UNIVERSITY OF CENTRAL FLORIDA

## PROTOCOL TITLE:

Crowdsourcing an open COVID-19 chest radiograph imaging repository for artificial intelligence research

## PRINCIPAL INVESTIGATOR:

Name: Dexter Hadley, M.D., Ph.D.
Department: Clinical Sciences
Telephone Number: 215-681-0268
Email Address: Dexter.Hadley@ucf.edu

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Version 1: 12/10/2020

## REVISION HISTORY

| Revision # | Version Date | Summary of Changes | Consent Change? |
|---|---|---|---|
| 1 | 12/10/2020 | Changes made as per clarifications requested after board review/approval | yes |

## Table of Contents

# 1.0 Study Summary

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|---|---|
| **Study Title** | Crowdsourcing an open COVID-19 chest radiograph imaging repository for artificial intelligence research |
| **Study Design** | Data repository. |
| **Primary Objective** | Assemble a crowdsourced, de-identified radiographic repository |
| **Secondary Objective(s)** | Train and validate existing COVID-NET deep learning diagnostic models |
| **Research Intervention(s)/ Investigational Agent(s)** | None |
| **IND/IDE #** | Not applicable. |
| **Study Population** | COVID-19 positive patients |
| **Sample Size** | 1,000 positive cases, 10,000-20,000 total cases |
| **Study Duration for individual participants** | Participants will remain in the study for as long as they remain users of the web portal. |
| **Study Specific Abbreviations/ Definitions** | AWS: Amazon Web Services<br>GCP: Google Cloud Platform<br>AI: Artificial Intelligence<br>DICOM: Digital Imaging and Communications in Medicine<br>HL7 FHIR: Fast Healthcare Interoperability Resources<br>CXR: Chest X-Ray<br>COVID-19: Corona Virus Disease 2019 |

## 2.0 Objectives

2.1 The objectives of this project are to (1) assemble a crowdsourced, de-identified radiographic repository; and (2) train and validate existing COVID-NET deep learning diagnostic models.

## 3.0 Background

3.1 The COVID-19 pandemic is laying bare the need for accessible curated datasets that researchers can use to build clinical-grade artificial intelligence (AI) models. Researchers in China recently used deep learning models of clinical-grade AI trained on radiographic imaging at an exponential scale to detect COVID-19 cases and optimize allocation of limited resources. (Jin S, Wang B, Xu H, et al. Ai-assisted ct imaging analysis for covid-19 screening: Building and deploying a medical ai system in four weeks. medRxiv. 2020:2020.2003.2019.20039354. doi: 10.1101/2020.03.19.20039354). This research platform is currently not possible in the United States because there are no large accessible radiographic imagesets of COVID-19 patients to leverage. Therefore, the purpose of this project is to launch an interactive and HIPAA-compliant web portal—CovidImaging.com—where patients can securely share their radiographic imaging data. This portal will serve as an imaging repository for the purpose of training, testing, and validating an AI model aimed at earlier and more accurate disease detection in this global fight against COVID-19.

On January 30, 2020 the World Health Organization designated the COVID-19 outbreak that originated in Wuhan, China as a global health emergency. Since then, the virus has rapidly spread across the world as a pandemic, unfavorably affecting health care systems at the expense of primary healthcare requirements.[1] Symptomatic cases of COVID-19 present with clinical symptoms similar to viral pneumonia such as fever, shortness of breath, chills, fatigue, cough, and dyspnea that can progress to acute respiratory distress syndrome, requiring critical care and ventilation.[2] Bronchoalveolar lavage analysis and electron microscopy identified the causative agent to be a novel, positive-sense RNA virus in the Coronaviridae family, with spiked peplomers attached to its envelope.[3] This family of viruses has also been associated with severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), which cause similar pneumonia-related mortality.

3.2 Preliminary reviews have been conducted to investigate the overlap of reported imaging features in SARS, MERS, and COVID-19 as it relates to onset of symptoms, progression of disease, and follow up. Early evidence suggests significant overlap in imaging features such as subpleural and peripheral areas of ground-glass opacity and consolidation, with initial chest imaging indicating abnormality in at least 85% of COVID-19 patients.[4]

In the absence of vaccines and specific therapeutic drugs for the prevention and treatment of COVID-19, detection of the disease plays a vital role in containment strategies that isolate infected people from the healthy population. Even though RT-PCR sensitivity for COVID-19 can be as low as 60-70%, it is currently the large-scale method of testing with its high specificity.[7] The low sensitivity of RT-PCR, along with limitations of sample collection, time delay, transportation, and lab equipment, means that not enough COVID-19 positive people are being identified in time to prevent progressive infection of this highly contagious virus.

Given the respiratory involvement in COVID-19 infections, chest radiography has played an important role in screening, diagnosing, and developing treatment plans for patients with COVID-19-related pneumonia. Therefore, combining imaging with clinical and laboratory findings could facilitate the early diagnosis of COVID-19.5 Early detection would speed up treatment and allow for early patient isolation. This is essential for the implementation of public health surveillance, containment, and response for a highly communicable disease in which transmission can occur prior to onset of symptoms.[6]Improving the precision of radiographic interpretation with AI models may improve detection rate and patient prognosis and thus help to reduce COVID-19 spread. As recently reported, chest CT demonstrates common radiographic features in almost all COVID-19 patients, including ground-glass 4 opacities, multifocal patchy consolidation, and/or interstitial changes with a peripheral distribution.8,9

Studies have also been conducted to compare the efficacy and diagnostic value of chest CT to RT-PCR tests in COVID-19 cases. A case report of 1014 patients in China concluded that chest CT has a high sensitivity for diagnosis of COVID-19, with 60% to 93% of cases showing initial positive CT diagnosis prior to the initial positive RT-PCR results.10 Another study with 51 patients having chest CT and RT-PCR assay within 3 days showed that the sensitivity of CT for

COVID-19 infection was 98%, compared to 71% RT-PCR sensitivity.11 These studies further indicate the diagnostic value of chest radiographs alongside clinical and laboratory findings. This project will develop a large radiographic image repository which will be used to train and validate an AI deep learning model.

This project necessarily involves not only designing and refining a deep learning model, but also curating a repository of donated chest radiographs that will be used to train the novel model. Using a secure and HIPAA-complaint online platform, as has been designed for this project, will allow this project to employ a big data approach to improve the accuracy of the model. Since patients from healthcare facilities around the country will have equal opportunity to participate in the project, this portal will also provide an opportunity to expand the demographic pool in a way that previous studies could not.

## 4.0 Study Endpoints

4.1 N/A. This is not an interventional study.

## 5.0 Study Intervention/Investigational Agent

5.1 N/A. This is not an interventional study.

## 6.0 Procedures Involved

6.1 This study will develop the computational infrastructure to study human participants who have been screened for COVID-19 with chest radiographic imaging. We will develop a secure web app hosted at https://CovidImaging.app on Amazon Web Services (AWS) to collect and store PHI, and we have confirmed that UCF has existing business associate agreements in place with AWS to fulfill HIPAA regulations managing electronic PHI. We have implemented multi-factor authentication to track users of the web app. The first authentication is the RSA-encrypted password that the user must generate to use the web application. The second authentication is email verification. Beyond this two-factor authentication to establish an account, we will also track all IP addresses of all database transactions as a precaution.

When a patient first logs on to the web app, they will be prompted to sign a terms and conditions form through the application portal's DocuSign interface. Next, they will use a HIPAA-compliant DocuSign interface to sign informed consent and provide medical release for every site at which their imaging was performed.

The subjects will be asked to provide informed consent and to sign a medical release for their images for each clinical site where their

imaging was performed. Once we have received medical release, we will generate a Transfer Ticket associated with a unique TransferID that will track the DICOM transfer for the specific user and site. The TransferID is not considered PHI and is used to keep any PHI we collect on the web app separate from the images that are transferred. The web app provides an administrative dashboard for study coordinators to manage / flag TransferIDs for manual transfer or follow up. However, to ensure PHI is protected, TransferIDs are the only public identifier to reference images.

HIPAA mandates that the imaging sites to fulfill the patient's requests to release images in a timely fashion. If the site is new to us, Nautilus Medical will onboard a specific site coordinator who will oversee install of their Matrix Ray software that allows secure peer-to-peer DICOM image transfer. It is entirely conceivable that the site may not use the MatrixRay software and may send a standardized CD/DVD to us that we can import into our MatrixRay pipeline. Once the site is onboarded and / or the data is made available on MatrixRay, our web app will directly email the site coordinator to alert them that a new transfer is available for medical data release.

TransferID means that no PHI is ever transmitted by email as the site coordinator must log on to our web app to retrieve the patients' medical release for the DICOM transfer.

The site coordinator will then transfer the requested DICOM imaging through MatrixRay. Every DICOM transferred through MatrixRay is associated with the unique TransferID. Once that TransferID is received, we close the Transfer Ticket. Unfulfilled Transfer Tickets remain queued in an administrative interface for manual follow up by our team. Therefore, the only reason we collect PHI is to initiate the DICOM transfer process. The internal TransferID will track DICOM transfer process from medical release to DICOM receipt. PHI is only used to initiate DICOM transfer process through MatrixRay. Our study coordinators only track PHI internally through the TransferID of the admin panel.

Nautilus Medical provides their MatrixRay technology for peer to peer DICOM transfer as free for our academic use. There is no other relationship with the team and Nautilus. The technology is routinely used to exchange DICOM imaging for clinical purposes among different clinical sites. The two sites exchanging DICOM imaging must download a windows client that establishes a secure peer to peer connection to transfer the DICOM files. Nautilus facilitates onboarding of the sites initially to sign BAAs and establish a site coordinator. Nautilus does not record any PHI. Nautilus only makes the MatrixRay client for DICOM transfer and will onboard hospital

sites. Once a site is onboarded, the clinical providers will require a HIPAA compliant medical release form signed by the patient to transfer the imaging.

The app collects this medical release form which is also PHI. Our app communicates the patient name, date of birth, imaging site, and MRN (when available) to the clinical provider to initiate the transfer. The medical release form collects PHI that will only be shared to initiate DICOM transfer. The clinical site ultimately sends the requested DICOM files, and we will specifically ask for all radiographic imaging for each potential COVID case. The patient will need to provide name and site, and MRN is optional. PHI (i.e. patient name) may be embedded on the delivered DICOM files. This is likely if clinical providers have scanned film with PHI labels embedded in images. We should not assume the clinical providers will strip the DICOM files because when Nautilus onboards the clinical provider, they become a business associate that can transfer PHI. This is a potential source of PHI leak on AWS. To address concerns, our study coordinators (as listed on the IRB application) will curate every image transferred to ensure no such images with PHI embedded are released for machine learning. Coordinators will annotate out the PHI manually before the image is released. We will use standard de-identification scripts to strip the DICOM files delivered to us of any PHI and integrate only raw .tiff or .png into our AWS web application.

We will keep/save the de-identified DICOMs on AWS to a secure S3 location, and MatrixRay will only communicate PHI to this AWS S3. AWS will only serve to coordinate PHI that we collect from the patient in EC2 instance independent from the S3 for imaging. EC2 serves to host our web applications and integrate imaging through transfer IDs. Once we receive their DICOM imaging, our app has a DICOM viewer that the patient can use to see their images. We will use MatrixRay on AWS to de-identify DICOM files by extracting images for machine learning. Only researchers and study coordinators approved by the IRB will curate de-identified images into labeled research imagesets that we will use for machine learning. PHI is not important to machine learning, so as a rule, we will keep all PHI we collect on AWS separate from any machine learning instances that will be either local at UCF or on Microsoft or Google clouds thereby protecting against any PHI leak.

To maintain the separation of images from PHI, the web interface never shows explicit PHI (such as the patient name or MRN) on the same screen as an Image which further reduces the leak of PHI tied to images by screen shots or other untoward attempt.

Within our AWS app, we have embedded a UCF-managed Qualtrics backend to issue interactive surveys within our web app. We have developed an initial COVID-19 questionnaire to learn

clinical outcomes to predict from de-identified imaging. Future surveys will be issued once IRB-approved as we grow our app-based community. These surveys may be interactive and will allow for a platform where researchers can longitudinally follow patients through the rapidly evolving pandemic. By keeping this Qualtrics backend managed by UCF, we also minimize any PHI leaks.

As we develop AI models, we will publish de-identified labeled imagesets on Zenodo, which issues digital object identifiers (DOI) that can be cited in our research, with tight integration with GitHub to store de-identified image assets. We may issue imagesets for machine learning based on clinical outcomes or other features learned from patient surveys. Once de-identified assets are registered on Zenodo/GitHub, they will be maintained as open and accessible pending funding. We have at least three years of funding from Dr. Hadley's startup to maintain this repository, and we will be seeking NIH grants to develop the resource for the AI community in perpetuity.

The process can be outlined as follows:

1. Patient visit the informational covidimaging.com which directs them to sign up for app at covidimaging.app
    a. Patient signs informed consent on DocuSign via app
    b. App collects patient's full name and date of birth
    c. App collects and validates patient's email address
2. Patient fills questionnaires about his/her imaging
    a. App collects name, date of birth, site of imaging, medical record number, and date of imaging if available
    b. Opens a new Transfer Ticket that serves to de-couple the PHI collected on the app from the imaging transferred
3. Patients fill out questionnaires about their COVID-19 course via app
    a. Questionnaire asks about patient's clinical course, including molecular diagnosis of infection and convalescence
4. Web app sends email to the imaging site initiate DICOM transfer
    a. No PHI is sent via email, just a notification that a new Transfer Ticket was created
    b. If known site, app emails the Transfer Ticket to the site coordinator
    c. If unknown site, app emails the Transfer Ticket to the Nautilus coordinator
        i. Nautilus onboards site to use MatrixRay
        ii. Nautilus emails the Transfer Ticket to site coordinator
5. Site coordinator transfers DICOM through MatrixRay to web app
6. Web app closes Transfer Ticket
7. Research team assembles de-identified imagesets for machine learning to Zenodo to issue digital object identifiers (DOI) with GitHub integration to store de-identified images. If applicable, the research team de-identifies images with PHI

8. Research team uses repository to train, test, and validate the open COVID-NET model on Microsoft, Google, or Amazon AI platforms to predict CXR outcomes.

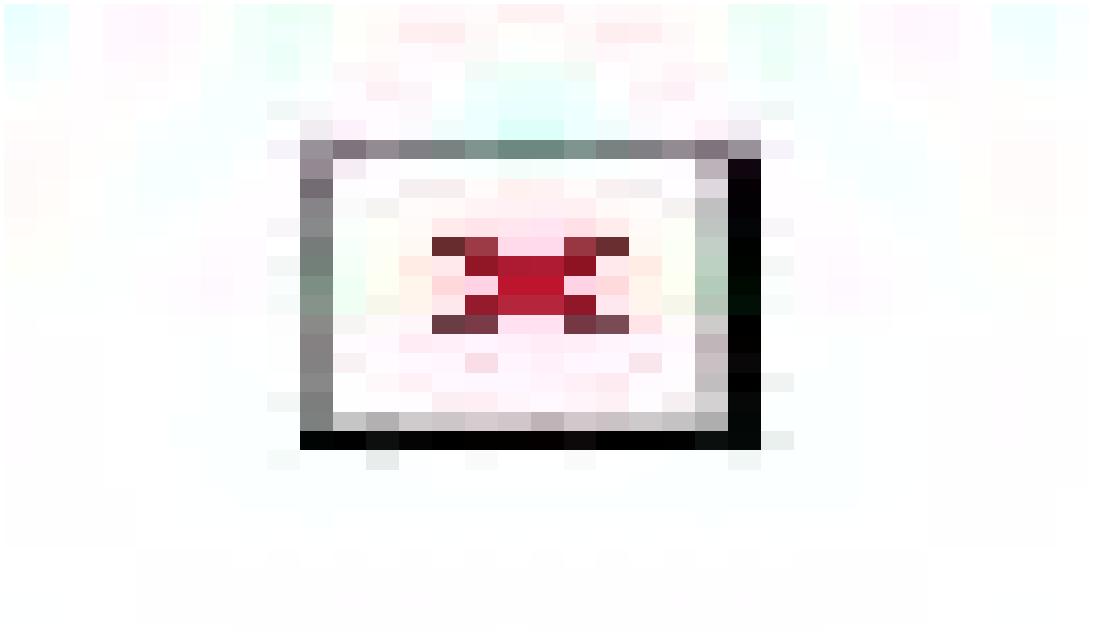

Figure: CovidImaging Data Flow diagram. Patients log on to the web app to sign informed consent and provide a medical release for each site they have had imaging. PHI data flows from patients on WWW network through the web interface hosted on AWS network. Coordinators at remote imaging sites are alerted to login to the web app and send imaging through MatrixRay to our AWS servers. Standard DICOM de-identification scripts on the MatrixRay receiving client will only save de-identified DICOMS to a secure S3 location. We will use a Qualtrics back end to issue surveys to participants about the clinical course of their disease. Study coordinators will be able to curate these images to publish de-identified, labeled imagesets on Zenodo with tight GitHub integration. AI platforms (such as Google Cloud and Microsoft Azure) will only access the de-identified imagesets to develop models for training, testing, and validating COVID-19 radiology models.

6.2

The only foreseeable risks posed to the study participants is the risk of exposure of their protected health information. To prevent this, all radiographic images will be de-identified and all patient information will be encoded as detailed above in this protocol.

6.3

We rely on AWS best practice workloads for securing patient data collected on the web app within the scope of the U.S. Health Insurance Portability and Accountability Act (HIPAA). All data collected is stored and encrypted behind password authentication. No PHI is ever exposed to an open network. When new imaging sites are onboarded, study coordinators at those sites are emailed.

6.4 We will collect the data through a survey questionnaire hosted on UCF's Qualtrics. *https://ucf.qualtrics.com/jfe/form/SV_9pdRxnqiKFvhsrP*

- There are no plans for long-term follow-up data collection (once all research related procedures are complete).

## 7.0 Data and Specimen Banking

7.1 PHI will be stored on AWS in perpetuity. There is ongoing research on COVID-19 for the foreseeable future and this repository can be used for further research inquiries. De-identified data will be stored on GitHub and Zenodo in perpetuity. PHI collected by the web app will remain on AWS relational databases. The PI and key personnel will have access to the PHI and de-identified images. Other researchers will only have access to de-identified images for machine learning. We anticipate collecting 1,000 positive cases, with a total of 10,000-20,000 cases. All PHI will be stored on AWS including Docusign Informed Consent and Medical Release Forms.

7.2 Data to be stored:

Survey questionnaire, Hospital site, and Deidentified DICOM imaging

7.3 Procedures to release data: Only GitHub data indexed by Zenodo will be shared to researchers. Only persons listed on the IRB will see PHI data on AWS.

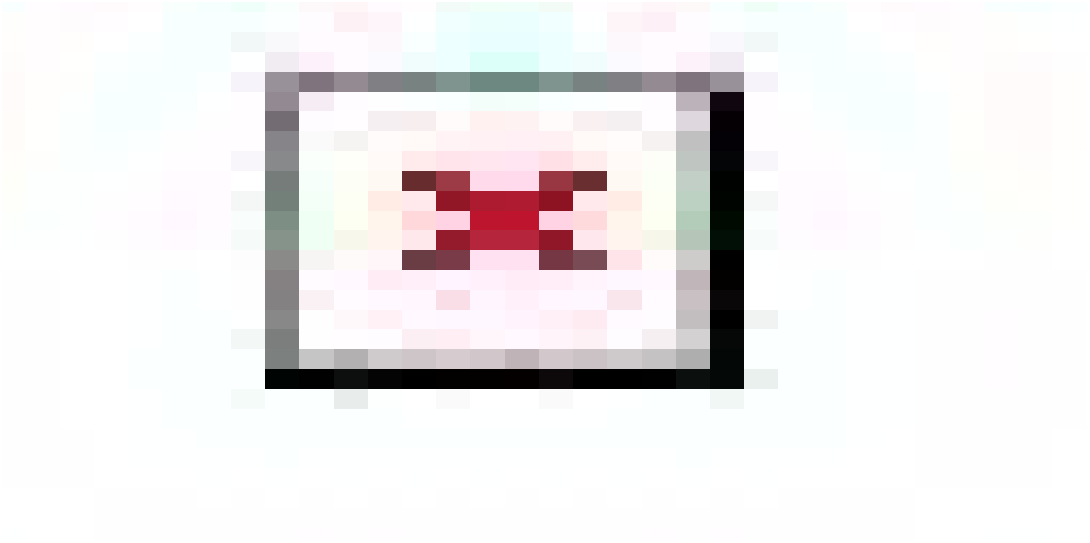

Figure 1: Data Sharing

## 8.0 Sharing of Results with Subjects

8.1 Results of the study will not be shared with the subjects; however, subjects can log on to https://CovidImaging.app and view their radiographic image in DICOM format for their personal use.

## 9.0 Study Timelines*

9.1

Duration of subject's participation in the study: Subjects will be asked to provide informed consent and provide a medical release for each imaging site (estimated time burden ≤ 30 minutes). Individual subjects can quickly fill out the surveys on the web app on their own time (estimated time burden ≤ 30 minutes). Unless they choose to withdraw, subjects will remain in study repository indefinitely. Subjects will have choice to withdraw from the study at any time and will have the ability to delete their data permanently at any time, including their DICOM images.

- Duration anticipated to enroll all study subjects: One year
- The estimated date for the investigators to complete this study (complete primary analyses): December 2021

## 10.0 Inclusion and Exclusion Criteria

10.1 This study will include anyone in the country who has been tested for COVID-19 with a chest radiograph image. Patients will provide informed consent through the web application portal. The study will exclude adults unable to consent, individuals who are not yet adults (infants, children, teenagers) pregnant women, and prisoners.

## 11.0 Vulnerable Populations

11.1 *N/A.* The study does not plan to recruit minors (under age 18), pregnant women, prisoners, or adults who are unable to provide consent.

## 12.0 Local Number of Subjects

12.1 Subjects will be sourced online at https://CovidImaging.app from all across the US. We plan to collect 1000 positive images, and about 20,000 total images.

12.2 *NA*

## 13.0 Recruitment Methods

Subjects will be recruited online using social media advertisement campaigns designed to inform the general public about the project and invite eligible participants to join the study. Recruitment materials will direct potential subjects to a www.covidimaging.com, which will provide both study details and access to registration.

Recruitment on website www.covidimaging.com is worded as follows: “Countries like China have trained AI on state-curated centralized data-stores of radiographic imaging as part of a strategy to effectively halt their COVID-19 epidemics. However, in the US, , privacy regulations, lack of interoperability and active health information blocking has curtailed the availability of data to train clinical grade AI. While no country can match China in terms of its population size or its surveillance reach, we are crowdsourcing a COVID-19 Imaging Registry for our own AI research in the fight against COVID-19. Patients may donate their chest x rays and clinical data to our IRB-approved study. Patients’ images and related protected health information will be immediately deidentified to protect privacy, and patients may choose how their data may be used for research. We will use patients’ anonymized data to develop and deploy AI for digital triage of COVID-19. Please sign up now for more information, including on how to sign up to participate in the COVID-19 Imaging Repository research study.”

13.1 We have an informational site up at https://CovidImaging.com. We have a live beta app up at https://CoidImaging.app. We will not begin to enroll patients until we have IRB approval.

## 14.0 Withdrawal of Subjects

14.1 At any time and for any reason subjects can delete their account on https://CovidIaging.app which will automatically withdraw them from the repository and delete all of their data. This is permanent and cannot be undone. However, subjects can re-enroll again and at any time.

14.2 Procedure for orderly termination: Subjects may log on to https://CovidImaging.app and delete their account.

14.3 If a subject withdraws from the study, all the subject's data and images will be permanently deleted from our servers including GitHub and Zenodo.

## 15.0 Risks to Subjects

15.1 Inherent in any web-based research platform is the possibility of public disclosure of the subject's protected health information and any physical or psychological anxiety that may be associated with this possibility. While extensive safeguards are in place to protect participants' PHI, there is a risk associated with the possibility of unauthorized access to PHI prior to de-identification and processing of images. This could lead to disclosure of signed consent, HIPAA authorization forms, personal contact information, and self-reported questionnaires. The risks posed by radiography are outside of the scope of this project and should be assumed by the imaging sites providing those radiographic services.

Data breach of PHI will be mitigated through the following efforts: We will ensure that all users who access patient data on the web platform are logged and available for review. The web app is hosted on Amazon Web Services using standard best practices for web security. Specific to HIPAA, the web app never exposes patient PHI without password protection. While email is used to communicate transfers with imaging sites, no PHI is every sent via email, and only links to log on to the secure web app. Amazon Web Services best practices has internal procedures in place to secure PHI, and this study will follow those procedures. The DICOM files are securely sent via the PACS communications protocol from the imaging site to our Microsoft Azure Healthcare platform where they are de-identified with HIPAA compliant protocols.

15.2 *N/A No current procedures have unforeseeable risks*

15.3 Radiographic imaging is not recommended for any pregnant women. For this reason, pregnant women will be excluded from the study.

15.4 *N/A No risks to others who are not subjects*

## 16.0 Potential Benefits to Subjects

16.1 At this stage in research utilizing AI in medicine, the benefit to the individual subjects is facilitated ownership and ready access of their radiographic data in a digital form. Future expansion and applications of AI research aim to benefit subjects by a) providing more accurate diagnostic measures that can lower the risk of false negative or false positive diagnoses, b) preventing unnecessary expenditure of financial resources due to false-positive follow-up care, c) increasing the speed at which physicians can perform their medical analyses, thereby saving subjects both time and financial resources.

16.2 The direct benefit to the patient will be from the app in facilitating personal access to a portable, digital copy of their chest images, part of their radiographic medical records, for their private use. With this, the patient can go from physician to physician with the images at their fingertips through this application.

## 17.0 Data Management and Confidentiality

17.1 Describe the data analysis plan: Data will be maintained on AWS according to best practices.

17.2 Steps that will be taken to secure the data: Data will be de-identified according to HIPAA Safe Harbor method. PHI collected by the web app will remain on AWS relational databases. This PHI will index de-identified images will be stored on AWS S3 in perpetuity. Per HIPAA, PHI will be stored for a minimum of 6 years. Storage duration for signed consent, PHI release, self-reported questionnaires, and contact information will be stored for at least 6 years. The PI and key personnel will have access to the PHI and de-identified images. Other researchers will only have access to de-identified images for machine learning.

17.3 Describe how any study/participant numbers, pseudonyms, etc. will be generated: All numbers will be alphanumeric and randomly generated. Subject ID numbers will be generated sequestional as C19AI001, C19AI002, …etc.

17.4 Identifiers will be stored in perpetuity or until the subject has deleted their account and withdrawn from the study.

Per UCF policy, de-identified data will be retained for a minimum of 5 years following study closure.

**Manual curation for quality control.**

(See CovidImaging Data Flow diagram)

## 18.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

This study does not involve more than minimal risk to subjects.

18.1

To address concerns of potential PHI leaks, our study coordinators (as listed on the IRB application) will curate every image transferred to ensure no such images with PHI embedded are released for machine learning. Coordinators will annotate out the PHI manually before the image is released. We will use standard de-identification scripts to strip the DICOMS delivered to us of any PHI and integrate only raw .tiff or .png into our AWS web application.

We will keep/save the de-identified DICOMs on AWS to a secure S3 location, and MatrixRay will only communicate PHI to this AWS S3. AWS will only serve to coordinate PHI that we collect from the patient in EC2 instance independent from the S3 for imaging. EC2 serves to host our web applications and integrate imaging through transfer IDs. Once we receive their DICOM imaging, our app has a DICOM viewer that the patient can use to visualize their imaging. We will use MatrixRay on AWS to de-identify DICOMS by extracting images for machine learning. Only researchers and study coordinators approved by the IRB will curate de-identified images into labeled research imagesets that we will use for machine learning. PHI is not important to machine learning, so as a rule, we will keep all PHI we collect on AWS separate from any machine learning instances that will be either local at UCF or on Microsoft or Google clouds thereby protecting against any PHI leak.

To maintain the separation of images from PHI, the web interface never shows explicit PHI like the patient name or MRN on the same screen as an Image which further reduces the leak of PHI tied to images by screen shots or other untoward attempt.

Within our AWS app, we have embedded a UCF-managed Qualtrics backend to issue interactive surveys within our web app. We have developed an initial COVID-19 questionnaire to learn clinical outcomes to predict from de-identified imaging. Future surveys will be issued once IRB-approved as we grow our app-based community. These surveys may be interactive and will allow for a platform where researchers can longitudinally follow patients through the rapidly evolving pandemic.

By keeping this Qualtrics backend managed by UCF, we also minimize any PHI leaks.

## 19.0 Provisions to Protect the Privacy Interests of Subjects

19.1 Amazon Web Services best practices has internal procedures in place to secure PHI, and this study will follow those procedures. The DICOMs are securely sent via the PACS communications protocol from the clinical site to our Microsoft Azure Healthcare platform where they are de-identified with HIPAA compliant protocols.

19.2 Patients are welcomed to ask questions about the study procedures, security, or the utilization of their data. Subjects can also delete their data and withdraw participation at any time without penalty.

19.3 Only the principal investigator and key personnel will access have to subject PHI. Otherwise de-identified data will be used for all research.

## 20.0 Compensation for Research-Related Injury

20.1 *N/A.* This is not an interventional study, and the subjects are not at risk for a research-related injury. The subjects will not be compensated for a research-related injury.

20.2 *N/A No contract related to compensation for research-related injury*

## 21.0 Economic Burden to Subjects

21.1 The patient will not bear any economic burden related to utilizing the web application or the associated third-party imaging transfer services. The only possible financial responsibility would be dependent on whether their individual imaging site requires a fee for medical records release. If the imaging site indicates that a fee is being levied on the patient, the transfer request will be cancelled.

## 22.0 Consent Process

22.1 Informed consent will be obtained through the web application through Qualtrics. There will be embedded questions to gauge comprehension and subjects will be able to go forward and backwards for review. See attached consent form for details and procedures.

## 23.0 Process to Document Consent in Writing

23.1 Consent will be documented online through the web application following SOP: written Documentation of Consent (HRP-091). Electronic signatures will be validated through Qualtrics.

23.2 *N/A We are not requesting a Waiver of Written Documentation of Consent*

## 24.0 Setting

24.1 The research team will recruit potential subjects using a web-based platform that can be found at www.covidimaging.org. All research procedures, including the collection and analysis of subject data and the distribution of radiographic images, will be performed online in a secure, HIPAA-complaint web application.

## 25.0 Resources Available

25.1 The web-based nature of this study opens participation to the broader population on a national scale. Access and opportunity to participate will be available to all individuals with internet access. The breadth of this reach supports the study's ability to achieve its target number of participants.

We will employ a database of coordinators to administer patients, hospitals and transfers through an admin panel. The research team will all have a current CITI Human Subjects training approval. Imaging site coordinators will also be onboarded with a training tutorial to demonstrate all the functionality of the web platform and admin panel. Admin panel functionality includes adding a new imaging site, monitoring DICOM transfers, viewing and updating informed consent and medical release documents, and Qualtrics survey management.

The initial onboarding experience will incorporate a mock transfer where a mock patient would enroll and have mock imaging sent from a mock site to simulate the entire experience. Coordinators will have to demonstrate competence with mock data before being allowed to access real subject data. All users who access patient data on the web platform will be logged and available for review.

All subject data is available until the subject elects to delete their account or we choose to dissolve the repository. The web app is hosted on Amazon Web Services using standard best practices for web security. Specific to HIPAA, the web app never exposes patient PHI without password protection. While

email is used to communicate transfers with imaging sites, no PHI is ever sent via email, and only links to log on to the secure web app. In the event of dissolution of the repository, all virtual machines and storage devices will be also be dissolved and subjects will be notified accordingly.

25.2 Ancillary reviews and approvals associated with the research:

- HIPAA Privacy, as this project collects Protected Health Information.
- Contracts IRB, UCF COM Legal

## 26.0 Multi-Site Research

*26.1 N/A*