

Vacuum vs Manual Drainage During Unilateral Thoracentesis

Study Protocol

NCT 03496987

Original Document Date: 11/17/15

SECTION I: ADMINISTRATIVE INFORMATION
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Title of Research Project: Thoracentesis using Manual Aspiration vs Vacuum Suction: A Study Comparing Pain and Complications			
Principal Investigator: Jonathan Puchalski, MD, MEd		Yale Academic Appointment: Associate Professor	
Department: Department of Medicine			
Campus Address: LCI 100D, 15 York St., New Haven, CT			
Campus Phone: 737-5699	Fax: 737-1666	Pager: 370-6396	E-mail: jonathan.puchalski@yale.edu
Protocol Correspondent Name & Address (if different than PI): Michal Senitko, MD, LCI 100D, 15 York St, New Haven, CT			
Campus Phone: 737-5699	Fax:	E-mail: michal.senitko@yale.edu	
Yale Cancer Center CTO Protocol Correspondent Name & Address (if applicable):			
Campus Phone:	Fax:	E-mail:	
Business Manager:			
Campus Phone :	Fax :	E-mail	
Faculty Advisor: (required if PI is a student, resident, fellow or other trainee) <input checked="" type="checkbox"/> NA		Yale Academic Appointment:	
Campus Address:			
Campus Phone:	Fax:	Pager:	E-mail:

Investigator Interests:

Does the principal investigator, or do any research personnel who are responsible for the design, conduct or reporting of this project or any of their family members (spouse or dependent child) have an incentive or interest, financial or otherwise, that may affect the protection of the human subjects involved in this project, the scientific objectivity of the research or its integrity? Note: The Principal Investigator (Project Director), upon consideration of the individual's role and degree of independence in carrying out the work, will determine who is responsible for the design, conduct, or reporting of the research.

See Disclosures and Management of Personal Interests in Human Research
<http://www.yale.edu/hrpp/policies/index.html#COI>

Yes **No**

Do you or does anyone on the research team who is determined by you to be responsible for the design, conduct or reporting of this research have any patent (sole right to make, use or sell an invention) or copyright (exclusive rights to an original work) interests related to this research protocol?

Yes **No**

If yes to either question above, list names of the investigator or responsible person:

The Yale University Principal Investigator, all Yale University co-investigators, and all Yale University individuals who are responsible for the design, conduct or reporting of research must have a current financial disclosure form on file with the University's Conflict of Interest Office. Yale New Haven Hospital personnel who are listed as co-investigators on a protocol with a Yale University Principal Investigator must also have a current financial disclosure form on file with the University's Conflict of Interest Office. If this has not been done, the individual(s) should follow this link to the COI Office Website to complete the form: <http://www.yale.edu/coi/>

NOTE: The requirement for maintaining a current disclosure form on file with the University's Conflict of Interest Office extends primarily to Yale University and Yale-New Haven Hospital personnel. **Whether or not they are required to maintain a disclosure form with the University's Conflict of Interest Office, all investigators and individuals deemed otherwise responsible by the PI who are listed on the protocol are required to disclose to the PI any interests that are specific to this protocol.**

SECTION II: GENERAL INFORMATION

1. **Performing Organizations:** Identify the hospital, in-patient or outpatient facility, school or other agency that will serve as the location of the research. Choose all that apply:

a. Internal Location[s] of the Study:

- | | |
|---|---|
| <input type="checkbox"/> Magnetic Resonance Research Center (MR-TAC) | <input type="checkbox"/> Yale University PET Center |
| <input type="checkbox"/> Yale Cancer Center/Clinical Trials Office (CTO) | <input type="checkbox"/> YCCI/Church Street Research Unit (CSRU) |
| <input checked="" type="checkbox"/> Yale Cancer Center/Smilow | <input type="checkbox"/> YCCI/Hospital Research Unit (HRU) |
| <input checked="" type="checkbox"/> Yale-New Haven Hospital | <input type="checkbox"/> YCCI/Keck Laboratories |
| <input type="checkbox"/> Cancer Data Repository/Tumor Registry | <input type="checkbox"/> Yale-New Haven Hospital—Saint Raphael Campus |
| <input checked="" type="checkbox"/> Specify Other Yale Location: Thoracic Oncology Program (TOP) Clinic | |

b. External Location[s]: N/A

- | | |
|---|--|
| <input type="checkbox"/> APT Foundation, Inc. | <input type="checkbox"/> Haskins Laboratories |
| <input type="checkbox"/> Connecticut Mental Health Center | <input type="checkbox"/> John B. Pierce Laboratory, Inc. |
| <input type="checkbox"/> Clinical Neuroscience Research Unit (CNRU) | <input type="checkbox"/> Veterans Affairs Hospital, West Haven |
| <input type="checkbox"/> Other Locations, Specify: | <input type="checkbox"/> International Research Site |

(Specify location(s)):

c. Additional Required Documents (check all that apply):

N/A

*YCCI-Scientific and Safety Committee (YCCI-SSC) Approval Date:

*Pediatric Protocol Review Committee (PPRC) Approval Date:

*YCC Protocol Review Committee (YRC-PRC) Approval Date:

*Dept. of Veterans Affairs, West Haven VA HSS Approval Date:

*Radioactive Drug Research Committee (RDRC) Approval Date:

YNHH-Radiation Safety Committee (YNHH-RSC) Approval Date:

Magnetic Resonance Research Center PRC (MRRC-PRC) Approval Date:

YSM/YNHH Cancer Data Repository (CaDR) Approval Date:

Dept. of Lab Medicine request for services or specimens form

Imaging on YNHH Diagnostic Radiology equipment request form (YDRCTO request) found at <http://radiology.yale.edu/research/ClinTrials.aspx>

**Approval from these committees is required before final HIC approval is granted. See instructions for documents required for initial submission and approval of the protocol. Allow sufficient time for these requests. Check with the oversight body for their time requirements.*

2. **Probable Duration of Project:** State the expected duration of the project, including all follow-up and data analysis activities.

Expected duration of the project is approximately 1 (one) year from approval, which includes follow up and data analysis activities expected to end December 31, 2017.

3. **Research Type/Phase: (Check all that apply)**

a. Study Type

Single Center Study

Multi-Center Study

Does the Yale PI serve as the PI of the multi-site study? Yes No N/A

Coordinating Center/Data Management

Other:

b. Study Phase N/A

Pilot Phase I Phase II Phase III Phase IV

Other (*Specify*) Two arm, prospective, randomized study

4. **Area of Research: (Check all that apply)** Note that these are overlapping definitions and more than one category may apply to your research protocol. Definitions for the following can be found in the instructions section 4c:

Clinical Research: Patient-Oriented

Clinical Research: Outcomes and Health Services

Clinical Research: Epidemiologic and Behavioral

Interdisciplinary Research

Translational Research #1 ("Bench-to-Bedside")

Community-Based Research

Translational Research #2 ("Bedside-to-Community")

5. Is this study a clinical trial? Yes No

NOTE the current ICMJE (International Committee of Medical Journal Editors) definition of a clinical trial: “any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.” Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events”

If yes, where is it registered? N/A

Clinical Trials.gov registry

Other (Specify)

Registration of clinical trials **at their initiation** is required by the FDA, NIH and by the ICMJE.

If this study is registered on clinicaltrials.gov, there is new language in the consent form and compound authorization that should be used.

For more information on registering clinical trials, including whether your trial must be registered, see the YCCI webpage, <http://ycci.yale.edu/researchers/ors/registerstudy.aspx> or contact YCCI at 203.785.3482)

1. Does the Clinical Trials Agreement (CTA) require compliance with ICH GCP (E6)?

Yes No N/A

7. Will this study have a billable service? *A billable service is defined as any service rendered to a study subject that, if he/she was not on a study, would normally generate a bill from either Yale-New Haven Hospital or Yale Medical Group to the patient or the patient’s insurer. The service may or may not be performed by the research staff on your study, but may be provided by professionals within either Yale-New Haven Hospital or Yale Medical Group (examples include x-rays, MRIs, CT scans, specimens sent to central labs, or specimens sent to pathology). Notes: 1. There is no distinction made whether the service is paid for by the subject or their insurance (Standard of Care) or by the study’s funding mechanism (Research Sponsored). 2. This generally includes new services or orders placed in EPIC for research subjects.*

Yes

If answered, “yes”, this study will need to be set up in OnCore, Yale’s clinical research management system, for Epic to appropriately route research related charges. Please contact oncore.support@yale.edu

8.. Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities? Yes x No *If Yes, please answer questions a through c and note instructions below. If No, proceed to Section III.*

a. Does your YNHH privilege delineation currently include the **specific procedure** that you will perform? Yes

b. Will you be using any new equipment or equipment that you have not used in the past for this procedure? No

c. Will a novel approach using existing equipment be applied? No

If you answered “no” to question 8a, or "yes" to question 8b or c, please contact the YNHH Department of Physician Services (688-2615) for prior approval before commencing with your research protocol.

*Please note that if this protocol includes Yale-New Haven Hospital patients, including patients at the HRU, the Principal Investigator and any co-investigators who are physicians or mid-level practitioners (includes PAs, APRNs, psychologists and speech pathologists) who may have direct patient contact with patients on YNHH premises must have medical staff appointment and appropriate clinical privileges at YNHH. If you are uncertain whether the study personnel meet the criteria, please telephone the Physician Services Department at 203-688-2615. **By signing this protocol as a PI, you attest that you and any co-investigator who may have patient contact has a medical staff appointment and appropriate clinical privileges at YNHH.***

SECTION III: FUNDING, RESEARCH TEAM AND TRAINING

1. **Funding Source:** Indicate all of the funding source(s) for this study. Check all boxes that apply. Provide information regarding the external funding source. This information should include identification of the agency/sponsor, the funding mechanism (grant or contract), and whether the award is pending or has been awarded. Provide the M/C# and Agency name (if grant-funded). If the funding source associated with a protocol is “pending” at the time of the protocol submission to the HIC (as is the case for most NIH submissions), the PI should note “Pending” in the appropriate section of the protocol application, provide the M/C# and Agency name (if grant-funded) and further note that University (departmental) funds support the research (until such time that an award is made).

PI	Title of Grant	Name of Funding Source	Funding	Funding Mechanism
Jonathan Puchalski	N/A	None	<input type="checkbox"/> Federal <input type="checkbox"/> State <input type="checkbox"/> Non Profit <input type="checkbox"/> Industry <input type="checkbox"/> Other For Profit <input type="checkbox"/> Other	<input type="checkbox"/> Grant-M# <input type="checkbox"/> Contract# <input type="checkbox"/> Contract Pending <input type="checkbox"/> Investigator/Department Initiated <input type="checkbox"/> Sponsor Initiated <input type="checkbox"/> Other, Specify:

Provide the Name and Address of the Sponsor Representative to whom the invoice should be sent. **Note: the PI’s home department will be billed if this information is not provided.**

Send IRB Review Fee Invoice To:

Name:

Company:
Address:

2. **Research Team:** List all members of the research team. Indicate under the affiliation column whether the investigators or study personnel are part of the Yale faculty or staff, or part of the faculty or staff from a collaborating institution, or are not formally affiliated with any institution. **ALL members of the research team MUST complete Human Subject Protection Training (HSPT) and Health Insurance Portability and Accountability Act (HIPAA) Training before they may be listed on the protocol. See NOTE below.**

NOTE: The HIC will remove from the protocol any personnel who have not completed required training.

	Name	Affiliation: Yale/Other Institution (Identify)	NetID
Principal Investigator	Jonathan Puchalski, MD, MEd	Yale Staff	JTP2
Role: Co-Investigator	Michal Senitko, MD	Yale Staff	MS3383
Role: Co-Investigator	Kyle Bramley, MD	Yale Staff	KB449
Role: Study Staff	Kelsey Johnson, PA	YNHH Staff	KMJ39
Role: Study Staff	Rachel Southard, APRN	YNHH Staff	RCS72

A personnel protocol amendment will need to be submitted when training is completed.

**SECTION IV:
PRINCIPAL INVESTIGATOR/FACULTY ADVISOR/ DEPARTMENT CHAIR AGREEMENT**

As the **principal investigator** of this research project, I certify that:

- The information provided in this application is complete and accurate.
- I assume full responsibility for the protection of human subjects and the proper conduct of the research.
- Subject safety will be of paramount concern, and every effort will be made to protect subjects' rights and welfare.
- The research will be performed according to ethical principles and in compliance with all federal, state and local laws, as well as institutional regulations and policies regarding the protection of human subjects.
- All members of the research team will be kept apprised of research goals.
- I will obtain approval for this research study and any subsequent revisions prior to my initiating the study or any change and I will obtain continuing approval of this study prior to the expiration date of any approval period.
- I will report to the HIC any serious injuries and/or other unanticipated problems involving risk to participants.
- I am in compliance with the requirements set by the University and qualify to serve as the principal investigator of this project or have acquired the appropriate approval from the Dean's Office or Office of the Provost, or the Human Subject Protection Administrator at Yale-New Haven Hospital, or have a faculty advisor.
- I will identify a qualified successor should I cease my role as principal investigator and facilitate a smooth transfer of investigator responsibilities.

PI Name (PRINT) and Signature

Date

As the **faculty advisor** of this research project, I certify that:

- The information provided in this application is complete and accurate.
- This project has scientific value and merit and that the student or trainee investigator has the necessary resources to complete the project and achieve the aims.
- I will train the student investigator in matters of appropriate research compliance, protection of human subjects and proper conduct of research.
- The research will be performed according to ethical principles and in compliance with all federal, state and local laws, as well as institutional regulations and policies regarding the protection of human subjects.
- The student investigator will obtain approval for this research study and any subsequent revisions prior to initiating the study or revision and will obtain continuing approval prior to the expiration of any approval period.
- The student investigator will report to the HIC any serious injuries and/or other unanticipated problems involving risk to participants.
- I am in compliance with the requirements set forth by the [University](#) and qualify to serve as the faculty advisor of this project.
- I assume all of the roles and responsibilities of a Principal Investigator even though the student may be called a PI.

Advisor Name (PRINT) and Signature

Date

Department Chair's Assurance Statement

Do you know of any real or apparent institutional conflict of interest (e.g., Yale ownership of a sponsoring company, patents, licensure) associated with this research project?

- Yes (provide a description of that interest in a separate letter addressed to the HIC.)
 No

As Chair, do you have any real or apparent protocol-specific conflict of interest between yourself and the sponsor of the research project, or its competitor or any interest in any intervention and/or method tested in the project that might compromise this research project?

- Yes (provide a description of that interest in a separate letter addressed to the HIC)
 No

I assure the HIC that the principal investigator and all members of the research team are qualified by education, training, licensure and/or experience to assume participation in the conduct of this research trial. I also assure that the principal investigator has departmental support and sufficient resources to conduct this trial appropriately.



Gary V Desir, MD

11/17/15

Chair Name (PRINT) and Signature

Date

Department of Medicine
Department

YNHH Human Subjects Protection Administrator Assurance Statement

Required when the study is conducted solely at YNHH by YNHH health care providers.

As Human Subject Protection Administrator (HSPA) for YNHH, I certify that:

- I have read a copy of the protocol and approve it being conducted at YNHH.
- I agree to notify the IRB if I am aware of any real or apparent institutional conflict of interest.
- The principal investigator of this study is qualified to serve as P.I. and has the support of the hospital for this research project.

YNHH HSPA Name (PRINT) and Signature

Date

SECTION V: RESEARCH PLAN

1. **Statement of Purpose:** State the scientific aim(s) of the study, or the hypotheses to be tested.

The purpose of the study is to assess if there is a difference in pain and complication rate between using a manual drainage system vs vacuum containers during thoracentesis of pleural effusions.

2. **Background:** Describe the background information that led to the plan for this project. Provide references to support the expectation of obtaining useful scientific data.

Patients with pleural effusions routinely undergo thoracentesis in which a catheter is placed into the pleural space to remove the fluid. In this setting, large amounts (often liters) of fluid are removed to palliate the patient's symptoms of breathlessness.

Thoracentesis is standardly performed using Safe T-Centesis™ Catheter Drainage Tray. After insertion of catheter to pleural space operator has two drainage system options. 1. Manual drainage that connects to drainage bag (figure 1) or 2. Drainage to vacuum bottle (figure2).

Pleural pressure (P_{pl}) is determined by the elastic recoil properties of the lung and chest wall. Normal pleural pressure is estimated to be -3 to -5 cm H₂O at functional residual capacity. During drainage of pleural fluid, negative pressure is applied either via syringe during manual drainage or via vacuum using vacuum drainage bottle. Hypothetically more negative pressure can translate to increased perception of pain or visceral pleural injury.

Two techniques (manual vs vacuum drainage) are used based on the operator preference and both are standard of care. To our knowledge there is no head to head comparison of two available systems of drainages during thoracentesis of pleural effusion.

Figure 1.

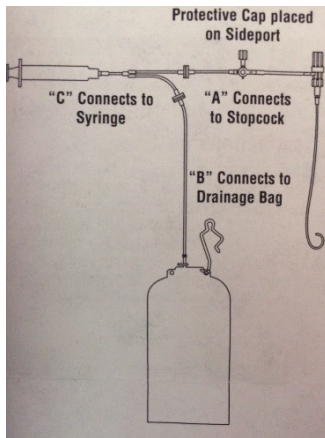
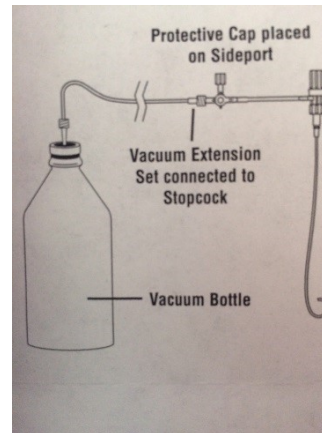


Figure 2.



3. **Research Plan:** Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. **Be sure to distinguish between standard of care vs. research procedures when applicable, and include any flowcharts of visits specifying their individual times and lengths.** Describe the setting in which the research will take place.

The interventional pulmonary team at Yale performs hundreds of thoracenteses per year. We have arbitrarily used the manual evacuation technique. However, use of a vacuum container could potentially save time for the patient and practitioner. Both methods of drainage are considered standard of care.

There are no research procedures performed in this study. During this study, we will simply methodically document which technique is performed, the patient's assessment of pain during the procedure, and complications (namely pneumothorax) based on randomization of which technique is performed.

Randomization will be done by block randomization to ensure an equal number of subjects in each group using a predefined key. (see Appendix 1: Research Randomizer Key).

Pain prior the initiation of the procedure and during the procedure will be assessed using The Numeric Pain Rating Scale (NPRS see Appendix 2). Patients' demographics (sex and age), the presumed etiology of pleural effusions, effusion laterality, volume removed, duration of procedure, reason for termination and complications will be recorded.

Investigators, study staff and patients will not be blinded to type of drainage system used.

4. Genetic Testing N/A

A. Describe

- i. the types of future research to be conducted using the materials, specifying if immortalization of cell lines, whole exome or genome sequencing, genome wide association studies, or animal studies are planned

- ii. the plan for the collection of material or the conditions under which material will be received
 - iii. the types of information about the donor/individual contributors that will be entered into a database
 - iv. the methods to uphold confidentiality
- B.** What are the conditions or procedures for sharing of materials and/or distributing for future research projects?
- C.** Is widespread sharing of materials planned?
- D.** When and under what conditions will materials be stripped of all identifiers?
- E.** Can donor-subjects withdraw their materials at any time, and/or withdraw the identifiers that connect them to their materials?
- i. How will requests to withdraw materials be handled (e.g., material no longer identified: that is, anonymized) or material destroyed)?
- F.** Describe the provisions for protection of participant privacy
- G.** Describe the methods for the security of storage and sharing of materials

5. **Subject Population:** Provide a detailed description of the types of human subjects who will be recruited into this study.

Patients with unilateral or bilateral pleural effusions who undergo thoracentesis by the Interventional Pulmonary team will be enrolled. These patients may be inpatient or outpatient and the procedure is performed throughout the hospital and clinic locations. Patients will be enrolled between January 1st 2015 through December 31st 2017.

6. **Subject classification:** Check off all classifications of subjects that will be specifically recruited for enrollment in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement. N/A

- | | | |
|--|--|--|
| <input type="checkbox"/> Children | <input type="checkbox"/> Healthy | <input type="checkbox"/> Fetal material, placenta, or dead fetus |
| <input type="checkbox"/> Non-English Speaking | <input type="checkbox"/> Prisoners | <input type="checkbox"/> Economically disadvantaged persons |
| <input type="checkbox"/> Decisionally Impaired | <input type="checkbox"/> Employees | <input type="checkbox"/> Pregnant women and/or fetuses |
| <input type="checkbox"/> Yale Students | <input type="checkbox"/> Females of childbearing potential | |

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects? Yes No (If yes, see Instructions section VII #4 for further requirements)

Subjects who may require additional safeguards or other considerations will not be enrolled in the study.

7. **Inclusion/Exclusion Criteria:** What are the criteria used to determine subject inclusion or exclusion?

Inclusion criteria:

1. Age > 18 y/o
2. Unilateral or bilateral pleural effusion

Exclusion criteria:

1. Patients with pleural effusions unable to be drained by thoracentesis
2. Adults who refuse to provide consent.
3. Patients unable to provide verbal feedback of their pain during the procedure. These include patients with an altered mental status and non-English speaking patients.

8. How will **eligibility** be determined, and by whom?

Once the consult for thoracentesis is received, the chart will be reviewed as part of standard practice. Eligibility for the study will be determined by the Interventional Pulmonary attending or fellow.

9. **Risks:** Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.

There is minimal to no risk for the study participant. The thoracentesis is standard of care. We will only be collecting data about pain (no risk to the patient) and complications of the procedure (no risk from study participation).

10. **Minimizing Risks:** Describe the manner in which the above-mentioned risks will be minimized.

Subject privacy risk will be minimized by using data collection tool where each subject will have a random number assigned. The medical record number will be available only to the Interventional Pulmonary Team involved in patient care and data will be de-identified as soon as the research data are entered to the data collection tool.

To protect against breaches of confidentiality, we will store all data on password protected computers and in locked file cabinets in key-card restricted areas. Data will be entered in computers associated with the Yale Program on Aging database.

11. **Data and Safety Monitoring Plan:** Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.) For more information, see the Instructions, page 24.

- a. What is the investigator's assessment of the overall risk level for subjects participating in this study? No risk

- b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study? N/A
- c. Include an appropriate Data and Safety Monitoring Plan. Examples of DSMPs are available here <http://www.yale.edu/hrpp/forms-templates/biomedical.html> for
 - i. Minimal risk
 - ii. Greater than minimal
- d. For multi-site studies for which the Yale PI serves as the lead investigator: N/A
 - i. How will adverse events and unanticipated problems involving risks to subjects or others be reported, reviewed and managed?
 - ii. What provisions are in place for management of interim results?
 - iii. What will the multi-site process be for protocol modifications?

The principal investigator is responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews quarterly. During the review process the principal investigator will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment.

The principal investigator, the Institutional Review Board (IRB) or, Yale Cancer Center Data and Safety Monitoring Committee (DSMC)] have the authority to stop or suspend the study or require modifications.

This protocol presents minimal risks to the subjects and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs), including adverse events, are not anticipated. In the unlikely event that such events occur, Reportable Events (which are events that are serious or life-threatening and unanticipated (or anticipated but occurring with a greater frequency than expected) and possibly, probably, or definitely related) or Unanticipated Problems Involving Risks to Subjects or Others that may require a temporary or permanent interruption of study activities will be reported immediately (if possible), followed by a written report within 5 calendar days of the Principal Investigator becoming aware of the event to the IRB (using the appropriate forms from the website) and any appropriate funding and regulatory agencies. The investigator will apprise fellow investigators and study personnel of all UPIRSOs and adverse events that occur during the conduct of this research project. Investigator will meet this obligation through the study meetings. The protocol's research monitor(s), Yale Cancer Center Data and Safety Monitoring Committee (DSMC), DSMBs, and regulatory agencies, and regulatory and decision-making bodies will be informed of any serious or life-threatening and unanticipated adverse events within 5 days of the event becoming known to the principal investigator.

12. Statistical Considerations: Describe the statistical analyses that support the study design.

The t-test will be used to analyze the difference in pneumothorax rate and pain assessment scales.

SECTION VI: RESEARCH INVOLVING DRUGS, BIOLOGICS, RADIOTRACERS, PLACEBOS AND DEVICES

If this section (or one of its parts, A or B) is not applicable, state N/A and delete the rest of the section.

A. DRUGS, BIOLOGICS and RADIOTRACERS

N/A

1. **Identification of Drug, Biologic or Radiotracer:** What is (are) the **name(s)** of the drug(s) biologic(s) or radiotracer(s) being used? Identify whether FDA approval has been granted and for what indication(s).

All protocols which utilize a drug, biologic or radiotracer **not** approved by, but regulated by, the FDA, or a radiotracer regulated by the RDRC, must provide the following information:

- a. What is the Investigational New Drug (IND) **number** assigned by the FDA?
- b. Who holds the IND?
- c. All protocols which utilize a radiotracer not approved by, but regulated by the FDA must provide the IND number: _____

Alternatively, use of the investigational radiotracer may be under RDRC/RSC oversight: (check if appropriate) _____

For all investigational radiotracers, attach a copy of the RDRC/RSC application (for radioisotopes used in the PET Center, PET Center personnel may complete this step)

Go to <http://rsc.med.yale.edu/login.asp?url=myApps.asp>. When you have logged in, complete the application and attach a copy to this submission.

Alternatively, an **exemption from IND filing requirements** may be sought for a clinical investigation of a drug product that is lawfully marketed in the United States. If there is no IND and an exemption is being sought, review the following categories and complete the category that applies (*and delete the inapplicable categories*):

Exempt Category 1

The clinical investigation of a drug product that is lawfully marketed in the United States can be exempt from IND regulations if all of the following are yes:

- i. The intention of the investigation is NOT to report to the FDA as a well-controlled study in support of a new indication for use or to be used to support any other significant change in the labeling for the drug. Yes No
- ii. The drug that is undergoing investigation is lawfully marketed as a prescription drug product, and the intention of the investigation is NOT to support a significant change in the advertising for the product. Yes No
- iii. The investigation does NOT involve a route of administration or dosage level or use in populations or other factor that significantly increases the risks (or decreases the acceptability of the risks)

- associated with the use of the drug product. Yes No
- iv. The investigation will be conducted in compliance with the requirements for institutional (HIC) review and with the requirements for informed consent of the FDA regulations (21 CFR Part 50 and 21 CFR Part 56). s No
- v. The investigation will be conducted in compliance with the requirements regarding promotion and charging for investigational drugs. Yes No

Exempt Category 2 (all items i, ii, and iii must be checked to grant a category 2 exemption)

- i. The clinical investigation is for an *in vitro* diagnostic biological product that involves one or more of the following (check all that apply):
- Blood grouping serum
 - Reagent red blood cells
 - Anti-human globulin
- ii. The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and
- iii. The diagnostic test is shipped in compliance with 21 CFR §312.160.

Exempt Category 3

- The drug is intended solely for tests in vitro or in laboratory research animals if shipped in accordance with 21 CFR 312.60

Exempt Category 4

- A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND.

2. **Background Information:** Provide a description of previous human use, known risks, and data addressing dosage(s), interval(s), route(s) of administration, and any other factors that might influence risks. If this is the first time this drug is being administered to humans, include relevant data on animal models.
3. **Source:** a) Identify the source of the drug or biologic to be used.
- b) Is the drug provided free of charge to subjects? Yes No
If yes, by whom?
4. **Storage, Preparation and Use:** Describe the method of storage, preparation, stability information, and for parenteral products, method of sterilization and method of testing sterility and pyrogenicity.

Check applicable Investigational Drug Service utilized:

YNHH IDS

CMHC Pharmacy

PET Center

Other:

Yale Cancer Center

West Haven VA

None

Note: If the YNHH IDS (or comparable service at CMHC or WHVA) will not be utilized, explain in detail how the PI will oversee these aspects of drug accountability, storage, and preparation.

5. Use of Placebo: **Not applicable to this research project**

If use of a placebo is planned, provide a justification which addresses the following:

1. Describe the safety and efficacy of other available therapies. If there are no other available therapies, state this.
- b. State the maximum total length of time a participant may receive placebo while on the study.
- c. Address the greatest potential harm that may come to a participant as a result of receiving placebo.
- d. Describe the procedures that are in place to safeguard participants receiving placebo.

6. Use of Controlled Substances:

Will this research project involve the use of controlled substances in human subjects?

Yes No *See HIC Application Instructions to view controlled substance listings.*

If yes, is the use of the controlled substance considered:

Therapeutic: The use of the controlled substance, within the context of the research, has the potential to benefit the research participant.

Non-Therapeutic: *Note, the use of a controlled substance in a non-therapeutic research study involving human subjects may require that the investigator obtain a Laboratory Research License. Examples include controlled substances used for basic imaging, observation or biochemical studies or other non-therapeutic purposes. See Instructions for further information.*

7. Continuation of Drug Therapy After Study Closure **Not applicable to this project**

Are subjects provided the opportunity to continue to receive the study drug(s) after the study has ended?

Yes If yes, describe the conditions under which continued access to study drug(s) may apply as well as conditions for termination of such access.

No If no, explain why this is acceptable.

B. DEVICES

N/A

1. Are there any investigational devices used or investigational procedures performed at Yale-New Haven Hospital (YNHH) (e.g., in the YNHH Operating Room or YNHH Heart and Vascular Center)? Yes No *If Yes, please be aware of the following requirements:*

- a. A YNHH New Product/Trial Request Form must be completed via EPIC: **Pull down the Tools tab in the EPIC Banner, Click on Lawson, Click on “Add new” under the New Technology Request Summary and fill out the forms requested including the “Initial Request Form,” “Clinical Evidence Summary, “ and attach any other pertinent documents. Then select “save and submit” to submit your request;** and
- b. Your request must be reviewed and approved **in writing** by the appropriate YNHH committee before patients/subjects may be scheduled to receive the investigational device or investigational procedure.

2. What is the name of the device to be studied in this protocol?

Has this device been FDA approved? Yes No

If yes, state for what indication.

3. **Background Information:** Provide a description of previous human use, known risks, and any other factors that might influence risks. If this is the first time this device is being used in humans, include relevant data on animal models.

4. **Source:**

a) Identify the source of the device to be used.

b) Is the device provided free of charge to subjects? Yes No

5. What is the PI’s assessment of risk level (significant or non-significant) associated with the use of the device?

Significant Risk (SR) Device Study: A study of a device that presents a potential for serious risk to the health, safety, or welfare of a participant and 1) is intended as an implant; 2) is used in supporting or sustaining human life; or otherwise prevents impairment of human health; 3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or 4) otherwise presents a potential for serious risk to the health, safety, or welfare of a participant.

Significant Risk Devices require an Investigational Device Exemption (IDE) issued by the FDA.

What is the **IDE number** assigned by the FDA?

Did the FDA approve this IDE as **Category A** (experimental/investigational) or as **Category B** (non-experimental/investigational)?

Who holds the IDE?

Non-Significant Risk (NSR) Device Study: A study of a device that does not meet the definition for a significant risk device and does not present a potential for serious risk to the health, safety, or welfare of participants. Note that if the HIC concurs with this determination, an IDE is not required.

6. **Abbreviated IDE or Exempt IDE:** There are abbreviated requirements for an IDE and there also are exemptions to the requirement for an IDE. *See the criteria in the HIC Application Instructions, Section VI.B.4 at http://www.yale.edu/hrpp/resources/docs/100FR1aHICProtocol_Application_Instructions5-25-11.pdf to determine if these pertain to this study.*

Abbreviated IDE or Exempt IDE – *If criteria set forth in the HIC Application Instructions are met, copy and paste the completed relevant section from the Instructions into this application.*

7. **Investigational device accountability:**

- a. State how the PI, or named designee, ensures that an investigational device is used only in accordance with the research protocol approved by the HIC, and maintains control of the investigational device as follows:

Maintains appropriate records, including receipt of shipment, inventory at the site, dispensation or use by each participant, and final disposition and/or the return of the investigational device (or other disposal if applicable):

Documents pertinent information assigned to the investigational device (e.g., date, quantity, batch or serial number, expiration date if applicable, and unique code number):

Stores the investigational device according to the manufacturer's recommendations with respect to temperature, humidity, lighting, and other environmental considerations:

Ensures that the device is stored in a secure area with limited access in accordance with applicable regulatory requirements:

Distributes the investigational device to subjects enrolled in the IRB-approved protocol:

SECTION VII: RECRUITMENT/CONSENT AND ASSENT PROCEDURES

1. **Targeted Enrollment: Give the number of subjects:**

- a. Targeted for enrollment at Yale for this protocol 100_
b. If this is a multi-site study, give the total number of subjects targeted across all sites
N/A

2. **Indicate recruitment methods below.** Attach copies of any recruitment materials that will be used.

- | | | |
|--|---|-------------------------------------|
| <input type="checkbox"/> Flyers | <input type="checkbox"/> Internet/Web Postings | <input type="checkbox"/> Radio |
| <input type="checkbox"/> Posters | <input type="checkbox"/> Mass E-mail Solicitation | <input type="checkbox"/> Telephone |
| <input type="checkbox"/> Letter | <input type="checkbox"/> Departmental/Center Website | <input type="checkbox"/> Television |
| <input type="checkbox"/> Medical Record Review | <input type="checkbox"/> Departmental/Center Research Boards | <input type="checkbox"/> Newspaper |
| <input type="checkbox"/> Departmental/Center Newsletters | <input type="checkbox"/> Web-Based Clinical Trial Registries | |
| <input type="checkbox"/> YCCI Recruitment database | <input type="checkbox"/> Clinicaltrials.gov Registry (do not send materials to HIC) | |

Other (describe): Patients with pleural effusion referred for thoracentesis will be invited to participate in this study. There is no specific advertising.

3. Recruitment Procedures:

a. Describe how potential subjects will be identified.

Any patient who needs thoracentesis as part of their routine medical care is eligible for this study.

b. Describe how potential subjects are contacted.

The study will be described to each patient at the time of the consent for the procedure.

c. Who is recruiting potential subjects?

Recruitment will be performed by Jonathan Puchalski, MD; Michal Senitko, MD; Kyle Bramley, MD; Kelsey Johnson PA and Rachel Southard APRN. All persons obtaining consent have experience with procedural consent.

4. Screening Procedures

a. Will email or telephone correspondence be used to screen potential subjects for eligibility prior to the potential subject coming to the research office? Yes No

b. If yes, identify below all health information to be collected as part of screening and check off any of the following HIPAA identifiers to be collected and retained by the research team during this screening process.

HEALTH INFORMATION TO BE COLLECTED:

HIPAA identifiers:

Names

All geographic subdivisions smaller than a State, including: street address, city, county, precinct, zip codes and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly-available data from the Bureau of the Census: (1) the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people, and (2) the initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.

Telephone numbers

Fax numbers

E-mail addresses

Social Security numbers

Medical record numbers

Health plan beneficiary numbers

Account numbers

All elements of dates (except year) for dates related to an individual, including: birth date, admission date, discharge date, date of death, all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older

Certificate/license numbers

Vehicle identifiers and serial numbers, including license plate numbers

Device identifiers and serial numbers

Web Universal Resource Locators (URLs)

Internet Protocol (IP) address numbers

Biometric identifiers, including finger and voice prints

Full face photographic images and any comparable images

Any other unique identifying numbers, characteristics, or codes

5. Assessment of Current Health Provider Relationship for HIPAA Consideration:

Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?

- Yes, all subjects
 Yes, some of the subjects
 No

If yes, describe the nature of this relationship.

The patients scheduled for thoracentesis will be asked to participate in this study. The PI and research staff will have a medical history of all patients based on the inherent relationship required for medical procedures

6. Request for waiver of HIPAA authorization: (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.)

Choose one:

- For entire study
 For recruitment purposes only
 For inclusion of non-English speaking subject if short form is being used

- i. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data;
- ii. If requesting a waiver of **signed** authorization, describe why it would be impracticable to obtain the subject's signed authorization for use/disclosure of this data;

By signing this protocol application, the investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

7. Required HIPAA Authorization: If the research involves the creation, use or disclosure of protected health information (PHI), separate subject authorization is required under the HIPAA Privacy Rule. Indicate which of the following forms are being provided:

- Compound Consent and Authorization form
 HIPAA Research Authorization Form

- 8. Consent Personnel:** List the names of all members of the research team who will be obtaining consent/assent.

Consent will be obtained by Jonathan Puchalski, MD; Michal Senitko, MD; Kyle Bramley, MD; Kelsey Johnson PA and Rachel Southard, APRN. All persons obtaining consent have experience with procedural consent.

- 9. Process of Consent/Assent:** Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.

At the time of outpatient or inpatient consult visit for thoracentesis, the study will be described to each patient. Only English speaking patients with a normal mental status will be enrolled.

Thoracentesis will be offered regardless to subjects' participation in the study. The procedure will be done in a standardized way.

- 10. Evaluation of Subject(s) Capacity to Provide Informed Consent/Assent:** Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.

All persons obtaining consent have experience with procedural consent and are trained to evaluate decision making capacity of the patients.

- 11. Documentation of Consent/Assent:** Specify the documents that will be used during the consent/assent process. Copies of all documents should be appended to the protocol, in the same format that they will be given to subjects.

The consent form as appended in Appendix 3 will be used to consent patients to participate in the study.

- 12. Non-English Speaking Subjects:** Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. If enrollment of these subjects is anticipated, translated copies of all consent materials must be submitted for approval prior to use.

N/A

12(a) As a limited alternative to the above requirement, will you use the short form* for consenting process if you unexpectedly encounter a non-English speaking individual interested in study participation and the translation of the long form is not possible prior to intended enrollment?

Note* If more than 2 study participants are enrolled using a short form translated into the same language, then the full consent form should be translated into that language for use the next time a subject speaking that language is to be enrolled.

Several translated short form templates are found on our website at: <http://www.yale.edu/hrpp/forms-templates/biomedical.html>. If the translation of the short form is not available on our website, then the translated short form needs to be submitted to the IRB office for approval via amendment prior to enrolling the subject. ***Please review the guidance and presentation on use of the short form available on the HRPP website.***

If using a short form without a translated HIPAA Research Authorization Form, please request a HIPAA waiver in the section above.

13. **Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed consent, or a full waiver of consent, depending on the study.** If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.

- Not Requesting a consent waiver**
- Requesting a waiver of signed consent**
- Requesting a full waiver of consent**

A. Waiver of signed consent: (Verbal consent from subjects will be obtained. **If PHI is collected, information in this section must match Section VII, Question 6)**

- Requesting a waiver of signed consent for Recruitment/Screening only**

If requesting a waiver of signed consent, please address the following:

a. Would the signed consent form be the only record linking the subject and the research?

Yes No

b. Does a breach of confidentiality constitute the principal risk to subjects?

Yes No

OR

c. Does the research activity pose greater than minimal risk?

Yes ***If you answered yes, stop. A waiver cannot be granted.*** Please note:

Recruitment/screening is generally a minimal risk research activity

No

AND

d. Does the research include any activities that would require signed consent in a non-research context? Yes No

- Requesting a waiver of signed consent for the Entire Study** (Note that an information sheet may be required.)

If requesting a waiver of signed consent, please address the following:

a. Would the signed consent form be the only record linking the subject and the research?

Yes No

b. Does a breach of confidentiality constitute the principal risk to subjects?

Yes No

OR

c. Does the research pose greater than minimal risk? Yes *If you answered yes, stop. A waiver cannot be granted.* No

AND

d. Does the research include any activities that would require signed consent in a non-research context? Yes No

B. Full waiver of consent: (No consent from subjects will be obtained for the activity.)

Requesting a waiver of consent for Recruitment/Screening only

a. Does the research activity pose greater than minimal risk to subjects?

Yes *If you answered yes, stop. A waiver cannot be granted.* Please note:

Recruitment/screening is generally a minimal risk research activity

No

b. Will the waiver adversely affect subjects' rights and welfare? Yes No

c. Why would the research be impracticable to conduct without the waiver?

d. Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date?

Requesting a full waiver of consent for the Entire Study (Note: If PHI is collected, information here must match Section VII, question 6.)

If requesting a full waiver of consent, please address the following:

a. Does the research pose greater than minimal risk to subjects?

Yes *If you answered yes, stop. A waiver cannot be granted.*

No

b. Will the waiver adversely affect subjects' rights and welfare? Yes No

c. Why would the research be impracticable to conduct without the waiver?

d. Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date?

SECTION VIII: PROTECTION OF RESEARCH SUBJECTS

Confidentiality & Security of Data:

a. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research?

Medical information as outlined in the Data Collection Tool (Appendix 3) will be collected. Data will be collected by interview and medical record abstraction. Medical record abstraction data will be directly entered into the data management software. All data will be entered with an ID code and no personal identifiers will be stored on computers. Consent Forms and contact information will be stored separately in locked file cabinets that will only be accessible by study staff.

b. How will the research data be collected, recorded and stored? Data will be collected from the patient's chart by investigators and research staff and will be recorded in Data Collection Tool. Data will be stored in secured server.

c. How will the digital data be stored? CD DVD Flash Drive Portable Hard Drive Secured Server Laptop Computer Desktop Computer Other

d. What methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the subject's participation in the study?

Do all portable devices contain encryption software? Yes No

If no, see <http://hipaa.yale.edu/guidance/policy.html>

e. What will be done with the data when the research is completed? Are there plans to destroy the identifiable data? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured.

Data will be stored in Secured Server.

f. Who will have access to the protected health information (such as the research sponsor, the investigator, the research staff, all research monitors, FDA, Yale Cancer Center Data and Safety Monitoring Committee (DSMC), SSC, etc.)? (please distinguish between PHI and de-identified data)

Only investigators and research staff will have access to the protected health information.

g. If appropriate, has a [Certificate of Confidentiality](#) been obtained? N/A

h. Are any of the study procedures likely to yield information subject to mandatory reporting requirements? (e.g. HIV testing – reporting of communicable diseases; parent interview - incidents of child abuse, elderly abuse, etc.). Please verify to whom such instances will need to be reported.

No.

SECTION IX: POTENTIAL BENEFITS

Potential Benefits: Identify any benefits that may be reasonably expected to result from the research, either to the subject(s) or to society at large. (Payment of subjects is not considered a benefit in this context of the risk benefit assessment.)

The potential benefit we expect from the study is to determine if there is a population of patients with pleural effusion who would benefit from using manual drainage rather than vacuum drainage.

SECTION X: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. **Alternatives:** What other alternatives are available to the study subjects outside of the research?

Patient will have thoracentesis done regardless of participating in the study.

2. **Payments for Participation (Economic Considerations):** Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.

No payments will be made to participating subjects.

3. **Costs for Participation (Economic Considerations):** Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.

There will be no extra cost to subjects participating in the study.

4. **In Case of Injury:** This section is required for any research involving more than minimal risk.

a. Will medical treatment be available if research-related injury occurs? N/A

b. Where and from whom may treatment be obtained? N/A

c. Are there any limits to the treatment being provided? N/A

d. Who will pay for this treatment? N/A

e. How will the medical treatment be accessed by subjects? N/A