Rapid Acceleration of Diagnostics: \textit{RADx (Tech + ATP)}

Bruce J. Tromberg, Ph.D.
Director, National Institute of Biomedical Imaging and Bioengineering (NIBIB)
April 24, 2020: $1.5B to NIH
$500 Million to NIBIB

RADx Tech – $500M
Highly competitive, rapid three-phase challenge to identify the best candidates 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 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

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

Rapid Scaling Up of Covid-19 Diagnostic Testing in the United States — The NIH RADx Initiative

Bruce J. Tromberg, Ph.D., Tara A. Schwetz, Ph.D., Eliseo J. Pérez-Stable, M.D., Richard J. Hodes, M.D., Richard P. Woychik, Ph.D., Rick A. Bright, Ph.D., Rachael L. Fleurence, Ph.D., and Francis S. Collins, M.D., Ph.D.

The first reports of an unusual cluster of pneumonia cases in the city of Wuhan, China, emerged in December 2019, heralding a global pandemic. As of July 13, 2020, more than 3.3 of RADx and their goals, and we end with a re-view of the challenges ahead.

On April 24, 2020, Congress appropriated $1.5 billion, from the $25 billion provided in the

National Institute of Biomedical Imaging and Bioengineering (NIBIB)
RADx Tech & ATP

NIH Office of the Director

Francis Collins  Rachael Fleurance  Larry Tabak  Tara Schwetz

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


April 29

National Institute of Biomedical Imaging and Bioengineering (NIBIB)

$307 M Partnership with BARDA
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

### Chart
- **Tests per Day (millions)**
- **U.S. Tests/day**
- **RADx Contribution**
- **Projected baseline**
- **August**
- **October**
- **Dec 2020**

### Source
Official sources collated by Our World in Data
RADx Innovation Funnel

Applications Started
~3000

Projects in each Phase
707
136
46
22 (Tech + ATP)

~$480M

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

5-6 Months

>6 M tests/day by end of year

DEPLOY MILLIONS of tests per week

Validation, Clinical Testing, Regulatory, Manufacturing, Distribution

NIH National Institute of Biomedical Imaging and Bioengineering
RADx Innovation Funnel

- Validation, Clinical Testing, Regulatory, Manufacturing, Distribution

~3000 Applications Started
Projects in each Phase: 707, 136, 46, 22 (Tech + ATP)

Rolling submission open April 29

>6 M tests/day by end of year

~$480M Innovation

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

NIH National Institute of Biomedical Imaging and Bioengineering
RADx Innovation Funnel

WP2 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)

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

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**Project Tech:**
1) Review  
2) Funding  
3) Expertise  
4) Testing

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

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

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

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

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

**Validation Core**
- 15 projects complete, 11 ongoing, >1500 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
Point-of-Care Technologies Research Network (POCTRN)

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Validation Core
Clinical Studies Core
Deployment Core
RADx Test Validation Core (Emory-Gtech)

15 projects complete, 11 ongoing

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 >1500 participants
Calculate sensitivity, specificity, positive and negative predictive values with input from our biostatistical core
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RADx Test Validation Core (Emory-Gtech)

15 projects complete, 11 ongoing

NIH score range: 1 (exceptional) to 9 (poor)
ACME POCT score: 2 (88% of respondents)
RADx Test Verification Core Recommendation: Proceed to WP2

Resume and Summary of Discussion: the RADx ACME POCT convened an internal study section on July 9th, 2020 to discuss the RADx Test Verification Core's analysis of Project #2244 in which the criteria for evaluation included: LOD, Sensitivity, Specificity, Repeatability, and Usability. The testing of this COVID-19 point-of-care (POC) PCR diagnostic test comprised of 1) LOD testing at several of our sites, including our Emory BT3 facility, Children's Healthcare of Atlanta clinical pathology laboratories, and laboratories in

OVERALL SUMMARY OF RESULTS ACROSS ACME POCT SITES

Prospective Clinical Results

<table>
<thead>
<tr>
<th>Virus Type</th>
<th>Lack of Cross-Reactivity?</th>
</tr>
</thead>
<tbody>
<tr>
<td>OC43 seasonal</td>
<td>+</td>
</tr>
<tr>
<td>Coronavirus</td>
<td>+</td>
</tr>
<tr>
<td>MERS (heat inactivated)</td>
<td>-</td>
</tr>
</tbody>
</table>

Sensitivity: 100%
Specificity: 100%
**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)
RADx Deployment Core (CIMIT)

Bridging NIH/USG, non-profit Foundations, Academia, and Industry

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
“When-to-Test” modeling tool: Match testing approaches w/needs; evaluate impact of risk reducing activities.

Inputs

<table>
<thead>
<tr>
<th>TEST OPTIONS (UNDER 'TYPICAL' CONDITIONS)</th>
<th>Test 1</th>
<th>Test 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turnaround time needed for test results</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Number of people to be tested in a day</td>
<td>111</td>
<td>91</td>
</tr>
<tr>
<td>Recommended max days between tests/person</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Number of instruments required</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Total instrument capital cost</td>
<td>$7,000</td>
<td>$30,000</td>
</tr>
<tr>
<td>Staff required</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Cost per test</td>
<td>$43.77</td>
<td>$47.03</td>
</tr>
<tr>
<td>Daily test cost</td>
<td>$4,858</td>
<td>$4,280</td>
</tr>
</tbody>
</table>
RADx Digital Health Networks: Integration

RADx POC Test

Wearables

Symptom Surveys

Cell Phone Reader

e.g. OpenRDT (Audere)

Digital Contact Tracing

EHR & Claims

Proof of Health Status

GATES foundation

RADx Tech/ATP: Accelerating innovation, Multiple platforms, Millions tests/day

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

RADx Partnerships:
- Guidelines: match & deploy tech and test protocols for range of use cases (what test/when?)
- Evaluate: performance, impact, efficacy; validate models
- Inspire: testing + DH platforms for widespread screening/surveillance