7.   CARDIAC MAGNETIC RESONANCE IMAGING (CMRI)

FREQUENT HEMODIALYSIS NETWORK

CARDIAC MAGNETIC RESONANCE IMAGING (CMRI)

MANUAL OF OPERATIONS

Version 3.1
June 10, 2011

Cardiovascular Imaging Core Laboratory (CICL)
for the Daily Hemodialysis Trial and the Nocturnal Hemodialysis Trials

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A. INTRODUCTION

A.1 Overview
This document is the manual of operation for the cardiac magnetic resonance imaging (CMRI) in the Daily Hemodialysis (DHD) Trial and the Nocturnal Hemodialysis (NHD) Trial. This manual is provided by the Cardiac Imaging Core Laboratory (CICL) to standardize the CMRI procedures among the clinical sites participating to the DHD and NHD trials. In particular, this manual of operation describes the procedures for CMRI scan execution, image acquisition, image submission, and image analysis.

A.2 Rationale for a Cardiac Imaging Core Laboratory (CICL)
As part of the DHD and NHD Trials, measurements obtained from CMRI scans in two separate intervals will be used to provide information on the efficacy of frequent dialysis on left ventricular mass regression (primary end-point) and in improvement of left ventricular volumes, functional indices and aortic stiffness (secondary end-points). These end-points (for CMRI, in particular) although highly reproducible and applicable to the clinical trial context are still subject to performance and measurement variability. The purpose of this manual is therefore to ensure a standardized approach to image acquisition and analysis.

A.3 Location and function of the CICL
The core lab is located in the OSU Division of Cardiovascular Medicine in Cardiac MR/CT Section The primary goal of the CICL is to assist for the acquisition of the data related to the primary and secondary end-points for both the trials. In brief, as part of this process the CICL will accomplish the following: 1. Determination of appropriate image acquisition parameters and scanning protocol; 2. Establishment of standards for the submission of images and data; 3. Assessment of the eligibility of sites to perform studies; 4. Certification of each site's readiness to begin imaging studies; 5. Training of participating sites in implementation of appropriate protocols for consistency; 6. Establishment of quality control measures; 7. Performance of studies in patients enrolled in investigator sites located in the CICL area; 8. Data analysis; 9. Quality Control; 10. Transmission of final results to the data-coordinating center.

A.4 Contact Information at the CICL

<div align="center">

Cardiac Imaging Core Laboratory (CICL) Coordinator
Floor 3, Room 398 Biomedical Research Tower
Ohio State University
460 West 12th Avenue
Columbus, OH 43210-1252
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B. PRELIMINARY SITE QUALIFICATION

Prior to enrolling any study subjects into the imaging study section of the trials, the appropriate CMRI hardware and software specifications should be confirmed as being acceptable. For CMRI, the magnet will need to have the following minimum gradient performance characteristics: peak strength $\geq$ 12 mT/m, slew rate $\geq$ 40 mTm/s (ideally $\geq$ 20 mT/m and $\geq$ 100mT/m/s, respectively). The pulse sequence employed for evaluation of ventricular mass and volumes will be steady state free precession (SSFP). This goes by a variety of proprietary names depending on the vendor: TrueFISP® (Siemens, Erlangen, Germany), FIESTA® (General Electric,Milawaukee, USA), BFFE® (Philips Medical Systems, Best, Netherlands). All images will need to be retrospectively triggered.

All candidate sites are required to submit test cases and Scanning parameters forms (Appendix 1 and 2) to the CICL to obtain site qualification.

B.1. Training Sessions

The CICL will conduct online training sessions on multiple occasions for sites on the protocol requirements and scanning procedure for Cardiac MRI in the trials. The tests will be provided based on demand (rate of inclusion of new imaging centers in the trial). The training sessions are designed by Drs. Rajagopalan and Sanz, and lead by Dr. Sanz. Multiple training sessions are held because of the different availability of the imaging centers, and the core lab. This is individualized with each imaging center(s). The success of the training will be determined by the test cases that each imaging center needs to submit to the core lab before certification for participation in the trial. These studies must be acquired and submitted according to the MOP specifications.

B.2 Test cases

The test cases should include CMRI images as specified in this manual. The submission of 2 CMRI test cases is required for inclusion as a CMRI site.

The images for these cases should be acquired in the format recommended in this manual. CMRI studies should be performed following the protocol specifications. The test cases submitted to the CICL can be past exams from your institution, as long as these cases have been performed in conformity with the required procedures. The instructions for test-cases image submission to the CICL are reported in section E (Images submission).

The Quality Review Laboratory of the CICL will process the images and the study site notified of the results. After the notification, the site may begin submitting CMRI from enrolled patients as specified in the study protocol. If the test images are not initially acceptable, the CICL will work with the site to identify solutions to improve image quality and protocol conformity (additional test cases will likely be requested). Specific training from the CICL is available for candidate centers.

Once two designated technicians have completed training in protocol specified image acquistion at each site, those persons can supervise other technicians in collecting scans according to the study protocol. The additional technicians are not required to go through the CICL training.

B.3 Scanning parameters form

Specific imaging parameters are required in this study. To assess the technical adherence of the candidate site to the prescribed parameters (see Sections C and D). CMRI Scanning Parameters Form (Appendix 1) should be completed for each of the test cases. These parameters will be updated on a yearly basis to ensure adherence to the protocol.

C. CMRI EXAMINATION

C.1 PATIENT PREPARATION FOR CMRI
This is detailed in Appendix 2, which also includes a list of contraindications for the procedure. As a general rule, subjects in whom CMRI studies are contraindicated will not be included in the trials. During the enrollment process, patients will be screened for the presence of such contraindications and an informed consent will be obtained. The imaging sites are however expected to perform a brief survey of contraindications (i.e. presence of metallic objects), following standard MRI safety procedures. Please also note the recommendations regarding patients with atrial fibrillation outlined in Appendix 2.

C.2 CMRI SCANNING PROTOCOL
The appropriate imaging hardware and software specifications should be confirmed as being acceptable and the designated imaging pulse sequence needs to be available on the CMRI scanner. Cross Vendor Lexicon reference is available at the website http://www.scmr.org/technologists/crossvendorlexicon.pdf. If it is necessary to deviate from the protocol due to equipment or software issues, the local investigators should contact the CICL prior to imaging a study patient.

Entry of patient ID number on the scanner: Enter the patient's Study Identification Number in the 'Last Name' and `Patient ID' fields on the scanner. The patient's Study Identification Number is the number that has been assigned to the patient when initially enrolled in the trial. If you do not know the patient's Study Identification Number, please contact your local study coordinator. In addition to the patient's Study Identification Number, please enter the date of the CMRI scan. All clinical (underlying diseases) and/or demographic data, such as age, gender or ethnicity, should be specifically excluded from the images.
ATTENTION: DO NOT ENTER INFORMATION THAT MAY DISCLOSE PATIENT IDENTITY.

Patient Positioning and ECG Gating (for patient preparation and scan time sequence see Appendices 2 and 3): Position the patient on the table with ECG leads applied and a phased-array receiver coil placed correctly on the chest for highest signal intensity cardiac imaging. It is crucial to achieve a high quality ECG signal to ensure accurate cardiac triggering and optimum image quality. If it is not possible to obtain adequate ECG gating, peripheral pulse gating with an appropriate plethysmographic device will be accepted as an alternative. This would need to be documented in the CMRI Mailing Form 251 (see Appendix 6).
THIS PROTOCOL DOES NOT REQUIRE IV ACCESS.

Breathing instructions: The patients should be advised to hold their breath at a relaxed point in end-expiration. The patients should not be instructed to "blow all the way out" or to hold their breath after forced end-expiration as this curtails the breath hold time. Test breathing instructions before starting the examination may be useful to confirm that the subjects understand what they are expected to do.

Brief protocol synopsis
Standard scout images leading to double oblique horizontal long axis (4-chamber view) of the heart
1.   Cine images of the horizontal long axis view of the heart (4-chamber view)
2.   Prescribed double oblique short axis view of the heart with the first slice above the insertion point of the mitral valve.

3. Cine images of the short axis of the left ventricle (LV) from the position in 3 (copy image position) extending proximal to this portion, to the apex to allow full and complete coverage of the LV.
4. Prescribed remaining long-axis views of the heart (2-chamber view, LV outflow tract view) and cine images from these positions.
5. Cine image of the LV outflow tract perpendicular to the 3-chamber view.
6. Cine image perpendicular to the ascending aorta for the evaluation of aortic stiffness.

Recommended sequence parameters and tips for optimal image quality
(for the complete list of scan parameters see Appendices 4 and 5)

Ventricular function (Appendix 4)
1. Steady state free precession (SSFP) imaging sequences [True-FISP (Siemens); FIESTA (GE); Balanced FFE (Philips)] should be retrospectively ECG-gated and performed in end-expiration.
2. Slice thickness of 8 mm with 2-mm gap between slices.
3. Temporal resolution <45 ms.
4. Flip angle maximized (>60°).
5. On obtaining the first short axis on a double oblique cut begin basally to the mitral valve (atrial level) to ensure full coverage of the LV for mass calculations.
6. Proceed to obtain sequential short axis cine loops of the entire LV all the way to the apex until the apex cannot be seen.

Aortic stiffness (Appendix 5)
1. Steady state free precession (SSFP) imaging sequences [True-FISP (Siemens); FIESTA (GE); Balanced FFE (Philips)] should be retrospectively ECG-gated and performed in end-expiration.
2. Slice thickness of 8 mm.
3. Temporal resolution ≤30 ms.
4. To ensure an adequate perpendicular orientation to the ascending aorta, prescribe your plane using both LV outflow tract cine views as references.
5. Check that the imaging plane remains above the sinotubular junction at all times during the cardiac cycle.

C.3 CMRI SCAN SEQUENCE
- Localizers and Cardiac Scout Images
Obtain initial multiplane thoracic localizer images (sagittal, coronal and transverse) with the heart at the center of the magnet bore. For higher accuracy it is preferable to have the localizer images acquired during a breath-hold. Confirm that all your coils are turned on and appropriate coverage of the area of interest is obtained. If not, reposition the coils and/or patient.

Two-Chamber Scout: Using the best axial (pseudo-4 chamber) localizer image, prescribe an imaging plane that bisects the LV taking care to ensure that the plane traverses the apex.
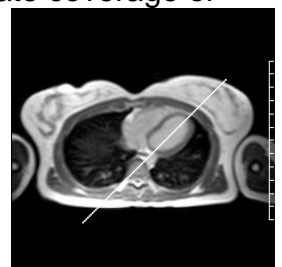
Short-axis Scout: Using the 2-chamber scout prescribe a plane parallel to the mitral plane and perpendicular to the LV long axis.
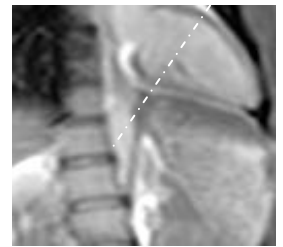
Four-chamber Scout. From the short-axis and two chamber scouts, prescribe a plane that transverses through the center of both ventricles, center of the mitral valve and the LV apex, to generate a double oblique horizontal long axis view (4-chamber).
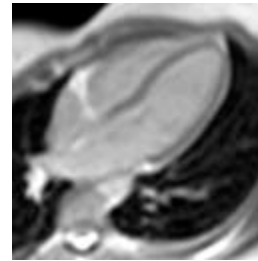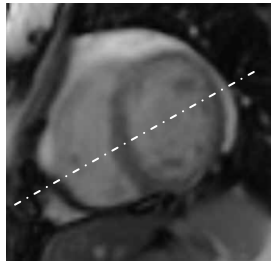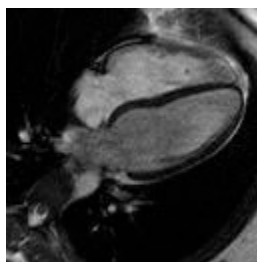

- ***Cine Images***
The sequence used for the cine mages is SSFP [True-FISP (Siemens); FIESTA (GE); Balanced FFE (Philips)] with retrospective ECG gating and breath-hold imaging. Prior to obtaining the cine images, the scan parameters should be checked on the scanner (see Appendix 4). It is recommended that once the participating sites have been certified by the CICL after submission of the test images, the imaging parameters are saved as a separate identifiable protocol on the scanner (e.g. frequentdialysis_CMRI). This will help minimize operator-dependent variability should different technologists perform the studies in various time-points.

Cine images are acquired once the desired 4-chamber localizer displayed above is obtained.

Four-Chamber Cine: This is acquired by copying the image position from the 4-chamber scout image and running the cine sequence using the parameters outlined in Appendix 4.

Short-axis cines: These are prescribed from the 4-chamber cine images. The short-axis images are to be correctly acquired as improperly oriented images may result in errors during analysis. A plane perpendicular to the interventricular septum is chosen. The short axis stack should begin above the level of the insertion points of the mitral valve (atrial level) and proceed towards the apex. Confirmation of the "double oblique" orientation as well as perpendicularity to the septum/anterior wall is recommended by simultaneously comparing the orientation on the 4-chamber and 2-chamber scouts. Once a single short axis cine-loop has been obtained at the most basal level, you may

proceed from this level in 8 mm (2-mm gap) intervals to the apex, ensuring complete ventricular coverage.
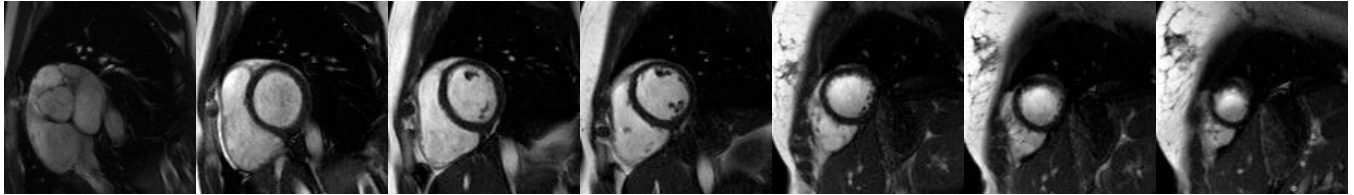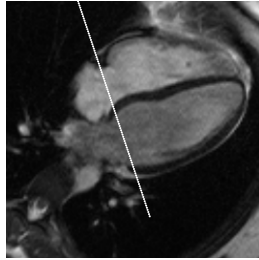
It is vitally important to provide complete anatomic coverage of the ventricle from the base to the apex. It is good idea to get images all the ways through till you do not see any apex. If one or more of the short axis slices are of sub optimal quality (due to motion artifacts, gating problem) please repeat the acquisition until adequate images are obtained. Indicate in the CMRI Data Acquisition Form (see Appendix 6) which series number is the "best" acquisition for a certain slice position.

Two-Chamber Cine: This can be obtained from the 4-chamber view by drawing a line that passes between the mitral valve leaflets and extending to the apex of the LV. On the short axis images this plane should pass through the anterior and inferior walls and should pass right through the apex. The orientation when correctly placed should not include the right chambers.
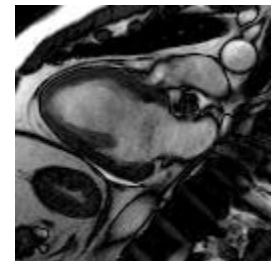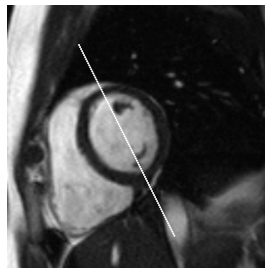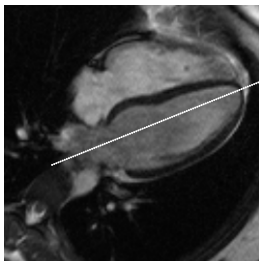
LV outflow tract view: This should be obtained by prescribing a plane that passes through the outflow tract on a short-axis cine movie-loop where one visualizes the outflow tract. The plane should pass through the apex and this can be confirmed in other views.
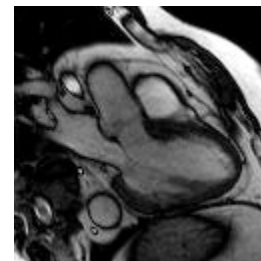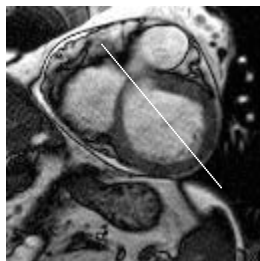
Cine image of the LV outflow tract: Obtain a cine loop perpendicular to the 3-chamber view, aligning your plane along the LV outflow tract and ascending aorta.
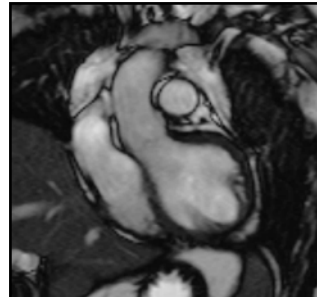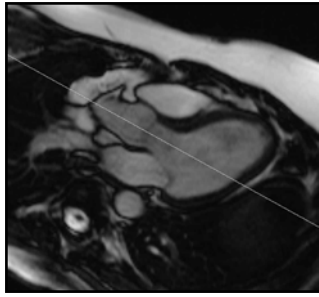
Ascending aorta: Prescribe a cine loop parallel to the plane of the aortic valve annulus and perpendicular to the ascending aorta using both LV outflow tract views as references. Ensure that this plane remains above the level of the sinotubular junction (defined as the junction between the sinuses of Valsalva and the tubular ascending aorta; dashed line on the image) at all times during the cardiac cycle. Remember that the scanning parameters for this acquisition differ from the prior cine loops (see Appendix 5). Because of more prolonged imaging time for this specific acquisition, it is a good idea to warn the patient that this breath-hold will be longer. If the subject cannot complete the breath-hold, repeat the acquisition using some of the tips outlined in Appendix 5 to reduce scanning time.
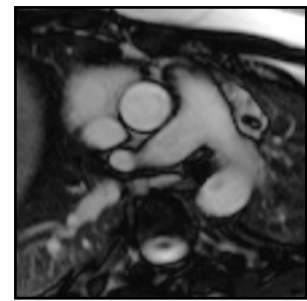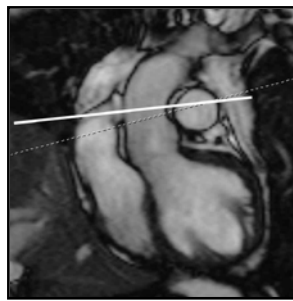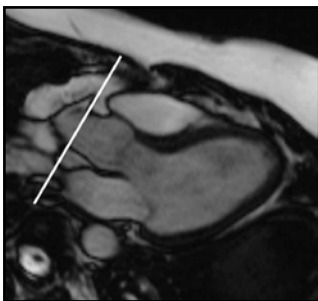
C.4 CMRI SAFETY GUIDELINES

Dialysis patients undergoing CMRI do not require specific safety measures above and beyond routine precautions that apply to the performance of CMRI in general. Updated information about biomedical devices that may impose a risk to patients undergoing MRI is available on the Internet at www.MRIsafety.com. Each clinical site should have written safety guidelines, practices and policies previously established for patients undergoing CMRI as well as for the personnel participating in patient care in the MRI department. All study patients should undergo the routine screening process for the presence of contraindications to MRI that is routinely used by the local department. In addition to the exclusion criteria specified in the protocol, patients with implanted biomedical devices that are not MRI safe or that may result in imaging artifacts are to be excluded. In addition, patients who have a history of claustrophobia who are unable to lie flat, hold their breath for at least 12 seconds or who are too large to fit in the bore of the scanner are to be excluded. General guidelines and standard practices should be followed. This would include institution of oxygen if needed, monitoring of heart rate and blood pressure.

D. IMAGES SUBMISSION
(See also section B.2)

The same protocol should be followed every time during submission of CMRI cases to the CICL.

Data Archiving and Submission: The complete CMRI studies (including scout images, repeated acquisitions for CMR) should be copied to a CD or DVD in DICOM compatible format. The only unique identifiers that should be included in this DICOM header are the center number, the patient ID number (will be assigned by the DCC) and the date of the scan. Prior to saving the DICOM file it is important to ensure that the patient name, social security number and hospital related identifiers are completely removed in order to protect patient confidentiality. In addition, there should be no other information contained in the DICOM header of the image or written on the CD/DVD that would disclose the identity of the patient for HIPAA compliance reasons (According to the United States Department of Health and Human Services, a covered entity [e.g. a hospital] may always use or disclose for research purposes, health related information which has been de-identified (in accordance with 45 CFR 164 502(d) and 164.514(a)-(c) of the rule; for more information visit www.os.dhhs.gov/ocr/hipaa/guidelines/research.pdf).

A copy of the CD should be maintained at the site.

CD/DVD Labeling: The CD/DVD should be labeled on the non-recording surface with a pen that has indelible ink. The data that should be included on the label is: center number, patient ID number and date of CMR scan.

Data Forms: Complete the CMRI Mailing Form 251 (Appendix 6). This Form will be provided to you by the local study coordinator. Return the CMRI Mailing Form 251 and the 2 CDs to your local study coordinator. The study coordinator will fax the CMRI Mailing Form 251 with the Data Submission Form (Appendix 7) to the CICL at 888-362-0639. This notifies the CICL coordinator that CD's from the site are to be expected soon.

In addition, the study coordinator will need to mail the CMRI Mailing Form 251 and the CD of the patient's study to the CICL.

Test cases: The images acquired for the initial test cases need to be sent using the same protocol described above. Each test case should be sent in DICOM format on a separate CD/DVD. The CD/DVD should be appropriately labeled with the patient's Study Identification Number (for the test cases: TEST-1 and TEST-2), Center Number and the date of study. A CMRI Mailing Form 251 should accompany each CD/DVD. In addition to the CD/DVD and CMRI Mailing Form 251, each test case must be accompanied by a CMRI Scanning Parameters Form (Appendix 1). The CMRI Scanning Parameters Form provides the CICL with technical data regarding the imaging protocol to ensure adherence to the Trial standards and reproducibility of imaging techniques amongst centers. The local study coordinator will mail the CD, CMRI Mailing Form 251 and the CMRI Scanning Parameters Form to the CICL for each test case. Prior to shipping the CD/DVD's and forms, the local study coordinator will also fax a copy of each Data Submission Form and CMRI Mailing Form 251 to the fax number above. These forms are identical to those that will be used for actual data submission and would provide a trial run for appropriate form submission as well

E. ANALYSIS PROTOCOLS FOR CARDIAC MR IMAGES
E.1 PRE-ANALYSIS LOGISTICS

MRI PERFORMANCE AND SHIPPING
On performance of an MRI, an email is sent to the core notifying that the CD was sent.

Pick up the mail package from the front desk of DHLRI room 110. Whitney Works is normally the receptionist who will inform you via email of when the package(s) would be available. The normal time for a package to come in is around 10 AM.

Confirm that envelope from site contains the following items:
    CMRI Mailing Form 251filled out, 2 pages.
    CD of exam that could be in DVD or CD format

Review the CMRI Mailing Form 251to make sure that the dates written on it are correct.
Fill out a 252A form with the corresponding information from the 251 Form, see Figure 1 below for a visualization of these entries:
1.   Participant ID#
2.   Alpha Code
3a.   Visit Type
3b.   Visit Number
4a.   Date of MRI: dd/mon/yyyy
5.   Heart rate as measured centrally (bpm)

Revision of 03/SEP/2008   Form #252A
                                                                          Page 1 of 1

Frequent Hemodialysis Network
MRI CENTRAL DATA ENTRY - FORM # 252A

This form is completed at the Cardiac MRI Core Laboratory (CICL). A staff member from the CICL will enter this into the study database. Many values will be calculated automatically and reported back to the Clinical Centers.

| 3 | 8 | 0 | 3 | 1 | 4 | Y | G | B | 0 | 1 | 0 | 3 | A | P | R | 2 | 0 | 0 | 9 |

1. Participant ID #   2. Alpha Code   3a. Visit Type   3b. Visit Number   4a. Date of MRI: dd/mon/yyyy

4b. Date this MRI read (dd/mon/yyyy)... 20/ARR/200 9

Hemodynamic (MRI scan)
  5. Heart rate as measured centrally (bpm) 120

Figure 1: 252A Form basic entries.

Take the CD along with Form 251 and 252A to the Argus Workstation located in the Ross Heart Hospital.

E.2 ARCHIVAL PROCEDURE

Make a copy of the CD/DVD of the exam. One copy of the CD/DVD is to be mailed out to Dr. Javier Sanz for wall motion reads. The original after below is saved in a folder for safekeeping. The CD/DVD's that are sent to Dr. Sanz at Mount Sinai will be stored in a locked cabinet, located in a locked office, located in secured area of the Mount Sinai Hospital Cardiovascular MR/CT Laboratory. They are organized in order of receipt. Dr. Sanz keeps a separate database that details the date each study was read, whether clinical findings were present, and if so, what findings were noted.

Import the study via the 'Import Function' on a SIEMENS ARGUS Workstation.

Once the study is imported, check to make sure that the study is de-identified. All studies should have the following format:

Patient's Name: 123456 (Participant ID#)
Patient's ID#: 123456 (Participant ID#)
Date of Exam: 12/22/2008 for example. Should match up with Question 4a from Form 252A

Remove any information on the MRI header that may identify the patients such as referring physician, date of birth, gender, etc.

Once the naming convention of the imported study is accomplished; push the study to WebPAX storage system. WebPAX is our centrally located server where we are able to store images for safe keeping.
> Select study that you want to send to WebPAX.
> Go to "Send" on the menu and select it.
> In the pop-up window, select WebPAX destination and click the Send button.
> The study should be sent to WebPAX, it may take 1 to 2 minutes to send all of the study to WebPAX. The duration depends on the size of the study. Be patient.

DETAILS ON WEBPAX AND BACK-UP FOR WEBPAX

The images for the Daily Dialysis and Nocturnal Dialysis trials are saved on a centralized web-based PACS system called WebPaxTM. WebPax has over 40TB of space currently available and is backed up regularly.

WebPAX stats as of April 27th 2009:
Storage Used (GB): 4096.000
Storage Available (GB): 4096.000

E.3 READING PROTOCOL

When the images are received in the Core Lab, they will be checked for quality and consistency, including appropriate anonymization, compliance with the imaging protocol and completeness of study. A scan may not be evaluable for measures due to a number of foreseeable circumstances:

• Damage of the images physical support (CD or DVD). The research coordinator at the original imaging center will be notified to submit another copy of the study

• Major violation of image protocol that precludes evaluation of the primary endpoint (LV mass), such as missing images, inadequate gating (prospective), gross motion or other artifacts. The imaging center will be immediately notified and the Core Lab will discuss the reason for failure with the imaging technologist. If the problem can be addressed, the Core Lab will request that the patient be called back for re-evaluation as soon as possible (within the enrollment window).

• Minor violations of imaging protocol that do not preclude evaluation of the primary endpoint (LV mass) will prompt notification to the imaging center but the images will be analyzed for the available parameters.

In all cases software-generated contours will not be accepted and that only hand-drown contours will be used.

Procedure to be followed for reading

Select the loaded exam. Look for the Short Axis cine series (SAX for short). Highlight the series and load them into Argus. The Patient Browser should look similar to Figure 2 below.
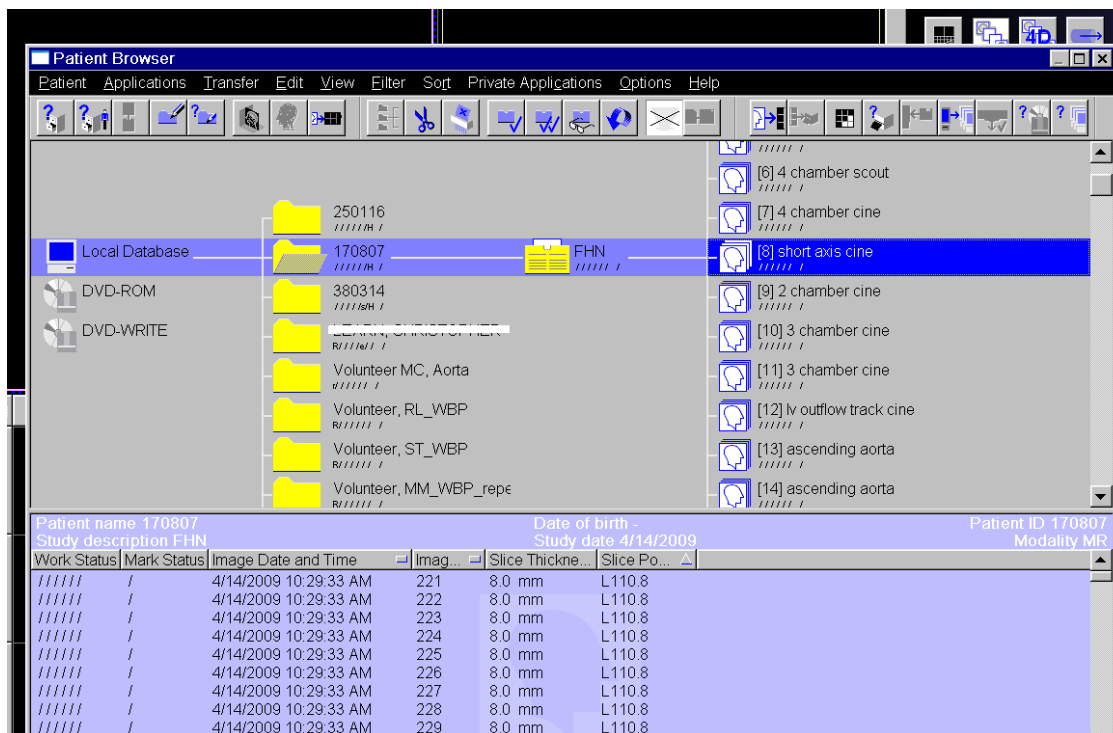
Figure 2: Siemens Workstation Leonardo Patient Browser window.

Make sure to check the slice location for all of the loaded series to see if there are any discrepancies. Sometimes there are multiple series that covered the same location of the heart (for example, the MRI technician repeated a series to try to obtain better image quality). Sometimes there is a skip in slice position. Note that the slice position should be 10 mm apart (8 mm thick slices with 2 mm gap). If there are repeat series that are loaded, unload the first series in that particular slice. If there are skipped slices Notify the imaging center in order to check whether not all images were sent to the Core Lab, or if not all slice positions were acquired (protocol violation)

Ensure that all of the requisite slice positions and aortic compliance was performed

Check Image quality and rate image quality on Form. The criteria for image quality are qualitative. The image quality is rated as excellent (3), acceptable (2) (for the purposes of contour analysis) and unacceptable (1).

Depending on the MRI system and/or protocol that was used to acquire the MRI images, you may or may not have to worry about loading multiple series into Argus. For example, GE Scanners typically acquire all short axis slices of the heart into one large series. In contrast, on the Siemens scanner it is typical to acquire each short axis slice as one series. It is also possible to acquire all of the short axis cuts in one series.

Select all of the images then zoom in and window the image. Figure 3 shows the icon where you can click to select all images (shown in red). Please note that the image selection functions like Microsoft Excel. Figure 4 shows the Zoom and Pan function.
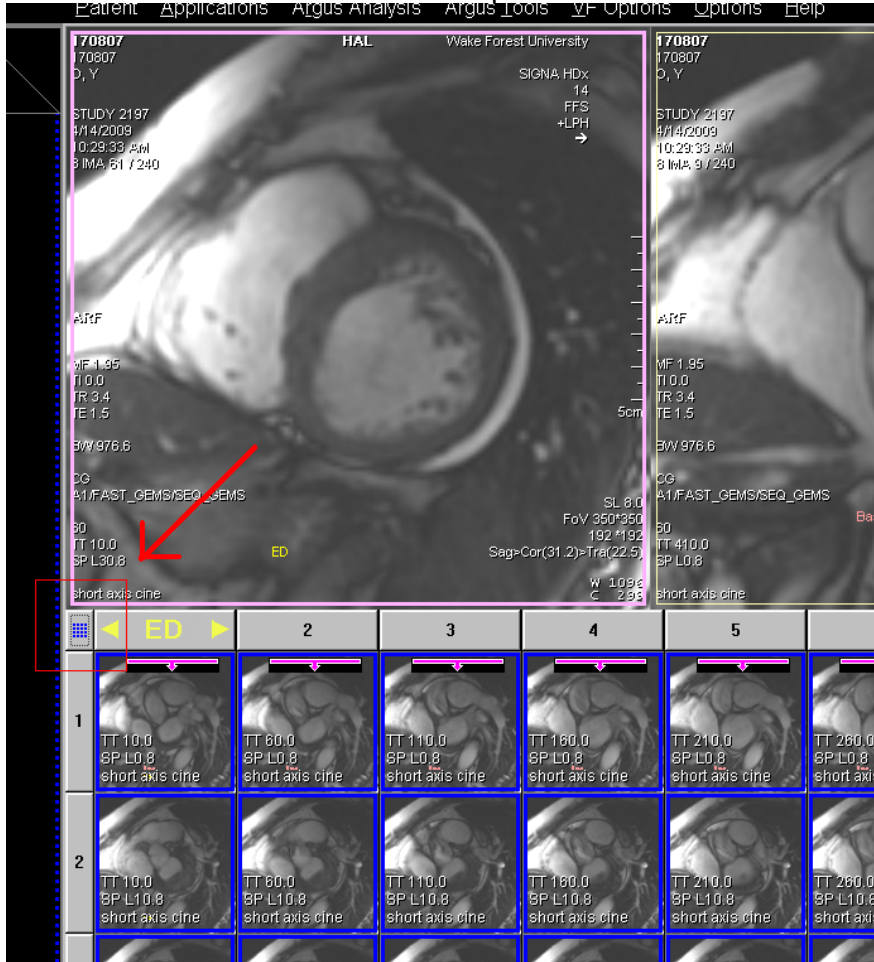
Figure 3: Select all images from Argus.
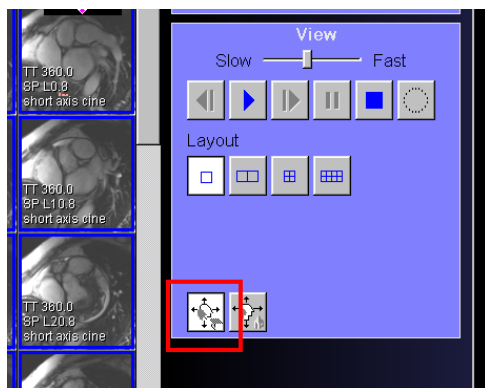
Figure 4: Zoom and Pan function.

Window-level settings
Brightness and contrast of the images are dependent, amongst other factors, on the type of magnet employed for the acquisition. Window settings will be manipulated manually and repeatedly to achieve, in every frame traced, good contrast between the LV cavity and the endocardial border, or between the epicardial border and surrounding fat/fluid.

Determining the Correct Phase for End-Diastole (ED) and End-Systole (ES)

Definition of ED: ED is defined as the phase corresponding to when the blood pool is largest (blood pool have brighter intensity than the bordering myocardium).

Definition of ES: ES is defined as the phase when the blood pool is smallest.

- ED and ES is defined visually based on:

    - Maximum (ED) and minimum cavity volume (ES) of the LV on playing the phases.

    - Valve position: mitral closes in ED, aortic closes in ES.

    - ED is in the vast majority of cases corresponds to the first or last phase in Argus.

Once you are able to determine which phases are ED and ES. Move the corresponding ED/ES tag like the one shown in Figure 4 to their corresponding columns.
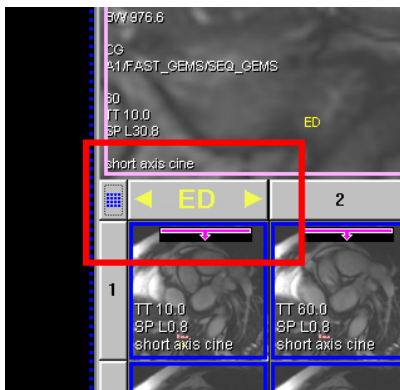
Figure 2: ED designation.

Tracings LV Epicardial and Endocardial Contours

- *Endocardial tracing*: Papillary muscles and trabeculations will be considered <u>part of the ventricular cavity</u> as a general rule (both in ED and ES). If a prominent trabeculation (as dense as the wall myocardium) is in contact with the wall <u>both</u> during ED and ES, it will be considered part of the wall.

- *Epicardial tracing*: <u>Do NOT include epicardial fat.</u> (lobulated, change the windowing)

Figure 5: Typical contour tracings.

- <u>Valves</u>: For LV and RV, anything below the aortic/pulmonary valve is ventricle.

- <u>Base</u>: For both ventricles it is defined based on wall thickness (higher for the ventricles than the atria), the motion of the wall (ventricles contract while atria dilate, and vice versa) and, in case of doubt, the position of the slice in the 4 chamber cine. <u>The base in ED is usually one level higher than in ES</u>.

-        For the **LV**, the first slice will be considered to be part of the LV if surrounded by ≥ 50 of ventricular myocardium. If the basal slice contains both ventricular and atrial myocardium, the contours will be drawn up to the junction and joined by <u>a straight line</u> (Figure).

-        For the **RV**, the outflow tract is often seen in the base together with the atrium (Figure).

- <u>Apex</u>: For both ventricles it is the last image where <u>cavity</u> can be identified.
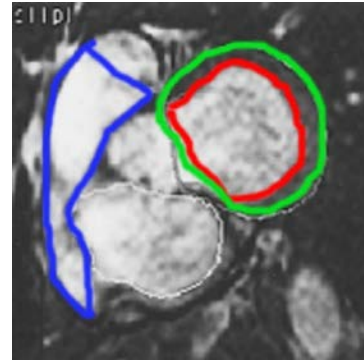
Click on the Volume box in the Result tab as seen in Figure 6 to get the results.
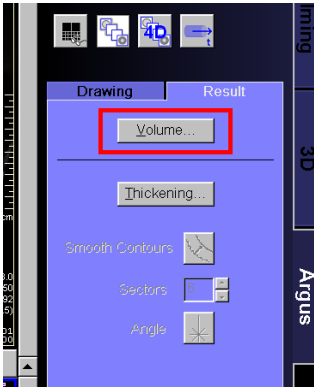
Figure 6: Volume and Mass Result.

The ARGUS workstation provides two LV Mass measurements: end-diastolic and average (representing the mean of end-diastolic and end-systolic measurements). For consistency, only the measurement at end-diastole will be recorded. This is because this is the common approach in clinical practice and it appears that end-systolic measurements overestimate LV mass with the 2D analysis method used in these trials (Swingen et al. J Cardiovasc Magn Reson 2004;6:829-35)

Determination of Systolic thickening

1. Eliminate slices where there is not a complete LV wall circumference.

2. There should be the same number of slices in ED and ES.

3. Go to the "thickening" card in Argus and do the analysis of 2 segments per slice. Add up all results and average them.

Click on the Thickening box in the Result tab as seen in Figure 7 to get the results.
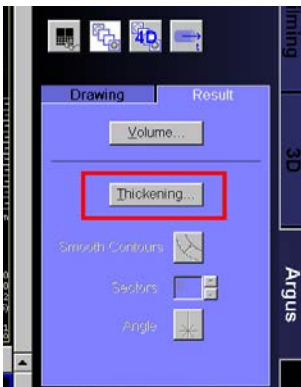
Figure 7: Thickening Result.

Aortic stiffness

1. Aortic series Images are loaded to Argus function.

2. Automatic contour detection is propagated.

3. The maximum and minimum areas are determined visually (ensure reasonable contours) and

with Argus "volumes" results.

4. These 2 frames are loaded to Viewing, where diameters and areas are traced.

Both diameters and areas are luminal, NOT wall-to-wall. The diameters are antero-posterior.

LV Thickening and Wall motion score index (to be performed Dr. Javier Sanz)

WMSI = ∑ scores 16 segments:

1.   Normal wall motion.

2.   Hypokinesia.

3.   Akinesia.

4.   Dyskinesia.

Dr. Sanz will determine the wall motion score index by adjudicating a category for contractility (1. normal wall motion, 2. hypokinesia, 3. akinesia, and 4. dyskinesia) to each of the standard 17 myocardial segments, as detailed in the MOP. Dr. Sanz will also review the studies for the presence of incidental findings that may pose significant risk to the patient and that may otherwise go undetected, including but not limited to cardiac or extracardiac tumors, aortic dissection, severe pericardial or pleural effusions, or wall motion abnormalities compatible with myocardial infarction/ischemia. These results are currently emailed to the core and then manually entered into the FHN database.

Dr. Sanz will proceed to the clinical reading of the studies within 3 working days upon receipt of the copies of the CD's from the Core Lab. If incidental findings considered to be of clinical relevance are noted, Dr. Sanz will immediately notify the Core Lab research coordinator, who in turn will fax a brief clinical report to the DCC.

F. RECORDING RESULTS INTO 252A FORM

Record the data obtained in the steps above into Form 252A like the one seen in Figure 8 below.

4b. Date this MRI read (dd/mon/yyyy)... 20/ABB/200 9

Hemodynamic (MRI scan)
5. Heart rate as measured centrally (bpm) 120

Global Left Ventricular Function
6. Left ventricular end-diastolic volume: (ml)... 76.5

7. Left ventricular end-systolic volume: (ml) 44.3

Left Ventricular Mass
8. Left ventricular mass: (gr) 89.2

Global Right Ventricular Function
9. Right ventricular end-diastolic volume: (ml).. 66.0

10. Right ventricular end-systolic volume: (ml).. 44.9

Segmental Left Ventricular Function
11. Absolute systolic thickening: (mm).. 2.6

12. Relative systolic thickening: (%).. 32.45

(Wall motion score index moved to Form 252B as Item #5.)

Aortic Stiffness
14. Maximal area: (cm²) 8.13

15. Minimal area: (cm²) 7.09

16. Maximal diameter: (cm²)... 3.10

17. Minimal diameter: (cm²)... 2.85

Figure 8: 252A Form measurement values.

Figure 9 shows a completed 252A Form with all of the patient information, recorded measurements, and person entering the data into the database.

Figure 9: Completed 252A Form.

G. ENTERING DATA INTO INTERNAL CORE DATA BASE
Enter Results from 252A Form into Core Database (Excel)

Fill in the corresponding values from the 252A Form into the Core Spreadsheet called DDialysisCore.xls. Figure 10 shows the fields that must be filled in. Please take extra care to make sure that you enter the number correctly from the 252A Form to the Excel Spreadsheet.

Figure   10:   DDialysisCORE.xls   spreadsheet.

H. QUALITY CONTROL MEASURES

The CICL has established quality assurance at multiple levels that will serve as a safeguard against error/bias in the trial.

1. <u>Sequence/protocol fidelity through the trial</u>: This will be ensured at sites prior to study initiation by requiring that the sequence for CMRI (SSFP) be saved as a separate identifiable protocol on the scanner.

2. <u>Scanner and site of performance</u>: The same scanner and site where the original MRI was performed will be adhered to through out the protocol for all patients. If any change is contemplated the site will contact the MRI core to approve any changes.

3. <u>Periodic surveillance of sites by CICL</u>: Sequence parameters specified in the MOP will be surveyed routinely during the review of the images. This will ensure uniformity of study performance at sites. In addition if there has been a change at a site with regards to hardware, software or technician at a site this will be required to be relayed to the CICL.

4. <u>Analysis of data in the trial</u>: Dedicated CMRI specialists will analyze CMRI end-points in the trial. The analysis of CMRI measurements will be performed for the most part by the same reader to reduce inter-reader variability. However in the event that the primary reader becomes unavailable, there will be a replacement reader who will take on the responsibility. The training of the reader has to fulfill the following criteria.

5. <u>Certification of New Reader</u>
The number of readers will be maintained at a minimum to reduce inter-reader variability. If a new reader needs to be introduced they will have the meet the following criteria.

•   The new reader goes through an exhaustive introduction and training of cardiac MR physics, scanning protocol (at the scanner) and exhaustive training on the workstation for analysis of cardiac MRI images over the course of 3 months. In the event of substantial cardiac MRI experience (>12 months experience scanning or /PhD level training in MR Physics with at least 6 months of scanning experience) this requirement for training in cardiac MR physics, on-scanner and workstation training may be waived

•   Approximately 60 unique cases will be read and verified over a period of 2 months. These cases will correspond to cases that have been previously read and will be assigned randomly so that the trainee is unaware of the previous results. The cases may be divided into phases that corresponds to the progression in skill set required for interpretative skills over a 2 month period (20 days each). In the event of substantial prior cardiac MRI experience the number of review cases will be limited to 20 over the course of 30 days. The original contours for these cases

•   The mean absolute difference between readers for LVMass (Reader 1 and Reader 2) will be estimated for these cases

•   Over the first 40 cases (20 in each set), the contours and volume analysis will be examined by a senior reader (Dr Rajagopalan or Dr. Sanz) and corrected resulting in an iterative learning process for the new reader

•   The final 20 or so cases will be interpreted with the assumption that these measurements would be as close as possible to the expected mean absolute difference as determined by published criteria.[†]

- If this assumption was not met (that is, if mean absolute LV mass difference is >5% in any of the 20 cases), additional sets of 20 cases will be analyzed till satisfactory agreement is accomplished

[†] Grothues et al [Am J Cardiol. 2002 Jul 1;90(1):29-34] showed that the mean absolute difference between scans for a "normal" population was 1.1± 4.2 grams. In the same study a hypertensive or heart failure population the variability was far more with a mean absolute difference ± SD of 2.4 ± 9 grams between measurements. When expressed as a % of the mean LV mass in this published study for the two populations this works out to 3% and 5% respectively.
In our preliminary analysis of over 300 cases for which we repeated measurements on 2 occasions, we established that the mean absolute difference was 2.8 ± 6 g. Based on this data and when expressed as a percent of the mean LV mass in the frequent dialysis population we estimated that a 5% variation between measurements would be an optimal trigger for review.

Quality control of data at CICL

The following procedures will be implemented on a periodic basis to ensure accuracy of data.

Parameter	Frequency	Procedure
CMRI Data Entry		
Lab Meetings	Every other week	Cases Reviewed; Contour Analysis reviewed in the event a new reader is introduced
Reproducibility of LV Mass and LVEDV	On every case Typically Done 1-2 months after initial tracing	Contours for LV Mass redrawn by same individual without knowledge of prior contours (not saved)
Reproducibility of LVESV and LVEF	Not recorded on all cases but on ≥5 % of cases	End-systolic contours redrawn

Lab meetings: Cases for review or where there is a question regarding analysis will be presented to the senior reader as and when these issues arise.

Protocol for Repeat Studies

A repeat LV Mass and LVEDV will be done for all cases. This step was implemented in June 2008 to ensure fidelity of measurements of the primary end-point LV MASS and LVEDV. This step is meant to reduce bias and will ensure reproducibility and performance measures to be derived.

- The repeat measurement will be typically done 30-60 days after the first measurement to ensure that there is no bias from the initial reading to the second reading. In addition, because traced contours are save only temporarily (for approximately 30 days), the second reading is repeated as if it is a brand new study. This reduces the bias of comparing first and second tracings by the reader and ensures independent analysis. The second reading will involve tracing contours in end-diastolic phases only, as these are the only ones needed to derive LV Mass.

- Cases requiring a repeat measurement are identified from the Case Log spreadsheet and pulled up on Webpax. The case-log sheet does not contain information on results of the MRI scans.

- Once cases have been identified they are then pushed to an Argus workstation where repeat measurements are done.

- The data ensuing from the second read will be entered into the corresponding fields in the Core Spreadsheet as seen below in Figure 11.

U	V	W	X	Y	Z	AA	AB	AC	AD	
			QC Repeat					Adjudicate		
EAD_USER	LVM Repeat	Repeat Date	Read User	Delta LVM	Delta %	Adj Date	Adj Reader	Adj Final Value	Reason	
KARIISM	246.1		KARIISM	-6.2	-2.6%					
KARIISM	128.3		KARIISM	3.7	2.8%					
KARIISM	108.3		KARIISM	2.3	2.1%					
KARIISM	125.1		KARIISM	1.3	1.0%					
KARIISM	89.2		KARIISM	43.8	39.4%		KARIISM	89.2	Measurement Error	

Figure 11: Quality Control fields in Core Spreadsheet.

Handling Of Discordant Values On Quality Control

- In the event that the first and second measurements (repeat) for LV Mass differ by more than 5%, this will trigger an evaluation by a senior reader. The contours are only temporarily saved and most tracings will be unavailable for review. Thus a third measurement will be made. In cases where the contours are available (<5% of cases) on ARGUS, then this second set of contours will be reviewed (in almost all cases only the second contour is available). If the second set of contours are unacceptable, the senior reader may request a third contour tracing. Although LVEDV is always measured twice in every patient (as its calculation is needed for the quantification of LV Mass), LVEDV will not be subject to the 5% criterion because it is not a primary endpoint in the trials.

- The third contour analysis will be reviewed by the senior reader (Dr. Sanz or Dr. Rajagopalan) in conjunction with the technician (for didactic purposes).

- The results on this analysis will be compared with the preceding measurements. There are several case scenarios.

  o   Scenario A. In the event that the third measurement of LVM (M3) varies by <5% from M1. M1 measurements will be retained.
  o   Scenario B. In the event that the third measurement of LVM (M3) varies by <5% from M2. M2 measurements (EDV, ESV and LVM)
  o   Scenario C. In the event that the third measurement of LVM (M3) varies by >5% from M1 and M2. M3 measurements will be used ((EDV, ESV and LVM)

- The new "adjudicated" values based on above will be recorded into the 'Adjudicate' fields of the Core Spreadsheet as seen in Figure 11.

- The QC procedure of LVESV will involve analysis of contours in 5% of cases to ensure internal consistency. In cases where the LVESV or LVEF vary by more than 10% a third measurement will be made. Cases for LVESV/LVEF reproducibility will be selected as the twentieth case of each set of 20 consecutive studies.

Appendix 1

CMRI Scanning Parameters Form
(To be filled out at study qualification)

FREQUENT DIALYSIS INVESTIGATORS

TEST CASE #:	SITE NUMBER:	DATE OF STUDY

Ventricular function

IMAGING PARAMETERS (SSFP)	VALUES	
TR (ms)		
TE (ms)		
Flip angle (degrees)		
Slice thickness (mm)		
Gap (mm)		
Field-of-view (mm)		
Matrix (lines)		
Averages (NEX)		
Lines (views) acquired per segment		
Reconstructed phases		
Bandwidth (Hz/pixel) or MHz		
Parallel imaging	Yes	No
View sharing	Yes	No

Aortic stiffness

IMAGING PARAMETERS (SSFP)	VALUES	
TR (ms)		
TE (ms)		
Flip angle (degrees)		
Slice thickness (mm)		
Field-of-view (mm)		
Matrix (lines)		
Averages (NEX)		
Lines (views) acquired per segment		
Reconstructed phases		
Bandwidth (Hz/pixel) or MHz		
Parallel imaging	Yes	No
View sharing	Yes	No

Please fax the completed form to the Cardiovascular Imaging Core Laboratory together with the CMRI Mailing Form 251 and Data Submission Form: 1-888-363-8923

Appendix 2

Patient Preparation for CMRI

1. A registered nurse or CMRI technician conversant with the procedure will conduct a brief survey of possible contraindications. These will include:
    a. Metallic implants incompatible with the magnetic field (pacemakers, defibrillators, aneurysm clips, etc). Intracoronary stents in particular are not a contraindication.
    b. Pregnancy (known or suspected)*.
    c. Severe obesity (weight > 200 kg)†.
    d. Severe claustrophobia.
    e. Unstable clinical condition or inability to lie flat.
    f. Inability to perform 8-12 second breath-holds
2. The patient will be instructed about the procedure (including purpose, estimated duration, steps and risks).
3. The patient's height and weight will be recorded for standardization of measurements according to the body surface area (BSA).
4. The absence of metallic objects will be confirmed and, if present, transdermal patches (such as those containing nitroglycerine) will be removed.
5. The patient will then be transported to the magnet room.
6. The patient will lie down on the CMRI examination table in the supine position (feet-first or head-first depending on the specific magnet).
7. CMRI-compatible ECG electrodes will be positioned on the precordial region of the chest for ECG monitoring and gating during the procedure. The ECG leads or plethysmography device will be connected to the magnet built-in monitoring system. In the event that the patient has markedly irregular atrial fibrillation (R-R interval variability >400 ms within 20 seconds) that precludes retrospective gating within a satisfactory breath-hold, the patient should be enrolled only after consultation with the CICL.
8. Dedicated surface coils will be placed and secured.
9. Headphones and/or earplugs will be provided for acoustic protection. During the full length of the procedure, visual and/or verbal contact with the patient will be maintained.

* In the event pregnancy is suspected, this will be ruled out by a pregnancy test.

† Maximum possible weight recommended by the manufacturer in a 1.5T *Magnetom Sonata*® magnet (Siemens Medical Systems, Erlangen, Germany). This figure may vary from site-to-site according to specific vendor-related specifications.

Appendix 3

CMRI Scan Time Sequence

- • *Pre-scan*   Patient preparation (see Appendix 2)
- • *Scan*
- - T=00 min   Patient preparation (see Appendix 2)
- - T=10 min   Start scan and acquisition of axial, sagittal and coronal localizer images
- - T=12 min   Two-chamber, short-axis and four-chamber localizer images
- - T=13 min   Four-chamber cine view (SSFP)
- - T=15 min   Short-axis cine sequences to assess ventricular function (SSFP)
- - T=24 min   Three-chamber and two-chamber cine imaging (SSFP)
- - T=26 min   End of study

Appendix 4

CMRI Parameters for Acquisition of Cine Images (Ventricular Function)

Parameters (SSFP Sequence)	Values
TR – Repetition time (ms)	3.2
TE - Echo time (ms)	1.6
Flip angle (degrees)	60-90
*Slice thickness (mm)**	8
*Interslice gap (mm)**	2
Typical field-of-view (mm) [†]	Minimal
Typical matrix (lines)	256 x 166
*Typical spatial resolution (mm)**	1.7 x 1.4
Averages (NEX)	1
*K Lines per segment**	11-15
*Typical temporal resolution (ms)**	33-45
Segments (number of heart beats)	11-15
Reconstructed phases	20-25
Bandwidth (Hz/pixel)	900-1000
Parallel imaging techniques	Allowed
View sharing [‡]	Allowed

The parameters provided in the Table are those typical of an LV function examination performed in the CICL (*TrueFISP*®, *Magnetom Sonata*® 1.5T, Siemens Medical Solutions, Erlangen, Germany).
* The asterisk denotes imaging parameters to be kept within restricted ranges between imaging sites.
  − Both the spatial and temporal resolution of the sequence have significant influence in the measured LV volumes and mass. The temporal resolution is inversely proportional to the number of k-space line acquired per segment and will be required to be < 50 ms. Similarly in-plane spatial resolution, which is determined by the field-of-view and matrix sizes, will be kept $\leq$ 2 mm.
[†] Orient the phase encoding axis of the field-of-view in the narrowest anatomic direction (typically anteroposterior for short-axis images). Minimize the field-of-view as much as possible but in the process ensure that you do not get wraparound artifacts, affecting the interpretation of images.
[‡] View sharing allows for a decrease in effective temporal resolution, although the "real" temporal resolution of the acquisition may still be suboptimal and result in inaccuracies in volume measurements. Consequently, maintain the acquired lines per segment within the limits established by the CICL to ensure adequate temporal resolution.

Appendix 5

CMRI Parameters for Acquisition of Cine Images (Aortic Stiffness)

Parameters (SSFP Sequence)	Values
TR – Repetition time (ms)	3.2
TE - Echo time (ms)	1.6
Flip angle (degrees)	60-90
Slice thickness (mm)	8
Typical field-of-view (mm)	Minimal
Typical matrix (lines)	256 x 123
Typical spatial resolution (mm)*	1.9 x 1.3
Averages (NEX)	1
K Lines per segment*	6-9
Typical temporal resolution (ms)*	20-30
Segments (number of heart beats)	18-28
Reconstructed phases	40
Bandwidth (Hz/pixel)	900-1100
Parallel imaging techniques	Allowed
View sharing[†]	Allowed

The parameters provided in the Table are those typical of an aortic stiffness examination performed in the CICL (*TrueFISP®, Magnetom Sonata® 1.5T*, Siemens Medical Solutions, Erlangen, Germany).

* The asterisk denotes imaging parameters to be kept within restricted ranges between imaging sites. In-plane spatial resolution, determined by the field-of-view and matrix sizes, will be kept ≤2 mm. Maintaining adequate temporal resolution is crucial when analyzing dynamic changes in aortic dimensions. The temporal resolution for this acquisition and will be required to be ≤30 ms (≤9 lines per segment or views per segment). This will result in a longer scanning (and breath-hold) time than for other cine images (12-25 s). Some tips for reducing scanning time without compromising the protocol requirements include:
  – Use parallel imaging if your scanner has that capability.
  – Orient the phase encoding axis of the field-of-view in the narrowest anatomic direction (typically anteroposterior). Minimize the field-of-view in this direction as much as possible, enabling wraparound artifacts. Make however sure that the artifact does not involve the ascending aorta.
  – Decrease slightly your matrix size, without violating the spatial resolution requirements.
  – Precede the breath-hold with a brief period of hyperventilation.
  – Oxygen supplementation may help some patients.

[†] View sharing allows for a decrease in effective temporal resolution, although the "real" temporal resolution of the acquisition may still be suboptimal and result in inaccuracies in volume measurements. Consequently, maintain the acquired lines per segment within the limits established by the CICL to ensure adequate temporal resolution.

Appendix 6 **Frequent Hemodialysis Network**
CARDIAC MRI MAILING FORM # 251

No technician may do an MRI on an FHN study patient until they have submitted two test case MRI's to the Cardiac MRI Core Laboratory (CICL) and received feedback that the test MRI's were performed and processed correctly. MRI's are assumed to have been done at the MRI site associated with the patient's participating dialysis unit as recorded in the study database. This form should be completed at the time of the MRI or (if *the MRI is not done*) at the end of the visit window for the MRI (if the MRI is not done, use the end date of the visit window as Date of MRI). If an MRI is done but is clearly of inadequate quality, repeat the MRI. Do not submit the MRI to the CICL and/or key enter a mailing form. When this form has been completed, it should be photocopied. The copy should be sent with the MRI images to the CICL; make sure it is a clear, clean copy. The original should be entered by a Clinical Center data entry person and kept with the patient's other completed study forms.

TO BE COMPLETED BY STUDY COORDINATOR:

									.								

1. Participant ID #   2. Alpha   3a. Visit   3b. Visit Number   4a. Date of MRI   dd/mon/yyyy
                                        Code   Type

5. Was the MRI done during the visit window? ....____

   1=Yes   5=No, logistic problem related to the FHN site
   2=No, patient refused   6=No, logistic problem related to the MRI site
   3=No, logistic problem related to the patient

If MRI done, continue. If not done, skip to item 200.

6.   Type of study...____
       1=Routine (in window)
       2=Make up for missed routine (in next window)
       3=Repeat

TO BE COMPLETED BY MRI TECHNICIAN:
Heart rate
7.   Heart Rate Measured at the Time of MRI (bpm) ....___ ___ ___

MRI

8.   Time of MRI ....(military) __ __ : __ __

9.   Was there sinus rhythm? (0 = No, 1 = Yes) ....__

10.   What was the gating? (1= ECG, 2 = pulse)..__

Left ventricular function

11. Position: 4-chamber view .... a. Series Number ____ ____   b. Slice position _____

Cine Short Axis

12. Position: Proximal to base .... a. Series Number ____ ____   b. Slice position _____

13. Position: Base .... a. Series Number ____ ____   b. Slice position _____

14. Next .... a. Series Number ____ ____   b. Slice position _____

15. Next .... a. Series Number ____ ____   b. Slice position _____

16. Next .... a. Series Number ____ ____   b. Slice position _____

17. Next .... a. Series Number ____ ____   b. Slice position _____

18. Next .... a. Series Number ____ ____   b. Slice position _____

19. Next .... a. Series Number ____ ____   b. Slice position _____

20. Next .... a. Series Number ____ ____   b. Slice position _____

21. Next .... a. Series Number ____ ____   b. Slice position _____

22. Next .... a. Series Number ____ ____   b. Slice position _____

23. Position: Apex .... a. Series Number ____ ____   b. Slice position _____

24. Position: Distal to Apex .... a. Series Number ____ ____   b. Slice position _____

Cine Long Axis

25. Position: 3-Chamber View .... a. Series Number ____ ____   b. Slice position _____

26. Position: 2-Chamber view .... a. Series Number ____ ____   b. Slice position _____

Aortic stiffness

27. Position: LV outflow tract .... a. Series Number ____ ____   b. Slice position _____

28. Position: Ascending aorta .... a. Series Number ____ ____   b. Slice position _____

----

29. Username of certified MRI tech who did this MRI. ....__ __ __ __ __ __ __ __

TO BE COMPLETED BY STUDY COORDINATOR:
30. Date shipped to CICL (dd/mon/yyyy).. __ __ /__ __ __ /__ __ __ __

200. Date this form completed (dd/mon/yyyy)……………………………….. __ __/__ __ __ /__ __ __ __

201. Username of person reviewing this form prior to data entry……………………__ __ __ __ __ __ __ __

FOR CLINICAL CENTER USE ONLY:
202. Username of person entering this form: __ __ __ __ __ __ __ __

203. Date Entered: (dd/mon/yyyy) __ __/__ __ __ /__ __ __ __

Appendix 7

Data Submission Form

FREQUENT DIALYSIS INVESTIGATORS

CENTER NUMBER

PATIENT STUDY IDENTIFICATION NUMBER

DATE OF CMRI
           (DD-MM-YYYY)   **TIME OF SCAN**

DATE SCAN SENT TO CORE LAB
                :   :

STUDY COORDINATOR SIGNATURE/DATE

_____

Please fax the completed form to the CICL together with the CMRI Mailing Form 251: 888-362-0639

Global left ventricular	Left ventricular end-dialstolic volume	**LVEDV**	155.90	mL
	Left ventricular end-diastolic volumne index	LVEDVI	66.06	mL/m^2
	Left ventricular end-systolic volume	**LVESV**	54.90	mL
	Left ventricular end-diastolic systolic index	LVESVI	23.26	mL/m^2
	Left ventricular stroke volume	LVSV	101.00	mL
	Left ventricular stroke volume index	LVSVI	42.80	mL/m^2
	Left ventricular ejection fraction	LVEF	64.79	%
	Left cardiac output	LCO	8,484.00	$L/m/m^2$
	Left cardiac index	LCI	3,595.14	L/m
Left ventricular mass	**Left ventricular mass**	**LVM**	139.50	g
	Left ventricular mass index	LVMI	59.11	g/m^2
Global right ventricular function	**Right ventricular end-diastolic volume**	**RVEDV**	94.00	mL
	Right ventricular end-diastolic volume index	RVEDVI	39.83	mL/m^2
	Right ventricular end-systolic volume	**RVESV**	33.00	mL
	Right ventricular end-diastolic systolic index	RVESVI	13.98	mL/m^2
	Right ventricular stroke volume	RVSV	61.00	mL
	Right ventricular stroke volume index	RVSVI	25.85	mL/m^2
	Right ventricular ejection fraction	RVEF	64.89	%
	Right cardiac output	RCO	5,124.00	$L/m/m^2$
	Right cardiac index	RCI	2,171.33	L/m
Segmental left ventricular	Absolute systolic thickening	AST	6.9	mm
	Relative systolic thickening	RST	88.97	%
	Wall motion score index	WMSI		
Aortic stiff	Maximal area	MAXA	5.18	cm^2
	Minimal area	MINA	4.64	cm^2
	Maximal diameter	MAXD	2.350	cm
	Minimal diameter	MIND	2.130	cm
	Compliance	C	0.0057	$cm^2/mmHg$
	Distensibility	D	0.0012	
	Elastic modulus	EM	833.33	
	Stiffness index	SI	6.81	
	Stiffness index (area method)	SIAREA	6.69	

Note: **Bold text** indicates measured value.