

Jackson Heart Study Protocol

Manual 6

Magnetic Resonance Imaging

Visit 3

Version 1.0

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FOREWORD

This manual is one of a series of protocols and manuals of operation for the Jackson Heart Study (JHS). The complexity of the JHS requires that a sizeable number of procedures be described, thus this rather extensive list of materials has been organized into the set of manuals listed below. Manual 1 provides the background, organization, and general objectives of the JHS. Manuals 2, 3, and 4 describe the Cohort Procedures, Blood Pressure and Central Laboratory and Specimen Repository Components of the study. Manuals 5 and 6 comprise Electrocardiography and Magnetic Resonance Image studies, respectively. Manual 7 comprises of Morbidity and Mortality Classifications. Manual 8 articulates the quality assurance and control activities of JHS Examination 3 components. Quality assurance includes activities that are designed to assure quality of data, which take place prior to the collection of data. Quality control relates to efforts during this study to monitor the quality of data. The Data Management System is described in Manual 9.

JHS Study Protocols and Manuals of Operation

MANUAL	TITLE
1	General Description and Study Management
2	Cohort Component Procedures
3	Blood Pressure
4	The Central Laboratory and Specimen Repository
5	Electrocardiography
6	Magnetic Resonance Imaging
7	Morbidity and Mortality
8	Quality Control
9	Data Management

Participant preparation (Page 2):

1. Blood Pressure
2. Patient setup

Brief scan overview:

1. Localizers (Scan 1-6)
2. Baseline white blood function (EF, morphometry- PIE software)
 - a. Four chamber (Scan 7)
 - b. Two chamber (Scan 8)
 - c. Three chamber (Scan 9)
 - d. Short axis stack (extend through atria) (Scan 10)
3. Short axis tagging – base, mid, apex with paired vertical and horizontal tags (results in 6 series- Intramyocardial strain use HARP software)
 - a. Base – horz & vertical (Scan 11 & 12)
 - b. Mid – horz & vert (Scan 13 & 14)
 - c. Apex –horz and vert (Scan 15 & 16)
4. Aorta Measurements
 - a. LAO Phase contrast (Scan 17)
 - b. Dark blood T2 aortic arch (Scan 18)
 - c. AX phase contrast aortic arch (Scan 19)
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 - h. AX phase contrast below renals (Scan 24)
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 - j. AX phase contrast above bifurcation (Scan 26)

Appendix ACardiac Magnetic Resonance Imaging with Contrast (pages 1-13)

Participant Preparation

1. Blood Pressure (measured after sitting 5 min).
2. Participant Setup for Cardiac scan
 - a. Place the three ECG leads on chest for Siemens Cardiac gating per training.
 - b. Attach PG sensor to finger.
 - c. Place headphones.
 - d. Place the two body matrix coils: one on chest, other on abdomen.
 - e. Instruct patient in proper breathing for scan: breathe in, breathe out, breathe in and hold it (not too deep).

Scan 1: 3-plane localizer Chest

Coil	Body Matrix
Plane	3-planes
FOV	400 mm
Slice thickness	7 mm
Spacing	
Averages	1
Matrix	240 x 384
Phase FOV	
Bandwidth	1130
TR	230
TE	1.1
Flip angle	65
Gating	cardiac
Sequence Variant	Tfi2dl_72
Sequence name	LOC_Trufi_MULTI Chest

Instructions: You should get a total of 11 images (1-3 sagittal, 4-6 coronal & 7-11 axial)

Scan 2: 3-plane localizer Abdomen

Coil	Body Matrix
Plane	3-planes
FOV	400 mm
Slice thickness	7 mm
Spacing	
Averages	1
Matrix	240 x 384
Phase FOV	
Bandwidth	1130
TR	230
TE	1.1
Flip angle	65
Gating	cardiac
Sequence Variant	Tfi2dl_72
Sequence name	LOC_Trufi_MULTIAbdomen

Instructions: You should get a total of 11 images (1-3 sagittal, 4-6 coronal & 7-11 axial)

Scan 3: localizer 2-Chamber (vertical long axis)

Coil	Body Matrix
Plane	oblique
FOV	400 mm
Slice thickness	7 mm
Spacing	
Averages	1
Matrix	144 x 192
Phase FOV	
Bandwidth	1130
TR	260
TE	1.1
Flip angle	65
Gating	
Sequence Name	LOC_Trufi_2CH

Instructions: 1 slice localizer plotted from the prior localizer which shows the left atrium and left ventricle.

Scan 4: localizer Short Axis (10 slices, base to apex)

Coil	Body Matrix
Plane	oblique
FOV	400 mm
Slice thickness	7 mm
Spacing	
Averages	1
Matrix	144 x 192
Phase FOV	
Bandwidth	1130
TR	260
TE	1.1
Flip angle	65
Gating	
Sequence Name	LOC_Trufi_SAX

Instructions: 10 slice localizer plotted from the 2 chamber localizer which shows the left atrium and left ventricle (only 4 of 10 shown below).

Scan 5: localizer 4-Chamber

Coil	Body Matrix
Plane	oblique
FOV	400 mm
Slice thickness	7 mm
Spacing	
Averages	1
Matrix	144 x 192
Phase FOV	
Bandwidth	1130
TR	260
TE	1.1
Flip angle	65
Gating	
Sequence Name	LOC_Trufi_4CH

Instructions: 1 slice localizer plotted from the prior short axis localizer.

Scan 6: localizer 3-Chamber

Coil	Body Matrix
Plane	oblique
FOV	400 mm
Slice thickness	7 mm
Spacing	
Averages	1
Matrix	144 x 192
Phase FOV	
Bandwidth	1130
TR	260
TE	1.1
Flip angle	65
Gating	
Sequence Name	LOC_Trufi_3CH_LOC

Instructions: 1 slice localizer plotted from the prior short axis localizer showing the left atrium, left ventricle and aortic root.

Scan 7: Cine 4 Chamber

Coil	Body Matrix
Plane	Oblique
FOV	400 mm
Slice thickness	7 mm
Spacing	20% 1.4 mm
Averages	1
Matrix	156 x 192
Phase FOV	81.3%
Bandwidth	930
TR	37.38
TE	1.13
Flip angle	82
Gating	cardiac
Option	
Sequence Variant	Tfi2d1_14
Sequence Name	Trufi_4CH_CINE

Instructions: 4 chamber CINE images (“true fisp” or trufi), one level, with ~ 25 images showing a beating heart.

Scan 8: Cine 2 Chamber

Coil	Body Matrix
Plane	Oblique
FOV	400 mm
Slice thickness	7 mm
Spacing	20% 1.4 mm
Averages	1
Matrix	156 x 192
Phase FOV	81.3%
Bandwidth	930
TR	37.38
TE	1.13
Flip angle	82
Gating	cardiac
Option	
Sequence Variant	Tfi2d1_14
Sequence Name	Trufi_2CH_CINE

Instructions: 2 chamber CINE images (“true fisp” or trufi), one level, with ~ 25 images showing a beating heart.

Scan 9:

Cine 3 Chamber

Coil	Body Matrix
Plane	Oblique
FOV	400 mm
Slice thickness	7 mm
Spacing	20% 1.4 mm
Averages	1
Matrix	156 x 192
Phase FOV	81.3%
Bandwidth	930
TR	37.38
TE	1.13
Flip angle	82
Gating	cardiac
Option	
Sequence Variant	Tfi2d1_14
Sequence Name	Trufi_3CH_CINE

Instructions: 3 chamber CINE images (“true fisp” or trufi), one level, with ~ 25 images showing a beating heart.

Scan 10: Cine Short Axis Stack – Entire LV

Coil	Body Matrix
Plane	Oblique (short Axis)
FOV	400 mm
Slice thickness	8 mm
Spacing	25% 2 mm
Averages	1
Matrix	109 x 192
Phase FOV	81.3%
Bandwidth	930
TR	45.54
TE	1.07
Flip angle	78
Gating	cardiac
Option	Concatenations = 12
Sequence Variant	Tfi2d1_18
Sequence Name	Trufi_SAX_Stack

Instructions: 2 chamber CINE images (“true fisp” or trufi), five levels from the apex of the LV through the left atrium (apex, mid, base, LA-Ao, LA posterior), resulting ~ 275 images (11 series of ~25 images each) showing a beating heart.

Scan 11 & 12: Tagging Cine Short Axis Base of LV

Coil	Body Matrix
Plane	Oblique (short Axis, Base of LV)
FOV	400 mm
Slice thickness	8 mm
Spacing	25% 2 mm
Averages	1
Matrix	192 x 256
Phase FOV	75%
Bandwidth	170
TR	60
TE	4
Flip angle	12
Gating	ECG trigger (prospective)
Segments	7
Option	
Sequence Variant	FI2d1r5
Sequence Name	TAG_Grid_Base_SAX of LV

Instructions: Short axis tagging image through the base of the Left ventricle. Be sure that the tag lines are clearly visible throughout the cardiac cycle, if not repeat.

Scan 13 & 14: Tagging Cine Short Axis Mid Cavity of left Ventricle

Coil	Body Matrix
Plane	Oblique (short Axis, Mid cavity of LV)
FOV	400 mm
Slice thickness	8 mm
Spacing	25% 2 mm
Averages	1
Matrix	144 x 256
Phase FOV	75%
Bandwidth	170
TR	41.1
TE	3.75
Flip angle	78
Gating	ECG trigger (prospective)
Option	
Sequence Variant	FI2d1r5
Sequence Name	TAG_Grid_Mid_SAX of LV

Instructions: Short axis tagging image through the Mid (Papillary muscle level) of the Left ventricle. Be sure that the tag lines are clearly visible throughout the cardiac cycle, if not repeat.

Scan 15 & 16: Tagging Cine Short Axis Apex

Coil	Body Matrix
Plane	Oblique (short Axis, Apex of LV)
FOV	400 mm
Slice thickness	8 mm
Spacing	25% 2 mm
Averages	1
Matrix	144 x 256
Phase FOV	75%
Bandwidth	170
TR	41.1
TE	3.75
Flip angle	78
Gating	ECG trigger (prospective)
Option	
Sequence Variant	FI2d1r5
Sequence Name	TAG_Grid_Apex_SAX of LV

Instructions: Short axis tagging image through the apical region of the Left ventricle. Be sure the tag lines are clearly visible throughout the cardiac cycle, if not repeat.

Scan 17: Phase contrast LAO Thoracic Aorta

Coil	Body Matrix
Plane	Oblique
FOV	460 mm
Slice thickness	8 mm
Spacing	0
Averages	1
Matrix	128 x 128
Phase FOV	100%
Bandwidth	387
TR	80.65
TE	3.45
Flip angle	15
Gating	Peripheral gating (PG)
Option	
Sequence Variant	FI2d1_6
Sequence Name	PC LAO Thoracic Aorta & PC LAO Thoracic Aorta_P

Instructions: This will be a CINE image of the “Candy-cane” view of the thoracic aorta plotted from the prior axial image. Two series of ~30 images will be generated (magnitude and velocity).

Scan 18: Dark Blood T2 Fatsat Thoracic Aorta

Coil	Body Matrix
Plane	Axial
FOV	300 mm
Slice thickness	6 mm
Spacing	0
Averages	1
Matrix	320 x 320
Phase FOV	80% (Phase encode A-P)
Bandwidth	179
TR	800
TE	89
Flip angle	180
Gating	cardiac
Option	Fat sat
Sequence Variant	Tse2d1_11
Sequence Name	DBT2 FS Ax DESC_AO-diaphragm

Instructions: plotted from the 3 plane localizer of the chest at the level of the right pulmonary artery.

Scan 19: Phase contrast Axial Thoracic Aorta

Coil	Body Matrix
Plane	Axial
FOV	360 mm
Slice thickness	8 mm
Spacing	0
Averages	1
Matrix	108 x 192
Phase FOV	75%
Bandwidth	389
TR	76.55
TE	3.14
Flip angle	15
Gating	ECG trigger, prospective
Option	
Sequence Variant	flfqshph
Sequence Name	PC AX Thoracic Aorta & PC AX Thoracic Aorta_P

Instructions: This will be at the same axial level through the ascending and descending aorta as the dark blood T2 images. CINE phase contrast images throughout the cardiac cycle will generate two series of ~30 images will be generated (magnitude and velocity).

Scan 20: TRUFI abd aorta localizer

Coil	Body Matrix
Plane	Coronal
FOV	440 mm
Slice thickness	7 mm
Spacing	0
Averages	1
Matrix	256 x 166
Phase FOV	81%
Bandwidth	977
TR	2.62
TE	1.11
Flip angle	70
Gating	nongated
Option	
Sequence Variant	tfi 2d1
Sequence Name	LOC_ABD_Aorta_trufi

Instructions: This will be a CINE image of the of the abdominal aorta plotted from localizers to include the aorta from the diaphragm through the aortic bifurcation. Typically you should oblique the image based on the sagittal image to center the abdominal aorta in the slice plane. Two series of ~30 images will be generated (magnitude and velocity).

Scan 21: Dark Blood T2 Fatsat Abdominal Aorta - diaphragm

Coil	Body Matrix
Plane	Axial
FOV	200 mm
Slice thickness	5 mm
Spacing	0
Averages	4
Matrix	320 x 320
Phase FOV	80% (Phase encode A-P)
Bandwidth	179
TR	800
TE	26
Flip angle	180
Gating	cardiac
Option	SPAIR Fat sat
Sequence Variant	Tse2d1_17
Sequence Name	DB T2 FS AX DESC_AO-diaphr

Instructions: Plotted at the diaphragm on the aorta localizer of the abdomen.
Non-breathheld.

NOTE:

Scan 22: Phase contrast Axial Abdominal Aorta - diaphragm

Coil	Body Matrix
Plane	Axial
FOV	360 mm
Slice thickness	4 mm
Spacing	0
Averages	1
Matrix	108 x 192
Phase FOV	75%
Bandwidth	389
TR	76.55
TE	3.14
Flip angle	15
Gating	ECG trigger, prospective
Option	
Sequence Variant	flfqshph
Sequence Name	PC AX DESC_AO-diaphragm & PC AX DESC_AO-diaphragm_P

Instructions: Plotted at the diaphragm, the same as the previous T2 scan. CINE phase contrast images throughout the cardiac cycle will generate two series of ~30 images will be generated (magnitude and velocity) for each location.

Scan 23: Dark Blood T2 Fatsat Abdominal Aorta - renals

Coil	Body Matrix
Plane	Axial
FOV	200 mm
Slice thickness	5 mm
Spacing	0
Averages	4
Matrix	320 x 320
Phase FOV	80% (Phase encode A-P)
Bandwidth	179
TR	800
TE	26
Flip angle	180
Gating	cardiac
Option	SPAIR Fat sat
Sequence Variant	Tse2d1_17
Sequence Name	DB T2 FS AX ABD AOR-renals

Instructions: Plotted 2cm below the renal arteries on the abdominal aorta localizer.

NOTE: Non-breathheld.

Scan 24: Phase contrast Axial Abdominal Aorta - renals

Coil	Body Matrix
Plane	Axial
FOV	360 mm
Slice thickness	4 mm
Spacing	0
Averages	1
Matrix	108 x 192
Phase FOV	75%
Bandwidth	389
TR	76.55
TE	3.14
Flip angle	15
Gating	ECG trigger, prospective
Option	
Sequence Variant	flfqshph
Sequence Name	PC AX DESC_AO-Renals & PC AX DESC_AO-Renals_P

Instructions: Plotted 2cm below renals, the same as the previous T2 scan. CINE phase contrast images throughout the cardiac cycle will generate two series of ~30 images will be generated (magnitude and velocity) for each location.

Scan 25: Dark Blood T2 Fatsat Abdominal Aorta - bifurcation

Coil	Body Matrix
Plane	Axial
FOV	200 mm
Slice thickness	5 mm
Spacing	0
Averages	4
Matrix	320 x 320
Phase FOV	80% (Phase encode A-P)
Bandwidth	179
TR	800
TE	26
Flip angle	180
Gating	cardiac
Option	SPAIR Fat sat
Sequence Variant	Tse2d1_17
Sequence Name	DB T2 FS AX ABD Aorta-Bifu

Instructions: Plotted 2cm above the aortic bifurcation.

NOTE: Non-breathheld.

Scan 26: Phase contrast Axial Abdominal Aorta - bifurcation

Coil	Body Matrix
Plane	Axial
FOV	360 mm
Slice thickness	4 mm
Spacing	0
Averages	1
Matrix	108 x 192
Phase FOV	75%
Bandwidth	389
TR	76.55
TE	3.14
Flip angle	15
Gating	ECG trigger, prospective
Option	
Sequence Variant	flfqshph
Sequence Name	PC AX ABD Aorta-bifurcati & PC AX ABD Aorta-bifurcati_P

Instructions: Plotted 2cm above aortic bifurcation, the same as the previous T2 scan. CINE phase contrast images throughout the cardiac cycle will generate two series of ~30 images will be generated (magnitude and velocity) for each location.

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Appendix A

**Jackson Heart Study (JHS) Exam 3
Cardiac Magnetic Resonance Imaging
Acquisition Protocol with Contrast****October 21, 2009****Overview**

The purpose of this cardiac MR protocol is to image the heart and aorta in ~5,000 African Americans located in the Jackson, Mississippi metropolitan area. The Jackson Heart Study (JHS) is a cohort study of community dwelling participants. They are not acutely ill but do reflect the spectrum of subclinical and clinical disease in the community. In this study we will gather data regarding left ventricular volumes/mass/ejection fraction, quantitative measures of left ventricular (LV) contraction (tagging), and measures of blood flow (vascular stiffness) and wall thickness in the thoracic aorta.

The protocol will measure the following domains of information:

1. Structural and functional measures of the heart, including ejection fraction, LV volumes, myocardial mass and thickness per myocardial segment.
2. Subclinical atherosclerosis in the aorta (wall thickness)
3. Vascular compliance and pulse wave velocity in the aorta
4. Regional (intramyocardial) motion and mechanical strain (Tagging)
5. Delayed Enhancement Imaging / Myocardial fibrosis (sub-study)

Generalizability of the CMR Protocol and Results:

To achieve the maximum benefit, the design of the JHS Cardiac Magnetic Resonance (CMR) protocol has been made consistent with previous NHLBI studies, specifically the Multi-Ethnic Study of Atherosclerosis (MESA). Both Drs. Carr and Hundley at Wake Forest are part of the MESA CMR imaging committee and participated in the development of the original baseline exam in 2000 as well as subsequent ancillary studies. Thus the JHS baseline protocol, including strain (aka "tagging") protocol is based on the MESA experience. Dr. Joao Lima of Johns Hopkins is the PI of the MESA exam 5 MRI reading center and a consultant to the JHS Reading center. Dr. David Bluemke, currently chair of Radiology at NIH intramural program and former PI of the MESA MRI reading center is a non-paid consultant for the Delayed Enhancement (DE) sub-study.

The study will be performed on a high-gradient, parallel-channel (TIM) cardiac MRI system (Siemens Espree) located at the Pavilion outpatient center of the University of Mississippi Medical Center. The participant will be scanned in a resting state and there is no need for the administration of medications or contrast agents unless the participant has been selected and consented to participate in the contrast sub-study. The protocol is

standardized so adherence to the protocol is mandatory. If a series or breath-hold is suboptimal the technologist should repeat the series making the appropriate adjustments.

Once proficient in scanning, the base protocol (without contrast) should be completed in less than 40 minutes. The delayed enhancement sub-study will require additional set-up and preparation time related to the administration of contrast as detailed subsequent; however, it is estimated that the actual room time required will only be an additional 10 minutes (total room time less than 50 minutes).

Timeline/Protocol Enhancements:

Exam 2: start June 2, 2008 - Dec, 2008 (n=263 exams) - protocol includes measures of LV structure-function, LV myocardial strain (tagging) and aortic wall thickness and pulse wave velocity/compliance.

Exam 3: start March 1, 2009 - protocol for exam 3 same as exam 2, with minor enhancements made to phase contrast sequences of the aorta to enhance pulse wave velocity measures.

Exam 3 + Myocardial Delayed Enhancement (Summer 2009) - a subset of of JHS participants will be consented to participate in post contrast imaging using delayed enhancement protocol.

Protocol Development

There is the capability on Siemens MRI systems to share protocols via a CD termed "Phoenixing". Basically the protocol can be built on a system, saved to CD media and then loaded as a protocol on similar systems. The Wake Forest Reading Center has a Siemen's Avanto cardiac MRI and Univ. Mississippi has a Siemen's Espree both upgraded to the the Siemens syngo B15 software and with the same advance cardiac package (ACP) pulse sequence library. We have successfully developed and transferred the based CMR protocols for JHS Exam 2 and Exam 3 and will follow a similar procedure for the DE sub-study protocol.

Gadolinium Safety Procedures Development:

Drs. Bluemke, Lima and Carr have participated in the development of the safety procedures (inclusion and exclusion criteria) for the administration of intravenous gadolinium DTPA for Exam 5 in MESA scheduled to being June 2010. As part of this process, the MESA nephrology working group and MRI imaging committee worked together to develop appropriate screening criteria for participants prior to injection of gadolinium based on the most current available data from the literature and FDA as of spring 2009 to minimize risk of Nephrogenic Systemic Fibrosis (NSF). We have incorporated these same criteria into the JHS safety procedures.

Potential Consent Language:

This language was approved for the MESA cardiac MRI exam which is very similar to the JHS CMR exam:

Magnetic resonance imaging (MRI): The MRI exam is limited to the evaluation of the size and function of your heart and aorta. No other organs or systems will be evaluated as a part of this study. For this exam, you will need to lie still on a table and be placed inside of a large device that takes pictures of your heart using magnetic fields and radiowaves (the exam takes about 30-40 minutes). The MRI machine does not use ionizing radiation (such as X-rays), and is considered safe. There is also no discomfort or physical pain. Prior to having the MRI exam, you will be asked questions about your medical history including whether you 1) have metal clips or fragments in your eyes, brain or spinal cord, 2) have a pacemaker, artificial heart valve, ear implant, or spinal cord stimulator, and 3) might be pregnant (if female).

MRI with Gadolinium Contrast Sub-Study:

If you are selected as part of the MRI contrast sub-study, we will ask additional questions and perform a blood test. The contrast agent used for the study, called gadolinium, is injected through a vein in your arm. It is widely used all over the world with MRI exams and has a good record of safety. However, in sick patients with severe kidney disease (kidney failure) a rare disease called Nephrogenic Systemic Fibrosis (NSF) has been observed. NSF has not been seen in people with normal or even slightly below normal renal function. As a precaution for this rare event we will make sure that your kidneys are working well and that you have not had major problems in the past with your kidneys. If you have had failure of your kidneys, a kidney transplant or liver failure you will not be eligible. Also, you will not be able to participate in the contrast MRI sub-study if you had an MRI with contrast in the past months. Before giving you the gadolinium contrast, we will draw a blood sample from your arm to check and measure how well your kidneys are filtering your blood, a measure called effective glomerular filtration rate (eGFR). Most people do not feel anything when the contrast agent is given.

Setup (15 minutes prior to scan & 105 minutes in MRI suite)

- Perform the MRI safety prescreening
- Greet and direct the participant into the MRI scanner suite
Attach ECG gating, respiratory bellows, Blood Pressure cuff, and pulse oximeter. (Note that ideally an external MRI compatible monitor is recommended to monitor during the exam and to serve as an alternative means for cardiac gating (ECG and pulse ox))
- Select the “JHS CMR protocol” and begin the exam
- Automatically network the exam to “WFUHS_Reading Center”
- Fax completed MRI Worksheet to the WFU JHS Reading Center
336.716.4340

Scanning Notes:

- All scans are performed during suspended inspiration (“holding the breath in”). It is critical that the technologist work with the participant to understand and perform breath holding appropriately. This will maximize image quality.
- If for some reason a sequence is suboptimal the technologist should immediately repeat that sequence.

Delayed Enhancement Imaging of the Myocardium

A subgroup of JHS participants in exam 3 will be recruited to participate in a sub-study designed to identify individuals with myocardial fibrosis from ischemic (myocardial infarction) and non-ischemic sources. This is based on the ability of cardiac MRI using a imaging after administration of gadolinium based contrast agents to identify delayed enhancement (DE). DE-CMR can with extremely high accuracy identify fibrosis and inflammation in the myocardium by location in the left ventricle and layer of the myocardium. This methodology was developed by Kim et. al. [1, 2] and applied in clinical and population-based studies [3]. This subgroup of participants will have to meet eligibility and exclusion criteria and sign an informed consent addendum that details the expanded protocol which consists of injection of intravenous gadolinium DTPA and additional imaging sequences of the heart requiring approximately 10 minutes.

Background on Delayed Enhancement (DE)**Scan Sequences Eligibility and Exclusion****Criteria**

If the participant meets the following criteria they will be eligible for the cardiac MRI with contrast sub-study

- Meets criteria eligible for MRI (JHS MRI safety Screening Form) - this is a two stage process initially performed by JHS clinic personnel prior to MRI scheduling and then repeated by the MRI technologist prior to entering the MRI suite. This includes all the standard exclusion criteria related to implanted devices and foreign bodies.

Additional Exclusion Criteria for Contrast MRI Sub-Study:

- 1 Have you ever had failure of your kidneys?
- 2 Have you had a kidney transplant?
- 3 Have you ever had liver failure?
Do you have a known allergy to MRI contrast agents - commonly referred to as “Gadolinium”?
- 4 Have you received MRI contrast (i.e., gadolinium) for another reason in the past month? If “Yes” to any of the questions above the participant will be excluded from the MRI contrast sub-study (If yes –exclude).

Rationale - Gadolinium contrast agents are cleared from the body by the kidney and to a lesser extent the liver. Individuals with a history of kidney and liver failure or kidney transplant are excluded from the research protocol as an

added margin of safety, without respect to their current level of renal function.

Additional Renal Function Testing Prior to Gadolinium Contrast Administration

Because of the small but potentially significant risk in individuals with extreme renal insufficiency or failure for the development of nephrogenic systemic fibrosis (NSF), we will test renal function in everyone prior to gadolinium administration to ensure that individuals with significant impairment in renal function are excluded from the MRI contrast sub-study. Rationale for using the eGFR is provided by the NIH's National Kidney Disease Education Program guidance to clinical laboratories:

"In adults ages 18 years and older the Modification of Diet in Renal Disease (MDRD) Study equation has been shown to be reliable in estimating GFR from serum creatinine, when the patient's age, gender, and race are also known.^{1,2} Use of the MDRD Study equation to estimate GFR is the best means currently available to more appropriately utilize serum creatinine values as a measure of kidney function. The MDRD Study equation has been validated extensively in Caucasian and African American populations with impaired kidney function (eGFR <60 mL/min/1.73m²), and ages between 18 and 70 years. The MDRD Study equation has shown good performance for patients with all common causes of kidney disease, including kidney transplant recipients.³"^[4]

- 1 The estimated glomerular filtration rate (eGFR) based on serum creatinine and the Modification of Diet in Renal Disease (MDRD) Study equation will be used to determine the current renal function of participants prior to MRI scan.
- 2 Following arrival at the MRI scan site, point of care testing will be performed and a serum creatine obtained. From the serum creatinine, the eGFR will be determined and recorded.
- 3 **Individuals with a eGFR \geq 45 ml/min/1.73m² will be eligible.**
- 4 If the eGFR is < 45 ml/min/1.73m² the participant will be excluded from contrast sub-study but is still eligible for the base JHS CMR exam protocol which does not require IV gadolinium contrast administration.
- 5 If for any reason the individual is unable to complete the MRI exam, the measurement of serum creatinine and eGFR should be repeated prior to proceeding with contrast administration if the time period is greater than 48 hours from the last measurement or unknown time interval.
- 6 The creatinine and eGFR will be recorded on the MRI worksheet, along with details of the contrast administration discussed below.

Intravenous (IV) injection protocol for administration of MRI contrast agent

The MRI technologists will complete the pre-exam screening procedures as detailed above. Then with the participant seated, identify an antecubital vein, cleanse the skin with alcohol and obtain intravenous access with a butterfly needle or equivalent (20-22 ga). Following confirmed IV access, 0.15 mmol / kg of body weight of gadopentetate dimeglumine (Magnevist) will be administered

IV manual push at a rate of 1 mL/sec followed by 20 mL of saline flush. The needle will be removed and cotton gauze applied. The volume and time of injection will be recorded on the MRI worksheet. The elapsed timer (provided by the reading center) will be started at the operator console.

15 minute wait period between injection and DE imaging sequences

The participants receiving the Gadolinium Injection will proceed with the standard JHS CMR protocol (see JHS CMR Exam 3 protocol for details). Once the elapsed time reaches 10 minutes, the technologists will stop the base protocol and execute the DE sequences detailed below. Note that the time of injection and time for TI scout start will be recorded on the MRI worksheet. Once the DE imaging sequences have been completed the base JHS CMR protocol will be completed.