Imaging for LAM
Find more accurate ways to improve LAM diagnostics and identifying new imaging biomarkers

Participants

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Preloaded Storyboard Ideas

Products/Trial Ideas

1. Widely accessible tool to estimate cyst volume % or texture
2. Method to quantify tumor burden for LAM PET
3. Methods to quantify very early disease (i.e. ^{129}Xe)

Needs that will be addressed by this innovation

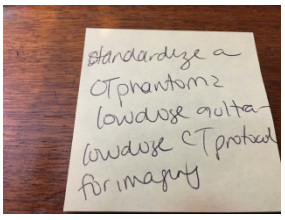
1. Actual measure of treatment response/disease progression
2. Limited endpoints available for trials
3. Endpoint for MILED and other early disease trials

Benefits of having it

1. Act as a complement to FEV1 in order to track disease. May also become a useful end point for clinical trials.
2. Surrogate end point for treatment outcome
3. Need to be able to measure outcomes in people with normal lung function

From the conference board

Products/Trial Ideas

- Standardize a CT phantom and low dosage or ultra low dosage CT protocol for imaging?
- 

- Can we use low dose CT to predict disease decline – i.e. do frequently to get more data points and use that to see if it correlates with FGV_1 decline
- How to disseminate low-dose CT algorithms and equipment?
- Widely accessible tool to estimate cyst volume % or texture
- Cyst score or other quantification by web portal
- Jonathan Chung needs to make a cystic lung disease module for his HRCTEduation.org website or work with the LAM Foundation/RLDC to make another similar education tool
- Can functional MRI be used to predict lung function decline?

- Combination of CALIPER CT, ^{129}Xe MRI, FEV, DLCO, exacerbations, pneumo in machine learning module
- Methods to quantify very early disease (i.e. ^{129}Xe)
- Deep learning for outcomes prediction using imaging
- Method to quantify tumor burden for LAM PET

Needs that will be addressed by this innovation

- Promote education of radiologists to be able to better diagnose LAM
- Endpoint for MILED and other early disease trials
- Limited endpoints available for trials
- Actual measure of treatment response or disease progression
- Prediction of treatment response and stability or decline

Benefits of having it

- Need to be able to measure outcomes in people with normal lung function
- Surrogate endpoint for treatment outcome
- Act as a complement to FEV1 in order to track disease. May also become a useful endpoint for clinical trials.
- Create a database or registry of clinical data to facilitate machine learning (deep learning)

Notes from Presentations

- In LAM patients
    - CT images correlate with spirometry
    - Patients have higher cyst score which correlates with more air trapped
    - Cyst score correlates with FEV1
    - More cysts leads to reduced exercise
- MMP activity around cyst leading to abnormal tissue, more emphysematous tissue around the cyst
- Vascular changes may occur in LAM
- Standard CT is equal to 30 chest x-rays. Dr. Chen's goal is to reduce dose to 1.5 chest xrays. Need image reconstruction software that can allow you to reconstruct at appropriate resolution to detect changes. It is available on new scanners. This will provide new opportunity for more frequent monitoring and therapeutic evaluation.
- MRI - provide structure, alveolar size, and function
    - UTE-MRI – structural use MRI to measure lung density
    - Xenon129 MRI – measures ventiliatory function, non-ionizing and non-radioactive, depict real-time ventilation
- Calipur software –
    - localize lung lobes and define areas as honeycombed, low attenuation, cyst, normal, etc. then create a picture and quantitate volume of various areas
    - As disease progresses the normal tissue decreases while the cysts and confluent areas increase in size.

- Calipur can quantify disease and also characterize disease progression, fast, slow

Long-term goal 5-10 years - **Machine learning** (deep learning)

- Train machine to accurately and appropriately diagnose patients based on images.
- Need CT scans (data) to put in to the machine so machine can "learn". Feed in data from LAM patients, normal, COPD, other cystic lung diseases – convolution of neural network will define important features of the disease groups
- Kaggle is a web-based tool that could help with this solution. Kaggle allows us to ask questions and create competitions for creative people to solve. We would upload 5000 CTs and ask the community to distinguish between patients.

Slides of the top 3 ideas for Presentation

#1: Education in Diagnosis of Cystic Lung Diseases

- Problem
  - lack of education/preparation of expert chest radiologists to adequately diagnose LAM
- What
  - Build interactive web-based program to train radiologists to properly diagnose various cystic lung diseases, distinguish LAM.
- How
  - Dr. Chung and National Jewish Health created program for the accurate interpretation of HRCT in the diagnosis of IPF (HRCTeducation.org). Replicate this for LAM.
  - Advertise program in pulmonary and radiology journals, Word of mouth, TLF and patients to distribute on social media and tweet program prior to national conferences
  - Small LAM foundation grant to achieve

#2: Standardization of Cystic Lung Disease CT Imaging Protocols

- Problem
  - lack of standardization of CT imaging protocols and issues/concerns with exposure to radiation
- What
  - Standardize low dose CT protocol for RLDC/LAM clinic centers
  - Identify centers capable of performing procedure on TLF website
  - Standardize imaging results using a validated cystic lung disease model
- How
  - Write standardized protocol using combination of available low and ultra-low dose protocols (Dr. Chen)
  - Obtain a cystic lung disease model so images can be standardized/validated between clinical sites. Could be built based on patient data and 3D printing.
  - LAM foundation purchases/maintains disease model, designed by imaging team, & supports QC at sites. Potential for TLF-designated centers: "TLF-approved imaging center"

#3: Biobank of Validated LAM Clinical Data for Deep

- Problem

    - Insufficient CT scans and clinical data that can be used to iteratively perform deep learning/machine learning to create software algorithms to accurately diagnosis LAM, predict response to therapy, prognosticate
- What
    - Use existing NIH LAM data (1000 scans!) to develop software models to accurately diagnosis LAM and predict prognosis or therapeutic benefit
    - Continue to build large cohort of patients and crowd-source efforts to develop techniques to best identify and characterize LAM.
- How
    - Develop model and standardize methods of cyst quantitation (Drs. Yao and Chen at the NIH).
    - Validate model with clinical datasets and begin to prognosticate outcomes
    - Investigate means/challenges with creating repository of data
    - Continue to develop LAM patient registry and data portal (“LAM 360”)