Rapid Acceleration of Diagnostics: $RADx \ (Tech + ATP)$

Bruce J. Tromberg, Ph.D.
Director, National Institute of Biomedical Imaging and Bioengineering (NIBIB)
NIH Office of the Director

RADx Tech – $500M
Highly competitive, rapid three-phase challenge to identify the best 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 24, 2020: $1.5B to NIH
$500 Million to NIBIB

April 29

National Institute of Biomedical Imaging and Bioengineering (NIBIB)

$307 M Partnership with BARDA

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

https://www.nih.gov/research-training/medical-research-initiatives/radx;
Tromberg, Collins et al. NEJM, 2020
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)

U.S. Tests/day

RADx Launch: ~250k/day

Source: Official sources collated by Our World in Data
Note: For testing figures, there are substantial differences across countries in terms of the units to which negative and pending tests are included and other aspects. Details for each country need to be considered.
RADx Tech/ATP Innovation Funnel

NATIONAL CALL FOR INNOVATIVE TECHNOLOGIES
Rolling submission open April 29

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

Applications Started
~3000

Projects in each Phase
707 136 46 22 (Tech + ATP) ~$480M

DEPLOY MILLIONS of tests per week
Validation, Clinical Testing, Regulatory, Manufacturing, Distribution

>6 M tests/day by end of year

5-6 Months
Manufacturing Expansion Summary

- **Type:** 17 Nucleic Acid, 5 Viral Antigen
- **Setting:** 8 POC, 3 “between”, 11 Lab
- **Regulatory:** EUA → 8 lab (+1), 3 POC (+2)
- **Impact:** ~2.5M tests/day (Dec)

- **Pipeline:** 21 POC (9 NAT, 11 An, 1 VOC)

22 (Tech + ATP) ~$480M

Table:

<table>
<thead>
<tr>
<th>NATIONAL CALL FOR INNOVATIVE TECHNOLOGIES</th>
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~3000

RADx Tech/ATP Innovation Funnel
### 22 Manufacturing Expansion

#### Innovation

1. Separation/concentration
2. μ-Fluidics
3. Chemistries, e.g. CRISPR, NGS
4. Labels, Reporters
5. Readout Tech
6. Miniaturization
7. Automation

#### Tens to 100,000 tests/day

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<thead>
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https://www.nibib.nih.gov/covid-19/radx-tech-program/radx-tech-phase2-awards
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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

RADx UP

Duke/UNC
CDCC
RADx UP
Coordinating Center

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

Validation Core
Clinical Studies Core
Deployment Core
RADx Leveraging NIH Proof of Concept (PoC) Network

~40 early-stage RADx-tech projects

Jodi Black      Matt McMahon
### 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

**15 projects complete, 11 ongoing**

RADx Test Validation Core (Emory-Gtech)

Wilbur Lam  Greg Martin  Oliver Brand

>1500 participants
**Feasibility**

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**RADx Test Validation Core (Emory-Gtech)**

15 projects complete, 11 ongoing

**OVERALL SUMMARY OF RESULTS ACROSS ACME POCT SITES**

- LOD (Limit of Detection)
  - Inactivated SARS-CoV-2
  - Live SARS-CoV-2 (WA1)

- Prospective Clinical Results
  - DiaSorin RT-PCR
    - Virus Type: OC43 seasonal coronavirus
    - Lack of Cross-Reactivity? +
    - Sensitivity: 100%
    - Specificity: 100%

* PNNS, pooled negative nasal swab
**Challenge:** Compare NAT and Antigen Test Performance

**Viral Antigen Test**
Lateral Flow Assay (LFA)
**LOD:** TCID$_{50}$/mL $\sim 10^3$-$10^4$/mL

**Nucleic Acid Test**
RT-PCR (Isothermal PCR)
**LOD:** Cp/mL $\sim 10^2$-$10^3$/mL
Understanding Screening/Surveillance Performance

Impact of LOD and Population Viral Load on Performance

Population Viral Loads from Ct values \((n = 4774)\)

- ~10 – 10^9 Cp/mL

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
Understanding Screening/Surveillance Performance

Impact of LOD and Population Viral Load on Performance

Population Viral Loads from Ct values \((n = 4774)\)

- Typical LOD \(\sim 10^6\) Copies/mL
- Sensitivity \(\sim 40\%\) for all population (symptomatic + asymptomatic)
- Sens/Spec \(\sim 90/95\%\) for symptomatic population (EUA: \(\sim 5\) days onset)

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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
Impact of LOD and Population Viral Load on Performance

Population Viral Loads from Ct values ($n = 4774$)

- Typical LOD > $\sim 10^2$ Copies/mL
- Sensitivity > $\sim 90\%$ for all population (symptomatic + asymptomatic)

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
Understanding Screening/Surveillance Performance

**Implications: NAT (PCR) vs LFA (An)**

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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Population Viral Loads from Ct values ($n = 4774$)

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

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Mission: Evaluate RADx platforms that advance to Phase 2 in rigorous clinical studies w/ diverse populations and settings.

Standard Trial Design: Master protocols, powered studies (~250 subjects), device-specific amendments, accelerate regulatory review

Eureka Digital Health Platform mobile app and website, participants enter own data

Data Safety Board and Single IRB for oversight and safety monitoring

Robust Research Center Network: POCTRN core center network for enrollment (w/Practice Based Research Network and Centers for Clinical and Translational Science assisting)
Mission
Provide support for successful commercialization and deployment of COVID-19 solutions in unique communities.

- Members: 32
- Nancy Gagliano, MD, Core Lead
- Brian Walsh, Commercialization Lead
- Sreeram Ramakrishnan, Data Solutions Lead
- Susan Moreira, Deployment Lead

Current Highlights
- Supply Chain continues to be core challenge
- Development of Testing Model has received international recognition
- User communities need end-to-end solutions to deploy COVID testing
- Design-a-thon scheduled to develop data solutions

www.poctrn.org
RADx webinars, tools

“When-to-Test” modeling tool:
Match tests w/needs; evaluate impact of risk reducing activities.
POC Comparison: *Performance Gap*

### POC RTPCR
- Visby Medical
- Mesa BioTech
- Visby Medical
- Mesa BioTech

### POC An (LFA/reader)
- Quidel Sophia
- Ellume
- Quidel Sophia
- Ellume

### POC An (LFA/visual)
- Maxim
- Maxim
- Maxim
- Maxim

**Cost**
- $$$
- $$
- $$
- $

**Speed**
- ~30 min
- <15 min

**Sens/Spec (EUA)**
- >90/95
- >90/95

**LOD**
- $\sim 10^3$ Cp/mL
- $\sim 10^6$ Cp/mL
POC Comparison: *Performance Gap*

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- **Cost**: $$$ | $ | $ | 0.5 $ |
- **Speed**: ~30 min | <15 min |
- **Sens/Spec (EUA)**: >90/95 | >90/95 |
- **LOD**: ~$10^3$ Cp/mL | ~$10^6$ Cp/mL |

**Tech to Bridge the Gap**
1) Separation/concentration
2) μ-Fluidics
3) Chemistries, e.g. CRISPR
4) Labels, Reporters
5) Readout/Sensing
6) ? (“Background” reduction)
RADx Digital Health Networks: Integration

RADx POC Test
Wearables
Digital Contact Tracing
Symptom Surveys
EHR & Claims
Proof of Health Status

Cell Phone Reader
e.g. OpenRDT (Audere)

GATES foundation

RADx Tech/ATP:
*Accelerating innovation, Multiple platforms, Millions tests/day*
Link NVBL to RADx network?

**Implementation Challenge:**
- Standard Medical Diagnostics: *accurately detect/diagnose disease in individuals*
- **COVID Paradox:** *rapidly assess +/- of disease in asymptomatic populations: Home?*  
- Barriers: *Economic, cultural, regulatory*

**Technical Challenges:**
- Match tests w/biology of infection; needs of user communities *(what/when/how often?)*
- Bridge Tech performance gap: *improve performance in low prevalence settings*
- Integrate: *tests, models, interventions, Apps/data, for personal and PH management*