Critical Path Score Card

CDRH FY18 Project Progress

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Project Title

High-throughput truthing of microscope slides to validate artificial intelligence algorithms analyzing digital scans of pathology slides: leveraging data collected in international "grand challenges"

What milestones have been accomplished so far? Also please provide any update or delays related to the project.
(Note: Text area expands and may run over the lines)

Objective 1: We determined the TUPAC data doesn't fit our needs. The glass slides are unavailable. I have engaged a new partner as a replacement, the TILS in breast cancer working group. They have added me to a funding proposal to the Breast Cancer Research Foundation to pay for creating infrastructure and data collection. I was also invited to contribute to an overview paper, Scoring of tumor-infiltrating lymphocytes: from visual estimation to machine learning," that was submitted to Seminars in Cancer Biology.
I met with the organizer of the Camelyon challenge at Pathology Informatics in May. He is still intent on sharing the slides and he is determining how many slides are from his hospital that he can share easily. These will likely be Camelyon17 cases instead of Camelyon16 cases as he has more authority over those. He invited me to present at the European Congress of Pathology on Sept. 9 on the topic of AI evaluation methods and our project plans. Our 348 sponsored travel request has been approved (small bureaucratic victory). The trip will also give us a chance to finalize plans for some glass slides from the Camelyon data set. We hope to have the MTA in the hands of the lawyers by then. The Camelyon IRB for the data can be added to our local IRB for the evaluation of anonymized images and their use in reader studies.
We also joined a proposal to the UK National Institute for Health Research with Darren Treanor from the UK NHS. Unfortunately, we just learned that we did not with the funding award.

Objective 2: I presented the study on the 14-head microscope at Pathology Informatics in May. MSKCC collaborators drafted a manuscript on a reader study comparing mitotic figure detection on four different WSI scanners to the microscope. They invited me and my assistant Qi Gong (who is funded by the CP award) to be coauthors. We helped them with the analyses. The manuscript's submission is imminent. This work is the foundation of the evidence module and future study designs and analyses.
In addition to Qi Gong, we have hired Weizhe Li, finishing an MPH in biostatistics from UMD with an internship with us. Weizhe also has a PhD in Biophysics from the Institute of Biophysics, Chinese Academy of Sciences. Beijing, China. He is part time with us and the NIH. He has downloaded most of the Camelyon data (~600 MB for Camelyon16 and 3TB for Camelyon 17). He has set up his work environment and has started to code the building blocks for training an algorithm that we can use to test our evaluation methods.
Our Cold Spring Harbor collaboration has been moving forward with the design of studies using our eeDAP system. They first executed registration accuracy studies that provide evidence supporting the context of use of the eeDAP MDDT. Since then we have been designing new work flows for eeDAP that allow the pathologist to evaluate slides on the microscope in a manner close to their clinical behavior while continuously recording the eyepiece view, stage coordinates, voice, and evaluation results (entered into the GUI). The workflows are faster because we will be able to map the results to the WSI after the fact. This collaborator has also sent us the green light (from their VP of Business Development and Technology Transfer) to begin the creation of a CRADA that will

How much funding has been utilized this year and on what? (Note: Text area expands and may run over the lines)

It's all be obligated to ORISE for Qi Gong and Weizhe Li.

If you have not utilized all your funding, how much do you have remaining?

How do you plan to use the remaining funds before the fiscal cut off?

Do you anticipate applying for FY19 CP funding? (•) Yes ( ) No ( ) Not Sure

CDRH Metrics Collection: Collaboration & Dissemination		
Metric	Description	Status/Fulfillment
Standards, studies, and guidances cited in applications	This demonstrates a broad understanding and acceptance of research.	
Research is cited in an expedited PMA	Research contributes to approval of a breakthrough medical device.	
Guidances impacted	Research helps the development of a new guidance document (the guidance cites the research).	
New regulations	Research contributes to the development of a new regulation.	
Licensures	Research results in a licensing agreement.	
Data sharing	Data generated from the research is shared externally.	
Web traffic to research outputs	Public-facing research has a site that generates hits or visits, or is found in internet searches.	
Impact of internal presentations related to the research	Research results are internally integrated, and reviewers are trained on the research results.	
Media coverage	Research is relevant and communicated well enough to be covered by the media.	
Submissions impacted	Research is cited in submissions to the FDA.	
Consults	Researchers receive consults related to the research.	
Potential standards impacted	Research is likely to contribute to standard development in areas of need.	
Research collaborations with external stakeholders	There is documented collaboration with external stakeholders.	1 presentation, 1 paper submitted, 2 proposals submitted
Input from industry stakeholders.	Industry stakeholders have had direct input into the need for, design of, or use of the research.	
External funding	External stakeholders provide additional funding	1 sponsor travel, 1 CRADA green light
Documented collaboration with internal stakeholders (scientific reviewer, stats, etc.)	Research has input from potential internal users, or is conducted in collaboration with internal users.	Provided update to Chen Cui (OIR/DMGP/MPCB)
Patents	Research results in a patent.	
Public meetings/workshops	Research is presented at a public meeting or workshop.	
Publications	Research is published in peer-reviewed journals.	
Presentations- external	Research is presented in a public capacity (not limited to internal use).	1 presentation
Attending conferences	Research is disseminated at conferences.	1 presentation
Miscellaneous high-impact communication with stakeholder	Center leadership incorporates research in communications.	
Expert training provided to review staff	Review staff is effectively prepared to evaluate the results of the research.	

CDRH Metrics Collection: Science Impact		
Metric	Description	Status/Fulfillment
External use of internally or collaboratively developed computational tools	The actual use of tools that are developed by CDRH. The tool both satisfies a need and is accessible.	eeDAP system, images/slides, and study design were used to collect the data for the MSKCC
Number of devices approved due to innovative computational models and clinical trials designs that enable a rebalancing of non- and post- clinical data	Research that facilitates the use of postmarket data, bench data, and animal data.	
Reliability and reproducibility of test and trial methods	Research protocol permits reproducibility; results are significant.	
Creation of or impact on postmarket registry	Research affects clinical data registries for devices on the market.	
Creation of test methods, tools, and computational models	Research affects the preclinical evaluation of device safety and effectiveness.	Data for eeDAP MDDT. New eeDAP workflows
Development of new or improved clinical endpoints; validation of biomarkers (MDDTs)	Research affects the clinical evaluation of device safety and effectiveness.	Data for eeDAP MDDT. New eeDAP workflows.
Creation of or impact on other surveillance systems	Research contributes to surveillance of medical device safety.	
Creation of infrastructure and methods for evidence generation, capture, synthesis, and analysis	Research contributes to better evidence for medical device evaluation and decision-making.	Data for eeDAP MDDT. New eeDAP workflows
Relevance to emerging technology forecast	Research builds internal capacity and expertise in novel, needed areas.	Obtaining Camelyon images and developing building blocks of code for training AI
Reverse translation	Taking a product or clinical insight and further developing the science behind it.	
Product code relevance	Research is tied to an existing or new product code.	
Relevance to common premarket deficiencies	Relevance to common premarket deficiencies	
Potential test methods developed (MDDTs)	Research is likely to contribute to the development of a medical device development tool, a preclinical test method that may be used in submissions.	
Potential development of new or improved clinical endpoints; validation of biomarkers (MDDTs)	Research is likely to contribute to the development of a medical device development tool, a clinical test method that may be used in submissions.	
Relevance of research to manufacturing processes (e.g. 3D printing)	Research contributes to better understanding of the safety considerations associated with a manufacturing process.	

CDRH Metrics Collection: Mission Relevance		
Metric	Description	Status/Fulfillment
Postmarket requirements and commitment studies impacted	Research affects the design and conduct of postmarket studies.	
Interactions with Congress	Research addresses a congressional requirement or request.	
Impact on a public health issue panel meeting	Research contributes to an advisory committee meeting.	
Progress in adverse events reporting and analysis	Research helps FDA track adverse events and address them.	
QALY	Research quantifiably contributes to an increase in quality-adjust life years for the public, per economic evaluation.	
Meets division/office/center/FDA priorities	See FDA priorities page for reference.	
Relevance to postmarket surveillance signal (ad hoc)	Research is in direct response to a device safety concern.	
Relevance to a public health risk (warning letters, recalls, seizures, injunctions)	Research is in direct response to an emergent public health issue.	
Related to voluntary recall	Research is in direct response to a voluntary recall.	
Compliance actions impacted or resolved	Research contributed to the resolution of a postmarket compliance concern.	
Translating bench-to-biology	Research bridges the gap between bench testing and biological effects.	
Translations from reduced biological model system to human	Research bridges the gap between the results of animal testing and the therapeutic and safety ramifications for patients.	

Is there any additional information you'd like to share regarding your progress?

Digital pathology Images are critical to this project. Most of the images are hosted on box, google cloud, or similar cloud services. We are struggling getting these images into the FDA to do our research because the websites are blocked. I have an FDA box account, and I have to use my home computer to download the images from the blocked websites and then upload them to the FDA box. I asked for help from ERIC and said the sites were blocked and they could not help. Can you?

Also, my UK collaborator has forwarded an opportunity for us to host PhD students as interns ... pretty much free of charge. They are kicking off a center for doctoral training in artificial intelligence. The challenge, in case you didn't already think of it, is security. FDA security for foreign visitors has gotten very challenging. Could we get a blessing from high up the chain of command to maybe get some exceptions? Seems like a win-win.