PVDOMICS

Chapter 60 & 70
Cardiac Echo & MRI
Imaging Core Lab Process

NHLBI Pulmonary Vascular Disease Phenomics Program

Funded by the National Heart, Lung, and Blood Institute of the National Institutes of Health with support from the Pulmonary Hypertension Association
CV Imaging Core

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Goals of Cardiac MRI

- Quantify cardiac volume and mass, fibrosis and scarring
- Evaluate perfusion and flow
- Compare CMR measures of RV performance to advanced echocardiographic measures.
- Help determine useful parameters to aid in early detection and reclassification of pulmonary hypertension.
MRI Protocol

**Cardiac Structure/Function**

**Rest Perfusion Imaging**

**Valvular Flow**

**DHE – Myocardial Scar**

Optional imaging:
- Pre-contrast MOLLI
- Pulmonary artery compliance/remodeling

Optional imaging:
- 4D flow

Optional imaging:
- Post-contrast MOLLI
## Cardiac MRI Imaging Schedule

<table>
<thead>
<tr>
<th>Imaging Visits</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qualification</td>
<td>Submit a qualification CMR to Core Lab before enrollment</td>
</tr>
<tr>
<td>Visit</td>
<td>Baseline CMR</td>
</tr>
</tbody>
</table>
Cardiac MRI Safety Process

• Preventive Maintenance (PM) Document
  - Prior to Qualification, a copy of the current annual PM document for each CMR scanner planned for use in the PVDOMICS trial, including serial number, must be submitted to the Imaging Core. This satisfies American College of Radiology (ACR) recommendations and ensures the mechanical integrity of the imaging system.
  - Sites must follow ACR Safe Practice Guidelines
Cardiac MRI Qualification Process

• Qualification Cardiac MRI (CMR)
  - All sites will submit a de-identified sample of a recently performed CMR exam completed at their institution.
  - The purpose of the qualification exam is to ensure viewer and analysis compatibility between the site and Core Lab prior to subject recruitment.

The Qualification process must be completed prior to sites submitting CMR exams of enrolled subjects.
CMR Contraindications

- Heart rate > 120
- Atrial fibrillation or irregular heart rate due to frequent ectopy
- Brain aneurysm clips or vascular clips (titanium or titanium alloy are acceptable)
- Cochlear implants
- PPM/ICD
- Insulin pumps
- Any metallic fragment or foreign body (metal shrapnel or bullets)
- Pregnant women
- Breast tissue expanders
- Aortic stent grafts

- Indwelling pulmonary artery catheter – (follow center’s protocol)
- Chronic Kidney Disease with GFR < 30 mL/min or known Gadolinium allergy are excluded from IV contrast, but can be enrolled for non-contrast CMR
- Patients with uncontrollable severe claustrophobia
- Patients in decompensated heart failure or with significant pleural effusions (moderate or more)
- Patients unable to hold their breath for 10 – 15 sec
Exceptions to Contraindications

CMR is safe with:
- Coronary stents
- Joint replacements
- ASD/PFO closure devices
- Sternal wires
- Most prosthetic heart valves
Anonymization Process

- The subject coordinator needs to supply the subject ID to the technologist.
- For purposes of confidentiality and to remain compliant with Health Insurance Portability and Accountability Act (HIPAA), all references to a specific subject must be made using the entire Subject ID.
- Site is responsible for correctly de-identifying clinical exams with the correct study assigned Subject ID within the AG Mednet application.
Cardiac MRI Qualification Process

- **AG Mednet**
  - Is the secure digital transfer service designated for this trial
  - The electronic CMR data transmittal form will be completed prior to transfer of the qualification exam (or any exam) to the Imaging Core via AG Mednet.

- **Qualification Status**
  - Site and Data Coordinating Center (DCC) will be notified of qualification status via email

- **Qualification Resubmission**
  - If the site does not qualify with the first submission, the Imaging Core will make recommendations for resubmission of another CMR Qualification study.
Cardiac MRI Quality Control

- **CMR Critique**
  - CMR images will be monitored for quality and adherence to the PVDOMICS imaging protocol.
  - The Imaging Core will provide feedback in the form of a critique to sites and the DCC via email for each CMR submitted.
  - The critique should be shared with the technologist performing the CMR exam to ensure the acquisition of research quality data and to help prevent the possibility of missing data.
  - The critique is a tool intended to standardize the collection of research quality data and to capture mistakes, if any, before they are repeated.
Archival Instructions

• Complete the electronic Data Transmittal Form carefully and completely. This is treated as a source document and is subject to audit by regulatory authorities.

• Archive the cardiac MRI scan to digital media (CD/DVD) immediately from the imaging system used to acquire the images prior to archiving to Picture Archiving and Communication System (PACS).
  - Make one copy of each CMR exam per disc and upload from this media to the AG Mednet website location. Retain disc copy of exam with site records.
Goals of Cardiac Echo

Echocardiography to assess:

• Cardiac anatomy and function
• Systolic and diastolic function
• Hemodynamic Assessment
  - Valvular pathology
  - Calculation of QP/QS
  - CVP and PAP estimate - TR and PR peak Velocities
Echo Protocol Recap

- Full diagnostic Echo/Doppler exam
- Each subject will have a saline bubble study to r/o a shunt with valsala maneuver
- Use contrast enhancement when necessary following ASE guidelines
- Optional 3D imaging section on LV and RV chambers
Echo Pre-Qualification

First Step:

• Submit a copy of the current Preventive Maintenance (PM) document for each ultrasound system planned for use in the trial (*including serial number*) to the Core Lab

• A copy of the PM document should be maintained at the site with the trial regulatory files
Echo Qualification Process

- All sites will be required to submit a de-identified sample echocardiogram to the Imaging Core Lab, via AG MEDNET for each sonographer participating in the trial.
- At a minimum a backup sonographer should be identified and follow the same qualification process.
- The qualification study performed should follow the PVDOMICS imaging protocol but may be performed on any subject.
Purpose of the Qualification Process

• To ensure compatibility between site Echo acquisition and Core Lab analysis tools
• To ensure moving image files play
• To ensure adherence to the imaging protocol
• To become familiar with the image anonymizing process
• To become familiar with the image upload and transfer process
The site coordinator will receive notification of the qualification results electronically in the form of a critique.

If a sonographer does not pass the initial qualification, the Imaging Core Lab will use the critique system to recommend changes for resubmission of another Echo qualification study.

All sonographers must pass qualification before performing a PVDOMICS exam.
Anonymization Process

- Coordinator to provide subject ID to the sonographer
- For purposes of confidentiality and to remain compliant with Health Insurance Portability and Accountability Act (HIPAA), all references to a specific subject must be made using the entire Subject ID
- Site is responsible for correctly de-identifying clinical exams with the correct study assigned Subject ID within the AG Mednet application
Echo Quality Control

Echo Critique

• Echo images will be monitored for quality and adherence to the PVDOMICS imaging protocol

• The Imaging Core will provide feedback in the form of an electronic critique to both the sites and the DCC for each echo exam submitted

• The critique should be shared with the sonographer performing the echo exam to ensure the acquisition of research quality data and to help prevent the missing data

• The critique is a tool intended to standardize the collection of research quality data and to capture mistakes, if any, before they are repeated
<table>
<thead>
<tr>
<th>Criteria To Meet</th>
<th>Completed Correctly</th>
<th>Additional Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Was the study de-identified?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was there a good quality EKG tracing?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Were adequate frame rates captured?</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Was the LVOT from PLAX measurable?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Were zoomed views of the Aortic Valve and the LVOT without color Doppler acquired?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Were zoomed views of the Aortic Valve and LVOT with color Doppler acquired?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was the Aortic Root from PLAX measurable?</td>
<td>No</td>
<td>Suggest repositioning the subject and/or moving the transducer to a higher intercostal space.</td>
</tr>
<tr>
<td>Was the Left Ventricle measurable?</td>
<td>No</td>
<td>Biplane LVEF not possible due to loss of endocardial definition. Recommend use of contrast in technically difficult studies.</td>
</tr>
<tr>
<td>Was the Right Ventricle measurable?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was the Right Atrium measurable?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was the Left Atrium measurable?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was the LVOT pulse wave Doppler peak velocity measurable?</td>
<td>No</td>
<td>Site used Doppler steering angle of greater than 10 degrees, could not analyze PW of LVOT.</td>
</tr>
<tr>
<td>Was the Aortic Valve Stent pulse wave Doppler peak measurable?</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Was the Aortic Valve continuous wave Doppler peak velocity measurable?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was the Pedoff probe used in three views (APEX/Subcostal, RSB, SSN)?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was Aortic Valve color Doppler acquired?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was Mitral color Doppler acquired?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was Pulmonary Vein pulse wave Doppler velocity acquired?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was Mitral inflow pulse wave Doppler acquired?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was Tricuspid Regurgitation color Doppler acquired?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was Tricuspid Regurgitation continuous wave Doppler velocity measurable?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was Tissue Doppler Imaging (TDI) acquired?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was Subcostal imaging of IVC with sniff acquired?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Was this a technically difficult study?</td>
<td>Yes</td>
<td>Biplane LVEF not possible due to loss of endocardial definition. Recommend use of contrast in technically difficult studies. Site used Doppler steering angle of greater than 10 degrees, could not analyze PW of LVOT. Do NOT use Doppler angle correct in Echocardiography.</td>
</tr>
</tbody>
</table>

**Criteria To Meet**

- Few measurements possible
- Biplane LVEF not possible due to loss of endocardial definition. Recommend use of contrast in technically difficult studies.
- Site used Doppler steering angle of greater than 10 degrees, could not analyze PW of LVOT. Do NOT use Doppler angle correct in Echocardiography.
Sites will enter required demographic data in electronic transfer system.

MRI Transmittal Form #251

- Study Coordinator Completes Questions 1-5.
  - Identification Number: 110002-AB
  - Date: 12/01/2015

- MRI Technologist Completes Questions 6-20.
  - Blood pressure measured at the beginning of cardiac MRI:
    - 1: Yes
      - If yes, blood pressure measures (mmHg): 110/070
  - Was there a cardiac rhythm disturbance during MRI?
    - 1: No
    - If yes, what type of rhythm disturbance?
      - 2: Bradycardia
  - Average heart rate collected during MRI?
    - 1: No
    - If yes, average heart rate during MRI (bpm):
      - 0.46
  - Was contrast agent used?
    - 0: No
      - If yes, total contrast volume (mL):
        - 2: Yes
          - 5: Dotarem: 4.0 mL

- MRI start time (24-hr clock): 12:01
- Injection start time (24-hr clock): 12:01
- Delayed enhancement sequence start time (24-hr clock): 12:01
- MOLLI sequence start time (24-hr clock): 12:01
- MRI end time (24-hr clock): 12:01

- Imaging Equipment Used for this Cardiac MRI
  - Manufacturer: 3
    - 1: GE
    - 2: Philips
    - 3: Siemens
  - Model #:
    - 1: Avanto
  - Serial Number #:
    - 1: 12345
  - Field Strength: Tesla (1: T1.5, 2: 3.0 T):
    - 1

- Transmission Details for Cardiac MRI to AG Mednet - Coordinator completes Q23 through end of form.
  - Method of transmission (1: Digital transfer, 2: Other, specify):
    - 3: Other
      - 12/01/2015

- Clinical Center Use Only
  - Date Form Entered (mm/dd/yyyy): 12/01/2015
  - Username of person entering this form: Smith CA

- Comments:
  - Username of MRI Technologist who performed cardiac MRI: Smith CA
  - Name of MRI Technologist who performed cardiac MRI: Smith CA
Echo Transmittal Form #250

PVDOMICS Study
Echocardiogram (ECHO) Transmittal Form #250

Revision: 01/18/2016
Page 2 of 2

Ultrasonic Equipment Used for this ECHO

10. Ultrasound manufacturer name: Philips

11. Model #: IE-33

12. Serial #: 12345

Transmission Details for ECHO to AG Mednet -- Coordinator completes Q3 through end of form.

13. Method of transmission (1=Digital, 2=Other, specify): 1

14. Date ECHO file transmitted (mm/dd/yyyy): 12/01/2015
   (Date file transmitted must be greater or equal to date the form is completed)
Digital Image Transfer
AG Mednet

- AG Mednet is a web-based diagnostic imaging network, enabling sites to send diagnostic image exams electronically and securely to the Imaging Core Lab.

  - AG Mednet will provide tools and training to anonymize exams, complete transmittal forms electronically and complete other trial specific tasks.

- Download the Cardiac MRI Transmittal Form #250 or Echo Transmittal Form #251 from the QHS website (http://qhsapps.ccf.org/pvdomics/). Completion of the hard copy data transmittal forms will aid in the completion of the AG Mednet Electronic Data Transmittal Form prior to exam upload.

- Please transfer exams as they are collected.
Example of Signature Log

PVDOMICS

AG Mednet Digital Image Transfer Training Completion Signature Page

AG Mednet WebEx: Recorded Session
Site Number: Site #: _______
Site Name: ________________________________
Training Session Date: ________________

<table>
<thead>
<tr>
<th>Print Name and Role:</th>
<th>Signature:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
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</tbody>
</table>
1. Complete account authorization
2. Register for an account on the AG Mednet Portal
3. Launch the Desktop Agent and log-in with your Username/Password
4. Submit an exam
   a) Import an image exam
   b) Review images (optional)
   c) Assign the exam to the trial
   d) De-identify the Pixel Data
   e) De-identify the DICOM data
   f) Complete the Data Transmittal Form
   g) Upload the exam
   h) Confirm successful exam submission
Data Clarification Process

- Query Notification
  - The study coordinator and the DCC will receive an email from the Imaging Core asking for resolution of any issues discovered during the quality control (QC) process. Prompt response is required from the study coordinator.
  - Query Data Clarification Form
    - Review the variable name, reported value and comments/suggestions
    - Record the corrected information in the resolution box
Data Clarification Form

PVDOMICS

Site Name: Brigham and Women's Hospital
Operator:
Exam Date: 12/1/2015
Visit: Baseline

Site Code: 11
Subject: 110001-AB
Modality: ECHO
Equipment: Philips IE-33
Exam Types: TTE

Media Critique
Digital Data stored in correct format?

Comment: The exam contains minimal images for this study. (29 images only).

Please re-upload the complete echo exam and forward to the Imaging Core Lab.

Sign and Date this DCF and return fax this query to the Imaging Core Lab as soon as possible for echo processing to be continued.

Response:

Signature: ____________________________ Date: ____________________________

Print Name: ____________________________
Data Clarification Form

C5Research

Data Clarification

PVDOMICS

Site Name: Brigham and Women’s Hospital  
Operator:  
Exam Date: 12/1/2015  
Visit: Baseline

Site Code: 11  
Subject: 110001-AB  
Modality: ECHO  
Equipment: Philips IE-33  
Exam Types: TTE

Media Critique
Digital Data stored in correct format?
Comment: The exam contains minimal images for this study. (29 images only).
Please re-upload the complete echo exam and forward to the Imaging Core Lab.
Sign and Date this DCF and return fax this query to the Imaging Core Lab as.

Response: 

Signature: ___________________________  
Date: ___________________________

Print Name: ________________________

Imaging Core Lab  
9500 Euclid Avenue JJ-65  
Cleveland, OH 44195  
Fax: 216-445-4419
Data Clarification Process Continued

- **Media Queries**
  
  - Review the issue and comments/suggestions
  
  - Record the corrected information and/or comments of action taken (Example: Sent Imaging Core new images via AG Mednet)
  
  - Please print your name, sign and date (DD/MMM/YYYY) in the space provided. The Core Lab will not consider corrections recorded on the DCF unless signed and dated by site personnel completing the form. A signature indicates agreement that the data should be changed as indicated on the DCF.

- **Questions?**
  
  - Contact an Imaging Core Team Member for assistance
CMR Data Clarification Process Continued

- **Resolution and Return of DCF**
  - The site contact person (coordinator) must fax the completed DCF to the Imaging Core within five business days at 1-216-445-4419. The site will keep a copy of the DCF with corresponding study files.

- **Unresolved Query Process**
  - If the Imaging Core does not receive the faxed resolution, a follow up email will be sent to the site study coordinator, and the DCC will be copied, for immediate attention/resolution of the DCF.
Replacement/Inactivation Process

- Imaging Core will initiate query to both site and DCC asking for clarification. Imaging Core will not process clarification received from site until sponsor (DCC) verifies the accuracy with signature on The Inactivation Form.
  - Site monitor or designee will verify the date and subject ID on the Inventory/Quality Report to ensure accuracy.
  - Imaging Core will update the Inventory/Quality Report, PACS system and C5Research Clinical Data Management.
Case Status Reports

• Report Distribution
  - Reports generated weekly
  - Designated DCC personnel

• Report Type
  - Qualification
  - Inventory/Quality
  - Incomplete Cases
  - Comprehensive Data Clarification
  - Outstanding Data Clarifications
# Quick Print Imaging Core

## Contact Information

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>email</th>
<th>phone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kathy Kassimatis</td>
<td>Project Manager</td>
<td><a href="mailto:kassimk@ccf.org">kassimk@ccf.org</a></td>
<td>216-445-5156</td>
</tr>
<tr>
<td>Margaret (Koko) Park</td>
<td>Imaging Specialist</td>
<td><a href="mailto:parkm@ccf.org">parkm@ccf.org</a></td>
<td>216-445-5175</td>
</tr>
<tr>
<td>Jeanne Drinko</td>
<td>Imaging Specialist</td>
<td><a href="mailto:drinkoj@ccf.org">drinkoj@ccf.org</a></td>
<td>216-445-5274</td>
</tr>
<tr>
<td>Annitta Flinn</td>
<td>Core Lab Manager</td>
<td><a href="mailto:flinna@ccf.org">flinna@ccf.org</a></td>
<td>216-445-7673</td>
</tr>
<tr>
<td>Dawn D’Eusanio</td>
<td>Research Coordinator</td>
<td><a href="mailto:deusand@ccf.org">deusand@ccf.org</a></td>
<td>216-444-8267</td>
</tr>
<tr>
<td>Jill Rusticelli</td>
<td>Project Specialist</td>
<td><a href="mailto:rusticj@ccf.org">rusticj@ccf.org</a></td>
<td>216-442-5231</td>
</tr>
<tr>
<td>Michelle Baksar</td>
<td>Project Specialist</td>
<td><a href="mailto:baksarm@ccf.org">baksarm@ccf.org</a></td>
<td>216-444-9872</td>
</tr>
<tr>
<td>Cathy McDowell</td>
<td>Research Coordinator</td>
<td><a href="mailto:mcdowec@ccf.org">mcdowec@ccf.org</a></td>
<td>216-445-7842</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AG Mednet Support</th>
<th><a href="mailto:support@agmednet.com">support@agmednet.com</a></th>
<th>1-888-9246336</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVDOMICS DCC Website</td>
<td><a href="http://qhsapps.ccf.org/pvdomics/">http://qhsapps.ccf.org/pvdomics/</a></td>
<td></td>
</tr>
</tbody>
</table>
Thank You!

Cleveland Clinic

Every life deserves world class care.