Accelerating Innovation and Technology Development through Engineering-Medicine Partnerships

Bruce J. Tromberg, Ph.D.

Director, National Institute of Biomedical Imaging and Bioengineering

National Institute of Biomedical Imaging and Bioengineering

Bioengineering at NIH

NIBIB and BME Growth

2000: *Creation of NIBIB*

Public Law 106–580
106th Congress

Dec. 29, 2000
[H.R. 1795]

An Act

To amend the Public Health Service Act to establish the National Institute of Biomedical Imaging and Bioengineering.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

National Institute of Biomedical Imaging and Bioengineering Establishment Act.
42 USC 201 note.
42 USC 285r note.

SECTION 1. SHORT TITLE.
This Act may be cited as the "National Institute of Biomedical Imaging and Bioengineering Establishment Act".

SEC. 2. FINDINGS.
The Congress makes the following findings:
(1) Basic research in imaging, bioengineering, computer science, informatics, and related fields is critical to improving health care but is fundamentally different from the research in molecular biology on which the current national research institutes at the National Institutes of Health ("NIH") are based. To ensure the development of new techniques and technologies for the 21st century, these disciplines therefore require an identity and research home at the NIH that is independent of the existing institute structure.

- 175+ accredited BME-related programs
- > 200 graduate programs

NIBIB established

Whitaker Fnd

ABET.org
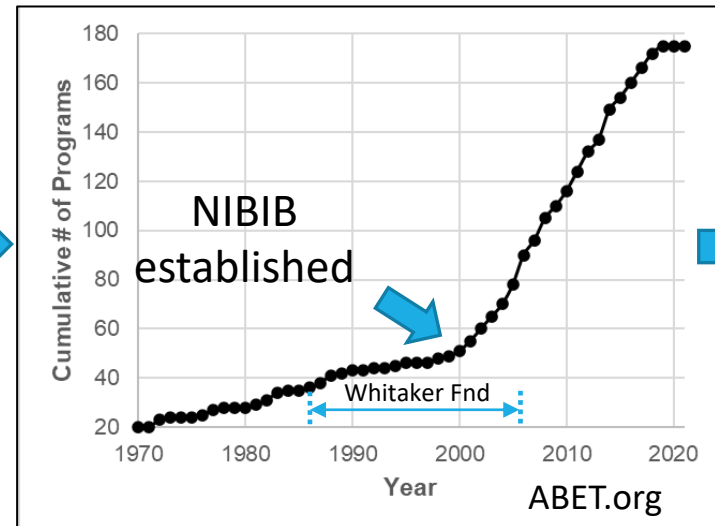
- **Human Health top priority of Engineering**

- **Medicine-Engineering partnerships:** *Physicianeers*

-BME Centers SOM/SOE
-University of Illinois Urbana-Champaign
-Texas A&M University
-Columbia (Dental School/ENG)
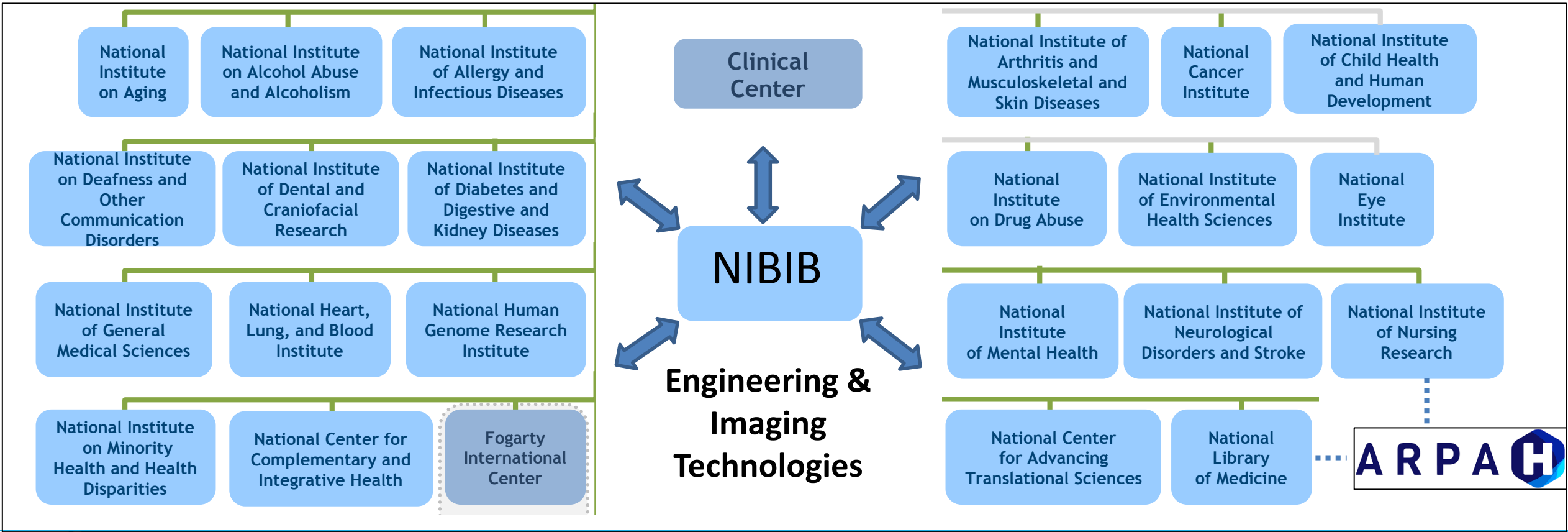
- *Drive Innovation, Entrepreneurship, Diversity*

https://blog.collegevine.com/us-colleges-with-biomedical-engineering-major/
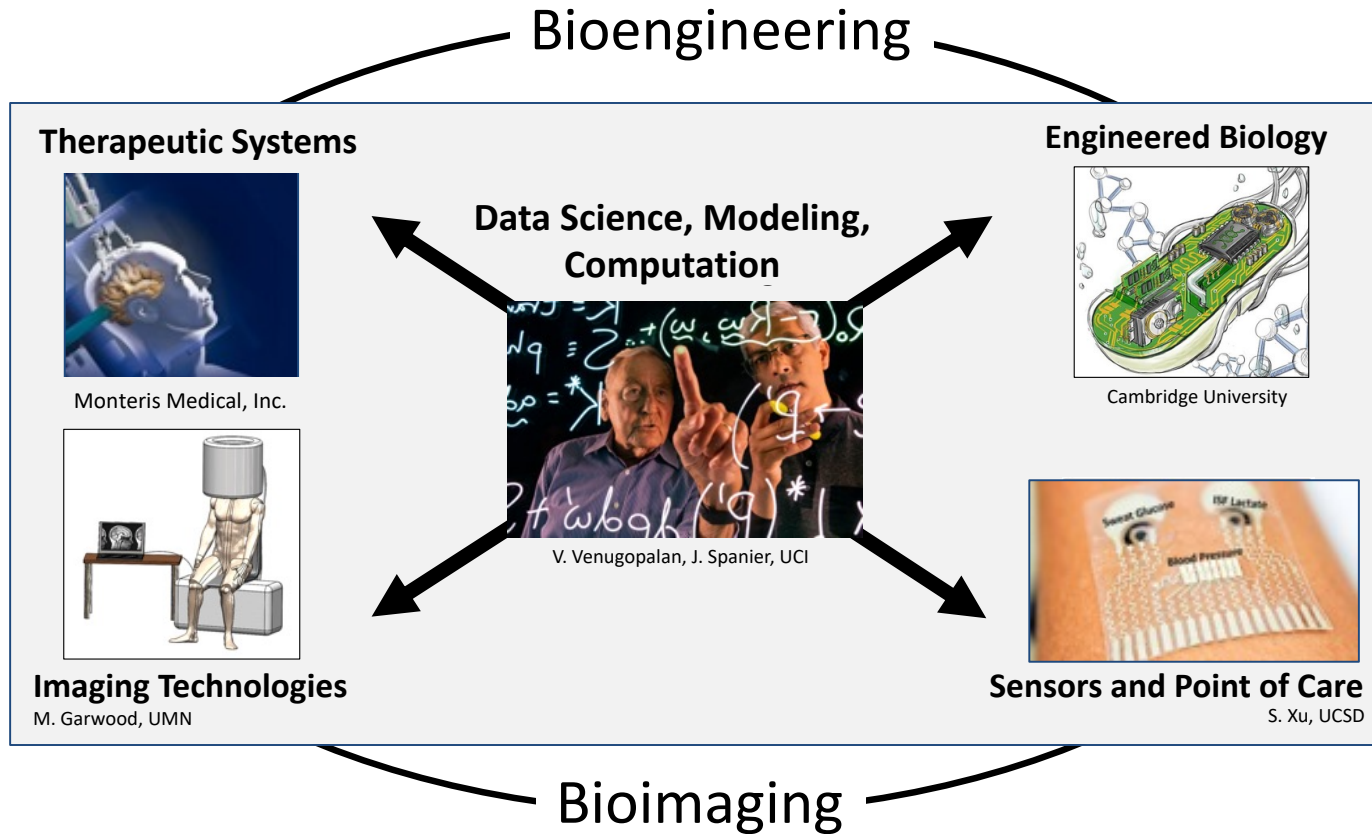
NIBIB @ NIH

Monica Bertagnolli, M.D.
- 17th NIH director: *11/9/2023*
- First surgeon, second woman
- Undergrad Chem Engineer

Structure: 27 Institutes & Centers, ~$47 Billion (FY23)

NIBIB: ~1% NIH Budget→ *Partnerships and Collaboration*

National Institute on Aging

National Institute on Alcohol Abuse and Alcoholism

National Institute of Allergy and Infectious Diseases

Clinical Center

National Institute of Arthritis and Musculoskeletal and Skin Diseases

National Cancer Institute

National Institute of Child Health and Human Development

National Institute on Deafness and Other Communication Disorders

National Institute of Dental and Craniofacial Research

National Institute of Diabetes and Digestive and Kidney Diseases

National Institute on Drug Abuse

National Institute of Environmental Health Sciences

National Eye Institute

National Institute of General Medical Sciences

National Heart, Lung, and Blood Institute

National Human Genome Research Institute

NIBIB

National Institute of Mental Health

National Institute of Neurological Disorders and Stroke

National Institute of Nursing Research

National Institute on Minority Health and Health Disparities

National Center for Complementary and Integrative Health

Fogarty International Center

Engineering & Imaging Technologies

National Center for Advancing Translational Sciences

National Library of Medicine

ARPA H

National Institute of Biomedical Imaging and Bioengineering

NIBIB: *Technology & Innovation Focus*

Bioengineering

Therapeutic Systems

Monteris Medical, Inc.

Imaging Technologies
M. Garwood, UMN

Data Science, Modeling, Computation

V. Venugopalan, J. Spanier, UCI

Engineered Biology

Cambridge University

Sensors and Point of Care
S. Xu, UCSD

Bioimaging

NIBIB: *No Disease Focus, Bio-hypothesis Not Needed*

- Understand, Prevent & Detect Disease
- Personalize Diagnosis and Treatment
- Extend Health-Span
- Reduce Tech Costs, Disparities, Barriers to Access
- Drive Innovation, Entrepreneurship, Partnerships

National Institute of Biomedical Imaging and Bioengineering
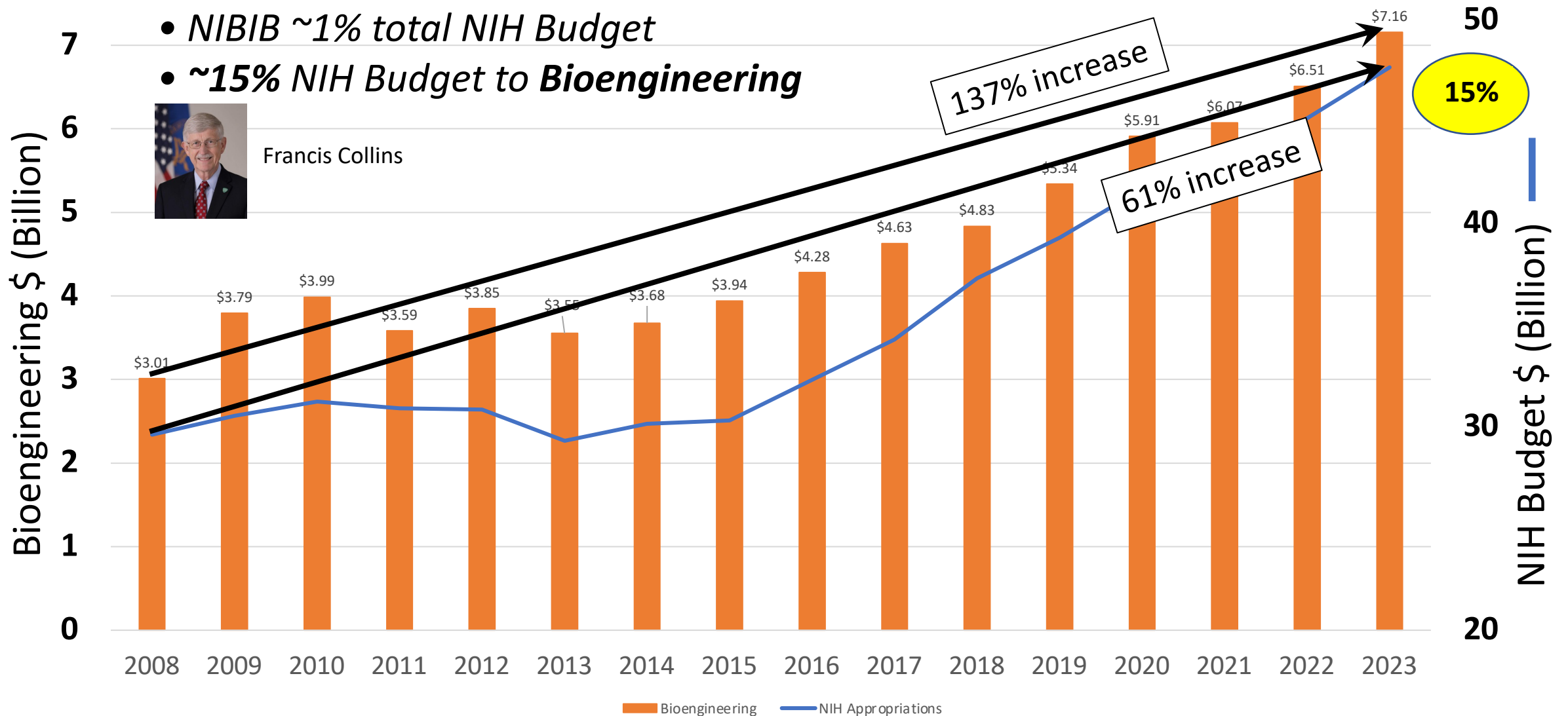
NIBIB Programs: *Pandemic Effect*

NIBIB *Core Programs*
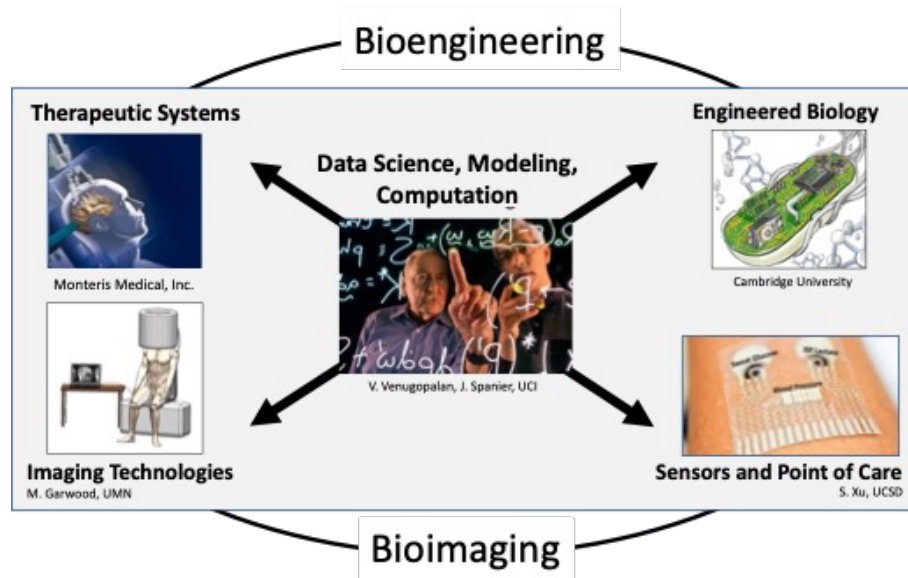
27 ICOs

+

Technology + Process Innovation

Pandemic Response

RADx Tech

- **Imaging and AI**
- **In Vitro Diagnostics**
- **Digital Health**

https://www.midrc.org

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

National Institute of Biomedical Imaging and Bioengineering

NIBIB Programs: *Pandemic Effect*

NIBIB Core Programs

Bioengineering

Therapeutic Systems
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Bioimaging

+

27 ICOs

NIH
National Institutes of Health

Technology + Process Innovation

MIDRC
MEDICAL IMAGING AND DATA RESOURCE CENTER.

- **Imaging and AI**
- *In Vitro Diagnostics*
- *Digital Health*

Radiologists limited resource

Need standardized, validated AI / ML

- Diagnose, assess extent disease
- Monitor therapy
- Detect complications
- Predict outcome
- Understand "long COVID"

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

NIH National Institute of Biomedical Imaging and Bioengineering

Medical Imaging and Data Resource Center

https://www.midrc.org

PI: Maryellen Giger, Ph.D., UChicago

24 core institutions
100+ investigators

Acute COVID

AI / ML

- Identify infection
- Diagnose disease
- Assess extent
- Monitor therapy
- Detect complications
- Predict outcome / PASC

Long COVID and Beyond

nature
Accelerated Article Preview

High-dimensional characterization of post-acute sequalae of COVID-19

2020
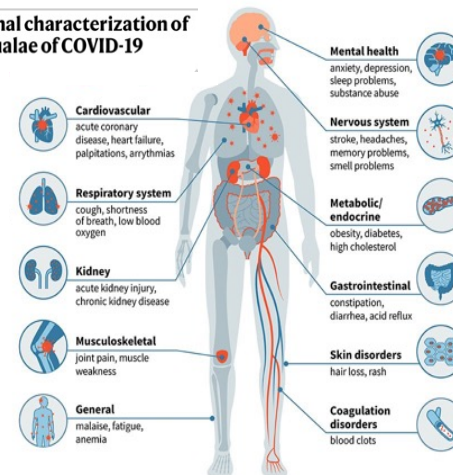
Early 2020

2023+

1. *Open Discovery Data Commons*

   Creation, testing, quality assurance, and data connectivity

2. *Machine Intelligence Computational Capabilities*

   Clinically relevant algorithms and software tools

Medical Imaging and Data Resource Center

https://www.midrc.org

PI: Maryellen Giger, Ph.D., UChicago

24 core institutions
100+ investigators

Acute COVID   Long COVID and Beyond

567,397 Imaging Studies Ingested	**177,079** Imaging Studies released to the Public	**390,318** Imaging Studies undergoing quality & harmonization	**58** Publications	**145+** Presentations	**31** Algorithms
272 Total Data Downloads this month	**73,714** Cases	**14.39 TB** Total size Published	**873** Registered Users	**100+** Investigators	**653** Collaborating Institutions

2020   Early 2020   2023+

Medical Imaging and Data Resource Center

MODEL EVALUATION ●
-Statistical Bias

DATA COLLECTION ●
-Data Acquisition &
 Aggregation Bias
-Biased Synthetic Data

-Population Bias ●●●
-Popularity/●●
 Patient-based Bias
-Temporal Bias ●●●●
-Sampling/
 Representation/Selection
 Bias
-Detection Bias
-Amplification Bias

-Training Data Bias ●●

-Cognitive Bias ●●●

-Institutional/Systemic Bias ●●●
-Activity Bias

-Presentation Bias ●●

DATA PREPARATION ●
-Content Production Bias

-Exclusion Bias ●●●

-Membership Bias
-Historical Bias
-Behavioral
 Bias

-Automation Complacency/
-Loss of Situational Awareness Bias ●●

-Annotator Bias ●●●●

MODEL DEPLOYMENT ●
-Deployment Bias
-Concept Drift/Emergent Bias
-User Interaction Bias

-Uncertainty Bias/Epistemic Uncertainty ●●

MODEL DEVELOPMENT ●
-Inherited/Error Propagation Bias

-Evaluation Bias ●●●
-Funding/Publication Bias

Major Bias Sources

- **Data Collection**
- **Data Preparation**
- **Model Development**
- **Model Evaluation**
- **Model Deployment**

Bias Awareness Tools
https://www.midrc.org

Essential for standardization and validation of muti-site, multi-platform data

Brad Brower   Kris Kandarpa   Rui de Sa
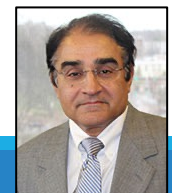
FDA Clearance for AI/ML Algorithms

AI/ML Enabled Devices Cleared by FDA (N=882 on 5/15/2024)

Chart: AI/ML Enabled Devices Cleared by FDA showing stacked bar graph (Radiology Panel in yellow, Other in blue) from 2014 to 2023/24, with an "Estimated" projection.

- 76% Radiology
- 10% Cardiovascular
- 3% Neurology
- 2% Hematology

Legend: Radiology Panel, Other
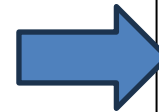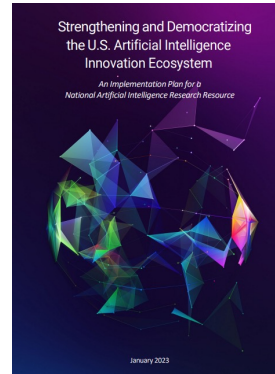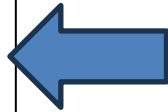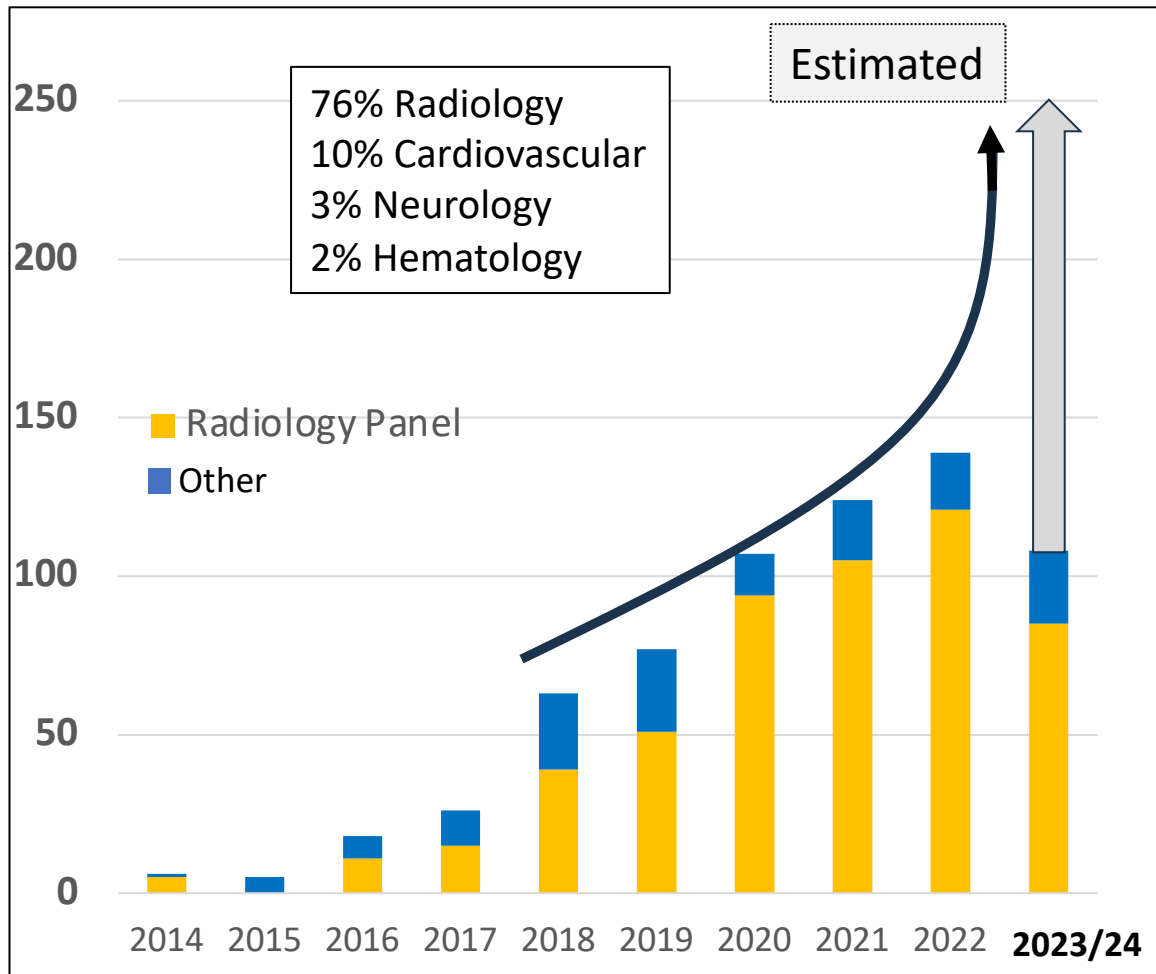
- *First authorization 11/08/1995*

- Radiology has highest number of submissions and steadiest growth rate vs. other specialties

- Models range in complexity from shallow ML to multilayer DL.

- Hybrid methods common: combine algorithmic approaches e.g one model to generate features, another to do classification.

- DeNovo rare: ~1-3%; drive family of 510ks (e.g. QuantX)

https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices

National Institute of Biomedical Imaging and Bioengineering

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76% Radiology
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Estimated

Radiology Panel
Other

2014 2015 2016 2017 2018 2019 2020 2021 2022 **2023/24**
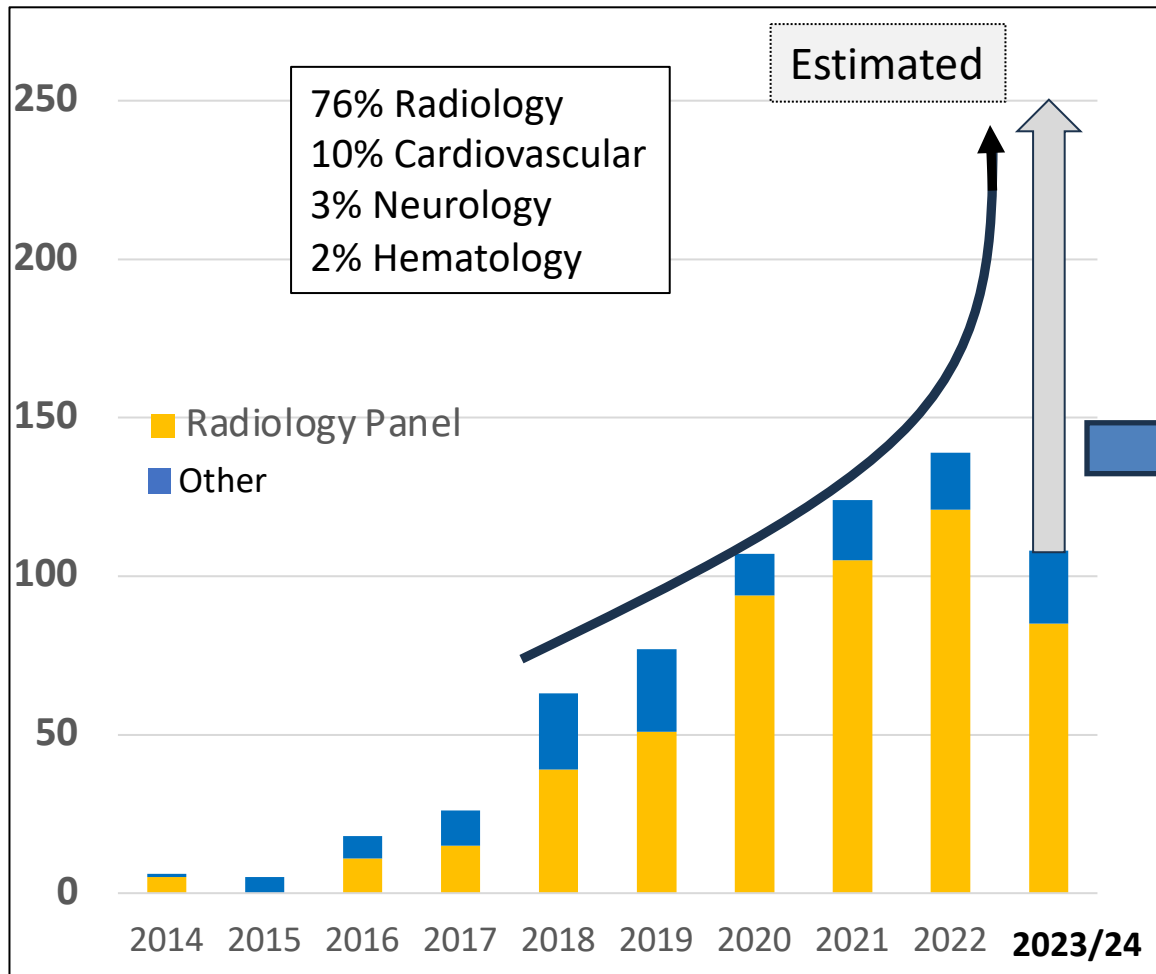
Driving Global Market Growth

AI IN HEALTHCARE MARKET
GLOBAL FORECAST TO 2029 (USD BN)

CAGR OF
48.1%

The AI in Healthcare market is expected to be worth USD 148.4 Billion by 2029, growing at a CAGR of 48.1% during the forecast period.

148.4

14.5   20.9

2023   2024   2029

North America   Europe   Asia-Pacific   Rest of the World

https://www.marketsandmarkets.com/Market-Reports/artificial-intelligence-healthcare-market-54679303.html

https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices

National Institute of
Biomedical Imaging
and Bioengineering

High-def ultrasound (US) microvasculature imaging (HDMI)

Thyroid
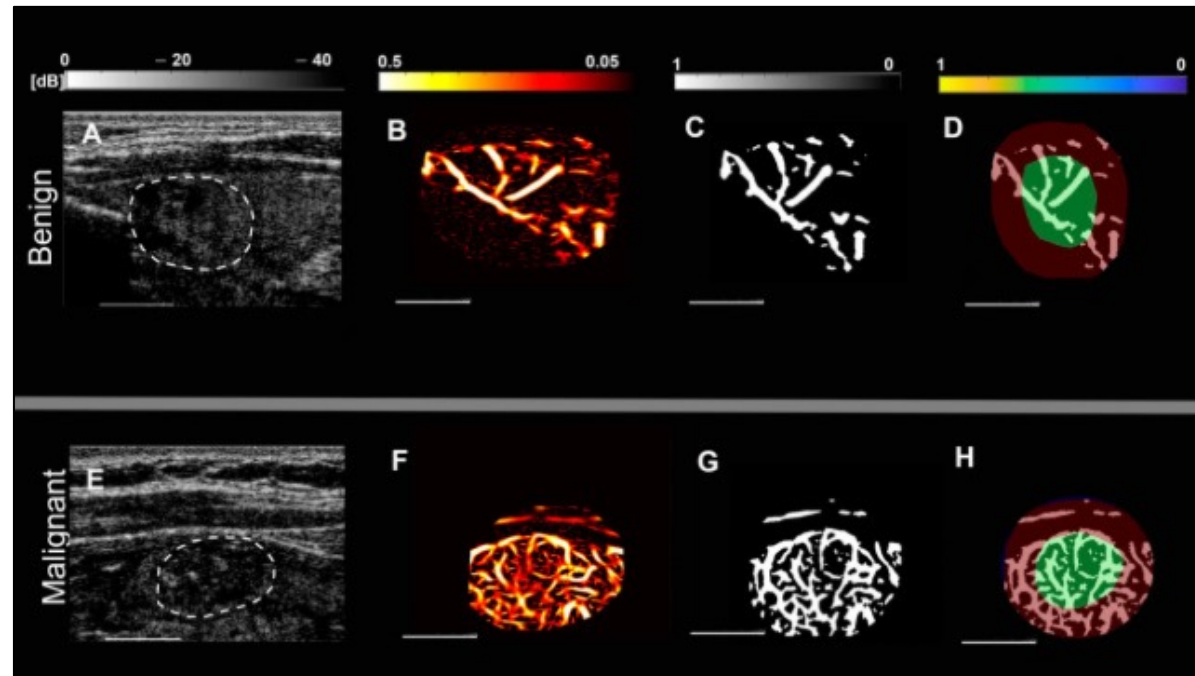
- Low-cost, noninvasive HDMI solution uses AI to accurately evaluate tumor microvasculature

- 600 fps model-based Doppler ultrasound technique renders vasculature and classifies tumor based on vessel features

- In study, ML algorithm generated a predictive model that accurately classified 89% of Thyroid cases

- Demos in Kidney, Liver, Thyroid, Breast
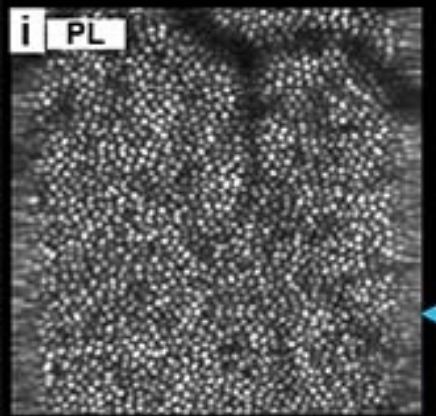

Azra Alizad and
Mostafa Fatemi team

National Institute of
Biomedical Imaging
and Bioengineering

Optical Coherence Tomography (OCT), AI and Adaptive Optics (AO)

Capillaries spanning INL-OPL boundary
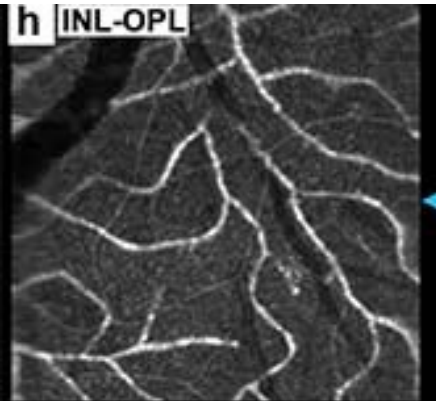
Photoreceptor layer

Retinal pigment epithelium
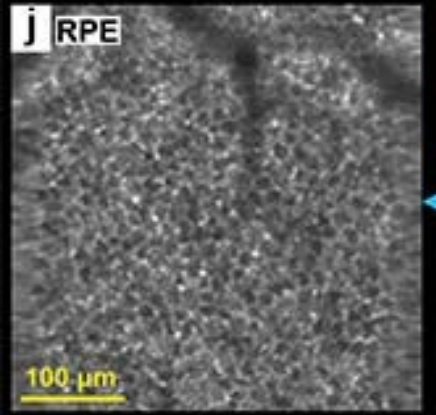
Zhuolin Liu and Daniel X. Hammer, FDA (with NIBIB support), Johnny Tam, NEI, Osamah Saeedi, University of Maryland.
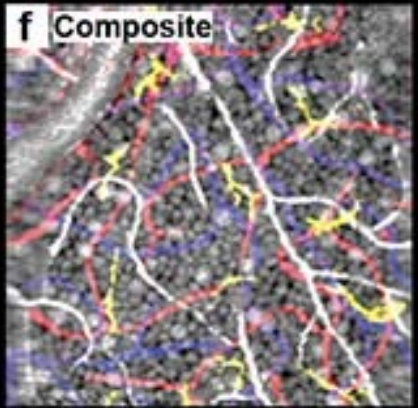
AO-OCT volume of the retina
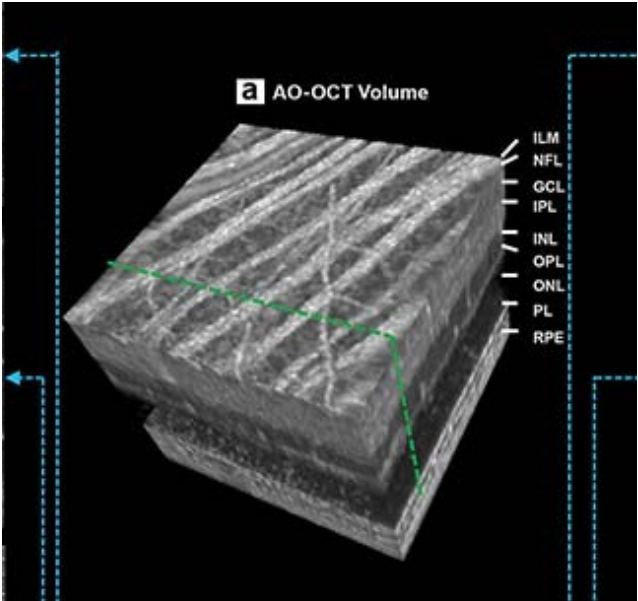
https://www.photonics.com/Articles/AO-OCT_Comes_into_Focus/a64316
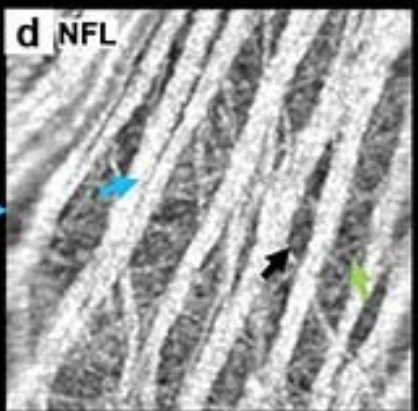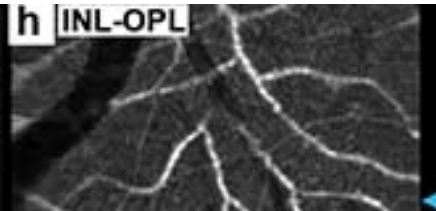
Retinal nerve fiber bundles

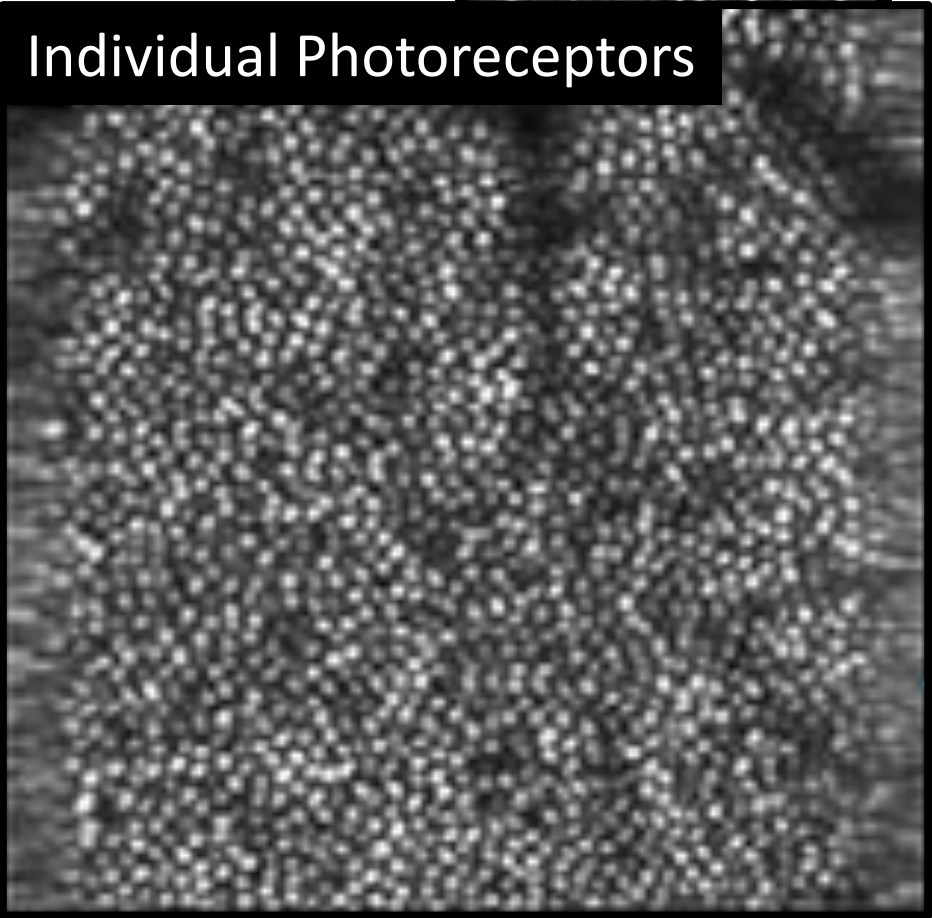Ganglion cell layer showing a mosaic of somas
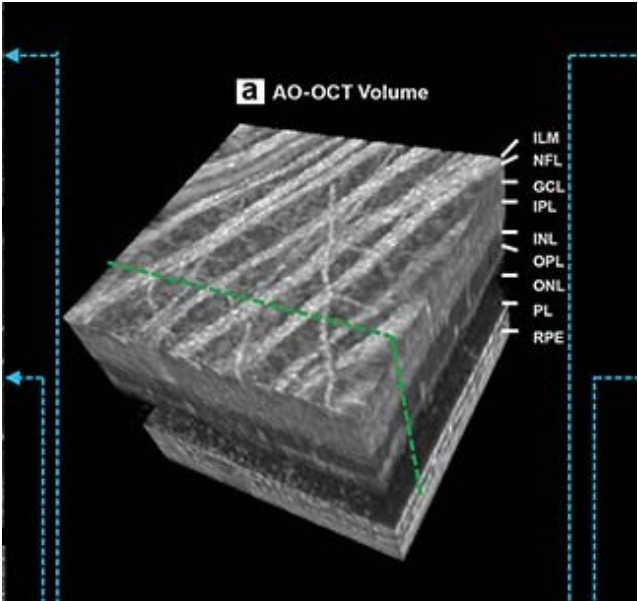
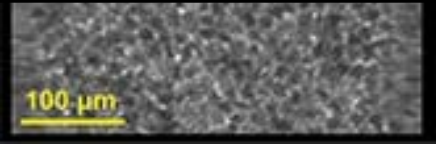Composite image overlaying multiple colorized layers

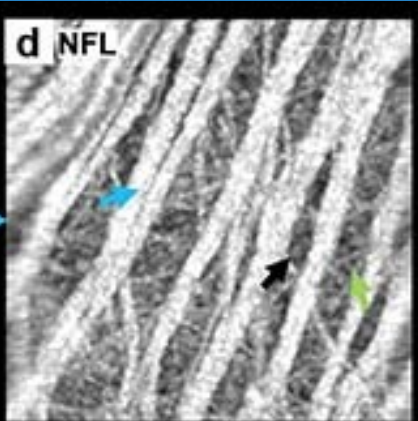# Optical Coherence Tomography (OCT), AI and Adaptive Optics (AO)

Individual Photoreceptors

Zhuolin Liu and Daniel X. Hammer, FDA (with NIBIB support), Johnny Tam, NEI, Osamah Saeedi, University of Maryland.
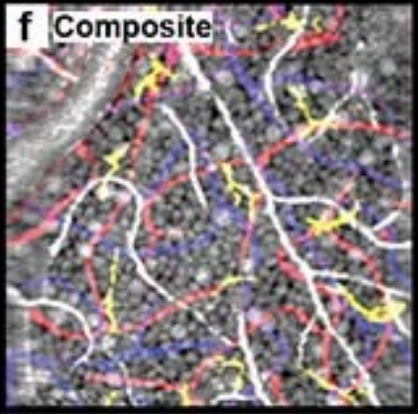
Retinal nerve fiber bundles

Ganglion cell layer showing a mosaic of somas

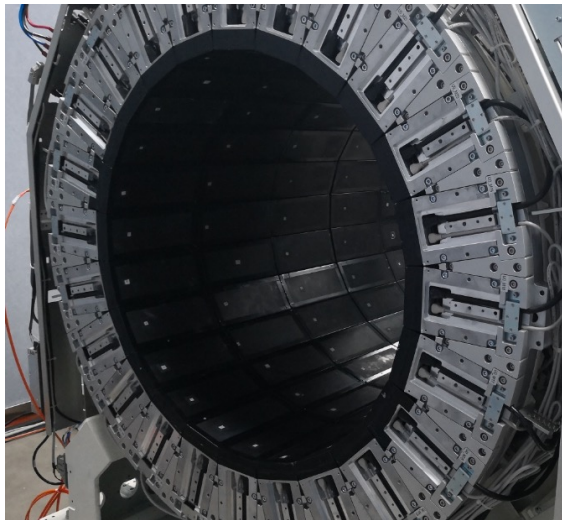https://www.photonics.com/Articles/AO-OCT_Comes_into_Focus/a64316

Particle Physics and AI: *Whole Body PET imaging*

The Compact Muon Solenoid (CMS) is a general-purpose electromagnetic calorimeter (EC) detector at the Large Hadron Collider (LHC). Applications range from studying the Standard Model (including the Higgs boson) to searching for extra dimensions and particles that could make up dark matter.
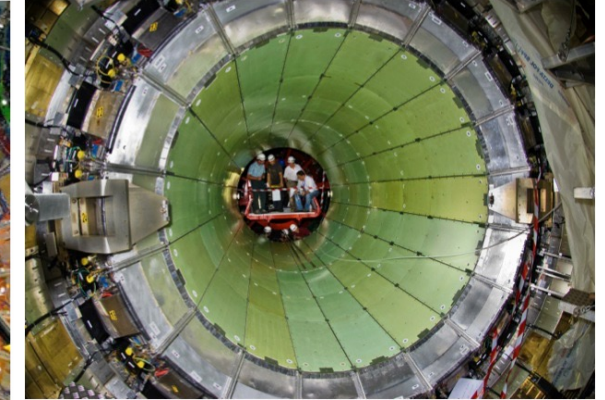
# of crystals: 75,848
# of photodetectors: 137,048
# of electronic channels: 75,848
Mass: ~100,000 kg

The EXPLORER Total Body Scanner uses similar design principles with massive parallelization of photodectectors and crystals to achieve the world's highest sensitivity positron emission tomography (PET) scanner.

# of crystals: 564,480
# of photodetectors: 53,760
# of electronic channels: 53,760
Mass: ~11,000 kg

Simon Cherry

UCDAVIS
EXPLORER MOLECULAR
IMAGING CENTER

https://health.ucdavis.edu/radiology/myexam/PET/Equipment/explorer.html

Particle Physics and AI: *Whole Body PET imaging*

Total FDG body image in 7 minutes

Female, 32y, BMI 21
310 MBq injection, ^{18}F-FDG
7 min acquisition
Scanned at **60 min p.i.**
2.34 mm voxels
~5 million voxels in total

Transformative R01 (2015)
Co-funded by NCI, NIBIB, OD
System completed 2018
FDA 510(k) clearance 2019
Commercialized 2019
~20 systems installed or ordered (2023)

Simon Cherry

UCDAVIS
EXPLORER MOLECULAR
IMAGING CENTER

https://explorer.ucdavis.edu

Dynamic FDG Movie

Age: 78
Gender: Male
Height: 170 cm
Weight: 71 kg

Tracer: FDG
Dose: 349 MBq (9.4 mCi)
60 min dynamic scan

0 min 1 s

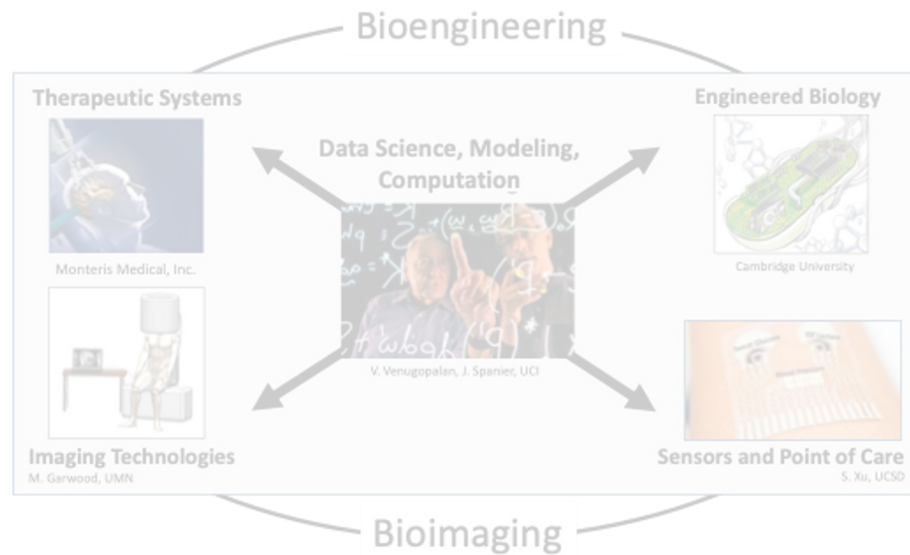Courtesy Yiran Wang, UC Davis

UC DAVIS
EXPLORER MOLECULAR IMAGING CENTER

NIBIB Programs: *Pandemic Effect*

NIBIB *Core Programs*

Bioengineering

Therapeutic Systems

Data Science, Modeling, Computation

Engineered Biology

Monteris Medical, Inc.

Cambridge University

V. Venugopalan, J. Spanier, UCI

Imaging Technologies
M. Garwood, UMN

Sensors and Point of Care
S. Xu, UCSD

Bioimaging

+

27 ICOs

NIH

National Institutes of Health

Technology + Process Innovation

Pandemic Response

RADx Tech

- • *Imaging and AI*
- • ***In Vitro Diagnostics***
- • ***Digital Health***
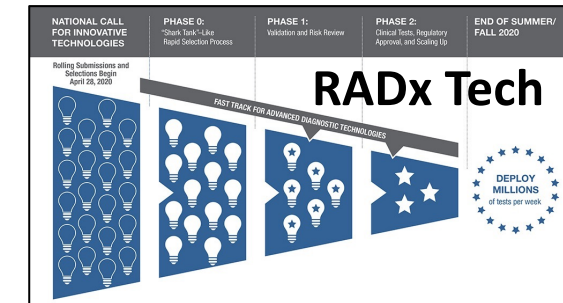
Meet Urgent National Need for COVID-19 Diagnostics

https://www.midrc.org

Effect

Cisco has pledged to positively impact 1 billion

Patti Tromberg

The Washington Post

Opinion: We need more covid-19 tests. We propose a 'shark tank' to get us there.

Opinion by **Lamar Alexander** and **Roy Blunt**

April 20, 2020 at 8:46 p.m. EDT

Lamar Alexander (R-Tenn.) is chairman of the Senate Health, Education, Labor and Pensions Committee. Roy Blunt (R-Mo.) is chairman of the Senate's health appropriations subcommittee.

There is no safe path forward to combat the novel coronavirus without adequate testing. To contain covid-19 and persuade
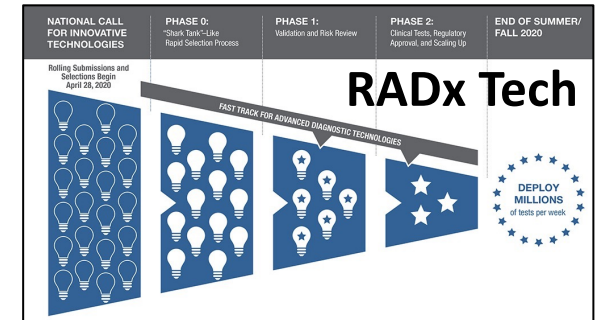
4ᵗʰ Congressional Supplement:
April 24, 2020 ($1.5B NIH)

RADx Launched: *April 29, 2020*

Goal: POC, OTC >> Lab

*10s Millions tests/month
By fall 2020*

Reimagine Safety   D

RADx Tech

ion: We need more covid-19 tests.
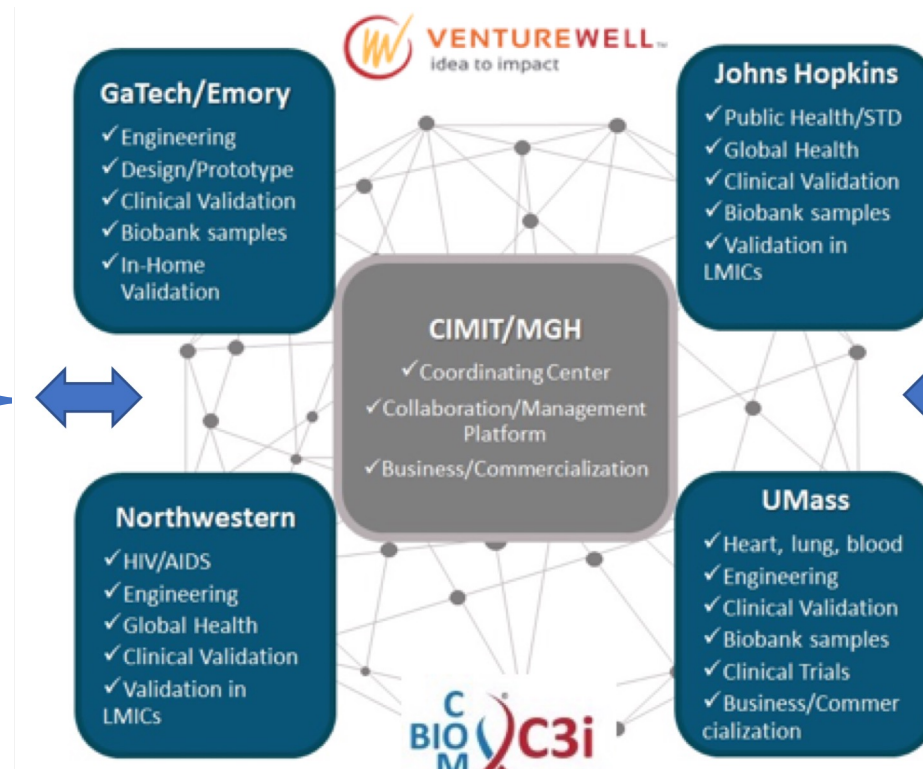ropose a 'shark tank' to get us

RADx Tech: *Structure*

NIBIB Point of Care Tech Research Network (POCTRN U54)
Expanded April 29, 2020: >900 RADx experts & contributors: (USG, Academia, Industry, NFP)

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

Innovation Funnel
(shark tank)
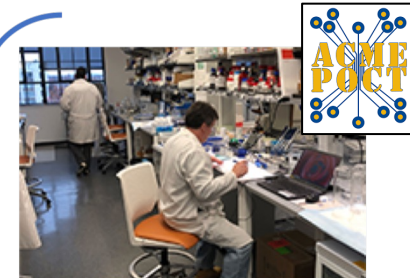
Validation Core

>1000 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

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
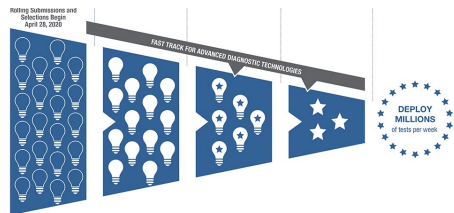
https://www.poctrn.org

RADx Tech: *Programs*

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Expanded April 29, 2020: >900 RADx experts & contributors: (USG, Academia, Industry, NFP)

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

Innovation Funnel

RADx MARS Digital Health

Variant Task Force *Project Rosa*

Independent Test Assessment (ITAP)

makemytestcount.org

Test Accessibility

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

Johns Hopkins
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https://www.poctrn.org

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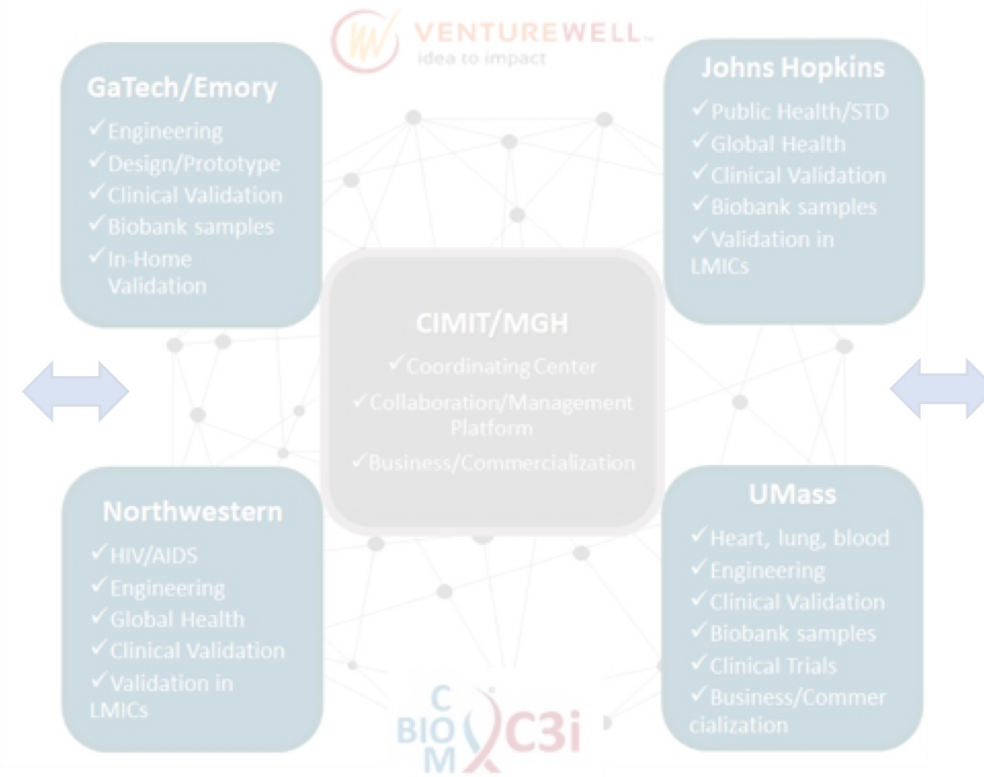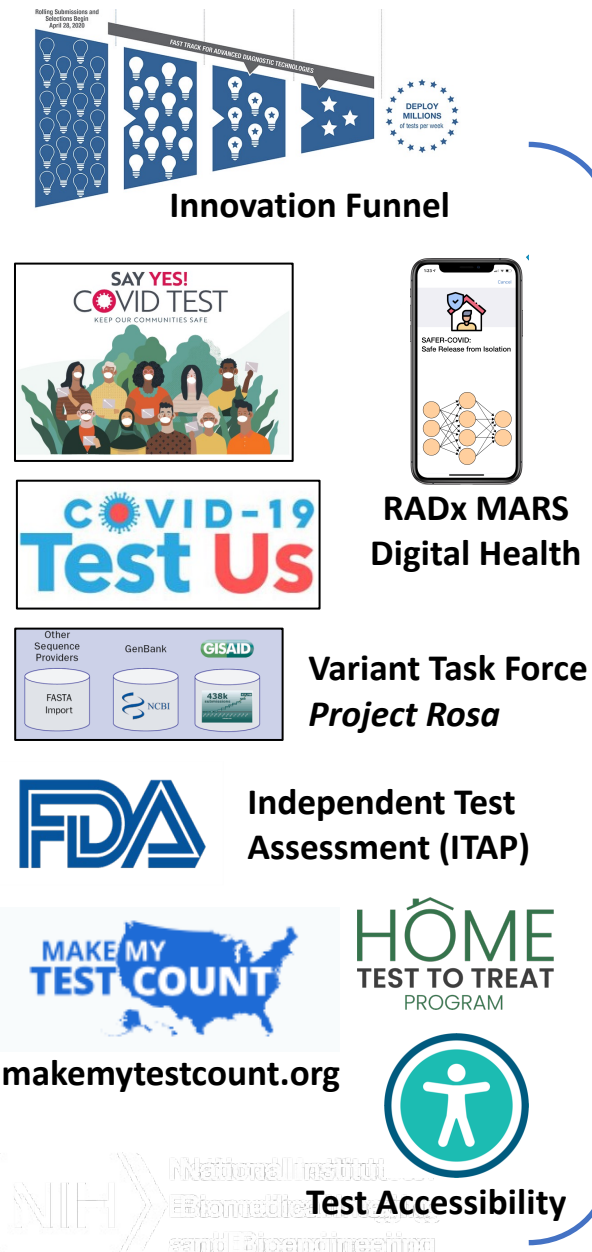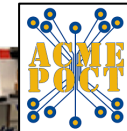Supply chain, Manufacturing, User Community, *whentotest.org* My COVID Toolkit
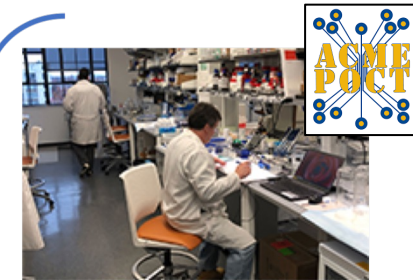
RADx Tech: *Impact*

Innovation Funnel

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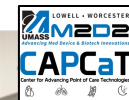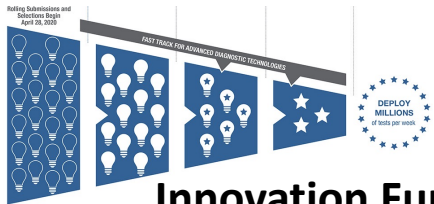1042 Applications→50 Phase 2

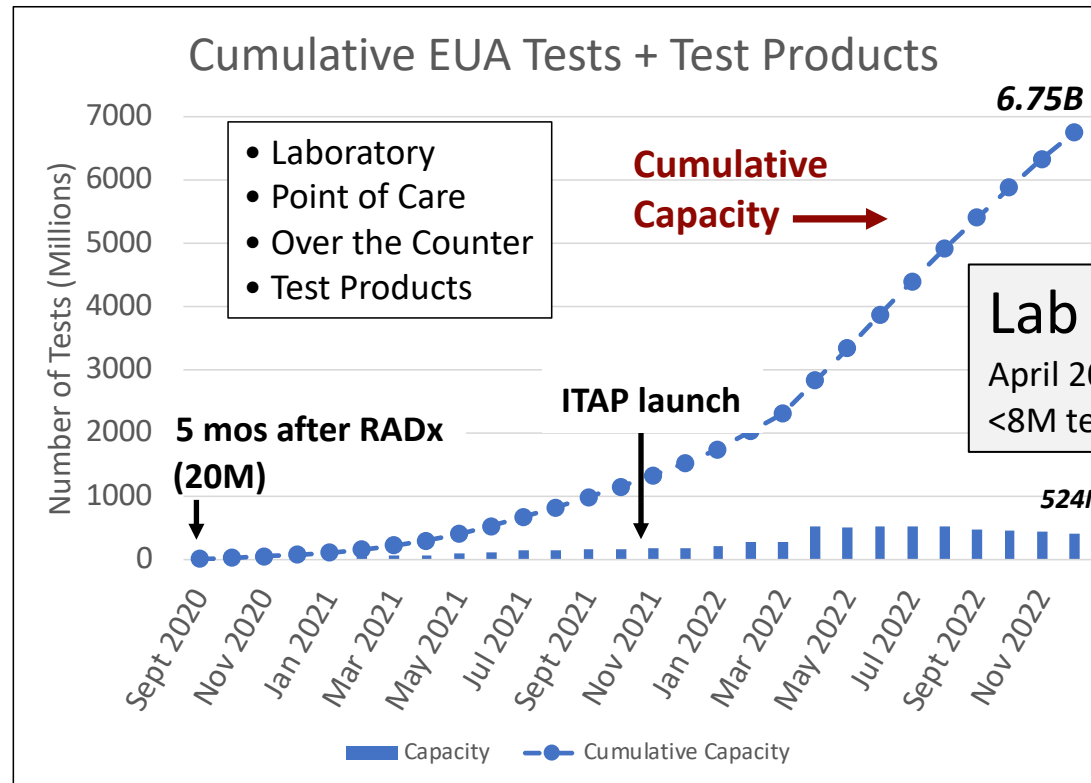- **7.8 B tot capacity →March 2023**
- **56 EUAs**: *19 OTC, 17 POC*

Independent Test Assessment (ITAP)

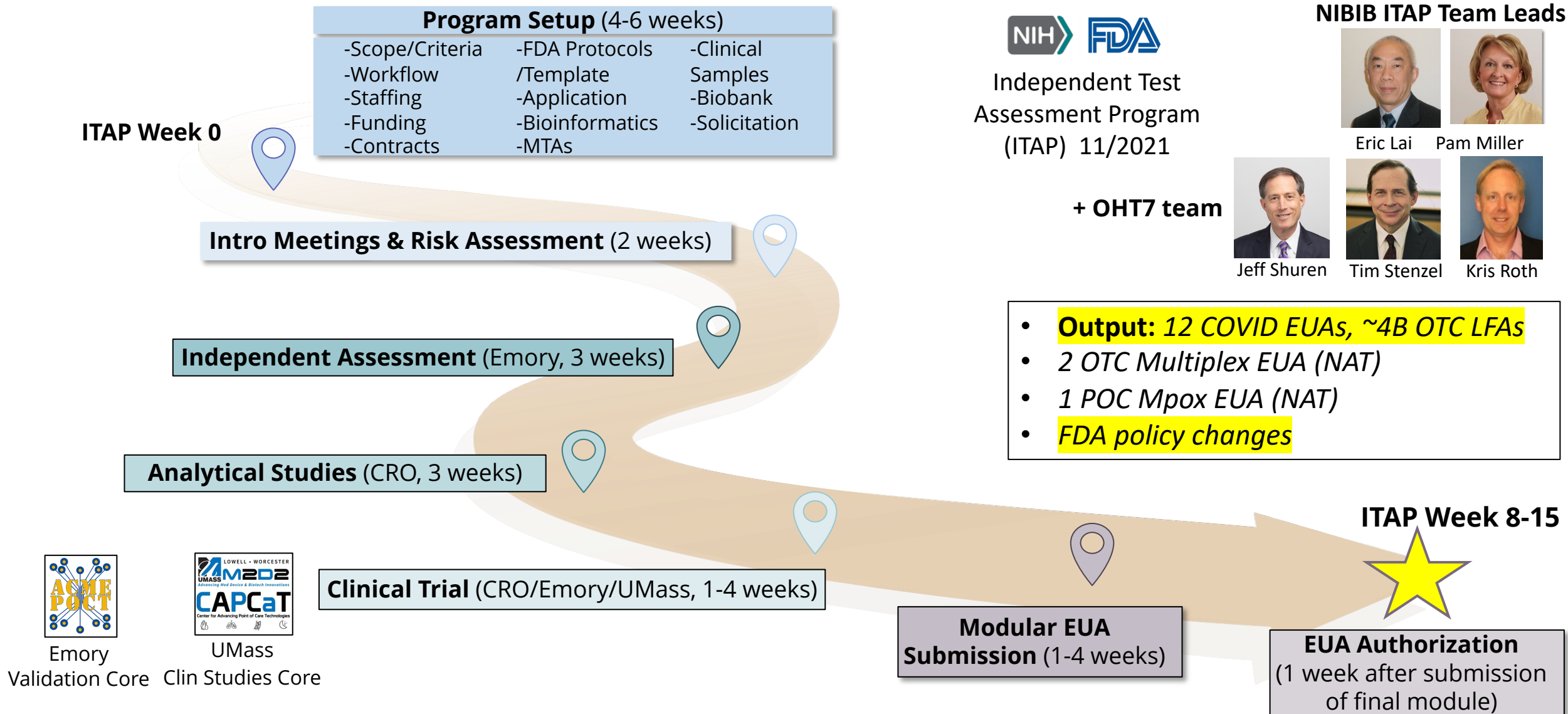**ITAP Team Leads**

Eric Lai   Pam Miller

EUA ~8-12 weeks

Cumulative EUA Tests + Test Products

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

Cumulative Capacity →

5 mos after RADx (20M)

ITAP launch

6.75B

524M

Capacity   Cumulative Capacity

Dx Paradigm Shift

Lab >> POC → OTC, POC >> Lab (~12%)

April 2020 <8M tests   Feb 2022 ~ 1B OTC tests

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

RADx Tech: *FDA Partnership*

Program Setup (4-6 weeks)

-Scope/Criteria	-FDA Protocols	-Clinical
-Workflow	/Template	Samples
-Staffing	-Application	-Biobank
-Funding	-Bioinformatics	-Solicitation
-Contracts	-MTAs	

ITAP Week 0

Intro Meetings & Risk Assessment (2 weeks)

Independent Assessment (Emory, 3 weeks)

Analytical Studies (CRO, 3 weeks)

Clinical Trial (CRO/Emory/UMass, 1-4 weeks)

Emory
Validation Core

UMass
Clin Studies Core

Modular EUA Submission (1-4 weeks)

NIH> FDA

Independent Test
Assessment Program
(ITAP) 11/2021

+ OHT7 team

NIBIB ITAP Team Leads

Eric Lai   Pam Miller

Jeff Shuren   Tim Stenzel   Kris Roth

- **Output:** *12 COVID EUAs, ~4B OTC LFAs*
- *2 OTC Multiplex EUA (NAT)*
- *1 POC Mpox EUA (NAT)*
- *FDA policy changes*

ITAP Week 8-15

EUA Authorization
(1 week after submission
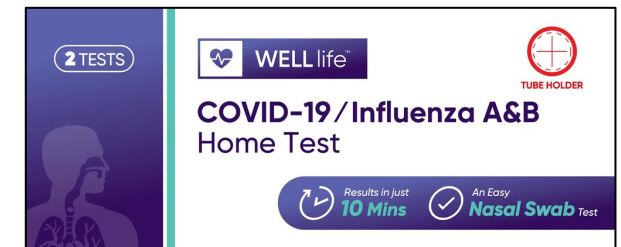of final module)

https://www.nibib.nih.gov/covid-19/radx-tech-program/ITAP

100% of FDA cleared 2023-2024 season COVID-Flu Multiplex Tests on Market Supported by RADx ITAP   (06/01/2024)

Lucira by Pfizer
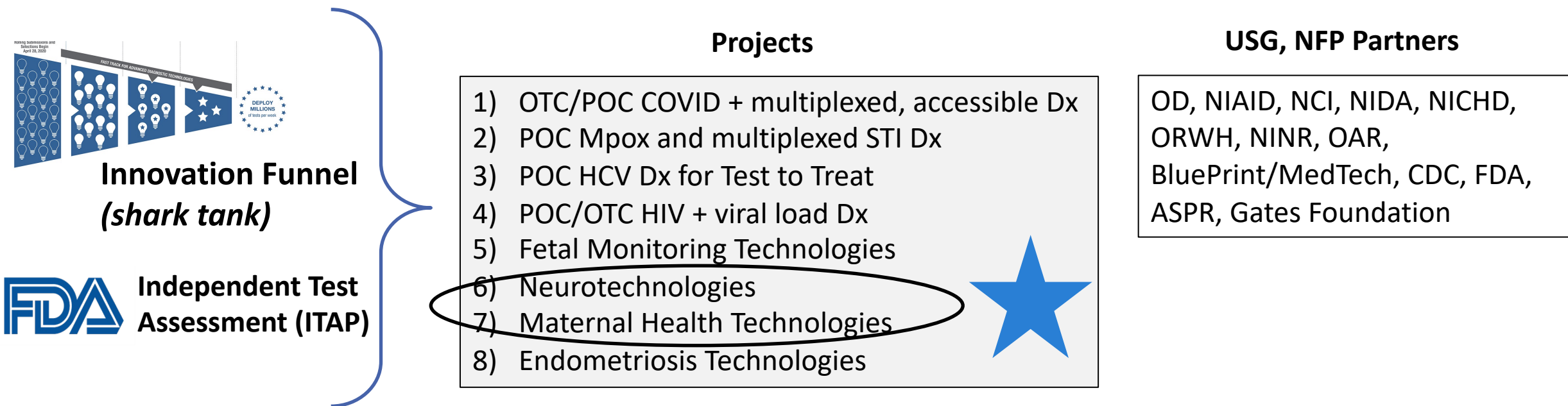Visby
Osom
CorDx
Osang
Wondfro
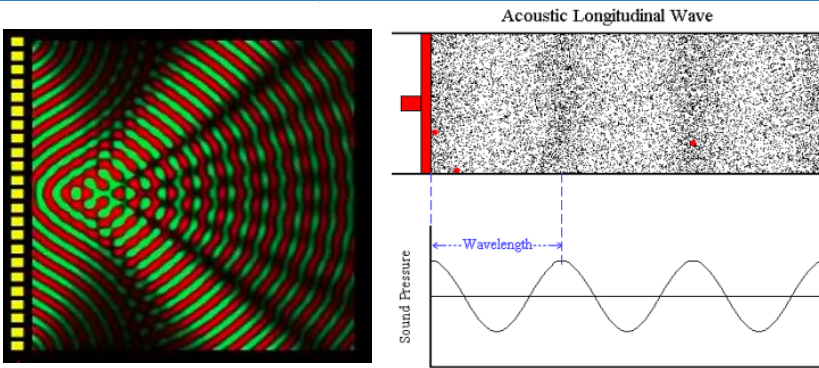iHealth
Watmind

OTC + POC weekly capacity ~46M
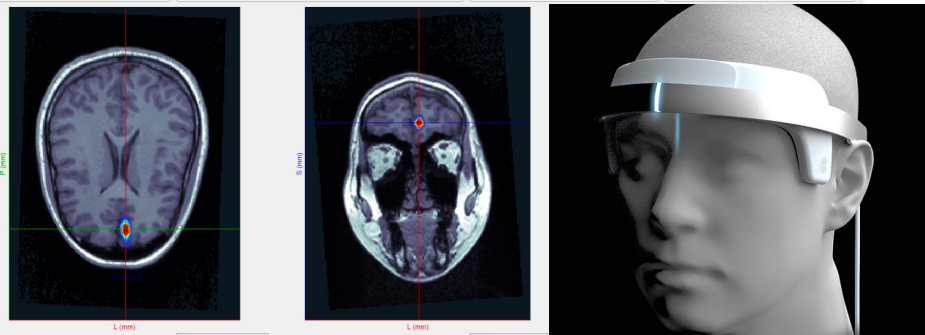
National Institute of Biomedical Imaging and Bioengineering

Neurotechnology projects (BRAIN and HEAL)

Array of transducers

High resolution neural activity and delivery of therapeutic stimulus (funded)

Non-addictive treatment for neuropathic pain, using low intensity focused ultrasound modulation of the dorsal root ganglia (funded)

BRAIN: novel non-invasive brain stimulation devices for the human CNS (sub-millimeter resolution at the cortical surface and depth)

HEAL: novel invasive or non-invasive devices for the diagnosis and/or treatment of pain and/or OUD

https://neuroscienceblueprint.nih.gov/neurotherapeutics/blueprint-medtech/blueprint-medtech-ics-and-contacts

RADx Tech for Maternal Health

Clinical Performance Assessment Phase
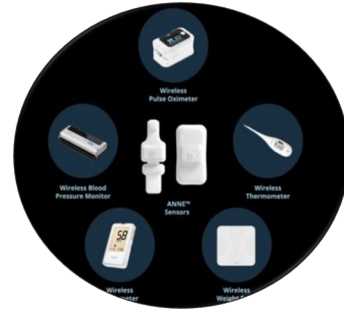
Sanguina	Sibel Health	Caretaker Medical	Global Access Dx	Dionysus Digital Health
Anemia mHealth	CV Monitor Wearable	CV Monitor Wearable	UTI Point of Care Dx	PPD Test + mHealth
PyrAmes	**CardieX**	**HemoSonics**	**Wash U St. Louis**	**MyLUA Health**
BP Monitor Wearable	BP Monitor Wearable	Hemorrhage Point of Care Dx	Hemorrhage Wearable	Care management mHealth
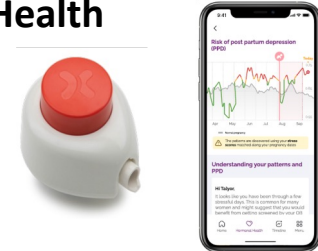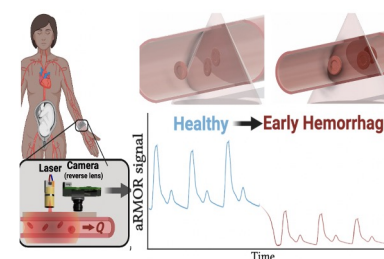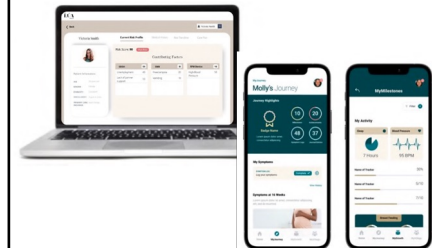
NIH NICHD

National Institute of Biomedical Imaging and Bioengineering

https://www.challenge.gov/?challenge=radx-tech-maternal-health

Summary

Tech Convergence: *Imaging, In Vitro Dx, Engineered Biology, AI*

Drivers: *Dx Tech advances during COVID; Home/POC markets for other pathogens, chronic diseases, prevention; Telehealth needs better Dx for "test to treat"*

Challenges: *How to standardize, validate, & regulate Dx info; integrate new approaches into healthcare (EHR, CMS, etc.), acquire Dx info on relevant biological timescales*

Opportunity: *Dx led precision medicine → personalize therapies, reduce time to treatments, Improve tech access & patient outcomes, empower broader communities*