A Collaborative Project to Produce Pathologist Annotations to Evaluate Viewers and Algorithms

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FDA, Center for Devices and Radiological Health,
Office of Science and Engineering Laboratories,
Division of Imaging, Diagnostics, and Software Reliability
AND
High-Throughput Truthing Project (HTT)

Data Collection Webinar agenda

FDA

- [High Throughput Truthing](#) (HTT) project
  - **Brandon D. Gallas**, PhD (15 min)

- Tumor Infiltrating Lymphocytes (TILs) clinical task. [Training slides are available here](#)
  - **Roberto Salgado**, MD (15 min)

- [Instructions](#) for data collection (Friday Feb. 28)
  - **Sarah Dudgeon**, MPH (15 min)

- Q&A (15 min)

> Wiki page with data-collection info (these presentations, informed consent, …) https://ncihub.org/groups/eedapstudies/wiki/HighThroughputTruthingYear3

HTT Collaborators

Project Management
- **Sarah Dudgeon**, MPH
  - FDA/CDRH/OSEL/DIDSR

caMicroscope team
- **Ashish Sharma**, PhD
  - Emory University Department of Biomedical Informatics
- **Joel Saltz**, MD PhD
  - Dept. of Biomedical Informatics, Stony Brook Medicine
- **Nan Li**, MS
  - Dept. of Biomedical Informatics, Stony Brook Medicine

PathPresenter team
- **Matthew Hanna**, MD
  - Memorial Sloan Kettering, New York, NY
- **Rajendra Singh**, MD
  - Icahn School of Medicine at Mt Sinai
- **Krushnavadan Acharya**, MCA
  - PathPresenter

Slides and Clinical
- **Roberto Salgado**
  - Peter Mac Callum Cancer Center; GZA-ZBA Hospitals
  - International Working Group for TILs in Breast cancer
- **Denis Larismont**
  - Institut Jules Bordet

Statistics
- **Si Wen**
  - FDA/CDRH/OSEL/DIDSR
- **Manasi Sheth**
  - FDA/CDRH/OPEQ/OCEA/Biostatistics
- **Chava Zibman**
  - FDA/CDRH/OPEQ/OCEA/Biostatistics
- **Weijie Chen**, PhD
  - FDA/CDRH/OSEL/DIDSR

HTT Collaborators

Committee

- **Mohamed Amgad**, MD, MSc
    – Emory University School of Medicine, Atlanta, GA
- **Rajarsi Gupta**, MD PhD
    – Renaissance School of Medicine and Dept. of Biomedical Informatics, Stony Brook Medicine
- **Steven N. Hart**, PhD
    – Mayo Clinic, Rochester, MN
- **Richard Huang**, MD, MS
    – Massachusetts General Hospital, Boston, MA
- **Giovanni Lujan**, MD
    – Computational Pathology Dept. at The Ohio State University Wexner Medical Center

Committee (cont.)

- **Anant Madabhushi**, PhD
    – Case Western Reserve University
- **Kyle J. Myers**, PhD
    – FDA/CDRH/OSEL/DIDSR
- **Joel Saltz**, MD, PhD
    – Stony Brook Department of Biomedical Informatics
- **Aparna Harbhajanka**, MD
   – Case Western Reserve University School of Medicine

Outline

- What are we doing?

- Why are we collecting data?

- When are we collecting data?

- Staying up to date

What are we doing?

Internal funding proposal title

- High-throughput truthing of microscope slides to **evaluate artificial intelligence** algorithms

- analyzing digital scans of pathology slides:

- **data (slides + images + annotations)** as an FDA-qualified medical device development tool (MDDT).
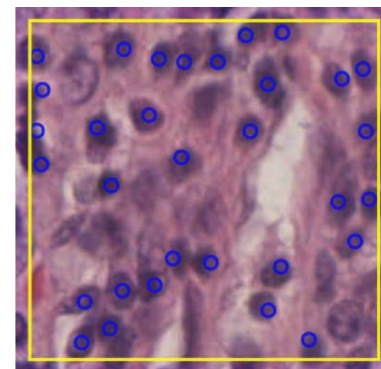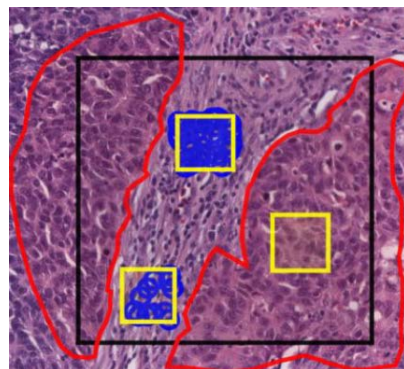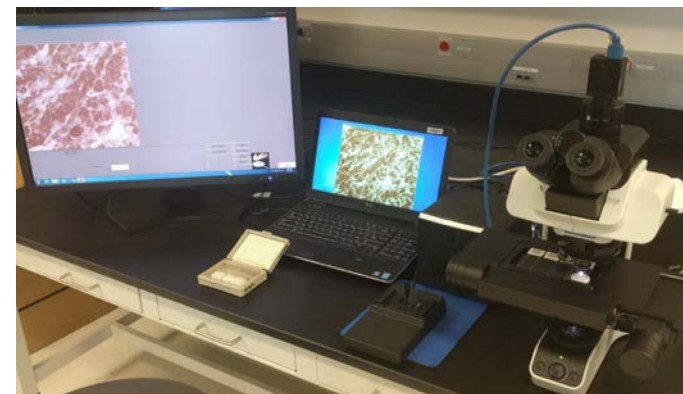
Standardized evaluation of Tumor-Infiltating Lymphocytes (TIL) in Breast Cancer for daily clinical and research practice or clinical trial setting

FDA
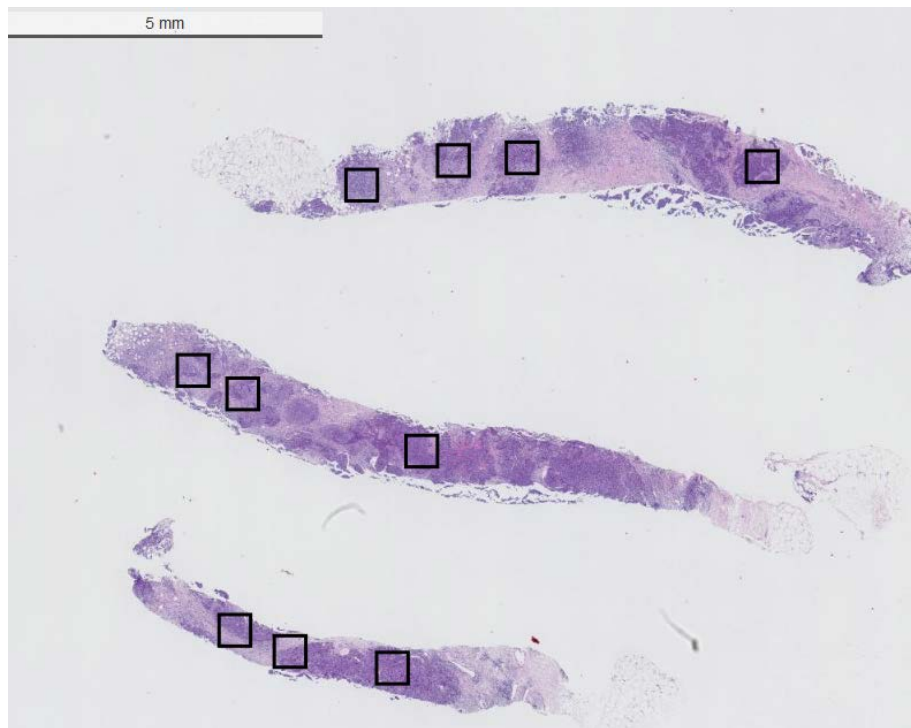
- A tutorial prepared by the International Working Group for TIL in breast cancer –2014 –adapted 2020

- Report percentage of tumor-associated stromal lymphocytes
  - Area of Lymphocytes / Area of Tumoral Stroma

- Report the average of the stromal area, do not focus on hot spots

Standardized evaluation of Tumor-Infiltating Lymphocytes (TIL) in Breast Cancer for daily clinical and research practice or clinical trial setting
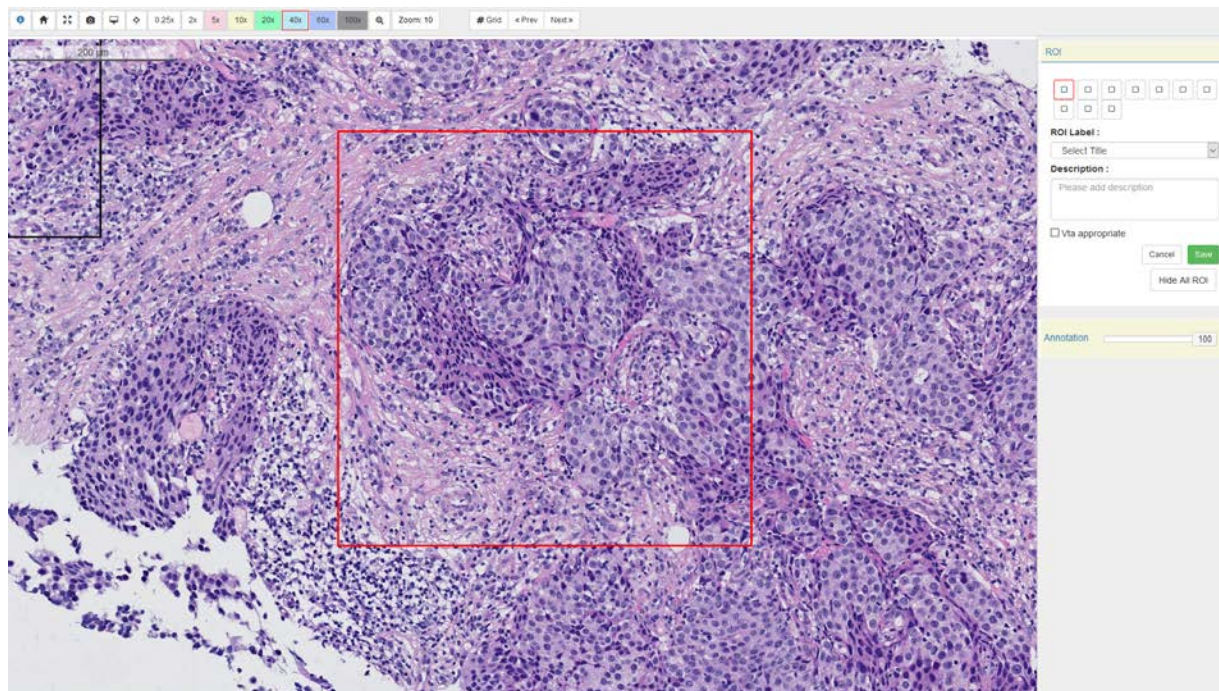
- Must zoom in to see tumor clusters, stroma, and TILs

- Evaluation happens on discrete areas

  - Fields of View (Microscope mode)

  - Regions of Interest (Digital mode)

- Evaluation can be done by a pathologist or an algorithm

Why are we collecting data?

Building a pathway

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.
Support and enable interoperability.

Why are we collecting data?

MDDT

Involve more stakeholders.

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

- ***Involve experts.***
- ***Involve the community.***

Impact

Give pathologists a voice, ownership of evaluation, and confidence to use.

- What should algorithms do?
- How should algorithms be evaluated?

- ***Create an example for stakeholders to follow.***
- ***Improve public health.***

When are we collecting data?

Recruiting Pathologists to Truth Images

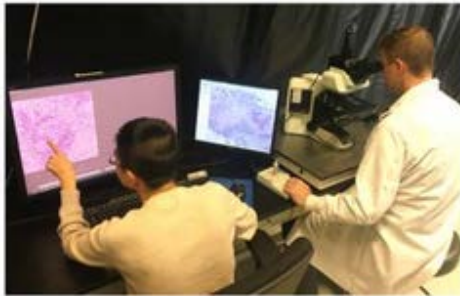### Data Collection Preceding USCAP at JW Marriot, Los Angeles
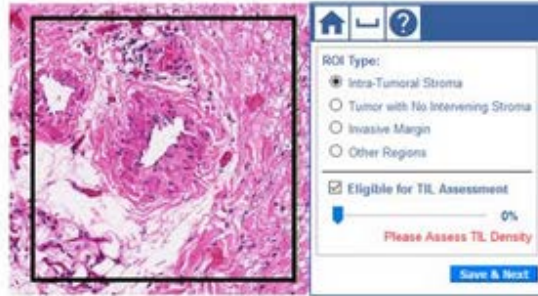- Friday, February 28th
- 30 min. sessions: 9am-5pm

Information Webinar
- Friday, February 19th, Noon EST

Evaluate in Microscope Mode

Evaluate in Digital Mode

Plan
- Board-certified Anatomic Pathologists and Residents

- Four workstations
  - 2 microscopes
  - 2 digital platforms

- 64 slides split into 8 batches of 8 slides

- 10 ROIs per slide

- 30 minute sessions

- **Looking for sites near DC for quick road trips.**
  - Let us know if you are interested.

https://nciphub.org/groups/eedapstudies/wiki/HighthroughputTruthingYear2

eeDAP studies ▸ Wiki

High-throughput Truthing - Year 2

by Brandon D. Gallas

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Year 2: High-throughput truthing validate artificial intelligence algo of pathology slides: data (images qualified medical device develop

- ↗ Link to full proposal submitted 10/19/2018. Decisions
- Here is an executive summary (four slides) of the projec
  - 20190402-HTTexecSummaryPublic.pdf (193 KB, up
- Here is a project overview presentation given Nov.-Dec.
  ↗ www.TILsinbreastcancer.org working group, project c
  - 20190402-HTToverviewPublic.pdf (348 KB, uploade
- Link to list of collaborators
- Link to updates

Project Overview

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https://nciphub.org/groups/eedapstudies/wiki

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Main Page

by Brandon D. Gallas

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Need help editing wiki? Scroll to bottom.

Projects

- eeDAP MDDT project description
- High throughput truthing of computational pathology al
- Here is a link to some device advice for AI and machine

Registration Accuracy

There is a discussion started. Check it out here.

Performance Endpoints

There is a discussion started. Check it out here

Hardware

There is a discussion started. Check it out here.

Funding Opportunities

There is a discussion started. Check it out here.

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https://nciphub.org/groups/eedapstudies/wiki/DeviceAdvice

eeDAP studies ▸ Wiki

Device Advice for AI and Machine Learning Algorith

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Here is a document of links pointing to FDA guidance documents and other forms of commu googling CDRH regulatory buzz words. We hope this document is useful. Caveat to all: You for your submission until you ask, try, and succeed.

Pre-submission meeting

In CDRH, the best advice is to know about pre-submission meetings.

- ↗ Slides: Pre-Submissions and Meetings with FDA Staff
- ↗ Guidance document: Requests for Feedback on Medical Device Submissions: The Pr Meetings with Food and Drug Administration Staff

IFU: Indications for Use

Part of the definition of your medical device are the indications for use.

- ↗ Webpage: Indications For Use.

It's never to early to start thinking about, researching, and crafting an IFU for your device.
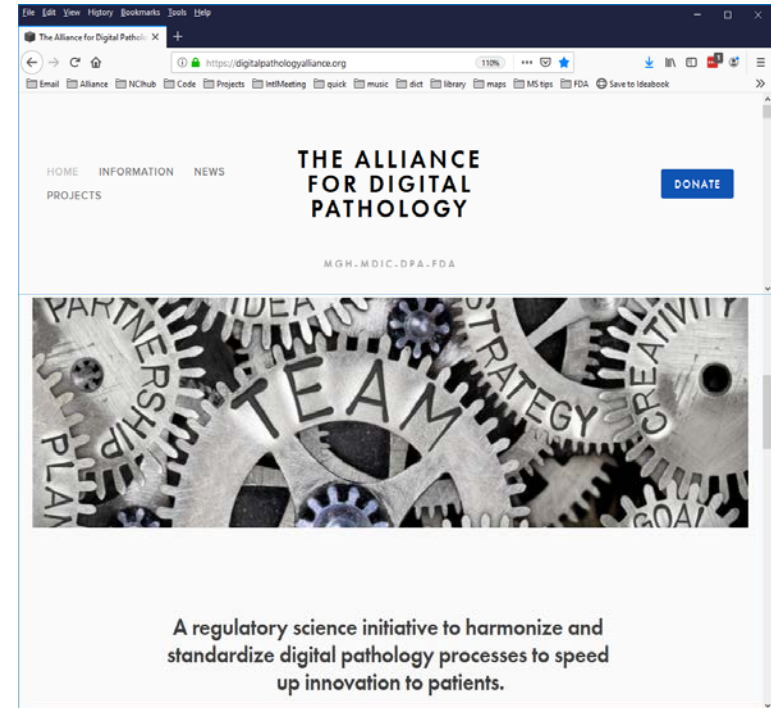
Comprehensive Regulatory Assistance

Collaboration Alliance

- **Objectives:**
  - Clarify and improve regulatory pathways

  - Develop evaluation tools, methods, and standards

  - Tackle large-scale projects in pre-competitive space

- Next meeting February 28, 2020
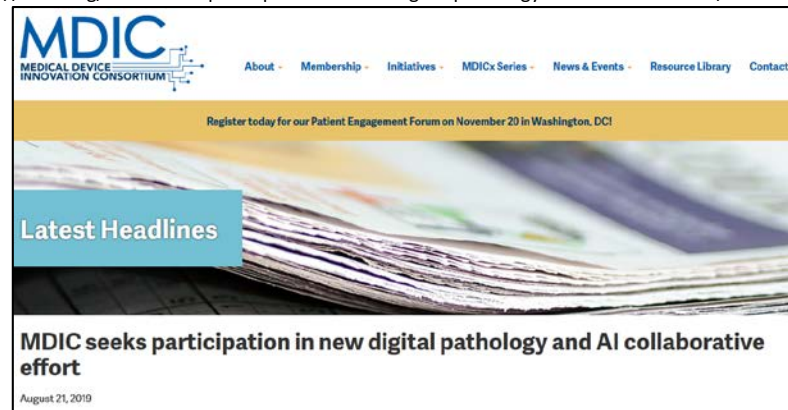 - Check out the fantastic agenda

https://digitalpathologyalliance.org/

THE ALLIANCE FOR DIGITAL PATHOLOGY

MGH.MDIC.DPA.FDA

A regulatory science initiative to harmonize and standardize digital pathology processes to speed up innovation to patients.

Collaboration Alliance

- Stakeholder participants (>250):
  - FDA, NIH, MDIC

  - Clinical societies:
    pathology (DPA, CAP)
    and radiology (ACR)!

  - Academic and clinical
    subject matter experts

  - Patient advocates

https://mdic.org/mdic-seeks-participation-in-new-digital-pathology-collaborative-effort/

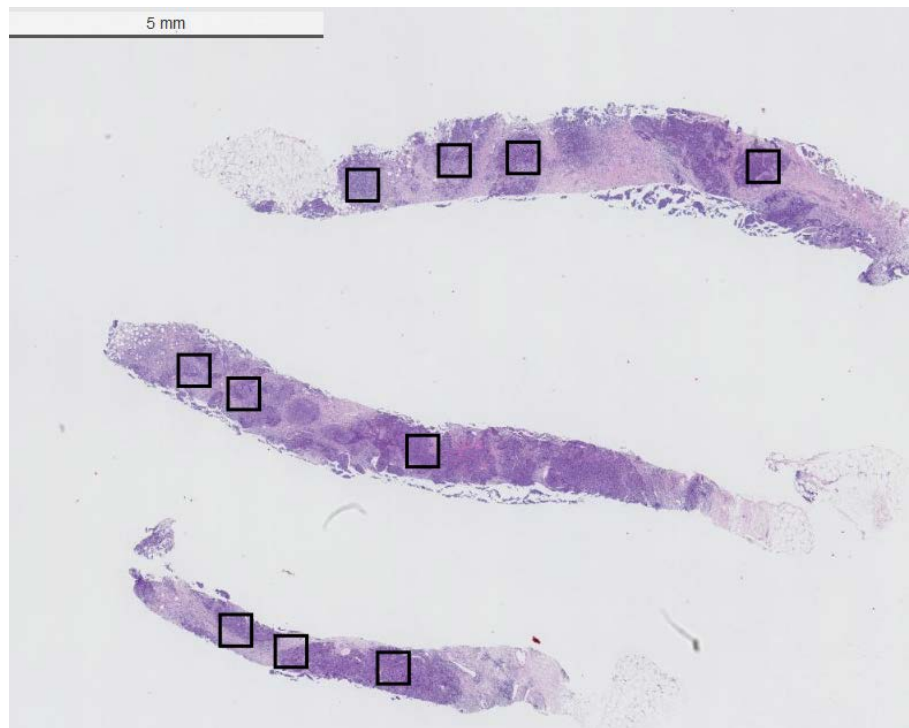https://digitalpathologyassociation.org/dpa-mdic-fda-alliance-meeting

Summary

- We are collecting data
  - To build collaborative relationships
  - To investigate methods and tools
  - To support the evaluation of AI/ML

- We hope to
  - Inform regulatory decision making
  - Improve submissions
  - Support and enable interoperability

Info

- Registration for Feb. 28 data-collection event
  - https://docs.google.com/forms/d/1Wf_h3pzFrrxy9r_nKUAjkXaRPxyrMQyptZSq6lblcQU/viewform

- Agenda for meeting of the Alliance for digital pathology (FREE)
  - https://docs.google.com/forms/d/1Wf_h3pzFrrxy9r_nKUAjkXaRPxyrMQyptZSq6lblcQU/viewform

- Email Brandon.Gallas@fda.hhs.gov with questions
  - Or if you don't have access to docs.google.com