RADx Tech: 2-year update and future perspective

RADx Tech Webinars

May 31th, 2022

Bruce J. Tromberg, Ph.D.
Director
National Institute of Biomedical Imaging and Bioengineering

**RADx Tech Program Leads @NIH:** Jill Heemskerk, Tiffani Lash, Todd Merchak, Mike Wolfson, Doug Sheeley, David George, Bill Heetderks, Shawn Mulvaney, Matt McMahon, Felicia Qashu, Tony Kirilusha, Andrew Weitz, Krishna Juluru, Taylor Gilliland, Jennifer Jackson, Ray MacDougall, Patty Wiley, Chris Cooper, **@Deloitte:** Mark Snyder, Adrienne Lane, Michael Walker, Frances Fernando
Call with Sen Alexander

- Can we get more testing?
- Oh, a Shark Tank!

ZOOM with POCTRN

- Can everyone change direction?
- Deliver millions of tests by fall!

4th Congressional Supplement

- 1.5 Billion to NIH for testing
- Unusual Opportunity

Press conference, Funnel Open!

- 400 applications started in 24 hours
- The race begins
Point-of-Care Technologies Research Network (POCTRN)

**NIBIB National Network:** NHLBI, NIAID, NCCIH, FIC, OBSSR, OAR, ODP

Established 2007, Expanded 2020: >900 RADx experts & contributors

- **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
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- **UMass**
  - Heart, lung, blood
  - Engineering
  - Clinical Validation
  - Biobank samples
  - Clinical Trials
  - Business/Commercialization
Rapid Acceleration of Diagnostics (RADx Tech)

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Innovation Funnel
824 Applications, 50 phase 2 awards

Innovation, Manufacturing, Distribution, Guidance, Regulatory

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https://www.poctrn.org

Validation Core
>100 projects complete,
>10,000 participants

Clinical Studies Core
Standard Trial Design, Digital Health Platform,
Single IRB, Center Network

Deployment Core
Supply chain, Manufacturing,
User Community,
whentotest.org
My COVID Toolkit
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Innovation, Manufacturing, Distribution, Guidance, Regulatory

Deployment Core

Validation Core

Clinical Studies Core

Deployment Core

RADx MARS

Variant Task Force

Project Rosa

Independent Test Assessment (ITAP)

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https://www.poctrn.org
RADx Funding: $500M ➞ $1.7 Billion
NIBIB Impact

NIBIB team:
Jill Heemskerk,
David George,
Jason Ford,
Deb Kelly,
Admin, Budget,
Grants
Management,
Communications,
Program,…

April 24, 2020 $1.5B
U.S. Congress to NIH

COVID/RADx total = $1.7B

<table>
<thead>
<tr>
<th></th>
<th>Millions</th>
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<tbody>
<tr>
<td>FY18</td>
<td>$377</td>
</tr>
<tr>
<td>FY19</td>
<td>$388</td>
</tr>
<tr>
<td>FY20</td>
<td>$405</td>
</tr>
<tr>
<td>FY21</td>
<td>$409</td>
</tr>
<tr>
<td>FY22*</td>
<td>$425</td>
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</table>

*projected

Direct
COVID
RADx Tech Impact: Capacity thru March 2022

Cumulative EUA Tests + Test Products

- Laboratory
- Point of Care
- Over the Counter
- Test Products

2.3B tot capacity thru March 2022

~260 M tests & products Mar 2022

44 EUAs: 9 “OTC”: 8 An, 1 RT-LAMP

5 months (20M)

1 year (300M)

260M

Innovation Funnel & ITAP

OTC Paradigm Shift Challenges:

1) **Reporting Cases**
2) **Use & Interpret Antigen Tests**

Establish **common standard** for over-the-counter (OTC) test results (iHealth 1st)

Promote **data hubs** to reduce complexity of reporting channels

**Free** for companies to report OTC test results

Help OTC app developers **navigate** reporting

---

**US Tests by Month**

- **OTC test growth**
- **Lab & POC Supply**
- **At-home Supply**
- **Lab, POC Reported**

**Tests reported** <100M/mo

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- **OTC Paradigm Shift Challenges:**
  - **1) Reporting Cases**
  - **2) Use & Interpret Antigen Tests**

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Promote **data hubs** to reduce complexity of reporting channels

**Free** for companies to report OTC test results

Help OTC app developers **navigate** reporting
Challenge: Use & Interpret An Tests

ROC Curves

BD, Binax, Quidel QV vs. Roche COBAS RTPCR

1) Variant Comparison

Delta: N = 262
Omicron: N = 501

Binax, BD, & QV

>7000 subject longitudinal serial antigen test study

2) Test Comparison

Omicron: N = 501

Binax, BD, & QV

https://doi.org/10.1101/2022.02.27.22271090
Antigen Test Performance: Variants and Platforms

1) Variant Comparison

2) Test Comparison

1) Antigen tests work equally well with Omicron and Delta

2) Antigen platforms have comparable performance

https://doi.org/10.1101/2022.02.27.22271090
Antigen Test Performance: *Platform PPA*

BD, Binax, Quidel QV vs. Roche COBAS RTPCR

For *high* viral loads, e.g. Ct $<~26$ ($\sim 10^6$ Cp/mL)

- Antigen PPA $\geq 80\%$
- Large changes in Ct, modest changes in PPA

https://doi.org/10.1101/2022.02.27.22271090
Antigen Test Performance: *Platform PPA*

**ROC Curves**

BD, Binax, Quidel QV vs. Roche COBAS RTPCR

For *intermediate* viral loads, e.g. Ct ~25 - 30

- Antigen PPA 31% - 81%
- Small changes in Ct = large changes in PPA

https://doi.org/10.1101/2022.02.27.22271090
Antigen Test Performance: Platform PPA

BD, Binax, Quidel QV vs. Roche COBAS RTPCR

For low viral loads, e.g. Ct 30 - 35 (weak positive)

- Antigen PPA 14% - 39%
- Small changes in Ct = modest changes in PPA

https://doi.org/10.1101/2022.02.27.22271090
Antigen Test Performance: **Platform PPA**

**BD, Binax, Quidel QV vs. Roche COBAS RTPCR**

- **Probability of turning An+ after weak RTPCR+**
  - **PPA**: 14% - 39%
  - **Ct**: 30 - 35

**Serial Testing**

**ROC Curves**

[Image of ROC curves showing probability and Ct values]

https://doi.org/10.1101/2022.02.27.22271090
### FDA Antigen Performance: Is there a difference?

1) EUA for serial testing
2) EUA PPA depends on study population

#### FDA IFU for Boson

<table>
<thead>
<tr>
<th>Primary Analysis</th>
<th>10% Low Positive</th>
<th>12.5% Low Positive</th>
<th>15% Low Positive</th>
<th>17.5% Low Positive</th>
<th>20% Low Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Positive Samples</td>
<td>52</td>
<td>52</td>
<td>52</td>
<td>52</td>
<td>52</td>
</tr>
<tr>
<td>Low Positive Samples</td>
<td>6</td>
<td>8</td>
<td>10</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Total Comparator Positive for PPA Calculation</td>
<td>58</td>
<td>60</td>
<td>62</td>
<td>64</td>
<td>65</td>
</tr>
<tr>
<td>Total Test Positives for PPA Calculation</td>
<td>48</td>
<td>48</td>
<td>48</td>
<td>48</td>
<td>48</td>
</tr>
</tbody>
</table>

#### PPA (%):
- 82.7%
- 80.0%
- 77.4%
- 75.0%
- 73.8%

**95% CI (XX% - XX%):**
- 71.1% - 90.4%
- 68.2% - 88.2%
- 65.6% - 86.0%
- 63.2% - 84.0%
- 62.0% - 83.0%

**NPA (%):** 99.1% (112/113)

**95% CI (XX%-XX%):** 95.2%-99.8%

*When all study participants are included, the PPA is 67.1% and the NPA is 99.1% with the 95% confidence interval bounds of 55.7% to 76.8% for the PPA and 95.2% to 99.8% for the NPA, respectively.*
FDA Antigen Performance: Is there a difference?

PPA

82.7

82.9

95.3

91.7

86.9

84.6

87.0

86.7

86.5

96.0

81.7

EUA PPA depends on clinical study population

PPA vs. % Weak Positives (Ct >30)

100.00

95.00

90.00

85.00

80.00

75.00

70.00

65.00

60.00

55.00

50.00

45.00

40.00

35.00

30.00

25.00

20.00

15.00

10.00

5.00

0.00

% PPA

% Weak Positive Subjects

100% strong positives

N = 58 – 65 from EUA

82.7% OTC EUA

80% OTC EUA bar

Boson LFA IFU

EUA

FDA antigen team, ITAP team

Eric Lai Pam Miller Richard Creager

FDA Antigen Performance

04/08/2022 Oxamni, LLC

04/24/2022 SD Biosensor, Inc.

04/24/2022 Hulka Labs, Inc.

04/24/2022 Abbott Diagnostics

05/30/2022 Mains Biomedical, Inc.

05/26/2022 Boston, Darkness and Company

05/25/2022 AccessBio, Inc.

05/23/2022 Collostrum USA, Inc.

05/23/2022 Siemens Healthcare

05/18/2022 Elanez Limited

05/16/2022 PHAGE Scientific International Ltd.

DiaChem COVID-19 Antigen Self Test

ProCOVID-19 Ag Home Test

Novakab COVID-19 Antigen Rapid Test

DiaSorin COVID-19 Antigen Self Test

CovTest COVID-19 Test

COVID-19 Antigen Home Test

COVID-19 Antigen Home Test

COVID-19 Antigen Self Test

Enter EUA

N = 58 – 65 from EUA

82.7% OTC EUA

80% OTC EUA bar

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FDA antigen team, ITAP team

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FDA Antigen Performance: Is there a difference?
RADx Tech Performance Challenges

<table>
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<tr>
<th>Lab RTPCR</th>
<th>POC RTPCR</th>
<th>POC An (LFA/reader)</th>
<th>OTC An (LFA/visual)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABL 7500</td>
<td>Mesa BioTech</td>
<td>Quidel Sophia</td>
<td>Ellume Dipstick LFA</td>
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- **Tech to Bridge the Gap?**

<table>
<thead>
<tr>
<th>Cost</th>
<th>Speed</th>
<th>Sens/Spec</th>
<th>LOD</th>
</tr>
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<tbody>
<tr>
<td>$$$$$</td>
<td>$$$$</td>
<td>&gt;90/95</td>
<td>&lt;10³ Cp/mL</td>
</tr>
<tr>
<td>$$$</td>
<td>~30 min</td>
<td>&gt;90/95</td>
<td>&lt;10³ Cp/mL</td>
</tr>
<tr>
<td>$$</td>
<td>&lt;15 min</td>
<td>&gt;90/95</td>
<td>&gt;10⁶ Cp/mL</td>
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RADx Tech: Better Performance

**Isothermal PCR (OTC)**
- Cue
- Lucira
- Detect
- Uh-Oh Labs

**RT PCR (POC)**
- Mesa/Thermo
- Visby

**Antigen w/PCR LOD**
- Qorvo
- Quanterix
Pre-Commercial: Palogen

3D Nano-electronic Biosensor

DNA Probes, Parallel Nucleic Acid Detection

High Density 3D-Biosensor Array

Sensing mechanism overview with DNA probes in 3D addressable sensor

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Ongoing Challenges

1) Improve Performance and Information Content

- **Accessibility**: vision, fine motor, cognitive impairments, etc.
- **Next gen performance**: POC/home tests w/lab performance; multiplex + variant capabilities; host response; Standard designs?
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3) **Sustainability:** COVID and Pandemic Preparedness; Cost and pay model (USG vs. consumer), leverage tech for other pathogens/diseases (e.g. TB, STD/HIV, Hep,...)
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4) Impact:  
   **Process:** RADx-ification at NIBIB/NIH; 
   **Practice:** OTC “Test to Treat” for diagnostic-led precision medicine
Thank You! National Policy Impact

POLITICS

Biden administration to launch website for free 500 million COVID-19 testing kits on Wednesday

Courtney Subramanian
USA TODAY
Published 2:55 p.m. ET Jan. 14, 2022 | Updated 5:02 p.m. ET Jan. 14, 2022

President Biden promises 'free' N95 masks and more at-home COVID tests

President Biden also announced that 1,000 military medical personnel will begin deploying to help overwhelmed medical facilities. 60494.png, USA TODAY

WASHINGTON — The Biden administration on Wednesday will launch a website where Americans can order up to four free COVID-19 testing kits per person, according to a senior administration official.

The New York Times

Biden announces 500 million more tests will be purchased for Americans.

By Michael D. Shear
Jan. 13, 2022

WASHINGTON — President Biden on Thursday stepped up his administration's response to a coronavirus surge driven by the Omicron variant, sending what he said is urgently needed help to overwhelmed hospitals and pledging to provide Americans with free tests and masks as the country enters the pandemic's third year.