MAESTRIA

Deliverable 4.3

Guideline for ECG, echocardiography, MRI and CT imaging acquisition, processing and storage of whole blood, EDTA plasma, SST serum.

Date: November 2021

HORIZON 2020 – RIA programme
Digital diagnostics – developing tools for supporting clinical decisions by integrating various diagnostic data

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Version	1

Abstract

Atrial fibrillation (AF) and stroke are major health care problems in Europe. They are most often the clinical expression of atrial cardiomyopathy, which is under-recognized due to the lack of specific diagnostic tools. Multidisciplinary research and stratified approaches are urgently needed to prevent, diagnose, and treat AF and stroke and preempt the AF-related threat to healthy ageing in Europe. MAESTRIA is a European consortium of 18 clinicians, scientists and Pharma industrials who are at the forefront of research and medical care of AF and stroke patients. It will create multi-parametric digital tools based on a new generation of biomarkers that integrate artificial intelligence (AI) processing and big data from cutting edge imaging, electrocardiography and omics technologies. It will develop novel biomarkers, diagnostic tools and personalized therapies for atrial cardiomyopathy. Digital Twin technologies, a rich data integrator combining biophysics and AI will be used to generate virtual twins of the human atria using patient-specific data. Unique experimental large-animal models, ongoing patient cohorts and a prospective MAESTRIA cohort of patients will provide rigorous validation for new biomarkers and newly developed tools. A dedicated core lab will collect and homogenize clinical data. MAESTRIA will be organized as a user-centered platform, easily accessible via clinical parameters routinely used in European hospitals. A Scientific Advisory Board comprising potential clinician users will help MAESTRIA meet clinical and market needs. Dissemination and visibility of the MAESTRIA consortium mission will benefit from participation of the German Competence Network on Atrial Fibrillation (AFNET), and support from the European Society of Cardiology, clinicians, scientists, and other professional societies. MAESTRIA will be ready to tackle the major challenges of data integration and personalized medicine focused on atrial cardiomyopathy, AF and stroke.

Contents

1. Introduction

The MAESTRIA (Machine learning and artificial intelligence for early detection of stroke and atrial fibrillation) project is an 18-partner Research and Innovation action (RIA) with the objective of developing and validating the first integrative diagnostic digital platform for atrial cardiomyopathy diagnosis. This platform will be designed to provide support for improved diagnostic accuracy that increases effectiveness and efficiency of treatments, as well as prevention of the complications of atrial cardiomyopathy, such as atrial fibrillation and stroke.

The WP4 is led by AFNET (Atrial Fibrillation NETwork), a German academic research organization integrating an interdisciplinary research network of clinicians, scientists, practices, hospitals and institutes, especially in German speaking countries.

The main goal of WP4 within MAESTRIA is to validate multimodality biomarkers of the atrial cardiomyopathy generated in the WP1, 2 and 3 and to test whether it could be used in the clinical practice. WP4 will analyse several large datasets from Investigator Initiated Trials (IITs) and registries by AFNET. In addition, a prospective cohort with the collection of relevant parameters as defined in WP1-3 will be set up (MAESTRIA-AFNET 10).

For MAESTRIA-AFNET 10 we are planning to recruit approximately 600 patients from 30 sites in 6 different countries (France, Germany, Greece, The Netherlands, Spain and United Kingdom). The participating sites will collect relevant clinical parameters for Atrial Fibrillation from patients: (digital-)ECGs, cardiac CT, MRI, echocardiograms and blood sampling for routine lab parameters and optional biobank sampling. Dedicated core labs will collect and homogenize the clinical data.

2. Purpose of this document

The purpose of this document is to provide the participating sites with a series of guidelines created by the core labs, describing ECG, echo, MRI and CT imaging acquisition, and the processing and storage of the blood samples for the MAESTRIA central Biobank.

3. Blood collection for MAESTRIA Central Biobank

The patients participating in this study will have the option to provide an extra blood sample at the time of the routine blood extraction. Given that this extra blood sample is optional, the patient will need to sign a separated informed consent form.

More details about the processing and storage of this extra blood collection can be found in the attached guideline on the following two pages.

Guideline for collection, processing and storage of blood samples for the MAESTRIA central Biobank

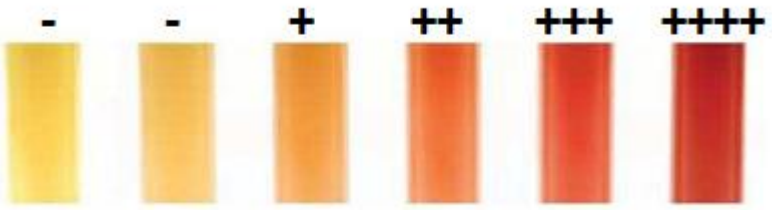
The patients participating in MAESTRIA-AFNET 10 can provide **extra blood** at the time of the routine blood extraction (they will need to sign a separated informed consent form).

The **extra blood volumen** would be **12ml** divided into 2 separate tubes : (A) 6ml for Serum preparation and (B) 6ml for Plasma preparation. The processing of the samples is described in detail below :

(A) 1 x 6 ml SST Tubes for Serum preparation

Process blood samples within 2 hours of collection.

1. Label cryotubes as indicated : XXXX (*) coding strategy is indicated below.
2. Leave SST blood tube to clot for at least 30 minutes at room temperature.
3. Centrifuge 10 minutes at 1500 g at room temperature
4. Aliquote serum into **12** aliquots of **200µL** using 2 ml screw cap tubes (x 12)
5. Please collect only non-hemolized samples (-) according to the scale below



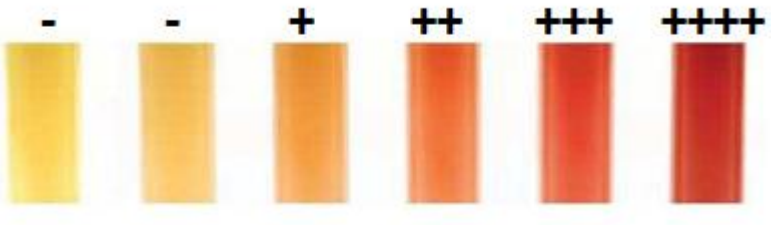
6. Freeze immediately at **- 80°C.** If a -80 °C ultrafreezer is not available at your site, please contact the central bank (SU-ICAN ; see below for full address) to arrange frequent shipments.

(B) 1 x 6ml EDTA Tubes for plasma preparation

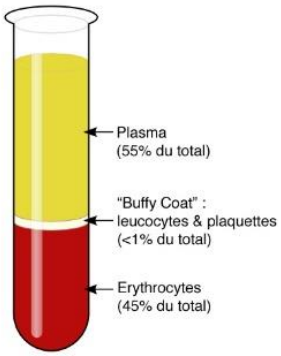
Process blood samples within one hour of collection. Keep blood samples at 4 °C until processed.

1. Label cryotubes as indicated : XXXX (*) coding strategy is indicated below.
2. Centrifuge 15 minutes at 2300 g at + 4 ° C
3. Collect plasma with a pipette without reaching the buffy coat
4. Aliquot plasma into 12 aliquots of 200µL using 2 ml screw cap tubes (x 12)

5. Please collect only non-hemolized samples (-) according to the scale below



6. Collect the buffy coat layer (see Figure) in a 2 ml tube
7. Freeze buffy coat and plasma samples immediately at **- 80°C.** If a -80 °C ultrafreezer is not available at your site, please contact the central bank (SU-ICAN ; see below for full address) to arrange frequent shipments.



(*)Coding strategy for the samples sent to Biobank:

The samples collected will be pseudonymized using a code that consists of the recruiting centre number + patient number (MAESTRIA ID) + 2 letters.

Location of the MAESTRIA central Biobank in France :

Biological Resources Centre Bio-ICAN
Institute of Cardiometabolism and Nutrition (ICAN)
IE3M, 47-83, boulevard de l'Hôpital
75013 Paris, France
CRB.Bio-ICAN@ican-institute.org
Bio-ICAN is certified ISO 9001:2015 and NF S96-900:2011

4. Guidelines from the Core Labs

In this section we include the guidelines prepared by the core labs (in their original format).

The guidelines appear in the following order:

- Guideline for ECG: Maastricht University and YourRhythmics.

- Guideline for CT scans: Oxford: UOXF & Caristo Diagnostics

- Guideline for MRI: AP-HP, LIB, SU-ICAN

- Guideline for echocardiography: AP-HP & Saint Antoine Hospital, Paris

Maastricht University and YourRhythmics

GUIDELINE for ECG:

MAESTRIA - Minimal requirements for ECG recordings and export
V 30.6.2021

1. Support of ECG recordings at the participating center:
- The availability of a contact person in the participating center willing to get familiarized with data export and anonymisation. This person will serve as contact point for technical questions around ECG recordings (noise management) and data export, storage, anonymisation and transfer.
- An ECG recording site initiation meeting will be held at each center before start of inclusion to make arrangements for optimal ECG recordings and noise monitoring and for data transfer incl. anonymisation.
- Detailed SOPs for ECG recording, anonymisation and transfer will be provided by Maastricht University and YourRhythmics.

2. ECG recordings
Minimum:
- standard 12-lead ECG configuration
- at least 5 minute recording (resting ECG)
- sampling frequency at least 500 Hz
- low-pass filter frequency: no filtering or at the lowest 150 Hz
- resolution at least 12 bit

Optional:
- additional leads (extended ECG lead placement as discussed during site initiation)

3. Storage and export:
Minimum:
- full disclosure storage
- export to a machine-readable format (text, xml, binary file with known file structure)
- no PDF or image.
- ECG must be anonymised before transfer (Maastricht University and YourRhythmics will provide procedures for this)

Some ECG devices from GE (CardioSoft) and Schiller (CardioVit) fulfil the full disclosure recording requirement of a 12-16 lead ECG. Export from the GE MUSE database system (to xml) requires a specific license, but is often limited to 10-second standard ECGs recorded with a GE MAC system.

Maastricht University and YourRhythmics will work with the participating center on a tailored solution, starting from what is available at that specific center.

Machine Learning Artificial Intelligence Early Detection Stroke Atrial Fibrillation (MAESTRIA)

Coronary CT Angiography (CCTA)

Core Laboratory Imaging Manual

Document Number V2.0

1 Contents

1. Introduction and Overview

The Oxford Cardiovascular Computed Tomography Core Laboratory (OXACCT Core Lab) will work in partnership with Caristo Diagnostics (a University of Oxford spinout company) to provide image management and advanced image analysis of CCTA data from within the MAESTRIA Study. The University of Oxford is a partner within the MAESTRIA Consortium.

CCTA data for the purposes of this manual refers to the original DICOM files for the CCTA scans. These data will be pseudo-anonymised or fully anonymised, and are not to contain any patient identifiable information.

This manual was created to serve as a guide to the individual sites for the acquisition and transfer of CCTA scans for the Maestria study. As an initial step in the imaging process, each site will receive a Site Questionnaire to complete. It requests important information about the site's available resources and equipment. Each site will also be required to successfully complete a certification process related to CT data acquisition and transmittal. Please refer to the certification section (Section 2) for details regarding these processes. Instructions for image acquisition and transfer are contained in this manual.

This manual also covers guidelines and instructions for submitting study CT scans to the Core Lab. This will be primarily accomplished by electronic submission via the Caristo portal, hosted by CIMAR.

Appendix 1 - Contact information for key personnel.

Appendix 2 - Cardiac CT guidelines for radiographers / technician in order to optimise the scans for analysis purposes.

Appendix 3 - CCTA Parameters Record Form (PRF)

Appendix 4 - Detailed instructions on how to upload research CT scans via the Caristo portal.

2. CCTA analysis

The OXACTT Core Lab will receive CCTA data from multiple sources within the MAESTRIA Consortium. The two primary work packages (WP) which will see CCTA data flow to the OXACCT Core Lab are WP1 and WP4. The exact data flow between the work packages will be different, however the analysis performed at the OXACCT will be identical.

As a summary, WP1 - 'Machine learning for multimodality atrial imaging' – will involve multiple hospital sites sharing anonymised CCTA data, up to 20'000 patients, with the core lab for the purposes of validation and refinement of the Atriomic AF & stroke algorithms. This is research orientated work. WP4 - 'Clinical cohorts for validation of new digital biomarkers' – will involve a smaller number, likely some 600 patients, shared from a number of different sites from both within and outside the MAESTRIA consortium for the purposes of demonstration and validation of AF risk calculation of technology developed within MAESTRIA. WP4 is traditional core lab analysis work and not for further research into the Atriomic algorithms as the results will be stand-alone and feed back to the WP4 leaders for their use in the project.

For the purposes of MAESTRIA, the analysis carried out on the CCTA scans will include the automated application of the Atriomic AF & stroke algorithm.

The outputs of WP1 will remain within the core lab for purposes of further refinement of the algorithms, as per MAESTRIA protocol.

The outputs of WP4 CCTA scans will flow back to the MAESTRIA datahub for incorporation and integration within the MAESTRIA demonstrator and validation work. This will be via sharing of databases via secure email or file transfer service.

3. Protocol

Ideally, all scans will be performed using each sites clinical CCTA protocol. We do not prescribe specific clinical CCTA acquisition protocols.

4. Image Transfer

All scans submitted must be in DICOM format, anonymised, and only site and subject-specific study ID's should be used.

Images are transferred using either a direct gateway link set up via your sites Picture Archiving and Communication (PACS) system or via the CIMAR image management platform.

The Cimar gateway is a small server that is installed within the University/Hospital network. It automatically and securely uploads imaging studies from DICOM devices or PACS to the Cimar cloud with minimal manual steps. There is no need to export images to a different system or storage device beforehand. It saves the person uploading studies considerable amount of time waiting for studies to be uploaded as the upload happens automatically in the background. The Cimar system can be configured to automatically de-identify patient information, and also automatically assign project-specific subject ID's.

The Cimar management platform is a web-based password protected service that supports the exchange of DICOM files. Studies will need to be exported from PACS to a storage device before upload. It will be configured to automatically anonymise all DICOM data before it is uploaded. Please refer to Appendix 5 for further information and instructions.

All site personnel that need to interact with the Cimar web-based platform will need their own account, which they must register before the study begins. A list of personnel and required access should be sent to ***sheena.thomas@cardiov.ox.ac.uk*** before the initial transfer. Additional user accounts can be requested at any time by contacting Sheena Thomas.

All submitted files uploaded via the CIMAR management platform must be accompanied by a Data Transmittal Form (DTF) and the CCTA Scanning Parameters Record Form (PRF). Please refer to Appendix 2 for details of which images / scan series to transfer.

Oxford Academic Cardiac CT Core Laboratory (OXACCT)

Division of Cardiovascular Medicine

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University of Oxford

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Email: sheena.thomas@cardiov.ox.ac.uk

Dr Henry West

Lead Researcher – MAESTRIA study at the University of Oxford

Phone 07401 931 003

Email: henry.west@cardiov.ox.ac.uk

OXACCT analysts who will work with MAESTRIA data within the core lab:

Ms Lucrezia Volpe, Ms Maria Lyasheva, Dr Michail Mavrogiannis

Appendix 2 – Cardiac CT Angiography Protocol – a guideline

Participant Positioning

Supine, Feet first

Participant Preparation

Cannulate the participant using an 18-gauge (green) cannula preferably in the right ACF.

Attach CT scanner compatible ECG monitoring – ensure good quality ECG is obtained. Clean the skin prior to electrode pad placement and adjust the amplitude if necessary.

Perform the initial observations – O2 saturations, Blood Pressure and Heart Rate (HR).

If HR > 60bpm then administer beta-blockers (unless contra indicated).

Give exact breathing instructions to the participant and have a practice run.

GTN (up to 800 µg) administered before the scan (unless contra indicated).

Ensure atropine is available if required.

Protocol

Calcium Score: If this is usual practice, then please ensure a wide FOV covering the entire thoracic skin edge is included as a recon. This may mean that you have to change the scan field of view to large / extra-large and then reduce the display field of view to the recommended size.

CCTA: Please use your department protocol as a baseline for the contrast enhanced scan.

- **kV** — 80, 100 or 120
- **Phase Range** — Cover 70 – 80% of the R-R interval (50% padding centred on 75% phase) at the minimum. If the heart rate / rhythm suggests a wider phase to be covered then cover as per departmental protocol.
  Please be aware of the dose limit set for the study (14mSv for the research scan)
- **Contrast** — As per the department protocol.
  Example – 120kV = 60-80mls @ 6mls /sec
  100kV = 50-60mls @ 5mls / sec
- **Coverage** — Position the volume(s) over the heart. **Ensure the coverage includes from the pulmonary trunk** (this may be slightly higher than the usual coverage) to below the apex of the

	left ventricle. Ensure both anterior and posterior borders of the heart are within the volume(s).

Reconstruction / Post processing to be sent to OXACCT Core Lab	
Calcium Score (if done)	Reconstructed to 2.5mm slices (Siemens = 2mm)
Lung	Whole scan field of view to be reconstructed to give skin edge to skin edge.
Cardiac Component	0.5/0.6/0.625 axial data
	Reconstructions at 5% of phase range (e.g. 70, 75 and 80%)
Lung	Widest field of view possible.
Bone equiv	Cardiac FOV
Detail / Edge	Cardiac FOV
STD (if not used for Cardiac)	Cardiac FOV
Soft (as used for abdominal imaging)	CardiacFOV

Please do not send any image captures/screen shots, because these do not de-identify using the Cimar portal.

CCTA Scanning Parameters Record Form (PRF)

Site ID		**Participant ID**	
Date of Scan		**Visit Nos**	
Name of Operator			

CT Scanner Used – Make and Model (if department has 2 or more scanners of the same make and model please use department identifier as well)	
kV	
mA	
Display Field Of View (DFOV)	
Scan Field of View (sFOV)- Max in cm	
Focal Spot Size (S, M, L)	
Phase Range Scanned (inc Prospective / Retro)	
Recon Kernal	
Contrast Type, Volume and Flow Rate	
Saline Volume and Flow rate	
Beta-blocker Name and Dose	
GTN Dose	
Total Study Radiation Dose (DLP) including Units	
Comments	

For OXACCT Lab:

Total Dose approved for VIP Study (2 scans)	**18 mSv**	Remaining Dose allowed for final CTCA	

The Oxford Academic Cardiovascular Computed Tomography Core Lab: Imaging Data Transmittal Form (DTF)

Section I: Image Data Demographics

Site Reference: **Participant ID Number:**

Scan Date: **Scan Time (as per image):**

Section II: Archival/Translation Information

Archive Media *(indicate type)*: ☐ DVD ☐ CD ☐ Electronic Transfer (File) ☐ Other-*specify*: _____
Please contact the OXACCT Core Lab to confirm compatibility – Ms. Sheena Thomas- *sheena.thomas@cardiov.ox.ac.uk / +447701050107*

Number of series included: _____
(For CT imaging please include all the different series (e.g. contrast and non-contrast, prospective or retrospective gating).

Instrument/Scanner Manufacturer: _____ **Model/Software Level:** _____
Indicate the scanner manufacturer (e.g. GE, Siemens, and Canon etc.) *(Indicate the Model Software level)*

Tube voltage (kVp): _____ **Slice thickness (mm):** _____

HR during acquisition: _____ **Arrhythmia: Y/N** **Heart Rhythm** _____

Prospective/Retrospective gating: _____ **Dose (DLP):** _____

Section III: Imaging Information

Timepoint *initial / follow-up / visit nos*	**Study Type** *(Please circle)*	**Anatomical Modality** *(Please circle all that apply per study date)*
	Non-contrast CCTA	Carotid Cardiac Chest Abdo Pelvis Other: _____
	Non-contrast CCTA	Carotid Cardiac Chest Abdo Pelvis Other: _____
	Non-contrast CCTA	Carotid Cardiac Chest Abdo Pelvis Other: _____

Instructions: For each imaging exam submitted, fill-out this form and include with the media shipment. For further information or questions contact Ms. Sheena Thomas +44(0)7701050107 or sheena.thomas@cardiov.ox.ac.uk

Additional Comments/Instruction: _____

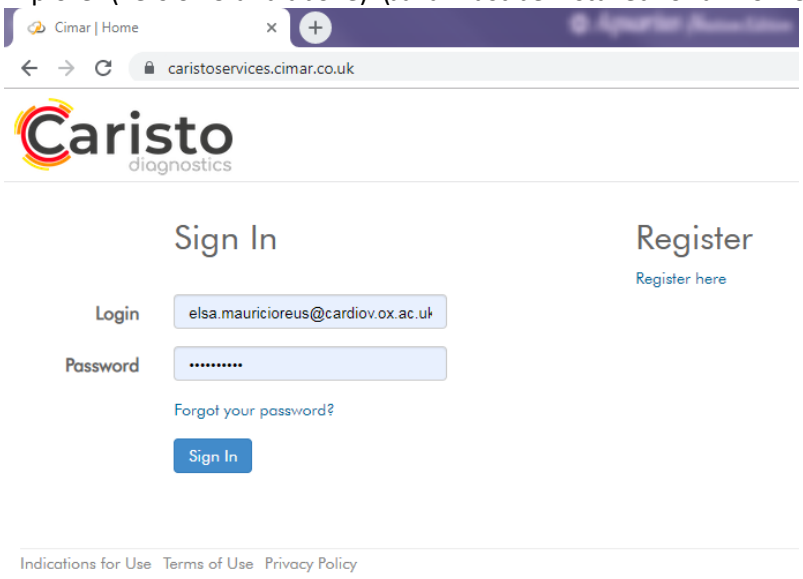
Form Completed By: _____
Email / Phone nos: _____ Date: _____
(This form MUST be completed by the site, signed and accompany all data submitted to OXACC CT Core Laboratory)

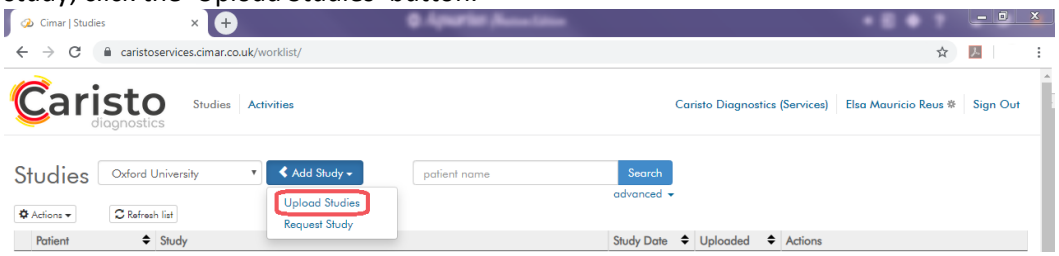
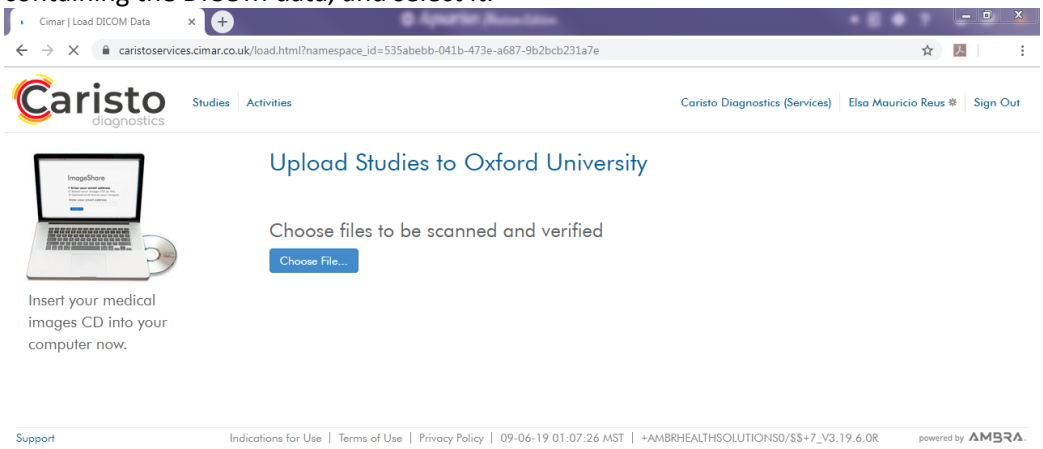
For OXACCT Core Lab Use Only:
Received By: _____
Date: _____
Process Completed By: _____
Date: _____

Oxford Academic Cardiovascular Computed Tomography Core Laboratory Data Transmittal Form (v3.0)

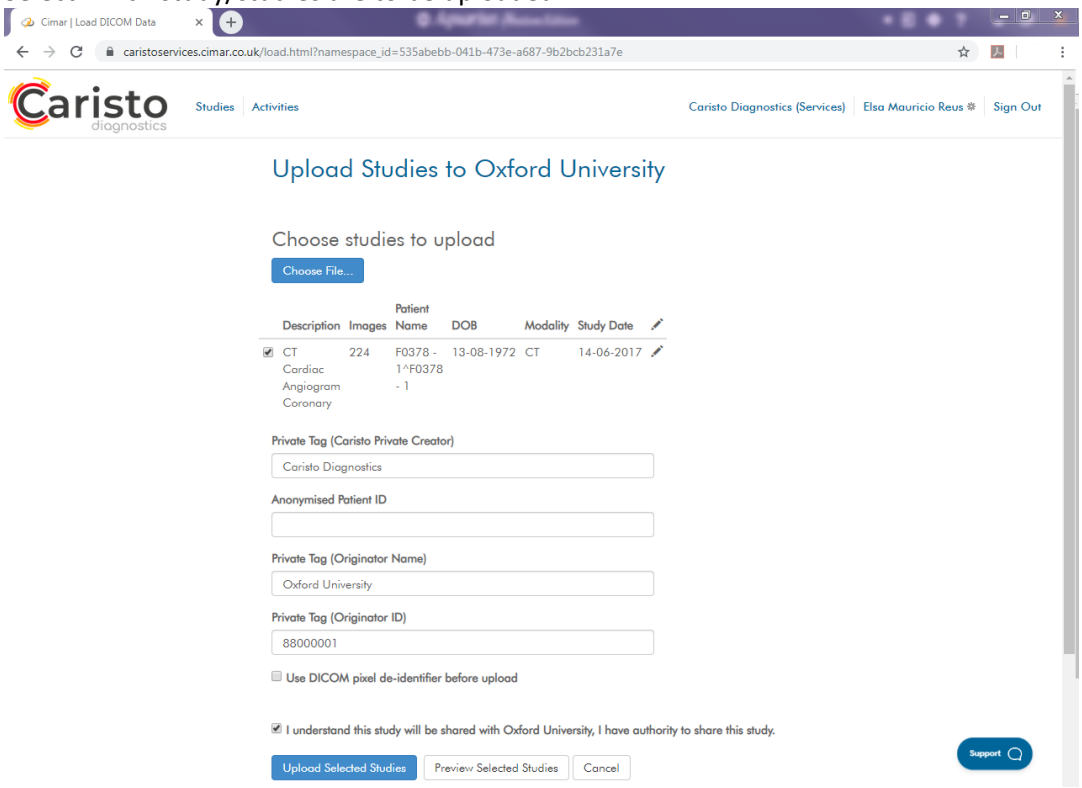
Appendix 5 – Uploading Files to Cimar

NOTE: The Cimar system automatically de-identifies DICOM data, replacing identifiers with the patient ID. The correct patient ID must be entered into Cimar when the files to transfer are selected.

Uploading Files to Caristo via Cimar Please ensure all DICOM files are accompanied by a DTF & PRF	Complete (tick ✓)
Preparing files for upload: Participant's images to be exported to a folder on a computer with external internet access Do not ZIP or archive the images Include the DTF and PRF within the folder (but note: these will need to be uploaded separately, after the DICOM images)	
Using the computer that has the image data on, log into the portal at https://caristoservices.cimar.co.uk/ Compatible web browsers include Google Chrome (preferred), Firefox, Safari and Internet Explorer (version 9 and above). (Java must be installed for all non-Chrome browsers).  You should have received instructions on how to register your unique username and set a password. If these have not been received please refer to the contact details in this manual.	
If asked, please review and accept terms of use / privacy agreement.	

The default view shows the studies uploaded for this project at your site. To upload a new study, click the 'Upload Studies' button. 	
Click the 'Choose File' button to select the data for upload. Navigate to the appropriate folder containing the DICOM data, and select it.  Once selected, the system will scan through the folder for DICOM files.	

Select which study/studies are to be uploaded.



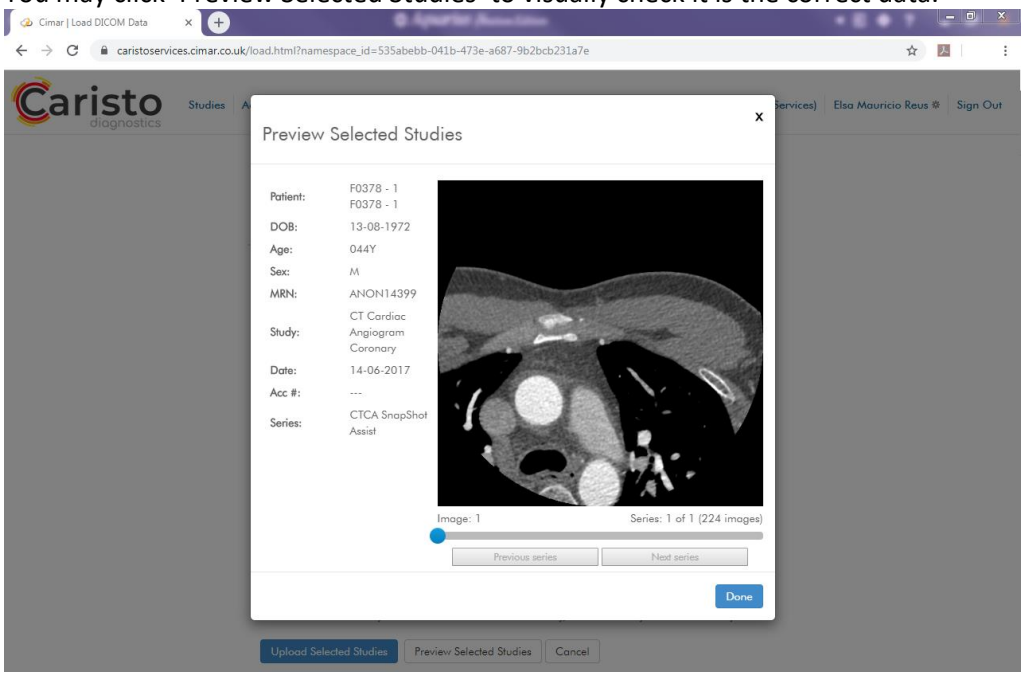
You must manually enter the patient ID in the fields above. The system will automatically de-identify the DICOM files using this information. Include radiation exposure summary or dose report images.

Ensure this information is correct before clicking 'Upload Selected Studies'.

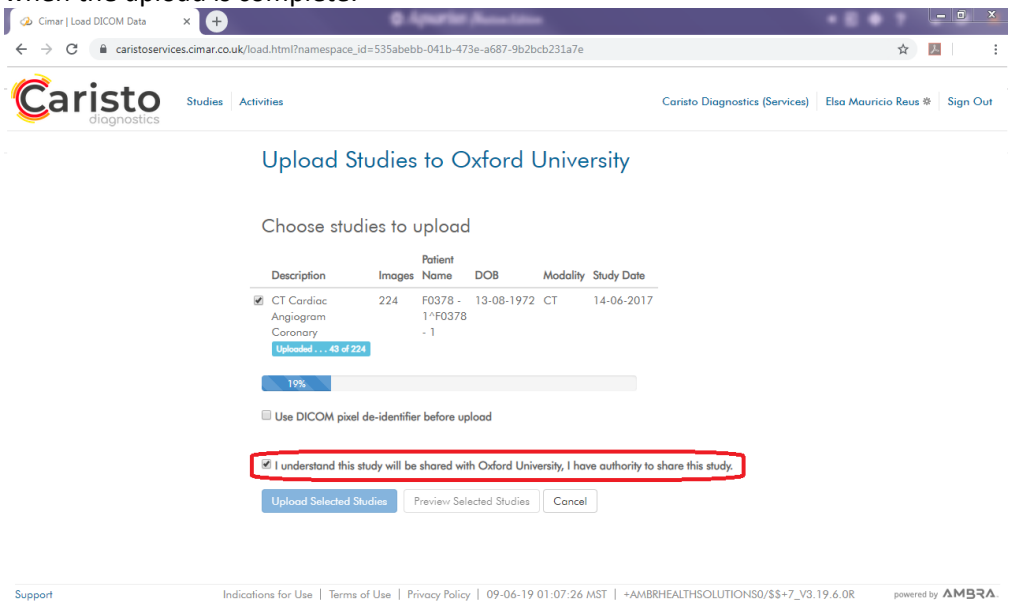
NOTE: some series may have PHI burned in to the images. Typically, these are not needed for upload. If you encounter a series that IS needed, and does have PHI burned in, you may check the 'Use DICOM pixel de-identifier before upload'. This will open a further dialog where you can drag masks over the images in question, so the PHI will be removed.

Do not check apply pixel de-identification box unless you are certain you need to use the pixel-level tool.

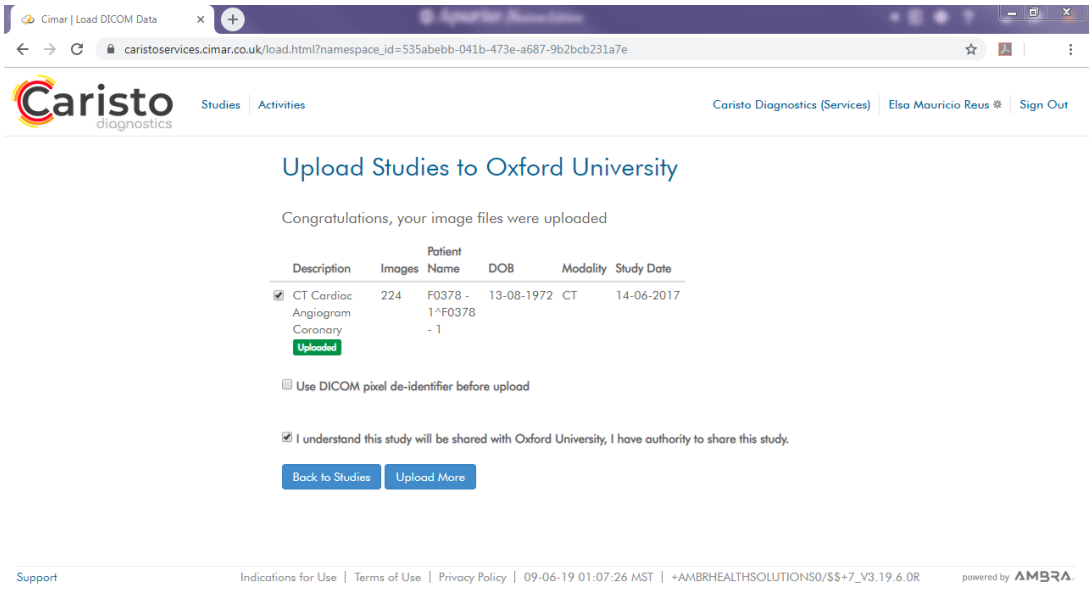
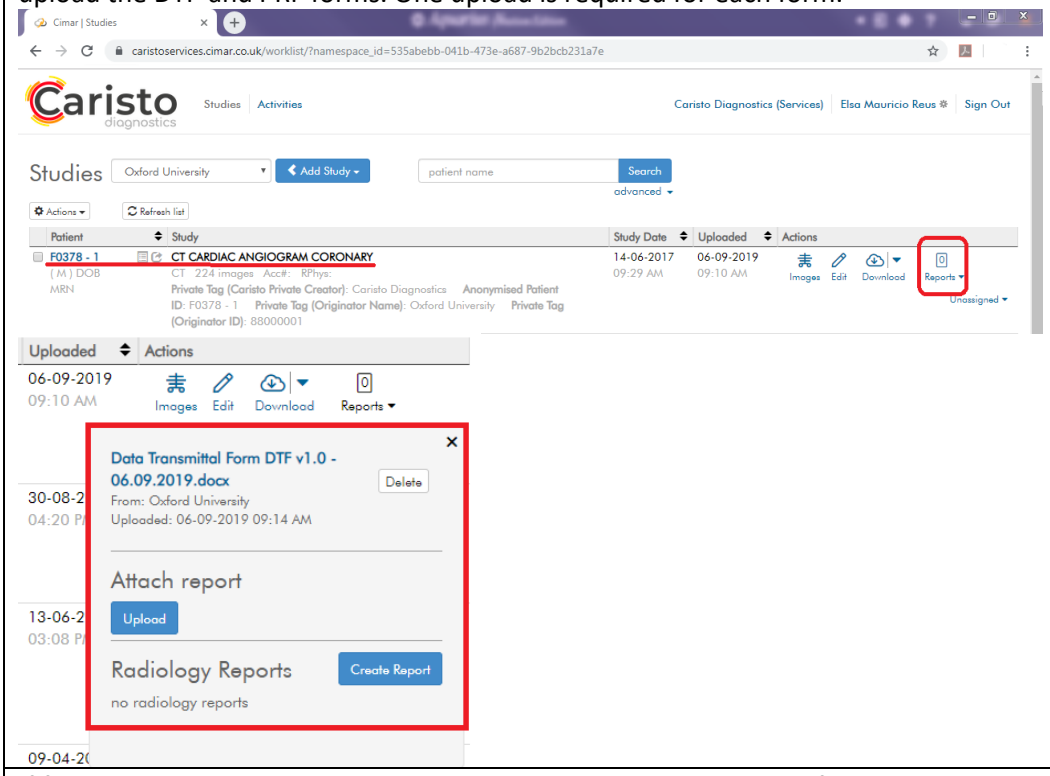
You may click ‘Preview Selected Studies’ to visually check it is the correct data.



Click ‘Upload Selected Studies’ to upload the DICOM data. A progress indicator will tell you when the upload is complete.



Ensure you have checked ‘I understand this study will be shared with Oxford University, I have authority to share this study’.

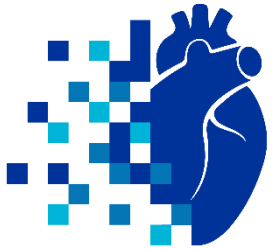
Click the 'Back to Studies' button to return to the main work list.  	
Locate the study that was just uploaded and click 'Reports' to pop up the reports panel and upload the DTP and PRF forms. One upload is required for each form.  	
If further data requires upload, go back to the work list and repeat from Step 4 above.	

Laboratoire d'Imagerie Biomédicale

ICAN IMAGING

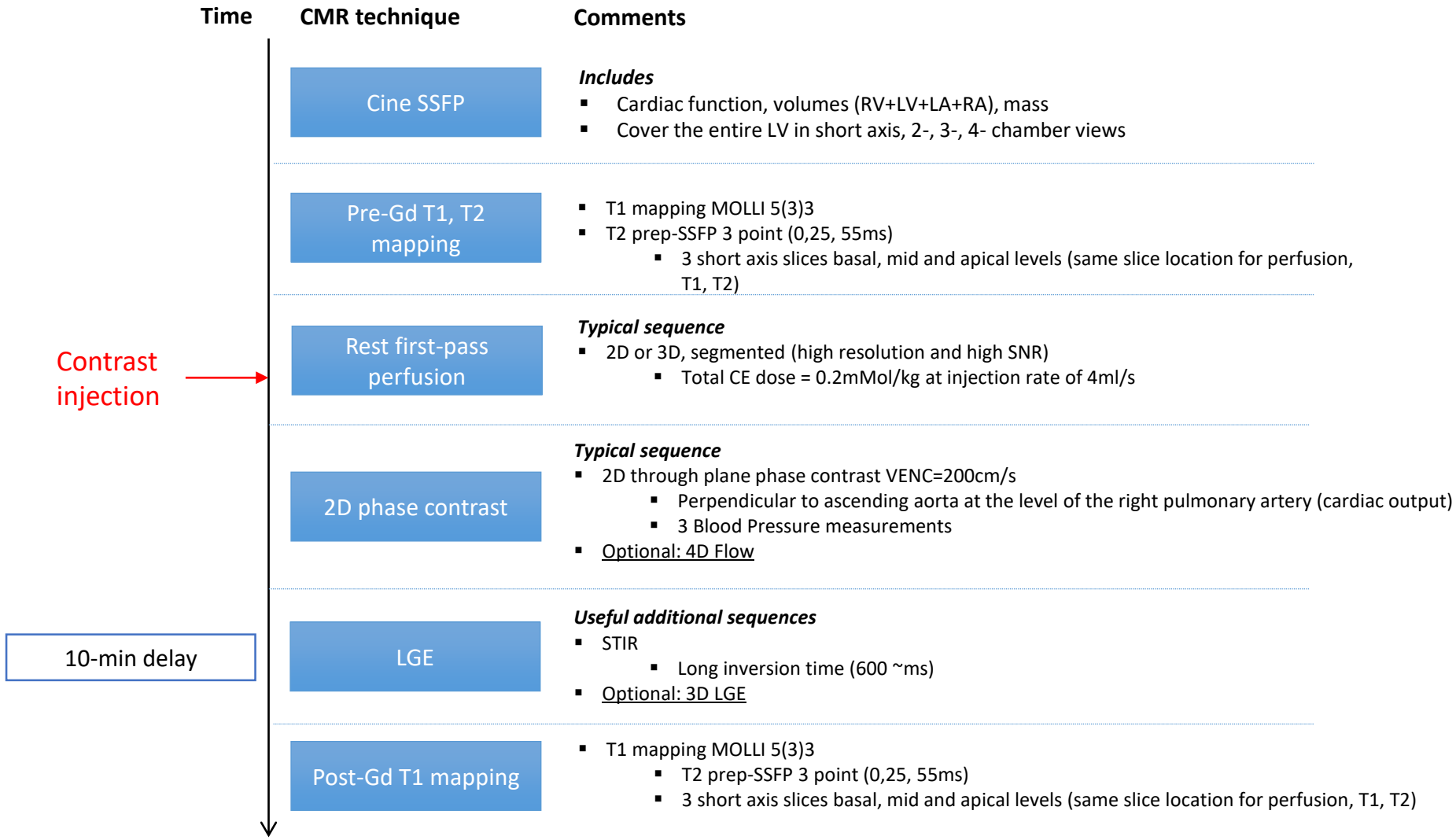
Cardiac MRI

19/11/2021



MAESTRIA

Cardiac MRI protocol

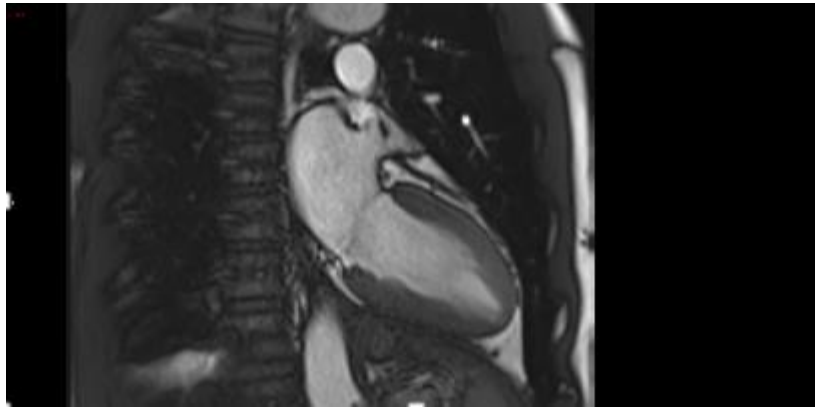


Cine imaging – Acquisition parameters

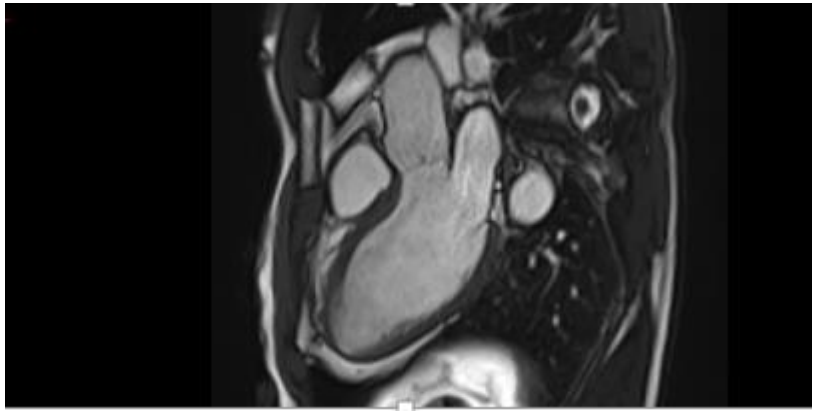
SSFP (Steady State Free Precession) imaging will be used for cine imaging:

- Slice thickness ≤ 7 mm; 0 mm gap short axis covering the entire left ventricle + 2,3,4- chamber views
- Voxel size: <= 1.8 mm
- FOV should cover the entire heart
- Temporal resolution should be < 30 ms with adjustement of number of views per segment according to heart rate: 40 real phases should be acquired
- Parallel imaging acceleration factor: 2.0

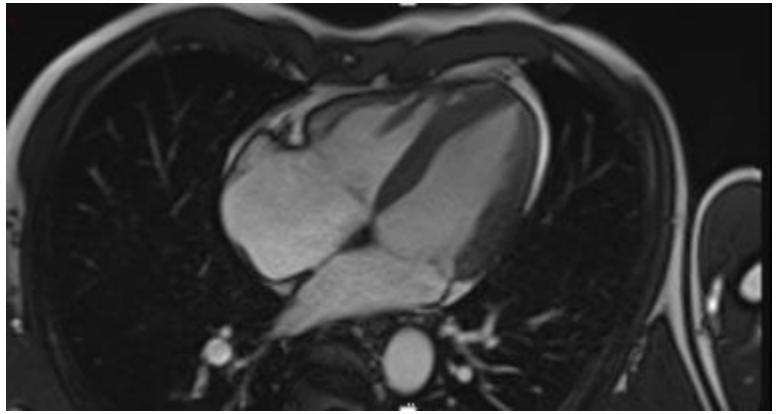
Cine imaging – Examples



2-chamber view

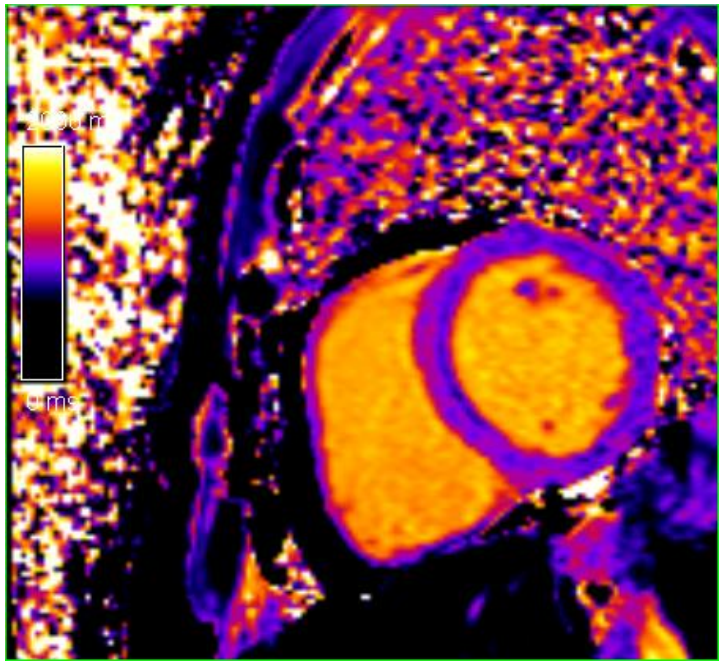


3-chamber view

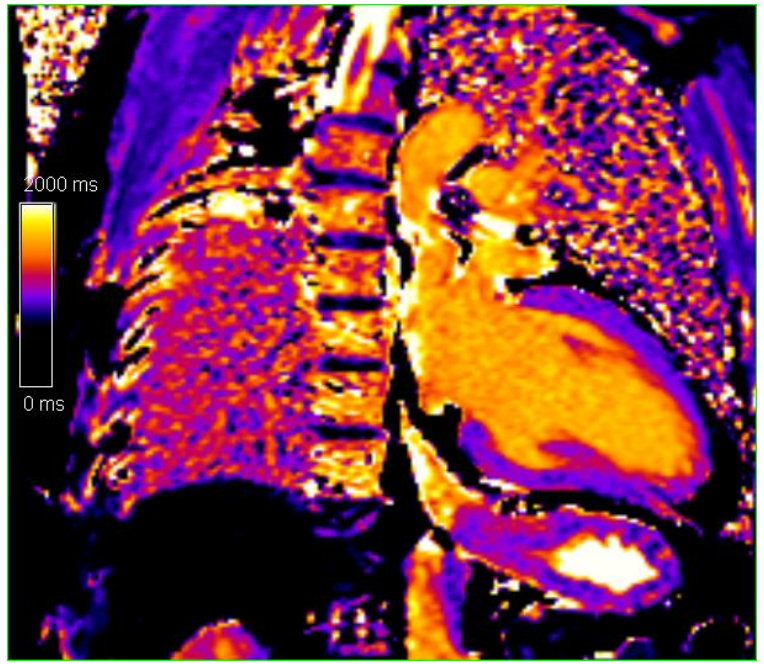


4-chamber view

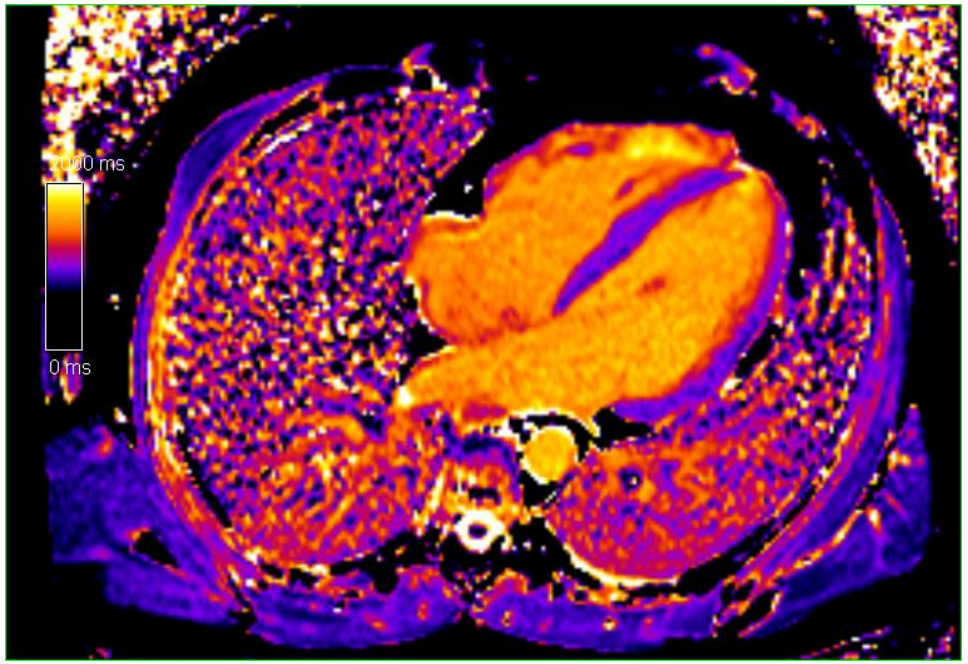
Mapping imaging – Examples



SA axis view



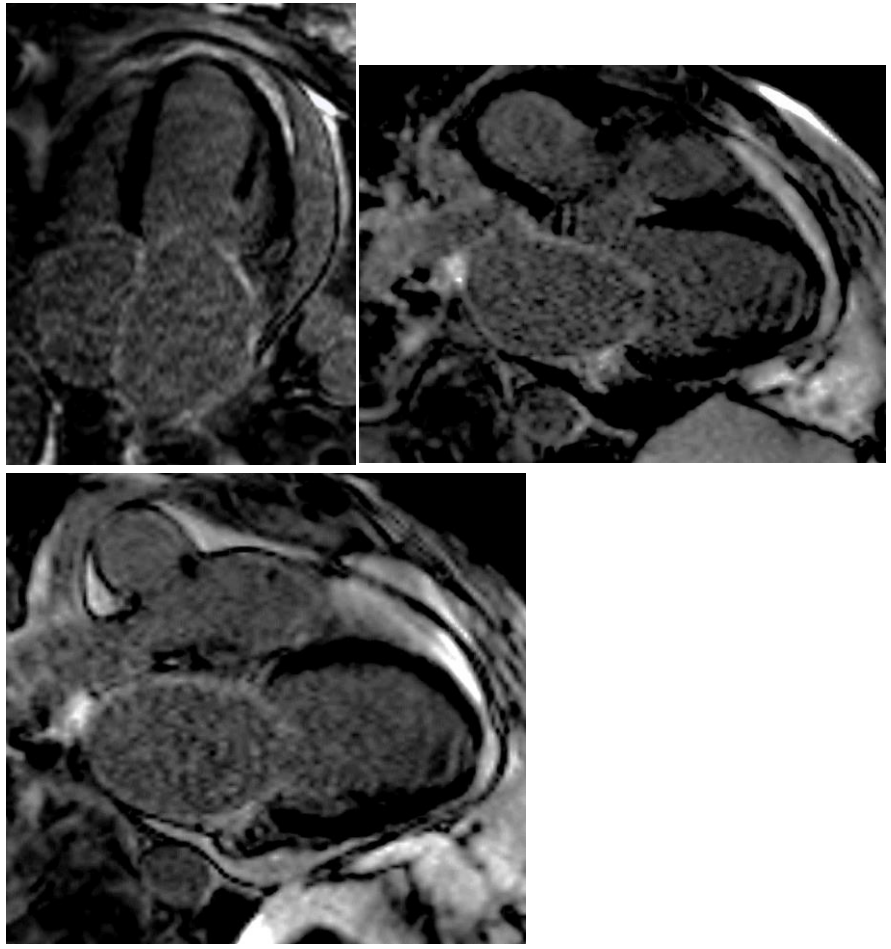
2-chamber view

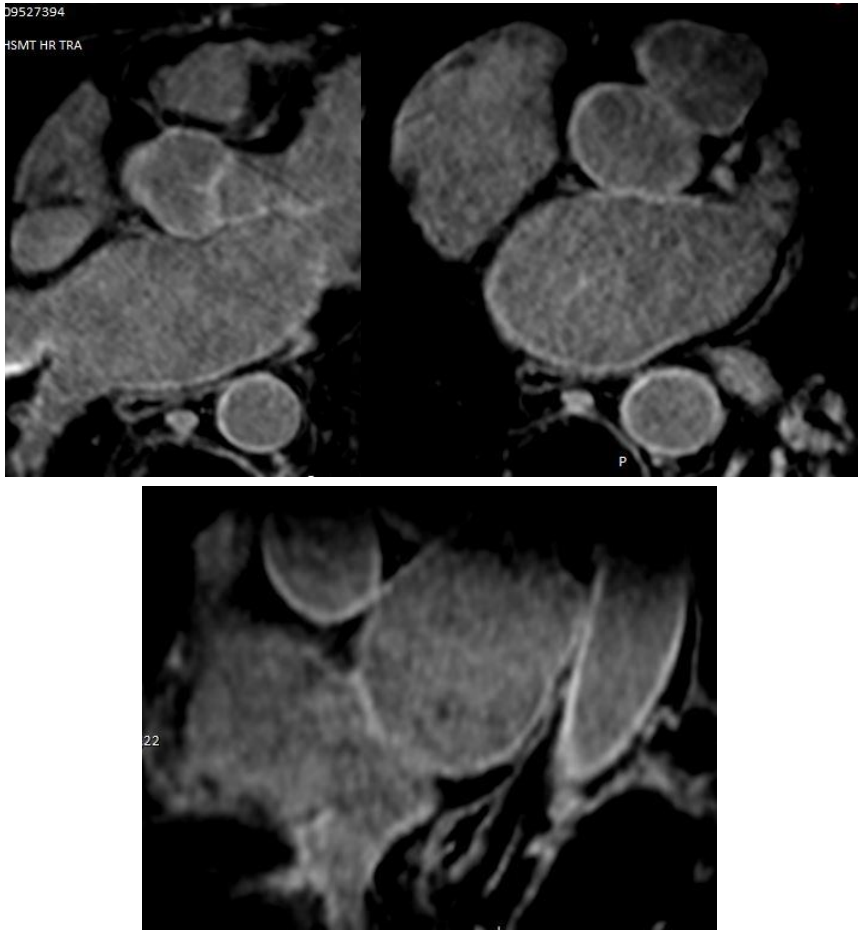


4-chamber view

LGE imaging – Examples

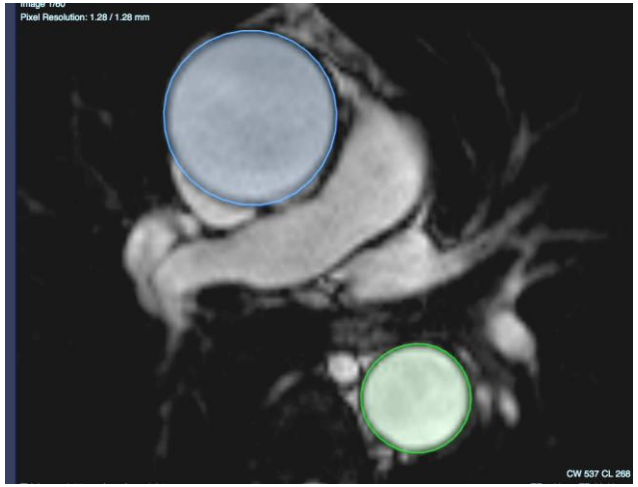
- 2D LGE IR sequence
- 3D nav LGE sequence

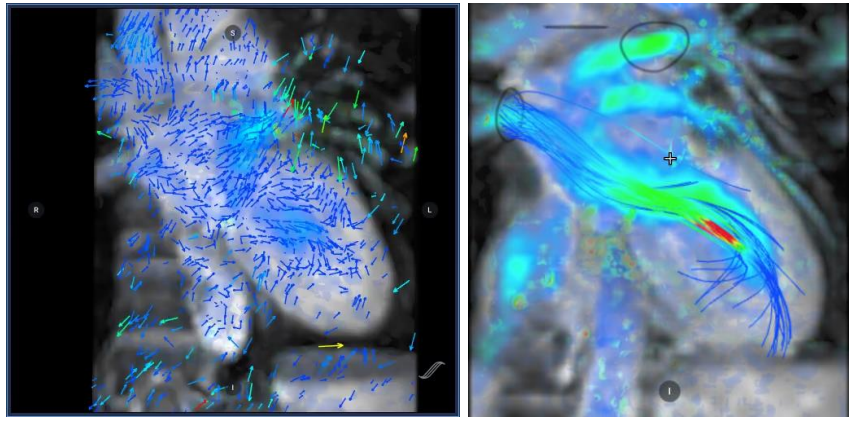


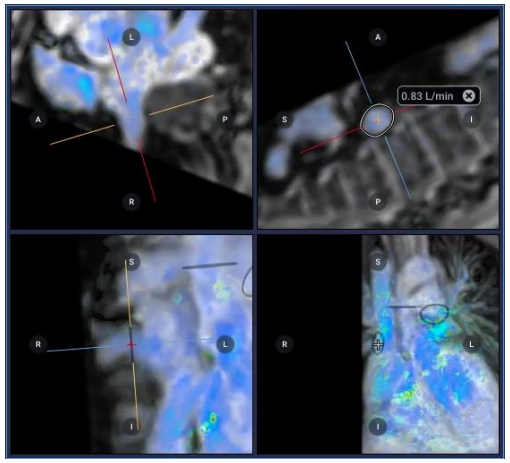


Flow imaging – Examples

- 2D
- 4D







Biomarkers from cardiac MRI

- Cardiac function parameters:
  - LA volumes, EF
  - LV masses, volumes, EF

- LA/LV deformation (strain): radial and longitudinal directions for LA and LV + circumferential for LV

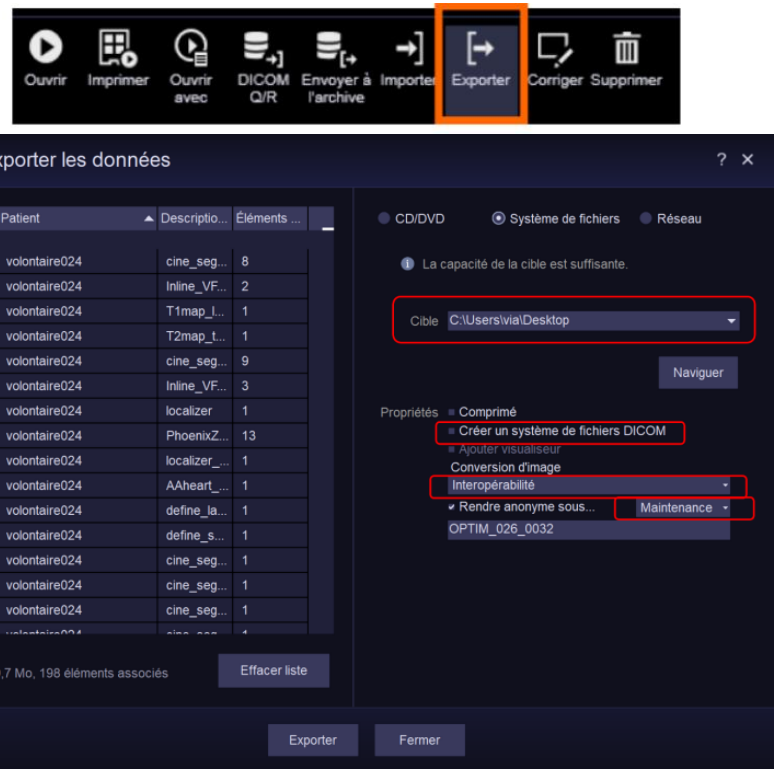
- Aortic parameters:
  - Ascending and descending aorta cross sectional areas
  - Aortic Strain / distensibility
  - Flow parameters: Net/Forward/Backward aortic flow

- LA fibrosis volume from 2D or 3D LGE images

/!\ Optional parameters

Data pseudo-anonymization

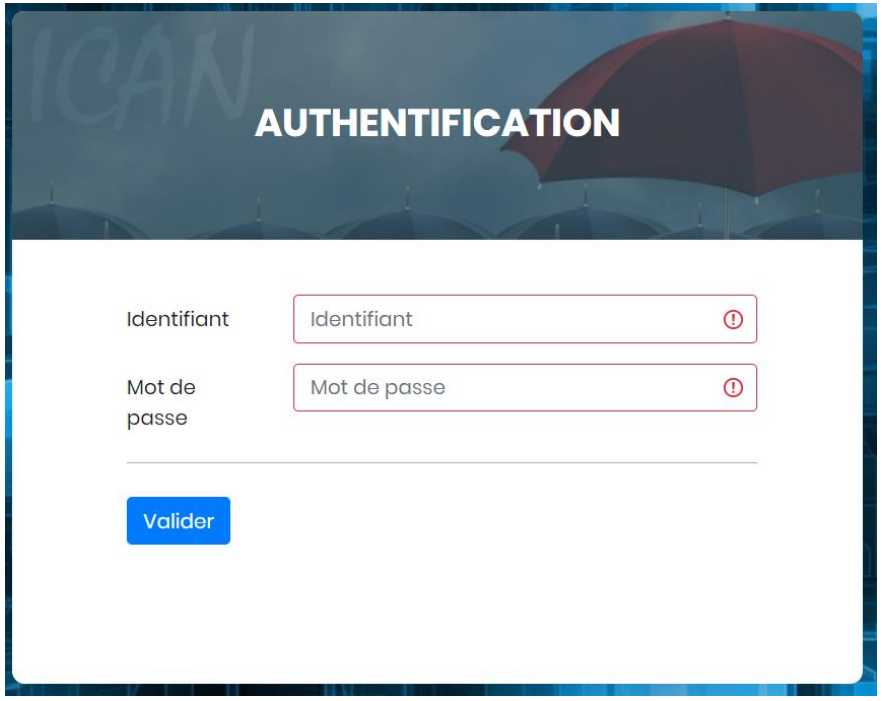
- All imaging data should be collected in a pseudo-anonymized manner
- Each patient will be given a unique MAESTRIA study ID: MAESTRIA_centerNumber_patientNumber
- For Siemens scanners:
  - Export the patient data
  - Choose « interoperability » and « maintenance » mode
- If a center is interested in LIB software* we can provide it!



*custom exe file running locally (in your instutution) on a PC

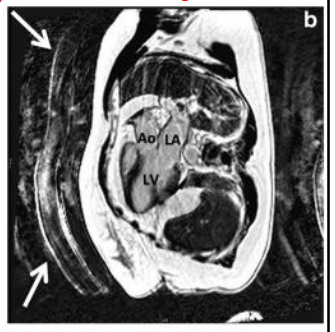
Data transfer

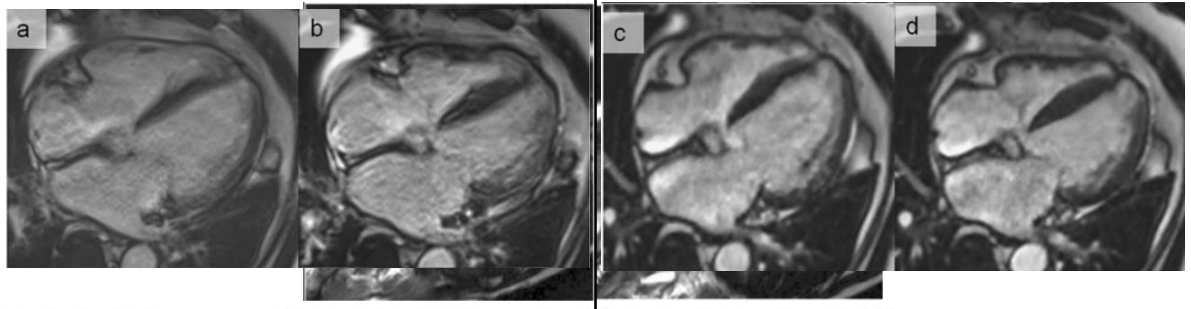
- Before data transfer, please check that a patient file size is around 1 Go and can be up to 2 Go when 4D flow images are acquired
- Images should be uploaded *via* a specific web portal
- The web portal will be password secured
- Only authorized people could have an access to the app

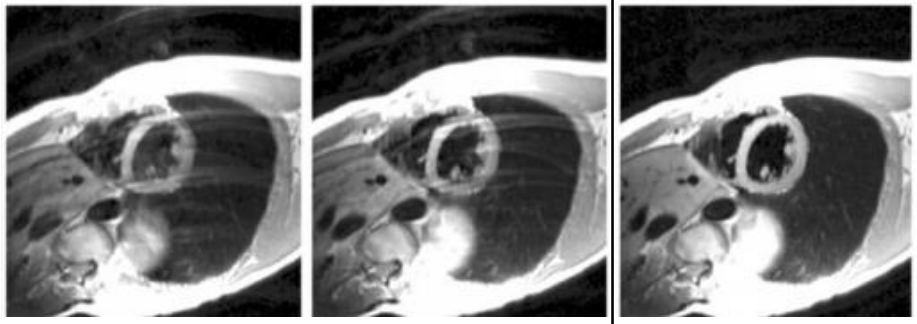


Motion artefacts

Unacceptable







Acceptable

Patient motion

- Radial k-space trajectories (Propeller, Multivane, BLADE)
- Navigators
- Shorten the scan time

Respiration

- Increase number of signal averages
- Respiratory gating
- Navigators
- Breath-hold

Pulsation

- Flow compensation
- Cardiac gating
- Saturation bands
- Change phase encode direction

Echocardiography Core Laboratory Imaging Analysis Protocol

MAESTRIA

Dr Laurie SOULAT DUFOUR, Pr Ariel COHEN

Cardiology Department, Saint Antoine and Tenon Hospitals, Sorbonne Université

Paris, France (Head: Pr Ariel COHEN)

Pr Stephane HATEM,

INSERM UMRS 1166, ICAN

Echocardiography Core Lab Maestria

- Location : Saint Antoine Hospital, Paris, France

- Director : Professor Ariel Cohen, MD, PhD, Professor of Medicine, Director of non- invasive cardiac laboratory
- Associate : Laurie Soulat Dufour, MD; Stephane Ederhy, MD

- Echocardiography Specialist : Laurie Soulat Dufour, MD; Stephane Ederhy, MD; Saroumadi Adavane-Scheuble, MD; Marion Chauvet-Droit, MD; Pascal Nhan, MD; Marie Liesse Jean, MD; Iris Kamami, MD; Rim Ben Said, MD; Pauline Issaurat, MD

- Maestria WP4, prospective cohort

Echocardiography Visit Schedule

- Inclusion
- Year 1
- Year 2
- Year 3
- Year 4
- Year 5

Role of the Echocardiography Core Lab

1. Create an imaging protocol with comprehensive instructions for the acquisition

2. Certify sonographer performing imaging studies

3. Assess each echocardiography and to provide feedback on image quality to each center

4. Provide full quantitative analysis of all the echocardiography

5. Answer to each sites for technical questions

Echocardiography Core Laboratory Imaging Analysis Protocol

MAESTRIA

Echocardiographic equipment, Sonographer Training, and Certification

Doppler Echo Protocol Acqusition

Transthoracic echocardiography

Transoesophageal echocardiography

Echocardiography equipment

1. All types of constructor of echo machines could be used
2. Echocardiography machines with dedicated cardiac imaging package which Doppler imaging, pulse wave and continuous wave spectral Doppler and tissue Doppler imaging should be used
3. The echo machines should have three-dimensional software to allow three-dimensional acquisition to study LV,LA,RV,RA cavities (cf echo protocol acquisition)
4. All images should be recorded in DICOM format and should be compatible with general DICOM analyzing programs
5. All images and cineloops are to be exported into DICOM format with “FULL FRAME RATE” (“FULL” or “maximum”,or “native” acquisition rate. (Please refer to Vendor specific instruction manual.)

Sonographer certification process

- Sites will be encouraged ideally to designate only 1 – 2 sonographers at their site to perform all examinations

- Sonographer certification is evaluated for each center after the study of the first exam transferred to the Core Lab (feedback within 3 business days)

Image transfer

- Each echocardiography exam should be anonymized in each site with a dedicate software (in progress, to be updated)
- Each anonymized echocardiography should be transferred by each site in the Data Hub (in progress, to be updated)
- In any case, store systematically an original copy of each echocardiogram at your site (DICOM) and don’t delete the original exam of the echocardiography machine until the agreement of the Core Lab

Echocardiography Core Laboratory Imaging Analysis Protocol

MAESTRIA

Echocardiographic equipment, Sonographer Training, and Certification

Doppler Echo Protocol Acqusition

Transthoracic echocardiography

Transoesophageal echocardiography

Doppler Echo Protocol Acqusition

General Comments

- The study imaging protocol included comprehensive views from the EACVI/ASE recommended adult exam

- In our center, the duration of transthoracic echocardiography is around 30-35 minutes and transoesophageal echocardiography around 10-15 minutes

Subject preparation

- Blood Pressure should be systematically collected after 3 minutes of rest at the beginning of each exam
- Heart rate should be collected at the beginning of each exam
- Electrocardiographic leads should be systematically present throughout the echocardiography exam
- All images must be acquired in left lateral decubitus position
- 3 to 5 beats acquisition should be recorded in atrial fibrillation patients

General Guidelines

- For 2D imaging maintain a frame rate of 50-80 frames per second (try to optimize imaging with depth and sector width)

- For doppler imaging ensure that the Doppler Nyquist limit is > 50-60cm/s

- No measurements should be recorded on the images acquired at the site

General Guidelines

- 3D acquisitions
  - Make sur to have the entire structure in the acquisition
  - 3 datasets for each structure

  - TTE
    - ✓ 3D obtained with frame rate ≥ 20 frames per second (try to optimize imaging with depth and sector width)
    - ✓ Prefer Heart Model acquisition
    - ✓ If Heart Model acquisition not available
      - Full Volume acquisition (at least 4 beats) or
      - High-volume rate acquisition could be used

  - TEE
    - ✓ 3D Zoom at least 1 beat, optimize the frame rate (try to optimize imaging with depth and sector width)
    - ✓ 3D live at least 1 beat could be used for the descending thoracic aorta

Echocardiography Core Laboratory Imaging Analysis Protocol

MAESTRIA

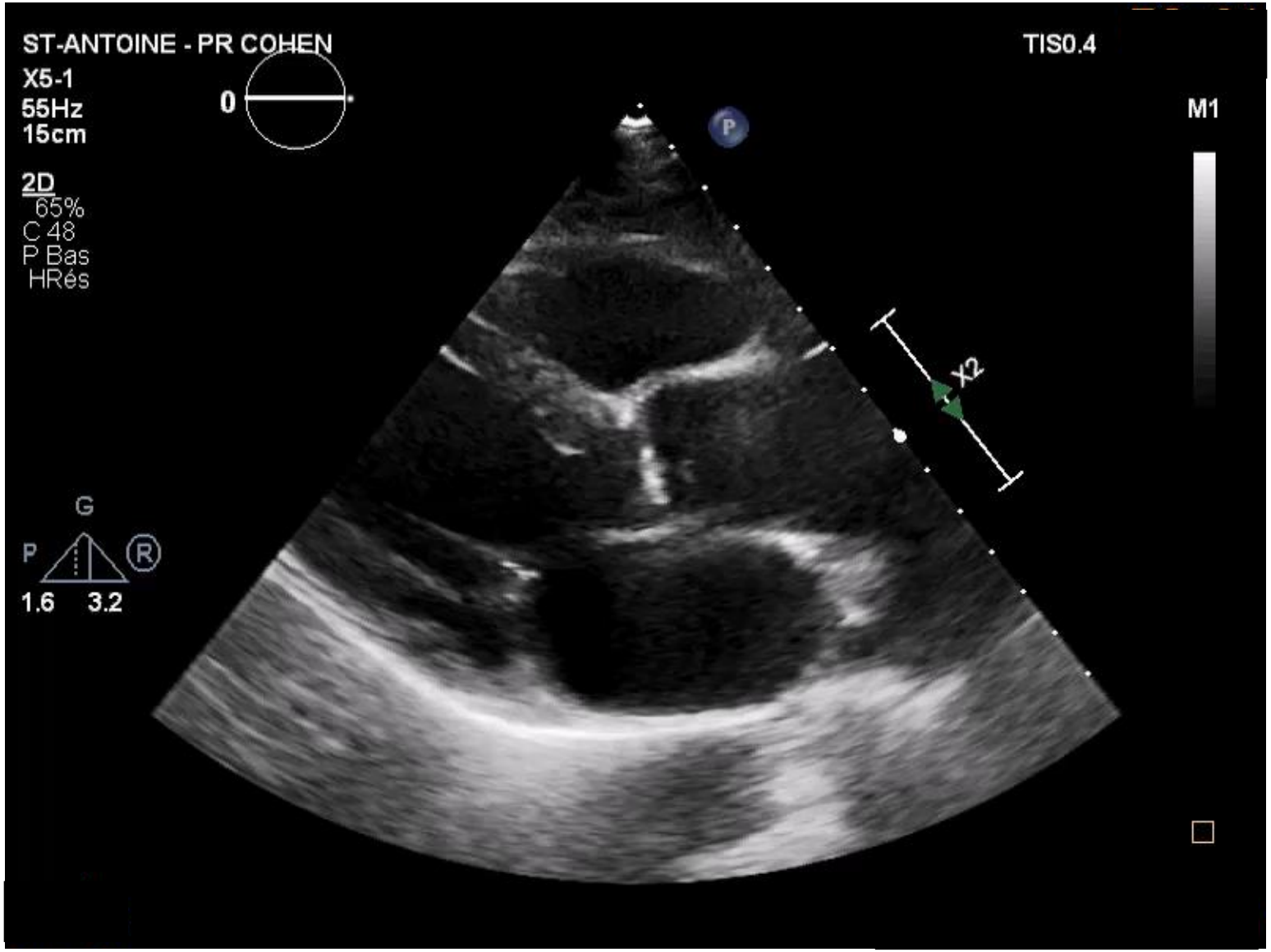
Echocardiographic equipment, Sonographer Training, and Certification

Doppler Echo Protocol Acqusition

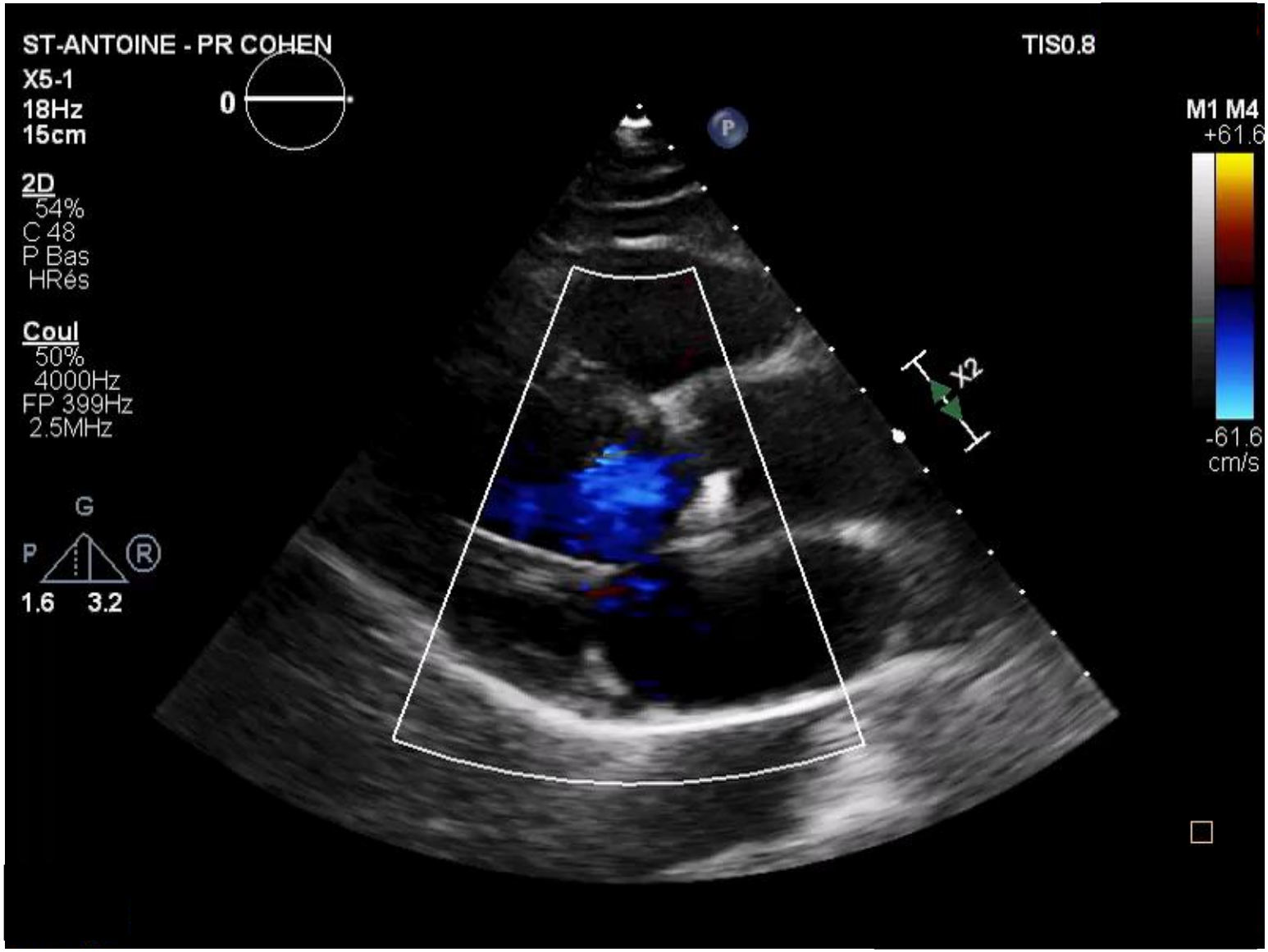
Transthoracic echocardiography

Transoesophageal echocardiography

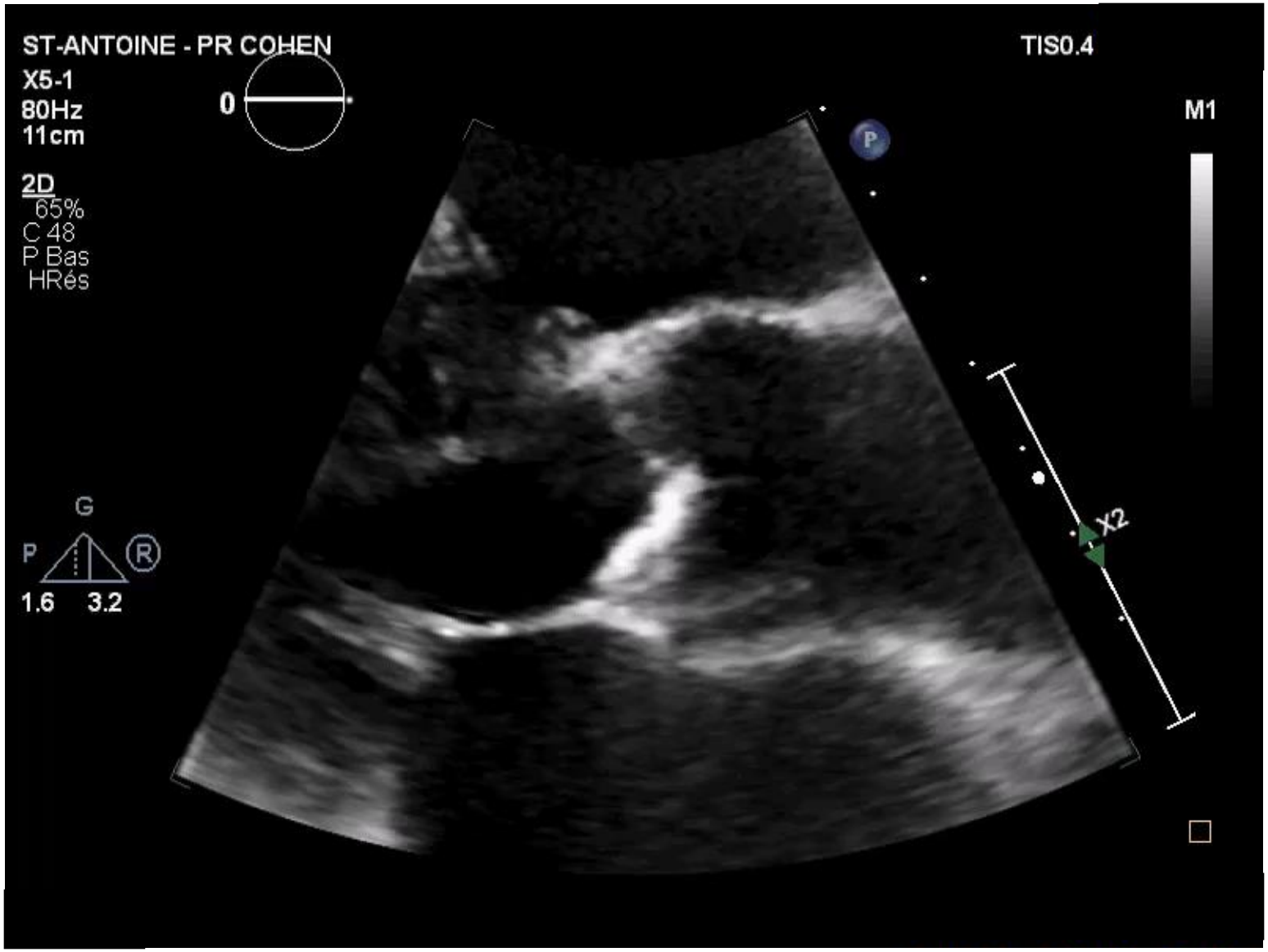
Parasternal long axis



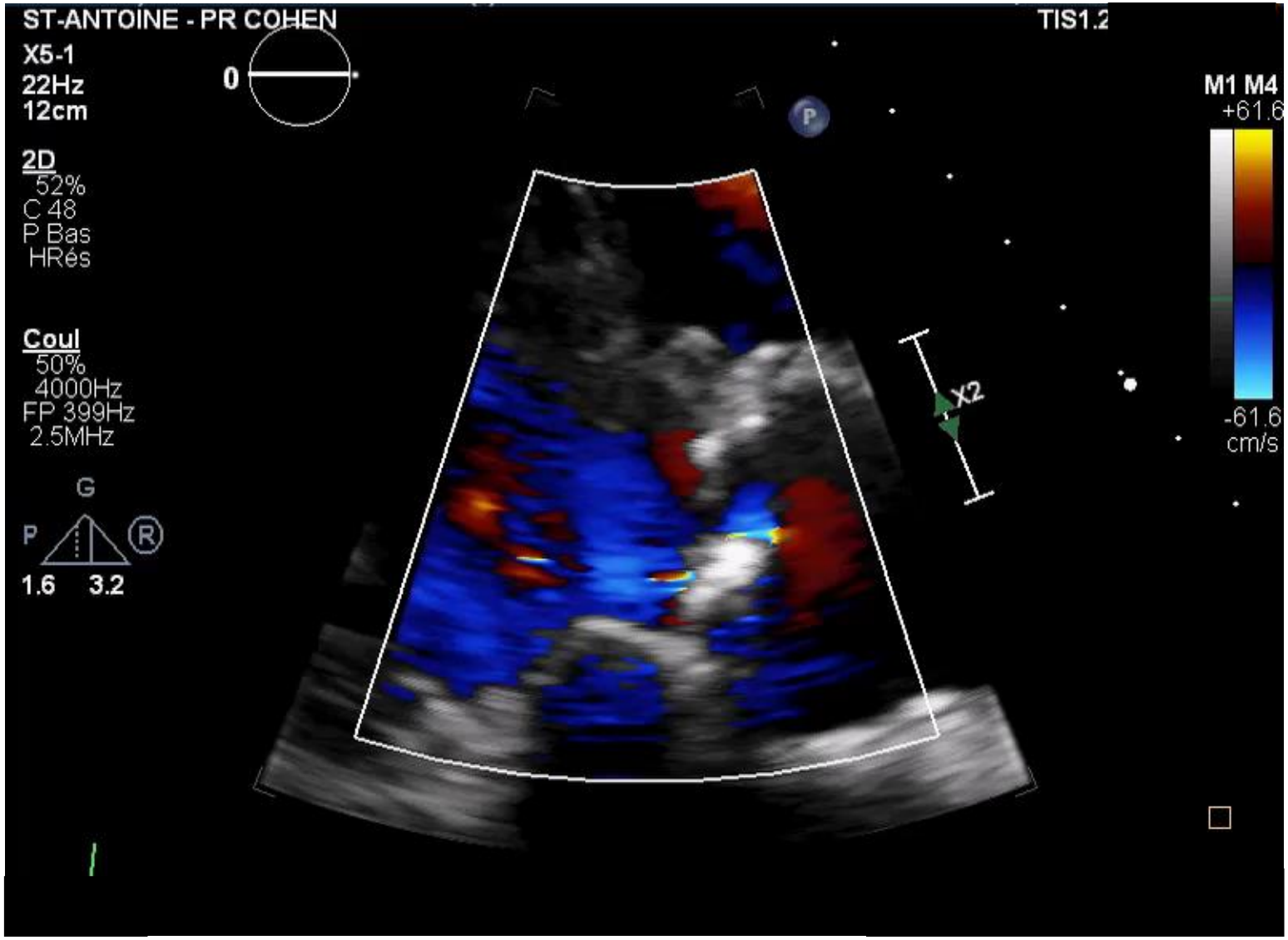
Parasternal long axis



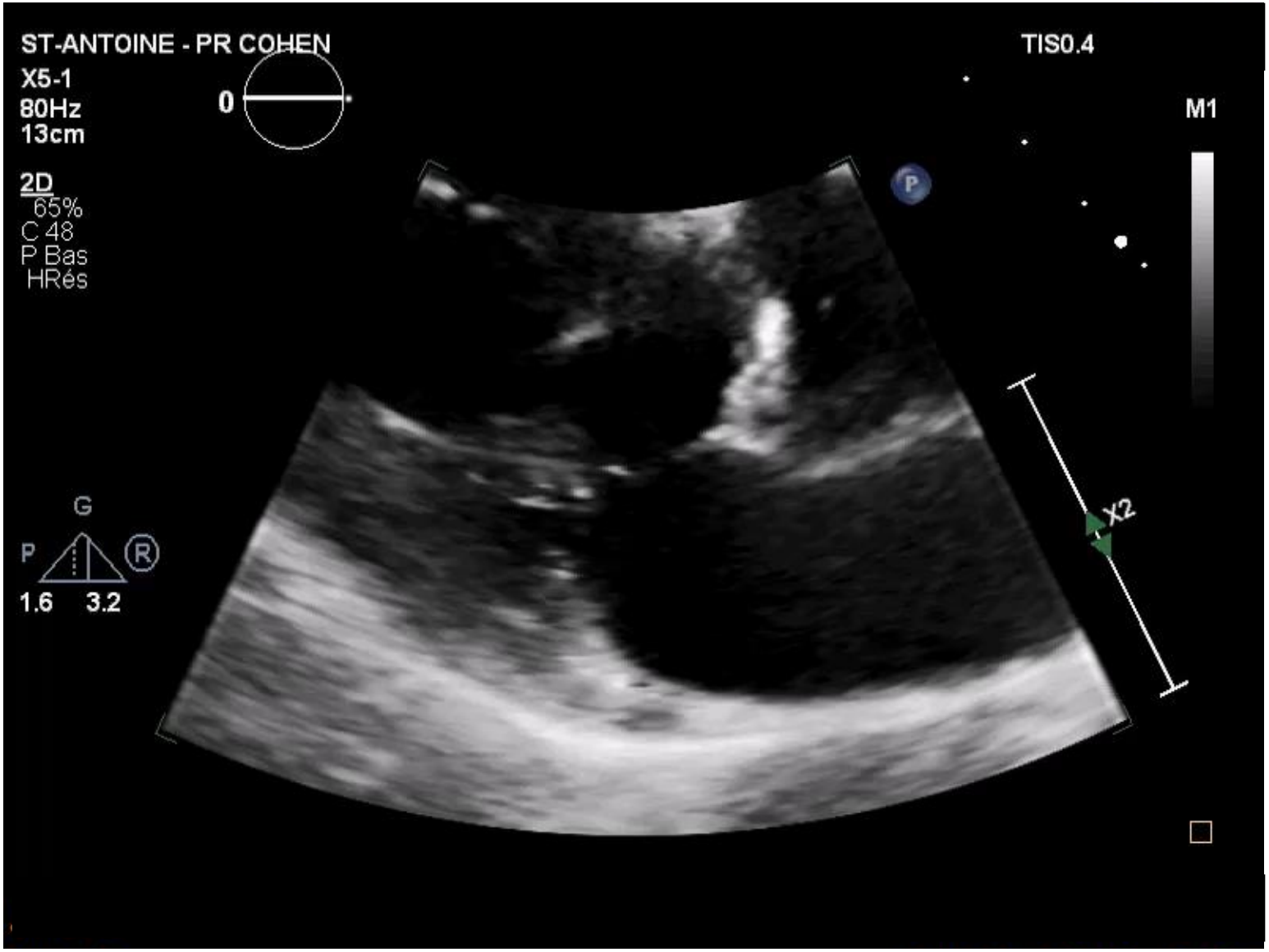
Parasternal long axis



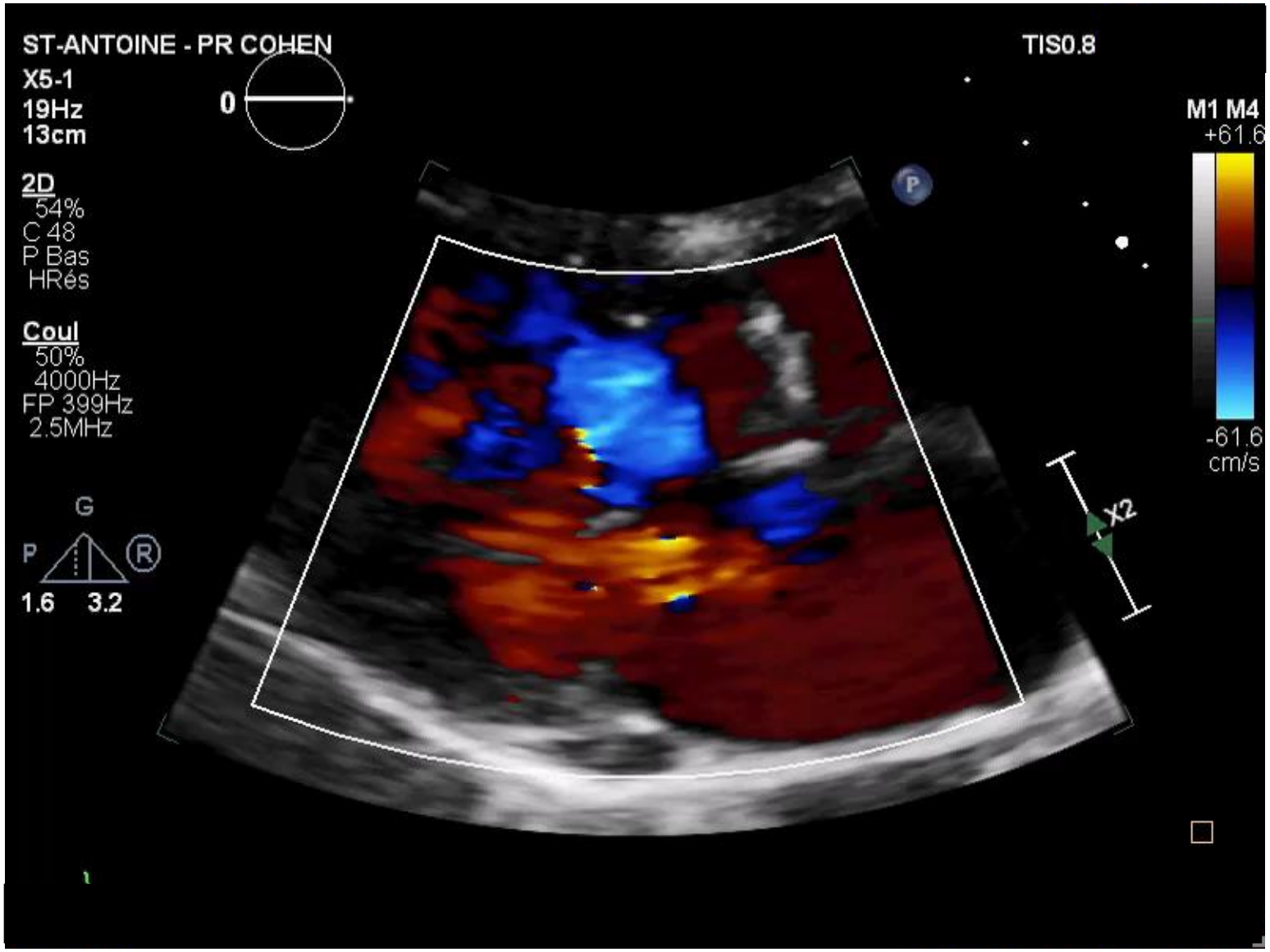
Parasternal long axis



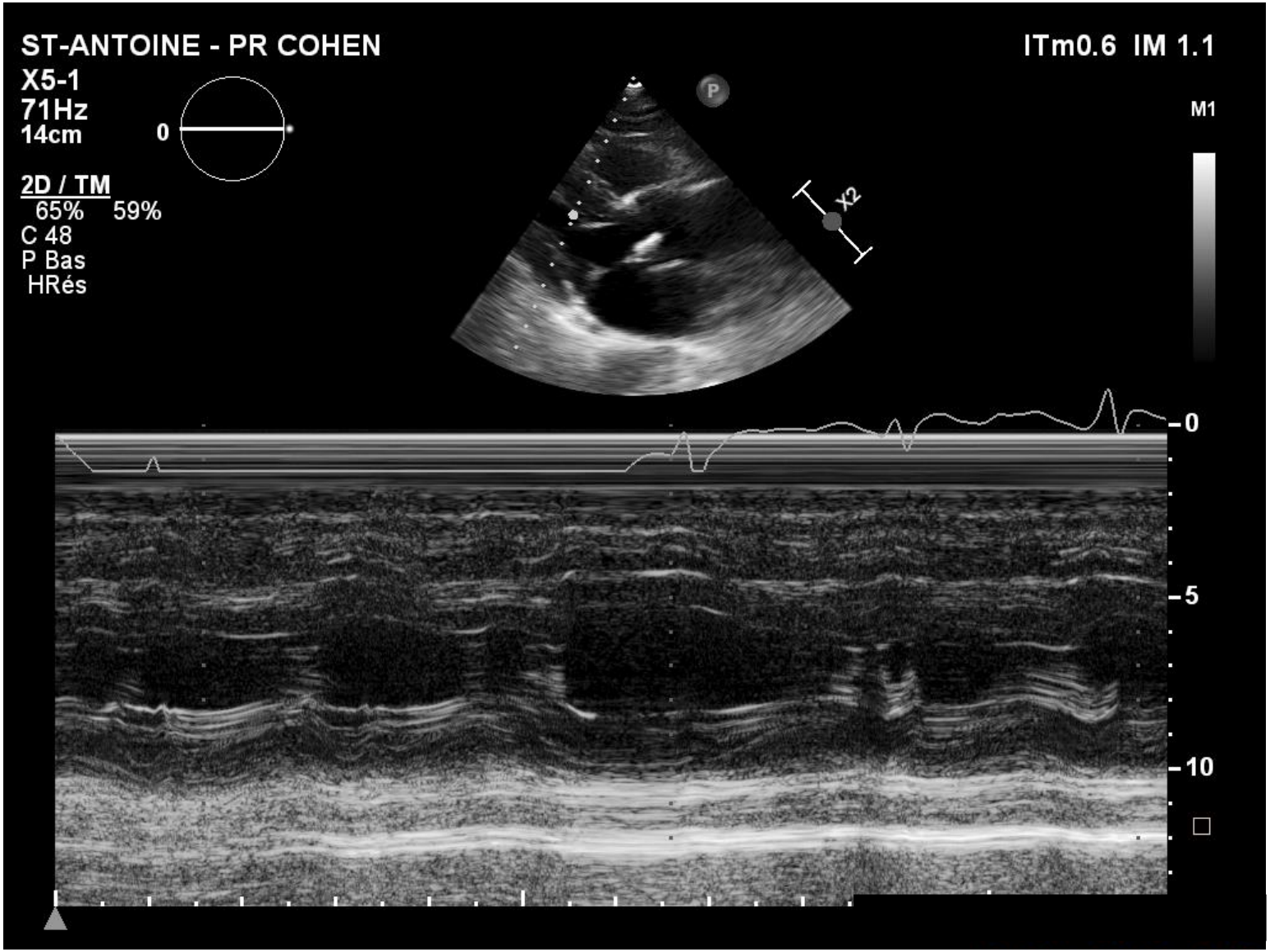
Parasternal long axis



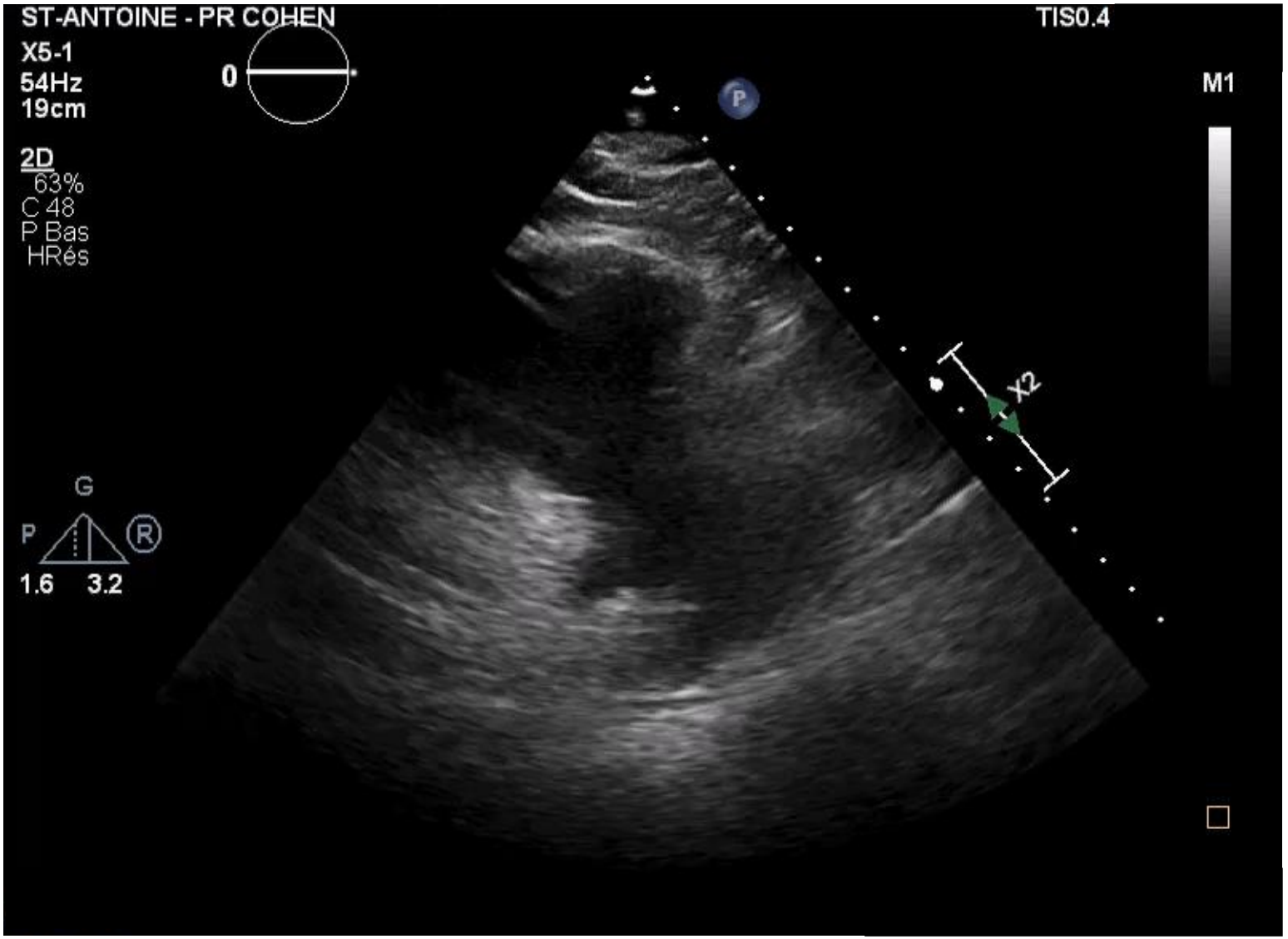
Parasternal long axis



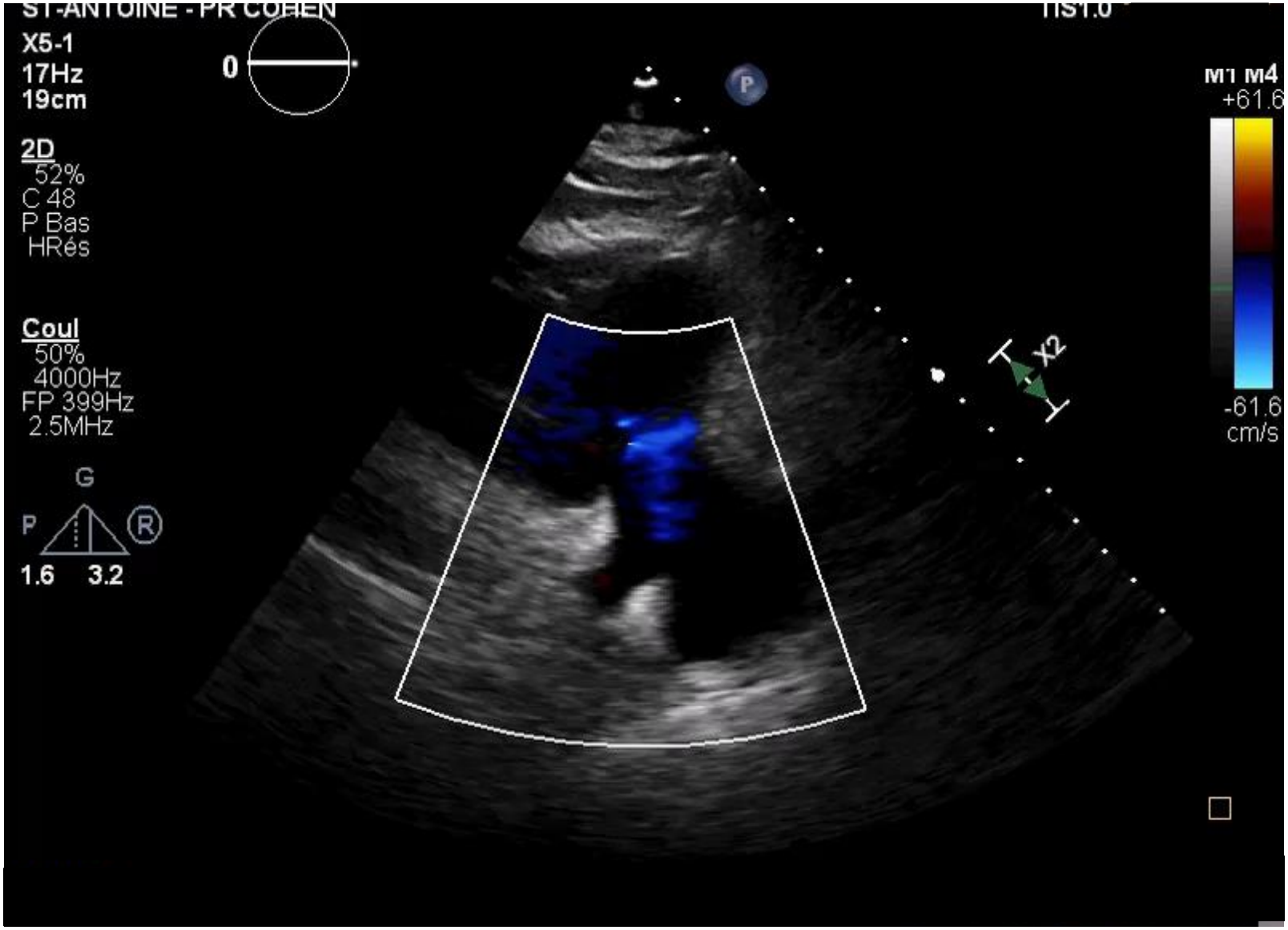
Parasternal long axis



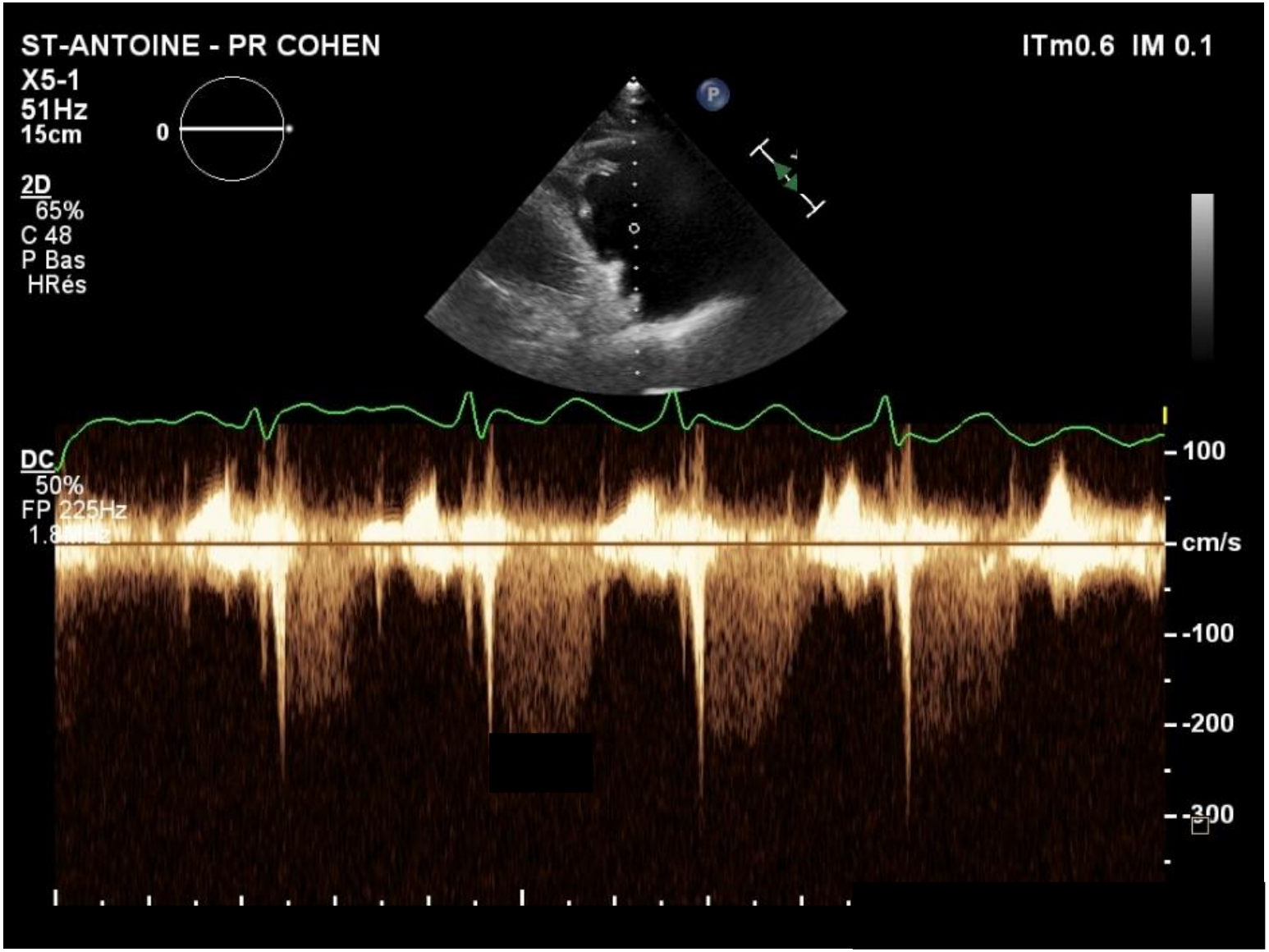
Parasternal long axis of RV inflow



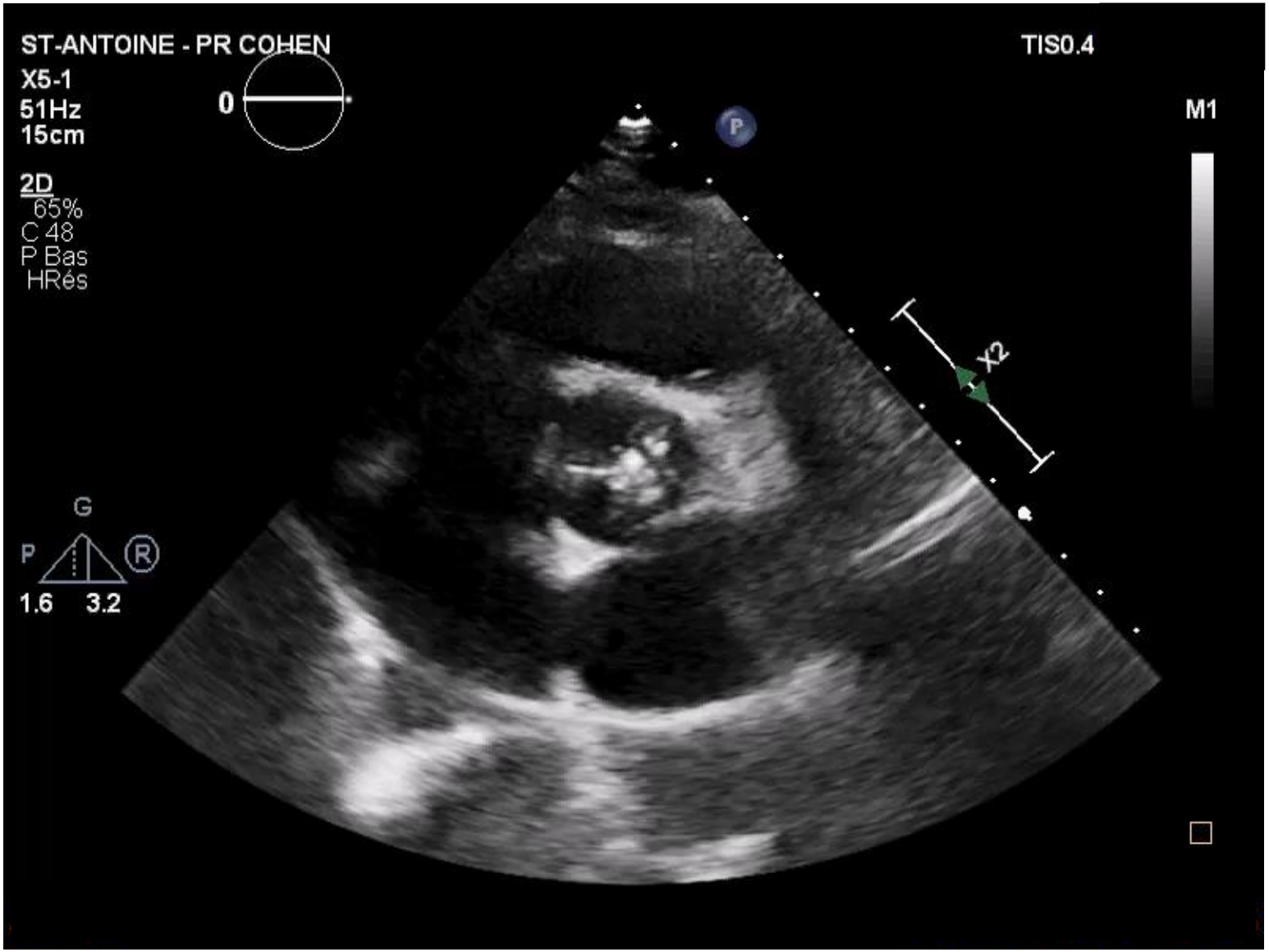
Parasternal long axis of RV inflow



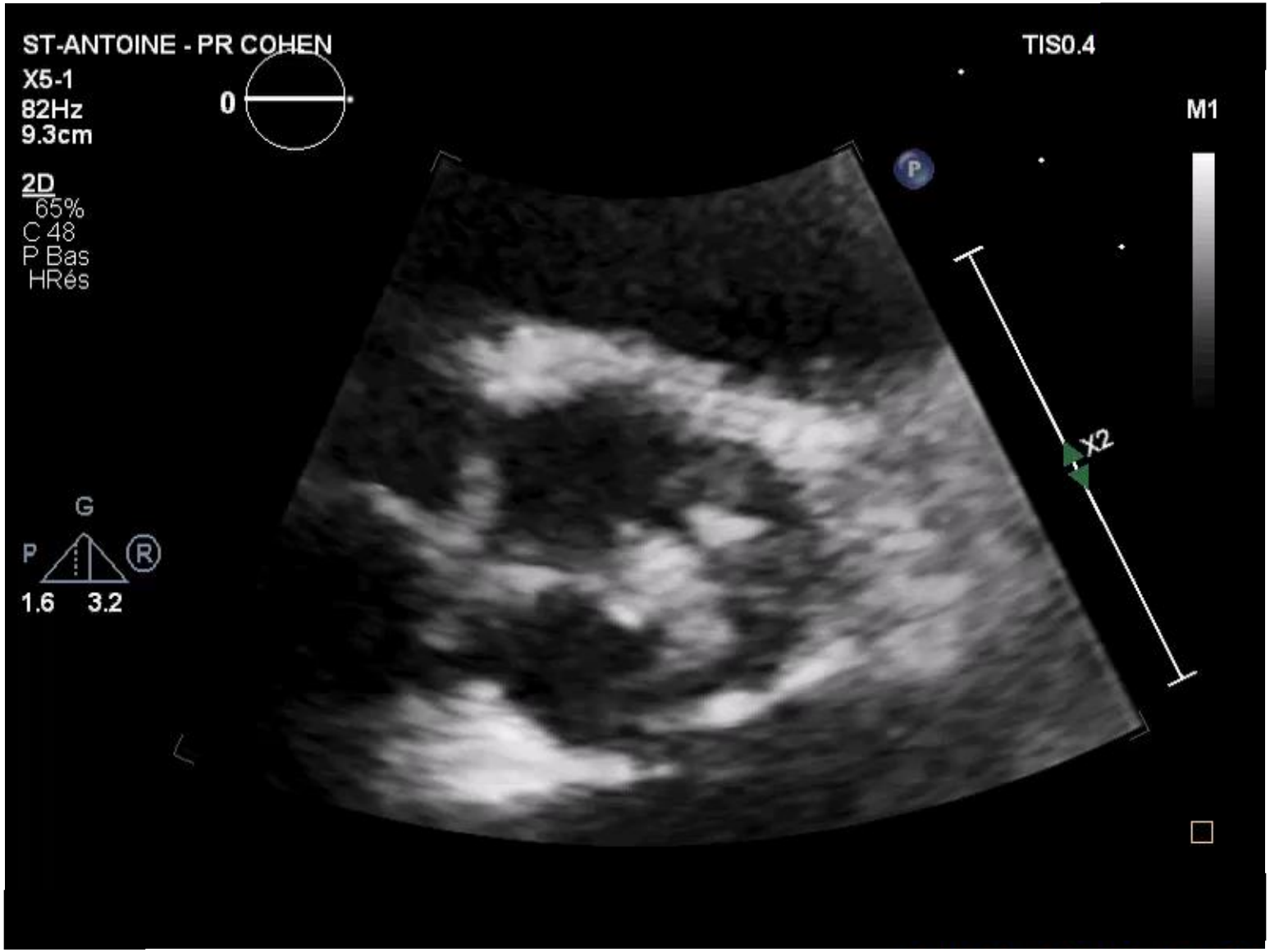
Parasternal long axis of RV inflow



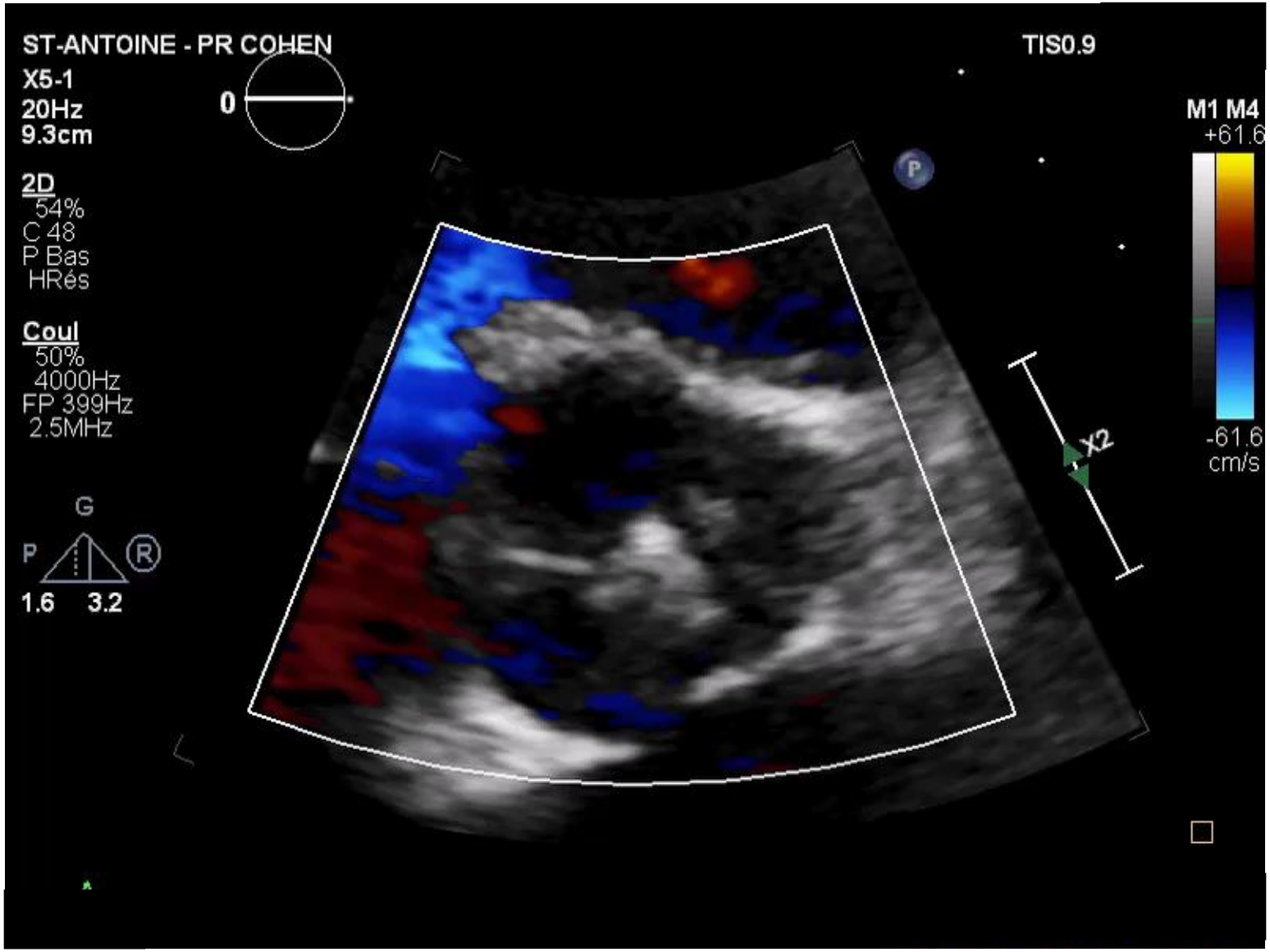
Parasternal short axis- Aortic valve level



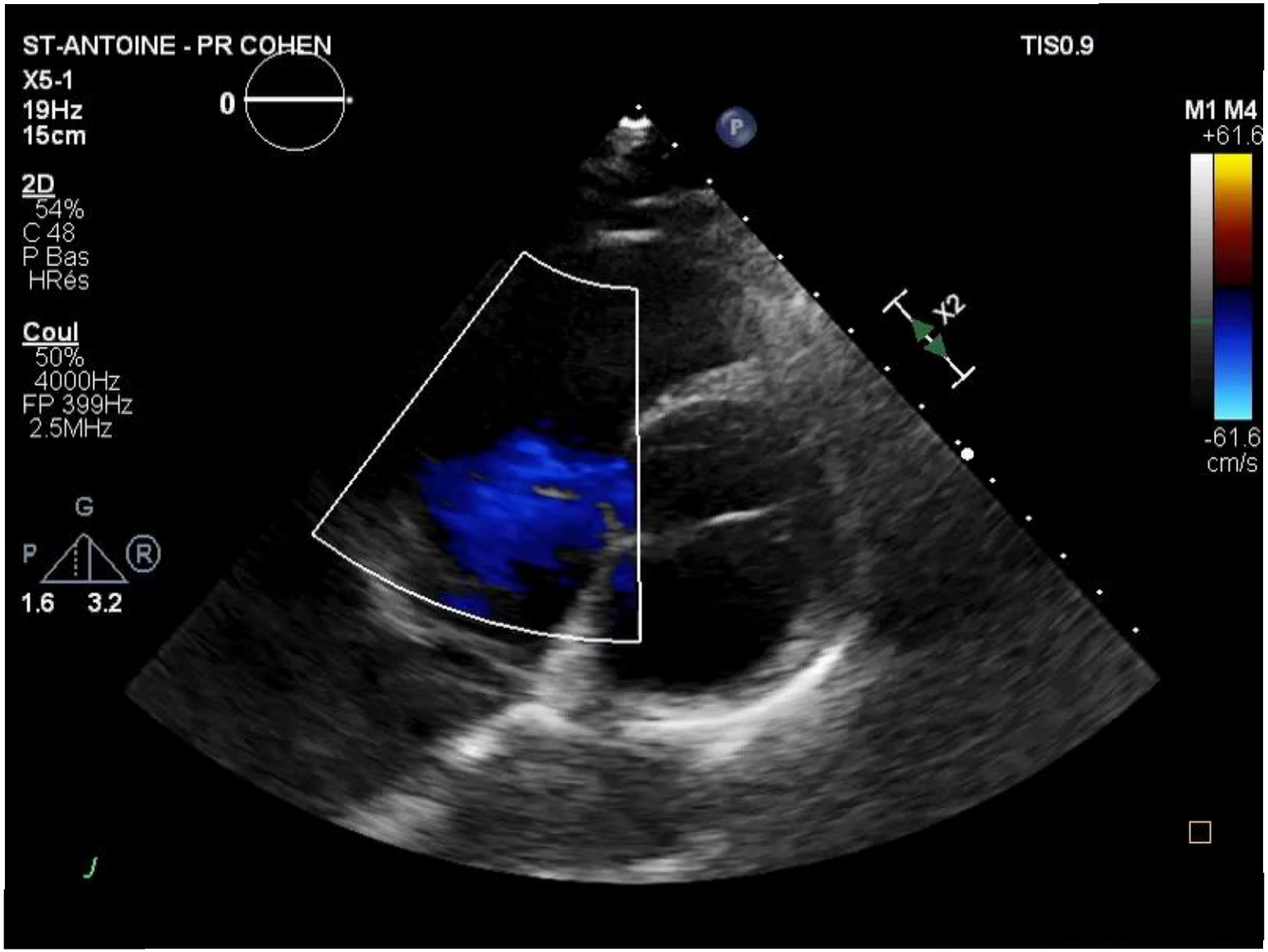
Parasternal short axis- Aortic valve level



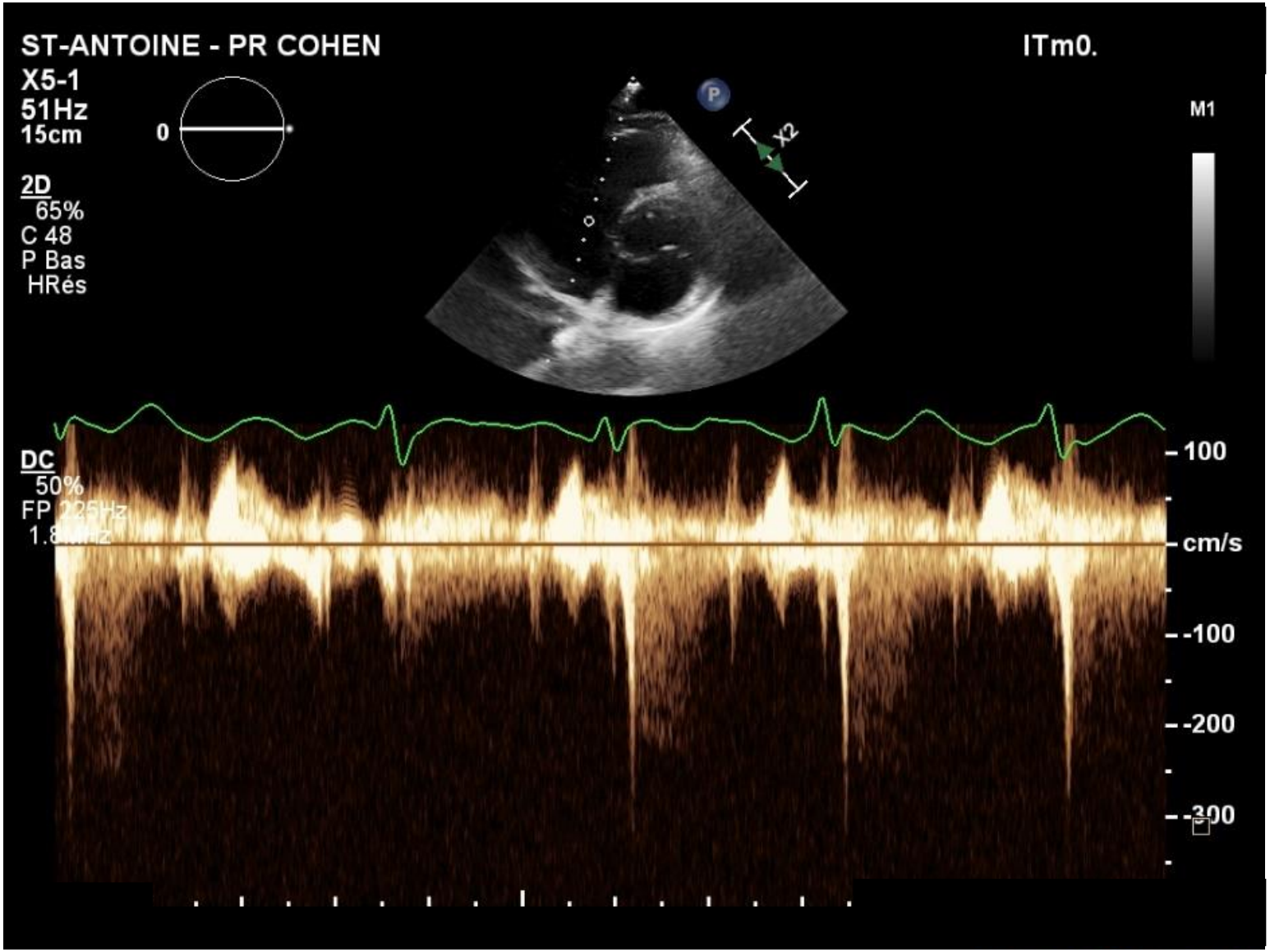
Parasternal short axis- Aortic valve level



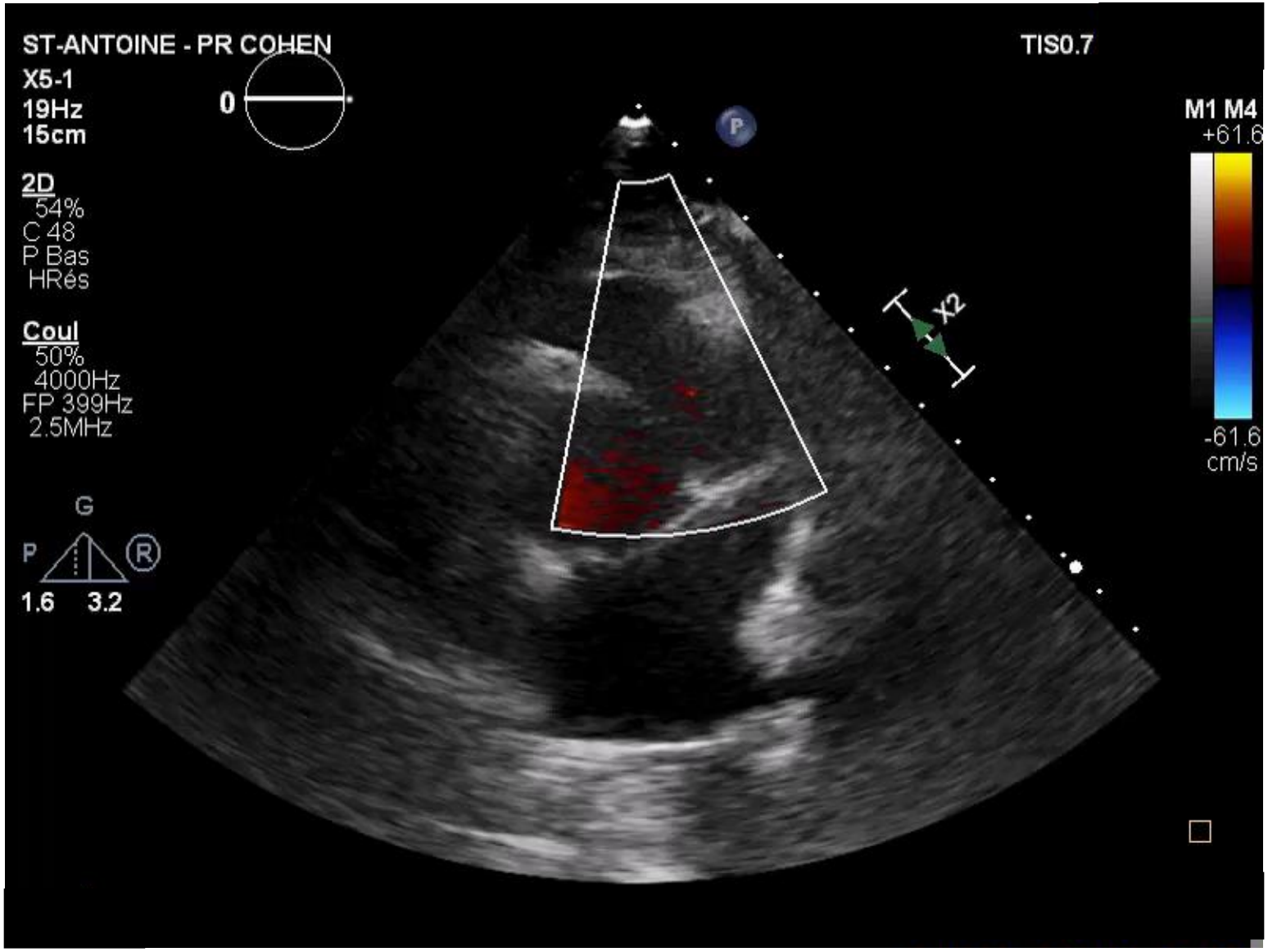
Parasternal short axis- Aortic valve level



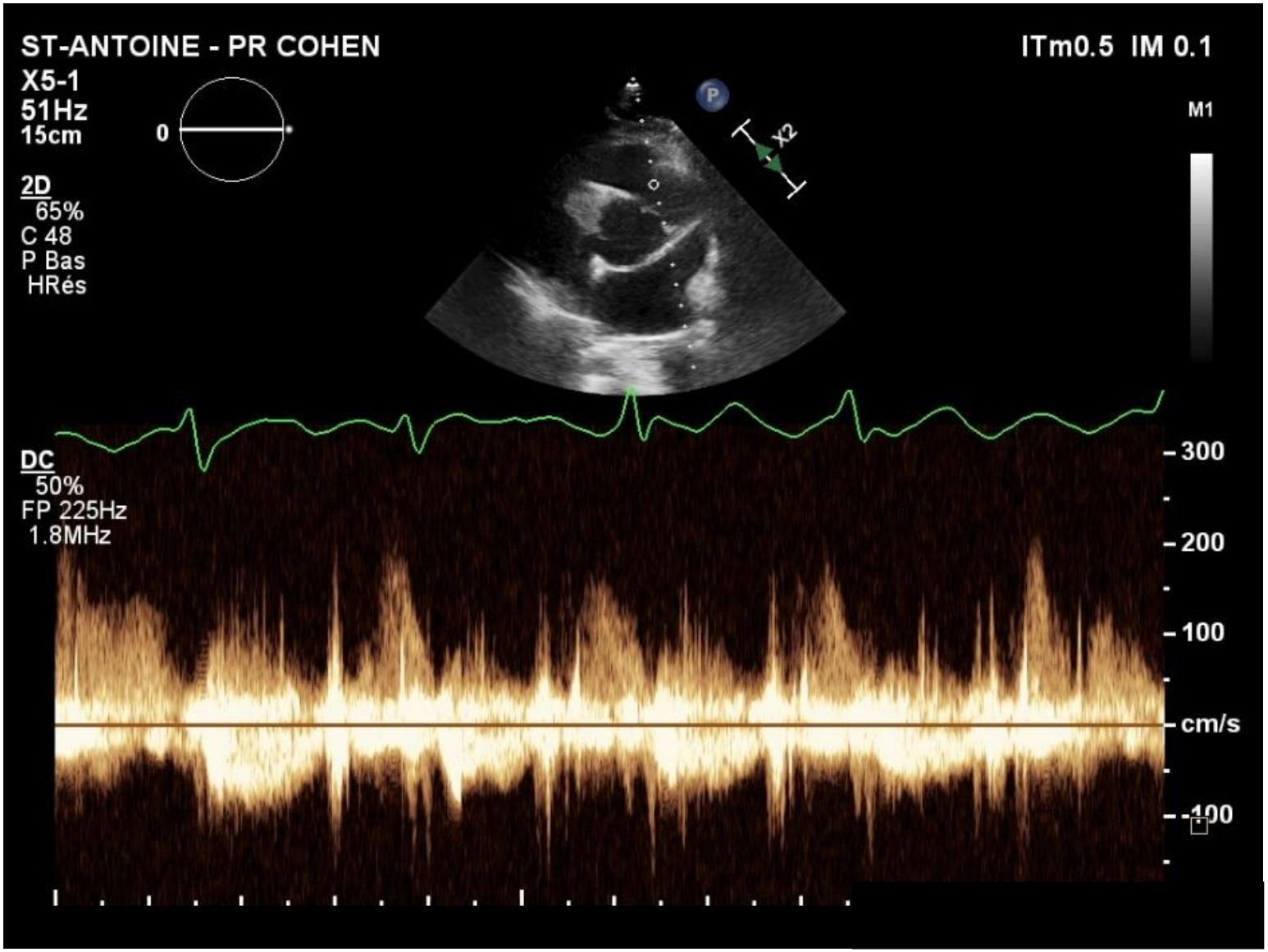
Parasternal short axis- Aortic valve level



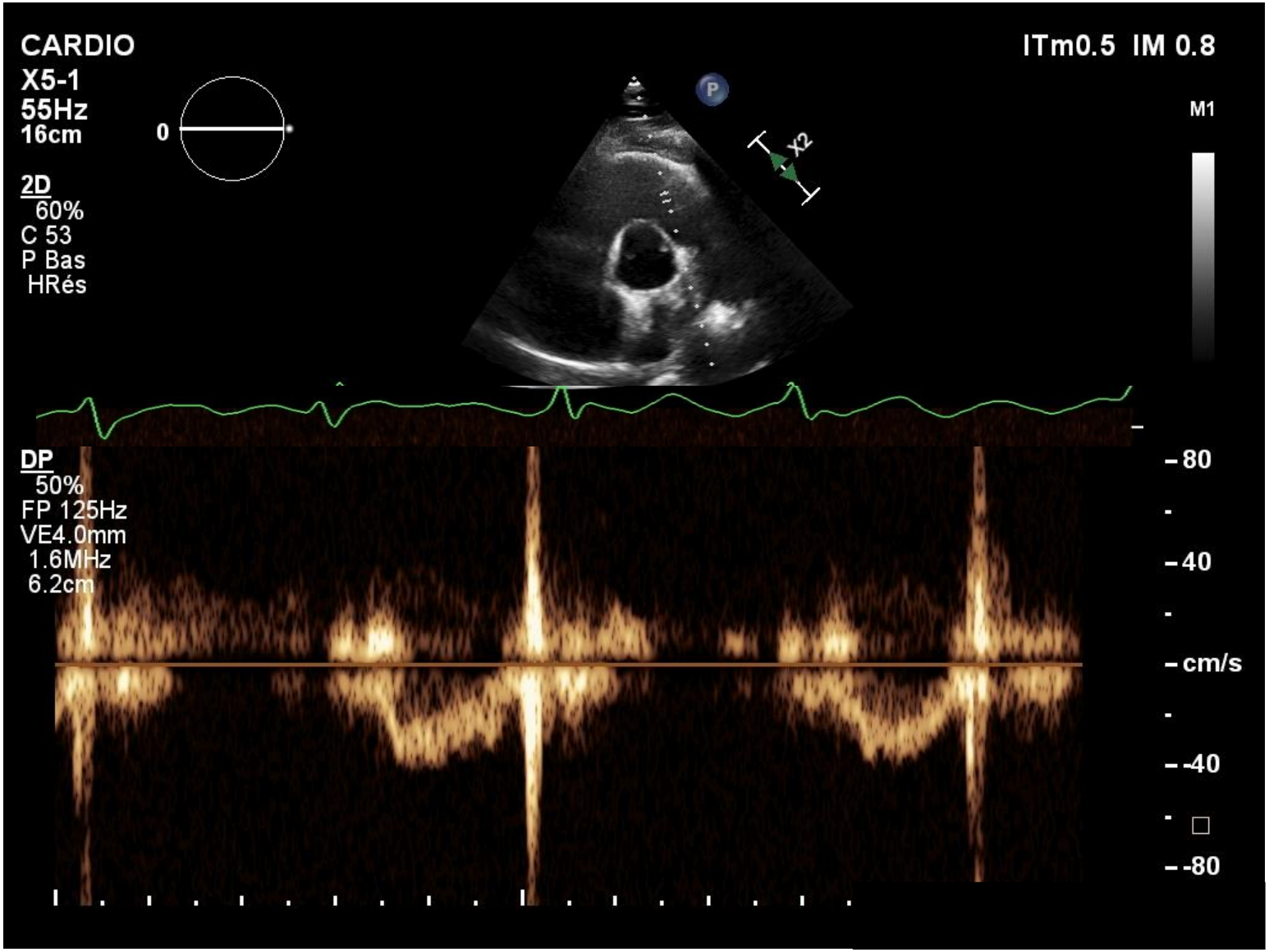
Parasternal short axis- Aortic valve level



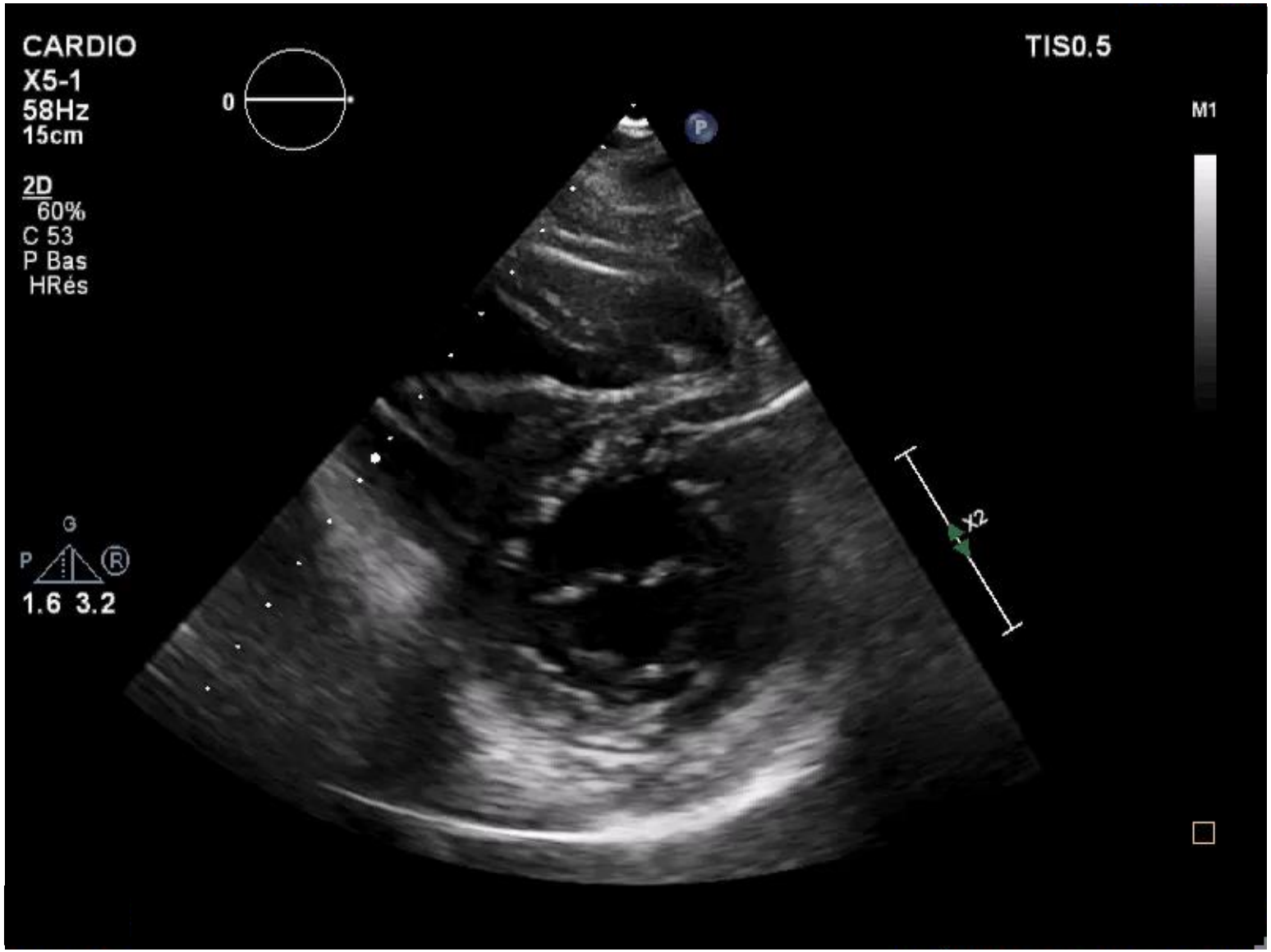
Parasternal short axis- Aortic valve level



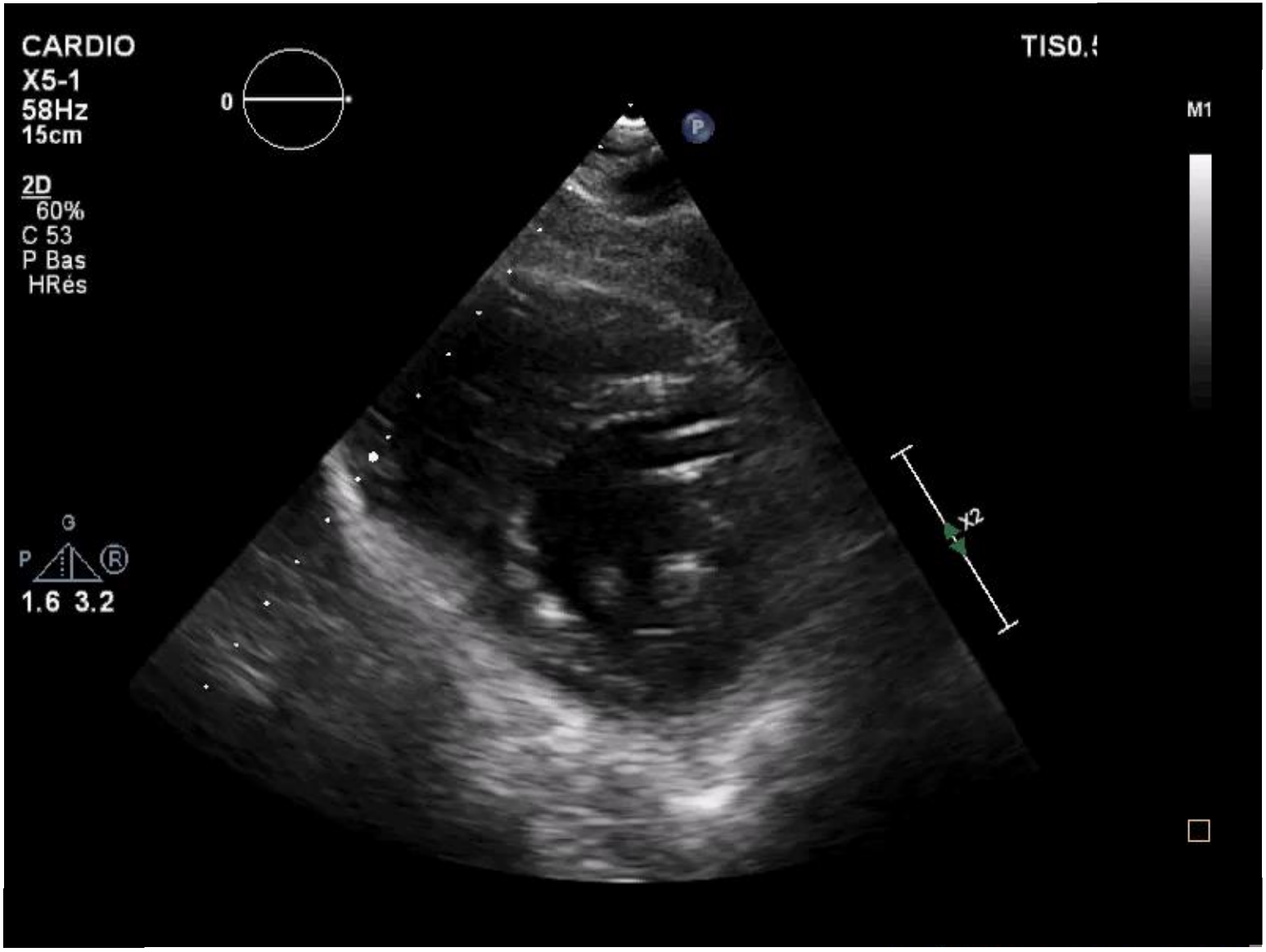
Parasternal short axis- Aortic valve level



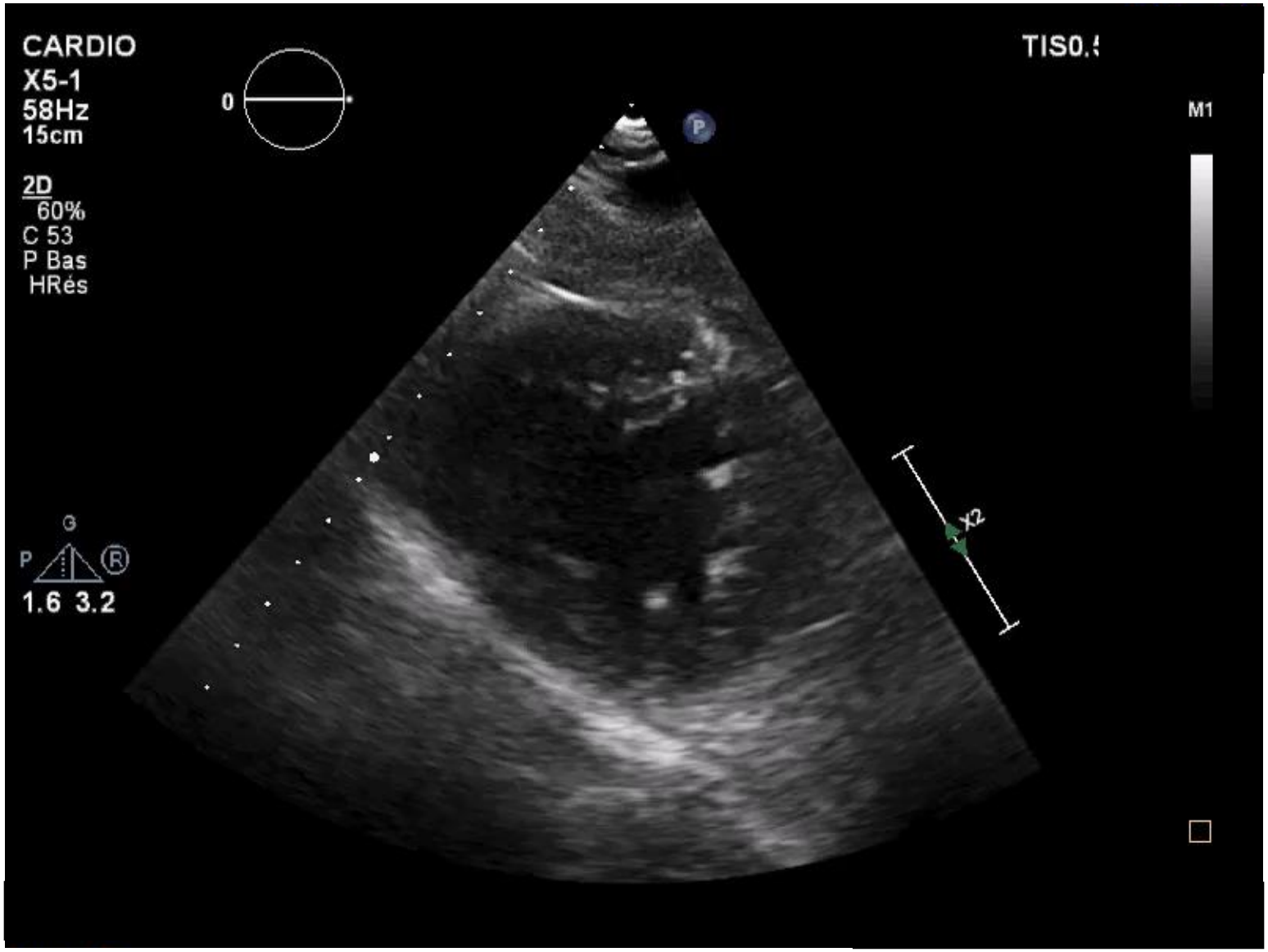
Parasternal short axis-Mitral Valve Level



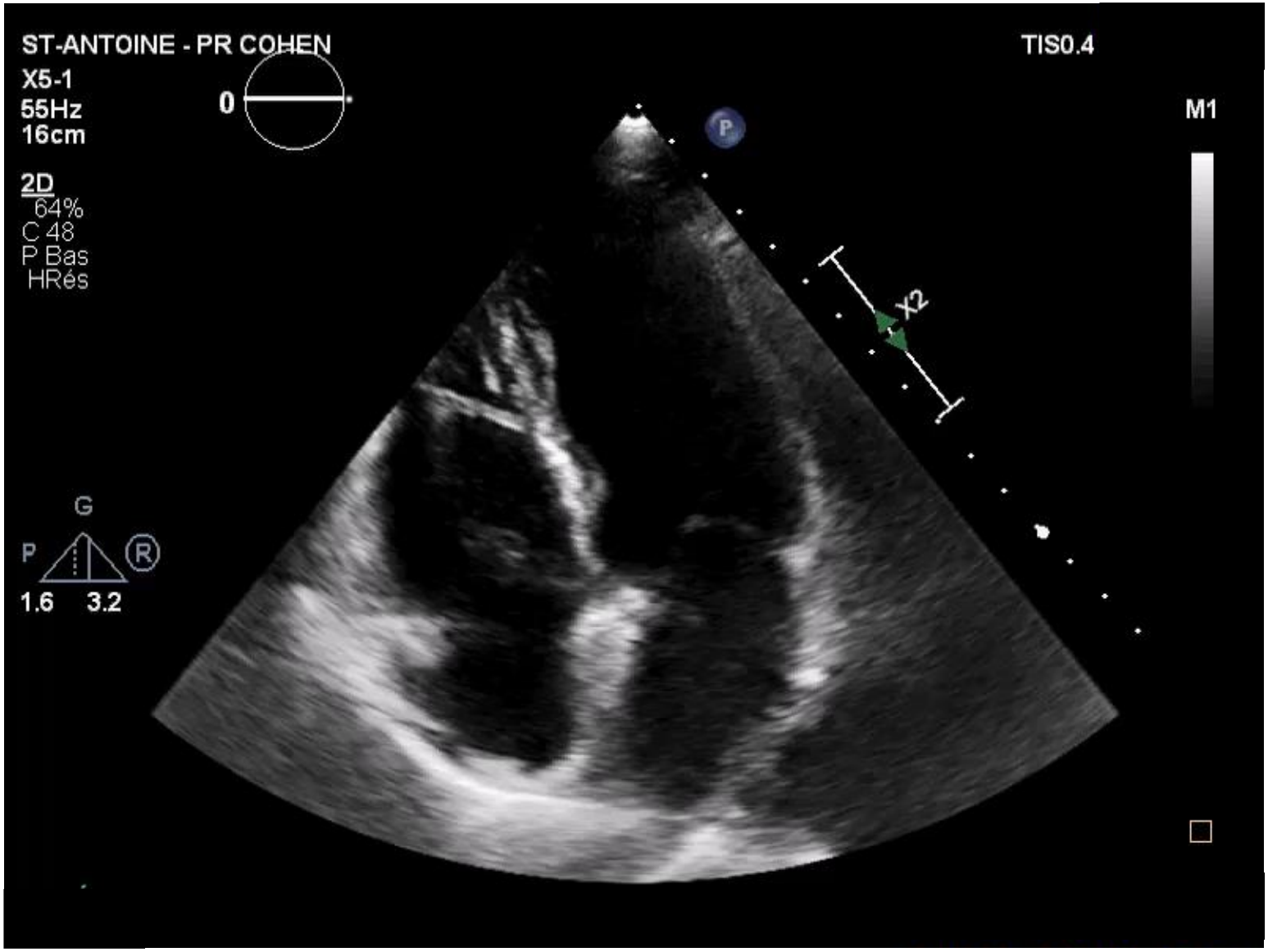
Parasternal short axis- Papillary muscle level



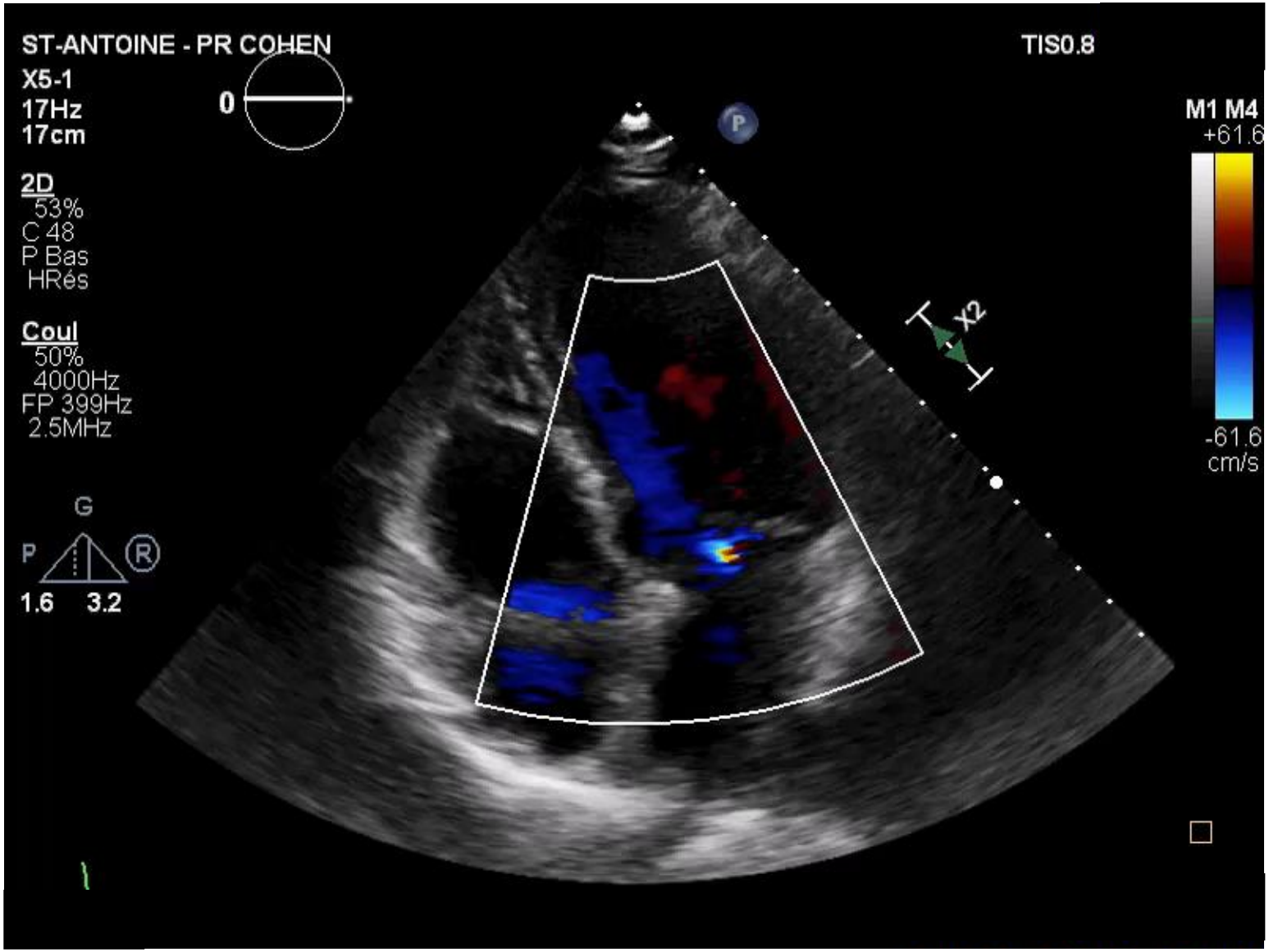
Parasternal short axis- LV apex



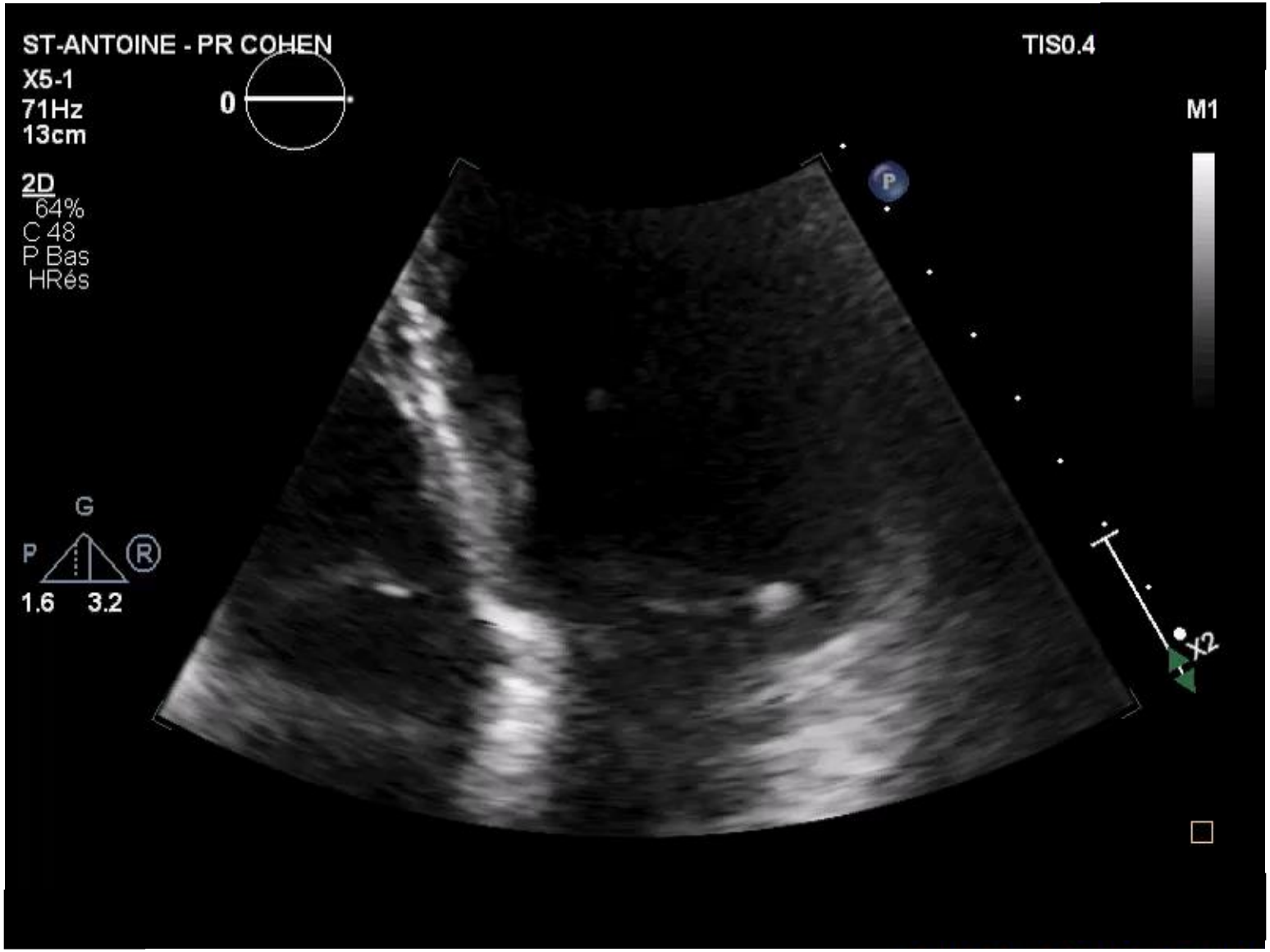
Apical 4 chamber view



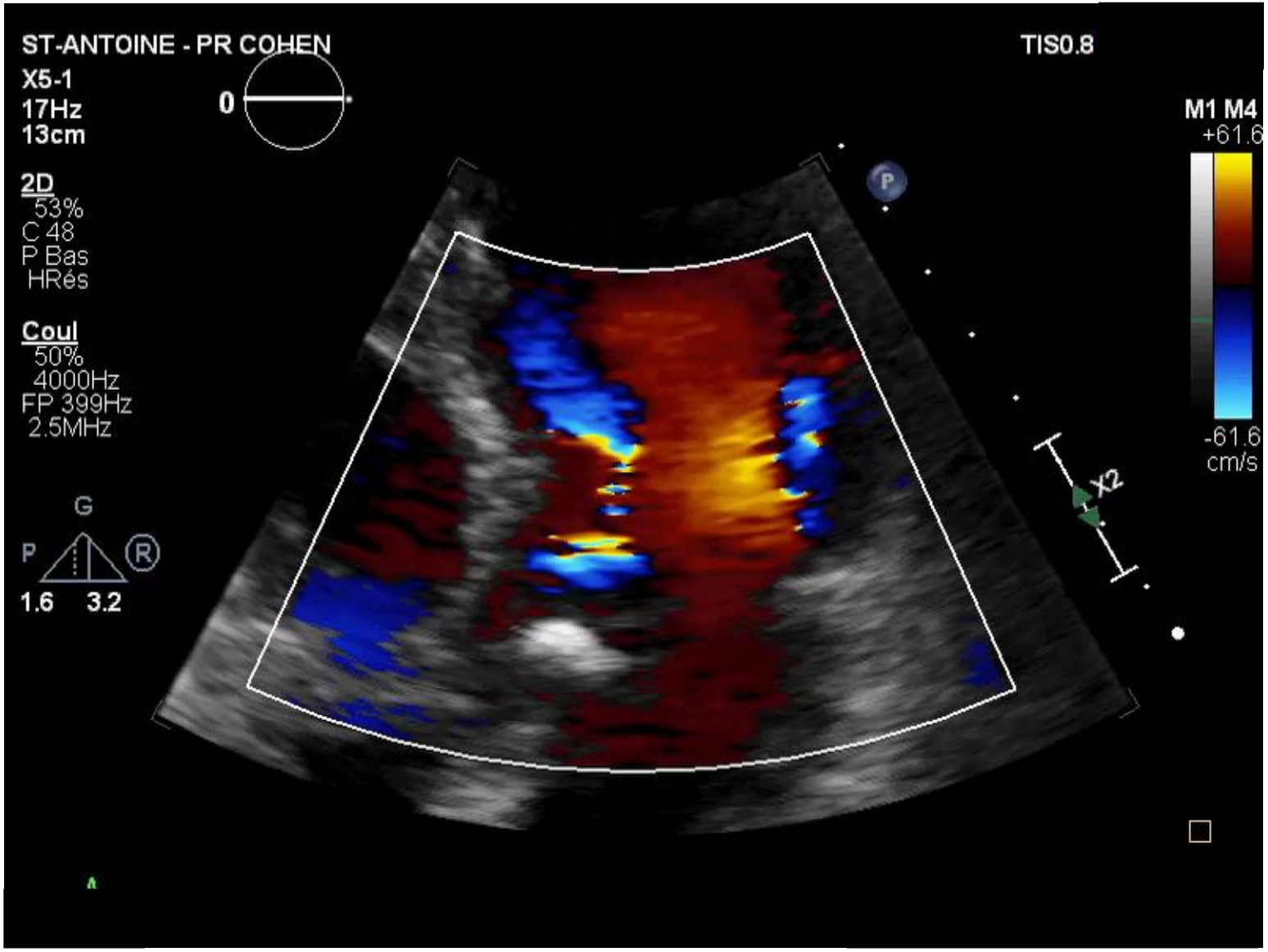
Apical 4 chamber view



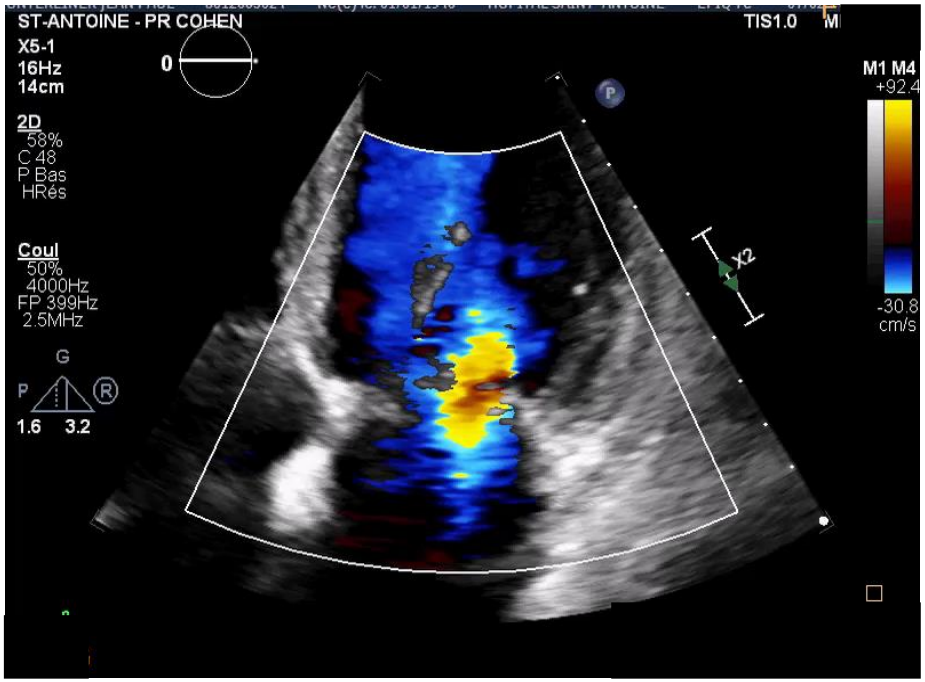
Apical 4 chamber view

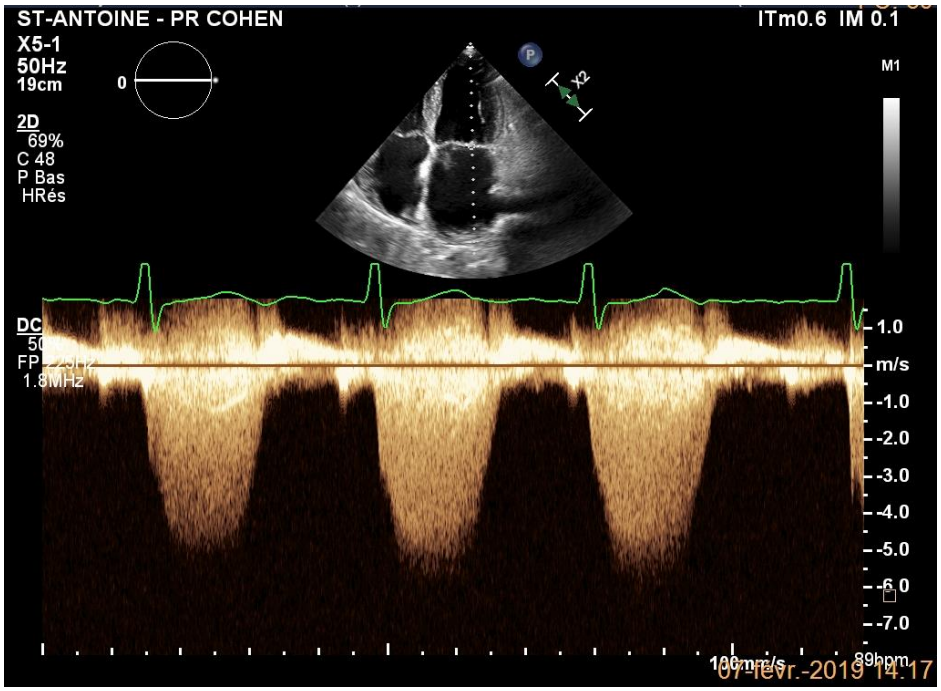


Apical 4 chamber view



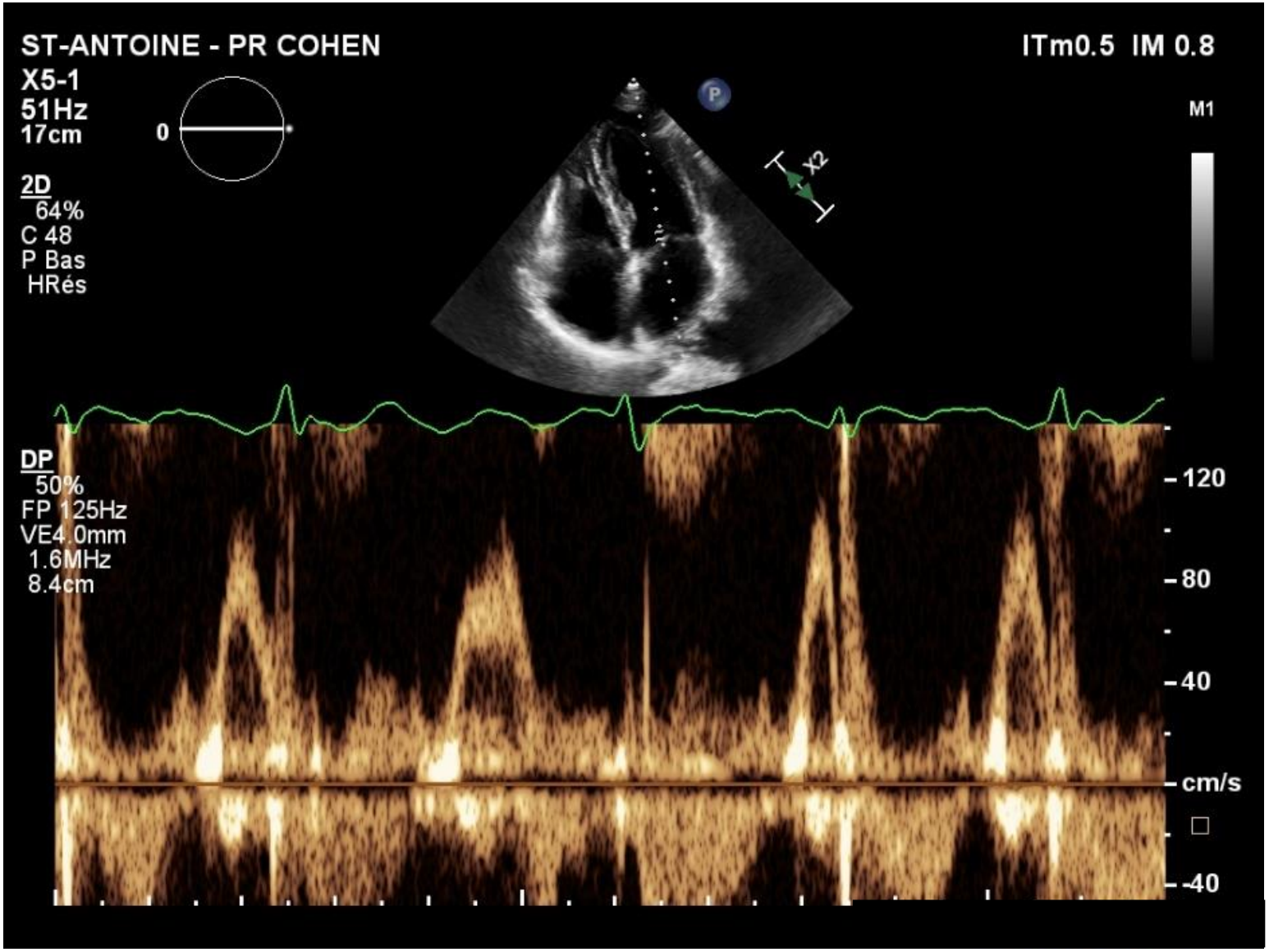
Apical 4 chamber view



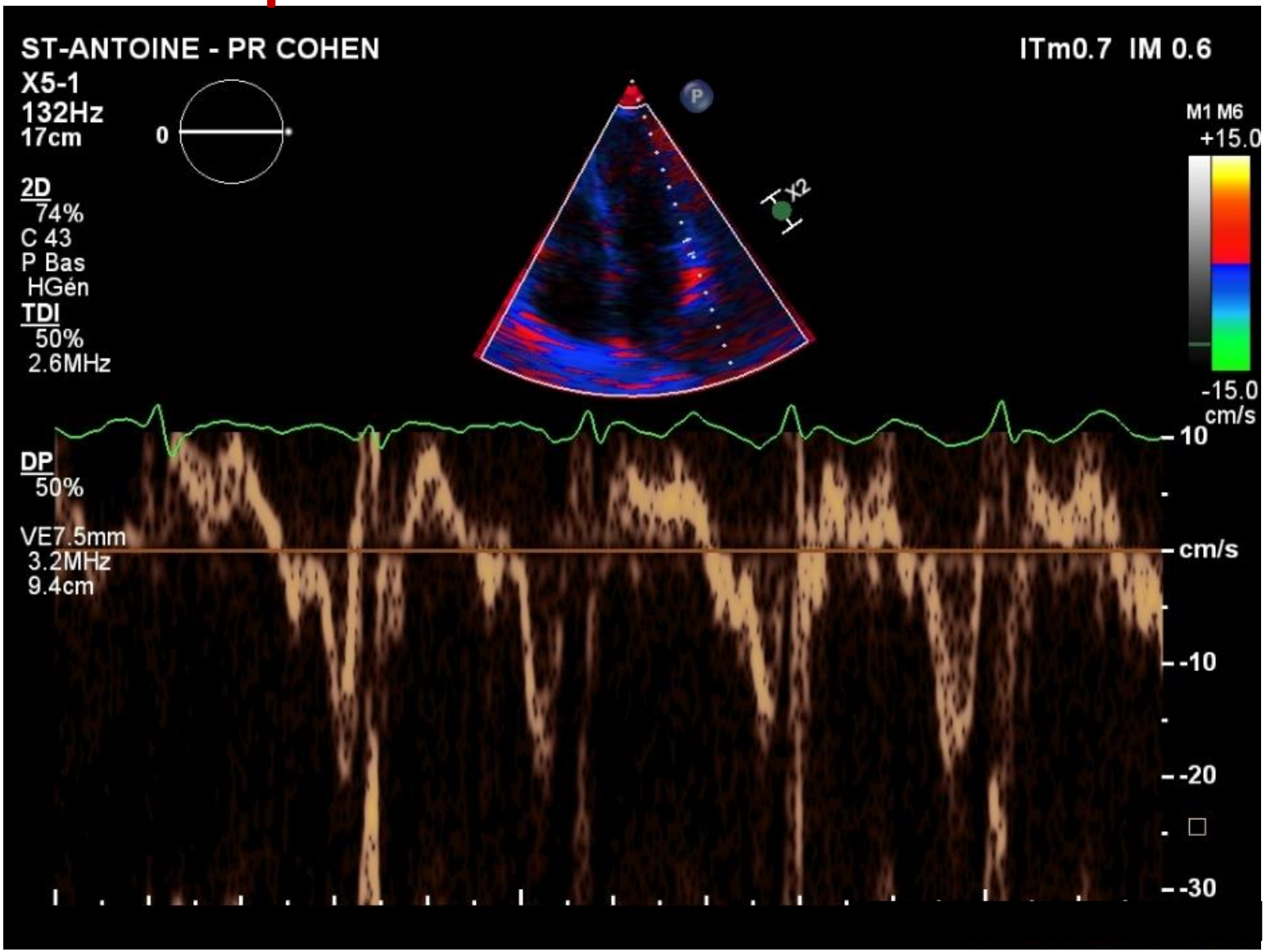


If valvular regurgitation ≥ mild, acquisition for ORE (color and continuous doppler)

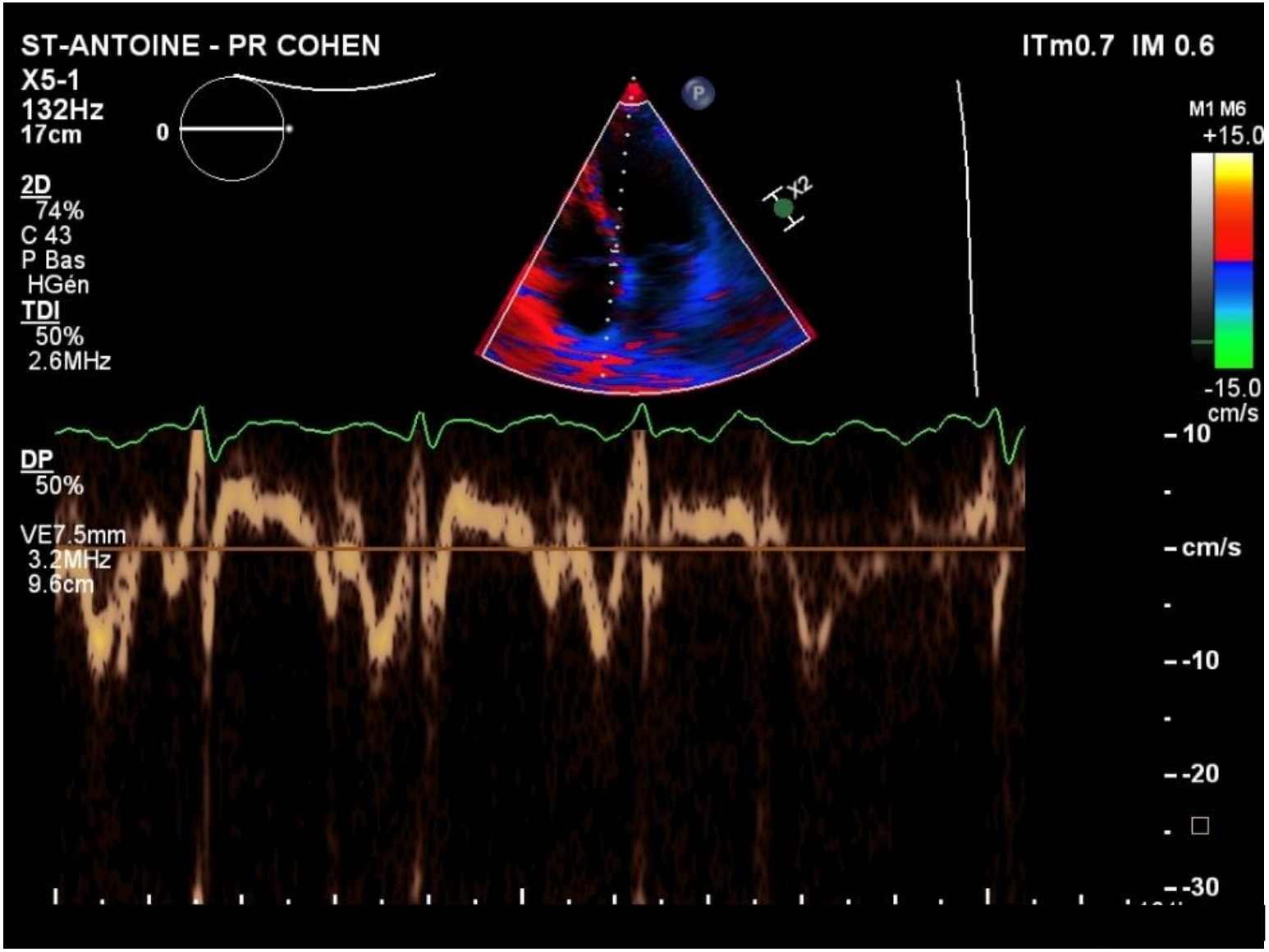
Apical 4 chamber view



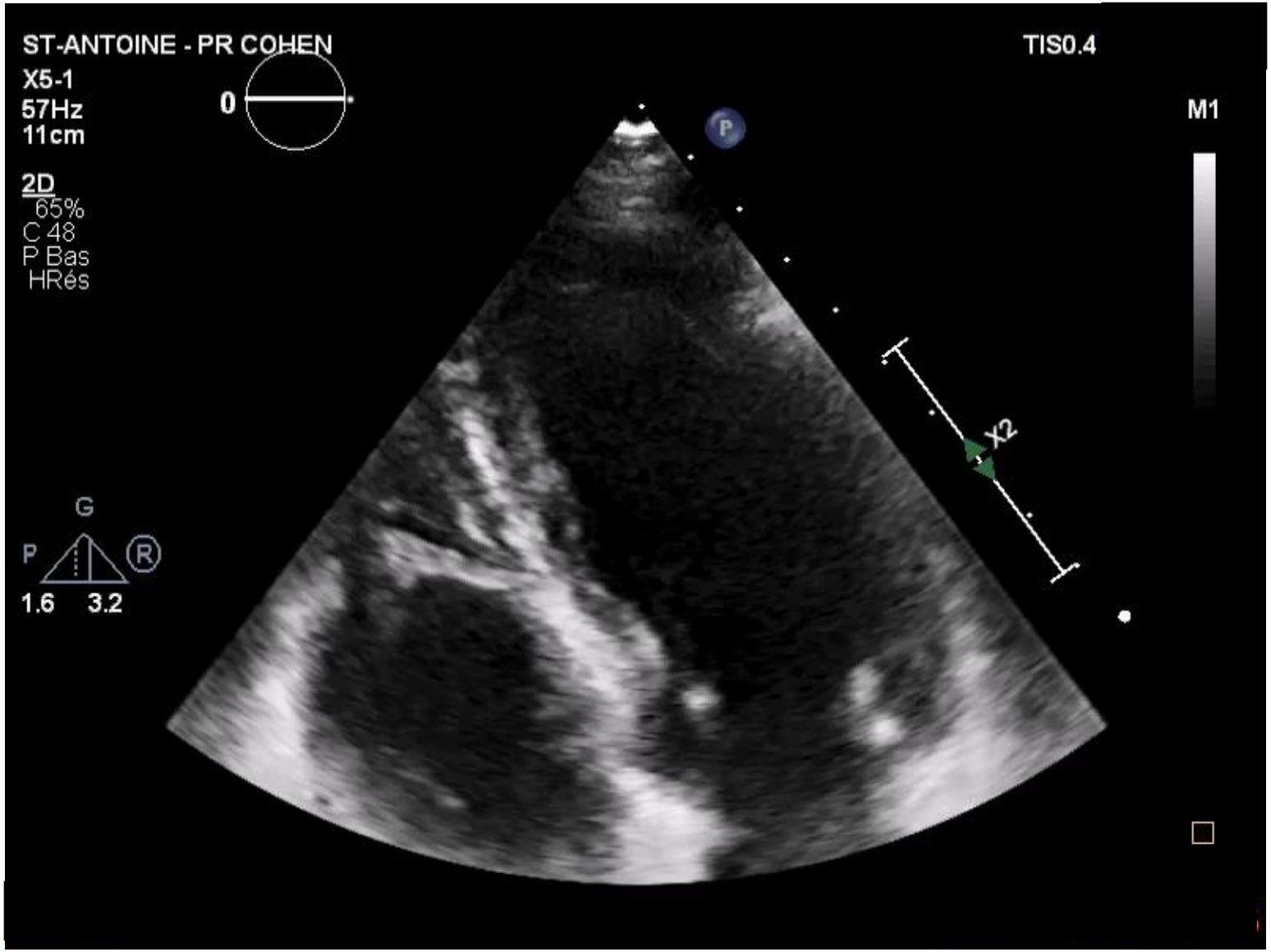
Apical 4 chamber view



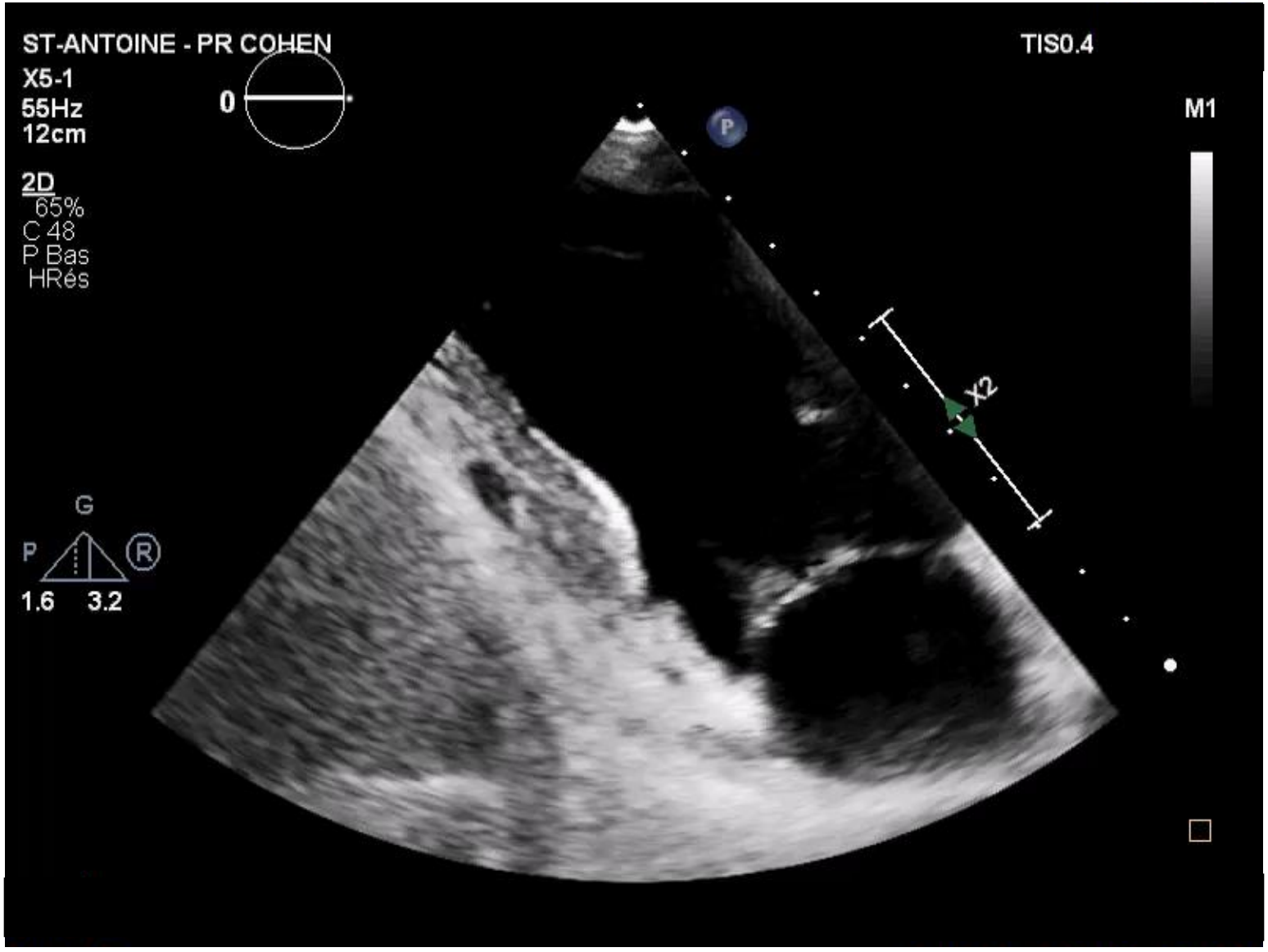
Apical 4 chamber view



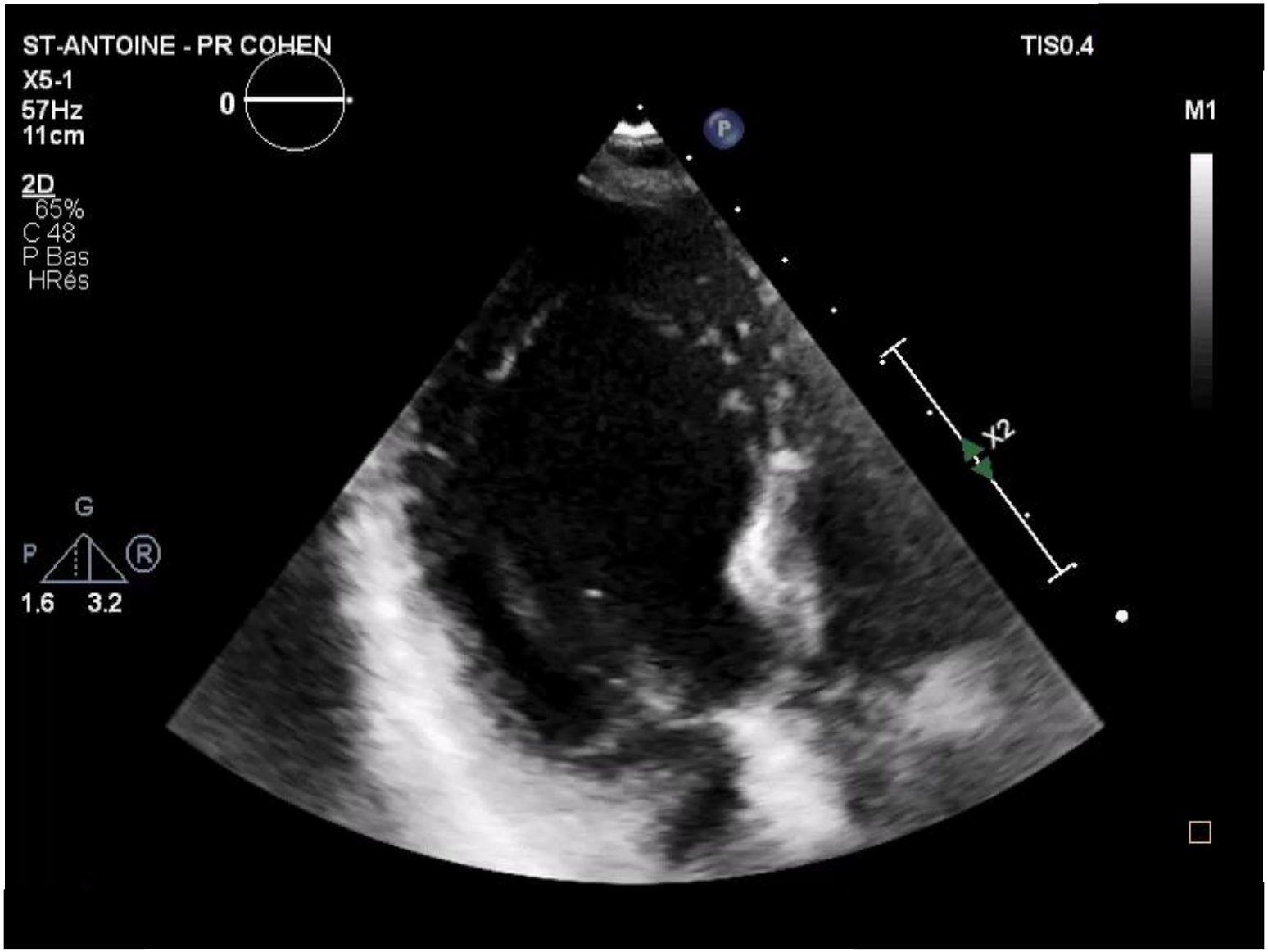
Apical 4 chamber focused on the left ventricle



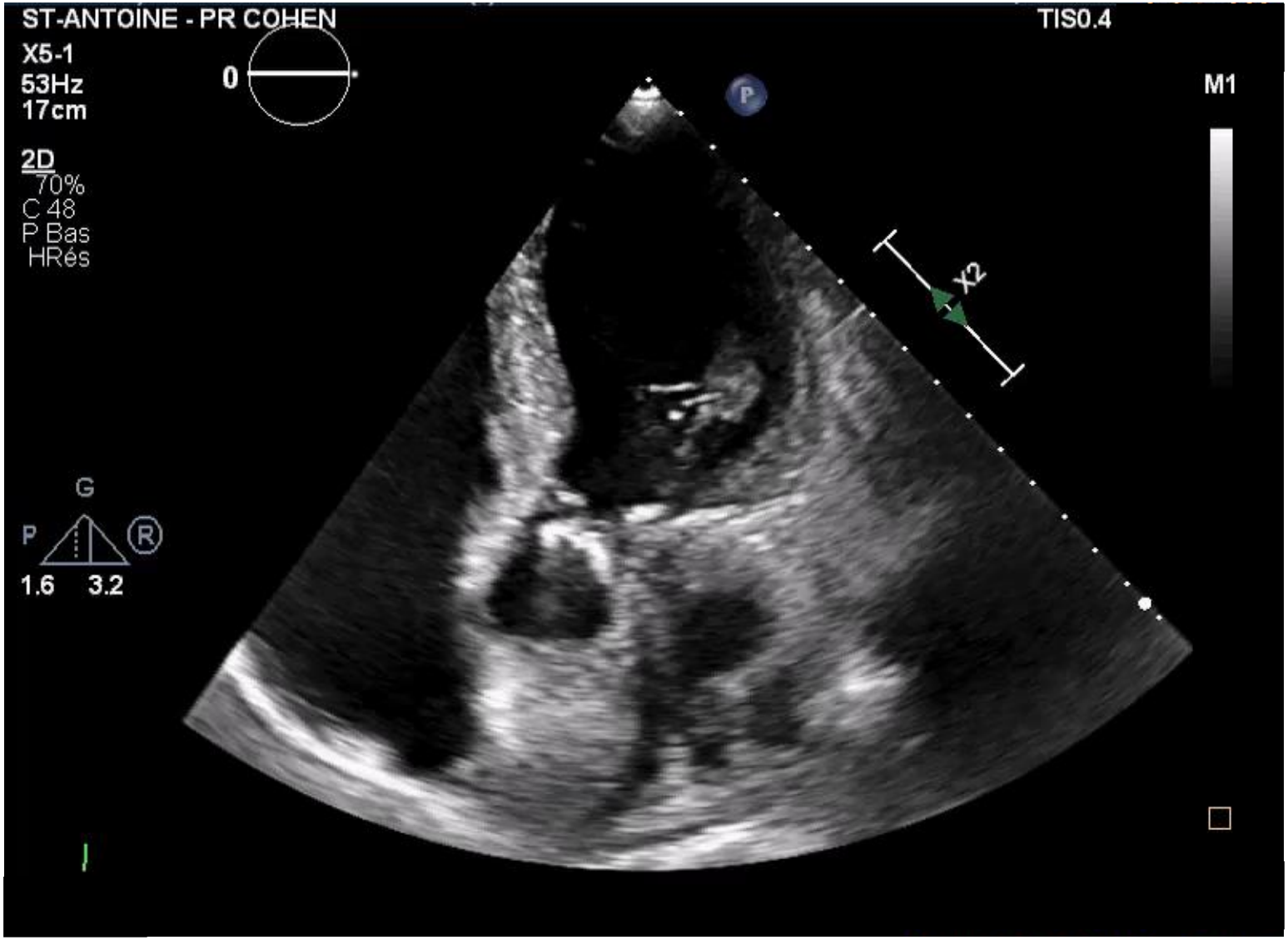
Apical 2 chamber focused on the left ventricle



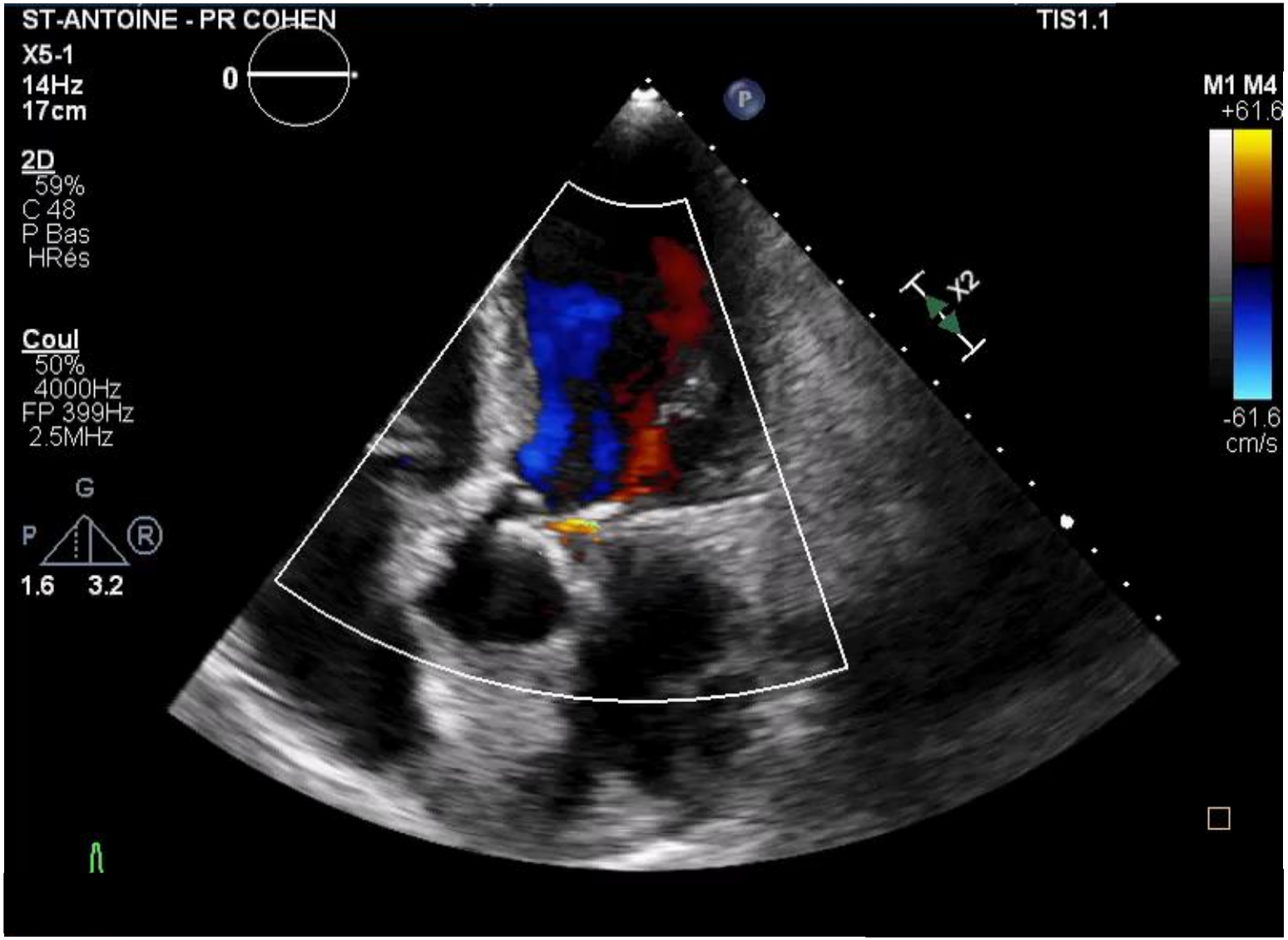
Apical 3 chamber focused on the left ventricle



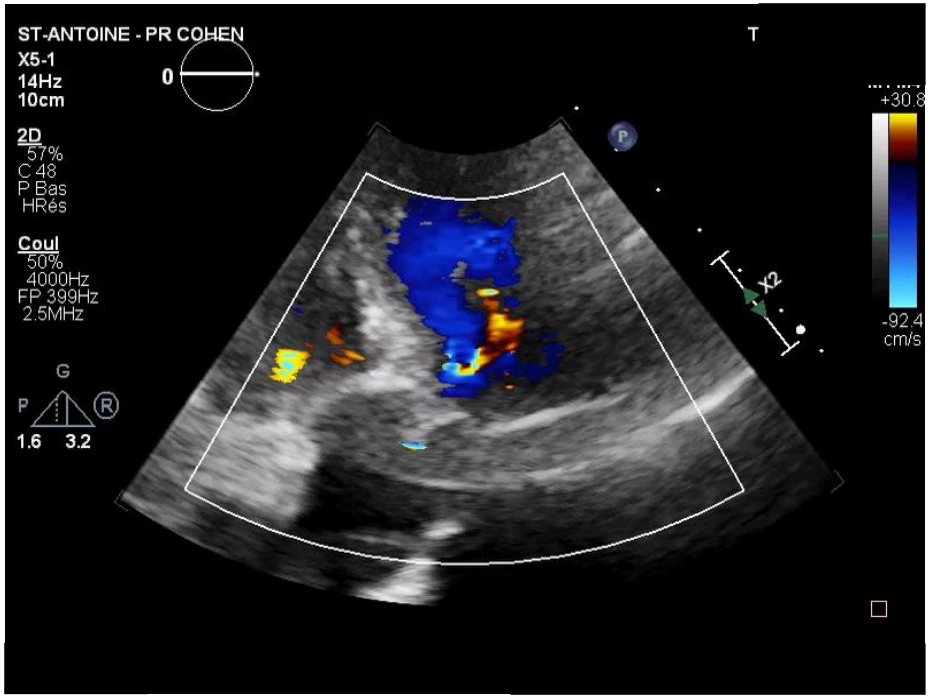
Apical 5 chamber view

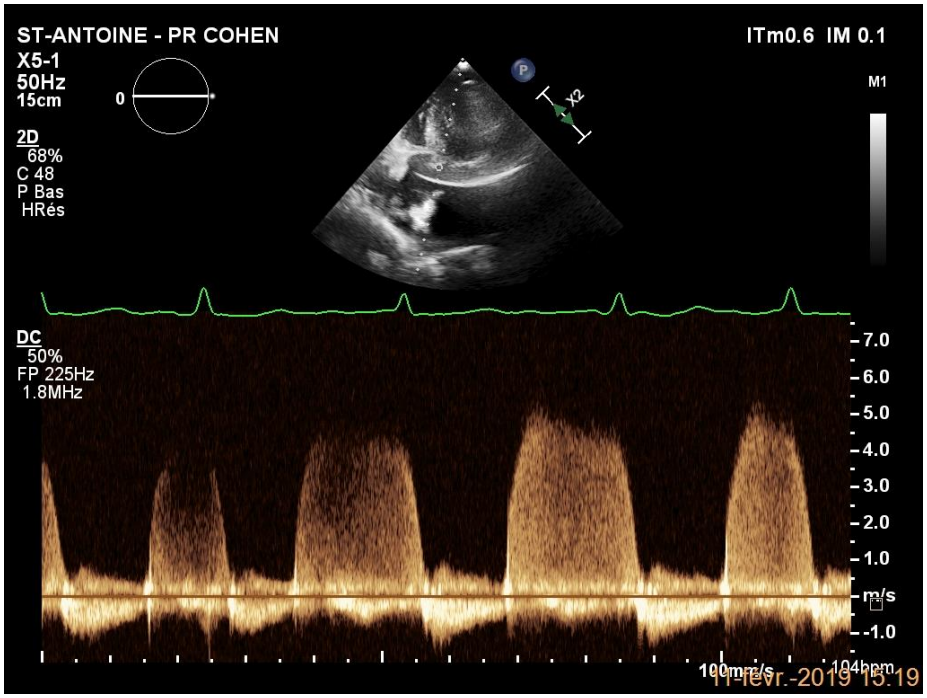


Apical 5 chamber view



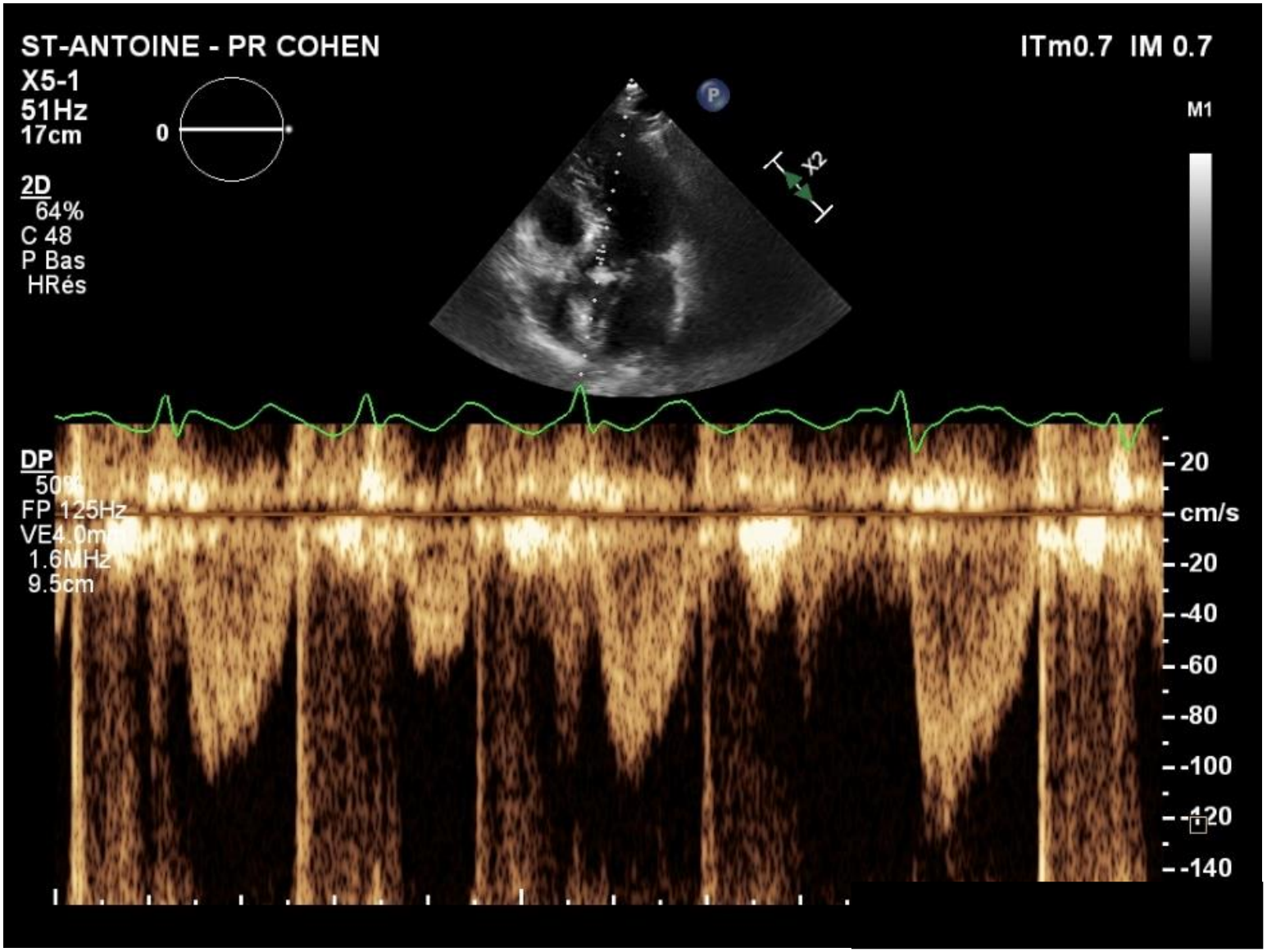
Apical 5 chamber view



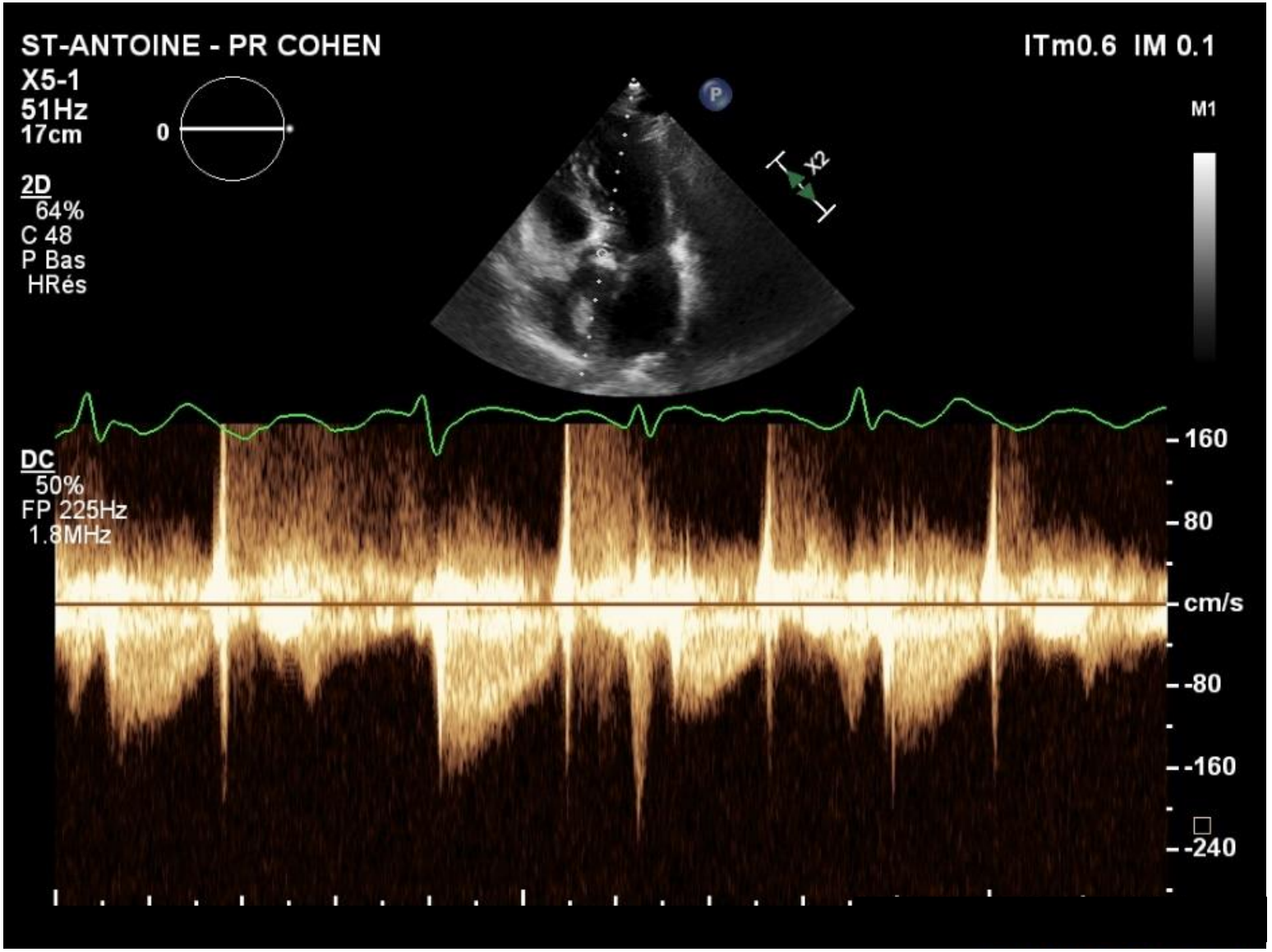


If valvular regurgitation ≥ mild, acquisition for ORE (color and continuous doppler)

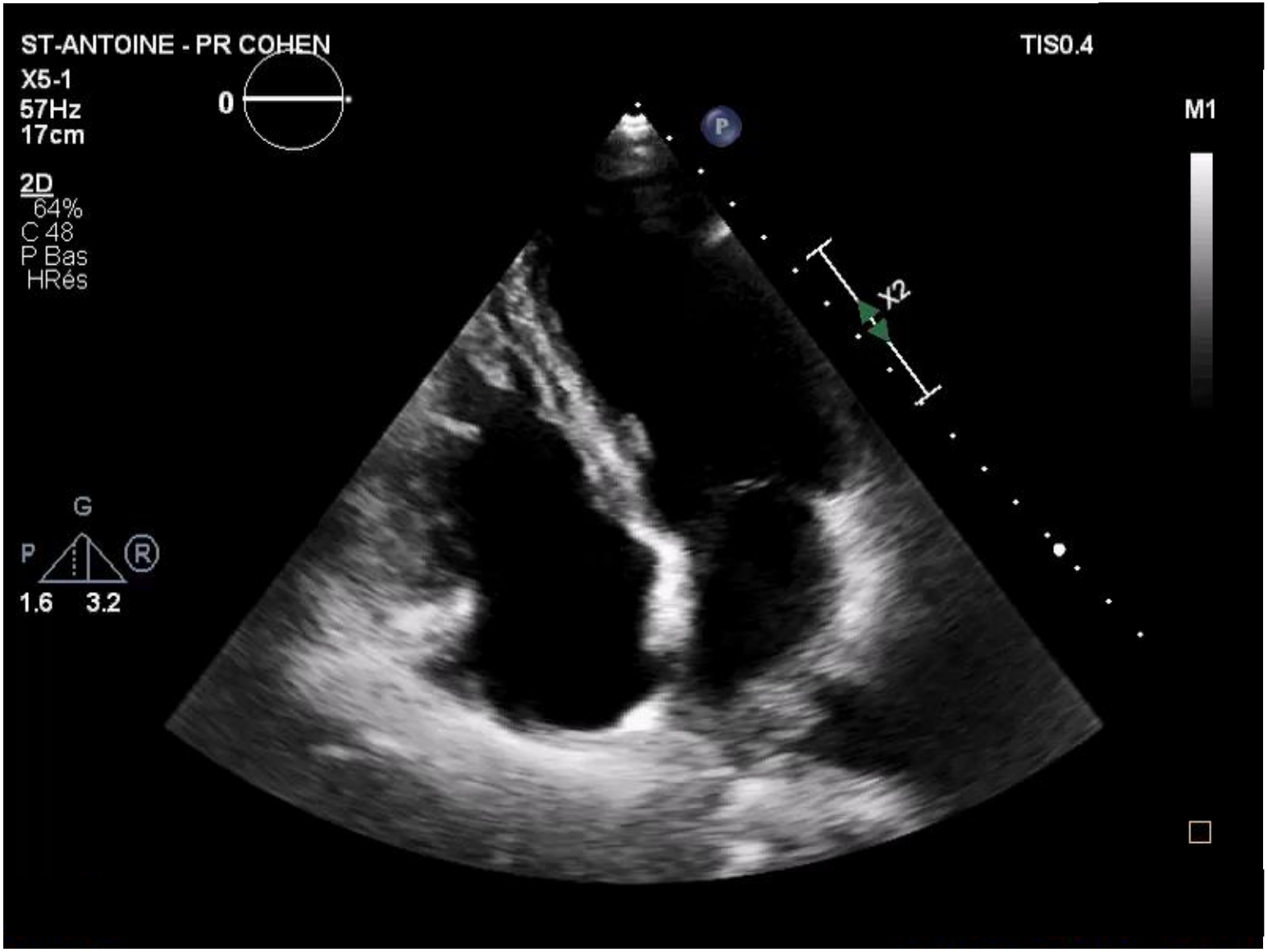
Apical 5 chamber view



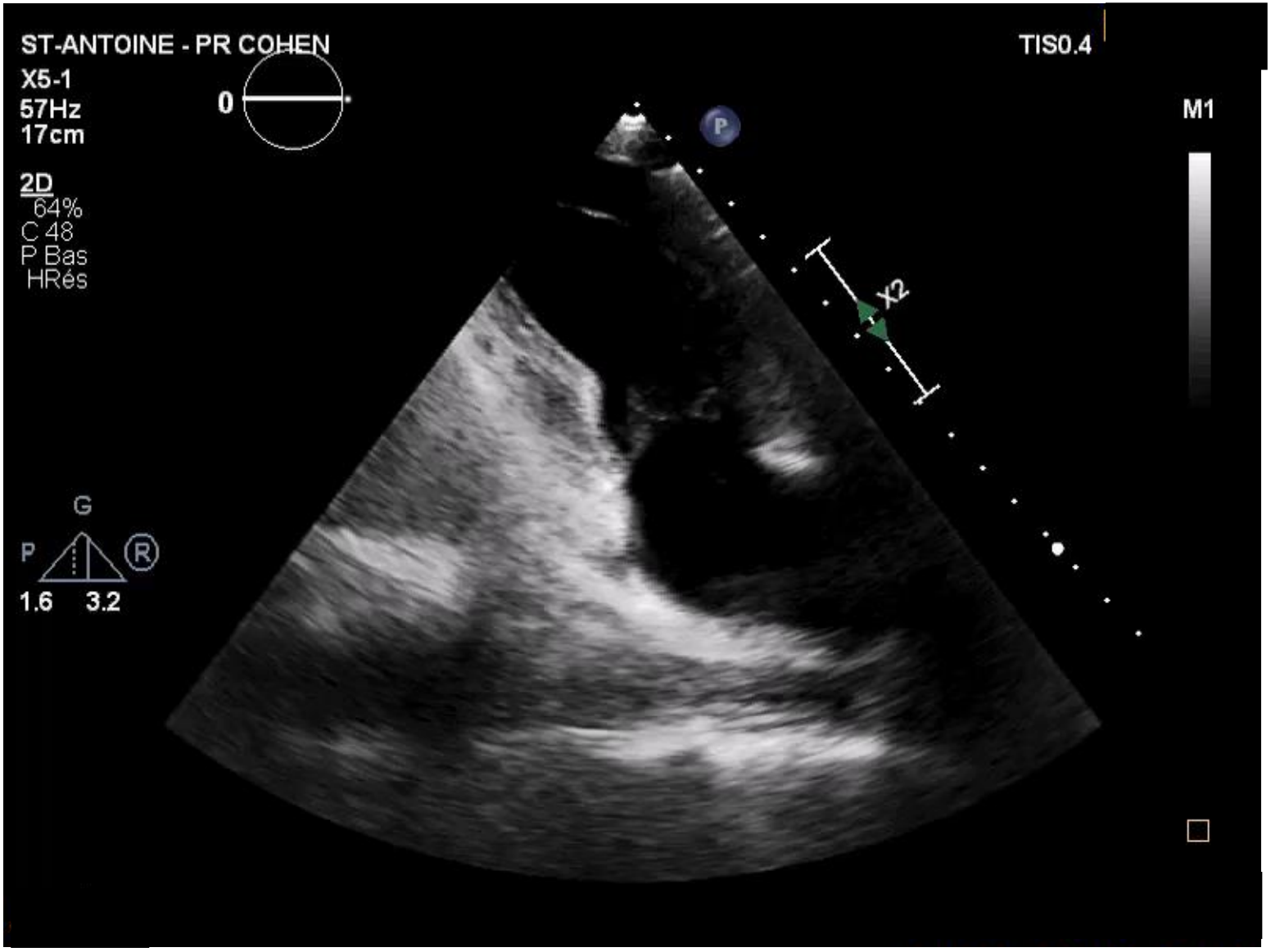
Apical 5 chamber view



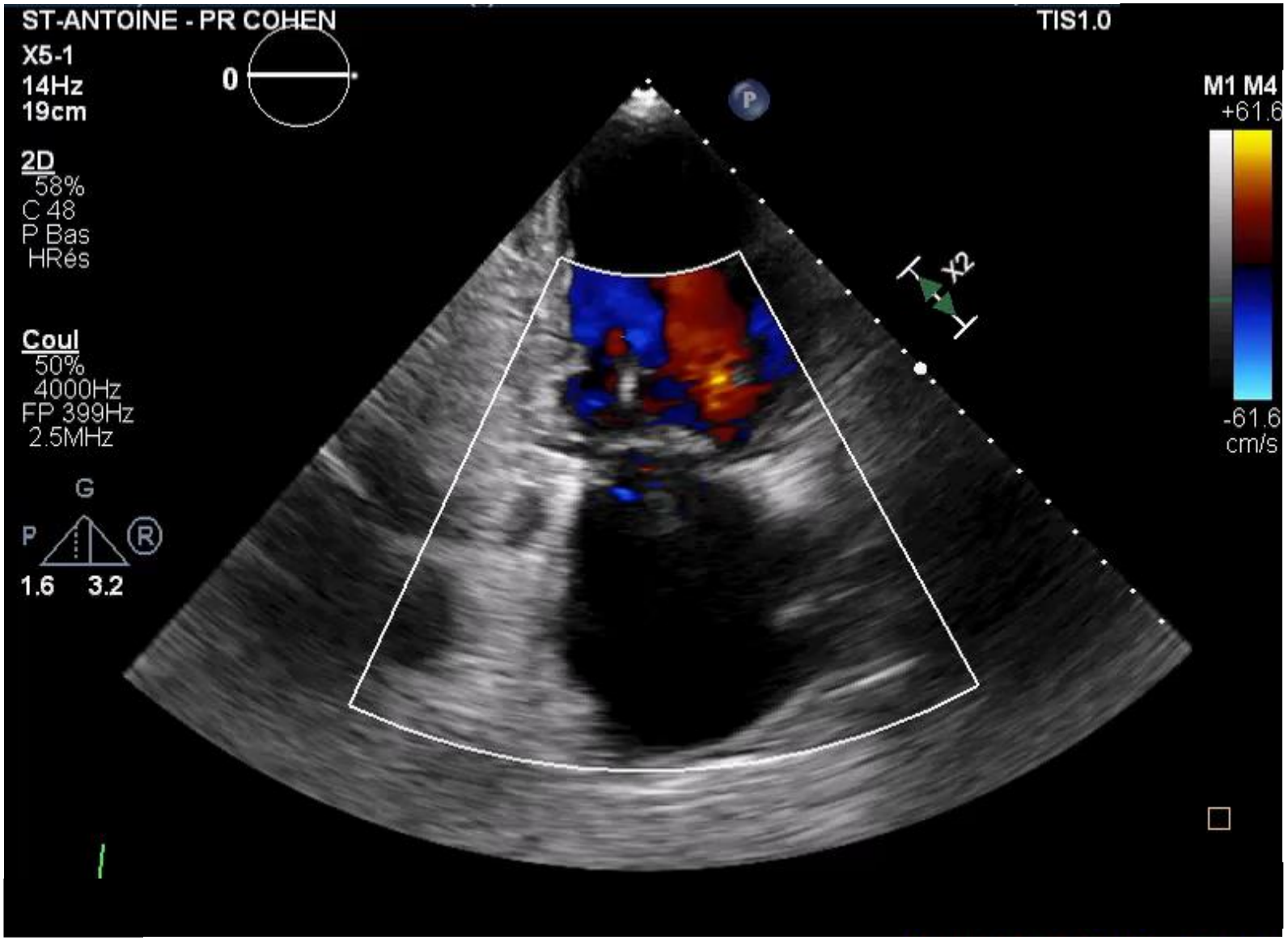
Apical 4 chamber focused on the left atrium



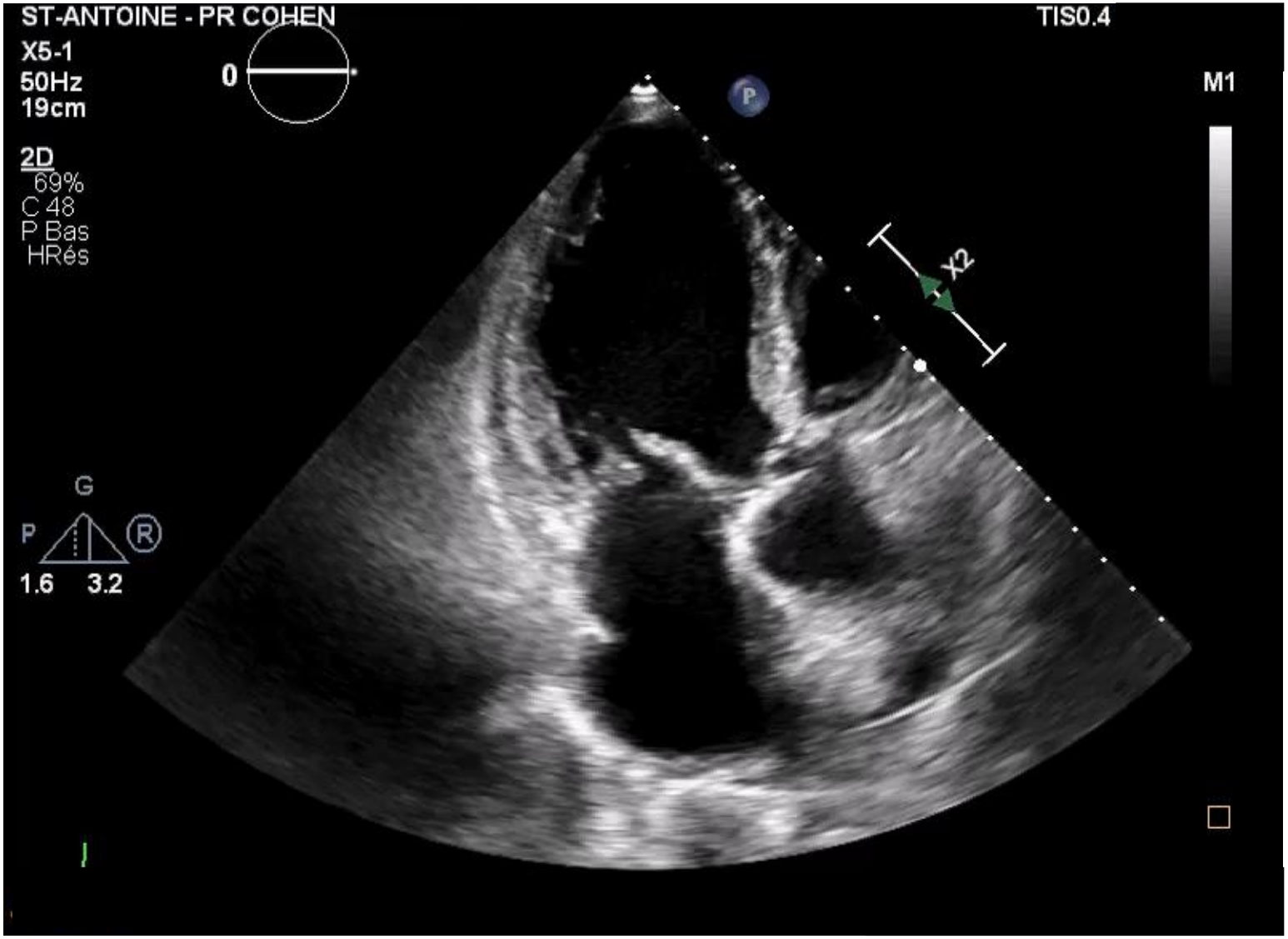
Apical 2 chamber focused on the left atrium



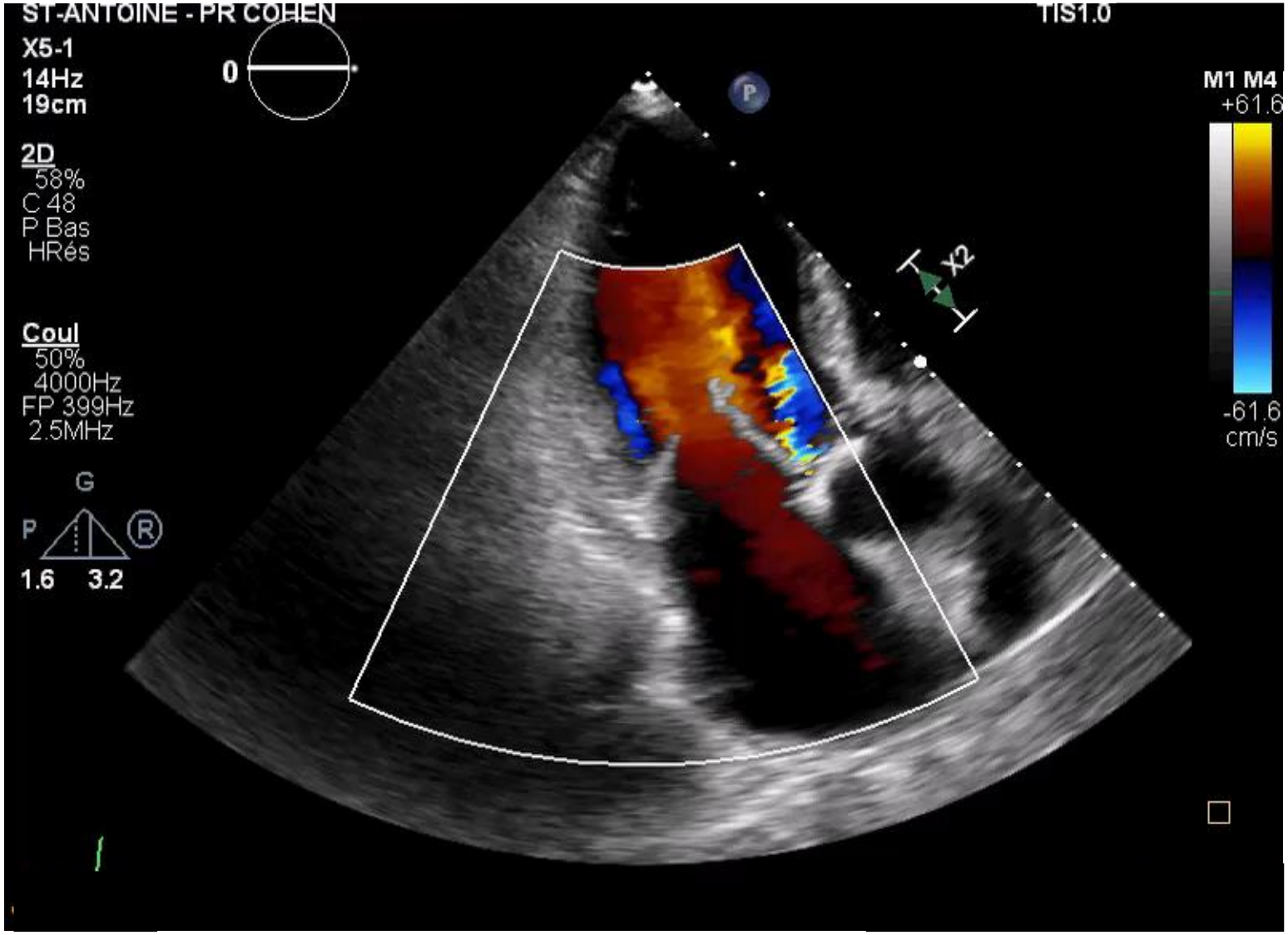
Apical 2 chamber focused on the left atrium



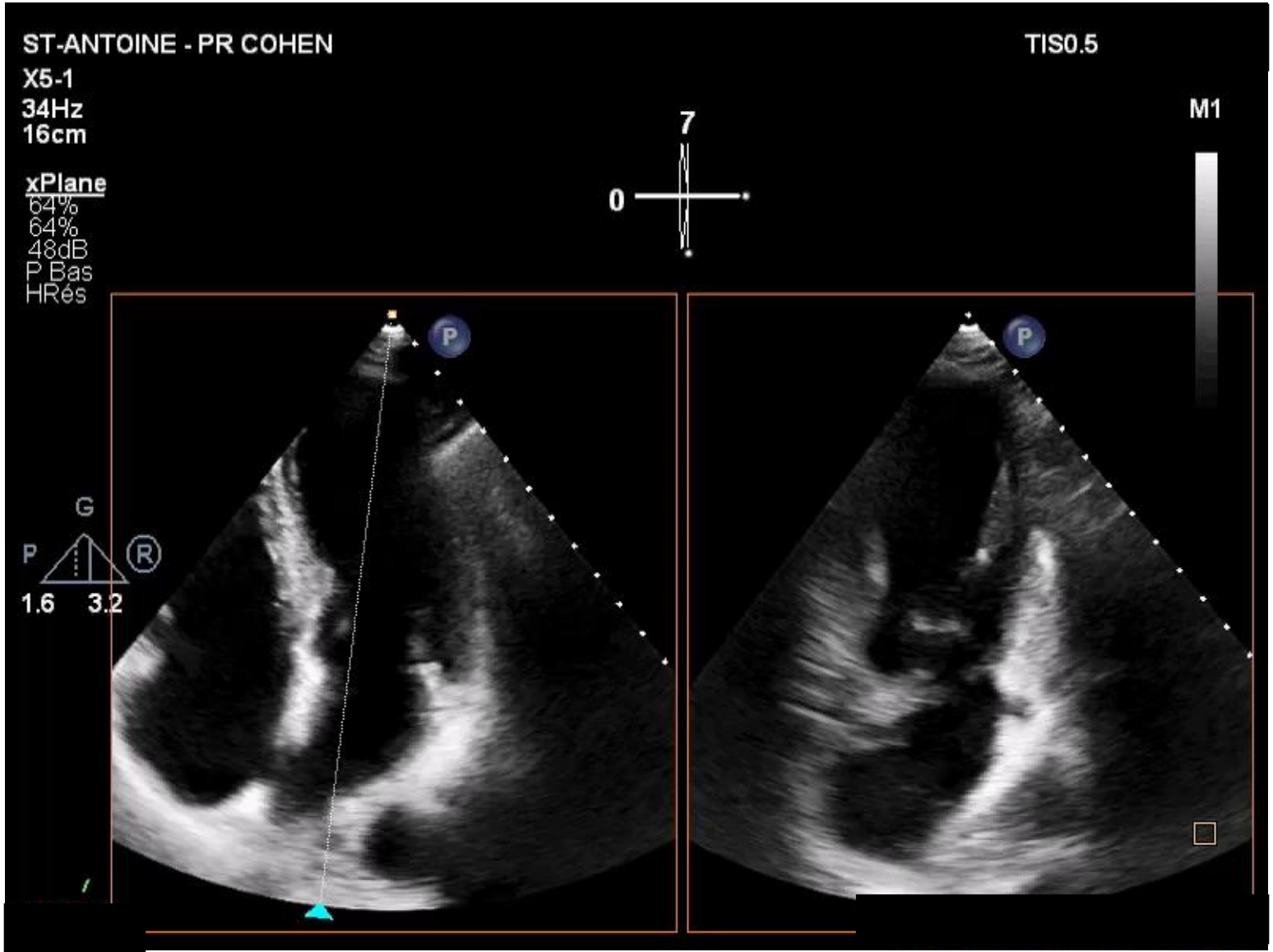
Apical 3 chamber focused on the left atrium



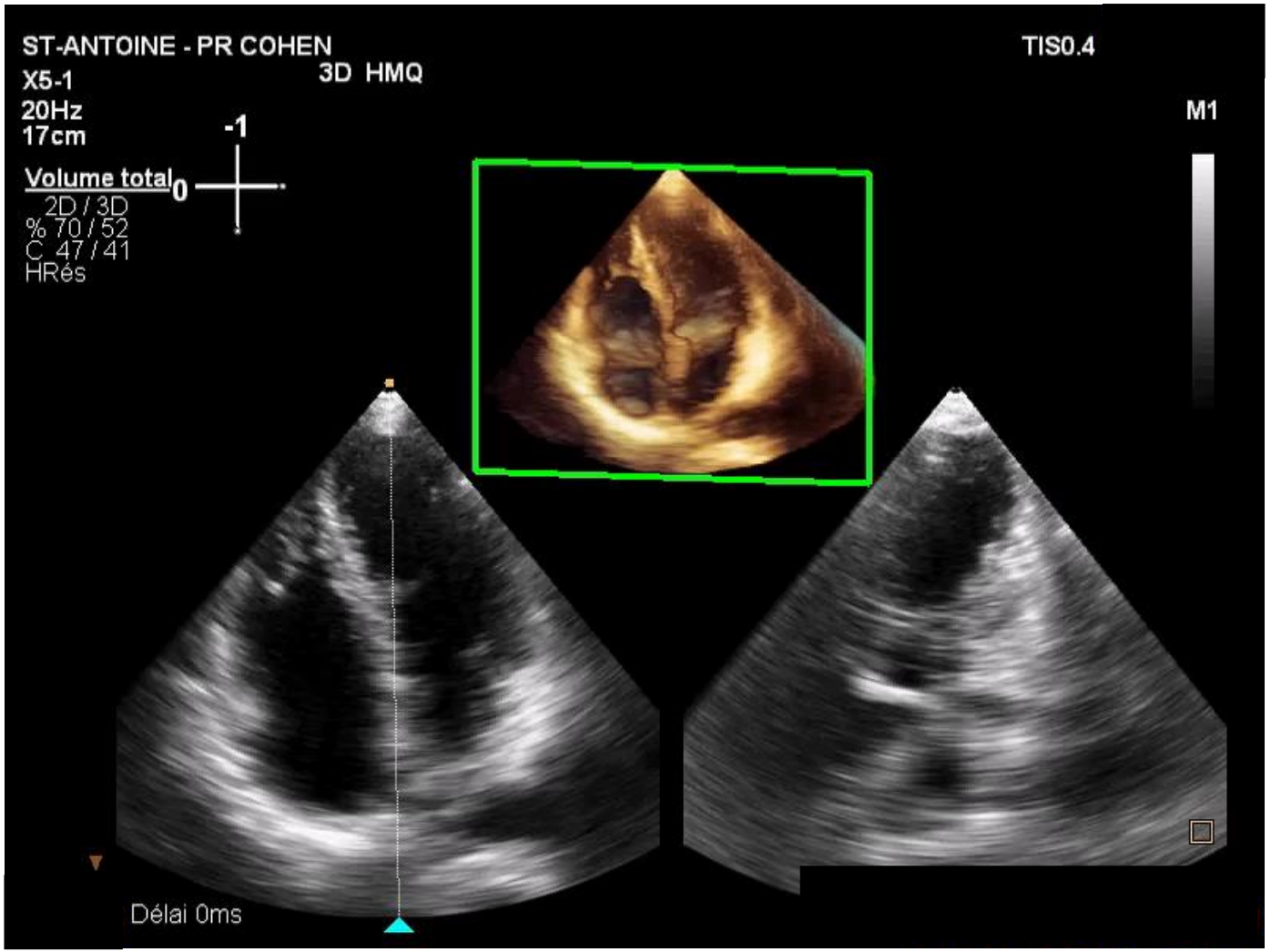
Apical 3 chamber focused on the left atrium



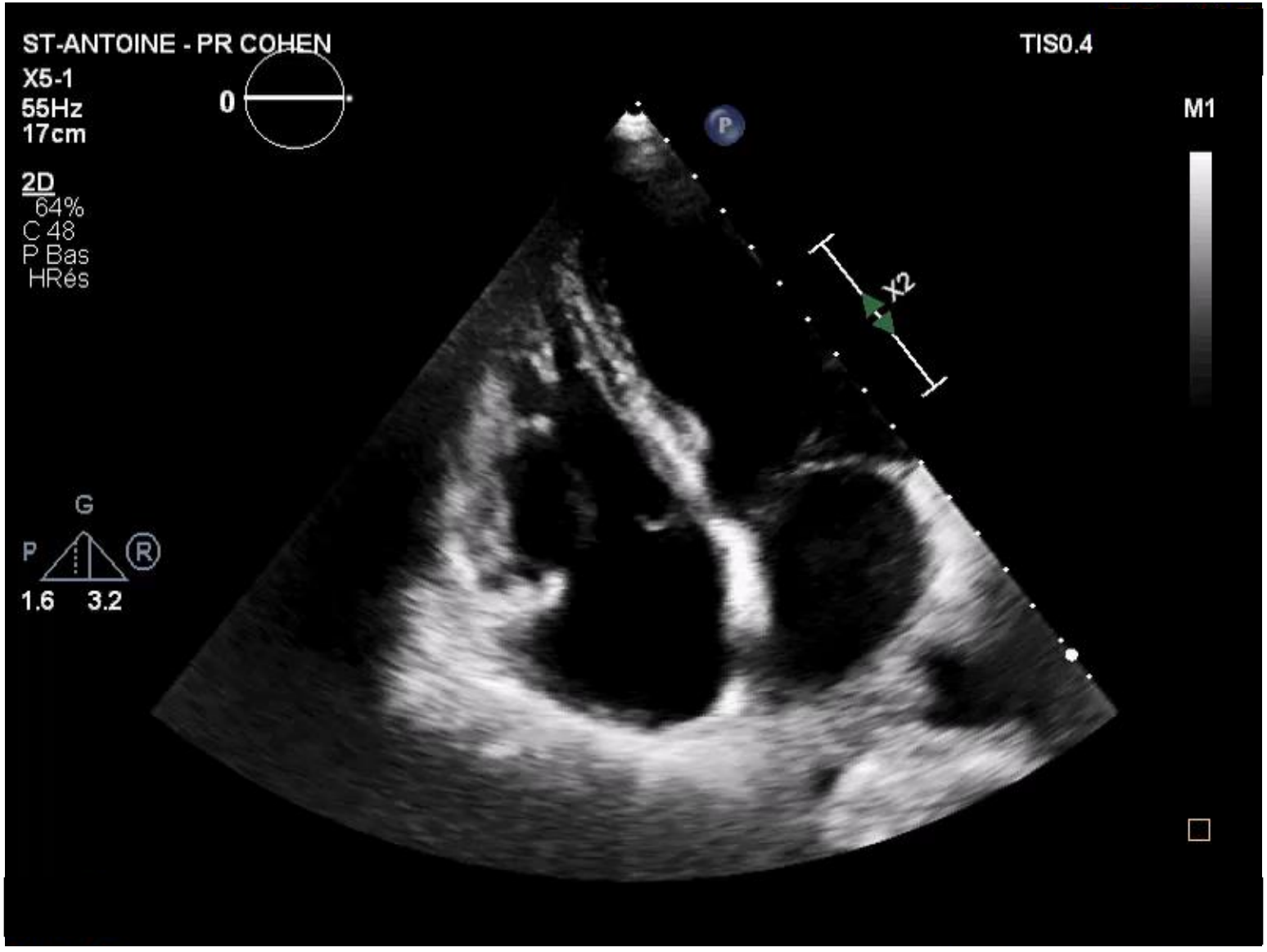
Apical 4 chamber focused on the left atrium-X plane



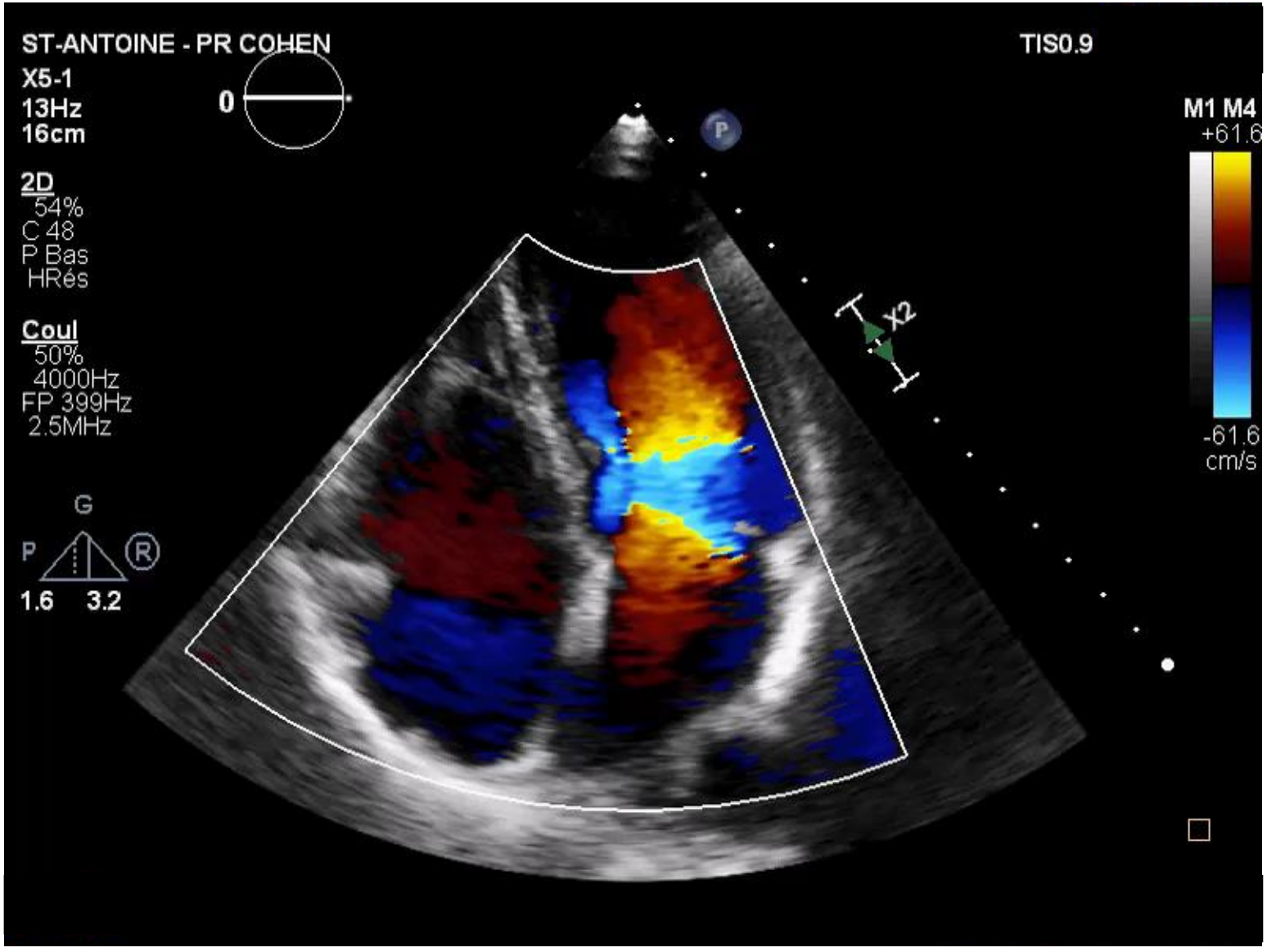
Apical 3D echocardiography focused on the left atrium and the left ventricle



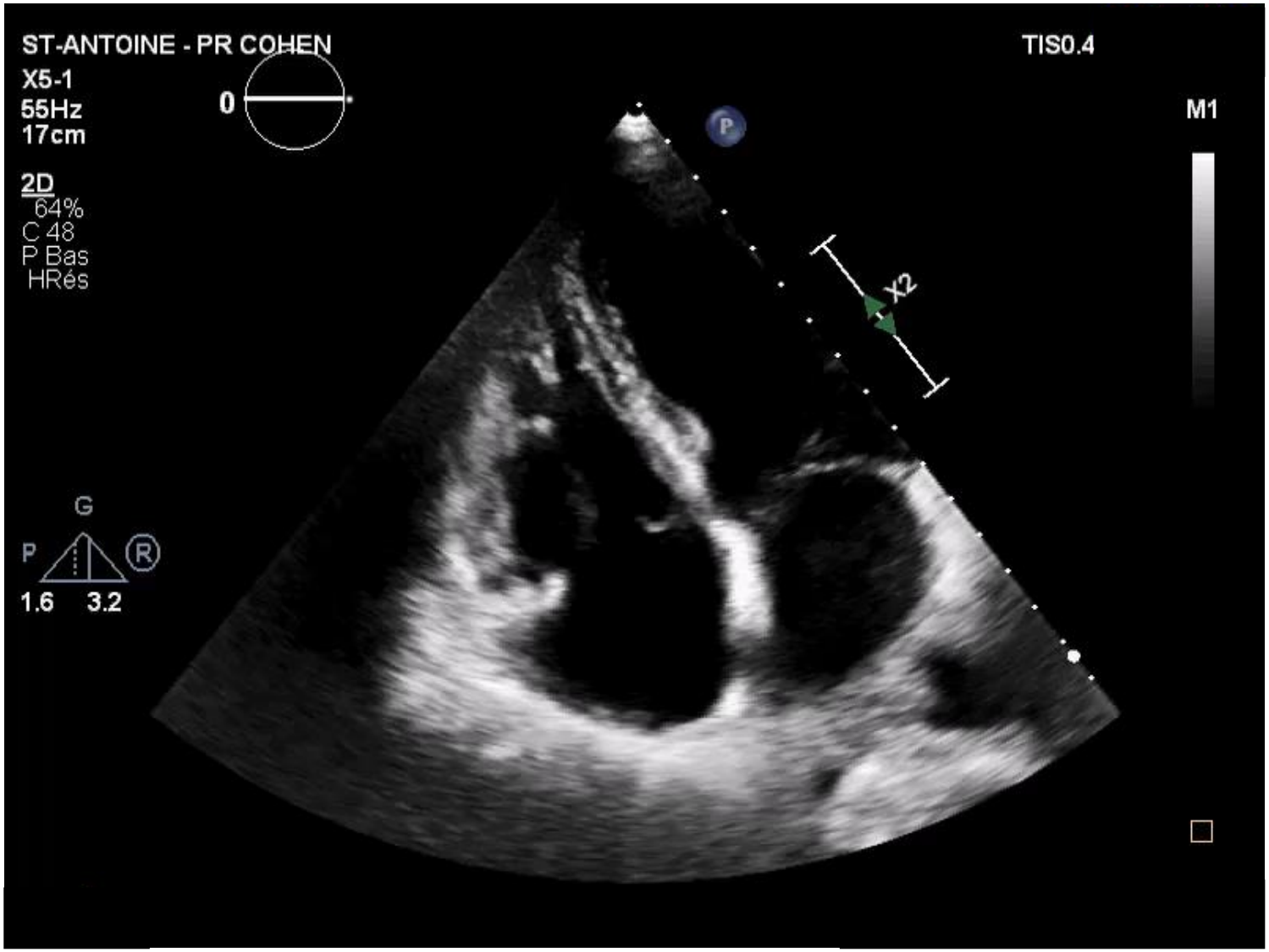
Apical 4 chamber interatrial septum



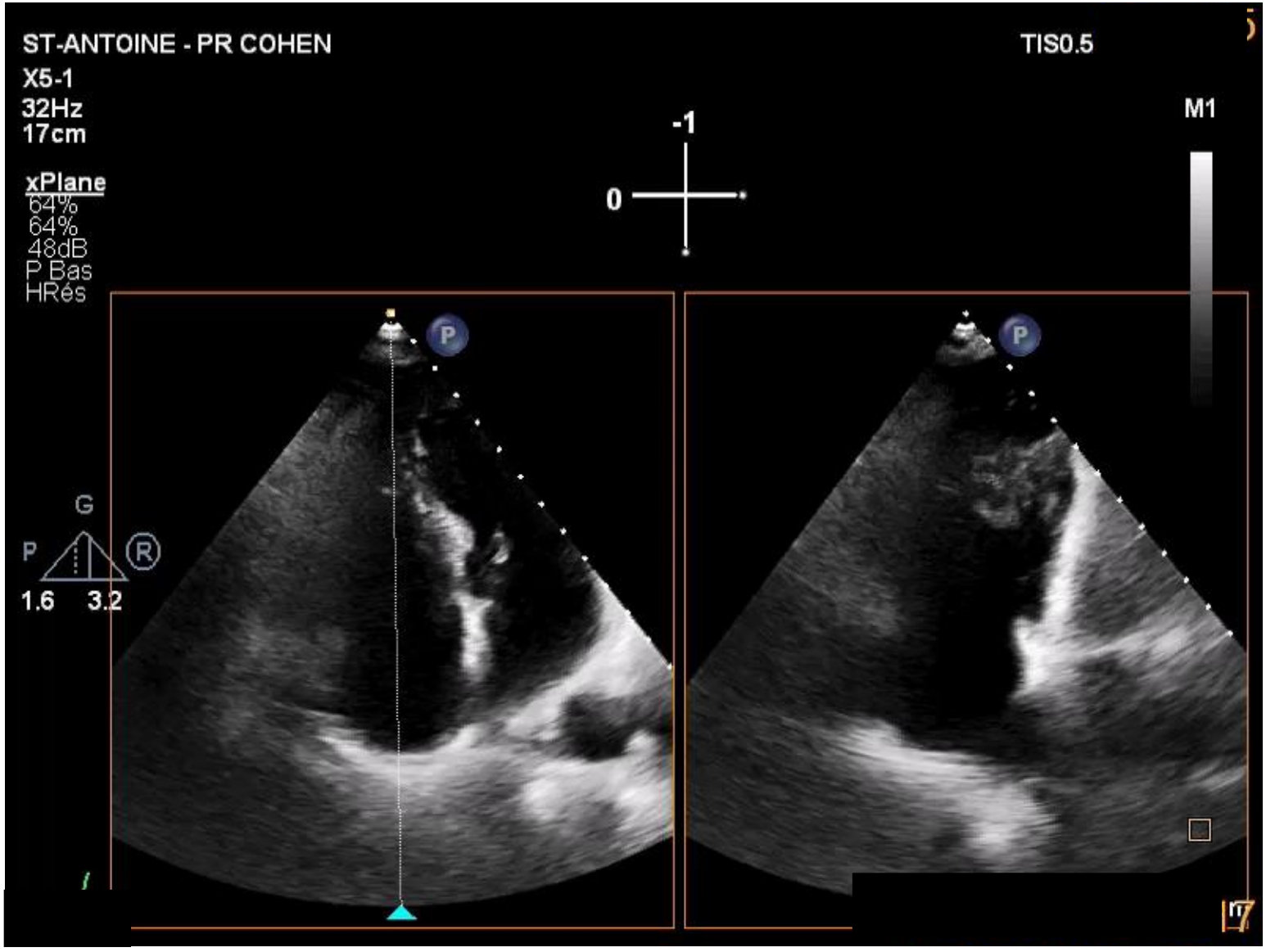
Apical 4 chamber interatrial septum



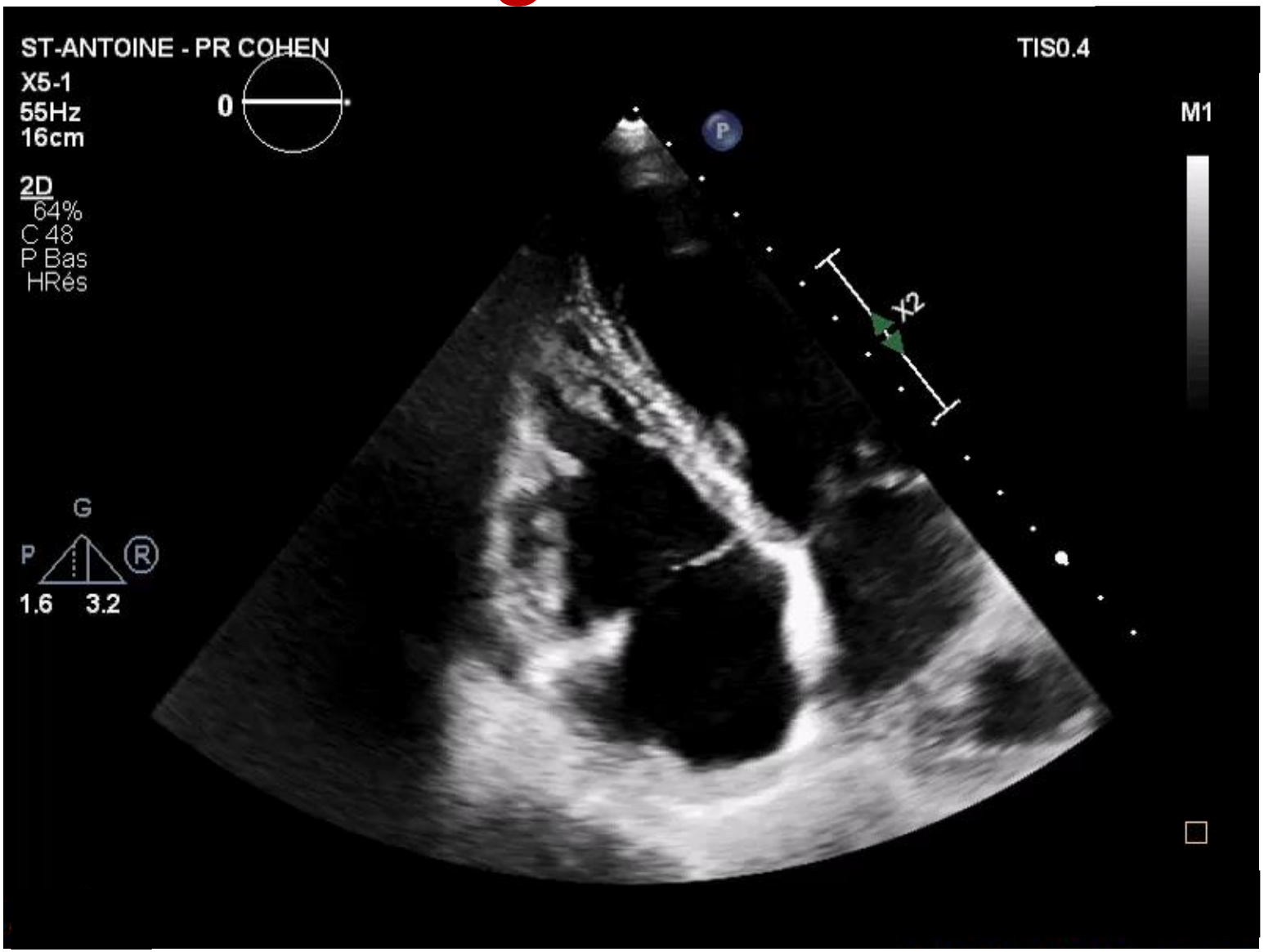
Apical 4 chamber focused on the right atrium



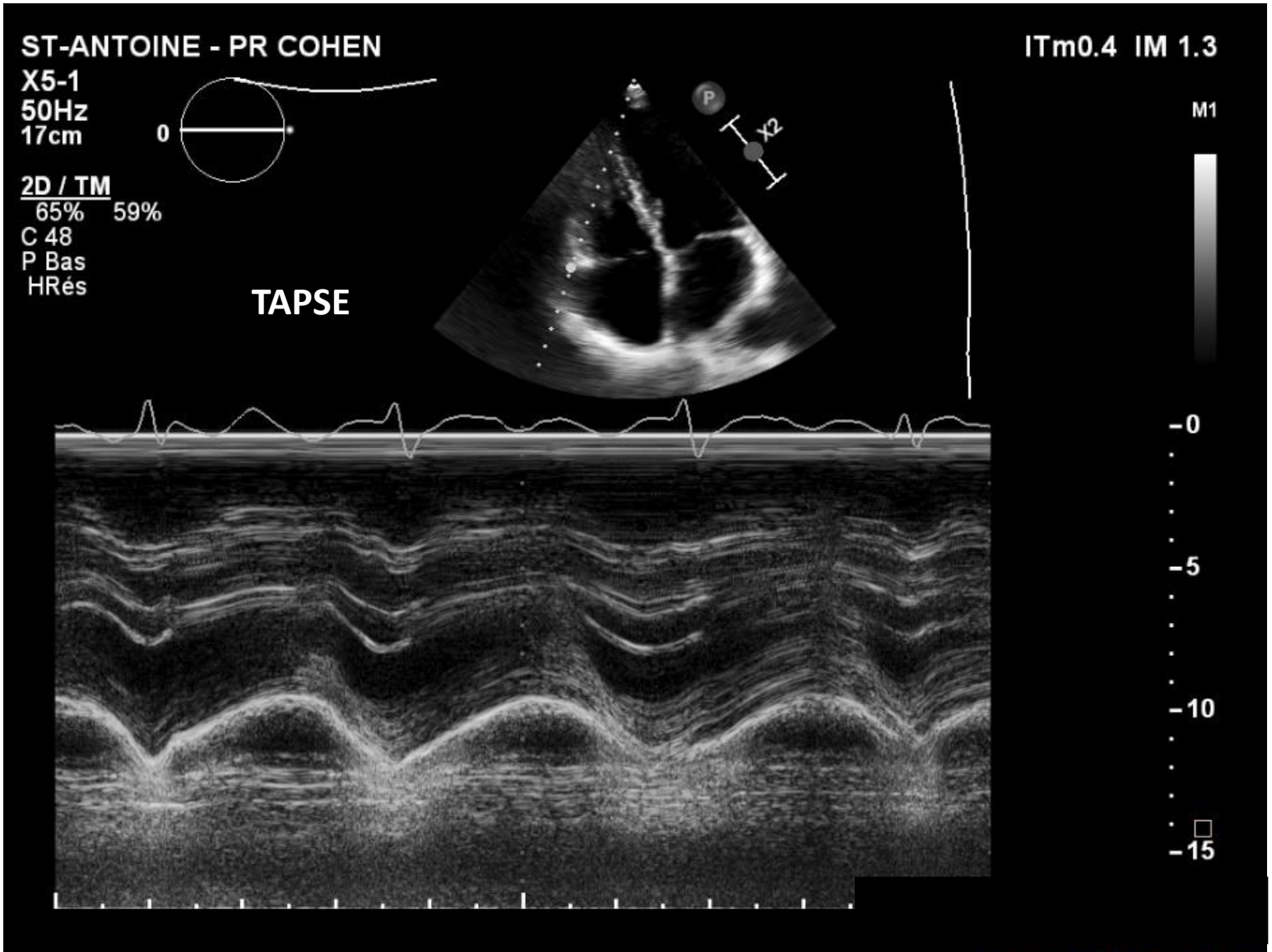
Apical 4 chamber focused on the right atrium- X plane



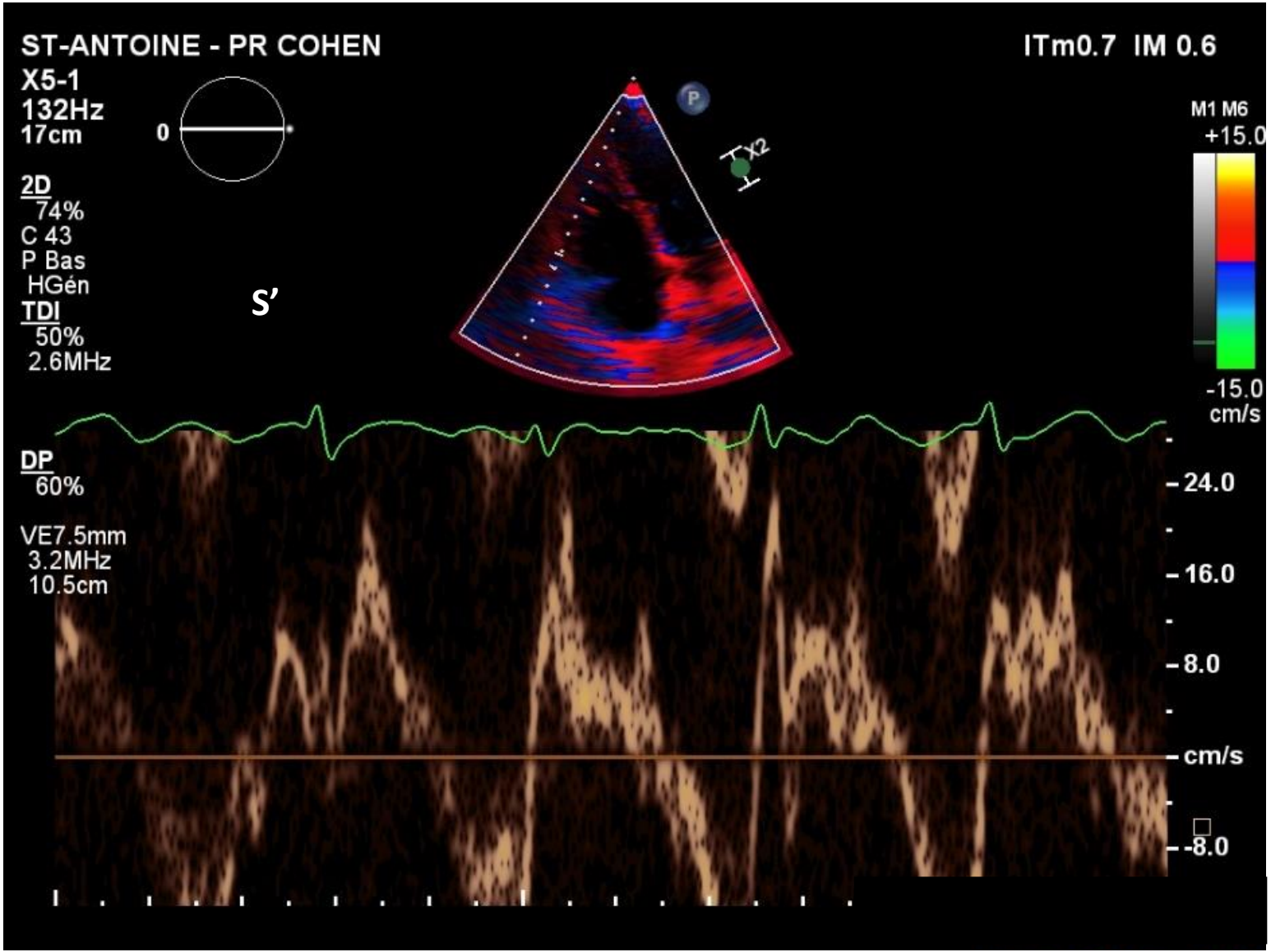
Apical 4 chamber focused on the right ventricle



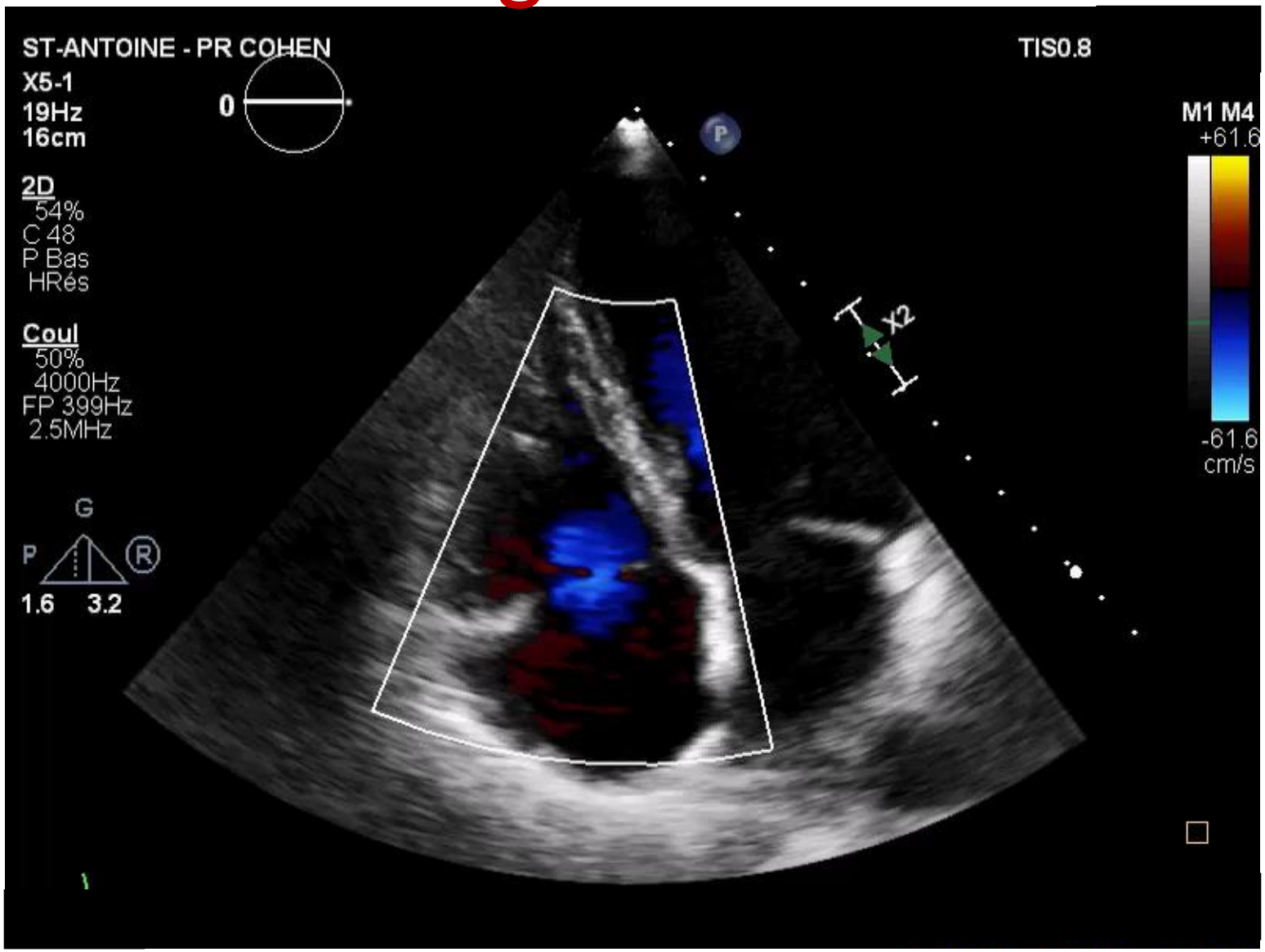
Apical 4 chamber focused on the right ventricle



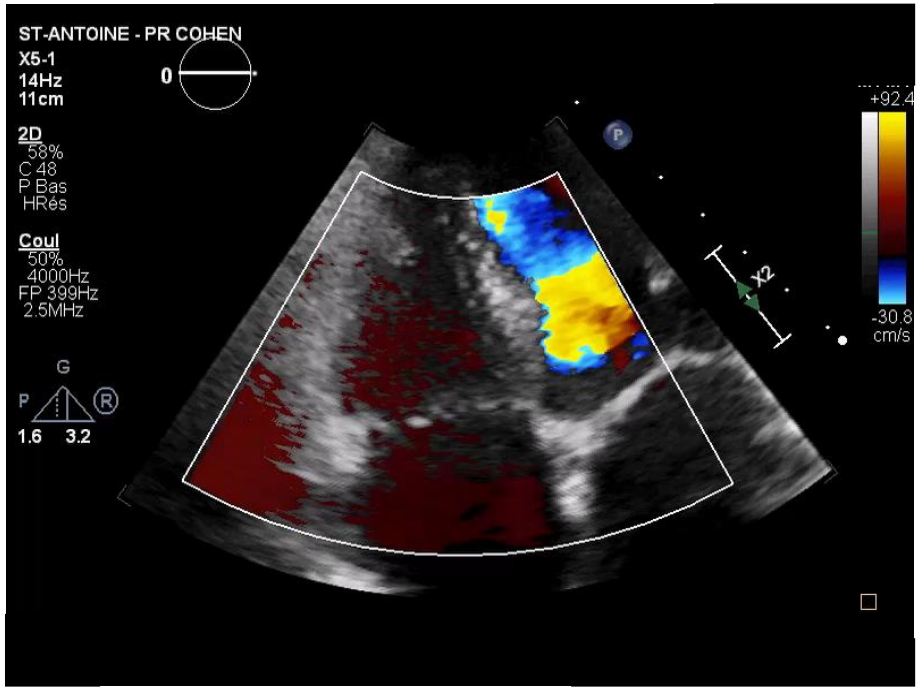
Apical 4 chamber focused on the right ventricle

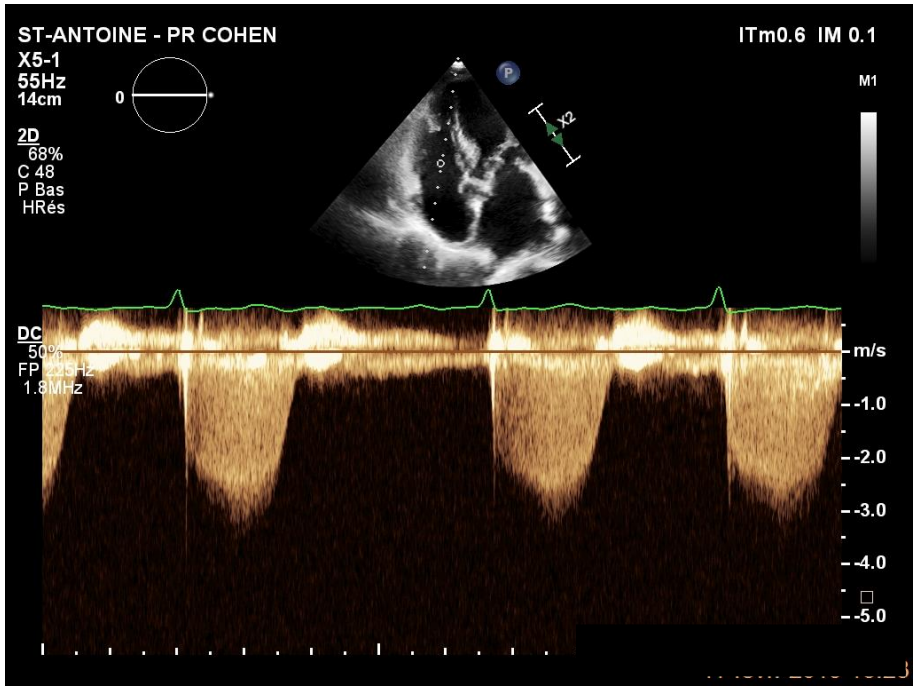


Apical 4 chamber focused on the right ventricle



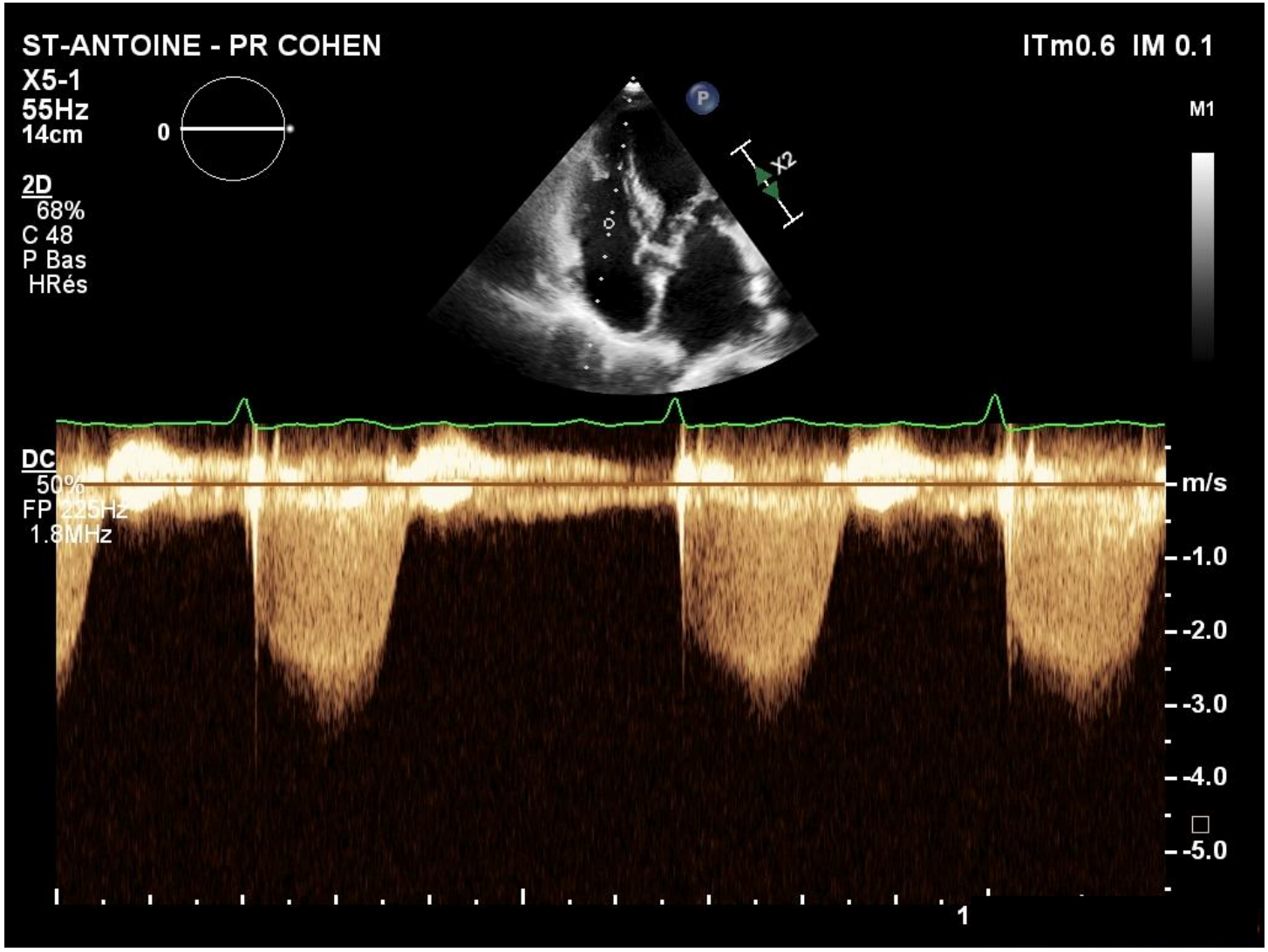
Apical 4 chamber focused on the right ventricle



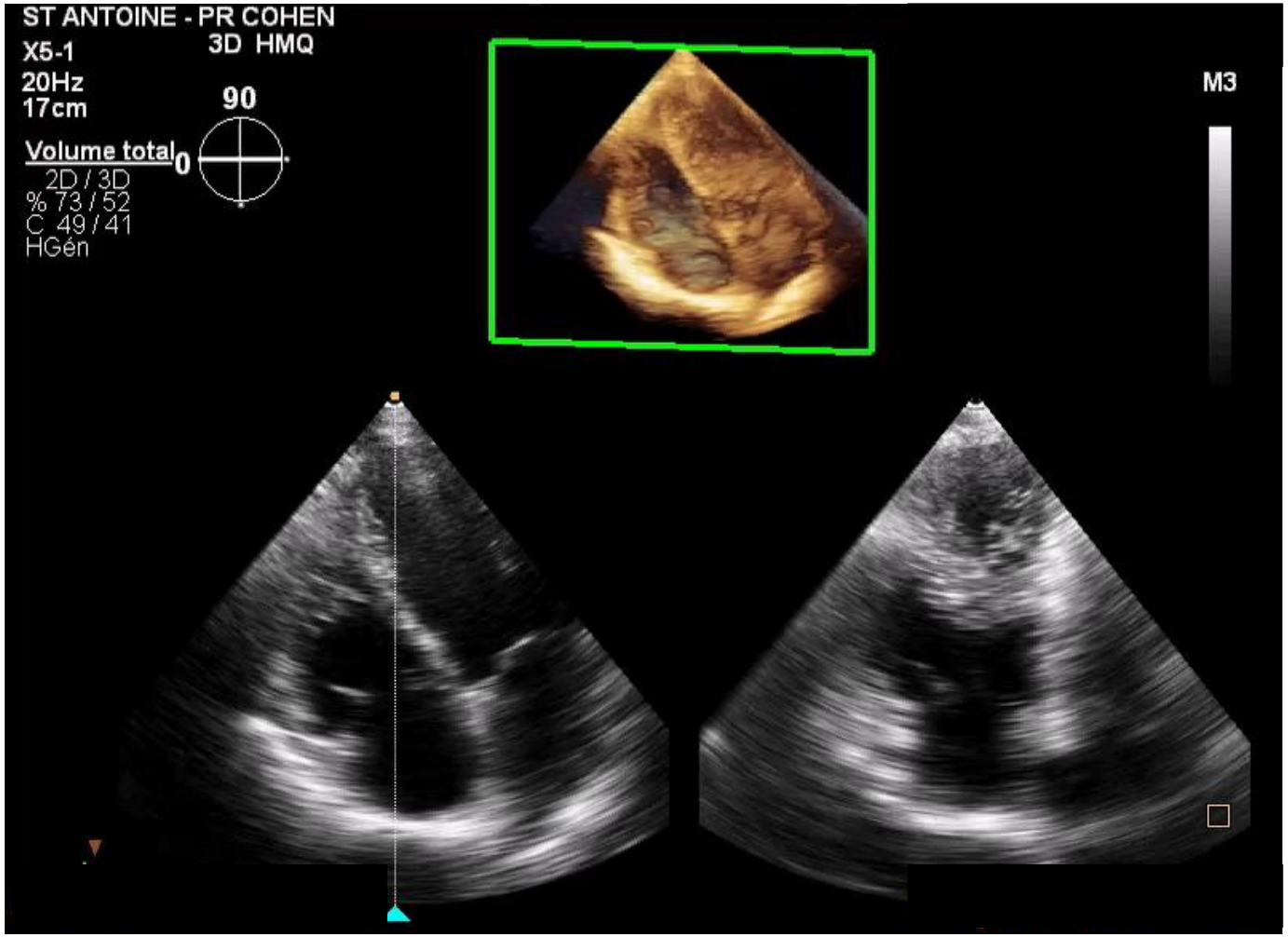


If valvular regurgitation ≥ mild, acquisition for ORE (color and continuous doppler)

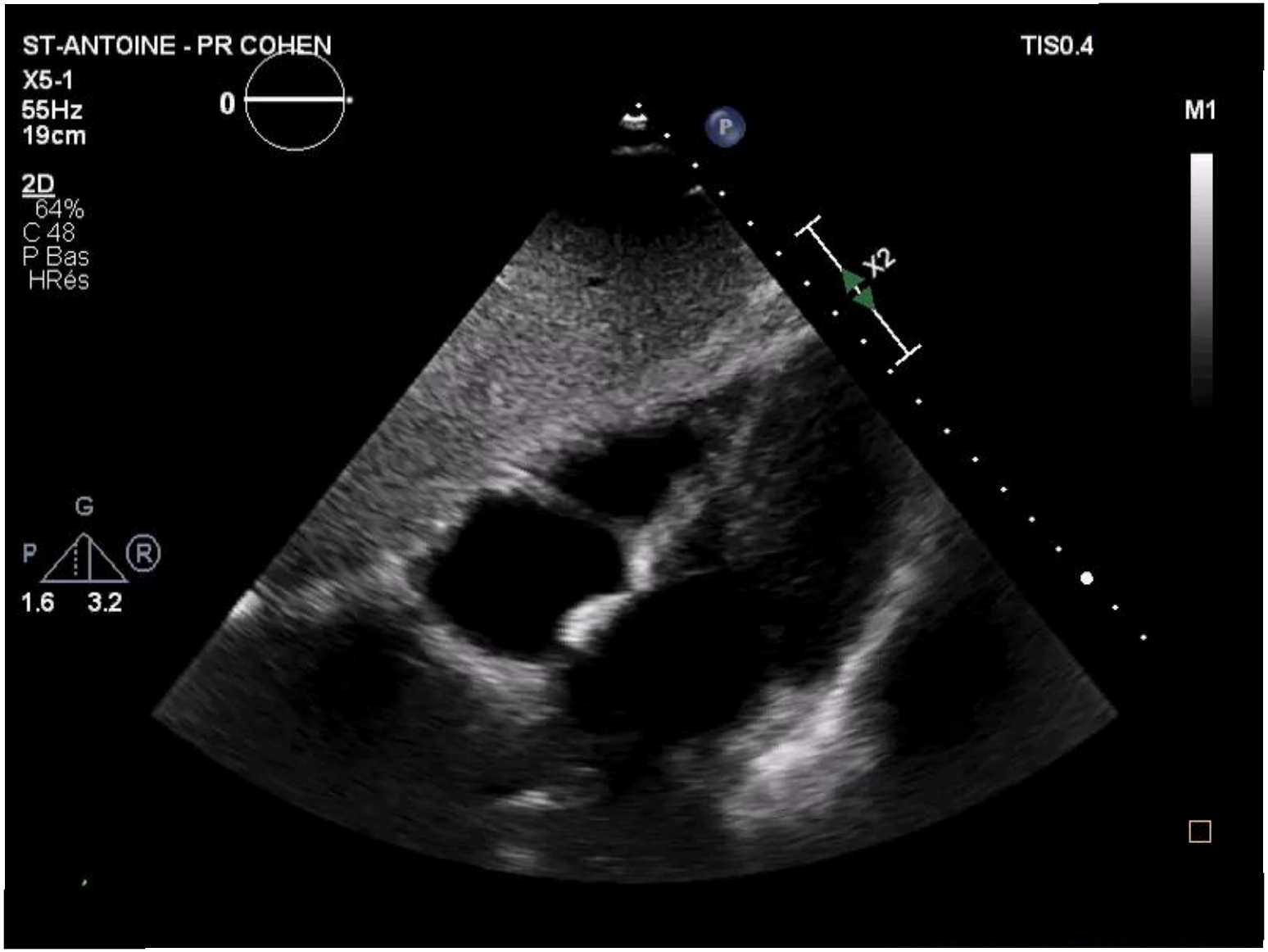
Apical 4 chamber focused on the right ventricle



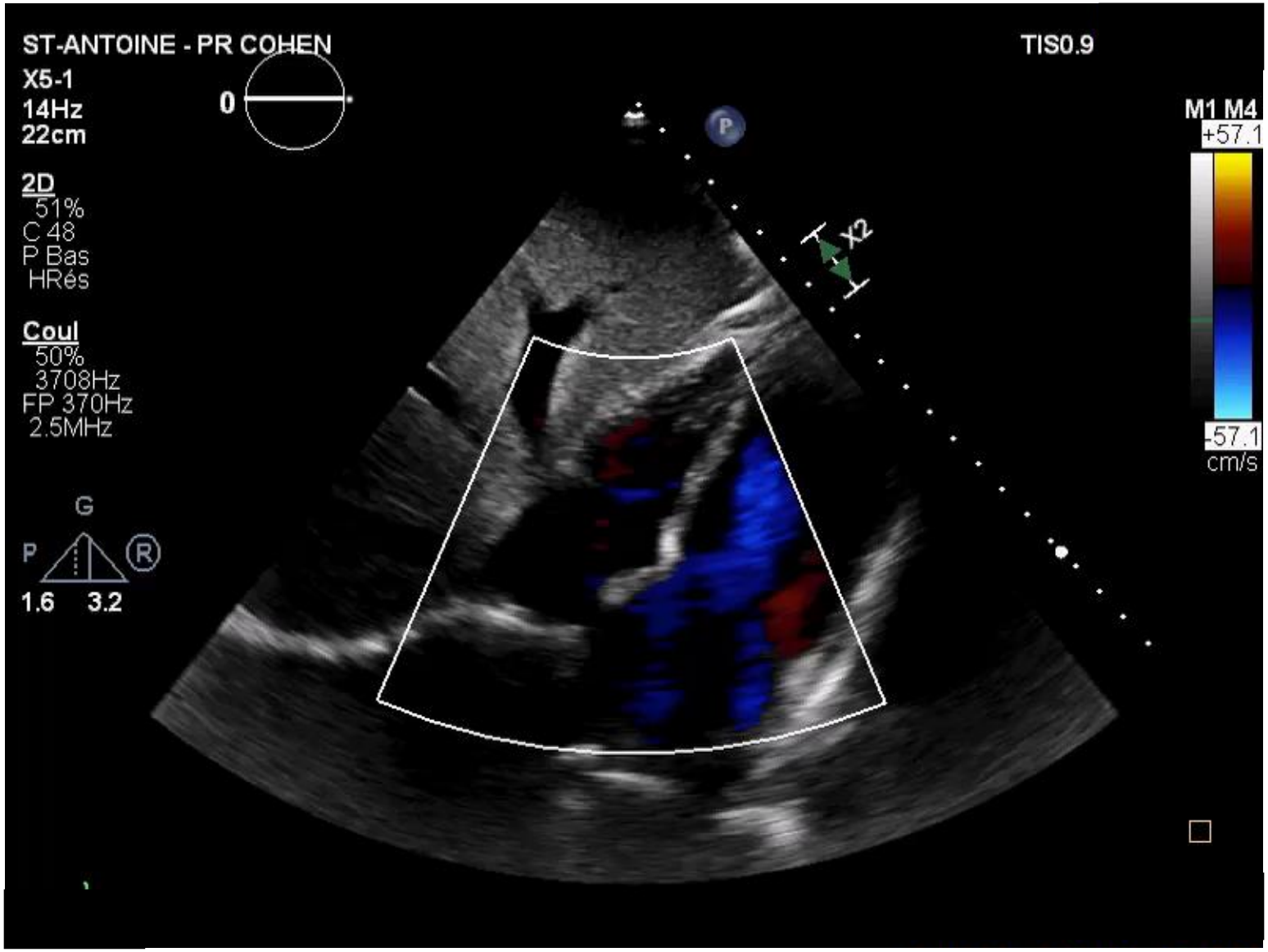
Apical 3 D echocardiography focused on the right atrium and right ventricle



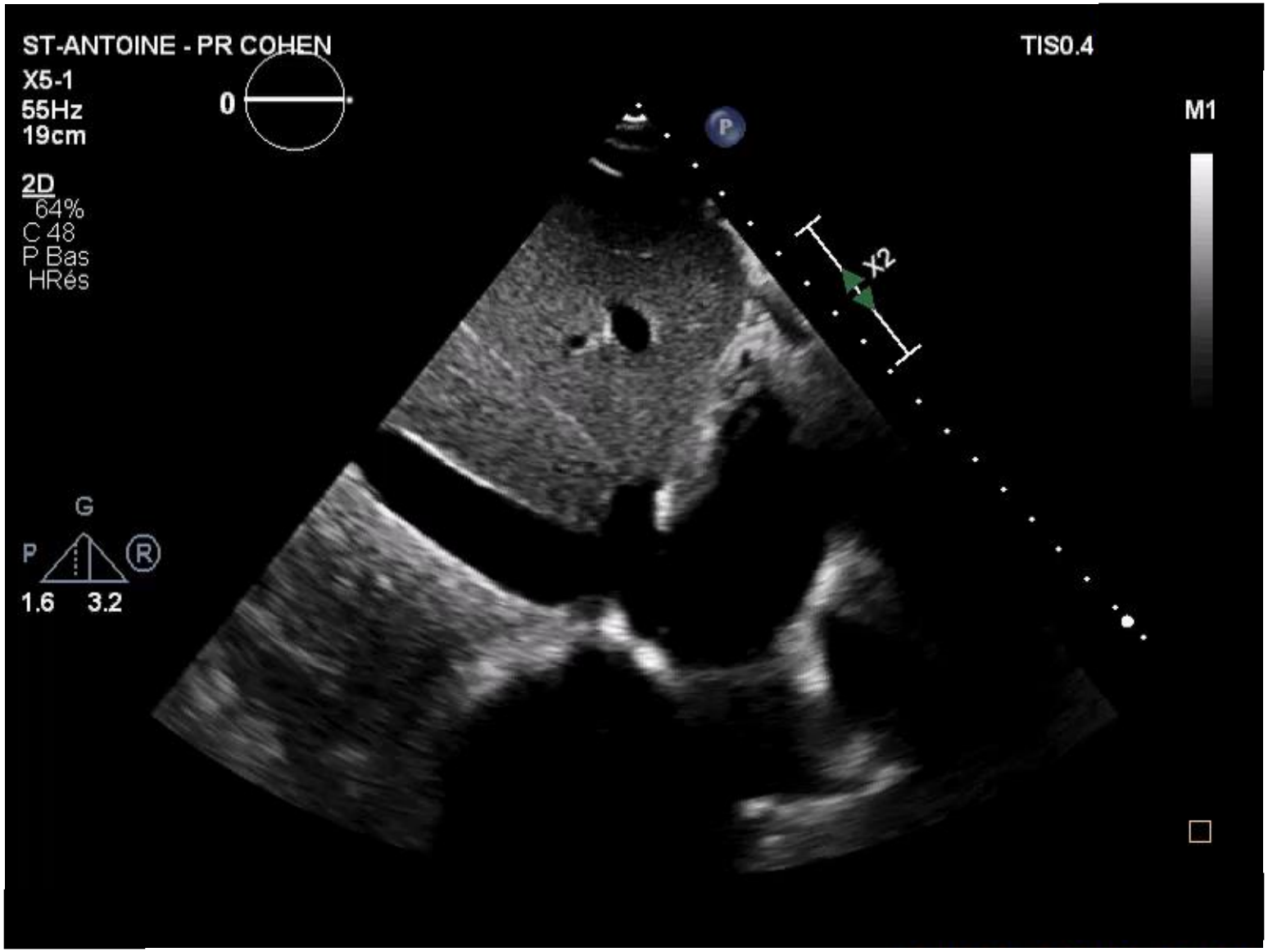
Sub costal view



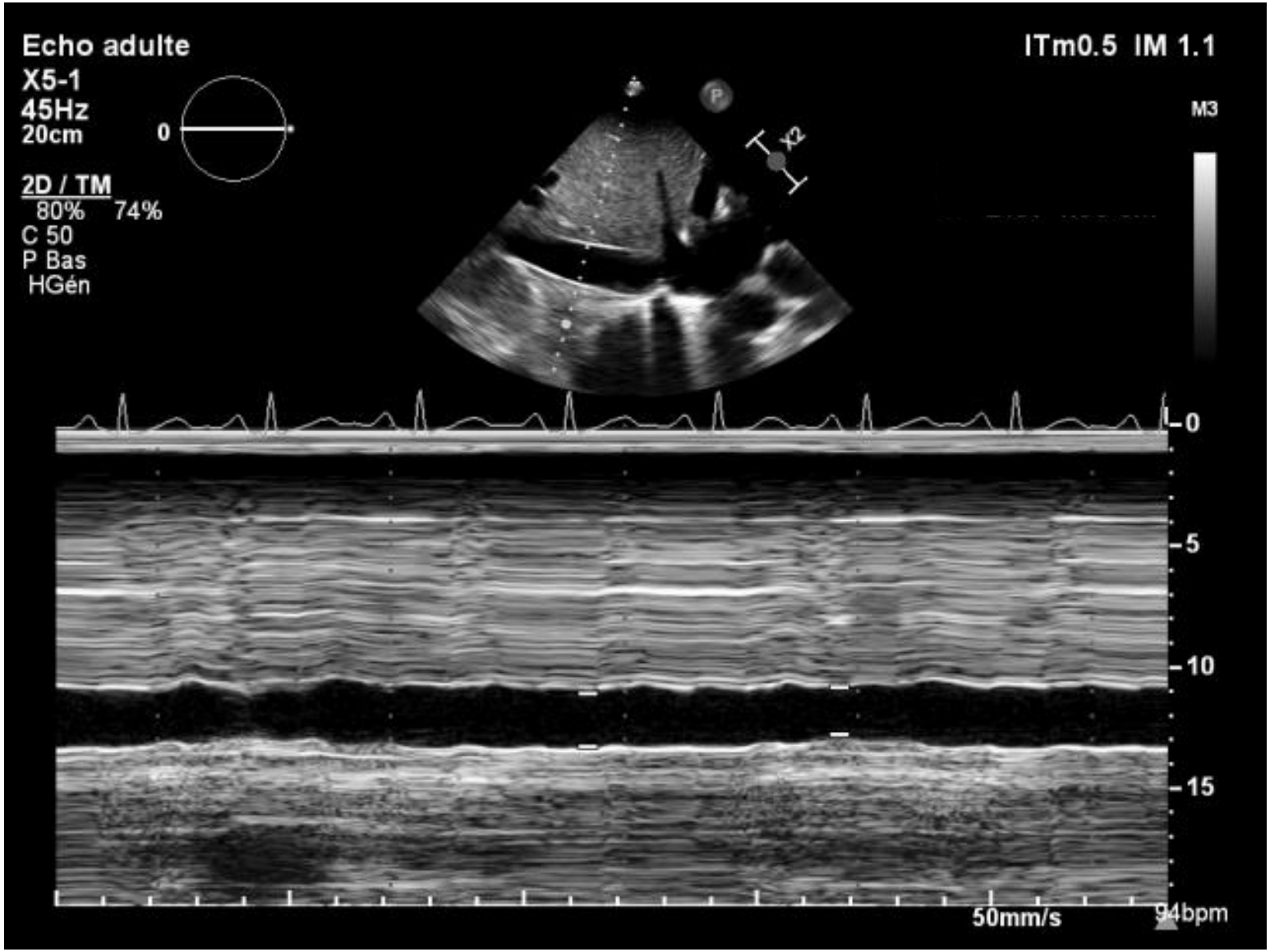
Sub costal view



Sub costal view



Sub costal view



TTE Short Protocol

Parasternal Position	
Parasternal long axis	2D imaging Color Doppler of AV and MV Color Doppler zoomed on AV Color Doppler zoomed on MV M Mode of the Left Ventricle
Parasternal long axis of RV inflow	2D imaging Color Doppler of TV Color Doppler zoomed on TV CW Doppler of tricuspid flow If valvular regurgitation ≥ mild, acquisition for ORE (color and continuous doppler)
Parasternal short axis – Aortic valve level	2D imaging of AV Color Doppler of AV Color Doppler zoomed on AV Color Doppler of TV CW Doppler of the TV Color Doppler of RVOT PW and CW Doppler of the RVOT
Parasternal short axis – Mitral valve level	2D imaging
Parasternal short axis – Papillary muscle level	2D imaging
Parasternal short axis – LV apex	2D imaging

TTE Short Protocol

Apical Position	
Apical 4 chamber view	2D imaging with all 4 chambers in 1 sector Color Doppler of MV 2D imaging zoomed on MV Color Doppler zoomed on MV PW Doppler of mitral flow TDI of septal and lateral mitral annulus If valvular regurgitation ≥ mild, acquisition for ORE (color and continuous doppler) 2D imaging of interatrial septum Color imaging of interatrial septum 2D imaging focused on LV without foreshortening: LV 4-chamber view 2D imaging focused on LA without foreshortening: LA 4-chamber view 2D imaging focused on RA without foreshortening
Apical 5 chamber view	2D imaging of apical 5 chamber view Color doppler of AV 2D imaging zoomed on AV Color Doppler zoomed on AV Color Doppler of LVOT PW wave of LVOT flow and CW of AV If valvular regurgitation ≥ mild, acquisition for ORE (color and continuous

TTE Short Protocol

Apical Position	
Apical 2 chamber view	2D imaging Color Doppler MV 2D imaging focused on LV without foreshortening: LV 2-chamber view 2D imaging focused on LA without foreshortening: LA 2-chamber view
Apical 3 chamber view	2D imaging Color Doppler MV/LA If valvular regurgitation ≥ mild, acquisition for ORE (color and continuous doppler) 2D imaging focused on LV without foreshortening: LV 3-chamber view 2D imaging focused on LA without foreshortening; : LA 3-chamber view
Apical 4 chamber – focused on the RV	2D imaging Color Doppler of tricuspid valve/RA CW Doppler of tricuspid regurgitation PW Doppler of tricuspid flow M-mode of the anterior tricuspid annulus TDI of anterior tricuspid annulus If valvular regurgitation ≥ mild, acquisition for ORE (color and continuous doppler)

TTE Short Protocol

Apical Position	
Apical 3D acquisitions	Make sur to have the entire structure in the acquisition 3D obtained with frame rate ≥ 20Hz: Xplane, Heart Model acquisitions If Heart Model acquisition not available Full Volume acquisition (at least 4 beats) or High-volume rate acquisition could be used Apical 4 chamber view: Xplane on LA Apical 4 chamber view: Xplane on RA 3 Heart Model datasets focused on LV LA 3 Heart Model datasets focused on RV RA
Subcostal Position	
Inferior vena cava	2D imaging with 4 chambers Color doppler on interatrial septum 2D imaging of IVC (for 5 sec acquisition) M Mode of IVC

Echocardiography Core Laboratory Imaging Analysis Protocol

MAESTRIA

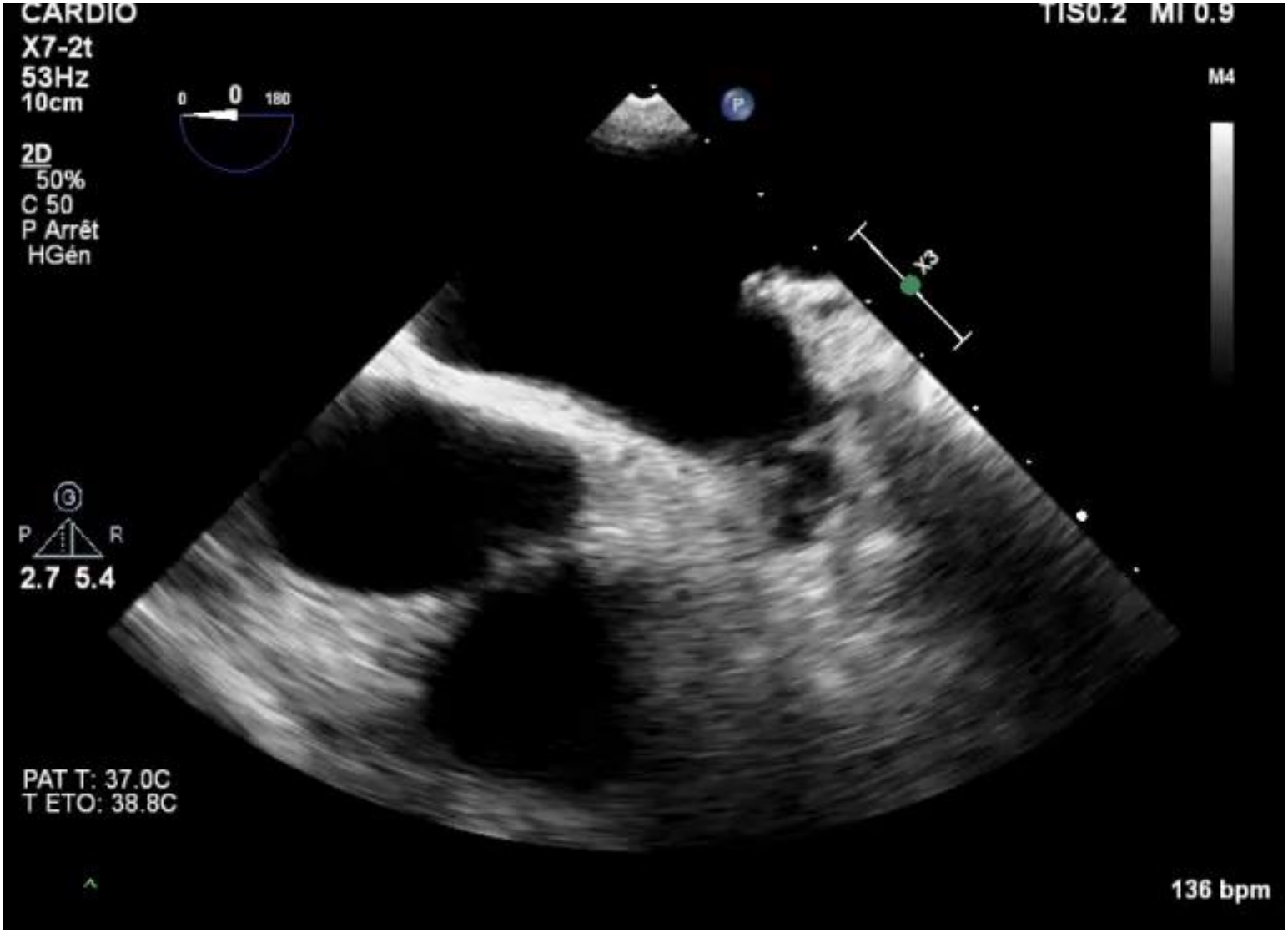
Echocardiographic equipment, Sonographer Training, and Certification

Doppler Echo Protocol Acqusition

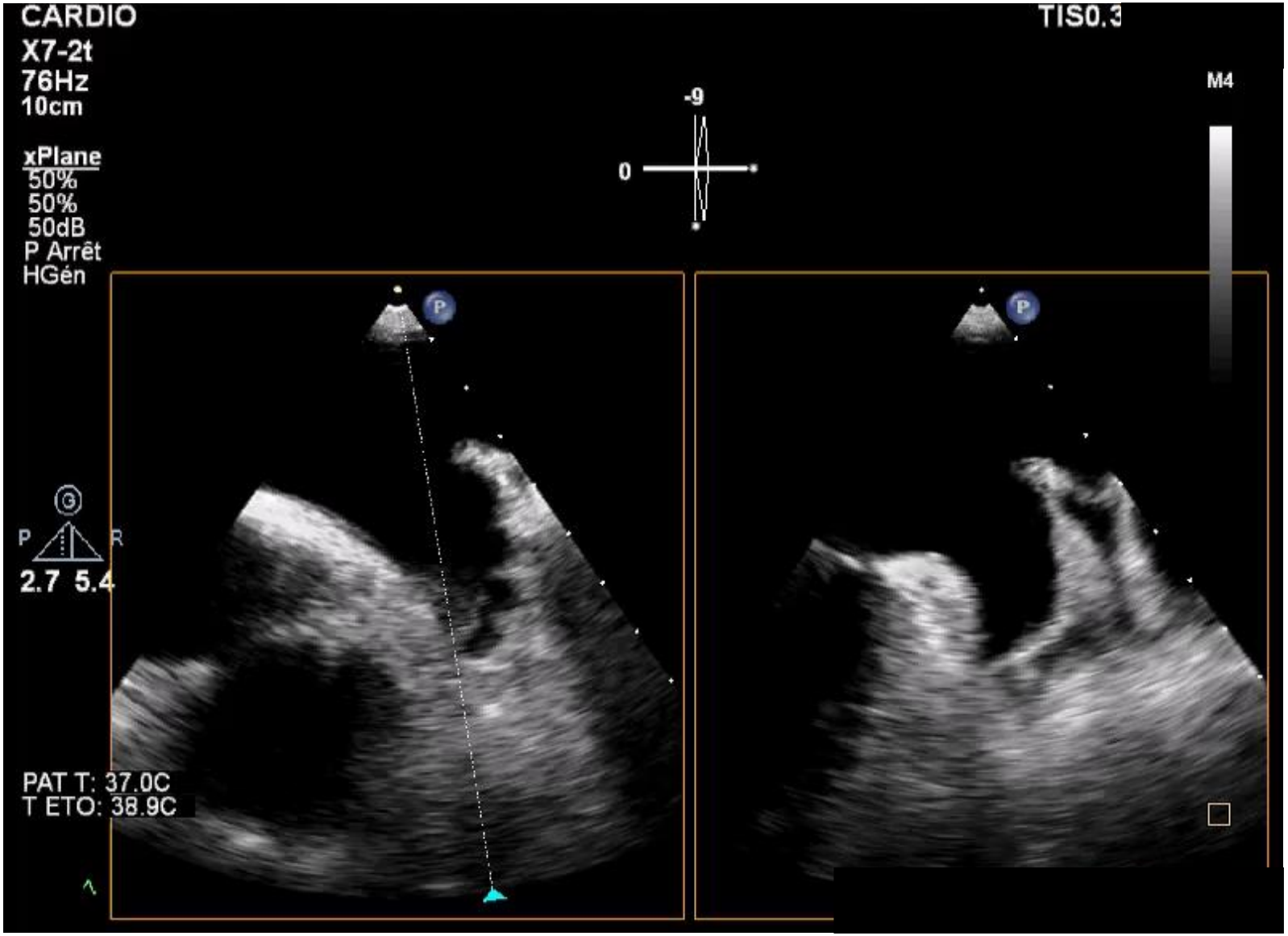
Transthoracic echocardiography

Transoesophageal echocardiography

Left atrial appendage 0°

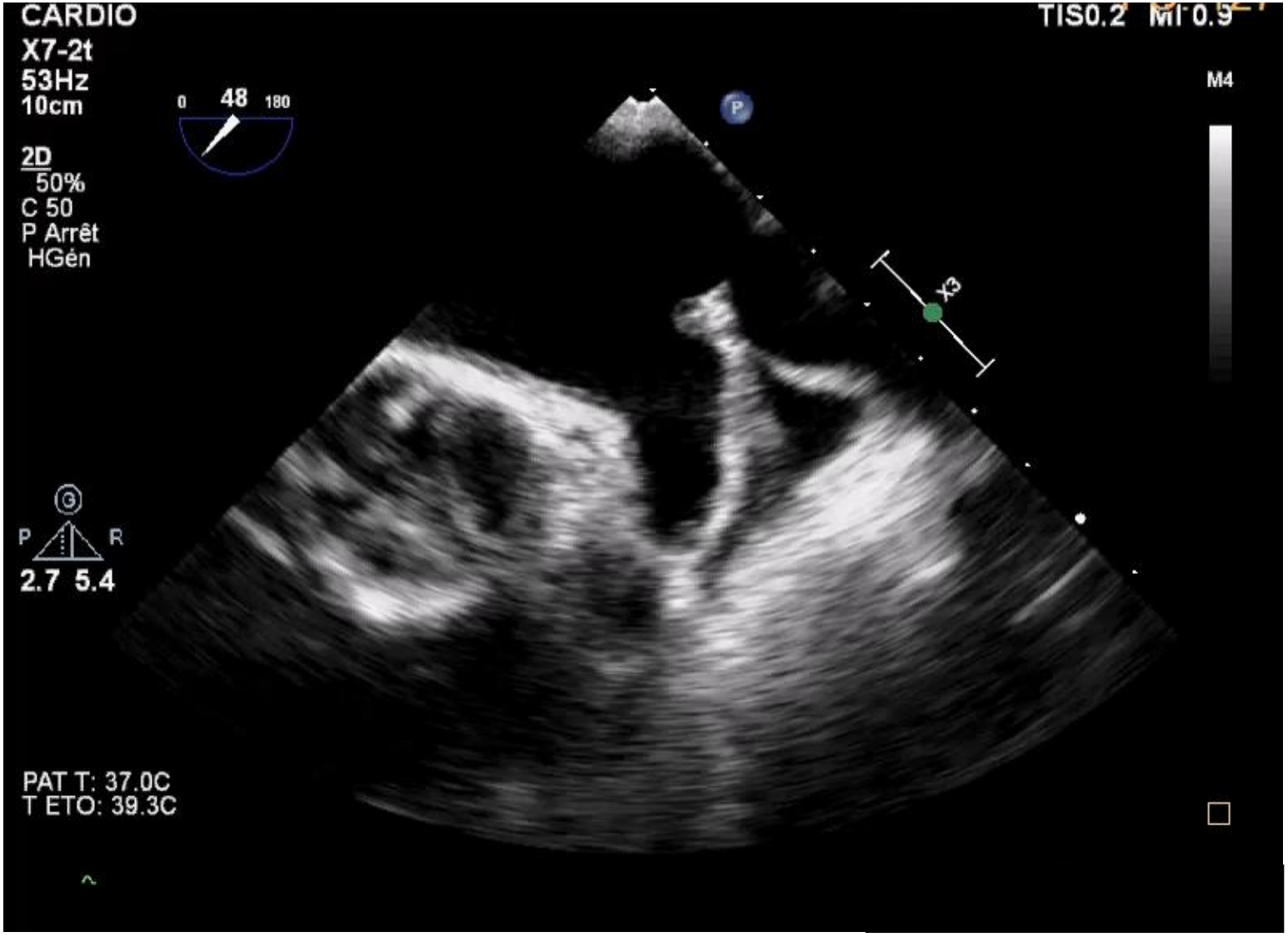


Left atrial appendage 0° X plane

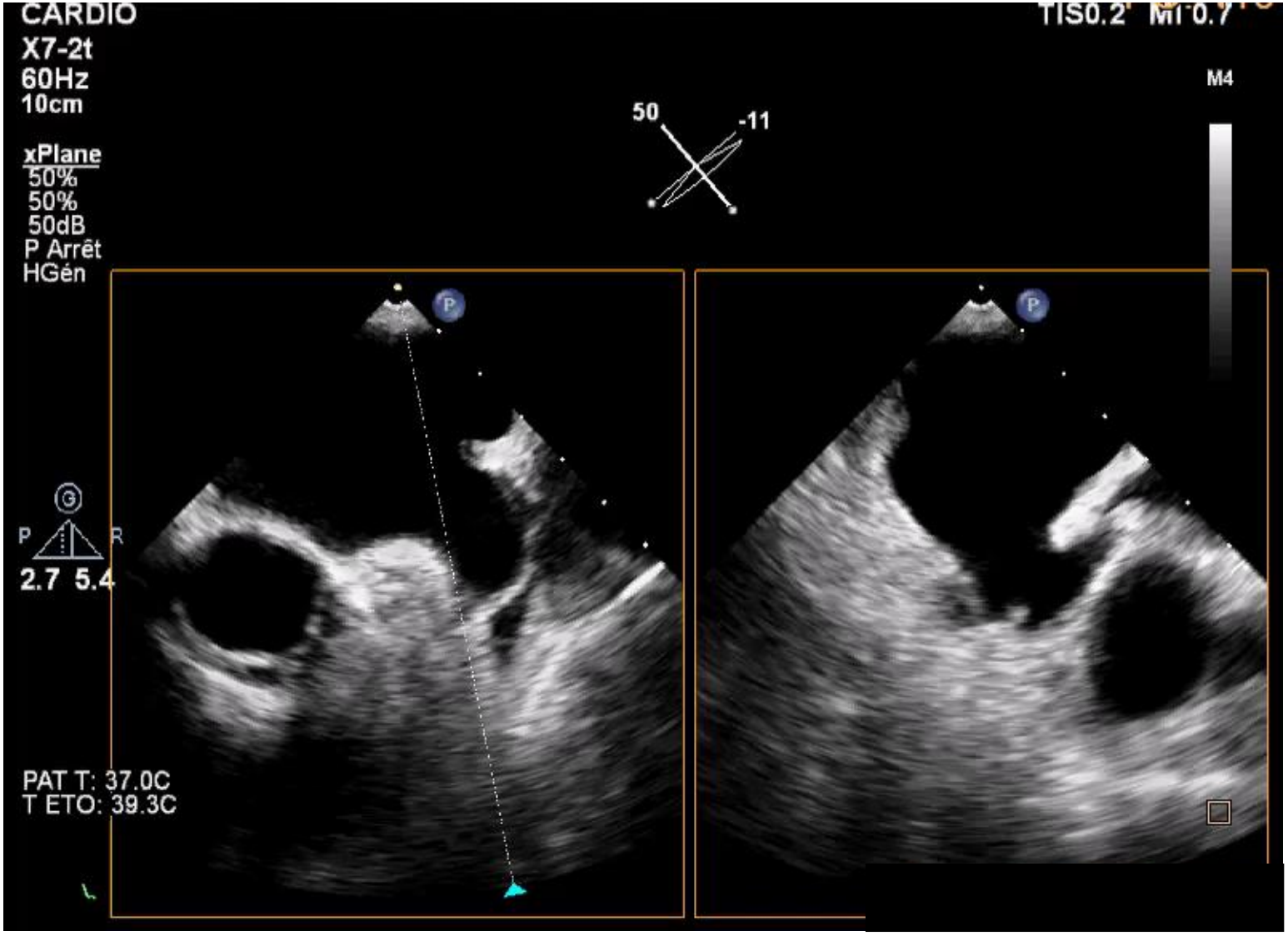


Left atrial appendage 0° 3D

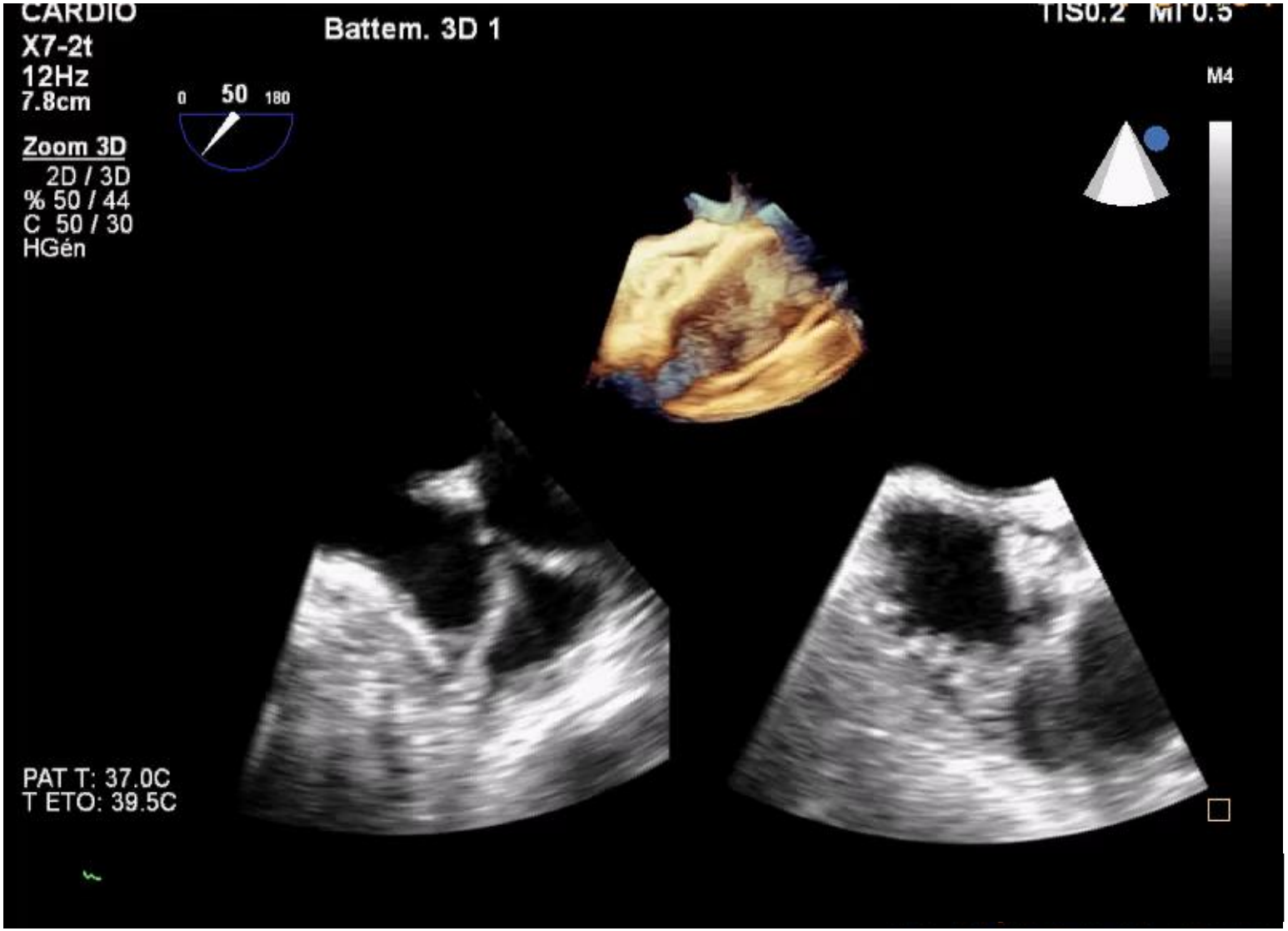
Left atrial appendage 45°



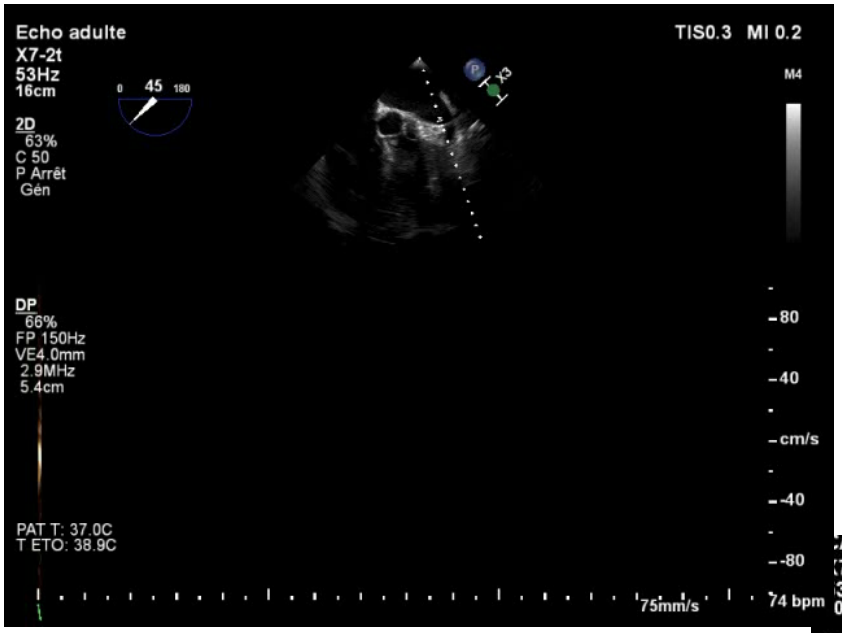
Left atrial appendage 45° X plane

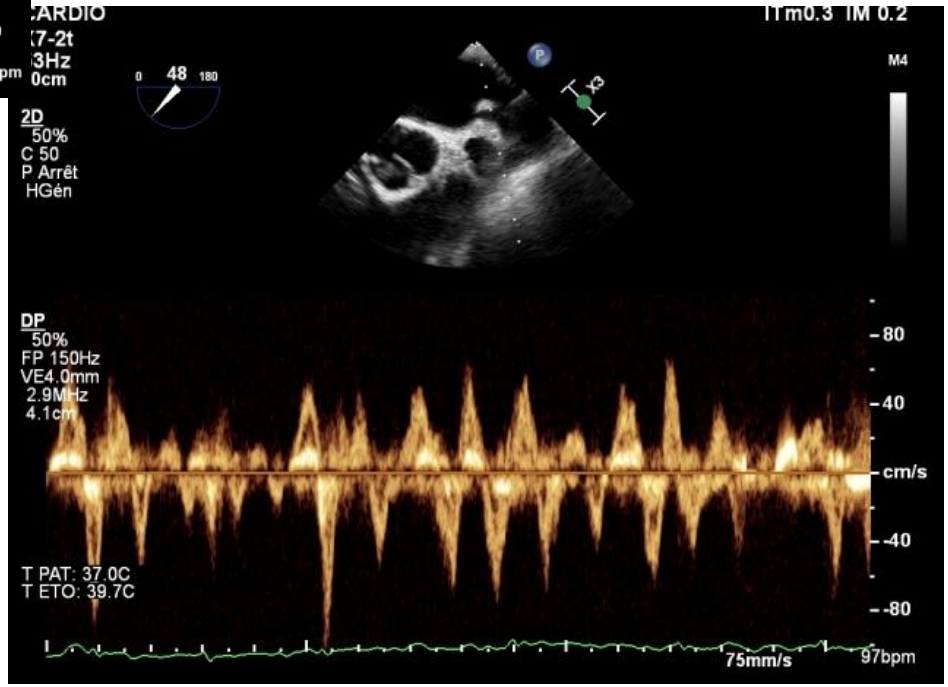


Left atrial appendage 45° 3D

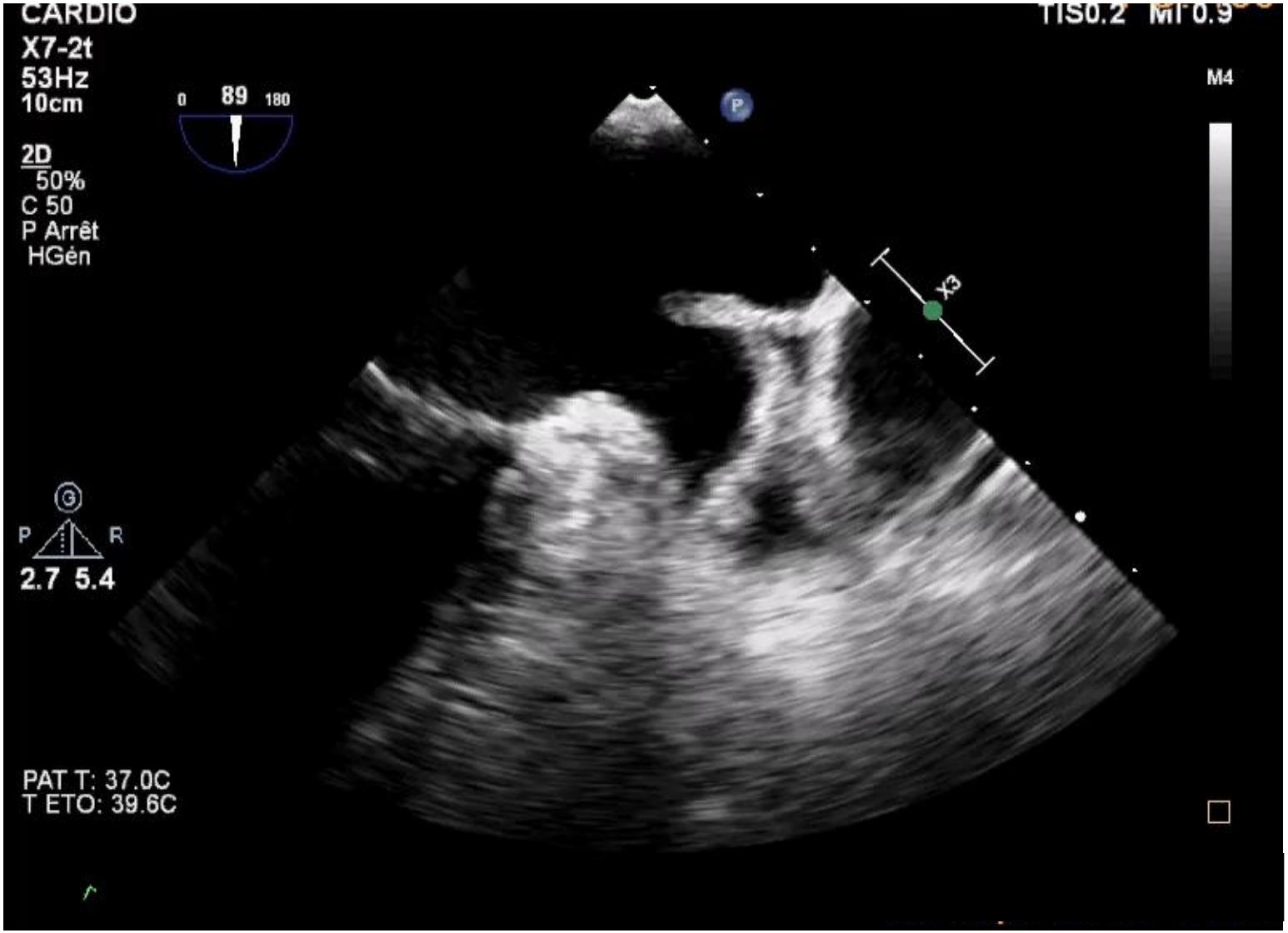


Left atrial appendage 45°

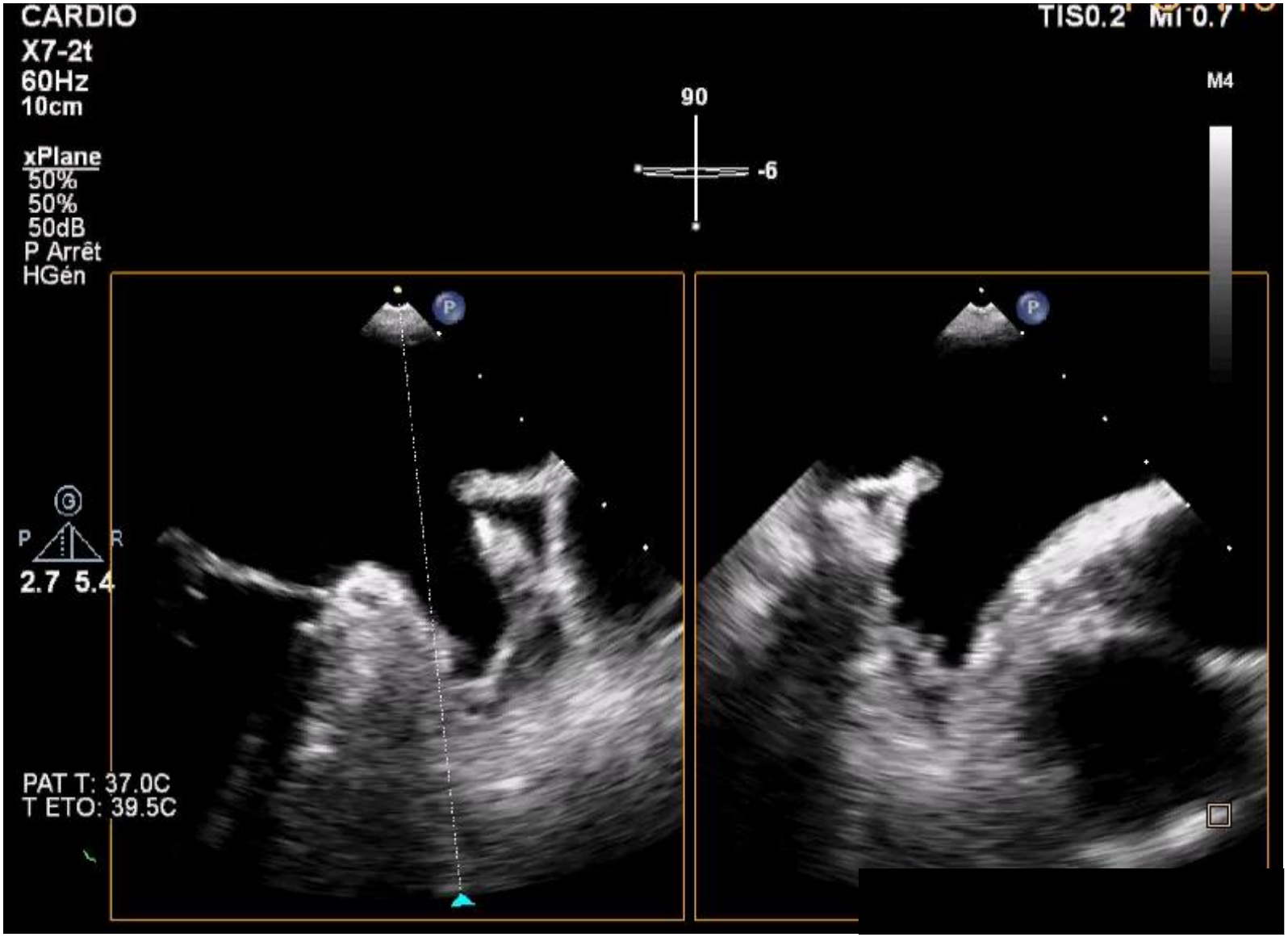




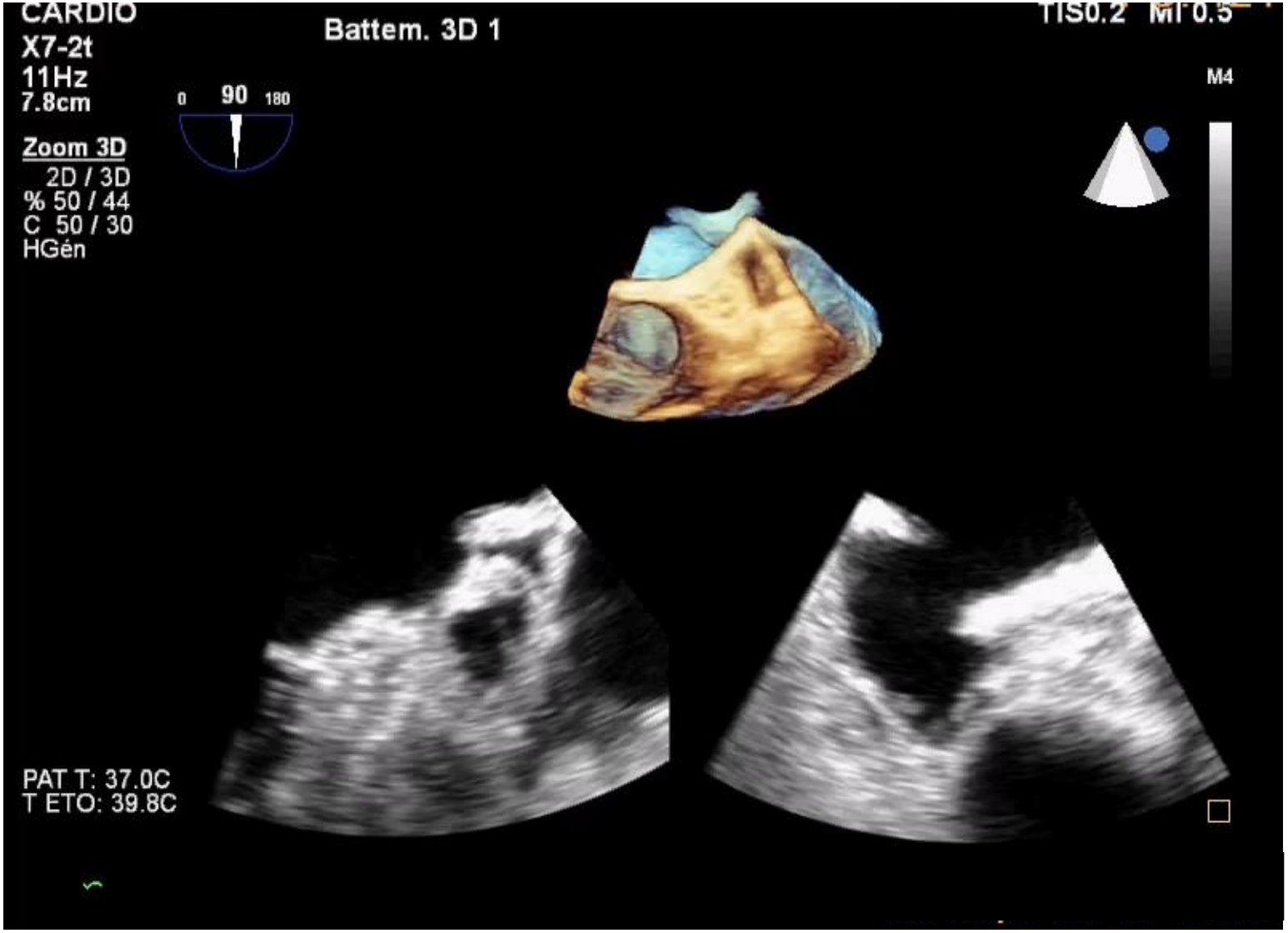
Left atrial appendage 90°



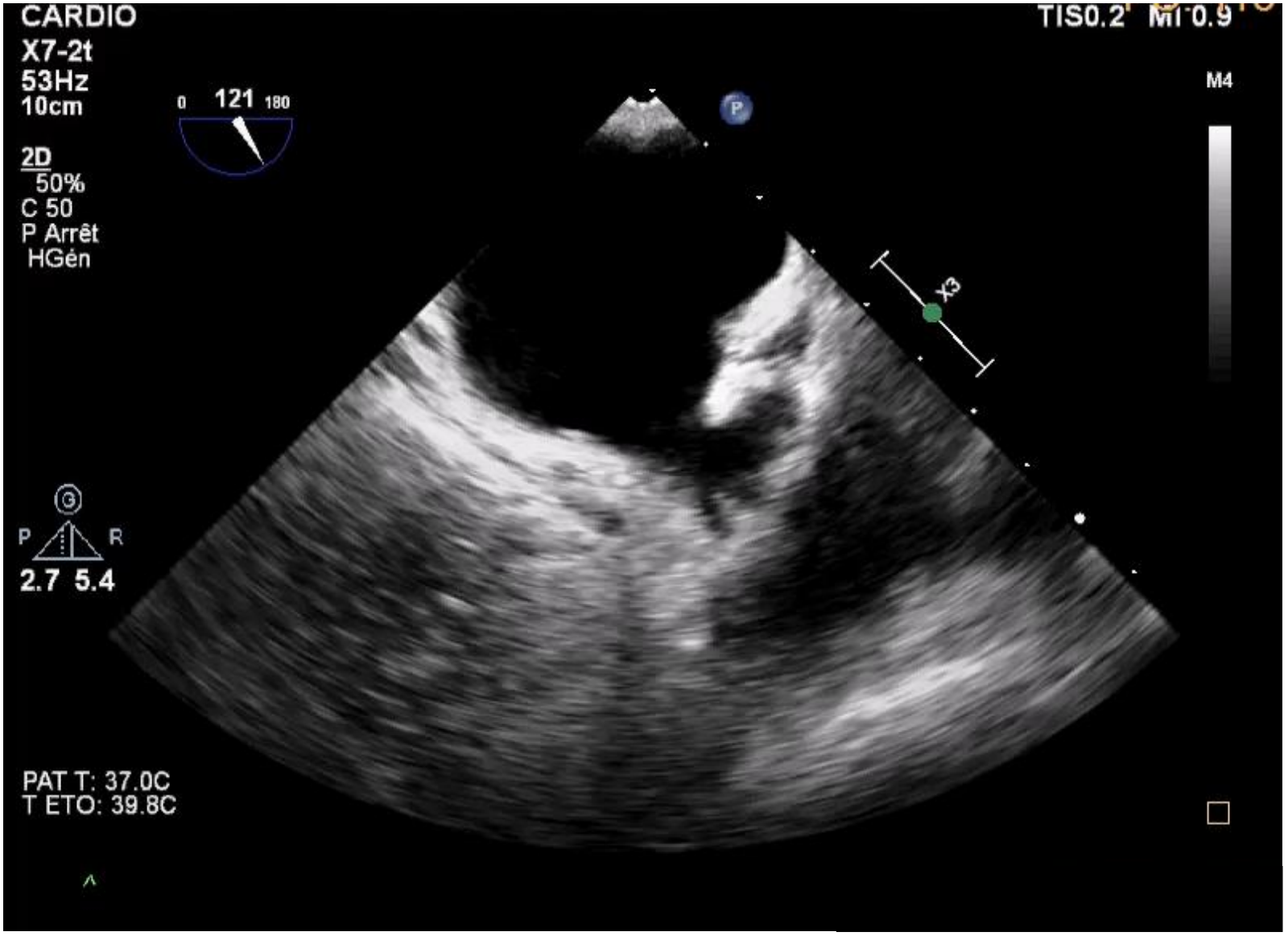
Left atrial appendage 90° X plane



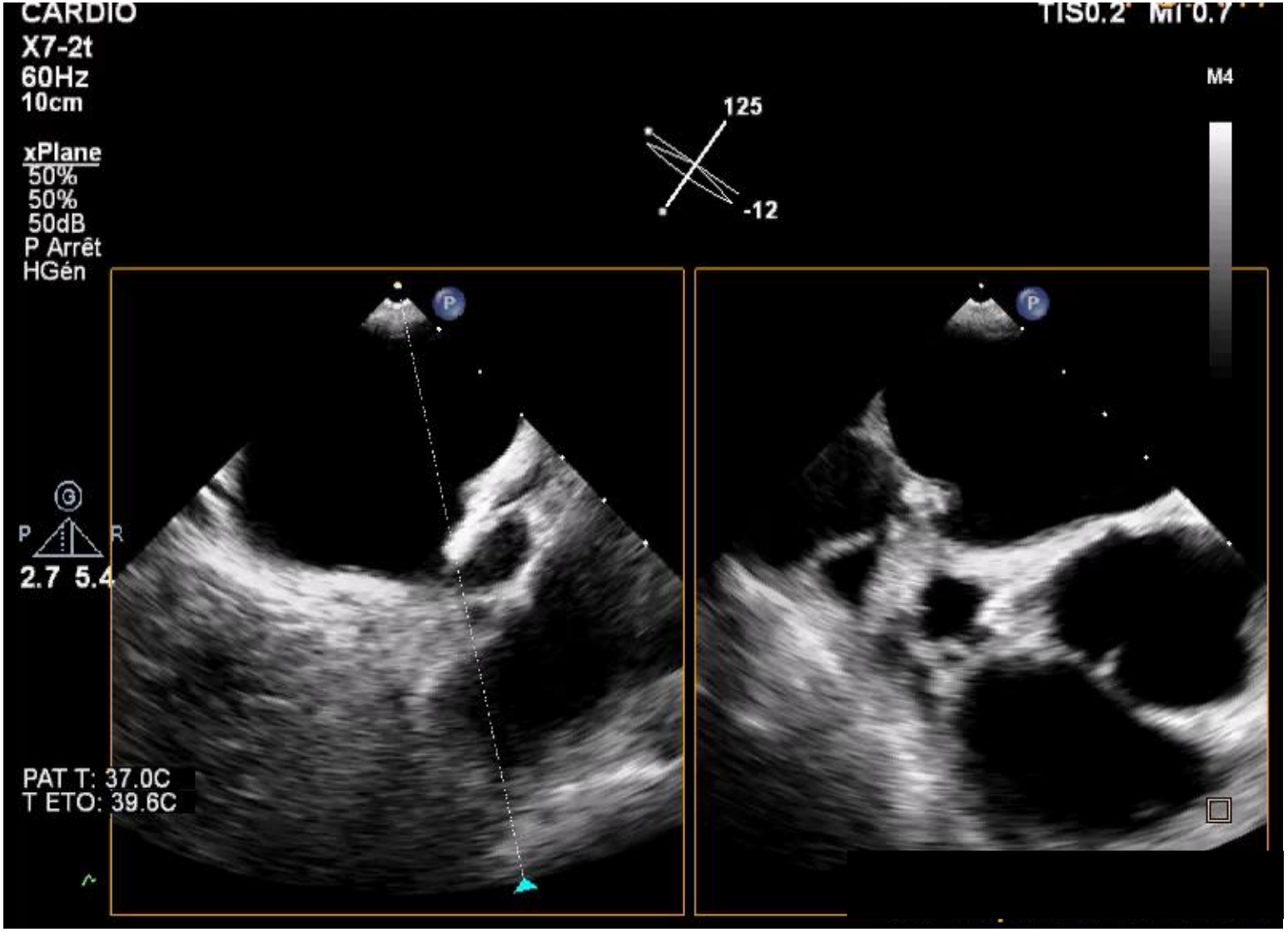
Left atrial appendage 90° 3D



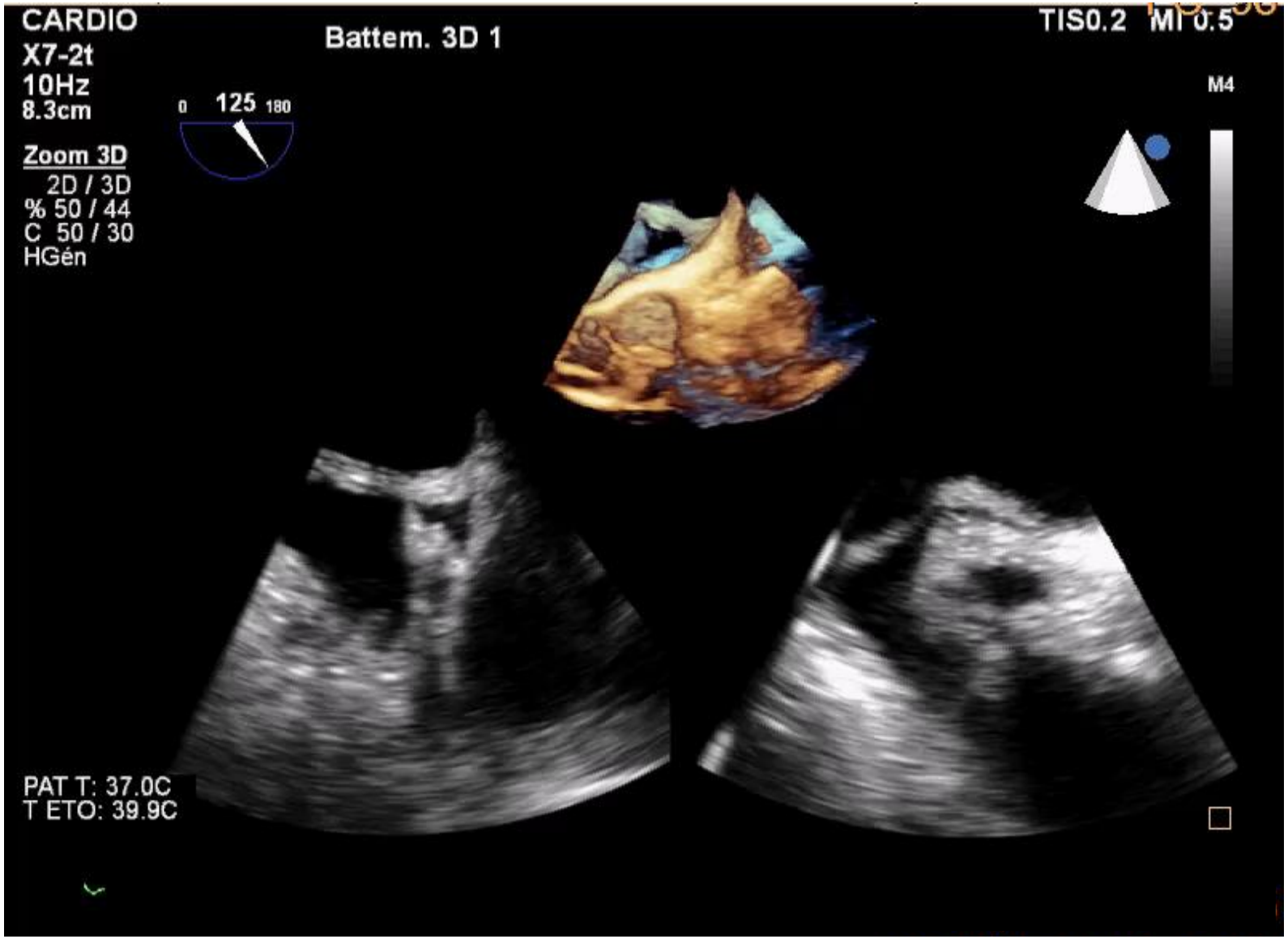
Left atrial appendage 120°



Left atrial appendage 120° Xplane

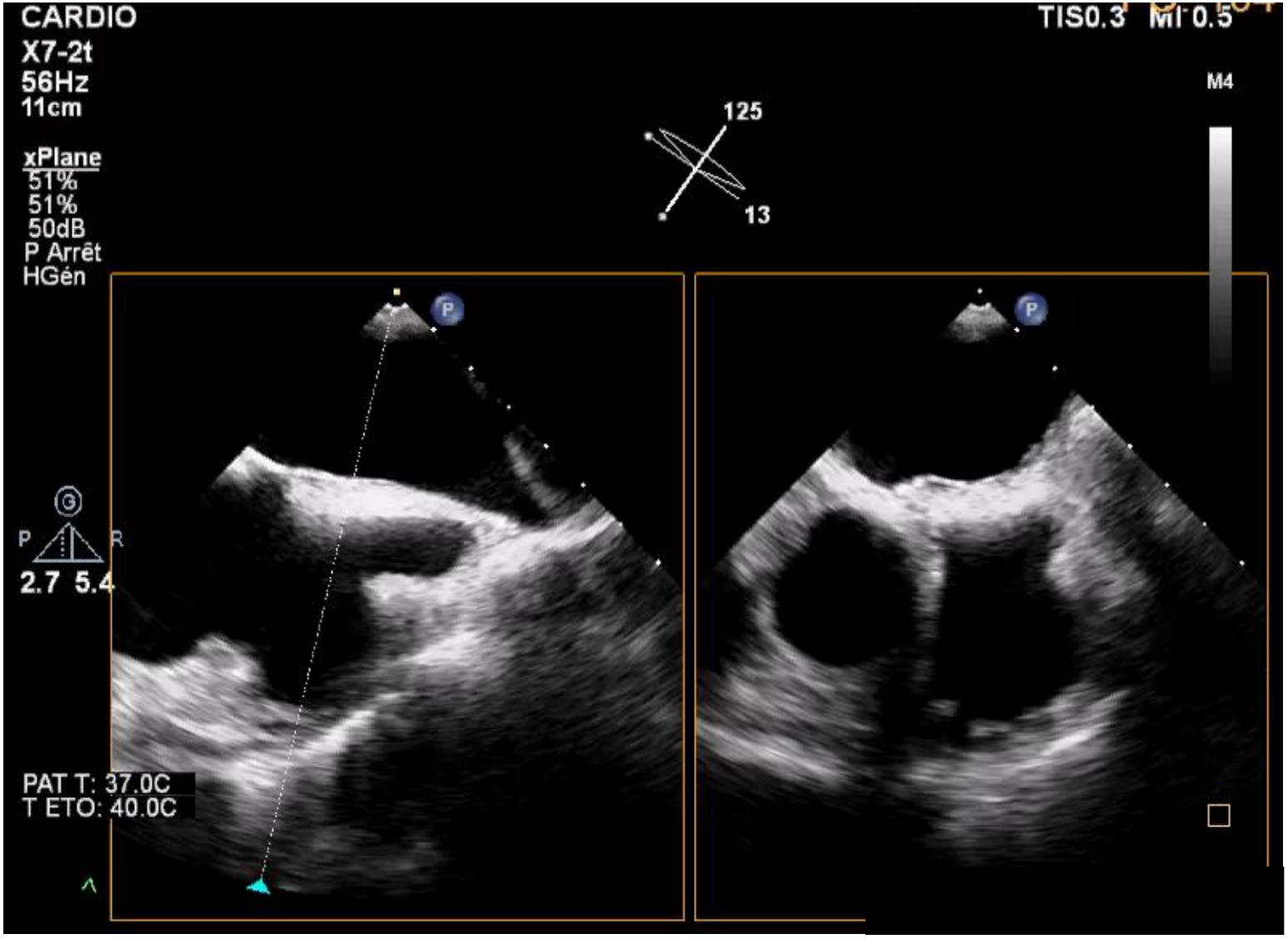


Left atrial appendage 120° 3D

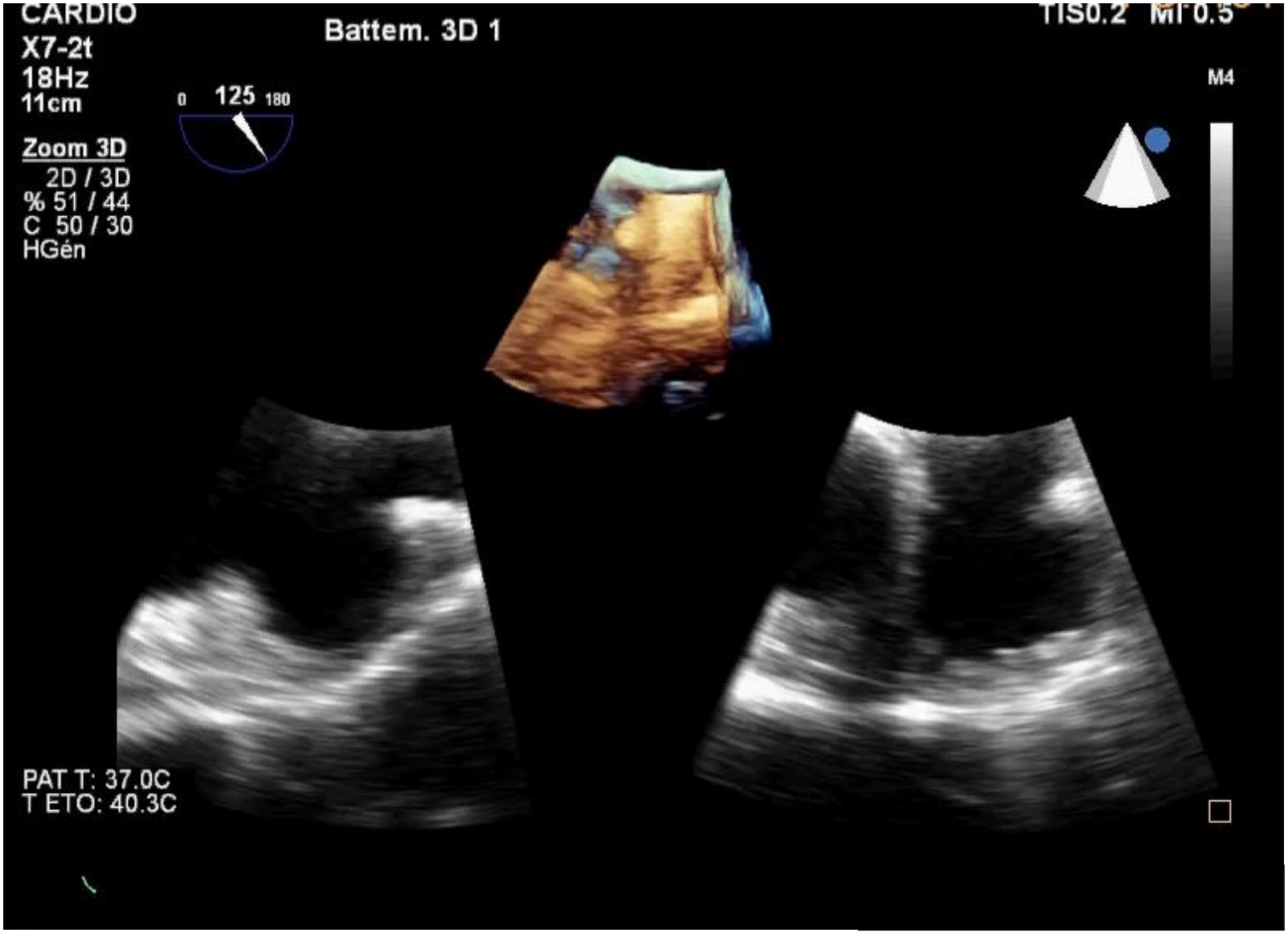


Right atrial appendage 120°

Right atrial appendage 120° Xplane

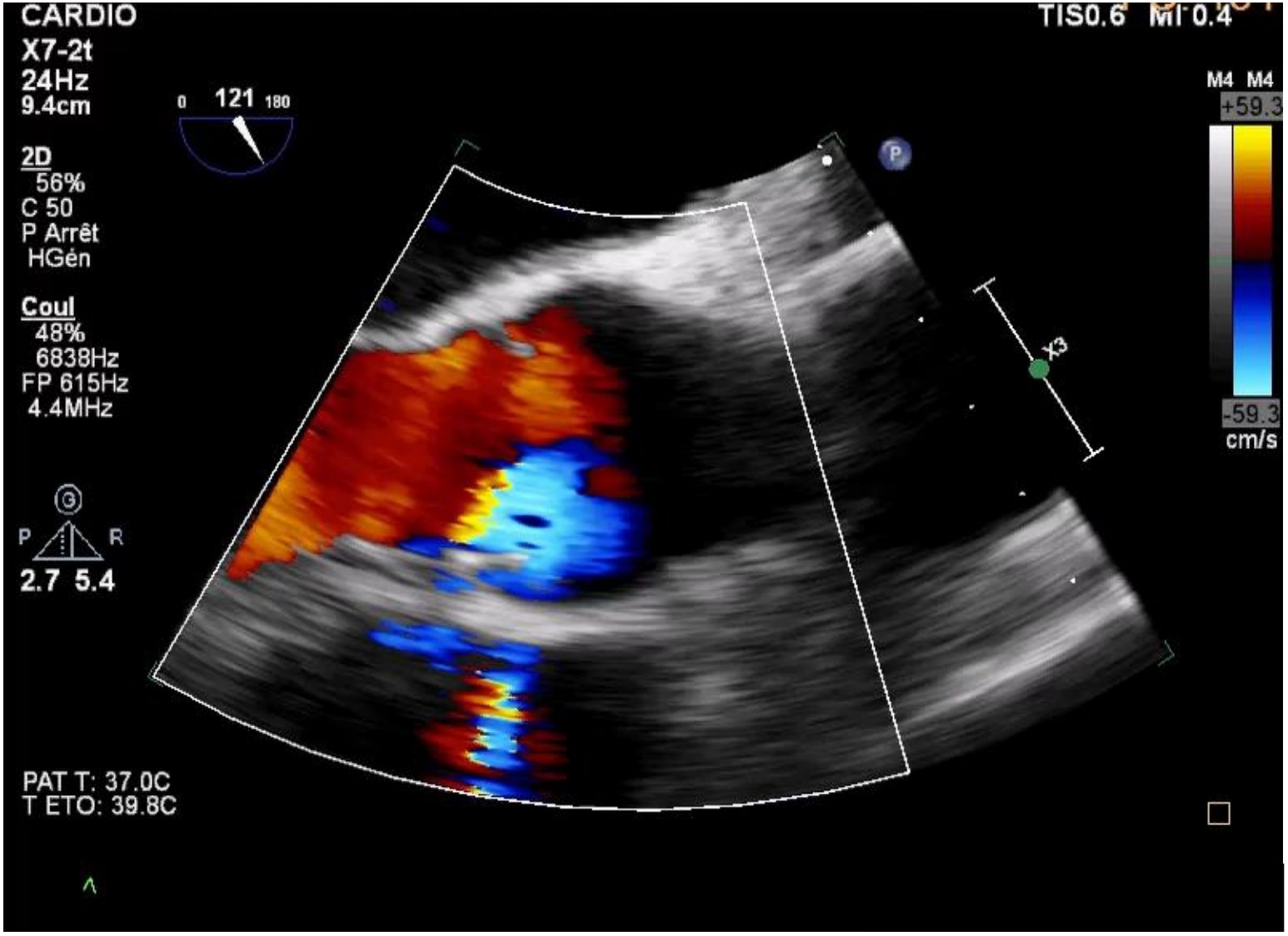


Right atrial appendage 120° 3D

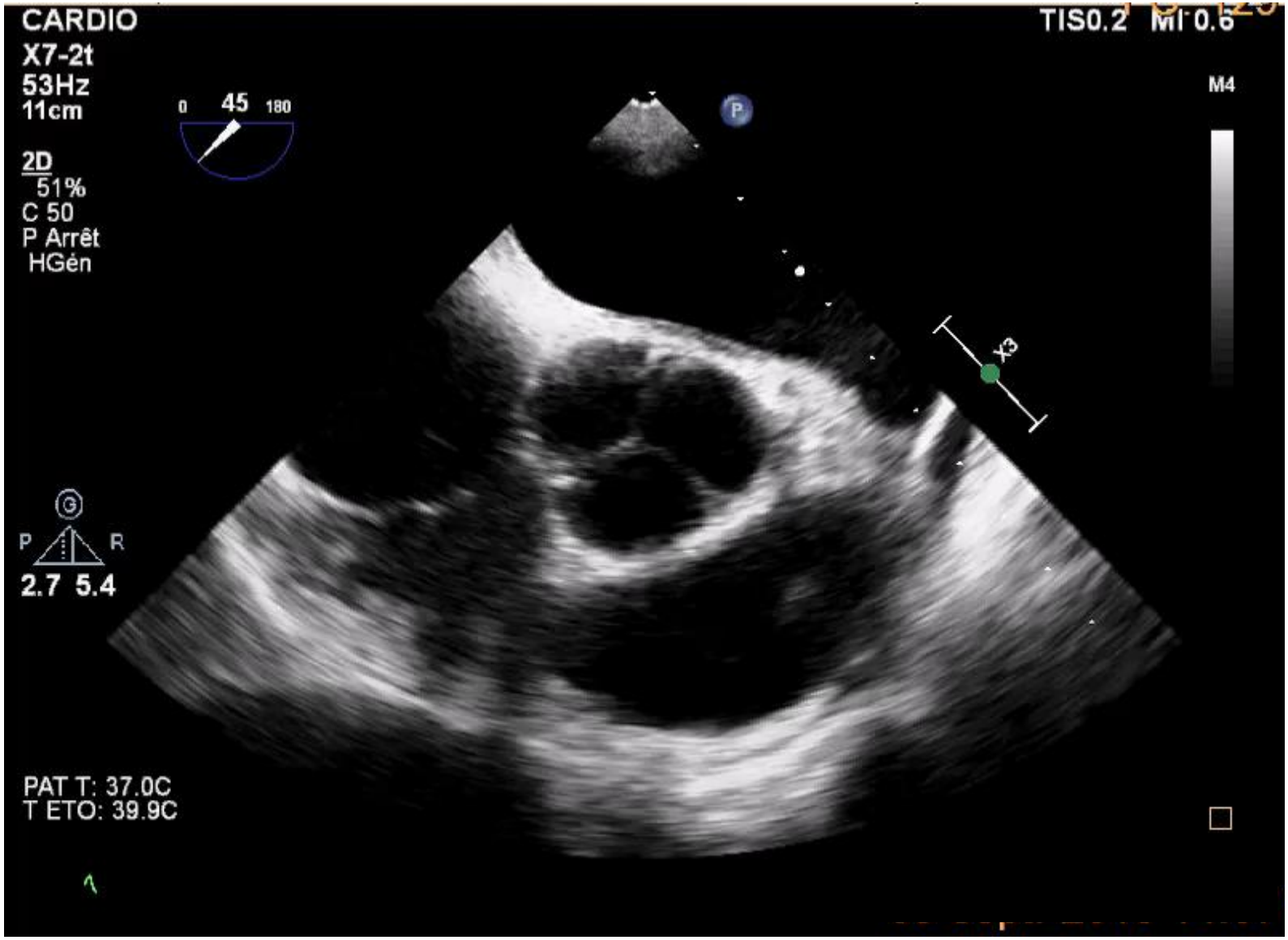


Aortic valve 120°

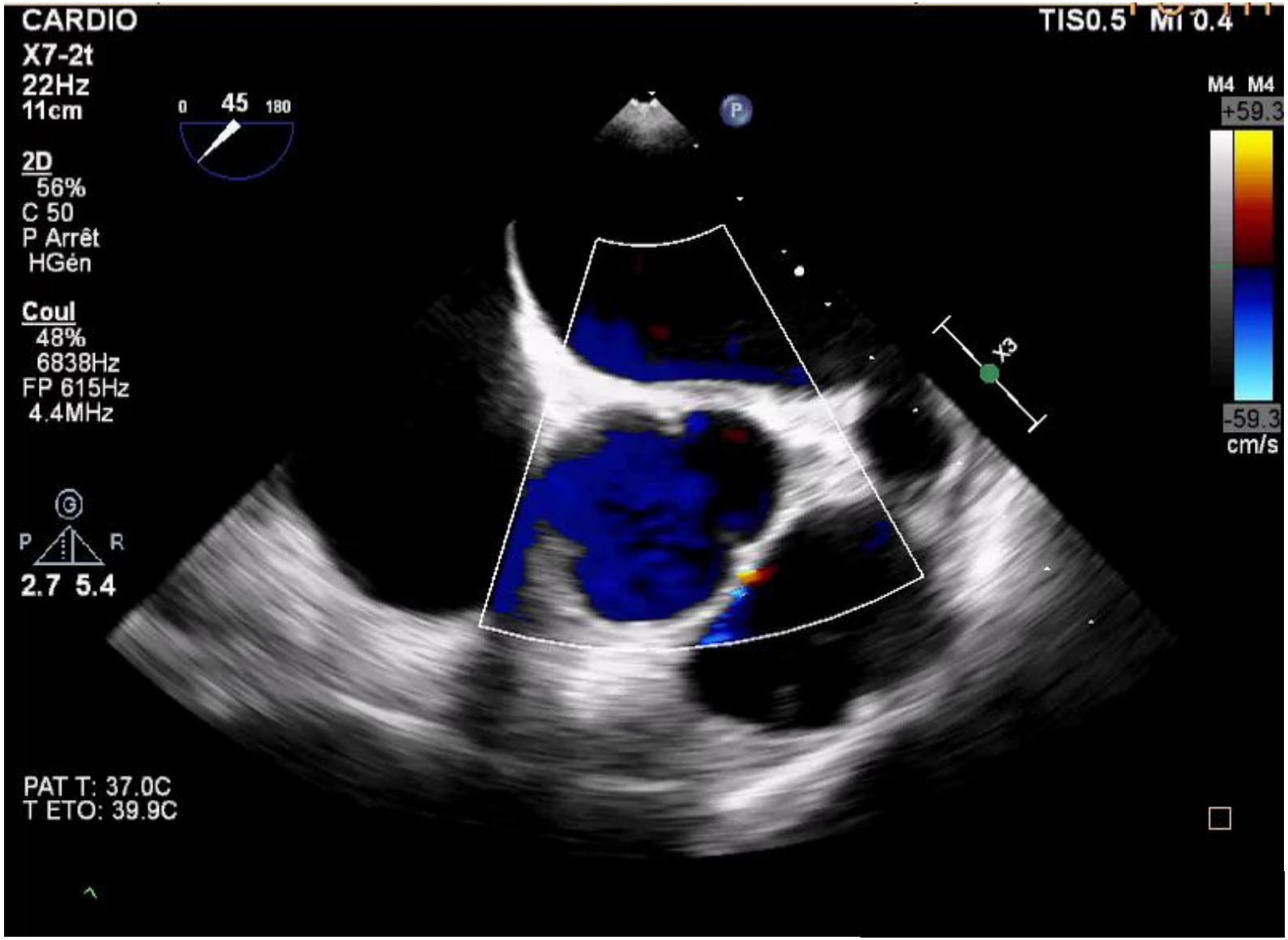
Aortic valve 120°



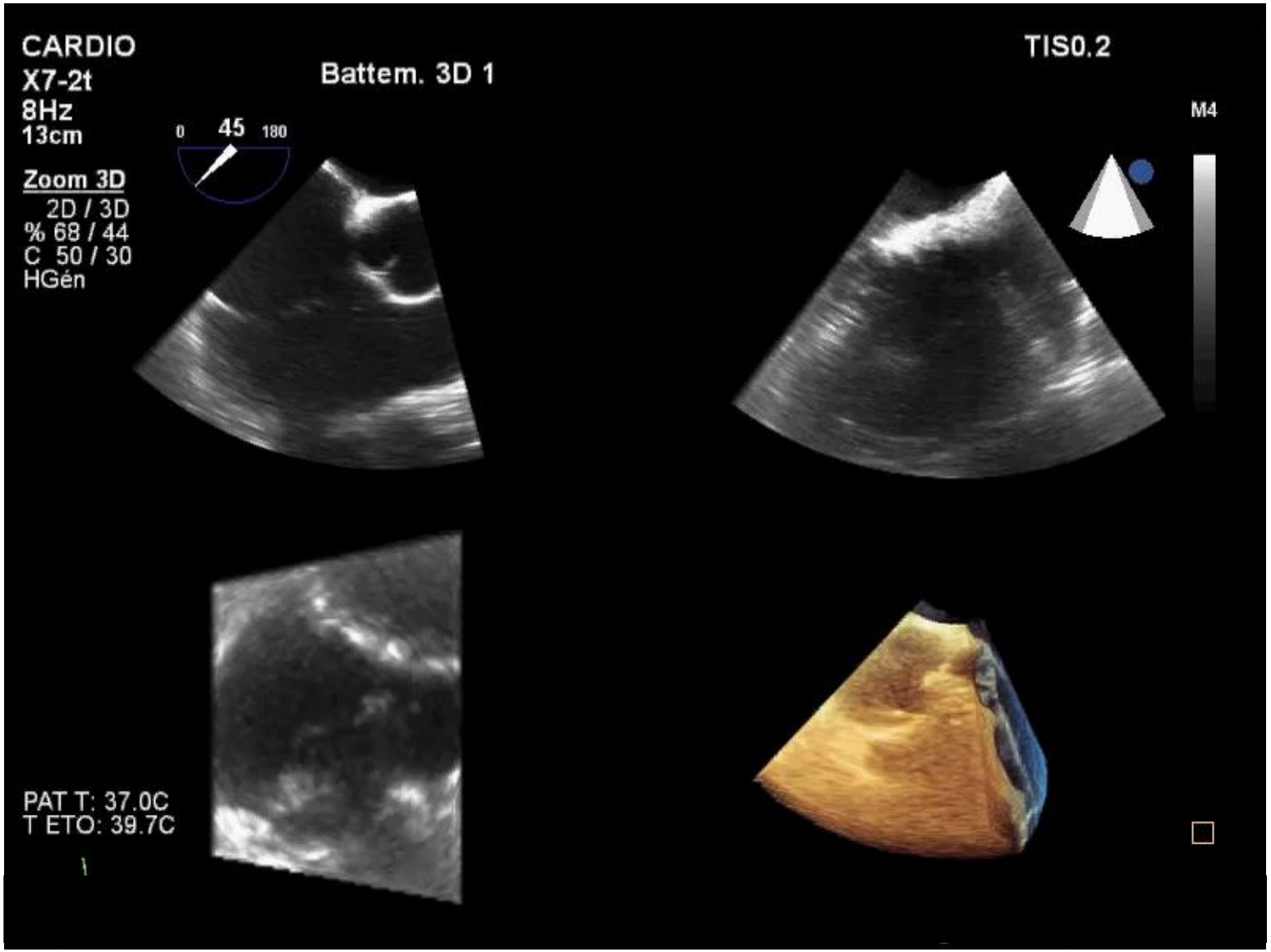
Aortic valve 45°



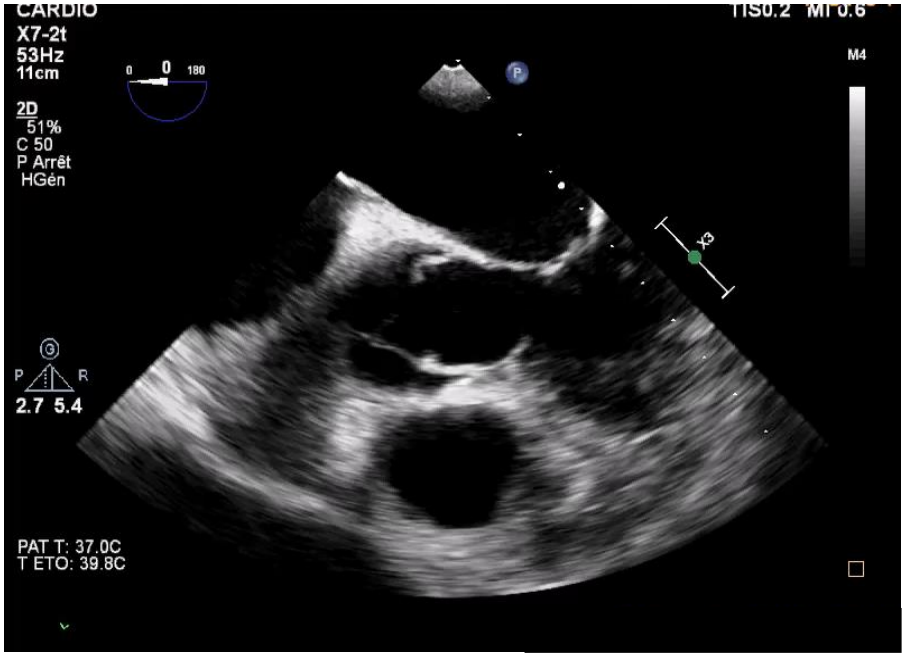
Aortic valve 45°

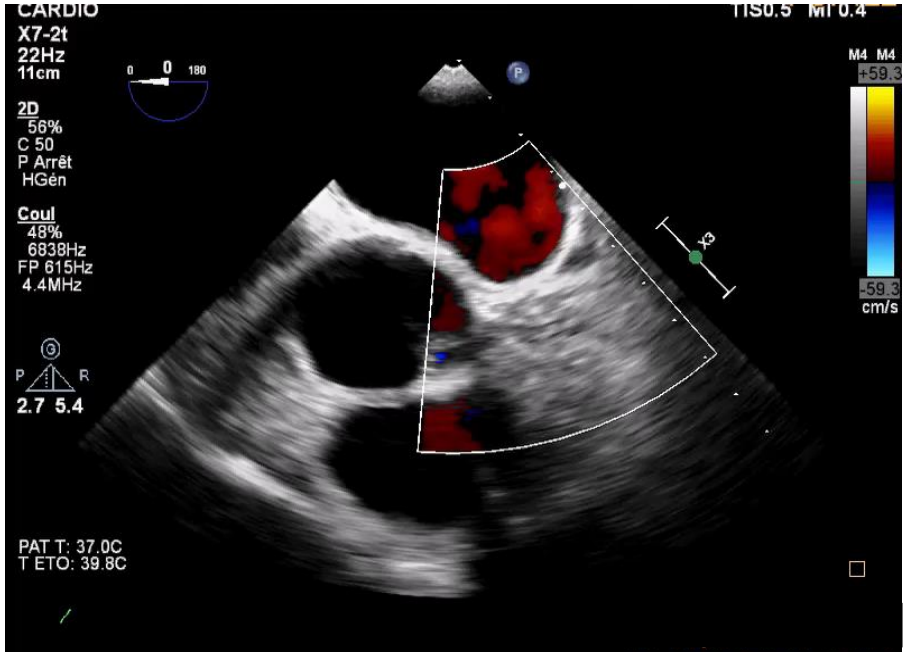


Tricuspid valve 3D

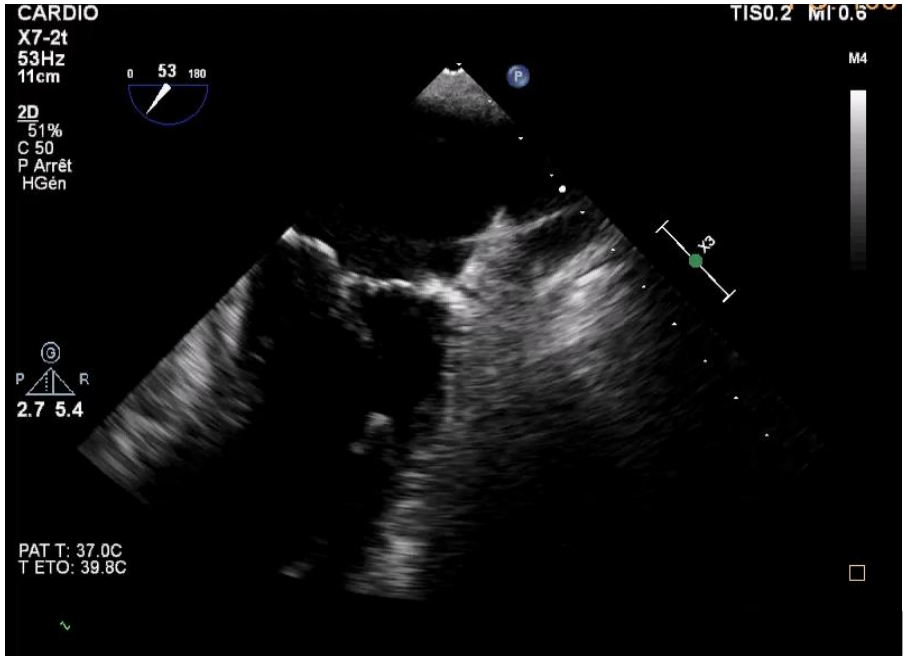


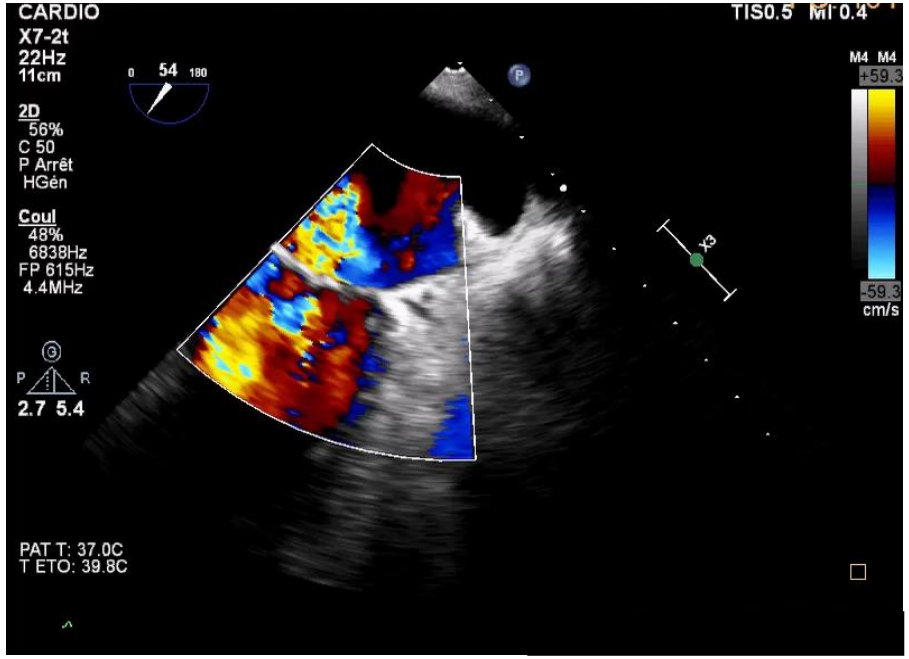
Mitral valve 0°



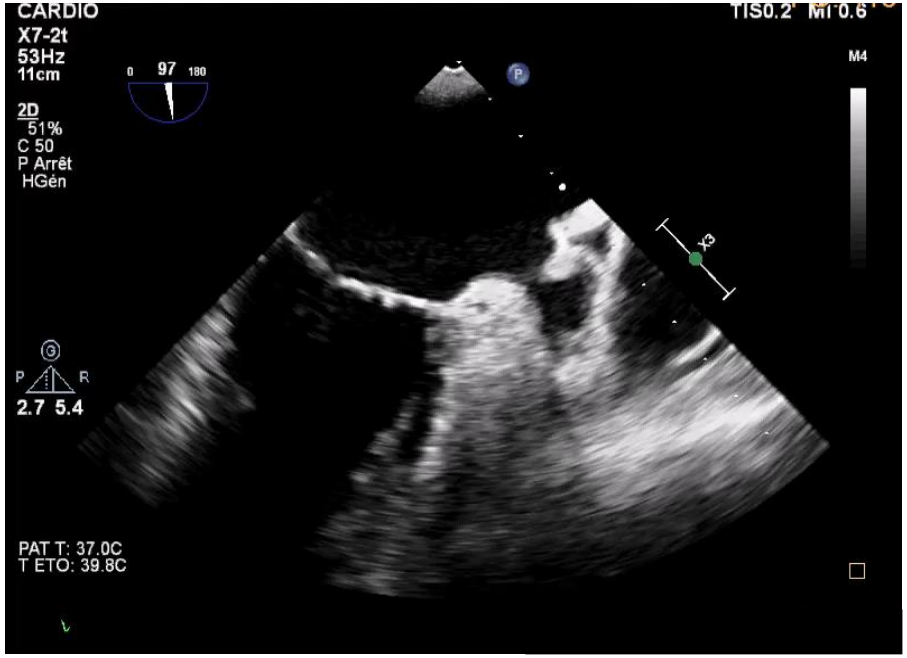


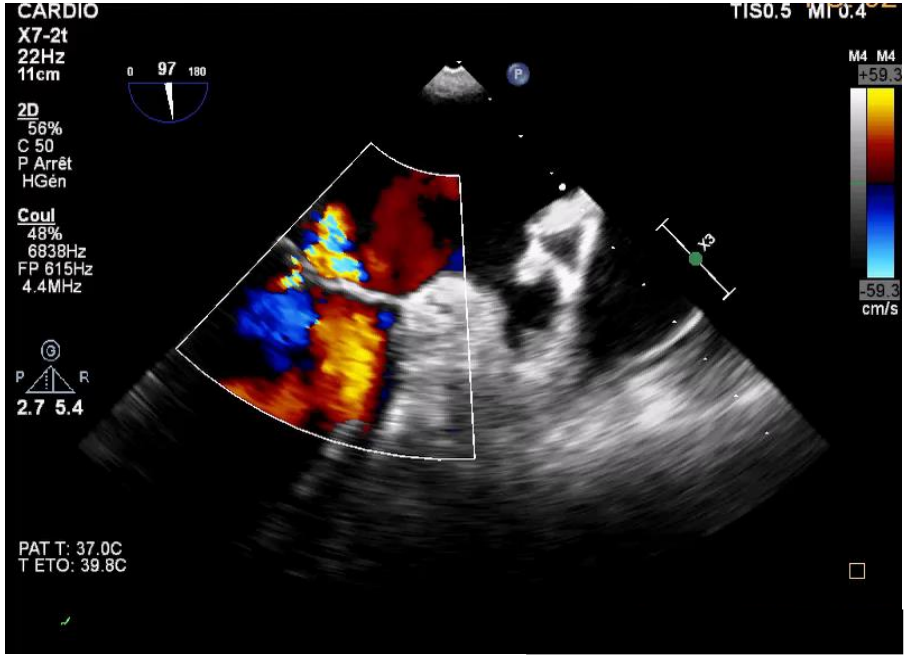
Mitral valve 45°



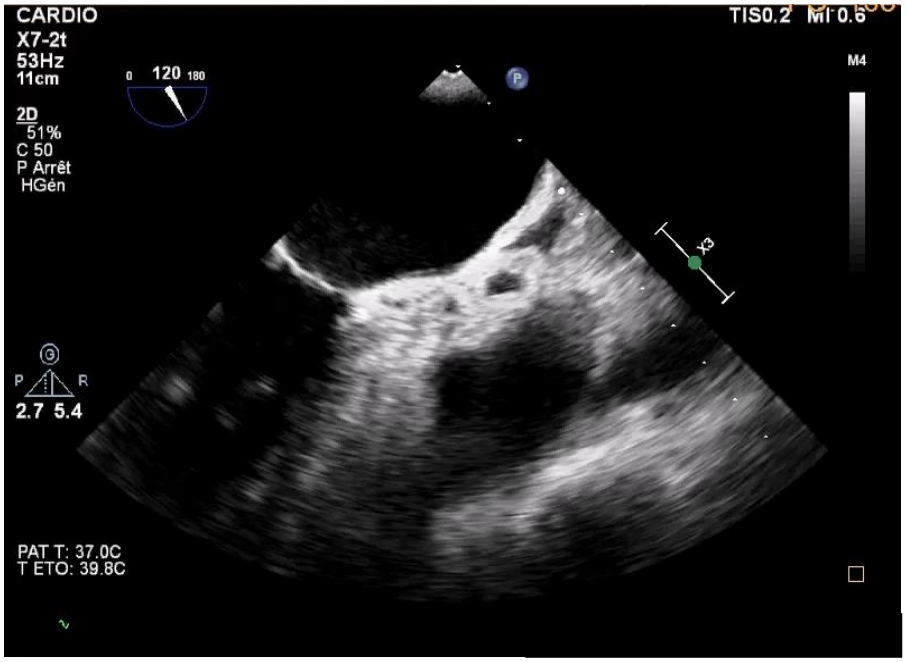


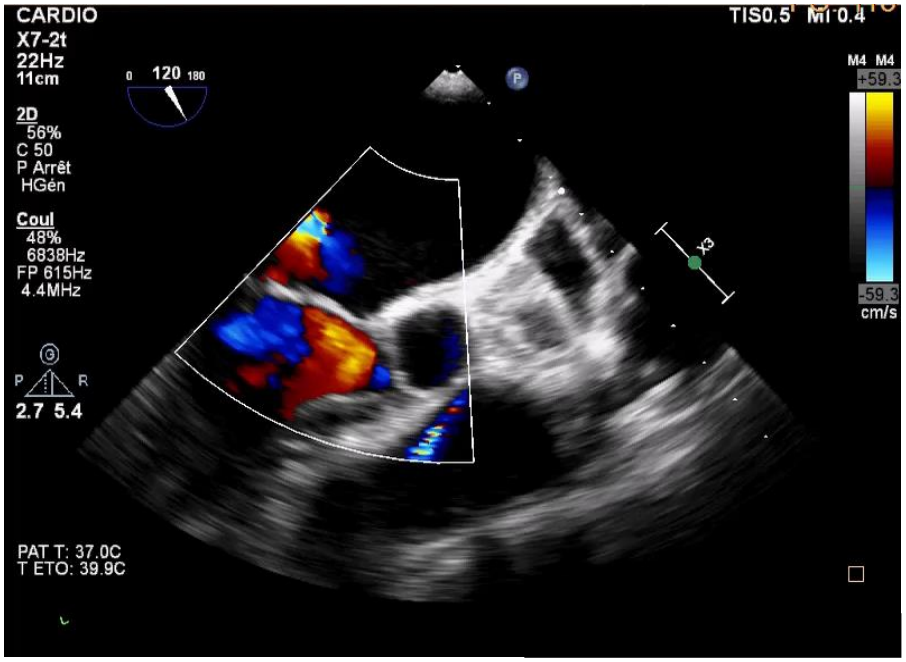
Mitral valve 90°



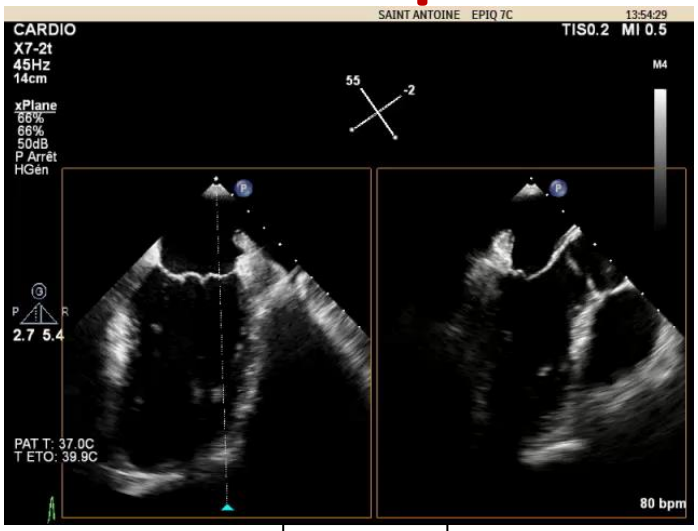


Mitral valve 120°

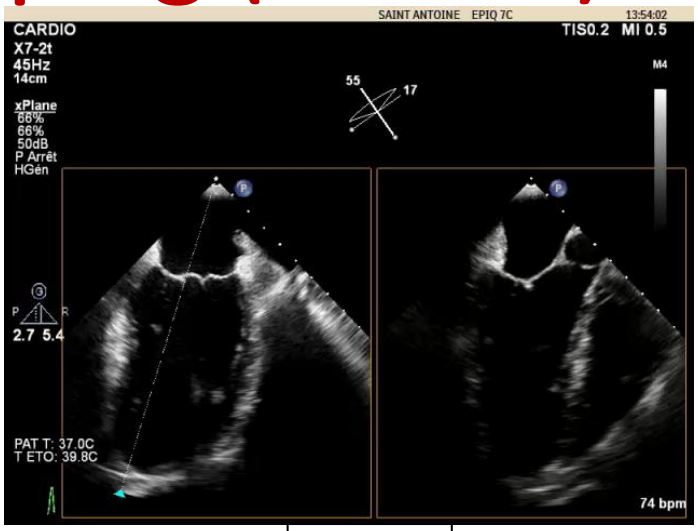




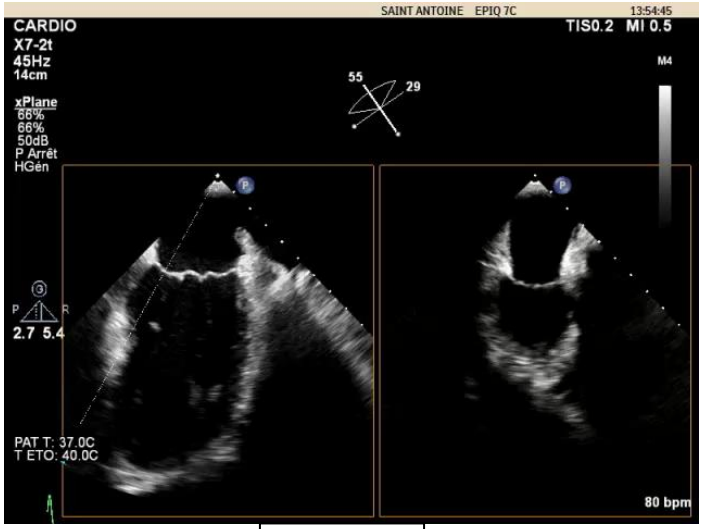
Mitral valve
X-plane sweeping (60-90°)



A1-P1

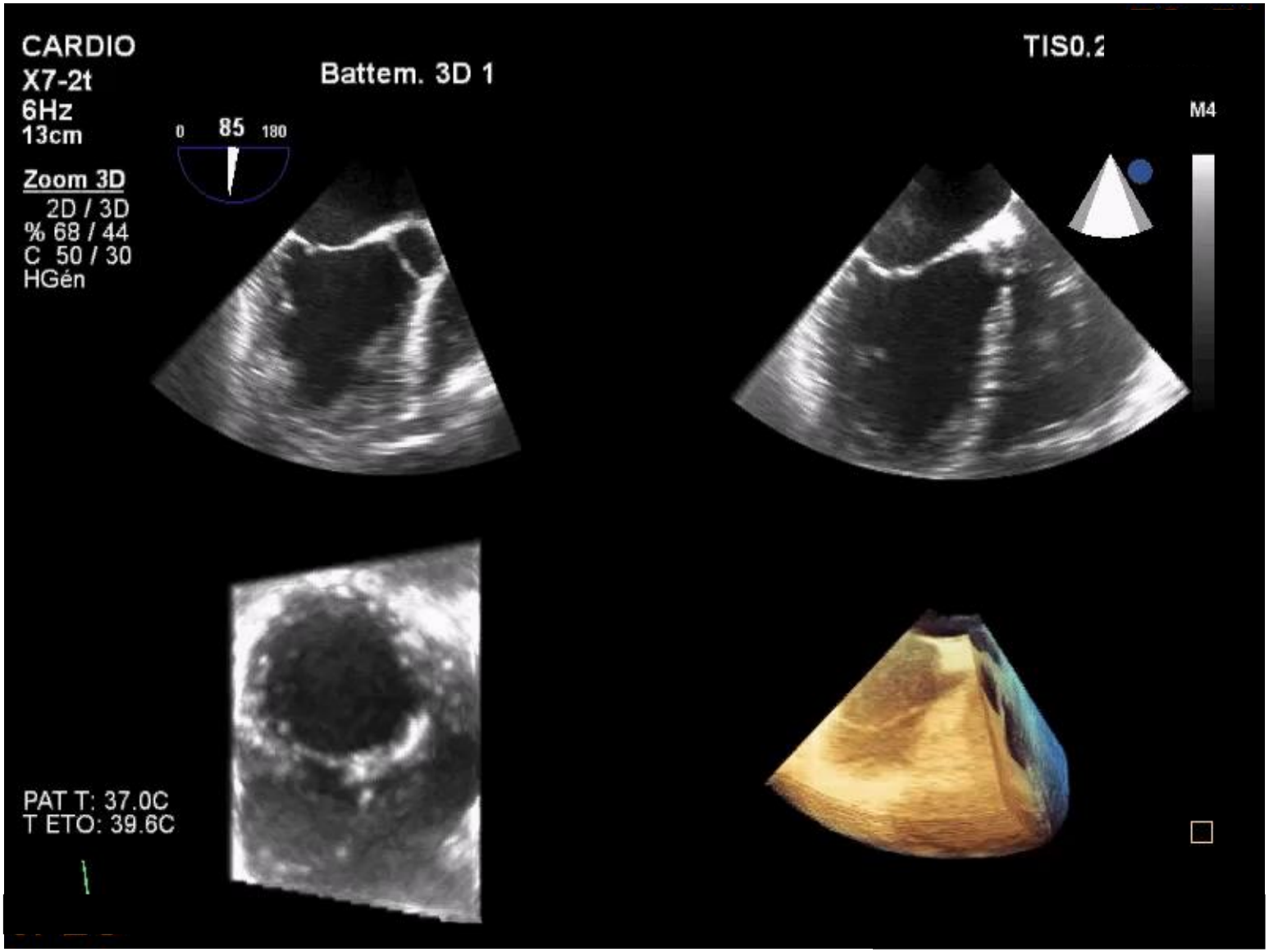


A2-P2

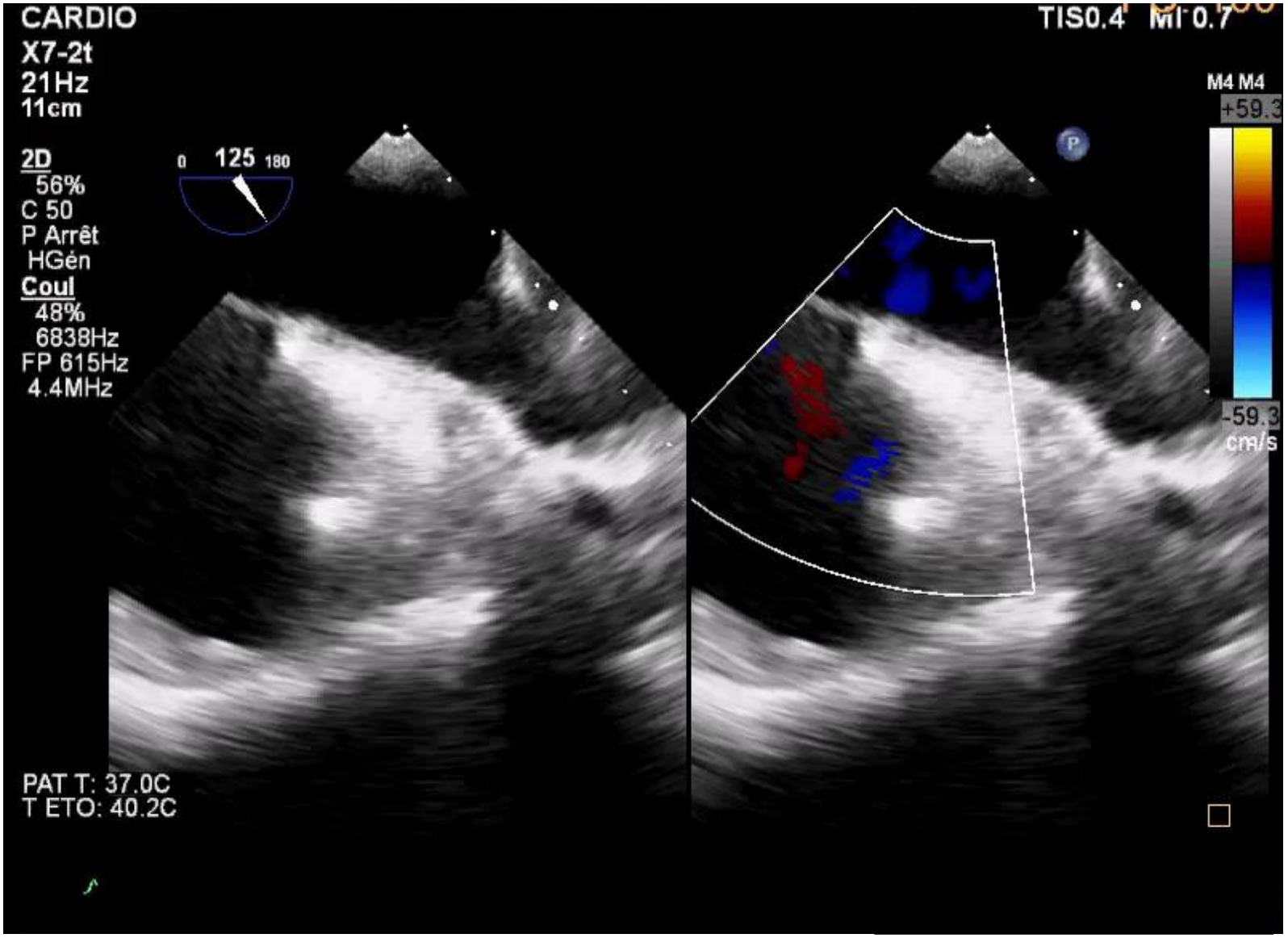


A3-P3

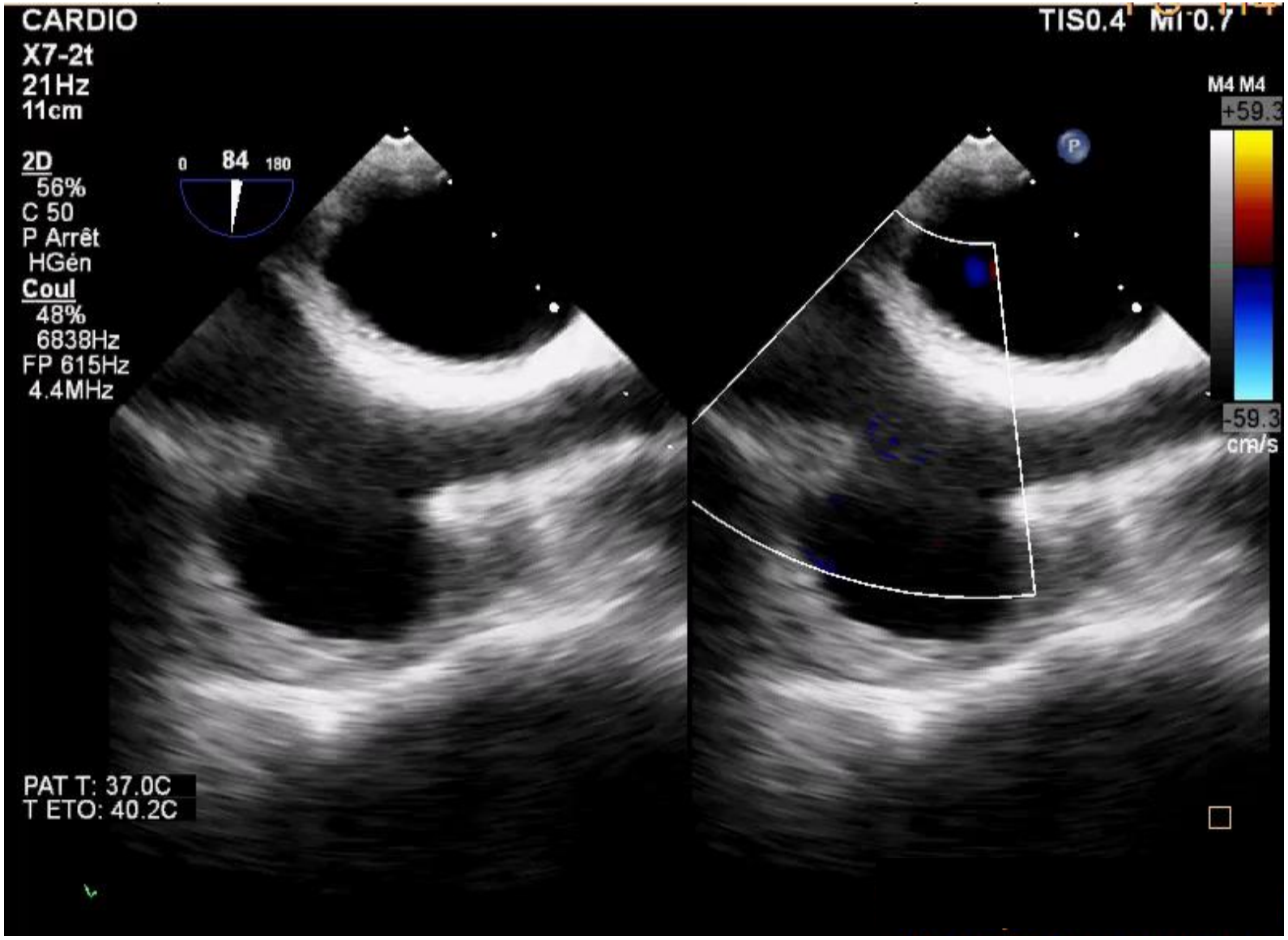
Mitral valve 3D



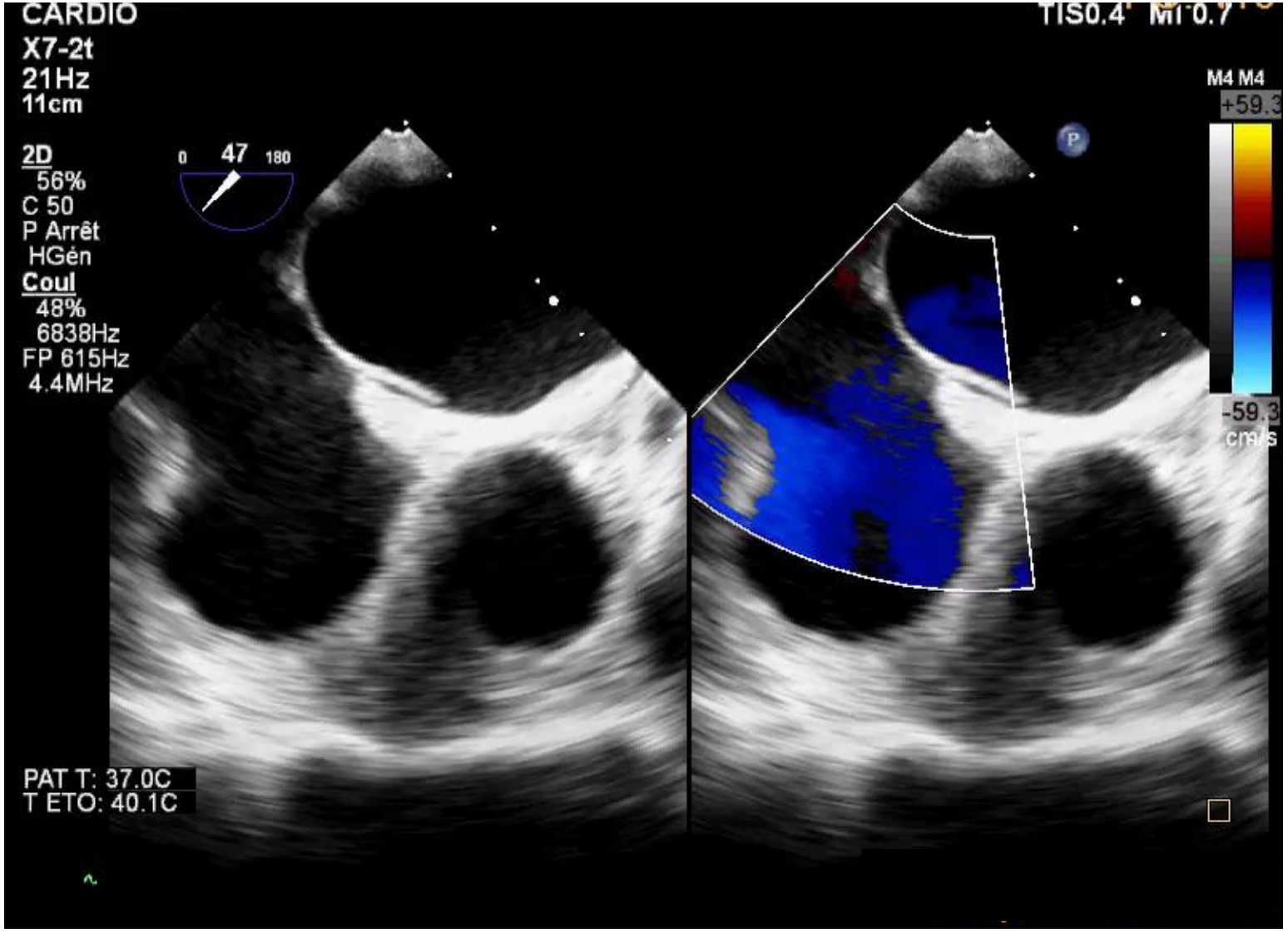
Inter atrial septum 120°



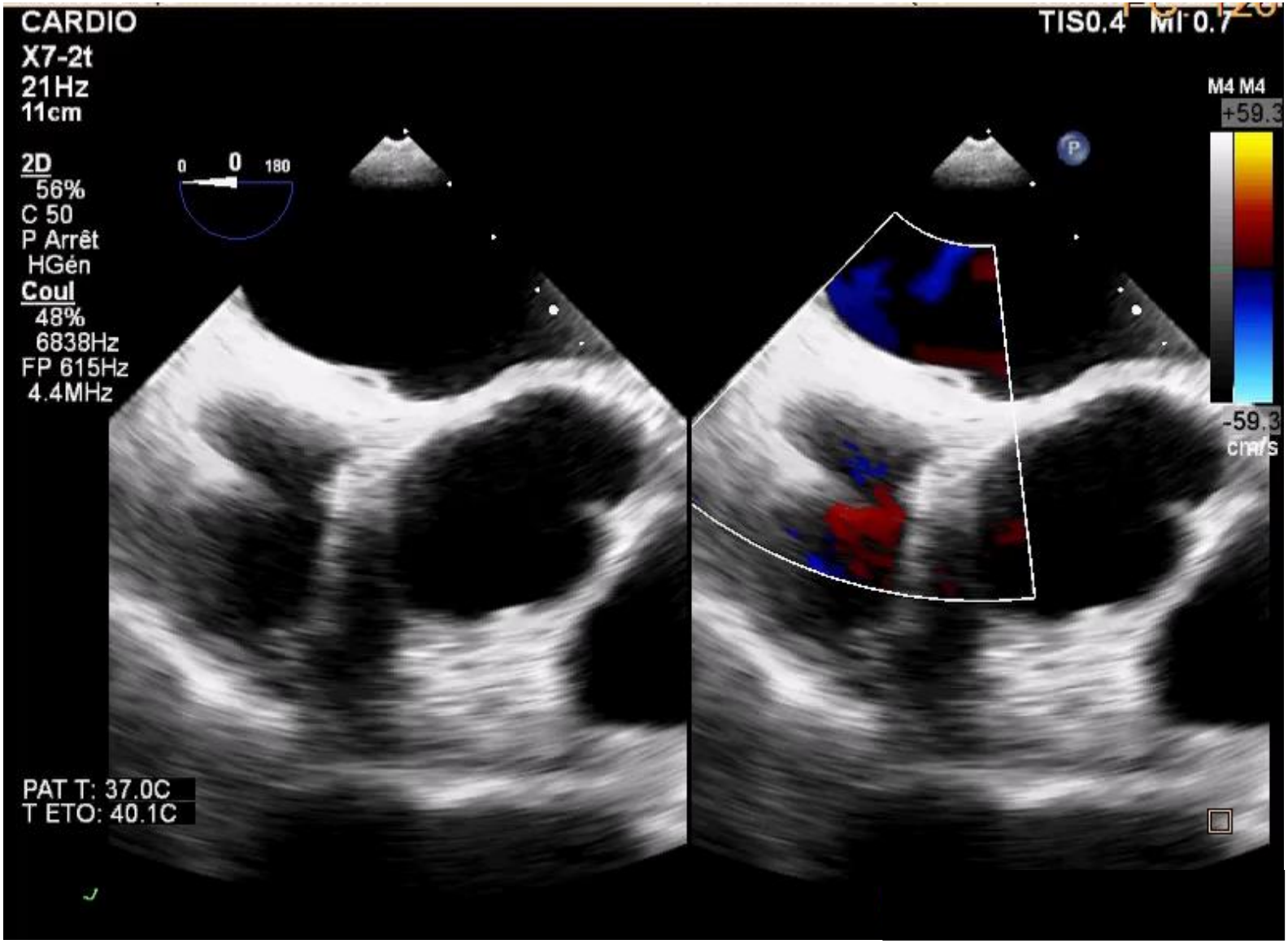
Inter atrial septum 90°



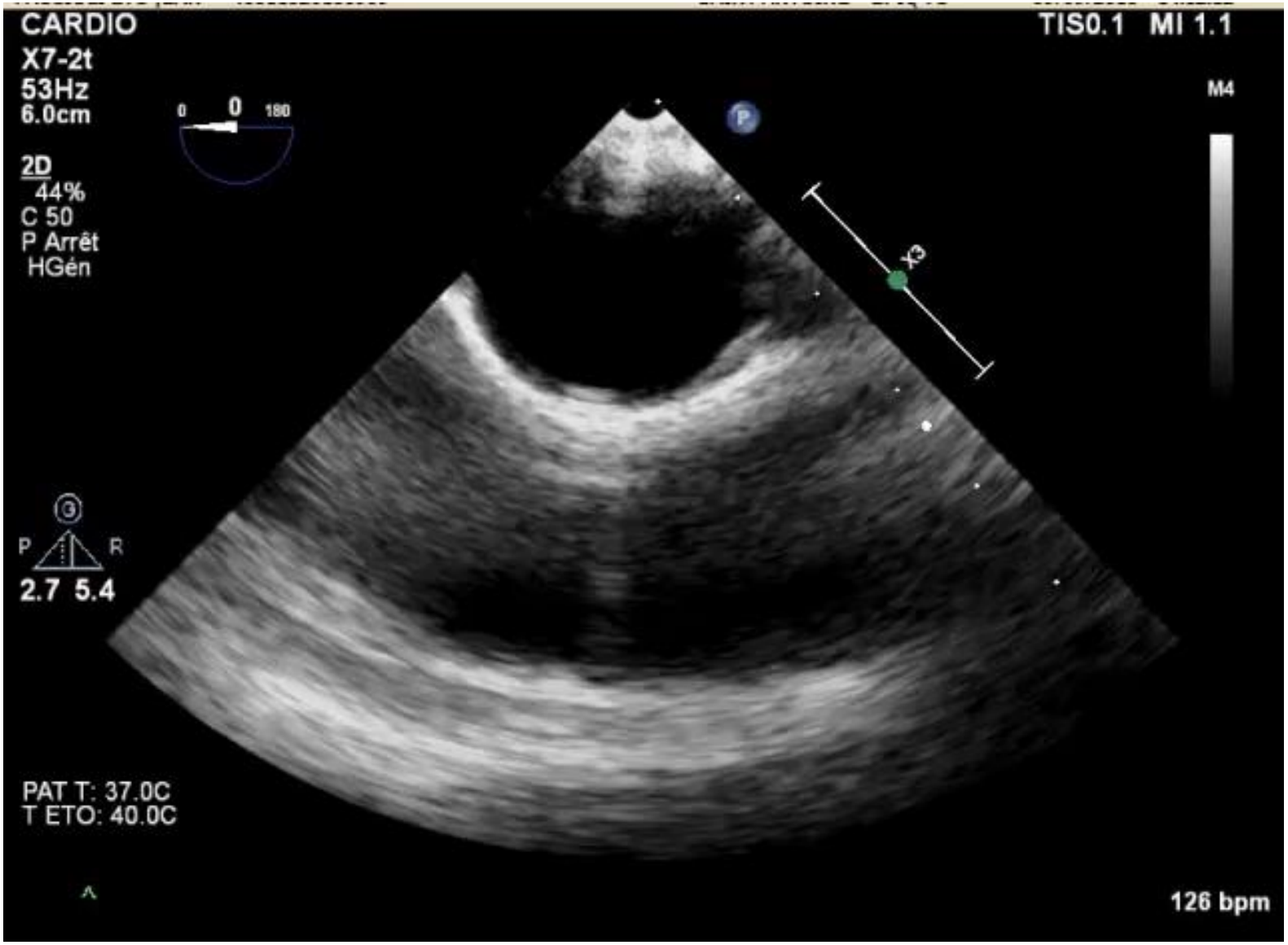
Inter atrial septum 45°



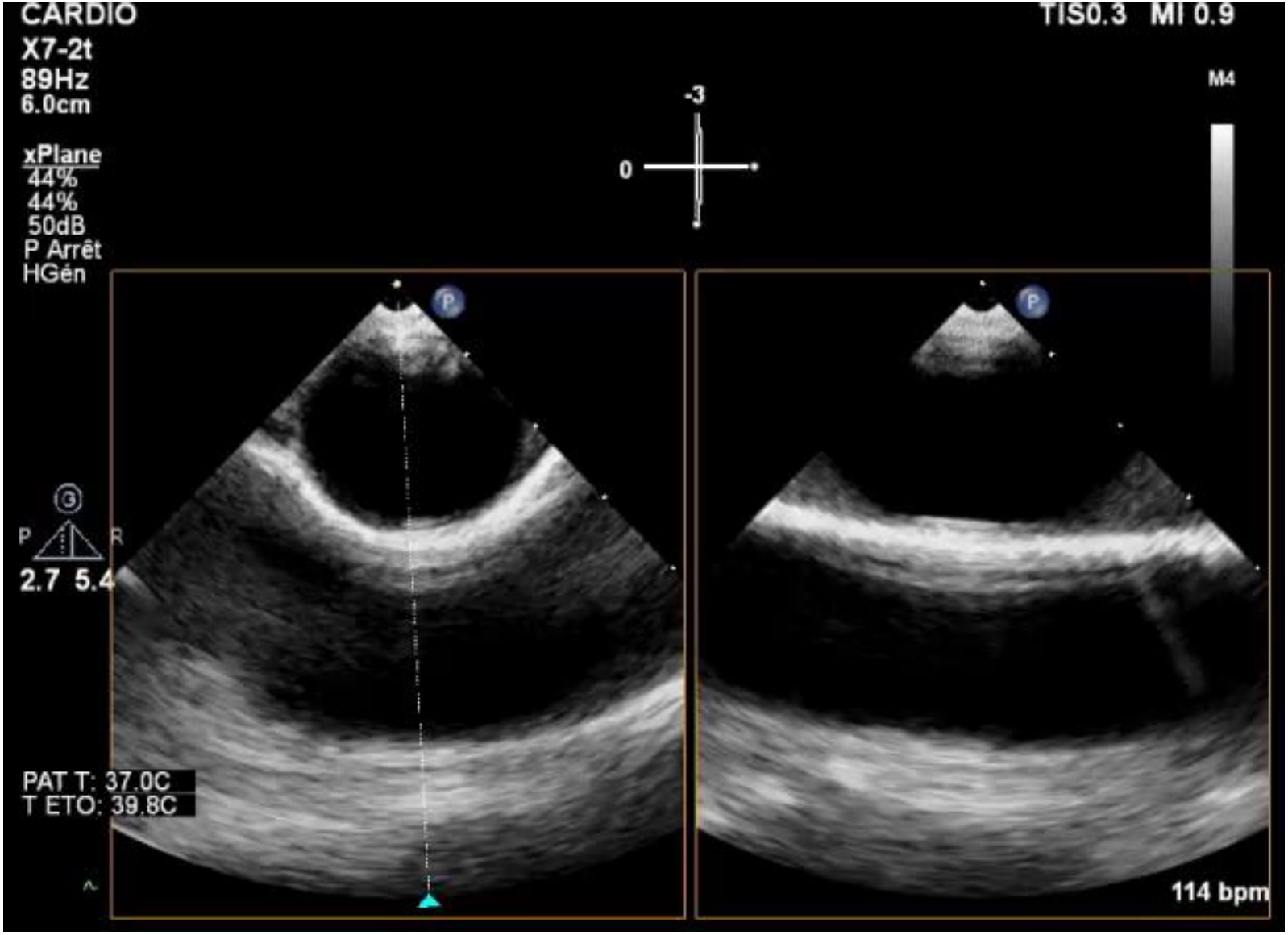
Inter atrial septum 0°



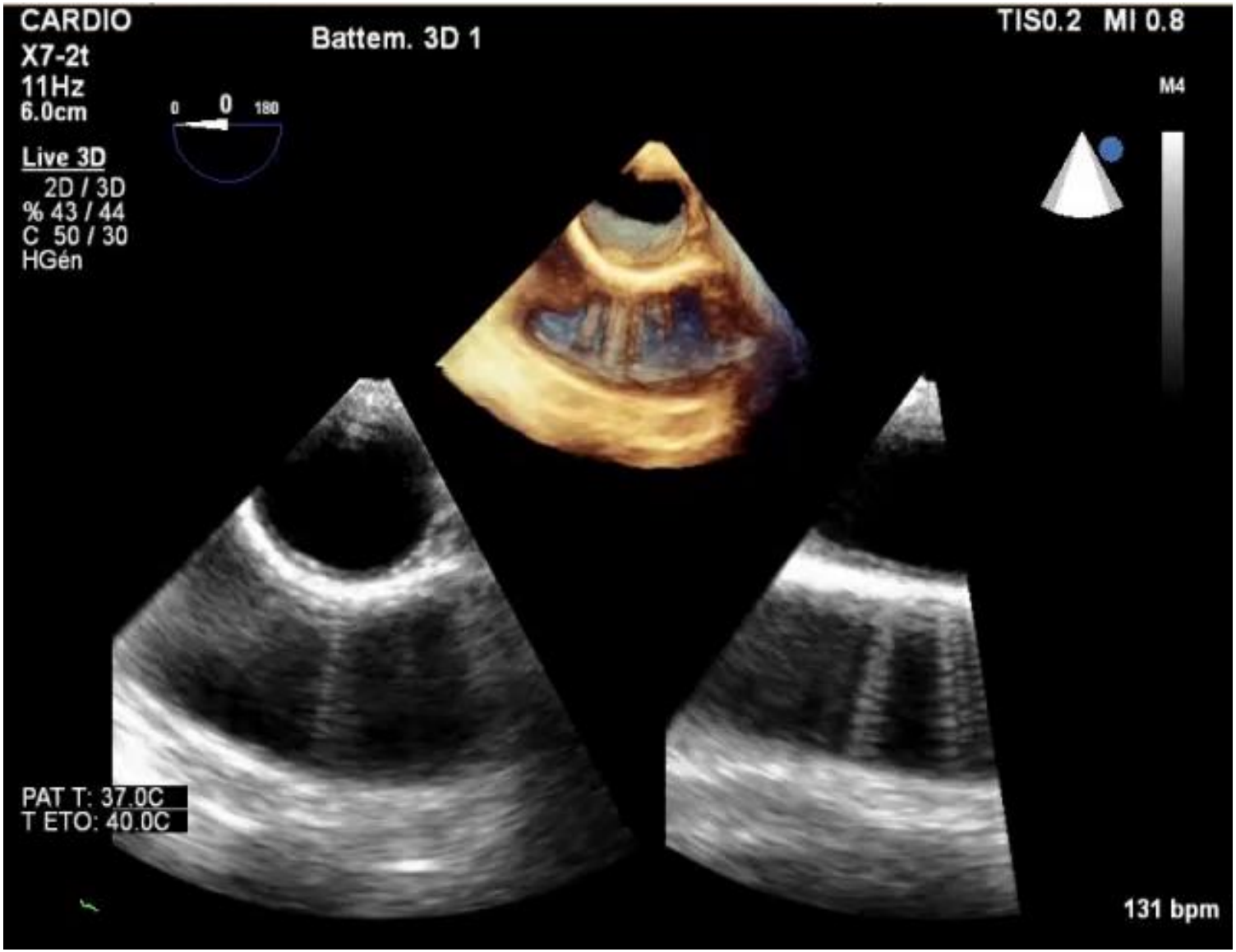
Thoracic Descending Aorta 0°



Thoracic Descending aorta X-plane



Thoracic Descending aorta 3D



TEE Short Protocol

TEE probe position	
0 degrees	2D imaging of left atrial appendage 2D imaging of interatrial septum Color imaging of interatrial septum 2D imaging of MV Color imaging of MV
45 degrees	2D imaging of left atrial appendage Velocity of the LAA (or at 90 degrees if the alignment is better) 2D imaging of interatrial septum Color imaging of interatrial septum 2D imaging of AV Color imaging of AV 2D imaging of MV Color imaging of MV
90 degrees	2D imaging of left atrial appendage Velocity of the LAA (or at 45 degrees if the alignment is better) 2D imaging of interatrial septum Color imaging of interatrial septum 2D imaging of MV Color imaging of MV

TEE Short Protocol

TEE probe position	
120 degrees	2D imaging of left atrial appendage 2D imaging of right atrial appendage 2D imaging of interatrial septum Color imaging of interatrial septum 2D imaging of AV Color imaging of AV 2D imaging of MV Color imaging of MV
Valvular regurgitation	If valvular regurgitation ≥ mild, acquisition for ORE (color and continuous doppler)

TEE Short Protocol

3D acquisitions	Make sur to have the entire structure in the acquisition X plane of the left atrial appendage at 0°, 45°, 90°, 120° X plane of the right atrial appendage at 120° X plane sweeping of the mitral valve (between 60° and 90°) X plane of the aorta at 0° 3 Zoom 3D datasets (at least 1 beat) focused on the left atrial appendage 3 Zoom 3D datasets (at least 1 beat) focused on the right atrial appendage 3 Live 3D datasets (at least 1 beat) of the aorta 3 Zoom 3D datasets (at least 1 beat) on the mitral valve 3 Zoom 3D datasets (at least 1 beat) on the tricuspid valve

THANK YOU

Echocardiography Core Laboratory Imaging Analysis Protocol

MAESTRIA

In case of any question please feel free to contact

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