Weighing Risks and Benefits of Laparoscopic Anti-Reflux Surgery in Patients With Idiopathic Pulmonary Fibrosis

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UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: WEIGHING RISKS AND BENEFITS OF LAPAROSCOPIC ANTI-REFLUX SURGERY IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS (WRAP-IPF): A PHASE II CLINICAL TRIAL

This is a medical research study. Your study doctor, Harold Collard, MD and/or his colleagues from the UCSF Department of Medicine, Division of Pulmonary Medicine, will explain this study to you.

Medical research studies include only people who choose to take part. Take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you have Idiopathic Pulmonary Fibrosis (IPF).

Why is this study being done?

You are being asked to take part in this research study to test the effect of Laparoscopic anti-reflux surgery on the clinical course of your IPF as measured by your lung function. This study will also try to understand some of the biology of IPF by testing fluids and cells before and after surgery.

Laparoscopic anti-reflux surgery is a minimally-invasive surgical procedure in which part of the stomach is wrapped around the valve connecting the stomach to the esophagus. This improves the valve's ability to keep the stomach contents from flowing back into the esophagus.

Many people with IPF (approximately 90%) also have some degree of abnormal gastroesophageal reflux (GER). Gastroesophageal reflux means that the contents of your stomach, including stomach acids, food particles, and fluids, can sometimes flow into your esophagus (the tube from your mouth to your stomach). This can cause symptoms like heartburn, cough, or difficulty breathing, but is often without symptoms. It is believed that breathing small amounts of your stomach contents into the lungs may be one of the possible causes of disease worsening in IPF.

Abnormal GER simply means that you have more episodes of GER in 24 hours than are seen in a normal person. The majority of patients with abnormal GER and IPF do not have typical symptoms of GER (heartburn and upset stomach) and many are without symptoms at all.

Anti-reflux surgery surgery is an approved (standard of care) treatment for severe GER, but its effect on lung function in patients with IPF is not known.

This study is being paid for by the National Institutes of Health (NIH). Dr. Collard will not receive any special payments for this study other than support of his regular salary to allow him to conduct the study and funds to complete some study tests and procedures.

How many people will take part in this study?

About 58 patients will take part in this study at five clinical centers across the United States. We expect about 12 patients to participate here at UCSF.

What will happen if I take part in this research study?

Before you begin the main part of the study...

You will need to have the following "screening" exams, tests or procedures to find out if you can be in the main part of the study. Your study doctor will ask you questions about your health and the medications, including any vitamins or herbal supplements, you are currently taking. Your doctor will confirm the diagnosis of IPF. You can expect the following during the screening period for participation in the study (Visit 1):

- You will review and sign this informed consent
- Your study doctor will go over your medical history and review certain parts of your medical history
- Physical examination including your vital signs (blood pressure, pulse, and breathing rate), weight, height, and amount of oxygen in the blood.
- Spirometry: Spirometry is a form of lung function test (Pulmonary function tests, or PFTs) that involves you breathing deeply and blowing into a tube that measure your air flows.
- About 5 teaspoons of blood will be drawn to measure levels of proteins in your blood (called biomarkers) and collect DNA.
- 6-minute walk test: this is a test that measures how far you can walk in 6 minutes. You are allowed to stop and rest during the test.
- Arterial Blood Gasses: Blood (about 1 teaspoon) will be drawn from an artery in your wrist to measure the amount of oxygen and other gases in your blood.
- You will have esophageal manometry performed if you have not had this test performed in the last 3 months in the same way as the one required for the study. Manometry involves testing your esophagus with a thin, flexible probe to measure its pressures and muscle movements. This helps doctors determine how best to perform additional testing and whether laparoscopic anti-reflux surgery is safe to perform on you.
- You will have 24 hour esophageal and pH testing performed if you have not had this test performed in the last 3 months in the same way as the one required for the study. You will have a thin, flexible catheter placed through your nose into your esophagus to measure the acid levels in your esophagus and record the number of reflux events that occur. This catheter will remain in place for 24 hours and then be removed. This helps doctors determine whether you have abnormal GER.
- You will be asked to complete questionnaires

The above tests will be reviewed by the study doctor. If you are eligible to participate in this study, you will be asked to return for the Enrollment Visit within 28 days.

During the main part of the study...

If the screening exams, tests or procedures show that you can continue to be in the study, and you choose to take part, then you will have the following tests and procedures done.

Enrollment Visit (Visit 2)

During this visit you can expect the following:

- You will have a brief physical examination including measurement of your blood pressure, pulse, and breathing rate, weight, height, and amount of oxygen in your blood.
- A detailed x-ray of your lungs (High-resolution Computed Tomography, or HRCT), if you have not had an HRCT scan done in the past 3 months in the same way as the one required for the study.
- Spirometry, (unless your screening visit happened within 28 business days). You will also have a second breathing test called the diffusion capacity. The diffusion capacity test involves breathing in a gas mixture and holding your breath approximately 10 seconds..
- 6-minute walk test: this is a test that measures how far you can walk in 6 minutes. You are allowed to stop and rest during the test, unless your screening visit happened within 28 business days.
- Blood (about 5 teaspoons) will be drawn to measure levels of proteins in your blood.
- You will be asked to complete questionnaires on your cough and your quality of life
- Home Spirometry Training: As part of this study, you will be given a hand held spirometer to take home with you and use on a regular basis. This spirometer is a miniature version of the machine used by your doctors to measure your breathing tests in the clinic. You will be asked to use this hand held spirometer every day to record your lung function. Similar to the office-based method, this involves you breathing deeply in and out through a tube. Your study doctor and staff will instruct you fully in the use of this spirometer. The spirometer will not display the values recorded (knowledge of the values could interfere with other aspects of this study) but will store them in its memory and will transfer them to the study database at different times during the study. The study staff will teach you how to do this task. You will have a brief physical examination including measurement of your vital signs (blood pressure, pulse, and breathing rate), weight, height, and amount of oxygen in your blood.

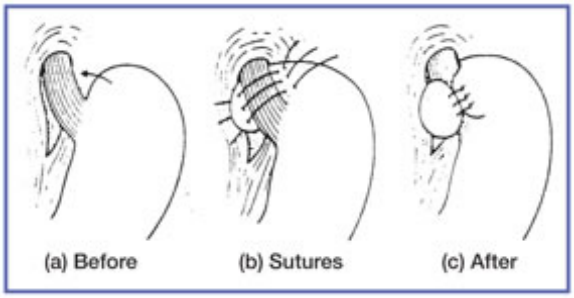
Following the above tests, you will be randomized to either receive anti-reflux surgery or receive intensive medical management. Randomization is like drawing numbers from a hat to decide whether you receive the surgery or not. You have an equal chance of being assigned to surgery or not.

Subjects randomized to surgery arm: If you are randomized to the surgery, we will contact your insurance provider to request pre-authorization for laparoscopic anti-reflux surgery and any other testing that the surgeon feels is necessary to ensure the surgery can be performed safely. If authorization for the surgery is not granted, you will not be able to undergo surgery as part of the study but will continue to participate in the study visits as described for the subjects not randomized to surgery. If authorization is granted, you will

undergo evaluation for laparoscopic anti-reflux surgery. You will meet with the surgeon and anesthesiologist before surgery to discuss the procedure in detail and undergo any additional testing that your doctors feel is necessary for your safety.

At the time of the surgery, you will undergo general anesthesia with a breathing tube in place. As part of the research protocol, you will have a bronchoscopy performed while you are anesthetized and before the surgery is performed (this will allow your study doctors to understand the biology of IPF and its relationship to GER). Bronchoscopy involves having a narrow tube fed into your lungs through your breathing tube for collection of salt-water washings and cells. Bronchoscopy is done routinely by your study doctors as part of the clinical care of patients with lung diseases.

During surgery, the surgeon will use a camera and other operative tools to take a part of your stomach muscle and wrap it around the opening between your stomach and your esophagus (see picture below for an illustration of this). This will allow the opening to close more effectively and keep the stomach contents from moving backwards into your esophagus and potentially into your lungs. In most cases, you will be hospitalized for 1-2 days after surgery. You will have instructions given to you after the operation and will have one or more post-operative follow up clinic visits with the surgeon to make sure that you are recovering well. Following surgery, you will be asked to halt the daily spirometry until you return for the week 12 visit.



Source: NIH/NDDIC website: digestive.niddk.nih.gov

Subjects randomized to medical therapy arm: If you are not randomized to receive surgery, you will continue with your usual medical care with close monitoring of your disease state throughout the clinical trial. Importantly, if you are in the non-surgical group and have progression of your IPF (a worsening of your lung function and shortness of breath as determined by the study doctor) at or after the week 24 visit, you will have the option to undergo laparoscopic anti-reflux surgery as a clinical procedure (in other words, not indicated or paid for by the study) while remaining in the clinical trial, assuming you and your treating doctor feel it is clinically indicated. If this happens, you will be asked to continue with your study visits as originally planned at the beginning of the study.

<u>Week 12 (Visit 3)</u>

During this visit you can expect the following:

- You will have a brief physical examination including measurement of your vital signs (blood pressure, pulse, and breathing rate), weight, height, and amount of oxygen in your blood.
- Spirometry, unless you have had surgery in the last 8 weeks. You will also have a second breathing test called the diffusion capacity. The diffusion capacity test involves breathing in a gas mixture and holding your breath approximately 10 seconds.

- You will again walk for up to 6 minutes under the supervision of study staff and the distance you walk will be recorded.
- About 5 teaspoons of blood will be drawn to measure levels of proteins in your blood (called biomarkers).
- You will be asked to complete questionnaires and forms on your shortness of breath, cough, and overall quality of life.
- About 1 teaspoon of blood will be drawn from an artery in your wrist to measure the amount of oxygen in your blood.

Week 24 (Visit 4)

During this visit you can expect the following:

- You will have a brief physical examination including measurement of your vital signs (blood pressure, pulse, and breathing rate), weight, height, and amount of oxygen in your blood.
- You will undergo spirometry, unless you have had surgery within the last 8 weeks and diffusion capacity tests again. The diffusion capacity involves breathing in a gas mixture and holding your breath approximately 10 seconds.
- You will again walk for up to 6 minutes under the supervision of study staff and the distance you walk will be recorded.
- About 5 teaspoons of blood will be drawn to measure levels of proteins in your blood (called biomarkers).
- You will undergo manometry and 24 hour pH monitoring to see whether and how much your GER has changed. Note: you will only do this if you were randomized to the surgery arm, and if it has been at least 12 weeks since your surgery.
- You will be asked to complete questionnaires and forms on your shortness of breath, cough, and overall quality of life.
- About 1 teaspoon of blood will be drawn from an artery in your wrist to measure the amount of oxygen in your blood.

Week 36 (Visit 5)

During this visit you can expect the following:

- You will have a brief physical examination including measurement of your vital signs (blood pressure, pulse, and breathing rate), weight, and amount of oxygen in your blood.
- You will undergo spirometry again, unless you have had surgery in the last 8 weeks.

- About 5 teaspoons of blood will be drawn to measure levels of proteins in your blood (called biomarkers).
- You will be asked to complete questionnaires and forms on your shortness of breath, cough, and overall quality of life.

Week 48 (Visit 6)

During this visit you can expect the following:

- You will have a brief physical examination including measurement of your vital signs (blood pressure, pulse, and breathing rate), weight, height, and amount of oxygen in your blood.
- You will undergo spirometry, unless you have had surgery within the last 8 weeks and diffusion capacity tests again. The diffusion capacity involves breathing in a gas mixture and holding your breath approximately 10 seconds.
- You will again walk for up to 6 minutes under the supervision of study staff and the distance you walk will be recorded.
- About 5 teaspoons of blood will be drawn to measure levels of proteins in your blood (called biomarkers).
- You will be asked to complete questionnaires and forms on your shortness of breath, GER symptoms, cough, and overall quality of life.
- About 1 teaspoon of blood will be drawn from an artery in your wrist to measure the amount of oxygen in your blood.
- You will undergo a second high-resolution computed tomography scan.
- Bronchoscopy- an optional procedure for surgical subjects- see " optional biological impact sub-study" below

Visit Overview

Below is a table providing an overview of the visit schedule, the parts of each visit, and approximately how long we estimate you will need to be at the study center for each visit.

Visit	**Procedures and Tests**	**Estimated time**
Screening (Visit 1)	• Informed consent • History and physical exam • Questionnaire • Spirometry • 6 minute walk test • Arterial blood gas • Blood draw	We estimate that the first 6 items will take 4-5 hours. The last item (24-hour pH monitoring and manometry) will require 2-3 hours in the laboratory on one day and a return to the laboratory the

	• Manometry • 24-hour pH/impedance monitoring	following day for a brief visit to remove the equipment.
Enrollment (Visit 2)	• Randomization • Physical exam • Spirometry* • Diffusion capacity (DLCO) • Computed tomography (CT) • 6 minute walk test* • Blood draw • Questionnaires *Only performed if Visit 2 occurs > 28 days after Visit 1	We estimate that this visit will take 5-6 hours.
Surgery and associated visits (only for those people randomized to surgery)	• Brief Physical Exam • Pre-operative evaluation and testing as necessary • Laparoscopic anti-reflux surgery • Post-operative follow-up as necessary	The amount of time required for this is hard to estimate, as it will vary for each patient significantly. In most cases, there will be 2-3 pre-operative clinic visits (1 hour each) and some associated testing; 2 days of hospitalization at the time of surgery; and 1-2 post-operative follow-up clinic visits (1 hour each).
Week 12 (Visit 3)	• Physical exam • Spirometry • Diffusion capacity (DLCO) • 6 minute walk test • Arterial blood gas • Blood draw • Questionnaires	We estimate that the first 6 items will take 3-4 hours.
Week 24 (Visit 4)	• Physical exam • Spirometry • Diffusion capacity (DLCO) • 6 minute walk test • Blood draw • Arterial blood gas • Questionnaires	We estimate this visit will take 3-4 hours. The last item (24 hour pH monitoring and manometry) will require 2-3 hours in the laboratory on one day and a return to the laboratory the following day

	• Manometry • 24 hour pH	for a brief visit to remove the equipment
Week 36 (Visit 5)	• Physical exam • Spirometry • Blood draw • Questionnaires	We estimate this visit will take 2-3 hours.
	• Bronchoscopy (optional with consent for patients randomized to surgery)	We estimate this visit will take 5-6 hours.

Phone Visits

Month 1, 2, 4, 5, 7, 8, 10, 11 and Week 52

• The site coordinator will call to see how you are doing and check for any adverse events that may have since your previous clinic visit.

Discontinuation of study

If you withdraw early from the study, you will be asked to return to complete the battery of assessments scheduled at week 48.

Optional Biological Impact Sub-study

An important part of this study is to understand how your lungs may have changed because of the laparoscopic anti-reflux surgery. To do this, we are asking patients randomized to laparoscopic anti-reflux surgery to consider undergoing a second bronchoscopy at the end of the study (around the week 48 visit) as part of a biological impact sub-study.

The optional second bronchoscopy would be performed as an outpatient by your study pulmonologist (or their co-investigator) in the same way bronchoscopy procedures are done for the clinical care of patients. Briefly, this involves having your mouth and throat numbed with an anesthetic (numbing) medicine and receiving medicine through an IV so you are comfortable. The study doctor will then insert a thin, flexible tube (called a bronchoscope) into your mouth and steer it into the lung where salt water will be washed in and out of a small part of your lung and a small brush will be used to collect some cells. The entire procedure takes about 2 hours from start to finish and you will be able to go home 1-2 hours after the procedure is completed.

If you agree to participate in the biological impact sub-study, you will check the “yes” box in the signature section of this consent form (it is at the end).

What you should do

While in this study you must:

- Come to your scheduled study visits
- Call your study doctor to let him or her know about anything that happens to you medically while in the study, such as illnesses, doctor visits, side effects, or hospitalizations
- Notify the study doctor if you are thinking about withdrawing from the research study
- Tell your primary care physician that you are participating in this study.

How long will I be in the study?

The entire study will last for about 3 years. You will be in the study for about 52 weeks.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely.

It is important to tell the study doctor if you are thinking about stopping so that your doctor can evaluate any risks from the stopping early and discuss what alternative follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. In some cases, side effects can be serious, long lasting, or may never go away. The primary risk to you in this protocol is from the laparoscopic fundoplication surgery. Additional risk is from the bronchoscopy, other study procedures, and from loss of privacy.

You should talk to your study doctor about any side effects you experience while taking part in the study.

Laparoscopic anti-reflux surgery

Laparoscopic anti-reflux surgery is widely used for treating patients with abnormal GER. It is generally considered a safe and effective procedure with a very low serious complication rate. The most common risks to patients include:

- Some difficulty swallowing right after surgery (20 out of 100), or long term (< 5 out of 100)

- Gas-bloat syndrome. . Some people subjected to fundoplication experience bloating, but other symptoms can include quickly feeling full when eating, nausea, upper abdominal pain, flatulence (passing gas), inability to belch, and inability to vomit. These effects have been reported in to up to 41 out of 100 and normally resolve in 2 to 4 weeks.
- Diarrhea (18 out of 100)
- Recurrent GER (10-15 out of 100)

Infrequent complications specific to the operation (< 3 out of 100)

- Injury to the esophagus or stomach during the procedure
- Injury to the vagus nerves (the nerves that control acid secretion and motility of the stomach)
- Injury to the spleen requiring repair or removal of the spleen
- Slipping or disruption of the wrap

Additional risks (which may occur with any operation) include post-operative pain, bleeding, pulmonary embolus, and infection, all of which are rare. There are risks when general anesthesia is used, but these are also rare. The risk of death from general anesthesia and laparoscopic anti-reflux surgery is less than 1 out of 100.

It is unknown if there are any additional risks from this surgery to patients with IPF.

Bronchoscopy

Bronchoscopy is a commonly performed clinical procedure and has a low risk (< 5 out of 100) of complications. In this study, bronchoalveolar lavage and endobronchial brushing will be performed. This may cause:

- local discomfort in the throat during the procedure
- fever lasting a short time (24 hours)
- short-term need for additional oxygen (24 hours to 1 week)

Serious but very rare complications include:

- air in the chest outside the lung
- bleeding
- acute exacerbation of IPF
- death

The sedatives that you will be given for the bronchoscopy may cause:

Likely

- Drowsiness, fatigue
- Nausea

Less Likely

- Short-term memory loss

Rare but serious

- Allergic reaction
- Irregular heart beat
- Hospitalization
- Death

Manometry and 24-hour pH monitoring

Both of these tests are commonly performed in the clinical setting and have a well-established safety profile. The most common risks to patients include pain and discomfort. There is a very small risk of:

- puncturing the esophagus
- bleeding
- infection
- death

Spirometry (home and office based) and diffusion capacity

Breathing tests are usually painless. Some of the tests may be tiring for people who have a lung disease. You may cough or feel lightheaded after breathing in or out rapidly, but you will be given a chance to rest between tests. You may find it uncomfortable to wear the nose clip. Breathing through the mouthpiece for a long period of time may be uncomfortable.

Six-Minute Walk Test

The 6-minute walking test may be tiring. Some people become lightheaded from walking for six minutes. There is a small risk of abnormal blood pressure (up or down) and disorders of the heartbeat (fast, slow or irregular). To minimize these complications you will walk at your own pace and let the staff know when you are uncomfortable. You will be able to stop at any time as needed. The staff giving you the 6-minute walk test will monitor and treat you if necessary.

Computed Tomography (CT)

Computed Tomography (CT) is a way to make x-ray images of the inside of the body. You will be exposed to a little more radiation than a regular x-ray. The amount of radiation from the chest CT scan has a low risk of harmful effects.

Radiation risks:

This research study involves exposure to radiation. This radiation exposure is not necessary for your medical care and is for research purposes only. The additional amount of radiation that you will receive as a result of participating in this study will be less than the yearly natural background radiation in the US, which is 3 mSv (a mSv, or milliSievert, is a measurement of radiation). This amount of radiation involves minimal risk. If you are pregnant or breast feeding, you SHOULD NOT participate in this study. If you have any questions regarding the use of radiation or the risks involved, please consult the physician conducting the study.

CT scan risks: CT scans involve the risks of radiation (see above).

Having a CT scan may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia when placed inside the CT scanner, or by lying in one position for a long time.

Blood Drawing
Risks associated with drawing blood from a vein in your arm by needle stick include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.

Risks of the Arterial Blood Gas test (ABG):
You may feel lightheaded, faint or dizzy while the blood is being taken from your artery. You may develop a small bruise at the site of the puncture. On rare occasions the needle may damage a nerve or an artery causing the artery to become blocked. A blocked artery can prevent blood from flowing to the hand, which can lead to damage. Because the arterial blood gas is slightly more painful than drawing blood from a vein, we may give you an injection of local anesthetic to numb the area.

Questionnaires
Some of the questionnaires may ask personal questions that may be uncomfortable to answer. You do not have to answer any questions that you do not want to answer.

- **Randomization risks:** You will be assigned to a treatment program by chance, and the treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.

- For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. This study will help doctors learn important information about treatment in IPF that will hopefully speed up finding an effective therapy for this disease.

What other choices do I have if I do not take part in this study?

Your other choices may include:

- Getting no treatment
- Getting standard treatment for your condition without being in a study.
- Getting a different experimental treatment/taking part in another study.

Please talk to your doctor about your choices before deciding if you will take part in this study.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Institutes of Health (study sponsor)
- The University of California
- The Food and Drug Administration (FDA), involved in keeping research safe for people
- Duke Clinical Research Institute and its representatives (coordinating center)

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. A medical record will be created because of your participation in this study. Your consent form and some of your research test results will be included in this record. Therefore, your other health care providers may see your test results and become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

This consent/authorization will be kept for at least 10 years from the date it was signed. Your study results will be kept in your research record for a minimum of 7 years after the end of the study. After that research information may be destroyed, or information that may identify you may be removed from the study records. If there is research information that has become part of your medical record, it will be kept indefinitely. If this information is revealed by anyone receiving it from us, it may no longer be covered by the federal privacy regulations. We will do everything possible to ensure that this does not occur. Information that could identify you will not be used if the results of this study are published.

What are the costs of taking part in this study?

Most of the costs associated with this study will be paid for by a research grant from the National Heart, Lung, and Blood Institute (NHLBI), which is one of the institutes in the National Institutes of Health (NIH). This means that the costs of the visits (including the cost of the research doctors and staff conducting the study) will not be billed to you or your insurance company. The anti-reflux surgery is being performed for your documented abnormal GER, and is therefore covered by most insurers in this context. If you are

randomized to the surgery, we will contact your insurance provider to request pre-authorization for laparoscopic anti-reflux surgery and any other testing that the surgeon feels is necessary to ensure the surgery can be performed safely. If authorization for the surgery is not granted, you will not be able to undergo surgery as part of the study, but will be asked to continue to participate in the study visits as described for the subjects not randomized to surgery. If authorization for surgery is granted, the cost of the surgery, the costs associated with additional visits and tests scheduled by the surgeon, and the costs of any complications of these procedures will be billed to your insurance, just like any medical procedure or test you receive in the clinic or hospital. This means that you will be responsible for any co-payments you may have and that you will ultimately be responsible for the costs associated with these procedures if your insurance company does not pay for them.

Will I be paid for taking part in this study?

You will receive reimbursement for your travel expenses of up to $250 for each study visit based on receipts and mileage (current government rate will be used per mile).

You will need to provide your social security number to receive a check. The check is usually received within 6 weeks after your visit.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Harold Collard, MD if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at 415-502-1958.

> **Treatment and Compensation for Injury:** If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415- 476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your study doctor Harold Collard, MD at 415-502-1958.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Office of the Committee on Human Research at 415-476-1814.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONSENT

You have been given signed and dated copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

Optional additional consents

You are being asked to consider the following optional consents that will allow additional scientific study and research to come from your participation in the WRAP-IPF study. These are completely voluntary and you decision whether or not to consent to these items will in no way affect your ability to participate in the main study.

Applicable to all "sub-studies:"

- The data and biological samples noted below in each sub-study may be kept for many years and "destroyed" when they are no longer needed.
- Specimens will be stored at UCSF
- The data and specimens may be used for future research in IPF or other diseases.
- Only researchers at UCSF, who are working on this study, will have access to your private information associated with the data and/or samples. Data and/or samples may be shared with researchers outside of UCSF only in anonymized form (i.e., coded so the researchers do not know any private information about you).

- Your privacy will be protected by storing the data and/or specimens in coded/anonymized form and on secure computer servers and locked offices and/or laboratories. Only UCSF researchers working on this study will have access to your private information.
- The data and/or specimens may be used in the development of tests, products, or discoveries that may have potential commercial value. You will not be paid or receive money for such developments.
- You may request destruction of stored samples in the future by contacting Harold Collard, MD at 415-502-1958, or via letter at UCSF, ILD Research 505 Parnassus Ave., Box 0111, San Francisco, CA 94143.

Optional Sub-Study 1: Biological Impact Sub-Study

Biological Impact Sub-study Consent (for patients randomized to surgery only)

□ Yes, I give my permission for a second bronchoscopy to be performed at the end of the study as part of the biological impact sub-study.

□ No, I do not give my permission for a second bronchoscopy to be performed at the end of the study at this time.

Optional Sub-Study 2: Consent to Share Data for Additional IPF Research

I give consent to my study doctor and the other WRAP-IPF study investigators to share data collected as part of the WRAP-IPF study with investigators studying IPF outside of the WRAP-IPF trial. I understand that all shared data will be anonymous (i.e. all potentially identifying information will be removed and kept securely by the WRAP-IPF study. I also understand that neither the study investigators, nor I will benefit financially from this sharing of data.

□ Yes, my data may be shared with researchers outside of the WRAP-IPF study that are investigating IPF.

□ No, my data may not be shared with researchers outside of the WRAP-IPF study that are investigating IPF.

Optional Sub-Study 3: Consent to Store and Use Biological Specimens for Additional IPF Research by WRAP-IPF Research Teams

I agree to allow my biological specimens (e.g. blood, urine, and lung washings and cells) collected as part of WRAP-IPF, and any product resulting from those specimens (e.g., plasma, serum), including specimens for genetic testing, to be stored and used for additional research into the cause and treatment of IPF by WRAP-IPF investigators. These samples will be stored until there is no more left, the investigators determine it is time to destroy the specimen(s), or I request in writing the specimen(s) be destroyed. All specimens will be studies anonymously using a bar code number for reference (i.e. all potentially identifying information will be removed).

□ Yes, my specimens may be stored and used for additional research purposes.

□ No, my specimens may not be stored and used for additional research purposes.

Optional Sub-Study 4: Consent to Store and Use Biological Specimens for Additional IPF Research by Researchers Outside WRAP-IPF

I agree to allow my biological specimens (e.g. blood, lung washings and cells, and any other specimens) collected as part of WRAP-IPF, and any product resulting from those specimens (e.g., plasma, serum), including specimens for genetic testing, to be shared with investigators outside of the WRAP-IPF study for additional research into the cause and treatment of IPF. All specimens will be studies anonymously using a bar code number for identification (i.e. all potentially identifying information will be removed). I understand that neither the study investigators, nor I will benefit financially from this sharing of data.

□ Yes, my biological specimens may be shared with investigators outside of the WRAP-IPF study, as described above.

□ No, my biological specimens may be shared with investigators outside of the WRAP-IPF study, as described above.

If you wish to participate in this study, you should sign below.

_____	_____
Date	Participant's Signature for Consent
	_____
	Printed Name of Participant
_____	_____
Date	Signature of Person Obtaining Consent
	_____
	Printed Name of Person Obtaining Consent
_____	_____
Date	Signature of Witness (only required if the participant is a non-English speaker)
	_____
	Printed Name of Witness

Experimental Subject's Bill of Rights

University of California, San Francisco

The rights below are the rights of every person who is asked to be in a research study. As an experimental subject I have the following rights:

1. To be told what the study is trying to find out,
2. To be told what will happen to me and whether any of the procedures, drugs, or devices is different from what would be used in standard practice,
3. To be told about the frequent and/or important risks, side effects, or discomforts of the things that will happen to me for research purposes,
4. To be told if I can expect any benefit from participating, and, if so, what the benefit might be,
5. To be told of the other choices I have and how they may be better or worse than being in the study,
6. To be allowed to ask any questions concerning the study both before agreeing to be involved and during the course of the study,
7. To be told what sort of medical treatment is available if any complications arise,
8. To refuse to participate at all or to change my mind about participation after the study is started. This decision will not affect my right to receive the care I would receive if I were not in the study,
9. To receive a copy of the signed and dated consent form,
10. To be free of pressure when considering whether I wish to agree to be in the study.

If I have other questions I should ask the researcher or the research assistant. In addition, I may contact the Committee on Human Research, which is concerned with protection of volunteers in research projects. I may reach the committee office by calling: (415) 476-1814 from 8:00 AM to 5:00 PM, Monday to Friday, or by writing to the Committee on Human Research, Box 0962, University of California, San Francisco, CA 94143.

Call 415 476-1814 for information on translations.