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

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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.

### Imaging Technologies

- M. Garwood, UMN

### Engineered Biology

- Cambridge University

### Modeling, Computation & Machine Intelligence

- V. Venugopalan, J. Spanier, UCI

### 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
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
Wearables for Monitoring and Detection

Digital Contact Tracing

GPS
Wi-Fi

Workforce

Integration with Test Results

Proof of Health Status

physIQ
pinpointIQ
physIQ
SAFER-COVID
IBM
UCSF

iCrypto

GATES foundation

NIH
NATIONAL CANCER INSTITUTE
NIH National Institute of Biomedical Imaging and Bioengineering
**Unexpected Opportunity**

**NIH Office of the Director**

Francis Collins  Rachael Fleurance  Larry Tabak  Tara Schwetz

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

**RADx Tech — $500M**  
Highly competitive, rapid three-phase challenge to identify the best new assays 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

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

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**April 29**

**National Institute of Biomedical Imaging and Bioengineering (NIBIB)**

Jill Heemskerk  Bruce Tromberg

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**$307 M Partnership with BARDA**

December 2020 Congress: $100,000,000

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

**POC > Lab**
- + >2 million/day LFA antigen tests unreported

**US tests/day**
- ~2M/day

[Source: Official sources collected by Our World in Data]
[Note: For testing figures, there are substantial differences across counties in terms of the units to which negative and pending tests are included and other aspects. Details for each country can be found in the referenced data sources.]
**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

[https://www.poctrn.org](https://www.poctrn.org)

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

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

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

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

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

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

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**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
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

- >6 M tests/day by end of year
- ~3000 Applications Started
- Rolling submission open April 29
- 5-6 Months
- ~$500M

- Projects in each Phase:
  - 716
  - 137
  - 47
  - 25 (Tech + ATP)

- Innovation, entrepreneur community

- Validation, Clinical Testing, Regulatory, Manufacturing, Distribution

- Small business: 353
- Academic: 153
- Start-up: 90
- Mid-size business: 51
- Large business: 38
- Other: 18
- Non-Profit Lab/CRO: 13

National Institute of Biomedical Imaging and Bioengineering
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 Tests/Products Produced and Sold in 2020

- **Cumulative Capacity**
- **Cumulative Sold**

5 months after launch

Tests (Millions)

- Sep
- Oct
- Nov
- Dec
RADx Leveraging NIH Proof of Concept (PoC) Network

- Matt McMahon, PhD

~50 early-stage RADx-tech projects

NIH SEED

Project Funding

Industry Coaching and Mentoring

Training and Resources

NIH Center for Accelerated Innovations at Cleveland Clinic

MBaRC MIDWEST BIOMEDICAL ACCELERATOR CONSORTIUM

CIMIT Consortia for Improving Medicine with Innovation & Technology

NIH Center for Accelerated Innovations at Cleveland Clinic

NIH Center for Accelerated Innovations at Cleveland Clinic
RADx Test Validation Core (Emory-Gtech)

~50 projects complete

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

>2000 participants
Challenges: **Screening/Surveillance LFA Performance**

Typical LOD ~10⁶ Copies/mL  
Sensitivity ~40% vs. RTPCR for only asymptomatic*

Vs.

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

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

Wide Population Viral Loads (n = 4774)

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

M. Mina et al, NEJM, DOI: 10.1056/NEJMp2025631
**Mission:** Evaluate Phase 2 RADx platforms in clinical studies to develop “real world” guidance on tech use, performance, digital health integration.

- **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?
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## RADx Tech: Bridging the Performance Gap

<table>
<thead>
<tr>
<th></th>
<th>POC RTPCR (Visby Medical, Mesa BioTech)</th>
<th>POC An (LFA/reader) (Quidel Sophia, Ellume)</th>
<th>POC An (LFA/visual) (Maxim)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>$$$</td>
<td>$$</td>
<td>$</td>
</tr>
<tr>
<td>Speed</td>
<td>~30 min</td>
<td>&lt;15 min</td>
<td></td>
</tr>
<tr>
<td>Sens/Spec (EUA)</td>
<td>&gt;90/95</td>
<td>&gt;90/95</td>
<td></td>
</tr>
<tr>
<td>LOD</td>
<td>&lt;10³ Cp/mL</td>
<td>&gt;10⁵ Cp/mL</td>
<td></td>
</tr>
</tbody>
</table>

**Tech to Bridge the Gap?**

**National Institute of Biomedical Imaging and Bioengineering**
POC RTPCR
- Visby Medical
- Mesa BioTech

POC An (LFA/reader)
- Quidel Sophia

POC An (LFA/visual)
- Ellume
- 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/](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

![COVID-19 Testing Impact Calculator](image)

ANETTE HOSOI, MIT  PAUL TESSIER, MGH
At-Home Challenges: *Digital Health*

**RADx POC Test**
- PCR
- LFA

**How to Use**
- OpenRDT (Audere)

**Wearables**
- Digital Contact Tracing

**Symptom Surveys**
- Cell Phone Reader
- GATES Foundation

**EHR & Claims**
- SYNC for Science
- HL7 FHIR
- Blue Button

**Proof of Health Status**

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Leverage, expand existing NIBIB network: *New processes introduced for unprecedented speed and impact.*
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Urgent need for new, purpose-driven tech: overcome limitations of “off the shelf” solutions.
Summary and Challenges

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

Urgent need for new, purpose-driven tech: overcome limitations of “off the shelf” solutions.

Bioengineering/tech engaged with new partners: Public Health, Policy.
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