Vanderbilt CVC 06-30-2020

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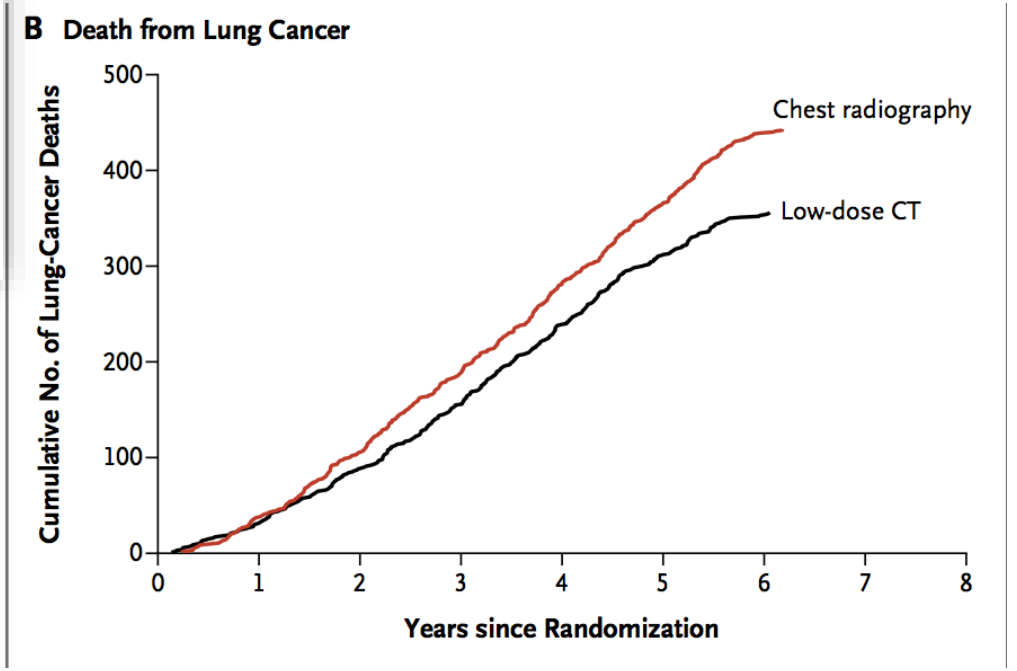
1. Personalized lung cancer screening in the underserved– Melinda Aldrich, Pierre Massion

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 4, 2011 VOL. 365 NO. 5

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*



Goals

1. To develop a high-risk cohort
2. To validate risk and diagnostic molecular biomarkers for lung cancer
3. To determine whether a surveillance program may lead to early diagnosis of lung cancer and improved outcomes
4. To develop an archive of biospecimens from at risk individuals and those with lung cancer for correlative studies within the EDRN

VANDERBILT-INGRAM CANCER CENTER

Department of Veterans Affairs Tennessee Valley Healthcare System

Nashville Lung Cancer Screening Trial

For more information, contact us at:
(800) 811-8480

VANDERBILT-INGRAM CANCER CENTER

Date of IRB Approval: 03/27/2019

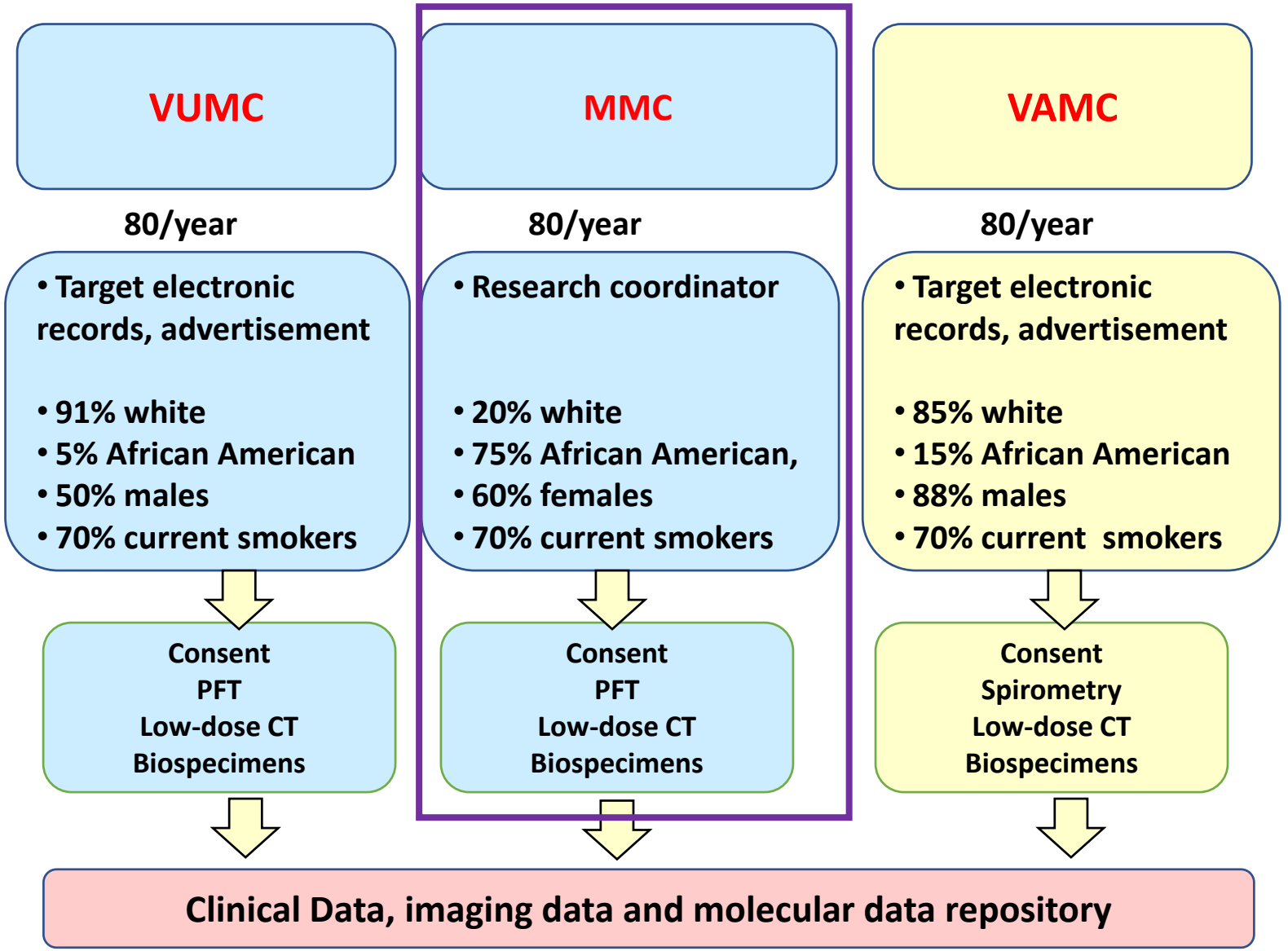
Institutional Review Board

Eligibility Criteria

- **Inclusion criteria:**
  - 55-80 years of age
  - Current smoker or former smoker (quit < 15 years)
  - 30 pack-year smoking history

- **Exclusion criteria:**
  - Diagnosis/treatment for lung cancer in prior 2 years
  - History of head/neck or esophageal cancer in the last year
  - Inability to provide informed consent

Populations and study sites



Recruitment

shade tree
CLINIC

FAITH FAMILY
MEDICAL CENTER

SILOAM
HEALTH

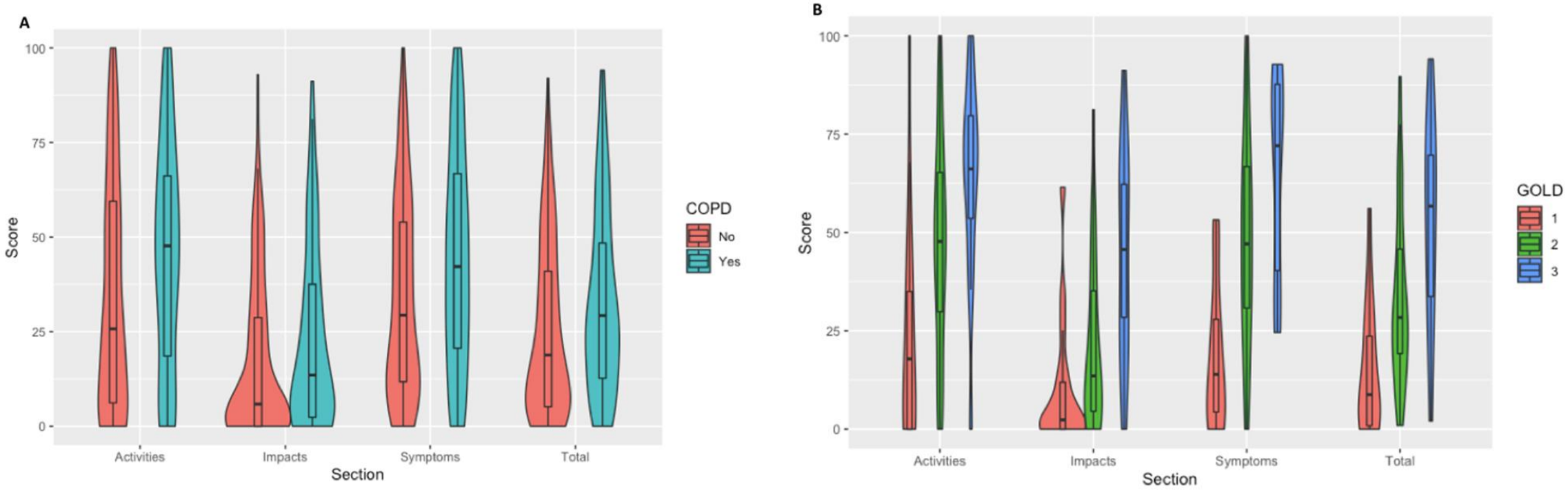
MEHARRY
MEDICAL COLLEGE

Demographic characteristics

Characteristics of consented patients, N=44	
Characteristic	N (%)
Mean age (SD), years	61.8 (5.3)
Sex	
Male	29 (66)
Female	15 (34)
Race	
Black	6 (14)
White	34 (77)
Other	4 (9)
Smoking history	
Former smoker	10 (23)
Current smoker	34 (77)

Sample collection, June 2020	
Sample type	N
Sputum	48
Nasal brushings	50
Buccal	51
Urine	51
Serum	52
Plasma	98
Cell-free plasma RNA	52

St. George Respiratory Questionnaire



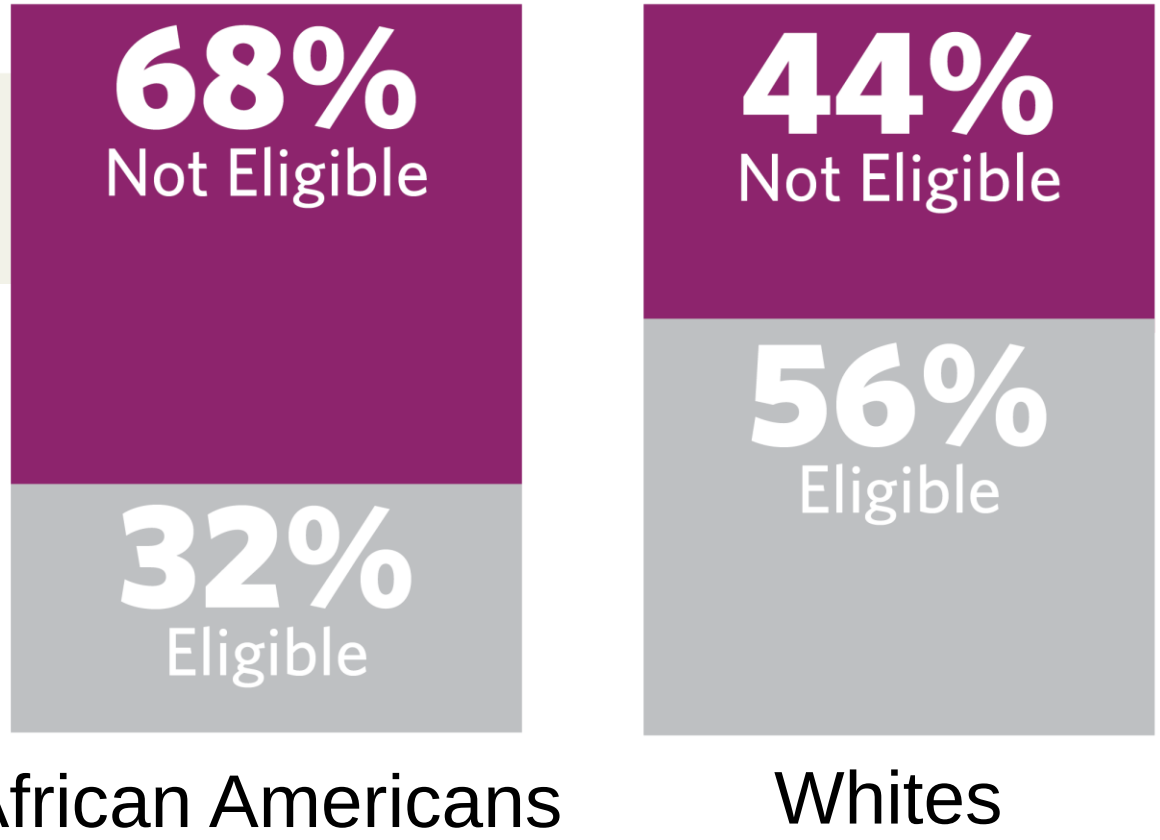
Research

JAMA Oncology | Original Investigation

Evaluation of USPSTF Lung Cancer Screening Guidelines Among African American Adult Smokers

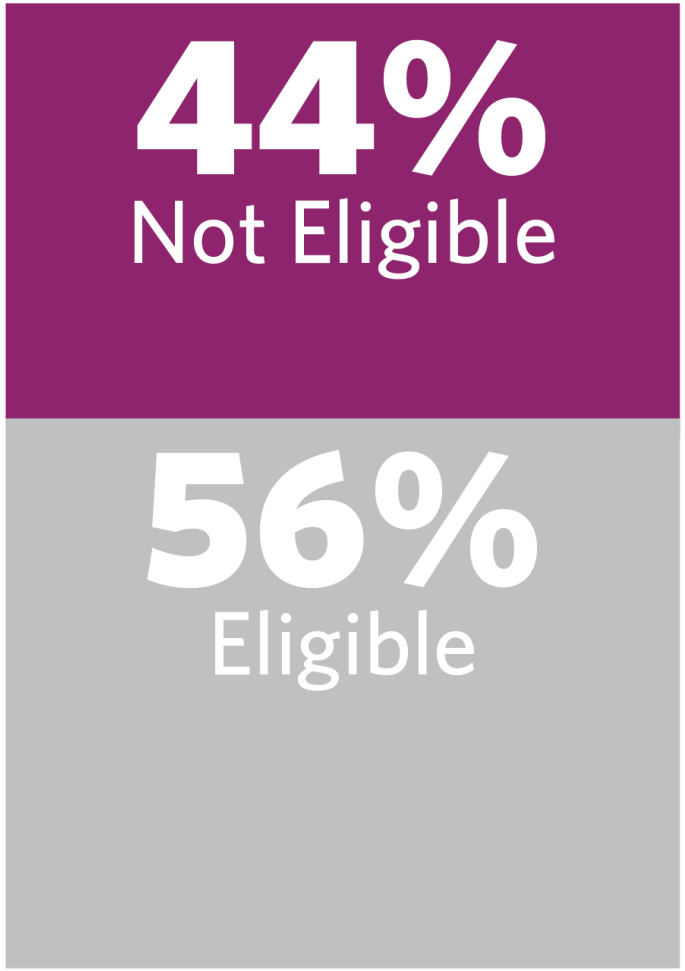
Melinda C. Aldrich, PhD; Sarah F. Mercaldo, PhD; Kim L. Sandler, MD; William J. Blot, PhD; Eric L. Grogan, MD; Jeffrey D. Blume, PhD

IMPORTANCE The United States Preventive Services Task Force (USPSTF) recommends low-dose computed tomography screening for lung cancer. However, USPSTF screening guidelines were derived from a study population including only 4% African American smokers, and racial differences in smoking patterns were not considered.



Revised Guidelines Reduces Eligibility Disparities
(Lower Smoking History & Age Criteria)

African Americans



Whites

Aldrich et al. JAMA Oncology 2019

Where do we go next?

<u>Address Barriers to LC Screening to Achieve Equity</u>:

- Current eligibility guidelines exclude certain populations
- Lack of awareness
- Cost concerns
- Skeptical of evidence
- Perception, fear, stigma
- Geographic access
- Shared decision making

National Quality Forum Report 2017

2. Management of Indeterminate pulmonary nodules. Steve Deppen Eric Grogan

Lung Atlas: Aid for Thoracic Diseases Diagnosis

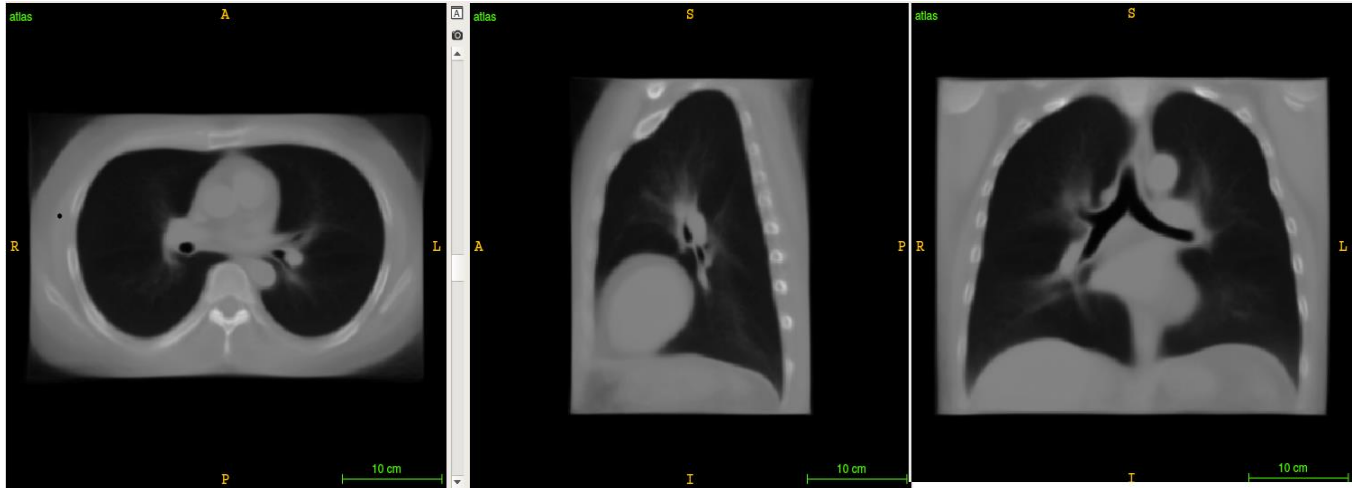


Figure 1: Grayscale Atlas

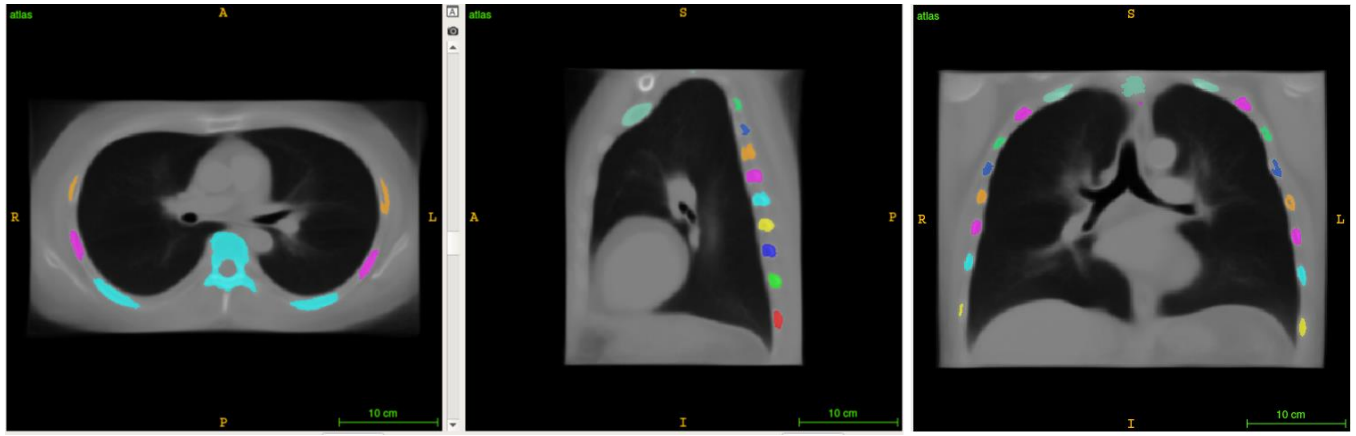


Figure 3: Grayscale Atlas with Rib Identification

Added Rib and Vertebral identification as quality of life improvement for radiologist readers (ease of report embedding)

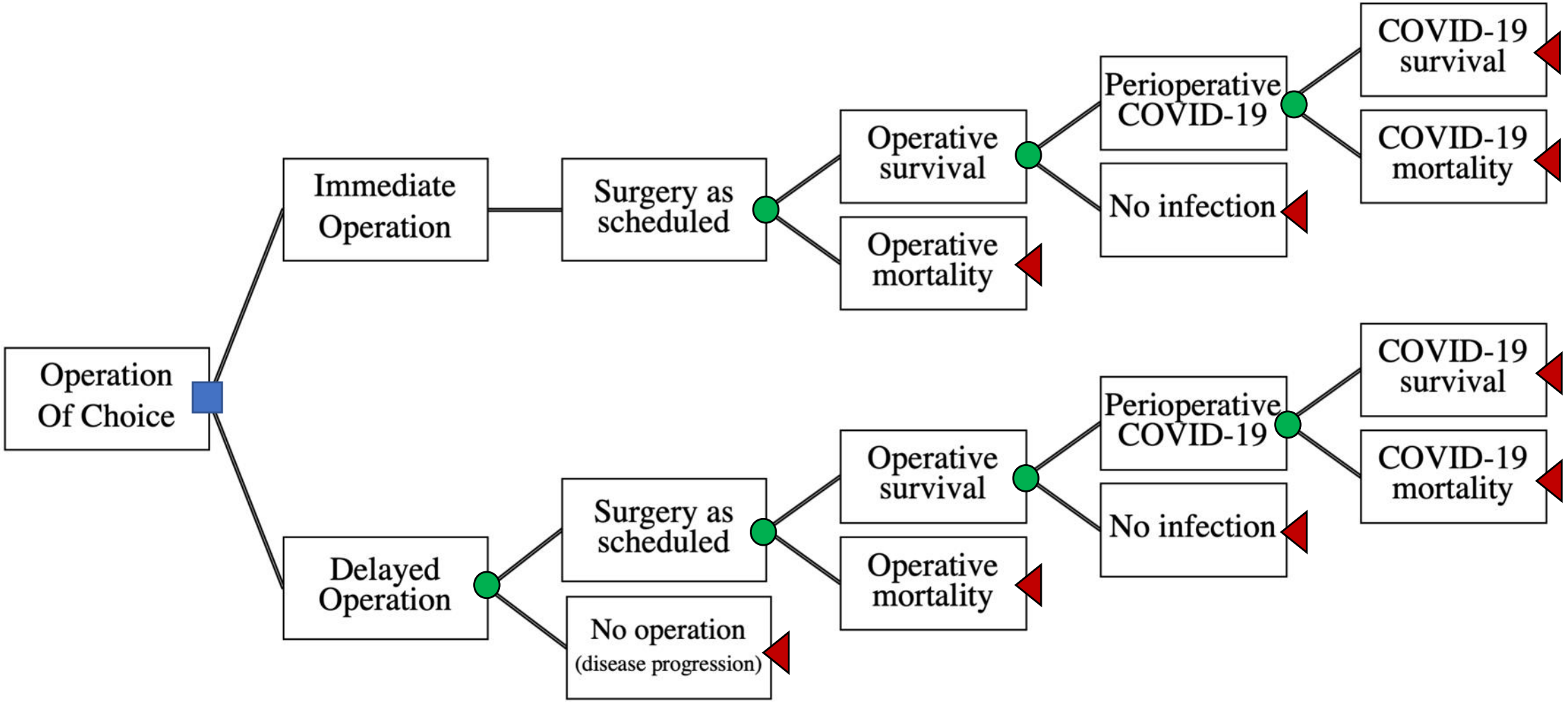
Multi-site validation of EIA histoplasmosis results

Test characteristics of histoplasma EIA

	IgG+				IgM+				IgG+ & IgM+			
	VUMC 1	VUMC 2	UPMC	Cinci	VUMC 1	VUMC 2	UPMC	Cinci	VUMC 1	VUMC 2	UPMC	Cinci
Positive tests	28	25	6	16	9	8	4	3	6	6	0	1
Sens	39%	32%	9%	54%	13%	11%	4%	8%	12%	8%	-	8%
Spec	89%	91%	92%	76%	97%	100%	92%	95%	100%	100%	-	100%
PPV	71%	66%	67%	44%	77%	100%	50%	33%	100%	100%	-	100%
NPV	69%	72%	35%	83%	63%	68%	34%	75%	63%	67%	-	76%

Shipe et al. Validation of Histoplasmosis Enzyme Immunoassay to Evaluate Suspicious Lung Nodules. Annals of Thoracic Surgery (in press)

COVID-19 Supplement: when to start cutting again? Decision-analysis of delaying surgery



Lung Nodule Results in the COVID 19 era

- For base case (65% likelihood of lung cancer), choosing **immediate surgery slightly favored**
  - 5-year survival: Immediate: 0.77
    Delayed: 0.74

- If COVID-19 **infection risk >13%,** delayed surgery favored
  - High COVID-19 related mortality
  - High risk of disease progression during delay

Shipe, Haddad, Deppen, Kozower, Grogan. "Delaying diagnosis of Lung Cancer in the Era of COVID-19: A Decision Analysis". Annals of Thoracic Surgery. Under review.

Sensitivity Analysis: COVID Infection Rates

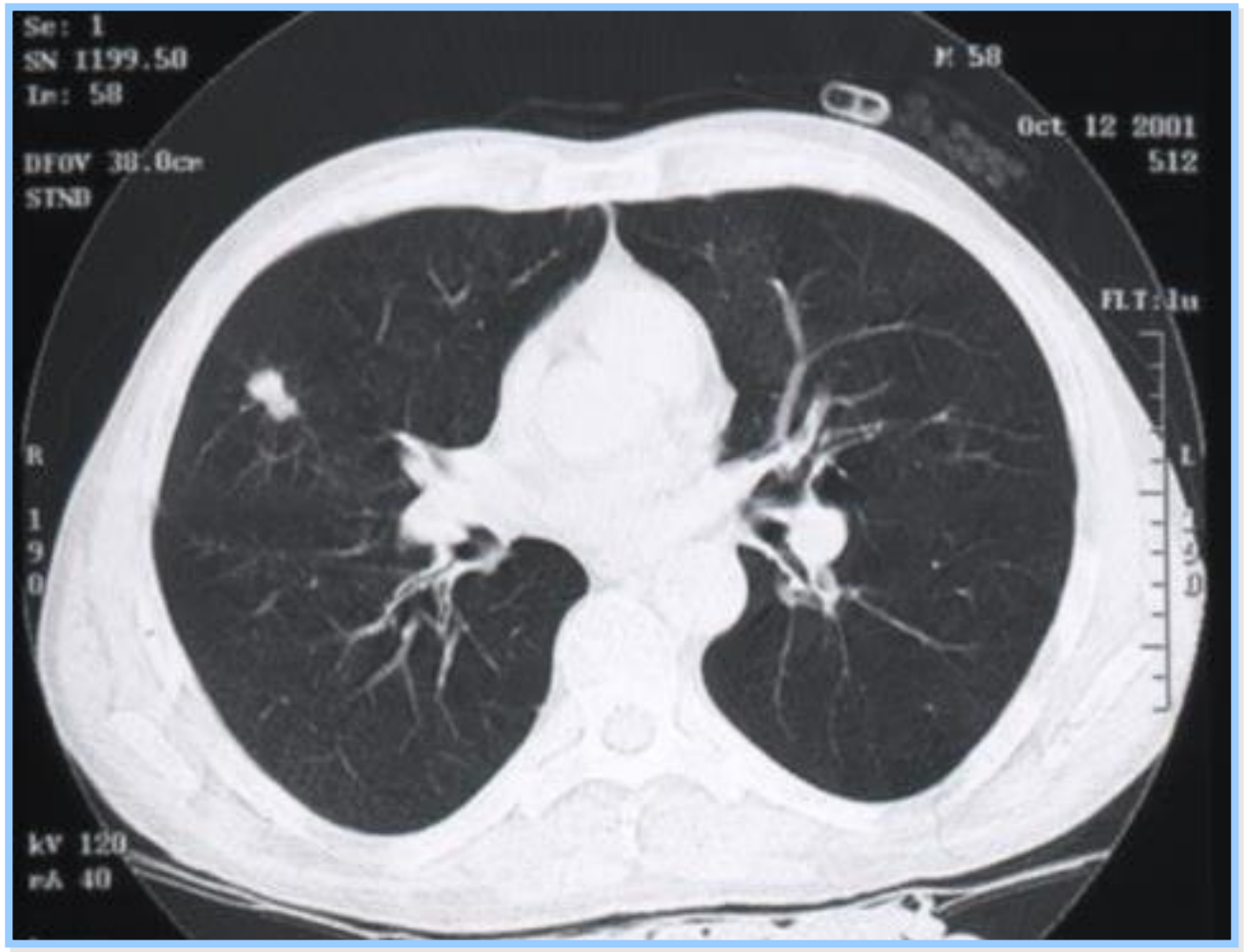
- Infection range with equivocal survival outcomes

	Immediate	Equivocal	Delayed
Bariatric surgery	0%	0.001-3%	>4%
Esophageal cancer	<2%	3-6%	>7%
LDKT	<1%	2-7%	>8%
Lung nodule	**<9%**	**10-12%**	**>13%**
TAVR low risk	<42%	43-46%	>47%
TAVR intermediate risk	<52%	53-54%	>55%
DCIS	<50%	51-96%	>97%

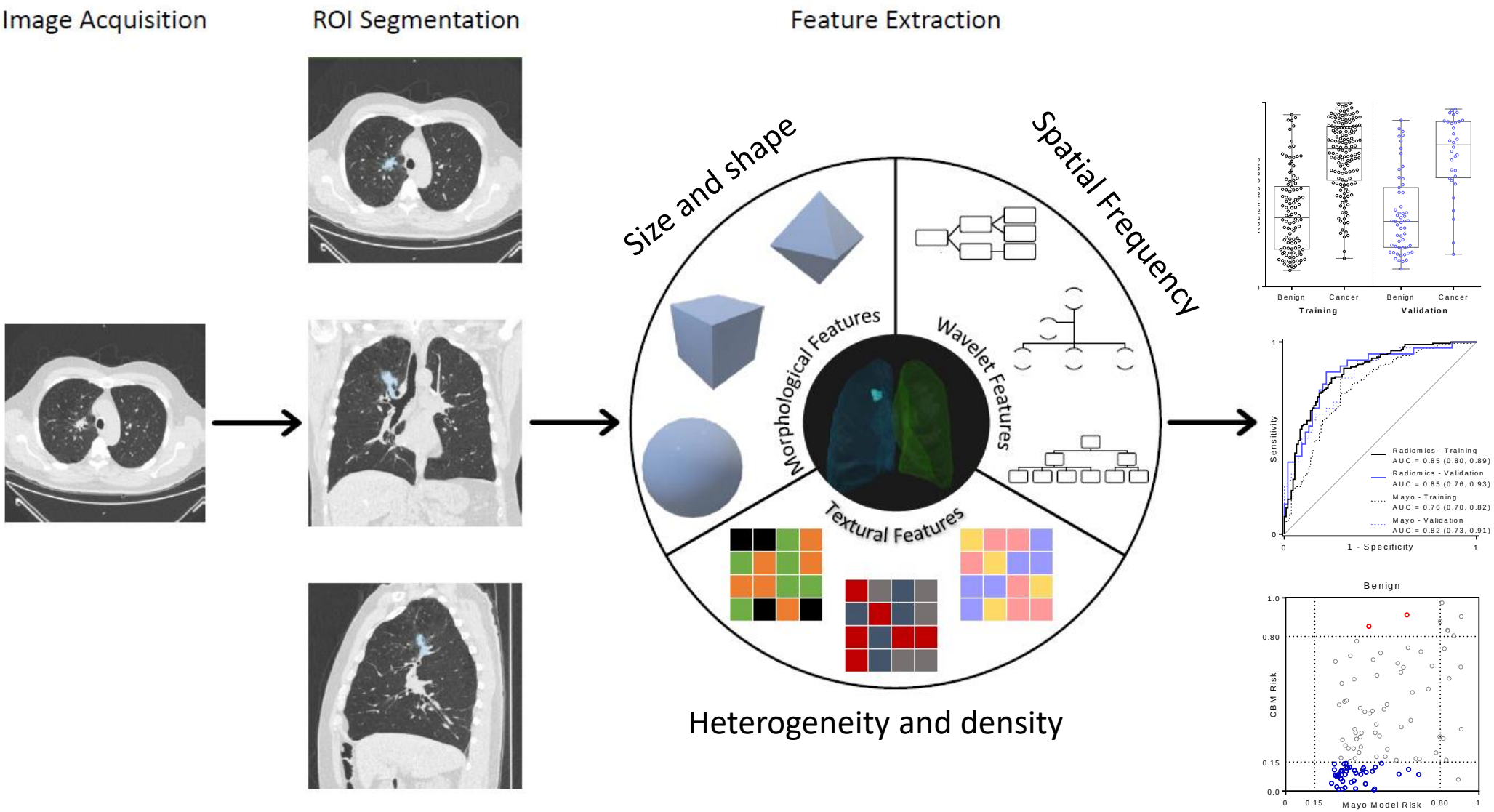
Survival could be impacted by patient selection

Management of indeterminate pulmonary nodule

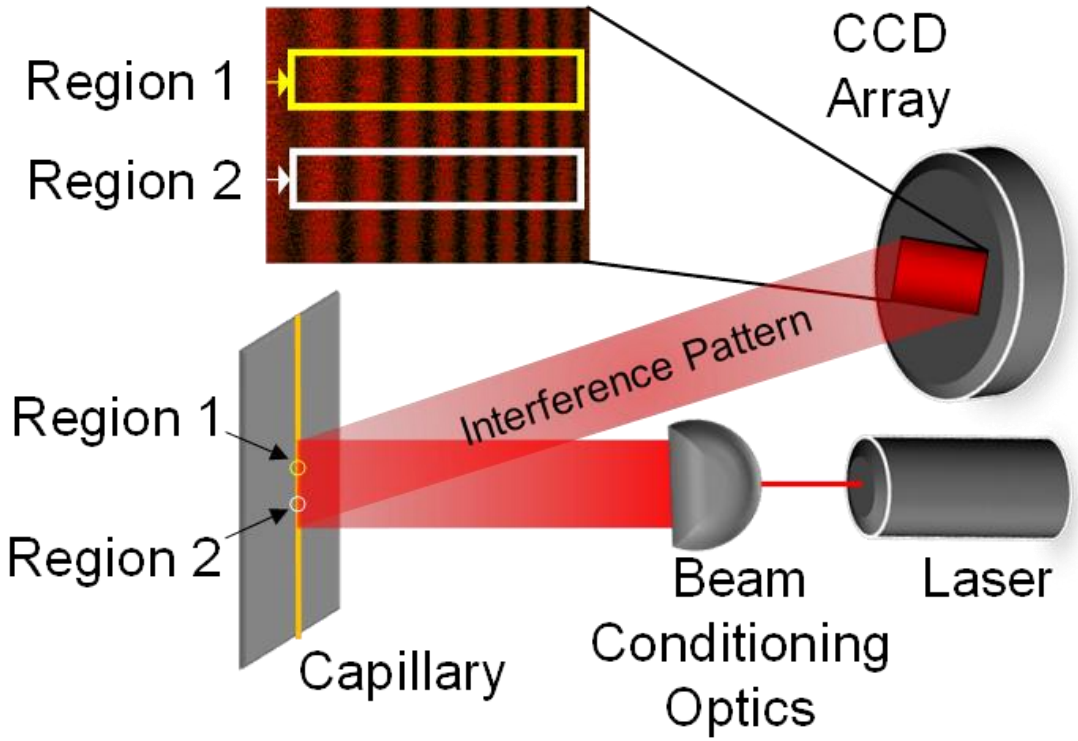
– Pierre Massion, Bennett Landman, Darryl Bornhop

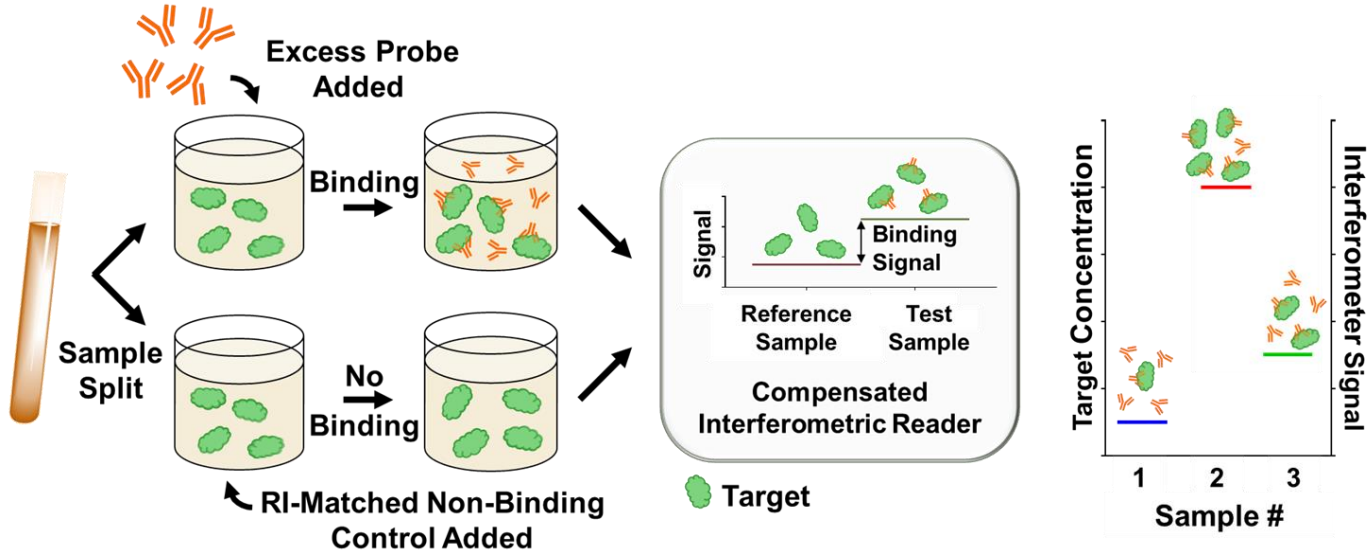


Quantitative imaging structural analysis



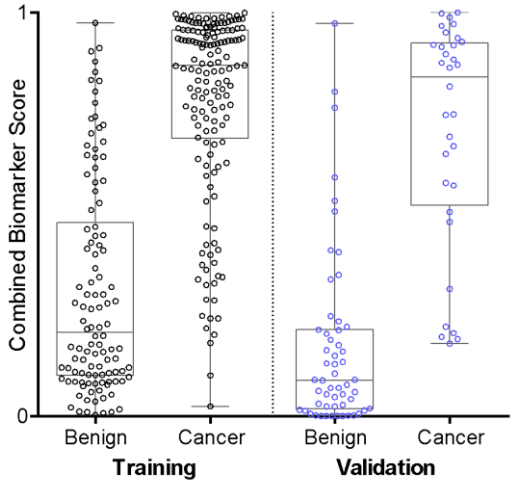
High sensitivity CYFRA 21-1 by Interferometry

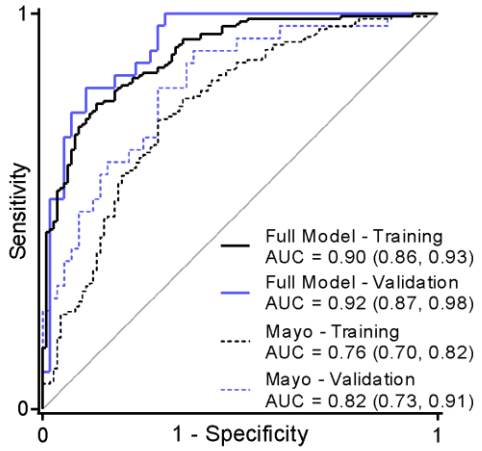




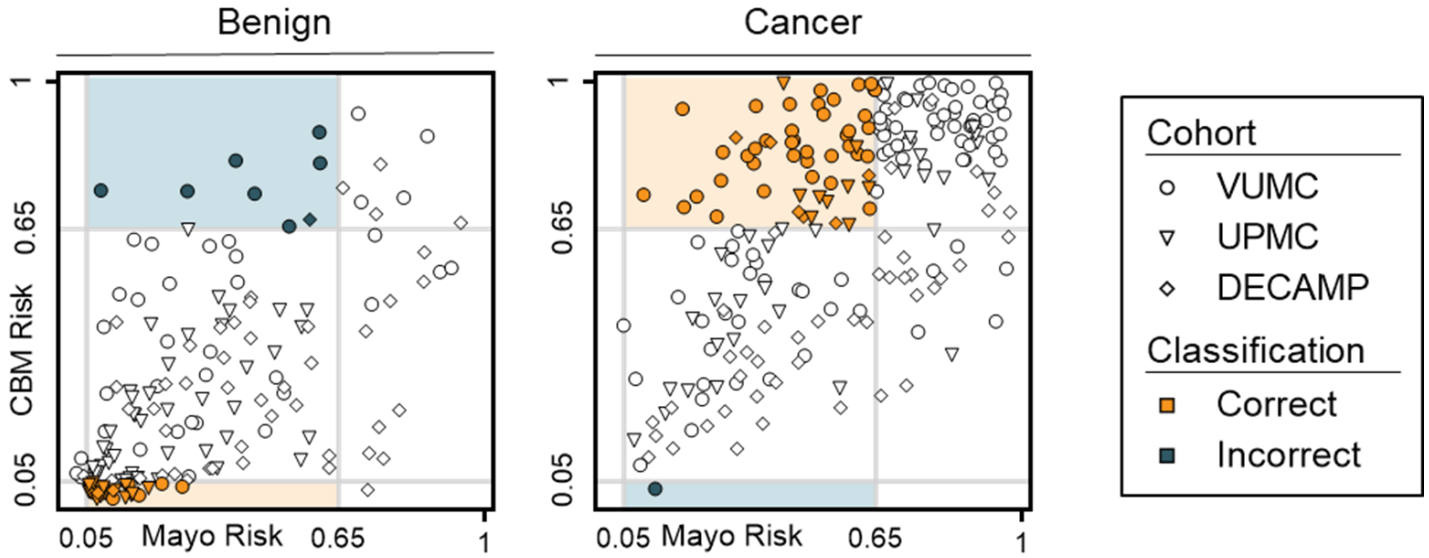
Kammer, et.al., ACS Sensors, (2018).
Kammer, et. al., Optics Letters (2018)
Kammer, et. al., ACS Combinatorial Science (2019)
US and PCT patents granted and pending.

The Combined Model Risk Reclassification
Clinical, Radiomics and CYFRA-21-1



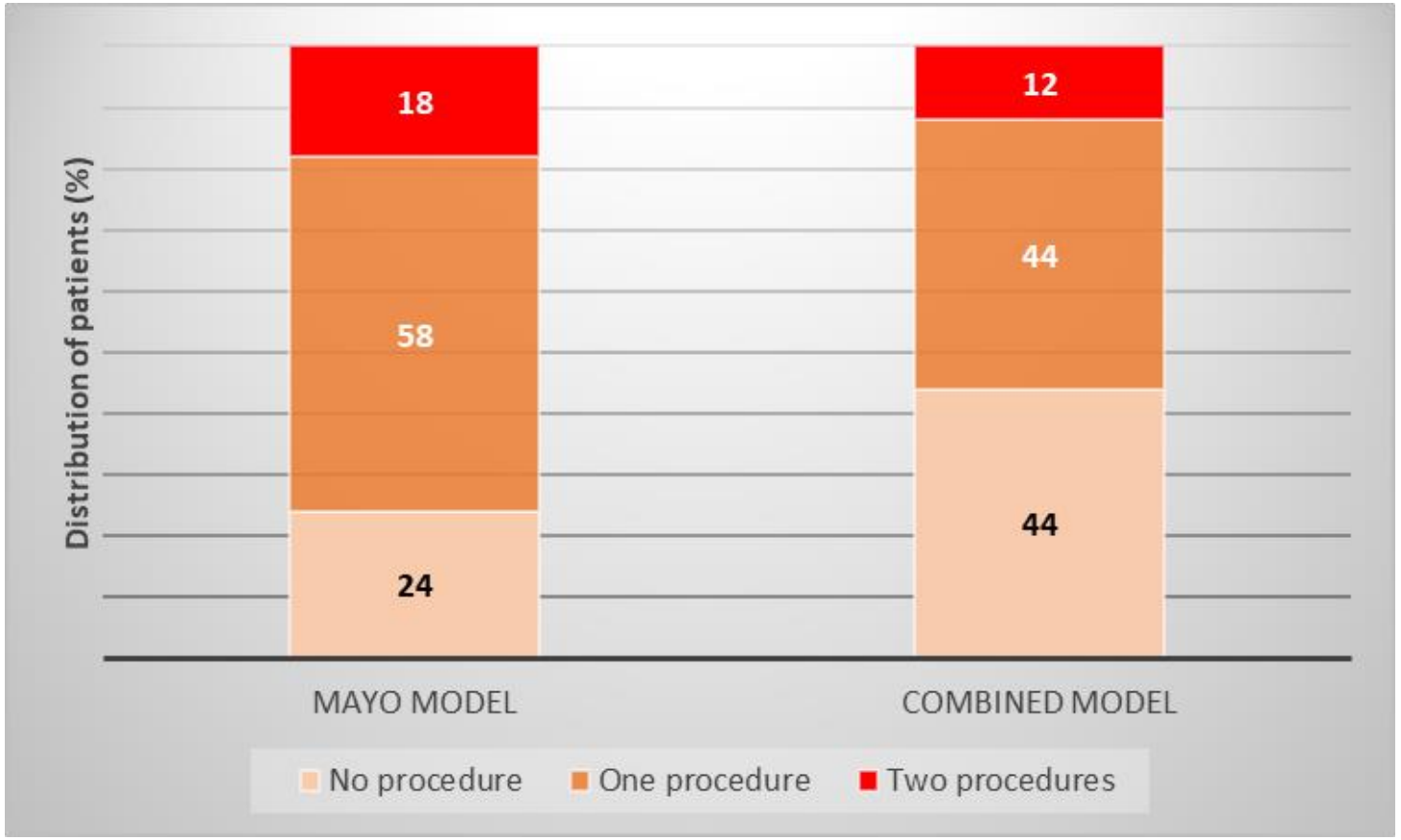


VUMC
UPMC
DECAMP

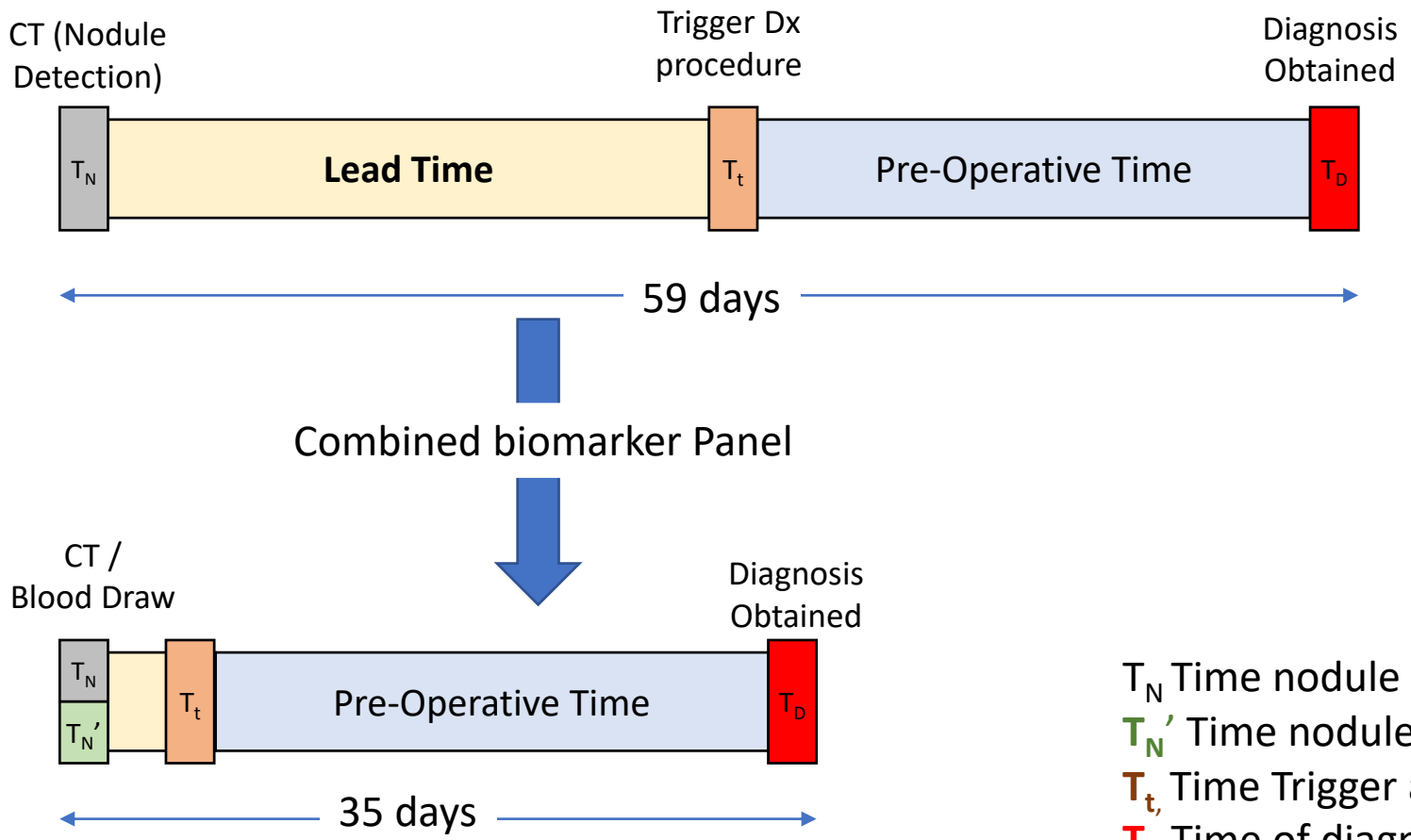


Clinical utility of the model: Decrease in invasive procedures tested on 106 IPNs from VUMC

Effect of CBM on % of patients with 0, 1 or 2 invasive procedures prior to Dx.



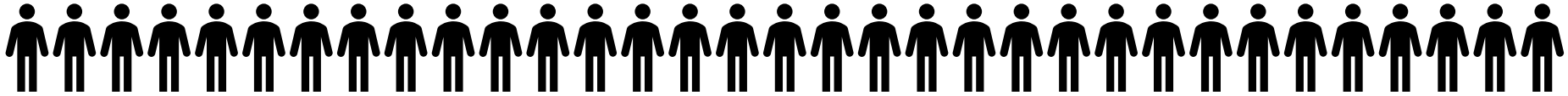
Clinical utility of the model: Reduced Time to diagnosis tested on 106 patients from VUMC.



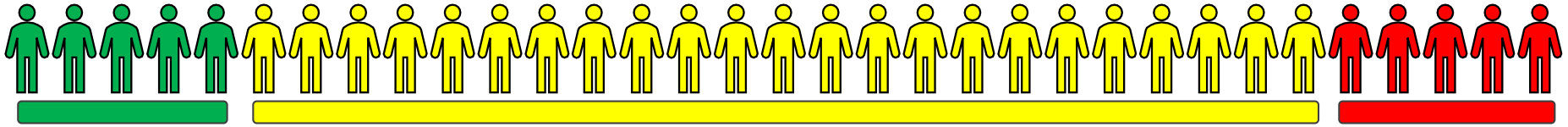
T_N Time nodule detection
T_N' Time nodule detection with BM
$T_{t,}$ Time Trigger a diagnostic procedure
T_D Time of diagnosis

Conclusions

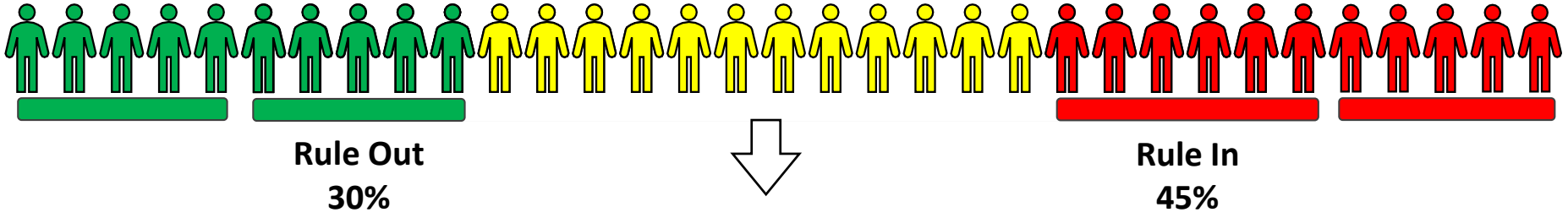
The incidentally detected IPN population: roughly 1.6 million per year



Clinical Risk Model



Combined Biomarker Model



Lower rate of unnecessary biopsy/thoracotomy/PET

On going validation studies

Validation

Meth ctDNA
UPMC

Auto Ab
Fred Hutch

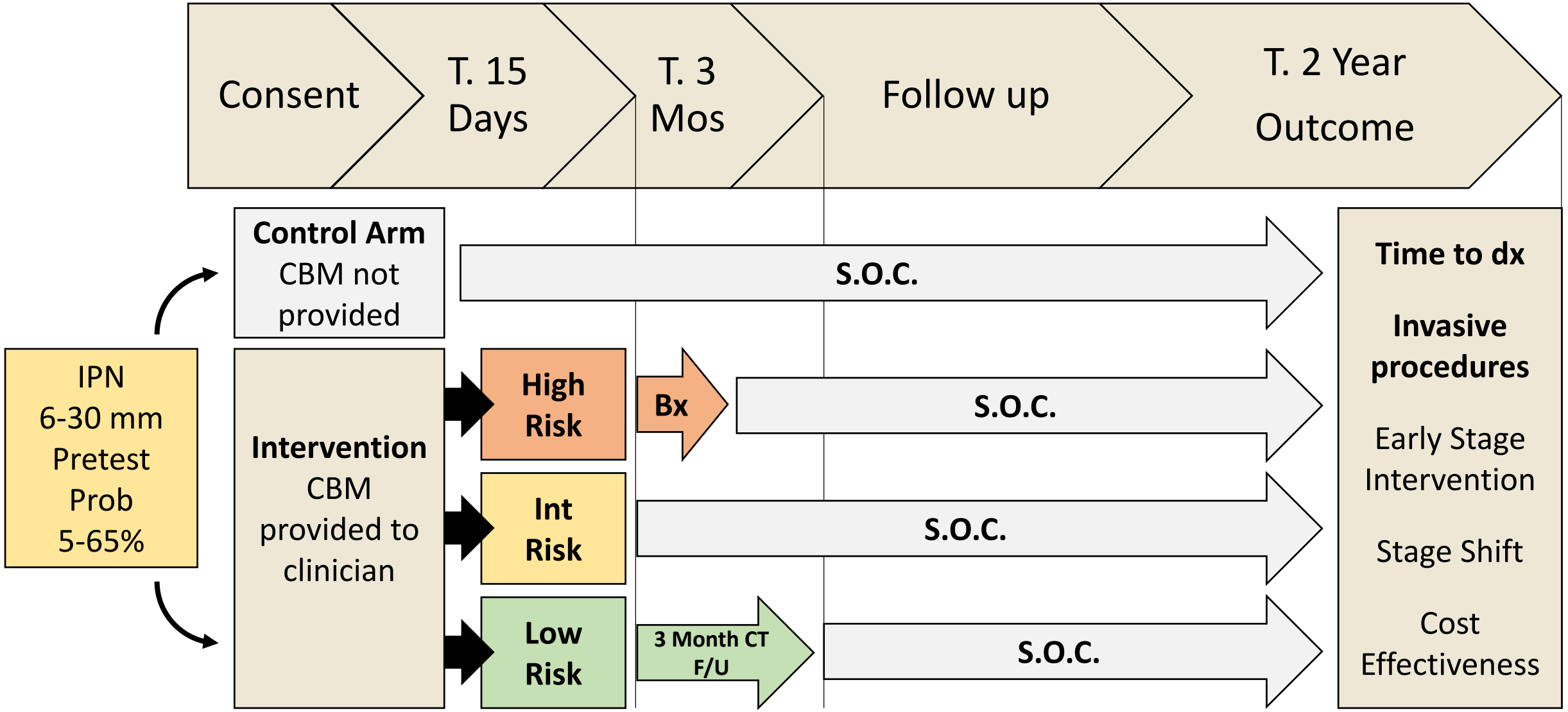
Biomarkers

-Deep Learning
-Autoantibodies
-Metabolites
-ctDNA

Clinical Trial

Planned

Biomarker driven management of IPN: RCT utility trial



Future of CVCs

Biomarkers tested Longitudinally

Interferometer/assay CLIA certification

EHR Prediction with Deep learning / AI

Diagnostic test application and utility

Expanding CIR assay targets

Total Lung Health using CT analysis

Personalized screening

Expanding CIR assay targets

Total Lung Health using CT analysis

Thank you!

Vanderbilt

VUMC
- Michael Kammer, PhD
- Melinda Aldrich, PhD
- Steve Deppen, PhD
- Eric Grogan, MD
- Shayan Mahapatra, MBBS
- Sanja Antic, MD
- Sarah Atmajoana

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- Chirayu Shah, MD PhD

Chemistry
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- Amanda Kussrow, PhD
- Rebekah Webster

Biostatistics
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- Sheau-Chiann Chen, PhD

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- Robert Gillies, PhD
- Yoganand Balagurunathan, PhD

UC Denver
- Anna Baron, PhD
- Alex Kaiser, PhD

University of Pittsburgh
- David Wilson, MD, MPH
- Brenda Diergaarde, PhD

DECAMP
- Avi Spira, MD
- Ehab Billatos, MD

HealthMyne
- Erin Prince
- Katie Dickerson

Questions?