Assessment of Lung Movement With Computed Tomography (CT)

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Application Number: _2006114
Application Title: Assessment of lung movement with CT in healthy subjects and Patients with ILD

Clinical Trial Protocol

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1. Abstract (problem, hypothesis and importance of research)

Interstitial lung disease (ILD) is a group of lung disorders in which the lung tissues become inflamed and then damaged. Idiopathic Pulmonary Fibrosis (IPF) is one of the subtypes of ILD which has characteristic histological and CT features. It is well known that microscopic fibrosis occurs in the lungs of IPF patients well before the structural changes of fibrosis become apparent on CT. By combining sophisticated image analysis with CT scans obtained at full inspiration, full expiration, and possibly during breathing, it may be possible to detect earlier changes of IPF than currently possible by looking at macro structural features alone. With the recent development of new and costly therapeutics for IPF, early detection of the disease and improved monitoring of treatment efficacy will become important. Using CT to assess regional lung compliance has the potential to become an easily translated clinical tool.

2. Objectives This is a pilot clinical trial to determine whether CT assessment of lung motion has the potential to be useful in the assessment of patients with ILD.

3. Background

In a prior research collaboration between the DoD and the University of Virginia, the airflow in healthy subjects and subjects with COPD was assessed using hyperpolarized gas MRI and CT imaging. In this project, one of the healthy subjects was found to have early (subclinical) idiopathic pulmonary fibrosis (IPF). Interestingly in this subject there was reduced lung motion on analysis of the CT in regions of the lung that are typically first affected by IPF but that still looked structurally nearly normal on CT. In a prior study, a correlation was found between honeycombing on CT (a classic feature of IPF) and pulmonary function tests (ref). In this project, we will assess lung motion on CT in both healthy subjects and patients with ILD to determine whether alterations of lung motion appear to precede alterations in lung structure (such as honeycombing) as seen on CT.

Experience with procedures: The pulmonary function testing and chest CT procedures will be completed according to the current clinical standards for the respective test.

Drug/device: None

4. Study Procedures

a. Study design, including the sequence and timing of study procedures (distinguish research procedures from those that are part of routine care).

20 subjects with Interstitial Lung Disease (ILD) and 20 age matched healthy normal subjects will be enrolled to undergo a non-contrast Chest CT and pulmonary function

testing (PFT). CT images will be collected with inspiration and expiration. Additional low radiation dose images may be collected during breathing. The CT images will be analyzed and compared with PFT results. A urine pregnancy test will be obtained for subjects of childbearing potential.

b. Study duration and number of study visits required of research participants.

The CT and PFTs can be completed in one 2 to 3-hour session, but may be scheduled on different days depending on the subject and clinic schedule. The CT scan takes approximately 10 minutes and the PFTs take approximately one hour.

c. Blinding, including justification for blinding or not blinding the trial, if applicable.
Not Applicable

d. Justification of why participants will not receive routine care or will have current therapy stopped.
Subject's routine care will not be disrupted or stopped.

e. Justification for inclusion of a placebo or non-treatment group.
Not Applicable

f. Definition of treatment failure or participant removal criteria.
- If there is a concern for the participant's health
- If the participant's underlying disease gets worse
- The study sponsor closes the study for safety, administrative or other reasons

g. Description of what happens to participants receiving therapy when study ends or if a participant's participation in the study ends prematurely.
Not Applicable

5. Inclusion/Exclusion Criteria

Inclusion Criteria:

- Subjects with ILD: Subjects must have a physician diagnosis of ILD and be in stable pulmonary condition at the time of the CT
- Healthy subjects: Subjects must have no history of pulmonary disease and smoked less than 100 cigarettes in their lifetime.

Exclusion Criteria:

- Subjects less than 18 years of age

6. Drugs/ Substances/ Devices

a. The rationale for choosing the drug and dose or for choosing the device to be used.
Not Applicable

b. Justification and safety information if FDA approved drugs will be administered for non-FDA approved indications or if doses or routes of administration or participant populations are changed.
Not Applicable

c. Justification and safety information if non-FDA approved drugs without an IND will be administered.
Not Applicable

7. Study Statistics

a. Primary outcome variable. This is a pilot study to determine whether alteration lung motion on CT may be an early indicator of ILD. We will assess the change in lung volume on CT from inspiration to expiration on a lobar basis.
b. Secondary outcome variables. A radiologist reader will assess the severity of structural changes in the lung on a lobar basis. Pulmonary function testing will also be performed (FEV1, FVC)
c. Statistical plan including sample size justification and interim data analysis. The lung motion, structural severity score and pulmonary function tests will be compared using a Spearmen correlation coefficient. As a small pilot study, we do not anticipate that any of the correlations will achieve statistical significance. The sample size was based on prior experience. No power calculation was performed as this is just a pilot study to determine whether this technique may warrant further study. The results from this study may be used to power a future study.
d. Early stopping rules. None

8. Risks

a. Medical risks, listing all procedures, their major and minor risks and expected frequency.

Risk of CT: The CT performed as part of the study is the same as a clinical CT scan. The total effective radiation dose a subject will receive from the CT study is approximately 7 mSv. For comparison, the dose from the CT is roughly 15% the annual radiation dose safely allowed for a radiation worker such as the person performing the CT scan. The precise risk from this dose is not known but is thought to be small.

Risk of PFT: Since pulmonary function testing requires blowing hard several times, the subject may cough or feel short of breath during or after the test.

b. Steps taken to minimize the risks. The CT parameters will be selected to achieve an appropriate balance between image quality and radiation dose and will be similar to the multicenter NIH funded COPD Gene trial CT scans.

c. Plan for reporting unanticipated problems or study deviations.
All unanticipated problems and deviations will be reported to the IRB within 5 business days of first learning of the event.

d. Legal risks such as the risks that would be associated with breach of confidentiality.
Unanticipated problems will be reported on the IRB event report within 5 days of learning of the event.

e. Financial risks to the participants.
None

9. Benefits

a. Description of the probable benefits for the participant and for society.

There are no direct benefits to the subject. This study may improve our understanding of alterations in lung compliance in patients with ILD. One potential offshoot of this study would be to assess whether alterations in lung compliance are an early indicator of response (or lack thereof) to treatments for ILD. Thus this study has the potential to benefit ILD patients in the future.

10. Payment and Remuneration

a. Detail compensation for participants including possible total compensation, proposed bonus, and any proposed reductions or penalties for not completing the protocol. Subjects will be paid $75 for CT and $25 for PFT.

In addition, for the healthy subjects, if the study CT indicates that a follow up CT is required, the follow up CT will be covered by study funds.

11. Costs

a. Detail costs of study procedure(s) or drug (s) or substance(s) to participants and identify who will pay for them.
There are no costs to participants for participating in the study. All study costs will be paid for by the sponsor.

12. References

a. List of references supporting research question.

Nakagawa H, Nagatani Y, Takahashi 3, Ogawa E, Tho NV, Ryujin Y, Nagao 1, Nakano Y,.Quantitative CT analysis of honeycombing area in idiopathic pulmonary fibrosis: Correlations with pulmonary function tests. Eur J Radiol. 2016 Jan;85(1):125-30. doi: 10.1016/j.ejrad.2015.11.011.

13. Data Sharing

Study data, including demographic information and imaging and pulmonary function test results collected by the University of Missouri will be shared with the Biotechnology High Performance Computing Software Applications Institute (BHSAI), a subordinate of the Telemedicine and Advance Technology Research Center (TATRC), which is part of the U.S. Army Medical Research and Materiel Command (MRMC) at Fort Detrick, Frederick, Maryland. Only investigators at the University of Missouri will have access to the codes that could be used to identify individual subjects. In all instances, data and images sent to collaborators will contain a code for each subject, and will not contain any subject PHI that could link the information to an individual subject enrolled at the University of Missouri. Data shared with the above research collaborators will be used for this study and possibly for future studies related to lung function or lung disease.