

The Use of Optison Echocardiography Contrast in the
Detection of Left Atrial Appendage Thrombus with
Transesophageal Echocardiography

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Protocol Summary

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University of Utah IRB #:	IRB_00058561
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Background and Introduction

Accurate determination of the presence or absence of left atrial appendage (LAA) thrombus has a large impact on the clinical course of patients with atrial fibrillation or ischemic stroke and has large financial implications as well. Misdiagnosing the presence of LAA thrombus can lead to unnecessarily cancelled procedures (cardioversion and atrial fibrillation ablation) and potentially hazardous, unnecessary changes in clinical care (such as prolonged Coumadin anticoagulation). Missing LAA thrombus can result in continuation of cardioversion or atrial fibrillation ablation procedures at a time when there is higher risk of subsequent embolic stroke.

The University of Utah is home to the CARMA Center (Comprehensive Arrhythmia Research and Management) and is a high volume center for the treatment of atrial fibrillation. Many of these patients require transesophageal echocardiography (TEE) performed by our echocardiography laboratory prior to cardioversion or atrial fibrillation ablation procedures, and most of them undergo cardiac MRI studies as well. There is opportunity to enroll most of these patients in our proposed study. There has been essentially no work published about the use of echo contrast materials in TEE (other than agitated saline), particularly the use of Optison. Thus, we will be exploring a new field in echocardiography and echo contrast.

Purpose and Objectives

Our objective is to determine if using Optison echocardiography contrast increases sensitivity and specificity of detecting left atrial appendage thrombus in transesophageal echocardiography studies as opposed to standard 2D and 3D TEE imaging without the use of echo contrast.

Study Population

Age of Participants: 18+

Sample Size:

At Utah:	500
All Centers:	500

Inclusion Criteria:

Patients referred to the University of Utah Echocardiography Lab for for a transesophageal echocardiography (TEE) will be included in the study.

Subjects must be

- (1) > 18 years old
- (2) Able to provide consent
- (3) Indicated for TEE as a standard clinical procedure to evaluate cardiac health status

Exclusion Criteria:

Patients will be excluded for meeting the contraindications for Optison administration.

1. Known right-to-left, or bi-directional cardiac shunts.
2. Hypersensitivity to perflutren, blood, blood products or albumin.
3. Women who pregnant (since Optison may have effects on the fetus that are currently unknown).
4. Removal of Left Atrial Appendage.
5. Not able to provide Informed Consent.

Design

Prospective Clinical Research

Study Procedures

Recruitment/Participant Identification Process:

Potential participants for the study will be recruited from the Cardiology/Electrophysiology (EP) clinic during normally scheduled clinic visits. No other recruitment procedures (phone call / recruitment letters) will be used in this study. In-person contact by the PI /sub-I or other cardiologists (made aware of study by word of mouth) who refer their patients into the study will be the primary mode of recruitment. Prior to approaching the subject, the PI/research staff will conduct a chart review to confirm that the potential subject fits the eligibility criteria for the study.

Potential participants will be screened by the PI/Co-PI and other cardiologists who are aware of the study and refer the subject to the study. When the patient is being seen in the clinic for a routine follow-up visit, if the patient fits with all the eligibility criteria during chart review (prior to clinician seeing the patient), then the PI/sub-I/ clinician will approach the potential participant and discuss the study with them.

If the potential subject is interested in participation, the PI/Co-PI will consent the subject or call the Study Coordinator (SC) /Clinical Research Manager (CRM) to conduct the informed consent process with the participant. The PI/sub-I may be present during the process. However, if they are not able to be physically present, the SC /CRM will report to the PI/Sub-I immediately after consent to confirm the appropriate conduct of the process.

Informed Consent:

Description of location(s) where consent will be obtained:

University of Utah Hospital and Clinics, specifically the ECHO clinic.

Description of the consent process(es), including the timing of consent:

Patients will be approached at the University of Utah Hospital and Clinics on the day that they are already scheduled to undergo their standard of care TEE for their specific clinical problem. If patients are found to fit with the eligibility criteria outlined for the study, they will be approached and the study discussed with them. The clinician may consent the patient themselves, or call the study coordinator / clinical research manager to conduct the consent process. The person who is conducting the consent process will provide a detailed description of the study, the study-related procedures, time that the participant will have to spend for the study, the benefits and risks of participation, the costs and compensations involved in the study, the contacts for the PI, IRB and the research participant advocate. The University of Utah's stand on research-related injuries will be explained and the participant's questions will be answered. The participant will be provided with a copy of the consent form and given as much time as they require to go over the consent and to make an informed decision. Participants who require extra time will be given the option to call the study team back. All this information and the consent process will be documented in the staff notes section of each participant's folder. If the study coordinator / clinical research manager conduct the informed consent process, then the PI / sub-I who identified the eligible participant will sign the informed consent form right below the signature of the person who conducted the informed consent process after confirmation that the informed consent process was completed in an appropriate and satisfactory manner.

Procedures:

1. Patients will be identified and pre-screened using electronic medical records. Final screening and consent will be conducted in clinic, generally on the day that they were already scheduled to undergo a standard of care TEE for their specific clinical condition.
2. If the patient is found to be eligible based on inclusion/exclusion criteria, the investigator and/or study coordinator will approach them and explain the study.
3. If the patient agrees to participate and provides informed consent, then we fill out an enrollment sheet, create their study file and gather the necessary information from the patient.

4. Patient will then undergo their scheduled TEE without optison contrast. The clinician will determine whether it is possible to clearly identify the presence or absence of left atrial appendage thrombus from the standard TEE images.

5. If the presence or absence of thrombus cannot be clearly determined with standard TEE, the clinician will administer optison contrast and then continue the examination to try to obtain a conclusive result.

6. Data will then be collected, including ECHO reports, cardiac MRI reports, medical history, adverse events etc. as compiled during the procedure visit. Data will only be collected if the patient receives Optison during the TEE procedure.

7. Three months following the TEE, the medical record of the patients that received Optison will be reviewed for any additional adverse events or thrombii detection via other method. The end point of the study will be the collection of pertinent data, three months following TEE.

Statistical analysis will be conducted utilizing the statistical resources available to us through the CCTS.

Optison will be used for its approved indications (as an ultrasound contrast agent) and in compliance with the U.S. Food and Drug Administration (FDA) safety guidelines. Optison is a contrast agent used in ECHO studies, and does not involve any radiation/radioactive substances. The ECHO procedure does not expose patients to ionizing radiation, and Optison or ultra sound contrast agents do not contain dye or increase a patient's risk of nephrotoxicity. Ultrasound contrast agents are safe and completely radiation-free diagnostic imaging tools.

Procedures performed for research purposes only:

Administration of Optison echocardiography contrast and re-imaging using standard 2 and 3D techniques will be the research-related procedure. The participant will be undergoing the Echocardiography for clinical indications and additional echo with optison contrast will be provided along with participant's clinical echo.

Statistical Methods, Data Analysis and Interpretation

Descriptive presentation of continuous variables and chi-squared / Fisher-exact tests for frequency variables. Since this study is a descriptive, pilot study to see utility of Optison in echocardiography, the contrast agent will be used in 100 patients to see at what

frequency the contrast agent is able to identify LAA thrombi. The contrast agent is already being used in echo, we are using it as it is approved by the FDA. A future larger RCT study will be construed using this pilot data.

While we intend to gather optison TEE data from 100 subjects, our enrollment cap has to be higher than that. Only those subjects whose standard TEE's are inconclusive will be administered optison, and subjects will need to be consented prior to the start of the standard TEE. Because only a minority of enrolled patients will receive optison, we plan to enroll 500 patients.