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A simplified stepwise approach to echo guidance during percutaneous mitral valve repair.

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TITLE:

A simplified stepwise approach to echo guidance during percutaneous mitral valve repair.

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Percutaneous mitral valve repair, mitral regurgitation, Mitra Clip, echocardiographic guidance, transesophageal echocardiography, stepwise, echocardiographic approach, transcatheter mitral valve repair (TMVR), edge-to-edge repair, minimal invasive mitral repair

SUMMARY:

This protocol presents in detail how to perform real-time echocardiographic guidance during transcatheter mitral valve repair. The fundamental views and the necessary measurements are described for each stage of the procedure.

ABSTRACT:

Percutaneous transcatheter edge-to-edge reconstruction of the mitral valve is a safe and well-established therapy for severe symptomatic mitral regurgitation in patients with high surgical risk. Echocardiographic guidance in addition to fluoroscopy is the gold standard and should be performed using a standardized technique.

This article lays out our reproducible step by step echocardiographic guide including views, measurements as well as highlighting possible difficulties that may arise during the procedure.

This article provides detailed and chronological echocardiographic views for each step of the procedure, especially preferences between 2D and 3D imaging. If needed, pulse wave, continuous wave and color doppler measurements are described. Furthermore, as there are no official recommendations for the quantification of mitral regurgitation during the percutaneous edge-to-edge-repair procedure, advice is also included for echocardiographic quantification after grasping the mitral leaflets and after device deployment. In addition, the article deals with

important echocardiographic views to prevent and deal with possible complications during the procedure.

Echocardiographic guidance during transcatheter mitral valve repair is mandatory. A structured approach improves the collaboration between interventionist and imager and is indispensable for a safe and effective procedure.

INTRODUCTION:

Mitral regurgitation (MR) is the second-most frequent indication for valve surgery in Europe[1]. Untreated, it may lead to severe heart failure and reduced quality of life[2,3,4]. The percutaneous mitral valve repair (PMVR) is a catheter-based technique, which mimics the Alfieri stitch surgical method to mitral repair by connecting the A2 and P2 scallops[5]. For patients with high surgical risk, this technique offers a minimally invasive approach for the treatment of severe MR. Data from several registries and trials has shown that the MitraClip procedure, a transcatheter mitral valve repair therapy, is an effective and safe method[6,7,8,9]. In 2019, a similar device, the PASCAL transcatheter valve repair system, was introduced to the market. It has shown feasibility and acceptable safety in the treatment of patients with severe MR[10]. The duration and success of the PMVR are dependent on the individual operator's skill and experience[11]. In contrast to other percutaneous techniques, like the percutaneous transvalvular replacement (TAVR), which can be done with fluoroscopy only, PMVR requires echocardiographic guidance[12,13].

This article describes step by step the echocardiographic approach during PMVR, including measurements, suggestions for intraprocedural quantification of the MR and important views to prevent periprocedural complications.

PROTOCOL:

The protocol follows the guidelines of our's institution's human research ethics committee.

1. Evaluation before intervention

1.1. Exclude pericardial effusion before transseptal puncture. If a small pericardial effusion is present, measure the maximal end-diastolic echolucent space in a four-chamber (4Ch) view with a focus on the right ventricle (RV), a mid-oesophageal right ventricular inflow-outflow view, and a long-axis (LAX) view.

1.2. Evaluate the pulmonary venous flow pattern with pulse wave doppler (PW) in the left upper pulmonary vein (LUPV) and exclude thrombus formation in the left atrial appendage (LAA). Show the short axis (SAX) view with focus on the LAA, sweep then at 40-60° and rotate the probe anti-clockwise to show the LUPV. Assess the flow in the right upper pulmonary vein (RUPV) by sweeping at 90-110° (**Figure 1** and **Supplementary Figure 1**).

[Place **Figure 1** here]

1.3. Ensure hemodynamic state is the same during pre- and post-procedural evaluation.

NOTE: AS MR is a dynamic valve disease, regurgitation may seem less severe under general anaesthesia. In this case, consult the operator and increase the afterload and/or the preload.

1.4. Find the best intercommissural view (50-70°). Take a perpendicular view (X-plane) in the three segments with and without color doppler and measure the length of the posterior mitral leaflet (PML). Then, check the leaflet morphology again (**Figure 2** and **Supplementary Figure 2**).

[Place **Figure 2**].

1.5. Assess the transmitral pressure gradient with continuous wave doppler (CW) in the long axis view (120-140°).

NOTE: A mean pressure gradient (MPG) > 5 mmHg is a relative contraindication for PMVR.

1.6. Take a 3D dataset with color doppler or a wide-sector zoom image with color and measure the 3D-vena contracta (3D-VCA) (**Figure 3**).

[Place **Figure 3 here]**

1.7. Without color, use the 3D volume to measure the mitral valve area (MVA) (**Supplementary Figure 3**).

NOTE: An area < 4 cm^2 is a relative contraindication, an area < 3 cm^2 an absolute contraindication to perform the procedure. Otherwise assess the MVA in the transgastric basal SAX view.

1.8. Show the 3D en-face surgical atrial view (aortic valve at 12 o'clock) of the mitral valve.

NOTE: The segments of the valve are named "lateral" for the segments 1 and "medial" for the segments 3. The sequence of the segments in the en-face surgical view, is inverse to the sequence in the commissural view. Perform a 180° clockwise rotation into the 3D en-face surgical view (aortic valve at 6 o'clock), that will result in an equal sequence of segments in both views (**Figure 4** and **Figure 5**).

[Place **Figure 4** and **Figure 5** here].

1.9. Finally, take a bicaval view (90-110°) with X-plane, to show the aortic valve (AV), for the transseptal puncture.

2. Strategy

2.1. Discuss the strategy with the operator before inserting the steerable guide catheter (SGC) and the clip delivery system (CDS) into the left atrium.

2.1.1. Evaluate a one device strategy if the orifice is < 1 cm wide and position the clip directly above the regurgitation jet if the orifice is circular.

2.1.2. Evaluate the implantation of ≥ 2 clips in case of large elliptic or multiple jets. Implant the device starting medially of the regurgitant orifice, as the positioning of a second device is often easier when the first has been implanted in this way, rather than after starting laterally (**Supplementary Figure 4**).

3. Transseptal puncture

3.1. Show a bicaval view combined with a SAX view. Ensure the AV is visible, to avoid aortic injury.

3.2. Make sure the puncture site is slightly superior and posterior (**Figure 6**).

[Place **Figure 6** here].

3.2.1. Choose a puncture height of 4-5 cm in case of degenerative MR (e.g., prolapse) and of > 3.5 in functional MR. Avoid a patent foramen ovale, as the entry is far too anterior.

3.3. Once the transseptal needle leads to tenting of the interatrial septum, measure the puncture height in the 4Ch view in mid-systole (**Supplementary Figure 5**).

NOTE: In patients with large atria, if the puncture site is too posterior the tenting cannot be visualized in the 4Ch view. In this case, retroflex and insert the probe deeper into the oesophagus.

3.4. After transseptal puncture, always exclude pericardial effusion in the 4Ch view.

3.5. Show a SAX view with a focus on the LAA and pulmonary vein to visualize the entering of the stiff guidewire into the LUPV.

4. Introduction of the SGC into the LA

4.1. Visualize the tenting and advancement of the SGC with the dilator in a SAX view with continuous 2D-echocardiography and fluoroscopic guidance to avoid injuries to the left atrial wall.

NOTE: The tip of the SGC is defined by a radiopaque and echo bright double ring (**Supplementary Figure 6**).

4.2. Show the operator the SAX view and the bicaval view (90-120°) to position the SGC in the direction of the left ventricle (LV).

5. Advancement of the CDS into the LA

5.1. Take a 3D-volume including the interatrial septum, the left lateral ridge and the MV and ensure that the left lateral ridge is visible because protrusion of the CDS is common (**Figure 7**).

[Place **Figure 7** here]

5.1.1. Otherwise choose the SAX view and the LAX view (X-plane) to ensure, the CDS does not have contact with the ridge and the LA-wall.

NOTE: The operator may ask the imager to show the interatrial septum and pull back the SGC a few millimetres to bypass the ridge. If the double ring in 3D cannot be visualized, switch to 2D and show the SGC in the SAX view.

5.2. Check that the CDS is positioned perpendicularly to the coaptation line to guarantee a correct trajectory.

5.2.1. Show the intercommissural view in 2D at ca. 60° to display the medial - lateral plane and the LAX view at 120-140° to identify the anterior - posterior plane of the MV (**Supplementary Figure 7**).

5.2.2. Alternatively optimize the medial, lateral, anterior, and posterior positioning of the CDS in the 3D en-face view (**Supplementary Figure 8**).

6. Orientation of the device above and below the MV

6.1. Take the 3D en-face view to show a perpendicular positioning of the arms to the coaptation line.

6.1.1. In the event of poor image quality, show an intercommissural view combined with a LAX view (**Figure 8** and **Figure 9**).

[Place **Figure 8 and Figure 9** here].

NOTE: The clip arms are visible only in the LAX view.

6.1.2. Adjust the intercommissural view angle for medially and laterally positioned devices to visualise the complete length of both arms. Sweep at ca. 30-45° for medially positioned devices and ca. 70-90° for laterally positioned devices.

6.2. Choose the intercommissural view combined with a LAX view to visualize the advancing of the CDS into the LV.

6.3. Ensure the CDS is placed just a few millimetres below the MV.

6.4. Verify in the 3D en-face view that the clip arms are still in the planned position, as a rotation of the clip while crossing the valve is frequent.

NOTE: If the position of the clip arms has changed, clockwise or anticlockwise rotation will be performed to obtain symmetric grasping. Be careful during this manoeuvre to minimize chordal and subchordal entanglement.

6.5. If gross reorientation of the device is necessary, show the intercommissural view with X-plane to visualize the inversion of the clip that will be retrieved into the LA.

7. Grasping of the mitral leaflets and assessment of MR before and after clip deployment

7.1. Record the grasping of the leaflets in the intercommissural view combined with the LAX view (X-plane) or in the LAX view only (**Supplementary Figure 9**).

7.2. Ask the anaesthesiologist to perform a breath-hold manoeuvre to reduce shifting during ventilation and to facilitate the grasping of the leaflets.

7.3. Ensure continuous visualisation of leaflet insertion to avoid rolling of the leaflets or the chordae.

NOTE: Grasping a rolled leaflet or a chorda may result in a partial leaflet detachment and/or an aggravation of the MR.

7.4. Carefully evaluate the regurgitation reduction before clip deployment. Ensure both, operator and imager analyse this crucial step.

7.4.1. Rotate the TEE probe medially and laterally to the clip or use X-plane with color doppler to find eccentric jets close to the clip (**Supplementary Figure 10**).

NOTE: Due to shadowing artifacts caused by the CDS underestimation of the MR may occur. Insert the probe deeper into the esophagus or show the transgastric view to visualize the residual insufficiency jets without shadowing artifacts.

7.4.2. Evaluate the PW flow in the pulmonary veins.

NOTE: if a previous systolic flow reversal changes into a systolic dominant pattern, a relevant reduction has probably occurred.

7.4.3. Measure the MPG across the mitral valve.

NOTE: A gradient > 5 mmHg is a relative contraindication for clip deployment (**Supplementary Figure 11** and **Supplementary Figure 12**).

7.4.4. Use the 3D en-face view of the MV or a transgastric SAX view of the MV to show the double orifice (**Figure 10**).

[Place **Figure 10** here].

7.4.5. Finally, if the result is satisfactory, check leaflet insertion in 2D.

7.5. After releasing the clip from the CDS, repeat the last five steps.

NOTE: Due to the tension of the system on the MV, the residual insufficiency jets after releasing the device may be aggravated.

7.6. Show when the delivery catheter tip is retrieved from the SGC in the LAX view with X-plane and ensure that the spike avoids contact with the LA (**Supplementary Figure 13**).

8. Final MR assessment

8.1. Show the intercommissural view with color doppler in combination with perpendicular X-planes in the residual insufficiency jets if present.

8.2. Calculate the 3D-VCA in a 3D-volume. NOTE: usually the orifices are not in the same plane. In this case measure separated planimetries of each orifice in the appropriate planes (**Supplementary Figure 14**).

8.3. Evaluate once again the pulmonary vein flow and the mean gradient across the mitral valve.

NOTE: continuous LA pressure monitoring may be a useful tool during transcatheter mitral valve repair.

8.4. Finally, show the 3D en-face view of the mitral valve.

9. Implantation of additional devices

9.1. Ensure MR reduction is sufficient.

NOTE: If the result is not satisfactory, evaluate the implantation of additional devices.

9.2. Ensure that the additional device does not contact the implanted device diving into the left ventricle.

NOTE: fluoroscopy is essential to show the real distance between the clips.

9.3. Show the 3D en-face view to visualize the commissural line, as it might be deferred after implantation of the first clip.

9.4. Repeat the five steps as explained in point 7.4 to evaluate MR after grasping the leaflets with the additional clip.

REPRESENTATIVE RESULTS:

Percutaneous edge-to-edge valve repair is an alternative to surgical valve repair or replacement in patients not eligible for surgery with symptomatic severe MR. The first clinical application of the MitraClip was investigated in the Endovascular Valve Edge-to-Edge Repair Study I (EVEREST I)[14] trial. Many other trials have proven the effectiveness of the procedure with an improvement of symptoms as well as low rates of hospital mortality and adverse events (ACCESS EU, TRAMI, EVEREST II)[15,16,17]. Percutaneous edge-to-edge procedures have been incorporated into the European guidelines for the intervention of primary and secondary MR[18]. Two randomized trials MITRA-FR and COAPT compared the MitraClip procedure with optimal medical therapy and verified the feasibility of this intervention in patients with secondary MR. Although MITRA-FR did not show any significant benefit for the MitraClip group concerning the composite endpoint (all-cause mortality and rehospitalization for heart failure) at 12 months[19] (**Supplementary Figure 15**), COAPT showed significant superiority of the MitraClip in terms of mortality and rehospitalization rates, compared to the conservative treatment alone at 24 months[20] (**Supplementary Figure 16**). Compared with patients in the COAPT trial, those enrolled in the MITRA-FR trial had substantially more left ventricular damage and less severe MR due to the use of different classifications of MR (**Supplementary Figure 17**). To classify severe MR MITRA-FR used the 2012 European guidelines[21], whereas COAPT used the 2006/2008 American guidelines[22], which may explain the different outcomes observed in these two trials.

Since 2019, another device for transcatheter mitral valve repair has become available. Compared to the MitraClip device, the PASCAL system has wider paddles. It can independently grasp leaflets, as the fourth generation MitraClip, in the presence of a central spacer. After a multi-centre, prospective, observational, first-in-man study[23] and the multi-centre early-feasibility trial of the PASCAL transcatheter mitral repair device (CLASP study), the PASCAL repair system received CE mark approval for the treatment of both primary and secondary MR. The early feasibility study of the PASCAL repair system showed high survival, low complication rates as well as improvements in functional status and quality of life (**Supplementary Figure 18**). Furthermore, the CLASP study showed a significant reduction of the MR with this device. As there are no head-to-head studies available yet, the preferred device related to the valve anatomy (e.g., larger flail segments, large prolapse, cleft, short posterior leaflet, mitral annular calcification) is still not defined. A head-to-head comparison trial of the MitraClip with the Pascal System (CLASP IID trial) started in 2018 and the estimated primary completion date is expected to be in 2023.

A critical appraisal of echocardiographic assessment of MR, especially a functional one, is still to be done.

Because of its complex structure, the MV is altered by dynamic changes[24] and quantification of

MR requires an understanding of the normal valve anatomy. The echocardiographic guidelines for the quantification of native valvular regurgitation have been updated in 2017.[25] Official recommendations for the quantification of valve regurgitation after percutaneous valve repair have been available since 2019.[26] Due to missing validation of 2D vena contracta and EROA in multiple jets, neither 2D vena contracta nor EROA and regurgitant volume/fraction by PISA is recommended after PMVR (**Supplementary Figure 19**). Thresholds for 3D-VCA were first introduced and 3D-VCA gained a relevant role for the quantification of valve regurgitations which is superior to the 2D PISA method[27,28]. 3D-VCA is highly dependent on good image quality. Therefore, semi-quantitative parameters such as the signal intensity of the CW doppler of the MR-jet, the pulmonary vein flow pattern and the mitral inflow pattern are still necessary[29].

Although the utility of 3D-VCA has not yet been fully validated to assess MR, further development of 3D technologies will probably improve its value.

Continuous hemodynamic monitoring may complement transesophageal echocardiography to assess and optimize percutaneous edge-to-edge mitral valve repair. Previous studies demonstrate the value of real-time monitoring of LA pressure during PMVR[30,31,32,33]. An increase in left atrial mean pressure is predictive of worse clinical outcomes at short-term follow-up, independent from echocardiographic findings.

FIGURE AND TABLE LEGENDS:

Figure 1: Modified SAX view: PW flow in the left upper pulmonary vein

Figure 2: 2D biplanar view of the MV with color doppler: medial insufficiency jet

Figure 3: Multiplanar reconstruction of the 3D dataset with color doppler: 3D-Vena contracta

Figure 4: Wide sector zoom image: 3D en-face surgical atrial view (aortic valve at 12 o'clock)

Figure 5: Wide sector zoom image: 3D en-face atrial view (aortic valve at 6 o'clock)

Figure 6: 2D biplanar view: transseptal puncture

Figure 7: Wide sector zoom image: SGC in the LA including the interatrial septum, the left lateral ridge and the MV

Figure 8: 2D biplanar view of the MV: positioning of the device over the mitral valve

Figure 9: Wide sector zoom image: positioning of the device over the mitral valve

Figure 10: Wide sector zoom image: double orifice of the MV after device deployment

Supplementary Figure 1: Modified bicaval view: PW flow in the right upper pulmonary vein

Supplementary Figure 2: 2D biplanar view of the MV: length of the PML

Supplementary Figure 3: Multiplanar reconstruction of the 3D dataset: mitral valve area in 3D

Supplementary Figure 4: 2D biplanar view of the MV with color doppler: medially implanted device and residual lateral insufficiency jet

Supplementary Figure 5: 4Ch view: puncture height

Supplementary Figure 6 SAX view in 2D: SGC with echo bright double ring

Supplementary Figure 7: 2D biplanar view of the MV: advancement of the CDS into the LA

Supplementary Figure 8: Wide sector zoom image: advancement of the CDS into the LA

Supplementary Figure 9: 2D biplanar view of the MV: grasping of the leaflets

Supplementary Figure 10: 2D biplanar view of the MV with color doppler: residual insufficiency jets

Supplementary Figure 11: LAX in 2D: transmitral pressure gradient before device deployment

Supplementary Figure 12: Intercommissural view in 2D: transmitral pressure gradient after device deployment

Supplementary Figure 13: 2D biplanar view of the MV: delivery catheter tip

Supplementary Figure 14: Multiplanar reconstruction of the 3D dataset with color doppler: 3D-VCA after device deployment

Supplementary Figure 15: MITRA-FR Trial: Kaplan–Meier Estimates of Survival without a Primary Outcome Event

Supplementary Figure 16: COAPT Trial: Primary Effectiveness and Safety End Points and Death

Supplementary Figure 17: MITRA-FR vs. COAPT: Similarities and differences between MITRAFR and COAPT with respect to baseline characteristics of the study populations

Supplementary Figure 18: CLASP Study: Functional and Clinical Paired Analyses at Baseline and 30 Days for the PASCAL Transcatheter Valve Repair System

Supplementary Figure 19: Guidelines for the Evaluation of Valvular Regurgitation After Supplementary Percutaneous Valve Repair or Replacement: Echocardiographic parameters and related comments in the assessment of MR severity with TTE after transcatheter MV interventions

DISCUSSION:

Echo-guidance for the PMVR is a safe method. Complications due to echocardiography may occur but rarely lead to significant damage. Nevertheless, esophageal lesions are possible after performing transesophageal echocardiography. This incidence is reduced with a shorter duration of the intervention[34]. On the contrary, several complications associated with the transcatheter edge-to-edge mitral valve repair are described[35,36]. Major bleeding is the most frequent major complication and blood transfusion after transcatheter valve procedures have been strongly associated with mortality[37]. Pericardial tamponade is rare and may occur during several steps of the procedure. Caution during transseptal puncture, insertion of the SGC into the left atrium and retrieving of the SGC-tip after clip deployment reduces the probability of this life-threatening complication. Rates of clip-specific complications, as embolization and partial clip detachment, are low and can be reduced by an accurate echocardiographic assessment during and after grasping of the leaflets.

Despite the carefulness during echocardiography, aggravation of the MR, may occur. Additional clip deployment in the medial and lateral position may increase the risk of entangling and rupturing of the chordae[38]. Furthermore, repeated grasping of the leaflets can lead to leaflet laceration and perforation. Residual MR is not only a determinant of procedural success but is also associated with poorer prognosis[39,40], especially when there is a concomitant transmitral pressure gradient >5 mm Hg[41,42]. Clear communication with the interventionist and a meticulous echocardiographic assessment are necessary to reduce peri-procedural clip-related complications.

The percutaneous edge-to-edge repair is not eligible for every pathomechanism of MR. For some determinants of MR, such as annulus dilatation, rupture of the chordae tendinae or severe calcifications of the mitral leaflets, the device reaches its limits. In this case, mitral ring dilation can be sutured surgically or percutaneously in place to provide annular stabilization. Polytetrafluoroethylene (PTFE) neochordae can be surgically sewed as new chordae tendinee. A MV with severe calcified leaflets may be replaced with a prosthetic valve. New percutaneous devices designed to address these aspects are under development.

A structured echocardiographic approach for the PMVR is mandatory. Several techniques of how to perform echoguidance for the PMVR procedure have been described[43,44,45,46,47,48.] In our opinion, it is important to define a detailed sequence of steps together with the interventionist, which should be performed during every intervention. Although the 3D en-face view is defined showing the aortic valve at 12 o'clock, many centres prefer the "cardiologist" 3D en-face view, which shows the aortic valve at 6 o'clock. There is no literature comparing both views during the PMVR. Several options for the assessment of specific views in 2D or 3D as well as for the quantification of MR are available. 3D transesophageal echocardiography allows the measurement of each orifice after edge-to-edge repair. The guidelines propose thresholds for 3D-VCA as $<0,2 cm^2$ for mild, $0,2-0,39\ cm^2$ for moderate and $\geq 0,4\ cm^2$ for severe regurgitation[26]. Previous studies have shown that improvement of clinical symptoms correlates to a significant reduction of the 3D-VCA, independently from an absolute value[49]. Furthermore, reduction of left atrial and ventricular volume is significantly greater in patients who show a reduction in 3D-VCA of more than a 50% after MV repair[50]. Our experience confirms this data. Nevertheless, the percentual reduction of the 3D-VCA required to significantly improve a severe MR has not been defined. Further validation of this method is needed and the assessment of other parameters for the adequate evaluation of residual MR remains indispensable. Due to possible mild mitral stenosis caused after clip implantation, the MV inflow pattern rarely gives additional information to the MR reduction. On the contrary, the pulmonary flow pattern is a reliable parameter and predicts recurrent MR and worse long-term outcomes.

In conclusion, percutaneous transcatheter mitral valve repair is fully dependent on transesophageal echocardiography. Both, the imager and the interventionist should have a fundamental understanding of echocardiographic assessment to achieve a successful and safe procedure.

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DISCLOSURES:
The authors have nothing to disclose.

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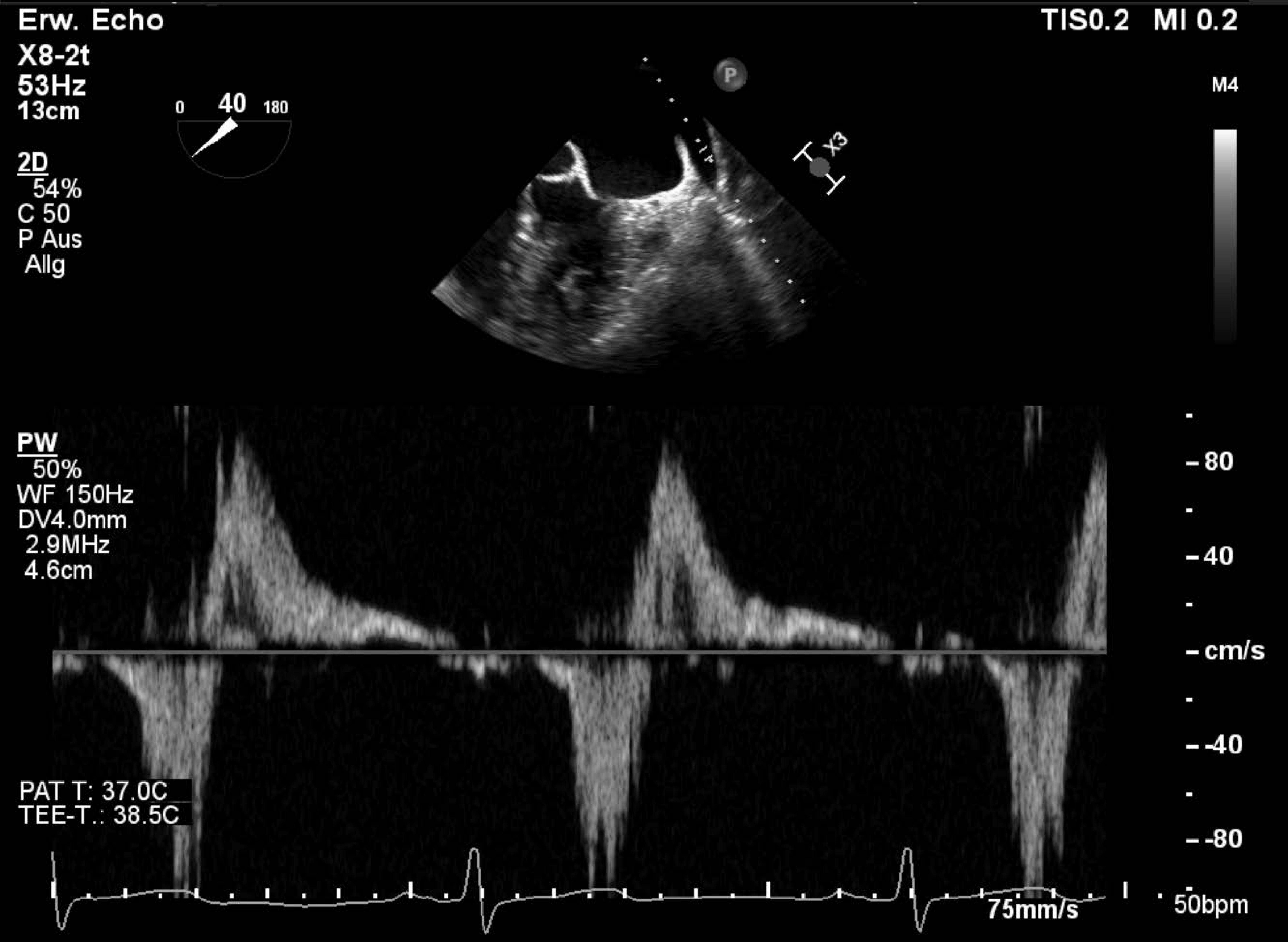
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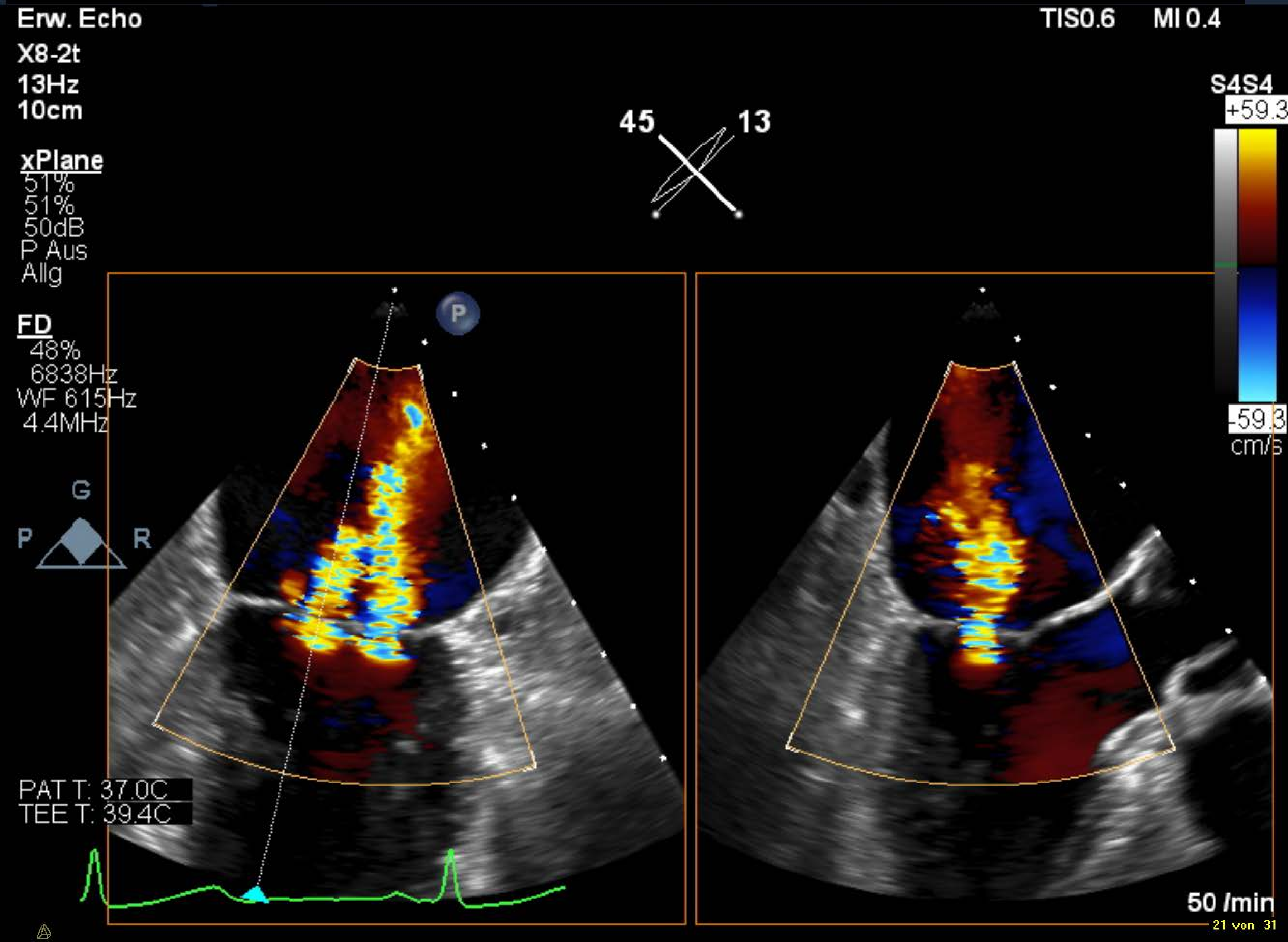
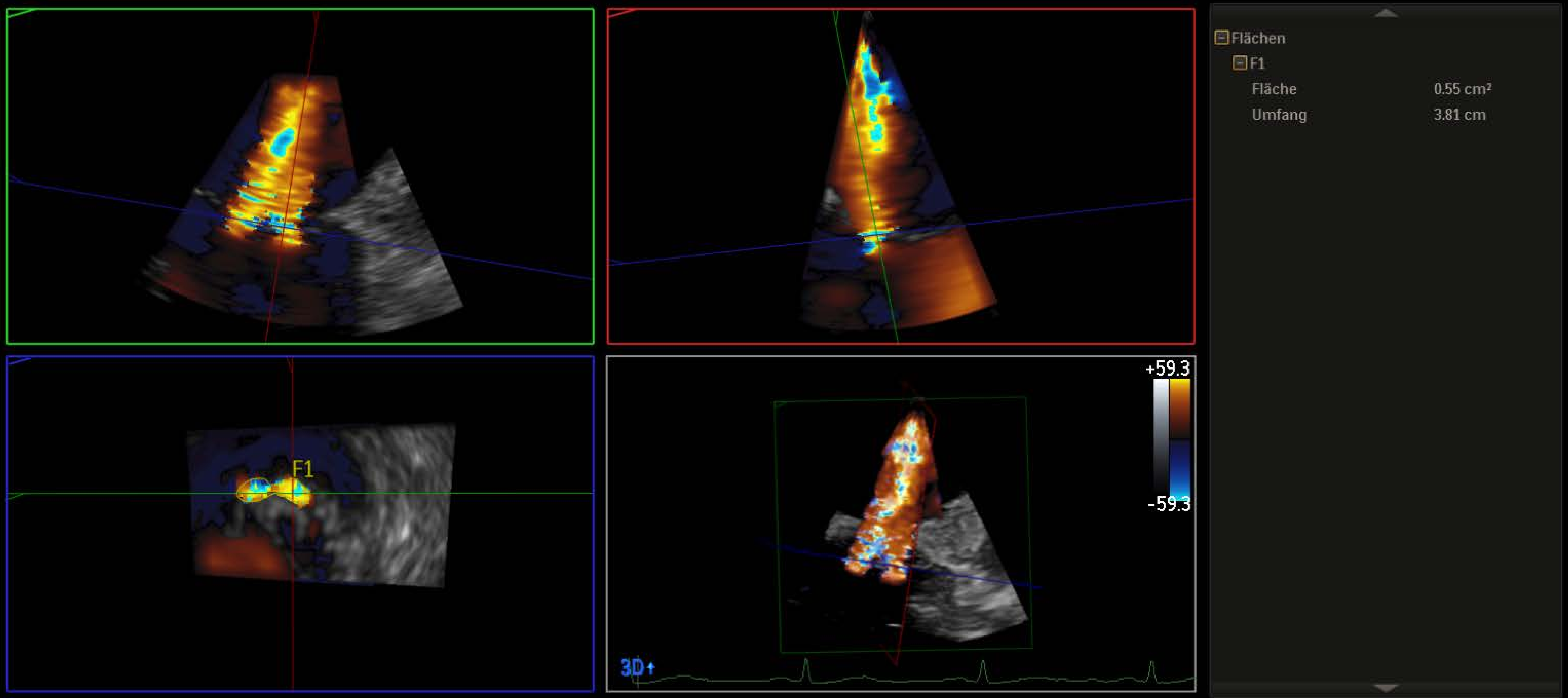
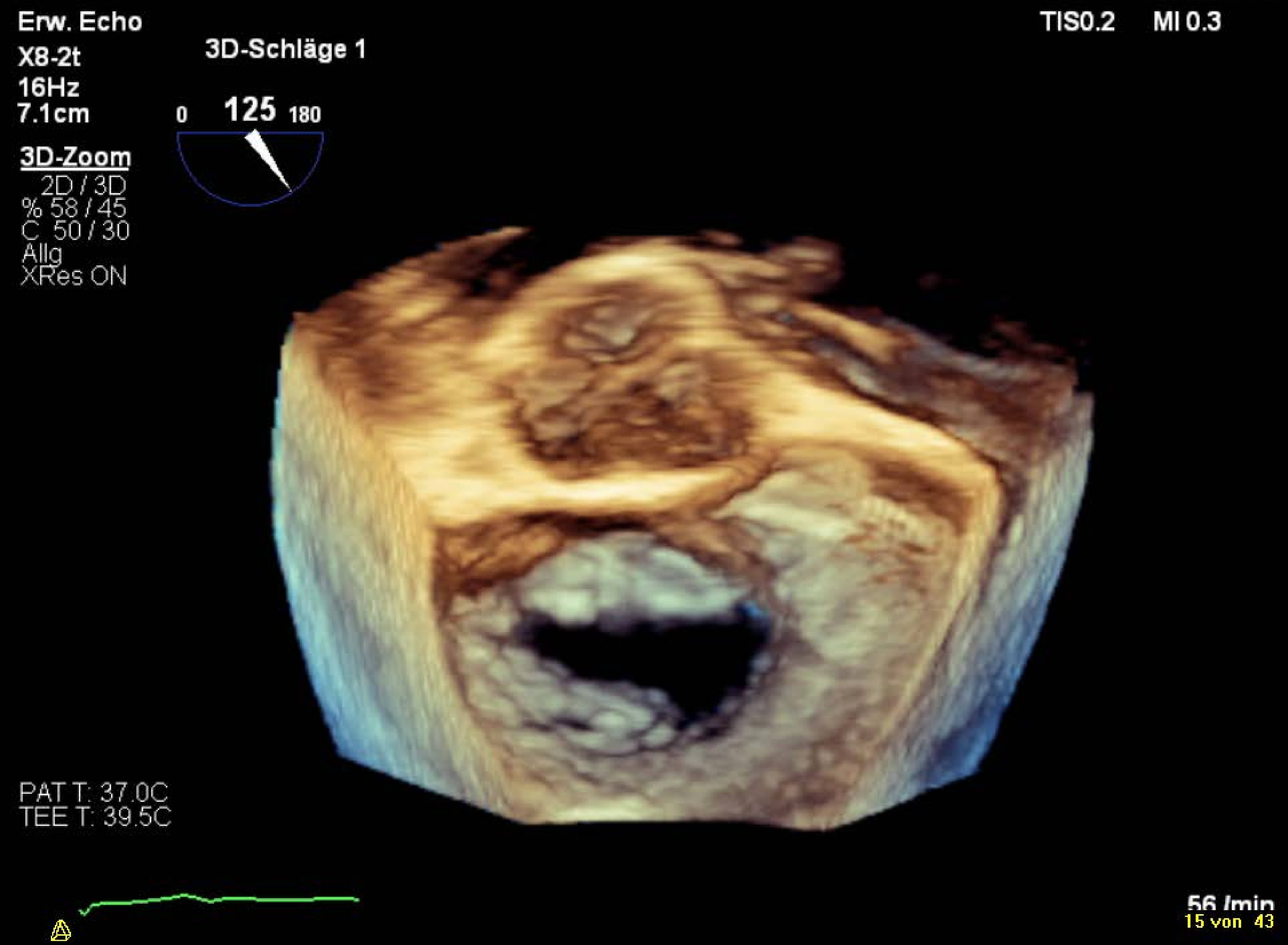
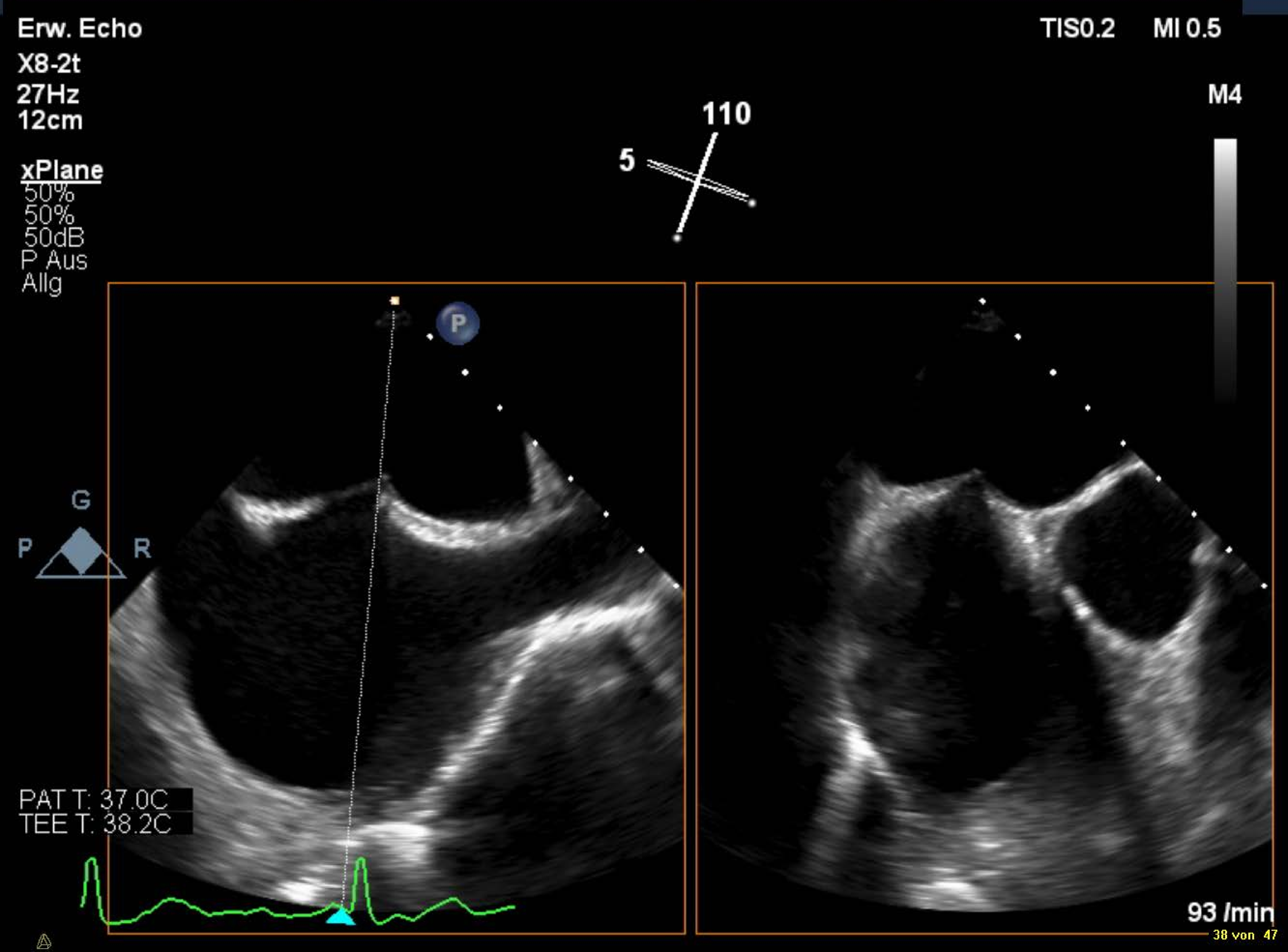
X8-2t
53Hz
13cm
0
40
180
TIS0.2 MI 0.2
P
X3
M4
2D
54%
C 50
P Aus
Allg
PW
50%
WF 150Hz
DV4.0mm
2.9MHz
4.6cm
80
40
cm/s
-40
-80
PAT T: 37.0C
TEE-T.: 38.5C
75mm/s
50bpm


Erw. Echo
X8-2t
13Hz
10cm
TIS0.6
MI 0.4
S4S4
+59.3
45
13
xPlane
51%
51%
50dB
P Aus
Allg
FD
48%
6838Hz
WF 615Hz
4.4MHz
-59.3
cm/s
G
P
R
P
PAT T: 37.0C
TEE T: 39.4C
50 /min
21 von 31

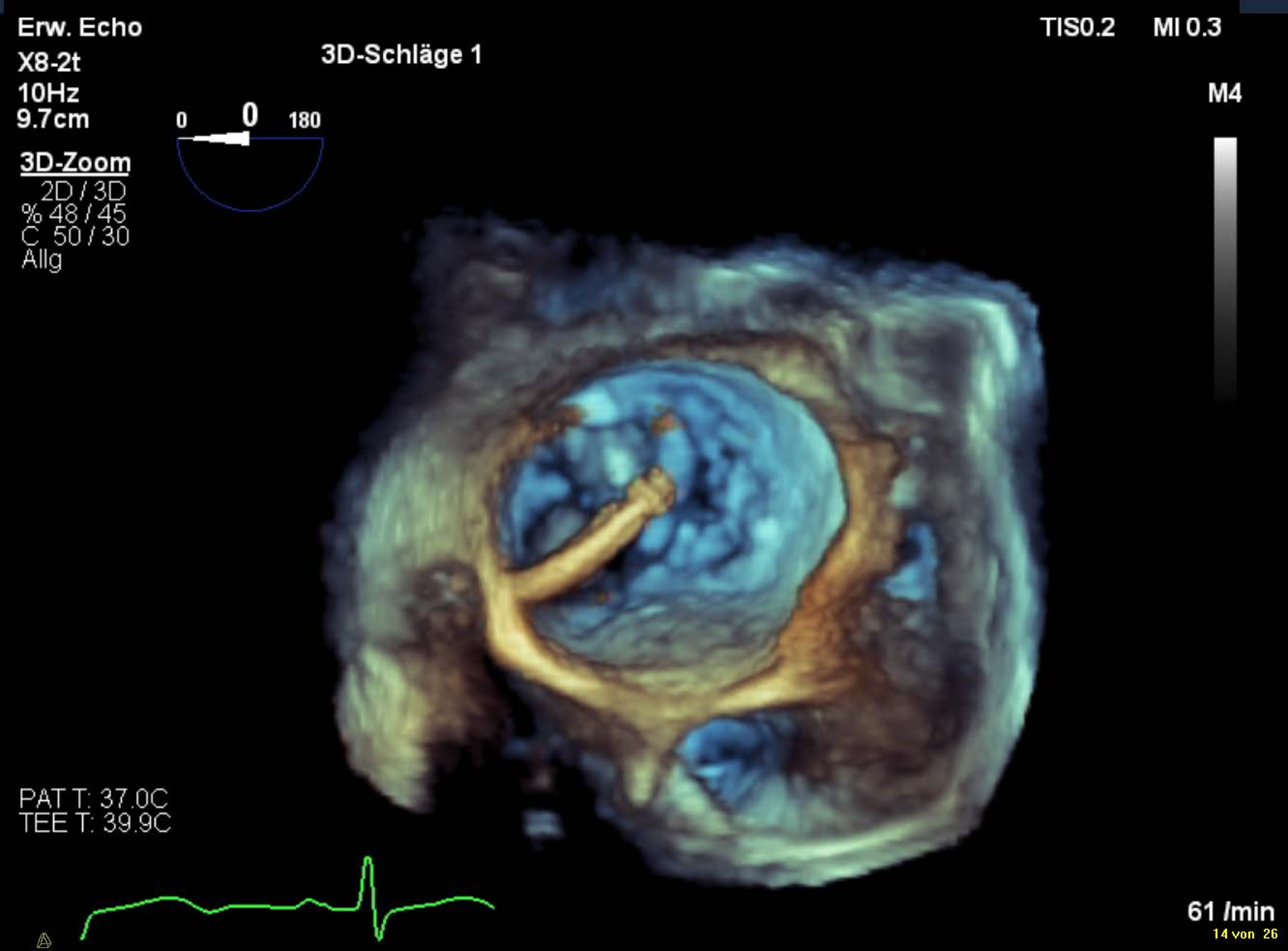

F1
+59.3
-59.3
3D
Flächen
F1
Fläche 0.55 cm²
Umfang 3.81 cm


JPEG CR 15:1
Erw. Echo
X8-2t
16Hz
7.1cm
3D-Schläge 1
0
125
180
TIS0.2
MI 0.3
3D-Zoom
2D / 3D
% 58 / 45
C 50 / 30
Allg
XRes ON
PAT T: 37.0C
TEE T: 39.5C
56 /min
15 von 43


Erw. Echo
X8-2t
16Hz
7.1cm
3D-Schläge 1
0
125
180
TIS0.2
MI 0.3
3D-Zoom
2D / 3D
% 53 / 45
C 50 / 30
Allg
XRes ON
medial
lateral
aortic valve
PAT T: 37.0C
TEE T: 39.7C
58 /min
7 von 27



Erw. Echo
X8-2t
27Hz
12cm
xPlane
50%
50%
50dB
P Aus
Allg
TIS0.2
MI 0.5
M4
110
5
P
G
P
R
PAT T: 37.0C
TEE T: 38.2C
93 /min
38 von 47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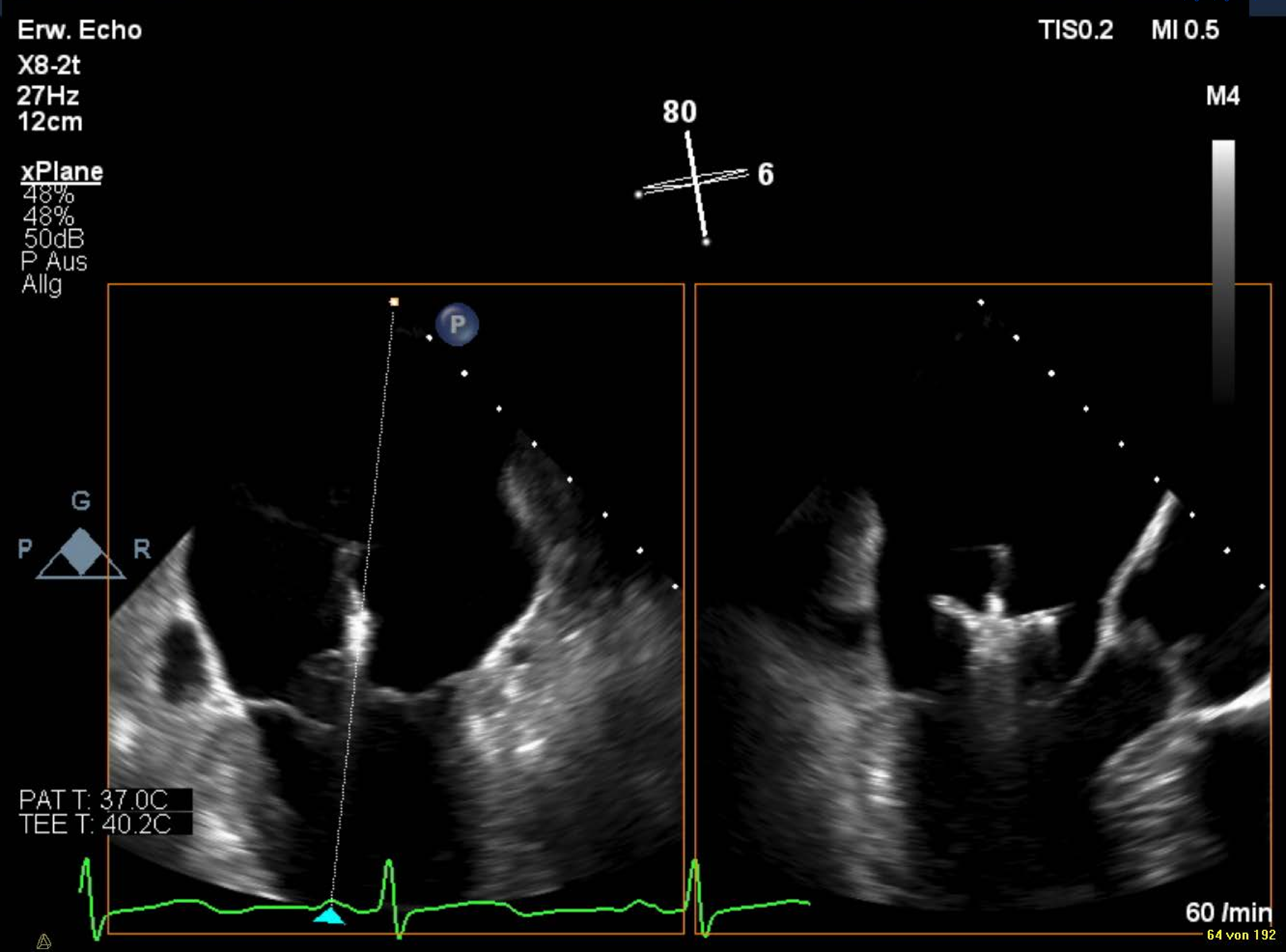
X8-2t
10Hz
9.7cm
3D-Schläge 1
0
0
180
3D-Zoom
2D / 3D
% 48 / 45
C 50 / 30
Allg
TIS0.2
MI 0.3
M4
PAT T: 37.0C
TEE T: 39.9C
61 /min
14 von 26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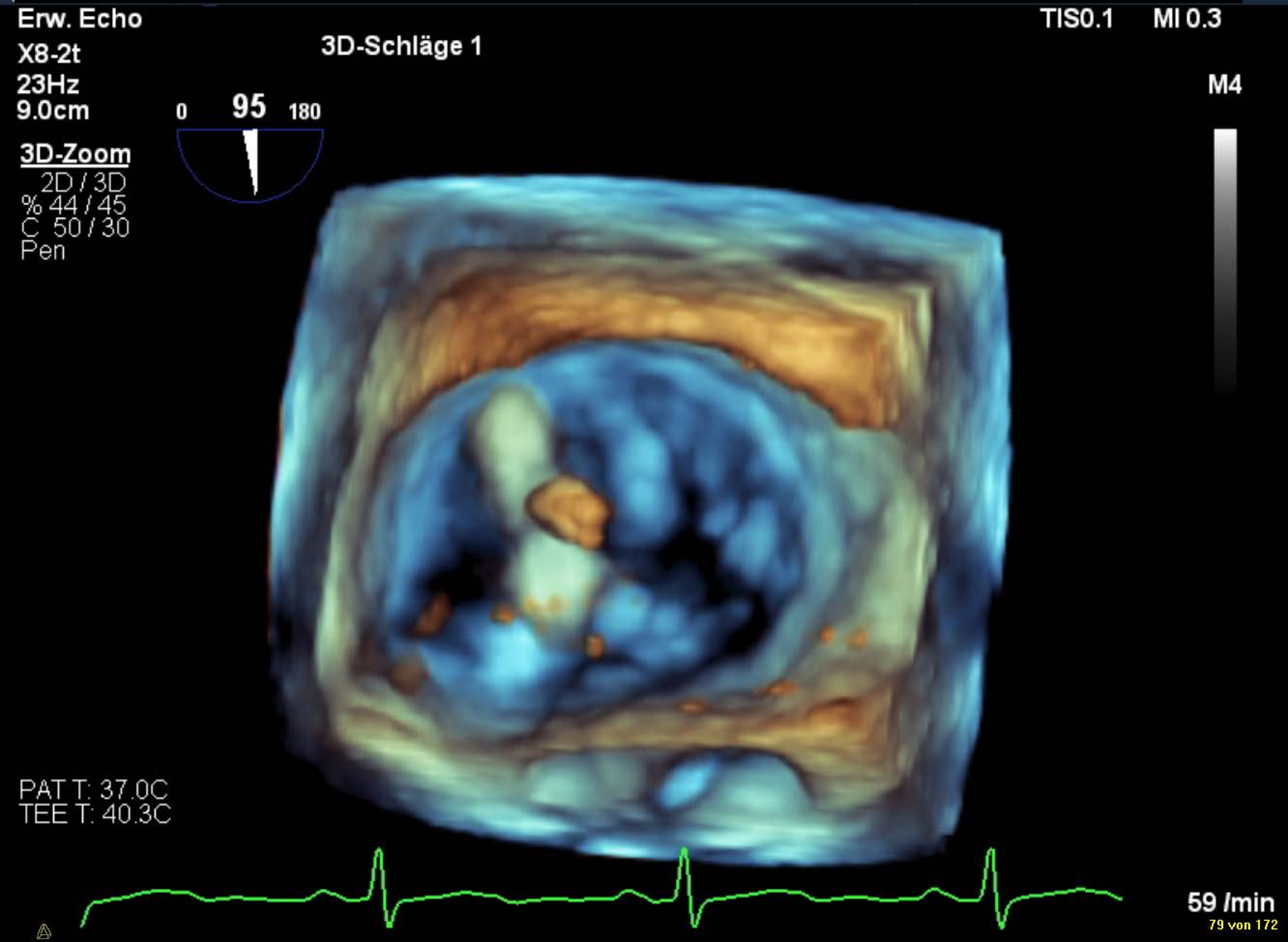
X8-2t
27Hz
12cm
xPlane
48%
48%
50dB
P Aus
Allg
TIS0.2
MI 0.5
M4
80
6
P
G
P
R
PAT T: 37.0C
TEE T: 40.2C
60 /min
64 von 192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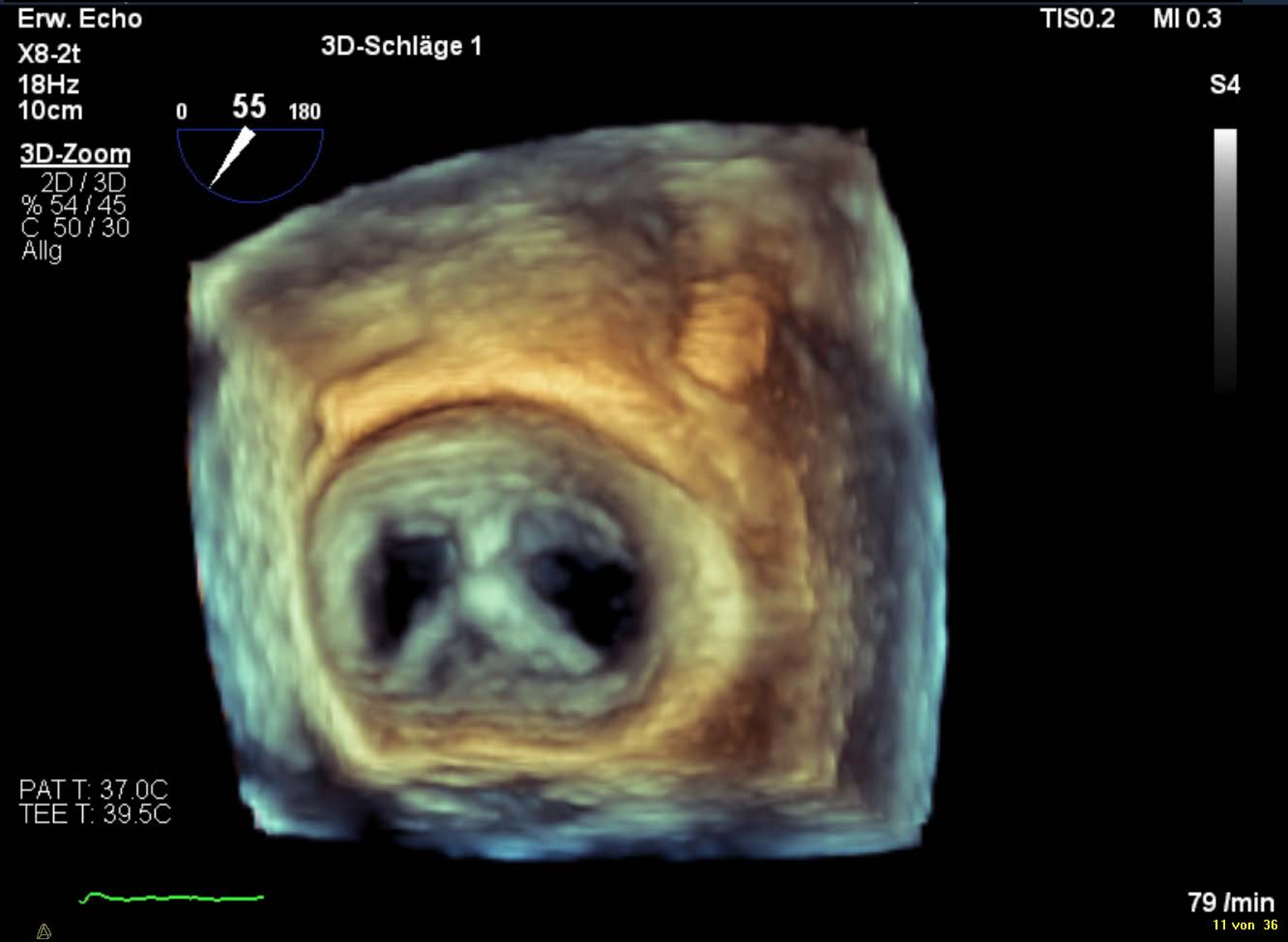
X8-2t
23Hz
9.0cm
3D-Schläge 1
0
95
180
3D-Zoom
2D / 3D
% 44 / 45
C 50 / 30
Pen
TIS0.1
MI 0.3
M4
PAT T: 37.0C
TEE T: 40.3C
59 /min
79 von 172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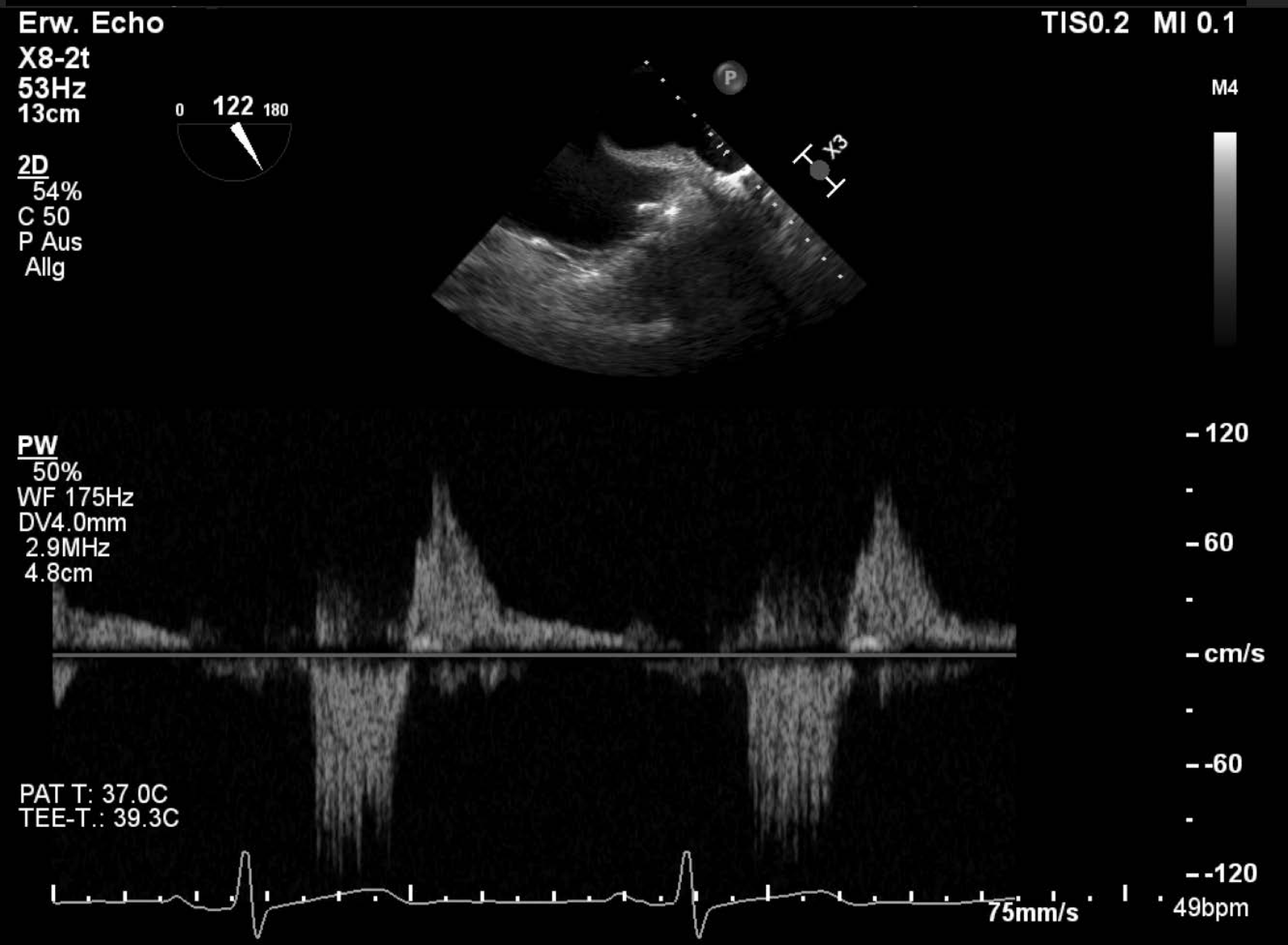
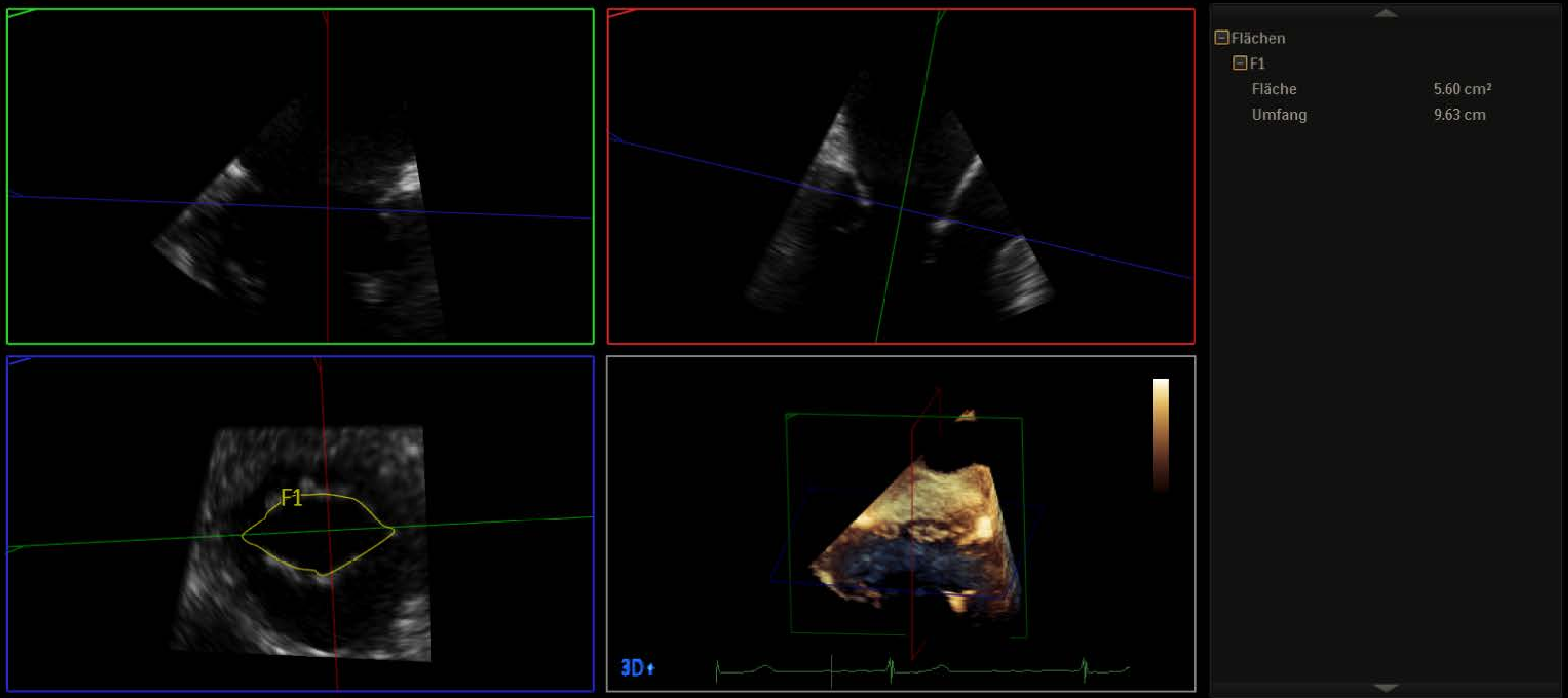
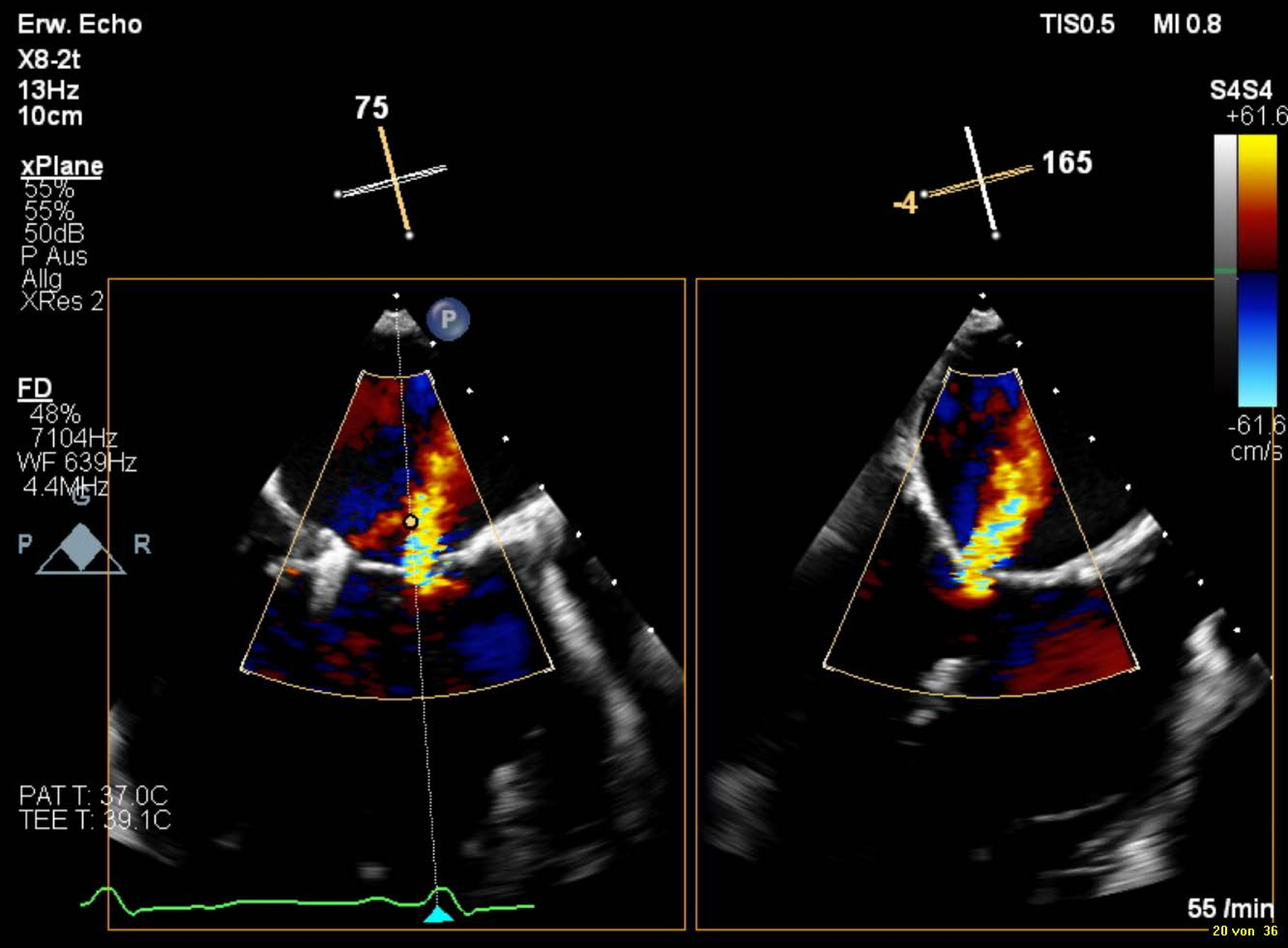
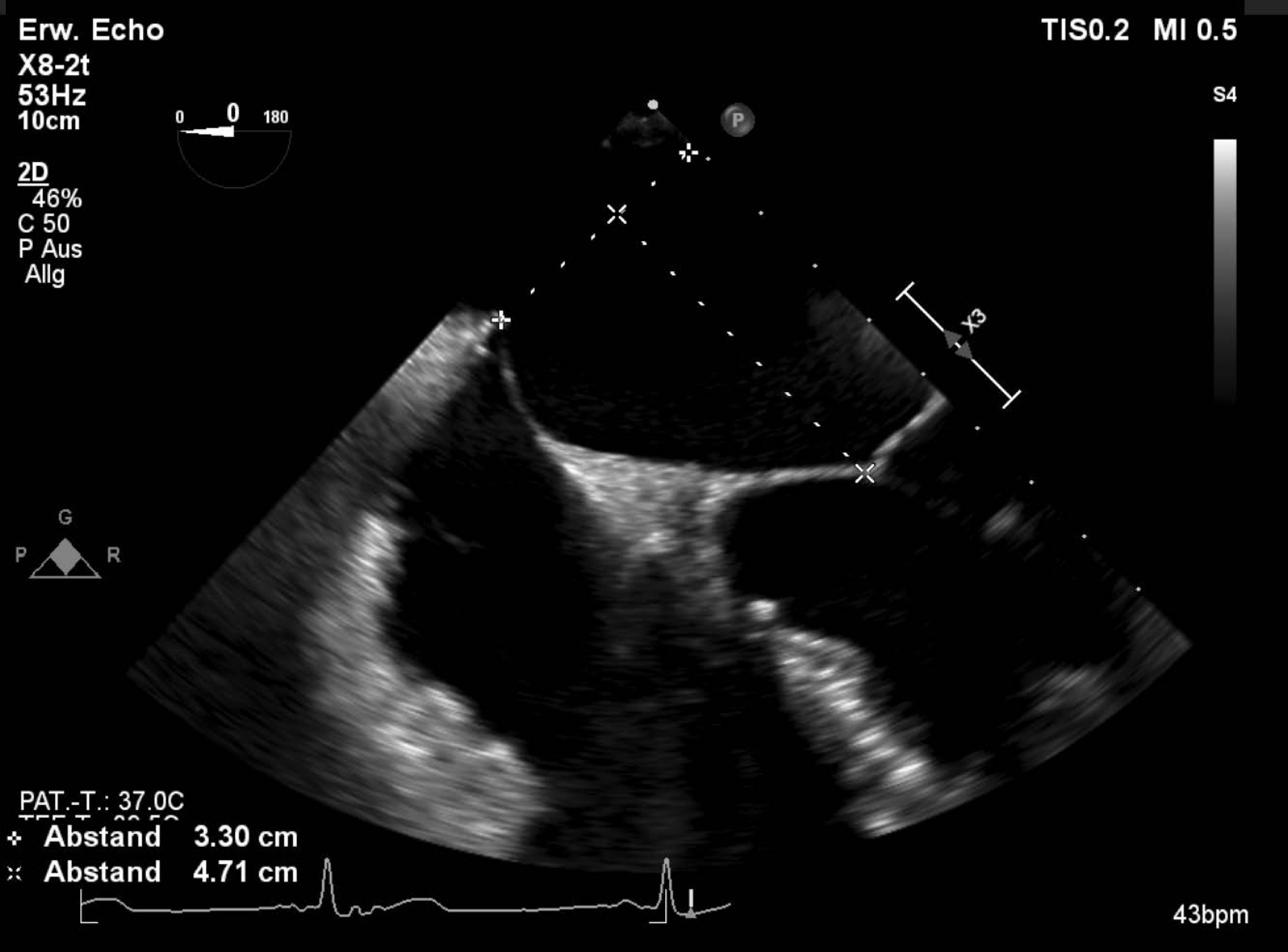
X8-2t
18Hz
10cm
3D-Schläge 1
TIS0.2
MI 0.3
S4
0
55
180
3D-Zoom
2D / 3D
% 54 / 45
C 50 / 30
Allg
PAT T: 37.0C
TEE T: 39.5C
79 /min
11 von 36

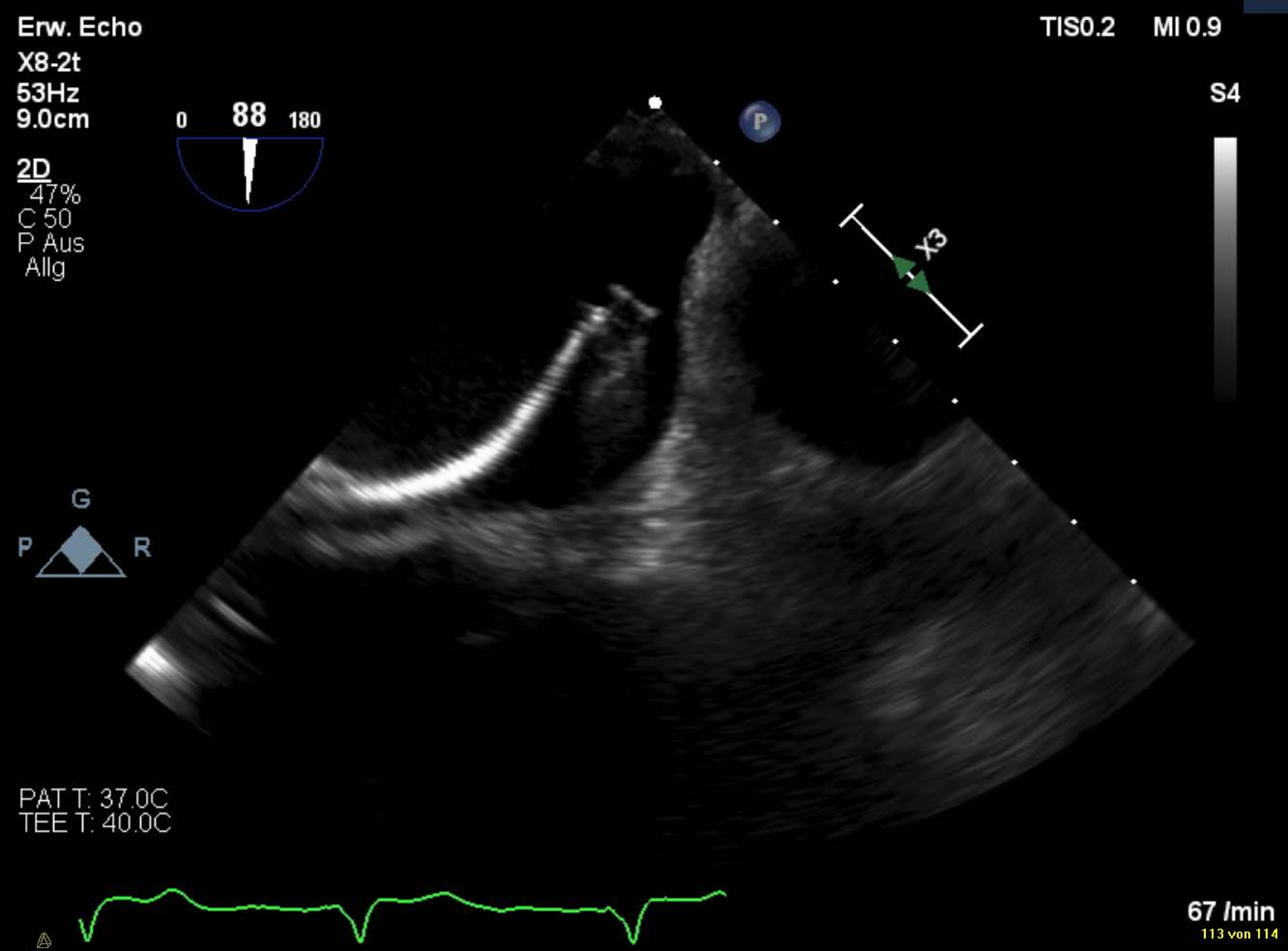

Erw. Echo
X8-2t
53Hz
13cm
0 122 180
2D
54%
C 50
P Aus
Allg
TIS0.2 MI 0.1
P
X3
M4
PW
50%
WF 175Hz
DV4.0mm
2.9MHz
4.8cm
PAT T: 37.0C
TEE-T.: 39.3C
120
60
cm/s
-60
-120
75mm/s
49bpm

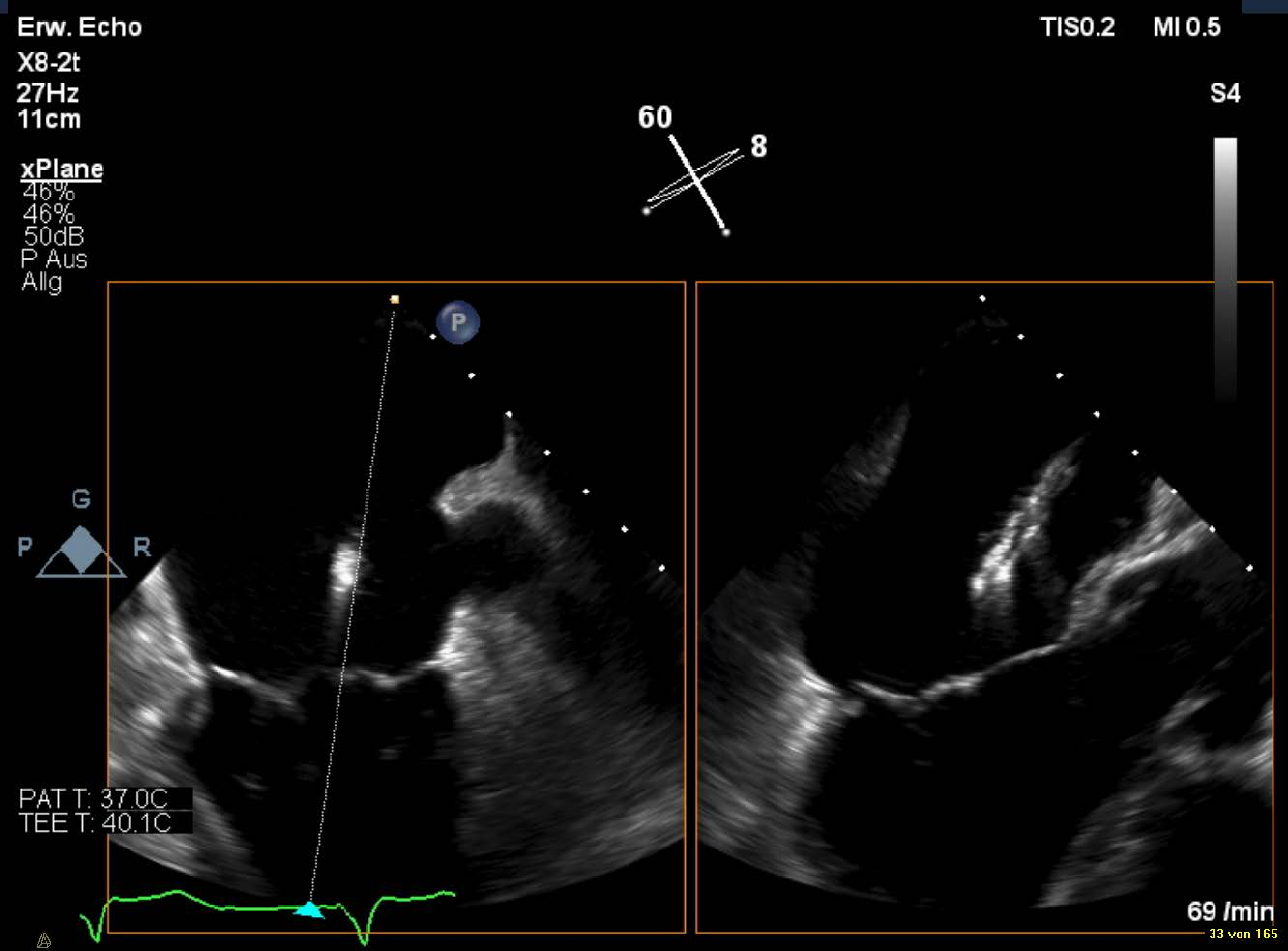

Erw. Echo
X8-2t
27Hz
9.0cm
xPlane
45%
45%
50dB
P Aus
Allg
TIS0.2 MI 0.5
S4
40
7
P
G
P
R
PAT.-T.: 37.0C
TEE-T.: 38.9C
Abstand 1.00 cm
51bpm

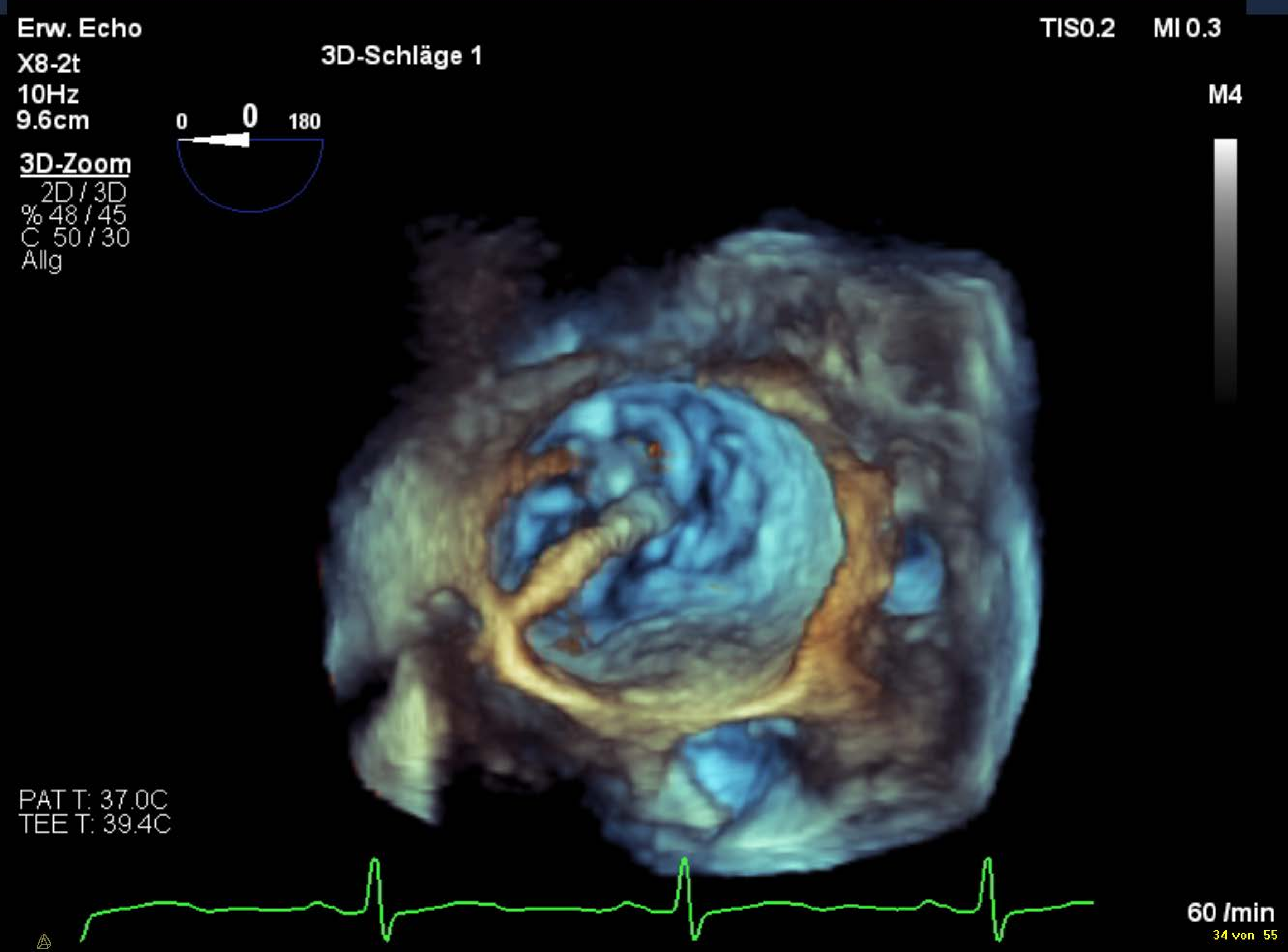

Flächen
F1
Fläche 5.60 cm²
Umfang 9.63 cm
F1
3D


Erw. Echo
X8-2t
13Hz
10cm
xPlane
55%
55%
50dB
P Aus
Allg
XRes 2
FD
48%
7104Hz
WF 639Hz
4.4MHz
P
R
PAT T: 37.0C
TEE T: 39.1C
75
165
-4
TIS0.5
MI 0.8
S4S4
+61.6
-61.6
cm/s
55 /min
20 von 36


Erw. Echo
X8-2t
53Hz
10cm
0
0
180
2D
46%
C 50
P Aus
Allg
TIS0.2 MI 0.5
S4
P
X3
G
P
R
PAT.-T.: 37.0C
Abstand 3.30 cm
Abstand 4.71 cm
43bpm


Erw. Echo
X8-2t
53Hz
9.0cm
0
88
180
2D
47%
C 50
P Aus
Allg
TIS0.2
MI 0.9
S4
P
X3
G
P
R
PAT T: 37.0C
TEE T: 40.0C
67 /min
113 von 114


Erw. Echo
X8-2t
27Hz
11cm
xPlane
46%
46%
50dB
P Aus
Allg
TIS0.2 MI 0.5
S4
60
8
P
G
P R
PAT T: 37.0C
TEE T: 40.1C
69 /min
33 von 165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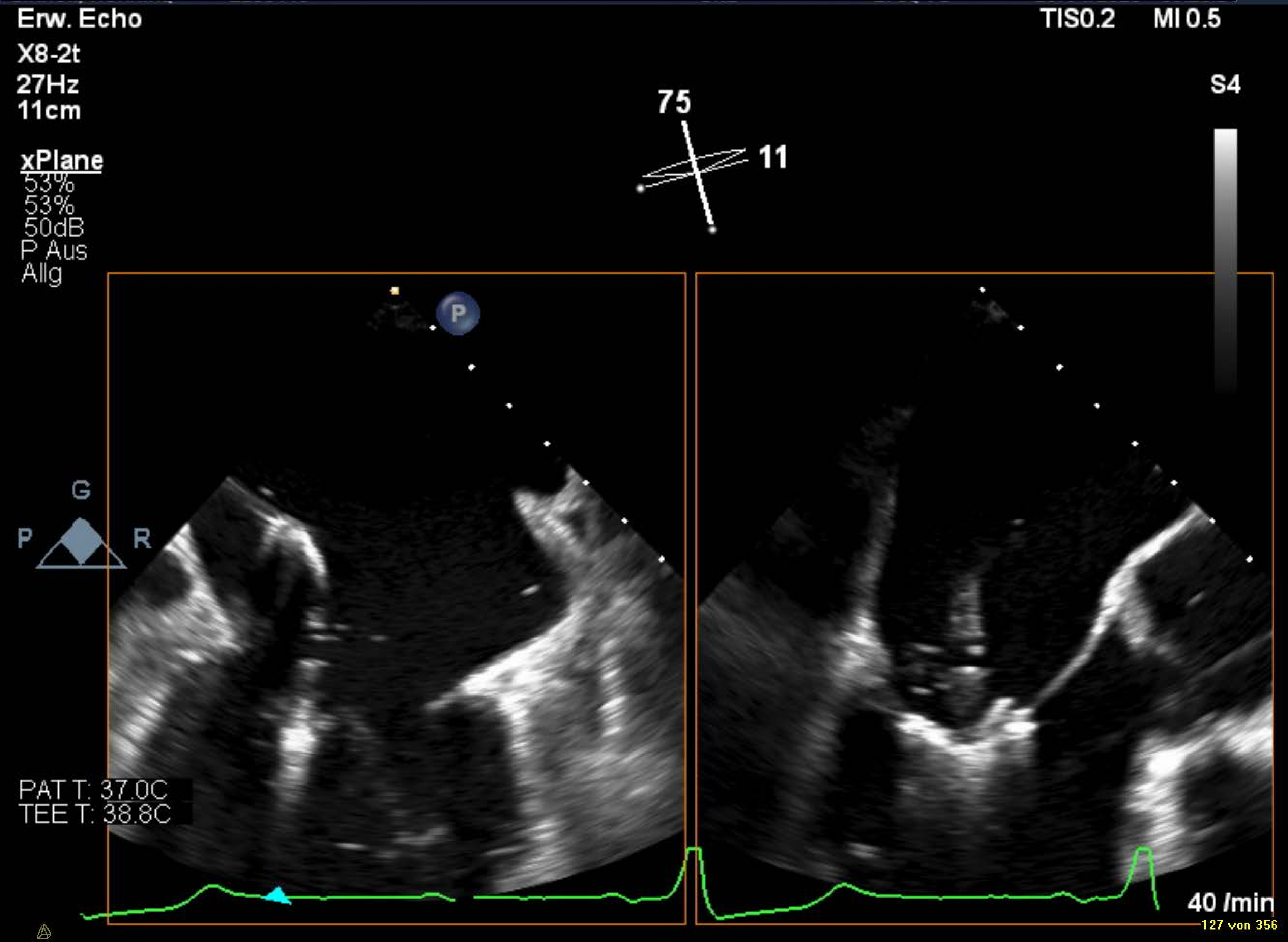
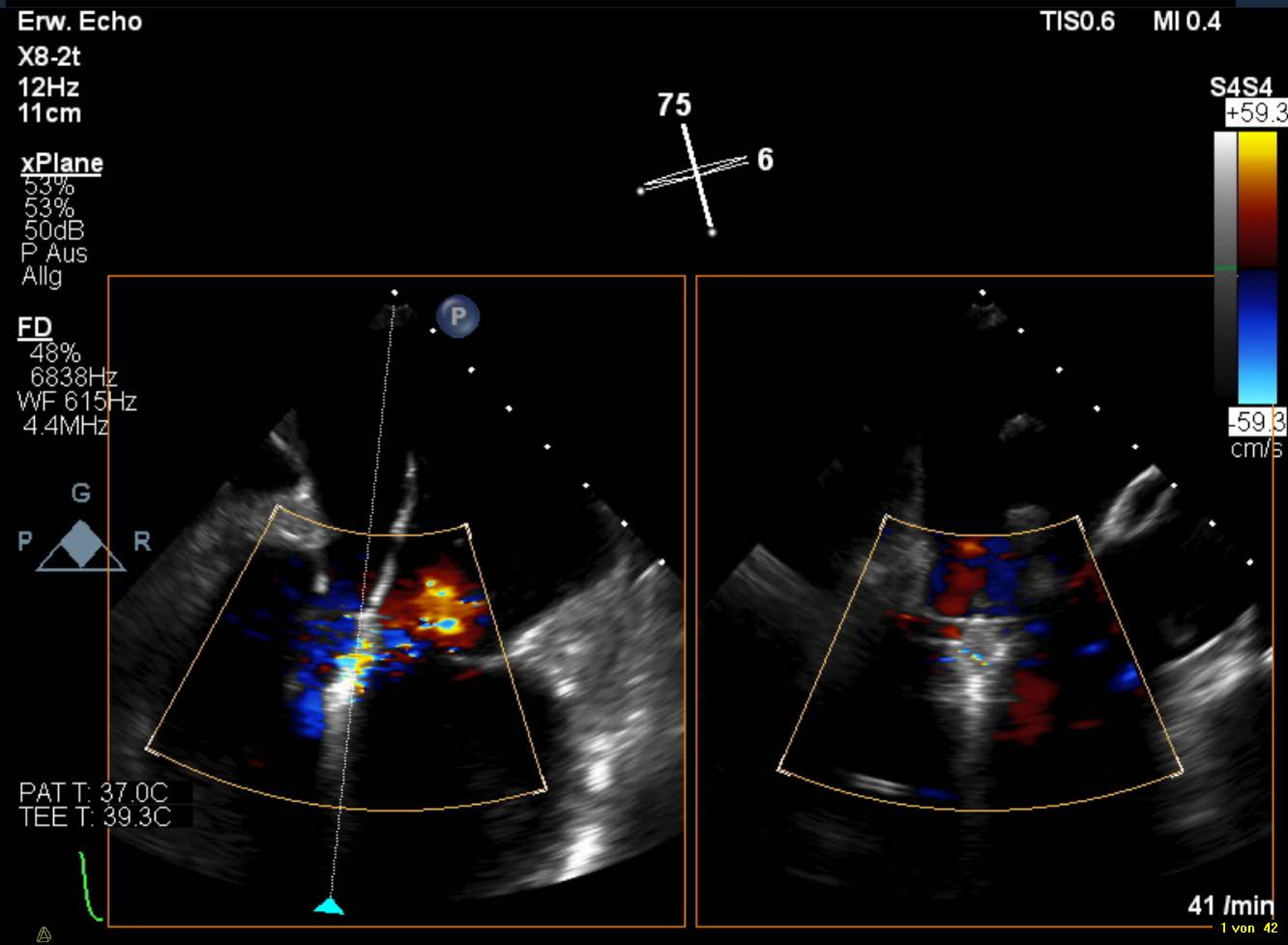
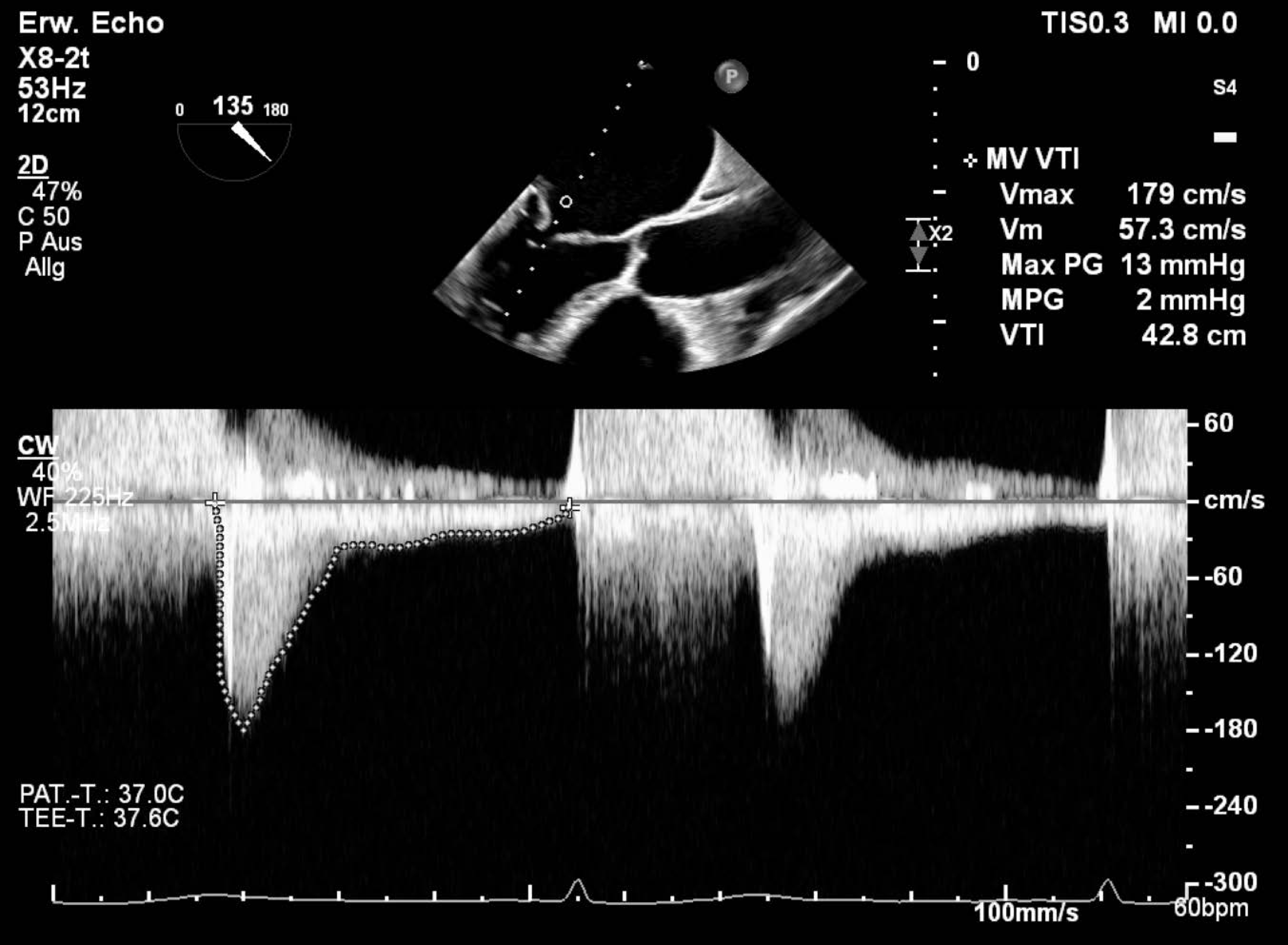
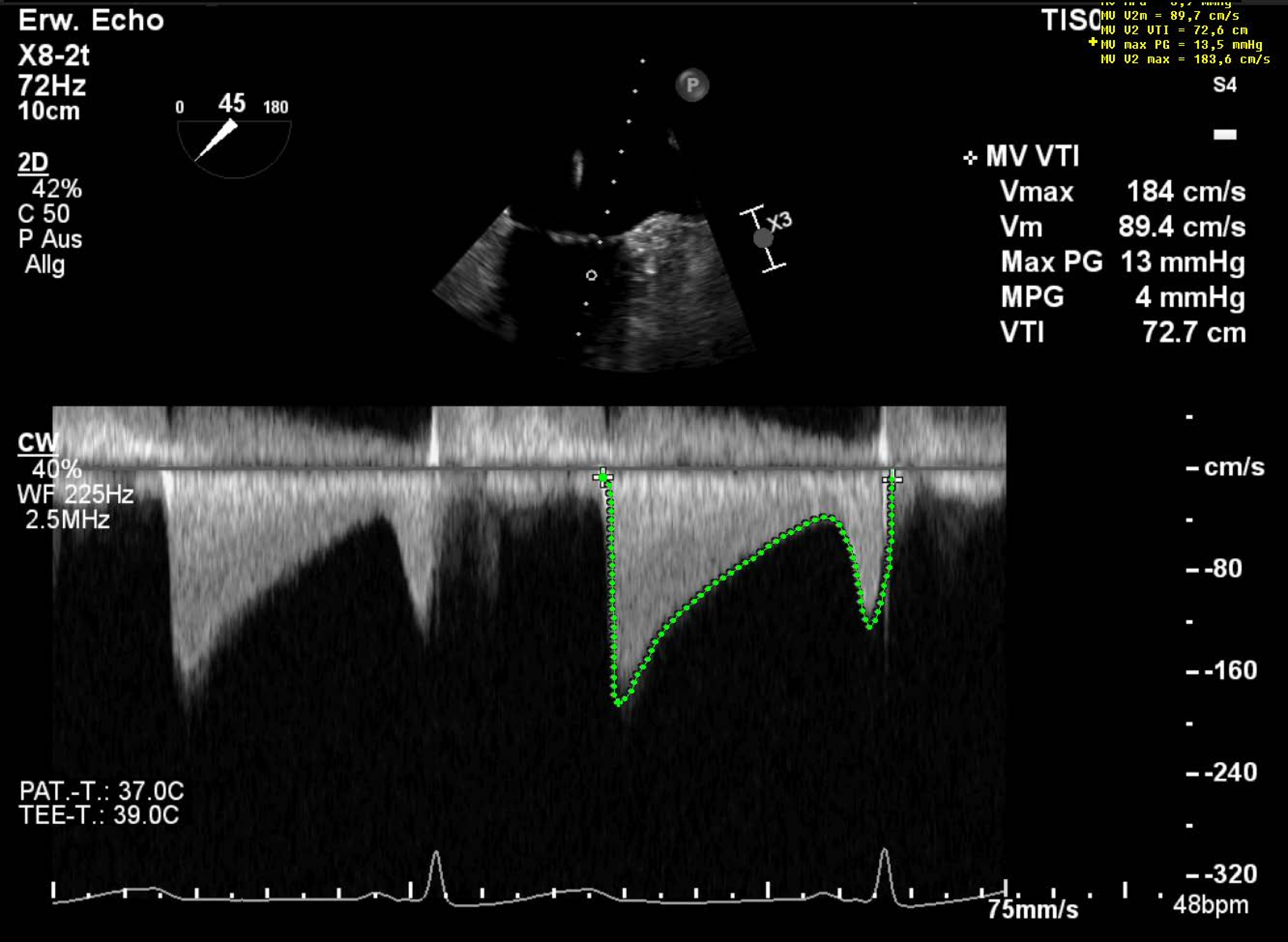
X8-2t
10Hz
9.6cm
3D-Schläge 1
0
0
180
TIS0.2
MI 0.3
M4
3D-Zoom
2D / 3D
% 48 / 45
C 50 / 30
Allg
PAT T: 37.0C
TEE T: 39.4C
60 /min
34 von 55

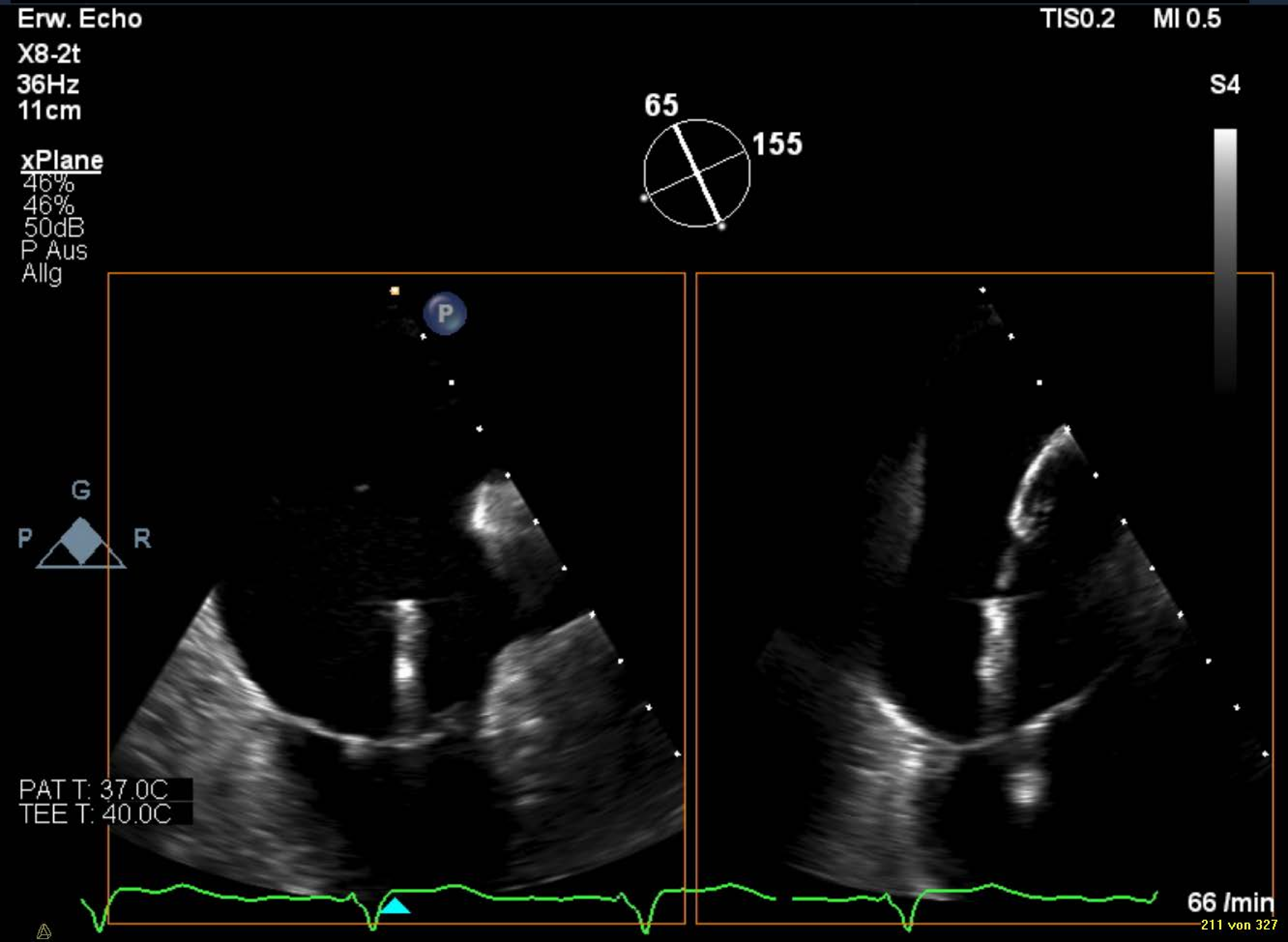


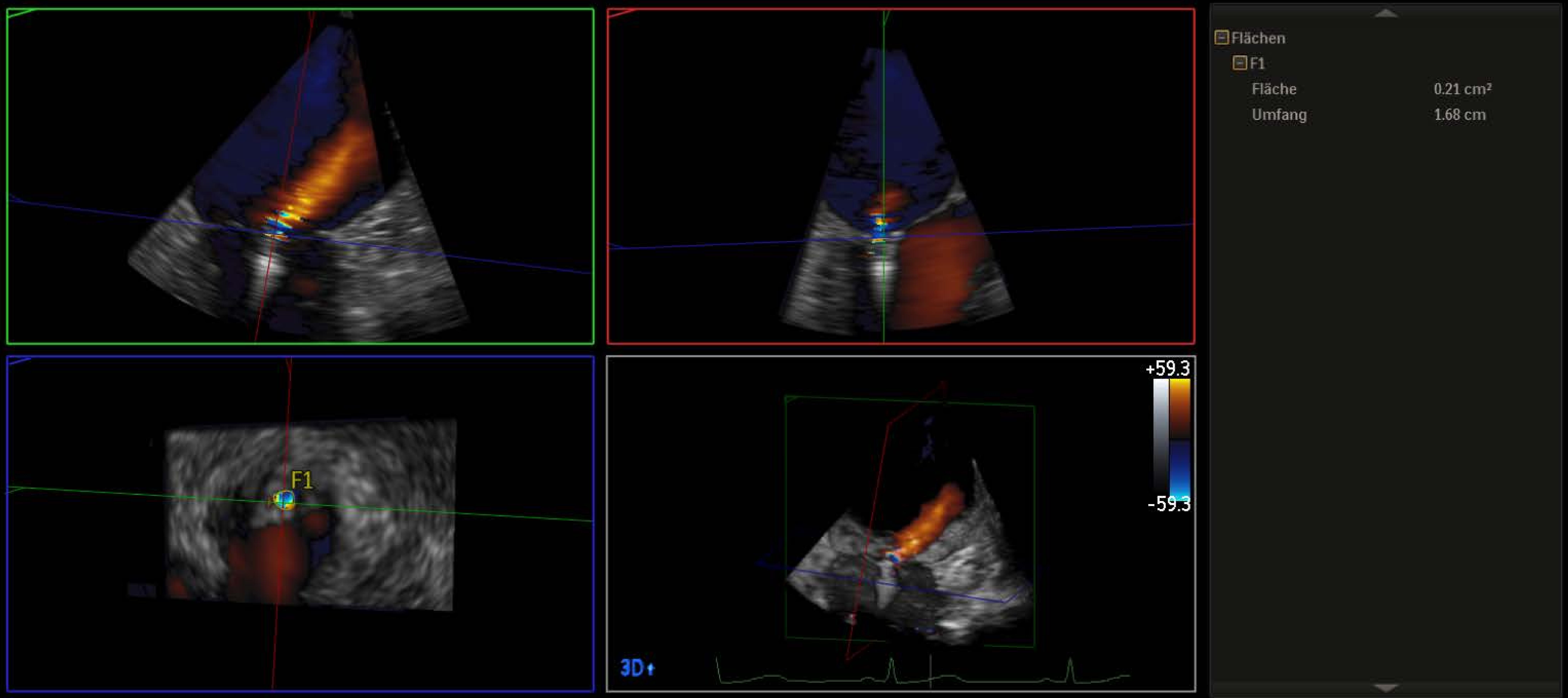
Erw. Echo
X8-2t
27Hz
11cm
xPlane
53%
53%
50dB
P Aus
Allg
TIS0.2
MI 0.5
S4
75
11
G
P
R
PAT T: 37.0C
TEE T: 38.8C
40 /min
127 von 356


Erw. Echo
X8-2t
12Hz
11cm
xPlane
53%
53%
50dB
P Aus
Allg
FD
48%
6838Hz
WF 615Hz
4.4MHz
G
P
R
PAT T: 37.0C
TEE T: 39.3C
TIS0.6
MI 0.4
75
6
S4S4
+59.3
-59.3
cm/s
P
41 /min
1 von 42


Erw. Echo
X8-2t
53Hz
12cm
0 135 180
2D
47%
C 50
P Aus
Allg
TIS0.3 MI 0.0
S4
MV VTI
Vmax 179 cm/s
Vm 57.3 cm/s
Max PG 13 mmHg
MPG 2 mmHg
VTI 42.8 cm
X2
CW
40%
WF 225Hz
2.5MHz
60
cm/s
-60
-120
-180
-240
-300
PAT.-T.: 37.0C
TEE-T.: 37.6C
100mm/s
60bpm


Erw. Echo
X8-2t
72Hz
10cm
0
45
180
2D
42%
C 50
P Aus
Allg
TIS0
MV V2m = 89,7 cm/s
MV V2 VTI = 72,6 cm
MV max PG = 13,5 mmHg
MV V2 max = 183,6 cm/s
S4
P
X3
MV VTI
Vmax 184 cm/s
Vm 89.4 cm/s
Max PG 13 mmHg
MPG 4 mmHg
VTI 72.7 cm
CW
40%
WF 225Hz
2.5MHz
cm/s
-80
-160
-240
-320
PAT.-T.: 37.0C
TEE-T.: 39.0C
75mm/s
48bpm


Erw. Echo
X8-2t
36Hz
11cm
TIS0.2
MI 0.5
S4
65
155
xPlane
46%
46%
50dB
P Aus
Allg
P
G
P
R
PAT T: 37.0C
TEE T: 40.0C
66 /min
211 von 327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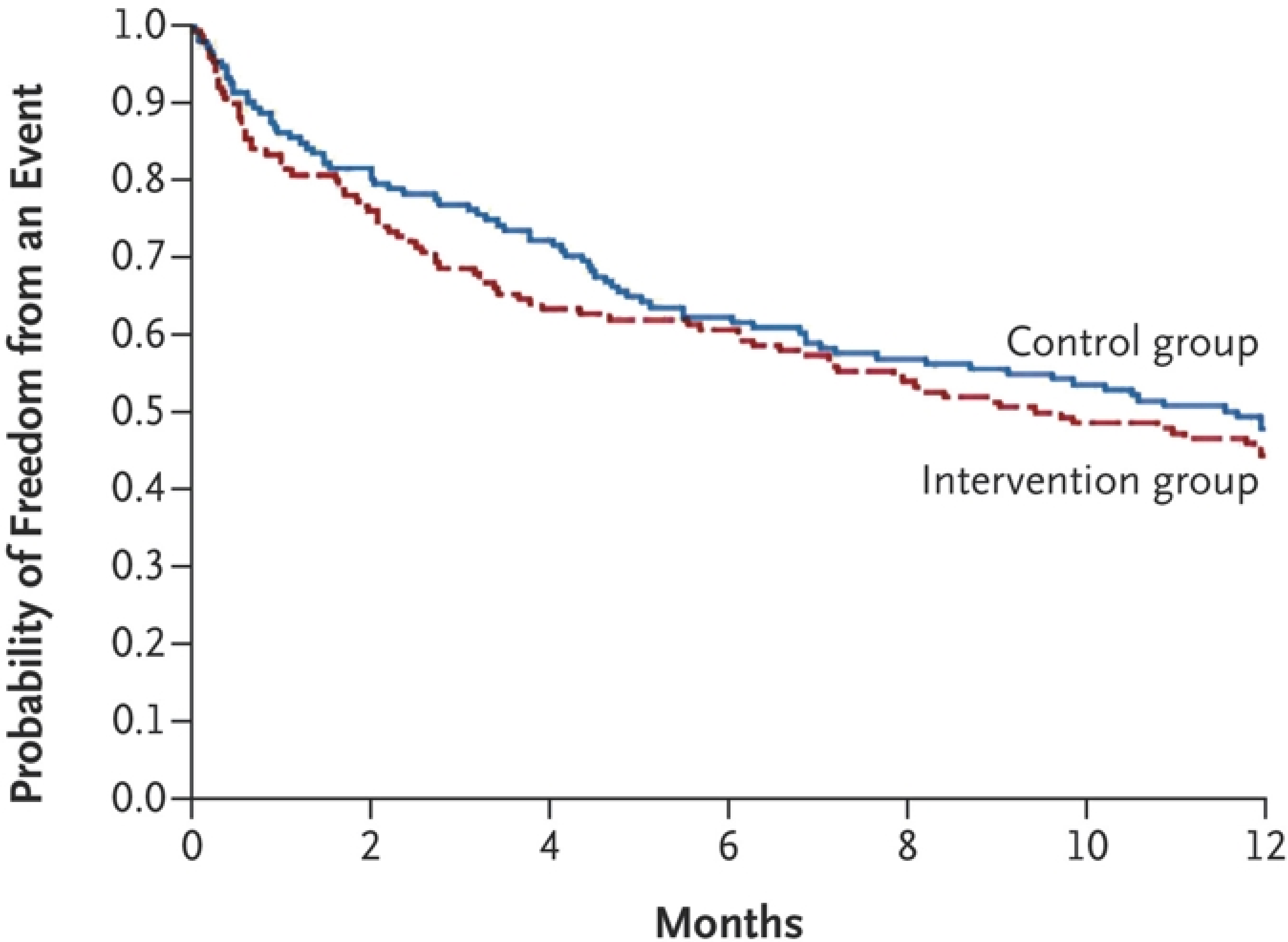
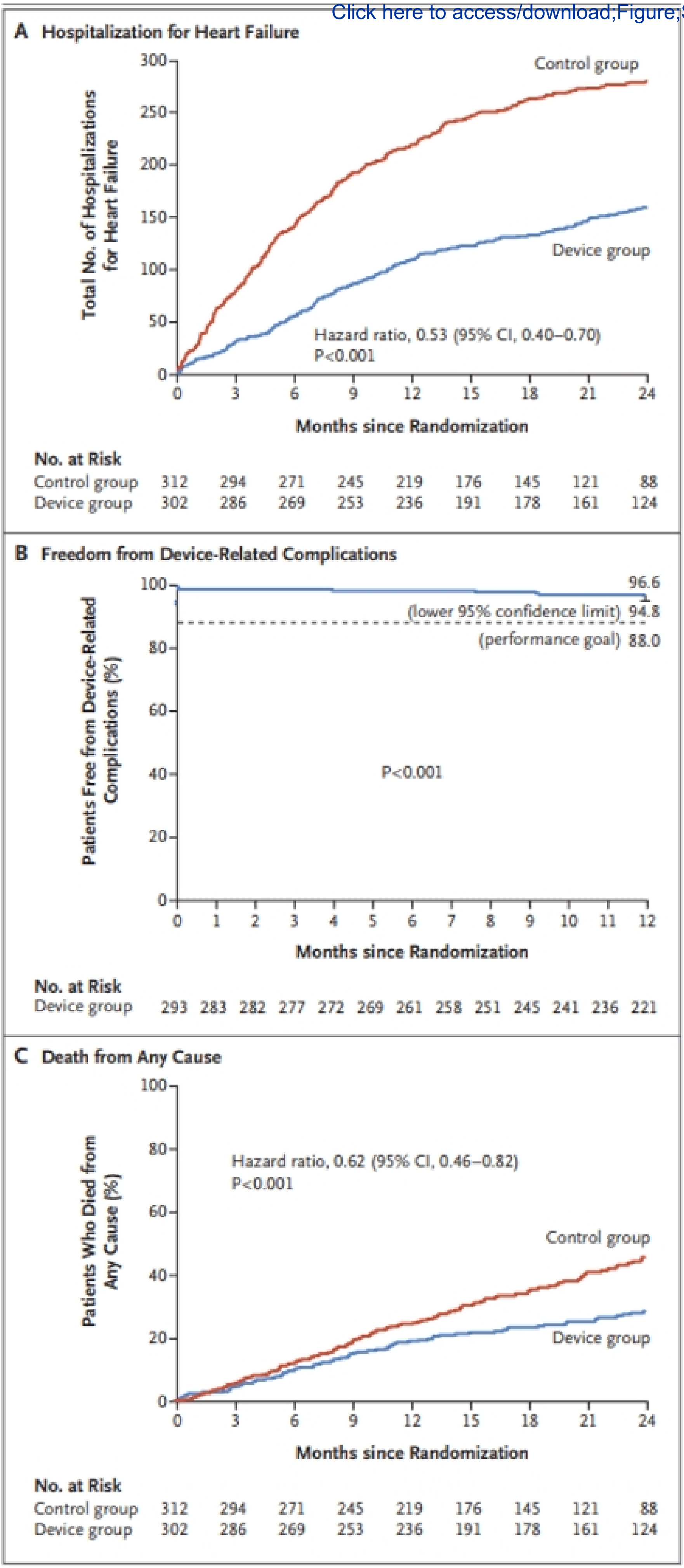
+59.3
-59.3
3D
Flächen
F1
Fläche 0.21 cm²
Umfang 1.68 cm



No. at Risk

Control group	152	123	109	94	86	80	73
Intervention group	151	114	95	91	81	73	67

Obadia JF et al; MITRA-FR Investigators. Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation. N Engl J Med. 2018 Dec 13;379(24):2297-2306. doi: 10.1056/NEJMoa1805374. Epub 2018 Aug 27. PMID: 30145927.



Stone GW et al.; COAPT Investigators. Transcatheter Mitral-Valve Repair in Patients with Heart Failure. N Engl J Med. 2018 Dec 13;379(24):2307-2318. doi: 10.1056/NEJMoa1806640. Epub 2018 Sep 23. PMID: 30280640.

Table 2 Similarities and differences between MITRA-FR and COAPT with respect to baseline characteristics of the study populations

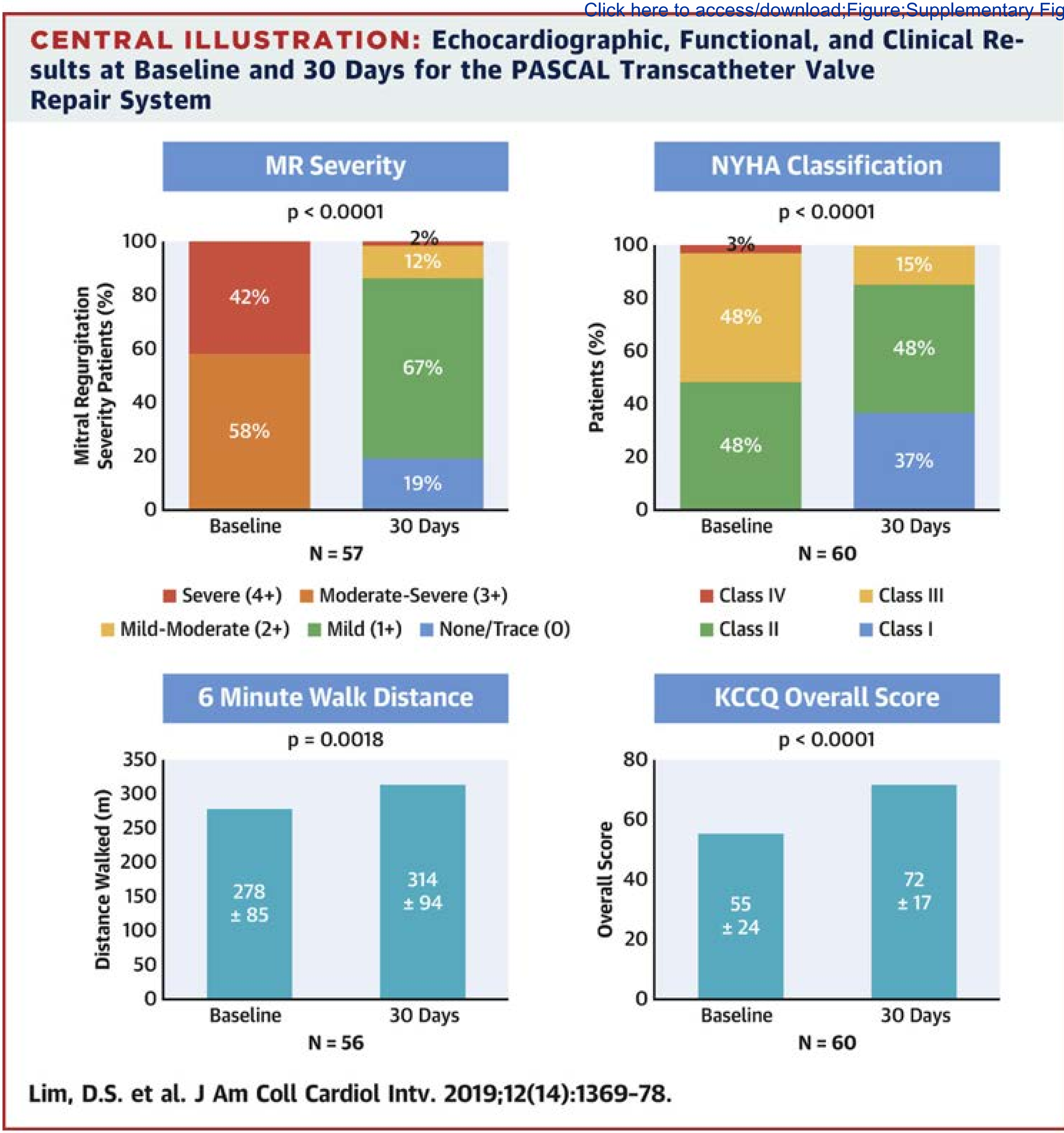
	MITRA-FR	COAPT
Baseline clinical characteristics		
Age, year	70 ± 10	72 ± 11
NYHA class, %		
I	0	0.2
II	32.9	39.0
III	58.5	52.5
IV	8.6	8.3
Surgical risk		
STS score ≥8%		42.7%
EuroSCORE II, median and IQR	6.2 (3.5–11.0)	
Baseline echocardiographic characteristics		
MR severity, %		
Moderate (EROA 20-29 mm^2)	52	14
Moderate-to-severe (EROA 30-39 mm^2)	32	46
Severe (EROA ≥ 40 mm^2)	16	41
EROA, mm^2	31 ± 10	41 ± 15
LV end-diastolic volume index, mL/m^2	135 ± 35	101 ± 34
LV ejection fraction, %	33 ± 7	31 ± 9

IQR, inter-quartile range; STS, Society of Thoracic Surgery. Other abbreviations as in *Table 1*.

Pibarot P et al. MITRA-FR vs. COAPT: lessons from two trials with diametrically opposed results. Eur Heart J Cardiovasc Imaging. 2019 Jun 1;20(6):620-624. doi: 10.1093/ehjci/jez073. PMID: 31115470; PMCID: PMC6529908.

Figure

Click here to access/download;Figure;Supplementary Figure 18.pdf



Lim DS et al. Transcatheter Valve Repair for Patients With Mitral Regurgitation: 30-Day Results of the CLASP Study. JACC Cardiovasc Interv. 2019 Jul 22;12(14):1369-1378. doi: 10.1016/j.jcin.2019.04.034. Epub 2019 Jun 26. PMID: 31255562.

Table 6 Echocardiographic parameters and related comments in the assessment of MR severity with TTE after transcatheter MV interventions

Parameter	Assessing residual MR after MV interventions
Color Doppler	
Color Doppler MR jet(s)	• Multiple jets can lead to overestimation of MR severity • MV device artifacts/shadowing may mask MR jet (TTE) or flow convergence (TEE). • PVR often difficult to identify, localize and quantify by TTE; TEE often needed • Eccentric jets difficult to evaluate and harder to detect (out of imaging plane)
Flow convergence	• Small, suggests mild MR; large suggests significant MR
Vena contracta width	• Often better defined with TEE • Not validated for multiple jets or various interventions
Vena contracta area (3D)	• Better defined with TEE • May be useful after edge-to-edge repair; likely a preferred method for CD quantitation but limited studies available
Spectral Doppler	
CW Doppler of MR jet	• Parabolic contour and soft density suggest mild MR • Dense and triangular velocity waveform suggests significant MR
Pulmonary vein flow pattern	• Systolic flow reversal specific for severe MR • Flow pattern influenced by multiple factors: LA pressure, LV filling pressure, atrial fibrillation • Difficult to record with prosthetic mitral valves
Mitral inflow pattern	• Mitral E-wave dominance affected by multiple factors: increased MR severity, LV filling pressure, and relative MV obstruction from implanted MV devices • Mitral A-wave dominance suggests mild MR
Quantitative parameters	
EROA and RVol by PISA	• Not recommended in the presence of MV devices, including edge-to-edge repair (not validated for multiple jets, double orifice MV, or eccentric jets)
Volumetric RVol and RF	• Requires excellent LV endocardial definition to quantitate LV stroke volume; best used with 3D echo or contrast echo so as not to underestimate LV stroke volume and hence RVol/RF • Cannot use mitral annulus site for flow because of MV devices (except MV annuloplasty) • Multiple measurements may compound errors • Not accurate if >mild aortic regurgitation or VSD present

VSD, Ventricular septal defect.
Other abbreviations as stated earlier.

Zoghbi WA et al. Guidelines for the Evaluation of Valvular Regurgitation After Percutaneous Valve Repair or Replacement: A Report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Angiography and Interventions, Japanese Society of Echocardiography, and Society for Cardiovascular Magnetic Resonance [published correction appears in J Am Soc Echocardiogr. 2019 Jul;32(7):914-917]. *J Am Soc Echocardiogr*. 2019;32(4):431-475. doi:10.1016/j.echo.2019.01.003

Click here to access/download
Table of Materials
Table of materials.xls

JoVE62053

„A simplified stepwise approach to echo guidance during the MitraClip procedure”

Dear Vineeta Bajaj,

We would like to thank the editorial team of JoVE for the opportunity to revise our manuscript. We would also like to thank the reviewers for their comments and ideas for further improvement of the manuscript. Below you will read our response to the reviewers´ comments along with the revised passages highlighted in blue.

Editorial and production comments:

Changes to be made by the Author(s):

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues.

The manuscript has been proofread from a native speaker.

2. Please remove the commercial term MitraClip from the title and use generic term instead. Please ensure that the title directly reflects the protocol being presented.

The title has been changed in:

A simplified stepwise approach to echo guidance during percutaneous mitral valve repair.

3. JoVE policy states that the video narrative is objective and not biased towards a particular product featured in the video. The goal of this policy is to focus on the science rather than to present a technique as an advertisement for a specific item. To this end, we ask that you please reduce the number of instances of "MitraClip" within your text. The term may be introduced once somewhere in the introduction but please use it when directly relevant. Otherwise, please refer to the term using generic language.

We reduced the instances of the term “MitraClip” within the text as much as possible. To present the study results concerning the MitraClip or the Pascal system, we preferred to not use the generic language for better understanding.

4. JoVE cannot publish manuscripts containing commercial language. This includes trademark symbols (™), registered symbols (®), and company names before an instrument or reagent. Please remove all commercial language from your manuscript and use generic terms instead. All commercial products should be sufficiently referenced in the Table of Materials and Reagents.

For example: MitraClips, (Abbott Laboratories, Melo Park, California, USA), PASCAL transcatheter, Edwards Lifesciences, Irvine, California, etc.

As mentioned before we reduced the term MitraClip or Pascal system within the text as much as possible and removed all trademark symbols (™) and registered symbols (®) within the text.

5. Please rephrase the Summary to clearly describe the protocol and its applications in complete sentences between 10-50 words: "This protocol presents…"

We rephrased the Summary as recommended.

This protocol presents in detail how to perform real-time echocardiographic guidance during transcatheter mitral valve repair. The fundamental views and the necessary measurements are described to each stage of the procedure.

6. Please expand the Introduction include all of the following with citation:

Echocardiography during a percutaneous mitral valve reconstruction procedure is mandatory. We want to explain the method of echocardiographic visualisation during this procedure. To the best of our knowledge, there are no studies of a percutaneous valve repair without echocardiography as there a no studies to prove that general anesthesia is necessary for open-heart surgery. Although there are various options how to perform general anesthesia, up to this point there is no alternative to echocardiographc visulisation during a percutaneous MV repair. Measurements such as 2D and 3D need to be performed during the procedure. There are different manufacturers of echocardiography machines, but these measurements are the same. All in all, performing percutaneous MV reconstruction without real-time echocardiography is not possible, so there are no studies comparing the procedure with and without echo. Thus, it is also not possible to describe whether echocardiography is the adequate method for performing MC.

a) A clear statement of the overall goal of this method

We added a clear statement of the overall goal of this method to the protocol.

Mitral regurgitation is the second-most frequent indication for valve surgery in Europe. Untreated, it may lead to severe heart failure and reduced life quality . The percutaneous transcatheter mitral valve repair is a catheter-based technique, that mimics the Alfieri stich surgical method to mitral repair by connecting together the A2 and P2 scallops.

b) The rationale behind the development and/or use of this technique

The percutaneous mitral valve repair (PMVR) is a catheter-based technique, which mimics the Alfieri stitch surgical method to mitral repair by connecting the A2 and P2 scallops.

c) The advantages over alternative techniques with applicable references to previous studies

The advantage of a percutaneous approach over an open-heart surgery is explained in the introduction.

For patients with high surgical risk, this technique offers a minimal invasive approach for the treatment of severe mitral regurgitation.

d) A description of the context of the technique in the wider body of literature

A description of the context of the technique in the wider body of the literature is in the introduction.

MitraClip has been the world's first transcatheter mitral valve repair therapy. Data of several registries and trials have shown, that the MitraClip procedure is an effective and safe method. In 2019 a similar device, the PASCAL transcatheter valve repair system was introduced to the market. It has shown feasibility and acceptable safety in the treatment of patients with severe mitral regurgitation.

e) Information to help readers to determine whether the method is appropriate for their application

This information is included in the paper in the introduction.

In contrast to other percutaneous techniques, like the percutaneous transvalvular replacement (TAVR), that can be done with fluoroscopy only, the transcatheter edge-to-edge repair of the mitral valve requires echocardiographic guidance. This review describes step by step the echocardiographic approach during transcatheter mitral valve repair, including measurements, suggestions for intraprocedural quantification of the mitral regurgitation and important views to prevent periprocedural complications.

7. Please include an ethics statement before the numbered protocol steps, indicating that the protocol follows the guidelines of your institution's human research ethics committee.

We added the phrase:

The protocol follows the guidelines of our's institution's human research ethics committee.

8. Please adjust the numbering of the Protocol to follow the JoVE Instructions for Authors. For example, 1 should be followed by 1.1 and then 1.1.1 and 1.1.2 if necessary.

We adjusted the numbering of the protocol to follow the Jove Instructions for authors.

9. Please ensure that all text in the protocol section is written in the imperative tense as if telling someone how to do the technique (e.g., "Do this," "Ensure that," etc.). The actions should be described in the imperative tense in complete sentences wherever possible. Avoid usage of phrases such as "could be," "should be," and "would be" throughout the Protocol. Any text that cannot be written in the imperative tense may be added as a "Note."

We changed the text and rewrote the sentences in the imperative tense.

10. The Protocol should contain only action items that direct the reader to do something.

We removed the information about the different clip sizes, as these are only available for the MitraClip System. This information does also not direct the reader to do something.

1. Strategy
    1.1. Discuss the strategy with the operator before inserting the steerable guide catheter (SGC) and the clip delivery system (CDS) into the left atrium.
        1.1.1. Evaluate a one device strategy if the orifice is < 1 cm wide and position the clip directly above the regurgitation jet if the orifice is circular.
        1.1.2. Evaluate the implantation of ≥ 2 clips in case of large elliptic or multiple jets. Implant the device starting medially of the regurgitant orifice, as the positioning of a second device is often easier when the first has been implanted in this way, rather than after starting laterally.

11. Please add more details to your protocol steps. Please ensure you answer the “how” question, i.e., how is the step performed? This can be done by including mechanical actions, button clicks, knob turns etc.

As recommended we have added more details to our protocol steps. We described mechanical actions e.g. “insert the probe deeper”, “retroflex the probe”, and “rotate the probe anti-clockwise”. In addition to that, we added information on button clicks e.g. “take an X-plane”, “asses xx with CW”, “take a 3D-colour data-set”, “take a wide sector zoom image”, “record..”

We described knob turns e.g. “sweep to degree..”, “Perform a 180° clockwise rotation into the 3D en-face surgical view..”

12. Please revise the protocol text to avoid the use of any personal pronouns in the protocol (e.g., "we", "you", "our" etc.).

We revised the protocol and deleted the personal pronouns.

Please include a single line space between each protocol step.

We included a single line space between each protocol step.

14. Please include a figure or a table in the Representative Results showing the effectiveness of your technique backed up with data. Example: Outcomes, before and after surgery tables.

Our protocol explains in detail the general method of echocardiographic visualization during a percutaneous mitral valve repair. Our goal of this paper was not the representation of any data. We did not produce any results, because, as already mentioned above, no comparing studies on echocardiography during percutaneous mitral valve reconstruction have been carried out. Nevertheless, we included slides with the results of previous studies of the percutaneous mitral valve repair as in the video.

15. Please include details about the patients (number, clinical symptoms, age, sex, etc) analyzed with this protocol.

Not applicable, general recommendation. Our protocol explains in detail the general method of echocardiographic visualization during a percutaneous mitral valve repair.

16. Please ensure that the results are described with respect to your experiment, you performed an experiment, how did it help you to conclude what you wanted to and how is it in line with the title.

Our protocol explains in detail echocardiographic visualisation during percutaneous mitral valve reconstruction. This is not an experiment, but a method that makes the intervention possible. In our case, the result of the method may be the change of the mitral regurgitation (reduced, increased, or absent). Under "Results" we described in detail the results of previous studies which examined the procedure and the quantification of the mitral valve regurgitation (result of the method) with the corresponding literature.

17. Each Figure Legend should include a title and a short description of the data presented in the Figure and relevant symbols.

We added a title and a short description to each Figure

18. Please obtain explicit copyright permission to reuse any figures from a previous publication. Explicit permission can be expressed in the form of a letter from the editor or a link to the editorial policy that allows re-prints. Please upload this information as a .doc or .docx file to your Editorial Manager account. The Figure must be cited appropriately in the Figure Legend, i.e. "This figure has been modified from [citation]."

We changed the previous figures with the original figures from the papers and complemented the citation of the original paper under the figures.

19. As we are a methods journal, please ensure that the Discussion explicitly cover the following in detail in 3-6 paragraphs with citations:
a) Critical steps within the protocol

Critical steps within the protocol were added to the paper.

Complications due to echocardiography may occur but rarely lead to significant damage. Nevertheless, esophageal lesions are possible after performing transesophageal echocardiography. This incidence is reduced with a shorter duration of the intervention[i]. On the contrary, several complications associated with the transcatheter edge-to-edge mitral valve repair are described. Major bleeding is the most frequent major complication and blood transfusion after transcatheter valve procedures have been strongly associated with mortality. Pericardial tamponade is rare and may occur during several steps of the procedure. Caution during transseptal puncture, insertion of the SGC into the left atrium and retrieving of the SGC-tip after clip deployment reduces the probability of this life-threatening complication. Rates of clip-specific complications, as embolization and partial clip detachment, are low and can be reduced by an accurate echocardiographic assessment during and after grasping of the leaflets.

b) Any modifications and troubleshooting of the technique

Despite the carefulness during echocardiography, aggravation of the MR, may occur. Additional clip deployment in the medial and lateral position may increase the risk of entangling and rupturing of the chordae. Furthermore, repeated grasping of the leaflets can lead to leaflet laceration and perforation. Residual MR is not only a determinant of procedural success but is also associated with poorer prognosis, especially when there is a concomitant transmitral pressure gradient >5 mm Hg. Clear communication with the interventionist and a meticulous echocardiographic assessment are necessary to reduce peri-procedural clip-related complications.

c) Any limitations of the technique

The percutaneous edge-to-edge repair is not eligible for every pathomechanism of MR. For some determinants of MR, such as annulus dilatation, rupture of the chordae tendinae or severe calcifications of the mitral leaflets, the device reaches its limits.

d) The significance with respect to existing methods

In this case, mitral ring dilation can be sutured surgically or percutaneously in place to provide annular stabilization. P*olytetrafluoroethylene* (PTFE) neochordae can be surgically sewed as new chordae tendinee. A MV with severe calcified leaflets may be replaced with a prosthetic valve.

e) Any future applications of the technique

New percutaneous devices designed to address these aspects are under development.

20. Please revise the table of the essential supplies, reagents, and equipment. The table should include the name, company, and catalog number of all relevant materials in separate columns in an xls/xlsx file.

We complemented the table of essential supplies.

Reviewer #1:

The manuscript by Gatti et al addresses a real clinical need about transcatheteter edge to edge MV repair: echocardiographic guidance is really mandatory and essential for procedural safety and success. As written in the manuscript, it is essential to build a shared planning between the imager and the interventionalist and the echo protocol should consider peculiarities related to the very single interventionalist and center.

We would like to thank reviewer # 1 for the recommended changes and the appreciation of our manuscript.

Title:
Avoid MitraClip in the title => percutaneous edge to edge repair; you speak also about

Pascal system in the text. It could be very useful to add peculiarities of echo guidance also for this novel device

The term MitraClip has been replaced with “mitral valve repair”.

A simplified stepwise approach to echo guidance during the percutaneous mitral valve repair.

Abstract:
check for typos; add also a sentence on shared standardization between imager and interventionalist=> useful for safety and efficacy.

We checked for typos and corrected possible mistakes. In the conclusion of the abstract and the discussion we mentioned that shared standardization between imager and interventionalist is indispensable for a safe and effective procedure.

A structured approach improves the collaboration between interventionist and imager and is indispensable for a safe and effective procedure.

Both, the imager and the interventionist should have a fundamental understanding of echocardiographic assessment to achieve a successful and safe procedure.

CW is not colour...but continuous

Thank you very much! We corrected the abbreviation CW.

There are official recommendations: Guidelines for the Evaluation of Valvular Regurgitation After Percutaneous Valve Repair or Replacement ASE https://doi.org/10.1016/j.echo.2019.01.003

As far as we know, there are no official recommendation for the evaluation of valvular quantification during the procedure of percutaneous valve repair. The official recommendations from ASE are allowed for the evaluation of valvular quantification after percutaneous valve repair. We quoted the Guidelines for the Evaluation of Valvular Regurgitation After Percutaneous Valve Repair or Replacement ASE in the text, when appropriate.

Protocol
Add more frequently/underline the role of X plane (es. for check perpendicularity)

We mentioned many times the role of X-plane without writing “X-plane” e.g when writing “choose a intercommissural view and a long axis view to ensure..” or “an intercommissural view combined with a long axis view to show perpendicular positioning....”.

We’ve added the role of X-plane in point 1.9.

Finally, take a bicaval view (90-110°) with X-plane, to show the aortic valve, for the transeptal puncture.

1. Measurement before intervention => better "evaluation";

We changed point 1. in

Evaluation before intervention

1.1 / 1.2 Also evaluation of pericardial effusion and PV flow pattern (not necessarily measure)

We think that it might be too many “evaluate” in series. We left “exclusion of the pericardial effusion” but changed the measurement in pulmonary vein flow in

Evaluate the pulmonary venous flow pattern in the left upper pulmonary vein…

1.4 hemodynamic state should not necessarily be kept during the procedure but at least at basal and final evaluation

We moved the changed phrase from 1.4 to point 1.3

Ensure hemodynamic state is the same at pre- and post-procedural evaluation.

Be consistent during protocol: always use for example keep or sentences without the verb

As recommended by the editor in chief of JOVE We changed the protocol into an imperative tone, which limited the number of verbs.

1.5 contraindication is MV area!!not gradient that coudl be influenced by MR;

As a transmitral pressure gradient > 5 mmHg is associated with poorer prognosis after percutaneous mitral valve repair, literature define this condition as a relative contraindication. We added the adjective “relative”.

A mean pressure gradient (MPG) > 5 mmHg is a relative contraindication for percutaneous mitral valve repair.

1.5 mean gradient should be measured by CW not PW!

PW can be alternatively used to CW. We changed the sentence into…

Assess the transmitral pressure gradient with CW in the long axis view (120-140°)

1.6 it is also possible (however less elegant) to directly measure it on the 3d volume rendering

We complemented the 3D-zoom-mode.

Take a 3D-colour doppler dataset or a wide-sector zoom image with colour and measure the 3D-vena contracta (3D-VCA).

1.7 add absolute and relative contraindication according to MV area

We changed the sentence into

An area < $4cm^2$ is a relative contraindication, an area < 3 cm^2 an absolute contraindication to the procedure.

1.8 however it is not the some for everybody! always state where aorta is => allign the view in accordance to your interventionist and use the same perspective as much as you can during the procedure to avoid confusion

We mentioned both views; the en-face surgical view and the “modified” en-face view, specifying the localisation of the aortic valve in both views.

Show the 3D en-face surgical atrial view (aortic valve at 12 o’clock) of the mitral valve. NOTE: The segments of the valve are named “lateral” for the segments 1 and “medial” for the segments 3. The sequence of the segments in the en-face surgical view, is inverse to the sequence in the commissural view. Perform a 180° clockwise rotation into the 3D en-face surgical view (aortic valve at 6 o’clock), that will result in equal sequence of segments in both views.

9. state that is for transeptal puncture

We changed point 1.9 in

Finally, take a bicaval view (90-110°) with X-plane for the transeptal puncture.

Clip strategy

To reduce the word “clip”, we changed point 2. In

2. Strategy

2. in front => above!

We changed the expression “in front” into “above”

“2.1.1…position the clip directly above the regurgitation jet..”

4. MitraClip Generation 4 introduced two additional clip sizes NTW and XTW (wider versions of NT and XT) => so 4 sizes are now available; add also a sentence on specificities about clip width

To make the article as neutral as possible, we decided to describe just the strategy and not the different types of the MitraClip devices.

2.1. Discuss the strategy with the operator before inserting the steerable guide catheter (SGC) and the clip delivery system (CDS) into the left atrium.

2.1.1. Evaluate a one device strategy if the orifice is < 1 cm wide and position the clip directly above the regurgitation jet, if the orifice is circular.

2.1.2. Evaluate the implantation of ≥ 2 clips in case of large elliptic or multiple jets. In this case, implant the device starting medially of the regurgitant orifice, as the positioning a second device is often easier than after starting laterally.

Transeptal puncture

State that SAX view at the base is useful for live monitoring to avoid aortic injury

We added information on the position of the aorta during transseptal puncture to avoid it´s injury.

3.1. Ensure the aortic valve is visible, to avoid aortic injury.

Advancement of CDS in the left atrium

one important point to be stressed is perpendicularity and trajectory

We changed the phrase into …

5.2. Check that the CDS is positioned perpendicularly to the coaptation line to guarantee a correct trajectory.

Orientation of the clip

1.1 an INTER-commissural view combined with a long axis view is required: role of X plane; specify how to check orientation in 2D (arms visible only in LAX)

Specification of orientation of the device in 2D was added to the paper:

6.1.1. In the event of poor image quality, show an intercommissural view combined with a long axis view.

6.1.2. Adjust the intercommissural view angle in medially and laterally positioned devices to visualise the complete length of both arms. Sweep at ca. 30-45° for medially positioned devices and ca. 70-90° for laterally positioned devices.

Point 1.1 has been changes in point 6.1.1. We completed point 6.1.1 with:

NOTE: the clip arms are visible only in the LAX.

3. also fluoroscopy could be useful for this purpose

That is right. But we want to describe the steps that are relevant for the echocardiographer. Nevertheless, we want to emphasise the role of fluoroscopy when echocardiography imaging is insufficient, as in point 9.2.

3.1 after gain reduction

Point 3.1. has been changed in 6.4. This depends on the adjustment of the echomachine at the beginning of the procedure and differs between the examiners.

3.2 if gross re-orientation is necessary, clip must be retrieved into LA

We totally agree with this statement and added this information to the protocol. Point 3.2. has been changed in 6.5.

If gross reorientation of the device is necessary, show the intercommissural view with X-plane to visualize the inversion of the clip that will be retrieved in the LA.

Grasping
3. detachment => attachment

What we ment, is not the single leaflet clip attachment, but a grasping of both leaflets resulting/ leading to a partial clip detachment.

4.2 not necessarily measure

We changed point 4.2. in 7.4.2.

Evaluate the PW flow in the pulmonary veins.

4.3 mean G > 5 is not necessarily a contraindication, as gradients are flow dependent => stress role of MV area

Point 4.3. has been changed in 7.4.3. We changed the sentence into…

A gradient > 5 mmHg is a relative contraindication for clip deployment.

4.4 or TG SAX of MV

Point 4.4. has been changed in 7.4.4.

Use the 3D en -face view of the mitral valve or a transgastric short axis view of the mitral valve to show the double orifice.

4.5 scanning the valve with X plane; rule out intraclip jet Check should be done after clip release! possible role of tension of the system

We described how to rule out intraclip jets in detail in point 7.4.1. and in the “Final MR Assessment” in point 9. The Check should be done before and after clips release. We mentioned the Check after clip release in point 7.5.

Rotate the TEE probe medially and laterally to the clip with colour doppler or use X-plane to find eccentrics jets close to the clip. NOTE: Due to shadowing artifacts caused by the CDS underestimation of the MR may occur. To avoid this, Insert the probe deeper into the esophagus or show the transgastric view to visualize the residual insufficiency jets without shadowing artifacts.

(In “final MR assessment”): Show the commissural view with colour doppler in combination with perpendicular X-planes in the residual insufficiency jets if present.

We added the role of the tension of the system in point 7.5.

NOTE: due to the tension of the system on the MV, the residual insufficiency jets after releasing the device may be aggravated.

Implantation of additional clips

deferred? what does it mean?

Point 8. Has been changed to Point 9.0. If a significant reduction of MR has not been achieved, implantation of additional clips is/may be required (if possible).

1.3 it is not clear => if necessary, reposition of the clip?

Point 1.3 has been changed to point 9.4. What we meant was that repositioning of the clip may be necessary in case of an aggravated MR. To avoid confusion, we changed the phrase in:

Repeat the five steps as explained in point 7.4 to evaluate MR after grasping the leaflets with the additional clip.

Final MR assessment

Stress role of technical settings for VCA role of hemodynamic monitoring: LA pressure and systemic arterial pressure

Point 9.0 has been changed in point 8.0. We added a NOTE in point 8.3

NOTE: continuous LA pressure monitoring may be a useful tool during transcatheter mitral valve repair.

line 272: also clip G4 has the possibility of independent grasping

The information on the possibility of independent grasping of the 4th generation Clip was rephrased in the paper.

"It can independently grasp leaflets, as the fourth generation MitraClip, in the presence of a central spacer."

line 279: A critical appraisal of echocardiographic assessment of mitral regurgitation, especially functional one, remains.

We changed the phrase as recommended.The nativ speaker changed the phrase in

A critical appraisal of echocardiographic assessment of MR, especially a functional one, is still to be done.

lines 290.. add role of hemodynamic data

We added:

Different studies demonstrate the value of real-time monitoring of LA pressure during percutaneous mitral valve repair. An increase in left atrial mean pressure is a predictive of worse clinical outcomes at short-term follow-up, independent from echocardiographic findings. Continuous hemodynamic monitoring may complement transesophageal echocardiography to assess and optimize percutaneous edge-to-edge mitral valve repair.

Figure 3: x plane view starting from..

We changed all titles of the figures as recommended from the Editorial team.

Figure 3 2D biplanar view of the MV with colour doppler: medial insufficiency jet

Figure 6: multiplanar reformatting

Figure 6 Multiplanar reconstruction of the 3D dataset: mitral valve area in 3D

Figure 20: PW is not correct

We choosed another figure for this title line 338 not only perforation => laceration

We added

Furthermore, repeated grasping of the leaflets can lead to leaflet laceration and perforation.

lines 343-348 add this part to the previous section when you speak about Pascal

We moved the paragraph to the result section where we speak about the Pascal system (line 250)

Since 2019, another device for transcatheter mitral valve repair is available. Compared to the MitraClip device, the PASCAL system has wider paddles. It can independently grasp leaflets, as the generation 4 MitraClip, in the presence of a central spacer. After a multicentre, prospective, observational, first-in-man study[ii] and the multicenter early-feasibility trial of the PASCAL transcatheter mitral repair device (CLASP study), the PASCAL repair system received CE mark approval for the treatment of both primary and secondary MR. The early feasibility study of the PASCAL repair system showed high survival, low complication rates as well as improvements in functional status and quality of life. Furthermore, the CLASP study showed a significant reduction of the MR with this device. As there are no head-to-head studies available yet, the preferred device related to the valve anatomy (e.g., larger flail segments, large prolapse, cleft, short posterior leaflet, mitral annular calcification) is still not defined. A head-to-head comparison trial of the MitraClip with the Pascal System (CLASP IID trial) started in 2018 and the estimated primary completion date is expected to be in 2023.

line 352: not only surgically but also percutaneously

We added

In this case, mitral ring dilation can be sutured surgically or percutaneously in place to provide annular stabilization.

line 362: cite guidelines

We added the citation of the current guidelines.

lines 374-376 => it is better to add this part as a conclusion

The structure of the article given by Jove does not contain a conclusion, but we added a conclusive sentence at the end of the discussion.

In conclusion percutaneous transcatheter mitral valve repair is fully dependent on transesophageal echocardiography. Both, the imager and the interventionist should have a fundamental understanding of echocardiographic assessment to achieve a successful and safe procedure.

Check for typos:

echo guidance,

oe/esophageal, manoeuvre..

british vs american english,

incorrect comas,

abbreviations should be consistent: es MR not always used; MC line 97 never explained

line 384: there is a bracket

The manuscript has been proofread from a native speaker.

Reviewer #2:

Manuscript Summary:

The below manuscript titled "A simplified stepwise approach to echoguidance during the MitraClip procedure", is a well written article. After careful review of the manuscript multiple times, I could not find any major flaws in the manuscript.

Major Concerns:

None upon multiple readings

Thank you very much. We are happy to hear this.

Minor Concerns:

page 2- line 69- please change the words to "..procedure are dependent on the individual operator's skill and experience. In c..."

We changed the phrase:

Duration and success of the percutaneous mitral valve repair are dependent on the individual operator’s skill and experience.

Reviewer #3:

The manuscript is well written and gives a brief and precise overview of the imaging strategy for MitraClipping. This topic is very important for interventional cardiologists. I have some minor comments:

Please acknowledge that many centers use the "cardiologist" view which shows the aortic valve at 6 o`clock.

We added this information in the discussion, line 353:

Although the 3D en-face view is defined showing the aortic valve at 12 o’clock, many centers prefer the “cardiologist” 3D en-face view, which shows the aortic valve at 6 o'clock. There is no literature comparing both views during the percutaneous mitral valve repair.

Please add to this section (2.4) accroding to MitraClip G4 device which is - to my knowledge - now available throughout Europe.

Jove' Editor demanded that we remove any commercial term. To make the article as neutral as possible, we decided to describe just the strategy and not the different types of the MitraClip devices.

2.1. Discuss the strategy with the operator before inserting the steerable guide catheter (SGC) and the clip delivery system (CDS) into the left atrium.

2.1.1. Evaluate a one device strategy if the orifice is < 1 cm wide and position the clip directly above the regurgitation jet, if the orifice is circular.

2.1.2. Evaluate the implantation of ≥ 2 clips in case of large elliptic or multiple jets. In this case, implant the device starting medially of the regurgitant orifice, as the positioning a second device is often easier than after starting laterally.

3.1.2. puncture height of >3.5cm is neccesarry instead of ca. 3.5

Point 3.2.1. We changed the phrase in

Choose a puncture height of 4-5 cm in case of degenerative MR (e.g. prolapse) and of > 3,5 in functional MR. Avoid a patent foramen ovale, as the entry is far too anterior.

I do not agree with a strict superiorly transseptal puncture. I would agree with "slightly superior".

Point 3.2. We changed the phrase in

Ensure the aortic valve is visible, to avoid aortic injury. Make sure the puncture site is slightly superiorly and posteriorly.

The resolution of the figures seems very low and especially 3D enface images are not nicely seen. Sometimes there may be a quality loss due to the editorial system. Please check and improve prior to publication.

Thank you for mentioning this, but the lower quality maybe due to the editorial system; the editors have accepted the quality of the mentioned images. Nevertheless, we improved image quality of every image.

Changes to be made by the Author(s) regarding the video:

1. Please increase the homogeneity between the video and the written manuscript. Ideally, all figures in the video would appear in the written manuscript and vice versa. The video and the written manuscript should be reflections of each other. Currently the results figures are missing from the text.

We complemented the figures of the results in the manuscript.

2. Furthermore, please revise the narration to be more homogenous with the written manuscript. Ideally, the narration is a word for word reading of the written protocol.

As we rewrote the text in the imperative tense, we also changed the narration.

3. Please ensure that the section highlight is same as that in the text.

We complemented the sections from the text.

4. Please include an ethics statement before the numbered protocol steps, indicating that the protocol follows the guidelines of your institution's human research ethics committee.

We added the ethic statement at the beginning of the protocol.

5. 2:00: Please zoom the monitor to not show the commercial name throughout the video.

The commercial name is not visible in the current version of the video.

6. Representative results: Please do not use commercial terms.

We minimized the commercial terms as much as possible.

7. Text

All the title looks more like a sentence. Please make each word have a capital letter to make it look more like a title: 00:00, 00:51, 03:06, 06:36
Please add a person caption with their name and affiliated lab to the left of the person: 00:11, 08:58, 09:12

The titles have been corrected and a person caption has been added as requested.

8. Pacing

00:09 - 00:09 The title doesn't need to be 10 seconds long. Please reduce this to about 5 seconds.

We reduced the length of the titles as requested.

00:34 - 00:34 There's a weird fade/dip to black that happens here that's very jarring. Please use a straight cut without any dissolve or flash/dip.

We made the requested changes.

00:55 - 00:55 The audio comes in a little late. Please have the narration happen right after the video fades up.

The narration starts right after the video fades up.

The narration ends and we hold on this shot for too long. Please move onto the next narration much sooner within these three spots: 01:26 - 01:31, 02:05 - 02:05, 02:45 - 02:53.

9. Audio

Interview audio should come out of both channels, instead of just the left. Please balance the audio so it can be heard equally left and right: 00:10 - 00:10, 08:56 - 08:56
00:57 - 00:57 Please remove any unnecessary sounds like breathing or paper rustling. I can here lip smacking here.

We made the requested changes.

I can hear background noise whenever certain clips are shown. Make sure the audio from any of the clips being shown are removed from the timeline in your editing program. We only want to hear the narration and nothing else please: 01:12 - 01:25, 01:50 - 02:04, 02:28 - 02:44, 03:52 - 03:59, 04:55 - 05:46, 05:55 - 06:10, 06:22 - 06:33

We deleted the background noise as requested.

10. Composition

00:35 - 00:35 The backdrop looks to be greenscreen. If so, I would recommend using a different backdrop to separate this interview from the previous. Maybe flipping the image so the person is on the left side of the screen would help as well.

The backdrop is not a greenscreen, but the official background requested from our hospital for portraits and interviews.
