**On-pump intraoperative echocardiography (OPIE)**


Principal Investigator: Daniel G. Swistel, M.D.
Associate Professor, Department of Cardiothoracic Surgery
Department of Cardiothoracic Surgery
NYU Langone Medical Center
530 First Avenue, Suite 9V
New York, NY 10016
Tel: (212) 263-5979
Email: daniel.swistel@nyumc.org

Sub-Investigator: Mark V. Sherrid, MD, FACC, FASE
Director, Hypertrophic Cardiomyopathy Program
Professor of Medicine
NYU Langone Medical Center
530 1st Avenue,
New York, NY 10016
Tel: (646) 501-0568
Email: mark.sherrid@nyumc.org



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**1. STUDY DESIGN**

In this pilot study we will use an ultrasound probe that is currently clinically used to assess pituitary anatomy, the Hitachi-Aloka high resolution pituitary transducer to measure left ventricular (LV) septal thickness during cardiopulmonary bypass in the performance of surgical septal myectomy. We will assess if septal thickness can be visualized during the procedure and if it is likely to improve the efficacy and safety of the procedure. The probe has FDA clearance for a variety of intra-operative surgical procedures but will be off-label for this cardiac surgical protocol. Attached is a memo from the manufacturer stating the device does not meet criteria of a "significant risk device" as per 21 CFR 812.3(m).

**2. OBJECTIVES**

The objective of this research project is to assess the utility an ultrasound probe that is currently clinically used to assess pituitary anatomy, the Hitachi-Aloka high resolution pituitary transducer to measure left ventricular (LV) septal thickness during cardiopulmonary bypass in the performance of surgical septal myectomy.

**3. RATIONALE**

There is currently no way to monitor the depth of surgical septal myectomy during the on-pump period in the OR. This is because the heart is empty of blood and transesophageal echocardiography (TEE) imaging is impossible. Also epicardial imaging is impossible. The brochure (attached separately) shows the probe we believe will let us image the septum. It may make the surgical procedure more accurate and decrease complications of "too little myectomy" or "too much myectomy". Both can decrease the need for reoperation which is currently a risk of myectomy 1-2%. The probe is a sterile one-time-use device. The transducer itself is 2.9 mm in diameter. We have tested the probe in a simulation similar to that we will encounter during Hypertrophic Cardiomyopathy (HCM) surgery and there was excellent visualization of muscular thickness with 1:1 correlation with conventionally measured muscular wall and the ultrasound visualized thickness.

**4. METHODS AND PROCEDURES**

Subjects will be volunteer patients with hypertrophic cardiomyopathy who will be undergoing myectomy from the HCM Program. Before cardiopulmonary bypass the anterior septal thickness at the point of mitral-septal contact will be measured by TEE in 120 degree view. The distance from the aortic annulus of this location will also be noted. With OPIE the PI will measure this thickness at the

site of mitral-septal contact as assessed by the location of the contact lesion (callous) and confirmed by the cm below the aortic annulus. After resection the residual thickness of the septum will be measured both by OPIE and by post-cardiopulmonary bypass TEE. The thickness of the surgical specimen will be measured. The differences between the OPIE and TEE measured septal thicknesses provide the primary data points for the statistical analysis.

We estimate that the cardiopulmonary bypass time of the OPIE will be prolonged 3 minutes. This may be offset by faster myectomy time gained by more confidence of septal thickening. Length of stay should not be prolonged.

We will enroll 10 subjects in this pilot study. Subject participation will be complete after their hospitalization for surgery. No follow-up visits are necessary, outside of the routine post-op care.

In general, results from studies, which use data, collected as part of this research will be preliminary, and the clinical implications of any findings may not be understood for years. Therefore, individual study results will not be disclosed to the patient and/or his or her healthcare provider(s). Data will be stored in a database housed within the Department of Cardiothoracic Surgery. The above mentioned database will be stored until the end of the study in a password protected secure computer server accessible only by the principle investigator, co-investigators and research staff listed for this project.

**Sample size and data analysis:**

Each of the 10 patients will have 4 measurements(OPIE & TEE before cardiopulmonary bypass and OPIE & TEE after cardiopulmonary bypass) in the septum using two techniques (TEE and OPIE Ultrasound Probe). Primary outcome is the the difference between TEE measured septal thickness and the OPIE measured thickness before and after cardiopulmonary bypass. Center tendency parameters(mean, standard deviation) will be reported for each outcome. For example: we will report the mean and standard deviation for the difference between TEE measured septal thickness and OPIE measured thickness before and after cardiopulmonary bypass. The OPIE and TEE measurements will be compared both before and after cardiopulmonary bypass for each of the outcome as well. Accurate myectomy residual thickness is vital for success of this operation. The clinical utility of the OPIE probe will be shown if there is a >= 2mm difference (either greater than or less than) between any single OPIE measurement and the TEE measurement either before cardiopulmonary bypass or after cardiopulmonary bypass. Given the critical nature of the assessment of septal thickness, even a 2-4 mm difference in just one patient (10% of patients) is deemed essential information.

**5. SUBJECTS POPULATION SELECTION**

Patients who are seen by in the Hypertrophic Cardiomyopathy (HCM) Clinic and will undergo surgical

myectomy for management of their HCM will be considered for this study.

### 5.1 Inclusion Criteria

All patients, inclusive of male and female and all racial/ethnic origins, age 18 or older who are scheduled to receive a septal myectomy.

### 5.2 Exclusion Criteria

Less than 18 years of age

### 5.3 Subject Withdrawal Criteria

Subjects may withdraw consent from the research and revoke authorization for the use and disclosure of protected health information at any time. Subjects may not revoke authorization for uses or disclosures that have already made or must make to complete analyses or report data from research in progress. If the subject withdraws consent but does not revoke authorization, the subject's health information may continue to be disclosed for research as described in this protocol.

To withdraw consent and/or revoke authorization, subjects may contact the Principle Investigator in writing.

## 6. POTENTIAL BENEFITS TO SUBJECTS

There will not be an immediate benefit to subjects enrolled in this study. This study seeks to improve the ability to monitor the depth of surgical septal myectomy during the on-pump period in the OR. This might lead to improved clinical care in the future.

## 7. POTENTIAL RISKS TO SUBJECTS

There are minimal risks to subjects. Although health information that is collected will be kept in a secure server, there is always the risk that it may be accessed by individuals not associated with this study. Efforts will be made to protect confidentiality as outlined in this protocol. We estimate that the cardiopulmonary bypass time of the OPIE will be prolonged by 3 minutes. This may be offset by faster myectomy time gained by more confidence of septal thickening. This potential increased confidence in performing the myectomy by knowing the thickness of the septum highlights the equipoise that provides the rationale for this research. Given the usual cardiopulmonary bypass time for HCM surgery

of 60 minutes a 3 minute prolongation of this time is clinically not significant. Therefore we believe that the OPIE procedure poses no clinical risk for the patients. However, we will monitor for risk by the procedures specified below. The device is small and is used under direct visualization without the need for any pressure against tissue, so there is no risk of perforation. The device is a sterile single-use object and therefore would have no additional risk of infection. The interior of the left ventricle, where the device would be used is full of blood and therefore there could not be any bleeding risk.

**8. Subject Recruitment and Compensation**

Subjects will be drawn from patients seen at the Hypertrophic Cardiomyopathy (HCM) Clinic and those scheduled to undergo septal myectomy cardio surgery within the New York University Langone Medical Center. These subjects will be under the care of both the PI and the co-investigator. The study will be described by the PI and consent will be obtained > 1 day after this initial description. Consent will be obtained by the PI or co-investigators in a private setting either in the PI office or co-investigators or in the hospital room. Informed consent will be obtained prior to the surgery. The subject will be given adequate time to read the consent form, ask questions, and consider study participation. All questions and/or clarifications, which the subject may have or need, will be addressed to their satisfaction before the consent is signed. Most of the patient's data will be gathered from the medical chart; however, the subject may be asked some questions regarding changes or latest updates in his/her current medications. Informed consent for this study, scanned into EPIC, will be confirmed at the time-out prior to surgery.

This study provides no additional cost to a subject. There are no interventions or procedures involved in this study that would be billable to the subject other than the standard of care. Subjects will not receive compensation for their participation in this project.

**9. STUDY MANAGEMENT AND PERSONNEL**

The Principle Investigator for this research project will analyze and store the data. The Principle investigator will store the data on a secure NYU server on a locked computer, where access will be restricted to the PI and other members of the study.

All Investigators and study personnel involved in this study have completed the appropriate human subjects' research training (NYU CITI module).

## 10. CONFIDENTIALITY

Data collected will also be de-identified and stored in the database using coded identification as well. The data will be linked to the subject's medical record number. Access to the key code linking the coded identification to the patient's medical record number will be restricted to the principle investigator, co-investigators and research staff. All data, including the key code, will be stored on a secure, password protected computer server housed in the Department of Cardiothoracic Surgery.

Data provided to requesting researchers will be stripped of identifiers. Only the principle investigator, co-investigators and research staff listed on this protocol will have access to the key code linking the specimen and data to the subject's medical record number. The de-identified information allowed to investigators will always be subject to prior IRB review and approval.

### Data Safety Monitoring Plan

Dr. Muhamed Saric, Director of Echocardiography will be responsible for monitoring the conduct and safety of the study. Dr. Saric is Associate Professor, Department of Medicine and Clinical Director, Non-Invasive Cardiology.

Dr. Saric will review the chart and clinical course of the patients to confirm safety of the performance of the protocol. He will review safety after every other case. All complications will be noted and he will evaluate whether there is relation to the OPIE: mortality, infection, cerebrovascular events. Complications will be determined to be either definitely related, possibly related, or definitely unrelated.

If there is a definite or possible relation of a complication to the OPIE, the adverse event will be reported to the IRB within a week of the operation.

It there is an adverse event that is deemed definitely related to the OPIE the study will be stopped pending comprehensive review.

Reports from Dr. Saric will be forwarded to the IRB after 6 cases and after 10 cases.

## 11. REFERENCES

Knappe UJ et al. Ultrasound-assisted microsurgery for Cushing's Disease. Exp Clin Endocrinol Diabetes 2011;119:191-200.