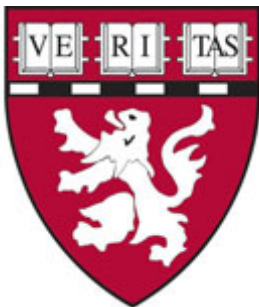


# ROMICAT II

ROMICAT II – Rule out Myocardial Ischemia/Infarction by  
Computer Assisted Tomography

## Operations Manual

Version 1.5  
Date: 05/20/2011



# Table of Contents (Operations Manual)

---

SIGNATURE APPROVAL.....	5
CONTACT LIST .....	6
STUDY PAGER .....	8
1.0 HOW TO PERFORM THE STUDY .....	10
1.1 Study Set-Up.....	10
1.2 Recruitment, Screening, Consent.....	10
1.2.1 Screening Process and Screen Failures .....	10
1.2.2 Consent .....	11
1.2.3 Advice for CRCs when explaining the risk benefit ratio of cardiac CT with respect to radiation exposure and iodinated contrast administration to subjects during the consenting process .....	12
1.2.4 Biomarker Ancillary Study .....	12
Goals .....	12
Procedures.....	13
1.3 Randomization .....	14
1.3.1 SOC.....	14
1.3.2 Cardiac CT.....	14
1.4 Follow-up.....	16
1.4.1 48-72 Hour Follow up after ED discharge .....	16
1.4.2 28 Day Follow up.....	16
1.4.5 Voluntary Withdrawal (by Subject):.....	16
1.4.6 Tips for optimizing Follow-up completion rates.....	17
1.5 Study Website .....	17
2.0 GLOSSARY OF ADJUDICATED EVENTS .....	17
3.0 DATA SAFETY MONITORING BOARD (DSMB) .....	20
4.0 Adverse & Serious Adverse Event Reporting Guidelines .....	21
4.1 Adverse Events: .....	21
4.2 Serious Adverse Events .....	21
5.0 Data Monitoring Plan.....	24
5.1 Training in Protection of Human Subjects.....	24
5.2 Site Monitoring Plan.....	24
6.0 Data Management .....	26
6.1 eCRF Data Entry.....	26
6.2 Randomization .....	26
6.3 Queries & Data Correction .....	29
7.0 Cost Data Retrieval Plan.....	30
8.0 Record Keeping .....	32
8.1 Study Tracking Logs.....	32
9.0 CASE REPORT FORMS (CRFs).....	36
9.1 GENERAL COMMENTS .....	37
9.2 SUBJECT & SITE ID NUMBERS .....	39
9.3 Screening Database CRF Instructions .....	41
SCREENING FORM.....	46
Demographics .....	46
Inclusion/Exclusion Criteria .....	46
9.4 Main Database CRF Instructions .....	48
SCREENING FORM.....	53
Demographics .....	53
Inclusion/Exclusion Criteria .....	53
ED Evaluation Timeline .....	56

Randomization & Consent.....	56
<i>CRF Page 6 – Medical History Form.....</i>	<i>57</i>
MEDICAL HISTORY FORM.....	59
Medical History .....	59
Pain Characteristics/Symptoms .....	59
<i>CRF Page 7 – ED Visit Form .....</i>	<i>60</i>
<i>CRF Page 8 - Laboratory Results.....</i>	<i>60</i>
<i>CRF Page 9 - Biomarker Testing.....</i>	<i>60</i>
ED VISIT FORM.....	62
Initial ED Vital Signs.....	62
ED Medications .....	62
Laboratory Results .....	62
Troponin Values.....	63
Biomarker Testing .....	63
<i>CRF Page 10 – ECG Form.....</i>	<i>64</i>
ECG FORM .....	64
Initial 12-Lead ECG Interpretation.....	64
<i>CRF Page 11 – CT Test Form .....</i>	<i>65</i>
CT FORM.....	67
CCTA Technical Assessment .....	67
<i>CRF Page 11 - CT Test Subject Physician Reading Form .....</i>	<i>69</i>
<i>CRF Page 12- Nuclear Imaging .....</i>	<i>71</i>
DIAGNOSTIC TESTING FORM .....	74
Nuclear Imaging.....	74
<i>CRF Page 13- Stress Echocardiogram.....</i>	<i>76</i>
Stress Echocardiogram.....	78
<i>CRF Page 14- Transthoracic Echocardiogram (rest).....</i>	<i>80</i>
Transthoracic Echocardiogram (rest).....	81
<i>CRF Page 15- Exercise ECG stress test (Non Imaging Only).....</i>	<i>82</i>
Exercise ECG Stress Test (Non-imaging only) .....	84
<i>CRF Page 16 - Cardiac Catheterization .....</i>	<i>86</i>
Cardiac Catheterization.....	87
<i>CRF Page 17 – Patient Discharge Information .....</i>	<i>88</i>
PATIENT DISCHARGE FORM.....	90
<i>CRF page 18 – 48-72 hour Follow Up .....</i>	<i>92</i>
48-72 HOUR FOLLOW UP FORM.....	95
48-72 HOUR FOLLOW UP SUPPLEMENT FORM .....	96
28 DAY FOLLOW UP FORM.....	101
28 DAY FOLLOW UP SUPPLEMENT FORM .....	103
<i>CRF page 20 – Adverse Event Form .....</i>	<i>105</i>
ADVERSE EVENT FORM.....	106
<i>CRF Page 21 – SERIOUS ADVERSE EVENT FORM .....</i>	<i>107</i>
SERIOUS ADVERSE EVENT FORM .....	109
<i>CRF page 22 – Protocol Deviation Form.....</i>	<i>111</i>
<i>CRF page 23 – Protocol Violation Form .....</i>	<i>111</i>
PROTOCOL DEVIATION FORM .....	112
PROTOCOL VIOLATION FORM .....	113
Appendix A: Physician Information Sheet .....	114
Appendix B: IRB Tracking Log .....	116
Appendix C: Protocol Deviation/Violation Tracking Log.....	117

Appendix D: SAE/AE Tracking Log.....	118
Appendix E: Note to File .....	119
Appendix F: Participation Information/Locator Sheet .....	120
Appendix G: Screen Failures Log (template) .....	122
Appendix H: Participant Contact Log.....	123
Appendix I: Troponin Values .....	124
Appendix J: Combination drugs for Diabetics.....	125
Appendix K: SPECT Examination Protocol.....	128
Pharmacologic Stress .....	136
Appendix L: Cardiac CT.....	139
Appendix M: Stress Testing – Echocardiography .....	143
Appendix N: Stress Testing – Exercise treadmill test (ETT) .....	150
Appendix O: Patient Interview Source Document.....	154

## **SIGNATURE APPROVAL**

---

This document has completed a final peer review and is understood and accepted by the following:

---

Signature of PI/CRC

Institution

Date

This document has been prepared by:

---

Pearl Zakrotsky  
Project Manager, ROMICAT II  
Massachusetts General Hospital

This document has been approved by:

---

Udo Hoffmann, MD, MPH  
Principal Investigator, ROMICAT II  
Massachusetts General Hospital

## CONTACT LIST

---

### **Principal Investigator Clinical Coordinating Center**

Udo Hoffmann, MD, MPH  
Massachusetts General Hospital  
Cardiac MR PET CT Program  
165 Cambridge Street, Suite 400  
Boston, MA 02114  
Phone: 617-726-5954  
Fax: 617-724-4152  
Email: [uhoffmann@partners.org](mailto:uhoffmann@partners.org)

### **Co-Investigator**

James Udelson, MD  
Tufts Medical Center  
800 Washington Street  
Boston, MA 02111  
Email: [judelson@tuftsmedicalcenter.org](mailto:judelson@tuftsmedicalcenter.org)

### **Co-Investigator Clinical Coordinating Center**

Quynh Truong, MD, MPH  
Massachusetts General Hospital  
165 Cambridge Street, Suite 400  
Boston, MA 02114  
Phone: 617-726-0798  
Fax: 617-724-4152  
Email: [qtruong@partners.org](mailto:qtruong@partners.org)

### **Principal Investigator Data Coordinating and Statistical Center (DCSC)**

David Schoenfeld, PhD  
Massachusetts General Hospital  
50 Staniford St, Suite 560  
Boston, MA 02114  
Phone: 617-726-6111  
Fax: 617-724-9878  
Email: [dschoenfeld@partners.org](mailto:dschoenfeld@partners.org)

### **Principal Investigator Clinical Events Committee**

Stephen Wiviott, MD  
Brigham and Women's Hospital  
75 Francis Street  
Boston, MA 02115  
Phone : 617-278-0145  
Fax : 617-734-7329  
Email : [swiviott@partners.org](mailto:swiviott@partners.org)

**Principal Investigator Cost Effectiveness and Decision Analysis (DACE)**

Scott Gazelle, MD, MPH, PhD

Massachusetts General Hospital

Phone: 617-726-4047

Email: [scott@mgh-ita.org](mailto:scott@mgh-ita.org)

**Cardiovascular Imaging Core Lab**

Project Manager

Nathan Sciortino

Massachusetts General Hospital

25 New Chardon Street, Suite 400B

Boston, MA 02114

Phone: 617-643-5308

Fax: 617-643-0111

Email: [nsciortino@partners.org](mailto:nsciortino@partners.org)

**Study Project Manager**

Pearl Zakrotsky

Massachusetts General Hospital

165 Cambridge Street, Suite 400

Boston, MA 02114

Phone: 617-643-0954

Fax: 617-724-4152

Email: [pzakrotsky@partners.org](mailto:pzakrotsky@partners.org)

## STUDY PAGER

---

We have established a study pager for immediate response to medical issues related to SAEs or **major** administrative or regulatory issues. If you need to call the pager, please dial 617-726-2000, pager # 13247. Between 09:00 and 17:00, the Project Manager (PM), Pearl Zakrotsky will respond within 1 hour of receipt and will triage medical issues to the study PI. After 17:00, please leave a voicemail at 617-643-0954 and your call will be returned as soon as possible.



**LIST OF ABBREVIATIONS**

ACS	Acute Coronary Syndrome
AE	Adverse Event
AMI	Acute Myocardial Infarction
CABG	Coronary Artery Bypass Graft
CAC	Coronary Artery Calcium
CAD	Coronary Artery Disease
CCC	Clinical Coordinating Center
CEC	Clinical Events Committee
COPD	Chronic Obstructive Pulmonary Disease
CP	Chest Pain
CK-MB	Creatine kinase-MB
CRF	Case Report Form
CRC	Clinical Research Coordinator
CT	Computed Tomography
DCSC	Data Coordinating and Statistical Center
DSMB	Data Safety Monitoring Board
ED	Emergency Department
FOV	Field Of View
HIPAA	The Health Insurance Portability and Accountability Act
HR	Heart Rate
ICF	Informed Consent Form
IRB	Institutional Review Board
IV	Intravenous
LBBB	Left bundle branch block
MACE	Major Adverse Cardiovascular Event
MI	Myocardial infarction/Ischemia
MSCT	Multi-slice Computed Tomography
NHLBI	National Heart, Lung, and Blood Institute
NIH	National Institute of Health
NTG	Nitroglycerin
PCI	Percutaneous coronary intervention
PI	Principal Investigator
PM	Project Manager
SAE	Serious Adverse Event
SOB	Shortness of Breath
SOC	Standard of Care
SOP	Standard Operations Procedure
SPECT	Single Proton Emission Computed Tomography
TIMI	Thrombolysis in Myocardial Infarction
ULN	Upper Limit of Normal
VT	Ventricular Tachycardia

## **1.0 HOW TO PERFORM THE STUDY**

---

The following are recommendations on how to perform the study. Each site will vary depending on their individual flow of patient care, unique departments, and standard operating procedures.

### **1.1 Study Set-Up**

The site PIs are encouraged to foster inter-departmental collaboration to ensure enrollment.

1. **Site Preparation for Conduction of the Trial:** At the 1st clinical investigator's meeting during the initiation period the DCSC will train participating site personnel in protocol specific procedures and data capture, including a review of Good Clinical Practices, HIPAA regulations, and protection of human subjects. The clinical sites will be trained by the PM/monitor of the DCSC to comply with reporting requirements in order to promote standardization of study related procedures.
2. **Protocol and Form Development:** The DCSC will guide sites in the preparation and submission of the local Ethical Boards and will keep track of approvals and amendments. The DCSC will develop all research protocols and forms for the trial and will review and test the Electronic Data Capturing System. During the initiation period, the DCSC will provide the updated study protocol (as approved by the NIH Clinical Trials Protocol Review Committee) to the clinical sites and will assist the clinical sites to obtain IRB approval.
3. **Set IT infrastructure:** The DCSC will develop and distribute a communication network (email list server, private network web site) and a data acquisition system where each site is responsible for entering its own data into an online Electronic Data Capture application (EDC). The EDC system consists of an electronic CRF, which will be tested during the initiation period, and components for remote data entry, remote monitoring, query system, audit trail, and data extract. To reach this purpose the DCSC will digitize of research protocol, informed consent form, and other study specific forms.

### **1.2 Recruitment, Screening, Consent**

The following is an overview of patient flow through the ED and suggestions that may be beneficial for your site.

#### **1.2.1 Screening Process and Screen Failures**

All patients presenting to the Emergency Department with chest pain or its equivalent (inclusion criterion #1) will be included in the REDCap Screening Database. For specific data entry instructions, please see Section 9.0 of this manual. Inclusion criterion #1: "Participant must have at least five minutes of chest pain or equivalent (chest tightness; pain radiating to left, right, or both arms or shoulders, back, neck, epigastrium,

jaw/throat; or unexplained shortness of breath, syncope/presyncope, generalized weakness, nausea, or vomiting thought to be of cardiac origin) at rest or during exercise within 24 hours of ED presentation, warranting further risk stratification, as determined by an ED attending.”

If subjects do not meet the remainder of the inclusion criteria, they will be considered Screen Failures. If subjects meet an exclusion criterion, they will also be considered Screen Failures.

Each site should keep a confidential list of Screen Failures including: Subject ID #, First Name, Last Name, and MRN. A template log can be found in Appendix G. The same information should be maintained for those subjects who are enrolled. These logs should be stored in a secure, locked location. If stored electronically, the logs should be password protected.

A report will be generated by the DCSC, providing sites with feedback concerning their enrollment status.

### **1.2.2 Consent**

The research team at each participating site typically includes the ED physicians, cardiologists, and radiologists as well as the clinical research coordinator and CT technologists. The principal investigator is responsible for timely enrollment and completeness of site-designated data submission. All clinical sites will perform screening Monday through Friday during daytime business hours (i.e.: 9am-5pm). However, specific screening hours can vary by site. Potential subjects will be identified by research coordinator/study nurse staff as soon as possible after ED presentation, usually after the initial ED evaluation consisting of: ECG, physical examination, clinical symptoms and presentation, review of immediate and past medical history, and screening for eligibility based on a checklist providing inclusion and exclusion criteria.

Eligible subjects will be approached and, if the subject considers participation, the Clinical Research Coordinator (CRC) will describe the rationale of the study and the study procedures with associated risks and benefits. A study physician/study nurse/CRC will speak directly with an ED physician caring for the patient to obtain an assessment of pretest probability for ACS and will verify that the ED physician feels that further observation or diagnostic testing is warranted in this patient.

If the subject agrees and further testing or observation is planned as SOC, key study personnel (typically a study physician or the attending ED physician) will review the study procedures, as well as all potential risks and discomforts and explain to the subject that he/she has the opportunity to decline or cease participation in the study at any time. Key study personnel will offer to answer any remaining questions and consent the subject.

Subjects can be consented but not randomized before the first troponin test result is available. Patients whose initial troponin level is markedly elevated (as defined prospectively by local standard of care – specified in Appendix I) will not be randomized.

Subjects can be consented but not randomized before a negative pregnancy test is available. Subjects with a positive pregnancy test will not be randomized. Subjects who are consented but not randomized will not be included in the intent to treat population.

Once consented, the CRC should obtain contact information for the subject using the Participant Information/Locator Sheet (Appendix F). If the subject should have any concerns about providing contact information, the CRC should remind him/her that all information will be kept completely confidential and will be stored separately from his/her Identification Number.

If a patient is consented but not randomized due to a markedly elevated troponin result or positive pregnancy test that patient will be considered a screen failure and should be captured under the screening database in REDCap. The reason for exclusion should be marked as “other” with an explanation of why in the text field. The site should keep the signed consent form on file. Every effort should be made to make sure that eligible patients are randomized once consented. If a situation arises where it is not possible for a patient to be randomized, the site should contact the CCC for further guidance.

### **1.2.3 Advice for CRCs when explaining the risk benefit ratio of cardiac CT with respect to radiation exposure and iodinated contrast administration to subjects during the consenting process**

#### Radiation Advice for CRCs if asked by subjects during consent:

Cardiac CT uses x-rays to make a 3-D picture of your heart. X-rays give off radiation. The radiation amount from a CT scan is about ~10-20% of the annual acceptable exposure. We will do everything possible to reduce the radiation dose you receive.

#### Renal advice for CRCs if asked by subjects during consent:

During your CT scan, you will receive contrast dye to let us to see the blood vessels of your heart. Contrast dye leaves your body through your kidneys. In rare cases contrast can decrease your kidney function but this is unlikely if your kidneys are healthy, which we just checked. You will be advised to drink as much water as possible after the scan to make sure the dye is flushed out of your body.

(Only for Diabetics on metformin or glucophage) If you have diabetes and are taking metformin (or glucophage), you will have to stop taking that drug for two days after the CT scan to prevent any side effects. See Appendix J for a list of combination drugs that contain metformin and/or glucophage.

### **1.2.4 Biomarker Ancillary Study**

#### **Goals**

The Biomarker ancillary study is an optional study that will be presented to subjects during the consent process. The goals of the study are to determine the most effective complimentary use of diagnostic testing for ACS and prediction of MACE, to determine

the behavior of high-sensitive troponin (hs-TnI) in the early stages of ACS and in those without ACS but “low level positives”, and to determine the association between hs-TnI and coronary artery disease by CT, left ventricular function (CT and echo), myocardial perfusion (CT and SPECT), and ECG changes. The blood samples will be analyzed for hs-TnI, standard TnI, and other analytics pending.

## Procedures

For all randomized subjects who consent to participate in the Biomarker Ancillary Study:

Time points for blood draws:

- 1) Baseline (T=0)
- 2) 90-155 minutes
- 3) 210-300 minutes or at discharge from ED, whichever is earlier

Tubes for the blood draws:

- 1) One serum (red top) – full draw
- 2) One EDTA (purple top) – full draw
- 3) One lithium-heparin (typically green) – full draw

Phlebotomy is to be done per standard research methods. Following phlebotomy, samples will be allowed 30-60 minutes to clot. Samples should be centrifuged for 15 minutes at an RPM of 2000-2500. It is ideal that the centrifuge is refrigerated. However, this is not necessary if a refrigerated centrifuge is not available at your site. Once spun, samples will be aliquoted into the provided daughter tubes (1 single daughter tube per colored tube with corresponding colored label attached; the remaining white label is for the phlebotomy form). This will equal 3 daughter tubes per blood draw for a total of 9 daughter tubes per subject. Following this, the aliquots should be stored at -80 degrees C, **until end of the study**, at which time the entire batch will be mailed on dry ice to the Clinical Coordinating Center. Dry ice and packaging materials will be the responsibility of the site. HazMat labeling is also the responsibility of the site.

NOTE: If tubes cannot be spun and aliquoted after each individual blood draw, they may be refrigerated, spun and aliquoted collectively after the 3<sup>rd</sup> blood draw.

All blood draw materials will be provided to sites. Each site will receive an initial shipment of 100 "specimen drawing kits" containing:

- 1) Three (3) 12 x75 mm polypropylene tubes with caps.
- 2) Label sheets with printed barcodes for tubes: two (2) identical barcode labels for each tube [one for the tube; one for the phlebotomy record]. See Section 9.0 of this manual for specific instructions for completing the eCRFs.

To order additional specimen drawing kits, contact the PM, Pearl Zakrotsky by email at [pzakrotsky@partners.org](mailto:pzakrotsky@partners.org). Please allow 2 weeks for shipment of additional kits. Phlebotomy records should be kept in the subject's binder.

## **1.3 Randomization**

After the subject has been consented, he/she will be randomized to either SOC or cardiac CT. For specific randomization procedures, refer to section 6.2 Randomization.

### **1.3.1 SOC**

Subjects will be evaluated according to each hospital's specific standard of care protocol to evaluate and manage patients with acute chest pain. Typically this will include:

- Past and current medical history
- Physical examination
- ECG
- Cardiac Biomarker (Troponin and CK-MB)
- Routine blood testing

All subjects will undergo each hospital's standard rule out myocardial ischemia protocol. This protocol typically consists of observation and monitoring including serial ECGs and repeated cardiac biomarker measurements as well as noninvasive stress test (often imaging based) to evaluate for myocardial ischemia. Sites will also perform routine nuclear perfusion imaging (SPECT) at rest and stress, and/or stress echocardiography, and/or exercise treadmill test (ETT).

Depending on results, subjects may undergo additional non-invasive testing (coronary angiography), and/or coronary revascularization during their hospital stay.

**Note:** Subjects may undergo cardiac CT as part of SOC, but only as a secondary diagnostic test.

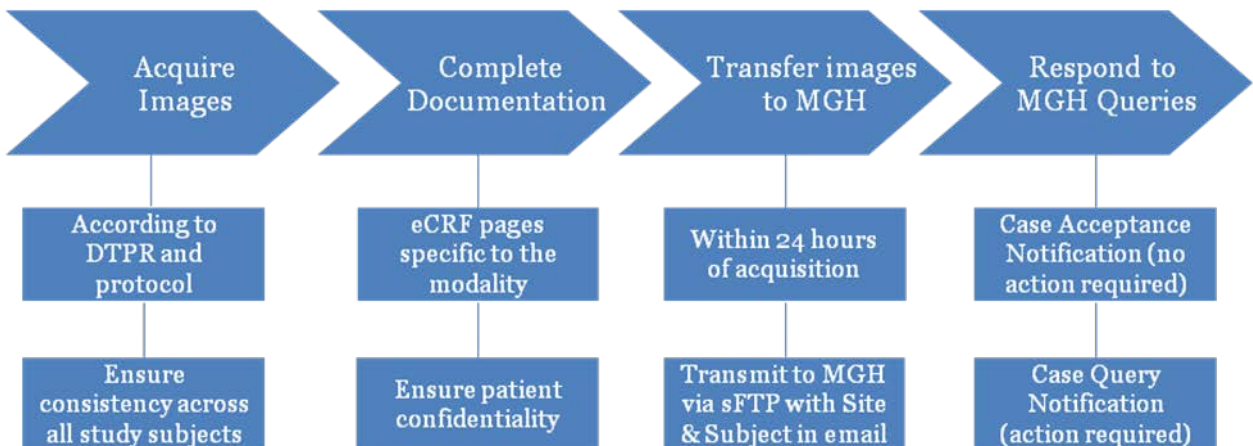
### **1.3.2 Cardiac CT**

Subjects will receive cardiac CT as a standard first diagnostic test. Caregivers will make any clinical decisions (e.g. need for further evaluation or admission) based upon their cumulative clinical assessment PLUS the results from the cardiac CT scan at their own discretion.

1. The Investigator Site will refer subjects to the Imaging Center for CT. CT exams must be conducted by trained Technologists in accordance with the ROMICAT II 'Diagnostic Testing Protocol Recommendations' (DTPR).
2. The Investigator Site, or a designee in the Imaging Center, will complete the 'CCTA Technical Assessment' page on the electronic case report form.
3. Imaging datasets must be anonymized before submission to CVIC according to the following guidelines:
  - i. Patient Name replaced with study ID
  - ii. Date of Birth and patient age may remain, if permitted by local regulation, and serve as a key identifier for the record
  - iii. Medical Record number replaced with a 7-digit standard code of zeros (e.g. 0000000)

- iv. Any other protected patient information removed from any additional fields
4. The complete and anonymized CT datasets will be sent to CVIC via secure File Transfer Protocol (sFTP) within 2 business days. CVIC will provide sFTP Data Transfer Instructions for details regarding submission of images. All images must be submitted in DICOM format.
  5. After CT images are received at CVIC, a Clinical Research Associate will confirm image set completeness and proper labeling/anonymization of images. Subject and time point information will be verified against eCRF submitted from site to Data Coordinating Center. A quality control (QC) will be performed to verify that the Study Imaging Procedures were followed. If the imaging associate finds an artifact that could impair the ability to interpret images, the nature of the artifact will be discussed with CVIC medical staff before being escalated to external study personnel.
  6. CVIC will notify the Imaging Centers of the results of the QC of each dataset submitted in the form of either a Case Acceptance or a Case Query Notification.
  7. The Case Acceptance Notification informs the Study Coordinator and Imaging Center that CT imaging for the time point is complete and of acceptable quality. Any deviation from the guidelines should be discussed with CVIC in advance. Any change in parameters should be pre-approved and noted on the Image Record Forms.
  8. If a Case Query Notification is issued, the notification will indicate actions that need to be taken by the Imaging Center. The site is required to resolve the query and/or send the missing/discrepant information to CVIC within 2 business days. If resolution of the query cannot be completed, the site will be required to notify CVIC (via phone or fax) within the two-business day time frame. This notification must include a definitive date for query resolution.

Once the query has been resolved, a Case Acceptance Notification will be issued to notify the Investigator Site and Imaging Center that the images are now complete and of acceptable quality.



## **1.4 Follow-up**

Subjects will be contacted by the CRC up to 4 times post discharge from the ED by phone as described below.

### **1.4.1 48-72 Hour Follow up after ED discharge**

Subjects who are discharged from the ED within 24 hours of presentation (for both randomization arms) will be contacted via telephone by the CRC between 48 and 72 hours after discharge to avoid ascertainment bias. During this call, subjects will be interviewed to determine whether they have had any recurrent symptoms suggestive of myocardial ischemia and/or whether they needed to seek further medical attention following their emergency department visit. If these phone attempts (4 attempts) at 48 and 72 hours are not successful, a final attempt will be made at 96 hours to contact the subject. If a subject is discharged on a Thursday, the 48-72 hour phone call may be extended to 96 hours. In the rare circumstance that a subject is discharged on a Thursday and the following Monday is a holiday, the follow-up call can be made during the next working business day. This will be recorded in a subject's contact log, which is kept at the local site (see Appendix H).

### **1.4.2 28 Day Follow up**

All subjects will be interviewed via a telephone call by the CRC at 28 days post ED discharge (+4 weeks) to determine the occurrence of MACE and healthcare utilization using a standardized questionnaire. Request of medical records for source documents will be obtained by the CRC and sent to the DCSC. All cases of recurrent chest pain, hospital admissions, and diagnostic testing must be collected by the CRC and will be verified by review of medical records by the CEC.

The CRC will send a reminder letter to participants two weeks prior to the 28-day follow up phone call.

**Note:** A reminder letter will be sent by the CRC to participants two weeks prior to the two year follow up phone call. **A minimum of five (5) phone attempts** will be made to contact each participant. If unable to contact the participant by phone, mortality will be assessed online using the SSDI website <http://ssdi.rootsweb.ancestry.com/> by the CRC.

### **1.4.5 Voluntary Withdrawal (by Subject):**

The subject who wishes to withdraw from the study in the absence of a medical need, as determined by the site PI is considered as a voluntary withdrawal. The subject must notify us of his/her withdrawal. Any written notification will be considered valid, including email. A copy of this note will be placed in the subject's source binder (see Section 8.0 Record Keeping).

This will only be considered a withdrawal if the subject explicitly says that he/she doesn't want his/her data used or that he/she does not want to ever be contacted again. You do not need to explain this option to him/her when he/she refuses their assigned treatment, as there is no risk to him/her of data collection.



### 1.4.6 Tips for optimizing Follow-up completion rates

- Try to get as much contact information as possible from the participant during the consenting process.
- Remind the participant that this information will be kept confidential and will not be shared with anyone else.
- Make sure to give the participant a study brochure (see template on the study website) with contact information and encourage him/her to call you if any of their contact information changes.
- Try calling the participant at different times of day and days of the week.
- If you still cannot reach the participant after making 5 attempts, try calling one of the locators listed on the Participant Information/Locator Sheet (see Appendix F).
- **Be persistent!**

## 1.5 Study Website

The most recent version of all study documents will be posted to the study website <http://www.romicat.org/>. The website will be updated on a regular basis. Study staff is therefore encouraged to visit the website often in order to see updated agendas, minutes, and news pertaining to the study. The website will also contain a Forum page in which study staff can post questions, comments, tips, and tricks.

### Login Information

Each staff member will receive an email containing a username and password for initial login. After initial log in, there will be a request to create a new password. Please visit the staff directory to make sure that all of the contact information is correct and up-to-date. If the contact information should change, please notify Pearl Zakrotsky at [pzakrotsky@partners.org](mailto:pzakrotsky@partners.org).

## **2.0 GLOSSARY OF ADJUDICATED EVENTS**

---

The Clinical Events Committee (CEC) will define and adjudicate efficacy and safety endpoints as well as serious adverse events in a consistent and unbiased manner throughout the entire course of the trial. Site will need to prepare relevant medical materials to be sent to the DCSC as described in Table 1: CEC Adjudication Forms Summary.

### Definitions

**Adverse events** are any unfavorable and unintended clinical events experienced by a study subject during his/her participation in the ROMICAT II trial. SAEs are defined as: 1) an out of hospital ACS in patients directly discharged from the ED, 2) death, 3) life-threatening event, 4) persistent or significant disability/incapacity, 5) an important clinical event that, in the PI's opinion, may jeopardize the subject's safety and may

require medical or surgical intervention to prevent one of the previously mentioned outcomes.

**Myocardial Infarction:** In subjects with no recent revascularization in whom normal biomarkers were never elevated or have been documented to return to normal after a qualifying (or recent) MI who meet the following criteria:

1. Typical cardiac biomarker rise and/or fall AND at least one of the following:
  - a) Ischemic discomfort at rest lasting  $\geq 10$  minutes
  - b) ECG changes indicative of ischemia (ST elevation  $\geq 0.1$  mV or ST depression  $\geq 0.05$  mV, or new T-wave inversions.

OR;

2. Development of new, abnormal Q waves ( $\geq 30$  msec in duration and  $\geq 1$  mm in depth) in  $>2$  contiguous precordial leads or  $\geq 2$  adjacent limb leads; or increase R amplitude in V1-V3 consistent with posterior infarction.

OR;

3. Pathologic findings of an acute MI
4. Sudden unexpected cardiac death, including cardiac arrest, often with symptoms suggestive of myocardial ischemia, accompanied by presumably new ST elevation, or new LBBB, or evidence of fresh thrombus in a coronary artery by angiography and/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood

In subjects with percutaneous coronary intervention within 48 hours, an elevation of CK-MB  $>3x$  ULN distinct from a prior event will be considered to be a procedural MI.

In subjects with CABG within 48 hours, an elevation of CK-MB  $> 10x$  ULN distinct from a prior event will be considered to be a procedural MI. For subjects with elevated cardiac biomarkers at the time of a suspected new event, the new event must be demonstrated to be distinct from a previous event including demonstration that cardiac biomarkers are falling and that the new event is associated with a rise in biomarkers of at least 50% above a the previous value.

For each MI identified by the CEC, a Type of MI will be assigned using the following guidelines:

Type 1: Spontaneous myocardial infarction related to ischemia due to a primary coronary event such as plaque erosion and/or rupture, fissuring, or dissection

Type 2: Myocardial infarction secondary to ischemia due to either increased oxygen demand or decreased supply, e.g. coronary artery spasm, coronary embolism, anemia, arrhythmias, hypertension, or hypotension

Type 3: Sudden unexpected cardiac death, including cardiac arrest, often with symptoms suggestive of myocardial ischemia, accompanied by presumably new ST elevation, or new LBBB, or evidence of fresh thrombus in a coronary artery by angiography and/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood

Type 4a: Myocardial infarction associated with PCI

Type 4b: Myocardial infarction associated with stent thrombosis as documented by angiography or at autopsy

Type 5: Myocardial infarction associated with CABG

**Unstable Angina:** An event not meeting the definition of myocardial infarction and with the following characteristics. Chest pain or anginal equivalent at rest or in accelerating pattern AND at least one of the following objective signs:

- a. New and/or dynamic ST-depression  $\geq 0.05$  mV, ST-elevation  $\geq 0.1$  mV, or symmetric T wave inversion  $\geq 0.2$  mV on a resting ECG.
- b. Definite evidence of ischemia on stress echocardiography, myocardial scintigraphy (e.g., an area of clear reversible ischemia), or ECG-only stress test (e.g., significant dynamic ST shift, horizontal or downsloping).
- c. Angiographic evidence of epicardial coronary stenosis of  $\geq 70\%$  diameter reduction and/or evidence for intraluminal arterial thrombus.
- d. Positive stress test without imaging resulting in increased anginal medication
- e. CT angiography showing  $> 50\%$  stenosis with regional LV dysfunction or  $> 70\%$  stenosis.

**Urgent Coronary Revascularization:** Ischemic discomfort or equivalent meeting the following criteria:

- a. Lasting  $\geq 10$  minutes at rest, or repeated episodes at rest lasting  $\geq 5$  minutes, considered to be myocardial ischemia upon final diagnosis

AND;

- b. Prompting coronary revascularization during an unscheduled visit to healthcare facility or during an unplanned (or prolonged) hospitalization for these symptoms.

### **3.0 DATA SAFETY MONITORING BOARD (DSMB)**

---

The DSMB consists of the following individuals:

- DSMB Chair: Robert Roberts, MD, FRCPC
- DSMB Member: Joseph P. Ornato, MD
- DSMB Member: Daniel Berman, MD
- DSMB Member: James Kirkpatrick, MD
- DSMB Member: Elisa T. Lee, PhD
- DSMB Executive Secretary: Nakela Cook, MD, MPH

The DSMB is an independent group advisory to the Director, NHLBI, and is required to provide recommendations about starting, continuing, and stopping the study. In addition, the DSMB is asked to make recommendations, as appropriate, to the NHLBI about:

- Efficacy of the study intervention (DSMB only)
- Benefit/risk ratio of procedures and participant burden
- Selection, recruitment, and retention of participants
- Adherence to protocol requirements
- Completeness, quality, and analysis of measurements
- Amendments to the study protocol and consent forms
- Performance of individual centers and core labs
- Participant safety
- Notification of and referral for abnormal findings

Meetings are usually held approximately twice a year, with additional meetings or conference calls scheduled as needed.

## 4.0 Adverse & Serious Adverse Event Reporting Guidelines

---

### 4.1 Adverse Events:

#### **Reportable Adverse Events**

Any untoward medical occurrence that occurs after randomization and prior to discharge from the ED should be evaluated by the site PI and reported to the DCSC by completing the electronic adverse event case report form within **24 hours**. Also, notify Pearl Zakrotsky within **24 hours** of knowledge of the event.

#### **Immediately Reportable Adverse Events**

Any adverse event that is judged by the site PI to be serious AND unexpected AND related to study procedures should be reported within **24 hours** of discovery of the event by phone or email to the PM, Pearl Zakrotsky. The local Institutional Review Board must also be notified in a timely manner.

#### **Coding AE terms:**

Use the following website as a resource for entering AE terms. The website will help ensure the standardization of coding AE terms.

<http://hedwig.mgh.harvard.edu/biostatistics/files/costart.html>

Any other AE which does not meet the above criteria should be entered electronically into REDCap using AE eCRF. As described in section 8, you also be faxing the SAE/AE Tracking Log to Pearl Zakrotsky every Monday. The fax number is listed on the SAE/AE Tracking Log form (Appendix D).

### 4.2 Serious Adverse Events

Serious adverse events are defined as cardiac ischemic events that occur between index hospitalization and 72 hours of hospital discharge. These may include, but are not restricted to:

- Death
- New ST elevation
- Elevated Biomarkers (troponin or CK-MB)
- New procedure related to cardiac ischemia
- Abnormal EKG
- Discharge Diagnosis of UAP/MI
- MACE within 72 hours of index hospitalization
- Major periprocedural complications
  - Bleeding
  - Stroke
  - Anaphylaxis
  - Renal Failure

All SAEs must be entered into the adverse event (SAE) eCRF. In addition, a copy of the relevant reports as listed in Table 1 (see below) must be sent to the DCSC. Also, notify Pearl Zakrofsky within **24 hours** of knowledge of the event.

SAEs will be adjudicated by the CEC to determine whether the event was or was not related to the study procedure. The study PI (Dr. Hoffmann) will report any SAEs deemed related to study procedure to the NIH and the DSMB within **15 business days**.

Investigators must also report Unanticipated Problems, regardless of severity, associated with the study procedures within **24 hours** to Pearl Zakrofsky. An unanticipated problem is defined as follows:

**Unanticipated Problem (UP):** any incident, experience, or outcome that meets all of the following criteria:

- Unexpected, in terms of nature, severity, or frequency, given the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and the characteristics of the subject population being studied;
- Related or possibly related to participation in the research, in this guidance document, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research;
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

In the event of a SAE or an immediately reportable AE, the sites should provide the DCSC with a packet containing the relevant medical record forms as outlined in Table 1.

Table 1: CEC Adjudication Forms Summary

<b>Case Report Forms (or summary report)</b>	<b>Source Documents*</b>
1. Hospitalization report (may not be applicable to some death events)  2. Event Report*, all appropriate pages will be sent.  3. Narrative for event	<p><b>Deaths</b></p> <ul style="list-style-type: none"> <li>a. Autopsy (if performed)</li> <li>b. Code summary (if available)</li> <li>c. Death/Hospital summary (if death occurred in-hospital)</li> </ul> <p><b>Cardiac Ischemic Events</b></p> <ul style="list-style-type: none"> <li>a. Admission History and Physical</li> <li>b. ECG tracings (prior to event, during event, and following event resolution)</li> <li>c. Cardiac biomarkers (all troponin/CK-MB results for hospitalization and prior 30 days) Record units, normal ranges, and myocardial necrosis and myocardial infarction reference limits)</li> <li>d. Other laboratory reports, if requested</li> <li>e. Procedure reports (Cardiac Catheterization, PCI, CABG)</li> </ul>

- |  |  |
|--|--|
|  | <ul style="list-style-type: none"><li>f. Other imaging reports (MRI, CTA, echocardiogram, Nuclear Medicine)</li><li>g. Discharge Summary</li></ul> <p><b>Cerebrovascular Events</b></p> <ul style="list-style-type: none"><li>a. Neurology Consult</li><li>b. Imaging reports (MRI, CT, or other imaging reports including transthoracic and/or transesophageal echocardiograms)</li><li>c. Discharge Summary</li></ul> <p><b>Coronary Revascularization Procedures</b></p> <ul style="list-style-type: none"><li>a. Procedure reports (Cardiac catheterization, PCI, CABG)</li><li>b. Cardiac biomarkers (all troponin/CK-MB results before and after procedure) Record units, normal ranges, and myocardial necrosis and myocardial infarction reference limits)</li><li>c. Discharge Summary</li></ul> <p><b>Bleeding Events</b></p> <ul style="list-style-type: none"><li>a. Admission history and physical</li><li>b. Laboratory Reports – CBC, bleeding and clotting time</li><li>c. Procedure Reports – (Transfusion, operative summary)</li><li>d. Discharge Summary</li></ul> <p><b>Renal Events</b></p> <ul style="list-style-type: none"><li>a. Admission History and Physical</li><li>b. Laboratory Reports – CBC, renal function (serum creatinine and eGFR)</li><li>c. Imaging Reports (CT including dose of contrast agent received, MRI, other imaging reports)</li><li>d. Discharge Summary</li></ul> <p><b>Anaphylaxis</b></p> <ul style="list-style-type: none"><li>a. Admission History and Physical</li><li>b. Laboratory Reports (CBC)</li><li>c. Imaging Reports</li><li>d. Procedure Reports (any intervention involving cardiovascular or respiratory support)</li><li>e. Discharge Summary</li></ul> |
|--|--|

## **5.0 Data Monitoring Plan**

---

All clinical sites will be visited by CCC and DCSC staff before and during the enrollment phase to ensure that the local research team is comfortable and familiar with all administrative, regulatory, scientific, and safety aspects of the study.

### **5.1 Training in Protection of Human Subjects**

Training in Protection of Human Subjects will be required from all site personnel. The DCSC will ensure site compliance by requesting a copy of a certificate of training completion prior to enrollment. The DCSC will recommend sites that do not regularly train their personnel in this area to complete the free, web-based course “Human Participant Protections Education for Research Teams” offered by the National Cancer Institute (<http://cme.cancer.gov/clinicaltrials/learning/humanparticipant-protections.asp>). A site will not be approved to start enrolling subjects until personnel’s certificates of training completion are provided to the DCSC. Safety of the participants in the trial is of paramount importance. Site monitoring, monitoring of each adverse event report as it occurs by a qualified clinician, an interim analysis, and the DSMB will assure safety of all subjects. Furthermore, the trial will be registered in accordance with previously published guidelines.

### **5.2 Site Monitoring Plan**

The DCSC has developed a monitoring plan to assess the progress of the study and to ensure that it is conducted in accordance with the protocol, GCP, and applicable local regulatory requirements. During the monitoring visit a member of the DCSC will verify that the rights and well-being of all participating human subjects are protected and the collected data are of the highest quality and integrity. The trial will conduct three different types of monitoring visits: a preoperational visit by the CCC, and an interim visit and closeout visit by the DCSC. Monitoring visits will take place during daytime on business days. They will be scheduled with the CRC and PI and their presence will be required at one point during the visit.

#### **5.2.1 Preoperational Visit:**

All clinical sites will receive a preoperational monitoring visit from the CCC by the end of the initiation period. The CCC will schedule the preoperational visit with the site PI and CRC during the first investigators’ meeting. A letter confirming the visit to the site PI and CRC stating the purpose of the visit will be sent. During this visit the CCC (PI, Co-PI) will ensure that the site set-up is suitable for study participation.

#### **5.2.2 Interim Monitoring Visit:**

All clinical sites will receive at least one interim monitoring visit from a DCSC monitor during the enrollment period. The DCSC monitor will contact the site at least 6 weeks prior to the visit. A letter confirming the visit to the site PI and CRC stating its purpose will be sent. At least two weeks prior to the visit, the DCSC monitor will notify the site CRC of all the documents that need to be available for the monitor upon arrival. In order



to determine if the site is conducting study in accordance with the protocol, GCP, and applicable local regulatory requirements, the DCSC monitor will: 1) review all Informed Consent Forms to verify proper procedures were followed, current version of IRB-approved form was used, and all signatures and dates were appropriately obtained. 2) Review a random sample (10 %) of enrolled subjects' source documents to verify eligibility, accuracy of data capture, and Adverse Event reporting. 3) Review all regulatory documentation to assure that all the required documents are present and, when applicable, appropriately submitted to the local IRB. Once interim monitoring visit is completed, the DCSC monitor will conduct a summary meeting with the PI and study personnel to review findings, site performance parameters, and any outstanding issues. If applicable, recommendations for improvement will be made. A written report listing an overall rating of items reviewed, based on the presence or absence of deficiencies found, and, if applicable, any corrective (remedial) plan will be completed and forwarded to the CCC for review within 14 business days of completion of the visit. Site personnel will receive a copy of the report approximately 2 weeks after completion of visit, once the CCC has reviewed it.

### **5.2.3 Close-Out Visit:**

All clinical sites will receive a close-out visit from the DCSC monitor. The purpose of this visit is to: 1. formally bring closure to the study at the site; 2. ensure that all data have been collected; 3. verify that the regulatory files are complete. The closeout monitoring visit will be scheduled after DCSC informs DCSC the site has completed all data capture and no data query remains unanswered or at the time the site PI is notified of the DCSC decision of terminating the site's participation in the study. The DCSC monitor will contact the site at least 6 weeks prior to the visit. A letter confirming the visit to the site PI and CRC stating its purpose will be sent. At least two weeks prior to the visit, the DCSC monitor will notify the site CRC of all the documents that need to be available for the monitor upon arrival. The closeout visit will be conducted as an interim monitoring visit. At the end of the visit, there would be a verbal communication of the findings to the PI and study personnel. A Close-Out Visit Report listing all findings and, if applicable, all outstanding issues will be completed by the DCSC monitor within 24 hours of the completion of the visit and forwarded to the CCC for review within 24 hours of completion of the visit. Site personnel will receive a copy of the report approximately 2 weeks after completion of visit, once the CCC has reviewed it.

## 6.0 Data Management

---

### 6.1 eCRF Data Entry

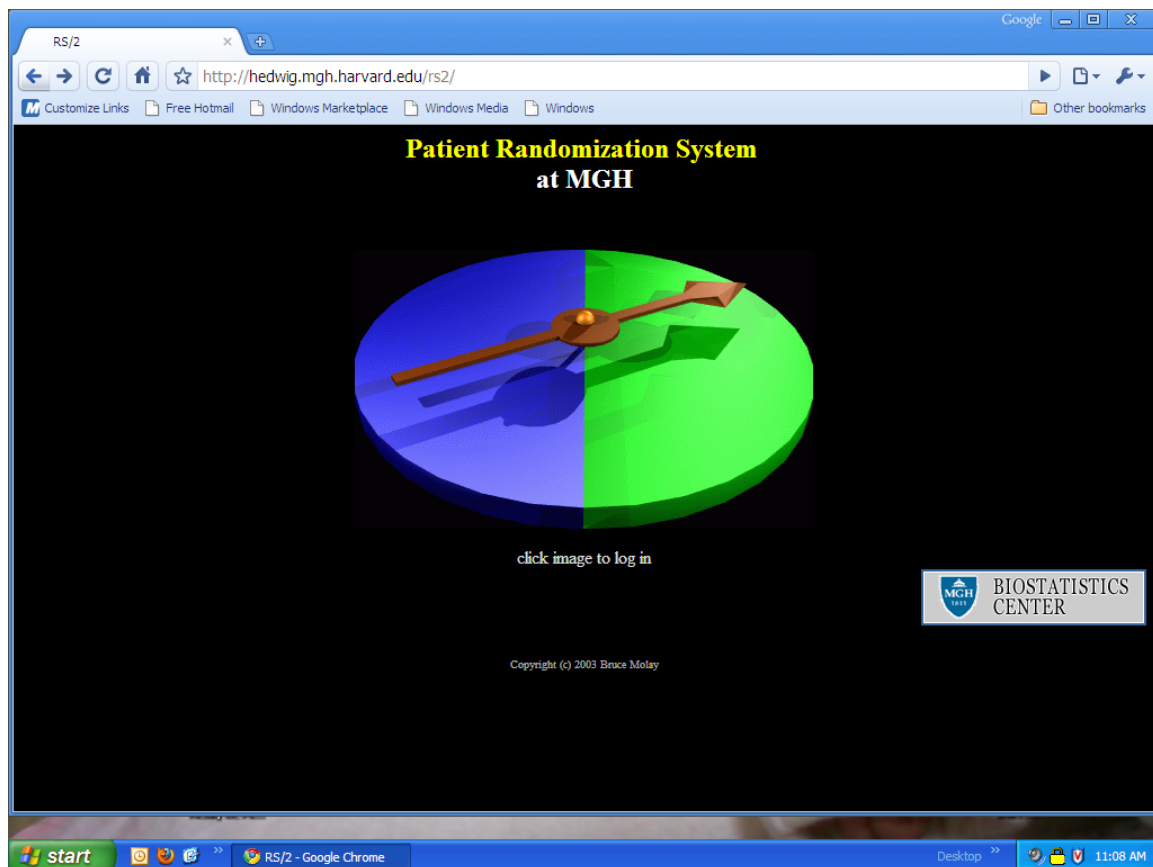
All data collected will be entered electronically by the CRCs into REDCap. Data entry should be completed within **30 days** of subject discharge.

### 6.2 Randomization

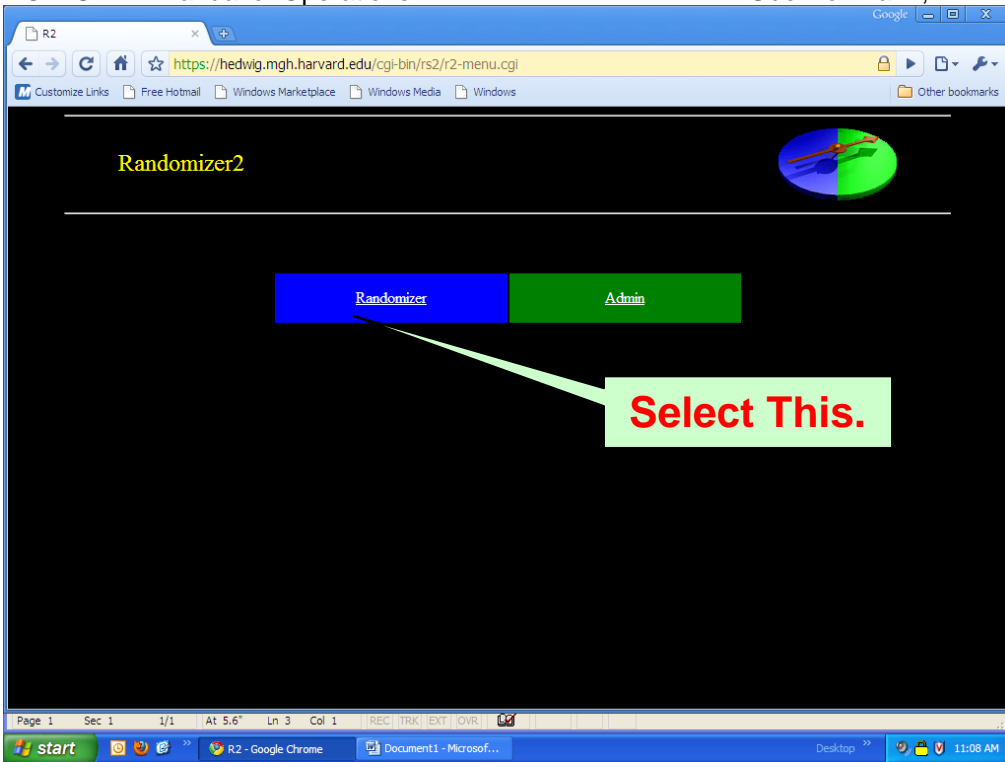
Randomization will be performed using the RS 2 software, which is accessible by the link: <http://hedwig.mgh.harvard.edu/rs2>

The CRC will be prompted to enter his/her username and password.

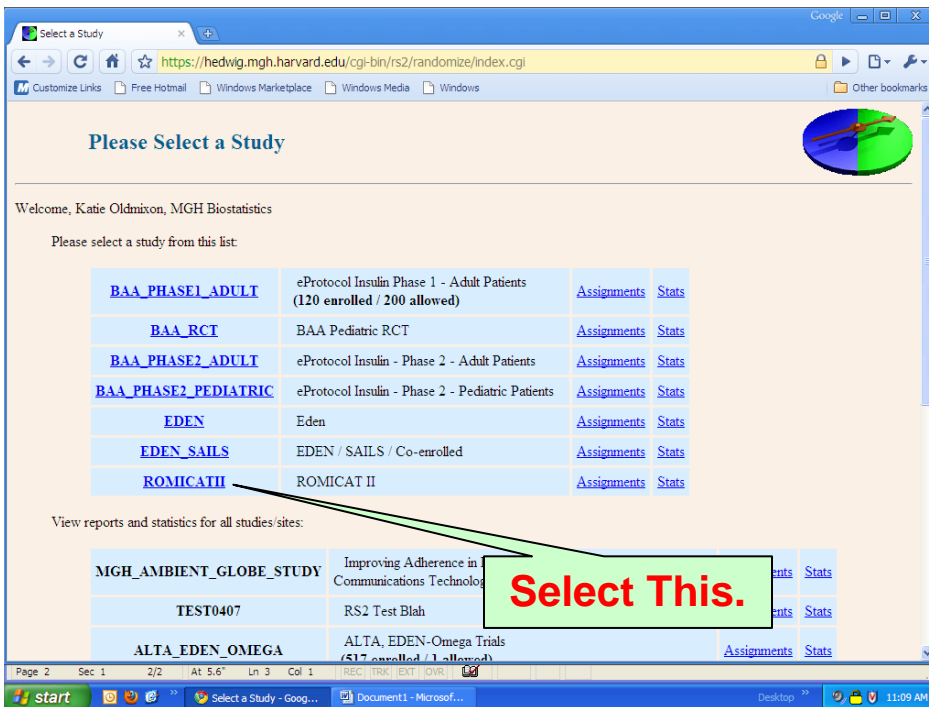
Below are screen shots of what the RS2 website will look like.



On the next screen, choose the box labeled “Randomizer”.



On the following screen, click on ROMICATII.



**Study romicatii**

Site: Katie Oldmixon, MGH Biostatistics  
Study: ROMICAT II

1. Please enter the patient id

2. Please enter the patients initials. If you wish not to enter the initials, please put a - in the field.

**Enter patient initials**

MGH_AMBIENT_GLOBE_STUDY	Improving Adherence in Hypertensive Patients - a novel use of Communications Technology	<a href="#">Assignments</a>	<a href="#">Stats</a>
TEST0407	RS2 Test Blah	<a href="#">Assignments</a>	<a href="#">Stats</a>
ALTA_EDEN_OMEGA	ALTA, EDEN-Omega Trials (517 enrolled / 1 Allowed)	<a href="#">Assignments</a>	<a href="#">Stats</a>

**Treatment Assignment**

Randomization Report for MGH BioStatistics

Date: Thu Mar 11 11:10:33 2010 (East Coast Time)  
PIN: 99906  
Study: romicatii  
Key:

Patient Initials: cfo  
Patient ID: 100001

Assignment

Randomization Number: RC999002  
Treatment: Standard of care

MGH_AMBIENT_GLOBE_STUDY	Improving Adherence in Hypertensive Patients - a novel use of Communications Technology	<a href="#">Assignments</a>	<a href="#">Stats</a>
TEST0407	RS2 Test Blah	<a href="#">Assignments</a>	<a href="#">Stats</a>
ALTA_EDEN_OMEGA	ALTA, EDEN-Omega Trials (517 enrolled / 1 Allowed)	<a href="#">Assignments</a>	<a href="#">Stats</a>

Next, a treatment assignment screen that records the date and time of randomization and the randomization code will be shown. Each participant will be assigned to either Interventional (CT) arm or Standard of care arm.

Shortly after randomization is complete, an email will be sent with this information to the CRC's email address. Please print a copy of this email and maintain this in each participant's binder.

### **6.3 Queries & Data Correction**

Once data entry is complete, each form not requiring additional information will need to be verified as complete using the pull down menu at the bottom of each CRF.

The DCSC will be regularly monitoring the data and generating queries for values that are missing, out of range, or completed incorrectly. A report will be sent to the site (PI and CRC) by the DCSC bi-weekly during the initial duration of the study. Following this initiation period, a report will be sent to the site monthly. Each site is expected to verify the data and make any corrections as indicated by the DCSC before generation of the next set of queries. Please follow the eCRF completion guidelines in this manual to help minimize data inconsistencies and query generation. If there are any questions about data entry or query reports, please contact the the Data Manager (Adrian Lagakos email: [alagakos@partners.org](mailto:alagakos@partners.org)).

## 7.0 Cost Data Retrieval Plan

---

CRCs are advised to contact the research finance department at your institution on a regular basis with a list of enrolled subjects' name and medical record number (MRN) and their date of admission and discharge. The items listed in the table below may be used as an example to retrieve the total cost of hospital stay for each subject. There may be additional costs which are not listed in the table below.

Item name	APC/CPT code
12 Lead ECG tracing	93005
Abdomen, Single AP view	74000
Amylase	82150
Apolipoprotein A-1	82172
Apolipoprotein B	82172
Basic Metabolic Panel	80048
Bilirubin, Direct	82248
Blood Culture	87040
Blood Glucose - ER	82962
B-Natriuretic Peptide	83880
CBC, Differential Smear	85025
CBC Hemogram	85027
Comprehensive Metabolic Panel	80053
Complete Blood Count	85027
Continuous Positive Airway Pressure (CPAP)	94660
CPK MB Fraction	82553
Creatine Kinase, Blood	82550
D-Dimer, Quantitative	85379
Extremity Vein Duplex Complete	85379
Emergency Drug Screen	80101
Emergency Level 1	99281
Emergency Level 4	99284
Emergency Level 5	99285
Erythrocyte Sedimentation Rate	85651
EST PT Level 4	99214
Fibrinogen Activity	85384
Free Thyroxine	84439
HCG-Pregnancy – Serum	84702
Hemoglobin A1c	83036
Hepatic Function Panel A	80076
Hydration IV Infusion, 31-60M	90760
Inhalation Treatment	94640
Injection –SubQ/IM	90772
IV Hydr EA ADD HR	90761
IV INF TX/DX to I HR SEQ	90767
IV Push 1 <sup>st</sup> /INIT DRUG	90774
IV Push 1 <sup>st</sup> /INIT DRUG	96374
IV Push 1 <sup>st</sup> /INIT DRUG	C8952

IV Push EA ADD NEW DRUG	90775
IV Push EA ADD NEW DRUG	96375
Lipase, Blood	83960
Lipid Panel	80061
Magnesium, Blood	83735
Partial Thromboplastin	85730
Phosphorus - Blood	84100
Prothrombin	85610
RAD.EXAM, CHEST, 1V, PA	71010
RADEX, CHEST, 2V, PA&LAT	71020
Rapid Strep A Test	87880
Strep Culture Only	87081
Free T3 - Blood	84481
Thrombin Time	85670
Thyroid Stimulating Hormone	84443
Troponin I	84484
Transthoracic Echocardiogram, Complete	93307
Doppler Color Flow	93325
Doppler, ECHO - Spectral	93320
Urinalysis, W/O MICRO	81003
Urinalysis AUTO W/MICRO	81001
Venipuncture	36415
Primary Care Outpatient Clinic Visit (Level 4)	99204
Outpatient Cardiology Evaluation (Level 4)	99204
Emergency Department Visit	80053, 85027, 71010, 85730, 85610, 84484, 99285, 93005, 36415
Hospital Admission with Cardiac Catheterization	DRG 143

## **8.0 Record Keeping**

---

For this study, electronic medical record will serve as the source document. All data entered into REDCap should be printed in paper format and stored in the subject's binder for site monitoring. We strongly recommend that each site keep blank copies of all of the eCRFs in the case that there are any technical issues with REDCap.

The only information that should be obtained through patient interview is listed on the one page Patient Interview Source Document (Appendix O) as well as the follow-up phone interviews. Any information gathered using patient interview should be documented by signing and dating the source document(s).

### **COPYING MEDICAL REPORTS AND PERSONAL PATIENT INFORMATION**

If it is necessary to copy a medical report or page from a medical record as a source document, the photocopy should be of good quality so that all relevant information is legible. Write the patient number and initials on the report. Mask-out all personal patient information such as first and last name and social security number. The patient's date of birth, sex, and race may be left unmasked.

It is recommended to first mask-out the personal information using a black permanent marker. Since the black marker does not necessarily completely mask-out the personal information, make a good quality photocopy of the document and use this as the source document filed with the CRF. Photocopies used as source documents should be signed and dated by the Investigator, Sub-Investigator, or Study/Nurse Coordinator.

Store any paper shadow documents in a designated, secure, locked area. This information does not need to be sent to the DCSC unless otherwise requested.

The CRC should maintain one binder with all consented subjects' informed consent forms and identifying information (i.e. address, phone number, locator information). Separate binders should be maintained for each subject, with a paper printout of his/her completed eCRFs, any de-identified medical records and contact logs (see Appendix H). These subject binders and source documents will be reviewed during site monitoring visits (see Section 5.2).

### **8.1 Study Tracking Logs**

Study Tracking Logs have been created to track IRB correspondence, AE/SAEs, Protocol Deviations and Violations, and Notes to File. These logs should be filed in your Regulatory Binder. Please see specific instructions for completing these logs below.

#### **IRB Tracking Log Instructions**

Utilize this log for tracking your IRB correspondence and fax an updated log to the CCC - Pearl Zakrotsky (617-724-4152) initially and as necessary. Keep a copy of this log with your regulatory documents. Please have the log accessible for review during site monitoring visits.



Complete the general information at the top of the page (Site Investigator Name and Site Number).

Initials

- Enter the Initials of the person submitting or receiving IRB documents

Date Submitted to IRB

- Enter the date the document was submitted to the IRB

Item Submitted

- Enter the name of the item submitted (i.e. Protocol, ICF, Ops Manual, etc.)

Date Received from IRB

- Enter the date of IRB response

Is a response necessary? Y/N

- Enter Y if the IRB requested a response before a document could be approved. If no changes were necessary, enter N

If Y, Reason

- If a response is necessary, enter the reason the IRB requested it

Date IRB approval received

- Enter the date of IRB approval

### **Protocol Deviation/Violation Tracking Log Instructions**

Utilize this log for tracking Protocol Deviations/ Violations at your site and fax an updated log to the CCC - Pearl Zakrotsky (617-724-4152) every Monday. If no events are listed we will assume that you have no new Protocol Deviations at your site since the previous Monday.

Complete the general information at the top of the page (Site Investigator Name and Site Number).

Subject #

- Enter the subject identification number

Description of Deviation/Violation

- Provide a description of the Protocol Deviation/Violation

Date & Time of Deviation/Violation

- Enter the date and time the Protocol Deviation/Violation occurred. For time please use military time.

Date notified CCC

- Enter the date you notified the CCC

**Date notified IRB**

- Enter the date you notified the IRB of the Protocol Deviation/Violation

**Date IRB acknowledgement received**

- Enter the date IRB acknowledgement of the Protocol Deviation/Violation was received at your site and fax a copy of IRB acknowledgement letter to the CCC

**Initials**

- Enter the initials of the person completing this form

**SAE/AE Tracking Log Instructions**

Utilize this log for the tracking of Serious Adverse Events and Adverse Events. Please fax the log on every Monday to Pearl Zakrofsky (617-724-4152). If no events are listed we will assume that you have no SAE/AE(s) at your site since the previous Monday.

Complete the general information at the top of the page (Site Investigator Name and Site Number).

**Subject #**

- Enter the subject identification number

**SAE/AE Report Description & Date of Event (Date PI signed Event)**

- Enter the SAE/AE report description, date of event, and date PI signed event

**Off Site Y/N**

- Enter yes or no as to whether the event was Off Site

**Date CCC was alerted**

- Enter the date the CCC was alerted about the SAE/AE

**Date SAE/AE Report sent to CCC**

- Enter the date the SAE/AE report was sent via fax to the CCC

**Date Follow-up SAE/AE sent to IRB/CCC**

- Enter the date the SAE/AE report was sent via fax to the CCC

**Date Follow-up SAE/AE sent to IRB/CCC**

- Enter the date the Follow-up SAE/AE IRB report was sent to the IRB & CCC

**Date Report sent to IRB**

- Enter the date SAE/AE report was sent to the IRB

**Date IRB acknowledgement received**

- Enter the date IRB acknowledgement of the SAE/AE was received at site and fax a copy of the IRB acknowledgement letter to the CCC

**Initials**

- Enter the initials of the person completing the form

**Note to File Form Instructions**

A Note to File is used to clarify or comment on many situations. For example, if a subject made an error when writing the date on one page of the consent. He/she entered the year “09” instead of “10”. The subject wrote the date correctly on the other pages. The CRC should write a Note to File. It should include the following fields listed below. A copy of the Note to File should be filed in the Regulatory Binder under Notes to File.

**IRB #**

- Enter the IRB # provided to you by your IRB

**Date**

- Enter the date of the Note to File in MM/DD/YYYY format

**Subject #**

- Enter the Subject Identification #

**Note**

- Enter explanation of the error

**Signature PI/CRC**

- The Site PI or CRC should sign the Note to File

Fax to the CCC – Pearl Zakrotsky (617-724-4152) at the end of each month

## **9.0 CASE REPORT FORMS (CRFs)**

---

9.1 General Comments

9.2 Subject ID & Site ID Numbers

9.3 CRF Instructions

CRF PAGE 1 PATIENT

CRF PAGE 2 SCREENING FORM

CRF PAGE 3 DEMOGRAPHICS

CRF PAGE 4 ED EVALUATION TIMELINE

CRF PAGE 5 RANDOMIZATION AND CONSENT

CRF PAGE 6 MEDICAL HISTORY FORM

CRF PAGE 7 ED VISIT FORM

CRF PAGE 8 LABORATORY RESULTS

CRF PAGE 9 BIOMARKER TESTING

CRF PAGE 10 ECG FORM

CRF PAGE 11 CT TEST FORM

CRF PAGE 12 NUCLEAR IMAGING

CRF PAGE 13 STRESS ECHOCARDIOGRAM

CRF PAGE 14 TRANSTHORACIC ECHOCARDIOGRAM (REST)

CRF PAGE 15 EXERCISE ECG STRESS TEST (NON-IMAGING ONLY)

CRF PAGE 16 CARDIAC CATHETERIZATION

CRF PAGE 17 PATIENT DISCHARGE FORM

CRF PAGE 18 48-72 HOUR FOLLOW UP FORM

CRF PAGE 19 28 DAY FOLLOW UP FORM

CRF PAGE 20 ADVERSE EVENT FORM

CRF PAGE 21 SERIOUS ADVERSE EVENT FORM

CRF PAGE 22 PROTOCOL DEVIATION FORM

CRF PAGE 23 PROTOCOL VIOLATION FORM

## **9.1 GENERAL COMMENTS**

CRCs, PIs and Administrators will be given access to the ROMICAT II eCRF software – REDCap, which will allow direct data entry of the electronic case report forms.

The ROMICAT II database will be divided into four databases –

ROMICAT II - Screening	1	33	
ROMICAT II - Core Lab	1	56	
ROMICAT II - CEC	0	8	
ROMICAT II - Main	1	1169	

For site CRCs:

- **ROMICAT II Screening:** Only screening information for Screen Failures\* will be entered here.
- **ROMICAT II Main:** All enrolled subject information will be entered here, including screening information for those enrolled.

For Core Lab:

- **ROMICAT II Core Lab:** This will be used for cardiac CT quality assurance and MD overread.

For CEC:

- **ROMICAT II CEC:** This will be used for adjudication of adverse events and serious adverse events and for adjudication of accuracy of patient discharge diagnosis.

General Information about REDCap:

- **\*Screen Failures:** Include subjects who do not meet all the inclusion criteria (except Inclusion #1) and who are not included due to meeting either an exclusion criteria or another reason. Screen Failures must be 18 years of age or older.
- CRCs will only have access to the ROMICAT II Screening and ROMICAT II Main databases.
- Dropboxes will open up depending on the choices entered on the eCRF.
- Data may be saved at any point of time and can be completed at a later stage.
- Data entry should be completed **within 30 days** of subject discharge.\*
- All dates should be entered in the format DD/MM/YYYY. DD is the two-digit day (i.e. 01 through 31), MM is the numerical order of the month in the calendar year (i.e. JAN=01 through DEC=12). YYYY is the four digit used to designate the year. You should use the calendar feature in REDCap to enter dates.
- All time stamps should be entered in the format HH:MM military format. HH refers to the two-digit hour (i.e. 00 through 24) and MM represents the two-digit minutes (i.e. 00 through 59). You should use the clock feature in REDCap to enter times.
- Range checks will be fired for numerical fields that are not within “normal” values. This does not mean that the value is incorrect or needs to be changed. These checks are simply intended to catch data entry errors. If a range check is

fired, please verify if the value entered is correct. If yes, hit the tab key and move to the next question.

- Do not use the enter key to move to the next field; press the tab key.
- Do not use the back or forward button on your web browser to move back and forth between forms. Click “save and move to next form” at the bottom of each form to ensure that data is saved.
- Enter the Randomization Number in all CAPS.
- For any questions with the option of “not reported”, consult the medical record first. If no information is provided in the medical record, select “not reported”.

\* The following fields are those which are time sensitive. Please complete fields that are bolded as soon as possible. For the remainder of the fields listed, please complete by the E.O.B. on Friday of each week.

**Main Database:**

**Demographics:**

Gender

Age

Ethnicity

Race

**ED Evaluation:**

**Date of ED presentation (need this to even be included in the weekly data report)**

**Time of ED presentation**

**Biomarker:**

Did the patient consent to testing?

Sample 1 collected and stored?

Sample 2 collected and stored?

Sample 3 collected and stored?

**CT:**

**Was CT done?**

**Reason not done if in interventional arm**

Prospectively gated

Retrospectively gated

**CT Quality Control:**

Total score

**CT Physician Reading:**

**Left main**

**LAD**

**LCX**

**RCA**

**Patient Discharge:**

**Date of discharge**

**Time of discharge**

**Primary dx**

48-72hr AND 28-day Follow Up:

**Contact date**

**Death (yes/no)**

**ED return (yes/no)**

**Chest pain recurrence (yes/no)**

**Screening Database:**

Demographics:

Gender

Age

Ethnicity

Race

Screening:

Need relevant exclusion reason

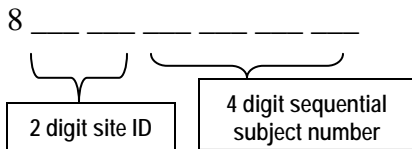
**9.2 SUBJECT & SITE ID NUMBERS**

Screened and enrolled subjects will have separate 7 digit subject ID numbers.

**Subject ID numbers for screened but NOT enrolled**

- The subject ID # for subjects who are **screened but not enrolled** will begin with the number 8, followed by the 2 digit site number, followed by the subject number (starting with 0001 till 9999)

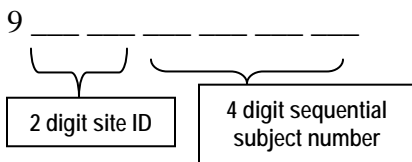
8010001 (first subject at site 1 who was screened but was not randomized)



**Subject ID numbers for those randomized/enrolled**

- The subject ID # for subjects who are **randomized/enrolled** will begin with the number 9, followed by the 2 digit site number, followed by the 4 digit subject number (starting with 0001 till 9999):

9010001 (first subject at site 1 who was enrolled)



Please refer to Table 2 for your site number.

Table 2. Site Name and Number

<b>Site Name</b>	<b>Site Number</b>
BIDMC	01
Baystate Medical Center	02
Kaiser Fontana	03
Washington University	04
Tufts Medical Center	05
University of Maryland	06
MGH	07
Cleveland Clinic	08
Northwestern University	09



### **9.3 Screening Database CRF Instructions**

As mentioned above, the Screening Database is only for data entry for those subjects that are screen failures. All information (including screening information) for enrolled subjects is to be captured under the Main Database (see section 9.4 Main Database CRF Instructions).

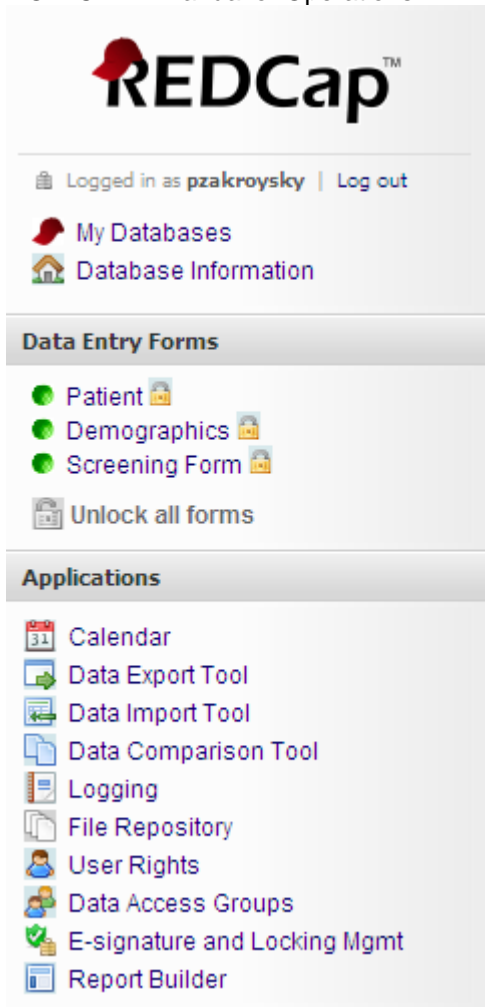
The instructions are provided in the order as they appear in REDCap. Forms may be filled out in any order.

A complete form will be shown by a green button next to the form. An incomplete one will be indicated by a red button.

Clicking directly on the dial will open the page of the subject of whom information is being entered. Clicking on the name of the document will open a fresh page, not related to the current case.

The only three forms that will need to be completed for screen failures are “Patient”, “Demographics”, and “Screening Form”.

Please enter the date a subject was screened as the Monday of the week he/she was screened.



The screenshot displays the REDCap web application interface. At the top, the REDCap logo is visible. Below it, the user is logged in as 'pzakroysky' with a 'Log out' link. The main navigation menu includes 'My Databases' and 'Database Information'. A section titled 'Data Entry Forms' lists 'Patient', 'Demographics', and 'Screening Form', each with a lock icon, and an 'Unlock all forms' option. Below this is an 'Applications' section with various tools: Calendar, Data Export Tool, Data Import Tool, Data Comparison Tool, Logging, File Repository, User Rights, Data Access Groups, E-signature and Locking Mgmt, and Report Builder.

### **CRF Page 1: Patient Form**

#### Instructions:

- Choose an existing Patient ID from the complete or incomplete patient record drop-down list to edit or review data; OR
- Type in a new patient ID and hit the TAB key to enter information about a new subject.
- Type in the date the patient was screened as the Monday of the week he/she was screened.

Mass General Hospital  
 Mass General Hospital  
 Biostatistics Center

**Romicat**

**Patient**  Download page as PDF

Incomplete Records	<input type="text"/>
Complete Records	<input type="text"/>
<b>OR type a new Patient ID and hit the TAB key</b>	
New Patient ID	<input type="text"/>

[Show Unverified Records above](#)

**Instructions:**

- Choose existing Patient ID to edit or review data; OR
- Type new Patient ID and hit the TAB key

- For each incomplete patient ID, you may choose one of the following form statuses: incomplete/unverified/complete.
- You should save the information intermittently as the system times out every 5 minutes.
- You may complete data entry at a later point in time, or you may save the information and continue to the next form.
- Once a form is locked, you may no longer edit the information under that record unless an administrator with Lock/Unlock privileges unlocks it.
- All data entry that is modified will be audited.

**ROMICAT II - Screening**

**Patient**

Re-assign this record to another Data Access Group?  
Site 01 BIDMC

Editing existing Patient ID "8010001"

<b>Patient ID</b>	8010001
<b>Monday (date) of week patient screened</b>	<input type="text"/> mm/dd/yyyy
<b>Form Status</b>	
<b>Complete?</b>	<input type="text"/> Complete
	<input type="checkbox"/> <b>Lock</b>
	<input type="button" value="Save Record"/>
	<input type="button" value="-- Cancel --"/>

**CRF Page 2: Demographics**

- 1. Gender:** Select male or female as appropriate
- 2. Age:** Enter age in years at last birthday
- 3. Ethnicity:** Select “Hispanic”, “non-Hispanic”, or “Unknown” as appropriate.
- 4. Race:** Select all that apply. If the race cannot be obtained by the patient, patients’ family or a source document, select “not reported.”

**CRF Page 3: Inclusion/Exclusion Criteria**

- 1. Select “yes” or” no” to indicate if patient met each of the inclusion criteria.**  
For a subject to be eligible for enrollment, the answer to all exclusions must be “Yes”.
- 2. Select “yes” or” no” to indicate if patient met each of the exclusion criteria?**  
For a subject to be eligible for enrollment, the answer to all exclusions must be “No”.

**Sinus Rhythm** - Sinus rhythm may include sinus bradycardia.

**New diagnostic ischemic ECG changes** are defined as ST-segment elevation or depression > 1 mm or T-wave inversion > 4 mm in two or more anatomically adjacent leads or left bundle branch block.

**History of CAD** – This includes a history of myocardial infarction (MI), percutaneous coronary intervention (PCI), coronary artery bypass grafts (CABG), or a catheterization report documenting >50% stenosis. This history may be documented or self reported.

**Impaired Renal Function** – based on the local standard of care (for example, measured serum creatinine >1.5 mg/dL).

**Markedly elevated Troponin** – based on the local standard of care - Refer to Appendix I for values at each institution.

**Hemodynamic or clinical instability** – including but not limited to systolic BP <80mmHg, persistent chest pain despite adequate therapy and atrial and ventricular arrhythmias.

**Acute Cocaine Use** - If acute cocaine use cannot be obtained from the medical record, please confirm this information with the caregiver. If the caregiver cannot provide this information, confirm with the patient and note on the Patient Interview Source Document (Appendix O).

**Woman of Child Bearing Potential:** defined as: < 2 years of menopause in the absence of hysterectomy or tubal ligation.

**Weight in Pounds**

	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	250
4'	30.5	33.6	36.6	39.7	42.7	45.8	48.8	51.9	54.9	58.0	61.0	64.1	67.1	70.2	73.2	76.3
4'2"	28.1	30.9	33.7	36.6	39.4	42.2	45.0	47.8	50.6	53.4	56.2	59.1	61.9	64.7	67.5	70.3
4'4"	26.0	28.6	31.2	33.8	36.4	39.0	41.6	44.2	46.8	49.4	52.0	54.6	57.2	59.8	62.4	65.0
4'6"	24.1	26.5	28.9	31.3	33.8	36.2	38.6	41.0	43.4	45.8	48.2	50.6	53.0	55.4	57.9	60.3
4'8"	22.4	24.7	26.9	29.1	31.4	33.6	35.9	38.1	40.4	42.6	44.8	47.1	49.3	51.6	53.8	56.0
4'10"	20.9	23.0	25.1	27.2	29.3	31.3	33.4	35.5	37.6	39.7	41.8	43.9	46.0	48.1	50.2	52.2
5'	19.5	21.5	23.4	25.4	27.3	29.3	31.2	33.2	35.2	37.1	39.1	41.0	43.0	44.9	46.9	48.8
5'2"	18.3	20.1	21.9	23.8	25.6	27.4	29.3	31.1	32.9	34.7	36.6	38.4	40.2	42.1	43.9	45.7
5'4"	17.2	18.9	20.6	22.3	24.0	25.7	27.5	29.2	30.9	32.6	34.3	36.0	37.8	39.5	41.2	42.9
5'6"	16.1	17.8	19.4	21.0	22.6	24.2	25.8	27.4	29.0	30.7	32.3	33.9	35.5	37.1	38.7	40.3
5'8"	15.2	16.7	18.2	19.8	21.3	22.8	24.3	25.8	27.4	28.9	30.4	31.9	33.4	35.0	36.5	38.0
5'10"	14.3	15.8	17.2	18.7	20.1	21.5	23.0	24.4	25.8	27.3	28.7	30.1	31.6	33.0	34.4	35.9
6'	13.6	14.9	16.3	17.6	19.0	20.3	21.7	23.1	24.4	25.8	27.1	28.5	29.8	31.2	32.5	33.9
6'2"	12.8	14.1	15.4	16.7	18.0	19.3	20.5	21.8	23.1	24.4	25.7	27.0	28.2	29.5	30.8	32.1
6'4"	12.2	13.4	14.6	15.8	17.0	18.3	19.5	20.7	21.9	23.1	24.3	25.6	26.8	28.0	29.2	30.4
6'6"	11.6	12.7	13.9	15.0	16.2	17.3	18.5	19.6	20.8	22.0	23.1	24.3	25.4	26.6	27.7	28.9
6'8"	11.0	12.1	13.2	14.3	15.4	16.5	17.6	18.7	19.8	20.9	22.0	23.1	24.2	25.3	26.4	27.5
6'10"	10.5	11.5	12.5	13.6	14.6	15.7	16.7	17.8	18.8	19.9	20.9	22.0	23.0	24.0	25.1	26.1
7'	10.0	11.0	12.0	13.0	13.9	14.9	15.9	16.9	17.9	18.9	19.9	20.9	21.9	22.9	23.9	24.9

<http://www.freebmicalculator.net>

Underweight
  Normal
  Overweight
  Obesity

You may determine the BMI of the subject from the chart shown above. To capture this more accurately, calculate it from the formula,  $BMI = \text{weight (kg)}/\text{height (m}^2\text{)}$  or use an online calculator to determine the BMI based on weight in pounds and height in inches.

# SCREENING FORM

## Demographics

Complete Questions 1-4 for all patients who are screened.

<b>1. Gender:</b>	<input type="checkbox"/> Male <input type="checkbox"/> Female
<b>2. Age in years:</b>	_____ years
<b>3. Ethnicity:</b>	<input type="checkbox"/> Hispanic or Latino <input type="checkbox"/> NOT Hispanic or Latino <input type="checkbox"/> Unknown
<b>4. Race:</b> Select ALL that apply.	NOTE: If the race(s) cannot be obtained from the patient, the patient's family, or from a source document, select <b>"not reported"</b> .
A. American Indian or Alaskan Native	<input type="checkbox"/>
B. Asian	<input type="checkbox"/>
C. White	<input type="checkbox"/>
D. Black or African Native	<input type="checkbox"/>
E. Native Hawaiian or Pacific Islander	<input type="checkbox"/>
F. Not reported	<input type="checkbox"/>

## Inclusion/Exclusion Criteria

To be completed on all patients who are screened.

<b>1. Please select yes or no to indicate whether patient meets the following inclusion criteria?</b>	
1) Participant must have at least five minutes of chest pain or equivalent (chest tightness; pain radiating to left, right, or both arms or shoulders, back, neck, epigastrium, jaw/throat; or unexplained shortness of breath, syncope/presyncope, generalized weakness, nausea, or vomiting thought to be of cardiac origin) at rest or during exercise within 24 hours of ED presentation, warranting further risk stratification, as determined by an ED attending.	<input type="checkbox"/> Yes <input type="checkbox"/> No
2) Participant is able to provide written Informed Consent	<input type="checkbox"/> Yes <input type="checkbox"/> No
3) Participant is <75 years of age, but ≥40 years of age	<input type="checkbox"/> Yes <input type="checkbox"/> No
4) Participant is able to perform a breath hold of at least 10 seconds	<input type="checkbox"/> Yes <input type="checkbox"/> No
5) Participant is in sinus rhythm	<input type="checkbox"/> Yes <input type="checkbox"/> No
<b>2. Please select yes or no to indicate whether patient meets the following exclusion criteria</b>	
1) New diagnostic ischemic ECG changes <i>ST-segment elevation or depression &gt; 1 mm or T-wave inversion &gt; 4 mm in two or more anatomically adjacent leads or left bundle branch block</i>	<input type="checkbox"/> Yes <input type="checkbox"/> No
2) Documented or self-reported history of CAD <i>MI, percutaneous coronary interventions [PCIs], coronary artery bypass graft [CABG], known significant coronary</i>	<input type="checkbox"/> Yes <input type="checkbox"/> No

<i>stenosis [&gt;50%]</i>	
3) Greater than 6 hours since presentation to ED to time of consent	<input type="checkbox"/> Yes <input type="checkbox"/> No
4) BMI >40 kg/m <sup>2</sup>	<input type="checkbox"/> Yes <input type="checkbox"/> No
5) Impaired renal function, as defined by local standard of care, for example, measured serum creatinine >1.5 mg/dL	<input type="checkbox"/> Yes <input type="checkbox"/> No
6) Markedly elevated troponin, as defined by local standard of care	<input type="checkbox"/> Yes <input type="checkbox"/> No
7) Hemodynamically or clinically unstable condition (BP systolic < 80 mm Hg, atrial or ventricular arrhythmias, persistent chest pain despite adequate therapy)	<input type="checkbox"/> Yes <input type="checkbox"/> No
8) Known allergy to iodinated contrast agent	<input type="checkbox"/> Yes <input type="checkbox"/> No
9) Currently symptomatic asthma	<input type="checkbox"/> Yes <input type="checkbox"/> No
10) Documented or self-reported cocaine use within the past 48 hours (acute)	<input type="checkbox"/> Yes <input type="checkbox"/> No
11) On Metformin therapy and unable or unwilling to discontinue for 48 hours after the CT scan	<input type="checkbox"/> Yes <input type="checkbox"/> No
12) Contraindication to beta blockers (taking daily antiasthmatic medication): This exclusion only applies to patients with a heart rate > 65 bpm at sites using a non-dual source CT scanner	<input type="checkbox"/> Yes <input type="checkbox"/> No
13) Participant with no telephone or cellphone number (preventing follow-up)	<input type="checkbox"/> Yes <input type="checkbox"/> No
14) Participant with positive pregnancy test within 24 hours prior to CT scan. <i>For woman of childbearing potential, defined as: &lt; 2 years of menopause in the absence of hysterectomy or tubal ligation.</i>	<input type="checkbox"/> Yes <input type="checkbox"/> No
15) Participant unwilling to provide written informed consent.	<input type="checkbox"/> Yes <input type="checkbox"/> No
16) Other	<input type="checkbox"/> Yes <input type="checkbox"/> No
17) Participant was eligible (i.e. met all inclusion criteria and no exclusion criteria). However, CRC could not consent participant because busy with enrolled participant(s).	<input type="checkbox"/> Yes <input type="checkbox"/> No

### **9.4 Main Database CRF Instructions**

The instructions are provided in the order as they appear in REDCap. Forms may be filled out in any order.

A complete form will be shown by a green button next to the form. An incomplete one will be indicated by a red button.

Clicking directly on the dial will open the page of the subject of whom information is being entered. Clicking on the name of the document will open a fresh page, not related to the current case.



The image shows a vertical sidebar menu from the REDCap web application. At the top is the REDCap logo. Below it, the user is logged in as 'pzakroysky' with a 'Log out' link. There are two main menu items: 'My Databases' and 'Database Information'. The 'Data Entry Forms' section is expanded, listing various forms such as Patient, Demographics, Screening Form, Ed Evaluation Timeline, Randomization And Consent, Medical History Form, Ed Visit Form, Laboratory Results, Biomarker Testing, Ecg Form, Ct Form, Ct Test Subject Physician Reading Form, Nuclear Imaging Form, Stress Echocardiogram Form, Transthoracic Echocardiogram Form, Exercise Ecg Stress Test, Cardiac Catheterization, Patient Discharge Form, Follow Up Form 48 To 72 Hour, Follow Up Form 48 To 72 Hour Supplement, Follow Up Form 28 Day, Follow Up Form 28 Day Supplement, Adverse Event Form, Serious Adverse Event Form, Protocol Deviation Form, Protocol Violation Form, and Ct Quality Control Case Report Form. The 'Applications' section is also visible at the bottom, containing a 'Calendar' link.

**REDCap™**

Logged in as **pzakroysky** | [Log out](#)

[My Databases](#)

[Database Information](#)

**Data Entry Forms**

- Patient
- Demographics
- Screening Form
- Ed Evaluation Timeline
- Randomization And Consent
- Medical History Form
- Ed Visit Form
- Laboratory Results
- Biomarker Testing
- Ecg Form
- Ct Form
- Ct Test Subject Physician Reading Form
- Nuclear Imaging Form
- Stress Echocardiogram Form
- Transthoracic Echocardiogram Form
- Exercise Ecg Stress Test
- Cardiac Catheterization
- Patient Discharge Form
- Follow Up Form 48 To 72 Hour
- Follow Up Form 48 To 72 Hour Supplement
- Follow Up Form 28 Day
- Follow Up Form 28 Day Supplement
- Adverse Event Form
- Serious Adverse Event Form
- Protocol Deviation Form
- Protocol Violation Form
- Ct Quality Control Case Report Form

**Applications**

- [Calendar](#)

Instructions:

- Choose an existing Patient ID from the complete or incomplete patient record drop-down list to edit or review data; OR
- Type in a new patient ID and hit the TAB key to enter information about a new subject.

Mass General Hospital  
Mass General Hospital  
Biostatistics Center

**Romicat**

**Patient** [Download page as PDF](#)

Incomplete Records

Complete Records

OR type a new Patient ID and hit the TAB key

New Patient ID

[Show Unverified Records above](#)

**Instructions:**

- Choose existing Patient ID to edit or review data; OR
- Type new Patient ID and hit the TAB key

- For each incomplete patient ID, you may choose one of the following form statuses: incomplete/unverified/complete.
- You should save the information intermittently as the system times out every 5 minutes.
- You may complete data entry at a later point in time, or you may save the information and continue to the next form.
- Once a form is locked, you may no longer edit the information under that record unless an administrator with Lock/Unlock privileges unlocks it.
- All data entry that is modified will be audited.

Mass General Hospital  
Mass General Hospital  
Biostatistics Center

**Romicat**

**Patient** [Download page as PDF](#) [PDF with saved data](#)

Editing existing Patient ID "13579"

Patient ID 13579

Form Status

Complete?

Lock this record for this form?  
If locked, no user will be able to edit this record on this form until someone with Lock/Unlock privileges unlocks it.

Incomplete

Incomplete  
Unverified  
Complete

Save Record  
Save and Continue  
Save and go to Next Form  
Cancel

**CRF Page 2: Demographics**

1. **Gender:** Select male or female as appropriate
2. **Age:** Enter age in years at last birthday
3. **Ethnicity:** Select “Hispanic”, “non-Hispanic”, or “Unknown” as appropriate.
4. **Race:** Select all that apply. If the race cannot be obtained by the patient, patients’ family or a source document, select “not reported.”

**CRF Page 3: Inclusion/Exclusion Criteria**

3. **Select “yes” or” no” to indicate if patient met each of the inclusion criteria.**  
For a subject to be eligible for enrollment, the answer to all exclusions must be “Yes”.
4. **Select “yes” or” no” to indicate if patient met each of the exclusion criteria?**  
For a subject to be eligible for enrollment, the answer to all exclusions must be “No”.

**Sinus Rhythm** - Sinus rhythm may include sinus bradycardia.

**New diagnostic ischemic ECG changes** are defined as ST-segment elevation or depression > 1 mm or T-wave inversion > 4 mm in two or more anatomically adjacent leads or left bundle branch block.

**History of CAD** – This includes a history of myocardial infarction (MI), percutaneous coronary intervention (PCI), coronary artery bypass grafts (CABG), or a catheterization report documenting >50% stenosis. This history may be documented or self reported.

**Impaired Renal Function** – based on the local standard of care (for example, measured serum creatinine >1.5 mg/dL).

**Markedly elevated Troponin** – based on the local standard of care - Refer to Appendix I for values at each institution.

**Hemodynamic or clinical instability** – including but not limited to systolic BP <80mmHg, persistent chest pain despite adequate therapy and atrial and ventricular arrhythmias.

**Acute Cocaine Use** - If acute cocaine use cannot be obtained from the medical record, please confirm this information with the caregiver. If the caregiver cannot provide this information, confirm with the patient and note on the Patient Interview Source Document (Appendix O).

**Woman of Child Bearing Potential:** defined as: < 2 years of menopause in the absence of hysterectomy or tubal ligation.

**Weight in Pounds**

	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	250
4'	30.5	33.6	36.6	39.7	42.7	45.8	48.8	51.9	54.9	58.0	61.0	64.1	67.1	70.2	73.2	76.3
4'2"	28.1	30.9	33.7	36.6	39.4	42.2	45.0	47.8	50.6	53.4	56.2	59.1	61.9	64.7	67.5	70.3
4'4"	26.0	28.6	31.2	33.8	36.4	39.0	41.6	44.2	46.8	49.4	52.0	54.6	57.2	59.8	62.4	65.0
4'6"	24.1	26.5	28.9	31.3	33.8	36.2	38.6	41.0	43.4	45.8	48.2	50.6	53.0	55.4	57.9	60.3
4'8"	22.4	24.7	26.9	29.1	31.4	33.6	35.9	38.1	40.4	42.6	44.8	47.1	49.3	51.6	53.8	56.0
4'10"	20.9	23.0	25.1	27.2	29.3	31.3	33.4	35.5	37.6	39.7	41.8	43.9	46.0	48.1	50.2	52.2
5'	19.5	21.5	23.4	25.4	27.3	29.3	31.2	33.2	35.2	37.1	39.1	41.0	43.0	44.9	46.9	48.8
5'2"	18.3	20.1	21.9	23.8	25.6	27.4	29.3	31.1	32.9	34.7	36.6	38.4	40.2	42.1	43.9	45.7
5'4"	17.2	18.9	20.6	22.3	24.0	25.7	27.5	29.2	30.9	32.6	34.3	36.0	37.8	39.5	41.2	42.9
5'6"	16.1	17.8	19.4	21.0	22.6	24.2	25.8	27.4	29.0	30.7	32.3	33.9	35.5	37.1	38.7	40.3
5'8"	15.2	16.7	18.2	19.8	21.3	22.8	24.3	25.8	27.4	28.9	30.4	31.9	33.4	35.0	36.5	38.0
5'10"	14.3	15.8	17.2	18.7	20.1	21.5	23.0	24.4	25.8	27.3	28.7	30.1	31.6	33.0	34.4	35.9
6'	13.6	14.9	16.3	17.6	19.0	20.3	21.7	23.1	24.4	25.8	27.1	28.5	29.8	31.2	32.5	33.9
6'2"	12.8	14.1	15.4	16.7	18.0	19.3	20.5	21.8	23.1	24.4	25.7	27.0	28.2	29.5	30.8	32.1
6'4"	12.2	13.4	14.6	15.8	17.0	18.3	19.5	20.7	21.9	23.1	24.3	25.6	26.8	28.0	29.2	30.4
6'6"	11.6	12.7	13.9	15.0	16.2	17.3	18.5	19.6	20.8	22.0	23.1	24.3	25.4	26.6	27.7	28.9
6'8"	11.0	12.1	13.2	14.3	15.4	16.5	17.6	18.7	19.8	20.9	22.0	23.1	24.2	25.3	26.4	27.5
6'10"	10.5	11.5	12.5	13.6	14.6	15.7	16.7	17.8	18.8	19.9	20.9	22.0	23.0	24.0	25.1	26.1
7'	10.0	11.0	12.0	13.0	13.9	14.9	15.9	16.9	17.9	18.9	19.9	20.9	21.9	22.9	23.9	24.9

<http://www.freebmicalculator.net>

Underweight
  Normal
  Overweight
  Obesity

You may determine the BMI of the subject from the chart shown above. To capture this more accurately, calculate it from the formula,  $BMI = \text{weight (kg)} / \text{height (m}^2\text{)}$  or use an online calculator to determine the BMI based on weight in pounds and height in inches.

# SCREENING FORM

## Demographics

Complete Questions 1-4 for all patients who are screened.

<b>5. Gender:</b>	<input type="checkbox"/> Male <input type="checkbox"/> Female
<b>6. Age in years:</b>	_____ years
<b>7. Ethnicity:</b>	<input type="checkbox"/> Hispanic or Latino <input type="checkbox"/> NOT Hispanic or Latino <input type="checkbox"/> Unknown
<b>8. Race:</b> Select ALL that apply.	NOTE: If the race(s) cannot be obtained from the patient, the patient's family, or from a source document, select <b>"not reported"</b> .
G. American Indian or Alaskan Native	<input type="checkbox"/>
H. Asian	<input type="checkbox"/>
I. White	<input type="checkbox"/>
J. Black or African Native	<input type="checkbox"/>
K. Native Hawaiian or Pacific Islander	<input type="checkbox"/>
L. Not reported	<input type="checkbox"/>

## Inclusion/Exclusion Criteria

To be completed on all patients who are screened.

<b>3. Please select yes or no to indicate whether patient meets the following inclusion criteria?</b>	
1) Participant must have at least five minutes of chest pain or equivalent (chest tightness; pain radiating to left, right, or both arms or shoulders, back, neck, epigastrium, jaw/throat; or unexplained shortness of breath, syncope/presyncope, generalized weakness, nausea, or vomiting thought to be of cardiac origin) at rest or during exercise within 24 hours of ED presentation, warranting further risk stratification, as determined by an ED attending.	<input type="checkbox"/> Yes <input type="checkbox"/> No
2) Participant is able to provide written Informed Consent	<input type="checkbox"/> Yes <input type="checkbox"/> No
3) Participant is <75 years of age, but ≥40 years of age	<input type="checkbox"/> Yes <input type="checkbox"/> No
4) Participant is able to perform a breath hold of at least 10 seconds	<input type="checkbox"/> Yes <input type="checkbox"/> No
5) Participant is in sinus rhythm	<input type="checkbox"/> Yes <input type="checkbox"/> No
<b>4. Please select yes or no to indicate whether patient meets the following exclusion criteria</b>	
1) New diagnostic ischemic ECG changes <i>ST-segment elevation or depression &gt; 1 mm or T-wave inversion &gt; 4 mm in two or more anatomically adjacent leads or left bundle branch block</i>	<input type="checkbox"/> Yes <input type="checkbox"/> No
2) Documented or self-reported history of CAD <i>MI, percutaneous coronary interventions [PCIs], coronary artery bypass graft [CABG], known significant coronary</i>	<input type="checkbox"/> Yes <input type="checkbox"/> No

<i>stenosis [&gt;50%]</i>	
3) Greater than 6 hours since presentation to ED to time of consent	<input type="checkbox"/> Yes <input type="checkbox"/> No
4) BMI >40 kg/m <sup>2</sup>	<input type="checkbox"/> Yes <input type="checkbox"/> No
5) Impaired renal function, as defined by local standard of care, for example, measured serum creatinine >1.5 mg/dL	<input type="checkbox"/> Yes <input type="checkbox"/> No
6) Markedly elevated troponin, as defined by local standard of care	<input type="checkbox"/> Yes <input type="checkbox"/> No
7) Hemodynamically or clinically unstable condition (BP systolic < 80 mm Hg, atrial or ventricular arrhythmias, persistent chest pain despite adequate therapy)	<input type="checkbox"/> Yes <input type="checkbox"/> No
8) Known allergy to iodinated contrast agent	<input type="checkbox"/> Yes <input type="checkbox"/> No
9) Currently symptomatic asthma	<input type="checkbox"/> Yes <input type="checkbox"/> No
10) Documented or self-reported cocaine use within the past 48 hours (acute)	<input type="checkbox"/> Yes <input type="checkbox"/> No
11) On Metformin therapy and unable or unwilling to discontinue for 48 hours after the CT scan	<input type="checkbox"/> Yes <input type="checkbox"/> No
12) Contraindication to beta blockers (taking daily antiasthmatic medication): This exclusion only applies to patients with a heart rate > 65 bpm at sites using a non-dual source CT scanner	<input type="checkbox"/> Yes <input type="checkbox"/> No
13) Participant with no telephone or cellphone number (preventing follow-up)	<input type="checkbox"/> Yes <input type="checkbox"/> No
14) Participant with positive pregnancy test within 24 hours prior to CT scan. <i>For woman of childbearing potential, defined as: &lt; 2 years of menopause in the absence of hysterectomy or tubal ligation.</i>	<input type="checkbox"/> Yes <input type="checkbox"/> No
15) Participant unwilling to provide written informed consent.	<input type="checkbox"/> Yes <input type="checkbox"/> No

## **CRF Page 4: ED Evaluation Timeline**

### **ED Evaluation timeline**

- 1. Date of ED presentation:** Use the pop-up calendar to indicate the date of ED presentation.
- 2. Time of ED presentation:** Use the pop-up clock to indicate the time of ED presentation. This is the time defined as the time of ED registration as marked in the medical record.
- 3. Date of Initial ED Evaluation:** Use the pop-up calendar to indicate the date of initial evaluation by the ED physician.
- 4. Time of Completion of Initial ED Evaluation:** Use the pop-up clock to indicate the time of completion of initial evaluation by the ED physician. This is the time point at which the ED physician puts in the 1<sup>st</sup> set of orders.

## **CRF Page 5: Randomization and Consent**

- 1. Date of Consent:** Enter the date the subject was consented using the pop-up calendar.
- 2. Time of Consent:** Enter the time the subject was consented using the pop-up clock.
- 3. Was the patient randomized?:** Select “yes” or “no” to indicate whether subject was randomized.
  - If randomized, select “SOC” or “Interventional arm” as appropriate. Enter the randomization number generated from the RS2 system.
  - If not randomized, select the reason why. If none of the available choices are applicable, select other and specify. Discontinue any further data entry.
- 4. Date of Randomization:** Enter the date of randomization using the pop-up calendar.
- 5. Time of Randomization:** Enter the LOCAL TIME of randomization using the pop-up clock. **Note:** the randomization email generated from the RS2 system will be in EASTERN TIME.

## ED Evaluation Timeline

1. Date of ED Presentation (mm/dd/yyyy):	
2. Time of ED Presentation (hh:mm):	
3. Date of Initial ED Evaluation (mm/dd/yyyy):	
4. Time of Completion of Initial ED Evaluation (hh:mm): (This is the time point at which the ED physician puts in the 1st set of orders.)	

## Randomization & Consent

1. Date of Consent (mm/dd/yyyy):	
2. Time of Consent (hh:mm):	
3. Was the patient randomized?	<input type="checkbox"/> Yes <input type="checkbox"/> No*  If yes, <input type="checkbox"/> SOC arm <input type="checkbox"/> Interventional arm  Randomization number _____  If no, reason: <input type="checkbox"/> <b>markedly</b> positive troponin <input type="checkbox"/> positive pregnancy test <input type="checkbox"/> patient withdrew consent <input type="checkbox"/> other, specify _____
4. Date of Randomization (mm/dd/yyyy):	
5. Time of Randomization (hh:mm):	



## **CRF Page 6 – Medical History Form**

### **Cardiac Risk Factors and Medications**

Fill out the data in this section based on patient reported data or medical records.

Note: If any risk factors or medications are not present in the medical records, enter as “not reported”.

**1. Hypertension** – history of hypertension (self-report or physician report) or current antihypertensive treatment

- Select “yes”, “no”, or “not reported” to indicate patient history of hypertension

**2. Diabetes Mellitus** – history of diabetes (self report or physician report) or treatment with a hypoglycemic agent

- Select “none” to indicate no patient history of diabetes
- Select “insulin requiring” or “non-insulin” as appropriate for those patients with a history of diabetes
- Select “not reported” if not listed

**3. Hypercholesterolemia/Hyperlipidemia** – history of hypercholesterolemia/hyperlipidemia (self report or physician report) or treatment with a lipid lowering medication documented in medical history

- Select “yes” or “no”, or “not reported” to indicate patient history of Hypercholesterolemia or Hyperlipidemia

**4. Cocaine Use** - select “never”, “former” or “recent (>48 hours)” to indicate subject’s history of cocaine use. (**NOTE:** Subjects with acute cocaine use within 48 hours are NOT eligible for enrollment. If subject already randomized, please fill out Protocol Violation form.)

**5. Tobacco Use** – select “never”, “former”, “current”, or “not reported” to indicate patient’s smoking history. Current smokers are defined as those who have smoked at least one cigarette per day in the year prior to the study.

**6. First degree relative with CAD/ACS/MI (men < 55 years, women < 65 years)** – defined as a subject having a first-degree female (<65 years) or male (<55 years) relative with a documented history of myocardial infarction or sudden cardiac death

- A **first degree relative** is defined as a parent, child or sibling of the patient

**7. Home Medications** – Select “yes” or “no” to indicate which medications the patient was taking prior to ED presentation

### **Medical History**

Fill out the data in this section based on medical records.

**1. Heart failure-**

- Select “yes”, “no”, or “not reported”

**2. Peripheral vascular disease-**

- Select “yes”, “no”, or “not reported”

**3. Chronic lung disease/COPD-**

- Select “yes”, “no”, or “not reported”

**4. Cerebrovascular event (stroke) -**

- Select “yes”, “no”, or “not reported”

**Pain Characteristics**

Fill out the data in this section based on patient reported data.

- 1. Chief Complaint** – Indicate the nature of the chest pain that the subject presented with to the hospital. If none of the available options are applicable, select “Other” and specify.
- 2. Most recent Episode** –
  - Enter the date of the most recent episode of chest pain or anginal equivalent using the pop-up calendar.
  - Enter the time of the most recent episode of chest pain or anginal equivalent using the pop-up clock.
  - Enter the duration in minutes of the most recent episode of chest pain or anginal equivalent.

# MEDICAL HISTORY FORM

## Cardiac Risk Factors and Medications

<b>1. Hypertension</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not Reported
<b>2. Diabetes mellitus</b>	<input type="checkbox"/> None <input type="checkbox"/> Insulin requiring <input type="checkbox"/> Non-insulin <input type="checkbox"/> Not Reported
<b>3. Hypercholesterolemia/hyperlipidemia</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not Reported
<b>4. Cocaine use</b>	<input type="checkbox"/> Never <input type="checkbox"/> Former <input type="checkbox"/> Recent (last use >48 hours)
<b>5. Tobacco use</b>	<input type="checkbox"/> Never <input type="checkbox"/> Former <input type="checkbox"/> Current <input type="checkbox"/> Not Reported
<b>6. First degree relative with CAD/ACS/AMI: (male &lt; 55 yrs, female &lt; 65 yrs)</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not Reported
<b>7. Home medications:</b>	
a. ACE-inhibitors/ARB	<input type="checkbox"/> Yes <input type="checkbox"/> No
b. Aspirin	<input type="checkbox"/> Yes <input type="checkbox"/> No
c. Nitrates	<input type="checkbox"/> Yes <input type="checkbox"/> No
d. Beta-blockers	<input type="checkbox"/> Yes <input type="checkbox"/> No
e. Calcium channel blocker	<input type="checkbox"/> Yes <input type="checkbox"/> No
f. Statins	<input type="checkbox"/> Yes <input type="checkbox"/> No
g. Niacin/fibrates	<input type="checkbox"/> Yes <input type="checkbox"/> No
h. Insulin	<input type="checkbox"/> Yes <input type="checkbox"/> No
i. Oral hypoglycemics	<input type="checkbox"/> Yes <input type="checkbox"/> No

## Medical History

<b>1. Heart failure</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not Reported
<b>2. Peripheral vascular disease</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not Reported
<b>3. Chronic lung disease/COPD</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not Reported
<b>4. Cerebrovascular event (stroke)</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not Reported

## Pain Characteristics/Symptoms

Patient reported data:

<b>1. Chief Complaint</b>	<input type="checkbox"/> Anginal Chest Pain or equivalent <input type="checkbox"/> Epigastric Pain <input type="checkbox"/> Arm/Jaw/Shoulder Pain <input type="checkbox"/> Shortness of Breath <input type="checkbox"/> Other: _____
<b>2. Most recent Episode</b>	Date (mm/dd/yyyy) Time (hh:mm) Duration (minutes): _____

**CRF Page 7 – ED Visit Form**

Data is collected by the CRC from the ED chart.

**Initial ED vital signs**

1. **Weight** – Enter to the nearest whole number in pounds
  2. **Height** – Enter to the nearest whole number in inches
  3. **Resting Heart Rate** -
  4. **Systolic BP**
  5. **Diastolic BP**
  6. **Presence of Rales?**
- } complete this information from  
the ED triage note

If presence of rales is not recorded, select “not reported”.

**ED Medications**

1. **Aspirin** - select whether or not administered during ED stay
2. **Nitrates** – select whether or not administered during ED stay
3. **Beta blocker** - select whether or not administered during ED stay
4. **Morphine** – select whether or not administered during ED stay
5. **Heparin/low molecular weight heparin/Fragmin/Lovenox** – select whether or not administered during ED stay
6. **Plavix** - select whether or not administered during ED stay

**CRF Page 8 - Laboratory Results**

Select “done” or “not done” to indicate whether the initial and 2 subsequent creatinine and CK-MB levels were obtained and to indicate if a D-Dimer was obtained.

If “done”, enter the date/time using the pop-up calendar and pop-up clock and result of available creatinine, CK-MB and D-Dimer. If values are reported with a < sign, enter values using a negative sign (-) before the number.

**Troponin Values**

Select “done” or “not done” to indicate if initial and 2 subsequent Troponin levels were obtained. If values obtained:

- Indicate Troponin classification as “T” or “I”
- Indicate date/time Troponin obtained using the pop-up calendar and pop-up clock
- Select “normal”, “markedly elevated”, or “borderline” to indicate the result based on your institution’s normal values (Appendix I). Enter you institution’s range for the chosen result.
- Enter Troponin result in ug/ml

**CRF Page 9 - Biomarker Testing**

Select “yes” or “no” to indicate if the subject consented to biomarker testing. If “yes”, enter the date/time (using the pop-up calendar and pop-up clock) the samples were collected for draws 1, 2, and 3. Mark whether or not each of the samples was collected and/or stored. For each of the 3 samples (red, purple, and green), enter the corresponding 8 digit Specimen ID# located on the printed label provided and indicate the number of

daughter tubes aliquoted. If less than 3 tubes were collected per blood draw, fill out the protocol deviation form.

# ED VISIT FORM

## Initial ED Vital Signs

Data collected by CRC from ED chart.

1. <b>Weight:</b>	lbs
2. <b>Height:</b>	inches
3. <b>Resting heart rate:</b>	bpm
4. <b>Systolic BP:</b>	mmHg
5. <b>Diastolic BP:</b>	mmHg
6. <b>Presence of rales?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not Reported

## ED Medications

Data collected from ED record. Select ALL that apply.

1. <b>Aspirin</b>	<input type="checkbox"/>
2. <b>Nitrates</b>	<input type="checkbox"/>
3. <b>Beta blocker</b>	<input type="checkbox"/>
4. <b>Morphine</b>	<input type="checkbox"/>
5. <b>Heparin/ Low molecular weight heparin/ Fragmin/ Lovenox</b>	<input type="checkbox"/>
6. <b>Plavix</b>	<input type="checkbox"/>

## Laboratory Results

Data collected from ED record.

Test	Date	Time	Result	Not done
Creatinine (initial)			mg/dL	<input type="checkbox"/>
Creatinine (2 <sup>nd</sup> )			mg/dL	<input type="checkbox"/>
Creatinine (3 <sup>rd</sup> )			mg/dL	<input type="checkbox"/>
CK-MB (initial)			ug/ml	<input type="checkbox"/>
CK-MB (2 <sup>nd</sup> )			ug/ml	<input type="checkbox"/>
CK-MB (3 <sup>rd</sup> )			ug/ml	<input type="checkbox"/>
D-Dimer			ng/ml	<input type="checkbox"/>

### Troponin Values

Test	Troponin classification	Date	Time	Result	Range	Not done
Troponin (initial)	T <input type="checkbox"/> I <input type="checkbox"/>			ug/ml	<input type="checkbox"/> Normal Enter Range:____ <input type="checkbox"/> Borderline Enter Range:____ <input type="checkbox"/> Elevated Enter Range:____	<input type="checkbox"/>
Troponin (2 <sup>nd</sup> )	T <input type="checkbox"/> I <input type="checkbox"/>			ug/ml	<input type="checkbox"/> Normal Enter Range:____ <input type="checkbox"/> Borderline Enter Range:____ <input type="checkbox"/> Elevated Enter Range:____	<input type="checkbox"/>
Troponin (3 <sup>rd</sup> )	T <input type="checkbox"/> I <input type="checkbox"/>			ug/ml	<input type="checkbox"/> Normal Enter Range:____ <input type="checkbox"/> Borderline Enter Range:____ <input type="checkbox"/> Elevated Enter Range:____	<input type="checkbox"/>

### Biomarker Testing

<b>Did the patient consent to biomarker testing?</b> <input type="checkbox"/> Yes <input type="checkbox"/> No
If yes,
Draw #1: Was blood collected and stored? If less than 3 tubes collected, fill out protocol deviation form. <input type="checkbox"/> Yes <input type="checkbox"/> No  Date (mm/dd/yyyy): _____ Time (hh:mm): _____  Red tube specimen ID no _____ How many daughter tubes? _____  Purple tube specimen ID no _____ How many daughter tubes? _____  Green tube specimen ID no _____ How many daughter tubes? _____
Draw #2: Was blood collected and stored? If less than 3 tubes collected, fill out protocol deviation form. <input type="checkbox"/> Yes <input type="checkbox"/> No  Date (mm/dd/yyyy): _____ Time (hh:mm): _____  Red tube specimen ID no _____ How many daughter tubes? _____

Purple tube specimen ID no _____ How many daughter tubes? _____
Green tube specimen ID no _____ How many daughter tubes? _____
Draw #3: Was blood collected and stored? If less than 3 tubes collected, fill out protocol deviation form. <input type="checkbox"/> Yes <input type="checkbox"/> No
Date (mm/dd/yyyy): _____ Time (hh:mm): _____
Red tube specimen ID no _____ How many daughter tubes? _____
Purple tube specimen ID no _____ How many daughter tubes? _____
Green tube specimen ID no _____ How many daughter tubes? _____

**CRF Page 10 – ECG Form**

1. **Date of initial ECG** – Enter the date of the initial ECG performed in the ED using the pop-up calendar.
2. **Time of initial ECG** - Enter the time of the initial ECG performed in the ED using the pop-up clock.
3. **ECG (electronic read)** -
  - Enter the HR based on the electronic ECG read results
  - Enter the QT based on the electronic ECG read results
  - Enter the QTc based on the electronic ECG read results.

**ECG FORM**

**Initial 12-Lead ECG Interpretation**

Information entered into eCRF by CRC.

<b>1. Date of initial ECG (mm/dd/yyyy):</b>	
<b>2. Time of initial ECG (hh:mm):</b>	
<b>3. ECG (electronic read)</b>	HR _____ bpm QT _____ ms QTc _____ ms



**CRF Page 11 – CT Test Form**

The information in this form should be entered by the CRC.

Indicate whether or not the CT was done. If not, mark the box next to the closest reason as to why it was not done.

**1. Was the CCTA performed?**

- Select “yes” or “no” to indicate whether the CCTA was performed

- Select “yes” if CCTA started even if not completed
- Select “no” if subject was randomized to SOC and move to next form

For Interventional arm

If “no”, select all reasons that apply for CCTA not being performed and fill out either the protocol deviation form or the protocol violation form, depending on the reason the CCTA was not performed.

- a. Select the Scanner Manufacturer/Model from the options. If none of the available options are applicable, select “other” and specify.
- b. Select “yes” or “no” to indicate whether hybrid imaging was performed
- c. As accurately as possible, enter the time the CCTA was ordered using the pop-up clock. This information should be available in the subject’s medical record.
- d. Enter the time the test was performed using the pop-up clock. This information should be gathered from the images (unless available from the report). The time refers to the start of the test.
- e. Enter the time the test was interpreted using the pop-up clock. This should be taken from the time stamp on the physician report of the results of the test.

**2. Calcium Scan**

Indicate whether calcium scan was done or not. If no, give reason and fill out protocol violation form

**3. CTA**

Select “yes” or “no” as appropriate.

**4. Intra – CCTA Vitals**

Indicate the average heart rate during the acquisition of the CCTA.

**5. Pre-procedure Medications:**

Select “yes” or “no” to indicate whether subject received **pre-procedure medications**

- If yes, indicate whether subject received IV beta blockers. If yes, select whether it was Metoprolol or other and indicate the dose.
- If yes, indicate whether subject received PO beta blockers. If yes, select whether it was Metoprolol or Atenolol and indicate the dose.
- If yes, indicate whether subject received Nitroglycerin SL. If yes, indicate the dose given.

**6. Contrast Agent:**

Select the contrast agent that was given from the available options. If none of the available options are applicable, select “other” and specify. If no contrast agent was given, fill out a Protocol Deviation Form.

**7. Concentration mg iodine per ml**

Select the concentration of iodine from the available options.

**8. Completion of the CT Scan**

Select “yes” or “no” to indicate whether the CCTA was COMPLETED

- If “no”, select all reasons that apply for CCTA not being completed. If none of the reason are applicable, select “other” and specify.

**9. Prospectively gated/triggered CT scan**

Select “yes” or “no” to indicate whether the scan was prospectively gated/triggered

**10. Retrospectively gated CT scan**

Select “yes” or “no” to indicate whether the scan was retrospectively gated/triggered

**11. Dose Length Product of CTA only:**

Enter the dose length product in mGY cm for CTA only.

**12. Total Dose Length Product**

Enter the dose length product in mGY cm for the entire CT scan.

**13. CTDI volume of CTA**

Enter the CTDI volume in mGy for CTA only.

# CT FORM

## CCTA Technical Assessment

To be entered into eCRF by CRC.

<p><b>1. Was CCTA performed</b></p> <p>For interventional arm: If not performed, please complete protocol deviation form or protocol violation form</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><b>If no</b>, indicate why not done:</p> <p><input type="checkbox"/> Definite ACS (positive troponin, ECG changes)</p> <p><input type="checkbox"/> Contrast extravasation</p> <p><input type="checkbox"/> Arrhythmias</p> <p><input type="checkbox"/> Claustrophobia</p> <p><input type="checkbox"/> Anaphylaxis</p> <p><input type="checkbox"/> ED physician decision</p> <p><input type="checkbox"/> Patient refusal/withdrawal</p> <p><input type="checkbox"/> Equipment failure</p> <p><input type="checkbox"/> Other: _____</p>
<p>A. Record Scanner Manufacturer/Model</p>	<p>Manufacturer: <input type="checkbox"/> Siemens  <input type="checkbox"/> GE  <input type="checkbox"/> Philips  <input type="checkbox"/> Other _____</p> <p>Model: <input type="checkbox"/> Somatom Sensation 64  <input type="checkbox"/> Lightspeed 64  <input type="checkbox"/> Lightspeed VCT  <input type="checkbox"/> Dual Source  <input type="checkbox"/> Flash  <input type="checkbox"/> ICT  <input type="checkbox"/> Other _____</p>
<p>B. Hybrid Imaging (SPECT or PET)</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No If yes, please provide copy of the report</p>
<p>C. Time CT ordered (hh:mm)</p>	
<p>D. Time CT performed (hh:mm)</p>	
<p>E. Time of CT interpretation (hh:mm)</p>	
<p><b>2. Calcium Scan</b> If no, give reason and fill out protocol violation form</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
<p><b>3. CTA</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
<p><b>4. Intra CCTA vitals:</b></p>	
<p>Average HR during scan:</p>	<p>bpm</p>
<p><b>5. Pre-procedure medications:</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
<p>a. Beta blocker IV</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, <input type="checkbox"/> Metoprolol  <input type="checkbox"/> Other _____                  dose: _____ mg</p>
<p>b. Beta blocker PO</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No  <input type="checkbox"/> Metoprolol  <input type="checkbox"/> Atenolol _____                  dose: _____ mg</p>
<p>c. Nitroglycerin SL</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, dose:</p>
<p><b>6. Contrast agent:</b></p>	<p><input type="checkbox"/> Isovue  <input type="checkbox"/> Omnipaque  <input type="checkbox"/> Optiray</p>

	<input type="checkbox"/> Vispaque <input type="checkbox"/> Other Specify: _____
a. concentration mg iodine per ml	<input type="checkbox"/> 300 <input type="checkbox"/> 320 <input type="checkbox"/> 350 <input type="checkbox"/> 370
<b>7. Completion of the CT scan</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If no, indicate why not done:  Medical reason <input type="checkbox"/> Patient refusal/withdrawal <input type="checkbox"/> Equipment failure <input type="checkbox"/> Other <input type="checkbox"/> If other, specify: _____
<b>8. Prospectively gated/triggered cardiac CTA scan</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<b>9. Retrospectively gated cardiac CTA scan</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<b>10. Dose Length Product of CTA only:</b>	mGY cm
<b>11. Total Dose Length Product</b>	mGY cm
<b>12. CTDI Volume of CTA</b>	mGy

**CRF Page 11 - CT Test Subject Physician Reading Form**

The information in this form should be entered by the CRC and signed by the Physician.

**1. Reading physician ID:**

Enter the ID number of the physician reading the scan (the ID number provided during the reader certification course). (Please have CT Reader initial paper CRF)

**2. Calcium Score**

Enter the calcium score.

**3. Coronary CTA**

This is based on visual assessment and a judgment call.

Normal: If no luminal narrowing is seen the segment can be labeled as normal despite the presence of plaque.

Indeterminate: If image quality is not optimal and no conclusive assessment can be made OR if you cannot decide for one of the other categories.

\*\*A stent will only be considered a PV if, upon revisiting the case, there is evidence of a stent in the subject's medical record.

**4. Overall study quality**

Interpretable: Check this when you can confidently rule out or rule in the presence of significant stenosis in a patient).

**5. LV functional analysis performed:**

Select "yes" or "no" to indicate whether LV functional analysis was performed

If "yes":

- Select "normal" or "abnormal" Global LV function
- Enter the Global LV function as a percent
- Select "yes" or "no" to indicate Regional Wall Motion ABNORMALITY
- If "yes" to Regional Wall Motion ABNORMALITY, select the applicable location(s)
- If yes, select "yes" or "no" to indicate whether this matches stenosis territory

**6. If retrospectively gated, was tube modulation technique or a similar radiation safety technique used**

Select "yes" or "no" to indicate whether the scan was retrospectively gated or not, and if so, whether tube current modulation was used or not

**7. Incidental Findings:**

Indicate if any of the listed incidental findings were noted on CT. Also indicate if any recommendations for follow-up imaging were made.

**Note:** For pulmonary nodules, please only report those in whom the CT Physician recommended follow-up imaging or biopsy.

# CT Test Subject Physician Reading Form

To be completed by CT reader with signature next to physician ID on paper CRF; information entered on form by CRC.

<b>1. Reading physician ID:</b> (Please have CT Reader initial paper CRF)	
<b>2. Calcium Score</b>	
<b>3. Coronary CTA</b> Fill out the appropriate box to indicate the level of stenosis. If level of stenosis equals stent, please fill out the protocol violation form.	
a. Left Main	<input type="checkbox"/> normal 0% <input type="checkbox"/> 1-49% (non-significant/mild or minor) <input type="checkbox"/> 50-99% (significant/severe) <input type="checkbox"/> 100% (occluded) <input type="checkbox"/> indeterminate <input type="checkbox"/> stent**
b. LAD (any)	<input type="checkbox"/> normal 0% <input type="checkbox"/> 1-49% (non-significant/mild or minor) <input type="checkbox"/> 50-69% (moderate) <input type="checkbox"/> 70-99% (significant/severe) <input type="checkbox"/> 100% (occluded) <input type="checkbox"/> indeterminate <input type="checkbox"/> stent**
c. LCX (any)	<input type="checkbox"/> normal 0% <input type="checkbox"/> 1-49% (non-significant/mild or minor) <input type="checkbox"/> 50-69% (moderate) <input type="checkbox"/> 70-99% (significant/severe) <input type="checkbox"/> 100% (occluded) <input type="checkbox"/> indeterminate <input type="checkbox"/> stent**
d. RCA (any)	<input type="checkbox"/> normal 0% <input type="checkbox"/> 1-49% (non-significant/mild or minor) <input type="checkbox"/> 50-69% (moderate) <input type="checkbox"/> 70-99% (significant/severe) <input type="checkbox"/> 100% (occluded) <input type="checkbox"/> indeterminate <input type="checkbox"/> stent**
<b>4. Overall study quality:</b>	<input type="checkbox"/> Interpretable: <input type="checkbox"/> Uninterpretable:
<b>5. LV functional analysis performed:</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No  Global LV function <input type="checkbox"/> Abnormal <input type="checkbox"/> Normal Global LV function in % _____ Regional Wall Motion Abnormality: <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, match stenosis territory <input type="checkbox"/> Anterior/apex/septal <input type="checkbox"/> Inferior/posterior <input type="checkbox"/> Lateral
<b>6. If retrospectively gated, was tube modulation technique or a similar radiation safety technique used?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<b>7. Incidental Findings</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, mark all that apply: <ul style="list-style-type: none"> <li>• Coronary anomaly <input type="checkbox"/></li> <li>• Cardiac finding <input type="checkbox"/></li> <li>• Pulmonary nodules requiring follow-up <input type="checkbox"/></li> <li>• Pulmonary Embolism <input type="checkbox"/></li> <li>• Pneumonia <input type="checkbox"/></li> <li>• Aortic Aneurysm <input type="checkbox"/></li> <li>• Other <input type="checkbox"/></li> </ul> *If yes, specify _____ If yes, specify, _____ Requires follow up imaging <input type="checkbox"/> Yes <input type="checkbox"/> No
**If stent is present, please check the medical record (MR). If evidence of a stent is documented in the MR, fill out the protocol violation form.	

**CRF Page 12- Nuclear Imaging**

This information should be entered by the CRC.

**1. Was nuclear imaging done?**

Select “yes” or “no” to indicate whether or not nuclear imaging was done.

**2. What are the initials of the physician who reported it?**

Type in the initials of the physician who reported the nuclear image

**3. Date/time test was ordered:**

Indicate the date and time the test was ordered using the pop-up calendar and pop-up clock. This information should be available in the subject’s medical record.

**4. Date/time test was performed:**

- Enter the date/time the test was performed using the pop-up calendar and clock. This information should be gathered from the images (unless available from the report). The time refers to the start of the test.

**5. Date/time of test interpretation:**

- Enter the date/time the test was interpreted using the pop-up calendar and clock. This should be taken from the time stamp on the report.

**6. Modality:**

- Select “Rest”, “Stress”, or “Rest & Stress” to indicate the modality of the nuclear imaging test conducted (If “Stress” or “Rest & Stress”, indicate whether ETT or pharmacologic)

**8. If ETT,**

- Select “Bruce”, “Modified Bruce”, “Naughton”, “Supine Bicycle” or “Upright Bicycle” to indicate modality
- Time to end of exercise: Enter the total amount of time of exercise (in minutes and seconds)
- Enter the METS achieved
- Enter the %MPHR (percentage of the maximum predicted heart rate attained)

**9. ECG changes meeting criteria for ischemia?**

- Select “yes” or “no” to indicate if ECG changes were observed during the test.
- Enter whether ST depression or ST elevation was present and the maximum ST segment deviation in mm.
- Ventricular arrhythmias are defined as at least 3 consecutive beats of non-sustained ventricular tachycardia, sustained ventricular tachycardia, or ventricular fibrillation.
- If other ECG changes, then specify.

**10. If pharmacological, list the agent used:**

- Select the agent(s) used from the available options

**11. Rest protocol tracer**

- Select the one tracer that was used and specify the administered activity/unit of activity
- 12. Stress protocol**
- Select the one tracer that was used and specify the administered activity/unit of activity
- 13. Was a ReInjection performed?**
- Select “yes” or “no” to indicate if a reInjection was performed. If yes, select the one tracer used and specify the administered activity/unit of activity.
- 14. Was a Rubidium test performed?**
- If the subject had a Rubidium protocol, indicate the administered activity/unit of activity at rest and at stress.
- 15. Completion of Protocol**
- Indicate whether or not the protocol was completed, the final heart rate, the maximum predicted heart rate and whether or not the subject reached the target. The target heart rate is 85% of the maximum predicted heart rate. If no, select whether or not is was converted to pharmacologic. If yes, select the agent used.  
\*For Rubidium – there is no target heart rate as pharmacological stress is used because of the short half life time.
- 16. If there were symptoms of possible CAD, enlist any other symptoms perceived by the patient.**
- Select “yes” or “no” to indicate if the subject had any chest pain.
  - If yes, select “yes” or “no” to indicate if the chest pain limited exercising capacity.
  - If yes, select if the subject experienced any of the remaining symptoms listed. If none of the available options are applicable select “other” and specify
- 17. Was the perfusion in the anterior/apical myocardial territory normal?**
- Select “yes” or “no”
- 18. Was the perfusion in the lateral myocardial territory normal?**
- Select “yes” or “no”
- 19. Was the perfusion in the infero-posterior myocardial territory normal?**
- Select “yes” or “no”
- 20. Resting gated LVEF**
- For rest exams only: Indicate whether rest left ventricular ejection fraction (LVEF) was normal (> 60%), abnormal ( $\leq 60\%$ ), or not done. Enter the actual value of the ejection fraction at rest.
- 21. Post stress gated LVEF**
- For rest and stress exams: Indicate whether rest left ventricular ejection



fraction (LVEF) was normal ( $> 60\%$ ), abnormal ( $\leq 60\%$ ), or not done. Enter the actual value of the ejection fraction at rest. Indicate whether the post-stress LVEF was normal or abnormal.

- For stress exams only: Indicate whether the post-stress LVEF was normal or abnormal.

**22. Transient Ischemic Dilatation**

- Select “yes” or “no” to indicate whether or not transient ischemic dilatation was present. If not present on the report, select “Not Mentioned”.

**24. Was additional nuclear imaging performed?**

- If the subject had another nuclear imaging stress test, select yes. A blank form will be generated automatically. Enter details as per the instructions shown above.

# DIAGNOSTIC TESTING FORM

## Nuclear Imaging

1. Was nuclear imaging done?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
2. What are the initials of the physician who reported it?		
3. Date/time test ordered:	Date (mm/dd/yyyy): Time (hh:mm):	
4. Date/time test was performed:	Date (mm/dd/yyyy): Time (hh:mm):	
5. Date/time of test interpretation:	Date (mm/dd/yyyy): Time (hh:mm):	
6. Modality:	<input type="checkbox"/> Rest <input type="checkbox"/> Stress <input type="checkbox"/> Rest & Stress If <u>stress</u> , select one of the following: <input type="checkbox"/> ETT (go to qs.7) <input type="checkbox"/> Pharmacologic (go to qs. 9)	
7. If ETT,	<input type="checkbox"/> Bruce <input type="checkbox"/> Modified Bruce <input type="checkbox"/> Naughton <input type="checkbox"/> Supine Bicycle <input type="checkbox"/> Upright Bicycle	Time to end of exercise _____min_____sec METS _____ %MPHR _____
8. ECG changes meeting criteria for ischemia?	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, specify changes: o ST depression <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, what is the maximum depression? _____mm o ST elevation <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, what is the maximum elevation? _____mm o Ventricular arrhythmias <input type="checkbox"/> Yes <input type="checkbox"/> No o Other <input type="checkbox"/> Yes <input type="checkbox"/> No, if yes, specify	
10. If pharmacological, list the agent used:	<input type="checkbox"/> Dobutamine <input type="checkbox"/> Dipyridamole <input type="checkbox"/> Adenosine <input type="checkbox"/> Regadenoson	
11. Rest protocol tracer:  administered activity /unit of activity	<input type="checkbox"/> Technetium <input type="checkbox"/> Tetrafosmin <input type="checkbox"/> Thallium _____(Mega Bq/millicuries)	
12. Stress Protocol tracer:  administered activity /unit of activity	<input type="checkbox"/> Technetium <input type="checkbox"/> Tetrafosmin <input type="checkbox"/> Thallium _____(Mega Bq/millicuries)	
13. Was a Reinjection performed?	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, fill out the following: Tracer <input type="checkbox"/> Technetium <input type="checkbox"/> Tetrafosmin	

<p><b>administered activity /unit of activity</b></p>	<p><input type="checkbox"/> Thallium _____(Mega Bq/millicuries)</p>
<p><b>14. Was a Rubidium test performed? rest stress</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No If yes, administered activity /unit of activity - _____(Mega Bq/millicuries) administered activity /unit of activity - _____(Mega Bq/millicuries)</p>
<p><b>15. Completion of Protocol</b></p>	<p><input type="checkbox"/> Not done <input type="checkbox"/> Done and completed <input type="checkbox"/> Performed but not completed Baseline Heart rate ____ bpm Peak Heart Rate _____ bpm Systolic Blood Pressure at rest _____ mmHg Diastolic Blood Pressure at rest _____mmHg Systolic Blood Pressure at peak stress ____ mmHg Diastolic Blood Pressure at peak stress ____mmHg Reached target HR?* <input type="checkbox"/> Yes <input type="checkbox"/> No If no, was it converted to pharmacologic? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, choose the agent used: <input type="checkbox"/> Dobutamine <input type="checkbox"/> Dipyridamole <input type="checkbox"/> Adenosine <input type="checkbox"/> Regadenoson  Did the patient develop symptoms of possible CAD (including CP, SOB) <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/>equivocal (if the answer is yes or equivocal, go to qs 15)</p>
<p><b>16. If there were symptoms of possible CAD, enlist any other symptoms perceived by the patient.</b></p>	<p>Chest Pain <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, did the chest pain limit exercising capacity? <input type="checkbox"/> Yes <input type="checkbox"/> No Shortness of Breath <input type="checkbox"/> Yes <input type="checkbox"/> No Hypotension <input type="checkbox"/> Yes <input type="checkbox"/> No VT or non sustained VT <input type="checkbox"/> Yes <input type="checkbox"/> No Patient request <input type="checkbox"/> Yes <input type="checkbox"/> No Abnormal BP response <input type="checkbox"/> Yes <input type="checkbox"/> No Other <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, specify:</p>
<p><b>17. Was the perfusion in the anterior/apical myocardial territory normal?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
<p><b>18. Was the perfusion in the lateral myocardial territory normal?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
<p><b>19. Was the perfusion in the infero-posterior myocardial territory normal?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
<p><b>20. Resting gated LVEF</b></p>	<p><input type="checkbox"/> Not done _____ EF % <input type="checkbox"/> Normal <input type="checkbox"/> Abnormal</p>
<p><b>21. Post stress gated LVEF</b></p>	<p>_____ EF % <input type="checkbox"/> Normal <input type="checkbox"/> Abnormal</p>
<p><b>22. Transient Ischemic Dilatation</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not Mentioned</p>
<p><b>23. Was additional nuclear imaging performed?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>

**CRF Page 13- Stress Echocardiogram**

This information should be entered by the CRC.

- 1. Was a stress echocardiogram performed?**
  - Select “yes” or “no” to indicate if a stress echocardiogram was performed
- 2. What are the initials of the physician who reported it?**
  - Enter the initials of the physician who reported it.
- 3. Date/time test ordered:**
  - Enter the date and time the test was ordered using the pop-up calendar and pop-up clock. This information should be available in the subject’s medical record.
- 4. Date/time test performed:**
  - Enter the date/time the test was performed using the pop-up calendar and clock. This information should be gathered from the images (unless available from the report). The time refers to the start of the test.
- 5. Date/time of test interpretation:**
  - Enter the date/time the test was interpreted using the pop-up calendar and clock. This should be taken from the time stamp on the report.
- 6. Modality:**
  - Indicate the modality of Stress Echocardiography performed.
- 7. If Exercise:**
  - If exercise, indicate the modality of testing used.
  - Determine the time the subject exercised until, the METS achieved and the percentage of the maximum predicted heart rate attained.
- 8. If Dobutamine:**
  - If dobutamine was used, indicate the maximum dose given, whether any provocative tests were used, the percentage of maximum heart rate achieved and whether or not the response was biphasic.
- 9. ECG changes:**
  - Indicate whether or not ischemic ECG changes were observed during the test.
  - Enter whether ST depression or ST elevation was present and the maximum ST segment deviation in mm. Ventricular arrhythmias are defined as at least 3 consecutive beats of non-sustained ventricular tachycardia, sustained ventricular tachycardia, or ventricular fibrillation. If other ECG changes, then specify.
- 10. Completion of protocol:**
  - Indicate whether or not the protocol was completed, the baseline and peak heart rate and blood pressure, and whether or not the subject reached the target. The target heart rate is 85% of the maximum predicted heart rate. If

not, was the test converted to a pharmacologic one? If yes, select the agent that was used from the available options.

**11. If there were symptoms of possible CAD, enlist any other symptoms perceived by the patient.**

- Select “yes” or “no” to indicate if the subject had any chest pain.
- If yes, select “yes” or “no” to indicate if the chest pain limited exercising capacity.
- If yes, select if the subject experienced any of the remaining symptoms listed. If none of the available options are applicable select “other” and specify

**12. Was the wall motion in the anterior/apical segment normal on stress?**

- Select “yes” or “no”

**13. Was the wall motion in the lateral segment normal on stress?**

- Select “yes” or “no”

**14. Was the wall motion in the infero-posterior segment normal on stress?**

- Select “yes” or “no”

**15. Resting LVEF**

- Enter the ejection fraction at rest and whether or not the overall function was normal or abnormal.
- Select “yes” or “no” to indicate whether or not there was a scar existing on the exam
- If yes, indicate whether the location was anterior/apical, inferior/posterior, or Lateral

**16. Stress LVEF**

- Enter the ejection fraction at stress and whether or not the overall function was normal or abnormal.
- If abnormal, select “yes” or “no” to indicate whether it was severely decreased (<35% EF)

**17. LV Dilatation at Peak Stress**

- Indicate whether or not there was LV dilatation at peak stress. If not present on the report, select “Not Mentioned”.

**18. ECHO Results:**

- Describe the overall ECHO result as normal or abnormal and if abnormal, choose the option that best suits the reason.

**19. Was another Stress Echocardiogram done?**

- If the subject had a repeat stress echocardiography test, select yes. A blank form will be generated automatically. Enter details as per the instructions shown above. Stress Echocardiogram

# Stress Echocardiogram

<p><b>1. Was a stress echocardiogram performed?</b></p>	<input type="checkbox"/> Yes <input type="checkbox"/> No	
<p><b>2. What are the initials of the physician who reported it?</b></p>		
<p><b>3. Date/time test ordered:</b></p>	Date (mm/dd/yyyy): Time (hh:mm):	
<p><b>4. Date/time test performed:</b></p>	Date (mm/dd/yyyy): Time (hh:mm):	
<p><b>5. Date/time of test interpretation:</b></p>	Date (mm/dd/yyyy): Time (hh:mm):	
<p><b>6. Modality:</b></p>	Select one of the following: <input type="checkbox"/> Exercise <input type="checkbox"/> Dobutamine <input type="checkbox"/> Other _____	
<p><b>7. If Exercise:</b></p>	<input type="checkbox"/> Bruce <input type="checkbox"/> Modified Bruce <input type="checkbox"/> Naughton <input type="checkbox"/> Supine Bicycle <input type="checkbox"/> Upright Bicycle	Time to end of exercise _____ min _____ sec METS _____ %MPHR _____
<p><b>8. If Dobutamine:</b></p>	Maximum dobutamine dose given:- _____ mcg/kg/min Atropine given?: <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, dose: _____ mg Handgrip use?: <input type="checkbox"/> Yes <input type="checkbox"/> No %MPHR _____ Biphasic response <input type="checkbox"/> Yes <input type="checkbox"/> No	
<p><b>9. ECG changes:</b></p>	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, specify changes: ST depression <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, what is the maximum depression? _____ mm ST elevation <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, what is the maximum elevation? _____ mm Ventricular arrhythmias <input type="checkbox"/> Yes <input type="checkbox"/> No Other _____ <input type="checkbox"/> Yes <input type="checkbox"/> No	
<p><b>10. Completion of protocol:</b></p>	<input type="checkbox"/> Not done <input type="checkbox"/> Done and completed <input type="checkbox"/> Performed but not completed Baseline Heart Rate _____ bpm (3 digits) Peak Heart Rate _____ bpm Systolic Blood Pressure at rest _____ mmHg Diastolic Blood Pressure at rest _____ mmHg Systolic Blood Pressure at peak stress _____ mmHg Diastolic Blood Pressure at peak stress _____ mmHg Reached target HR? <input type="checkbox"/> Yes <input type="checkbox"/> No If no, was it converted to pharmacologic? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, choose the agent used: <input type="checkbox"/> Dobutamine <input type="checkbox"/> Dipyridamole <input type="checkbox"/> Adenosine <input type="checkbox"/> Regadenoson Did the patient develop symptoms of possible CAD (including CP, SOB, C/yes, No <input type="checkbox"/> equivocal (if the answer is yes or equivocal, go to qs 11)	

<p><b>11. If there were symptoms of possible CAD, enlist any other symptoms perceived by the patient.</b></p>	<p>Chest Pain <input type="checkbox"/>Yes <input type="checkbox"/>No                  If yes, did the chest pain limit exercising capacity? <input type="checkbox"/>Yes <input type="checkbox"/>No                  Shortness of Breath <input type="checkbox"/>Yes <input type="checkbox"/>No                  Hypotension <input type="checkbox"/>Yes <input type="checkbox"/>No                  VT <input type="checkbox"/>Yes <input type="checkbox"/>No                  Patient request <input type="checkbox"/>Yes <input type="checkbox"/>No                  Abnormal BP response <input type="checkbox"/>Yes <input type="checkbox"/>No                  Other <input type="checkbox"/>Yes <input type="checkbox"/>No                  If yes, specify:</p>
<p><b>12. Was the wall motion in the anterior/apical segment normal on stress?</b></p>	<p><input type="checkbox"/>Yes <input type="checkbox"/>No</p>
<p><b>13. Was the wall motion in the lateral segment normal on stress?</b></p>	<p><input type="checkbox"/>Yes <input type="checkbox"/>No</p>
<p><b>14. Was the wall motion in the infero-posterior segment normal on stress?</b></p>	<p><input type="checkbox"/>Yes <input type="checkbox"/>No</p>
<p><b>15. Resting LVEF</b></p>	<p>____ EF% <input type="checkbox"/>Normal <input type="checkbox"/>Abnormal                  Scar existing on rest exam <input type="checkbox"/>Yes <input type="checkbox"/>No                  If yes, <input type="checkbox"/> Anterior/apical <input type="checkbox"/> inferior/posterior <input type="checkbox"/> Lateral</p>
<p><b>16. Stress LVEF</b></p>	<p>____ EF% <input type="checkbox"/>Normal <input type="checkbox"/>Abnormal                  If abnormal, severely decreased (&lt;35% EF) <input type="checkbox"/>Yes <input type="checkbox"/>No</p>
<p><b>17. LV Dilatation at Peak Stress</b></p>	<p><input type="checkbox"/>Yes <input type="checkbox"/>No <input type="checkbox"/>Not Mentioned</p>
<p><b>18. ECHO Results:</b></p>	<p><input type="checkbox"/>Normal <input type="checkbox"/>Abnormal                  If abnormal, specify:  <input type="checkbox"/> Inducible ischemia  <input type="checkbox"/> MI/scar (no ischemia)  <input type="checkbox"/> Both</p>
<p><b>19. Was another Stress Echocardiogram done?</b></p>	<p><input type="checkbox"/>Yes <input type="checkbox"/>No</p>

**CRF Page 14- Transthoracic Echocardiogram (rest)**

This information should be entered by the CRC.

1. **Was a resting transthoracic echocardiogram performed?**
  - Select “yes” or “no” to indicate whether or not a transthoracic echocardiogram was performed
2. **What are the initials of the physician who performed the test?**
  - Enter the initials of the physician who performed the test
3. **Date/time test ordered:**
  - Enter the date and time the test was ordered using the pop-up calendar and pop-up clock. This information should be available in the subject’s medical record.
4. **Date/time test performed:**
  - Enter the date/time the test was performed using the pop-up calendar and clock. This information should be gathered from the images (unless available from the report). The time refers to the start of the test.
5. **Date/time of test interpretation:**
  - Enter the date/time the test was interpreted using the pop-up calendar and clock. This should be taken from the time stamp on the report.
6. **Was the wall motion in the anterior/apical segment normal?**
  - Select “yes” or “no”
7. **Was the wall motion in the lateral segment normal?**
  - Select “yes” or “no”
8. **Was the wall motion in the infero-posterior segment normal?**
  - Select “yes” or “no”
9. **LV function (Ejection fraction %)**
  - Record the ejection fraction.
10. **Results:**
  - Indicate whether the overall result was normal or abnormal, and if abnormal, please specify.
11. **Was a resting transthoracic echocardiogram done again?**
  - If the subject had a repeat rest echocardiography test, select yes. A blank form will be generated automatically. Enter details as per the instructions shown above.



## Transthoracic Echocardiogram (rest)

To be entered on form by CRC

1. Was a resting transthoracic echocardiogram performed?	<input type="checkbox"/> Yes <input type="checkbox"/> No
2. What are the initials of the physician who performed the test?	
3. Date/time test ordered:	Date (mm/dd/yyyy): Time (hh:mm):
4. Date/time test performed:	Date (mm/dd/yyyy): Time (hh:mm):
5. Date/time of test interpretation:	Date (mm/dd/yyyy): Time (hh:mm):
6. Was the wall motion in the anterior/apical segment normal?	<input type="checkbox"/> Yes <input type="checkbox"/> No
7. Was the wall motion in the lateral segment normal?	<input type="checkbox"/> Yes <input type="checkbox"/> No
8. Was the wall motion in the infero-posterior segment normal?	<input type="checkbox"/> Yes <input type="checkbox"/> No
9. LV function (Ejection fraction %)	_____%
10. Results:	<input type="checkbox"/> Normal <input type="checkbox"/> Abnormal If abnormal, specify:
11. Was a resting transthoracic echocardiogram done again?	<input type="checkbox"/> Yes <input type="checkbox"/> No

**CRF Page 15- Exercise ECG stress test (Non Imaging Only)**

This information should be entered by the CRC.

- 1. Was an exercise ECG stress test performed?**
  - Select “yes” or “no” to indicate whether or not an exercise ECG stress test was performed.
- 2. What are the initials of the physician who performed the test?**
  - Enter the initials of the physician who performed the test
- 3. Date/time test ordered:**
  - Enter the date and time the test was ordered using the pop-up calendar and pop-up clock. This information should be available in the subject’s medical record.
- 4. Date/time test performed:**
  - Enter the date/time the test was performed using the pop-up calendar and clock. This information should be gathered from the images (unless available from the report). The time refers to the start of the test.
- 5. Date/time of test interpretation:**
  - Enter the date/time the test was interpreted using the pop-up calendar and clock. This should be taken from the time stamp on the report.
- 6. Type of Exercise protocol**
  - Select the modality of exercise test performed from the available options
- 7. Functional Capacity**
  - Enter the time the subject exercised until (time to end of treadmill), the METS achieved and the percentage of the maximum predicted heart rate (MPHR) attained.
- 8. Completed protocol?**
  - Indicate whether or not the protocol was completed, the baseline and peak heart rate and , and whether or not the subject reached the target. If not, was the test converted to a pharmacologic one? If yes, select the agent that was used from the available options.
- 9. If there were symptoms of possible CAD, enlist any other symptoms perceived by the patient.**
  - Select “yes” or “no” to indicate if the subject had any chest pain.
  - If yes, select “yes” or “no” to indicate if the chest pain limited exercising capacity.
  - If yes, indicate whether it was ischemic or equivocal
  - If yes, select if the subject experienced any of the remaining symptoms listed. If none of the available options are applicable select “other” and specify
- 10. Results:**
  - Indicate whether the results were negative, positive, or borderline

- If positive or borderline, select “yes” or “no” to indicate whether there was ST depression, ST elevation, Ventricular arrhythmias, or Other. If ST depression or ST elevation, enter the maximum. If other, specify.

**11. Was exercise ECG stress test done again?**

- If the subject had a repeat exercise treadmill test, select yes. A blank form will be generated automatically. Enter details as per the instructions shown above.

## Exercise ECG Stress Test (Non-imaging only)

To be entered on form by CRC.

<p><b>1. Was an exercise ECG stress test performed?</b></p>	<p><input type="checkbox"/>Yes <input type="checkbox"/>No</p>
<p><b>2. What are the initials of the physician who performed the test?</b></p>	<p></p>
<p><b>3. Date/time test ordered:</b></p>	<p>Date (mm/dd/yyyy): Time (hh:mm):</p>
<p><b>4. Date/time test performed:</b></p>	<p>Date (mm/dd/yyyy): Time (hh:mm):</p>
<p><b>5. Date/time of test interpretation:</b></p>	<p>Date (mm/dd/yyyy): Time (hh:mm):</p>
<p><b>6. Type of Exercise protocol</b></p>	<p><input type="checkbox"/>Bruce <input type="checkbox"/>Modified Bruce <input type="checkbox"/>Naughton <input type="checkbox"/>Supine Bicycle <input type="checkbox"/>Upright Bicycle</p>
<p><b>7. Functional Capacity</b></p>	<p>Time to end of Treadmill _____min_____sec METS _____ %MPHR _____</p>
<p><b>8. Completed protocol?</b></p>	<p><input type="checkbox"/> Not done <input type="checkbox"/> Done and completed <input type="checkbox"/> Performed but not completed Peak Heart Rate _____ bpm (3 digits) Baseline Heart Rate _____ bpm Reached target HR? <input type="checkbox"/>Yes <input type="checkbox"/>No <input type="checkbox"/>NA If no, was it converted to pharmacologic? <input type="checkbox"/>Yes <input type="checkbox"/>No If yes, choose the agent used: <input type="checkbox"/> Dobutamine <input type="checkbox"/> Dipyridamole <input type="checkbox"/> Adenosine <input type="checkbox"/> Regadenoson  Symptoms of possible CAD (including CP, SOB) <input type="checkbox"/>Yes <input type="checkbox"/>No <input type="checkbox"/>equivocal (If the answer is yes or equivocal, go to qs. 9)</p>
<p><b>9. If there were symptoms of possible CAD, enlist any other symptoms perceived by the patient.</b></p>	<p>Chest Pain <input type="checkbox"/>Yes <input type="checkbox"/>No If yes, did the chest pain limit exercising capacity? <input type="checkbox"/>Yes <input type="checkbox"/>No If yes, <input type="checkbox"/>Ischemic <input type="checkbox"/>Equivocal Shortness of Breath <input type="checkbox"/>Yes <input type="checkbox"/>No Hypotension <input type="checkbox"/>Yes <input type="checkbox"/>No VT or non sustained VT <input type="checkbox"/>Yes <input type="checkbox"/>No Patient request <input type="checkbox"/>Yes <input type="checkbox"/>No Abnormal BP response <input type="checkbox"/>Yes <input type="checkbox"/>No Other <input type="checkbox"/>Yes <input type="checkbox"/>No If yes, specify:</p>
<p><b>10. Results:</b></p>	<p><input type="checkbox"/>Negative <input type="checkbox"/>Positive <input type="checkbox"/>Borderline If positive or borderline, select as appropriate: <input type="checkbox"/> ST depression <input type="checkbox"/>Yes <input type="checkbox"/>No If yes, what was the maximum? _____ <input type="checkbox"/> ST elevation <input type="checkbox"/>Yes <input type="checkbox"/>No</p>

	If yes, what was the maximum? _____ <input type="checkbox"/> Ventricular arrhythmias <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Other <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, specify: _____
<b>11. Was exercise ECG stress test done again?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No

**CRF Page 16 - Cardiac Catheterization**

This information should be entered by the CRC.

- 1. Was Cardiac Catheterization done?**
  - Select “yes” or “no” to indicate whether cardiac catheterization was done.
- 2. Initials of physician who interpreted test:**
  - Enter the initials of the physician who interpreted the test.
- 3. Date/time test ordered:**
  - Enter the date and time the test was ordered using the pop-up calendar and pop-up clock. This information should be available in the subject’s medical record.
- 4. Date/time test performed:**
  - Enter the date/time the test was performed using the pop-up calendar and clock. This information should be gathered from the images (unless available from the report). The time refers to the start of the test.
- 5. Date/time of test interpretation:**
  - Enter the date/time the test was interpreted using the pop-up calendar and clock. This should be taken from the time stamp on the report.
- 6. Were there any complications to the procedure (as per cath lab ACC/NCDR instruction)?**
  - Indicate if there were any complications during the procedure. If yes, fill out the Adverse Event form.
- 7. Mark the appropriate box to indicate the level of stenosis in each vessel:**
  - Record the appropriate number to indicate the level of stenosis in each vessel. If multiple stents were placed, please fill out the note field.
- 8. Did subject undergo revascularization?**
  - Select “yes” or “no” to indicate whether the subject underwent revascularization
  - If yes, indicate whether it was PCI or CABG
- 9. Radiation Exposure**
  - Record the fluoroscopy time, the number of cine runs, and the radiation dose. Please provide all values and units available. If multiple values available, please enter all values and units separated using a “;”. For example, if both the fluoro and dosimeter are available, enter: dosimeter: 300 mrem/mrad; fluoro: 10,000 cGycm<sup>2</sup>.
- 10. Cardiac Catheterization done again?**
  - If the subject had a repeat cardiac catheterization, select yes. A blank form will be generated automatically. Enter details as per the instructions shown above.

# Cardiac Catheterization

To be entered by the CRC

<b>1. Was Cardiac Catheterization done?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<b>2. Initials of physician who interpreted test:</b>	
<b>3. Date/time test ordered:</b>	Date (mm/dd/yyyy): Time (hh:mm):
<b>4. Date/time test performed:</b>	Date (mm/dd/yyyy): Time (hh:mm):
<b>5. Date/time of test interpretation:</b>	Date (mm/dd/yyyy): Time (hh:mm):
<b>6. Were there any complications to the procedure (as per cath lab ACC/NCDR instruction)?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No  If yes, fill out <b>adverse event form</b> .
<b>7. Mark the appropriate box to indicate the level of stenosis in each vessel:</b>	
a. Left Main	<input type="checkbox"/> normal 0% <input type="checkbox"/> 1-49% (non-significant/mild or minor) <input type="checkbox"/> 50-99% (significant/severe) <input type="checkbox"/> 100% (occluded) <input type="checkbox"/> indeterminate <input type="checkbox"/> stent   note: _____
b. LAD (any)	<input type="checkbox"/> normal 0% <input type="checkbox"/> 1-49% (non-significant/mild or minor) <input type="checkbox"/> 50-69% (moderate) <input type="checkbox"/> 70-99% (significant/severe) <input type="checkbox"/> 100% (occluded) <input type="checkbox"/> indeterminate <input type="checkbox"/> stent note: _____
c. LCX (any)	<input type="checkbox"/> normal 0% <input type="checkbox"/> 1-49% (non-significant/mild or minor) <input type="checkbox"/> 50-69% (moderate) <input type="checkbox"/> 70-99% (significant/severe) <input type="checkbox"/> 100% (occluded) <input type="checkbox"/> indeterminate <input type="checkbox"/> stent note: _____
d. RCA (any)	<input type="checkbox"/> normal 0% <input type="checkbox"/> 1-49% (non-significant/mild or minor) <input type="checkbox"/> 50-69% (moderate) <input type="checkbox"/> 70-99% (significant/severe) <input type="checkbox"/> 100% (occluded) <input type="checkbox"/> indeterminate <input type="checkbox"/> stent note: _____
e. LV Gram	<input type="checkbox"/> Normal <input type="checkbox"/> Abnormal
<b>8. Did subject undergo revascularization?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, type of revascularization: <input type="checkbox"/> PCI <input type="checkbox"/> LM <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> LAD <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> LCX <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> RCA <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> CABG
<b>9. Radiation Exposure</b>	Fluoro time ____ Min/sec Cine runs ____ Number Radiation Dose ____
<b>10. Cardiac Catheterization done again?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No

**CRF Page 17 – Patient Discharge Information**

This information should be entered by the CRC.

**1. Disposition:**

- Select the disposition of the subject. If “Died prior to ED discharge”, fill out an SAE form. If “left against medical advice”, fill out Protocol Deviation form.

**2. Date/time of index hospital discharge:**

- Enter the date and time of study hospital discharge using the pop-up calendar and pop-up clock. This is the time at which the hospital staff makes the decision to discharge the patient. This time is reflected by the physician discharge order.

**3. Was the subject admitted to the hospital? If so where?**

- Select “yes” or “no” to indicate whether the subject was admitted to the Hospital. If yes, indicate which unit of the hospital the subject was admitted to

**4. Primary discharge diagnosis (Choose One):**

- Indicate the primary ED diagnosis.
- **Cardiac Chest Pain not meeting ACS:** Select if the subject had chest pain that was most likely coronary but does not meet the definition of ACS. For example, this could be someone with borderline test findings, non-obstructive CAD, or vasospasm. If unclear, please review with your Site PI for guidance.

**5. If Non cardiac Chest Pain, (Choose one):**

- If the pain was non-cardiac in nature, choose the option that most closely resembles the cause. If none of the available options are applicable, select “other” and specify

**6. If, Non coronary cardiac chest pain, (Choose One):**

- If the pain was non-coronary in nature, choose the option that most closely resembles the cause. If none of the available options are applicable, select “other” and specify

**7. If Acute Coronary Syndrome, (Choose One):**

- If the subject had an ACS, indicate if it was a Myocardial Infarction (MI) or Unstable Angina (UAP). If MI, enter the peak biomarker levels, units, and the local laboratory upper limit of normal (ULN) values.

**8. Did the subject have any peri-procedural complications?**

- Indicate if the subject had any peri-procedural complications.
- **Stroke** is defined as an acute focal neurological deficit of sudden onset, not reversible within 24 hours, or that resolves in <24 hrs with clear evidence of a



new stroke on cerebral imaging.

- **Bleeding** is defined as major based on one or more of the following:
  - Transfusion of at least 2 units heterologous packed red blood cells or whole blood
  - Decrease in hemoglobin level by at least 2.0 g/l
  - Need for re-operation or invasive intervention (*e.g.* Evacuation of wound hematoma)
  - Bleeding at a critical anatomic site (intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial, or intramuscular with compartment syndrome)
- **Renal failure** is defined as:
  - increase in serum creatinine by 0.5mg/dL AND at least >1.5 mg/dL or
  - The requirement of renal replacement therapy (hemodialysis)
- **Anaphylaxis** defined as severe contrast reaction resulting in:
  - Anaphylactic shock
  - Intubation
  - Management of respiratory distress symptoms with epinephrine

# PATIENT DISCHARGE FORM

## Patient Discharge Information

<p><b>1. Disposition:</b></p>	<p><input type="checkbox"/> Direct ED Discharge</p> <p><input type="checkbox"/> Observational Unit admission</p> <p><input type="checkbox"/> Hospital admission</p> <p><input type="checkbox"/> Died prior to ED discharge; (If so, fill out SAE form)</p> <p style="padding-left: 20px;">Date of death (mm/dd/yyyy):</p> <p style="padding-left: 20px;">Time of death (hh:mm):</p> <p><input type="checkbox"/> Left against medical advice (If so, fill out Protocol Deviation form)</p> <p><input type="checkbox"/> Other, specify:</p>
<p><b>2. Date/time of index hospital discharge:</b></p>	<p>Date (mm/dd/yyyy):</p> <p>Time (hh:mm):</p> <p><input type="checkbox"/> Yes    <input type="checkbox"/> No</p>
<p><b>3. Was the subject admitted to the hospital? If so where?</b></p>	<p><input type="checkbox"/> Medical/surgical unit</p> <p><input type="checkbox"/> Step down unit</p> <p><input type="checkbox"/> ICU/CCU</p> <p><input type="checkbox"/> Telemetry</p>
<p><b>4. Primary discharge diagnosis (Choose One):</b></p>	<p><input type="checkbox"/> Noncardiac chest pain</p> <p><input type="checkbox"/> Non coronary cardiac chest pain</p> <p><input type="checkbox"/> Acute Coronary Syndrome</p> <p><input type="checkbox"/> Cardiac chest pain not meeting Acute Coronary Syndrome</p>
<p><b>5. If Non cardiac Chest Pain, (Choose one):</b></p>	<p><input type="checkbox"/> Pulmonary embolism</p> <p><input type="checkbox"/> Pneumonia</p> <p><input type="checkbox"/> GERD</p> <p><input type="checkbox"/> Gastrointestinal</p> <p><input type="checkbox"/> Musculoskeletal</p> <p><input type="checkbox"/> Aortic dissection</p> <p><input type="checkbox"/> Non cardiac CP without clear alternate diagnosis</p> <p><input type="checkbox"/> Other, specify</p>
<p><b>6. If, Non coronary cardiac chest pain, (Choose One):</b></p>	<p><input type="checkbox"/> Pericarditis/Myocarditis</p> <p><input type="checkbox"/> Valvular</p> <p><input type="checkbox"/> Cardiomyopathy</p> <p><input type="checkbox"/> Other _____</p>
<p><b>7. If Acute Coronary Syndrome, (Choose One):</b></p>	<p><input type="checkbox"/> Myocardial Infarction (defined as 1 and 2)</p> <p style="padding-left: 20px;">1. Anginal equivalent &gt; 10 minutes AND</p> <p style="padding-left: 20px;">2. Typical rise and fall of cardiac biomarkers</p> <p style="padding-left: 40px;">(record peak cTn _____</p> <p style="padding-left: 40px;">or peak CK-MB _____)</p> <p style="padding-left: 20px;">(Provide Units and ULN: _____)</p> <p><input type="checkbox"/> Unstable Angina (defined as 1 and 2)</p> <p style="padding-left: 20px;">1. Chest pain or anginal equivalent at rest or in an accelerating pattern</p> <p style="padding-left: 20px;">2. At least one objective sign : (check all signs that apply)</p> <p style="padding-left: 40px;">a. <input type="checkbox"/> New ST-segment changes (ST-depression <math>\geq</math>0.05mV or ST-elevation <math>\geq</math>0.1 mV)</p>

	<ul style="list-style-type: none"> <li>b. <input type="checkbox"/> New TWI <math>\geq 0.2V</math> on a resting ECG (if yes, please provide ECG)</li> <li>c. <input type="checkbox"/> Positive stress-test with imaging showing ischemia</li> <li>d. <input type="checkbox"/> Positive stress test without imaging resulting in increased anginal medication</li> <li>e. <input type="checkbox"/> Cath <math>&gt;70\%</math> stenosis or thrombus</li> <li>f. <input type="checkbox"/> CT angiography with <math>&gt;50\%</math> stenosis and LV dysfunction or <math>&gt;70\%</math> stenosis</li> </ul>
<p><b>8. Did the subject have any peri-procedural complications?</b></p>	<p>Stroke <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>Bleeding <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>Renal failure <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>Anaphylaxis <input type="checkbox"/> Yes <input type="checkbox"/> No</p>

**CRF page 18 – 48-72 hour Follow Up**

This information should be entered by the CRC. This form should only be filled for those subjects who were discharged from the hospital within 24 hours of presentation to the ED.

If answers to all questions below are “No” (i.e. the subject did not return to the ED or have any testing), then complete only this form, leave the 48-72 Hour Follow Up Supplement Form blank and mark as complete. If “Yes” was selected for any questions, enter detailed information on the 48-72 Hour Follow Up Supplement Form.

- 1. Was the 48-72 hour follow-up call completed?**
  - Select “yes”, “no”, or “Not Applicable” to indicate if the follow-up interview was completed.
  - If no, did the subject withdraw from the study? If yes, enter the reason the subject withdrew.
  
- 2. Date of contact (mm/dd/yyyy):**
  - Select the date the subject was initially contacted using the pop-up calendar
  
- 3. Time of contact (hh:mm):**
  - Select the time the subject was initially contacted using the pop-up clock
  
- 4. How many attempts were made to reach the patient?**
  - Select the number of attempts that were made to reach the subject
  
- 5. Did subject die?\***
  - Select “yes” or “no” to indicate whether the subject died. \*If yes, indicate the date and time of death using the pop-up clock and pop-up calendar. Also, fill out an SAE form.
  
- 6. Did subject have recurrence of chest pain or anginal equivalent?**
  - Select “yes” or “no” to indicate if the subject had recurrence of symptoms.
  - If yes, provide the duration of the longest episode of symptoms.
  
- 7. Did subject return to ED?**
  - Select “yes” or “no” to indicate if the subject returned to the ED.
  - If the subject returned to the ED, indicate the date, time, institution and reason for return. If the reason for return to the ED was recurrent chest pain, fill out an SAE form
  - Provide a copy of the medical records for revisits. Indicate the date and time of discharge.
  
- 8. Did subject return to OPD (since index hospitalization/last contact)?**
  - Select “yes” or “no” to indicate if the subject returned to the OPD.
  - If the subject returned to the OPD, indicate the date, time, institution and reason for return. If the reason for return to the OPD was recurrent chest pain, defined as cardiac in origin, fill out an SAE form.
  - Provide a copy of the medical records for revisits. Indicate the date and time of discharge.

- 9. Was the patient admitted to the hospital?**
- Select “yes” or “no” to indicate if the subject was admitted to the hospital.
  - If the subject was admitted to the hospital, indicate the date, time, institution and reason for return. If the reason for the admission was recurrent chest pain, defined as cardiac in origin, fill out an SAE form
  - Provide a copy of the medical records for revisits. Indicate the date and time of discharge.
- 10. Was an ongoing hospitalization prolonged for ischemic signs/symptoms?**
- Select “yes” or “no” to indicate if the index hospitalization was prolonged due to ischemic signs/symptoms.
- 11. Did subject have ECG changes (since index hospitalization/last contact)? \***
- Select “yes” or “no” to indicate if the subject had ECG changes since index hospitalization/last contact
  - \* If yes, fill out SAE form
- 12. Were Cardiac biomarkers obtained (since index hospitalization/last contact)?**
- Enter the peak biomarker levels, units, and the local laboratory upper limit of normal (ULN) values for cTn and CK-MB, if collected.
- 13. Was a stress test performed?**
- Select “yes” or “no” to indicate if a stress test was performed. If yes, provide report and fill out an SAE form. If yes, select whether it was ETT or Nuclear Imaging and complete subsequent questions.
- 14. Was a coronary angiogram performed?**
- Select “yes” or “no” to indicate whether a coronary angiogram was performed. If results were positive fill out an SAE form. If yes, provide report and complete subsequent questions.
- 15. Was a PCI performed?**
- Select “yes” or “no” to indicate whether a PCI was performed. If yes, fill out an SAE form. If yes, provide report and complete subsequent questions.
- 16. Did subject undergo heart revascularization?**
- Select “yes” or “no” to indicate whether the subject underwent heart revascularization.  
If yes, provide report and fill out an SAE form. If yes, complete subsequent questions.
- 17. Did the subject have any peri-procedural complications? \***
- Indicate if the subject had any peri-procedural complications. If yes, fill out SAE form.
  - **Stroke** is defined as an acute focal neurological deficit of sudden onset, not reversible within 24 hours, or that resolves in <24 hrs with clear evidence of a new stroke on cerebral imaging.
  - **Bleeding** is defined as major based on one or more of the following:
    - Transfusion of at least 2 units heterologous packed red blood cells or whole

blood

- Decrease in hemoglobin level by at least 2.0 g/l
- Need for re-operation or invasive intervention (*e.g.* Evacuation of wound hematoma)
- Bleeding at a critical anatomic site (intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial, or intramuscular with compartment syndrome)
- **Renal failure** is defined as:
  - increase in serum creatinine by 0.5mg/dL AND at least >1.5 mg/dL or
  - The requirement of renal replacement therapy (hemodialysis)
- **Anaphylaxis** defined as severe contrast reaction resulting in:
  - Anaphylactic shock
  - Intubation
  - Management of respiratory distress symptoms with epinephrine

**18. What source documents have been provided by site?**

- Select all applicable source documents that need to be obtained and provide the source documents to the DCSC. De-identify and keep the source documents in the subject's binder.

**48-72 HOUR FOLLOW UP FORM****48-72 Hour Follow Up**

Complete only for patients discharged within 24 hours of ED presentation.

<b>1. Was the 48-72 hour follow-up call completed?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> NA If No, Did the subject withdraw from the study? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, reason: _____
<b>2. Date of contact (mm/dd/yyyy):</b>	
<b>3. Time of contact (hh:mm):</b>	
<b>4. How many attempts were made to reach the patient?</b>	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> >5
<b>5. Did subject die?*</b> If yes, fill out SAE form.	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, death reported how? <input type="checkbox"/> Relative <input type="checkbox"/> SSDI <input type="checkbox"/> Medical record
a. Date of death (mm/dd/yyyy):	
b. Time of death (hh:mm):	
c. Cause of death:	<input type="checkbox"/> CV death due to coronary heart disease <input type="checkbox"/> CV death not directly due to coronary heart disease <input type="checkbox"/> Non CV_death <input type="checkbox"/> Other _____
<b>6. Did subject have recurrence of chest pain or anginal equivalent?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, provide, duration of longest episode: _____
<b>7. Did subject return to ED?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, complete supplement form
<b>8. Did subject return to OPD (since index hospitalization/last contact)?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, complete supplement form
<b>9. Was the patient admitted to the hospital?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, complete supplement form
<b>10. Was an ongoing hospitalization prolonged for ischemic signs/symptoms?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, complete supplement form
<b>11. Did subject have ECG changes (since index hospitalization/last contact)? *</b>	<input type="checkbox"/> Yes * <input type="checkbox"/> No If Yes, complete supplement form
<b>12. Were Cardiac biomarkers obtained (since index hospitalization/last contact)?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If Yes, complete supplement form
<b>13. Was a stress test performed?*</b> If yes, fill out SAE form	<input type="checkbox"/> Yes * <input type="checkbox"/> No If yes, complete supplement form and provide report.
<b>14. Was a coronary angiogram performed?*</b> If positive, fill out SAE form.	<input type="checkbox"/> Yes* <input type="checkbox"/> No If yes, complete supplement form and provide report.
<b>15. Was a PCI performed?*</b> If yes, fill out SAE form.	<input type="checkbox"/> Yes * <input type="checkbox"/> No If yes, complete supplement form and provide report.
<b>16. Did subject undergo heart revascularization?</b> *If yes, fill out SAE form	<input type="checkbox"/> Yes * <input type="checkbox"/> No If yes, complete supplement form and provide report.
<b>17. Did the subject have any peri-procedural complications? *</b> If yes, fill out SAE form	<input type="checkbox"/> Yes * <input type="checkbox"/> No If yes, complete supplement form and provide report.
<b>18. What source documents have been provided by site?</b>	<input type="checkbox"/> Discharge summary <input type="checkbox"/> Exercise testing report <input type="checkbox"/> Death note, certificate <input type="checkbox"/> Cardiac Cath/PCI report <input type="checkbox"/> Cardiology consultation note <input type="checkbox"/> CABG report <input type="checkbox"/> Biomarker report <input type="checkbox"/> Other, specify <input type="checkbox"/> ECG, during & after event

# 48-72 HOUR FOLLOW UP SUPPLEMENT FORM

<p><b>1. Was the 48-72 hour follow-up call completed?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> NA                  If No, Did the subject withdraw from the study? <input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, reason: _____</p>
<p><b>2. Date of contact (mm/dd/yyyy):</b></p>	
<p><b>3. Time of contact (hh:mm):</b></p>	
<p><b>4. How many attempts were made to reach the patient?</b></p>	<p><input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> &gt;5</p>
<p><b>5. Did subject die?*</b> If yes, fill out SAE form.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, death reported how?  <input type="checkbox"/> Relative  <input type="checkbox"/> SSDI  <input type="checkbox"/> Medical record</p>
<p>a. Date of death (mm/dd/yyyy):</p>	
<p>b. Time of death (hh:mm):</p>	
<p>c. Cause of death:</p>	<p><input type="checkbox"/> CV death due to coronary heart disease  <input type="checkbox"/> CV death not directly due to coronary heart disease  <input type="checkbox"/> Non CV_death  <input type="checkbox"/> Other _____</p>
<p><b>6. Did subject have recurrence of chest pain or anginal equivalent?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, provide, duration of longest episode:</p>
<p><b>7. Did subject return to ED?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes,                  a. Date of return (mm/dd/yyyy):                  b. Time of return (hh:mm):                  c. Institution:                  d. Reason:  <input type="checkbox"/> Recurrent chest pain*  <input type="checkbox"/> Other, specify _____                  *Fill out SAE form</p> <p>Discharged?  <input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes,                  e. Date (mm/dd/yyyy):                  f. Time (hh:mm):</p>
<p><b>8. Did subject return to OPD (since index hospitalization/last contact)?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes,                  a. Date of return (mm/dd/yyyy):                  b. Time of return (hh:mm):                  c. Institution:                  d. Reason:  <input type="checkbox"/> Recurrent chest pain*  <input type="checkbox"/> Other, specify _____                  *Fill out SAE form</p> <p>If yes,                  Discharged?  <input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes,                  e. Date (mm/dd/yyyy):                  f. Time (hh:mm):</p>



<p><b>9. Was the patient admitted to the hospital?</b></p>	<p><input type="checkbox"/> Yes    <input type="checkbox"/> No</p> <p>If yes,</p> <p>a. Date of admission (mm/dd/yyyy):</p> <p>b. Institution:</p> <p>c. Reason:</p> <p><input type="checkbox"/> Recurrent chest pain*</p> <p><input type="checkbox"/> Other, specify _____</p> <p>*Fill out SAE form</p> <p>Discharged?</p> <p><input type="checkbox"/> Yes    <input type="checkbox"/> No</p> <p>If yes,</p> <p>d. Date (mm/dd/yyyy):</p> <p>e. Time (hh:mm):</p>
<p><b>10. Was an ongoing hospitalization prolonged for ischemic signs/symptoms?</b></p>	<p><input type="checkbox"/> Yes    <input type="checkbox"/> No</p> <p>If yes,</p> <p>a. Date of admission (mm/dd/yyyy):</p> <p>b. Institution:</p>
<p><b>11. Did subject have ECG changes (since index hospitalization/last contact)?</b> *</p>	<p><input type="checkbox"/> Yes *    <input type="checkbox"/> No</p> <p>If Yes, check appropriate boxes below and fill out SAE form:</p> <p><input type="checkbox"/> ST elevation &gt;1mm</p> <p><input type="checkbox"/> ST depression &gt;1mm</p> <p><input type="checkbox"/> TWI &gt;1mm</p>
<p><b>12. Were Cardiac biomarkers obtained (since index hospitalization/last contact)?</b> If yes, <b>Peak cTn result?</b></p> <p><b>Peak CK-MB result?</b></p>	<p><input type="checkbox"/> Yes    <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes    <input type="checkbox"/> No</p> <p>Provide peak cTn result: _____</p> <p>Provide cTn units: _____</p> <p>Provide cTn ULN: _____</p> <p><input type="checkbox"/> Yes    <input type="checkbox"/> No</p> <p>Provide peak CK-MB result: _____</p> <p>Provide CK-MB units: _____</p> <p>Provide CK-MB ULN: _____</p>
<p><b>13. Was a stress test performed?*</b> If yes, fill out SAE form</p>	<p><input type="checkbox"/> Yes *    <input type="checkbox"/> No</p> <p>If yes, provide report.</p> <p>If yes, was it ETT <input type="checkbox"/> or nuclear imaging? <input type="checkbox"/></p> <p>If yes, you will need to fill out the ETT or Nuclear imaging questions.</p>
<p><b>14. Was a coronary angiogram performed?*</b> If positive, fill out SAE form.</p>	<p><input type="checkbox"/> Yes*    <input type="checkbox"/> No</p> <p>If yes, you will need to fill out the coronary angiogram questions and provide report.</p>
<p><b>15. Was a PCI performed?*</b> If yes, fill out SAE form.</p>	<p><input type="checkbox"/> Yes *    <input type="checkbox"/> No</p> <p>If yes, you will need to fill out the PCI questions and provide report.</p>
<p><b>16. Did subject undergo heart revascularization?</b> *If yes, fill out SAE form</p>	<p><input type="checkbox"/> Yes *    <input type="checkbox"/> No</p> <p>If yes, provide report.</p> <p>If yes, select method of revascularization:</p> <p><input type="checkbox"/> CABG</p> <p><input type="checkbox"/> Stent</p> <p><input type="checkbox"/> Unknown</p>
<p><b>17. Did the subject have any peri-procedural complications? *</b> If yes, fill</p>	<p>Stroke            <input type="checkbox"/> Yes    <input type="checkbox"/> No</p> <p>Bleeding        <input type="checkbox"/> Yes    <input type="checkbox"/> No</p>

out SAE form	Renal failure <input type="checkbox"/> Yes <input type="checkbox"/> No Anaphylaxis <input type="checkbox"/> Yes <input type="checkbox"/> No
<b>18. What source documents have been provided by site?</b>	<input type="checkbox"/> Discharge summary <input type="checkbox"/> Death note, certificate <input type="checkbox"/> Cardiology consultation note <input type="checkbox"/> Biomarker report <input type="checkbox"/> ECG, during & after event

**CRF page 20 – 28 Day Follow Up**

This information should be entered by the CRC.

If answers to all questions below are “No” (i.e. the subject did not return to the ED or have any testing), then complete only this form, leave the 28 Day Follow Up Supplement Form blank and mark as complete. If “Yes” was selected for any questions, enter detailed information on the 28 Day Follow Up Supplement Form.

- 1. Was the 28 day follow-up call completed?**
  - Select “yes” or “no” to indicate if the follow-up interview was completed.
  - If no, did the subject withdraw from the study? If yes, enter the reason the subject withdrew.
  
- 2. Date of contact (mm/dd/yyyy)**
  - Select the date the subject was initially contacted using the pop-up calendar
  
- 3. How many attempts were made to reach the patient?**
  - Select the number of attempts that were made to reach the subject
  
- 4. Did subject die (since index hospitalization/last contact)?**
  - Select “yes” or “no” to indicate whether the subject died. If yes, indicate the date and time of death using the pop-up clock and pop-up calendar.
  
- 5. Did subject have recurrence of chest pain or anginal equivalent (since index hospitalization/last contact)?**
  - Select “yes” or “no” to indicate if the subject had a recurrence of chest pain or anginal equivalent. If yes, provide duration of longest episode.
  
- 6. Did subject return to ED (since index hospitalization/last contact)?**
  - Select “yes” or “no” to indicate if the subject returned to the ED.
  - If the subject returned to the ED, indicate the date, time, institution and reason for return.
  - Provide a copy of the medical records for revisits. Indicate the date and time of discharge.
  
- 7. Did subject return to OPD (since index hospitalization/last contact)?**
  - Select “yes” or “no” to indicate if the subject returned to the OPD.
  - If the subject returned to the OPD, indicate the date, time, institution and reason for return.
  - Provide a copy of the medical records for revisits. Indicate the date and time of discharge.
  
- 8. Was the patient admitted to the hospital (since index hospitalization/last contact)?**
  - Select “yes” or “no” to indicate if the subject was admitted to the hospital.
  - If the subject was admitted to the hospital, indicate the date, time, institution

and reason for return.

- Provide a copy of the medical records for revisits. Indicate the date and time of discharge.
- 9. Was an ongoing hospitalization prolonged for ischemic signs/symptoms?**
    - Select “yes” or “no” to indicate if the index hospitalization was prolonged due to ischemic signs/symptoms.
  - 10. Did the subject have ECG changes (since index hospitalization/last contact)?**
    - Select “yes” or “no” to indicate if the subject had ECG changes since index hospitalization/last contact
  - 11. Were Cardiac biomarkers obtained (since index hospitalization/last contact)?**
    - Enter the peak biomarker levels, units, and the local laboratory upper limit of normal (ULN) values for cTn and CK-MB, if collected. If cTn were normal, enter “no” for “Peak cTn result?”
  - 12. Was a stress test performed (since index hospitalization/last contact)?**
    - Select “yes” or “no” to indicate if a stress test was performed. If yes, provide report. If yes, select whether it was ETT or Nuclear Imaging and complete subsequent questions.
  - 13. Was a coronary angiogram performed (since index hospitalization/last contact)?**
    - Select “yes” or “no” to indicate whether a coronary angiogram was performed. If yes, provide report and complete subsequent questions.
  - 14. Was a PCI performed (since index hospitalization/last contact)?**
    - Select “yes” or “no” to indicate whether a PCI was performed. If yes, provide report and complete subsequent questions.
  - 15. Did subject undergo heart revascularization (since index hospitalization/last contact)?**
    - Select “yes” or “no” to indicate whether the subject underwent heart revascularization. If yes, provide report and complete subsequent questions.
  - 16. What source documents have been provided by site?**
    - Select all applicable source documents that need to be obtained and provide the source documents to the DCSC. De-identify and keep the source documents in the subject’s binder.

## 28 DAY FOLLOW UP FORM

<p><b>1. Was the 28 day follow-up call completed?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If No, Did the subject withdraw from the study? <input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, reason: _____</p>
<p><b>2. Date of contact (mm/dd/yyyy)</b></p>	
<p><b>3. How many attempts were made to reach the patient?</b></p>	<p><input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> &gt;5</p>
<p><b>4. Did subject die (since index hospitalization/last contact)?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, death reported how?  <input type="checkbox"/> Relative  <input type="checkbox"/> SSDI  <input type="checkbox"/> Medical record                  If yes, provide death note, certificate.</p>
<p>d. Date of death:</p>	
<p>e. Time of death (hh:mm):</p>	
<p>f. Cause of death:</p>	<p><input type="checkbox"/> CV death due to coronary heart disease  <input type="checkbox"/> CV death not directly due to coronary heart disease  <input type="checkbox"/> Non CV death  <input type="checkbox"/> Other _____</p>
<p><b>4. Did subject have recurrence of chest pain or anginal equivalent (since index hospitalization/last contact)?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, provide, duration of longest episode:</p>
<p><b>5. Did subject return to ED (since index hospitalization/last contact)?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, complete supplement form and provide report</p>
<p><b>6. Did subject return to OPD (since index hospitalization/last contact)?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, complete supplement form and provide report</p>
<p><b>7. Was the patient admitted to the hospital (since index hospitalization/last contact)?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, complete supplement form and provide report</p>
<p><b>8. Was an ongoing hospitalization prolonged for ischemic signs/symptoms?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, complete supplement form and provide report</p>
<p><b>9. Did the subject have ECG changes (since index hospitalization/last contact)?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If Yes, complete supplement form and provide a copy of the ECG</p>
<p><b>10. Were Cardiac biomarkers obtained (since index hospitalization/last contact)?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, complete supplement form</p>
<p><b>11. Was a stress test performed (since index hospitalization/last contact)?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, complete supplement form and provide report</p>
<p><b>12. Was a coronary angiogram performed (since index hospitalization/last contact)?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, complete supplement form and provide report</p>
<p><b>13. Was a PCI performed (since index hospitalization/last contact)?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, complete supplement form and provide report</p>
<p><b>14. Did subject undergo heart revascularization (since index hospitalization/last contact)?</b></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No                  If yes, complete supplement form and provide report</p>
<p><b>15. What source documents have been provided by site?</b></p>	<p><input type="checkbox"/> Discharge summary <input type="checkbox"/> Exercise testing report  <input type="checkbox"/> Death note, certificate <input type="checkbox"/> Cardiac Cath/PCI report  <input type="checkbox"/> Cardiology consultation note <input type="checkbox"/> CABG report</p>

<input type="checkbox"/> Biomarker report	<input type="checkbox"/> Other, specify:
<input type="checkbox"/> ECG, during & after event	

**28 DAY FOLLOW UP SUPPLEMENT FORM**

1. Was the 28 day follow-up call completed?	<input type="checkbox"/> Yes <input type="checkbox"/> No If No, Did the subject withdraw from the study? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, reason: _____
2. Date of contact (mm/dd/yyyy)	
3. How many attempts were made to reach the patient?	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> >5
4. Did subject die (since index hospitalization/last contact)?	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, death reported how? <input type="checkbox"/> Relative <input type="checkbox"/> SSDI <input type="checkbox"/> Medical record If yes, provide death note, certificate.
g. Date of death:	
h. Time of death (hh:mm):	
i. Cause of death:	<input type="checkbox"/> CV death due to coronary heart disease <input type="checkbox"/> CV death not directly due to coronary heart disease <input type="checkbox"/> Non CV death <input type="checkbox"/> Other _____
4. Did subject have recurrence of chest pain or anginal equivalent (since index hospitalization/last contact)?	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, provide, duration of longest episode:
5. Did subject return to ED (since index hospitalization/last contact)?	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, a. Date of return (mm/dd/yyyy): b. Time of return (hh:mm): c. Institution: d. Reason: <input type="checkbox"/> Recurrent chest pain <input type="checkbox"/> Other, specify _____ If yes, Discharged? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, please provide a copy of the report e. Date (mm/dd/yyyy): f. Time (hh:mm):
6. Did subject return to OPD (since index hospitalization/last contact)?	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, a. Date of return (mm/dd/yyyy): b. Time of return (hh:mm): c. Institution: d. Reason: <input type="checkbox"/> Recurrent chest pain* <input type="checkbox"/> Other, specify _____ *Please provide a copy of the report
7. Was the patient admitted to the hospital (since index hospitalization/last contact)?	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, a. Date of admission (mm/dd/yyyy): b. Institution: c. Reason: <input type="checkbox"/> Recurrent chest pain <input type="checkbox"/> Other, specify _____

	If yes, Discharged? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, please provide a copy of the report d. Date (mm/dd/yyyy): e. Time (hh:mm):
<b>8. Was an ongoing hospitalization prolonged for ischemic signs/symptoms?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, please provide a copy of the report a. Date of admission: b. Institution:
<b>9. Did the subject have ECG changes (since index hospitalization/last contact)?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If Yes, please provide a copy of the ECG If Yes, check appropriate boxes below <input type="checkbox"/> ST elevation >1mm <input type="checkbox"/> ST depression >1mm <input type="checkbox"/> TWI >1mm
<b>10. Were Cardiac biomarkers obtained (since index hospitalization/last contact)?</b> If yes, Peak cTn result?  Peak CK-MB result?	<input type="checkbox"/> Yes <input type="checkbox"/> No  <input type="checkbox"/> Yes <input type="checkbox"/> No Provide peak cTn result: _____ Provide cTn units: _____ Provide cTn ULN: _____  <input type="checkbox"/> Yes <input type="checkbox"/> No Provide peak CK-MB result: _____ Provide CK-MB units: _____ Provide CK-MB ULN: _____
<b>11. Was a stress test performed (since index hospitalization/last contact)?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, provide report. If yes, Was it <input type="checkbox"/> ETT <input type="checkbox"/> Nuclear Imaging If yes, fill out questions about ETT and Nuclear Imaging
<b>12. Was a coronary angiogram performed (since index hospitalization/last contact)?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, fill out questions about the coronary angiogram and provide report.
<b>13. Was a PCI performed (since index hospitalization/last contact)?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, fill out questions about the PCI and provide report.
<b>14. Did subject undergo heart revascularization (since index hospitalization/last contact)?</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, fill out questions and provide report. Select method of revascularization: <input type="checkbox"/> CABG <input type="checkbox"/> Stent <input type="checkbox"/> Unknown
<b>15. What source documents have been provided by site?</b>	<input type="checkbox"/> Discharge summary <input type="checkbox"/> Exercise testing report <input type="checkbox"/> Death note, certificate <input type="checkbox"/> Cardiac Cath/PCI report <input type="checkbox"/> Cardiology consultation note <input type="checkbox"/> CABG report <input type="checkbox"/> Biomarker report <input type="checkbox"/> Other, specify: <input type="checkbox"/> ECG, during & after event



**CRF page 20 – Adverse Event Form**

This information should be entered by the CRCs.

Fill this form out only if the subject had an adverse event (defined in the glossary).

**1. AE Number**

- Mention if this is the first event or a subsequent one.

**2. Event Code**

- Use the following url to find standardized coding terms for AEs:  
<http://hedwig.mgh.harvard.edu/biostatistics/files/costart.html>

**3. Event Description**

- Describe the nature of the event.

**4. Start Date (mm/dd/yyyy):**

- Enter the start date of the event using the pop-up calendar.

**5. End Date (mm/dd/yyyy):**

- Enter the end date of the event using the pop-up calendar. Select “continuing” if still ongoing.

**6. Grade (1-4)**

- Describe the severity of this event.

**7. SAE?**

- Was this a serious adverse event? If so, fill out the SAE form.

**8. Was patient withdrawn from study due to AE?**

- Select “yes” or “no” to indicate whether the subject was withdrawn from the study due to the AE

**9. Relationship to study procedure**

Determine the relation of the event to the procedure

**10. Relationship to contrast (1-5)**

- Determine the relation of the event to the contrast agent

**11. Relationship to underlying disease**

- Determine the relation of the event to the underlying disease.

**12. Action (1-5)**

- Describe the action taken.

**13. Outcome (1-5)**

- Describe the final outcome of the event.

**14. Did the subject have another AE?**

- If the subject had another AE, select yes. A blank form be generated automatically. Enter details as per the instructions shown above.

**ADVERSE EVENT FORM**

1) AE Number	
2) Event Code	
3) Event Description	
4) Start Date (mm/dd/yyyy):	
5) End Date (mm/dd/yyyy):	<input type="checkbox"/> Continuing
6) Grade (1-4)	<input type="checkbox"/> 1 - Mild <input type="checkbox"/> 2 - Moderate <input type="checkbox"/> 3 - Severe <input type="checkbox"/> 4 - Life-threatening
7) SAE?	<input type="checkbox"/> Yes <input type="checkbox"/> No
8) Was patient withdrawn from study due to AE?	<input type="checkbox"/> Yes <input type="checkbox"/> No
9) Relationship to study procedure	<input type="checkbox"/> 1 - Not related <input type="checkbox"/> 2 - Unlikely Related <input type="checkbox"/> 3 - Possibly Related <input type="checkbox"/> 4 - Probably Related <input type="checkbox"/> 5 - Definitely Related
10) Relationship to contrast (1-5)	<input type="checkbox"/> 1 - Not related <input type="checkbox"/> 2 - Unlikely Related <input type="checkbox"/> 3 - Possibly Related <input type="checkbox"/> 4 - Probably Related <input type="checkbox"/> 5 - Definitely Related
11) Relationship to underlying disease	<input type="checkbox"/> 1 - Not related <input type="checkbox"/> 2 - Unlikely Related <input type="checkbox"/> 3 - Possibly Related <input type="checkbox"/> 4 - Probably Related <input type="checkbox"/> 5 - Definitely Related
12) Action (1-5)	<input type="checkbox"/> 1 - No Action Taken <input type="checkbox"/> 2 - Medication Given <input type="checkbox"/> 3 - Non-drug therapy given <input type="checkbox"/> 4 - ED visit <input type="checkbox"/> 5 - Hospitalization /prolonged hospitalization
13) Outcome (1-5)	<input type="checkbox"/> 1 - Recovered <input type="checkbox"/> 2 - Recovered with sequelae <input type="checkbox"/> 3 - Ongoing <input type="checkbox"/> 4 - Death <input type="checkbox"/> 5 - Unknown
14) Did the subject have another AE?	<input type="checkbox"/> Yes <input type="checkbox"/> No

**CRF Page 21 – SERIOUS ADVERSE EVENT FORM**

This information should be entered by the PI

- 1. Type of Report:**
  - Indicate whether the event occurred during the index hospitalization (initial report – during index hospitalization) or during the 48-72 hour follow up period.
- 2. Date of this report (dd/mm/yyyy):**
  - Enter the date of the report using the pop-up calendar.
- 3. Did the subject receive contrast?**
  - Determine whether or not the subject received contrast agent. If so, list the name and dose.
- 4. Time to onset after injection:**
  - Enter the time to onset after injection of the contrast agent.
- 5. Indicate the nature of the diagnosis that best describes the event.**
  - Describe the nature of the diagnosis that best describes the event. If none of the available options are applicable, enter the details under the option, “other”
- 6. Date of onset (dd/mm/yyyy):**
  - Enter the date of onset using the pop-up calendar
- 7. Time of onset of event:**
  - Enter the time of onset of the event using the pop-up clock
- 8. Date of outcome (dd/mm/yyyy):**
  - Enter the date of outcome using the pop-up calendar
- 9. Time of outcome:**
  - Enter the time of outcome using the pop-up clock
- 10. Seriousness**
  - Describe how serious the event was.
- 11. Was this an unexpected SAE (not listed in the informed consent)**
  - Select “yes” ff this was an unexpected event (one which is not mentioned in the ICF).
- 12. What was the relationship of the SAE to the procedure?**
  - Determine the relation of the event to the procedure.

**13. What was the relationship of the SAE to the contrast?**

- Determine the relation of the event to the contrast agent.

**14. What was the relationship of the SAE to underlying disease?**

- Determine the relation of the event, to the underlying disease.

**15. Describe the event:**

- Describe the nature of the event

**16. Describe the action taken:**

- Describe the action taken

**17. Outcome:**

- Describe the final outcome of the event.

**18. Attached documentation:**

- Select all of the attached supporting documents from the list.

**19. Did the subject have another SAE?**

- If the subject had another SAE, select yes. A blank form be generated automatically. Enter details as per the instructions shown above.

**SERIOUS ADVERSE EVENT FORM**

<b>Event Information</b>	
1. Type of Report	<input type="checkbox"/> Initial Report <input type="checkbox"/> 48-72 hour follow up
2. Date of this report (dd/mm/yyyy)	
<b>Contrast Information</b>	
3. Did the subject receive contrast? If yes, complete the following: Contrast agent: Dose	<input type="checkbox"/> Yes <input type="checkbox"/> No  _____ ml _____ ml
4. Time to onset after injection:	_____
<b>Event Details</b>	
5. Indicate the nature of the diagnosis that best describes the event.	<input type="checkbox"/> Myocardial Infarction <input type="checkbox"/> Bleeding <input type="checkbox"/> Stroke <input type="checkbox"/> Renal Failure <input type="checkbox"/> Anaphylaxis <input type="checkbox"/> Death <input type="checkbox"/> Other medically important events <input type="checkbox"/> Other, _____
6. Date of onset (dd/mm/yyyy):	
7. Time of onset of event:	
8. Date of outcome (dd/mm/yyyy):	
9. Time of outcome:	
10. Seriousness	<input type="checkbox"/> Death : Date _____ Time : _____ <input type="checkbox"/> Resulted in a life-threatening illness or injury <input type="checkbox"/> Resulted in a permanent impairment of a body structure or function <input type="checkbox"/> Resulted in a hospitalization or prolongation of an existing hospitalization <input type="checkbox"/> Required medical or surgical intervention to prevent permanent impairment or damage <input type="checkbox"/> Congenital anomaly or birth defect in offspring of the subject
11. Was this an unexpected SAE (not listed in the informed consent)	<input type="checkbox"/> Yes <input type="checkbox"/> No
12. What was the relationship of the SAE to the <b>procedure</b> ?	<input type="checkbox"/> Not related <input type="checkbox"/> Possibly related <input type="checkbox"/> Probably related <input type="checkbox"/> Definitely related <input type="checkbox"/> Unable to determine
13. What was the relationship of the SAE to the <b>contrast</b> ?	<input type="checkbox"/> Not related <input type="checkbox"/> Possibly related <input type="checkbox"/> Probably related <input type="checkbox"/> Definitely related <input type="checkbox"/> Unable to determine
14. What was the relationship of the SAE to underlying disease?	<input type="checkbox"/> Not related <input type="checkbox"/> Possibly related <input type="checkbox"/> Probably related <input type="checkbox"/> Definitely related <input type="checkbox"/> Unable to determine

15. Describe the event:	
16. Describe the action taken:	
17. Outcome:	<input type="checkbox"/> Resolved : Date (DD/MM/YYYY) <input type="checkbox"/> Ongoing <input type="checkbox"/> Improved <input type="checkbox"/> Unchanged <input type="checkbox"/> Worsened <input type="checkbox"/> Death - Was an autopsy performed? <input type="checkbox"/> Yes <input type="checkbox"/> No
18. Attached documentation:	<input type="checkbox"/> Lab report (s) <input type="checkbox"/> ECG (s) <input type="checkbox"/> Discharge Summary <input type="checkbox"/> Admission History and Physical <input type="checkbox"/> Death Certificate <input type="checkbox"/> Other _____
19. Did the subject have another SAE?	<input type="checkbox"/> Yes <input type="checkbox"/> No

**CRF page 22 – Protocol Deviation Form**

In the event of a protocol deviation, defined as any deviation from this protocol except if intended to eliminate a hazard to subjects or to protect the life or well being of subjects in an emergency, you should fill out the protocol deviation form.

Enter the date and time of occurrence of the protocol deviation, along with the code that best describes the reason for deviation. If the deviation does not fall under category 1-5, enter the reason in the field described as other. In addition, describe the reason for deviation in the free text box.

You should fax a copy of this form to the attention of Pearl Zakrotsky at 617-724-4152 within 24 hours of the event. The local IRB should also be notified, as required, based on each site's policy.

**CRF page 23 – Protocol Violation Form**

A protocol violation is defined as any protocol deviation that is not approved by the IRB prior to its initiation or implementation.

A major violation: May impact subject safety, affect the integrity of study data and/or affect subject's willingness to participate in the study.

A minor violation: A violation that does not impact subject safety, compromise the integrity of study data and/or affect subject's willingness to participate in the study.

**REPORTING REQUIREMENTS**

All major protocol violations must be reported to the IRB within ten (10) working days of discovery. Minor violations are to be reported at continuing review. It is the responsibility of the Site Principal Investigator (PI) to determine whether a violation is major or minor and to ensure proper reporting to the IRB.

Enter the date and time of occurrence of the protocol violation, along with the code that best describes the reason for violation. If the deviation does not fall under category 1-10, enter the reason in the field described as other. In addition, describe the reason for violation in the free text box.

You should fax a copy of this form to the attention of Pearl Zakrotsky at 617-724-4152 within 24 hours of the event. The local IRB should also be notified, as required, based on each site's policy.

# PROTOCOL DEVIATION FORM

<p>A. Date of protocol deviation: (dd/mm/yyyy)    ____ - ____ - ____</p> <p>Time of protocol deviation: (military time)    ____: ____</p> <p>B. Deviation code: _____ (from list below)</p> <p>C. Reason for Deviation: (i.e. lost to follow-up) _____</p>
<b>Possible Deviation Codes</b>
1 – CT Group – CT not performed (i.e. subject refusal)
2 – CT Group – (i.e. CT malfunction)
3 – Subject left hospital against medical advice (post-randomization)
4 – 2-3 day follow-up call was done out of window
5 – 28 days follow-up call was done out of window
6 – Other: (specify) _____
Did the subject have another Protocol Deviation? <input type="checkbox"/> Yes <input type="checkbox"/> No

*Note: Protocol Deviations must be reported to Pearl Zakrotsky ([pzakrotsky@partners.org](mailto:pzakrotsky@partners.org)) immediately after deviation occurs. Deviations should also be reported, as required, according to site IRB policy.*



# PROTOCOL VIOLATION FORM

<p>A. Date of protocol violation: (dd/mm/yyyy)    ____ - ____ - ____</p> <p>Time of protocol violation: (military time)    ____: ____</p> <p>B. Violation code: _____ (from list below)</p> <p>C. Reason for Violation: (i.e. subject underwent CT with sent in place ) _____</p>
<b>Possible Violation Codes</b>
1 – Subject was randomized but did not meet incl/excl criteria (specify which criteria): _____
2 – CT Group – CT not performed (i.e. no staff available to perform CT scan)
3 – Failure to sign informed consent
4 – Pregnancy test was not performed in applicable subject
5 – Qualifying labs not performed
6 – Qualifying ECG not performed
7 – Calcium scan not performed
8 – Contrast agent was not given
9 – Coronary CTA – stent was present
10 – 2-3 day follow-up call was not done
11 – Other: (specify) _____
Did the subject have another Protocol Violation? <input type="checkbox"/> Yes <input type="checkbox"/> No

*Note: Protocol Violations must be reported to your IRB, as required, according to site IRB policy. PVs must also be reported to Pearl Zakrofsky ([pzakrofsky@partners.org](mailto:pzakrofsky@partners.org)) immediately after knowledge of the event.*

## Appendix A: Physician Information Sheet

### Design:

A multicenter (7 US tertiary centers), randomized controlled diagnostic trial with 1000 subjects

### Patient Population:

Acute Chest Pain (ACP) Patients in Emergency Department (ED) and Intermediate Likelihood for Acute Coronary Syndrome (ACS)

### Intervention:

Coronary Computed Tomography Angiogram (CTA) as part of the early ED evaluation assessing:

- Plaque Burden / • Significant Coronary Stenosis / • Global and Regional LV Function

### Measure:

Utility of CTA to improve triage of patients with ACP

### CTA Literature

#### Accuracy for the detection of significant stenosis in comparison to Invasive Coronary Angiography

- Safely excludes significant stenosis (>50%), sensitivity of 85-99%, specificity of 64-90%, PPV of 64-91%, and NPV of 83-99% using retrospective-gating<sup>1-3</sup>
- Using prospective gating (no information on left ventricular function) and new scanners, sensitivity and specificity remain high, at 96% and 99% respectively, and image quality is not degraded<sup>4-6</sup>

#### **Association of coronary CT findings with Clinical outcomes of Patients with ACP**

- No CAD by coronary CT safely and accurately excludes ACS (100% Sensitivity and NPV)<sup>7-8</sup>
- Detection of significant stenosis on CTA is associated with 20 times increased risk for ACS (specificity: 87%)<sup>9</sup>
- ACS in non-obstructive plaque is rare (<5%) and is either small NSTEMI (second troponin positive) or UAP.<sup>9</sup> Risk of MACE over two years in patients with non-obstructive plaque is 1%<sup>10</sup>
- In patients with significant stenosis, regional LV dysfunction has a sensitivity of 89% and a specificity of 86% for ACS. With non-diagnostic CT, regional LV dysfunction has a sensitivity of 60% and a NPV of 92% for ACS, PPV is near 100% if it matches the location of a stenosis<sup>11</sup>

#### **Association of coronary CT findings with results of stress testing**

- Patients without CAD in CT have a negative stress test (100% Sensitivity and NPV) for myocardial perfusion abnormalities<sup>7</sup>
- The overwhelming majority of patients with non-obstructive CAD have negative stress tests<sup>12</sup>

#### **Coronary CT in the Emergency Room**

- Early discharge of 50% of ACP patients from the ED is safe<sup>9</sup>
- 75% of ACP patients with CT immediately are discharged and none have cardiovascular death or nonfatal MI within 30 days<sup>13</sup>

#### **Potential CT associated Risks**

- Radiation (median across multiple vendors = 12 mSv): comparable to standard stress test (average 10mSv but range up to 20mSV) - marginal increase of risk for cancer during lifetime<sup>14-15</sup>
- Average radiation dose using prospective gating is 4 mSv<sup>4</sup>
- Iodinated Contrast Agent: very rare contrast-induced nephropathy in patients with a normal renal function

### Contacts:

insert local PI

### References

1. Budoff MJ, Dowe D, Jollis JG, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. *J Am Coll Cardiol* 2008;52:1724-32.
2. Meijboom WB, Meijjs MF, Schuijff JD, et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. *J Am Coll Cardiol* 2008;52:2135-44.
3. Miller JM, Rochitte CE, Dewey M, et al. Diagnostic performance of coronary angiography by 64-row CT. *N Engl J Med* 2008;359:2324-36.
4. Maruyama T, Takada M, Hasuike T, et al. Radiation dose reduction and coronary assessability of prospective electrocardiogram-gated computed tomography coronary angiography: comparison with retrospective electrocardiogram-gated helical scan. *J Am Coll Cardiol* 2008;52:1450-5.

5. Achenbach S, Marwan M, Ropers D, et al. Coronary computed tomography angiography with a consistent dose below 1 mSv using prospectively electrocardiogram-triggered high-pitch spiral acquisition. *Eur Heart J* 2009.
6. Raff GL, Chinnaiyan KM, Share DA, et al. Radiation dose from cardiac computed tomography before and after implementation of radiation dose-reduction techniques. *Jama* 2009;301:2340-8.
7. Esteves FP, Sanyal R, Santana CA, et al. Potential impact of noncontrast computed tomography as gatekeeper for myocardial perfusion positron emission tomography in patients admitted to the chest pain unit. *Am J Cardiol* 2008;101:149-52.
8. Rubinshtein R, Halon DA, Gaspar T, et al. Impact of 64-slice cardiac computed tomographic angiography on clinical decision-making in emergency department patients with chest pain of possible myocardial ischemic origin. *Am J Cardiol* 2007;100:1522-6.
9. Hoffmann U, Bamberg F, Chae CU, et al. Coronary computed tomography angiography for early triage of patients with acute chest pain: the ROMICAT (Rule Out Myocardial Infarction using Computer Assisted Tomography) trial. *J Am Coll Cardiol* 2009;53:1642-50.
10. Schlett CL, Banerji D, Siegel EL, et al. Abstract 308: Computed Tomography Angiography Results Predict Long-term Major Adverse Cardiac Events in Patients With Chest Pain From the Emergency Department: Two-year Outcome of the ROMICAT (Rule Out Myocardial Infarction Using Computer Assisted Tomography) Trial. *Circulation* 2009;120:S317-.
11. Seneviratne SK, Rogers IS, Bamberg F, et al. Abstract 5745: Resting Regional Left Ventricular Function by 64-slice Cardiac CT adds Incremental Value to Coronary Plaque and Stenosis in Predicting Acute Coronary Syndrome in Patients with Acute Chest Pain. *Circulation* 2008;118:S\_993-a-.
12. Hoffmann U, Nagurny JT, Moselewski F, et al. Coronary multidetector computed tomography in the assessment of patients with acute chest pain. *Circulation* 2006;114:2251-60.
13. Hollander JE, Chang AM, Shofer FS, et al. Coronary computed tomographic angiography for rapid discharge of low-risk patients with potential acute coronary syndromes. *Ann Emerg Med* 2009;53:295-304.
14. Hausleiter J, Meyer T, Hermann F, et al. Estimated radiation dose associated with cardiac CT angiography. *JAMA* 2009;301:500-7.
15. Einstein AJ, Moser KW, Thompson RC, et al. Radiation dose to patients from cardiac diagnostic imaging. *Circulation* 2007;116:1290-305.









## Appendix F: Participation Information/Locator Sheet



### Participant Information/Locator Sheet

Site: \_\_\_\_\_

Participant's Name: \_\_\_\_\_

Primary Address: \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

Alternate Address: \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

Home Phone Number: \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

Is it ok to leave a voicemail?  Yes  No

Is it ok to speak with someone else who may answer the phone?  Yes  No

Is it ok to leave a message with someone else?  Yes  No

Best day/time to reach on this number: \_\_\_\_\_

Cell Phone Number: \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

Is it ok to leave a voicemail?  Yes  No

Is it ok to leave a message with someone else?  Yes  No

Best day/time to reach on this number: \_\_\_\_\_

Work Phone Number: \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

Is it ok to leave a voicemail?  Yes  No

Is it ok to leave a message with someone else?  Yes  No

Best day/time to reach on this number: \_\_\_\_\_

Preferred Phone Number:  Home  Cell  Work

Would it be ok to contact you by email?  Yes  No

If yes, Email address: \_\_\_\_\_





### Locator Information Sheet

We are asking that you also provide the name and contact information for another person or doctor(s) we may contact, who knows about your health, should you be unavailable to provide any information. We will not share any confidential information with your locators; we will only mention that we are trying to reach you as part of a research study.

#### **Locator #1**

Name: \_\_\_\_\_

Relationship to you: \_\_\_\_\_

Address: \_\_\_\_\_

\_\_\_\_\_

Phone Number: \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

Is it ok to leave a voicemail?  Yes  No

Best day/time to reach on this number: \_\_\_\_\_

#### **Locator #2**

Name: \_\_\_\_\_

Relationship to you: \_\_\_\_\_

Address: \_\_\_\_\_

\_\_\_\_\_

Phone Number: \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

Is it ok to leave a voicemail?  Yes  No

Best day/time to reach on this number: \_\_\_\_\_

**Appendix G: Screen Failures Log (template)**

Subject ID Number	MRN	Subject's Last Name	Subject's First Name
8070001			
8070002			
8070003			
8070004			
8070005			
8070006			
8070007			
8070008			
8070009			
8070010			
8070011			
8070012			
8070013			
8070014			
8070015			
8070016			
8070017			
8070018			
8070019			
8070020			
8070021			
8070022			
8070023			
8070024			
8070025			
8070026			
8070027			
8070028			
8070029			
8070030			
8070031			
8070032			
8070033			
8070034			
8070035			
8070036			
8070037			
8070038			
8070039			
8070040			
8070041			
8070042			
8070043			
8070044			
8070045			

## Appendix H: Participant Contact Log

### Participant Contact Log

Follow Up	Date	Time	Staff Initials	Contact Reason	Contact Type	Contact Results	Comments
2-3 days							
28 days							
1 year							
2 years							

**Codes:**

Contact Reason:

1. Inquiry
2. Schedule FU
3. Re-schedule FU
4. Update contact info
5. Other

Contact Type:

1. Call to
2. Call from
3. Mail sent
4. Mail received
5. Email sent
6. Email received
7. Other

Contact Results:

1. FU scheduled
2. FU re-scheduled
3. FU interview completed
4. Left voicemail
5. Left message with other
6. No contact
7. Phone disconnected/NIS
8. Contact info updated
9. Other

## Appendix I: Troponin Values



Site	Troponin Assay	Normal Value	Borderline Value	MI Value
Baystate	Troponin T	0-0.02 ng/mL	0.03-0.1 ng/ml	>0.1 ng/mL
BIDMC	Troponin T (Roche – ECLIA)			
Kaiser	Troponin I (Beckman)	<0.04 ng/mL	0.04-0.5 ng/mL	>0.5 ng/mL
MGH	Troponin T (Roche)	0-0.03 ng/mL	0.04-0.09 ng/ml	>0.09 ng/mL
Tufts	Triage Cardiac Panel	<0.4 ng/mL		≥0.04 ng/ml
University of Maryland Medical Center	Troponin I (Beckman)	<0.07 ng/mL	none	≥0.07 ng/mL
Washington University	Troponin I	<0.07 ng/mL	0.07-0.25 ng/ml	>0.25 ng/mL
Cleveland Clinic				
Northwestern	Troponin I	<0.4 ng/mL		≥0.04 ng/ml

## Appendix J: Combination drugs for Diabetics

Metformin Combinations	Actoplus Met Xr Actoplus Met Competact (Uk)	Avandamet Glucovance Janumet	Efficib® - Eu Only Metaglip Prandimet
Generic Metformin Combinations	Glipizide / Metformin	Glyburide / Metformin	
Metformin	Formet Glumetza	Glucophage Glucophage Xr	RIOMET
Generic Regular Metformin	Apo-Metformin Gen-Metformin	Glycon Novo- Metformin	Nu-Metformin
Generic Extended Release Metformin	Metformin ER		
Other Biguanides (not US approved – used in other countries)	Phenformin	Buformin	
Metformin Combinations In Phase 3 Clinical Trials	Amaryl M Slow Release	Metgluna	

Appl No	<a href="#">RLD</a>	Active Ingredient	Dosage Form	Strength	Proprietary Name	Company
---------	---------------------	-------------------	-------------	----------	------------------	---------

### Metformin Combinations

<a href="#">N022386</a>	N	Metformin Hcl; o Pioglitazone Hcl	Tablet, Extended Release; Oral	1GM;EQ 15MG BASE 1GM;EQ 30MG BASE	<b>Actoplus Met Xr</b>	Takeda Global
<a href="#">N021410</a>	No	METFORMIN HCL; PIOGLITAZON E HCL	TABLET; ORAL	500MG;EQ 15MG BASE 850MG;EQ 15MG BASE	<b>Actoplus Met Competact (Uk)</b>	Takeda Global
<a href="#">N021410</a>	No	METFORMIN HCL; ROSIGLITAZO NE MALEATE	TABLET; ORAL	1GM;EQ 2MG BASE 1GM;EQ 4MG BASE 500MG;EQ 1MG BASE 500MG;EQ 2MG BASE 500MG;EQ 4MG BASE	<b>Avandamet</b>	Sb Pharmco
<a href="#">N021178</a>	No	GLYBURIDE; METFORMIN HCL	TABLET; ORAL	1.25MG;250MG 2.5MG;500MG 5MG;500MG	<b>Glucovance</b>	Bristol Myers Squibb

Appl No	<b>RLD</b>	Active Ingredient	Dosage Form	Strength	Proprietary Name	Company
<a href="#">N022044</a>	Yes	METFORMIN HCL; SITAGLIPTIN PHOSPHATE	TABLET; ORAL	500MG;EQ 50MG BASE 1GM;EQ 50MG BASE	<b>Janumet</b> <b>Efficib® - Eu Only</b>	Merck
<a href="#">N021460</a>	No	GLIPIZIDE; METFORMIN HCL	TABLET; ORAL	2.5MG;250MG 2.5MG;500MG 5MG;500MG	<b>Metaglip</b>	Bristol Myers Squibb
		REPAGLINIDE AND METFORMIN HCL	TABLET; ORAL	1 MG/500 MG 2 MG /500MG	<b>Prandimet</b>	

### Metformin Combinations In Phase 3 Clinical Trials

		GLIMEPIRIDE METFORMIN HCL, SLOW RELEASE	TABLET; ORAL		<b>Amaryl M Slow Release</b>	Sanofi-Aventis
		MITIGLINIDE METFORMIN HCL	TABLET; ORAL		<b>Metgluna</b>	Elixir Pharmaceuticals

**OTHER BIGUANIDES** - still used in other countries, not approved in US. These carry a higher risk of lactic acidosis (with a 50% death rate) than metformin.

		PHENFORMIN - Has also been found in Chinese "herbal products"	TABLET; ORAL	Available in: 1. Italy, 2. Brazil, 3. Uruguay, 4. China, 5. Poland, 6. Greece 7. Portugal	<b>Phenformin</b>	Jinan Shengruixiang Pharmaceutical R&D Co.,Ltd, China B&K Technology Group (China) Co., Ltd
		BUFORMIN	TABLET; ORAL	Available in: 1. ROMANIA 2. SPAIN.	<b>Buformin</b>	Grünenthal

### Generic Metformin Combinations

<a href="#">A077507</a>	No	GLIPIZIDE; METFORMIN HCL	TABLET; ORAL	2.5MG;250MG 2.5MG;500MG 5MG;500MG	<b>Glipizide And Metformin Hcl</b>	Caraco , Corepharma, Mylan, Teva Pharms
<a href="#">A076716</a>	No	GLYBURIDE; METFORMIN HCL	TABLET; ORAL	1.25MG;250MG 2.5MG;500MG 5MG;500MG	<b>Glyburide And Metformin Hcl</b>	Actavis Elizabeth Aurobindo Pharma, Corepharma Dr Reddys Labs Inc, Ivax Sub Teva Pharms

Appl No	<a href="#">RLD</a>	Active Ingredient	Dosage Form	Strength	Proprietary Name	Company
<b>Metformin</b>						
		Metformin Hcl	Tablet, Extended Release; Oral	500MG 1000MG	<b>Formet</b>	Shionogi Pharma, Inc. (Formerly Sciele Pharma)
<a href="#">A07624</a>	Yes	Metformin Hcl	Tablet, Extended Release; Oral	500MG 1GM	<b>Glumetza</b>	Depomed Inc
<a href="#">N02035</a>	Yes	Metformin Hcl	Tablet; Oral	500mg 850mg 1gm	<b>Glucophage</b>	Bristol Myers Squibb
A076818	No	Metformin Hcl	Tablet, Extended Release; Oral	500MG 750MG	<b>Glucophage XR</b>	Bristol Myers Squibb
		Metformin Hcl	Metformin Oral Solution	500MG/ 5ml	<b>Riomet®</b>	Ranbaxy Laboratories Inc
<b>Generic Regular And Extended Release Metformin</b>						
<a href="#">N021202</a>	No	Metformin Hcl	Tablet, Extended Release; Oral	500mg 750mg	<b>Metformin ER</b>	Barr, Impax Labs, Ivax Sub Teva Pharms, Mylan, Neurosci Inc, Nostrum, Ranbaxy, Sandoz, Sun Pharm Inds (In), Teva, Torrent Pharm, Watson Labs Florida, Zydus Pharms Usa
<a href="#">A075969</a>	No	Metformin Hcl	Tablet; Oral	500MG 625MG 750MG 850MG 1GM Not all companies make all the above strengths, but all make 500mg/ 850mg/ 1000mg doses	<b>Metformin Hcl</b> 1. Apo-Metformin 2. Gen-Metformin 3. Glycon 4. Novo-Metformin 5. Nu-Metformin	Alphapharm, Alvogen, Amneal Pharms Ny, Apotex, Aurobindo, Caraco, Dr Reddys Labs Inc, Genpharm, Glenmark Generics, Indicus Pharma, Ipca Labs Ltd, Ivax Sub Teva Pharms, Ivax Sub Teva Pharms, Mutual Pharma, Mylan, Provident Pharm, Sandoz, Teva, Torrent Pharms, Watson Labs, Watson Labs Florida, Zydus Pharms Usa

## Appendix K: SPECT Examination Protocol

### 1. General Considerations

This document details guidance based on professional society standards, and encourages the use of such standard practices, even though adherence to the stipulations of this guidance is not required by protocol. Stress myocardial perfusion studies should be performed in accordance with best practice standards as delineated in the imaging guidelines of the American Society of Nuclear Cardiology<sup>77</sup>. Below is a summary of the standard that should be considered at each institution in the trial.

### 2. Patient Preparation

#### Day Prior to SPECT MPI Study

As some patients will be undergoing a vasodilator pharmacologic stress test (including those who start to exercise but may not reach an adequate heart rate), it is important that the patient understands that they are to have NO CAFFEINE after midnight on the day of the exam. A phone call reminder is strongly recommended the day or night before the study. Instruct patient to remain NPO at least 4 hours prior to the start of testing. It is also standard before pharmacologic stress tests to hold any “methylxanthine” containing medications for 24 hours prior to testing, which include any theophylline or aminophylline preparations. Patients who cannot hold these medications due to concomitant conditions (i.e. asthma) cannot undergo a pharmacologic stress test with adenosine, dipyridamole or regadenoson. Also, patients with history of significant reactive airways disease and bronchospasm should not undergo pharmacologic stress testing with these agents. In this situation, a dobutamine pharmacologic stress test should be performed.

#### Summary Instructions

- Review and obtain medical history and make sure there is no contraindication for proceeding with a stress test.
- List patient’s current medication regimen and whether or not meds were withheld.
- Prepare the patient’s skin in accordance with standard ETT practice
- The limb leads should be placed in the torso modified position for stress testing
- Obtain supine and standing ECG and BP.
- During the test, the subject may gently rest their hands on the treadmill railing. When obtaining BP, have subject raise hand off the railing and place on shoulder of person obtaining BP to minimize electronic noise.

#### 1. MPI Imaging Protocols

For the purposes of this study, sites may use any of the following imaging protocols:

1. One-day rest stress dual isotope (Thallium 201 rest/Tc99m Sestamibi stress or Tetrofosmin stress)



2. Two-day rest stress dual isotope (Thallium 201 rest/Tc99m Sestamibi stress or Tetrofosmin stress)
3. One-day rest/stress Tc99m Sestamibi or Tetrofosmin
4. Two-day rest/stress Tc99m Sestamibi or Tetrofosmin
5. One-day stress/rest Tc99m Sestamibi or Tetrofosmin
6. One-day stress-redistribution Thallium 201 optional 18-24 hour images
7. One-day stress - reinjection Thallium 201

#### For Dual-Isotope Studies

##### Rest Imaging Study

Isotope: Thallium201

Dose: 3-4 mCi

Wait 10-15 minutes after injection before beginning the rest SPECT images. Monitor the patient throughout the exam to gauge motion. If significant motion has occurred during the exam, immediately begin acquisition on a repeat exam.

Acquisition parameters: 64x64 matrix, 8 bit pixel depth. Thirty (30) seconds per stop for the thallium201 acquisition, however this can be adjusted to ensure at least 50-100K counts/stop, based on body size. For single or multi-headed cameras, at least 64 stops/180 degrees should be acquired. Dosing should follow all local regulations re dose limits.

Please follow Stress Techniques described in Section 0 of this document.

##### Stress Imaging Study – gated SPECT

Isotope: Tc-99m Sestamibi or Tc-99m Tetrofosmin

Dose: 25-30 mCi, weight adjusted as per local lab standards to achieve high count high quality images.

**AFTER EXERCISE STRESS, IMAGING IS TO BEGIN NO EARLIER THAN 15 MINUTES AFTER ISOTOPE INJECTION, TO MINIMIZE HEPATIC ACTIVITY.**

**AFTER PHARMACOLOGIC STRESS, IMAGING IS TO BEGIN NO EARLIER THAN 60 MINUTES AFTER ISOTOPE INJECTION, TO MINIMIZE HEPATIC ACTIVITY.**

Monitor the patient throughout the exam to gauge motion. If significant motion occurs during the exam, immediately begin a repeat acquisition.

Acquisition Parameters: 64x64 matrix, 8 bit pixel depth. Twenty-five (25) seconds per stop for the Tc-99m acquisition, adjusted for body size to ensure at least 300-500K counts/stop. Gating will be performed at 8 or 16 frames per cycle according to your laboratory's standard practice of using bad-beat rejection and setting the R-to-R window or no bad-beat rejection with a 100% R-to-R window. For single or multi-headed cameras, at least 64 stops/180 degrees should be acquired. After completion of the acquisition and before releasing the patient review the raw projection data in cine format and repeat acquisition if there is significant patient motion or hot activity adjacent to the heart that obscures myocardial activity.

#### For Single Isotope Studies (Technetium)

##### Rest Imaging Study

Isotope: Tc-99m Sestamibi or Tc-99m Tetrofosmin

Dose: 7-15 mCi if the rest study is being done as part of a 1 day protocol

Dose: 25-40 mCi if the rest study is being done as part of a 2 day protocol

**IMAGING IS TO BEGIN NO EARLIER THAN 45 MINUTES AFTER ISOTOPE INJECTION, TO MINIMIZE HEPATIC ACTIVITY.**

Monitor the patient throughout the exam to gauge motion. If significant motion occurs during the exam, immediately begin a repeat acquisition.

Acquisition parameters: 64x64 matrix, 8 bit pixel depth. Twenty-five (25) seconds per stop for the thallium201 acquisition, however this can be adjusted to ensure at least 50-100K counts/stop, based on body size. For single or multi-headed cameras, at least 64 stops/180 degrees should be acquired. After completion of the acquisition and before releasing the patient review the raw projection data in cine format and repeat acquisition if there is significant patient motion or hot activity adjacent to the heart that obscures myocardial activity. Dosing should follow all local regulations re dose limits.

Stress Imaging Study – gated SPECT

Isotope: Tc-99m Sestamibi or Tc-99m Tetrofosmin

Dose: 25-30 mCi, weight adjusted as per local lab standards to achieve high count high quality images.

**AFTER EXERCISE STRESS, IMAGING IS TO BEGIN NO EARLIER THAN 15 MINUTES AFTER ISOTOPE INJECTION, TO MINIMIZE HEPATIC ACTIVITY.**

**AFTER PHARMACOLOGIC STRESS, IMAGING IS TO BEGIN NO EARLIER THAN 60 MINUTES AFTER ISOTOPE INJECTION, TO MINIMIZE HEPATIC ACTIVITY.**

Monitor the patient throughout the exam to gauge motion. If significant motion occurs during the exam, immediately begin a repeat acquisition.

Acquisition Parameters: 64x64 matrix, 8 bit pixel depth. Twenty-five (25) seconds per stop for the Tc-99m acquisition, adjusted for body size to ensure at least 300-500K counts/stop. Gating will be performed at 8 or 16 frames per cycle according to your laboratory's standard practice of using bad-beat rejection and setting the R-to-R window or no bad-beat rejection with a 100% R-to-R window. For single or multi-headed cameras, at least 64 stops/180 degrees should be acquired. After completion of the acquisition and before releasing the patient review the raw projection data in cine format and repeat acquisition if there is significant patient motion or hot activity adjacent to the heart that obscures myocardial activity. The gating frame rate should be the same at the follow-up serial study time point (i.e., 8 or 16 frames/cycle). Dosing should follow all local regulations re dose limits.

For Single Isotope Studies (Thallium201)

Stress/Redistribution

Stress Imaging Study – gated SPECT

Isotope: Thallium201

Dose: 2.5-4.0 mCi, weight adjusted as per local lab standards to achieve high count high quality images.

**AFTER EXERCISE STRESS, IMAGING IS TO BEGIN 10-15 MINUTES AFTER ISOTOPE INJECTION**

**AFTER PHARMACOLOGIC STRESS, IMAGING IS TO BEGIN 10-15 MINUTES AFTER ISOTOPE INJECTION**

Monitor the patient throughout the exam to gauge motion. If significant motion occurs during the exam, immediately begin a repeat acquisition.

Acquisition Parameters: 64x64 matrix, 8 bit pixel depth. Forty (40) seconds per stop for the Thallium201 acquisition, adjusted for body size to ensure at least 125-175K counts/stop. Gating will be performed at 8 or 16 frames per cycle according to your laboratory's standard practice of using bad-beat rejection and setting the R-to-R window or no bad-beat rejection with a 100% R-to-R window. For single or multi-headed cameras, at least 64 stops/180 degrees should be acquired. Dosing should follow all local regulations re dose limits.

#### Redistribution Imaging Study

Isotope: Thallium201

**IMAGING BEGINS 2.5-4.0 HOURS AFTER STRESS THALLIUM201 ISOTOPE INJECTION,**

Monitor the patient throughout the exam to gauge motion. If significant motion occurs during the exam, immediately begin a repeat acquisition. Acquisition parameters: 64x64 matrix, 8 bit pixel depth. Forty (40) seconds per stop for the thallium201 acquisition, however this can be adjusted to ensure at least 50-100K counts/stop, based on body size. For single or multi-headed cameras, at least 64 stops/180 degrees should be acquired

Optional 18-24 hr images.

**IMAGING BEGINS WHEN PATIENT ARRIVES.**

Monitor the patient throughout the exam to gauge motion. If significant motion occurs during the exam, immediately begin a repeat acquisition. Acquisition parameters: 64x64 matrix, 8 bit pixel depth. Forty (40) seconds per stop for the thallium201 acquisition, however this can be adjusted to ensure at least 50-100K counts/stop, based on body size. For single or multi-headed cameras, at least 64 stops/180 degrees should be acquired

#### Thallium201 Stress/Reinjection

Stress Imaging Study – gated SPECT

Isotope: Thallium201

Dose: 2.5-4.0 mCi, weight adjusted as per local lab standards to achieve high count high quality images.

AFTER EXERCISE STRESS, IMAGING IS TO BEGIN 10-15 MINUTES AFTER ISOTOPE INJECTION

AFTER PHARMACOLOGIC STRESS, IMAGING IS TO BEGIN 10-15 MINUTES AFTER ISOTOPE INJECTION

Monitor the patient throughout the exam to gauge motion. If significant motion occurs during the exam, immediately begin a repeat acquisition.

Acquisition Parameters: 64x64 matrix, 8 bit pixel depth. Forty (40) seconds per stop for the Thallium201 acquisition, adjusted for body size to ensure at least 125-175K counts/stop. Gating will be performed at 8 or 16 frames per cycle according to your laboratory's standard practice of using bad-beat rejection and setting the R-to-R window or no bad-beat rejection with a 100% R-to-R window. For single or multi-headed cameras, at least 64 stops/180 degrees should be acquired. Dosing should follow all local regulations re dose limits.

Rest (Redistribution) Imaging Study

Isotope: Thallium201

IMAGING BEGINS 2.5-4.0 HOURS AFTER STRESS THALLIUM201 ISOTOPE INJECTION,

Monitor the patient throughout the exam to gauge motion. If significant motion occurs during the exam, immediately begin a repeat acquisition. Acquisition parameters: 64x64 matrix, 8 bit pixel depth. Forty (40) seconds per stop for the thallium201 acquisition, however this can be adjusted to ensure at least 50-100K counts/stop, based on body size. For single or multi-headed cameras, at least 64 stops/180 degrees should be acquired

Reinjection Study

Isotope: Thallium201

Dose: 1.0-2.0 mCi, weight adjusted as per local lab standards to achieve high count high quality images. Thallium201 injected after rest/redistribution study.

Wait 10-15 minutes after injection before beginning the rest SPECT reinjection images. Monitor the patient throughout the exam to gauge motion. If significant motion has occurred during the exam, immediately begin acquisition on a repeat exam.

Acquisition parameters: 64x64 matrix, 8 bit pixel depth. Thirty (30) seconds per stop for the thallium201 acquisition, however this can be adjusted to ensure at least 50-100K counts/stop, based on body size. For single or multi-headed cameras, at least 64 stops/180 degrees should be acquired. Dosing should follow all local regulations re dose limits.

Acquisition Parameters

Dual Isotope Acquisition Parameters

<u>Acquisition Parameter</u>	<u>Rest Study</u>	<u>Stress Study</u>
Dose*	3.0 – 4.0mCi (111 – 148 MBq)* <sup>201</sup> Thallium	25-30mCi (925 – 1110 MBq)* <sup>99m</sup> Tc- Sestamibi or Tetrofosmin
Energy window(s)	70 KeV 30% and 167 KeV 20%	140 KeV 20%
Collimator	Low-energy, high resolution	Low-energy, high resolution
Patient Position	Supine	Supine
Orbit	180°/360°	180°/360°
Total Number of projections	Minimum 64 Per 180°	Minimum 64 Per 180°
Matrix	64 X 64	64 X 64
Time/Projection	25 seconds (minimum)	20 seconds (minimum)
ECG gated <sup>1</sup>	No	Yes
Frames / R-R Interval	NA	8 or 16

<sup>1</sup>Gated acquisition on the stress study is mandatory, unless technically not feasible (e.g., atrial fibrillation, consistent variable heart rate, bigeminy).

\*Dosing should follow all local regulations re dose limits.

## Single Isotope Sestamibi or Tetrofosmin Acquisition Parameters

### 99mTc Same Day – Rest/Stress Acquisition

<u>Acquisition Parameter</u>	<u>Rest Study</u>	<u>Stress Study</u>
Dose*	7-15mCi (259 – 555 MBq)* <sup>99m</sup> Tc- Sestamibi or Tetrofosmin	25-40mCi (925 – 1480 MBq)* <sup>99m</sup> Tc- Sestamibi or Tetrofosmin
Energy window(s)	140 KeV 20%	140 KeV 20%
Collimator	Low-energy, high resolution	Low-energy, high resolution
Patient Position	Supine	Supine
Orbit	180°/360°	180°/360°
Total Number of projections	Minimum 64 Per 180°	Minimum 64 Per 180°
Matrix	64 X 64	64 X 64
Time/Projection	25 seconds (minimum)	20 seconds (minimum)
ECG gated <sup>1</sup>	No	Yes
Frames / R-R Interval	NA	8 or 16

<sup>1</sup>Gated acquisition on the stress study is mandatory, unless technically not feasible (e.g., atrial fibrillation, consistent variable heart rate, bigeminy).

\*Dosing should follow all local regulations re dose limits.

### 99mTc Two Day–Acquisition Parameters

<u>Acquisition Parameter</u>	<u>First Day Study</u>	<u>Second Day Study</u>
Dose*	15-40mCi (925 – 1480 MBq)* <sup>99m</sup> Tc-Sestamibi or Tetrofosmin	25-40mCi (925 – 1480 MBq)* <sup>99m</sup> Tc-Sestamibi or Tetrofosmin
Energy window(s)	140 KeV 20%	140 KeV 20%
Collimator	Low-energy, high resolution	Low-energy, high resolution
Patient Position	Supine	Supine
Orbit	180°/360°	180°/360°
Total Number of projections	Minimum 64 Per 180°	Minimum 64 Per 180°
Matrix	64 X 64	64 X 64
Time/Projection	20 seconds (minimum)	20 seconds (minimum)
ECG gated <sup>1</sup>	Yes if stress	Yes if stress
Frames / R-R Interval	8 or 16	8 or 16

<sup>1</sup>Gated acquisition on the stress study is mandatory, unless technically not feasible (e.g., atrial fibrillation, consistent variable heart rate, bigeminy).

\*Dosing should follow all local regulations re dose limits.

**Tl-201 Same Day – Stress/Redistribution Acquisition, Stress/Redistribution/Reinjection**

Acquisition Parameter	Stress Study	Redistribution	Study
Reinjection Study			
Dose*	2.5-4.0mci (93 -148 MBq)* 201Thallium	201Thallium	1-2mci (37-74MBq)* 201Thallium
Energy windows	70 KeV 30% and 167 KeV 20%	70 KeV 30% and 167 KeV 20%	70 KeV 30% and 167 KeV 20%
Collimator	Low-energy, high resolution	Low-energy, high resolution	Low-energy, high resolution
Patient Position	Supine	Supine	Supine
Orbit	1800/3600	1800/3600	1800/3600
Total Number of Projections	Minimum 64 Per 1800	Minimum 64 Per 1800	Minimum 64 Per 1800
Matrix	64 X 64	64 X 64	64 X 64
Time/Projection	40 seconds (minimum)	40 seconds (minimum)	30 seconds (minimum)
ECG gated*	YES	NO	NA
Frames / R-R	8 or 16	NO	NA

## Interval

1Gated acquisition on the stress study is mandatory, unless technically not feasible (e.g. atrial fibrillation, consistent variable heart rate, bigeminy)

\*Dosing should follow all local regulations re dose limits.

## Exercise Treadmill Testing

The ETT will be supervised by an attending physician or his/her designee. Prior to proceeding with any exercise test, make sure that the subject has not recently exhibited any unstable cardiac symptoms. Testing should be symptom limited only and not stopped for simply reaching 85% maximum predicted HR. For patients who do not reach or exceed 85% maximum predicted HR or who do not reach a symptomatic end-point in the test, pharmacologic stress should then be employed.

Recognizing that stress test labs and stress imaging labs will incorporate different protocols for exercise, the diagnostic core lab recommends using the Standard Bruce Protocol for the exercise treadmill test (ETT) whenever safe and feasible for the patient. For patients requiring a more gentle or “warm up” period and/or rate of progression and in those in whom shorter stages are more suitable the Modified Bruce, Naughton, or Balke protocols are recommended.

## Standard Bruce Protocol

The Standard Bruce Protocol requires patients to begin walking at a speed of 1.7 miles per hour at a 10% grade. The grade and speed are changed every 3 minutes as specified in the table below.

<b>Stage</b>	<b>Stage Speed (MPH)</b>	<b>Elevation (% Grade)</b>	<b>Duration (min)</b>
1	1.7	10	3
2	2.5	12	3
3	3.4	14	3
4	4.2	16	3
5	5.0	18	3
6	5.5	20	3
7	6.0	22	3

## Modified Bruce Protocol

The first stage of the protocol is performed at 1.7 MPH and 0% grade for 3 minutes; and the second stage is performed at 1.7 MPH and 5% grade for 3 minutes. Subsequent stages follow the Standard Bruce Protocol starting at the 1st stage (1.7 MPH, 10% grade for 3 minutes and on).

## Summary Instructions

### Exercise

- Total exercise time should be reported on the ETT Worksheet.
- The clock should start at the beginning of the protocol.
- Continuous 12 lead ECG monitoring should be performed throughout both exercise and recovery periods, until the test is terminated.
- Obtain a BP towards the end of each stage (every 2 or 3 minutes, depending on ETT protocol used).
- Exercise should be terminated based on symptoms, safety parameters or at the subject's request.
- The reason for exercise termination should be documented.

### Immediately Post Exercise

- As soon as the test stops, the clock should be reset to zero and recovery time begins.
- Continuous ECG monitoring should continue throughout recovery.
- Obtain a BP immediately upon termination of the ETT.

### Recovery

- Patients are to be monitored for a minimum of 10 minutes into recovery or until symptoms and/or ECG changes resolve to pre-test condition.
- Continuous ECG monitoring should continue throughout the recovery period.
- BP should be obtained at minutes 1, 3, 5, 7 and 10 (or as often as clinically needed).

### Pharmacologic Stress

Pharmacologic agents are used in patients who are unable to exercise and are combined with imaging of the myocardium. Nuclear perfusion imaging can be performed with a variety of pharmacologic agents described below. Pharmacologic stress echocardiography is performed with Dobutamine.

#### Adenosine stress

This will take place using adenosine as the stressor. The following represents the standard FDA-approved protocol. Adenosine is infused over a 6 minute time period at 140 µg/kg/min, with simultaneous monitoring of HR, BP, and the ECG as per the laboratory's standard procedure. Isotope injection (sestamibi or tetrofosmin, 25-30 mCi) takes place 3 minutes after start of the infusion (i.e., at minute 3 of the 6 minute infusion). Other widely used protocols that have validation in the literature and are described in the American Society of Nuclear Cardiology Guidelines include a 4 minute infusion protocol, with isotope injected at 2 minutes, and an "adeno-walk" protocol, in which low-level exercise is performed during the adenosine infusion.

#### Dipyridamole stress

This will take place using dipyridamole as the stressor, as per the ASNC Imaging Guidelines. This is preferably infused or can be given manually 0.56 mg/kg over a 4-minute time period with simultaneous monitoring of HR, BP, and the ECG as per the laboratory's standard procedure. Isotope injection (sestamibi or tetrofosmin 25-30 mCi) takes place 3-5 minutes after the completion of the dipyridamole administration.



Intravenous aminophylline (125-250 mg) may be required to reverse the dipyridamole side effects.

### Regadenoson Stress

This will take place using Regadenoson as the stressor. The following represents the standard FDA-approved protocol and the ASNC Imaging Guidelines. Regadenoson is injected into a peripheral vein as a rapid bolus (approximately 10 seconds) at 0.4 mg/5 ml followed by a 5 ml saline flush with simultaneous monitoring of HR, BP, and the ECG as per the laboratory's standard procedure. Isotope injection (sestamibi or tetrofosmin, 25-30 mCi) (thallium, 2.5-4.0 mci) takes place 10-30 seconds after the 5 ml saline flush. A 22-gauge or larger catheter or needle is used and the radionuclide may be injected directly into the same catheter as the Regadenoson.

### Dobutamine Stress

The pharmacologic stressor agent dobutamine may be used if adenosine or dipyridamole is contraindicated, as per the ASNC Imaging Guidelines. Dobutamine is also used as the stressor agent in pharmacologic stress echocardiography. This is infused incrementally using an infusion pump starting at a dose of 5-to10 ug/kg/min, which is increased at 3-minute intervals to 20, 30 up to a maximum of 40 ug/kg/min, with simultaneous monitoring of HR, BP, and the ECG as per the laboratory's standard procedure. Dobutamine titration is ramped up with the intention of exceeding 85% of the maximum predicted heart rate. If the maximum dose of dobutamine is reached without reaching 85% of MPPHR, then atropine and or isometric exercise may be given. Isotope injection (sestamibi, 25-30 mCi) takes place 1 minute into the highest dobutamine dose, and dobutamine infusion should be continued for 2 minutes post sestamibi injection.

### SPECT Reporting

While recognizing that each site will have their own method and template for reporting the results of stress SPECT MPI studies to referring MDs, it is important for the purposes of the ROMICAT II trial that essential elements of the results are uniformly reported to the decision making referring MDs across trial sites.

The elements in a structures report have been summarized in the American Society of Nuclear Cardiology Imaging Guidelines for Nuclear Cardiology Procedures document entitled: "Structured Reporting of Radionuclide Myocardial Perfusion and Function". (1) The elements of a report relevant to the ROMICAT II trial patients, who may be referred for stress SPECT MPI, can be listed as follows (1):

### Table of Structured Data Elements

- Site administrative data
- Study demographics
- Patient demographics
- Clinical information
- Stress testing data
- Resting and Stress ECG data
- Imaging acquisition parameters
- Myocardial perfusion
- Perfusion quantitation (if performed)

- LV function parameters
- Miscellaneous data
- Overall impression

#### ETT Parameters to be reported

1. Mode of stress (exercise (and type of exercise) or pharmacologic (and specific pharmacologic agent))
2. Functional capacity
3. Total exercise time
4. Reason for terminating test (patient must be limited by angina related symptoms), including: angina, fatigue, shortness of breath, hypotension, ECG changes, other
5. ECG changes from continuous 12 lead ECG monitoring
6. HR and BP response measured towards the end of each stage
7. Baseline medications
8. Resting and peak heart rate
9. Resting and peak systolic and diastolic blood pressure
10. peak dose of dobutamine and atropine
11. Arrhythmia, bundle branch block or pacemaker activity on resting ECG, during exercise or during recovery monitoring.
12. documentation of any complications, treatment and outcome of these

#### Imaging Parameters to be reported

The description of the perfusion abnormality is particularly important, as the extent and severity of perfusion abnormality is associated with subsequent outcomes. That element and the degree of reversibility (ischemia) usually drive physician decision making. Perfusion abnormalities should be described as to their location (either by segment, wall or vascular territory), as well as by their extent (how much territory is involved), and also by severity (“depth” of perfusion abnormality, described as mild, moderate or severe), for each distinct defect. Each perfusion defect should also be described as to its reversibility, indicating ischemia or infarct.

Gated SPECT evaluation of LV function is a routine component of the stress/rest SPECT MPI study, and information on regional wall motion abnormalities and quantitated global function should be routinely provided. The “overall impression” at the end of the report is a summary of the findings of the study, described in clinically relevant language (i.e., described as “ischemia” or “infarct” rather than “reversible defect” or “fixed defect” respectively).

#### References

1. Tilkemeier PL, et al. American Society of Nuclear Cardiology Imaging Guidelines for Nuclear Cardiology Procedures. Structured Reporting of Radionuclide Myocardial Perfusion and Function. <http://www.asnc.org/imageuploads/ImagingGuidelinesReportingJuly2009.pdf>

## Appendix L: Cardiac CT

### 1. General Considerations

This document details guidance based on professional society standards, and encourages the use of such standard practices, even though adherence to the stipulations of this guidance is not required by protocol. Cardiac computed tomography will be performed and interpreted in accordance with best practice standards as delineated in the imaging guidelines of the Society of Cardiovascular Computed Tomography using at least 64 slice technology and interpreted by physicians at least COCATS level 2 or equivalent Society of Cardiovascular Computed Tomography level 2 or the Certification Board of Computed Cardiovascular Tomography (CBCCT). For this trial both prospective and retrospective ECG gating/triggering are permitted. The assessment of LV function is optional. Below is a summary of the standard that should be considered at each institution in the trial.

### 2. Patient Preparation

- Contraindications
  - Absolute
    - Iodinated contrast allergy not amenable to pre-treatment
    - Pregnancy
  - Relative
    - Renal insufficiency
    - Inability to perform breathhold  $\geq 10$  seconds
    - Cardiac rhythm: frequent ectopy/arrhythmia
    - Unwillingness to hold metformin 48 hour after the CT examination
  
- Prior to arrival
  - May continue usual intake of liquids and solids
  
- In the scanner
  - Patient positioning - Heart should be centered within the gantry
  - Appropriate placement of ECG leads
  - Perform a test breath hold to monitor heart rate to decide on beta blocker requirement and usage of prospective vs. retrospective gating
  - Use of iv or oral beta blockers if heart is above 60 bpm (e.g. 5 to 20 mg Metoprolol, I.V. or 50-100 mg Atenolol one hour before) – exceptions can be made for CT scanners with high temporal resolution such as Dual Source or Flash
  - Use of nitroglycerin for coronary vasodilation (e.g. 400-800 mcg sublingual nitroglycerin – one to two tabs)
    - Important: If phosphodiesterase inhibitors for 48 hours before the test, no nitrates to be given during CT scan acquisition

### 3. CT Imaging Protocol

- Iodinated contrast agent with at least 320 (or 300) mg Iodine per ml
- Injection rate of contrast agent: minimum rate of 5ml/sec
- Determination of optimal contrast timing using either a test bolus or a bolus trigger technique
- AMOUNT OF CONTRAST: DURATION OF SCAN BUT AT LEAST 10 SECONDS Injection
- Minimizing the radiation exposure by choosing an appropriate scan coverage in the Z-direction (at the level of the carina to the dome of the diaphragm)

#### Steps

##### 1. Scout

- Topogram ap and/or lateral

##### 2. Coronary Calcium Assessment

- Prospective ECG gated/triggered, low dose non-contrast CT scan to determine Coronary artery calcification

##### 3. Assessment of coronary atherosclerotic plaque and stenosis

- Prospective ECG triggered or retrospective ECG gated CT imaging using tube modulation technique
  - Using maximal temporal and spatial resolution of the equipment
  - **Candidates for prospective triggering:** regular heart rate <62 bpm during breath hold after beta blockade, no cardiac arrhythmias or extrasystolic beats prior or during test breath hold
  - **Adjusting kvp to BMI**
    - 100 kvp if BMI <30 kg/m<sup>2</sup> AND body weight is below 220 pounds
    - 120 kvp if BMI > 30 kg/m<sup>2</sup>
  - For retrospective gating – use **radiation safety options** according to the manufacturers guidelines (i.e. tube current modulation, width of the full tube current according to heart rate, hybrid techniques such as padding)
  - Image reconstruction
    - perform ECG editing in patients with extrasystolic beats
    - reconstruct with approximately 50% overlap (Eg. 0.75 mm slice thickness with 0.4 mm increment or 0.6 slice thickness with 0.3 mm overlap)
    - reconstruct the number of series necessary to eliminate motion artifacts, typically two data sets, but more if required (i.e. for the RCA) in mid diastole(65-80%) and end systole (35-45%) if retrospective technique was used.

##### 4. LV function (optional)

- a. If retrospective ECG gating is performed to assess the coronary arteries LV data on global and regional LV function should be collected and assessed
- b. Typically 1.5mm thick axial images are reconstructed at 10% increments (10 phases) for single source CT scanners or 5% increments (20 phases) for dual source CT scanners throughout the cardiac cycle
- c. USE REDUCED PIXEL MATRIX (256x256)

**5. Full field of view**

- d. For assessment of incidental findings – a data set of 3 mm thick axial images, covering the portions of the thorax acquired during the cardiac CT scan is reconstructed
- e. Reconstruction of a field of view optimized for coverage of the heart

**6. Documentation of Radiation Exposure**

- f. document radiation exposure - this page can usually be stored once the reconstruction is finished

**4. CT Parameters to be reported****1. Beta blocker and nitrate administration****2. Imaging sequences performed****3. Overall contrast administration including which contrast agent****4. Overall radiation dose****5. Coronary evaluation including:**

- a. Artery distribution (right or left dominant, co-dominant)
- b. Overall image quality as interpretable/uninterpretable optimally specify non-evaluable segments/arteries with reason
- c. presence and extent of coronary atherosclerotic plaque (none, calcified, non-calcified, both) according to AHA classification per vessel and optionally per 17-coronary segments
- d. presence and severity of a significant coronary stenosis (>70% luminal narrowing) per vessel and optionally per coronary segments and classify severity of stenosis as

**Left Main**

- i. Normal: 0%
- ii. Non-significant/Mild or Minor Disease: 1-49%
- iii. Significant/Severe Severe Disease: 50-99%
- iv. Occluded: 100%

**All others Vessels**

- i. Normal: 0%
- ii. Non-significant/Mild or Minor Disease: 1-49%
- iii. Moderate Disease: 50-69%
- iv. Significant/Severe Severe Disease: 70-99%
- v. Occluded: 100%

**6. Optional: Evaluation of the left ventricle**

- a. Regional LV dysfunction including wall motion and wall thickening of the myocardium assessed qualitatively based on the AHA/ACC/ASE 17-segment model<sup>27</sup>
- b. Whether the location of regional dysfunction matches the stenosis location
- c. Regional LV dysfunction has to be present in at least two contiguous myocardial segments or in one segment visualized in two different views to be considered a true positive finding.
- d. Each LV segment graded as normal, hypokinetic (impaired contraction), akinetic (absent contraction), dyskinetic (paradoxical outward wall motion during systole without aneurysmal formation in diastole) or aneurysmal.

- e. Global LV function as normal, mildly, moderately or severely impaired

**7. Non-cardiac finding assessment includes, but is not limited to**

- a. aortic dissection
- b. pulmonary embolism
- c. pulmonary nodules
- d. pneumonia
- e. pneumothorax
- f. pericardial effusion
- g. hiatal hernia
- h. rib fractures

## **Appendix M: Stress Testing – Echocardiography**

### **1. General Considerations**

This document details guidance based on professional society standards, and encourages the use of such standard practices, even though adherence to the stipulations of this guidance is not required by protocol. The stress echocardiogram is typically performed with 1) exercise – either a) treadmill or b) bicycle (supine or upright) or 2) Dobutamine. All sonographers and echo physicians involved in this study should review the ASE Guidelines for Performance of Stress echocardiography and adhere to these recommendations (<http://www.asecho.org/i4a/pages/index.cfm?pageid=3317>) (Pellikka PA, et al. American Society of Echocardiography Recommendations for Performance, Interpretation, and Application of Stress Echocardiography. J Am Soc Echocardiogr 2007;20:1021-1041). Each site will be responsible for the patient's safety, quality of patient preparation, reports, data collection, ECG tracings and timely forwarding of test results.

### **2. Patient Preparation**

A 12-lead system, modified for use in the exercising patient, is then applied. Resting 12-lead electrocardiograms are generally obtained in a supine or scanning position. In order to interpret the ETT-ECG tracing with the highest accuracy, the patient's skin must be prepared properly. There should be no electrical distortion/artifact on the ETT-ECG. Patients are instructed to come to the stress laboratory dressed comfortably with lightweight shoes and the exercise laboratory should be kept at a comfortable temperature ranging from 68 - 74 degrees F with 40-60% humidity. The supervisor of the test must obtain a careful history and a brief physical examination should be performed, focusing on the cardiopulmonary system. The supervisor of the test must evaluate its purpose and carefully consider indications and contraindications to testing. The entire testing procedure should be explained to the patient in detail, including a review of the treadmill or bike system. The patient should be instructed to immediately report unusual or significant symptoms, e.g. chest pain, dizziness, lightheadedness, etc. The patient may request the termination of exercise prematurely whenever necessary. Laboratories must have guidelines, protocols and equipment in place for treatment of patients who become unstable or have a change in status during or after stress. Cardiopulmonary resuscitation equipment including a defibrillator and commonly used emergency cardiac drugs is essential and must be readily available. Medical as well as paramedical personnel working in the exercise laboratory should be capable of providing cardiopulmonary resuscitation.

### **Summary Instructions**

- Review and obtain medical history and make sure there is no contraindication for proceeding with a stress test.
- List patient's current medication regimen and whether or not meds were withheld.
- Prepare the patient's skin in accordance with standard ETT practice
- The limb leads should be placed in the torso modified position for stress testing

- Obtain supine and standing ECG and BP.
- During the test, the subject may gently rest their hands on the treadmill railing. When obtaining BP, have subject raise hand off the railing and place on shoulder of person obtaining BP to minimize electronic noise.

### **3. Test Protocol (s)**

#### **Exercise Stress Echocardiography Using Treadmill**

The ETT will be supervised by an attending physician or his/her designee. Prior to proceeding with any exercise test, make sure that the subject **has not recently exhibited any unstable cardiac symptoms**. Testing should be symptom limited only and not stopped for simply reaching 85% maximum predicted HR. For patients who do not reach or exceed 85% maximum predicted HR or who do not reach a symptomatic end-point in the test, pharmacologic stress should then be employed.

Recognizing that stress test labs and stress imaging labs will incorporate different protocols for exercise, the diagnostic core lab recommends using the Standard Bruce Protocol for the exercise treadmill test (ETT) whenever safe and feasible for the patient. For patients requiring a more gentle or “warm up” period and/or rate of progression and in those in whom shorter stages are more suitable the Modified Bruce, Naughton, or Balke protocols are recommended.

#### **Standard Bruce Protocol**

The Standard Bruce Protocol requires patients to begin walking at a speed of 1.7 miles per hour at a 10% grade. The grade and speed are changed every 3 minutes as specified in the table below.

<b>Stage</b>	<b>Stage Speed (MPH)</b>	<b>Elevation (% Grade)</b>	<b>Duration (min)</b>
1	1.7	10	3
2	2.5	12	3
3	3.4	14	3
4	4.2	16	3
5	5.0	18	3
6	5.5	20	3
7	6.0	22	3

If patients are elderly or sedentary, the ECG core lab recommends a Modified Bruce Protocol. The first stage of the protocol is performed at 1.7 MPH and 0% grade for 3 minutes; and the second stage is performed at 1.7 MPH and 5% grade for 3 minutes. Subsequent stages follow the Standard Bruce Protocol starting at the 1st stage (1.7 MPH, 10% grade for 3 minutes and on).

#### **Exercise Stress Echocardiography Using Supine Bike**



The following are the standard protocols used for evaluation of ischemia with supine bike exercise. Each have 2 minute stages which allow sufficient time for echo imaging for LV wall motion.

### Standard

	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Stage 6	Stage 7	Stage 8	Stage 9	Stage 10
WATTS	25	50	75	100	125	150	175	200	225	250
METS	2.5	3.7	4.9	6.1	7.3	8.6	9.8	11.0	12.2	13.5
Stage duration (mins)	2	2	2	2	2	2	2	2	2	2
Accumulated time (mins)	2	4	6	8	10	12	14	16	18	20

### For those expected to have good functional capacity

	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Stage 6	Stage 7	Stage 8	Stage 9	Stage 10
WATTS	50	75	100	125	150	175	200	225	250	275
METS	3.7	4.9	6.1	7.3	8.6	9.8	11.0	12.2	13.5	14.7
stage duration (mins)	2	2	2	2	2	2	2	2	2	2
Accumulated time (mins)	2	4	6	8	10	12	14	16	18	20

### Summary Instructions

#### Rest

- Review and obtain medical history and make sure there is no contraindication for proceeding with a stress test.
- List patient's current medication regimen and whether or not meds were withheld.
- Prepare the patient's skin in accordance with standard ETT practice
- The limb leads should be placed in the torso modified position for stress testing
- Obtain supine and standing ECG and BP.
- During the test, the subject may gently rest their hands on the treadmill railing. When obtaining BP, have subject raise hand off the railing and place on shoulder of person obtaining BP to minimize electronic noise.

#### Exercise

- Total exercise time should be reported on the ETT Worksheet.
- The clock should start at the beginning of the protocol.
- Continuous 12 lead ECG monitoring should be performed throughout both exercise and recovery periods, until the test is terminated.
- Obtain a BP towards the end of each stage (every 2 or 3 minutes, depending on ETT protocol used).

- Exercise should be terminated based on symptoms, safety parameters or at the subject's request.
- The reason for exercise termination should be documented.

### **Immediately Post Exercise**

- As soon as the test stops, the clock should be reset to zero and recovery time begins.
- Continuous ECG monitoring should continue throughout recovery.
- Obtain a BP immediately upon termination of the ETT.

### **Recovery**

- Patients are to be monitored for a minimum of 10 minutes into recovery or until symptoms and/or ECG changes resolve to pre-test condition.
- Continuous ECG monitoring should continue throughout the recovery period.
- BP should be obtained at minutes 1, 3, 5, 7 and 10 (or as often as clinically needed).

### **Pharmacologic Stress Echocardiography - Dobutamine Stress Echocardiography**

Pharmacologic agents are used in patients who are unable to exercise and are combined with imaging of the myocardium. Pharmacologic stress echocardiography is typically performed with Dobutamine. This is infused incrementally using an infusion pump starting at a dose of 5-to10 ug/kg/min, which is increased at 3-minute intervals to 20, 30 up to a maximum of 40 ug/kg/min, with simultaneous monitoring of HR, BP, and the ECG as per the laboratory's standard procedure. Dobutamine titration is ramped up with the intention of exceeding 85% of the maximum predicted heart rate. If the maximum dose of dobutamine is reached without reaching 85% of MPPHR, then atropine and or isometric exercise may be given. Patients are studied in the supine position; no exercise is performed.

- Atropine 0.25 - 0.5 mg aliquots IV up to a maximum dose of 2 mg may be given at the discretion of the test supervisor if the heart rate response to Dobutamine is well below 85% predicted maximum heart rate.
- Metoprolol 2.5-10.0 mg may be given by slow IV push (suggested rate: 1mg/minute) to reverse Dobutamine-related side effects or ischemic ECG changes. BP should be measured following each dose of metoprolol.

### **Dobutamine Infusion Protocol for evaluation of Ischemia without resting wall motion abnormalities**

<b>Stage</b>	<b>Dose</b>	<b>Duration (min)</b>
1	05 mcg/kg/min	3
2	10 mcg/kg/min	3
3	20 mcg/kg/min	3
4	30 mcg/kg/min	3
5	40 mcg/kg/min	3
6 (optional)	50 mcg/kg/min	3 (given at discretion of supervisor)
7 (optional)	0.25-2.0 mg atropine	(described below)

**Note:** For evaluation of Ischemia with resting wall motion abnormalities the protocol is same as above except for stage 1 where the duration is 5 minutes.

### **Echocardiography Imaging Protocol**

TTE images of the LV are acquired from the parasternal long axis, parasternal short axis (mid LV), apical 4 chamber and apical 2 chamber windows. Monitor for wall motion abnormalities and vital signs during each stage of the exercise protocol. Images are recorded at baseline, low dose dobutamine, peak stress, and recovery. Images must be obtained within 90 seconds of completion of exercise.

For each view, the gain and compression should be optimized so that the best echocardiographic image of the endocardial borders is obtained. The selection of harmonics or fundamental frequency should depend upon which yields the best definition of structures. The depth should be selected which allows visualization of all of the structures of interest in that view. All images should have a good quality ECG tracing on the screen and clear calibration markings on the imaging sector.

The main focus is on the left ventricle, thus depth and sector size for each of the views should be optimized so that the left ventricle occupies most of the sector. It is critical that at a minimum the common four views of the LV be obtained at baseline and peak stress (or immediate post-stress) – parasternal long axis, parasternal short axis (mid LV/papillary muscle), apical four chamber and apical two chamber. While only 1 beat of each view is displayed at each stage, if more images are performed at each stage, these should be included in the image transfer to the image processing center when ever possible. If sites wish to also include a set of recovery images for each view then the software protocol should be set up as a quad screen format and only 3 of the four cells will include images.

For treadmill exercise stress echo, the four images are obtained at baseline and immediately after exercise and are displayed in a “side by side” or “split screen” format. Imaging is performed while the patient lies on a bed and the bed should be positioned close to the treadmill so that images can be obtained quickly after the treadmill stress. It is critical that the immediate post-exercise images be obtained quickly since stress induced ischemic LV wall motion abnormalities may resolve quickly after the stress is stopped and the heart rate recovers. For acquisition of the immediate post-exercise images, it is recommended that the apical views be obtained first since these display segments of the LV that cover all coronary territories and this window may be found quickly once the patient moves from treadmill to imaging bed.

If visualization of the LV endocardial border is inadequate then an approved contrast agent should be administered and harmonic imaging with low to intermediate mechanical index should be performed. Recommendations for echo contrast use are detailed in the ASE Contrast Consensus Document (<http://www.asecho.org/files/public/ContrastConsensusStatement.pdf>). Contrast for LV opacification is typically recommended when greater than or equal to 2 contiguous LV segments are not visualized from apical views.

Supine or upright bicycle stress echo differ from treadmill stress echo in that the imaging of the LV can be performed during the stress and thus the peak stress images should be performed during rather than immediately after the stress. For both treadmill and bicycle stress, if there are no wall motion abnormalities noted at peak stress, it is valuable to also image several minutes later as delayed wall motion abnormalities can occur with myocardial ischemia.

For Dobutamine stress echo, continuous imaging is feasible since the patient is lying on the bed throughout the test. Thus the peak stress images should be obtained either during the peak dose of Dobutamine (+/- Atropine) or immediately after the IV infusion is stopped.

For all modes of stress echo, if wall motion abnormalities are noted at peak stress, then recovery images should be obtained to document that the stress-induced LV regional dysfunction resolved.

#### **4. Test Reporting**

##### **ETT Parameters to be reported**

1. Mode of stress (exercise (and type of exercise) or pharmacologic (and specific pharmacologic agent))
2. Functional capacity
3. Total exercise time
4. Reason for terminating test (patient must be limited by angina related symptoms), including: angina, fatigue, shortness of breath, hypotension, ECG changes, other
5. ECG changes from continuous 12 lead ECG monitoring (ST depression, elevation, VT)
6. HR and BP response measured towards the end of each stage
7. Baseline medications
8. Resting and peak heart rate
9. Resting and peak systolic and diastolic blood pressure
10. peak dose of dobutamine and atropine
11. Arrhythmia, bundle branch block or pacemaker activity on resting ECG, during exercise or during recovery monitoring.
12. documentation of any complications, treatment and outcome of these

##### **Echocardiography**

At rest and peak stress (or immediate post-stress, if treadmill exercise) LV size (qualitative or quantitative), global LV function, (LVEF either qualitative or quantitative) and regional LV function (qualitative) are assessed and compared. If resting wall motion abnormalities are noted on the dobutamine stress echo then assessment of regional LV function should be performed also at low dose (5 or 10 mcg/kg/min).

Regional function is assessed by the extent of endocardial inward motion, the extent of systolic thickening and the timing of systolic thickening by vessel territory. Vessel territory is defined as LAD (anterior, apical), LCX (lateral), RCA (inferior). Segmental function is classified as either normal, mildly hypokinetic, severely hypokinetic, akinetic, or dyskinetic. The entire segment must demonstrate the degree of wall motion to be classified as such otherwise the milder degree of wall motion is coded for that segment. During peak stress, a normal segmental response is considered to be hyperkinetic.

The stress echo report should include:

1. Presence and location of regional LV wall motion at rest.
2. Presence of new regional LV wall motion abnormalities with stress or presence of stress-induced global LV dysfunction by vessel territory.
3. Location of stress-induced regional LV wall motion abnormalities.
4. For dobutamine testing if resting wall motion: presence of myocardial viability in dysfunctional segments.
5. Presence of stress-induced LV cavity dilation
6. Interpretation:
  - a. No inducible ischemia at appropriate workload
  - b. No inducible ischemia at sub-maximal workload
  - c. Inducible ischemia and location(s)
  - d. Viable myocardium (for dobutamine testing when resting wall motion present)

## **Appendix N: Stress Testing – Exercise treadmill test (ETT)**

### **1. General Considerations**

This document details guidance based on professional society standards, and encourages the use of such standard practices, even though adherence to the stipulations of this guidance is not required by protocol. For exercise ECG – below is a summary of techniques to be considered in concordance with ACC/AHA Exercise Stress Testing Guidelines<sup>75</sup>. Each site will be responsible for the patient's safety, quality of patient preparation, reports, data collection, ECG tracings and timely forwarding of test results.

### **2. Patient Preparation**

Patients should be contacted prior to the day of ETT and instructed on whether or not to take medications, to remain NPO for at least 3 hours prior to ETT, to avoid exertion prior to ETT, and to dress in casual clothing suitable for exercise. A basic history and physical exam should be used to screen relative contraindications to exercise, such as resting hypertension, severe aortic stenosis, or active symptoms of angina or heart failure. A resting ECG prior to exercise, ideally for comparison to a prior ECG, is generally examined for rate, rhythm and morphology to further ensure both the safety and the suitability of proceeding. Orthostatic blood pressure on standing is also a widely recommended practice prior to exercise.

Informed consent with regard to the goals, procedure and risks/benefits of the ETT is an essential process. Patients should also be introduced to how to step on, walk on and step off the treadmill, preferably through demonstration by the technician. While walking on the treadmill patients should be encouraged to keep arms lightly rested on the railing.

In addition to the above the most critical aspect of patient preparation is the connection to the ECG monitoring system. The two basic principles of such connection are: skin preparation and lead positioning. For most ETT recordings, 10 electrodes should be positioned to produce the standard 12-lead waveform array. Precordial lead positions are identical to those used for diagnostic ECGs, positioned by counting rib interspaces and identification of the mid-clavicular and axillary lines. Limb leads are generally moved to torso positions (shoulders or clavicles for upper extremity limb leads, iliac crests or hypogastrium for lower extremity leads). Torso lead positions may result in rightward QRS axis shift and the appearance or disappearance of inferior Q-waves, changing the morphology relative to true diagnostic ECGs, nonetheless the stability of the torso lead positions is generally favored due to the profound impact on motion artifact during exercised.

Skin preparation is perhaps the most critical technical feature of patient preparation. Skin preparation has two main features: adherence and impedance. For optimal adherence, hair should be generously shaved, skin oils should be removed using isopropyl alcohol or some equivalent, and fresh electrodes, ideally designed for ETT, should be used. Impedance to signal transmission from the source myocardial cells to the ETT amplifier

is primarily mediated through the waxy epidermis. Resting impedance of normal skin is >50,000 ohms. Gentle abrasion of the epidermis with an abrasive, or using ETT electrodes specifically designed for this purpose, can reduce impedance to <5,000 ohms, with a 10-fold increase in signal/noise waveform quality.

## Summary Instructions

### Rest

- Review and obtain medical history and make sure there is no contraindication for proceeding with a stress test.
- List patient's current medication regimen and whether or not meds were withheld.
- Prepare the patient's skin in accordance with standard ETT practice
- The limb leads should be placed in the torso modified position for stress testing
- Obtain supine and standing ECG and BP.
- During the test, the subject may gently rest their hands on the treadmill railing. When obtaining BP, have subject raise hand off the railing and place on shoulder of person obtaining BP to minimize electronic noise.

### 3. Test Protocol (s)

#### Exercise treadmill Testing

The ETT will be supervised by an attending physician or his/her designee. Prior to proceeding with any exercise test, make sure that the subject **has not recently exhibited any unstable cardiac symptoms**. Testing should be symptom limited only and not stopped for simply reaching 85% maximum predicted HR. For patients who do not reach or exceed 85% maximum predicted HR or who do not reach a symptomatic end-point in the test, pharmacologic stress should then be employed.

Recognizing that stress test labs and stress imaging labs will incorporate different protocols for exercise, the diagnostic core lab recommends using the Standard Bruce Protocol for the exercise treadmill test (ETT) whenever safe and feasible for the patient. For patients requiring a more gentle or "warm up" period and/or rate of progression and in those in whom shorter stages are more suitable the Modified Bruce, Naughton, or Balke protocols are recommended.

#### Standard Bruce Protocol

The Standard Bruce Protocol requires patients to begin walking at a speed of 1.7 miles per hour at a 10% grade. The grade and speed are changed every 3 minutes as specified in the table below.

<b>Stage</b>	<b>Stage Speed (MPH)</b>	<b>Elevation (% Grade)</b>	<b>Duration (min)</b>
1	1.7	10	3
2	2.5	12	3
3	3.4	14	3
4	4.2	16	3
5	5.0	18	3
6	5.5	20	3
7	6.0	22	3

### **Modified Bruce Protocol**

The first stage of the protocol is performed at 1.7 MPH and 0% grade for 3 minutes; and the second stage is performed at 1.7 MPH and 5% grade for 3 minutes. Subsequent stages follow the Standard Bruce Protocol starting at the 1st stage (1.7 MPH, 10% grade for 3 minutes and on).

### **Summary Instructions**

#### **Exercise**

- Total exercise time should be reported on the ETT Worksheet.
- The clock should start at the beginning of the protocol.
- Continuous 12 lead ECG monitoring should be performed throughout both exercise and recovery periods, until the test is terminated.
- Obtain a BP towards the end of each stage (every 2 or 3 minutes, depending on ETT protocol used).
- Exercise should be terminated based on symptoms, safety parameters or at the subject's request.
- The reason for exercise termination should be documented.

#### **Immediately Post Exercise**

- As soon as the test stops, the clock should be reset to zero and recovery time begins.
- Continuous ECG monitoring should continue throughout recovery.
- Obtain a BP immediately upon termination of the ETT.

#### **Recovery**

- Patients are to be monitored for a minimum of 10 minutes into recovery or until symptoms and/or ECG changes resolve to pre-test condition.
- Continuous ECG monitoring should continue throughout the recovery period.
- BP should be obtained at minutes 1, 3, 5, 7 and 10 (or as often as clinically needed).



**4. Test Reporting**

ETT Parameters to be reported

1. Functional capacity
2. Total exercise time
3. Reason for terminating test (patient must be limited by angina related symptoms), including: angina, fatigue, shortness of breath, hypotension, ECG changes, other
4. ECG changes from continuous 12 lead ECG monitoring (ST- elevation, ST- depression, VT)
5. HR and BP response measured towards the end of each stage
6. Baseline medications
7. Resting and peak heart rate
8. Resting and peak systolic and diastolic blood pressure
9. Arrhythmia, bundle branch block or pacemaker activity on resting ECG, during exercise or during recovery monitoring

## Appendix O: Patient Interview Source Document

The items on this form are the **ONLY** data fields that should be completed using direct patient interview. Any other data points that you are not able to obtain from the medical record should be left blank.

For those items that you obtain using direct patient interview, please initial in the right column and sign and date the bottom of the form.

\*If acute cocaine use cannot be obtained from the medical record, please confirm this information with the caregiver. If information cannot be confirmed with the caregiver, confirm with the patient and note on this form.

### Demographics

### CRC Initials

<b>Ethnicity:</b>	Hispanic or Latino NOT Hispanic or Latino Unknown	
-------------------	---	--

### Inclusion/Exclusion Criteria

Please select yes or no to indicate whether patient meets the following inclusion criteria			
Participant must have at least five minutes of chest pain or equivalent (chest tightness; pain radiating to left, right, or both arms or shoulders, back, neck, epigastrium, jaw/throat; or unexplained shortness of breath, syncope/presyncope, generalized weakness, nausea, or vomiting thought to be of cardiac origin) at rest or during exercise within 24 hours of ED presentation, warranting further risk stratification, as determined by an ED attending.	Yes	No	
Participant is able to perform a breath hold of at least 10 seconds	Yes	No	
Please select yes or no to indicate whether patient meets the following exclusion criteria			
Documented or self-reported history of CAD <i>MI, percutaneous coronary interventions [PCIs], coronary artery bypass graft [CABG], known significant coronary stenosis [&gt;50%]</i>	Yes	No	
BMI >40 kg/m <sup>2</sup>	Yes	No	
Known allergy to iodinated contrast agent	Yes	No	
*Documented or self-reported cocaine use within the past 48 hours (acute)	Yes	No	
On Metformin therapy and unable or unwilling to discontinue for 48 hours after the CT scan	Yes	No	

### Pain Characteristics/Symptoms

<b>Chief Complaint</b>	Anginal Chest Pain or equivalent Epigastric Pain Arm/Jaw/Shoulder Pain Shortness of Breath Other: _____	
<b>Most recent Episode</b>	Date (mm/dd/yyyy) Time (hh:mm) Duration (minutes): _____	

### Initial ED Vital Signs

<b>Weight:</b>	lbs	
<b>Height:</b>	inches	

**Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_