BRIGHAM AND WOMEN'S HOSPITAL
HARVARD MEDICAL SCHOOL

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ATHEROSCLEROSIS RISK IN COMMUNITIES

ARIC

VISIT 7

ECHOCARDIOGRAPHY
FIELD CENTER MANUAL OF OPERATIONS

Version: 01-07-2018

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I. Introduction

Approximately 6,200 participants in the NHLBI Atherosclerosis Risk in the Communities (ARIC) study underwent comprehensive echocardiography between 2011-2013 at the fifth study visit. Repeat echocardiography will now be performed at the seventh study visit according to the protocol outlined in this manual. Serial echocardiograms in elderly participants, performed on average 5 years apart, will permit quantification of longitudinal changes in cardiac structure and function, definition of the factors predicting these changes, and determination of the association of these longitudinal changes with heart failure symptoms and hospitalization. These findings will clarify the pathophysiology leading to heart failure in the elderly. Given the key importance of longitudinal changes in echocardiographic measures, a high priority of the imaging protocol at Visit 7 is comparability to the imaging approach employed at Visit 7. To this end, the same echocardiography equipment (machines, probes) will be used as at Visit 5.

The Brigham & Women's Hospital Cardiac Imaging Core Laboratory (CICL) in Boston, Massachusetts will serve as the Echocardiography Reading Center for the ARIC Visit 7. This manual contains key information Field Centers need to perform high quality study echocardiograms.

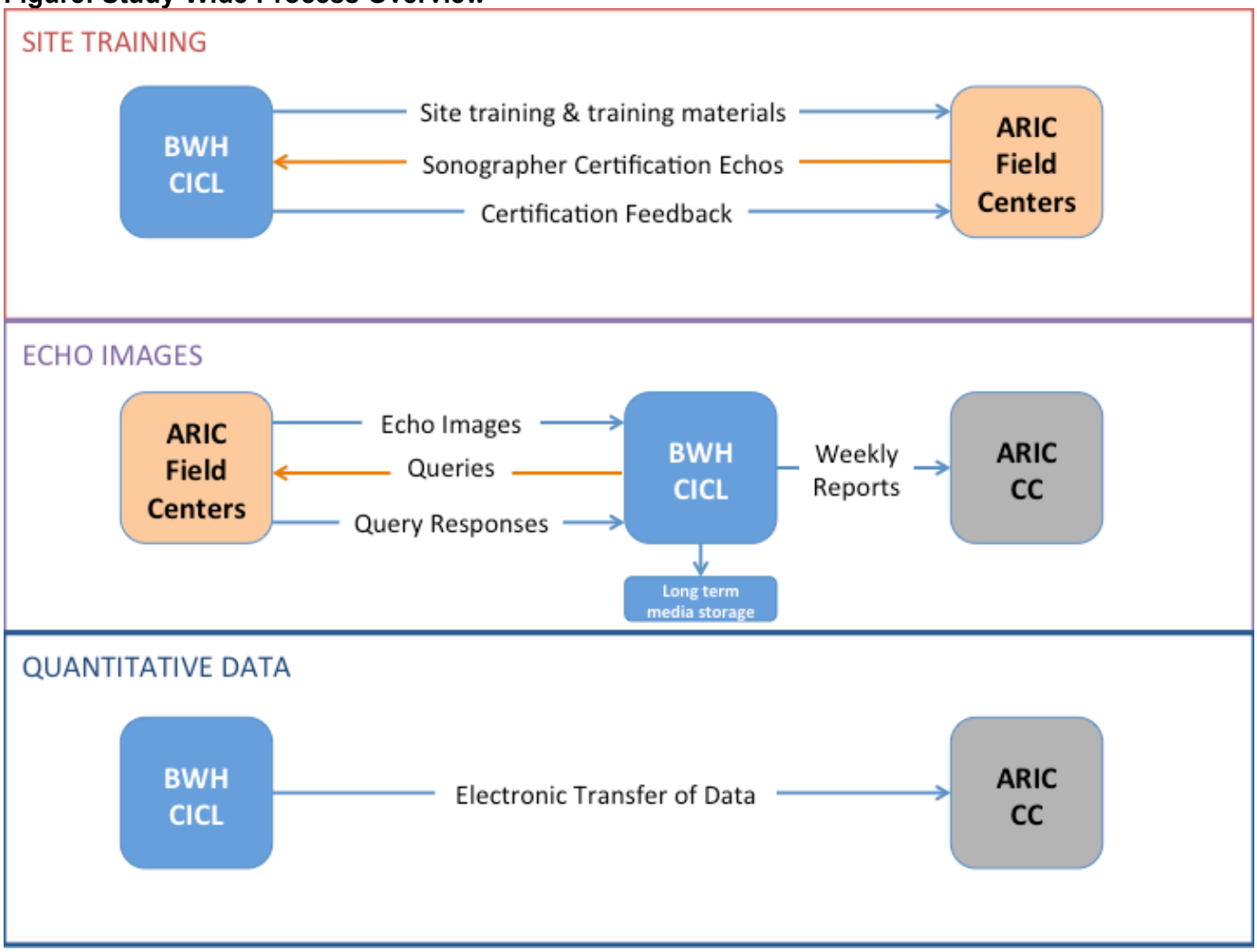
OBJECTIVES	
Cardiac Imaging Core Lab	• To provide high quality reproducible quantitative analysis of study echocardiograms
Site Instruction Manual	• To instruct field centers on how to perform and send study echos to the Cardiac Imaging Core Lab (CICL).

ROLES AND RESPONSIBILITIES	
Field Centers Sonographers	• Perform highest-quality study echocardiograms per the protocol contained in this document • Participate in monthly ARIC Echocardiography Sonographer calls
Field Center Sonographers, Study Coordinators, and PIs	• Ensure that the CICL stays informed of study-wide changes and updates as the study progresses. • Serve as the primary liaison between the CICL and field centers for study deficiencies, chronic poor quality studies and other issues related to overall site performance. • Provide oversight and support, as required, for the entire process
Cardiac Imaging Core Lab	• Receive, review and analyze study echos. • Train and certify each field center sonographer. • Provide field centers feedback on poor quality echos, and queries for technical/process improvement. • Serve as a resource for sites for all echo-related questions.

II. Study-Wide Process Overview

Field centers will electronically transmit echos directly to the Cardiac Imaging Core Lab (CICL). Below is a basic diagram to describe the study wide process that will occur.

Figure: Study-Wide Process Overview



III. Site Training

Sonographers at each Field Center will undergo the following on-site training:

1. Two days of dedicated Philips training as in-service on the features and functionality of the iE33 machines, use of the pre-programmed ARIC protocol, image optimization approaches, and 3D-image acquisition
2. Two days of ARIC Visit 7 echocardiography-specific training performed by ERC PI (Dr Amil Shah) and the CICL Chief Sonographer (Dr Jose Rivero). Training will focus on the ARIC Visit 7 imaging protocol (including live supervised scanning on models), electronic image transfer, procedures for handling potential clinical alerts based on echocardiographic findings.

Following on-site training, and prior to submission of certification echocardiograms (section IV below), Field Center sonographers will be required to perform the complete ARIC Visit 7 imaging protocol on 4 volunteers, and to transmit these studies to the CICL.

IV. Sonographer Certification

The purpose of certification is to ensure consistency in how echocardiograms are performed study-wide and to ensure performance of the highest quality echocardiograms. Any sonographer who will be performing study echocardiograms must first submit two certification studies performed in accordance with the protocol described in this manual and transferred electronically to the CICL for review and certification.

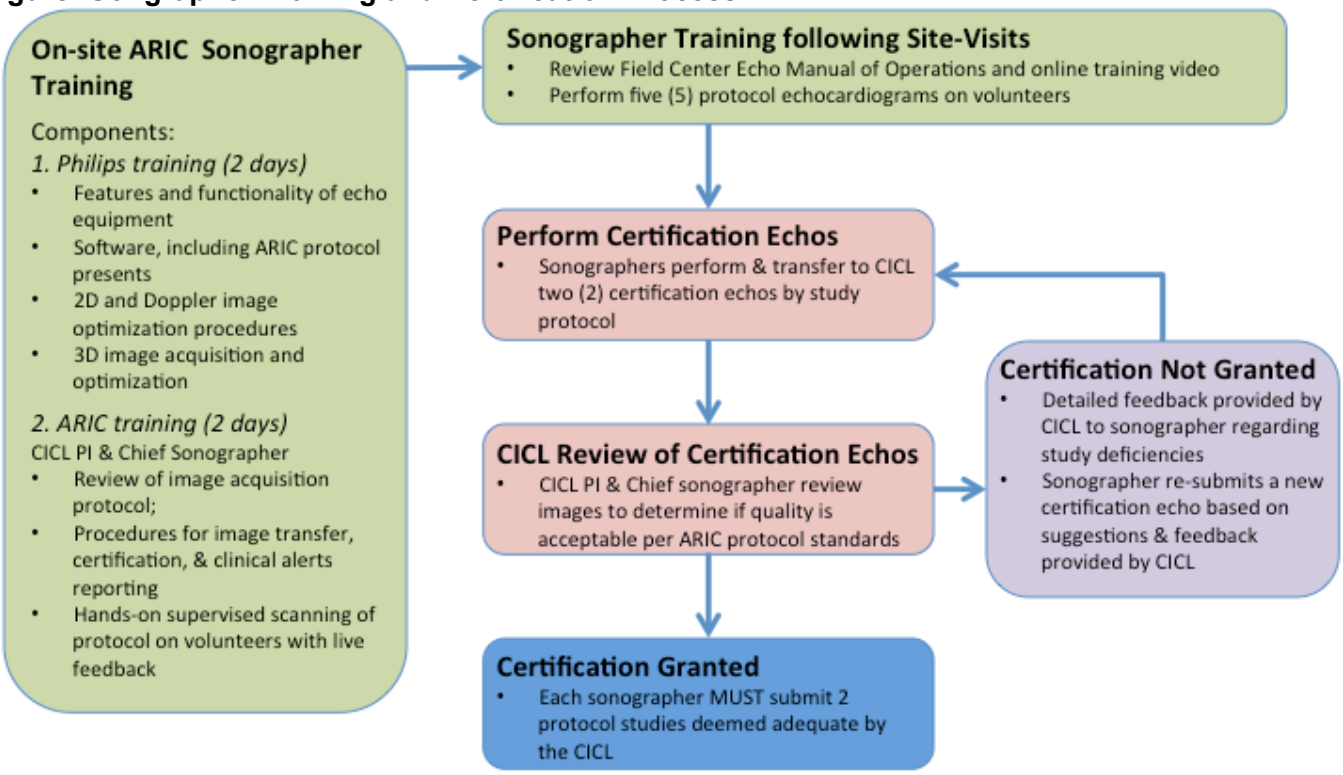
Studies will be scrutinized for adherence to protocol, acquisition of all required views, and image quality. Itemized direct written feedback and suggestions from the technical project manager will be provided for each study submitted. This is intended to address any individual equipment or operator dependent problems that may arise. Sonographers will have the opportunity to re-submit a sample protocol study should the initial submission be inadequate. Following submission of an adequate sample study, the sonographer will be officially certified and will receive feedback documenting this.

New Field Center sonographers starting during the study period will be required undergo the certification process outlined above by submitting 2 sample protocol studies in order to demonstrate the ability to perform a technically adequate protocol study and the knowledge to successfully transmit this data to the CICL.

A general outline of the process is outlined below. Prior to performing and submitting a sample study for certification, the following steps are recommended:

1. Read and review this Site Manual of Operations and refer to the ARIC Visit 7 Echo Pocket Guide during performance of the echocardiogram. The instructional video available on the ARIC Visit 7 Echocardiography Reading Center website is an additional resource. This is considered supplemental and is not a requirement to receive certification.
2. Contact the CICL for any questions before performing and submitting the certification echo to the CICL.
3. Send the certification echo to the CICL – per the instructions provided in this manual.

Figure: Songrapher Training and Certification Process



V. Submission of Studies from the Field Center to the Reading Center

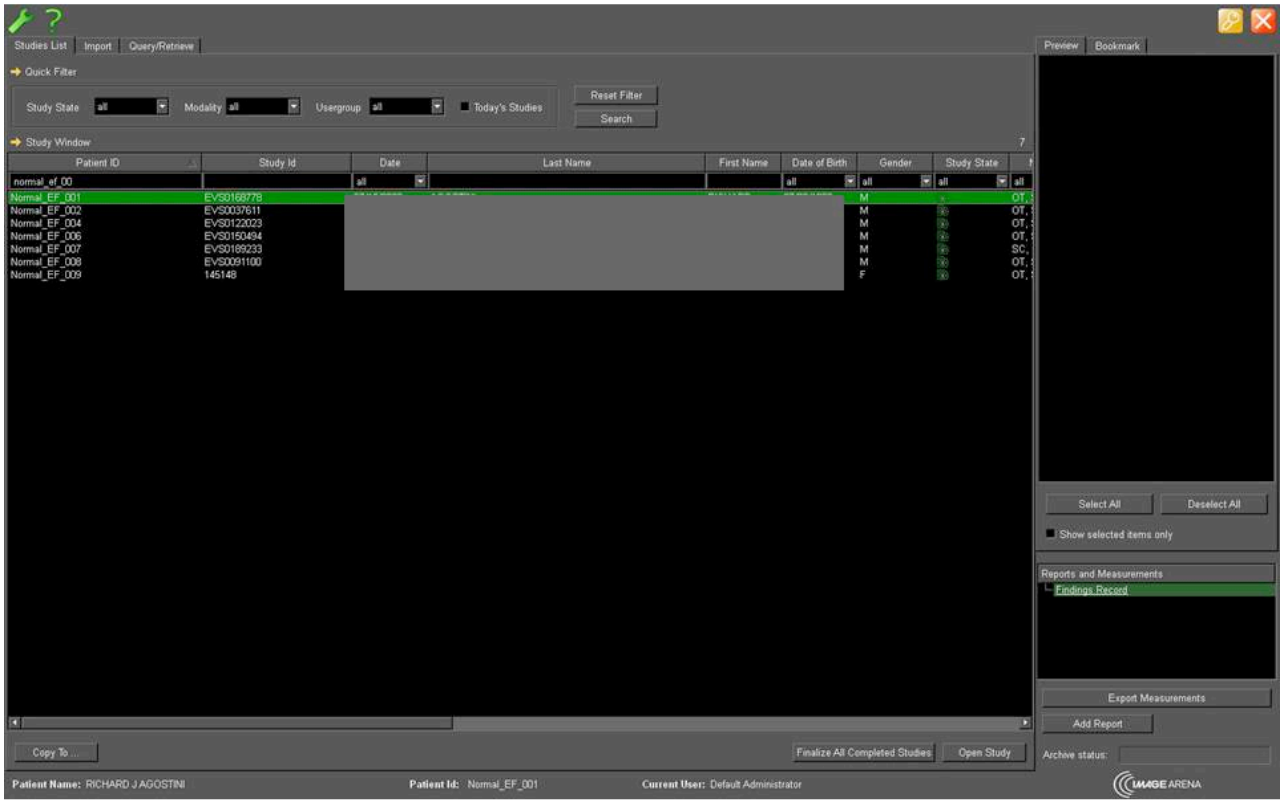
All ARIC Visit 7 echocardiograms will be transmitted electronically from Field Centers to the Echocardiography Reading Center via a secure web transfer system as detailed below. Field center staff will receive electronic confirmation (by email) upon successful receipt of each echocardiogram by the Reading Center.

V.a. Instructions for Electronic Transfer of Studies to the Reading Center

Echocardiograms will be transferred from Field Centers to the Reading Center electronically via direct VPN tunnel from the field center to the reading center server at the Brigham and Women's Hospital. Transfer of completed studies to the Reading Center has **2** components:

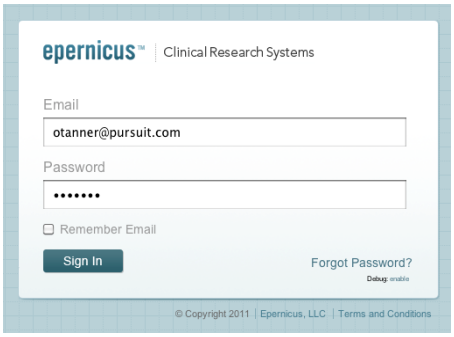
(1) Transfer of Image Files

Upon finalizing and closing a study on the iE33 machine, studies will be automatically transferred to the Field Center PC which houses the Tomtec Image Arena software. This will act as a local temporary PACs for recent studies performed at the Field Center. Image Arena will be configured such that studies will automatically transfer to the BWH server. If the Field Center prefers, studies may alternatively be manually selected for transfer by site sonographer from Image Arena to the BWH server. The user interface for the Tomtec Image Arena software is demonstrated in the figure below.



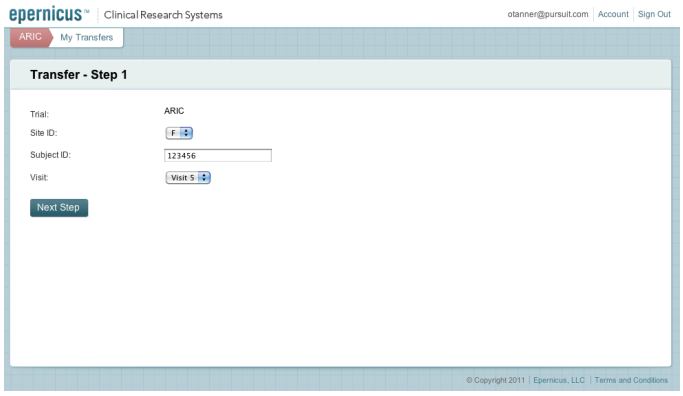
(2) Transfer of the Echocardiogram Electronic Transfer Form (ETF)
For each Echocardiogram study performed and transmitted to the Reading Center, the sonographer must also ***separately*** submit an Electronic Transfer Form (ETF) to the Reading Center as outlined below. This form provides a notification for the Reading Center to expect the study images and provides important demongraphic and physiologic (heart rate, blood pressure) information necessary in analyzing the echo studies.

1. Sign in: Navigate to https://cicl.clinicalresearchsystems.com and sign in with your email address and password (provided to you by the Reading Center)

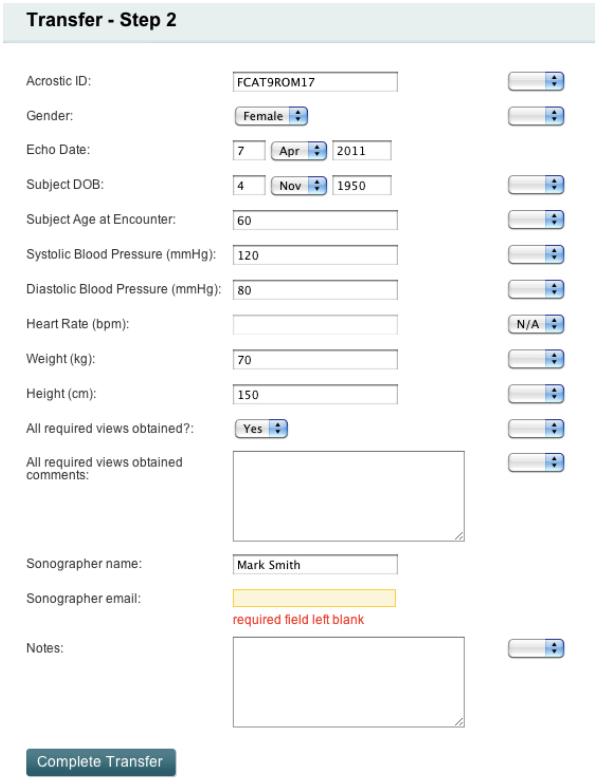


2. Initiate new ETF: Click on “New Transfer” to begin process

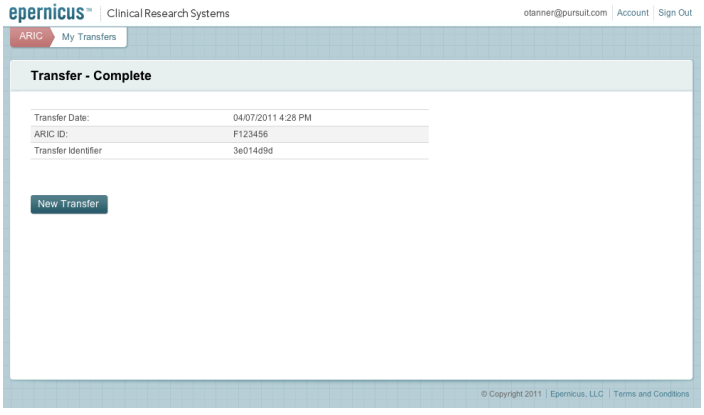
3. Enter participant ARIC ID
   - You will select your site identifier (one of ‘F’, ‘J’, ‘M’ and ‘W’) and enter the 6 digit Subject ID. Visit will default to the only available option (‘Visit 7’)



4. Enter required data
    - All fields are required, and are validated according to type. If certain fields are unavailable, you can select 'N/A' from the menu to the right side of that field to indicate that it is intentionally left blank.



5. Complete transfer by clicking the 'Complete Transfer' button
6. 'Transfer compete' confirmation screen
    - You can initiate another transfer, click on "My Transfers" to view your transfer history



For questions regarding either study performance or submission, the Reading Center has an established "hot line" channel of communication, which is listed within the Field Center Manual of Operations.

VI. Reading Center Feedback to Field Centers

The CICL will continuously monitor the adequacy and quality of all studies received according to the criteria outlined in the table below:

Criteria for Evaluating Image Quality		
View	**Score**	**Criteria**
Parasternal long axis view	2 points	• Image is on axis and endocardial border well visualized in all anatomic segments of the main structures imaged (e.g. all 4 segments of the LV)
	1 point	• Image is not completely on axis (e.g. low parasteranal view), or the endocardial border is well visualized in most but not all anatomic segments of the main structures imaged (e.g. only 3/4 anatomic segments of the LV)
	0 points	• Image is completely off axis, or endocardial border not well visualized >25% of anatomic segments of the main structures imaged
Parasternal short axis, mid-ventricular level	2 points	• Image is on axis and endocardial border well visualized in all anatomic segments of the main structures imaged (e.g. all 6 segments of the LV)
	1 point	• Image is not completely on axis, or endocardial border is well visualized in most but not all anatomic segments of the main structures imaged (e.g. only 5/6 anatomic segments of the LV)
	0 points	• Image is completely off axis or endocardial border not well visualized >15% of anatomic segments of the main structures imaged (e.g. there is dropout of ≥2 (of 6) anatomic segments of the LV)
Apical 4 chamber view	2 points	• Image is on axis and endocardial border well visualized in all anatomic segments of the main structures imaged (e.g. all 6 segments of the LV)
	1 point	• Image is not completely on axis, or endocardial border is well visualized in most but not all anatomic segments of the main structures imaged (e.g. only 5/6 anatomic segments of the LV)
	0 points	• Image is completely off axis, or endocardial border not well visualized >15% of anatomic segments of the main structures imaged (e.g. there is dropout of ≥2 (of 6) anatomic segments of the LV)
Apical 2 chamber view	2 points	• Image is on axis and endocardial border well visualized in all anatomic segments of the main structures imaged (e.g. all 6 segments of the LV)
	1 point	• Image is not completely on axis, or endocardial border is well visualized in most but not all anatomic segments of the main structures imaged (e.g. only 5/6 anatomic segments of the LV)
	0 points	• Image is completely off axis or endocardial border not well visualized >15% of anatomic segments of the main structures imaged (e.g. there is dropout of ≥2 (of 6) anatomic segments of the LV)
Doppler views	2 points	• Clear signals captured over at least 3 cardiac cycles for all Doppler measures
	1 point	• Clear signals captured over at least 2 cardiac cycles for most Doppler measures
	0 points	• Absent or unclear signals captured for most Doppler measures

Scoring Criteria	
Grading	**Total Points**
Good quality	9-10 points
Acceptable quality	6-8 points
Fair quality	4-5 points
Poor quality	≤3 points

For each echocardiogram received by the Reading Center, quality feedback will be provided via email to the performing sonographer, in addition to the appropriate Field Center Coordinator. Quality feedback will include the quality score – defined as above – in addition to directed feedback regarding parasternal and apical view

foreshortening, endocardial border definition, missing views, spectral and Tissue Doppler quality, and quality of 3D image acquisitions.

In situations where concerns arise regarding the quality of a study submitted by the Field Center, this feedback will include technical instructions for quality improvement. Additionally, if any queries arise at the Reading Center regarding images submitted, the Field Center coordinator and sonographer will receive a CICL- Query via email. The query email will contain easy to follow instructions for the Field Centers on how to resolve the query. Field Centers should respond to queries as soon as possible but latest within 10 business days. Field Centers should contact the Reading Center with questions related to queries received.

A pattern of inadequate or poor-quality studies will prompt directed discussion by CICL staff with the Field Center PI and/or sonographer and, possibly, retraining. The CICL will also hold monthly teleconferences with study sonographers to review common or persistent quality issues with study echocardiograms, and receive feedback from sonographers.

VII. Instructions for Conducting Studies

A. Echocardiographic Equipment

All echocardiograms will be performed using dedicated Philips iE33 Ultrasound systems. All echocardiogram examinations will be performed using the X5-1 xMatrix transducer, for 2D, Doppler, and 3D data acquisition. An acquisition default for the ARIC study will be programmed in each study echocardiography machine, incorporating the imaging parameters detailed in this section. All examinations should be performed using the 'ARIC' default for subjects in sinus rhythm and the 'ARIC AF' default for subjects in atrial fibrillation. All machines will also be programmed with an ARIC protocol to guide sonographers through the study protocol and ensure that all protocol required views are obtained.

Default settings for ARIC are as follows:

2D images	Color Doppler	Spectral Doppler
• H pen • Xres: ON • Elevation compounding: ON • Chroma: 1 • Gray scale: 4 • Persistence: low • Re-speed in the midline	• Gain: 65 • Map: 4 • Smoothing: 3 • Persistence: OFF	• Compress: 4 • Reject: 4 • Speed:100 mm/sec

Default acquisition time will be 4 cardiac cycles. For patients in atrial fibrillation, default acquisition time will be 5 seconds (automatic in protocol preset).

All images and cineloops are to be exported into DICOM format with "FULL FRAME RATE" (DICOM storage properties of maximum frame rate to be configured to "FULL" or "maximum", "native", "acquisition rate" instead of "30".

B. Review of Key Echo Views from Visit 5

Given the key importance of longitudinal changes in echocardiographic measures from Visit 5 to Visit 7, sonographers should make every effort to obtain images at Visit 7 that are comparable to those obtained at Visit 5. To this end, the CICL will provide all study sonographers will access to a file containing key imaging views from all participants at Visit 5. For each study participant, .avi files will be provided for the following views: (1) parasternal long axis; (2) apical 4 chamber; (3) apical 4 chamber RV-focused view; (4) apical 2 chamber. Prior to scanning each study participant, sonographers should review these views from that participant at Visit 5. To accomplish this:

1. Open the 'Visit 5 images' folder
2. Open the appropriate site sub-folder ('Site M', 'Site J', 'Site W', 'Site F')
3. Open the sub-folder with the appropriate subject ARIC ID
4. Double click on each .avi file to play

On the ETF for each study echocardiogram, sonographers will be required to certify that they reviewed the appropriate Visit 5 .avi images prior to exam performance.

C. Subject Identification on Recorded Images

The CICL should receive no subject identifiers, such as the name, on actual echo recordings. **Record only the subject's study ID.**

D. Subject Preparation

The subject's blood pressure should be taken with 30 minutes of starting the echocardiogram and after the subject has been resting for 5 minutes. Be sure to record the blood pressure and initial heart rate on the Echo Electronic Transfer Form (ETF). *Note: Although blood pressure is annotated on some of the images in this MOO, do NOT annotate the participant's blood pressure on the echo images for the ARIC exam.*
Fill in *all* of the information on the Echo Transfer Form including heart rate, blood pressure, height, weight, and subject date of birth.

Electrocardiographic leads (3-lead) should be placed on the subject prior to imaging. An adequate ECG signal in which the QRS complex is clearly identifiable should be visible on the echocardiographic monitor must be present throughout the imaging exam duration.

The subject should be placed in the steep left lateral decubitus position unless this position is not possible.

Echocardiograms should be obtained in a manner that is most consistent with good subject care. Subject care issues, including subject comfort, should always supersede research interests. Indeed, subject cooperation and comfort are extraordinarily important in obtaining the highest quality echocardiographic examination.

VIII. Guidelines for Image Optimization

Quantitative measurements entail manually tracing the endocardium and Doppler envelopes at various periods in the cardiac cycle. Even when images are of good quality, this can be extremely difficult, and it is therefore critically important that the best possible endocardial definition and Doppler signal are obtained. Guidelines for obtaining optimal quality 2D, color Doppler, Spectral Doppler, and Tissue Doppler acquisitions are outlined in this section.

A. General

For patients in sinus rhythm, at least three full cardiac cycles must be recorded for each protocol specified view. For subjects in atrial fibrillation, (at least 1) 5 second acquisition per view must be recorded. Recording should start when the view is optimized and end after the required number of cardiac cycles have been recorded per view.

The echocardiographic exam should be performed in the order listed in section IX: Echocardiogram Protocol: Required Views.

No measurements should be recorded on the images acquired at the Field Center. All measurements will be performed centrally at the Echocardiography Reading Center.

B. 2D Imaging

Throughout the course of the echo exam, both imaging depth and sector with should be continuously optimized to maintain a frame rate of 50-80 frames per second.

Ensure that the entire cardiac structure of interest is within the echo sector throughout both the systolic and diastolic periods. Optimal visualization of endocardial borders is essential for quantitative analysis. If necessary, increase 2D gain to optimally demonstrate left ventricular endocardial borders, particularly in the apical views. In general, tissue harmonic imaging should be used, except in the unusual situation where \this worsens endocardial border definition. Adjustment of sector width, imaging depth, 2D gain, and use of tissue harmonic imaging from the ARIC protocol defaults may be necessary to optimize image quality and will be at the discretion of the sonographer performing the examination.

Meticulous efforts to avoid foreshortening of imaging planes is essential to the integrity of the quantitative analysis performed on these studies. Utilize the landmarks detailed in the following sections to ensure on axis image acquisition.

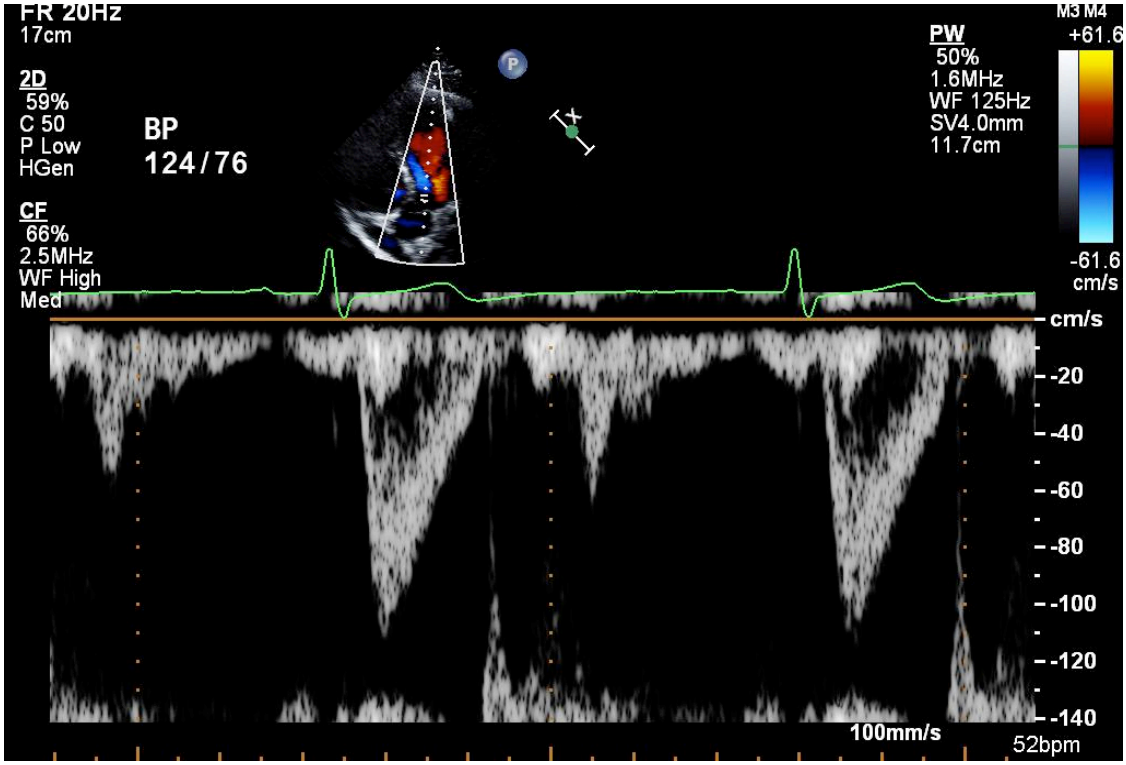
C. Color Doppler Imaging

For all color Doppler imaging, the color Doppler Nyquist limit should be at 64 cm/sec. Color Doppler gain should be set at a level just below the level at which random background noise is seen. Neither color Doppler gain nor the Nyquist limit should be adjusted by the sonographer from the ARIC protocol default. Color Doppler variance display will not be utilized in this examination.

For all color Doppler acquisitions, be sure to make the color Doppler sample window large enough to encompass the structure of interest, but no larger than necessary.

D. Spectral Doppler

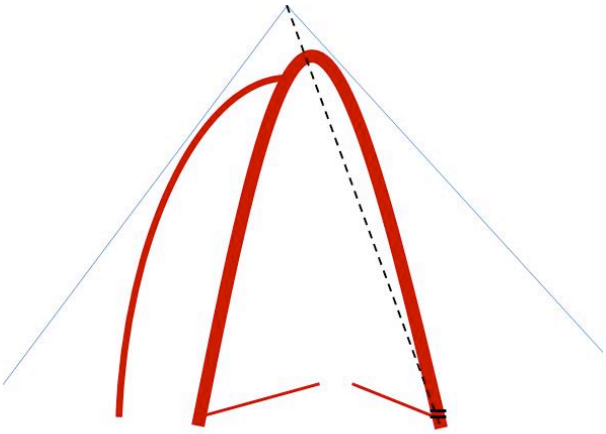
By the Doppler equation, velocity is inversely related to the cosine of the intercept angle between the ultrasound beam and the direction of blood flow. Therefore, the key principle in all spectral Doppler acquisitions (both pulsed wave and continuous wave) is to optimally align the ultrasound beam parallel to the direction of blood flow of interest. Good quality spectral Doppler tracings demonstrate clear onset and end of flow. For pulsed wave Doppler, gain should be optimized such that a well-defined envelop is visible, with a sharp peak and a lucent center. For both continuous and pulsed wave Doppler, sonographers will need to optimize the baseline shift and velocity range such that the spectral envelope occupies approximately three-fourths of display. The following ARIC protocol defaults will be set and should not be altered: (1) sweep speed 100 cm/sec, and (2) sample volume length 3mm [for pulsed wave Doppler].



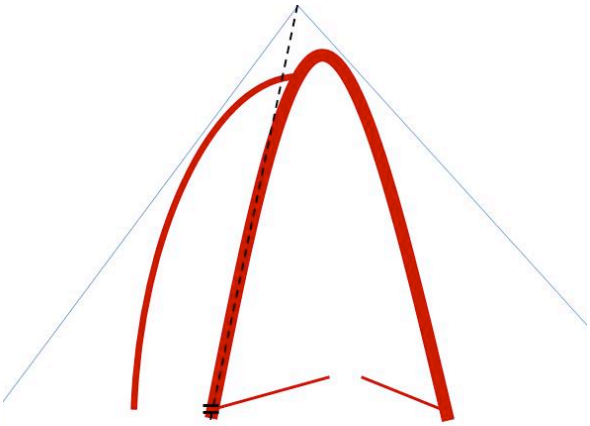
E. Tissue Doppler Imaging

Tissue Doppler imaging measures the velocity of myocardial tissue, which is low velocity and high amplitude. In contrast, the motion of blood is high velocity and low amplitude and these signals must be filtered. For this protocol, tissue Doppler imaging will be employed to measure annular velocities at both the mitral and tricuspid annulus (described in detail in the sections below). Like standard Doppler, the accuracy of tissue Doppler is dependent on a parallel angle of incidence of myocardial motion with the ultrasound beam. Optimally align the longitudinal motion of the ventricle with the ultrasound beam. Placement of the tissue Doppler sample volume appropriately at the level of annular (mitral or tricuspid depending on the view being obtained) is essential for high quality data and is reviewed in detail below. Sonographers will need to optimize the baseline shift and velocity range such that the spectral envelope occupies approximately three-fourths of display. The following ARIC protocol defaults will be set and should not be altered: (1) sweep speed 100 cm/sec, (2) sample volume length 5mm, and (3) filter setting of 100 Hz.

Proper positioning of sample volume for mitral annular TDI:



Lateral



Septal

F. 3D Echocardiography

Three 3D Volumetric datasets will be acquired in this imaging protocol: (1) parasternal long axis focusing on the mitral and aortic valves; (2) apical 4 chamber view focusing on the LV and LA; (3) apical 4 chamber view focusing on the RV and RA. Each volumetric dataset is acquired over 4-continigous cardiac cycles. The following are essential to ensure adequate quality 3D data:

1. Optimal 2D image quality. 3D quality will only be as good as the associated 2D images
2. Inclusion of the entire structure of interest in the 3D volume set being acquired. If even a portion of the structure of interest is not included in the volumetric acquisition (e.g. exclusion of apical lateral segment for the LV/LA focused acquisition), the entire dataset is not useable.
3. Absence of 'stitch' artifacts, which are due to change in the position of the heart relative to the probe during the 4-beat volumetric acquisition. Stitch artifacts can therefore be due to: (1) participant motion, commonly due to respiration; (2) sonographer movement of the ultrasound probe; or (3) abrupt change in the R-R interval during acquisition (e.g. due to a PVC or APC). Stitch artifacts can be recognized by the sonographer at the time of image acquisition. If present, the acquisition should be rejects and another attempt made. Datasets with stitch artifacts are not useable.

To optimize chances of obtaining adequate quality 3D volumetric datasets, the following steps should be taken for each acquisition:

1. Optimize the 2D image quality of the structure of interest, adjusting the sector width and depth to achieve the highest frame rate possible while being sure to include all structures of interest.
2. Once optimized, click 'xPlane' to view the structure of interest in 2 orthogonal planes (0 degrees and 90 degrees) simultaneously. Ensure that the entire structure of interest is included in the imaging sector in both planes.
3. Activate "Full Volume" and ensure that "4 Beat Full Volume" is selected on the bottom of the right touch screen.
4. Wait for the 4 quadrants of the volumetric images to 'fill'
5. Ask the subject to hold their breath in order to minimize motion of the chest. If the subject is unable to hold their breath, then ask him/her to take very shallow breaths. Hold the image absolutely steady.
6. Once no 'stitch' artifacts are seen, count 6 cardiac cycles then press 'Acquire'
7. The acquired volumetric dataset will automatically playback on the screen. Review this for (a) presence of stitch artifact; and (b) exclusion of any portion of the anatomic structures of interest. If either of these are present, repeat to acquisition.

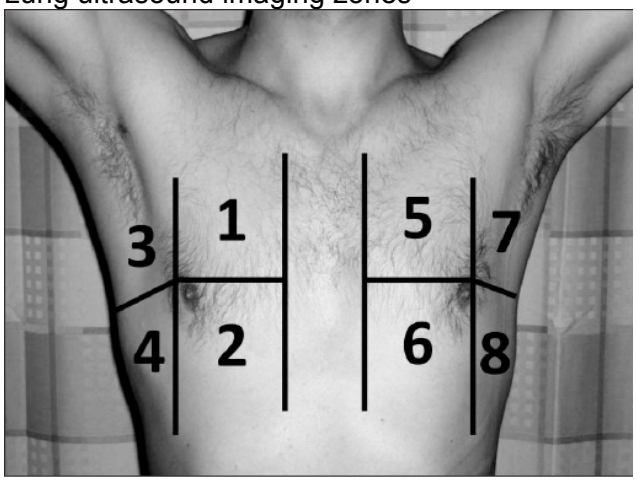
G. Lung Ultrasound

Lung ultrasound is a non-invasive method to detect and semi-quantitatively assess extravascular lung water, a marker of pulmonary congestion that may precede frank pulmonary edema. While the lung parenchyma typically cannot be imaged by ultrasound, a specific type of imaging artifact – B-lines (also known as comet-tail artifacts or ultrasound lung comets) – have been shown to reflect the presence of extravascular lung water. By placing the phased array transducer between the intercostal space of the anterior and lateral chest wall, the hyper-echoic pleural line can be visualized. B-lines refer to hyper-echoic vertical signals that fan out from the pleural line, extend to the entire depth of the imaging sector, and move with respiration. The assessment of B-lines by lung ultrasound involves acquisition of such images from 8 locations: two intercostal spaces anteriorly and two laterally on right and left sides. By convention, 6-second clips will be acquired for each imaging location at a depth of 18 cm.

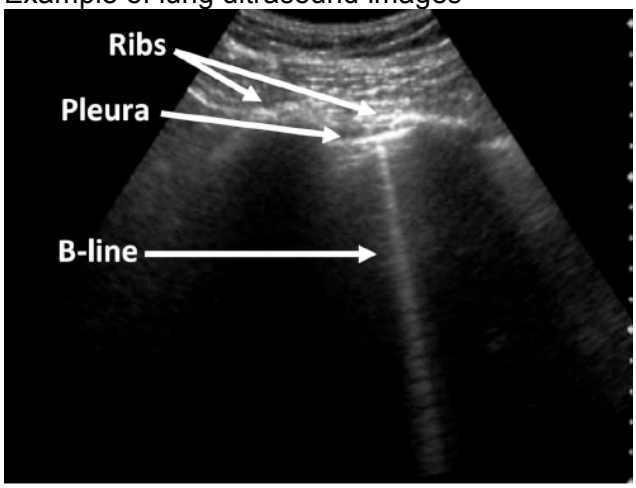
Key considerations to ensure optimal quality lung ultrasound images for this protocol include:

1. Be sure to acquire lung ultrasound images in the order specified in the image above (intercostal spaces #1 through #8)
2. For each lung ultrasound in this protocol, be sure to change the acquisition from '4 cycles' to '6 seconds' [unfortunately, this will need to be done for *each* lung ultrasound acquisition in this protocol].
3. Ensure imaging depth is at 18 cm.
4. Orient the imaging probe vertically in the intercostal space with the probe marker facing the participant's feet
5. Identify the following key anatomic landmarkers: (1) two rib shadows in short axis, flanking (2) the hyper-echoic pleural line in the near field. Ensure that heart, liver, or other organs are not visible in the imaging field.
6. Optimize gain for each acquisition

Lung ultrasound imaging zones*



Example of lung ultrasound images*



*Lung ultrasound images from Anderson KL et al. *J Ultrasound Med* 2013;32:115-120.

For ARIC Visit 7, lung ultrasound images will be acquired as a separate 'study' following the acquisition of the cardiac images. Sonographers will employ the 'LUS' protocol, which will default to an imaging depth of 18 cm and 10 second acquisition time.

IX. Echocardiogram Protocol: Required Views

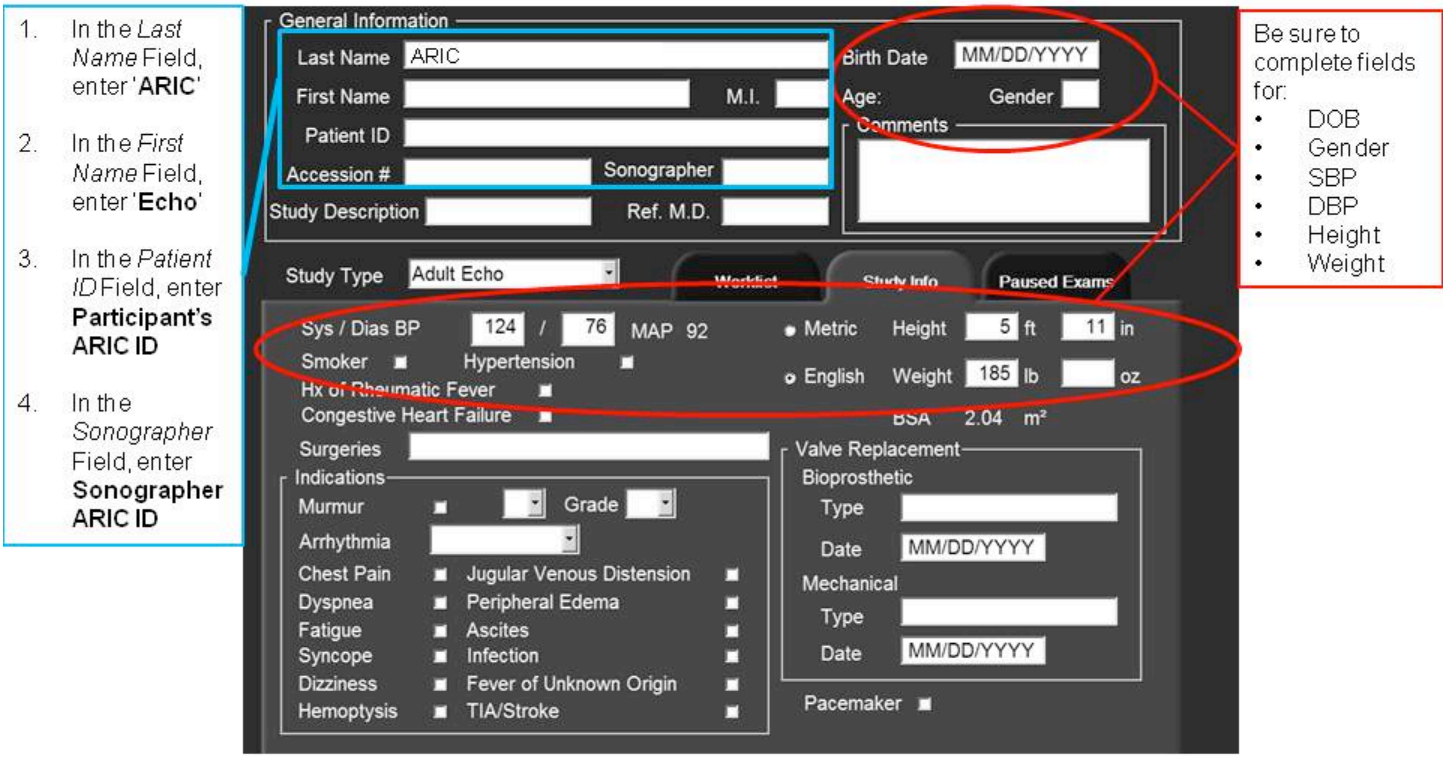
A. Brachial Blood pressure	♦ Ensure that BP obtained within 30 min of the echo examination
B. Parasternal Position	
☑ *Parasternal long axis*	♦ 2D imaging (at deep depth) ♦ 2D imaging (at shallow depth) ♦ Color Doppler of the mitral and aortic valves
☑ *Parasternal RV inflow view*	♦ 2D imaging of TV ♦ Color Doppler of TV ♦ CW of TV regurgitation
☑ *Parasternal RV outflow view*	♦ 2D imaging of RVOT and PV ♦ Color Doppler of PV ♦ PW of RVOT ♦ CW Doppler of PV, being sure to include full PR envelope
☑ *Parasternal short axis – Aortic valve level*	♦ 2D imaging of AV ♦ Color Doppler of AV ♦ 2D imaging of TV ♦ Color Doppler of TV ♦ CW Doppler of tricuspid regurgitation ♦ 2D imaging of right ventricular outflow tract ♦ Color Doppler of right ventricular outflow tract and PV ♦ PW Doppler of the RVOT ♦ CW Doppler of PV, being sure to include full PR envelope
☑ *Parasternal short axis – Mitral valve level*	♦ 2D imaging
☑ *Parasternal short axis – Papillary muscle level*	♦ 2D imaging
☑ *Parasternal short axis – LV apex*	♦ 2D imaging
C. Apical Position	
☑ *Apical 4 chamber view*	♦ 2D imaging ♦ 2D imaging, focused on LV ♦ 2D imaging, zoomed on LA ♦ Color Doppler of mitral valve/LA ♦ PW Doppler of mitral flow at leaflet tips ♦ PW Doppler of mitral flow at mitral annulus ♦ CW Doppler of mitral inflow ♦ TDI color and PW of lateral mitral annulus ♦ TDI color and PW of septal mitral annulus
☑ *Apical 4 chamber – focused on the RV*	♦ 2D imaging ♦ Color Doppler of tricuspid valve/RA ♦ PW Doppler of tricuspid inflow flow at tricuspid annulus ♦ CW Doppler of tricuspid regurgitation ♦ M-Mode of lateral tricuspid annulus ♦ TDI of lateral tricuspid annulus

☑ *Apical 5 chamber view*	♦ 2D imaging ♦ Color Doppler of LV, including MV and AV ♦ Color Doppler of left ventricular outflow tract and AV ♦ Pulse wave of LVOT flow ♦ CW of transaortic flow
☑ *Apical 2 chamber view*	♦ 2D imaging ♦ 2D imaging focused on LV ♦ 2D imaging zoomed on LA ♦ Color Doppler MV/LA
☑ *Apical 3 chamber view*	♦ 2D imaging ♦ color Doppler LVOT/AV
D. Subcostal View	
☑ *Inferior vena cava*	♦ 2D imaging (5 second acquisition)
☑ *4 chamber view*	♦ 2D imaging
E. 3D Imaging (pause protocol)	
☑ *Apical Position*	♦ 3D full volume acquisition of LV ♦ 3D full volume acquisition of RV
☑ *Parasternal Position*	♦ 3D full volume acquisition of MV and TV

Seperate Protocol: Lung Ultrasound	
☑ *Lung ultrasound*	♦ 8 zone acquisitions, each 6 second duration

IX. Detailed Review of Protocol Required Views

Beginning the Exam
Complete the subject information screen on the iE33 as detailed in the figure below:



Be sure to acquire an image of this screen.

A. Brachial Blood Pressure

The participant's brachial blood pressure should be measured within 30 minutes of the start of the echo examination. The subject's blood pressure should be taken after the subject has been resting for 5 minutes. Blood pressure should be performed at baseline in both arms. The highest reading should be recorded and subsequent measure should be done on the arm with the highest reading. Be sure to record the blood pressure and initial heart rate on the ETF. *Note: Although blood pressure is annotated on many of the images in this MOO, do NOT annotate the participant's blood pressure on the echo images for the ARIC exam.*

B. Parasternal Views

The following parasternal views will be obtained:

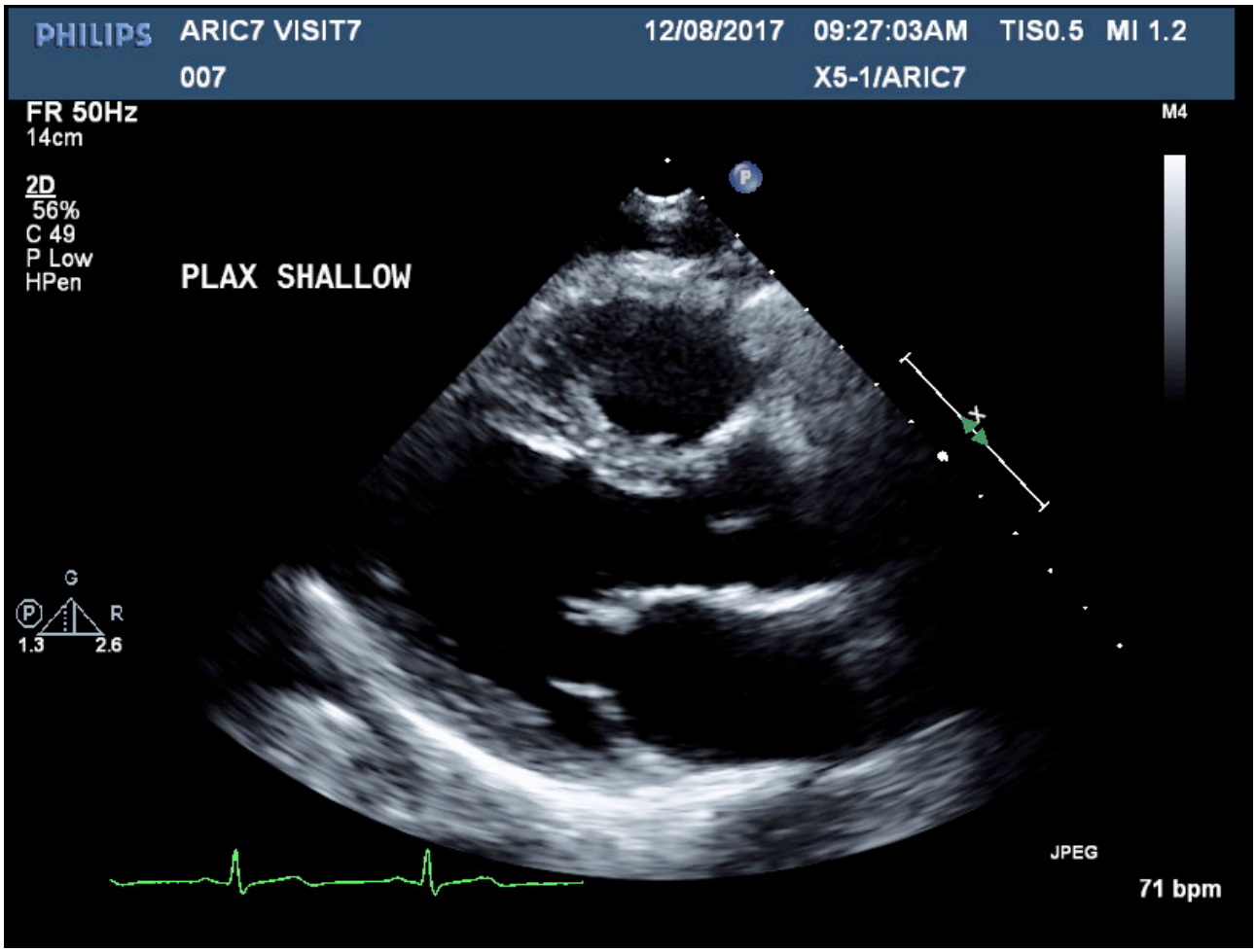
- Parasternal long axis view (section B.1.)
- Parasternal right ventricular inflow view (section B.3.)
- Parasternal right ventricular outflow view (section B.4.)
- Parasternal short axis view at 4 levels as detailed below (section B.5.)

At the Reading Center, these veiws will be used for calcuation of left ventricular mass and geometry (based on linear measures in the parasternal long axis views), LV circumferential strain and torsion (based on parasternal short axis views), and pulmonary arterial pressure and resistance (based on RV inflow and outflow views).

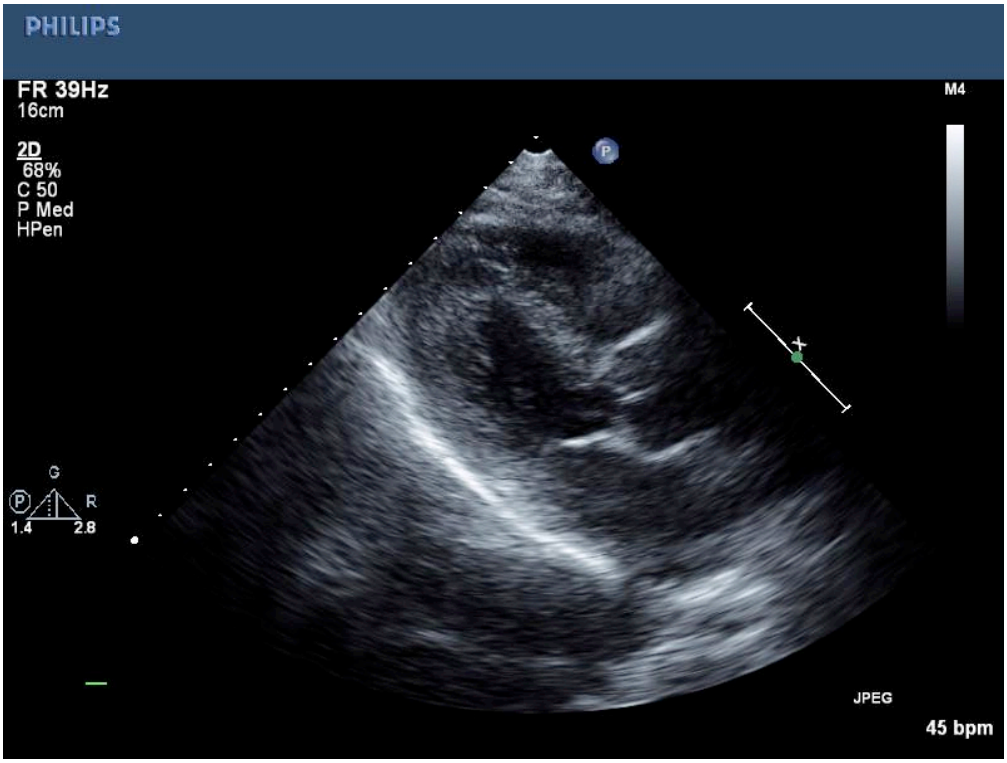
B.1. Parasternal Long Axis View

B.1.i. Parasternal Long Axis View – 2D imaging

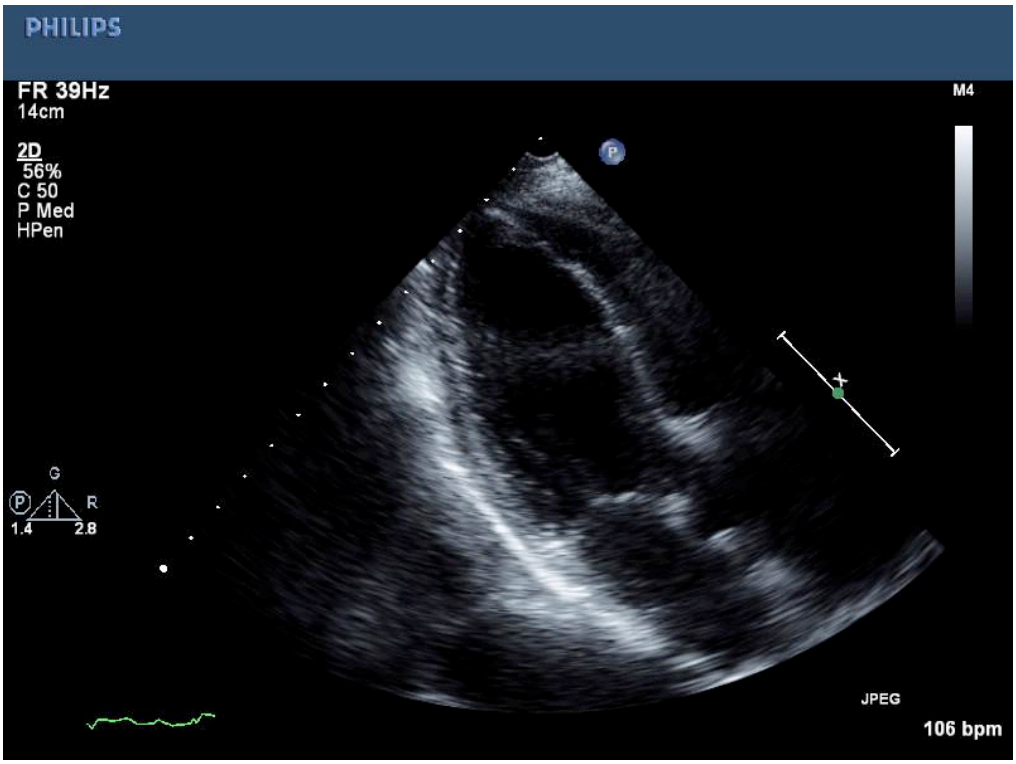
- Imaging should be performed initially at deep depth, then at shallow depth
- The LV endocardium at the septum and the posterior wall should be well delineated.
- The proximal interventricular septum should be horizontal and continuous with the aortic root.
- The anterior and the posterior mitral valve leaflets, and the right and noncoronary aortic valve leaflets should all be visible.
- The left ventricular apex should not be visualized.



Avoid obtaining shortened or low parasternal views:



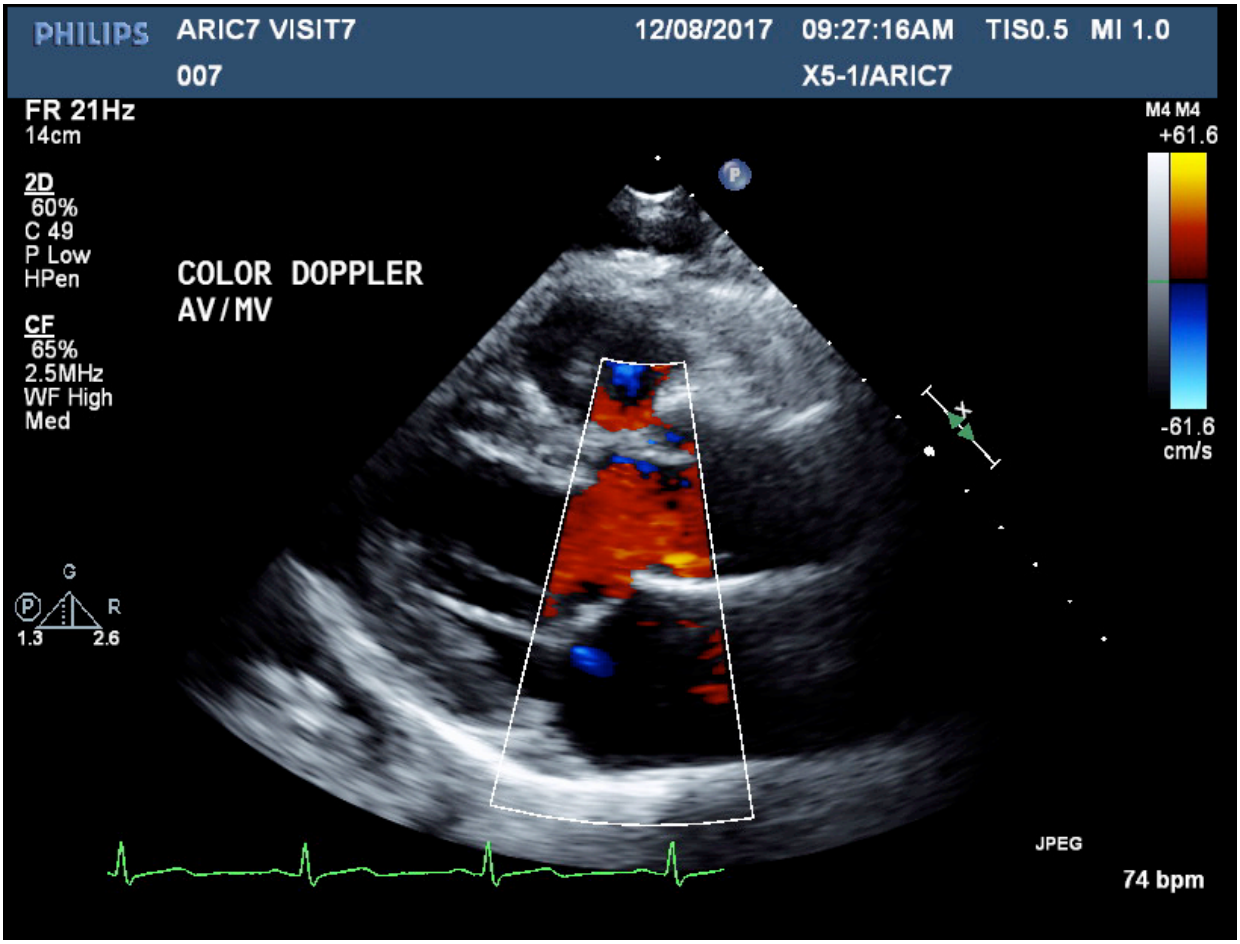
Grossly forshortened PLAX View



Low PLAX View

B.1.ii. Parasternal Long Axis View with color Doppler

- Assure that the color Doppler sample box fully encompasses the mitral valve, proximal left atrium, LVOT, aortic valve, and proximal aortic root
- Assure the color Doppler Nyquist limit is 60-65 cm/sec

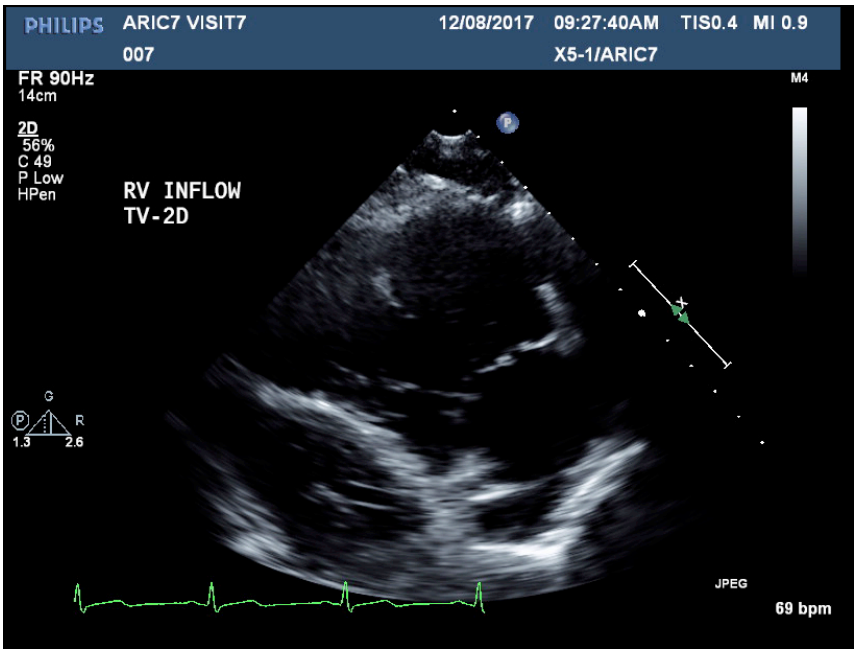


B.2. Parasternal RV Inflow View

- Assure that the tricuspid valve, right atrium, and right ventricle are all well visualized
- The following views will be obtained: 2D imaging, color Doppler of the tricuspid valve and RA, and CW Doppler of tricuspid regurgitation.

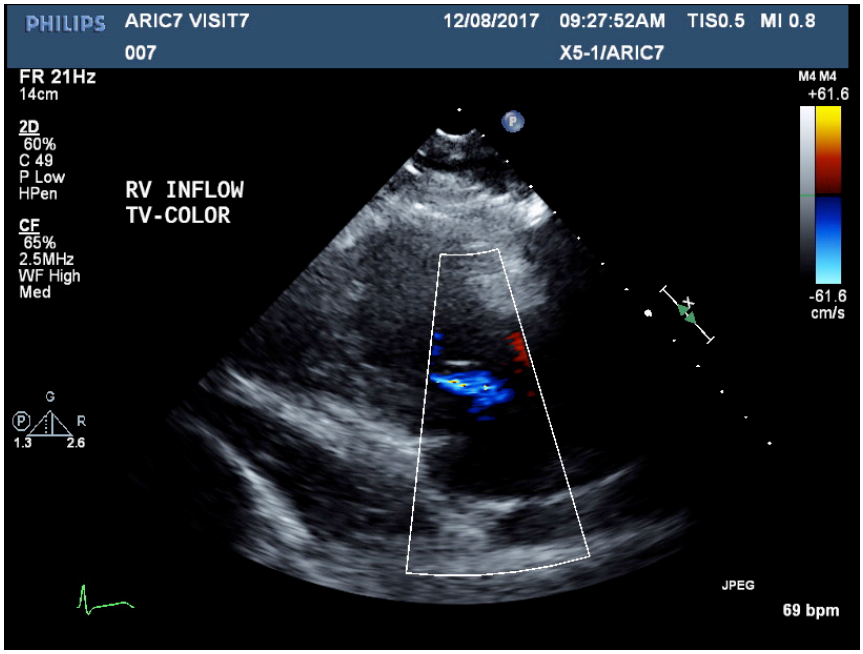
B.2.i. Parasternal RV Inflow View – 2D imaging

- Assure that the tricuspid valve, right atrium, and right ventricle are all well visualized



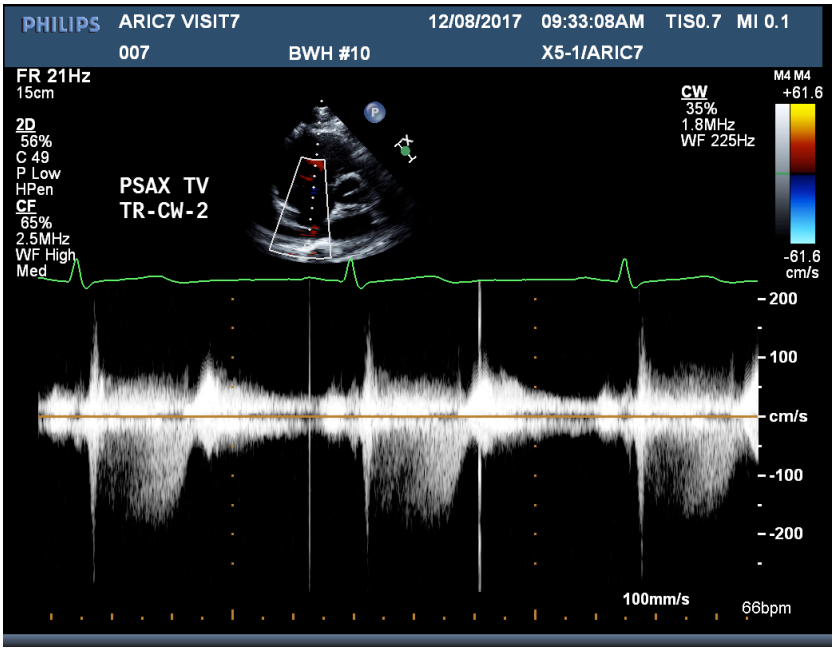
B.2.ii. Parasternal RV Inflow View – color Doppler

- Assure that the color Doppler sample window includes the entire tricuspid valve and RA



B.2.iii. Parasternal RV Inflow View – CW Doppler

• Position the interrogation line as parallel to tricuspid regurgitant flow as possible. Adjust the baseline and scale to capture the peak TR velocity. Aim to obtain a parabolic spectral Doppler envelope that is visible for >two-thirds of the systolic period. Record at least 3 (10 for subjects in atrial fibrillation) full representative systoles at sweep speed of 100 mm/sec.

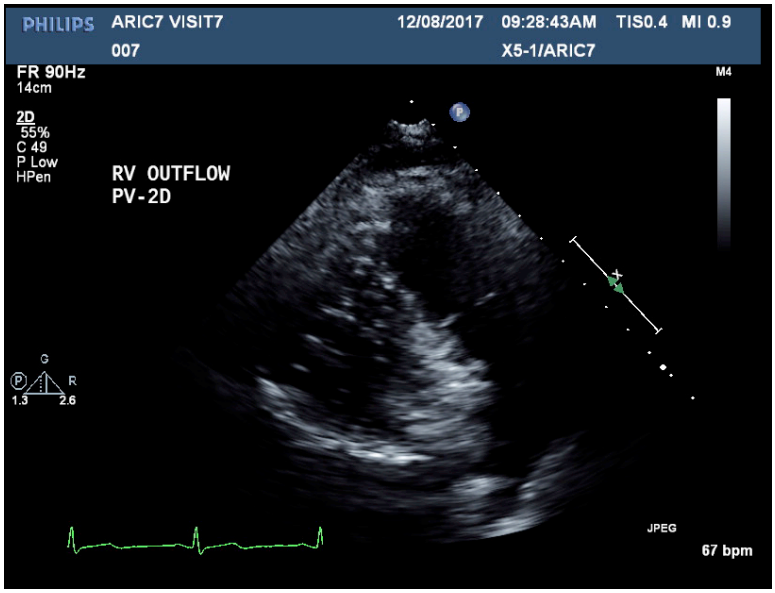


B.3. Parasternal RV Outflow View

- Assure that the RVOT, pulmonic valve, and proximal PA are all well visualized
- The following views will be obtained: 2D imaging, color Doppler of the RVOT and pulmonic valve, PW Doppler of the RVOT, and CW Doppler of pulmonic valve ensuring optimal visualization of both the systolic ejection flow and diastolic regurgitant flow (if present) envelopes.

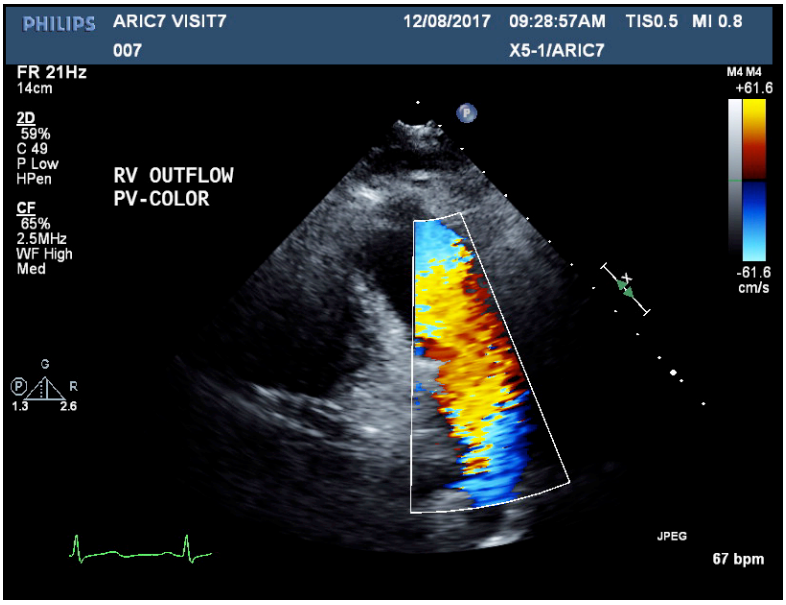
B.3.i. Parasternal RV Outflow View – 2D imaging

- Assure that the RVOT, pulmonic valve, and proximal PA are all well visualized



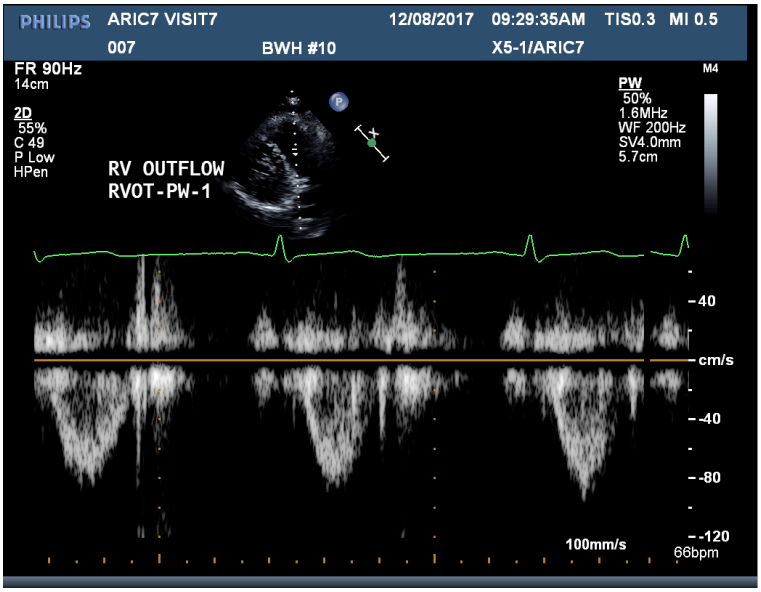
B.3.ii. Parasternal RV Outflow View – color Doppler

- Assure that the color Doppler sample window includes the RVOT, pulmonic valve, and PA



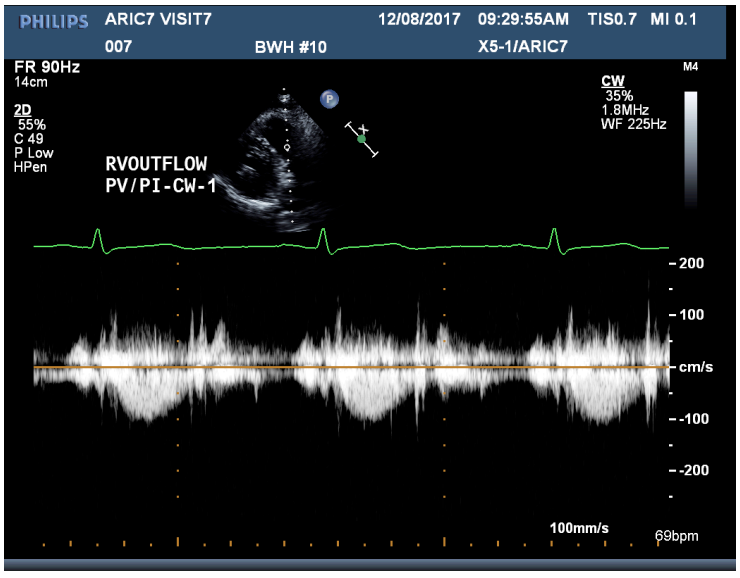
B.3.iii. Parasternal RV Outflow View – PW Doppler

• Ensure that the sample is in the right ventricular outflow tract (RVOT) approaching the pulmonic valve, just prior to the level of flow acceleration and spectral broadening. Record a minimum of 3 cardiac cycles (10 for subjects in atrial fibrillation) at a sweep speed of 100 mm/sec.



B.3.iv. Parasternal RV Outflow View – CW Doppler

• Ensure that the velocity scale and baseline are optimized so as to optimize complete visualization of both the systolic ejection flow and diastolic regurgitant flow (if present) envelopes. Record a minimum of 3 cardiac cycles (10 for subjects in atrial fibrillation) at a sweep speed of 100 mm/sec.



B.4. Parasternal Short Axis View

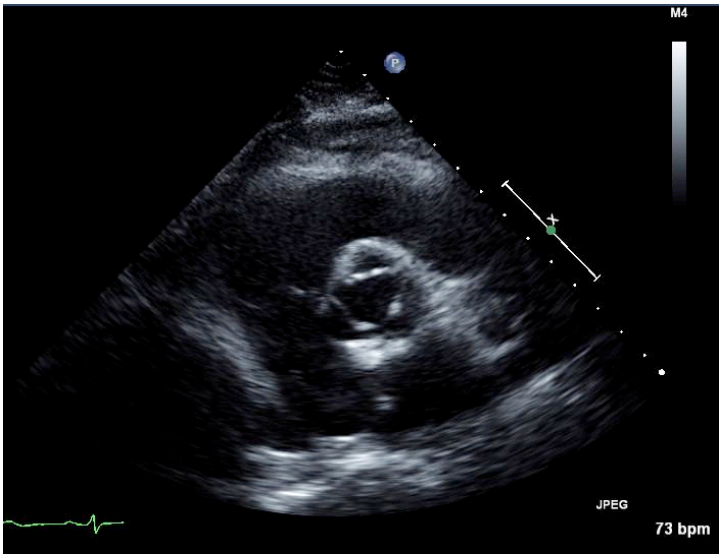
Parasternal short axis view will be obtained at four levels:

1. At the aortic valve level with the RVOT and pulmonic valve visible.
2. At mitral valve when both anterior and posterior mitral valve leaflets are visualized.
3. At the mid-papillary muscle level with the papillary muscles visible.
4. At the left ventricular apex.

B.4.i. Aortic Valve Level

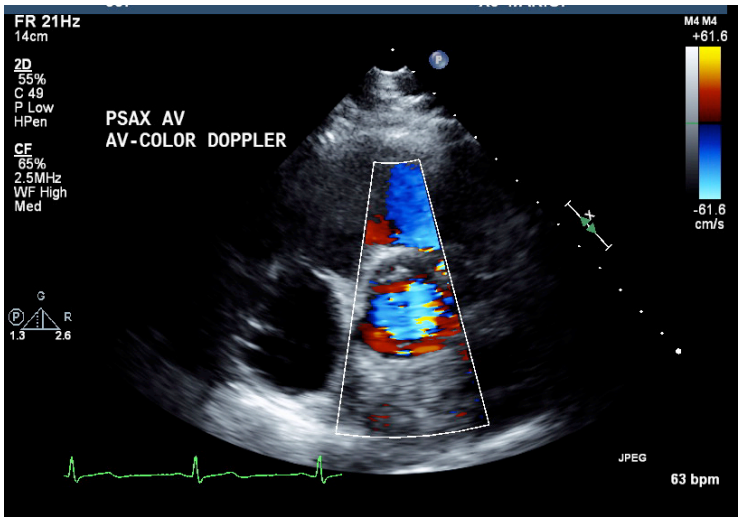
(a) 2D Imaging

- All 3 cusps of the aortic valve are visible, with a clear upside down triangle pattern during systole.
- The tricuspid valve and interatrial septum are visible.



(b) Color Doppler Imaging

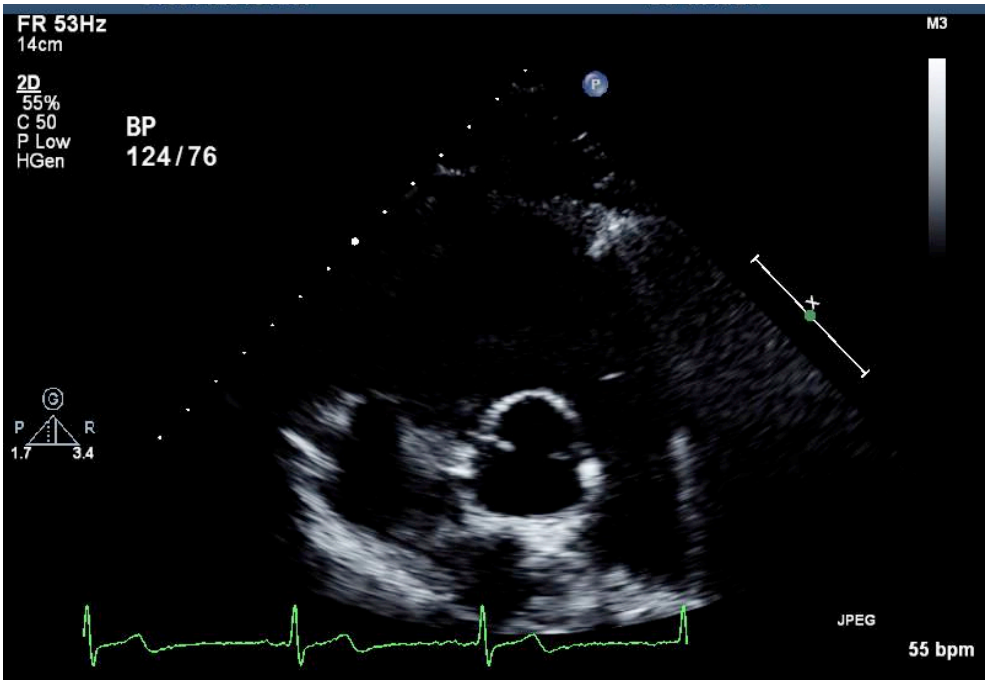
- Assure that the color Doppler sample box fully encompasses the aortic valve, including the entire valve annulus
- Assure the color Doppler Nyquist limit is 60-65 cm/sec



(c) Focused view of the RVOT and pulmonic valve

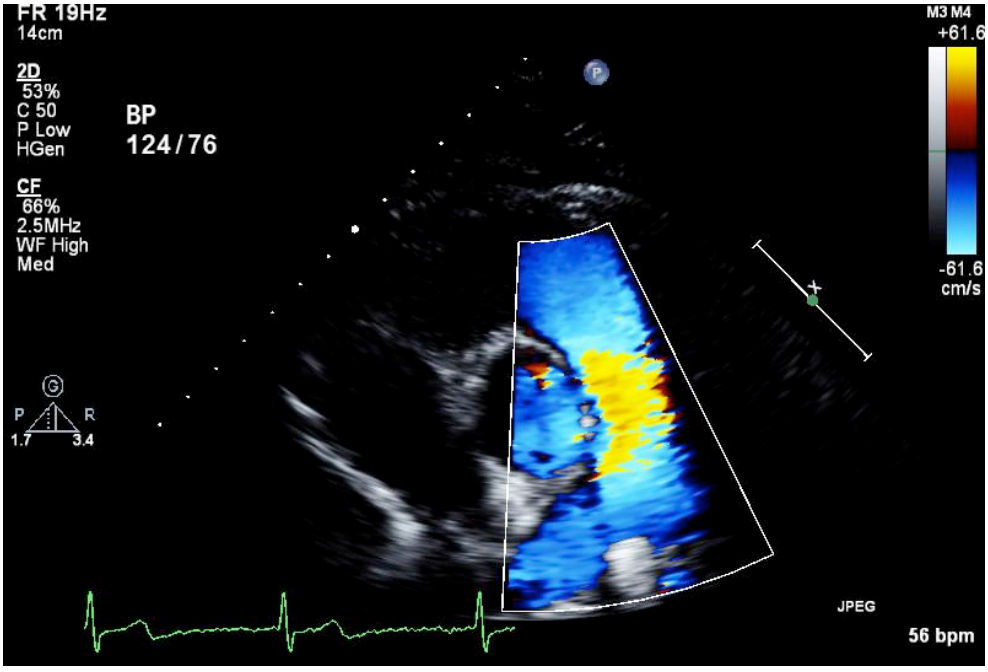
2D imaging

- Assure that the RVOT, pulmonic valve, and proximal PA are all well visualized



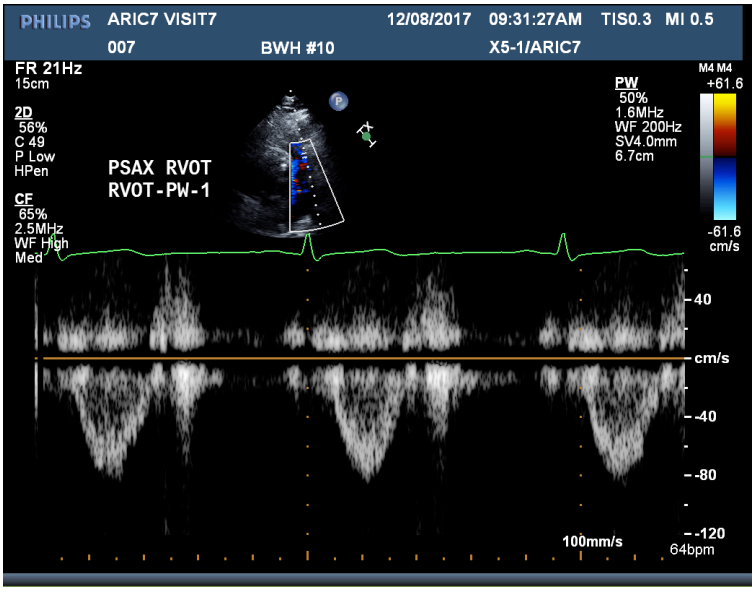
Color Doppler imaging

- Assure that the color Doppler sample window includes the RVOT, pulmonic valve, and PA



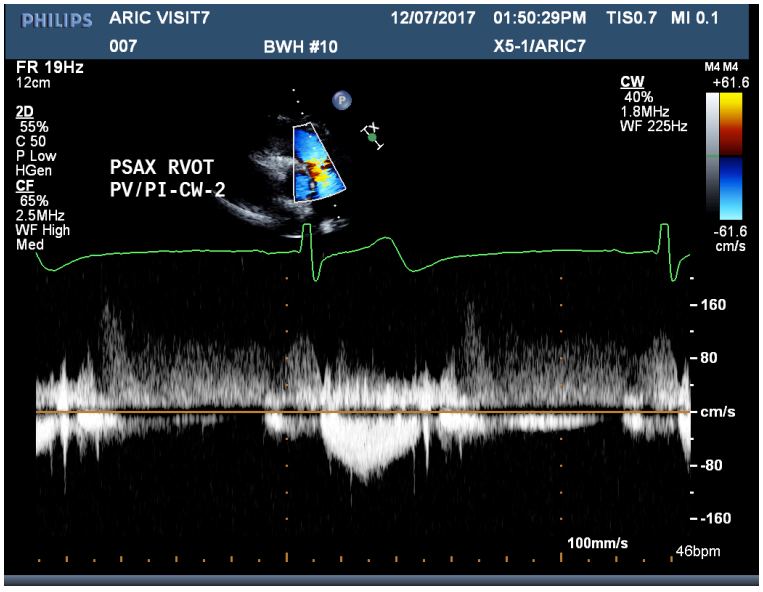
PW Doppler of RVOT

• Ensure that the sample is in the right ventricular outflow tract (RVOT) approaching the pulmonic valve, just prior to the level of flow acceleration and spectral broadening. Record a minimum of 3 cardiac cycles (10 for subjects in atrial fibrillation) at a sweep speed of 100 mm/sec.



CW Doppler of Pulmonic Valve

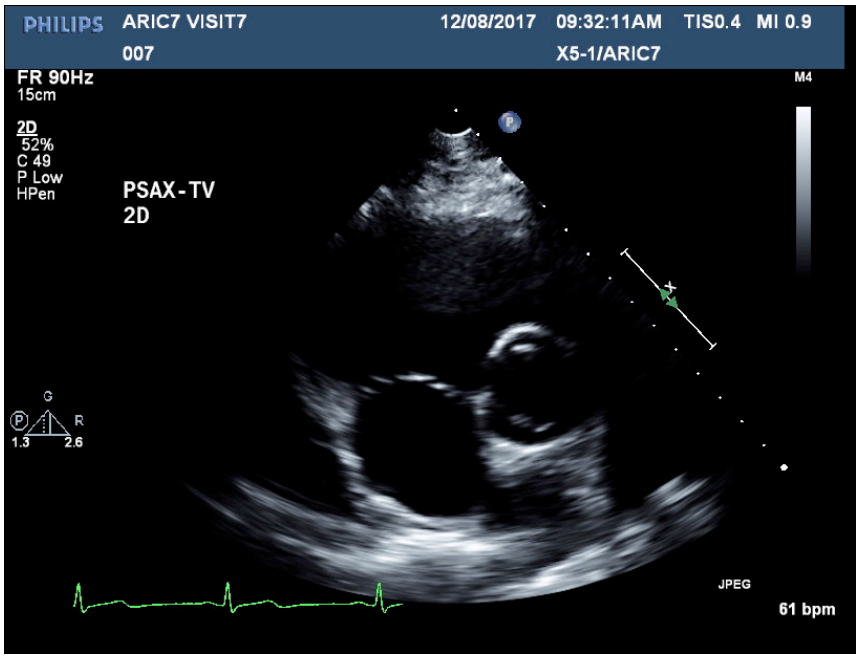
• Ensure that the velocity scale and baseline are optimized so as to optimize complete visualization of both the systolic ejection flow and diastolic regurgitant flow (if present) envelopes. Record a minimum of 3 cardiac cycles (10 for subjects in atrial fibrillation) at a sweep speed of 100 mm/sec.



(d) Focused view on the tricuspid valve

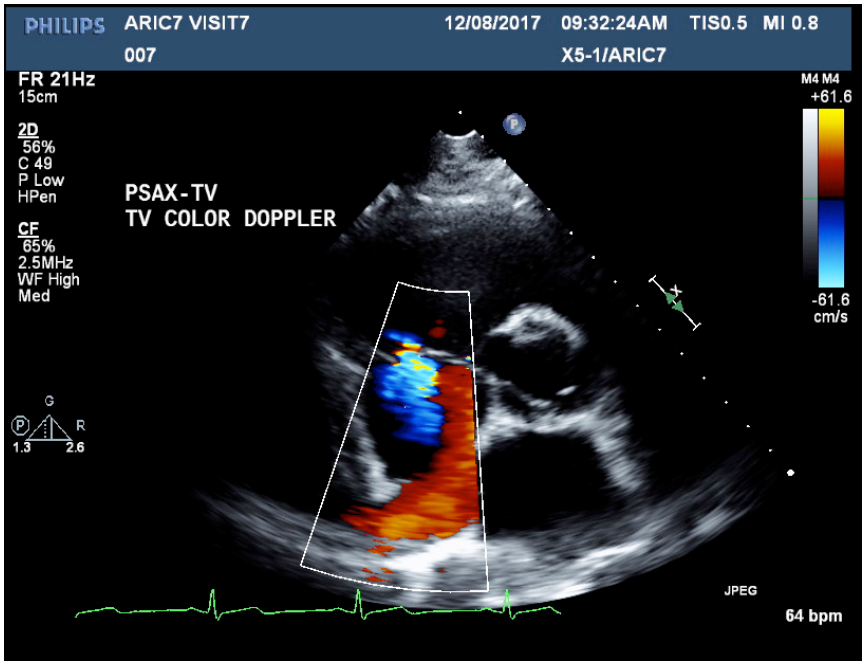
2D imaging

• Assure that the tricuspid valve, right atrium, and right ventricle are all well visualized



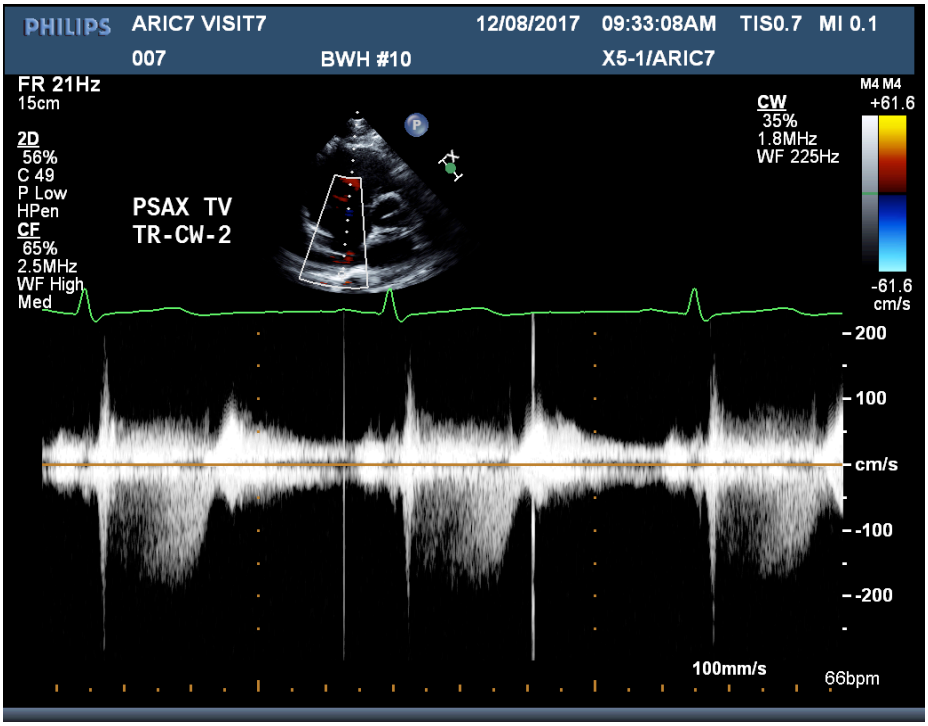
Color Doppler of the tricuspid valve and RA

• Assure that the color Doppler sample window includes the entire tricuspid valve and RA



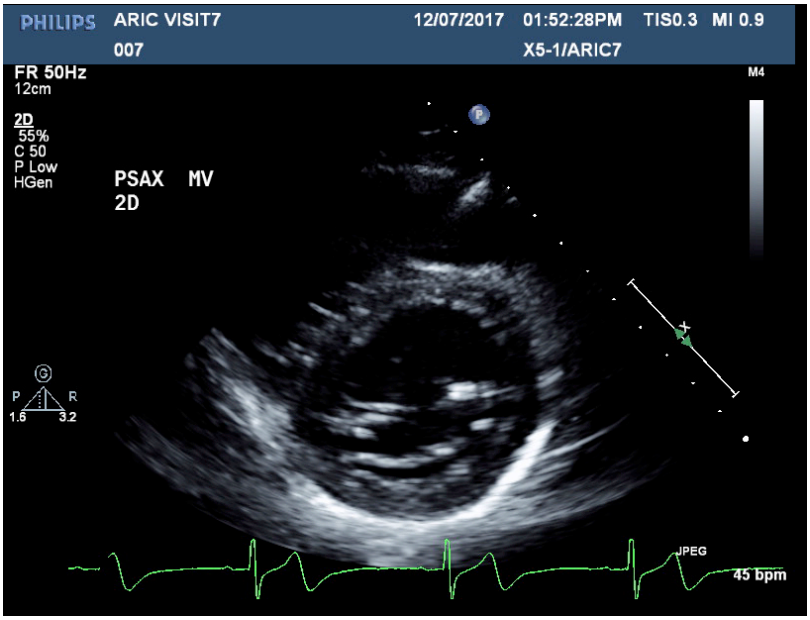
CW Doppler of tricuspid regurgitation

• Position the interrogation line as parallel to tricuspid regurgitant flow as possible. Adjust the baseline and scale to capture the peak TR velocity. Aim to obtain a parabolic spectral Doppler envelope that is visible for >two-thirds of the systolic period. Record at least 3 (10 for subjects in atrial fibrillation) full representative systoles at sweep speed of 100 mm/sec.



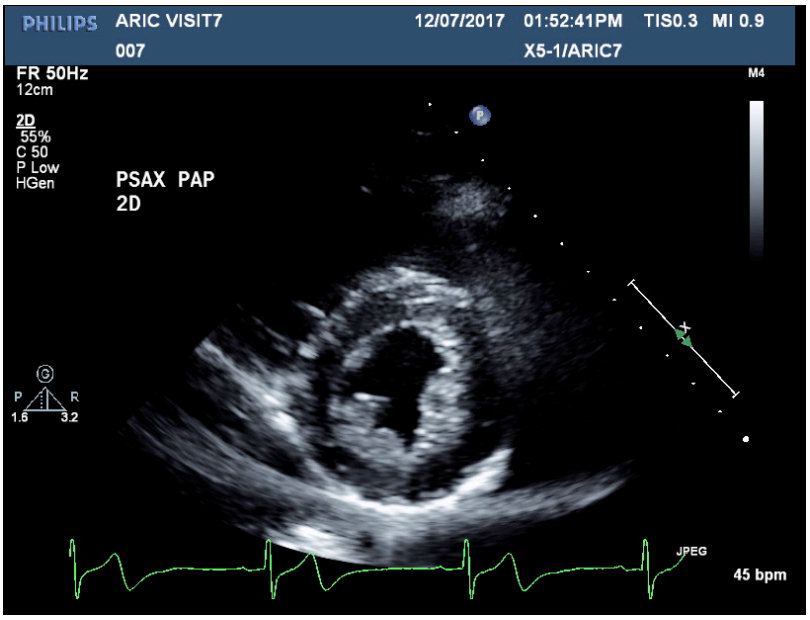
B.4.ii. Mitral valve level

- In the absence of prior infarction, the left ventricle should have a circular shape in the short axis – an elliptical shape suggests off-axis/tangential cut through the ventricle.
- Use internal LV landmarks to ensure imaging at consistent planes in the short axis, which at the mitral valve level includes visualization of the anterior and posterior mitral leaflets
- Adjust sector width and imaging depth to ensure acquisition frame rate of 50 to 70 frames per second.



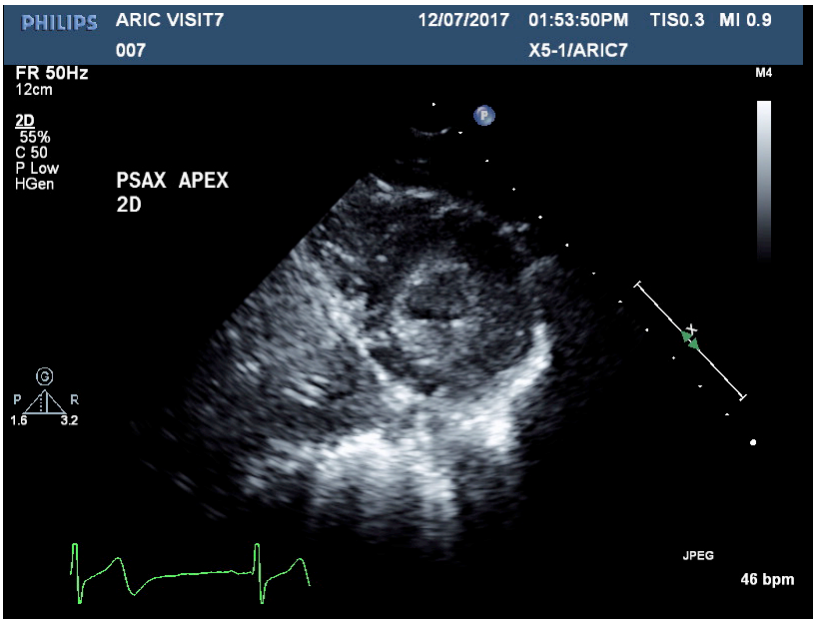
B.4.iii. Mid-papillary Level

- The left ventricle should have a circular shape in the short axis – an elliptical shape suggests off-axis/tangential cut through the ventricle.
- Use internal LV landmarks to ensure imaging at consistent planes in the short axis, which at the mid-papillary level includes visualization of both papillary muscles for the mid-papillary level
- Adjust sector width and imaging depth to ensure acquisition frame rate of 50 to 70 frames per second.



B.4.iv. Apical Level

- The left ventricle should have a circular shape in the short axis – an elliptical shape suggests off-axis/tangential cut through the ventricle.
- Adjust sector width and imaging depth to ensure acquisition frame rate of 50 to 70 frames per second.



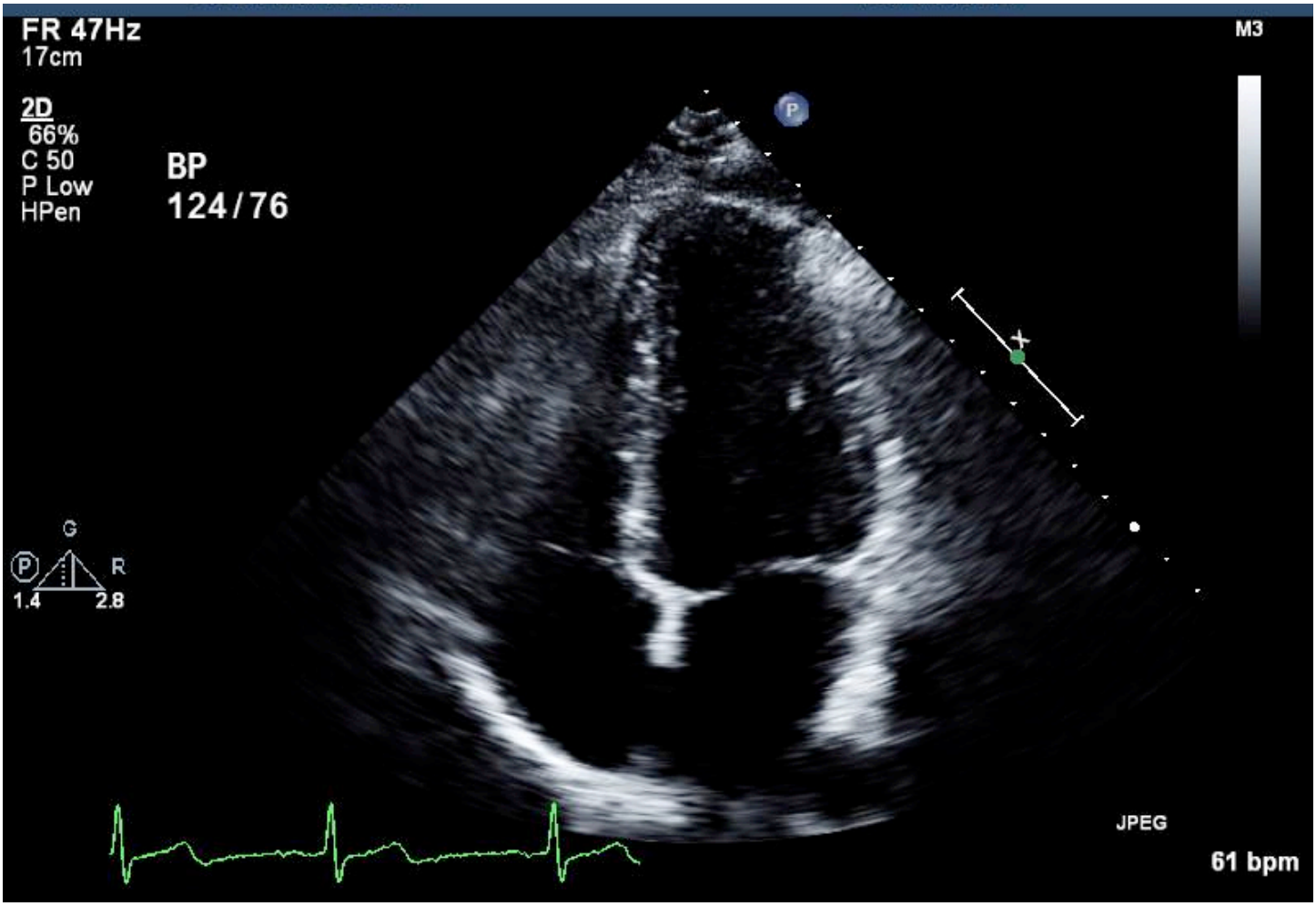
C. Apical Views

Five apical views will be obtained:

- The standard apical four-chamber focused on the LV
- The apical four-chamber dedicated to optimal imaging of the RV
- The five-chamber view
- The two-chamber view
- The three-chamber view

At the Reading center, left ventricular and atrial areas and volumes will be measured from these views (i.e. using Simpson's method). Therefore, in all apical views, special attention should be paid to properly align the image and capture the left ventricle and atrium in full. Avoid either foreshortening or elongating the chambers by transducer angulation.

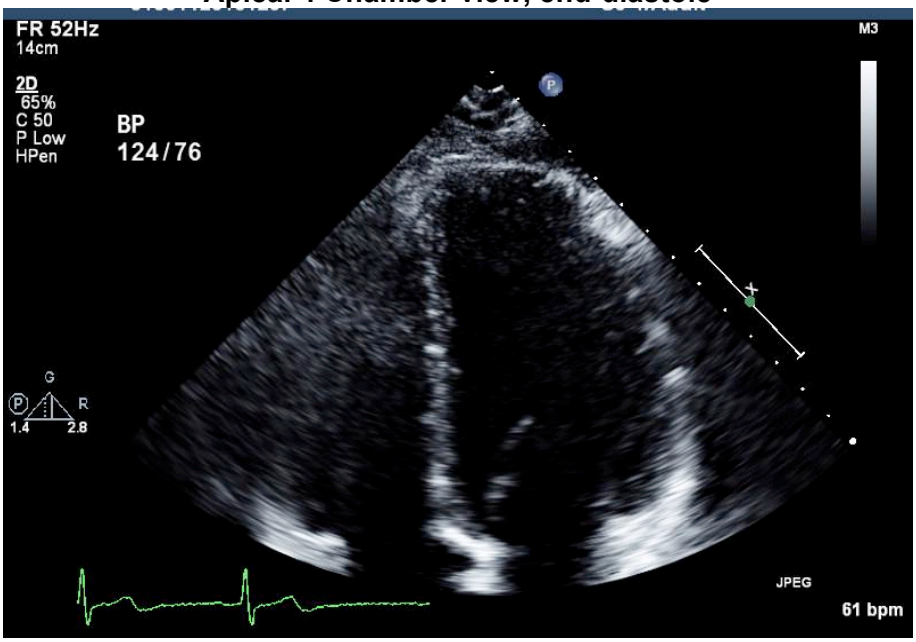
C.1. Apical 4-Chamber View



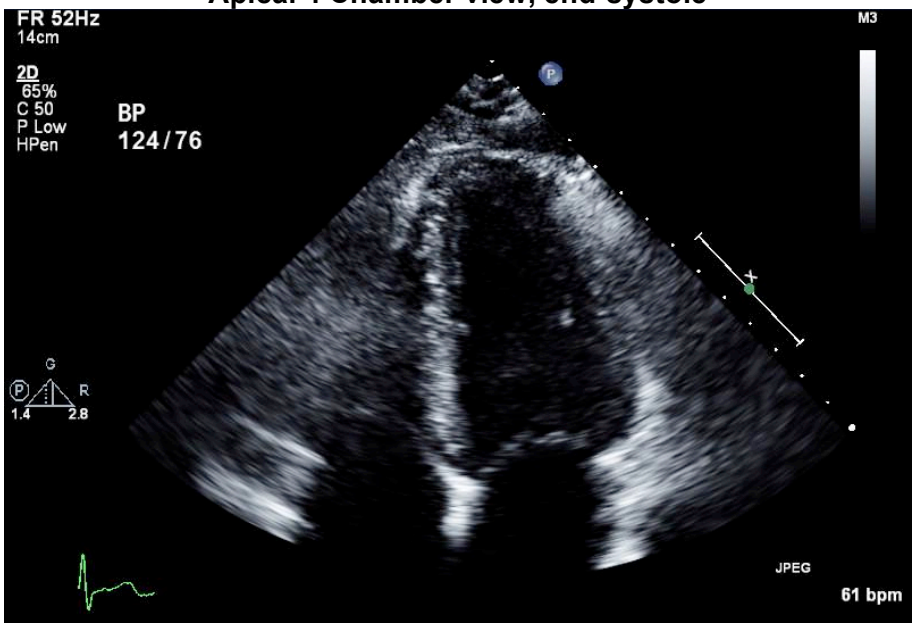
C.1.i. Apical 4-Chamber View Focused on LV

- Obtain 1 clip optimizing visualization (including imaging depth) of the left ventricle during systole and diastole.
    - Maximize LV length and be careful not truncate the true long axis.
    - The entire LV endocardium must be within the imaging sector in both end-diastole and end-systole. Pay special attention to the apex and the lateral LV free wall, which are often the most difficult areas to visualize.
    - Adjust sector width and imaging depth to ensure acquisition frame rate of 50 to 70 frames per second.

Apical 4 Chamber view, end-diastole

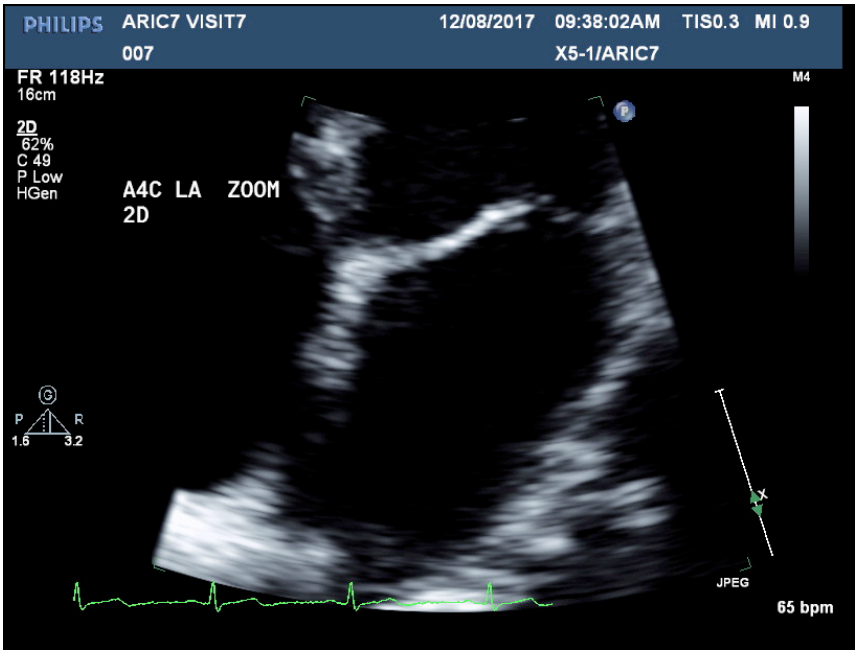


Apical 4 Chamber view, end-systole



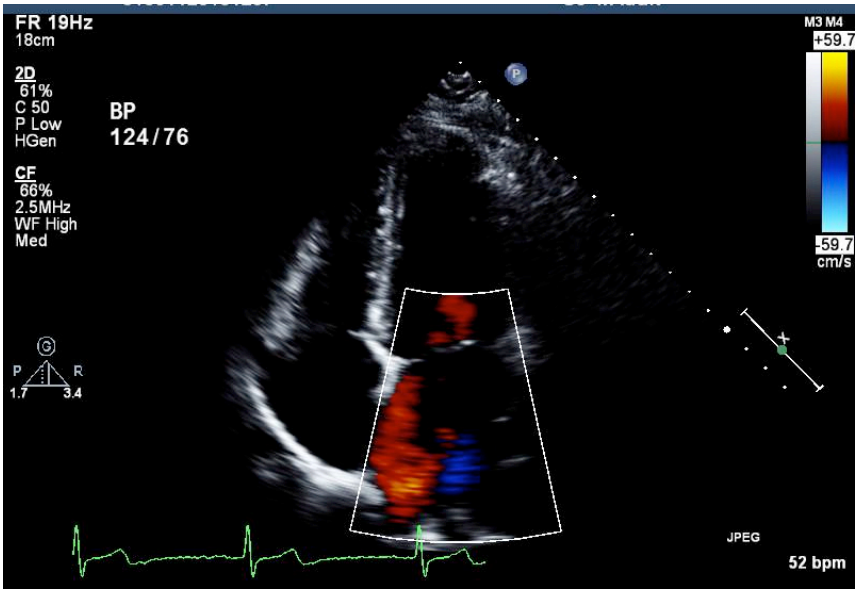
C.1.ii. Apical 4-Chamber view zoomed on LA

- Obtain 1 clip zooming in on the left atrium, and optimizing visualization of the left atrium during systole and diastole.
    - Properly align the image and capture the left atrium in full. Avoid any foreshortening of the chamber.



C.1.iii. Color Flow Doppler for Mitral Regurgitation

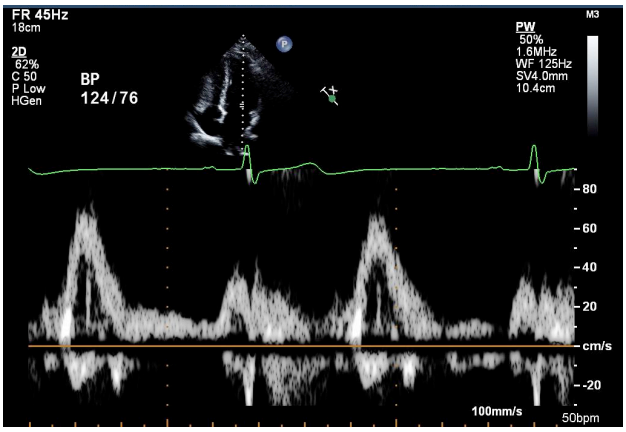
- Adjust color Doppler sample sector over the mitral valve and include the entire LA cavity. To optimize frame rate, keep the color sector scan as narrow as possible, while including the entire LA. Ensure that the color Nyquist limit is 60-65 cm/s.



C.1.iv. Spectral Doppler of Mitral Inflow

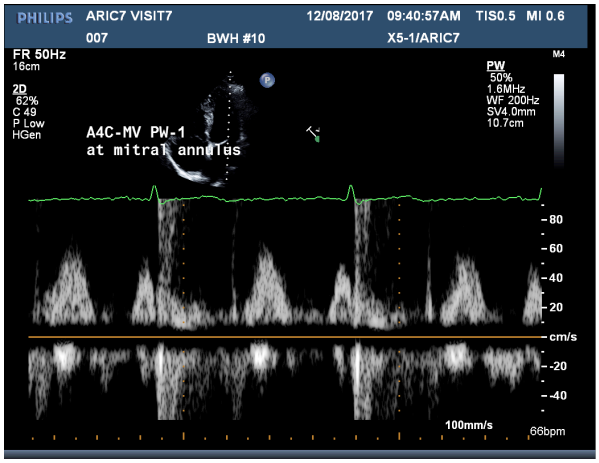
(a) PW Doppler at the mitral leaflet tips

- From the apical four chamber view record the mitral inflow velocity curve with the pulsed-wave Doppler sample volume positioned at the tips of the mitral leaflets during quiet respiration for 30 seconds (or at least five cardiac cycles). Adjust the baseline and Doppler scale to visualize the peak E and A wave velocities. Record a minimum of 3 cardiac cycles (10 for subjects in atrial fibrillation) at a sweep speed of 100 mm/sec.



(b) PW Doppler at the mitral annulus

- From the apical four chamber view record the mitral inflow velocity curve with the pulsed-wave Doppler sample volume positioned at the mitral annulus during quiet respiration for 30 seconds (or at least five cardiac cycles). Adjust the baseline and Doppler scale to visualize the peak E and A wave velocities. Record a minimum of 3 cardiac cycles (10 for subjects in atrial fibrillation) at a sweep speed of 100 mm/sec.



(c) CW Doppler of mitral inflow

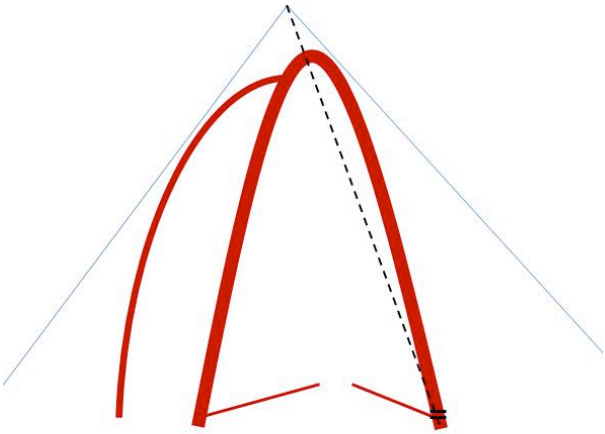
- From the apical four chamber view record the mitral inflow velocity curve with the continuous-wave Doppler sample volume positioned through the mitral annulus during quiet respiration for 30 seconds (or at least five cardiac cycles). Adjust the baseline and Doppler scale to visualize the peak E and A wave velocities. Record a minimum of 3 cardiac cycles (10 for subjects in atrial fibrillation) at a sweep speed of 100 mm/sec.

C.1.v. Tissue Doppler Imaging (TDI) of Mitral Annulus (lateral and septal)

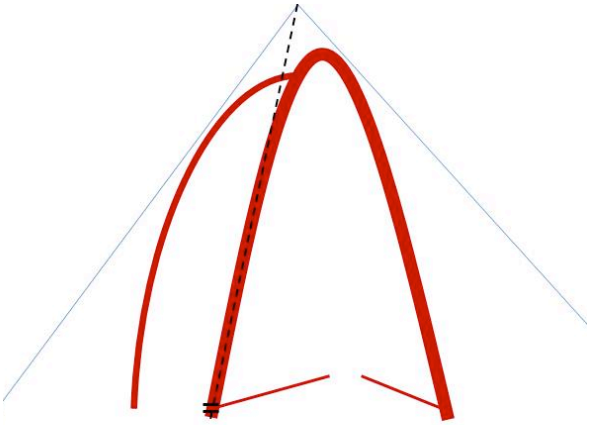
- Guildelines of TDI image acquisition and optimization

1. Decrease image depth (to include the LV and a small part of the LA, ideal depth approximately 16 cm) and optimize the 2D image for the LV, focusing on the lateral wall and the mitral annular region.
2. Adjust the image to orient the motion of the lateral wall parallel to the cursor. Both gains and filter settings should be set low (100 Hz or less) to obtain the best images.
3. Initiate 2D color DTI and position the sample volume on the ventricular side of the lateral mitral annulus at the junction of the LV wall with the mitral annulus of the lateral myocardial segment; the myocardium should stay within the sample volume for as much of the cardiac cycle as possible.
4. Before the data is acquired, check that only the region to be sampled is moving through the sample volume.
5. Switch to PW spectral DTI and set the scale to 20 cm/sec with a sweep speed of 100 mm/sec.
6. Before collecting data, set the Pulsed Doppler velocity range to avoid velocity aliasing (a velocity range of +/- 24 cm/sec is normal though subjects with high heart rates may require a higher setting).
7. Once a clear pattern is obtained, record at least 10-20 beats during quiet respiration (or preferably during breath holding at end-expiration).
8. Record a minimum of 3 cardiac cycles (10 for subjects in atrial fibrillation) at a sweep speed of 100 mm/sec.
9. Repeat this process for the septal mitral annulus

Proper positioning of sample volume for mitral annular TDI:



Lateral

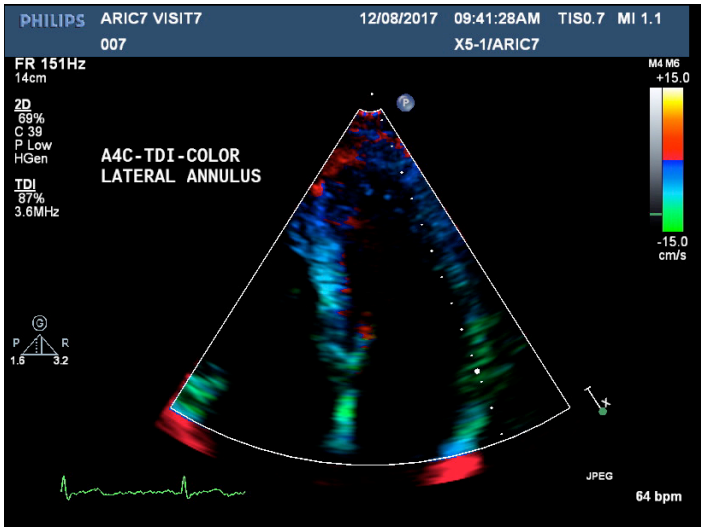


Septal

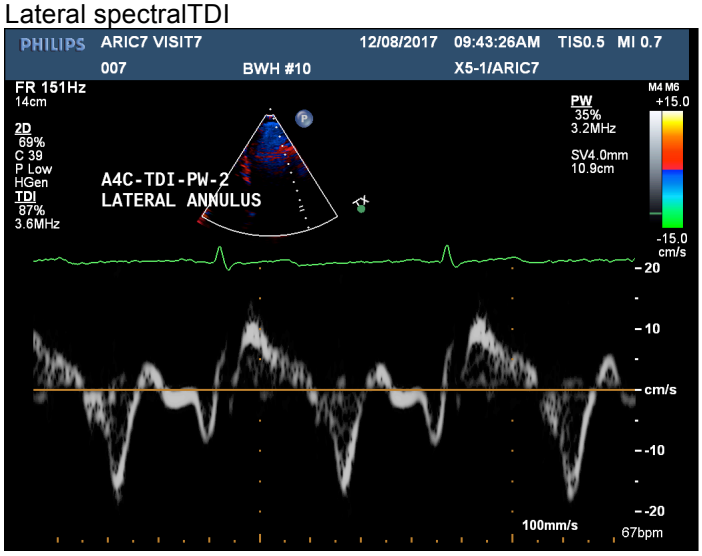
For both septal and lateral TDI acquisition, acquire 1 clip of color TDI demonstrating placement of the spectral Doppler sample volume, prior to acquisition of TDI spectral Doppler.

Tissue Doppler imaging at the lateral mitral annulus

Lateral color TDI

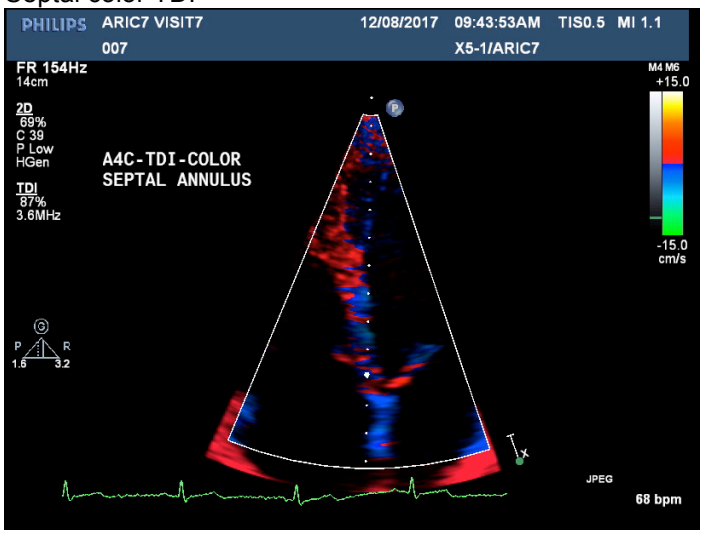


Lateral spectralTDI

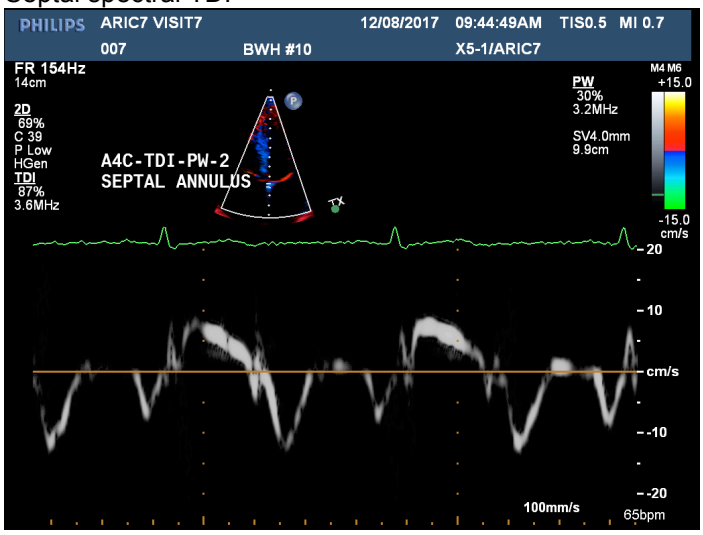


Tissue Doppler imaging at the septal mitral annulus

Septal color TDI



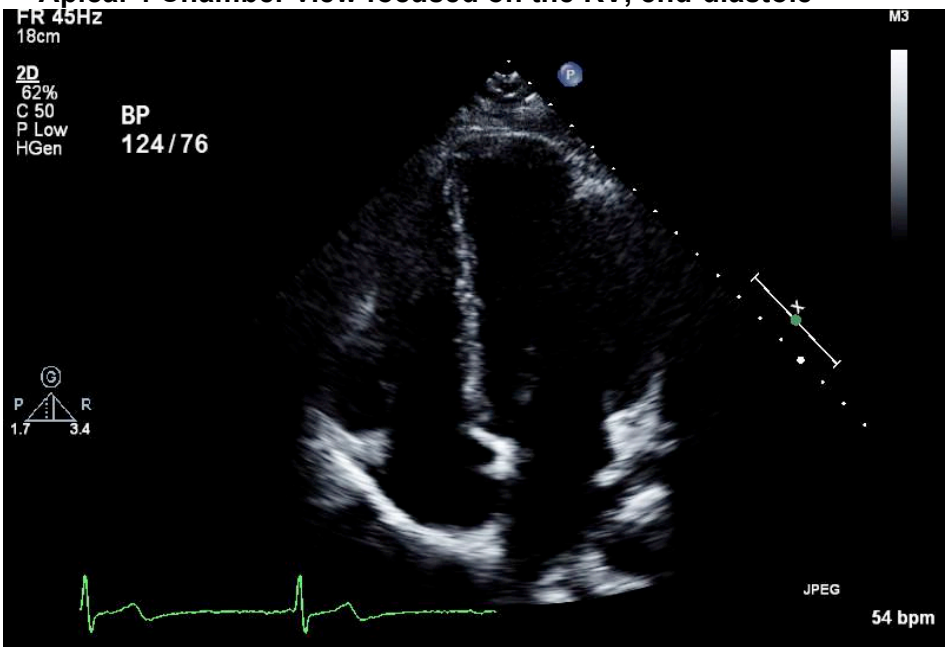
Septal spectral TDI



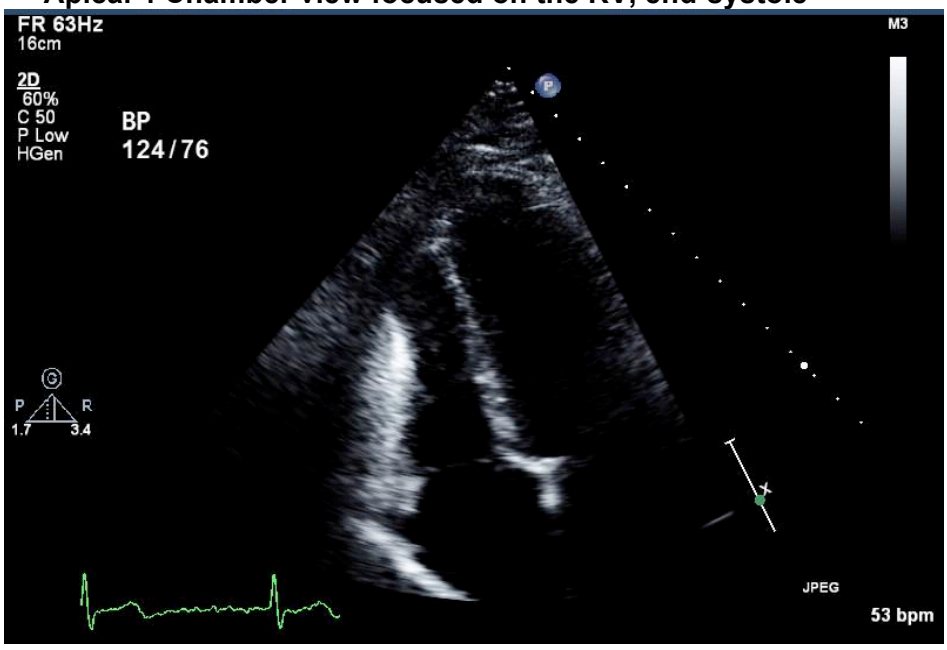
C.2. Apical 4-Chamber View (Focused on the Right Ventricle)

- The right ventricular length is maximized and the right ventricular apex is clearly visualized. The entire RV endocardium must be within the sector scan in both end-diastole and end-systole.

Apical 4 Chamber view focused on the RV, end-diastole

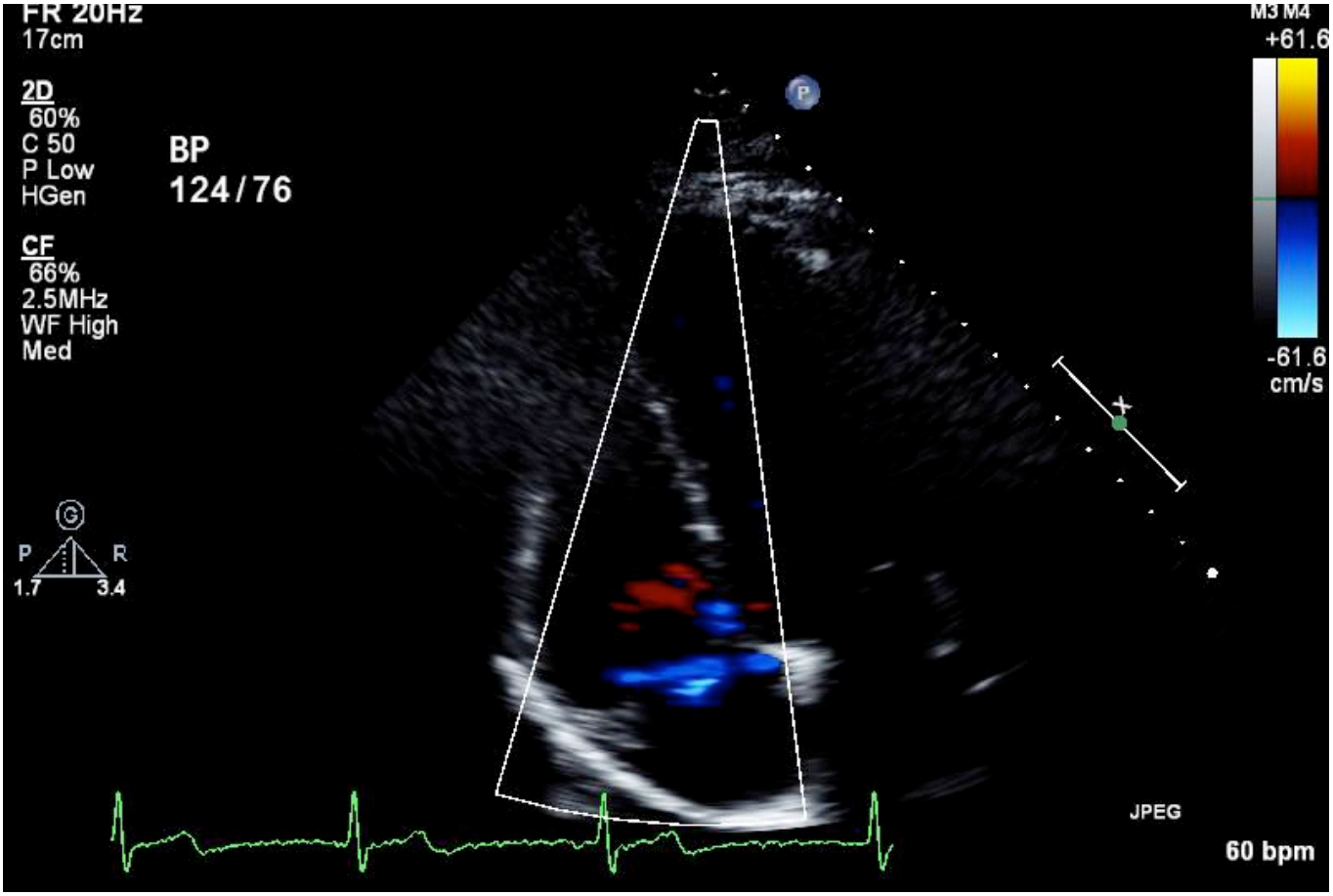


Apical 4 Chamber view focused on the RV, end-systole



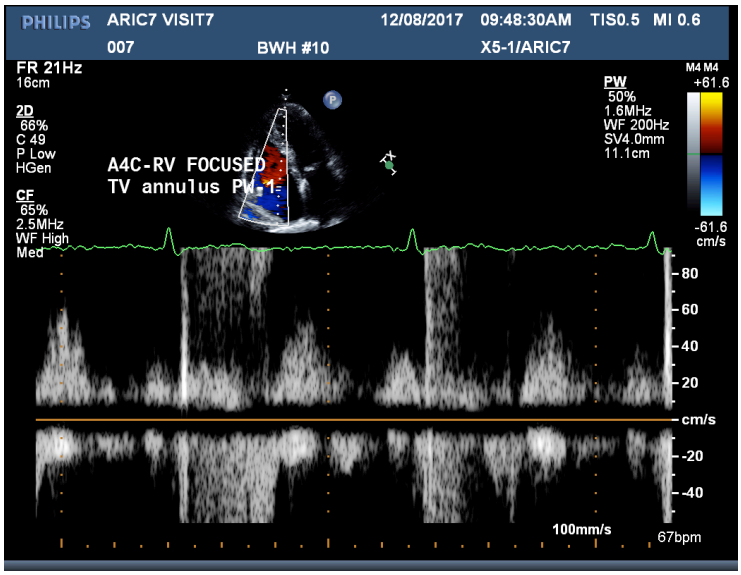
C.2.i. Color Doppler of tricuspid inflow and regurgitation

- Adjust color Doppler sample sector over the tricuspid valve and include the entire RA cavity. The color Nyquist limit sure be 60-65 cm/sec.



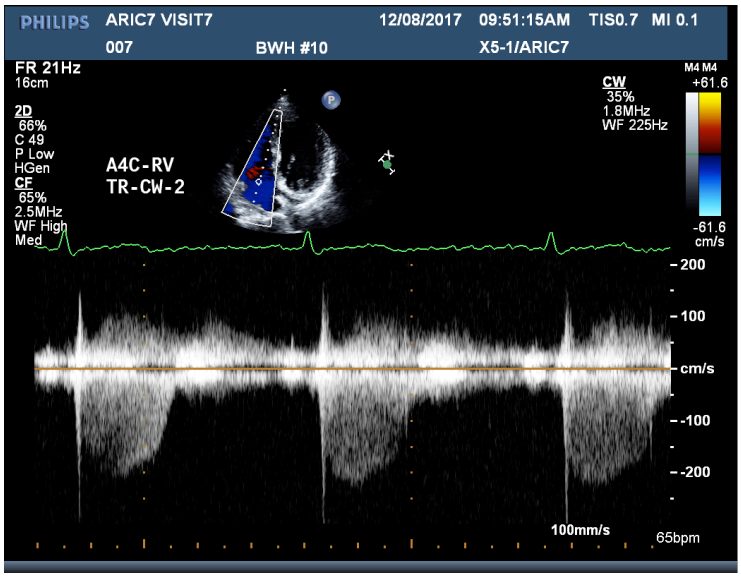
C.2.ii. Pulse Wave Doppler at tricuspid annulus

Record the tricuspid inflow velocity curve with the pulsed-wave Doppler sample volume positioned at the tricuspid annulus during quiet respiration for 30 seconds (or at least five cardiac cycles). Adjust the baseline and Doppler scale to visualize the peak E and A wave velocities. Record a minimum of 3 cardiac cycles (10 for subjects in atrial fibrillation) at a sweep speed of 100 mm/sec.



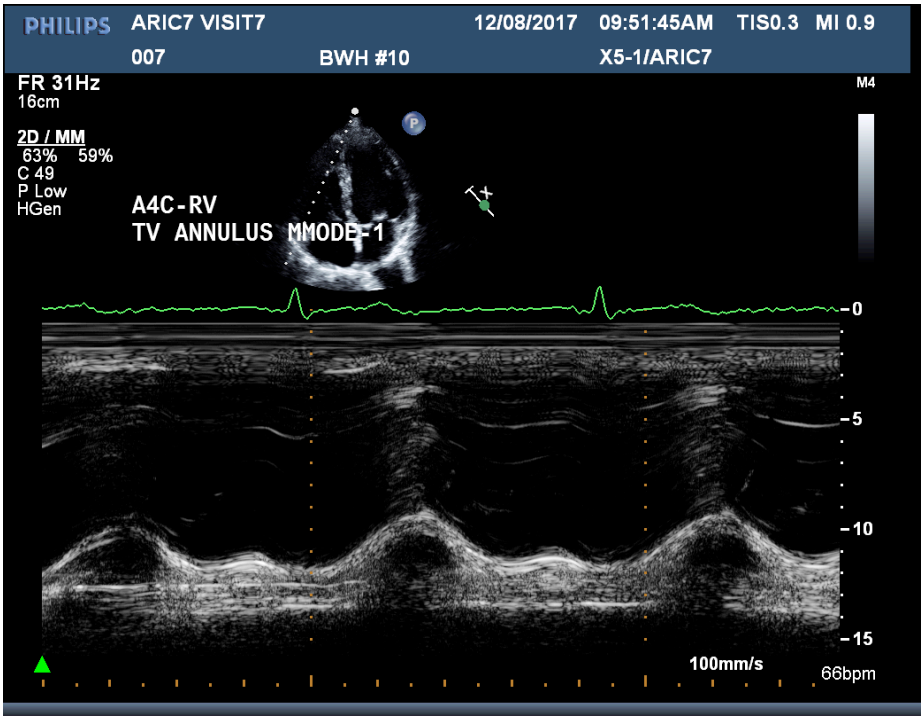
C.2.iii. CW Doppler of Tricuspid Regurgitation

- Position the interrogation line down the right ventricle and atrium as parallel to tricuspid regurgitant flow as possible. Adjust the baseline and scale to capture the peak TR velocity. Aim to obtain a parabolic spectral Doppler envelope that is visible for >two-thirds of the systolic period. Record at least 3 (10 for subjects in atrial fibrillation) full representative systoles at sweep speed of 100 mm/sec.



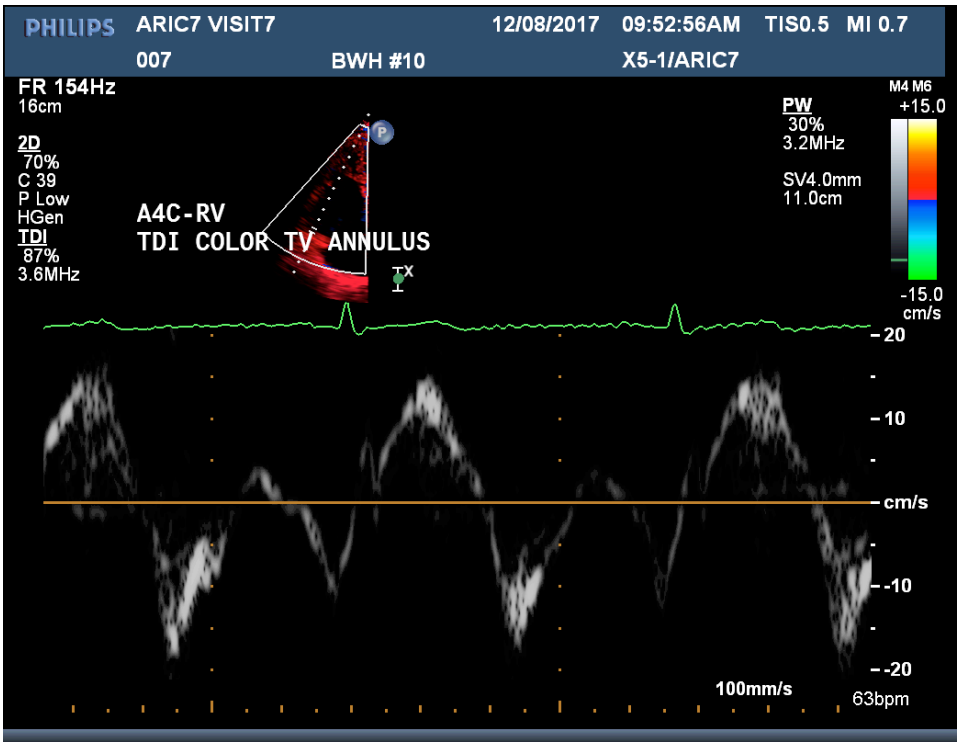
C.2.iv. M-mode imaging of the lateral tricuspid annulus (for TAPSE assessment)

- Decrease image depth to include the RV and a small part of the RA (optimal depth approximately 16 cm) and optimize the 2D image for the RV, focusing on the tricuspid annular region.
- Adjust the image to orient the motion of the lateral tricuspid annulus parallel to the cursor. Both gains and filter settings should be set low to obtain the best images.
- Initiate M-mode and ensure that M-mode cursor remains on axis with movement of the lateral tricuspid annulus



C.2.v. Tissue Doppler imaging at the lateral tricuspid annulus

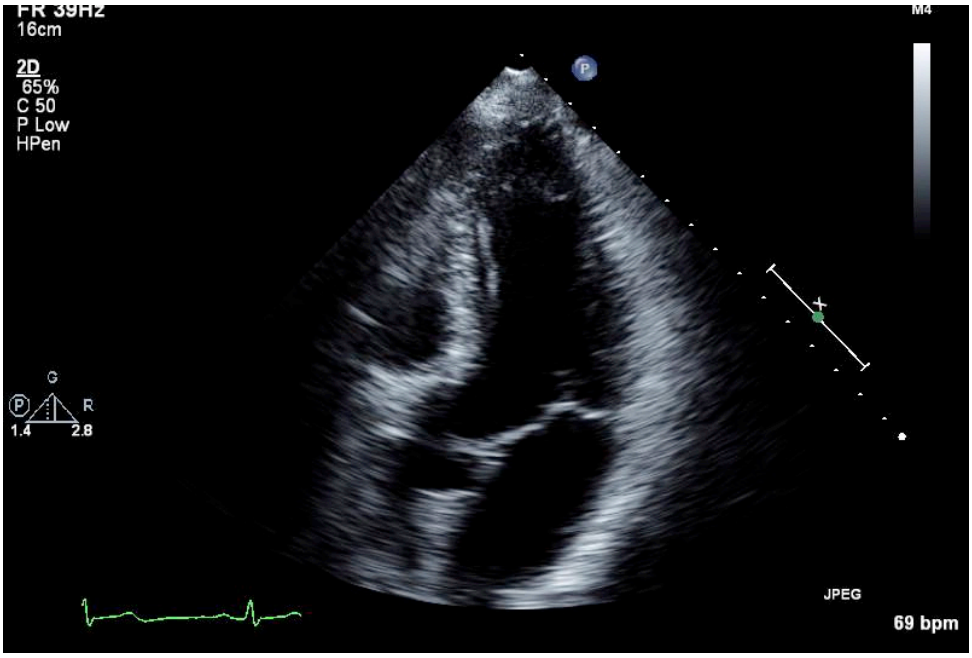
- Decrease image depth to include the RV and a small part of the RA (optimal depth approximately 16 cm) and optimize the 2D image for the RV, focusing on the tricuspid annular region.
- Adjust the image to orient the motion of the lateral tricuspid annulus parallel to the cursor. Both gains and filter settings should be set low to obtain the best images.
- Initiate 2D color DTI and position the sample volume on the ventricular side of the lateral tricuspid annulus at the junction of the RV wall with the tricuspid annulus: the myocardium should stay within the sample volume for as much of the cardiac cycle as possible.
- Switch to PW spectral DTI and set the scale to 20 cm/sec with a sweep speed of 100 mm/sec. Once a clear pattern is obtained, record at least 10-20 beats during quiet respiration (or preferably during breath holding at end-expiration).
- Record a minimum of 3 cardiac cycles (10 for subjects in atrial fibrillation) at a sweep speed of 100 mm/sec.



C.3. Apical 5-Chamber View

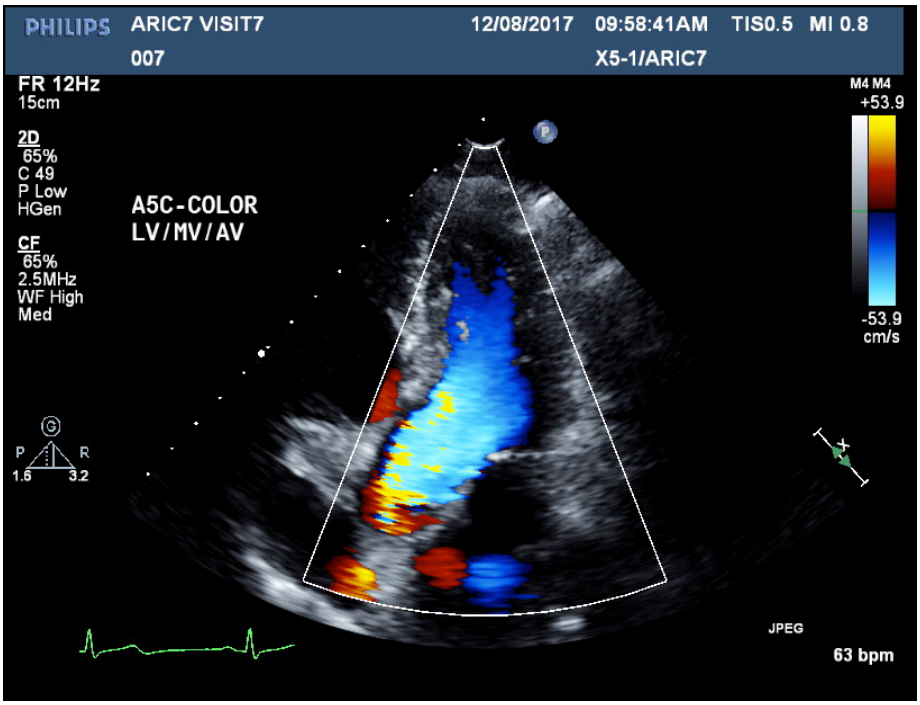
C.3.i. 2D imaging

- Maximize LV length, making sure not to truncate the true long axis



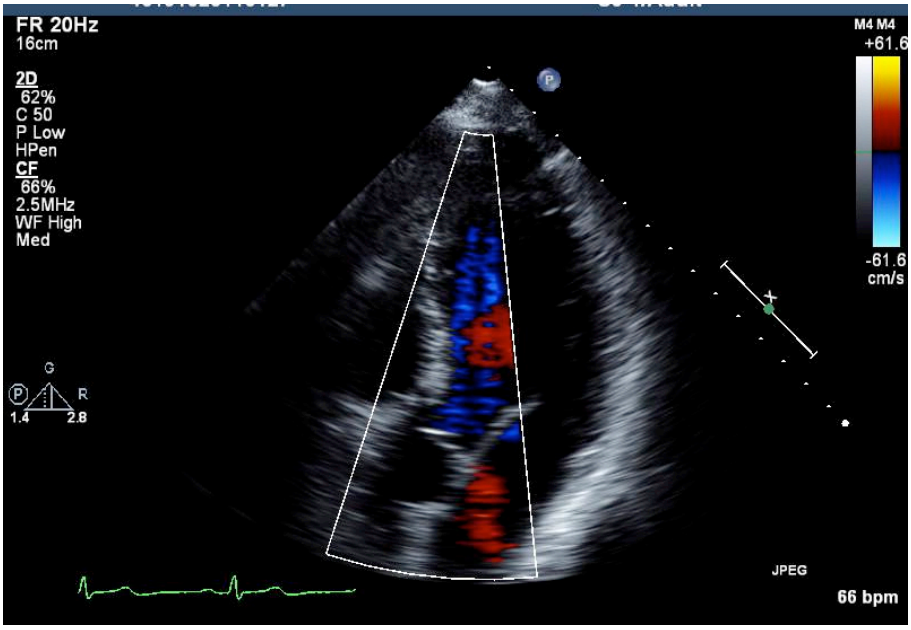
C.3.ii. Color Doppler of the MV, LV, and AV

- Ensure that the color Doppler sample window is wide and includes the entire MV, LV, LVOT, AV, and proximal aortic root
- Ensure the Nyquist limit is 60-65 cm/sec.



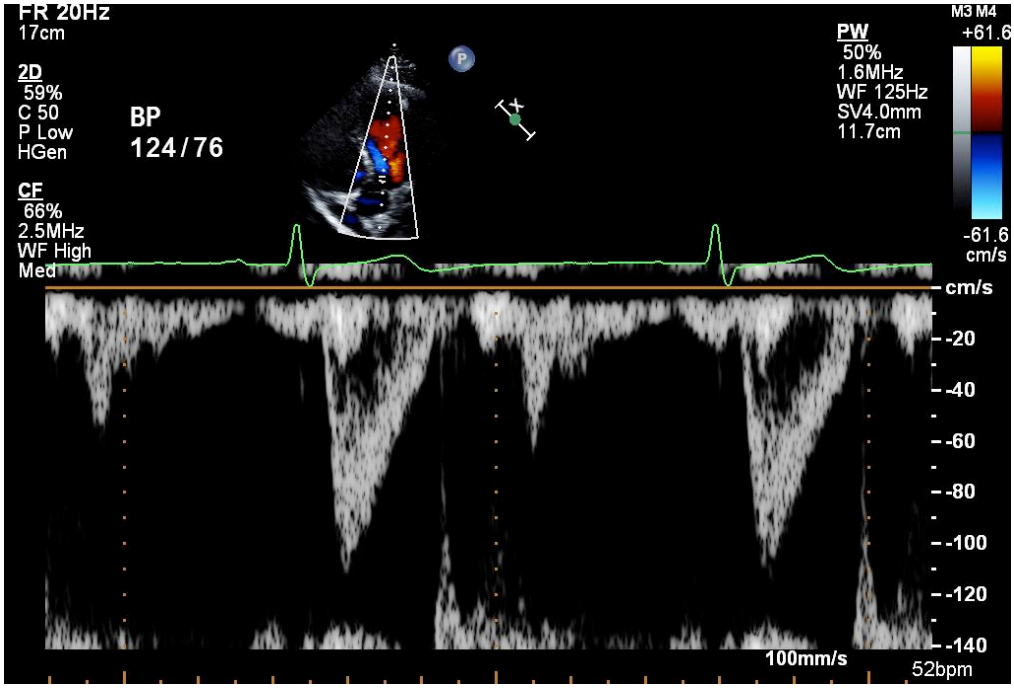
C.3.iii. Color Doppler of the LVOT and AV

- Narrow the color Doppler sample window to include the LVOT, AV, and proximal aortic root
- Ensure the Nyquist limit is 60-65 cm/sec.

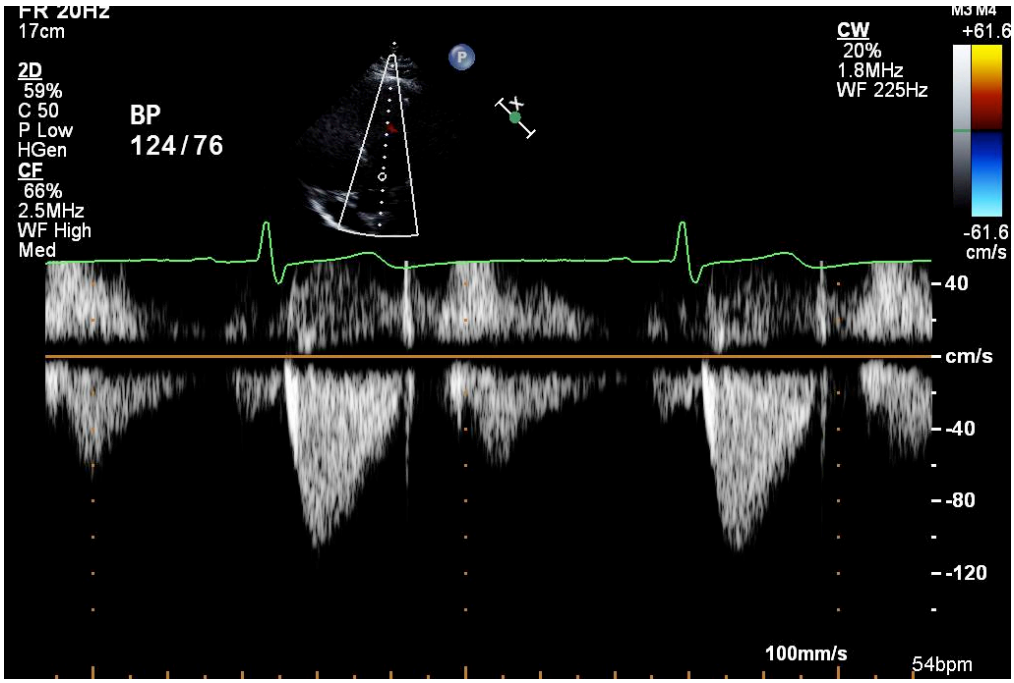


C.3.iv. Pulsed wave Doppler at the left ventricular outflow tract

- For pulse wave acquisition, ensure that the sample is in the left ventricular outflow tract (LVOT) approaching the aortic valve, just prior to the level of flow acceleration and spectral broadening. Record a minimum of 3 cardiac cycles (10 for subjects in atrial fibrillation) at a sweep speed of 100 mm/sec.



C.3.v. Continuous wave Doppler across the aortic valve

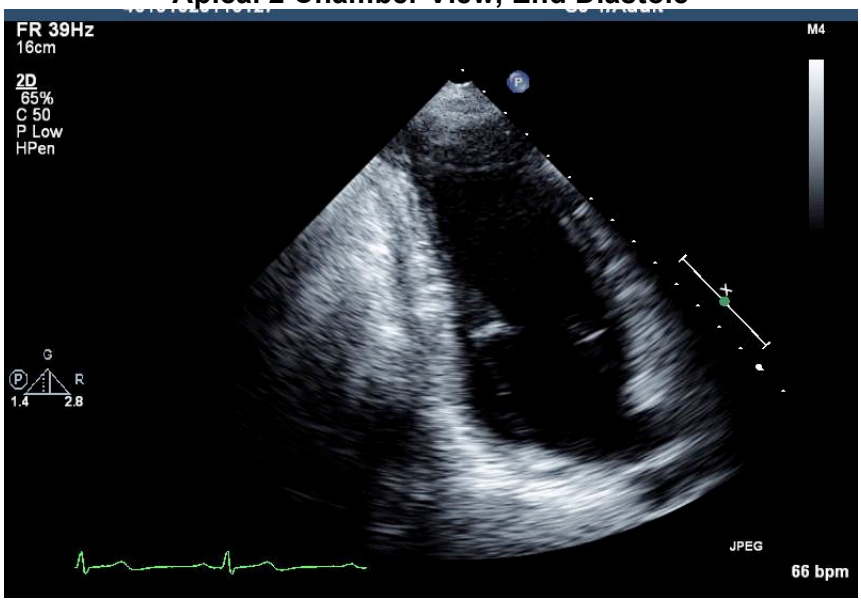


C.4. Apical 2-Chamber View

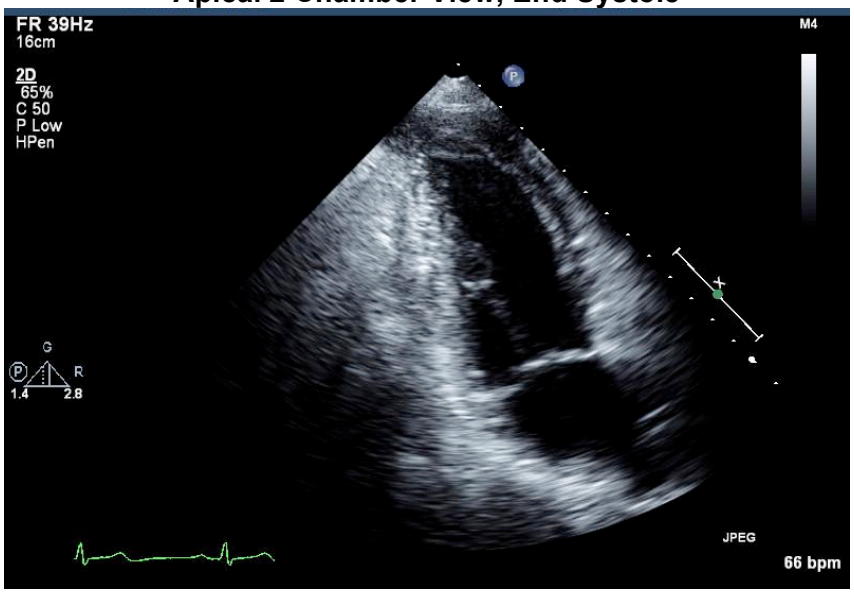
C.4.i. Apical 2-Chamber View focused on the LV

- Obtain 1 clip optimizing visualization of the left ventricle during systole and diastole.
  - Maximize LV length and be careful not truncate the true long axis.
  - The scan plane transects the anterior and inferior LV walls, with neither the RV nor the LV outflow tract visualized.
  - The most difficult areas in which to visualize the endocardium are usually the anterior LV wall and the apex; pay particular attention to these walls**.** Visualization of both anterior and inferior wall endocardium will be essential to accurately calculate left ventricular volume by Simpson's formula.
  - Adjust sector width and imaging depth to ensure acquisition frame rate of 50 to 70 frames per second.

Apical 2 Chamber View, End Diastole

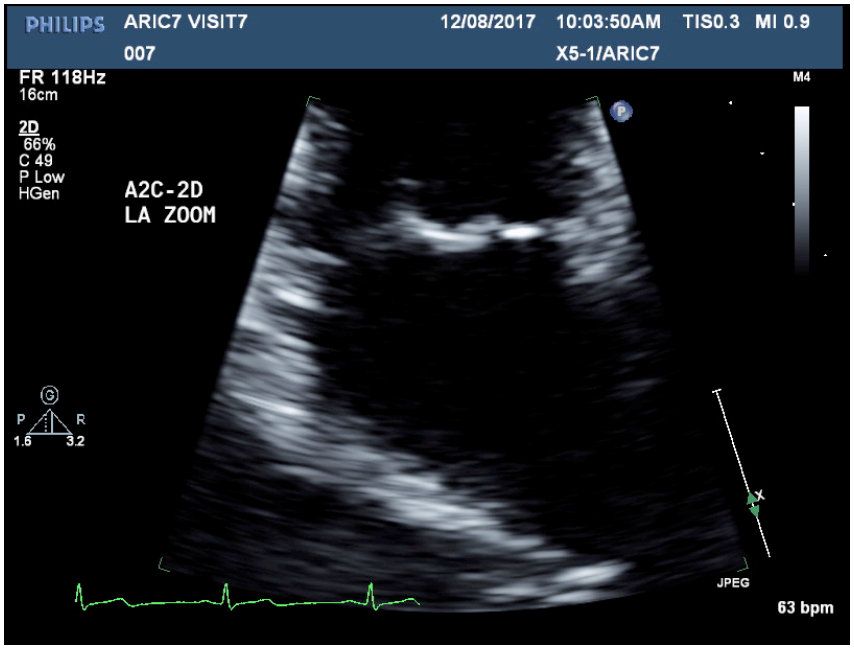


Apical 2 Chamber View, End Systole



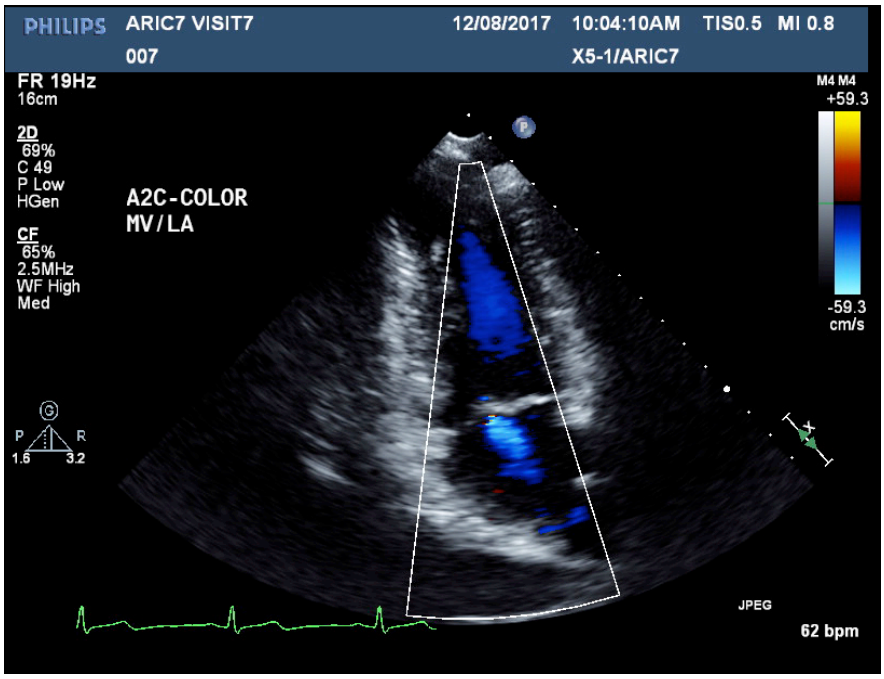
C.4.ii. Apical 2-Chamber View zoomed on the LA

- Obtain 1 clip zooming in on the left atrium, and optimizing visualization of the left atrium during systole and diastole.
    - Properly align the image and capture the left atrium in full. Avoid any foreshortening of the chamber.



C.4.iii. Color Flow Doppler for Mitral Regurgitation

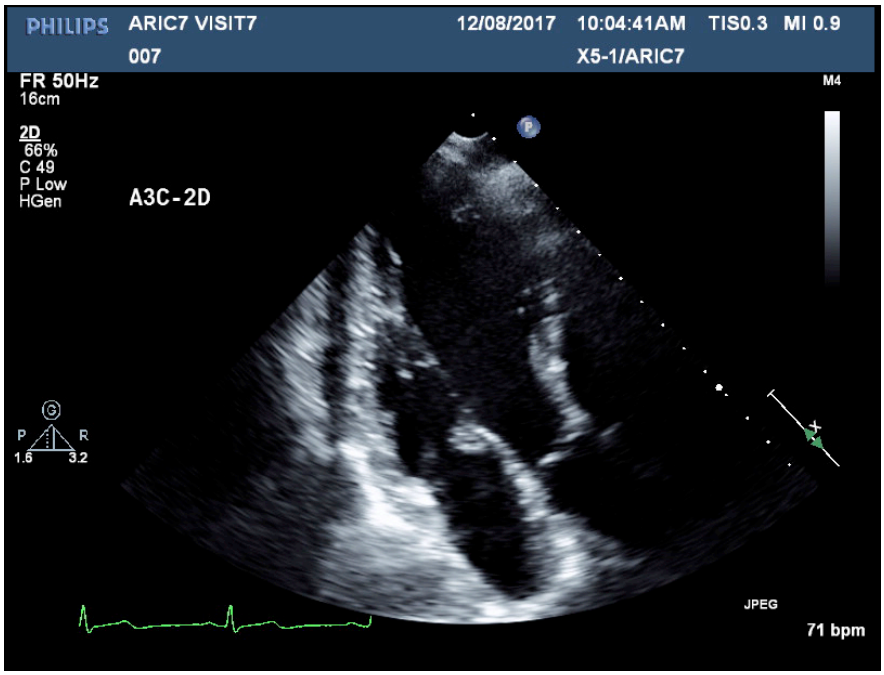
Adjust color Doppler sample sector over the mitral valve and include the entire LA cavity. To optimize frame rate, keep the color sector scan as narrow as possible, while including the entire LA. Ensure that the color Nyquist limit is 60-65 cm/s.



C.5. Apical Three Chamber View

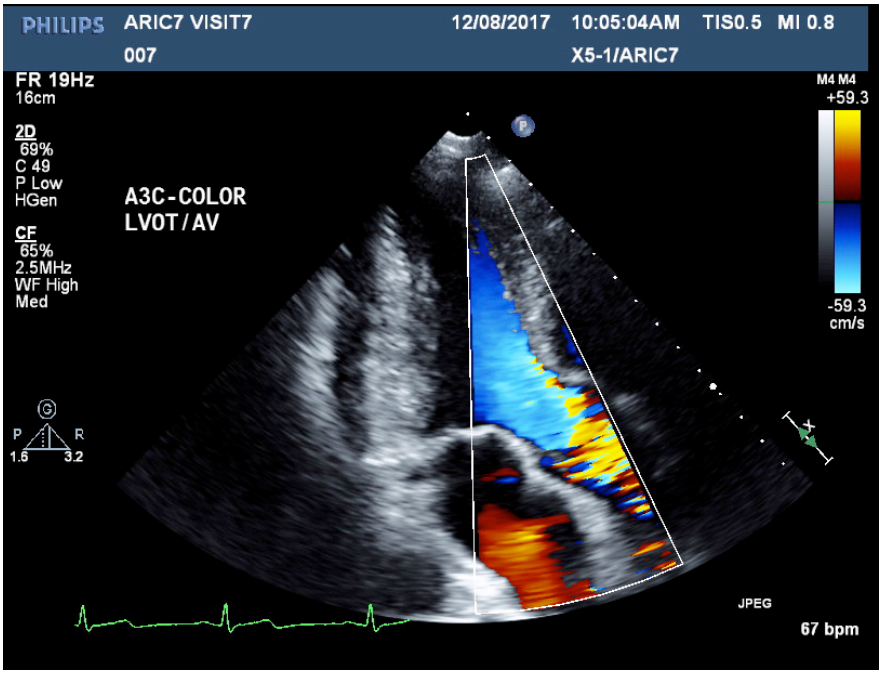
C.5.i. Apical 3-chamber view – 2D imaging

- Obtain a 2D image, including the entire LA and LV and mitral valve



C.5.ii. Apical 3-Chamber view – color Doppler

- Ensure the color Doppler sample window to include the LVOT, AV, and proximal aortic root
- Ensure the Nyquist limit is 60-65 cm/sec.



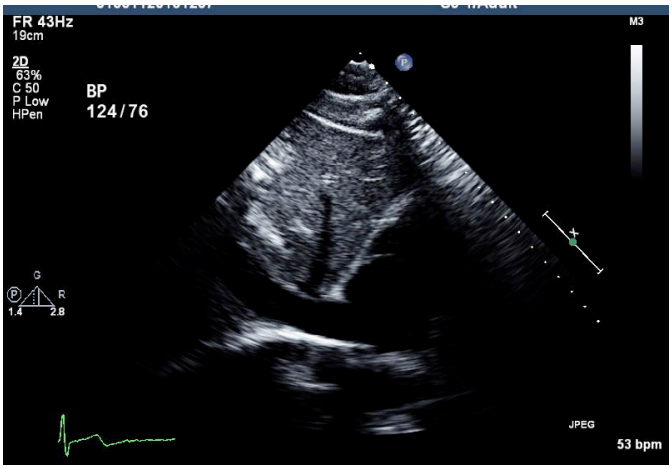
D. Sub-costal View

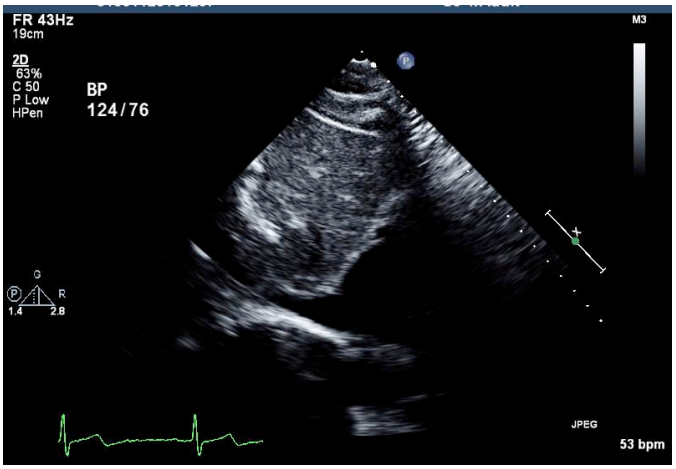
Two views will be obtained from the subcostal position:

- Imaging of the inferior vena cava (IVC)
- The subcostal four-chamber view

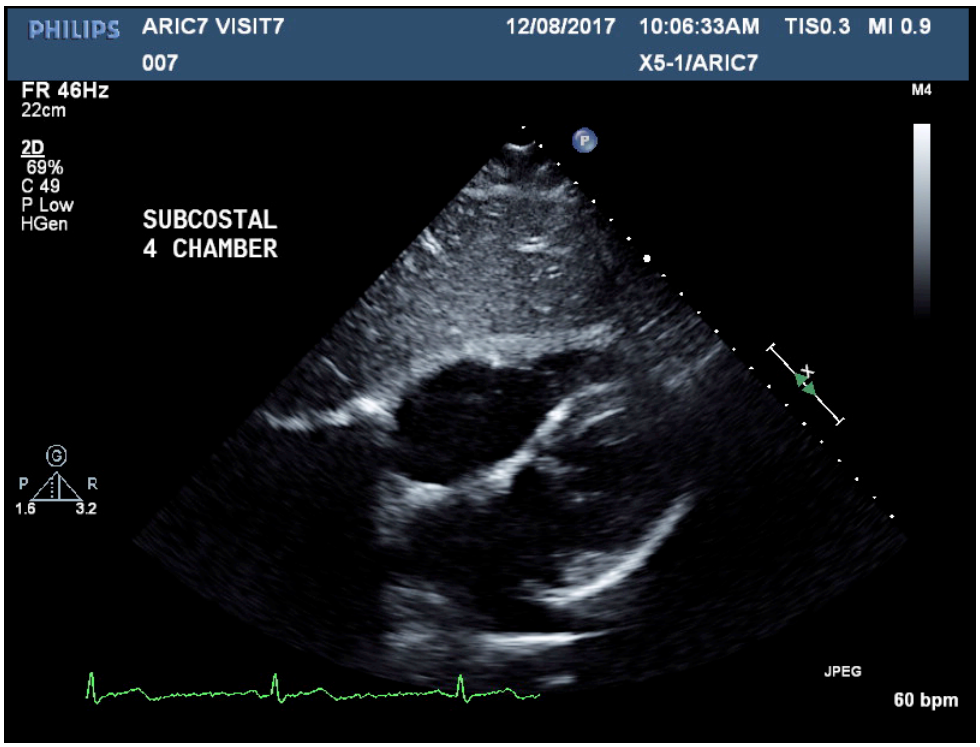
D.1. Subcostal imaging of the IVC

- This view is obtained from the sub-xiphoid position with the transducer manipulated to visualize the proximal inferior vena cava where it meets the right atrium. Approximately 5-10 beats should be acquired in this view to allow for assessment of both IVC size and compressibility with respiration.





D.2. Subcostal 4-Chamber View

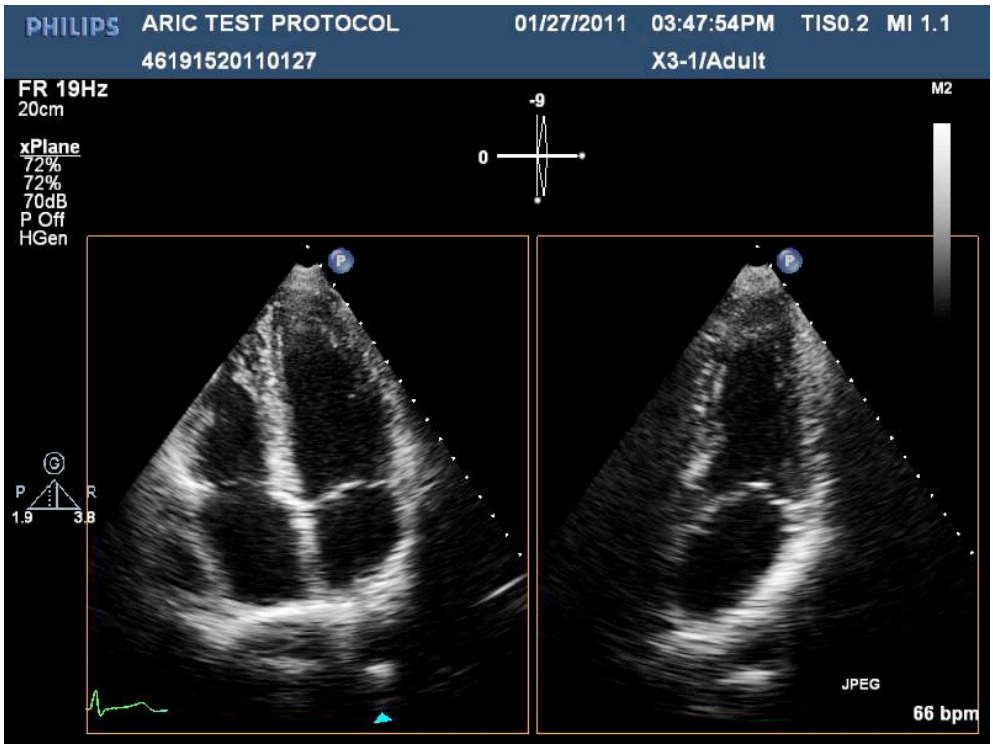


E. 3D Acquisition

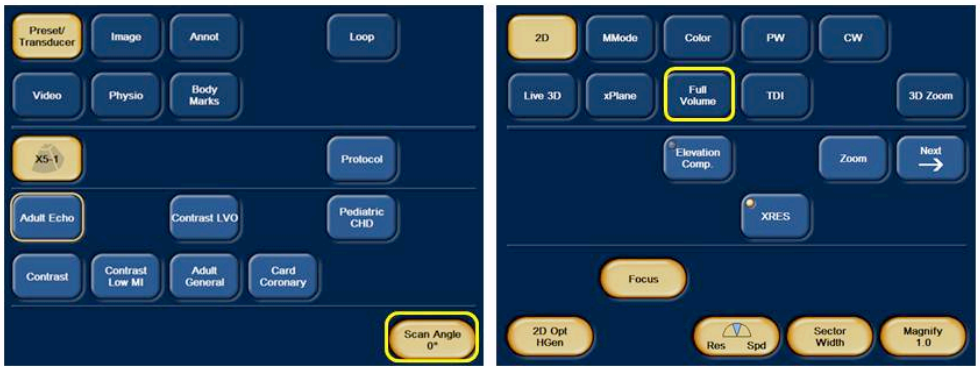
Pause the imaging protocol by clicking ‘Pause Protocol’ prior to acquiring 3D volumetric datasets. All 3D acquisitions are full volume acquisition.

E.1. 3D full volume acquisition of the Left Ventricle

1. Optimize the apical 4 chamber view 2D image, including the entire LV and LA in the image. Adjust the sector width and depth to achieve the highest frame rate possible while being sure to include the entire LV and LA in the image.
2. Once optimized, click ‘xPlane’ to view the structure of interest in 2 orthogonal planes (0 degrees and 90 degrees) simultaneously. Ensure that the entire structure of interest is included in the imaging sector in both planes.



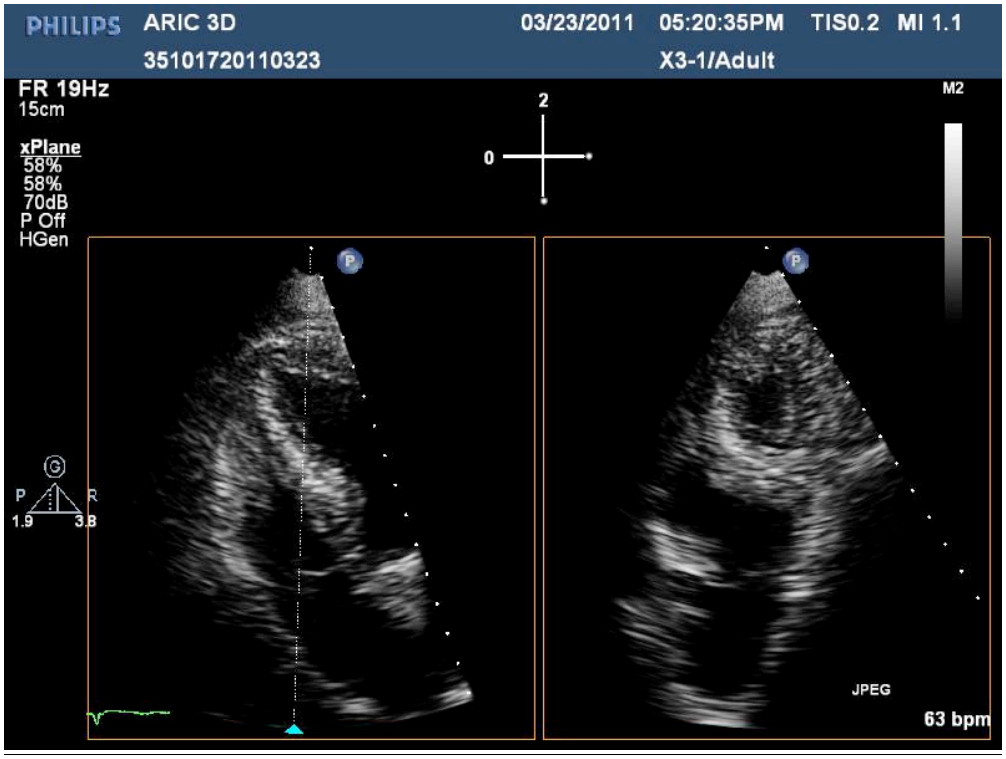
3. Activate “Full Volume” and ensure that “4 Beat Full Volume” is selected on the bottom of the right touch screen. Scan Angle will need to be set to 0 degrees.



4. Wait for the 4 quadrants of the volumetric images to ‘fill’
5. Ask the subject to hold their breath in order to minimize motion of the chest. If the subject is unable to hold their breath, then ask him/her to take very shallow breaths. Hold the image absolutely steady.
6. Once no ‘stitch’ artifacts are seen, count 6 cardiac cycles then press ‘Acquire’
7. The acquired volumetric dataset will automatically playback on the screen. Review this for (a) presence of stitch artifact; and (b) exclusion of any portion of the anatomic structures of interest. If either of these are present, repeat to acquisition.

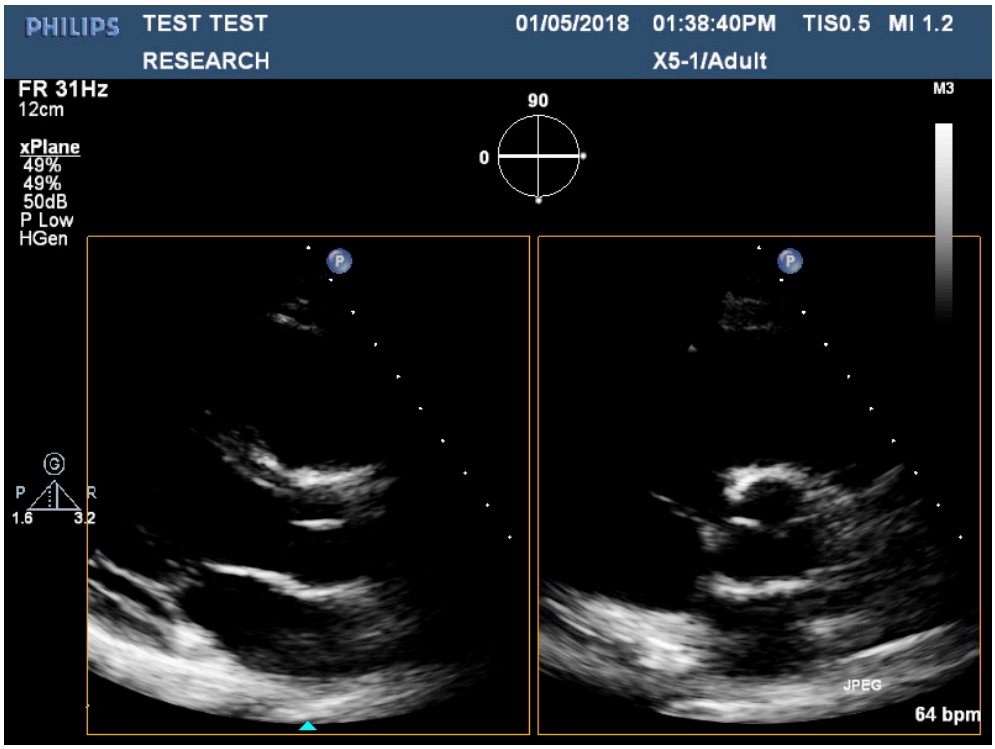
E.2. 3D full volume acquisition of the Right Ventricle

Follow the steps outlined above, focusing on the right ventricle in the apical 4-chamber view. The ideal reference 2D image when acquiring the 3D full volume acquisition of the right ventricle is demonstrated below.



E.3. 3D full volume acquisition of the Mitral and Aortic Valves

Follow the steps outlined above, focusing on the mitral and aortic valves in the parasternal long axis view. The ideal reference 2D image when acquiring the 3D full volume acquisition of the mitral and aortic valves is demonstrated below.



Once all 3D acquisitions of complete, un-pause the imaging protocol by clicking 'Pause Protocol' again.

Then end the study by first clicking 'Accept Protocol', then 'End Study'.

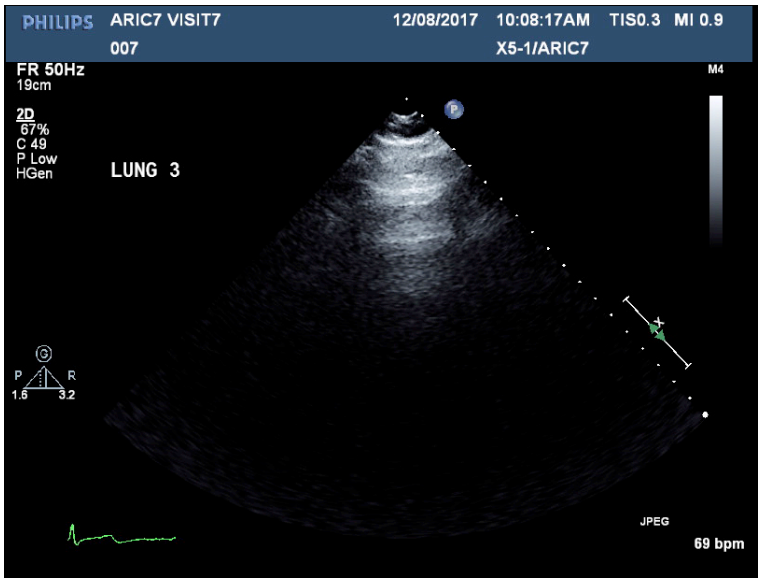
F. Lung Ultrasound

Lung ultrasound will be acquired as a separate imaging study/protocol. Select 'LUS' protocol. On the iE33 subject information screen, enter:

- 'ARIC' in the *Last Name* Field
- 'LUS' in the *First Name* Field
- Participant ARIC ID in the *Patient ID* Field
- Sonographer ARIC ID in the *Sonographer* Field

Acquire and image of this screen. The protocol will default to an 18 cm depth and 10 second acquisition duration. Images will be obtained from 8 intercostal spaces in the order specified in the image below (#1 through #8). Key image quality features for lung ultrasound are as follows:

- Orient the imaging probe vertically in the intercostal space with the probe marker facing the participant's feet
- Identify the following key anatomic landmarkers: (1) two rib shadows in short axis, flanking (2) the hyper-echoic pleural line in the near field
- Optimize gain for each acquisition



Once all 8 images are complete, accept the protocol and end the study.

XI. Reporting of Critical Results

Sonographers performing echocardiographic studies will occasionally identify abnormalities that they consider important and will alert site investigators directly. These findings will include, but are not limited to, tamponade, aortic dissection, thrombosed or frankly dysfunctional prosthetic valve, pseudoaneurysm, intracardiac abscess or obvious vegetation, intracardiac thrombus, ventricular septal defect, and intracardiac mass/tumor. The Echocardiography Reading Center will also be informed via a "critical alert" checkbox and a free text field in the electronic Echocardiography Transmittal Form (ETF) to facilitate an expedited analysis of the study. Site investigators will be responsible for handling alert findings (either as alerts requiring emergency/immediate referral, urgent referral, or routine referral as they deem appropriate), including relaying findings to study participant and, where consent has been provided, to the participant's treating provider. We recommend that each site establish a system that allows the site sonographer to communicate directly with the local consultant cardiologist (in person or by phone) with joint review of the echo images, as needed, to verify presence of a possible critical alert and coordinate with clinic staff the most appropriate course of action for the participant. Possible and/or verified critical alerts will be expedited for review by the Echocardiography Reading Center.

Other abnormalities that may be detected by the sonographer (in conjunction with the consultant cardiologist, as needed) that would be considered a non-critical alert include: a) low EF <=30%; b) pericardial effusion > 1cm, without hemodynamic compromise; c) flail MV leaflet with severe mitral regurgitation; d) other severe valvular disease (aortic, mitral, tricuspid, or pulmonic); e) hypertrophic cardiomyopathy with evidence of obstruction; f) severe pulmonary HTN with PASP >70 mmHg; g) large aortic aneurysm with ascending aorta >50 mm diameter; and, h) complex congenital heart disease. These findings are not considered true critical alerts but, if identified, will also be expedited for review by the Echocardiography Reading Center.

Over-reading cardiologists at the Echocardiography Reading Center may identify critical abnormalities that would require emergent notification and arrangements for care. Such findings will be reported within 24 hours of review by the Reading Center to the Data Coordinating Center and will be communicated to the field centers as an Immediate Alert Notification. Abnormalities that would trigger a critical result include, but are not limited to a) tamponade, b) aortic dissection, c) thrombosed or frankly dysfunctional prosthetic valve, d) pseudoaneurysm, e) intracardiac abscess or obvious vegetation, f) intracardiac thrombus, g) ventricular septal defect, and, h) intracardiac mass/tumor. Each field center should have a plan for handling these types of alerts, including relaying findings to study participant and, where consent has been provided, to the participant's treating provider.

Over-reading cardiologists at the Echocardiography Reading Center may identify specific non-critical abnormalities that would be important for a patient and physician to be aware of, but that don't necessarily require emergent care. These findings will be incorporated into the routine data transfers from the Echocardiography Reading Center directly to the Data Coordinating Center. Such findings include the items listed above as "non-critical" alerts in addition to: a) moderate or greater mitral regurgitation, b) moderate or greater mitral stenosis, c) moderate or greater obstructive lesions of left ventricular outflow, including aortic stenosis and dynamic left ventricular outflow tract obstruction, d) moderate or greater aortic regurgitation, e) moderate to severe pulmonary hypertension, f) severe right ventricular enlargement.

Limited quantitative data will be included in the routine reporting letter generated by the data coordinating center for all participants. This will include three commonly used measures of cardiac structure and function: a) left ventricular ejection fraction, b) left ventricular diastolic diameter, c) left ventricular wall thickness. These data will be presented in a table with reference values (see example below).

Parameter	Value	Sex	Low Normal	Mildly Abnormal	Moderately Abnormal	Severely Abnormal
LV ejection fraction (%)	[VALUE]	Both	50 – 54	45 – 49	30 – 44	<30
LV diastolic diameter (cm)	[VALUE]	Men		6.0-6.3	6.4-6.8	≥6.9
		Women		5.4-5.7	5.8-6.1	≥6.2
LV wall thickness (cm)	[VALUE]	Men		1.1-1.3	1.4-1.6	≥1.7
		Women		1.0-1.2	1.3-1.5	≥1.6

Reference values are based on practice guidelines published by the American Society of Echocardiography.[1]

[1] Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;28:1-39.

XII. Contact Information

For technical echo-related questions, please direct all questions and inquiries to the Brigham and Women's Hospital Cardiac Imaging Core Lab:

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Fax:	1-617-582-6027
Email:	echocore@rics.bwh.harvard.edu ARIC Study Cardiac Imaging Core Lab PBB Ground Rm A-100 20 Shattuck Street Boston, MA 02115 USA