Current Research Led By FDA

High-throughput truthing of microscope slides to validate artificial intelligence algorithms analyzing digital scans of same slides

- Partnership with academia, clinicians, and industry through Medical Device Innovation Consortium (MDIC)
- Focus on truth by pathologists, the microscope and TILs in breast cancer
- Status: Creating project structure, workgroups and leadership

- Key Deliverables:
  1. FDA qualified dataset for algorithm validation
  2. MDDT or mock 510(k) submission for
     - WSI viewer
     - TILs in breast cancer algorithm

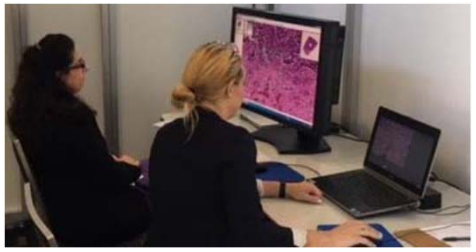
Work to be done in the public domain.

MDDT:
Medical Device Development Tool
https://www.fda.gov/medicaldevices/scienceandresearch/medicaldevicedevelopmenttoolsmddt/

510(k):
Premarket submission for Class II medical devices
https://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/premarketsubmissions/premarketnotification510k/default.htm

High Throughput Truthing for AI Validation

1. **FDA qualified dataset for algorithm validation**
   - Collect slide annotation data at pathology conferences and other high-volume settings
   - Use microscope and system that records evaluation locations
     - Scanner agnostic: map annotations to any digital scan of the slides
   - Also collect annotations from WSI's to support viewer and algorithm deliverables
   - Multiple readers per slide/ROI (5 to 15, not 2+1)
   - Dataset as a Medical Device Development Tool (MDDT)
   - Available to developers (in a controlled way) to use in FDA submissions
2. **MDDT or mock 510(k) submission for WSI viewer**
   - The WSI viewer is an enabling technology that has been developed by many groups.
   - Goal: Demonstrate regulatory pathway to allow innovation enabled by different viewers.
   - Use MDDT data (deliverable 1). Share process publicly. Community follows the example.
3. **MDDT or mock 510(k) submission for TILs in breast cancer algorithm**
   - Create an algorithm use case (= FDA Indications for Use).
   - Validate algorithm with MDDT data (deliverable 1).
   - Share process publicly. Community follows the example.



Data Collection At ASCP 2018

Why is the FDA doing this?

"help encourage more developers to translate advances into clinically actionable tools to benefit patients"
Scott Gottlieb, Commissioner FDA, "Transforming FDA's Approach to Digital Health."

MDDT

Medical Device Development Tool

New pathway. New mechanism.

- Reduce burden to sponsors
  - Use MDDT data in the submission
  - Replace 40 pages of a submission with, "Using the MDDT dataset, our algorithm performance is …"
- Reduce burden to FDA
  - Approve data once to support multiple sponsors

New stakeholders.

- Not just industry
- Pathologists, Academia, Health Providers
- Associations, Societies, Colleges (CAP, USCAP, ASCP)

Create an example for stakeholders to follow.

Impact

Build consensus. Build tools. Disseminate.

- High-throughput data-collection tools and protocols
- Standardize annotation formats for humans and algorithms
- Statistical methods and software for algorithm performance evaluation

→ Improve submissions. Enable interoperability.

Give pathologists ownership and confidence.

- What the algorithms should do
- The validation process

→ Improve clinical practice

Shift effort to community.

→ Reduce FDA workload

High-Throughput Truthing for AI Validation

How can your team get updates or get involved ?

Info and Updates

- Browse this wiki page: https://nciphub.org/groups/eedapstudies/wiki/HighthroughputTruthingYear2
- Join this group: https://nciphub.org/groups/eedapstudies

Use Case Development

- Outline use cases appropriate for novel AI algorithms, provide clinical guidance for industry R&D

Conference Logistics

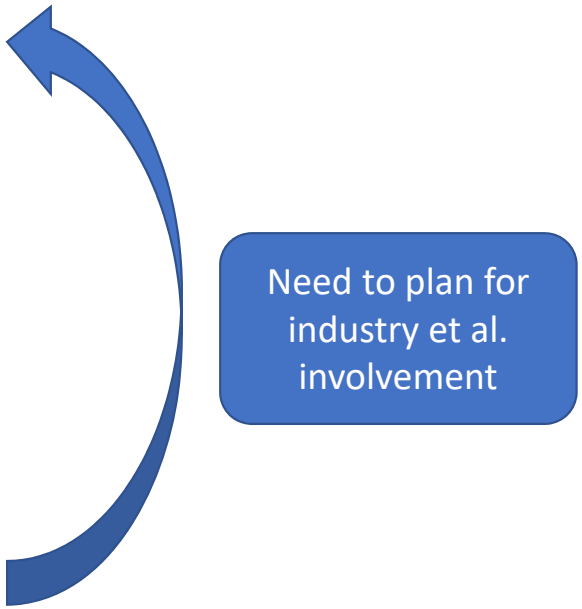
- Logistics and operations knowledge of pathology conferences, a primary source of pathologist recruitment

Pathologist Recruitment, Management, and Training

- Use-case training, biotechnology informatics

Big Tent project

- Plans will be shared with NCIPhub groups (eeDAPstudies and wsi_working_group) and then to the public
  - Join!
- Want workgroups to welcome the community (scale up)
  - Leaders get to steer and make decisions.
  - Leverage skills and resources of team.
  - Leaders cultivate the spirit to share and advance science
- Preparing to be adopted as MDIC project (MDIC board meeting June 12)
  - Looking for board champion
- MDIC will bring
  - Industry participation
  - Resources
  - Exposure
- Industry will
  - Join teams … and possibly leadership
  - Add deliverables



Funding

- ITCR administrative supplements
- ITCR grant for the Viewer MDDT/510k
- Need to tap NCI Cancer Imaging Program

- FTE positions available at FDA
- Intern positions at FDA (part time and summer)
- UK Research Institute Centre for Doctoral Training in AI for Medical Diagnosis and Care

Project Workgroups

- Slides
- Conference Logistics
- MDDT (Use-case) Development
- Infrastructure and Viewer
- Stats
- Annotation Data: Human
- Annotation Data: Algorithm
- Algorithm
- Pathologist Recruitment and Training

Workgroup Leadership

Slides

Anant Madabhushi

- F. Alex Nason Professor II of Biomedical Engineering, Case Western Reserve University and Research Health Scientist, Louis Stokes Cleveland Veterans Health Administration Medical Center, Cleveland, OH, US

Hannah Gilmore

- Division of Anatomic Pathology, University Hospitals Cleveland Medical Center, Case Western Reserve University

Conference Logistics

Jithesh Veetil

- MDIC: Medical Device Innovation Consortium

MDDT Development (Use-case)

Sarah Dudgeon

- FDA, CDRH, Office of Science and Engineering Laboratories, Division of Imaging, Diagnostics, and Software Reliability, Silver Spring, MD, US

Raj Gupta

- Stony Brook Medicine

Infrastructure and Viewer

Ashish Sharma

- Emory: viewer caMicroscope

Joel Saltz

- Dept. of Biomedical Informatics and Dept. of Pathology Stony Brook Medicine, Stony Brook, NY, US

Workgroup Leadership

Human Annotations

Darren Treanor

- NPIC: Northern Pathology Imaging Co-operative, Leeds Teaching Hospitals, NHS Trust, Leeds, UK

Bethany Williams

- Leeds Teaching Hospitals, NHS Trust, Leeds, UK

Algorithm Annotations

Lee Cooper

- Dept. of Biomedical Informatics, Emory University School of Medicine, Atlanta, GA, US

Mohamed Amgad

- Dept. of Biomedical Informatics, Emory University School of Medicine, Atlanta, GA, US

Algorithm

Roberto Salgado

- Department of Pathology, GZA-ZNA, Antwerp, Belgium; Division of Research, Peter Mac Callum Cancer Centre, Melbourne, Australia

Jeroen van der Laak

- Radboud University, The Netherlands

Stats

Weijie Chen

- FDA, CDRH, Office of Science and Engineering Laboratories, Division of Imaging, Diagnostics, and Software Reliability, Silver Spring, MD, US

Pathologist Recruitment, and Training

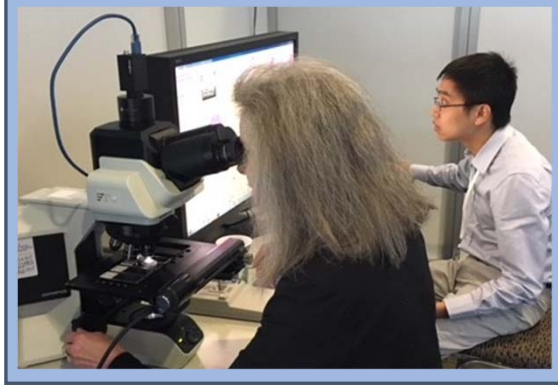
Opportunity!

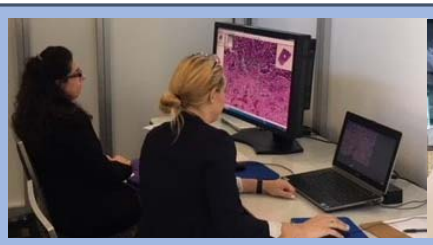
High-throughput Truthing

Go where thousands of pathologists go … Annual Society Meetings

Data-collection event (Demonstration)

Baltimore 2018.
Local destination.
Low cost.





TILs: Tumor Infiltrating Lymphocytes

Pathologists evaluated regions of interest:

- Stromal TILs density task
- TIL marking task

Microscope and digital modes

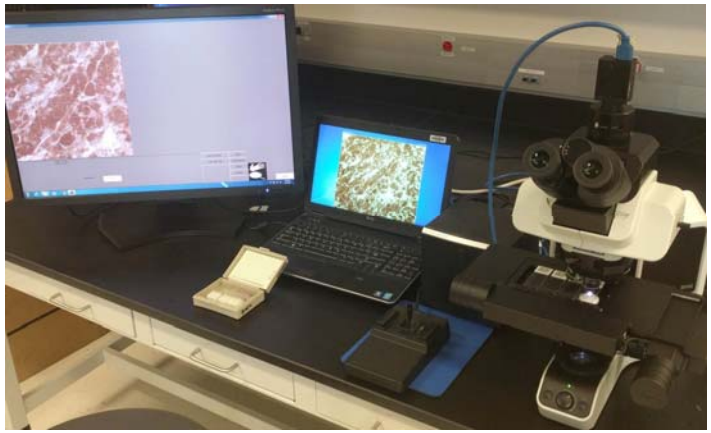
26 pathologists; 13 collection hours total.

eeDAP:

Evaluation Environment for Digital and Analog Pathology

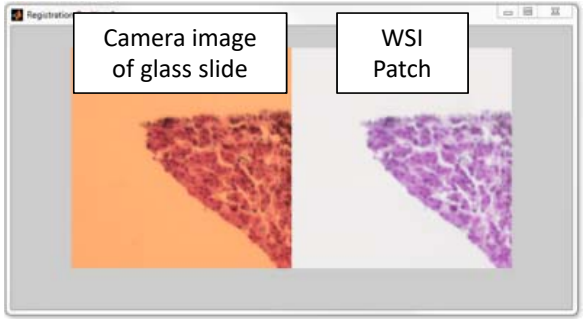
Microscope Mode

Monitor, Computer,
motorized stage with joystick,
microscope with mounted camera,
reticle in eyepiece



https://github.com/DIDSR/eeDAP

Register glass slide and WSI



Allow pathologists to create annotations using microscope … **scanner agnostic annotations**.

Then map annotations to ***any*** WSI

Possible Data Collection Events

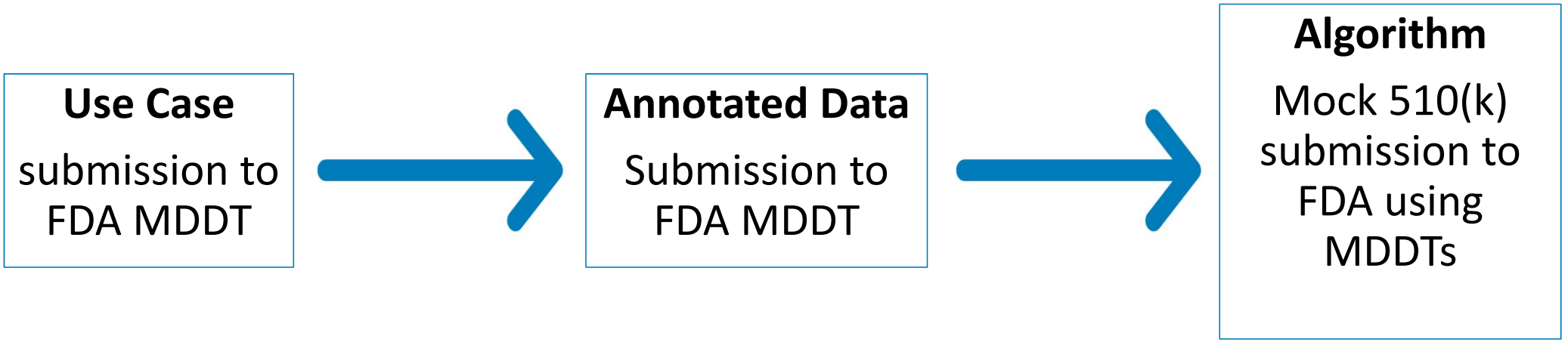
- FDA
  - 10?, 17? July, Silver Spring, MD
- ECP
  - 7-11 September, Nice, France
- ASCP
  - 11-13 September, Phoenix, AZ
- CAP
  - 21-25 September, Orlando, FL

- Complimentary web-based studies

<u>Default Plan</u>

- Four workstations
  - 2 microscopes + 2 digital mode
- Semi-private space on exhibit floor or a small conference room
- Need advertising for recruiting ahead of and during conference
- Opportunity to organize a session of speakers about the different project elements

Borrowing ACR's Pathway



ACR's Data Science institute's Senior Director has shared their first use-case MDDT submission with the HTT project.

What is a “Use Case?”

- Sets framework for the way which AI is expected to perform
- Ensures AI for specified context is both clinically relevant and implementable
- Dictates dataset development

- Specifies the following

The inputs to the algorithm.
Number of sections/slides required.
The evaluation area: entire WSI or pathologist identified regions of interest (ROIs)?

Patient inclusion and exclusion criteria: organ, disease.
Procedures or referrals that yield the appropriate specimen.
Imaging specifications: magnification, stain.
Other diagnostic results that are required.
The outputs from the algorithm.

How is the Use Case drafted?