Artificial Intelligence in Imaging

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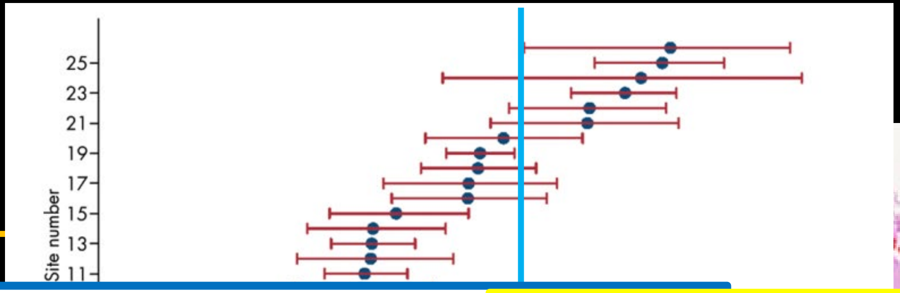
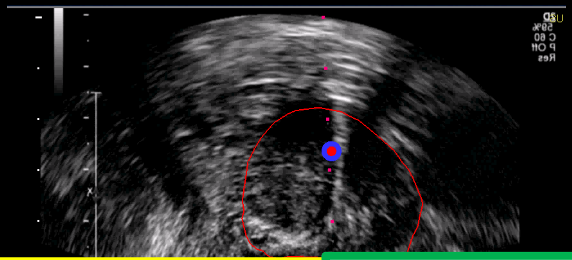
Disclosures

- CRADA: NVIDIA
- CRADA: Philips
- Royalties from NIH
- Patents in the field of AI
- Research samples of an MRI artificial intelligence (AI) algorithm developed in NCI in collaboration with NVIDIA will be shown in this talk

Prostate Cancer

- Most common cancer type among biologically male individuals in the entire World.
- Top 3 leading cause of cancer related deaths (lung, prostate, colorectal).
- Complex disease course:
  - Localized
  - Biochemical recurrence
  - Metastatic
    - ADT sensitive
    - ADT resistant





- EM tracking
- Fixed arm
- Image-image fusion
- In-bore

Eur Radiol (2012) 22:746–757
DOI 10.1007/s00330-011-2377-y

UROGENITAL

ESUR prostate MR guidelines 2012

Jelle O. Barentsz · Jonathan Richenberg · Richard Clements · Peter Choyke · Sadhna Verma · Geert Villeirs · Olivier Rouviere · Vibeke Logager · Jurgen J. Fütterer

Received: 16 October 2011 / Revised: 23 November 2011 / Accepted: 2 December 2011 / Published online

Abstract The aim was to develop clinical guidelines for multi-parametric MRI of the prostate by a group of prostate MRI experts from the European Society of Urogenital Radiology (ESUR), based on literature evidence and consensus expert opinion. True evidence-based guidelines could not be formulated, but a compromise, reflected by "minimal" and "optimal" requirements has been made. The scope of these ESUR guidelines is to promulgate high quality MRI in acquisition and evaluation with the correct indications for prostate cancer across the whole of Europe and eventually outside Europe. The guidelines for the optimal technique and three protocols for "detection", "staging" and "node and bone" are presented. The use of endorectal coil vs. pelvic phased array coil and 1.5 vs. 3 T is discussed. Clinical indications and a PI-RADS classification for structured reporting are presented.

Key Points
- *This report provides gu*
  imaging (MRI) in prost
- *Clinical indications, an*
  acquisition protocols ar
- *A structured reporting sy*

Keywords Prostate cance
ESUR

Introduction

In their lifetime, 1 in 6 me
prostate cancer. This acc

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available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Prostate Cancer
Editorial by Jelle O. Barentsz, Jeffrey C. Weinreb, Sadhna Verma et al on pp. 41–49 of this issue

PI-RADS Prostate Imaging – Reporting and Data System: Version 2

Jeffrey C. Weinreb [a,†,], Jelle O. Barentsz [b,†], Peter L. Choyke [c], Francois Cornud [d], Masoom A. Haider [e], Katarzyna J. Macura [f], Daniel Margolis [g], Mitchell D. Schnall Faina Shtern [i], Clare M. Tempany [j], Harriet C. Thoeny [k], Sadna Verma [l]*

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EUROPEAN UROLOGY 76 (2019) 340–351

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European Association of Urology

Review – Prostate Cancer

Prostate Imaging Reporting and Data System Version 2.1: 2019 Update of Prostate Imaging Reporting and Data System Version 2

Baris Turkbey [a,†,], Andrew B. Rosenkrantz [b,†,*], Masoom A. Haider [c], Anwar R. Padhani [d], Geert Villeirs [e], Katarzyna J. Macura [f], Clare M. Tempany [g], Peter L. Choyke [a], Francois Cornud [h], Daniel J. Margolis [i], Harriet C. Thoeny [j], Sadhna Verma [k], Jelle Barentsz [l,‡], Jeffrey C. Weinreb [m,‡]*

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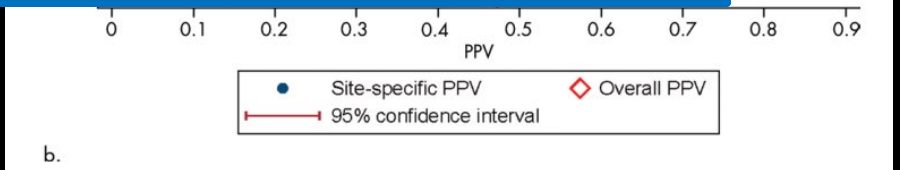


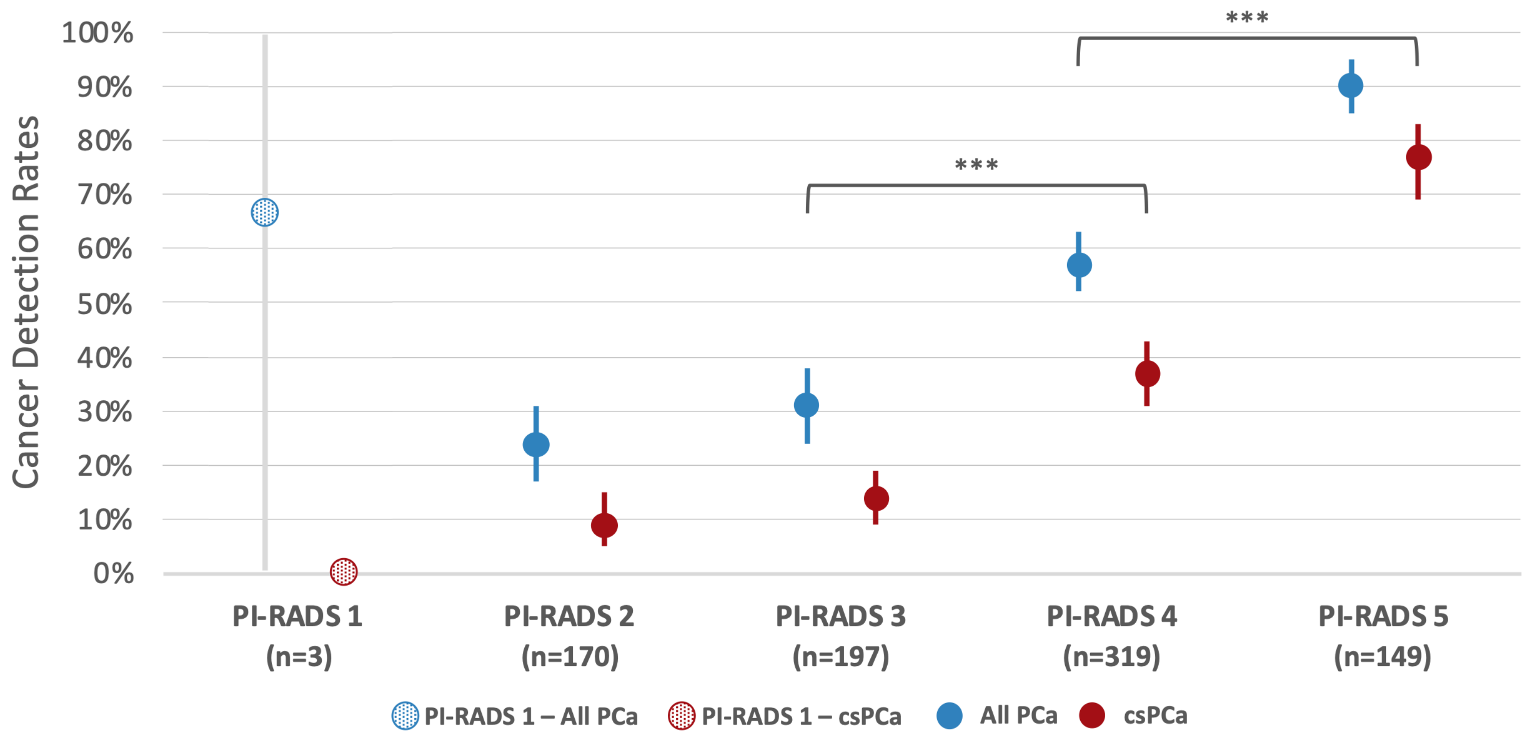
Figure 4: Forest plots show site-specific median positive predictive values (PPVs) of **(a)** Prostate Imaging Reporting and Data System (PI-RADS) score greater than or equal to 3 and **(b)** PI-RADS score greater than or equal to 4. The overall estimated PPV for all sites is also shown.

- AUA guidelines x2
- EAU guidelines x2
- ISUP guidelines x2
- CAP guidelines x2

SAR Article (Radiology 2020)

PI-RADS Category	No. of Lesions	No. of PCa	PCa Rate (%)	95% CI	*P* value	No. of csPCa	csPCa Rate (%)	95% CI	*P* value
1	3	2	67	0 - 100	-	0	0	0 - 0	-
2	170	40	24	17 - 31	.3	16	9	5 - 15	.13
3	197	61	31	24 - 38	.06	27	14	9 - 19	.11
4	319	183	57	52 - 63	<.001	118	37	31 - 43	<.001
5	149	134	90	85 - 95	<.001	114	77	69 - 83	<.001

Lesion-based Cancer Detection Rates



- Higher performance compared to other academic centers and community practice
- Radiologist
- Urologist
- Interventional Radiologist
- Pathologist
- Engineer

Yilmaz EC, et al. Accepted for publication in Radiology (2023)

Can we replicate this performance using AI?

Original Investigation

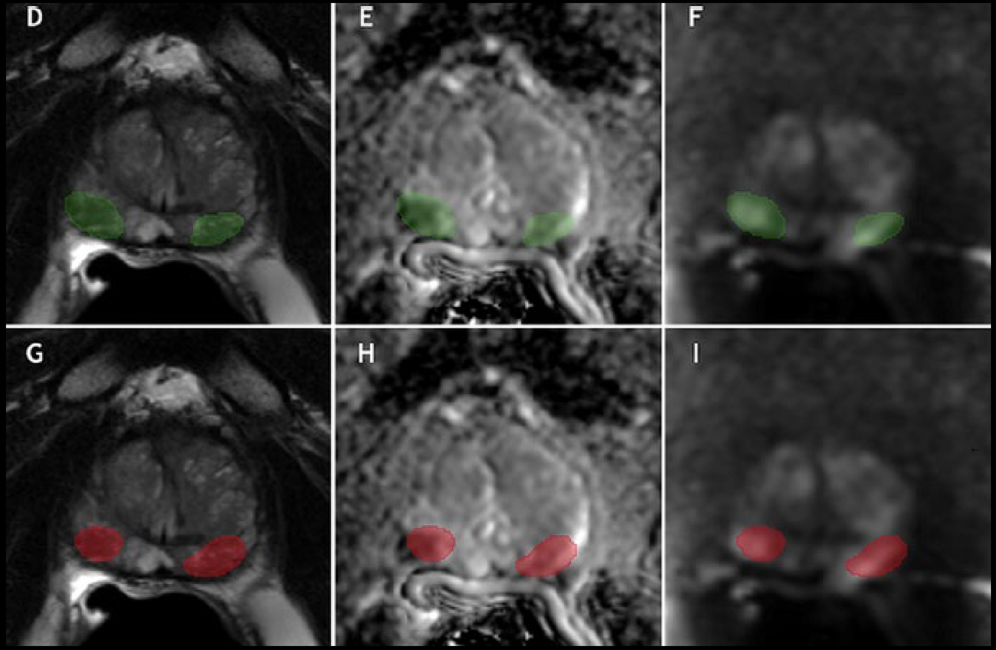
A Cascaded Deep Learning–Based Artificial Intelligence Algorithm for Automated Lesion Detection and Classification on Biparametric Prostate Magnetic Resonance Imaging

Sherif Mehralivand, MD, Dong Yang, PhD, Stephanie A. Harmon, PhD, Daguang Xu, PD, Ziyue Xu, PhD, Holger Roth, PhD, Samira Masoudi, PhD, Thomas H. Sanford, MD, Deepak Kesani, DO, Nathan S. Lay, PhD, Maria J. Merino, MD, Bradford J. Wood, MD, Peter A. Pinto, MD, Peter L. Choyke, MD, Baris Turkbey, MD

- 1390 patients (n=350 outside NIH)
  - train/test (89%/11%)
- Lesions were contoured + assigned PI-RADS category
- 3D U-Net: lesion detection and segmentation
- Two 3D residual neural network: PI-RADS categorization

Radiologist

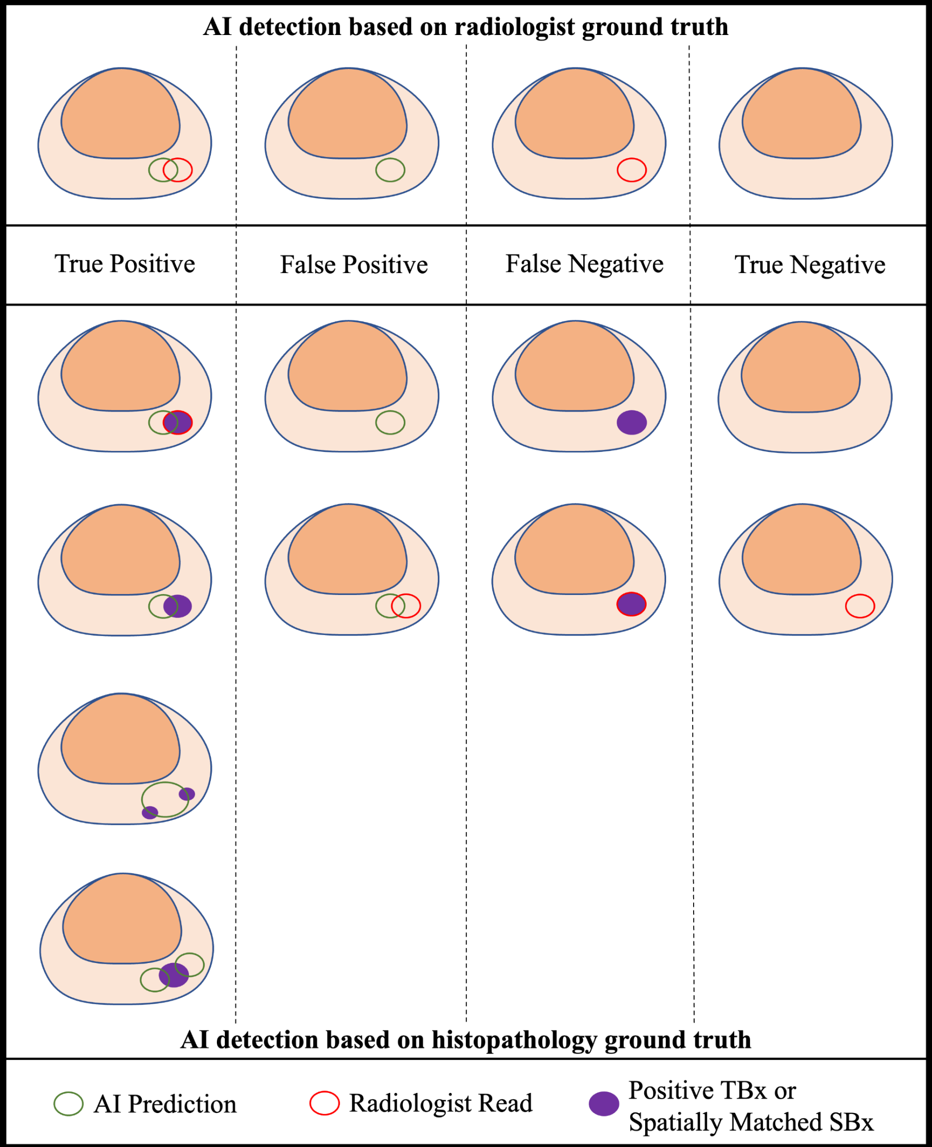
AI



- PPV (CDR) = 63%
- False positives/patient = 0.44 lesion/patient
  - TP= 82% were cancer
  - FP=51% were benign
- Lesion segmentation (DSC) = 0.36
- PI-RADS classification accuracy=58%

Can we replicate this performance using AI?

- April 2019-September 2022
- 658 patients (median age=67 years, PSA=6.7ng/ml)
  - 1029 lesions
  - 31% biopsy naïve
  - 78% Caucasian
  - 40% positive family history of prostate cancer



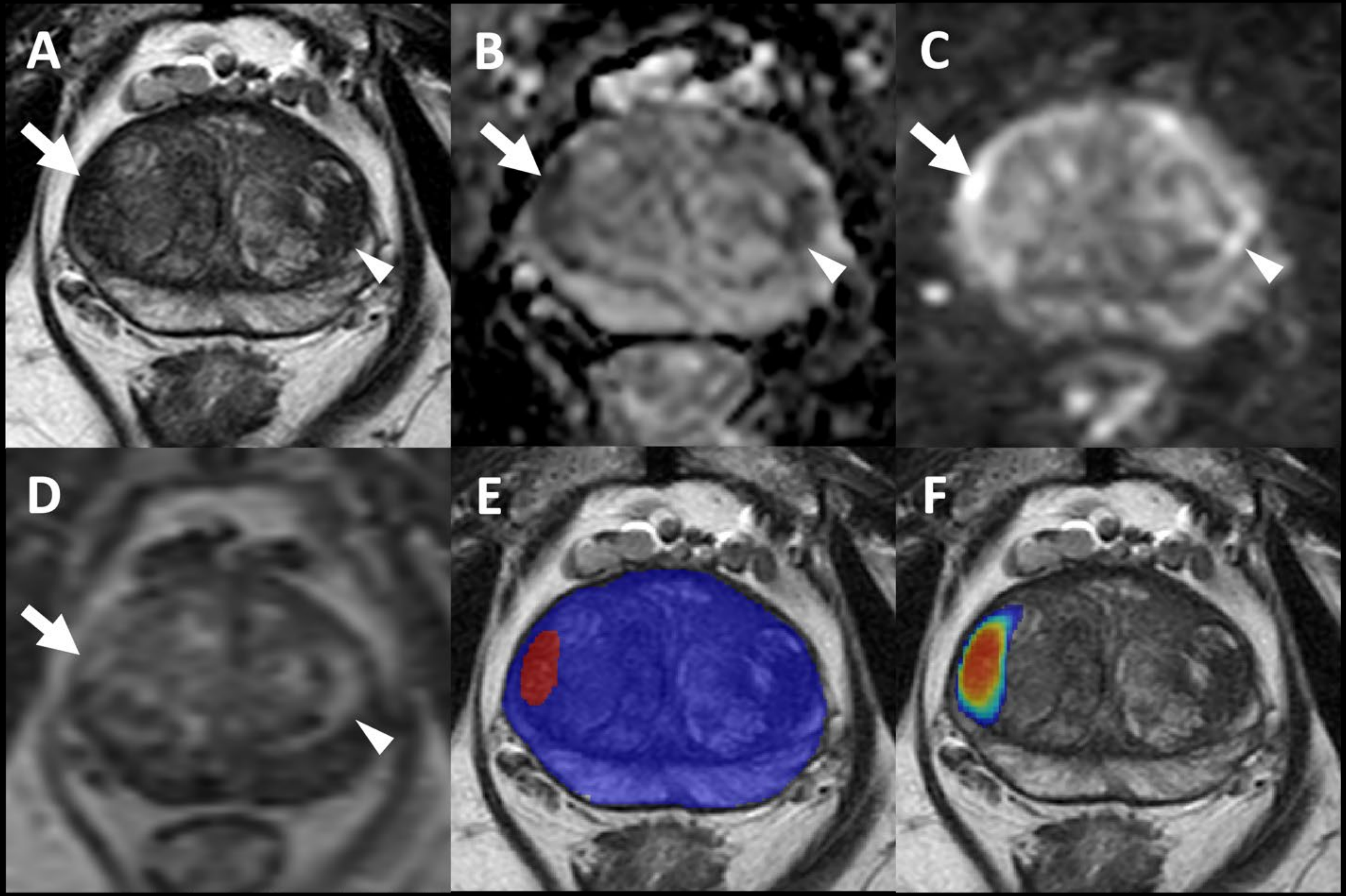
Lin Y, et al. Prepared to be submitted to Radiology (2023)

Can we replicate this performance using AI?

Analysis	TP	FN	FP	TN	Sensitivity		PPV		FDR		Specificity		DSC
					%	95% CI	%	95% CI	%	95% CI	%	95% CI	
Lesion-level	566	463	370	NA	55 (566/1029)	52, 58	60 (566/936)	57, 64	40 (370/936)	36, 43	NA	NA	0.29
Participant-level	519	41	72	23	93 (519/559)	90, 95	88 (519/591)	85, 90	12 (72/591)	10, 15	23 (23/98)	15, 32	0.34

- Mean number of false positive lesions per participant= 0.56 (range 0–3).
- CDR for GG>1 Prostate cancer:
    - AI=96% (281/294; 95% CI: 94, 98) vs. Radiologist= 98% (287/294; 95% CI: 96, 99) (p = 0.24).
    - GG1=84% (103/122)
    - GG2=96% (152/159)
    - GG3=96% (47/49)
    - GG4=95% (38/40)
    - GG5=98% (45/46)

Lin Y, et al. Prepared to be submitted to Radiology (2023)



72-year-old male PSA= 9.1ng/mL

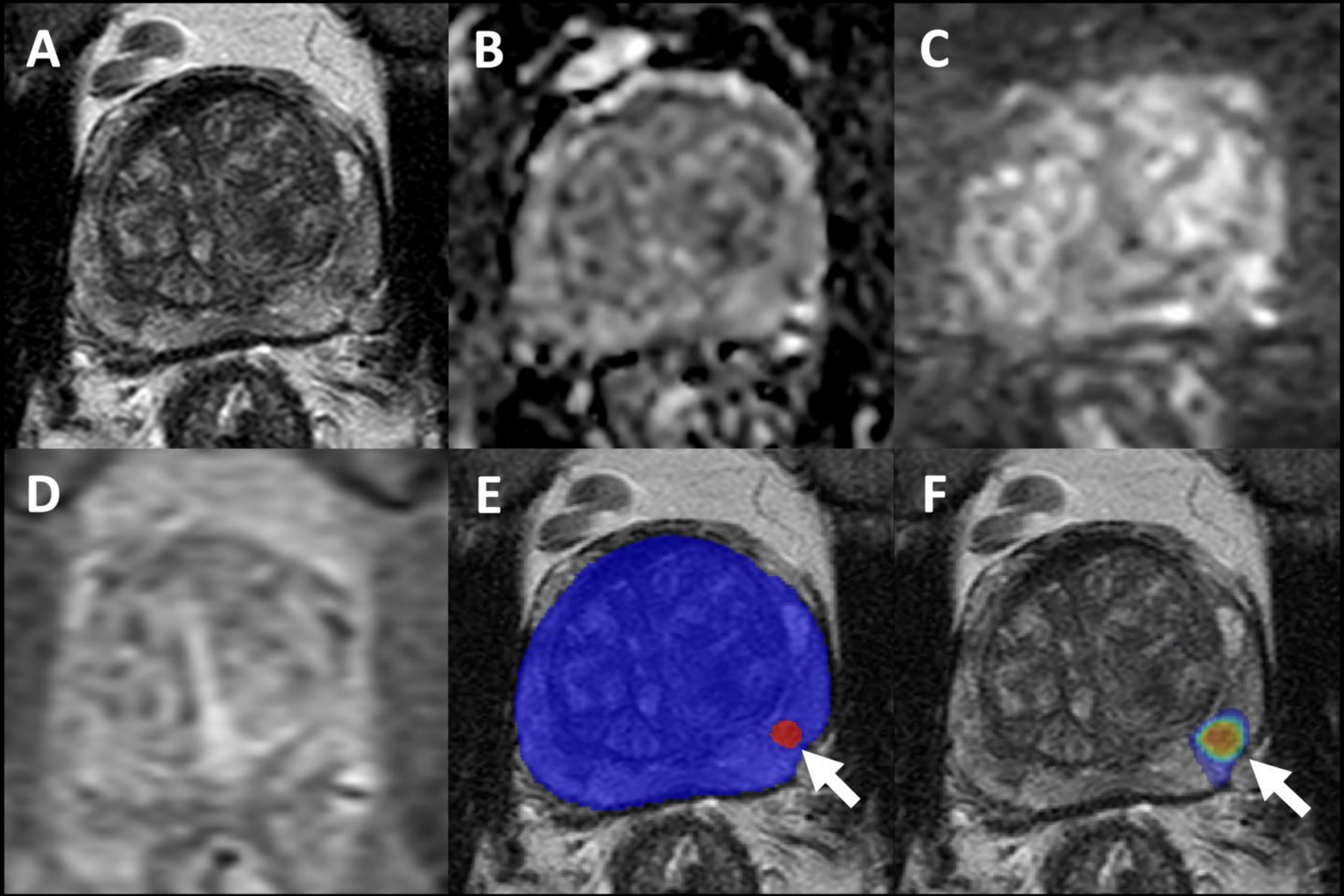
Two distinct lesions were detected by the radiologist representing the ground truth

Lesion 1 (arrow) PI-RADS 4
Bx=Gleason score 7 (3+4)

Lesion 2 (arrow heads) PI-RADS 3
Bx=benign

Radiologist vs. AI: 1-1

Lin Y, et al. Prepared to be submitted to Radiology (2023)



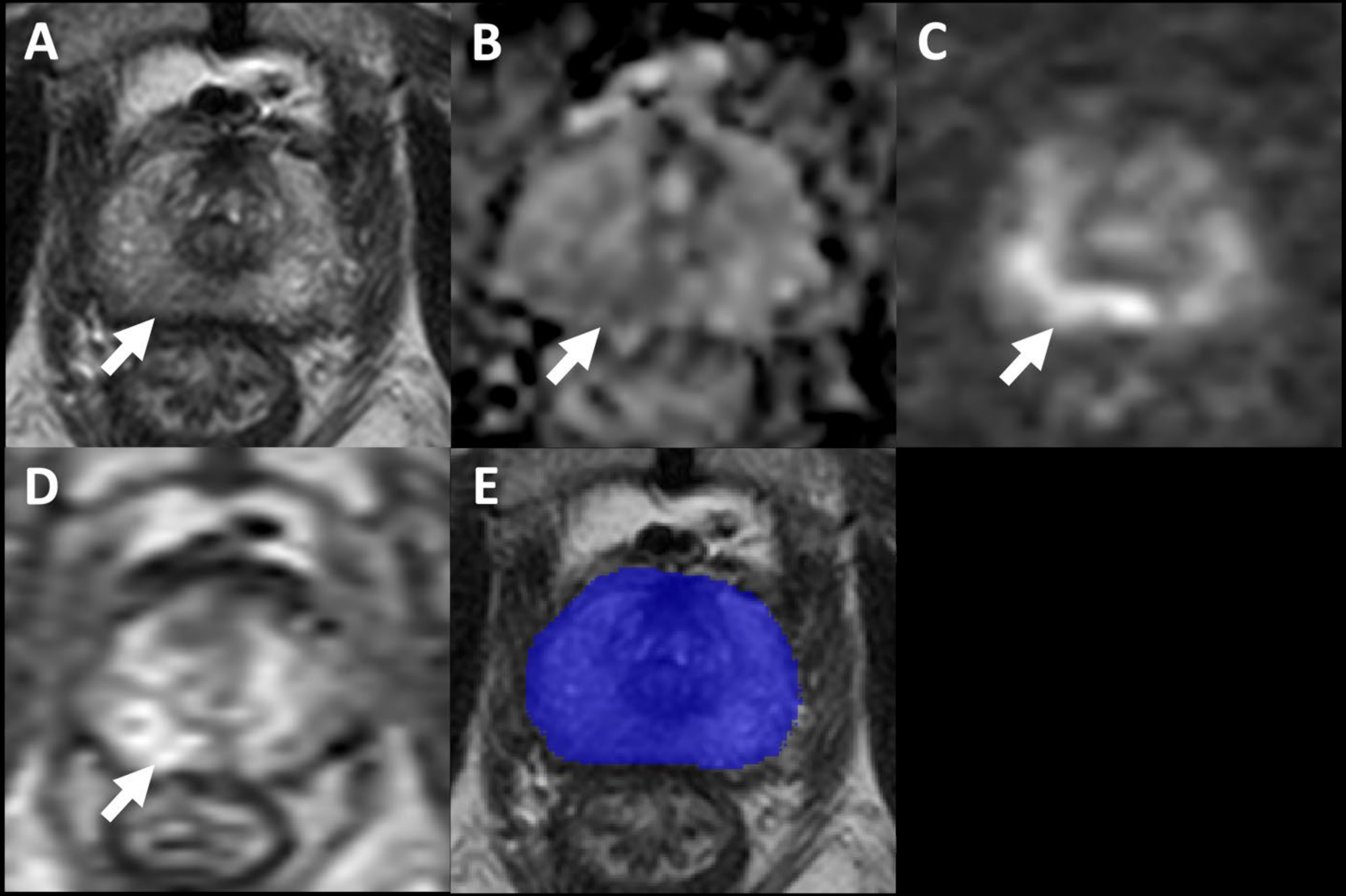
64-year-old male PSA= 8.1ng/mL

No distinct lesion was detected by the radiologist

AI detected left mid PZ lesion
Bx=Gleason score 7 (3+4)

Radiologist vs. AI: 0-1

Lin Y, et al. Prepared to be submitted to Radiology (2023)



74-year-old male PSA= 12.9ng/mL

One distinct lesion was detected by the radiologist representing the ground truth

Lesion 1 (arrow) PI-RADS 4
Bx=Gleason score 7 (3+4)

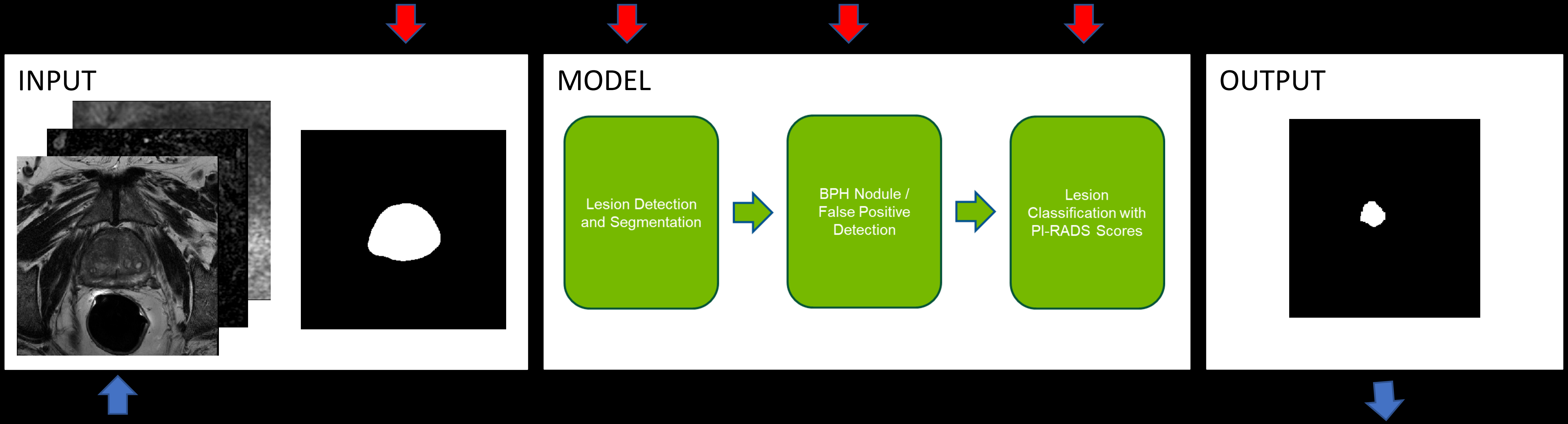
AI did not detect this lesion

Radiologist vs. AI: 1-0

Lin Y, et al. under revision with Radiology (2023)

AI Available for Daily Clinical Use

Four sequential 3D DL models



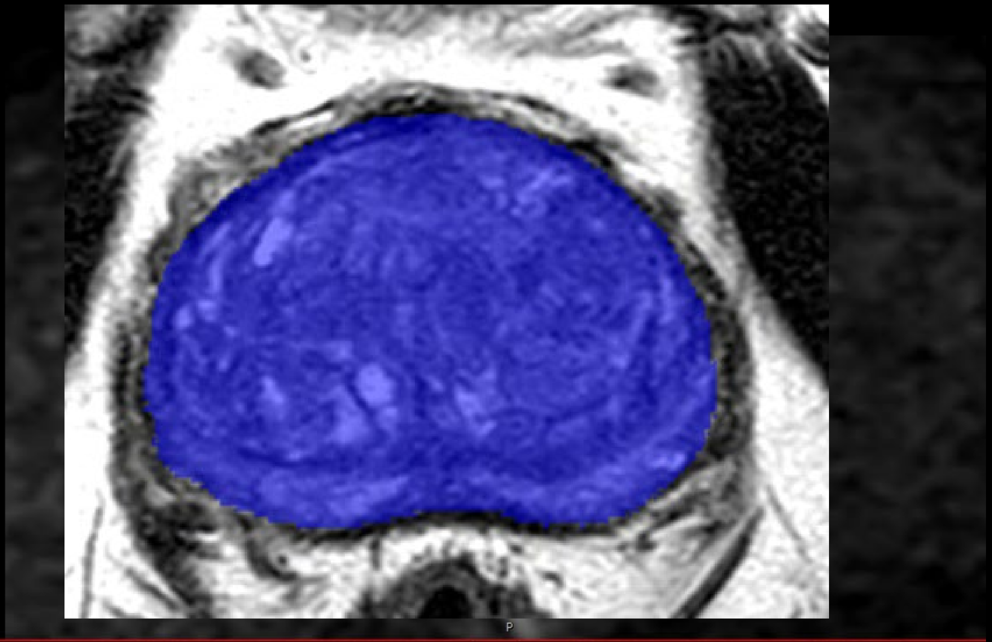
Clinical workflow

- Patient study identified as prostate MR
- Appropriate sequences selected for processing
- Pipeline called from PACS for execution
- Sequences sorted for AI input

Clinical workflow

- Results viewable in PACS
- Modifiable by user for downstream procedures

Stephanie Harmon, Jesse Tetreault



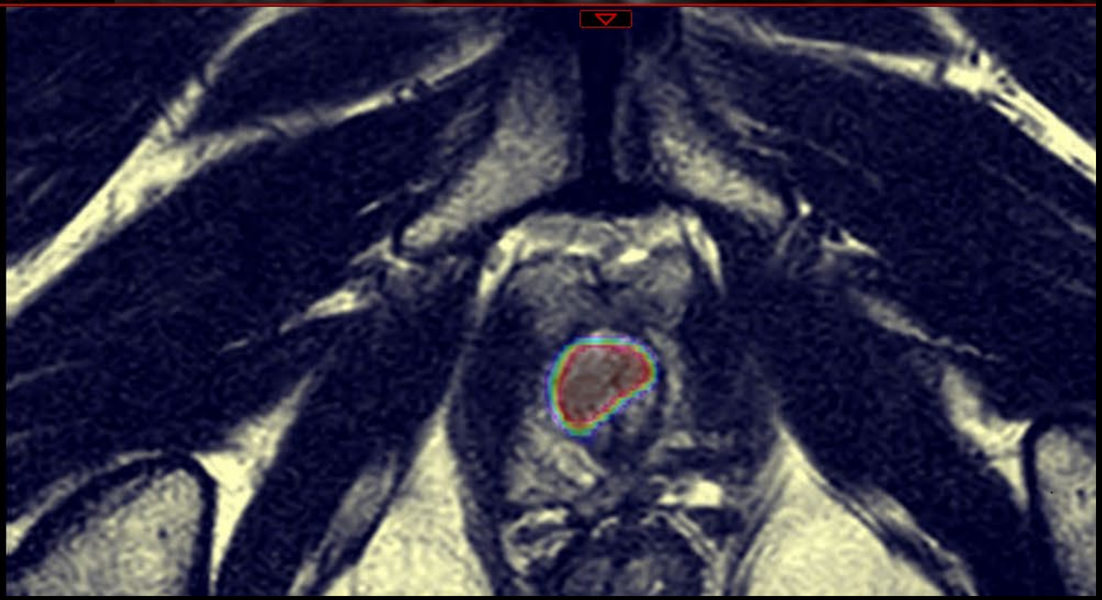
Clara Deploy Generated Observations

CAUTION: Not for diagnostic use. Limited by Federal (or United States) law to investigational use.

This research use only software has not been cleared or approved by FDA or any regulatory agency.

- Lesion_ID: 1 Major_Axis_Length: 22.48422032726106 PI_RADS: 5 Volume: 1460.25

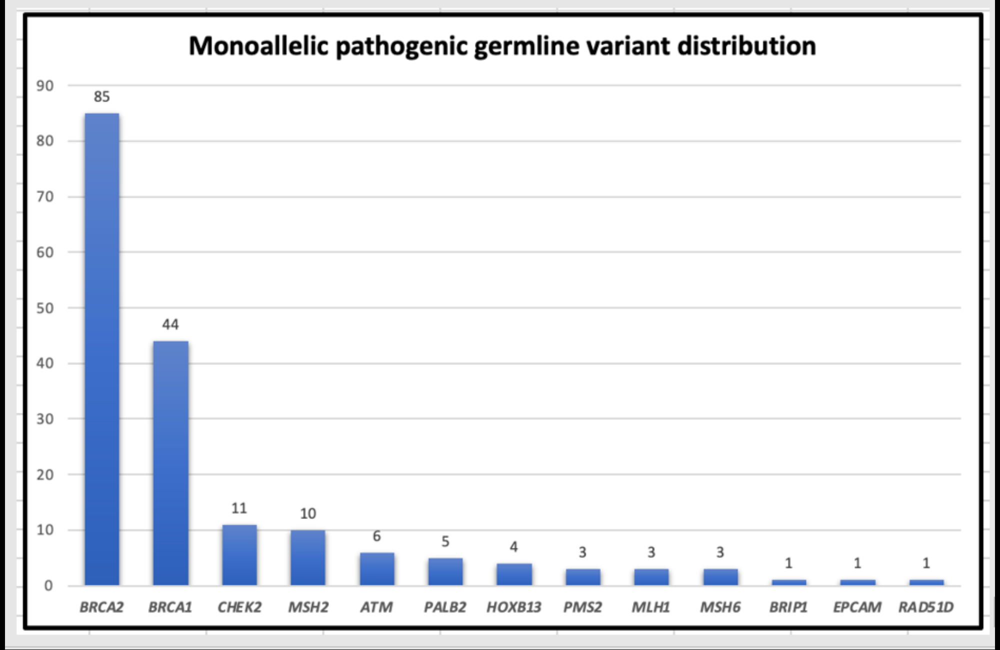
Gleason 3+4 with cribriform pattern

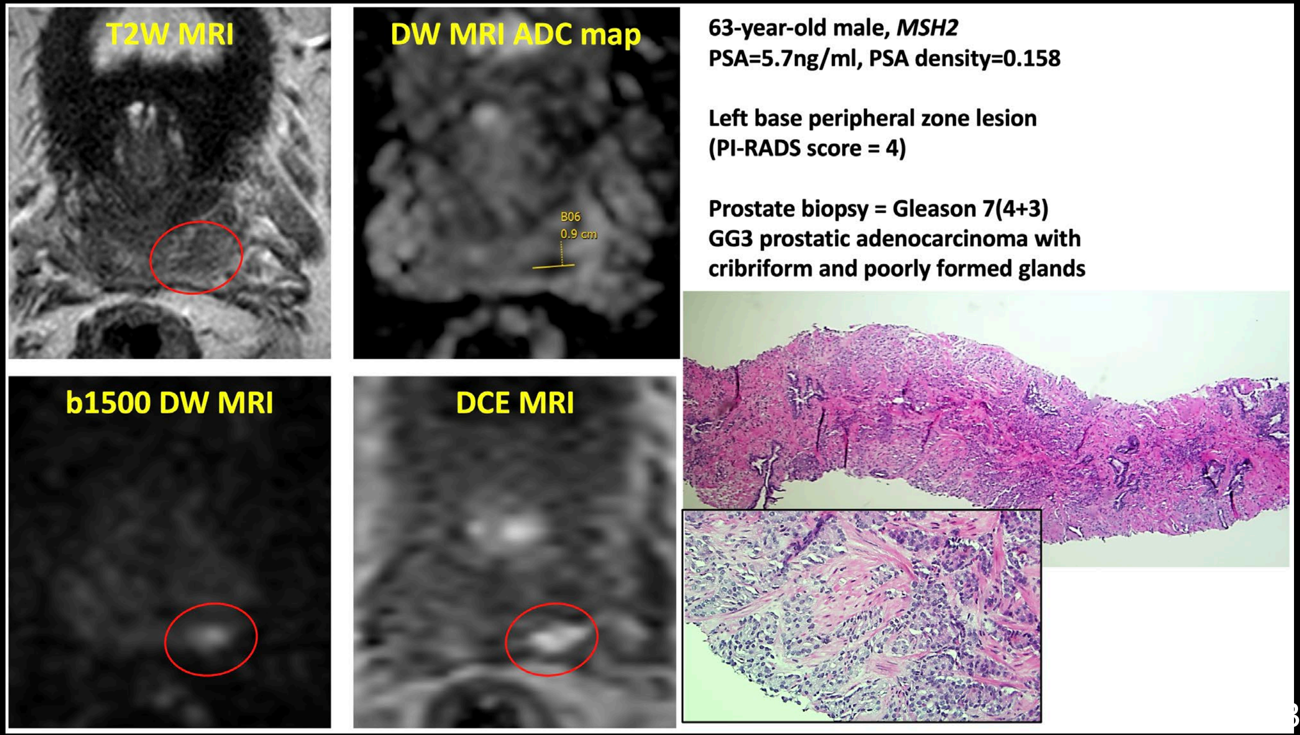


Harmon S, et al. Manuscript in preparation (2023)

Natural history of men with high-risk genetics using multiparametric MRI

- To date, 210 participants have enrolled (median age=47 years, PSA<3ng/ml).
- 26.3% of participants had biopsy: 28/46 (61%) MRI findings, 12/46 (26%) elevated PSA (median=2.8 ng/mL), 6/46 (13.0%) clinical discretion.
- Prostate cancer diagnosis=17/46 (37%) biopsies:
  - Median age at diagnosis=59 years.
  - 11/17 (65%) participants had a PSA <3 ng/ml at diagnosis.
  - Nine participants were diagnosed with ISUP G





3)

Prostate Cancer Imaging in MIB

Localized Disease
(2005-today)
- 20-30 MRIs/week
- 1-2 PET/CTs/week
- 5-10 Biopsies/week
- 1-3 Surgeries/week
- 1-2 xRT/month

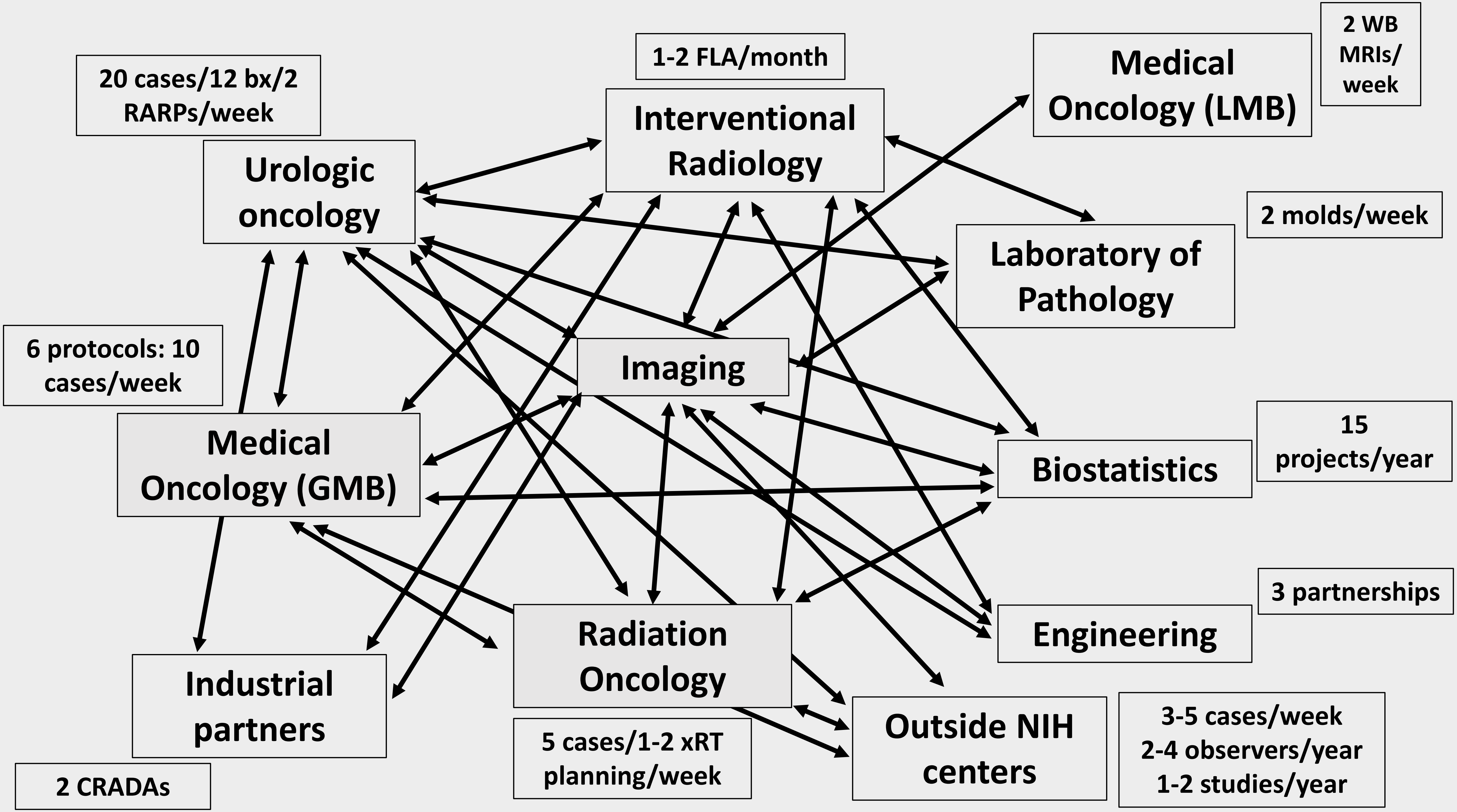
Biochemical Recurrence (BCR)
(2015-today)
- 1-3 MRIs/week
- 1-3 PET/CTs/week
- 1-2 salvage therapies/month

Metastatic Disease
(2009-today)
- 1-2 PET/CTs/week
- PSMA targeted radioligand therapy

  - Research use
- Integrated departmental structure:
  - Radiology-Pathology-Informatics

Make the imaging available as easy as possible for novel scientific goals

Yolanda McKinney, Juanita Weaver, Joy Zou, Bryanna Frith, Tieu Hoa, Dagane Daar, Chris Leyson, Mona Cedo, Linda Burke Prout, Inna Shamis, Philip Eclarinal


20 cases/12 bx/2 RARPs/week
1-2 FLA/month
2 WB MRIs/ week
Urologic oncology
Interventional Radiology
Medical Oncology (LMB)
2 molds/week
Laboratory of Pathology
6 protocols: 10 cases/week
Imaging
Medical Oncology (GMB)
Biostatistics
15 projects/year
3 partnerships
Radiation Oncology
Engineering
Industrial partners
Outside NIH centers
3-5 cases/week
2-4 observers/year
1-2 studies/year
5 cases/1-2 xRT planning/week
2 CRADAs

Why was AIR formed?

- AI (Computer Vision) is becoming a standard tool for:
  - Automating routine tasks
  - Improving reliability of subjective tasks
  - Discovering new information contained in images
- Lack of centralized resources in AI at NIH
- Large unexplored data sets in CCR
- **Idea**: Form a team of AI scientists to tackle new problems of relevance to CCR and develop new methods of AI analysis

Artificial Intelligence Resource-CCR

- Apply ML and DL algorithms to real world research problems generated within the Center for Cancer Research:
  - Medical Imaging:
    - Human MRI,CT, PET, US etc.
    - Preclinical PET, MRI
  - Digital Pathology Imaging
    - Human digital pathology and immunohistochemistry
    - Preclinical pathology
  - High Throughput Microscopy
    - Changes in cancer cell cultures after exposure to drugs in high throughput manner
    - Dynamic changes in transcription, cell division etc. in response to drugs

Baris Turkbey MD
Head

G. Thomas Brown MD PhD
Staff Clinician

Nathan S. Lay PhD
Staff Scientist

Stephanie A. Harmon PhD
Stadtman Investigator

Abdul Kader Sagar PhD
Staff Scientist

Fahmida Haque PhD
Post-doc Fellow

Sushant Patkar PhD
Post-doc Fellow

Alex Chen BS
Post-bac Fellow

Affiliated AIR Members:
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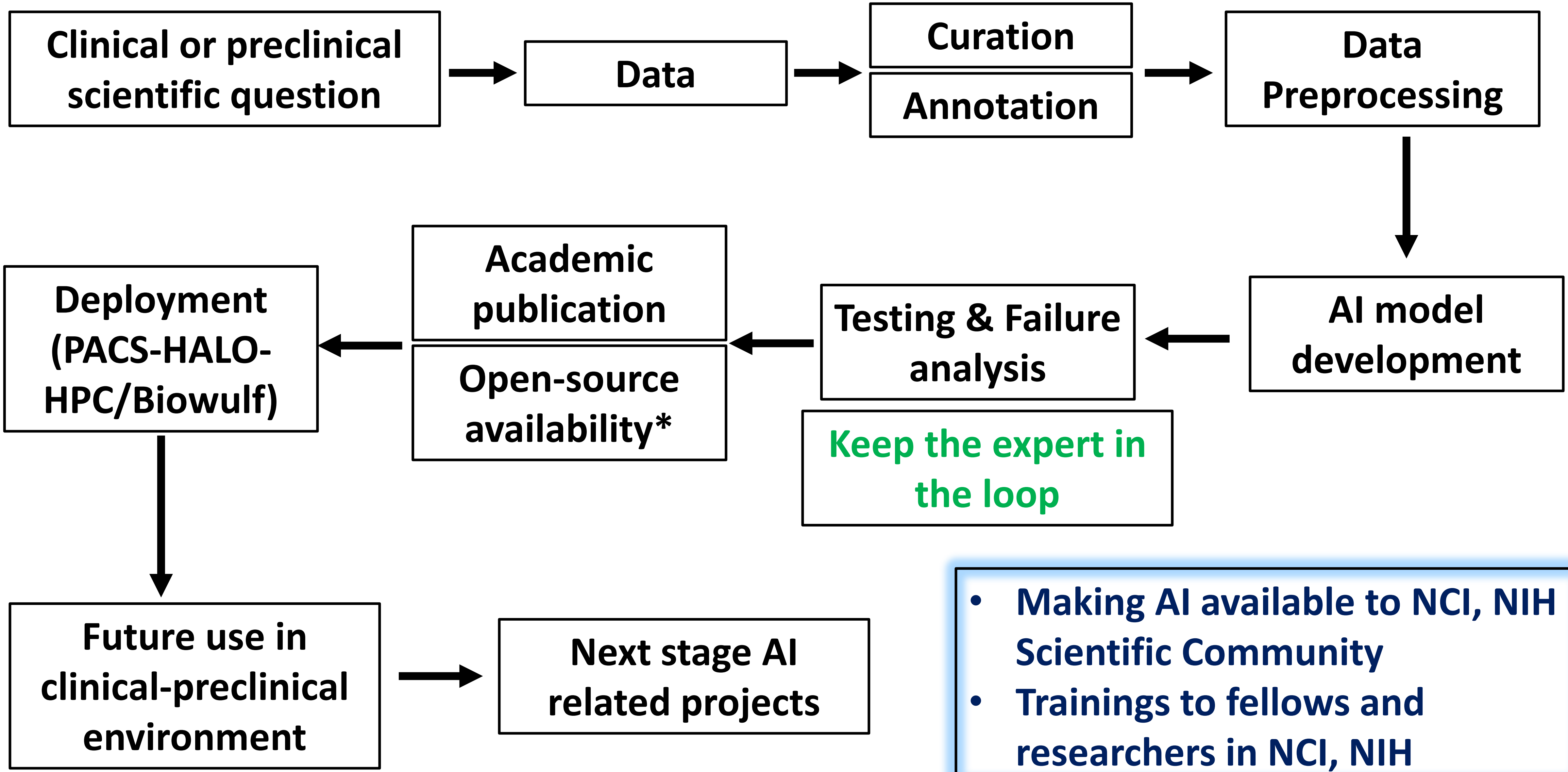
Kutsev Ozyoruk PhD, MIB post-doc Fellow
Zhijun Chen PhD, SH post-doc Fellow
Sophia Ty BS, MIB post-bac Fellow
Katie Merriman BS, MIB post-bac Fellow
Enis Yilmaz MD, MIB post-doc Fellow
David Gelikman BS, MRSP Fellow
Benjamin Simon, NIH-OxCam PhD Student
Nicole Tran, Summer Student
Philip Eclarinal NMT, IT Support
Chris Leyson NMT, AIR Volunteer
Anita Ton, AIR Pathology Slide Scanning Tech
Mason Belue BS, MIB Volunteer
Yue Lin, AB, MIB Volunteer

Admin Support:
Beth Hardisty, AO
Karen Wong, MIB (purchase)
Betty Garcia, MIB (travel)

Steering Committee:
Brad Wood, CC
Steve Hewitt, NCI
Clem McDonald, NLM
Ulas Bagci, Northwestern
Peter Choyke, NCI
Baris Turkbey, NCI

AIR Workflow



- Making AI available to NCI, NIH Scientific Community
- Trainings to fellows and researchers in NCI, NIH

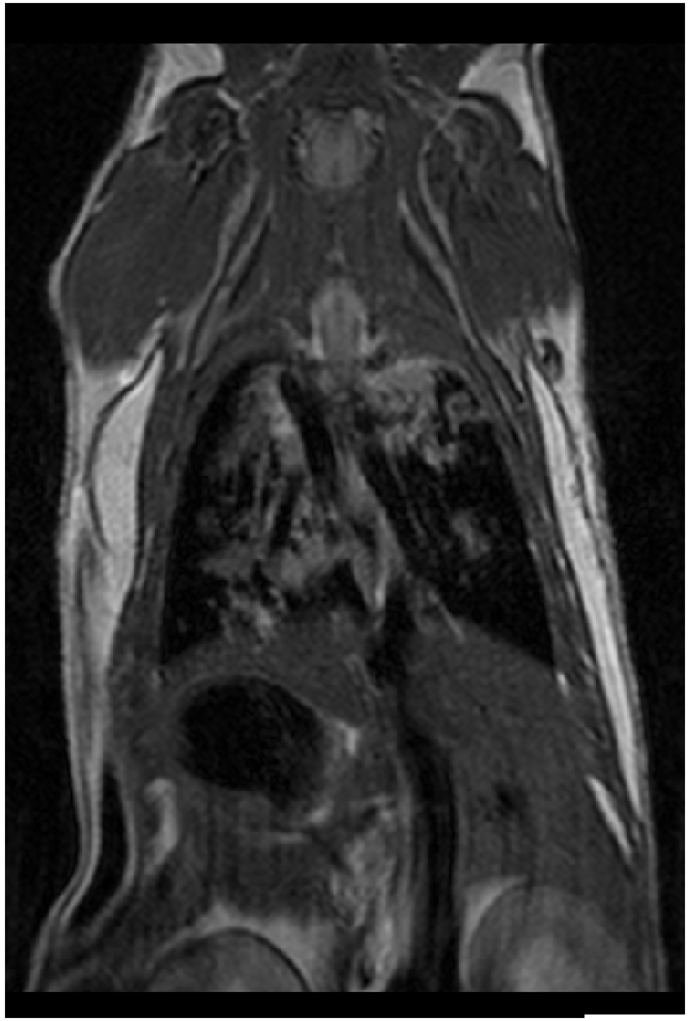
Study Name	PI/Branch/Institute	Data preparation	Model development	Test	Failure Analysis	Model refinement	Paper/ Abstract	Code available to PI
Automated dosimetry from positron imaging using AI	Mike Green/MIB	✓	✓	✓	✓	✓	✓	✓
Automated tumor burden estimation in pre-clinical models of lung cancer	Chen Zhao/NCI	✓	✓	✓	✓	✓	✓	✓
HRCC AI project	Ashkan Malayeri/CC	✓	✓	✓	✓	✓	✓	✓
Canine osteosarcoma AI project	Jess Beck, Amy LeBlanc/MIB	✓	✓	✓	✓	✓	✓	✓
Lymphoma subtyping at histopathology using AI	UNC/Malawi	✓	✓	✓	✓			
Identification and characterization of ovarian follicles	Veronica Gomez Lobo/NICHD	✓	✓	✓	✓		✓	
PET AI project for PSMA imaging	Esther Mena/MIB	✓	✓	✓	✓	✓	✓	
Detection, segmentation, and phenotype classification of SCLC liver metastases	Part Desai, Anish Thomas/NCI	✓	✓	✓	✓	✓	✓	✓
Automated detection, grading, and outcome prediction of prostate cancer	Joel Moncur/WRMMC	✓	✓	✓	✓	✓	✓	
HCC early detection in Chronic Hepatitis using surveillance ultrasonography	Christine Hsu-Theo Heller/NIDDK	✓	✓					
Detection and imaging-based scoring of HCC on MRI	Veterans Administration/VA							
GBM Radiotherapy Response Project	Andra Krauze/ROB	✓	✓	✓	✓	✓	✓	✓
Glioma Immunotherapy Response Project	Jing Wu/NOB	✓	✓	✓	✓	✓	✓	
Multi-organ segmentation on micro-CT imaging	Noriko Sato/MIB							
Automated segmentation of lung tumors at rodent MRI	Chenran Zhao/NCI	✓	✓	✓	✓	✓	✓	
Automated lesion detection at CT in thymoma patients	Chen Zhao/NCI	✓	✓	✓	✓	✓	✓	
AI assisted quantification of soft tissue sarcoma tumor burden at radiology imaging	Rosie Kaplan/NCI	✓						
Endoscopy AI project for GDH1 mutation patients	Jeremy Davis/NCI	✓						

Segmentation of Lung Tumors in preclinical MRI studies

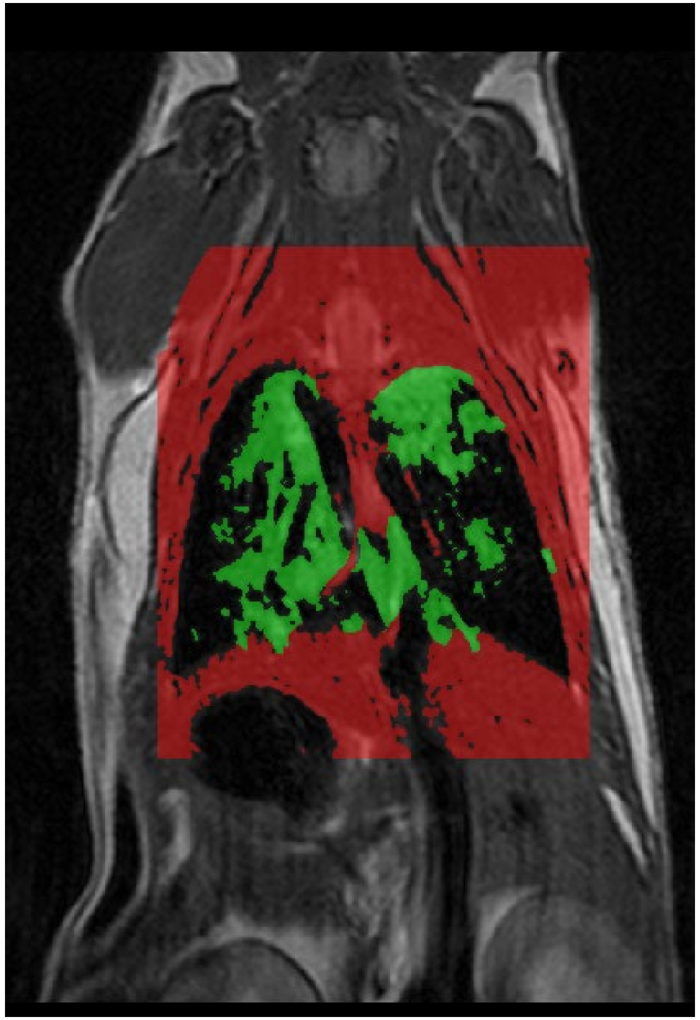
- Animal models are important for studying disease initiation and sensitivity to various targeted therapeutics
- Measuring lung-tumor burden (manuel or semiautomated) for monitoring progression of tumors in mouse models is time-consuming and prone to inter-reader variability

Objective: To develop an AI algorithm for automated lung lesion segmentation

MRI



Semi-automated manual annotations



Katie Merriman Stephanie Harmon Chenran Zhang

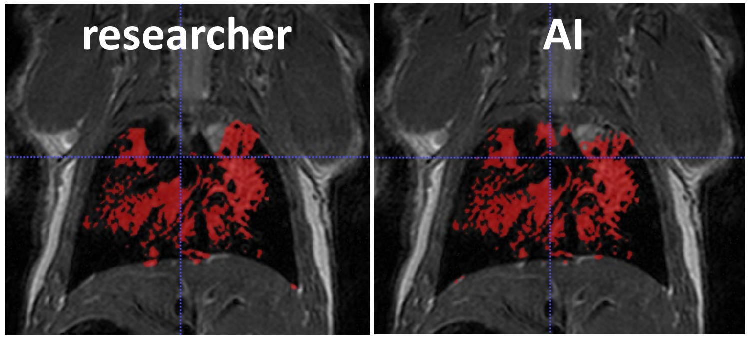
Segmentation of Lung Tumors in preclinical MRI studies

- 3D binary segmentation algorithm trained:
  - 224x224x16 VOIs
  - 3:1 ratio background:lung to reduce false positives
  - Ensemble of SegResNet, UNET, UNETR
  - Optimized via Dice loss
- Mean DSC in validation set: 0.568 for ensemble
- Final comparison to histopathological ground truth from sub-set of unlabeled test cohort

Training and Validation:

183 images from 6 experimental studies, 2 experimental set-ups

Supervised training



Unlabeled test set:

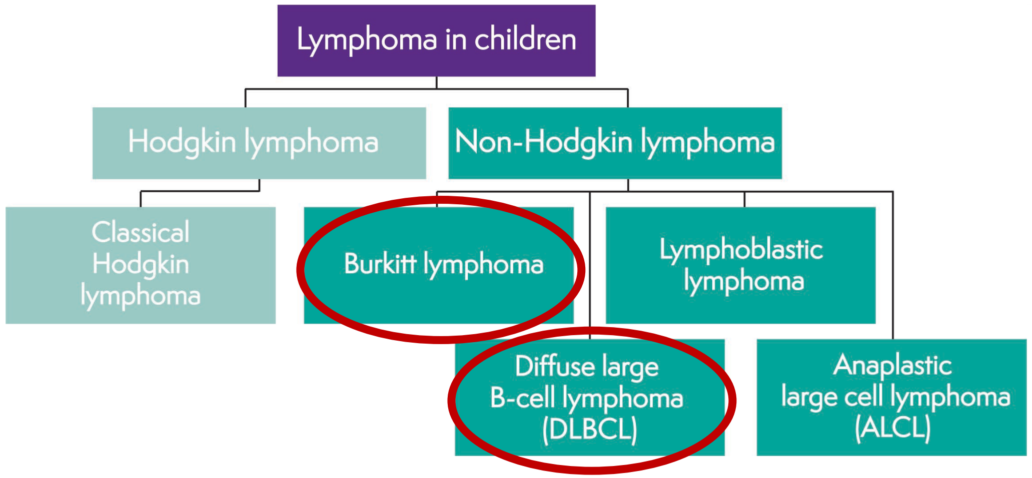
47 images from single study

Final comparison:
1. Semi-automated (manual)
2. Fully automated (AI alone)
3. Semi-automated (AI)

Katie Merriman Stephanie Harmon Chenran Zhang

Developing an AI Algorithm to Differentiate Diffuse Large B-cell Lymphoma (DLBCL) from Burkitt Lymphoma at Digital H&E Pathology

- Sub-Saharan Africa: 1 million new cancer cases vs. 0.8 million cancer related deaths by 2030
  - NHL is the 6th most common cancer
  - HIV epidemic (30-70%)
- UNC Project Malawi Cancer Program has a registry of lymphoma patients in Malawi
- Shortage of pathologists (1 pathologist/1 million)
- AI algorithm can be used to help carry out diagnosis and can be optimized to be used in low-resource setting



G. Tom Brown Alena Arlova Sophie Roush Yuri Fedoriw

Data Enrichment and AI Development Strategy

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- 74 Bu
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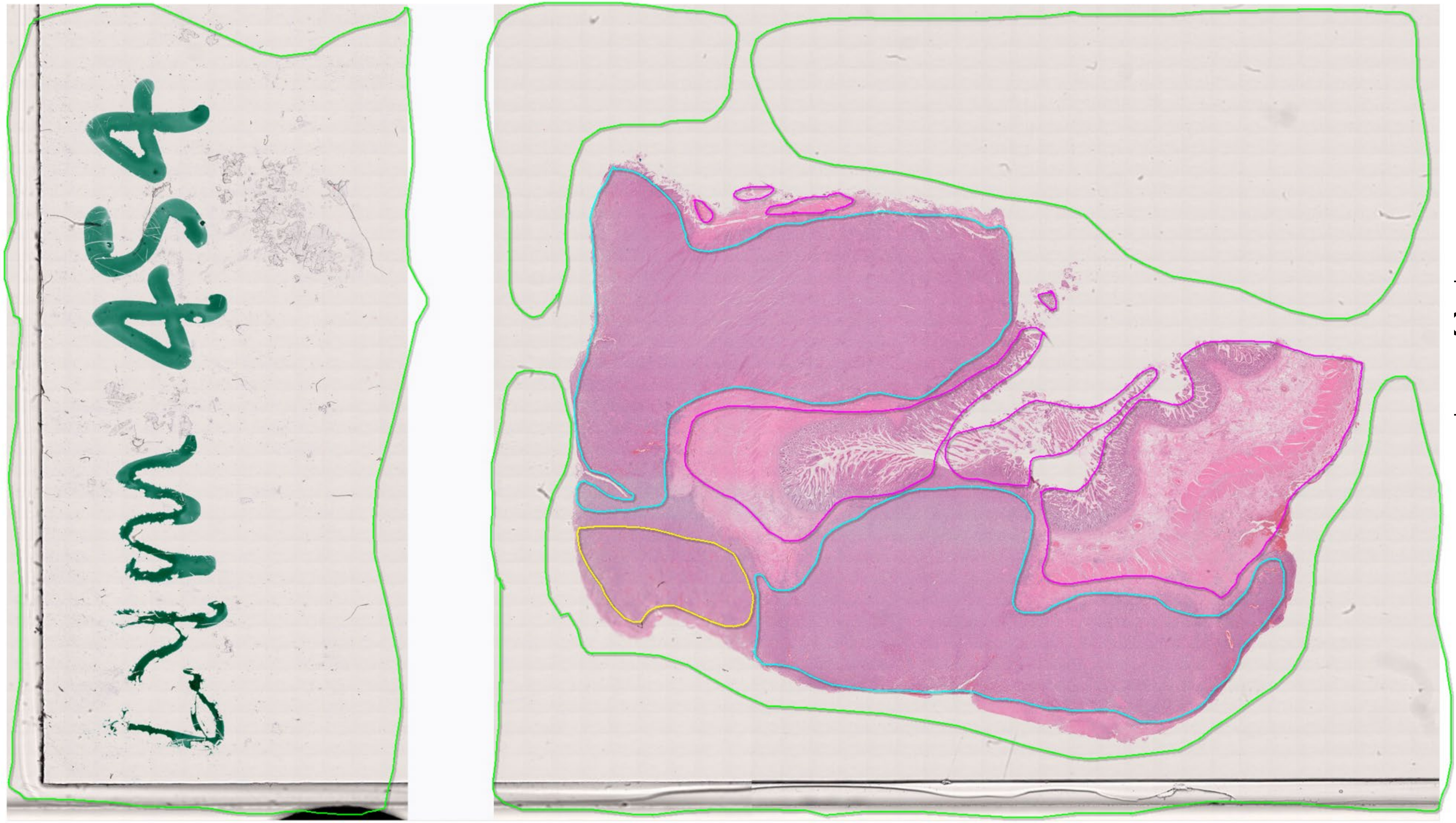
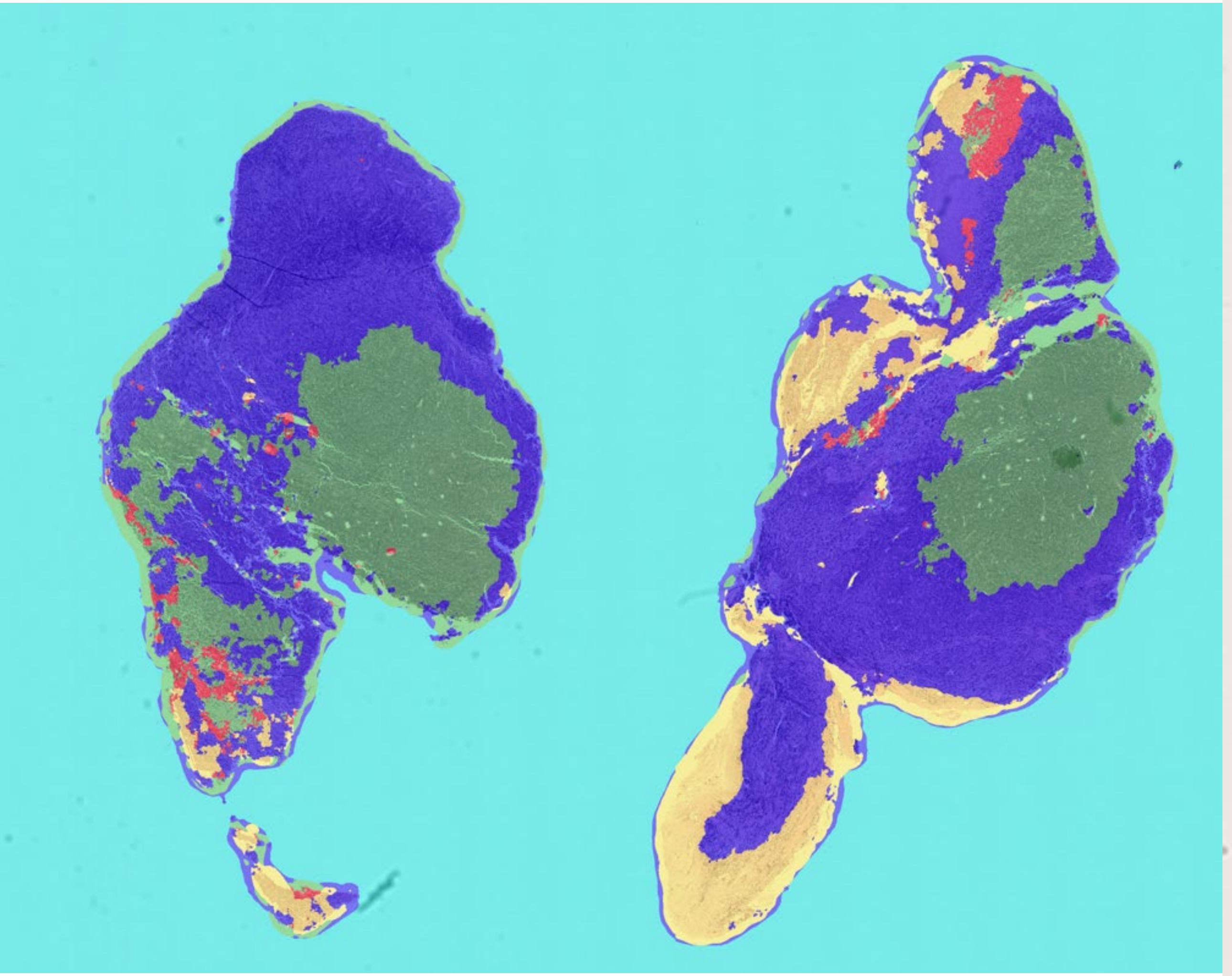
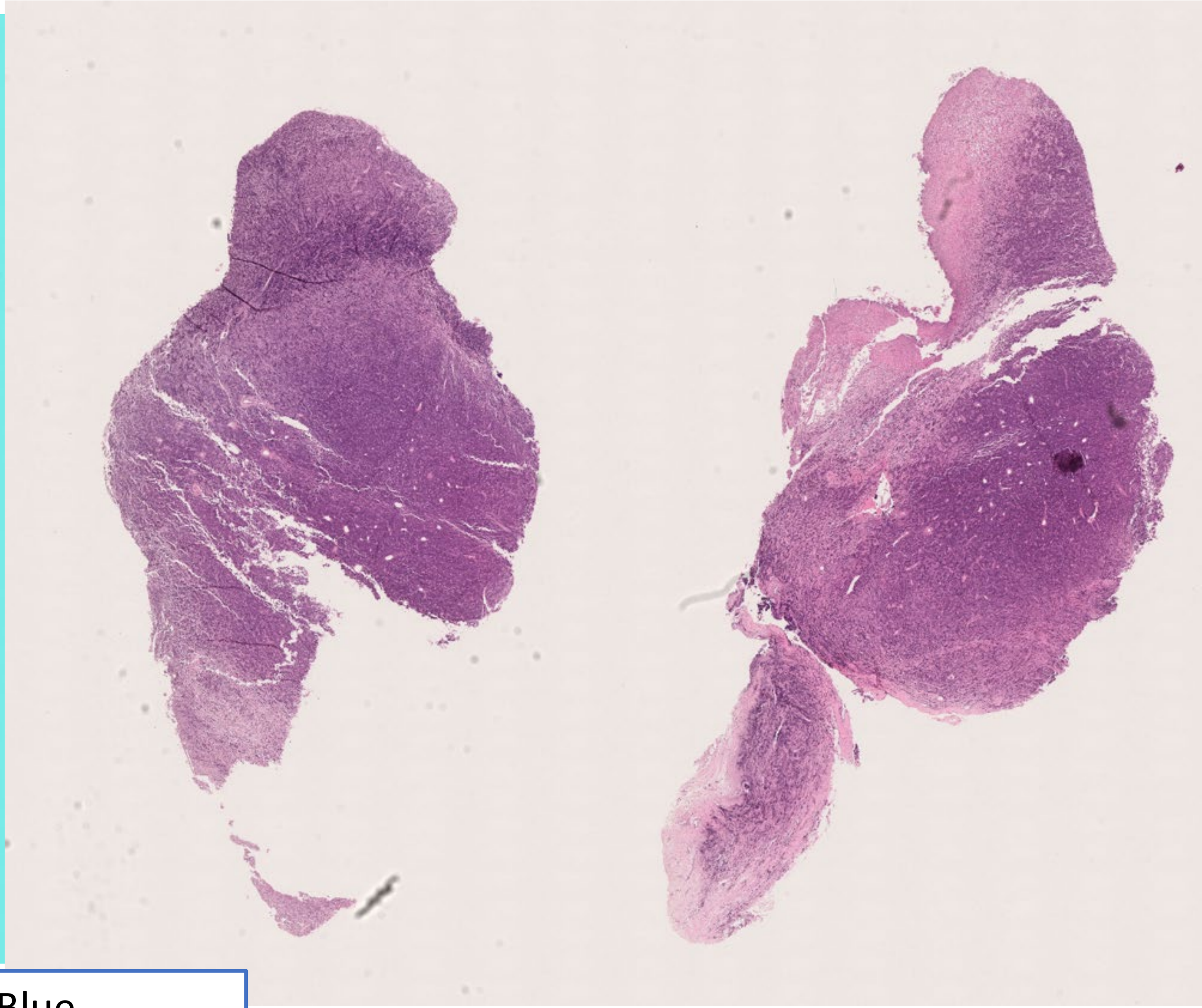


chitecture
AI)

G. Tom Brown Alena Arlova Sophie Roush Yuri Fedoriw

Correct - Burkitt lymphoma (93% BL; 7% DLBCL)





DLBCL = Red
BL = Green
Stroma = Yellow
Unsat = Blue
Background = Cyan

G. Tom B

Yuri Fedoriw

Data Enrichment and AI Development Strategy

- 84 lymphoma slides (WSI) from Malawi
- 74 Burkitt lymphoma slides (WSI) from NCI (originally from Kenya)

- Expert annotations
  - Tumor: DLBCL vs. BL
  - Stroma: non-tumor tissue
  - Background: glass, dust, labels, edges
  - Unsatisfactory: crushed cells, fold, wrinkles

  By Dr. G .Tom Brown

DenseNet Architecture (HALO AI)

Current accuracy=91.66%

Failure analysis

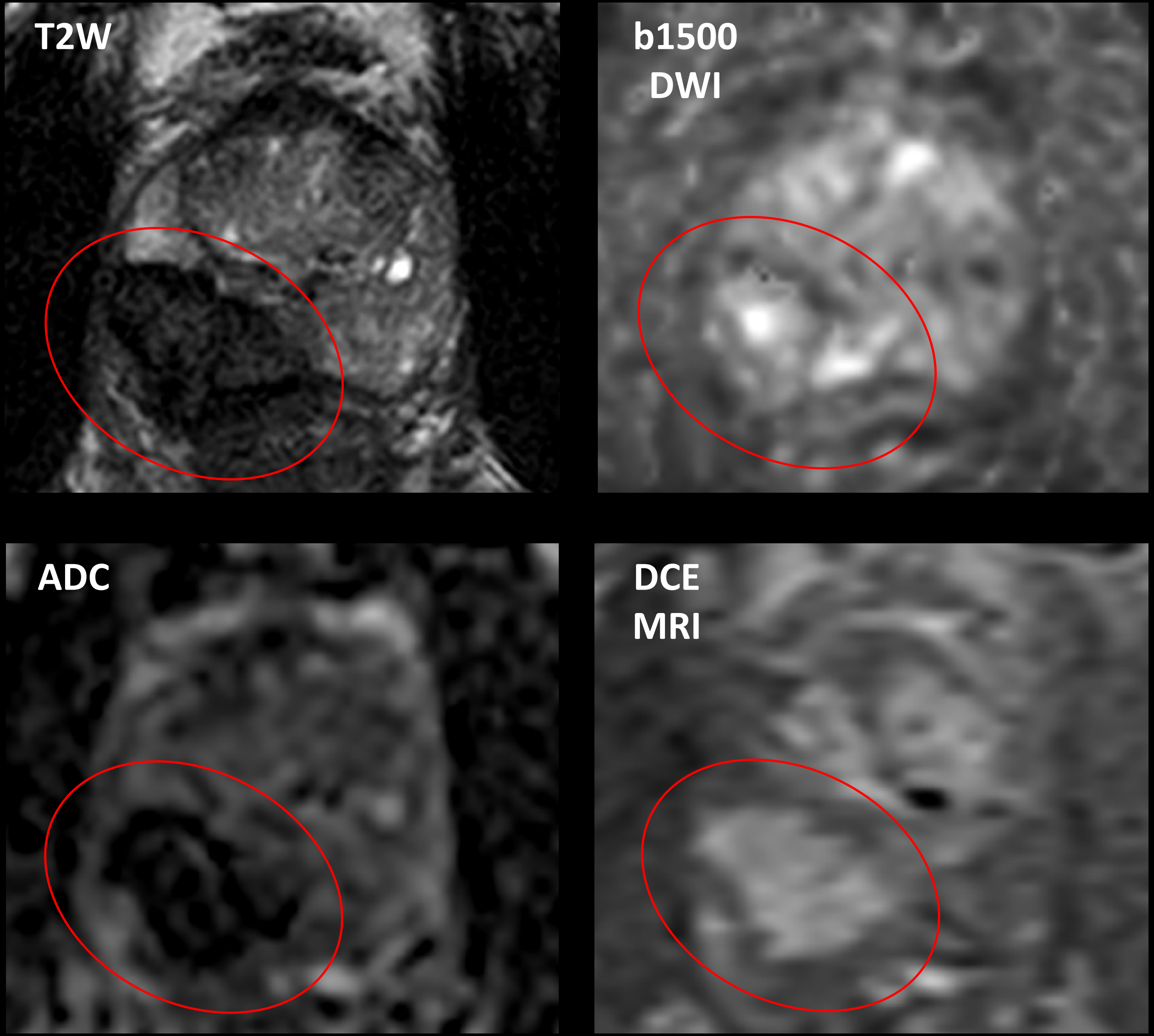
Model optimization

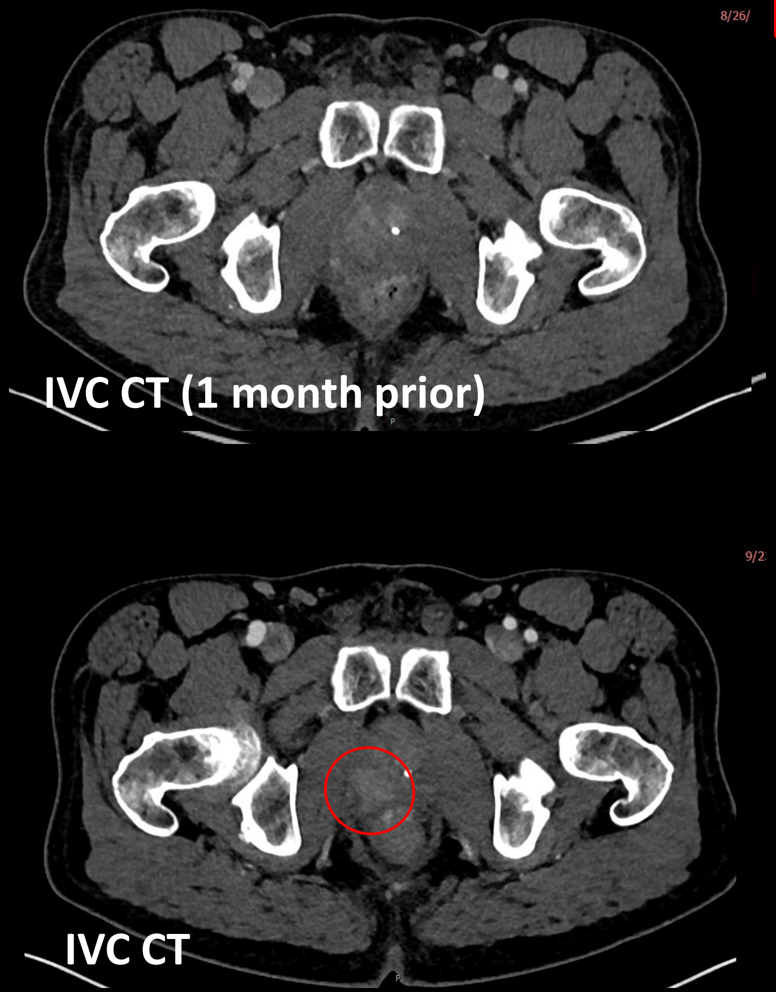
Deployment to Malawi

G. Tom Brown   Alena Arlova   Sophie Roush   Yuri Fedoriw

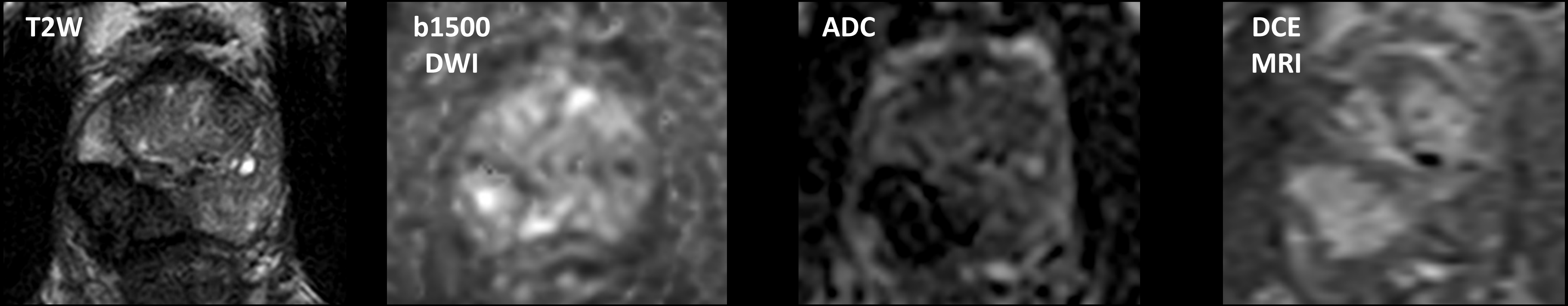
62-year-old African American male, PSA=2.8ng/ml, Aplastic anemia, dysuria

- Right apical-mid peripheral zone
- Acute prostatitis
- Unlikely to represent cancer

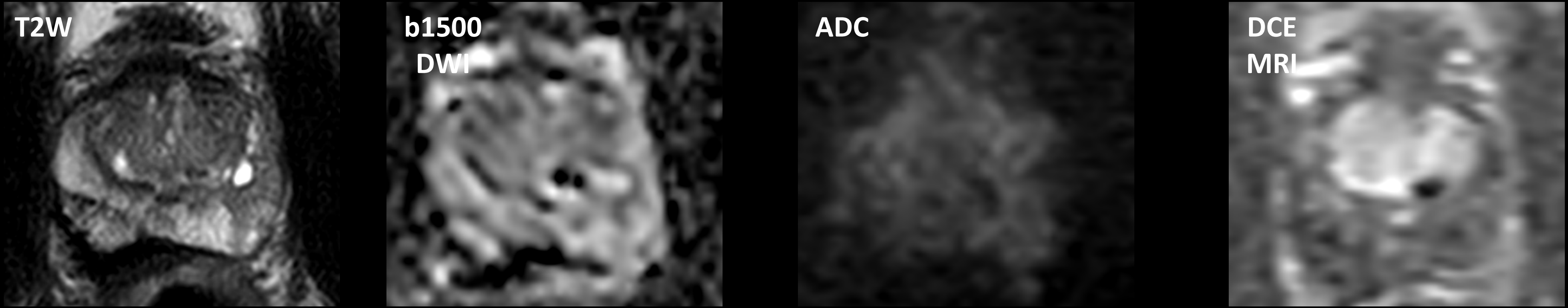




62-year-old African American male, PSA=2.8ng/ml, Aplastic anemia, dysuria

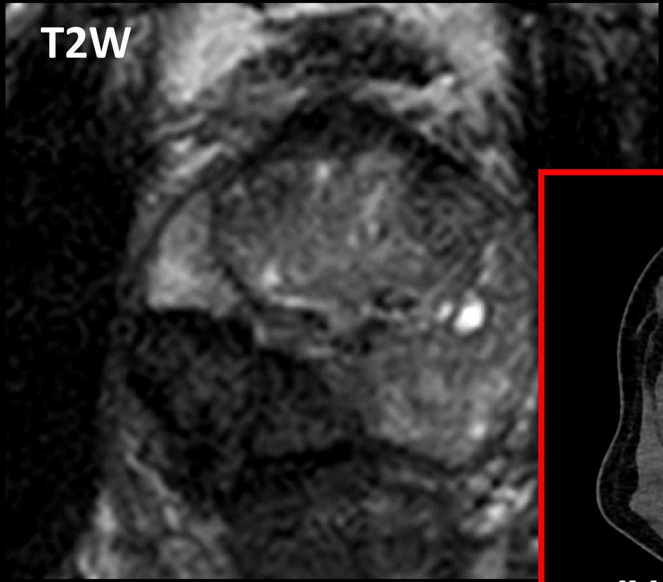


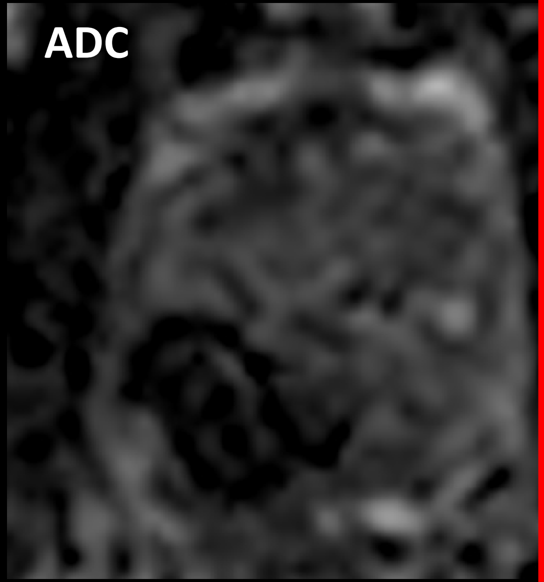
4 weeks: Meropenem + Levofloxacin

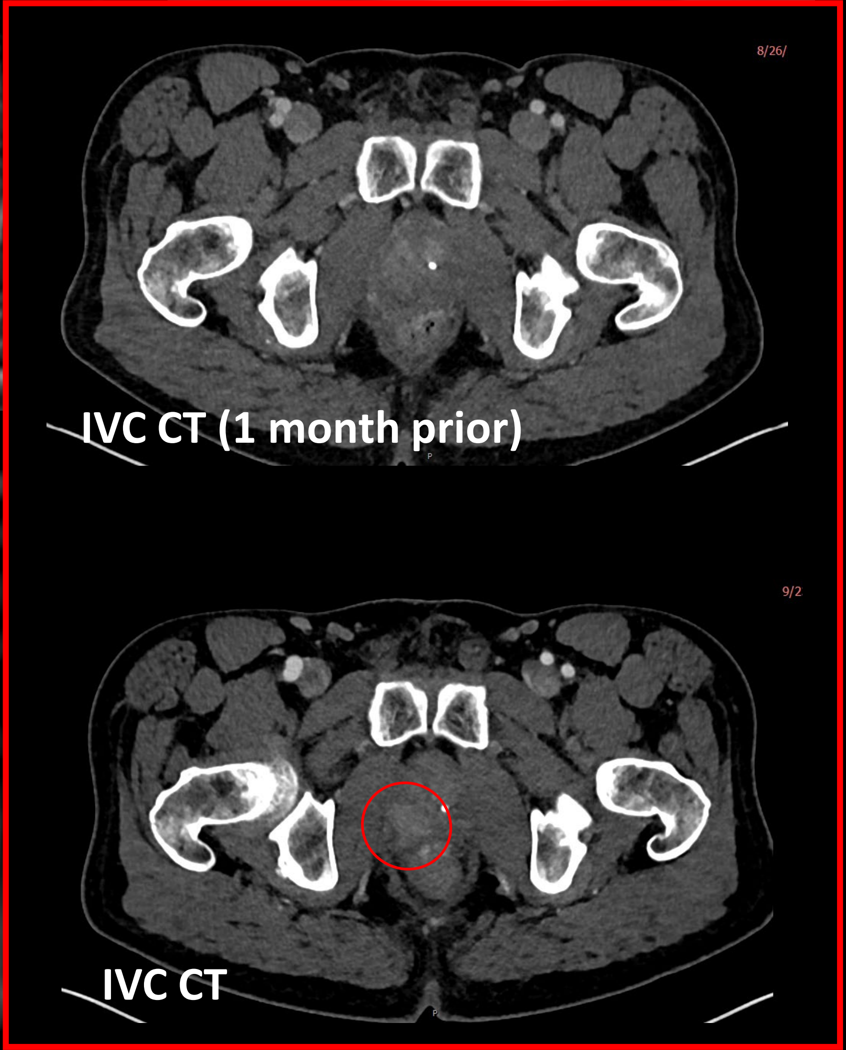


62-year-old African American male, PSA=2.8ng/ml, Aplastic anemia, dysuria

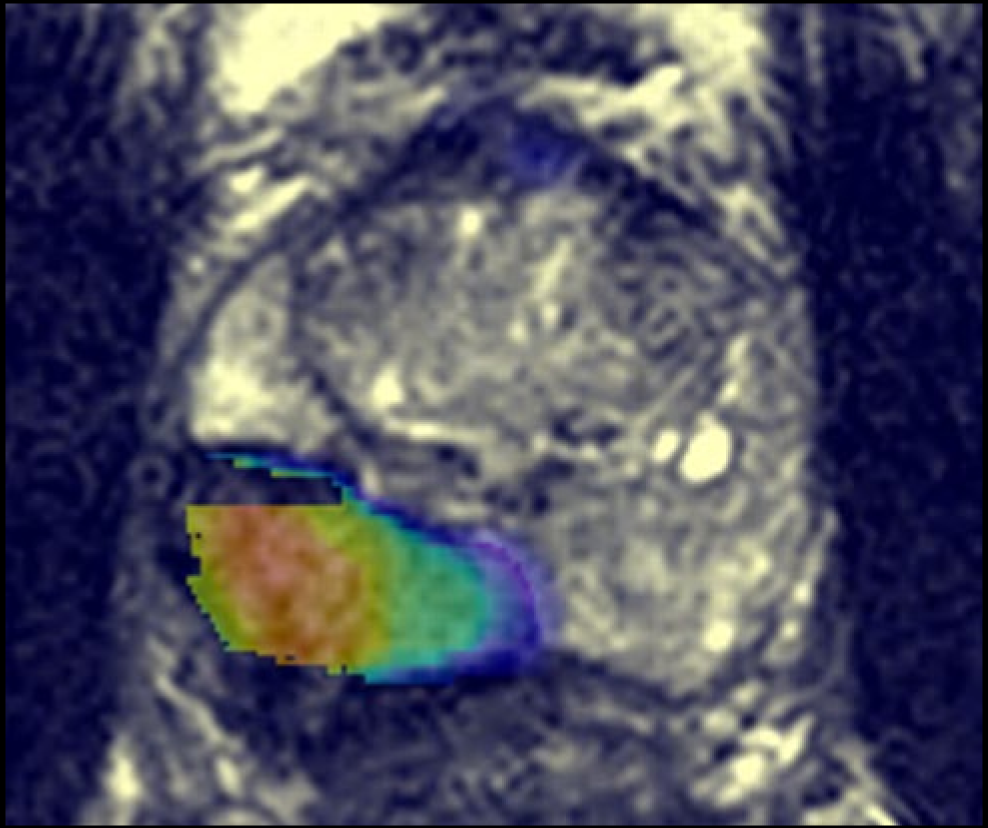
- Right apical-mid peripheral zone
- PI-RADS 5/5
- Extraprostatic extension

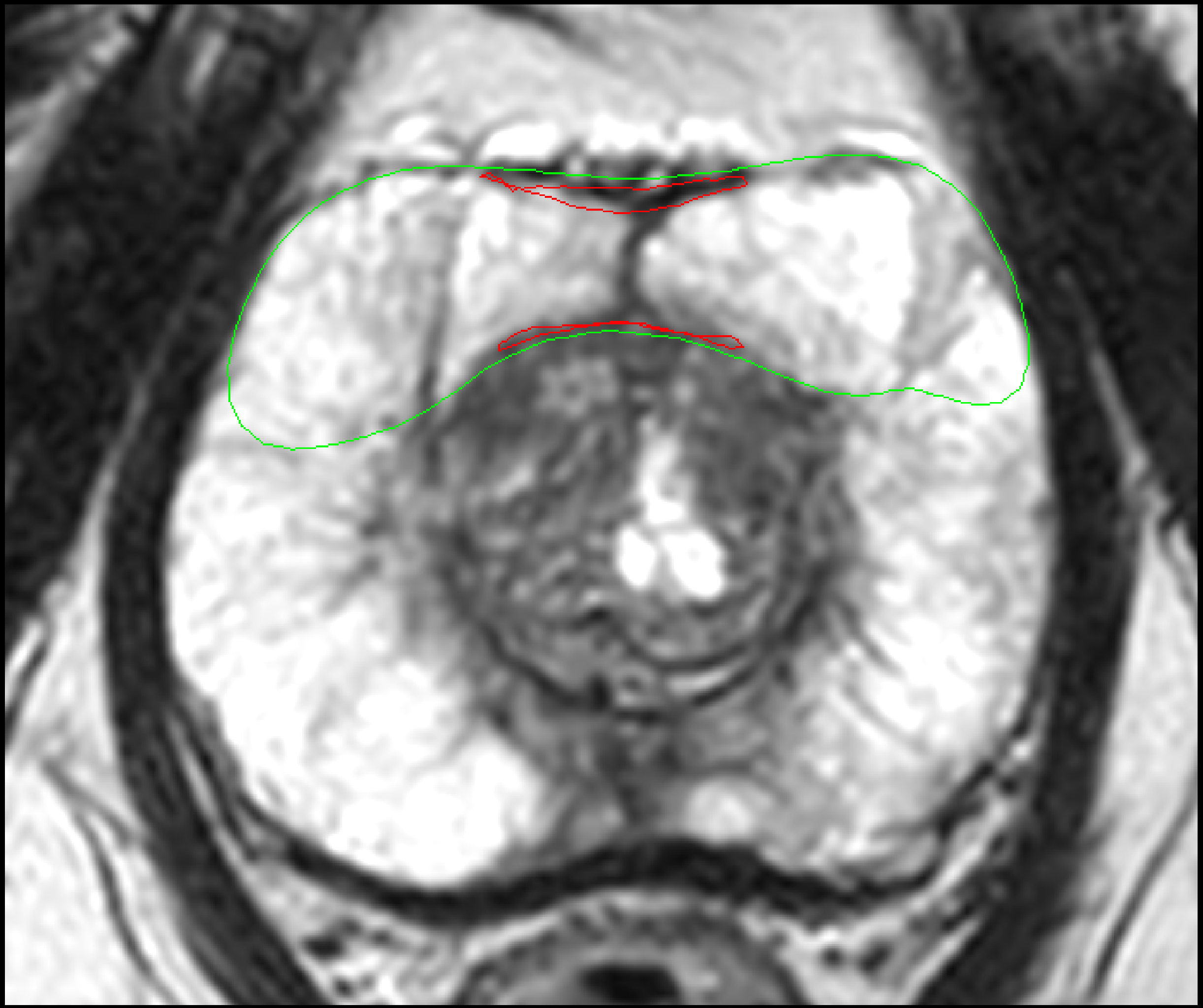




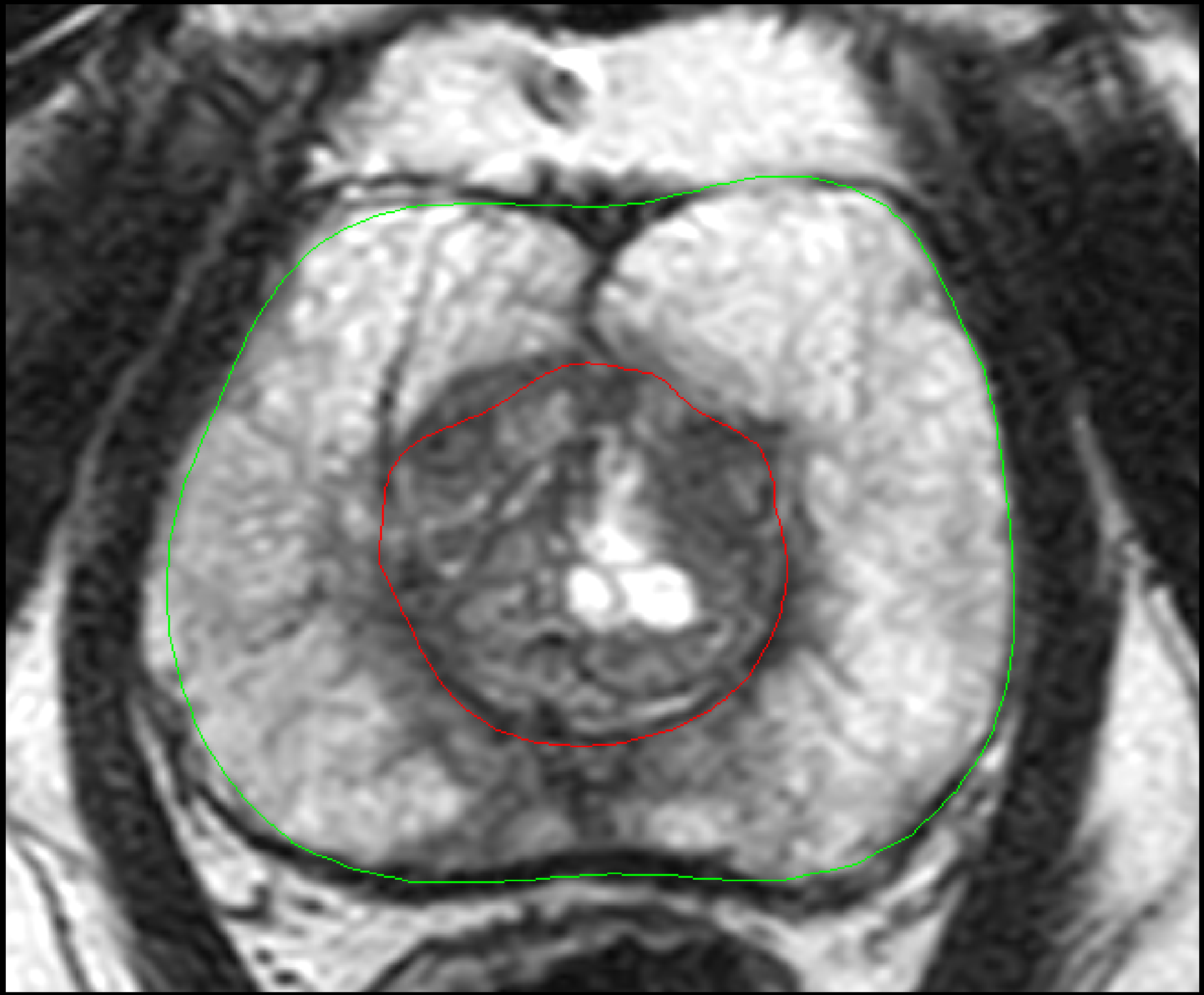


X





03/02/2023



10/13/2021

What happened in the interval?

Latrice Johnson

Stephanie Harmon

Where should we go with AI?

- Strong AI models can be trained with big data
- Even strong AI models can focus on solving one problem
  - Cascaded model can handle multiple problems
- Almost all AI models are using unidimensional data
  - e.g., prostate AI model does not consider lab results, age, prior imaging history
- AI model's results are not connected to each other
  - e.g., google translate does the work sentence by sentence (no reading comprehension)
- AI models' results are not stable
  - Even subtle adverse factors can impact the performance
- While we keep doing translational AI in NCI, we should also focus on multi-dimensional AI and smart AI

MIB

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Yue Lin
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Thank you…

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