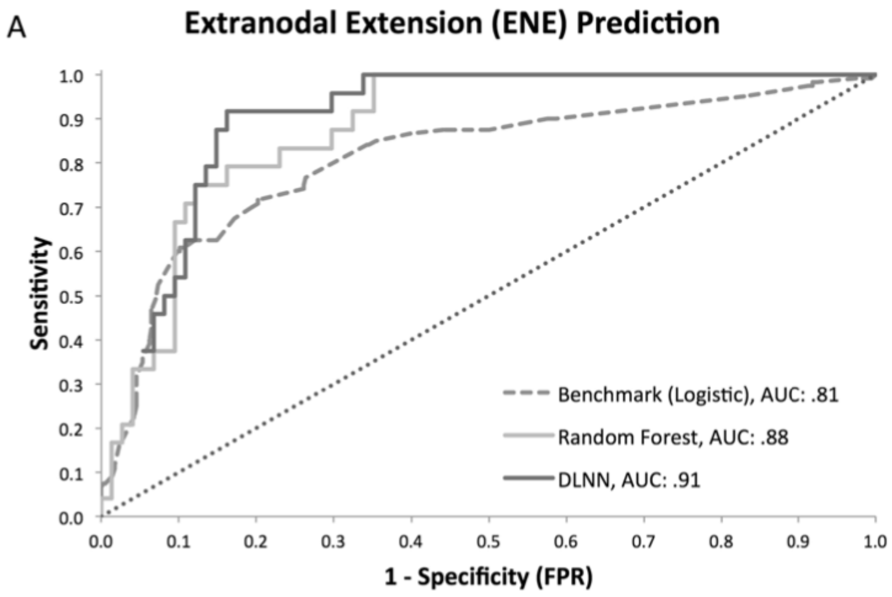


Figure 3. (**A**,**B**) Test Set ROC Curve Comparisons for Extranodal Extension (ENE) and Nodal Metastasis Prediction for Deep Learning Neural Network (DLNN), Radiomic Feature Random Forest, and Benchmark Logistic Model.

Imaging Biomarkers
Lymph Node Classification

EXTERNAL VALIDATION

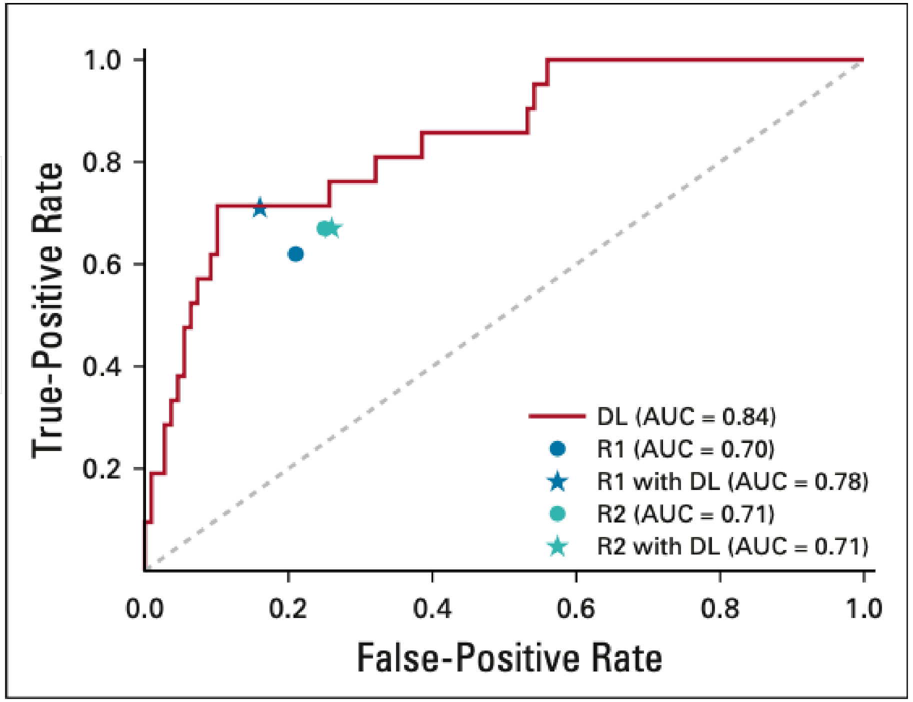


FIG 2. Receiver operating characteristic plots for extranodal extension identification for deep learning (DL [DualNet]) algorithm and radiologists (R1, R2): Mount Sinai Patients. AUC, area under the curve.

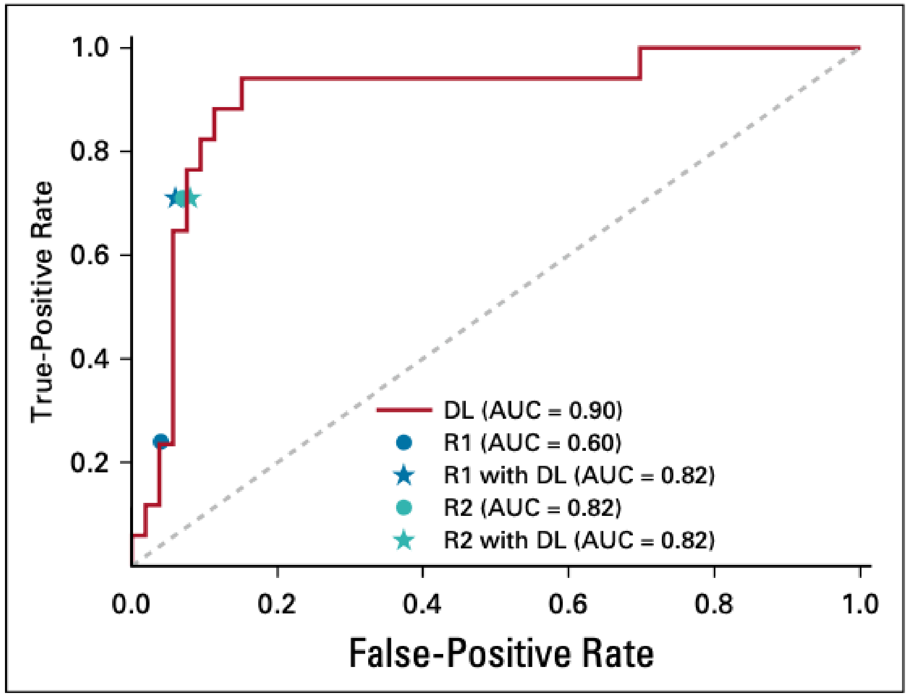


FIG 3. Receiver operating characteristic plots for extranodal extension identification for deep learning (DL [DualNet]) algorithm and radiologists (R1, R2): The Cancer Imaging Archive–The Cancer Genome Atlas patients.

Imaging Biomarkers
Lymph Node Classification

EXTERNAL VALIDATION

TABLE 2. DL Algorithm Performance for ENE Identification and Radiologist Comparisons on External Test Sets

Performance Metric	Internal Test Set (n = 98)	Mount Sinai Validation (n = 130)			TCIA-TCGA Validation (n = 70)		
	DL	DL	R1	R2	DL	R1	R2
AUC (95% CI)	0.91 (0.86 to 0.96)	0.84 (0.75 to 0.93)	0.70 (0.59 to 0.82)	0.71 (0.60 to 0.82)	0.90 (0.81 to 0.99)	0.60 (0.49 to 0.71)	0.82 (0.71 to 0.94)
Accuracy, %	85.7	83.1	76.2	73.8	88.6	78.6	88.6
Sensitivity	0.88	0.71	0.62	0.67	0.82	0.24	0.71
Specificity	0.85	0.85	0.79	0.75	0.91	0.96	0.94
PPV	0.66	0.48	0.36	0.34	0.74	0.67	0.80
NPV	0.95	0.94	0.91	0.92	0.94	0.80	0.91
Youden index	0.73	0.56	0.41	0.42	0.73	0.20	0.65
Cohen κ score			0.43			0.29	

Abbreviations: AUC, area under the curve; DL, deep learning (DualNet algorithm); ENE, extranodal extension; NPV, negative predictive value PPV, positive predictive value; R, radiologist.

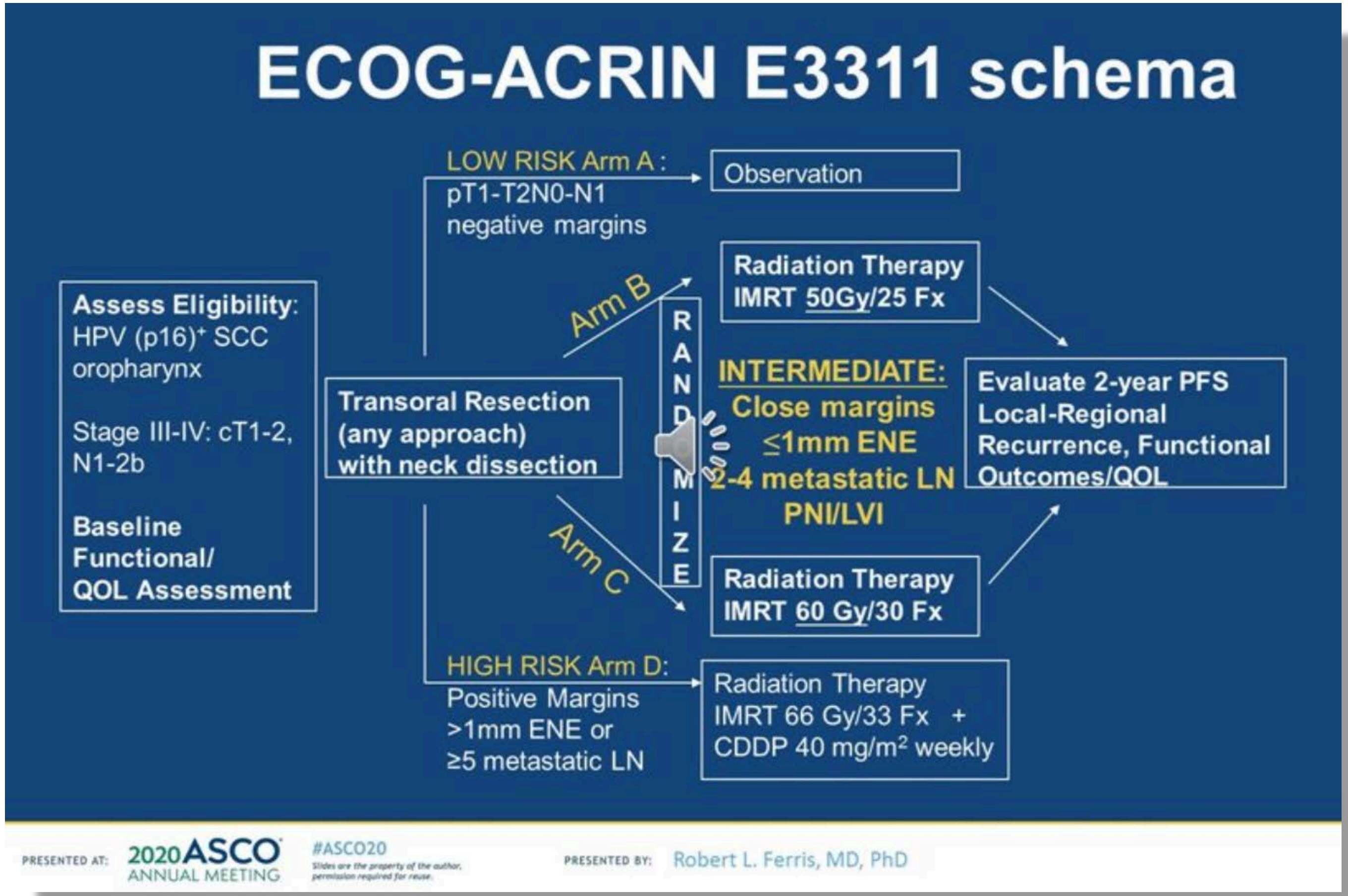
TABLE 3. Radiologist Performance With DL Assistance

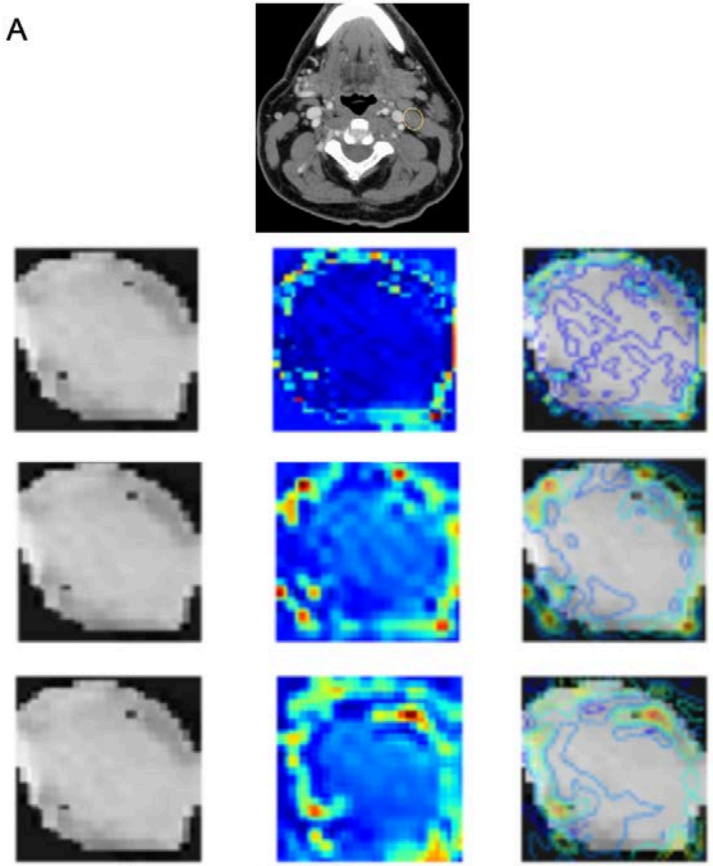
Performance Metric	Mount Sinai Validation		TCIA-TCGA Validation	
	R1 With DL	R2 With DL	R1 With DL	R2 With DL
AUC (95% CI)	0.78 (0.67 to 0.88)	0.71 (0.59 to 0.82)	0.82 (0.71 to 0.94)	0.82 (0.71 to 0.94)
Accuracy	82.3	73.1	88.6	88.6
Sensitivity	0.71	0.67	0.71	0.71
Specificity	0.84	0.74	0.94	0.94
PPV	0.47	0.33	0.80	0.80
NPV	0.94	0.92	0.91	0.91
Youden index	0.55	0.41	0.65	0.65
Cohen κ score	0.74		0.75	

Abbreviations: AUC, area under the curve; DL, deep learning (DualNet algorithm); NPV, negative predictive value; PPV, positive predictive value; R, radiologist.

Imaging Biomarkers
Lymph Node Classification

SURVEILLANCE & VULNERABILITY STUDIES





Final Thoughts

Quantitative imaging methods appear to have utility in clinical oncology

-Non-invasive risk stratification

-Clinical decision aids

Despite enthusiasm for machine learning methods, there are necessary steps before clinical implementation

-Rigorous external validation

-Interpretability and vulnerability studies

Questions

sanjay.aneja@yale.edu
www.aneja-lab.org

Github: Aneja-Lab-Yale

Department of Therapeutic Radiology

Department of Statistics and Data Science

Center for Outcome Research and Evaluation