Bioengineering for COVID-19: *Rapid Acceleration of Diagnostics (RADx) at Unprecedented Speed and Scale*

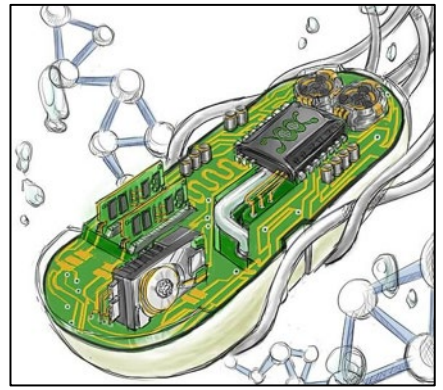
Bruce J. Tromberg, Ph.D.
Director, National Institute of Biomedical Imaging and Bioengineering (NIBIB)
PI, Section on Biomedical Optics, NICHD

NIBIB Vision: *Engineering the Future of Health*

Therapeutic Devices

Monteris Medical, Inc.

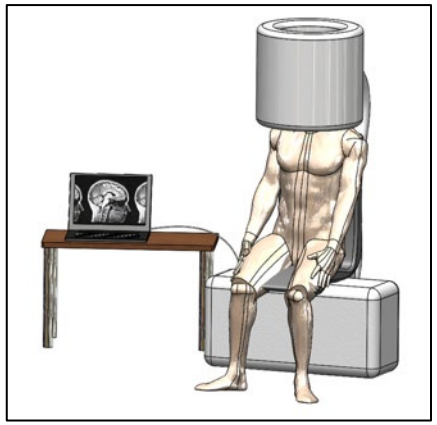
Engineered Biology



Cambridge University

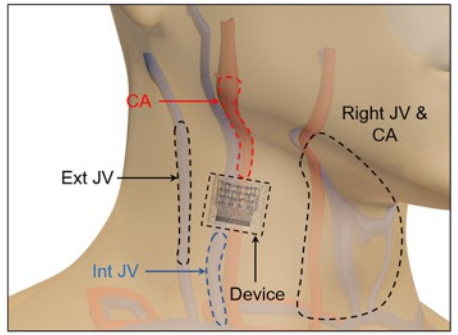
Modeling, Computation & Machine Intelligence

V. Venugopalan, J. Spanier, UCI



Imaging Technologies

M. Garwood, UMN

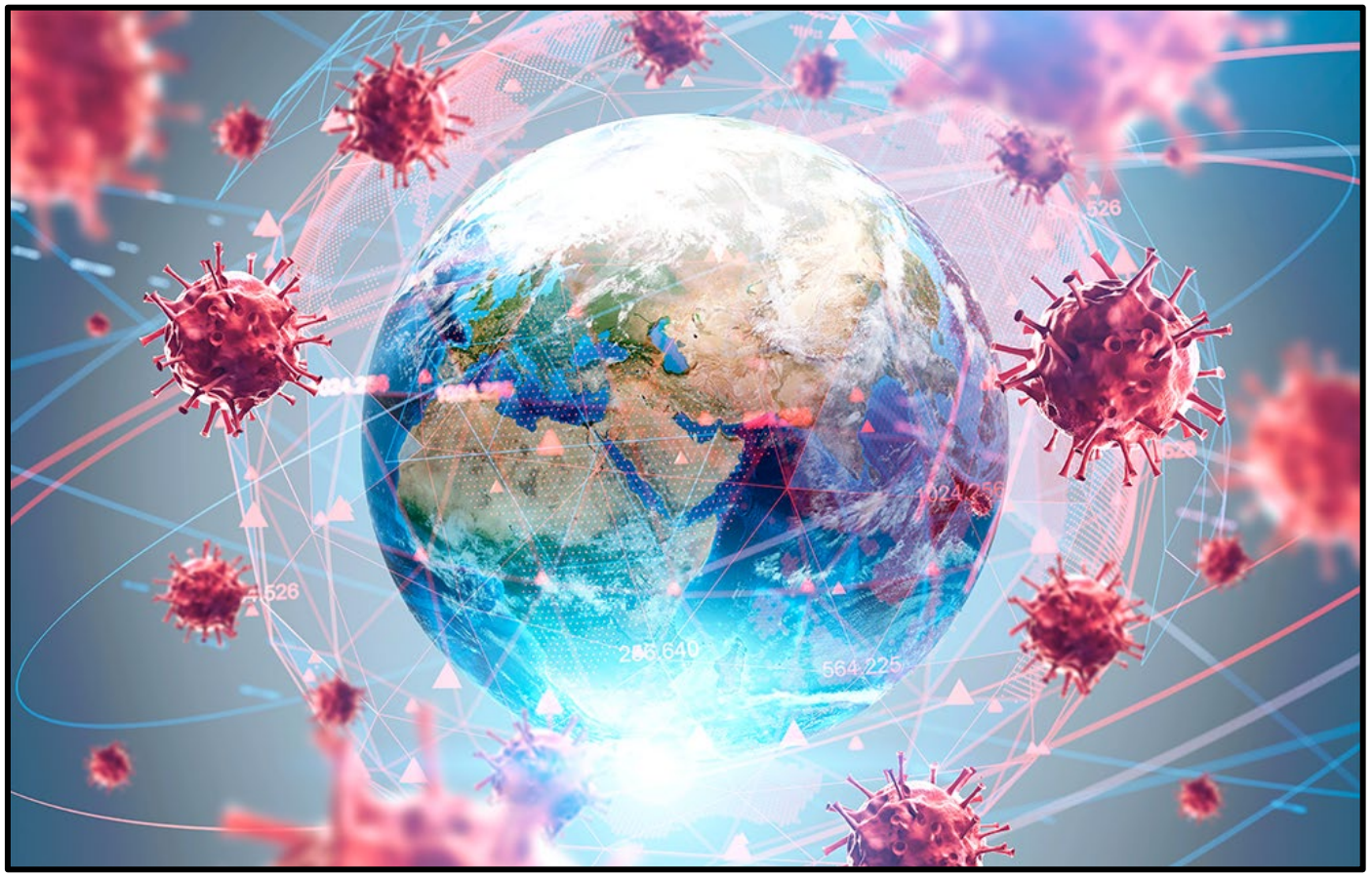


Sensors and Point of Care

S. Xu, UCSD

Bioengineering for COVID-19

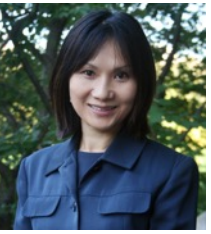
NIBIB Strategy



1) Imaging and AI
2) Digital Health Platforms
3) **Diagnostic Test Technologies**

Medical Imaging and Data Resource Center (MIDRC)

Kris Kandarpa
Chair



Guoying Liu
Scientific Program Lead

Behrouz Shabestari
NIBIB National Technology Center Program Director

Maryellen Giger (PI)
AAPM, University of Chicago

https://www.nibib.nih.gov/news-events/newsroom/nih-harnesses-ai-covid-19-diagnosis-treatment-and-monitoring

Two-year, $20M contract: Medical Imaging/Data Science

Thoracic imaging and clinical data repository for COVID 19

Develop, validate ML/AI for detection, diagnosis, Tx

60,000 curated COVID-19 chest radiographs and CTs+clinical data

THE UNIVERSITY OF CHICAGO

RSNA® Radiological Society of North America

ACR® American College of Radiology

AAPM

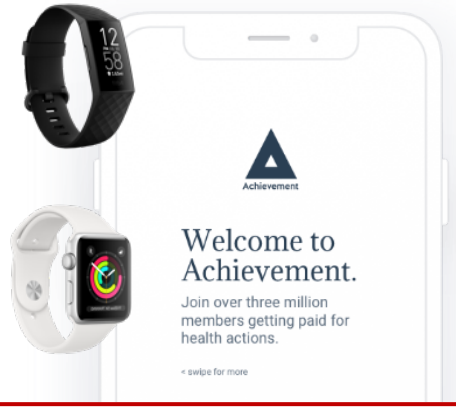
NIH National Institute of Biomedical Imaging and Bioengineering

Wearables for Monitoring and Detection

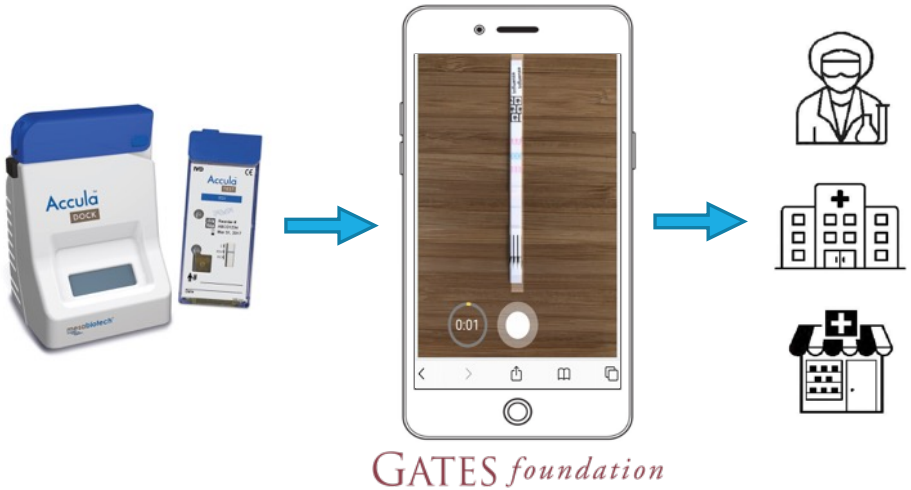
physIQ

pinpoint IQ

evidation

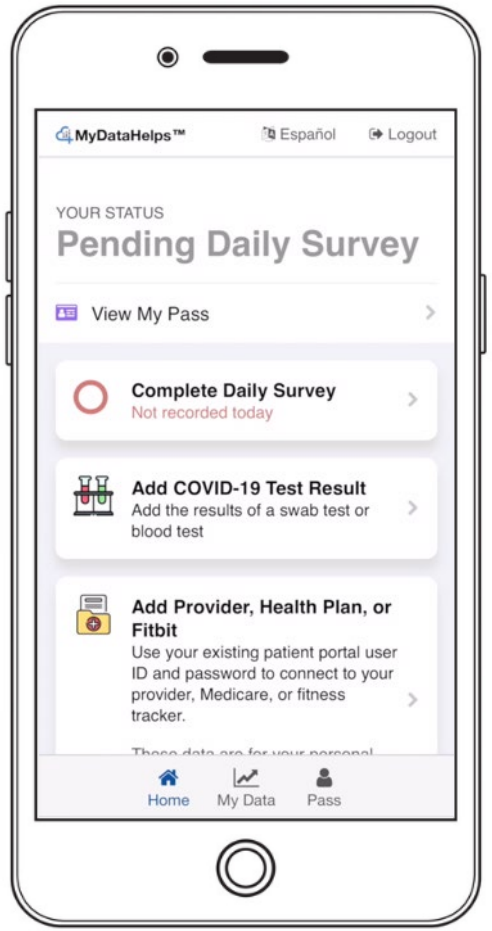


Integration with Test Results



GATES foundation

SAFER-COVID



careevolution
HEALTHCARE TECHNOLOGY

Digital Contact Tracing

IBM

Workforce

UCSF

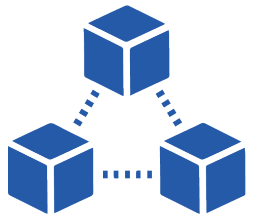
GPS

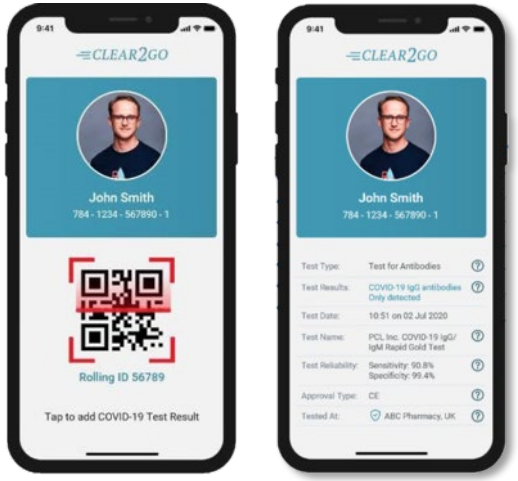
Wi-Fi

vibrent

Proof of Health Status

iCrypto





Unexpected Opportunity

NIH Office of the Director


Francis Collins


Rachael Fleurance


Larry Tabak


Tara Schwetz

RADx Tech – $500M
Highly competitive, rapid three-phase challenge to identify the best c… for at-home or point-of-care tests for COVID-19

RADx Advanced Technology Platforms (RADx-ATP) – $230M
Rapid scale-up of advanced technologies to increase rapidity and enhance and validate throughput – create ultra-high throughput machines and facilities

RADx Radical (RADx-Rad) – $200M
Develop and advance novel, non-traditional approaches or new applications of existing approaches for testing

RADx Underserved Populations (RADx-UP) – $500M
Interlinked community-based demonstration projects focused on implementation strategies to enable and enhance testing of COVID-19 in vulnerable populations

April 29

April 24, 2020: $1.5B to NIH
$500 Million to NIBIB


Jill Heemskerk.


Bruce Tromberg

National Institute of Biomedical Imaging and Bioengineering (NIBIB)

$307 M Partnership with BARDA

December 2020 Congress: ***$100,000,000***

Tech/ATP Team Leads: Tiffani Lash, Todd Merchak, Taylor Gilliland, Kate Egan, Mike Wolfson, Doug Sheeley, Gene Civillico

OASH FDA CMS CDC

https://www.nih.gov/research-training/medical-research-initiatives/radx

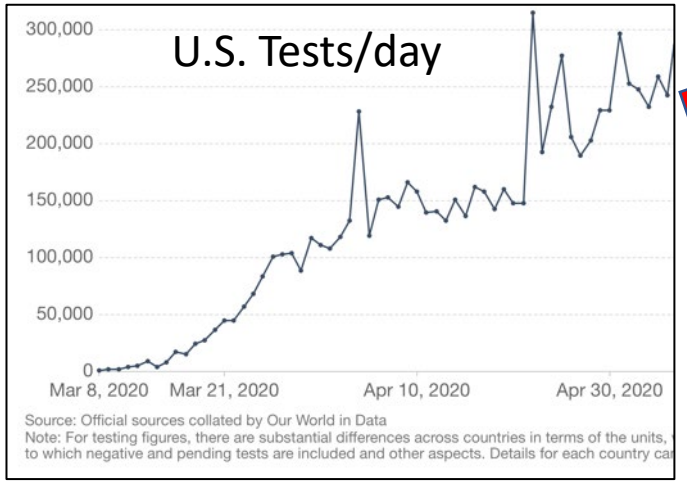
RADx Tech & ATP Goals

1) Expand COVID-19 Testing Technologies: *Number, Type and Access*

2) Optimize Performance: *Technologic and Operational; Match Community Needs*

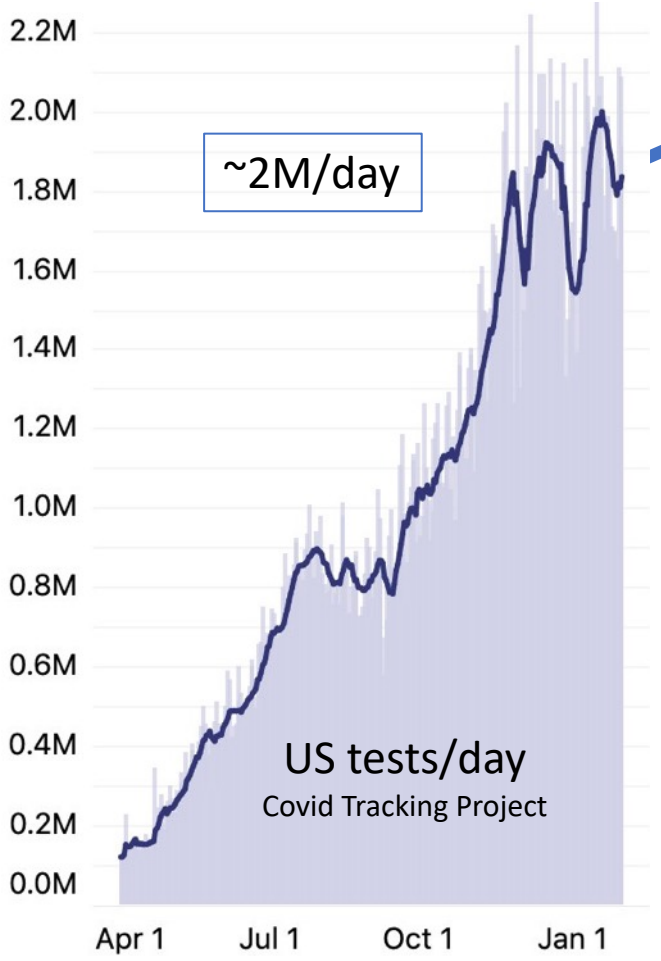
Test Settings

- Home-based
- Point of Care (POC)
- Laboratory (CLIA, research)



RADx Launch: *~250k/day*

Lab > POC



POC > Lab

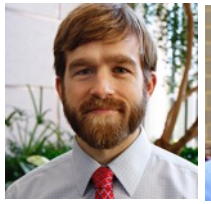
+ >2 million/day LFA antigen tests unreported

https://www.theatlantic.com/health/archive/2021/01/rapid-antigen-covid19-tests-unreported/617668/

Point-of-Care Technologies Research Network (POCTRN)

NIBIB National Network: *5-6 years for new POC technologies*

Established 2007, Expanded 2020: >1000 RADx experts & contributors


Todd Merchak


Tiffany Lash

https://www.poctrn.org

VENTUREWELL™ idea to impact

GaTech/Emory
- ✓Engineering
- ✓Design/Prototype
- ✓Clinical Validation
- ✓Biobank samples
- ✓In-Home Validation

Johns Hopkins
- ✓Public Health/STD
- ✓Global Health
- ✓Clinical Validation
- ✓Biobank samples
- ✓Validation in LMICs

CIMIT/MGH
- ✓Coordinating Center
- ✓Collaboration/Management Platform
- ✓Business/Commercialization

Northwestern
- ✓HIV/AIDS
- ✓Engineering
- ✓Global Health
- ✓Clinical Validation
- ✓Validation in LMICs

UMass
- ✓Heart, lung, blood
- ✓Engineering
- ✓Clinical Validation
- ✓Biobank samples
- ✓Clinical Trials
- ✓Business/Commercialization

C BIO M C3i

Operations:
- Review & Fund
- Test & Validate
- Expert Guidance

Validation Core

>50 projects complete, ~2000 participants

Clinical Studies Core

Standard Trial Design, Digital Health Platform, Single IRB, Center Network

Deployment Core

Supply chain, Manufacturing, User Community, End to end solutions

National Institute of Biomedical Imaging and Bioengineering

RADx Tech/ATP Innovation Funnel

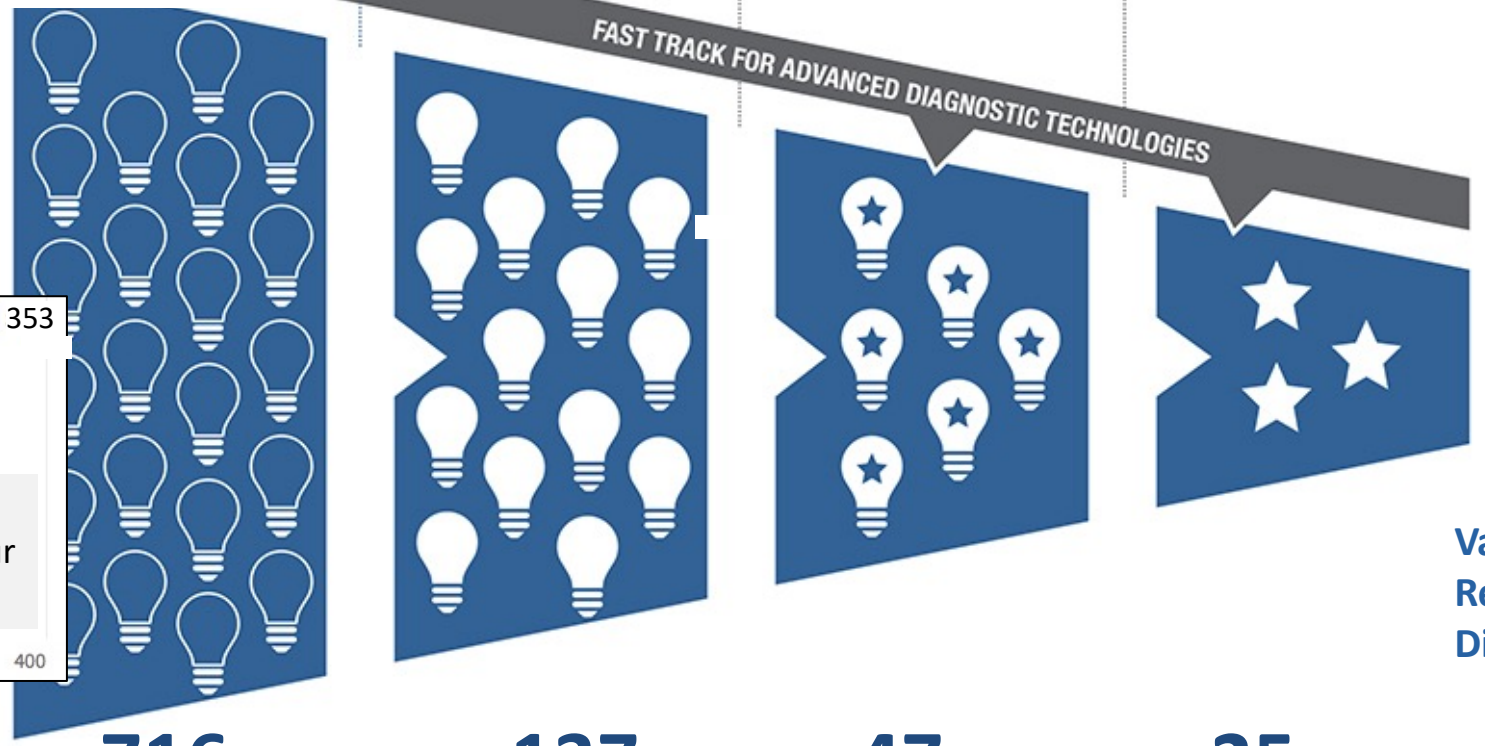
NATIONAL CALL FOR INNOVATIVE TECHNOLOGIES	PHASE 0: "Shark Tank"–Like Rapid Selection Process	PHASE 1: Validation and Risk Review	PHASE 2: Clinical Tests, Regulatory Approval, and Scaling Up	END OF SUMMER/ FALL 2020

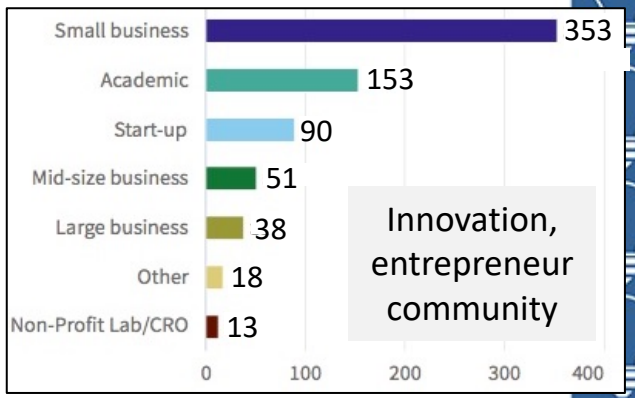
Rolling submission open April 29

5-6 Months

~3000
Applications Started

FAST TRACK FOR ADVANCED DIAGNOSTIC TECHNOLOGIES





Innovation, entrepreneur community

>6 M tests/day by end of year

DEPLOY MILLIONS of tests per week

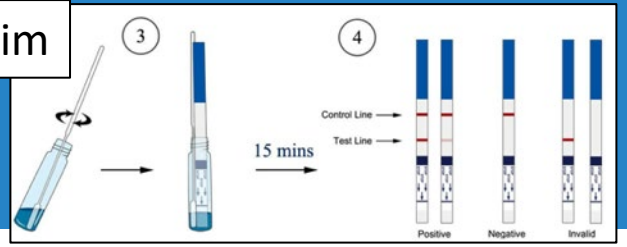
Validation, Clinical Testing, Regulatory, Manufacturing, Distribution

Projects in each Phase

716 | **137** | **47** | **25** (Tech + ATP) | **~$500M**

Mesa BioTech

Maxim



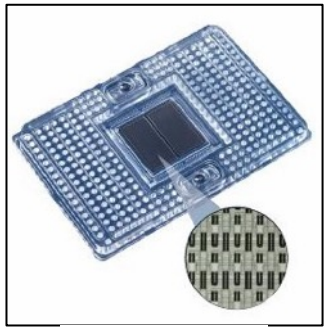
14 EUAs issued

Visby Medical

Ubiquitome

Quidel Sophia

Yukon Swabs

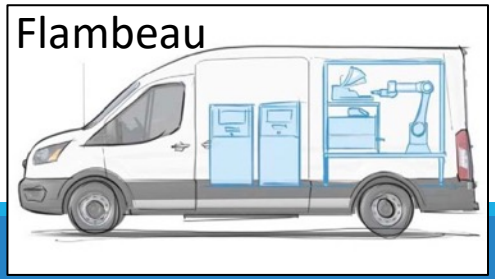


Fluidigm

Luminostics

Ellume

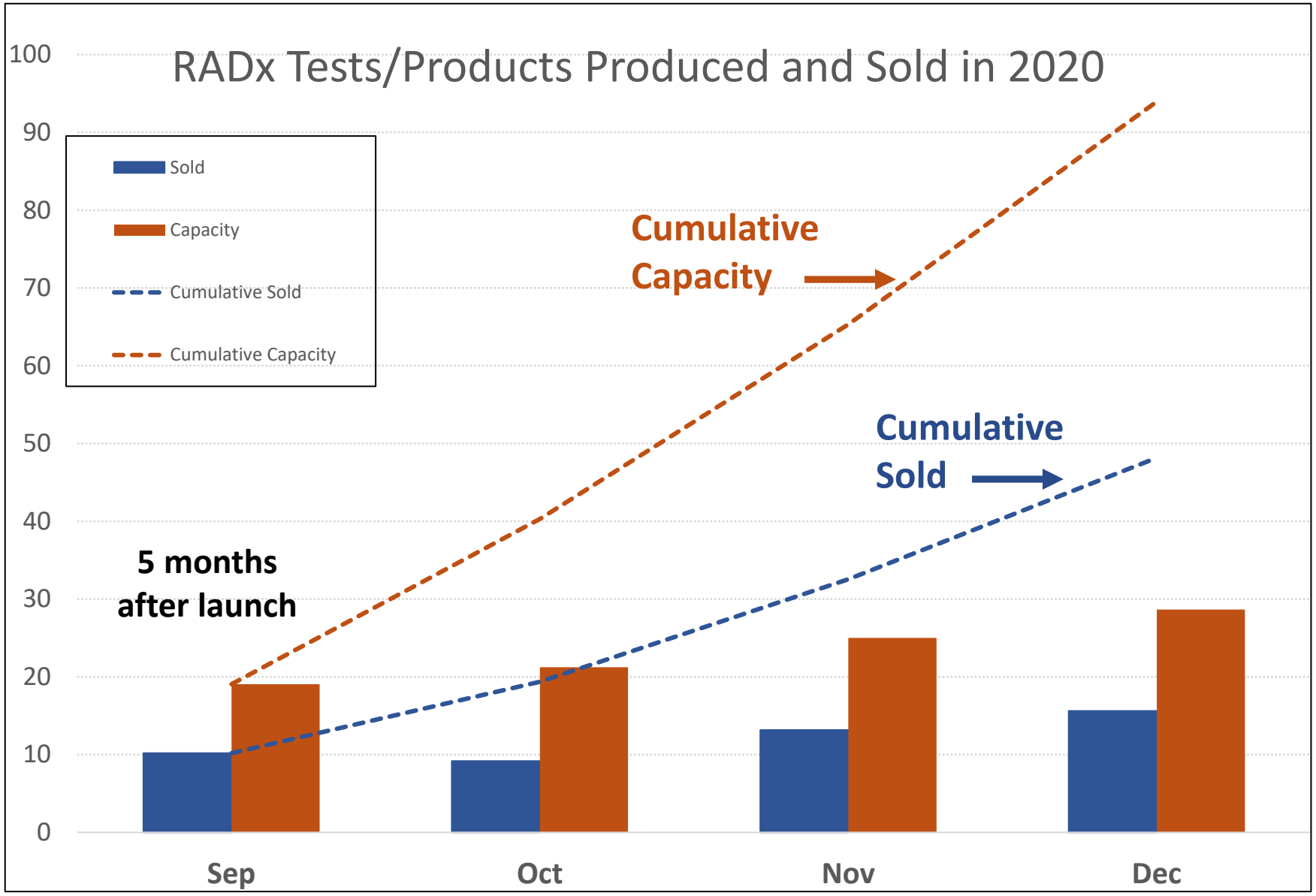
Flambeau



ANP

Point of Care & Home	
Visby	RTPCR
Mesa	RTPCR
Microgem	RTPCR
Talis	ISO-PCR
MatMaCorp	RTPCR
Ubiquitome	RTPCR
Quidel Sophia	An-LFA
Quidel QuickView	An-LFA
Luminostics	An-LFA
ANP	An-LFA
Ellume	An-LFA
Laboratory	
Flambeau	PCR-mobile
Fluidigm	RTPCR
Broad Inst	RTPCR
Illumina	NGS
Helix	NGS/RTPCR
Gingko	NGS/RTPCR
Sonic Healthcare	RTPCR
PathGroup	RTPCR
Aegis	RTPCR
Quanterix	SIMOA (An)
Lab Products	
Mammoth Biosci	CRISPR
Ceres Nanosciences	Beads/Conc
Yukon	Swabs

RADx Impact in 2020



- **~94 million capacity in 2020**
- **~48 million sold in 2020**
- ~950k tests/day produced Dec 2020; ~550k/day sold
- ~14 EUAs and 1st OTC EUA
- ~150 Companies supported, 25 “Phase 2”
- **Feb 2021**: Project millions OTC LFA tests/day
- **March 2021:** Project >2.5M tests/day

RADx Leveraging NIH Proof of Concept (PoC) Network

NIH SEED

Matt McMahon, PhD

~50 early-stage RADx-tech projects

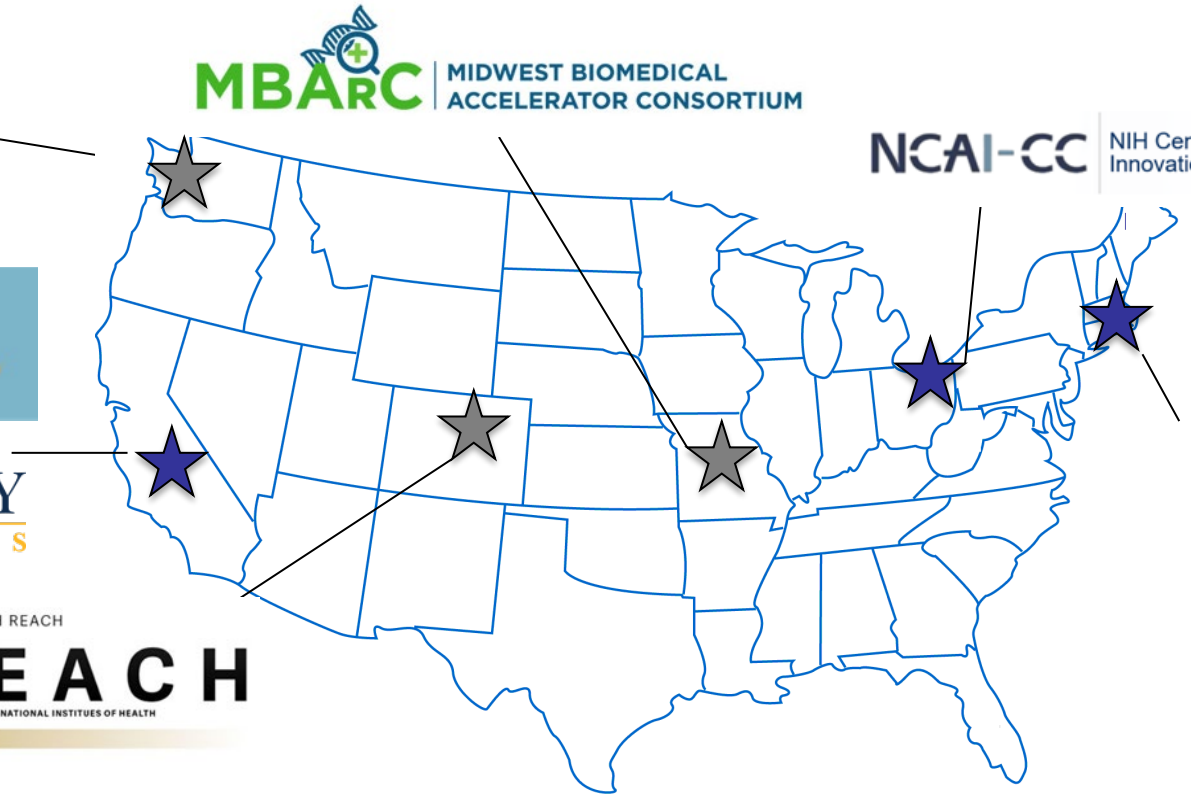
- **Project Funding**
- **Industry Coaching and Mentoring**
- **Training and Resources**

WASHINGTON ENTREPRENEURIAL RESEARCH EVALUATION & COMMERCIALIZATION HUB
WE-REACH
Bridge to Medical Impact

MBARC | MIDWEST BIOMEDICAL ACCELERATOR CONSORTIUM

NCAI-CC | NIH Center for Accelerated Innovations at Cleveland Clinic

UC CAI
University of California Center for Accelerated Innovation



CIMIT®
Consortia for Improving Medicine with Innovation & Technology

ULP UNIVERSITY LAB PARTNERS

B-BIC: Translating Discoveries Into Products

SPARK IS NOW POWERED BY NIH REACH
SPARK | REACH
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS | NATIONAL INSTITUTES OF HEALTH
COLORADO

NIH National Institutes of Health
Office of Extramural Research

RADx Test Validation Core (Emory-Gtech)

~50 projects complete



Wilbur Lam Greg Martin. Oliver Brand

Feasibility

Ensure positive control (provided or commercial) is positive

Ensure negative matrix (i.e. saliva, patient sample or commercial) is negative

Ensure negative matrix spiked with live and/or inactivated SARS-CoV-2 virus is positive

Contrived samples

Verify the limit of detection (LOD) via live and/or inactivated SARS-CoV-2 virus by serial dilution using correct matrix

Test non-SARS-CoV-2 coronaviruses (test specificity/cross-reactivity)

Test different strains of SARS-CoV-2 (strain variation)

Patient samples

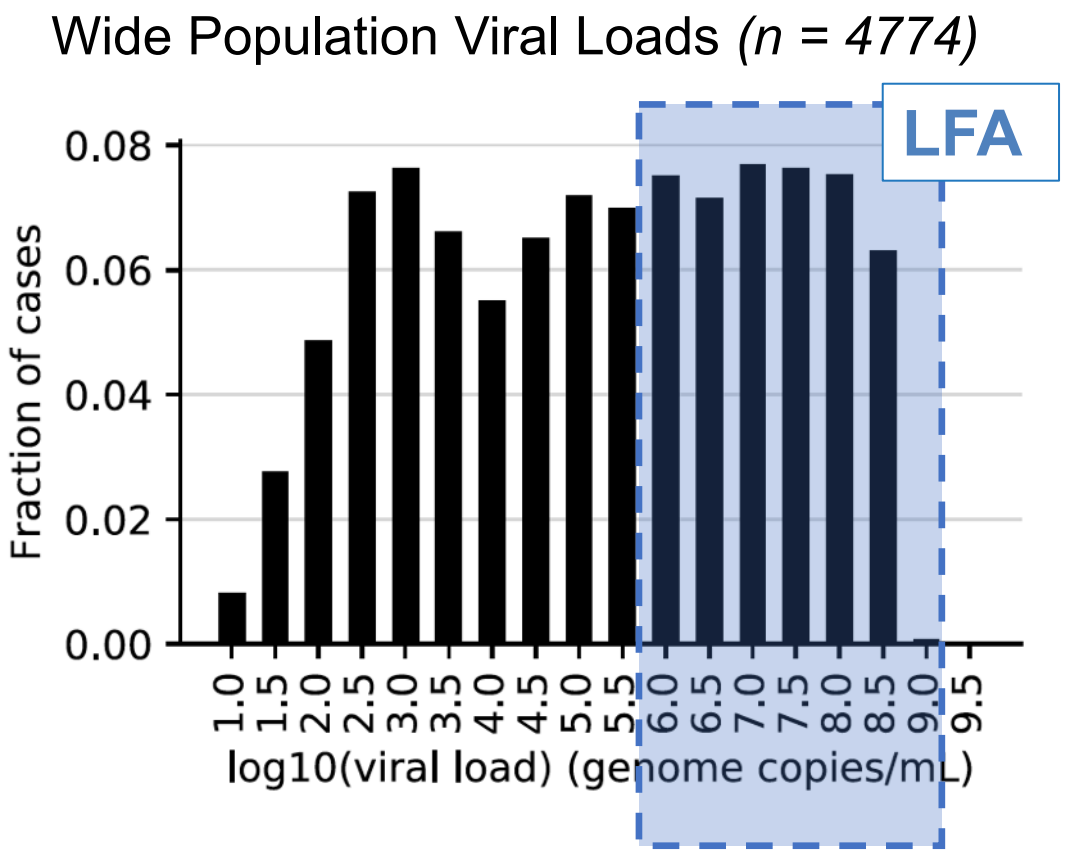
Test banked patient samples (adult and pediatric) with concomitant testing on reference method to determine concordance

Test prospective patient samples using collection sites

>2000 participants

Calculate sensitivity, specificity, positive and negative predictive values with input from our biostatistical core

Challenges: *Screening/Surveillance LFA Performance*



Typical LOD ~10^6 Copies/mL
Sensitivity ~40% vs. RTPCR for only asymptomatic*

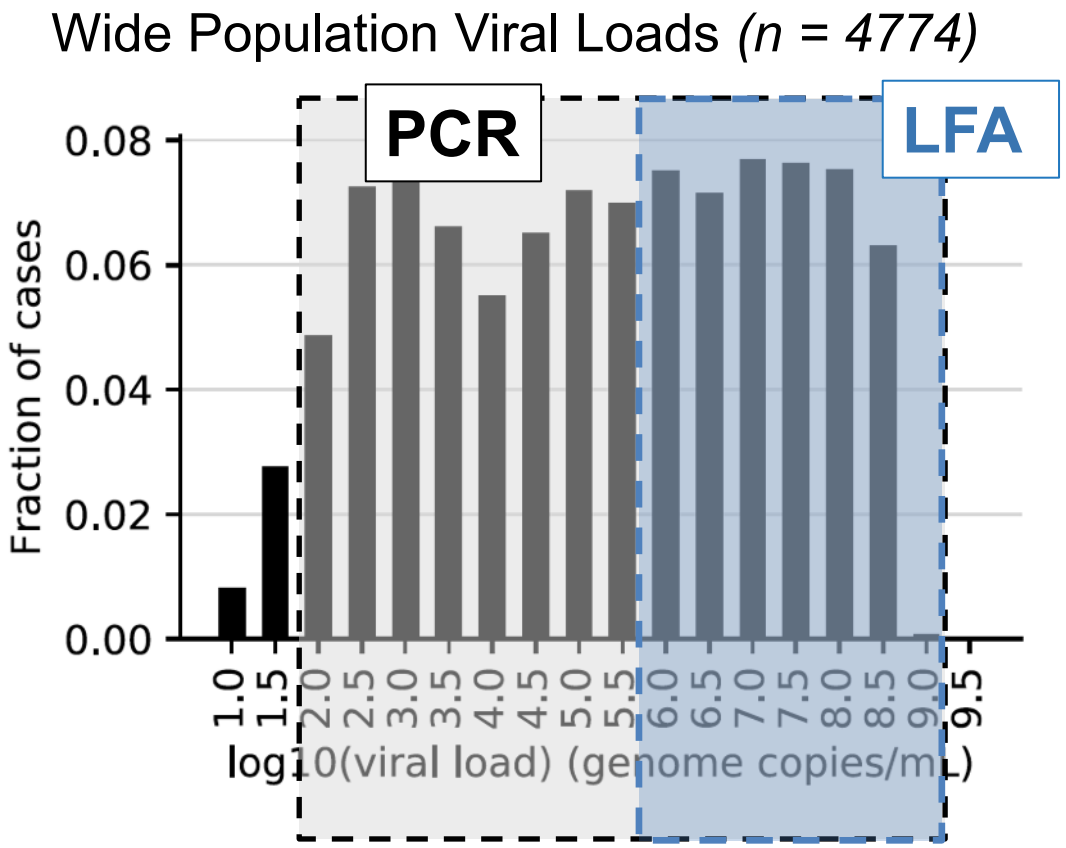
Vs.

Sens/Spec ~90/95% for symptomatic population (EUA: ~5 days post-onset)

Ramy Arnaout, James E. Kirby, et al., **SARS-CoV2 Testing: The Limit of Detection Matters**
bioRxiv 2020.06.02.131144; doi: https://doi.org/10.1101/2020.06.02.131144

*Pray IW, et al. Morb Mortal Wkly Rep 2021;69:1642–1647.
DOI: http://dx.doi.org/10.15585/mmwr.mm695152a3

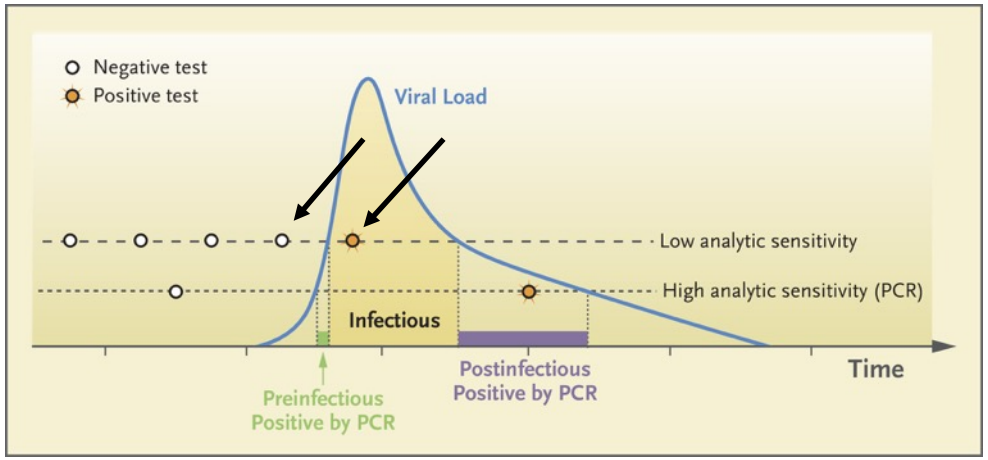
Challenges: *Screening/Surveillance LFA Performance*



1) Use LFA within ~5-7 days of symptoms
   - Elevated viral load (>90% sens, spec)

2) "Off Label" LFA in Asymptomatics:
   - Backup PCR w/positive in low prevalence
   - Backup PCR w/negative recently exposed

3) ***Sequential LFA tests***



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bioRxiv 2020.06.02.131144; doi: https://doi.org/10.1101/2020.06.02.131144

M. Mina et al, NEJM, DOI: 10.1056/NEJMp2025631

RADx Clinical Studies Core (UMass)

Mission: *Evaluate Phase 2 RADx platforms in clinical studies to develop "real world" guidance on tech use, performance, digital health integration.*

Laura Gibson, MD

David McManus, MD

- **LFA Multisite study:** ***UMass, UIUC, JHU in progress (n=100)***
  - Longitudinal sequential Lateral Flow Assay (LFA) assessment (2 weeks)
  - RTPCR, saliva, + viral infectiousness assay
- **LFA home testing study:** ***UMass and Northwestern, Jan 25 (n=100)***
  - At home, Self sampling, Digital health platforms
- **LFA large population study, planning w/public health (n>200,000)**
  - Regular frequent tests break chain of transmission?

COVID-19 Test US

COVID-19 SHIELD Target TEST Tell

UMassMemorial Health Care

UCSF Health

Northwestern Medicine

Eureka

Participant ID & Enrollment

JOHNS HOPKINS MEDICINE

EMORY HEALTHCARE

The CTSA Trial Innovation Network

Connecting: NIH Institutes, Industry, Researchers, and Participants

Investigators at CTSA Hubs across the U.S.

Trial Innovation Centers (TICs)

Request Support and Advice for Success

Recruitment Innovation Centers (RICs)

RADx Clinical Studies Core (UMass)

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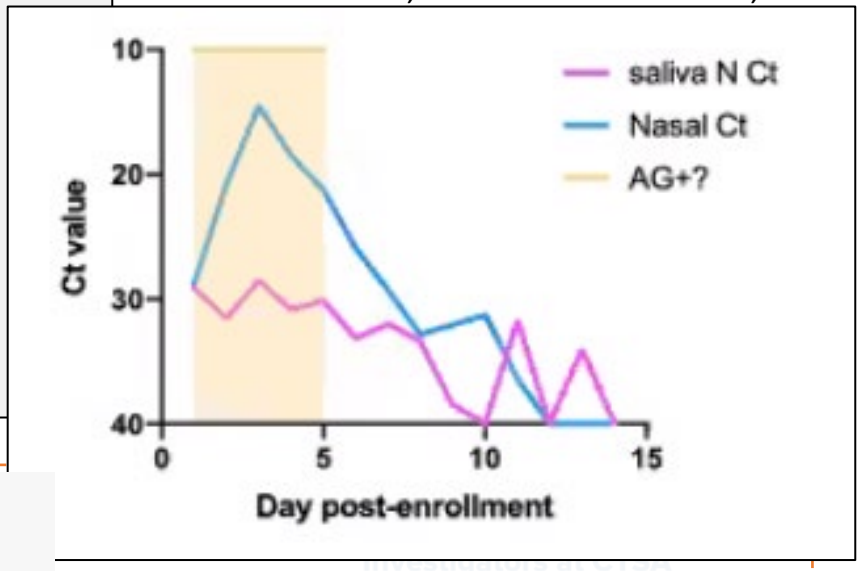

COVID-19 SHIELD Target TEST Tell

UMassMemorial Health Care

UCSF Health

JOHNS HOPKINS MEDICINE

Eureka
Participant ID & Enrollment

Northwestern Medicine

EMORY HEALTHCARE

Investigators at 33 Hubs across the U.S.

Trial Innovation Centers (TICs)

Request Support and Advice for Success

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RADx Tech: *Bridging the Performance Gap*

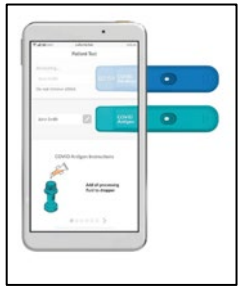
POC RTPCR

Visby Medical

Mesa BioTech

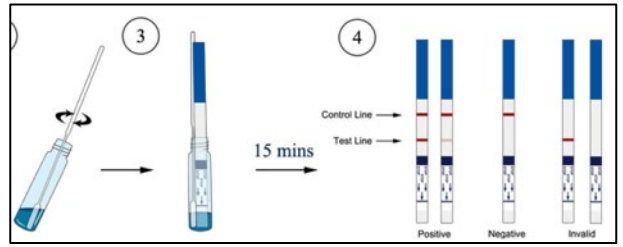
POC An (LFA/reader)

Quidel Sophia



Ellume

POC An (LFA/visual)



Maxim

Cost	$$$	**Tech to Bridge the Gap?**	$$	$
Speed	~30 min	<15 min		
Sens/Spec (EUA)	>90/95	>90/95		
LOD	<10^3 Cp/mL	>10^5 Cp/mL		

RADx Tech: *Bridging the Performance Gap*

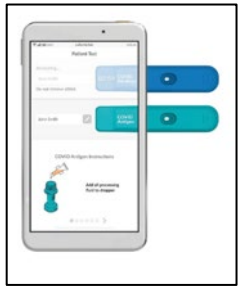
POC RTPCR

Visby Medical

Mesa BioTech

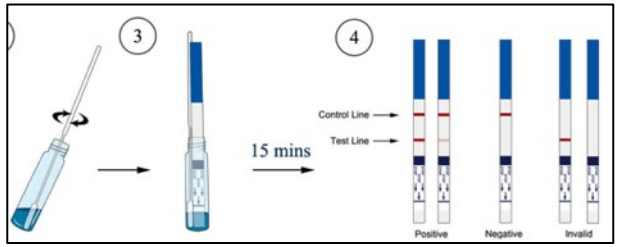
POC An (LFA/reader)

Quidel Sophia



Ellume

POC An (LFA/visual)

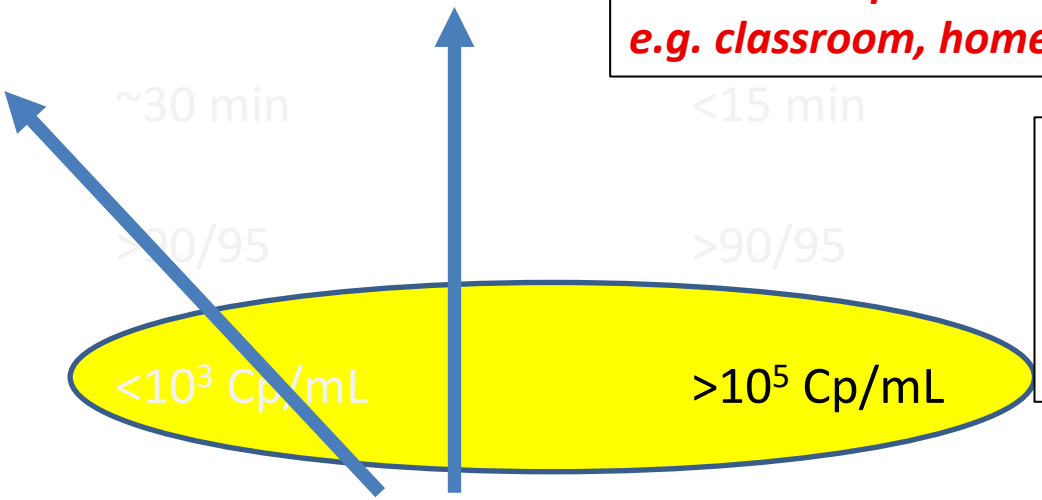


Maxim

New Protocols

Pool "social pod"
e.g. classroom, home, etc.

New Technology
- CRISPR
- Microfluidics
- Nanoparticles
- Single Molecule
- ASICs
- Waveguides

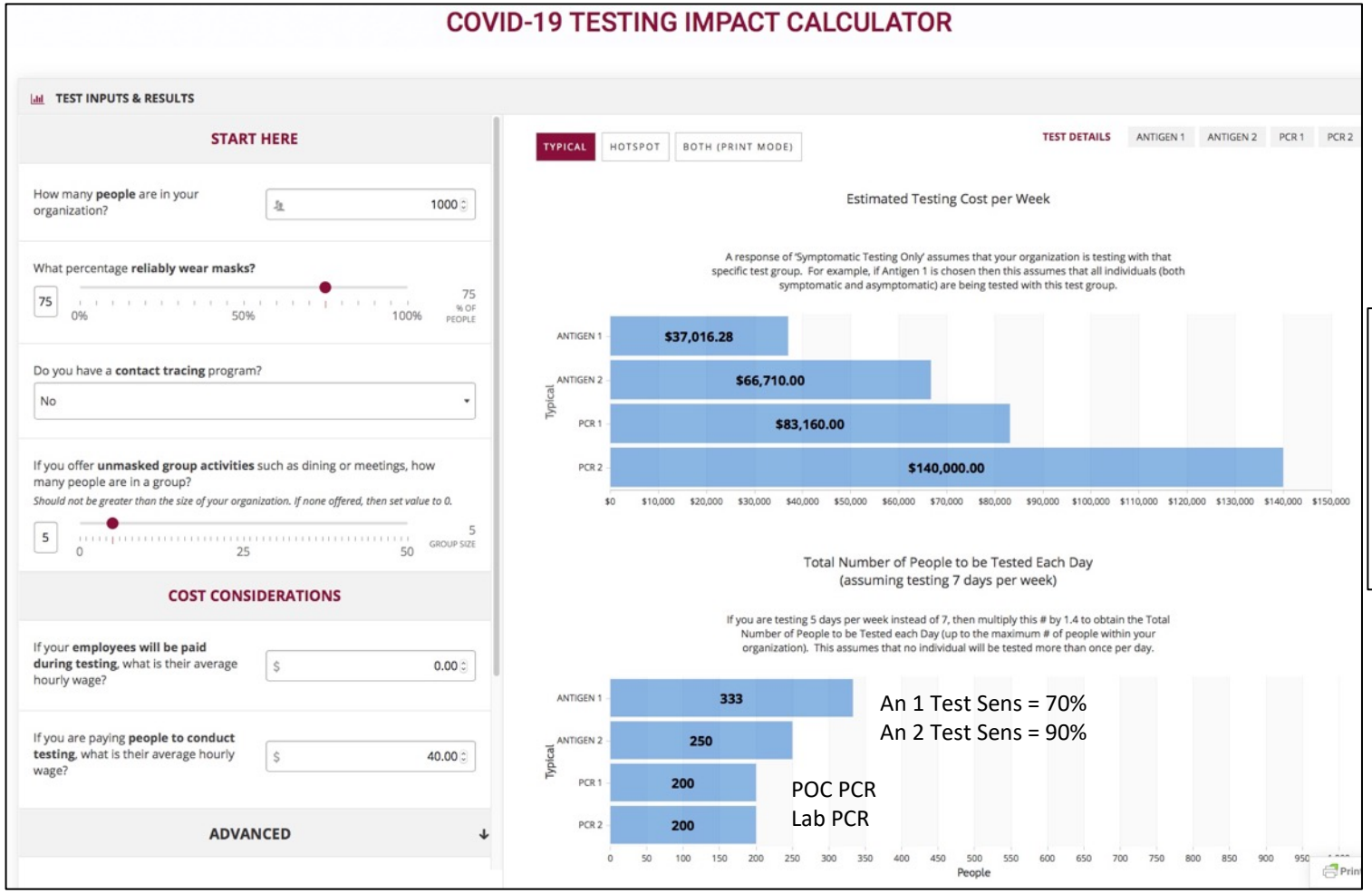


Pooling of POC PCR
- Slight reduction in LOD, optimized for infectiousness
- Fast turnaround (<30 min)
- 3-5X reduced cost ($)
- Rapid test, report, isolate entire "social pod"

RADx Tech Deployment Core: *CIMIT/MGH*

"When-to-Test" https://whentotest.org/ Match tests w/needs; evaluate impact of risk reducing activities.

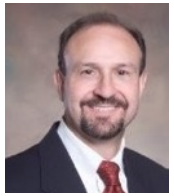
Bridging NIH/USG w/non-profits (Rockefeller, BMGF, FIND, APHL, APC) Academia, and Industry



Nancy Gagliano, MD
Deployment core lead
CIMIT/MGH

- **Create** Playbooks: *K-12, College/Uni, Business*
- **Connect** purchasers with vendors
- **Coordinate** supply chain solutions
- **Collaborate** with RADx UP
- **Organize** trans-RADx core task force on variants

Anette Hosoi, MIT

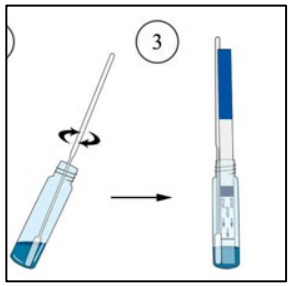


Paul Tessier, MGH

At-Home Challenges: *Digital Health*

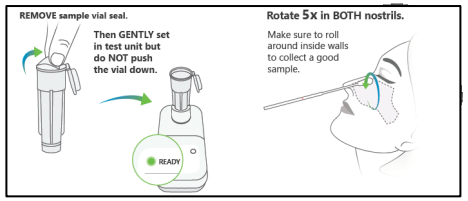
RADx POC Test

PCR



LFA

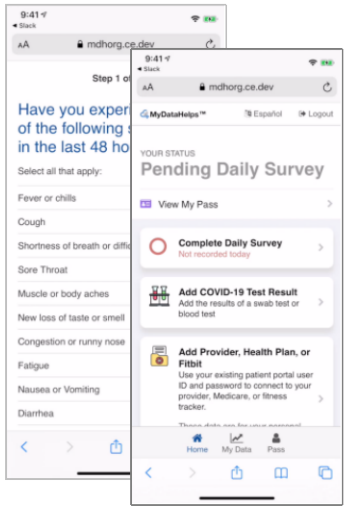
How to Use

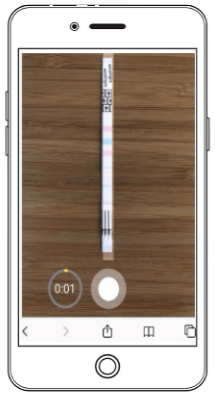


Wearables

Digital Contact Tracing

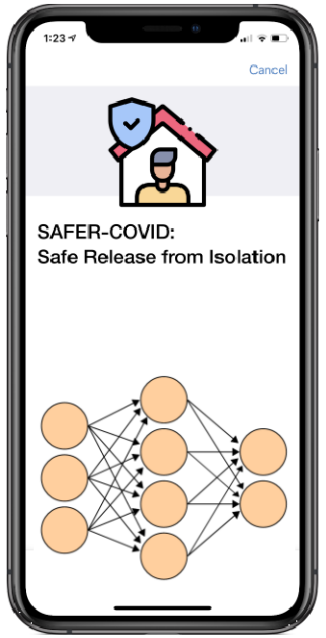
Symptom Surveys





Cell Phone Reader

e.g. OpenRDT (Audere)



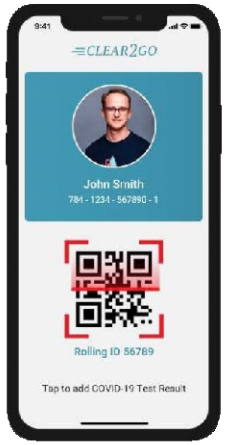
EHR & Claims

SYNC FOR SCIENCE

HL7 FHIR

Blue Button Download My Data

Proof of Health Status



GATES foundation

NIH National Institute of Biomedical Imaging and Bioengineering

NIH NATIONAL CANCER INSTITUTE

https://www.nibib.nih.gov/news-events/newsroom/nih-awards-contracts-develop-innovative-digital-health-technologies-covid-19

Summary and Challenges

Leverage, expand existing NIBIB network: *New processes introduced for unprecedented speed and impact.*

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Ongoing challenges:

1) Leverage $1B+ investment in Dx tech for other diseases and future pathogens;
2) US Regulatory, Health Care, Reimbursement Systems *optimized for detecting disease in individuals, not screening/surveillance (prevention) in populations.*
3) RADx general platform for acceleration: embed in NIBIB structure, disseminate to NIH & beyond