

Chapter 70 Cardiac MRI

70.1 Core Lab Contacts

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AG Mednet Support:

US Toll Free: 1-888-924-6336

Email: support@agmednet.com

70.2 Hours of Operation

70.2.1 Hours of Operation

The Imaging Core Lab is open Monday through Friday, 8:00 AM to 4:30 PM, Eastern Standard Time.

70.2.2 2016-2019 Holidays

The Imaging Core Lab is closed on the following dates for holidays:

2016

Memorial Day	May 30, 2016
Independence Day	July 4, 2016
Labor Day	September 5, 2016
Thanksgiving	November 24-25, 2016
Christmas	December 23-26, 2016

2017

New Year's Day	January 2, 2017
Memorial Day	May 29, 2017
Independence Day	July 4, 2017
Labor Day	September 4, 2017
Thanksgiving	November 23-24, 2017
Christmas	December 25-26, 2017

2018

New Year's Day	January 1, 2018
Memorial Day	May 28, 2018
Independence Day	July 4, 2018
Labor Day	September 3, 2018
Thanksgiving	November 22-23, 2018
Christmas	December 24-25, 2018

2019

New Year's Day	January 1, 2019
Memorial Day	May 27, 2019
Independence Day	July 4, 2019
Labor Day	September 2, 2019
Thanksgiving	November 28-29, 2019
Christmas	December 24-25, 2019

70.3 Abbreviations and Acronyms

ACR	American College of Radiology
AF	Atrial Fibrillation
AHA/ACC	American Heart Association/American College of Cardiology
C5R	C5 Research
MRI	Magnetic Resonance Imaging
DICOM	Digital Imaging and Communications in Medicine
DTF	Data Transmittal Form
ECV	Extracellular Volume
GCP	Good Clinical Practice
GFR	Glomerular Filtration Rate
HIPAA	Health Insurance Portability and Accountability Act
ICL	Imaging Core Lab
LGE	Late Gadolinium Enhancement
Mfr	Manufacturer
MOLLI	Modified Look Inversion Recovery
MRA	Magnetic Resonance Angiography
MRI	Magnetic Resonance Imaging
MRN	Medical Record Number
NA	Not Applicable
NHLBI	National Heart Lung and Blood Institute
PACS	Picture Archiving and Communication System
PM	Preventive Maintenance
PPM/ICD	Permanent Pacemaker/Implantable Cardioverter Defibrillator
QC	Quality Control
SAEs	Serious Adverse Events

70.4 Document Revision History

70.4.1 V1.0_09Sep2016

This document is the first approved version. Amended versions will be described in this section and include a history of changes.

Version	Changes Made	Effective Date
1.0	Original	09Sep2016
2.0	1. Section 70.10.1.3, page 70.15: Clarification provided recommending sites to administer contrast within dose range (0.1 - 0.2 mmol/kg, 3–7 ml/s) according to GFR results. 2. Section 70.10.1.3, page 70.15, Added CMR Dosing Table #2 to summarize recommended dose range according to GRF results.	25Jan2017

Note to sites:

The Imaging Core Lab analysis results are intended for research purposes only and should not be used for clinical patient management.

Each site must have a plan for ensuring that clinically relevant findings are observed and managed at the site level.

70.5 Study Overview

70.5.1 Purpose

The purpose of this C5Research (C5R) Imaging Manual is to instruct sites in: 1) protocol-specific image acquisition requirements; 2) necessary documentation, image data transfer instructions and data storage; and 3) the query resolution process for any clerical discrepancies and/or non-compliant data.

The goal of the Cardiac MRI (CMR) portion of this trial is to quantify cardiac volume and mass, fibrosis and scarring, perfusion and evaluation of flow. The inherent 3-dimensional nature of CMR makes it particularly well suited for the evaluation of the RV, which is difficult to assess with other imaging modalities due to its complex shape and variable morphology. Advanced echocardiographic measures of right ventricular performance will be compared to cardiac MRI.

70.5.2 Study Synopsis (from PVDOMICS Protocol V1.1 May 12, 2016)

It is recognized that patients with various forms of heart and lung disease exhibit varying degrees of pulmonary vascular disease, leading to pulmonary vascular remodeling, pulmonary hypertension, and right ventricular dysfunction. The genetic, molecular, and cellular processes driving these phenomena are not well understood. Rapid advances in high throughput omic methodology, combined with powerful bioinformatics and network biology capability, have created the opportunity to conduct studies that broadly search for homologies and differences across the spectrum of disease states associated with pulmonary hypertension and determinants of the spectrum of pulmonary vascular disease and RV compensation that accompanies these conditions.

The 2010 NHLBI Pulmonary Vascular Strategic Plan identified the

development of a comprehensive cohort to define phenotypes integrating Omics technologies and systems approaches as a top priority. The current WHO PH classification, based solely on clinical/hemodynamic subsets, limits the ability to customize treatment for an individual patient, or to assign meaningful clinical phenotype designations, *e.g.*, Long-term survivor or Maladaptive RV Hypertrophy. **The overall goal of the PVDOMICS network is to perform comprehensive pheno-typing (demographic, physiologic, clinical chemistries, and imaging) and endophenotyping (genomic, proteomic, metabolomic, coagulomic, cell and/or tissue based) across the World Health Organization (WHO) classified PH clinical groups 1 through 5 as well as intermediate phenotypes (including those without overt PH) in order to deconstruct the traditional classification and define new meaningful subclassifications of patients with PVD. The long-term goal is utilization of endophenotypes/biomarkers for early diagnosis, at-risk screening, and personalized approaches for interventions and/or preventions of PVD.**

The PVDOMIC protocol is designed to lead to this comprehensive understanding of patients with pulmonary vascular disease based on phenotypes and endophenotypes.

The first aim will be a natural product of the protocol, to identify the molecular basis of pulmonary vascular disease regardless of WHO clinical classification, by comparison of current subsets of PH patients with healthy subjects and with non-PH diseased comparators. The second aim is to discover biological measures of disease and therapeutic responses that may be useful not only in diagnosis but also as outcome measures in treatment and possibly prevention trials.

70.6 CMR Qualification Process, Quality Control Process, and Visit Schedule

70.6.1 CMR Qualification Submission Process

70.6.1.1 Prior to Qualification, a copy of the current annual Preventive Maintenance (PM) document for each CMR scanner planned for use in the trial must be submitted to the Imaging Core (including serial number). A copy of the PM document(s) should be maintained at the site with the trial regulatory files. This satisfies the American College of Radiology recommendations and ensures the mechanical integrity of the imaging system.

70.6.1.1.1 Sites must follow American College of

Radiology (ACR) Safe Practice Guidelines

70.6.1.2 The qualification process must be completed prior to sites submitting CMR exams of enrolled subjects.

All participating sites will submit to the Imaging Core Lab a de-identified sample of a recently performed CMR exam completed in their institution. The purpose of the Site CMR Qualification Process is to ensure viewer and analysis compatibility between the site and the Core Lab prior to subject recruitment.

70.6.1.3 The electronic CMR data transmittal form will be completed by choosing the “Qualification” visit type prior to transferring the study to the Imaging Core lab via AG Mednet

70.6.1.4 The site and Data Coordinating Center (DCC) will be notified of the qualification status of the CMR qualification scan via email or fax.

70.6.1.5 If the site does not qualify with the first submission, the Imaging Core Lab will make recommendations for resubmission of another CMR Qualification study.

70.7 CMR Quality Control

70.7.1 CMR Critique

7.1.1.1 CMR images will be monitored for quality and adherence to the PVDOMICS imaging protocol. Imaging Core will provide feedback in the form of a critique to sites and the DCC via email for each CMR performed.

70.7.2 CMR Imaging Schedule

7.2.2.1 Acquire images at the time points listed in Table 1. The same CMR scanner should be used throughout the trial duration.

Table 1: CMR Imaging Schedule

Imaging Visits	Description
Qualification	Submit a qualification CMR to Core Lab before enrolment
Visit	Baseline CMR

70.8 CMR Contraindications (Exclusions)

- ☐ Heart rate > 120
- ☐ Atrial fibrillation or irregular heart rate due to frequent ectopy
- ☐ Brain aneurysm clips or vascular clips (however, titanium or titanium alloy clips are acceptable)
- ☐ Cochlear implants
- ☐ PPM/ICD
- ☐ Insulin pump, drug pumps
- ☐ Any metallic fragment or foreign body (Metal shrapnel or bullets)
- ☐ Pregnant women
- ☐ Indwelling pulmonary artery catheter
- ☐ 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
- ☐ Breast tissue expanders
- ☐ Aortic stent grafts
- ☐ Patients in decompensated heart failure or with significant pleural effusions (moderate or more)
- ☐ Patients who are not able to hold their breath for 10-15 seconds at a time

Exceptions:

CMR is safe with coronary stents, joint replacements, ASD/PFO closure devices, sternal wires and most prosthetic heart valves.

70.9 Anonymization Process and Cardiac CMR Protocol

70.9.1 Anonymization Process

70.9.1.1 Before beginning imaging exam (CMR), **secure the study assigned subject ID from the site coordinator.** In the system ID last name field, type PVD. In the MRN field type: Site ID (2 digits) and Subject ID (4 digits) for a 6 digit subject identifier- followed by Alpha (2) assigned by the DCC. Ex: 110002-AB. For purposes of confidentiality and Health Insurance Portability and Accountability Act (HIPAA), all references to a specific subject must be made using the entire Subject ID. Please do not use subject names or initials to label the exam.

70.9.1.1.1 Exams clinically indicated, labeled with PHI, must be anonymized before sending to the Core Lab through AG Mednet (see section 11 for instructions)

70.9.1.2 Acquire images per study protocol keeping subject positioning optimal throughout image acquisition.

70.9.1.3 Download the study in DICOM format to CD/DVD.

70.9.1.4 Sites are to use the digital transmission method for submitting CMR exams. Follow AG Mednet instructions (see section 15) for digital transmission to the Core Lab.

70.9.1.5 Make one copy of each CMR study per disc and upload from this media to the AG Mednet website location. Retain disc copy of the study with site records.

70.9.1.6 Please copy only one CMR study per disc.

70.10 Cardiac CMR Protocol and Image Acquisition Instructions

70.10.1 Core Exam Components

70.10.1.1 Cardiac Structure/Function: Cine-CMR will be used to assess cardiac structure and function. Cine-CMR will employ an ECG gated steady state free precession (SSFP) sequence. Images will be acquired in contiguous short axis (throughout the left and right ventricle), left ventricular (2, 3, and 4 chamber) and right ventricular long axis orientations. Cine- CMR will be performed using a slice thickness of 8.0mm (inter- slice gap =0). (See Figure 1 and 2.)

Figure 1

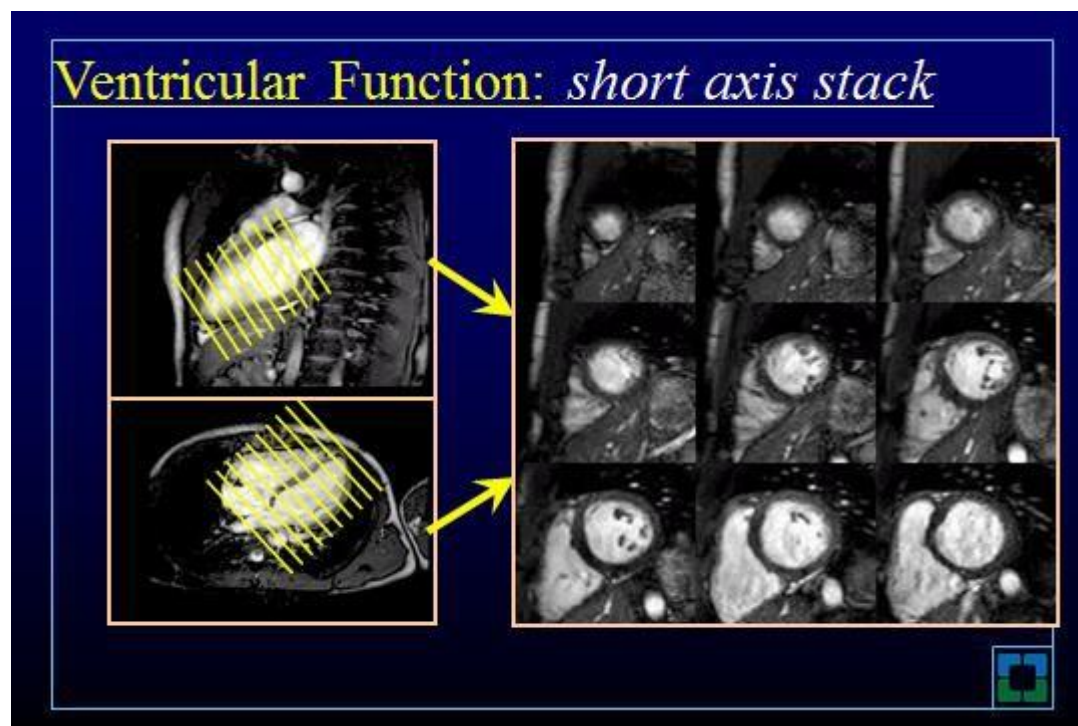
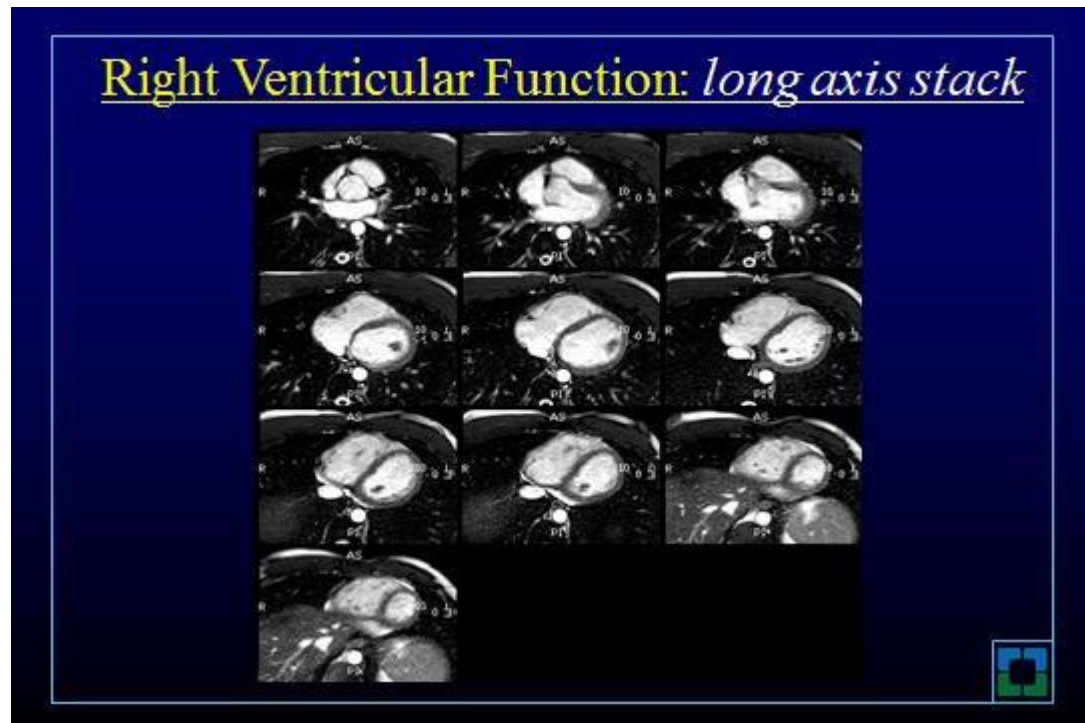


Figure 2



70.10.1.2 Valvular Flow: Phase velocity encoded CMR will be used to assess valvular flow. Images will be acquired through the aortic valve as well as the pulmonic valve (i.e. two separate images will be acquired). Images will be acquired “en-face” valve orientation at the level of the aortic and pulmonic valve leaflet tips. Making certain the temporal resolution is adequate, < 35ms, will ensure accuracy in flow data. Peak velocity encoding (VENC) limits will be tailored to avoid aliasing (typically 1.5 m/sec). **Recommend careful assessment for aliasing, and increasing the VENC level as needed (i.e. 2 m/sec or greater as needed). VENC is important to not travel too high away from the normal values on each patient.** In addition, flow quantification will be assessed of the right and left pulmonary arteries. (See Figure 3 and 4)

Figure 3

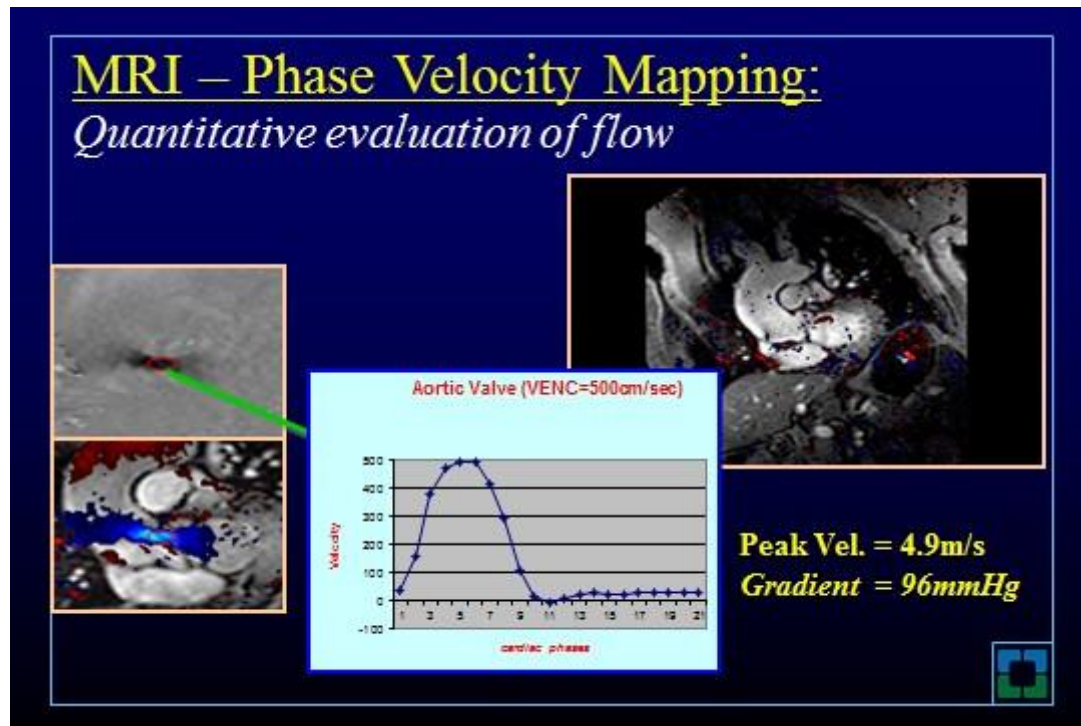
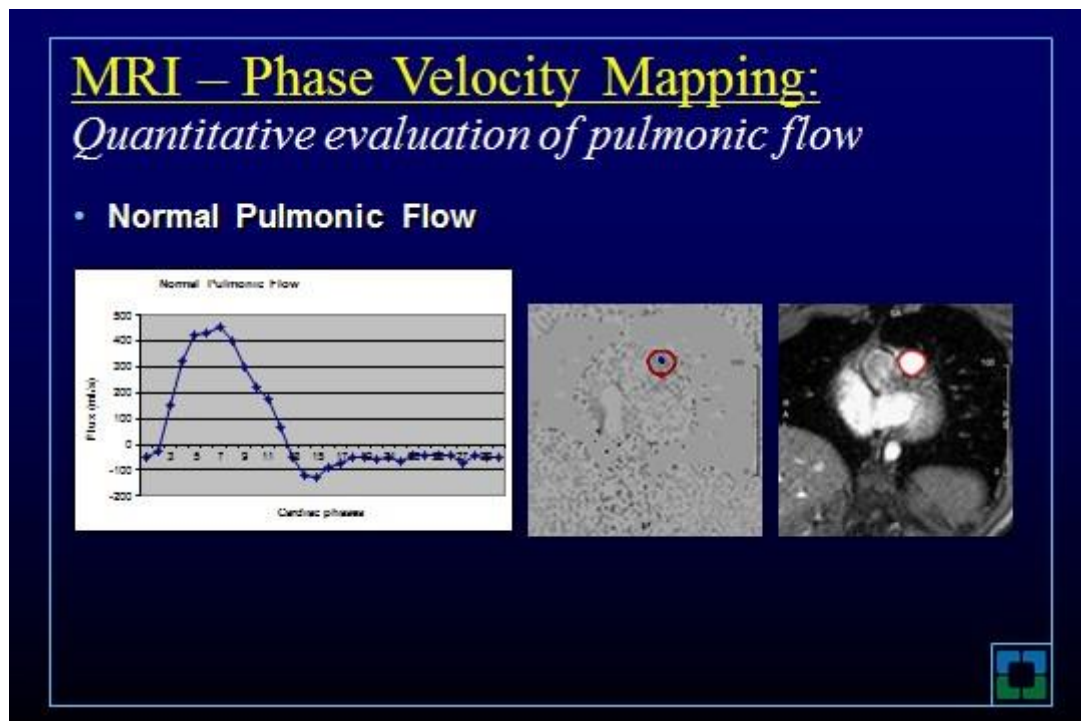


Figure 4

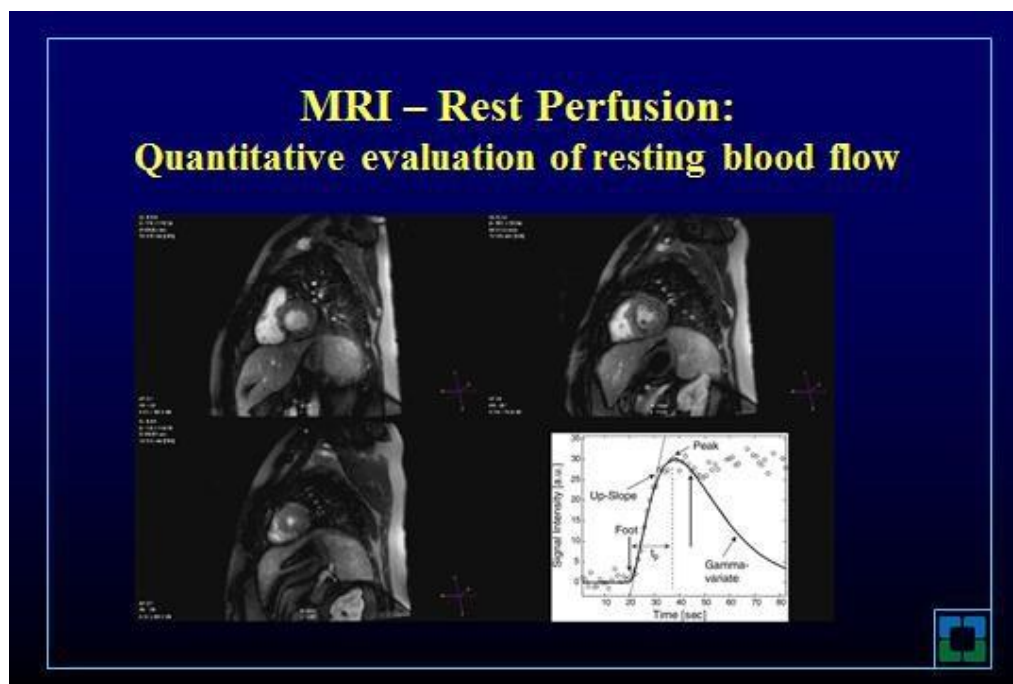


70.10.1.3 Resting Perfusion Imaging: Saturation-recovery imaging will be used to assess resting myocardial perfusion. Short-axis images will be acquired (at least 3 slices per heart beat), using a slice thickness of 8 mm and parallel imaging, 2-fold acceleration, if available with in-plane resolution, $\sim < 3$ mm. Readout temporal resolution $\sim 100 - 125$ ms or shorter as available. Contrast will be given (0.1 - 0.2 mmol/kg, 3–7 ml/s) followed by at least 30 ml saline flush (3–7 ml/sec). Breath hold will start during early phases of contrast infusion before contrast reaches the LV cavity. Images will be acquired for 40-50 heart beats to ensure that the contrast has passed through the LV myocardium. (See figure 5.)

Table 2: CMR Dosing

GFR (mL/min/1.73m ²)	Gadolinium Dosage (mmol/kg)
<30	Non contrast exam
30-60	0.10
>60	0.20
Option	If necessary follow site's institutional guidelines

Figure 5



70.10.1.4 Myocardial Scar/Infarction: Delayed enhancement (DE)-CMR will be used to assess for myocardial infarction/scar. Imaging will be performed using an inversion recovery pulse sequence (Look-Locker), for which images **will be 10-20 minutes post contrast**. DE-CMR inversion times (TI) will be tailored to null viable myocardium (~300msec). DE-CMR will be acquired in both short and long axis orientations, matched to pre-contrast cine-CMR. **Short axis delayed images should match exactly with Cine-CMR short axis stack, acquired with a slice thickness of 8.0mm (inter-slice gap=0).**
(See Figure 1 and 2.)

Segmented (breath-held) will be required as part of the CMR protocol. Ancillary DE-CMR approaches (i.e. single shot, 3D navigator) can be used as an adjunctive (optional) approach if available at participatory sites. In addition, contiguous short axis stack of images as well as a 4 chamber image will be acquired using single shot pulse sequence with a TI of 600ms to assess for RV/LV thrombus. (See Figures 6 and 7.)

Figure 6

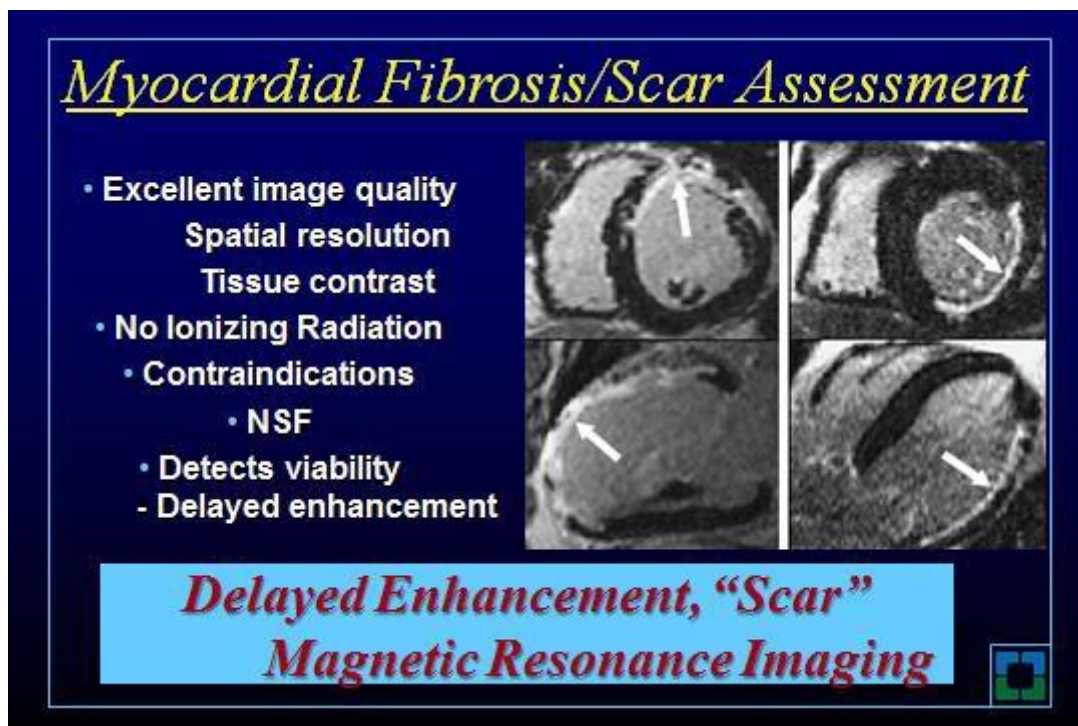
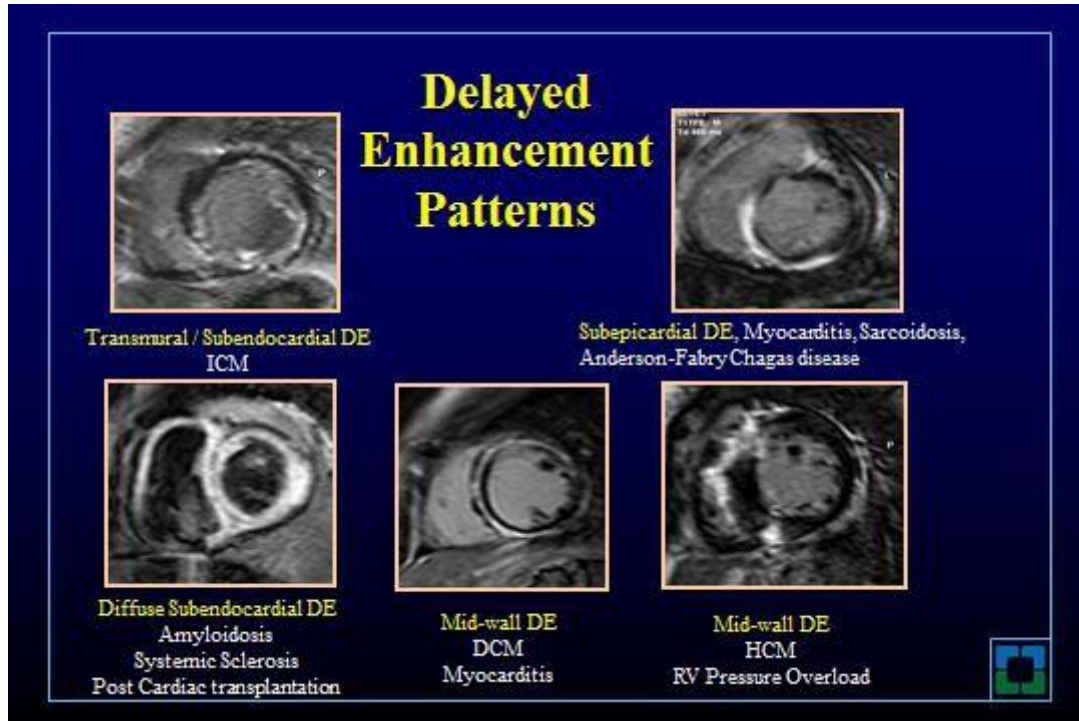


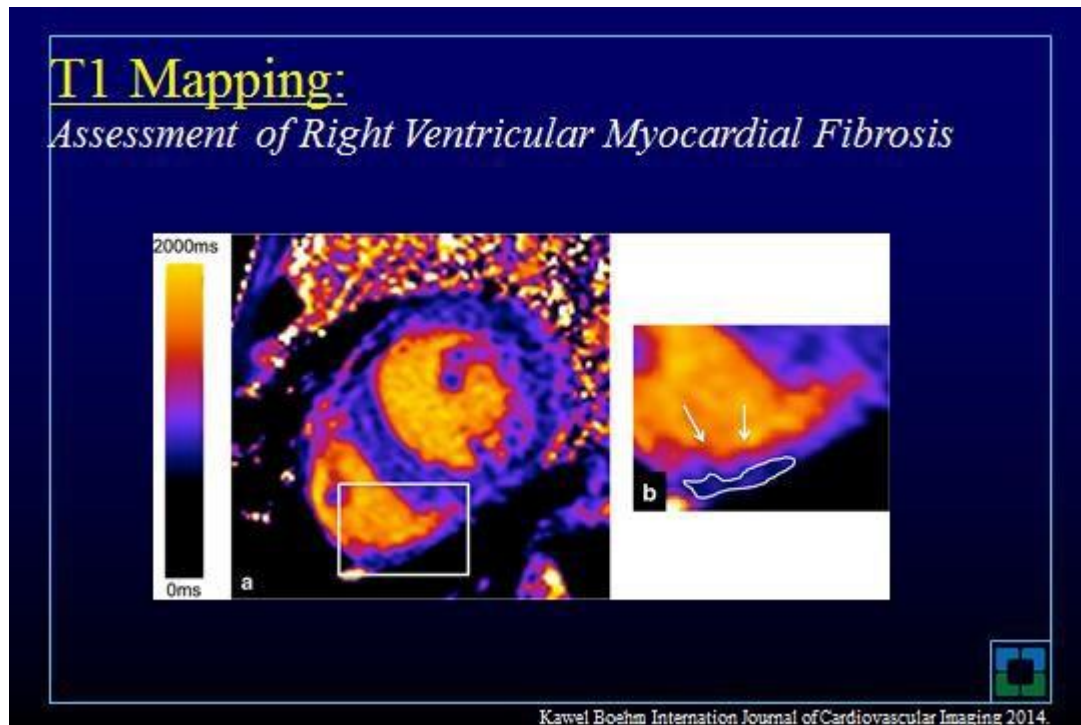
Figure 7



70.10.2 Optional

70.10.2.1 Extracellular Volume Fractionation: Pre-contrast T1 mapping will be performed to quantify myocardial extracellular volume (ECV). T1 mapping imaging will use a modified look inversion recovery (MOLLI) pulse sequence, which will be acquired in 3 short axis locations in the basal, mid, and distal left ventricle (corresponding to 16 of 17 segments within AHA/ACC segmental model). **Imaging acquired 5, 10, and at least 15 minutes** post-contrast in spatially matched locations for calculation of ECV, which will be quantified in accordance with established convention $[ECV = (1 - \text{hematocrit}) * [(1/T1_{\text{myo post}} - 1/T1_{\text{myo pre}}) / (1/T1_{\text{blood post}} - 1/T1_{\text{blood pre}})]]$. **Recommend also acquiring high resolution MOLLI with in plane resolution of 1-2mm for T1 mapping/ECV quantification of the right ventricle.** (See figure 8.)

Figure 8



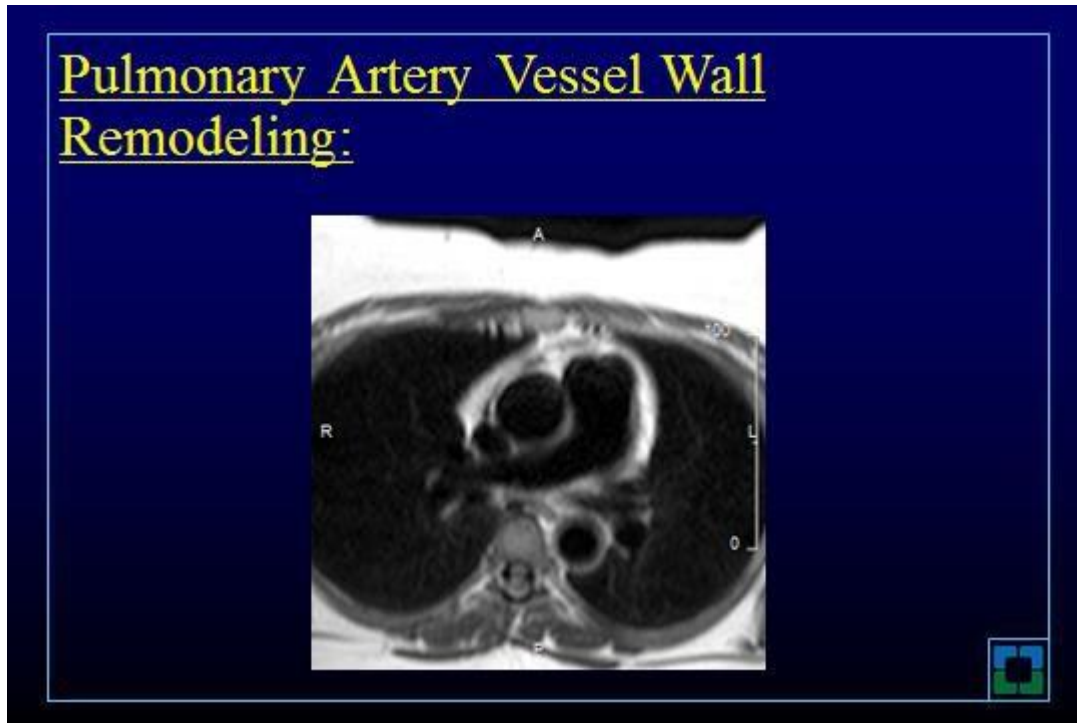
70.10.2.2 Pulmonary Artery Compliance: High temporal resolution cine-CMR (temporal resolution < 50 msec) will be performed to assess vascular compliance. Cine-CMR will be acquired in three pre-specified locations – (1) main pulmonary artery (1.0cm proximal to bifurcation), (2, 3) left and right pulmonary arteries (1.0 cm distal to bifurcation). Images will be acquired in double oblique orientation (i.e. orthogonal to the PA vessel wall, as oriented based off cine images). (See Figure 9)

Figure 9



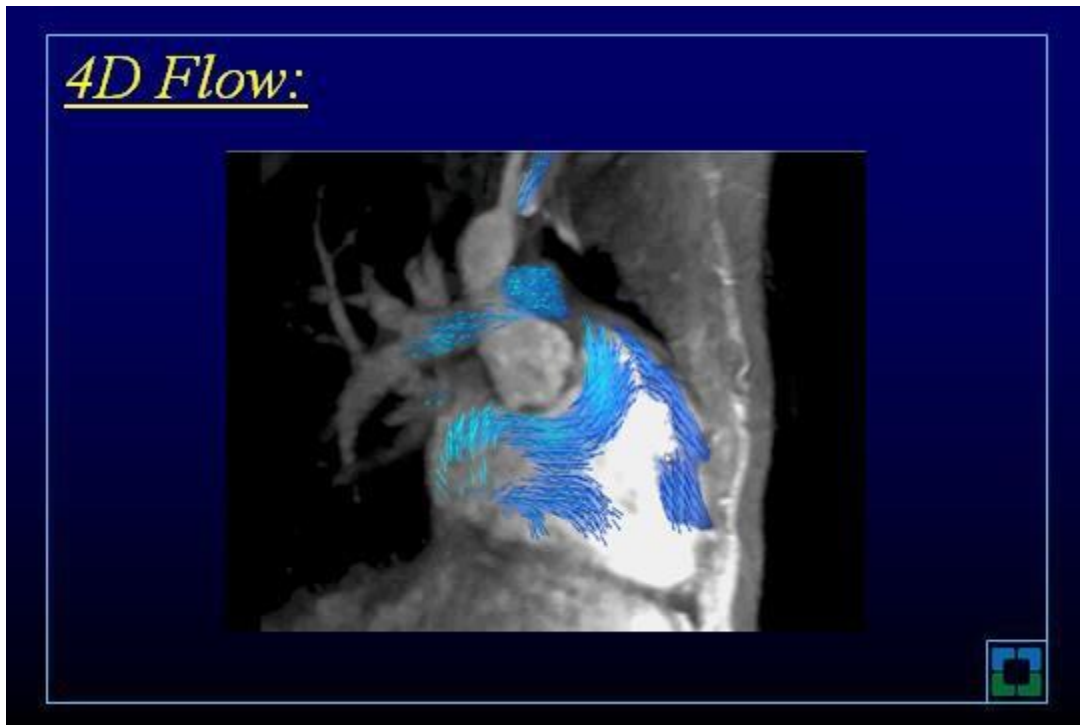
70.10.2.3 Pulmonary Artery Vessel Wall Remodeling: High anatomic resolution black blood imaging (typical in-plane resolution 1-2 mm) will be performed to assess pulmonary arterial vessel wall thickness at spatially matched locations corresponding to high temporal resolution cine-CMR (main, left, right pulmonary artery). (See Figure 10)

Figure 10



70.10.2.4 4D Flow: Anisotropic 4D segmented k-space phase contrast gradient echo sequence with retrospective ECG gating with navigator-gating of respiratory motion will be performed to assess three-directional blood flow velocity information to visualize blood flow patterns qualitatively in normal and pathological hemodynamic conditions. 3D volume will cover the apex of the heart to the aortic arch, the sternal border and spine, and the main stem of the right and left pulmonary artery until further branching in the right-to-left will be acquired (typical in-plan resolution 2-3mm). ***If this sequence is available, it should be performed immediately after the resting perfusion sequence. (See figure 11).***

Figure 11



70.10.3 Image Acquisition Sequence

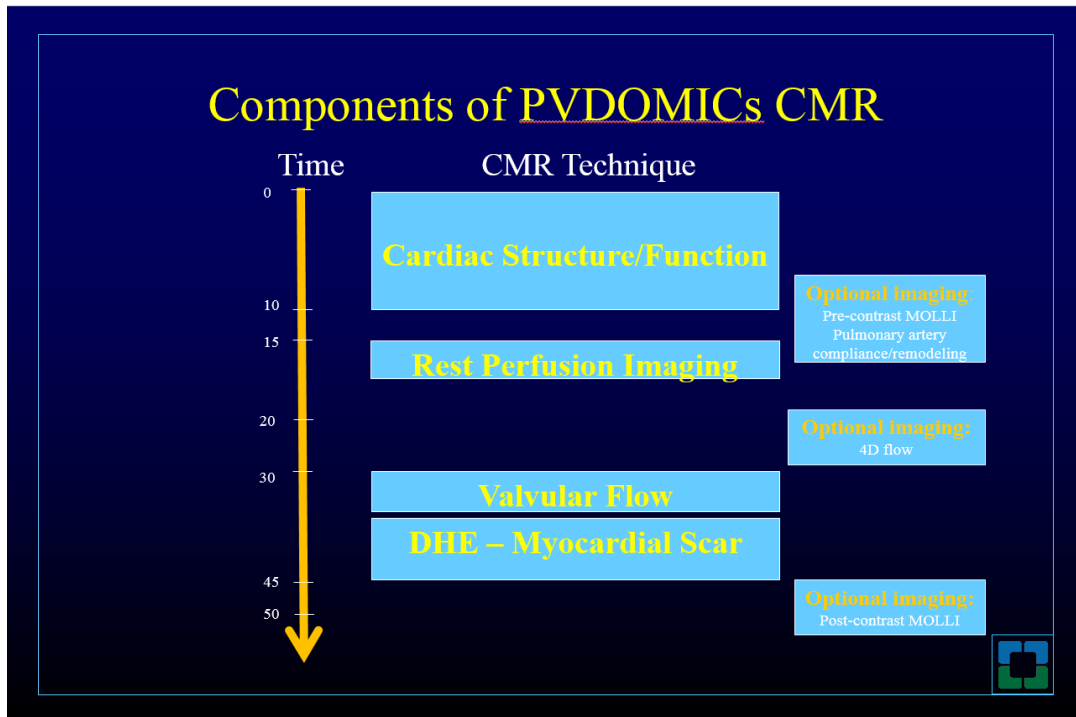


Image Acquisition Instructions

1. Acquire images using consistent imaging parameters.
 - a. Subject positioning and plane orientations must remain consistent throughout the study.
2. All subjects will be examined in the supine position.
3. EKG monitoring will be performed; lead placement is critical. Poorly placed leads result in blurred images and inaccuracies in data. Breath holding must be consistent. Placement of slices can be off as much as 2 cm when inconsistency with breath holds occurs.
4. Three-plane scout
5. Localizer: Axial single-shot blood (HASTE) images through the chest
6. 8 mm thick, spaced to cover the aortic arch through the diaphragm
7. **Acquisition during breath-hold is optimal for accuracy.**
8. Localizer: Axial bright blood images through the chest
9. Single-shot SSFP
10. (8 mm thick slices) spaced to cover the aortic arch through diaphragm
11. SSFP cine imaging (3 orientations)
12. Vertical long-axis orientation (2 chamber)
13. Horizontal long-axis orientation (4 chamber)
14. Left ventricular outflow tract (LVOT) orientation (3 chamber view)
15. Common sequence parameters for cine imaging
16. 8-mm slice thickness
17. 2.3 mm minimum spatial resolution (for both phase and frequency encoding directions)
18. 25-35 ms temporal resolution preferred; can be obtained by dropping views per segment captured between R to R intervals.
19. CMR with Late Gadolinium Enhancement (LGE)

Delayed short axis and long axis views should match slice locations of SSFP cine images. Copying the slice location is an industry standard. Cine images can be ordered to select the end diastolic trigger time by simply scrolling through a short axis image slice location. The selected time for end diastole can be entered into the actual trigger delay time prior to acquiring the delayed image set. This will enable a more accurate representation of the tracing to copy.

20. Segmented Inversion-Recovery Sequence
21. Should be acquired during breath hold approximately 10 minutes post IV administration of 0.15 mmol/kg of gadolinium chelate to optimize blood pool contrast myocardium nulling. If possible, capture a second set of late SAX stack of delays in single breath, acquiring 2 and long axis in between.
22. Inversion Time (TI) optimized by Look-Locker sequence (TI scout) to null normal myocardium. Proper selection of TI time for optimal nulling cannot be over emphasized.
23. Contiguous LV short axis stack to cover complete LV
 - a. myocardium from valve plane to apex. (0 mm inter-slice gap)
24. Vertical long-axis orientation (2 chamber)
25. Horizontal long-axis orientation (4 chamber))
26. Left Ventricular outflow tract (LVOT) orientation (3 chamber view)
27. Common sequence parameters for cine imaging
28. Recommended LGE Imaging Parameters
29. TR 4.3 ms
30. TE 2.1 ms
31. Flip Angle 45 degrees to optimize effectiveness of contrast agent
32. FOV 300-350 mm
33. Matrix 128 x 256
34. 8 mm slice thickness
35. 0 mm inter-slice gap (for contiguous stack)

70.11 Image Transmittal Instructions

70.11.1 CMR Transmittal Instructions

70.11.1.1 AG Mednet is a web-based diagnostic imaging network, which enables 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.

70.11.1.2 The electronic Cardiac MRI Transmittal-DCC Form #251 (see example 11.2) should be downloaded and completed by

the site technologist, then submitted to the study coordinator (or designee) for use in completing the electronic transmittal form prior to uploading the study to AG Mednet.

70.11.1.3 No fields may be left blank. You will be unable to upload images to AG Mednet until all required fields on the electronic transmittal form are complete.

70.11.1.4 In accordance with Good Clinical Practices (GCP), errors on the hard copy should be crossed out with a single line, not obliterated, with the correction inserted, and the change initialed and dated.

70.11.1.5 If you have questions about completing the electronic data form, refer to the Data Transmittal Form example or contact AG Mednet Support for assistance. (See contact information on page 2)

70.11.1.6 An ICL Study Team Contact Information sheet is located in the front of this manual for reference.

It is important to transfer image exams to the core lab as they are collected. This practice will prevent a backlog of analysis at the core lab. Please, no bulk sending.

70.11.2 Cardiac MRI Transmittal Form #251 Example

Revision of 01/15/2016



PVDOMICS Study Cardiac MRI Transmittal Form #251

Form #251
Page 1 of 2

Instructions: This form is used for both uploading data to AG Mednet for the Imaging Core Lab (ICL) and uploading data to the DCC database. Review MOP Chapter 70 prior to testing.

Study Coordinator Completes Questions 1-5.

1	1	0	0	0	2	-	A	B	1	2	0	1	2	0	1	5
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---

1. Identification Number

2. Alphacode

3. Date of Cardiac MRI (mm/dd/yyyy)

4. Gender (0=Male, 1=Female)..... 0
5. Visit Type..... 2
1=Qualification, 2=Baseline, 3=Follow-up

MRI Technologist Completes Questions 6-20.

6. a. Blood pressure measured at the beginning of cardiac MRI?..... 1
0=No, BP measures not collected, 1=Yes
- b. If yes, blood pressure measures (mmHg) (systolic/diastolic) 110 / 070
7. a. Was there a cardiac rhythm disturbance during MRI? (0=No, 1=Yes)..... 1
- b. If yes, what type of rhythm disturbance? 2
1=Atrial fibrillation
2=Bradycardia
8=Other, specify _____
8. a. Was average heart rate collected during MRI? (0=No, 1=Yes)..... 1
- b. If yes, average heart rate during MRI (bpm) 046
9. a. Was contrast agent used? 2
0=No contrast agent used
1=Ablabar (gadofosveset trisodium)
2=Magnevist (gadopentetate dimeglumine)
3=MultiHance (gadopentetate dimeglumine)
4=OptiMARK (gadoversetamide)
5=Dotarem (gadoterate meglumine)
6=Omniscan (gadodiamide)
7=ProHance (gadoteridol)
8=Other, specify _____
- b. Total contrast volume (mL)..... 40

(continued on next page)

Cardiac MRI Transmittal Form Example, page 2

Revision of 01/15/2016 Pt ID 110002 AC AB Date of MRI 12/01/2015

Form #251
Page 2 of 2

10. MRI start time (24-hr clock) (hh:mm) 08:00
11. Injection start time (24-hr clock) (hh:mm) 08:15
12. Look-Locker sequence start time (24-hr clock) (hh:mm) 08:28
13. Delayed enhancement sequence start time (24-hr clock) (hh:mm) 08:30
14. MOLLI sequence start time (24-hr clock) (hh:mm), if performed 08:35
15. MRI end time (24-hr clock) (hh:mm) 09:00

Comments _____

16. a. Username of MRI Technologist who performed cardiac MRI SMITHCA
b. Name of MRI Technologist who performed cardiac MRI Cathy Smith

Imaging Equipment Used for this Cardiac MRI

17. MRI manufacturer 3
1=GE 8=Other, specify _____
2=Philips
3=Siemens
18. Model # Avanto
19. Serial Number # 12345
20. Field Strength: Tesla (1=1.5 T, 2=3.0 T) 1

Transmission Details for Cardiac MRI to AG Mednet- Coordinator completes Q21 through end of form.

21. Method of transmission (1=Digital transfer, 8=Other, specify _____) .. 1
22. Date MRI file transmitted to AG Mednet (mm/dd/yyyy) 12/01/2015
(Date file transmitted must be greater or equal to the date the form is completed.)
200. Date this form completed (mm/dd/yyyy) 12/01/2015
201. Username of person completing/reviewing completeness of this form SMITHCA

Clinical Center Use Only

Date Form Entered (mm/dd/yyyy) ____/____/_____
Username of person entering this form _____

70.12 Cardiac MRI Archival Instructions

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

70.12.1.2 Archive the cardiac MRI scan to digital media (CD/DVD) immediately from the imaging system that was used to acquire the images (before archiving to Picture Archiving and Communication System [PACS]).

Please retain the CMR discs with the subject research records.

70.13 CMR Data Clarification Process

70.13.1 Query Notification

70.13.1.1 The study coordinator (or designee) and the DCC will receive an email from the C5R ICL asking for the resolution of any issues that were found during the quality control (QC) process. Prompt response is required from the site study coordinator.

70.13.1.2 Data Tracking Form Queries

- Review the variable name, reported value, and comments/suggestions
- Record the corrected, missing, or illegible information in the resolution box

70.13.1.3 Media Queries

- Review the issue and comments/suggestions
- Record the corrected information and/or comments of action taken (Example: Sent Imaging Core Lab new images via AG Mednet).

70.13.1.4 Please print your name, sign and date (DD/MMM/YYYY) in the space provided. The C5R ICL will not consider corrections recorded on the DCF unless signed and dated by site personnel completing the form. A signature indicates your

agreement that the data should be changed as indicated on the DCF.

70.13.1.5 Ensure all fields of the DCF are complete.

70.13.1.6 If you have questions about completing the form, refer to the Data Clarification Form (see example 13.4), send an email, or telephone a Core Lab team member for assistance.

70.13.1.7 An ICL Study Team Contact Information sheet is located in the front of this manual for reference.

70.13.2 Resolution and Return of DCF

70.13.2.1 The study center contact person must fax the completed Data Clarification Form to the Core Lab within five business days at +1 216.445.4419. The study center will keep a copy of the DCF with the corresponding study files.

70.13.3 Unresolved Query Process

70.13.3.1 If the ICL does not receive the faxed resolution, a follow up email will be sent to the site study coordinator and copied to the DCC indicating a second request for immediate attention/resolution of the DCF.

70.13.3.2 If the DCF is returned and all the issues are not resolved, the Imaging Core Lab will re-send an updated DCF to resolve the outstanding issues. The study center will complete the form, sign it, and fax it to the ICL.

70.13.3.3 Site will save a copy of this DCF with the site study records.

70.13.3.4 Site will ensure all fields of the DCF are complete.

70.13.3.5 If you have questions about completing the form, refer to the Data Clarification Form example, send an email, or telephone an ICL team member for assistance.

70.13.3.6 An ICL Study Team Contact Information sheet is located in the front of this manual for reference.

70.13.4 Data Clarification Form (DCF) Example

 C5Research Cleveland Clinic Coordinating Center for Clinical Research	Imaging Core Lab 9500 Euclid Avenue JJ-65 Cleveland, OH 44195 Fax: 216-445-4419
Data Clarification	
PVDOMICS	
Site Name: Brigham and Women's Hospital Operator: Exam Date: 12/1/2015 Visit: Baseline	Site Code: 11 Subject: 110002-AB Modality: MRI Equipment: Siemens Avanto Exam Types: Cardiac

Data Form
Data Form is complete?

Comment: MRI Baseline Date Clarification is needed.

The Baseline MRI exam has been previously received at the Imaging Core Lab with a date of 11/30/2015.

A second Baseline MRI exam has been received with a date of 12/1/2015.

Please confirm MRI Baseline exam date for processing of the study to be continued.

Baseline MRI Date: _____

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

Response: _____

Signature: _____ **Date:** _____

Print Name: _____

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70.14 Imaging Core Replacement/ Inactivation Process

In the event that an image exam must be replaced or inactivated due to a submission error, this process will be followed:

- i. ICL to initiate query to site and DCC designee asking for clarification. ICL will not process clarification received from site until sponsor designee(s) verifies the accuracy with signature on inactivation form.
- ii. The site monitor or designee will verify the date and subject ID on the Inventory/Quality Report to ensure accuracy.
- iii. ICL will update the Inventory Report, PACS system and C5Research Clinical Data Management (CDM).
 1. Rename incorrect CMR as INACTIVE.
 2. Proceed with normal processing of replacement CMR, i.e. check-in, import and analysis.
- iv. Prior to data transfer, ICL will send DCC's Data Management team and C5Research CDM Replacement CMR spreadsheet containing cumulative list of studies that have been renamed.
 1. DCC will update their DM team in preparation for successful receipt of transfer.

70.15 Electronic Submission Overview

70.15.1 AG Mednet

70.15.1a AG Mednet is a web-based diagnostic imaging network which enables sites to send diagnostic image exams electronically and securely to the Imaging Core Lab

70.15.1b AG Mednet will provide tools and training to:

- ☐ De-identify exams
 - o Site is responsible for correctly de-identifying study within the AG Mednet portal.
- ☐ Complete transmittal forms electronically

- Complete other trial-specific tasks

70.15.2 Electronic Submission Process

70.15.2.1 All data should be acquired in DICOM format and submitted electronically via a web-based interface to the Imaging Core Lab using the AG Mednet Desktop Agent.

70.15.2.2 Upload time is dependent on site speed network connection, but the transfer runs in the background so site staff can leave the computer running or work on other applications.

70.15.2.3 Sites are informed via email of electronic submission success as soon as transfer has completed.

70.15.2.4 AG Mednet is an intuitive system and can run from a networked PC with Java 8 plug-in installed. This plug-in ensures AG Mednet will run within the web browser. It is likely that you already have Java 8 installed.

70.16 Forms

70.16.1 CMR Data Tracking Forms

70.16.1a Hard copy transmittal forms should be downloaded from QHS website and used as worksheets, at site's discretion, in preparation for electronic data transfer. Link to the PVDOMICS webpage: <http://qhsapps.ccf.org/pvdomics/>. Click on information page and select forms from choices.

70.17 References

American College of Radiology—North American Society for Cardiovascular Imaging Society for Pediatric Radiology Practice Parameter for the Performance and Interpretation of Cardiac Magnetic Resonance Imaging (MRI). Amended 2014 (Resolution 39)*).

ACCF/ACR/AHA/NASCI/SCMR, 2010 Expert Consensus Document on Cardiovascular Magnetic Resonance. Journal of the American College of Cardiology Vol 55, No. 23, 2010