The role of CMR in Arrhythmogenic Cardiomyopathy

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CMR sequences

- **Cardiac morphology and function (systolic and diastolic)** (ie black blood, white blood SSFP, myocardial tagging, transmitral velocities, FT stain)
- **Quantification of chambers and mass**
- **Tissue characterisation**

FSE sequences -/+ saturations pulses

T2W sequences (STIR)-increased water content- oedema infiltration infarction

Precontrast T1 T2 mapping, post contrast T1 mapping, ECV

Multiecho T2* GE

LGE inversion recovery sequence and gadolinium contrast agent- areas with expanded interstitial fibrosis necrosis infiltration

EGE

- **Perfusion** ischaemia/microvascular obstruction
- **Flows**
- **Intracardiac features**
- **Extracardiac findings**

ARVC

Characterized by a broad phenotypic spectrum

- loss of myocytes in the right ventricular myocardium,
- Fatty or fibrofatty replacement
- Frequent involvement of the LV
- Association with myocarditis
- Genetics: ARVC is a desmosomal cardiomyopathy- defective cell-adhesion proteins

JUP—plakoglobin, *PKP2*—plakophilin

desmosomal cadherins (*DSG2*—desmoglein-2

DSC2—desmocollin-2)

plakins (*DSP*—desmoplakin)

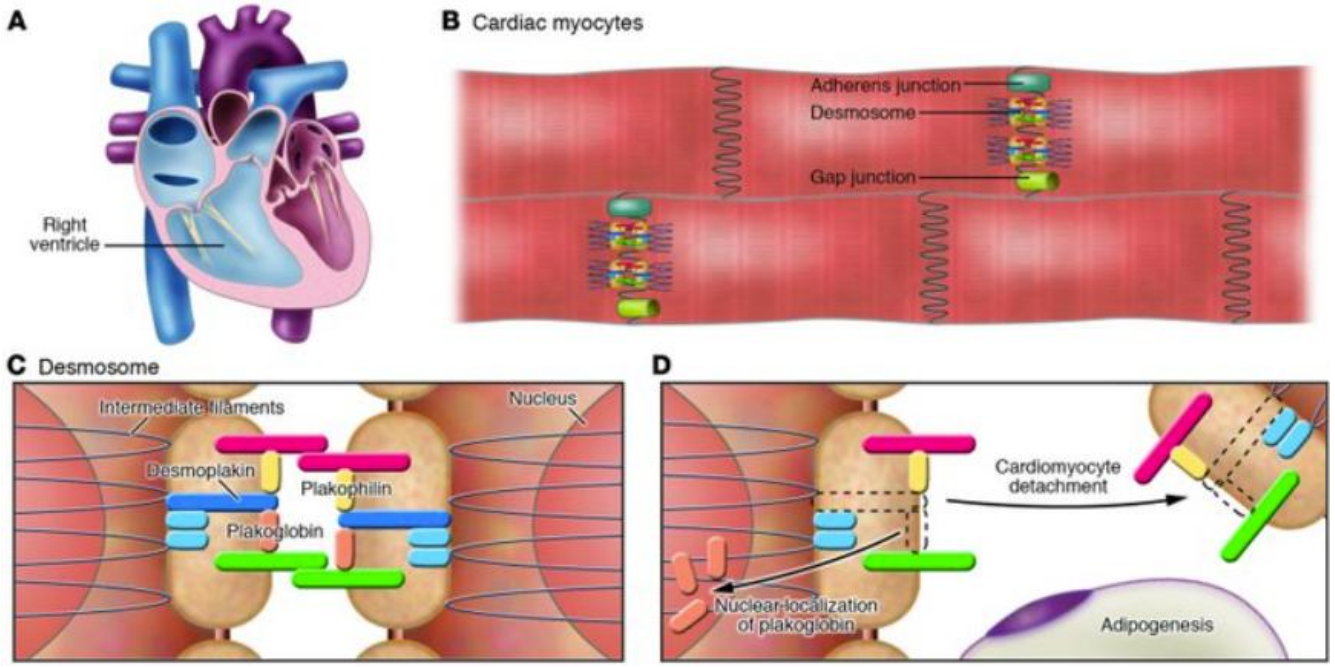
- Non-desmosomal genes

alpha T-catenin (CTNNA3),

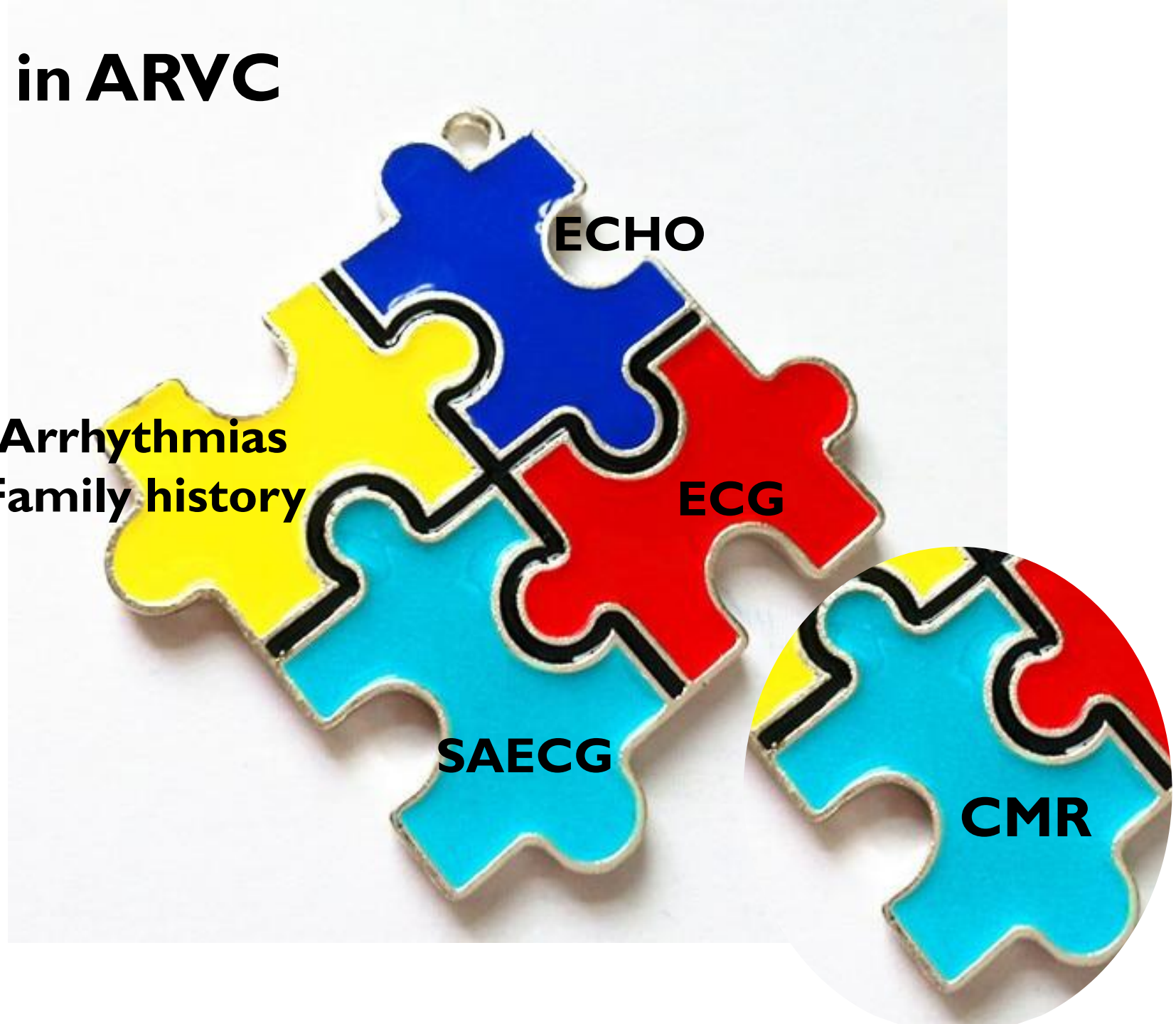
N-cadherin (CDH2)

transmembrane protein 43 (TMEM43)

ryanodine-receptor type 2 (RYR2)



Diagnosis in ARVC



Arrhythmogenic Cardiomyopathy

- "Arrhythmogenic Cardiomyopathy" is currently defined as a genetic heart muscle disease which affects the **RV, the LV**, **or both**, whose most distinctive phenotypic feature is myocardial scar **(fibro or fibrofatty myocardial replacement**) which **underlies global and/or regional** ventricular dysfunction and predisposes to potentially lethal scar-related ventricular arrhythmias, regardless of the severity of the systolic ventricular dysfunction (*autosomal dominant and recessive PKP2, DSG2, DSP, DSC2, and JUP LMNA, TMEM43, PLN, SCN5A, TGFB3)*

(i) the ***"dominant-right"*** variant, i.e., the classic ARVC phenotype characterized by the predominant RV involvement, with no or minor LV abnormalities

(ii) the ***"biventricular disease"*** variant characterized by the parallel involvement of the RV and LV

(iii) the ***"dominant-left "***variant (also referred to as "arrhythmogenic left ventricular cardiomyopathy; ALVC") characterized by the predominant LV involvement, with no or minor RV abnormalities

- ✓ RV assessment (volumes, wall thickness, function, RWMAs)
- ✓ Risk stratification

Screening 1-2 years probands and family members

Revised ARVC Diagnostic Criteria 2010

Original Task Force Criteria	Revised Task Force Criteria
I. Global or regional dysfunction and structural alterations*	
Major	
• Severe dilatation and reduction of RV ejection fraction with no (or only mild) LV impairment • Localized RV aneurysms (akinetic or dyskinetic areas with diastolic bulging) • Severe segmental dilatation of the RV	**By 2D echo:** • Regional RV akinesia, dyskinesia, or aneurysm • *and* 1 of the following (end diastole): — PLAX RVOT ≥32 mm (corrected for body size [PLAX/BSA] ≥19 mm/m²) — PSAX RVOT ≥36 mm (corrected for body size [PSAX/BSA] ≥21 mm/m²) — *or* fractional area change ≤33% **By MRI:** • Regional RV akinesia or dyskinesia or dyssynchronous RV contraction • *and* 1 of the following: — Ratio of RV end-diastolic volume to BSA ≥110 mL/m² (male) or ≥100 mL/m² (female) — *or* RV ejection fraction ≤40% **By RV angiography:** • Regional RV akinesia, dyskinesia, or aneurysm
Minor	
• Mild global RV dilatation and/or ejection fraction reduction with normal LV • Mild segmental dilatation of the RV • Regional RV hypokinesia	**By 2D echo:** • Regional RV akinesia or dyskinesia • *and* 1 of the following (end diastole): — PLAX RVOT ≥29 to <32 mm (corrected for body size [PLAX/BSA] ≥16 to <19 mm/m²) — PSAX RVOT ≥32 to <36 mm (corrected for body size [PSAX/BSA] ≥18 to <21 mm/m²) — *or* fractional area change >33% to ≤40% **By MRI:** • Regional RV akinesia or dyskinesia or dyssynchronous RV contraction • *and* 1 of the following: — Ratio of RV end-diastolic volume to BSA ≥100 to <110 mL/m² (male) or ≥90 to <100 mL/m² (female) — *or* RV ejection fraction >40% to ≤45%

I. Imaging
II. Pathology
III. ECG
IV. Ventricular arrhythmias
V. Family history

Definite diagnosis: (2M or 1M+2m or 4m)

- ***New techniques***
- ***More sensitive for familial and mild disease***
- ***Early and greater involvement of LV in parallel or exceed the severity or RV involvement***

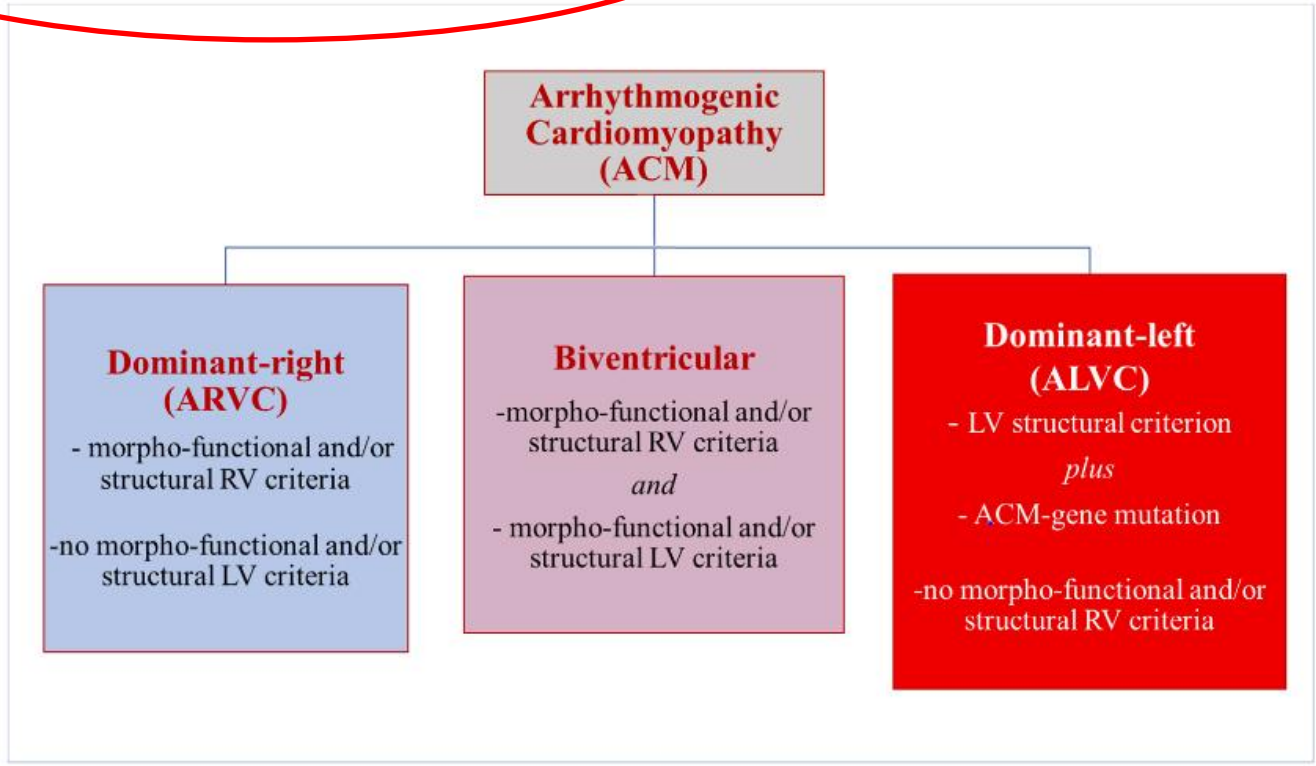
The Padua Criteria 2020

- Tissue characterization by CE-CMR for detection of fibro-fatty myocardial replacement of both ventricles.

- New ECG criteria, including depolarization/ repolarization abnormalities and ventricular arrhythmias, specific for the LV involvement.

"Padua criteria" for diagnosis of Arrhythmogenic Cardiomyopathy.

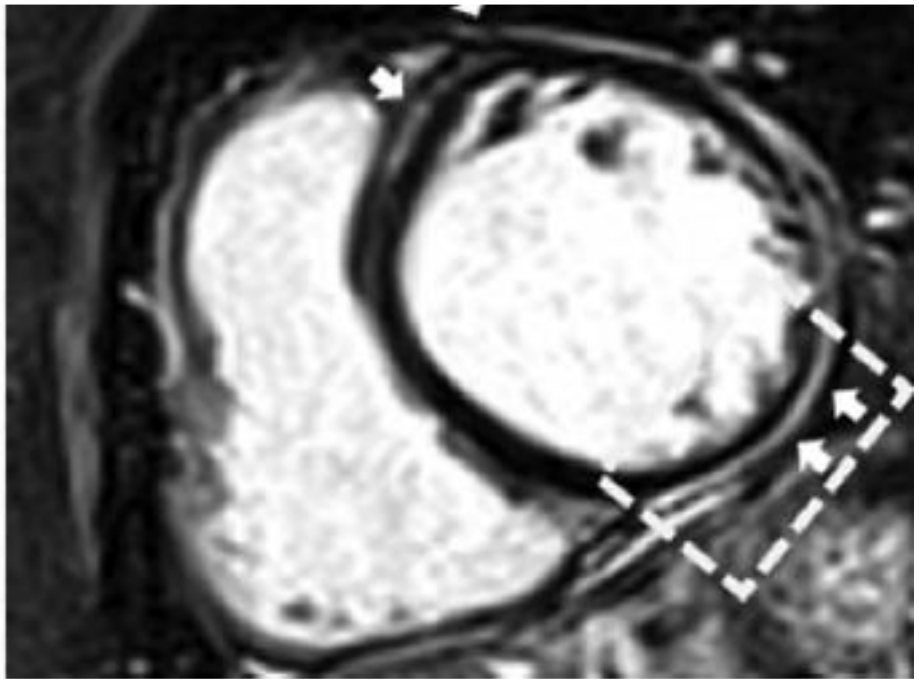
Category	Right ventricle (upgraded 2010 ITF diagnostic criteria)	Left ventricle (new diagnostic criteria)
I. Morpho-functional ventricular abnormalities	*By echocardiography, CMR or angiography:* *Major* • Regional RV akinesia, dyskinesia, or bulging *plus* one of the following: - global RV dilatation (increase of RV EDV according to the imaging test specific nomograms) - global RV systolic dysfunction (reduction of RV EF according to the imaging test specific nomograms) *Minor* • Regional RV akinesia, dyskinesia or aneurysm of RV free wall	*By echocardiography, CMR or angiography:Minor* • Global LV systolic dysfunction (depression of LV EF or reduction of echo-cardiographic global longitudinal strain), with or without LV dilatation (increase of LV EDV according to the imaging test specific nomograms for age, sex, and BSA) *Minor* • Regional LV hypokinesia or akinesia of LV free wall, septum, or both
II. Structural myocardial abnormalities	*By CE-CMR:Major* • Transmural LGE (stria pattern) of ≥1 RV region(s) (inlet, outlet, and apex in 2 orthogonal views) *By EMB (limited indications):Major* • Fibrous replacement of the myocardium in ≥1 sample, with or without fatty tissue	*By CE-CMR:Major* • LV LGE (stria pattern) of ≥1 Bull's Eye segment(s) (in 2 orthogonal views) of the free wall (subepicardial or midmyocardial), septum, or both (excluding septal junctional LGE)



Corrado D et al. *Int J Cardiol.* 2020

Diagnosis of arrhythmogenic cardiomyopathy: The Padua criteria

Domenico Corrado [a,*], Martina Perazzolo Marra [a], Alessandro Zorzi [a], Giorgia Beffagna [a], Alberto Cipriani [a], Manuel De Lazzari [a], Federico Migliore [a], Kalliopi Pilichou [a], Alessandra Rampazzo [b], Ilaria Rigato [a], Stefania Rizzo [a], Gaetano Thiene [a], Aris An[illegible] [c], [illegible] [d], [illegible] [e], Kristine H. Haugaa [f], Francis E. Marchlinsk[illegible], Antonio Pelliccia [k], Christian Schmied [l], Sa[illegible]



Category	Right ventricle (up[illegible] 2010 ITF diagnosti[illegible]	
I. Morpho-functional ventricular abnormalities	*By echocardiograph[illegible]* *Major* • Regional RV aki[illegible] - global RV dilata[illegible] specific nomog[illegible] - global RV systol[illegible] imaging test sp[illegible] *Minor* • Regional RV akinesia, dyskinesia or aneurysm of RV free wall	
II. Structural myocardial abnormalities	*By CE-CMR:Major* • Transmural LGE (stria pattern) of ≥1 RV region(s) (inlet, outlet, and apex in 2 orthogonal views) *By EMB (limited indications):Major* • Fibrous replacement of the myocardium in ≥1 sample, with or without fatty tissue	*By CE-CMR:Major* • LV LGE (stria pattern) of ≥1 Bull's Eye segment(s) (in 2 orthogonal views) of the free wall (subepicardial or midmyocardial), septum, or both (excluding septal junctional LGE)

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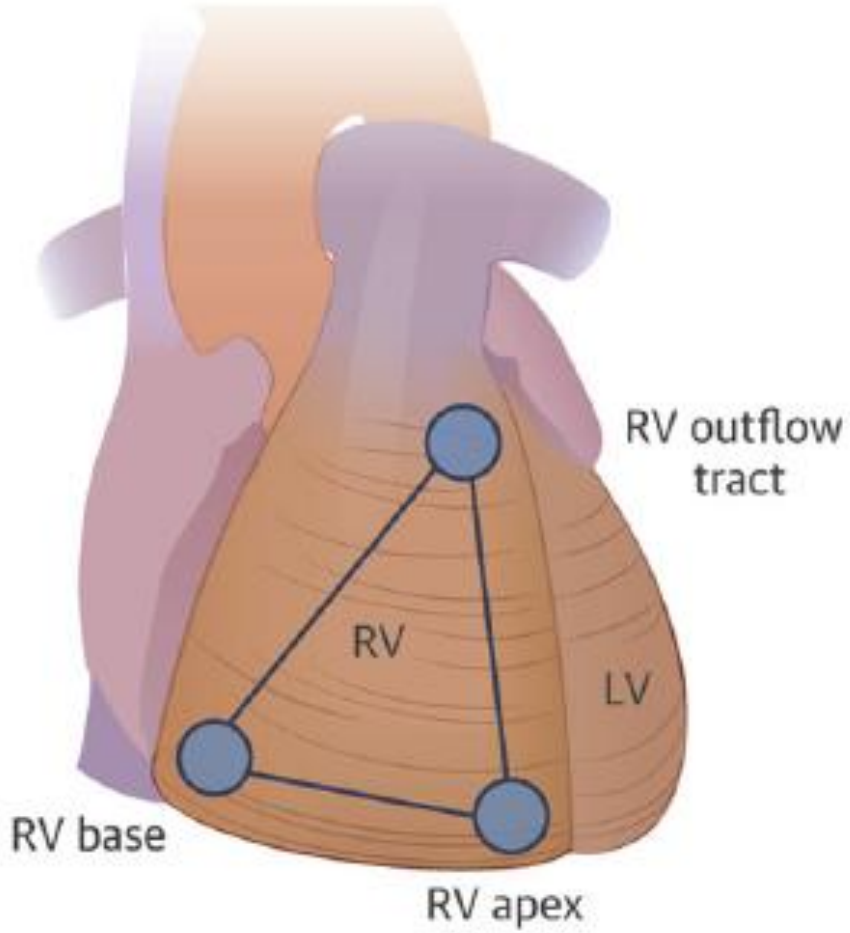
Arrhythmogenic cardiomyopathy in CMR

- **Akinesia:** Lack of motion (10% wall thickening)
- **Hypokinesia:** <40% wall thickening
- **(Focal) wall thinning**
- **Dyskinesia**
- **(Micro)-Aneurysm**: Persistent bulging in both systole and diastole.
- **Dyssynchrony**: Regional peak contraction occurring at different times in adjacent myocardium.
- **Accordion sign:** specific area/segment of free RV wall myocardium with dyssynchronous micro contraction.

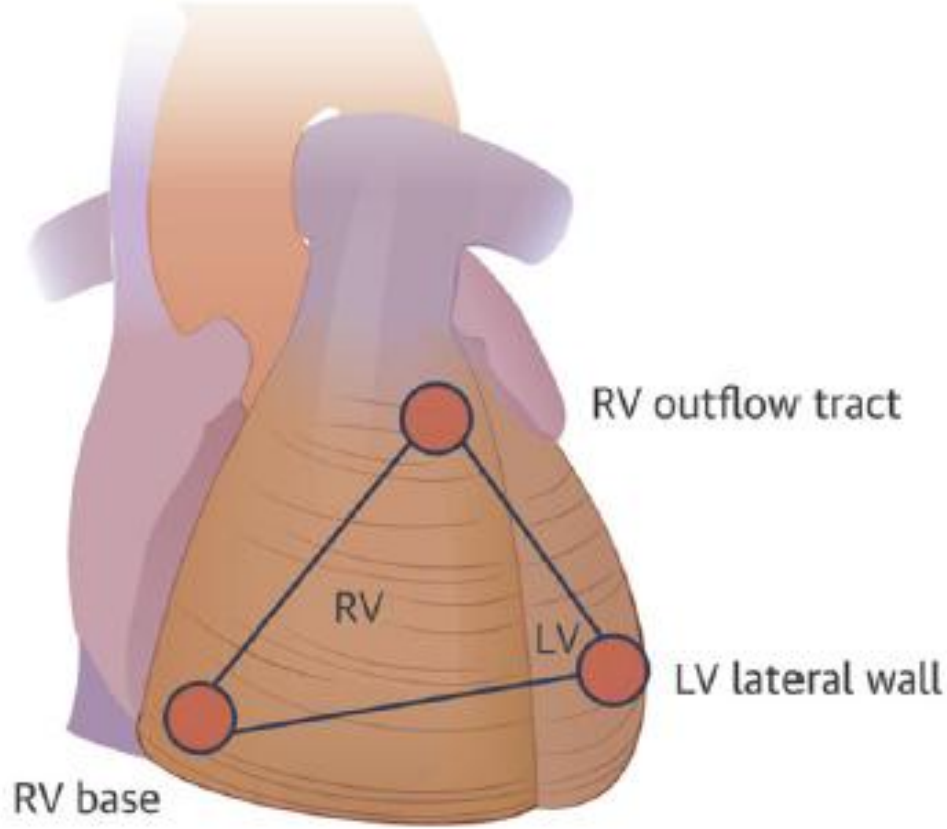
TRADITIONAL MODEL OF ARVD/C

2D Visualization of Structural Substrate, Triangle of Dysplasia

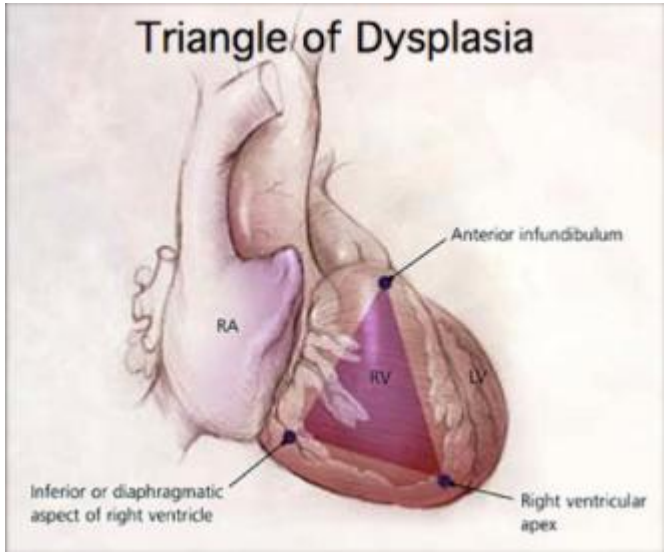


CONTEMPORARY MODEL OF ARVD/C

Multiplane Visualization of Electrical and Structural Substrate, Triangle of Dysplasia Displaced

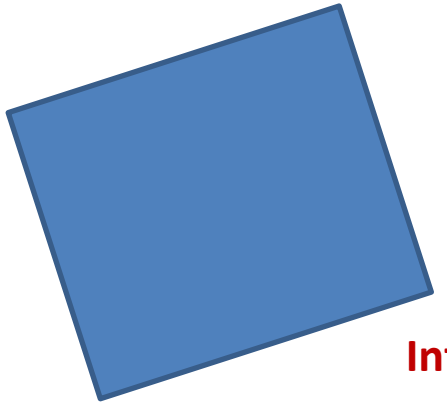


te Riele et al, JACC CV imaging 2015



RV sub tricuspid

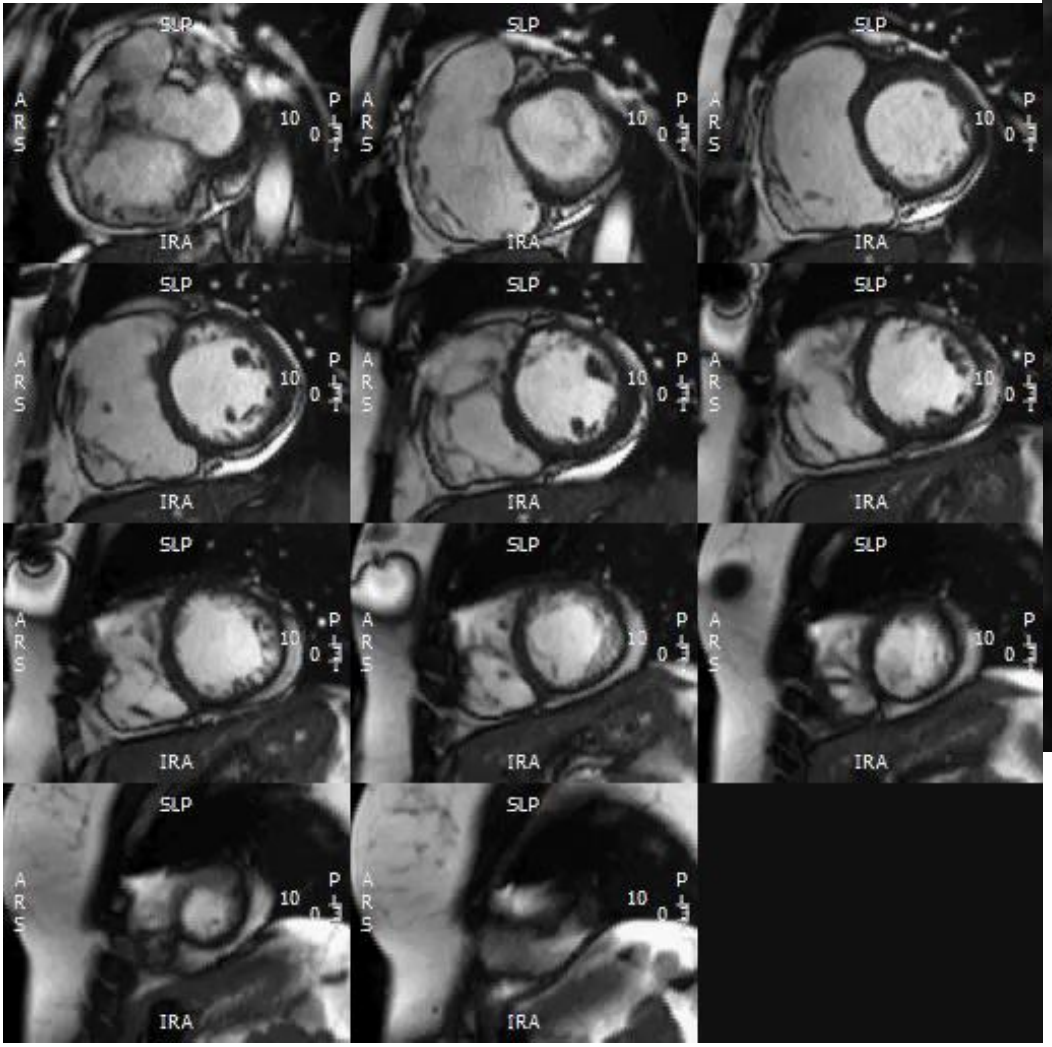
Infundibulum



Inferolateral LV

RV apex

Case 1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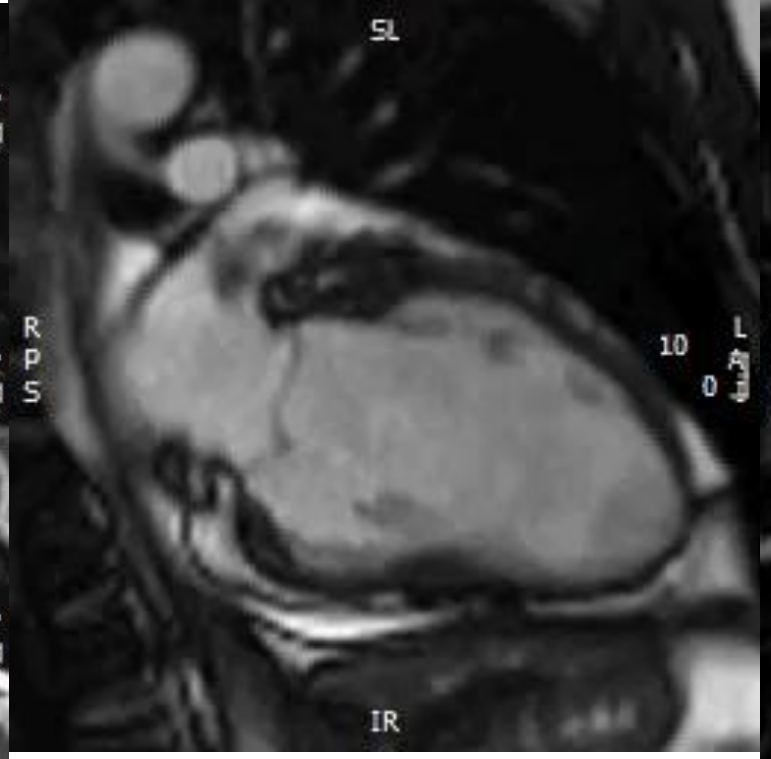
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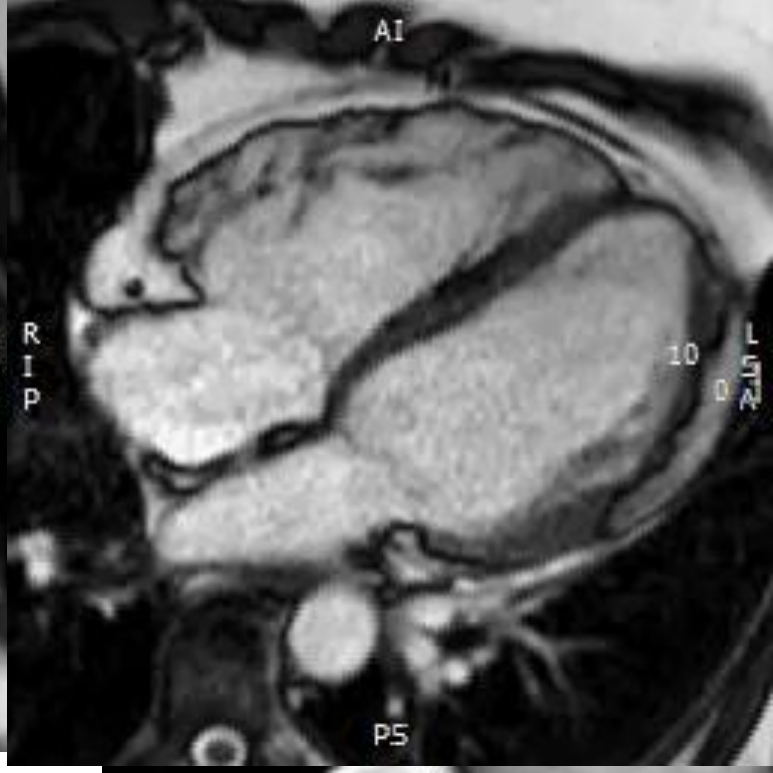
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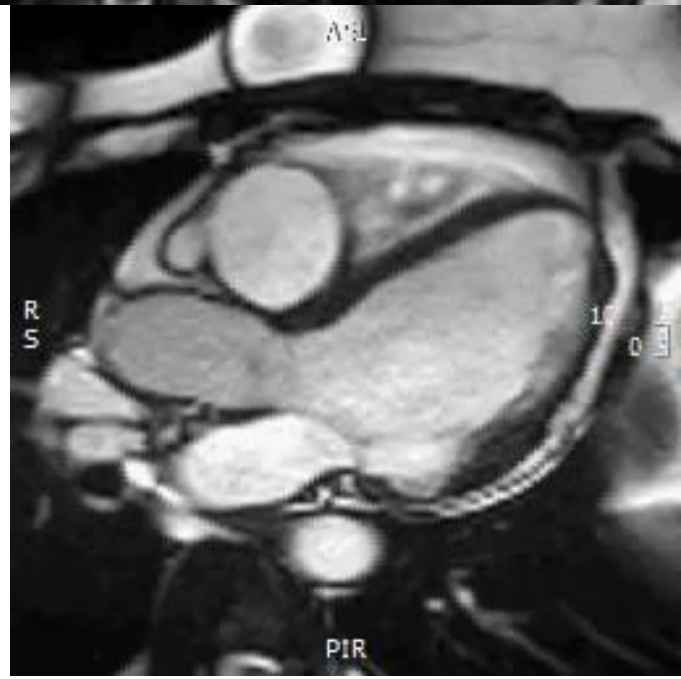
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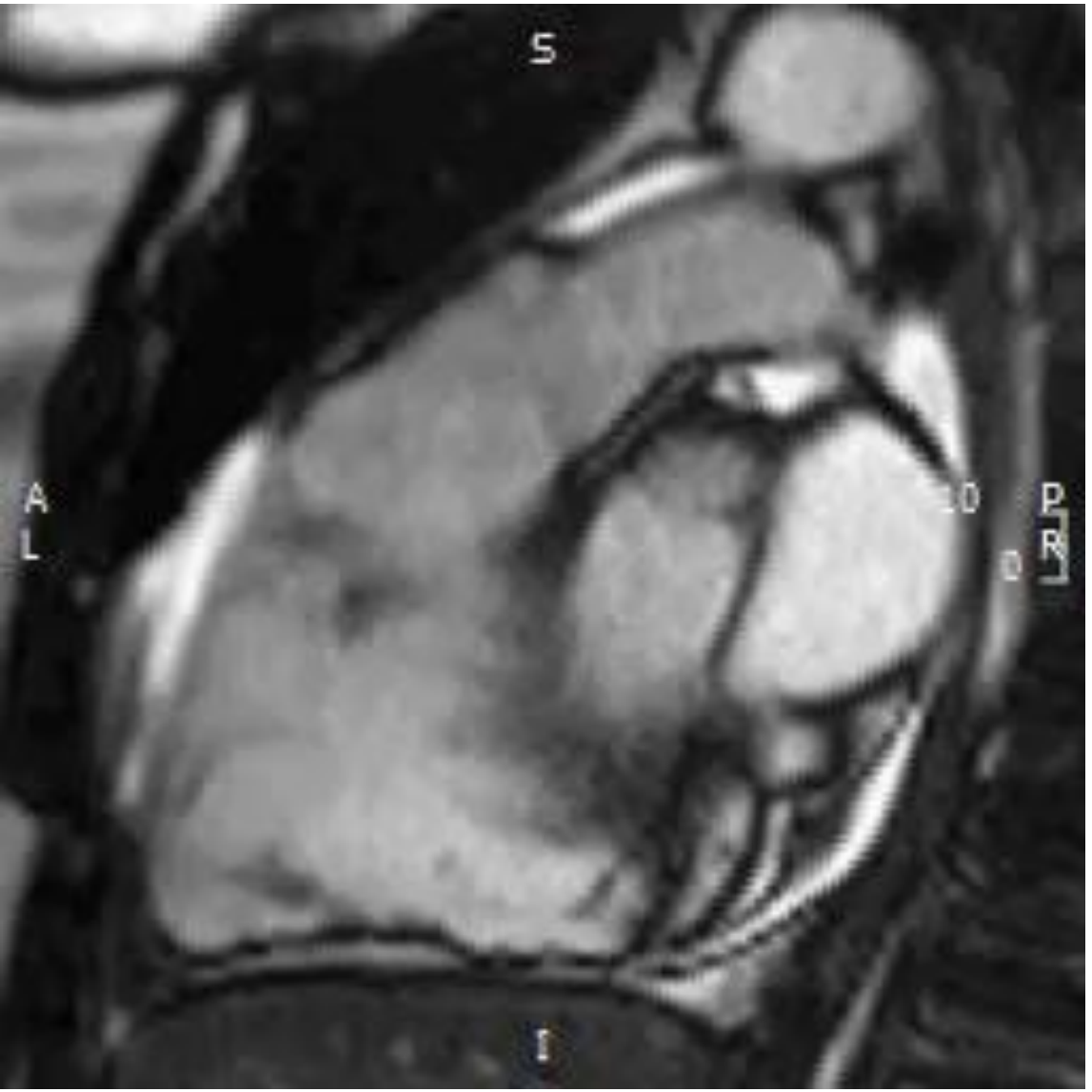
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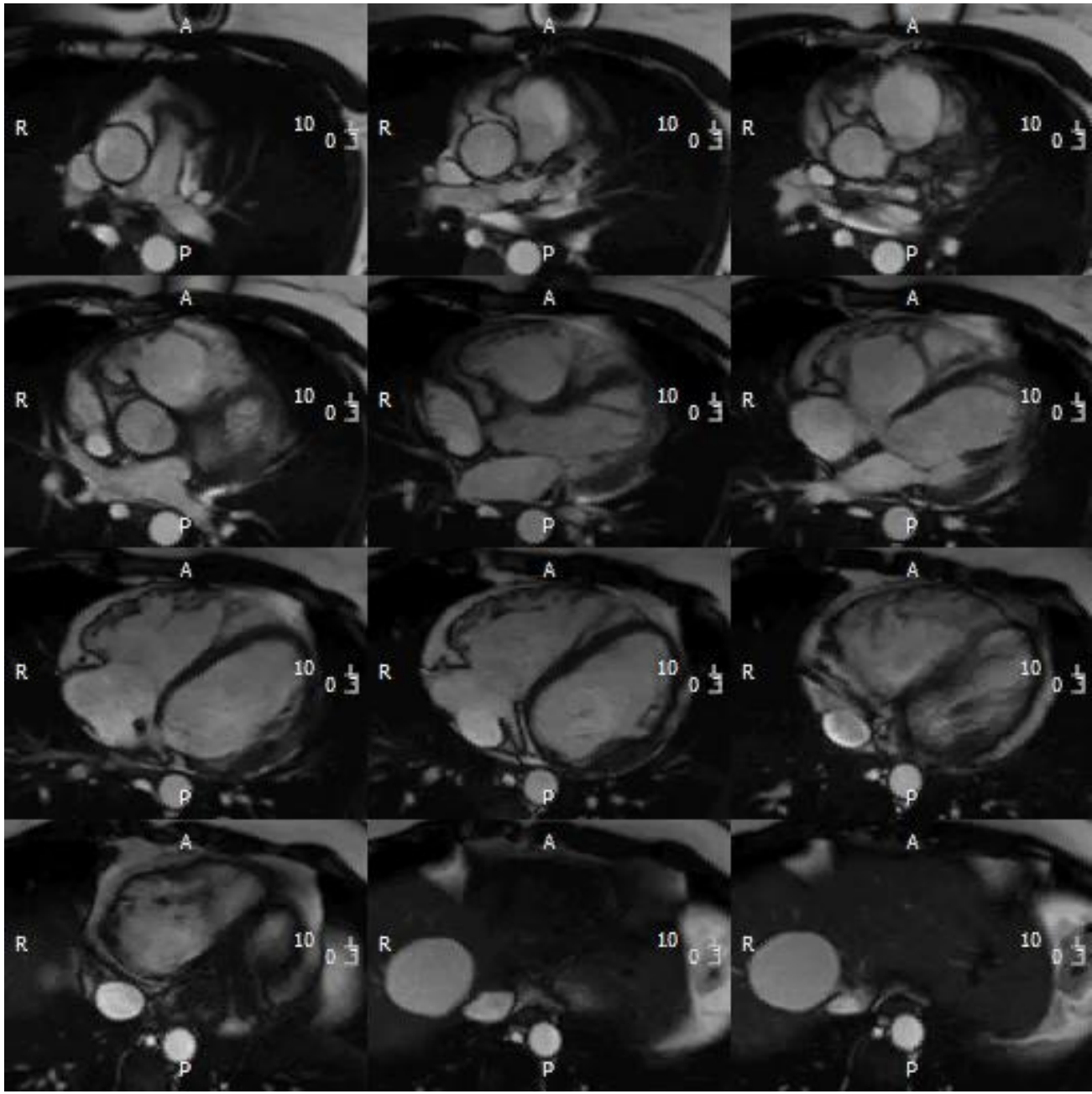
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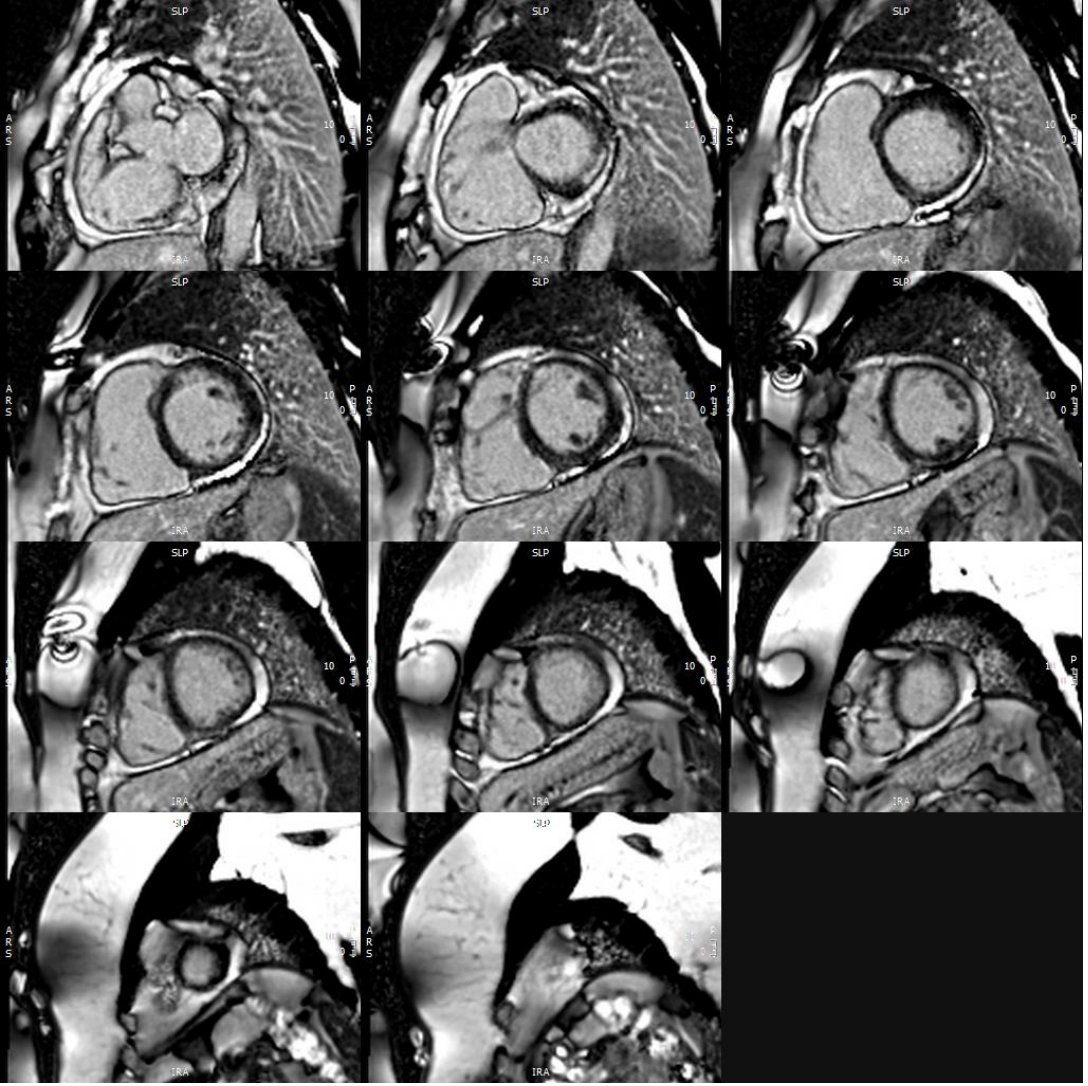
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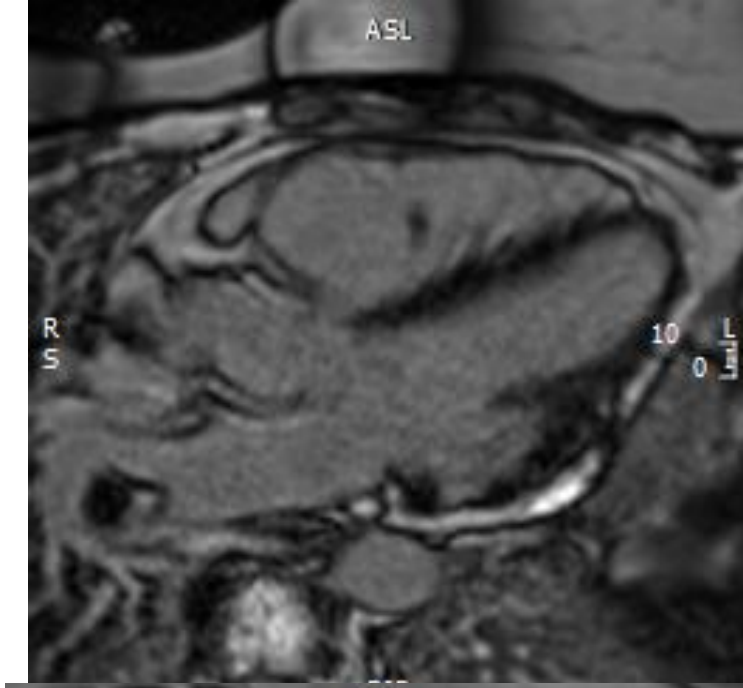
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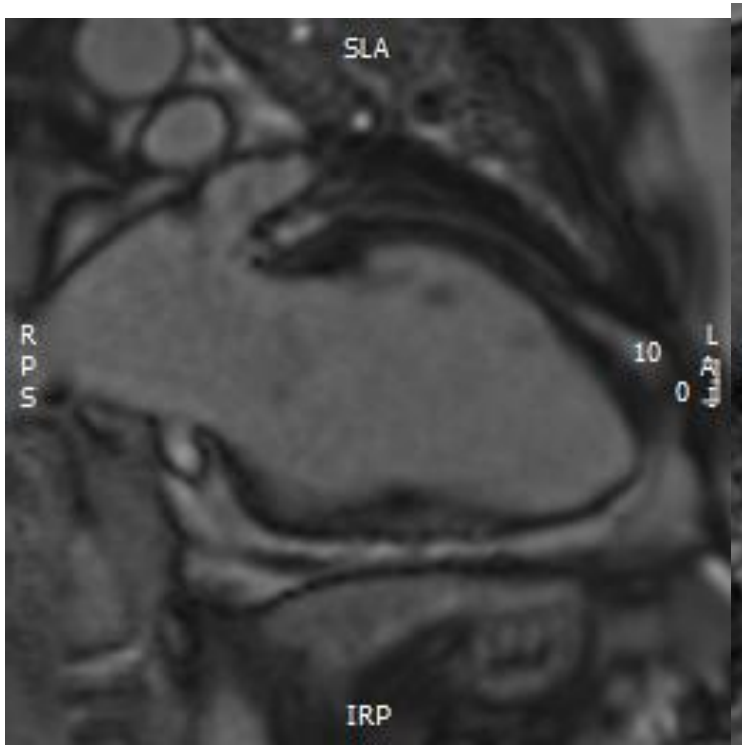
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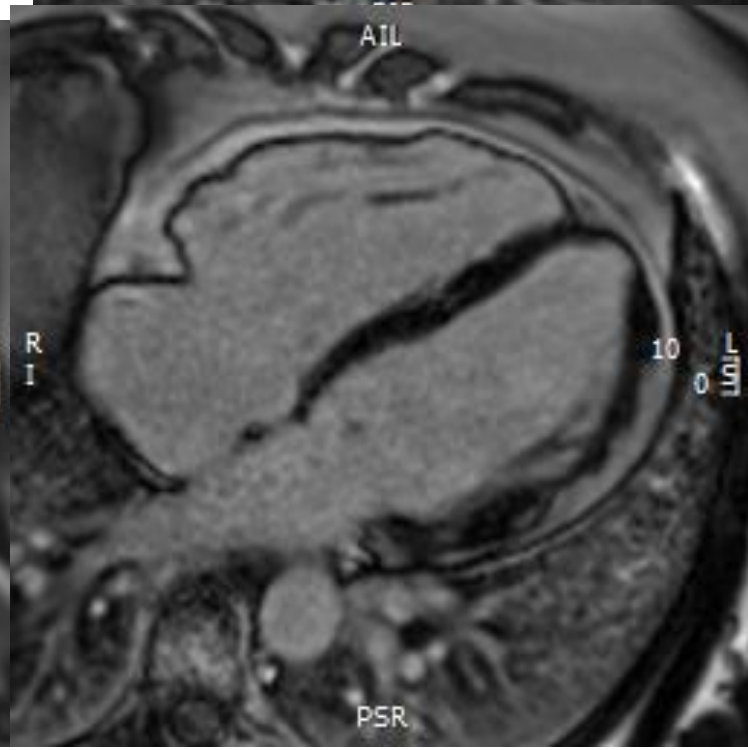
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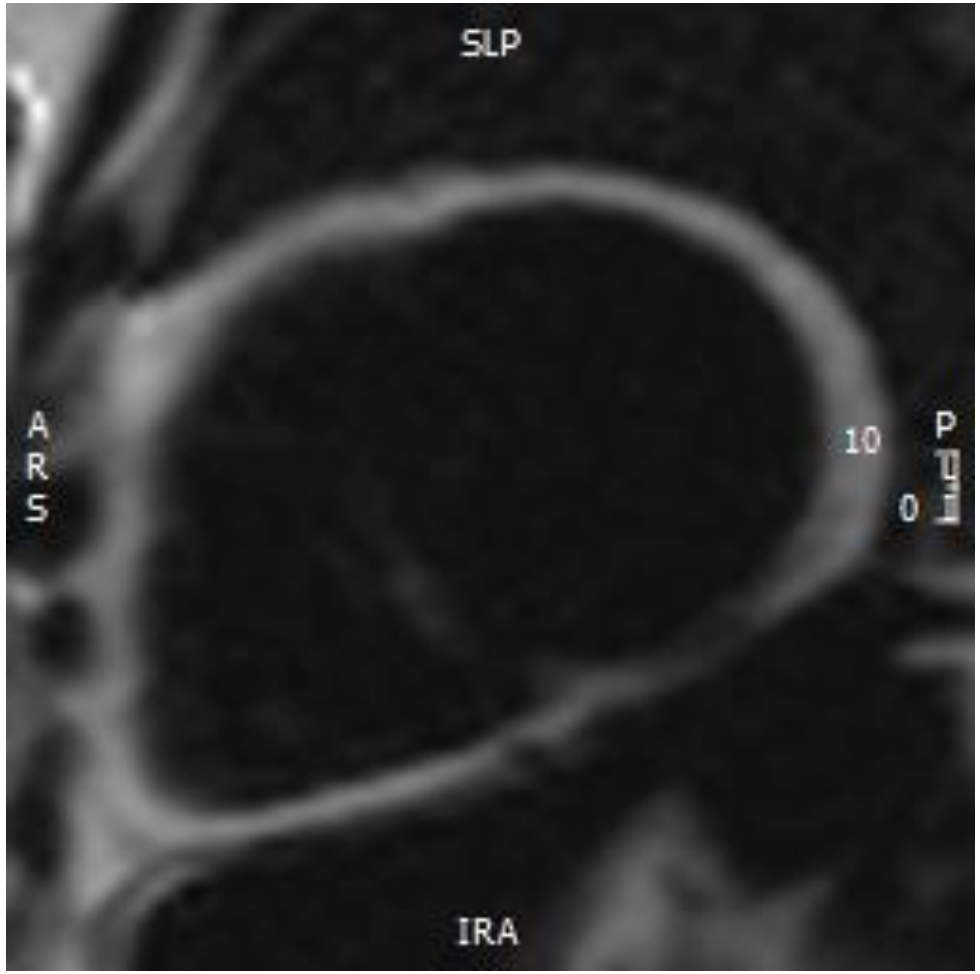
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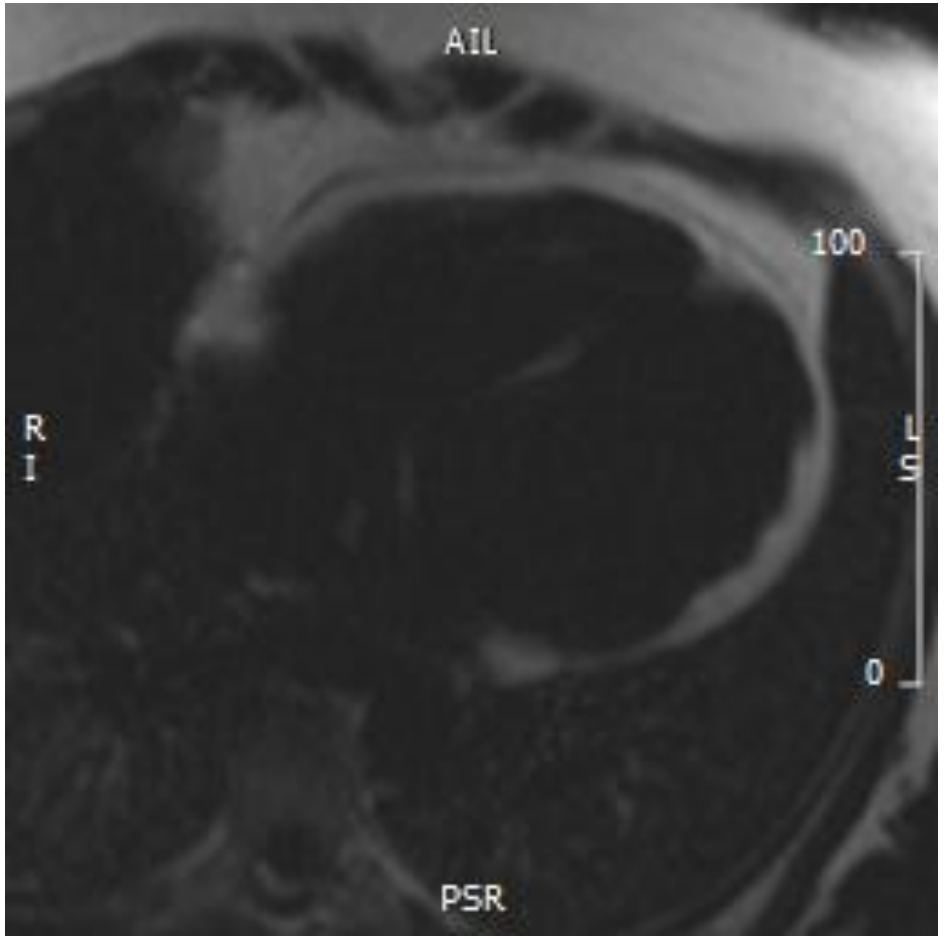
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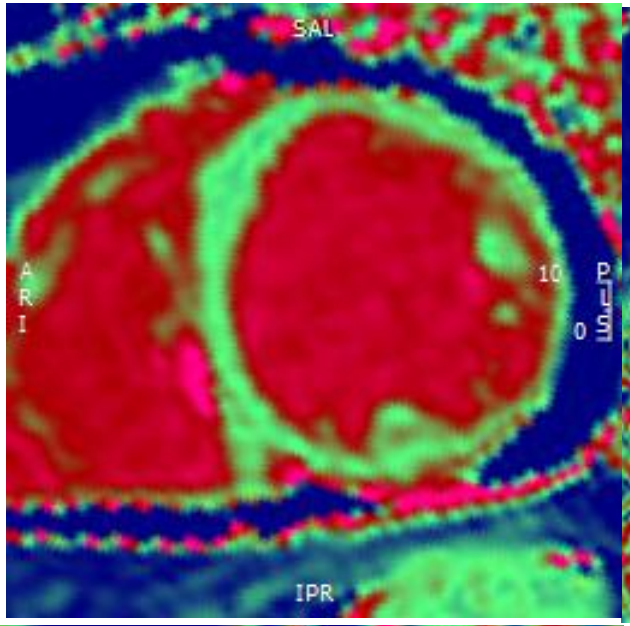
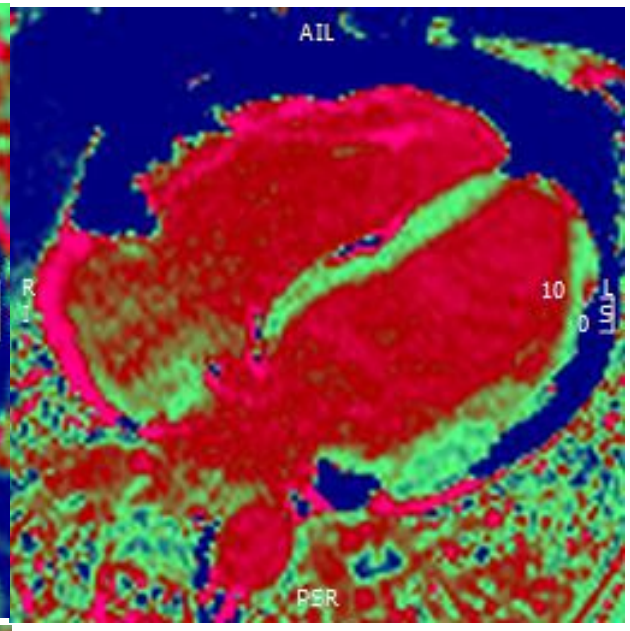
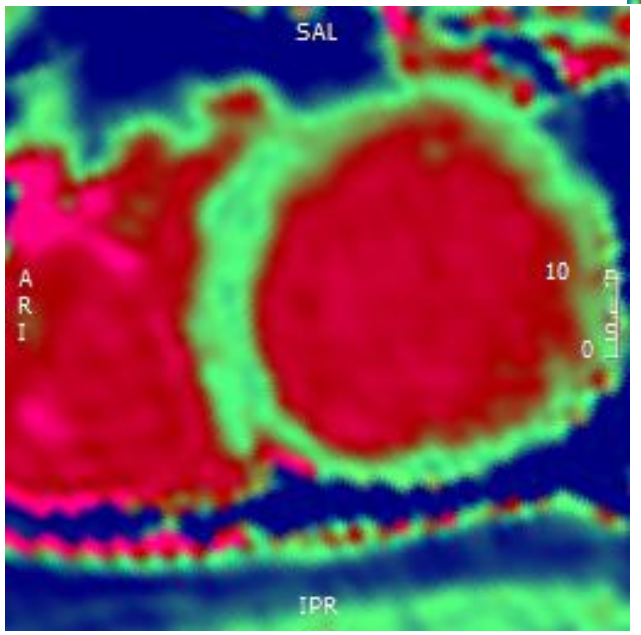
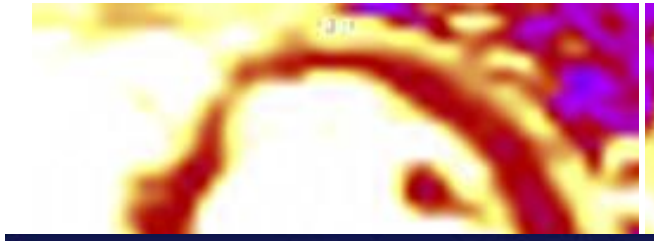
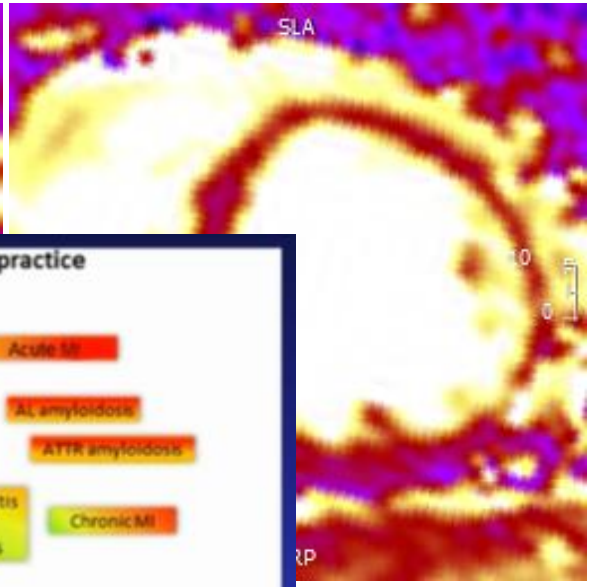


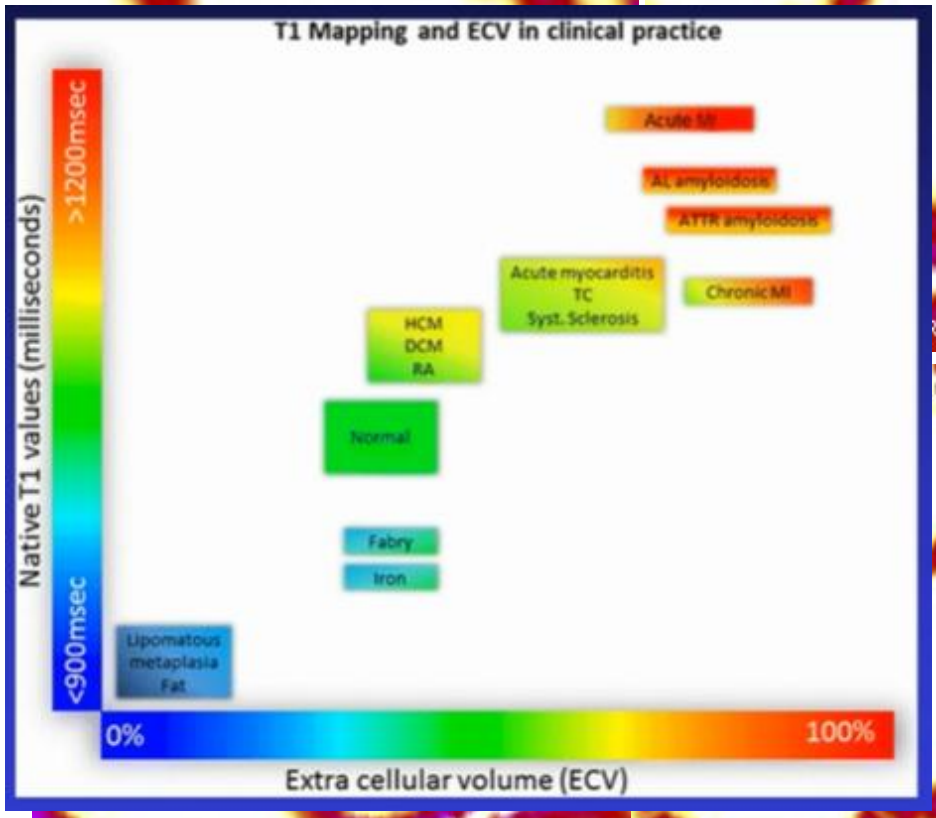


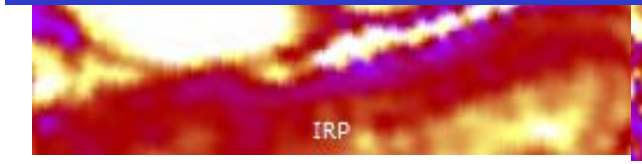


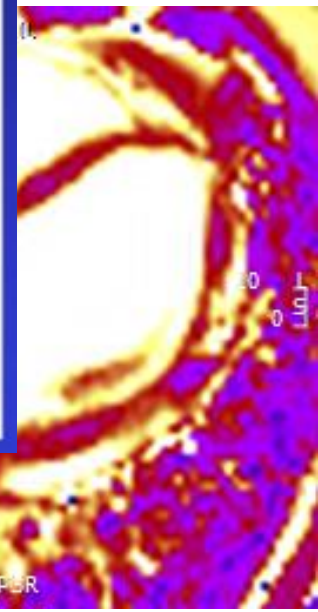
Be aware of "HOT" Phases







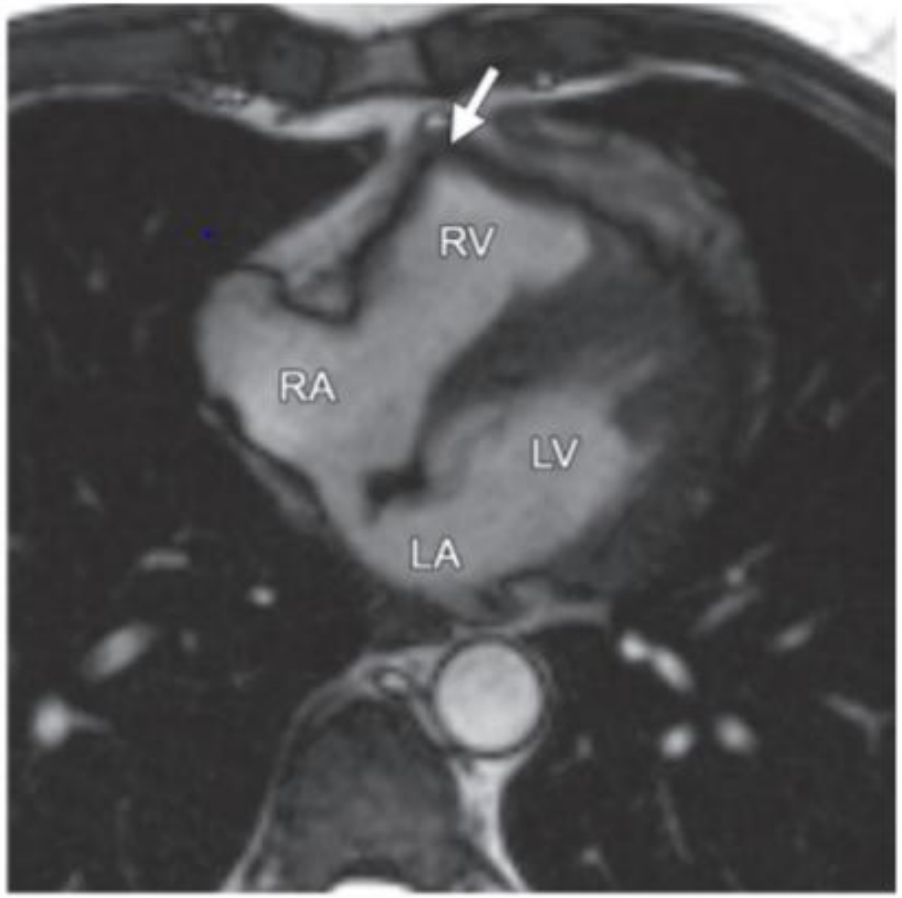


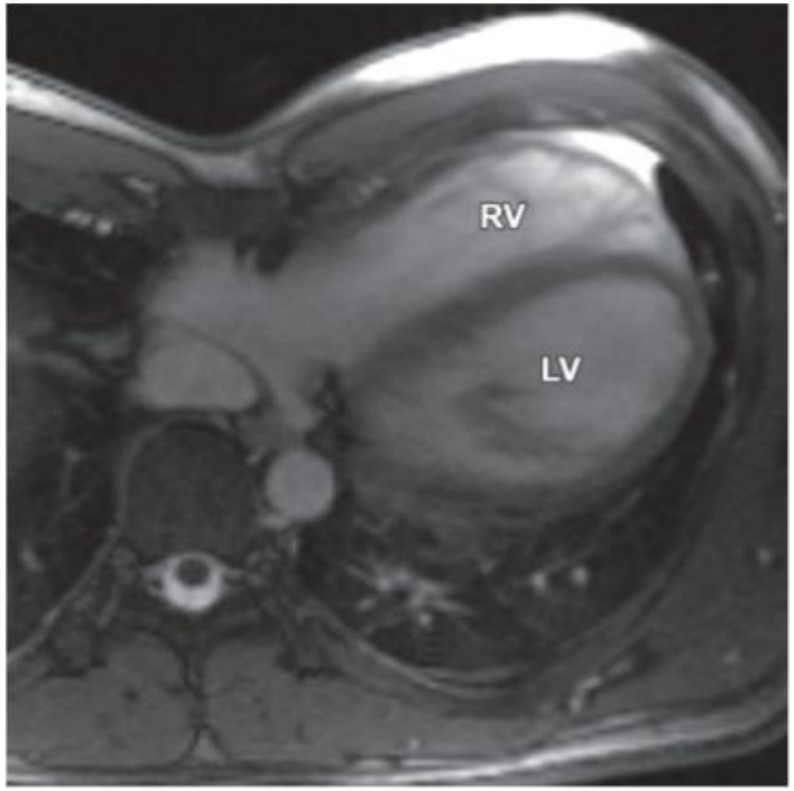


Pitfalls in imaging of ARVC

Fatty infiltration

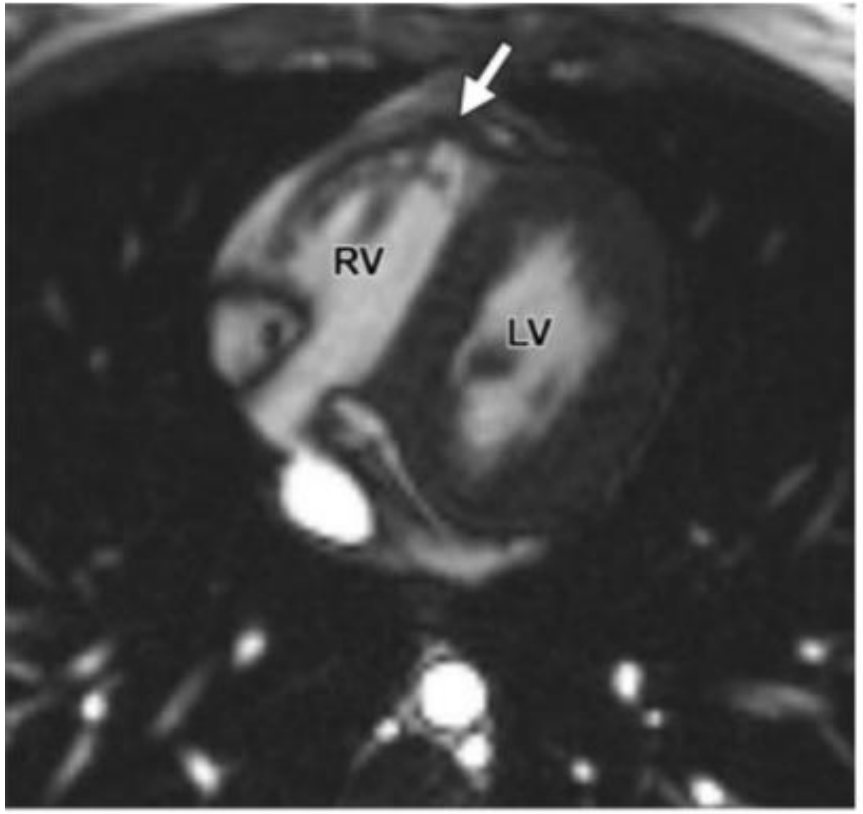
Free wall tethering



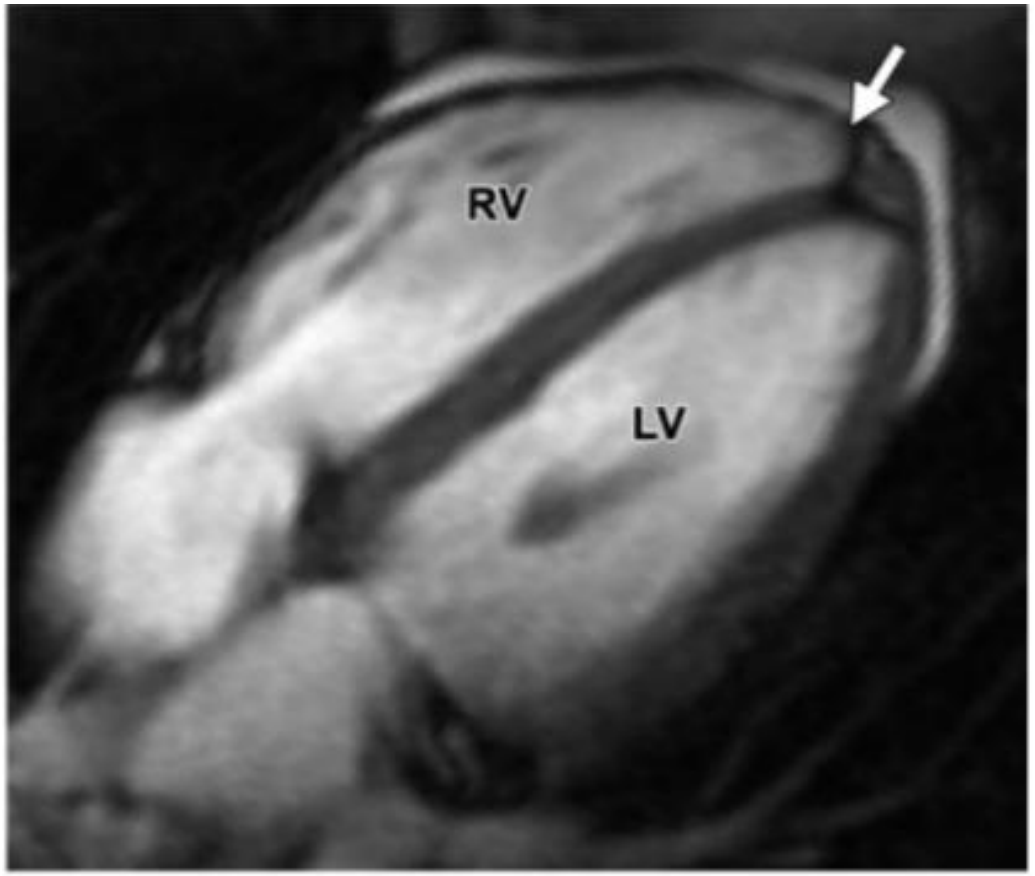


Pectus excavatum

Apicolateral bulge



Butterfly apex



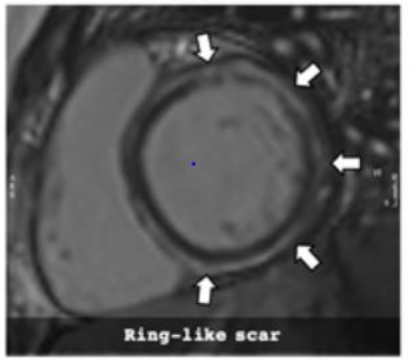
Correlation of phenotype with genotype

Lamin A/C 6% of DCM

Filamin C

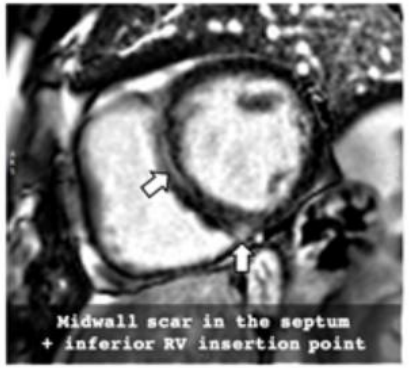
DSP

Desmoplakin



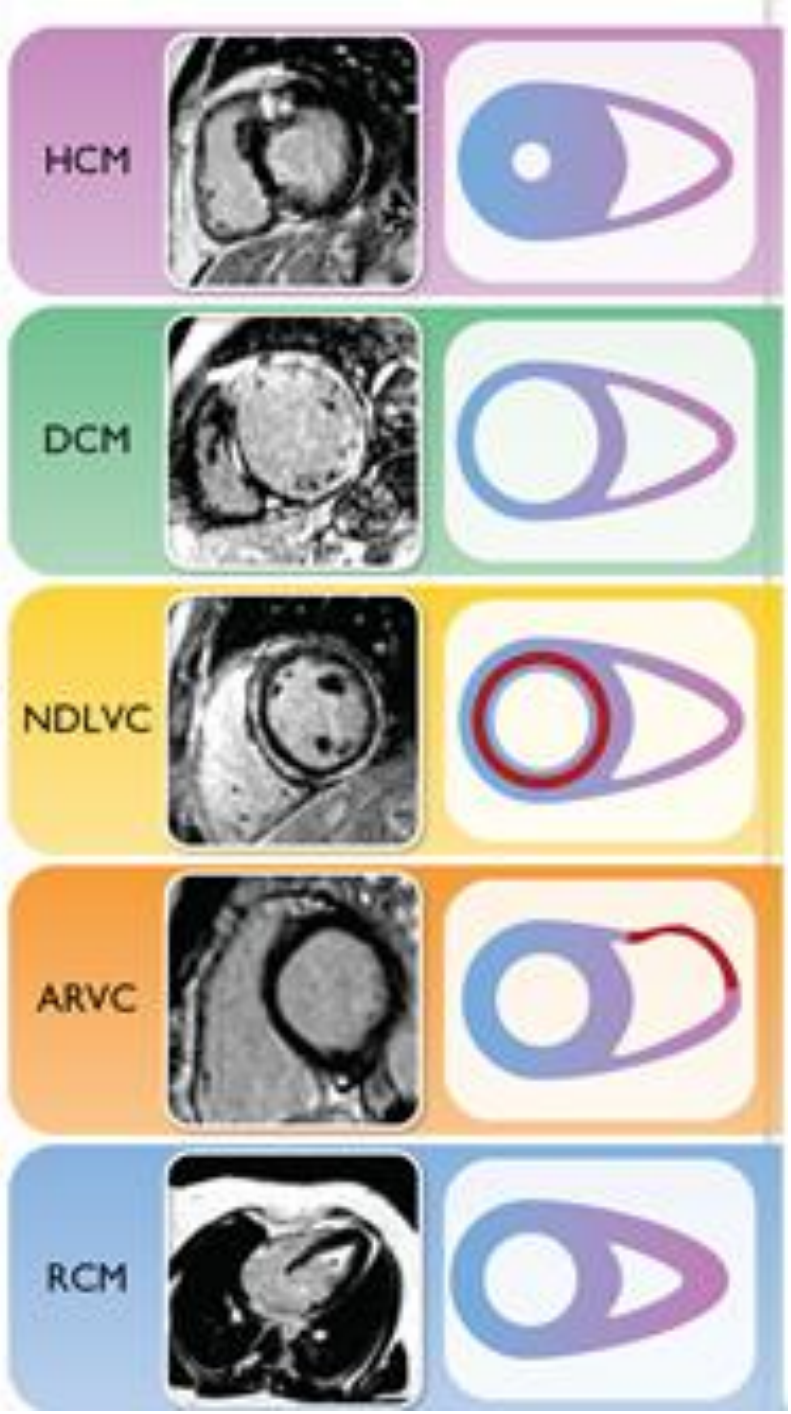
Filamin C

Lamin A/C



Augusto JB, et al. Dilated cardiomyopathy and arrhythmogenic left ventricular cardiomyopathy: a comprehensive genotype-imaging phenotype study. *Eur Heart J Cardiovasc Imaging*. 2020;21(3):326-336.

5 Phenotypes



Non Dilated Left Ventricular Cardiomyopathy (NDLVC)

- Presence of Non ischaemic LV scar/ Fatty replacement WITH or WITHOUT global/regional wall motion abnormalities
- Isolated GLOBAL LV hypokinesia WITHOUT scarring

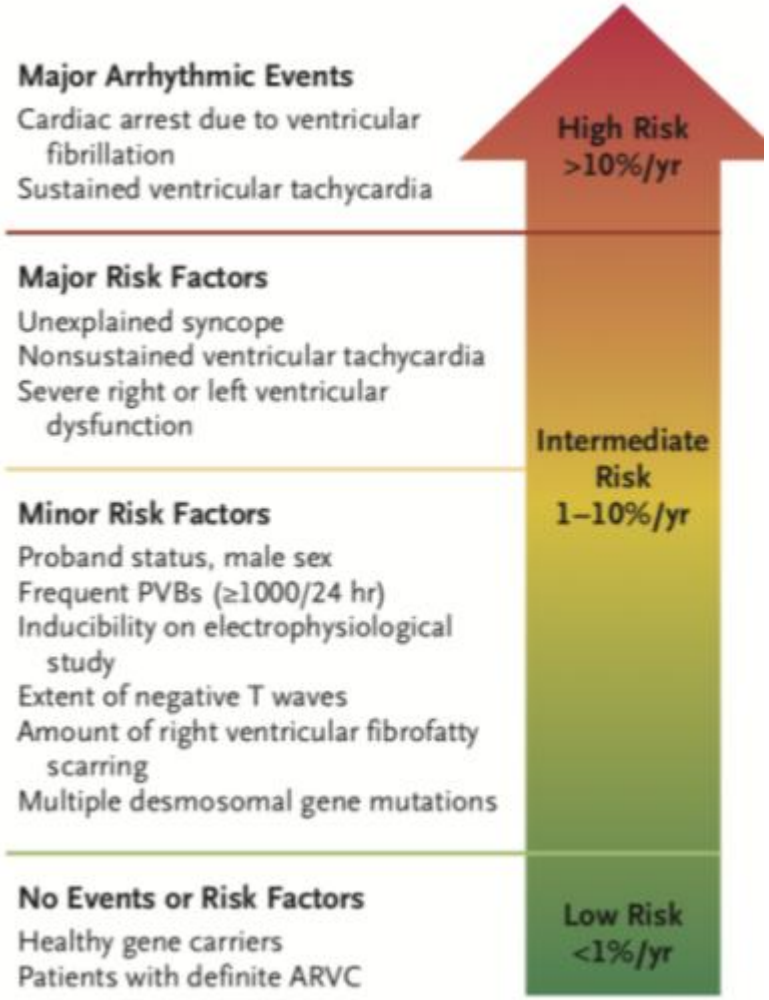
DCM (NO LV dilation)

ALVC

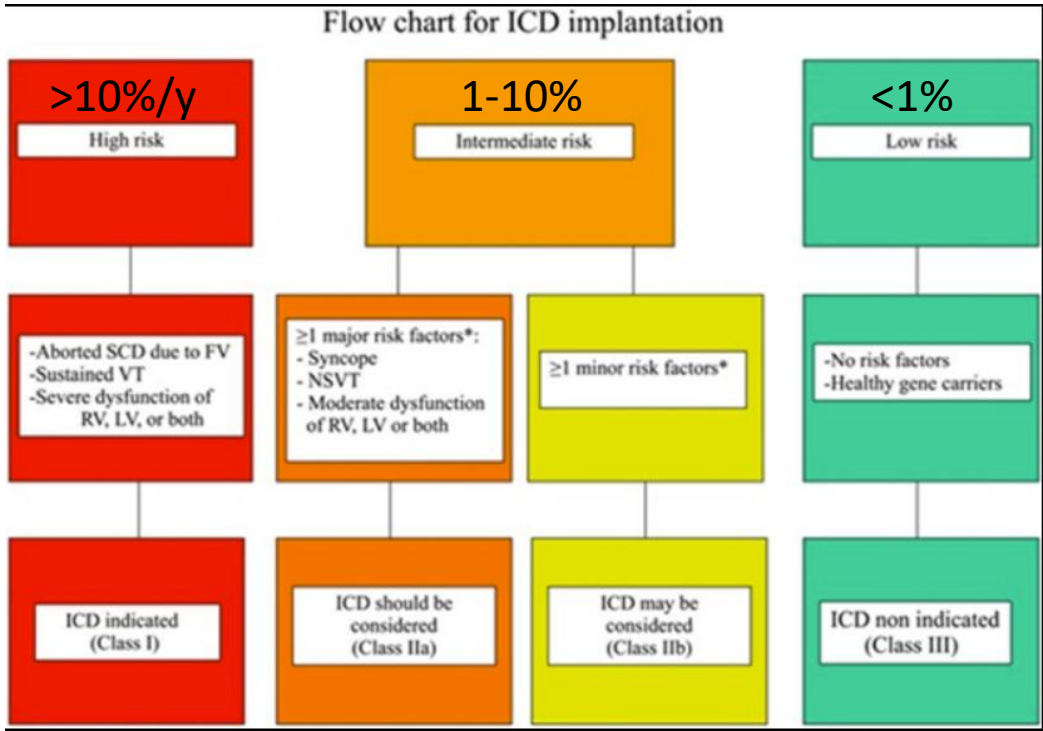
Left dominant ARVC

Arrhythmogenic DCM

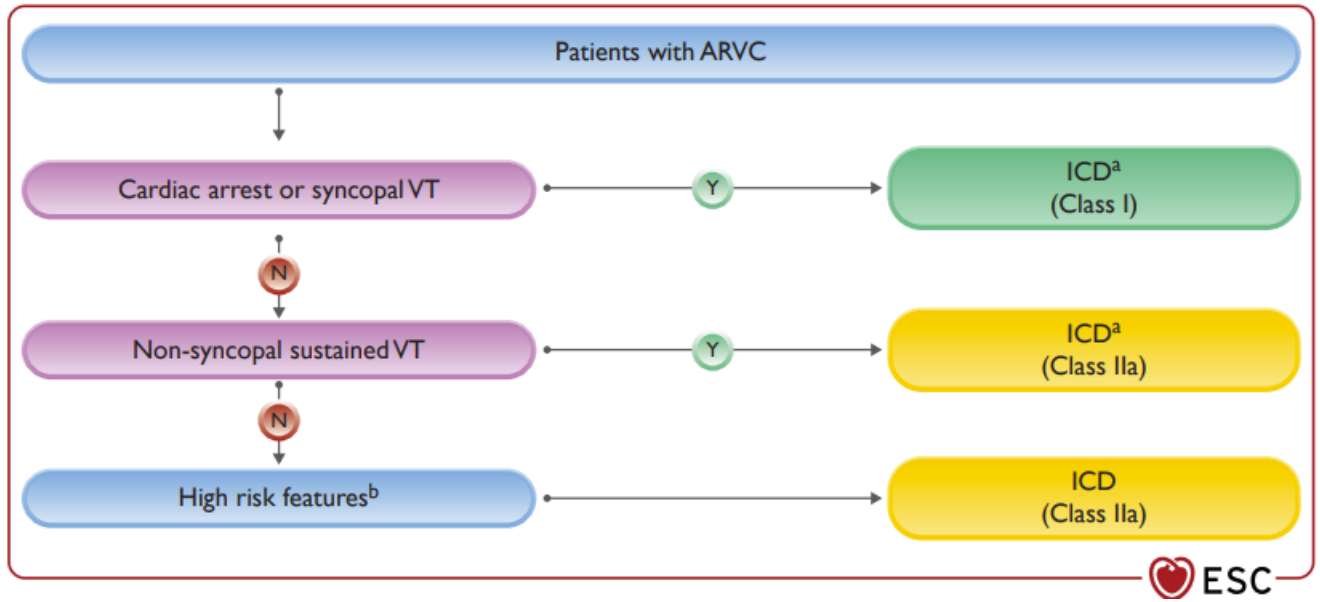
This is NOT the diagnosis



Corrado D. et al N Engl J Med 2017;376:61-72



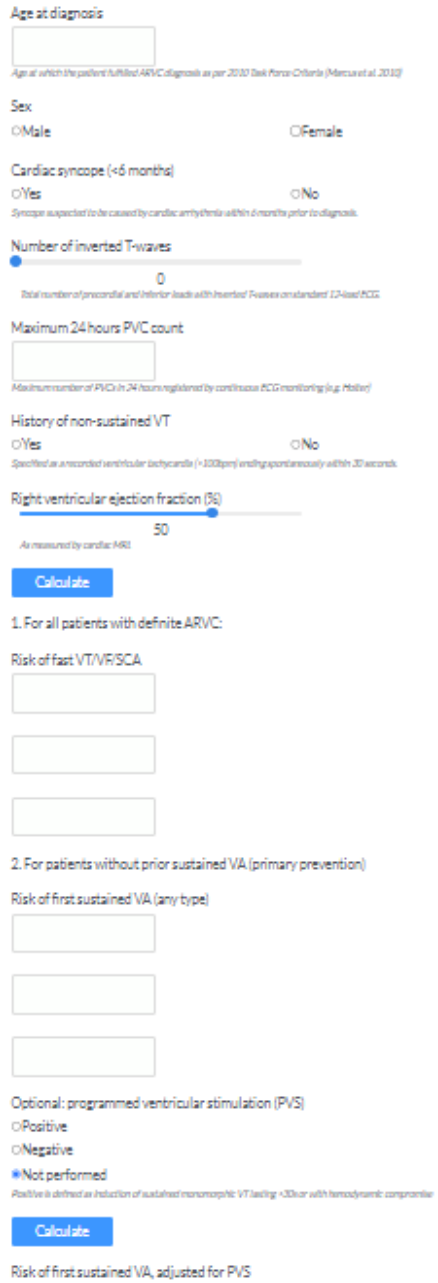
ARVC-SCD



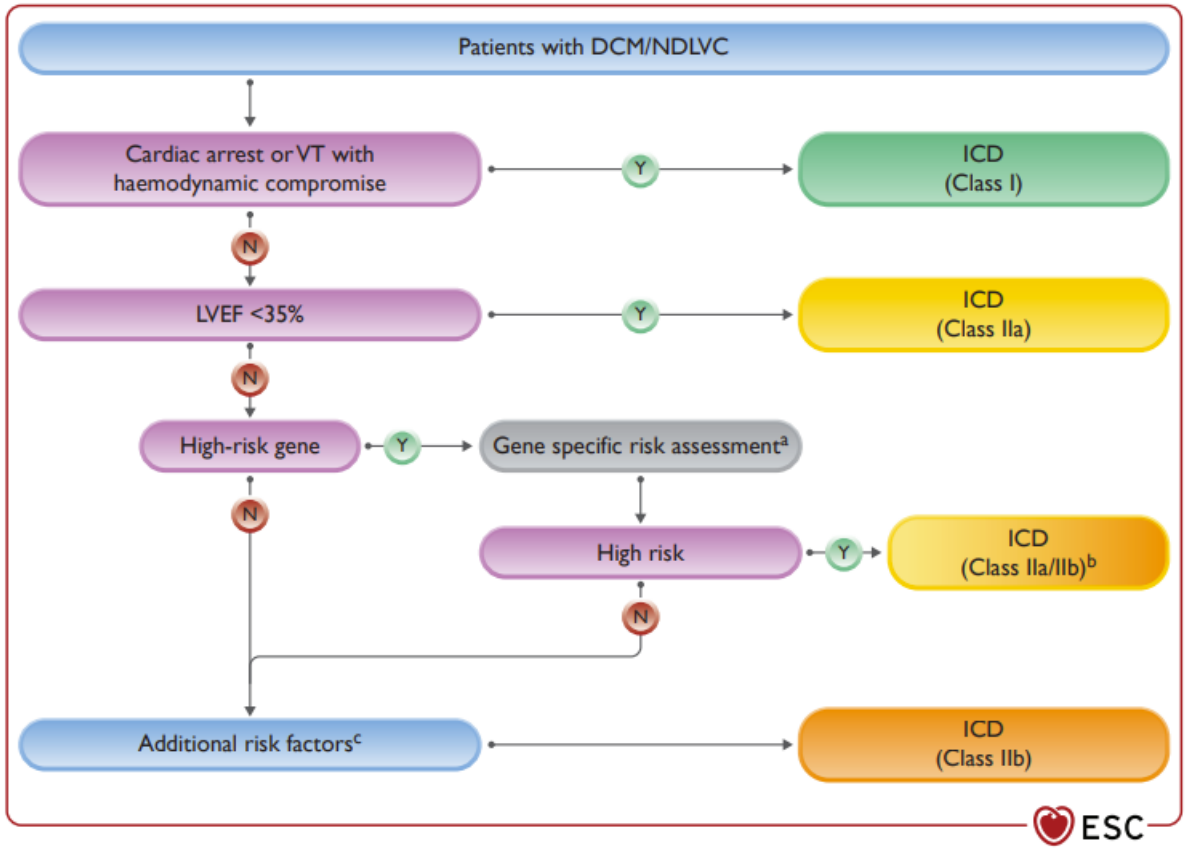
- Better for certain genotypes (ie PKP2 vs gene elusive)
- High-risk features are defined as either cardiac syncope

NSVT, RVEF<40%, LVEF<45%, SMVT at PES

ICD implantation should be considered in symptomatic[d] patients with definite ARVC, moderate right or left ventricular dysfunction, and either NSVT or inducibility of SMVT at PES.	IIa
In ARVC patients with indication for ICDs, a device with the capability of ATP programming for SMVT up to high rates should be considered.	IIa



DCM/NDLVC-SCD



- Syncope IIb
- LGE IIb

➢Gene specific approach (IIa)

- Variant Specific calculators

Primary prevention		
An ICD should be considered to reduce the risk of sudden death and all-cause mortality in patients with DCM, symptomatic heart failure, and LVEF ≤35% despite >3 months of OMT.[861,885]	IIa	A
The patient's genotype should be considered in the estimation of SCD risk in DCM.[185,186,869,886]	IIa	B
An ICD should be considered in patients with DCM with a genotype associated with high SCD risk and LVEF >35% in the presence of additional risk factors (see *Table 21*).[541,542,867,869,873,878,881,886]	IIa	C
An ICD may be considered in selected patients with DCM with a genotype associated with high SCD risk and LVEF >35% without additional risk factors (see *Table 21*).[869,873,881,886]	IIb	C
An ICD may be considered in patients with DCM without a genotype associated with high SCD risk and LVEF >35% in the presence of additional risk factors.[c,138,873,874]	IIb	C

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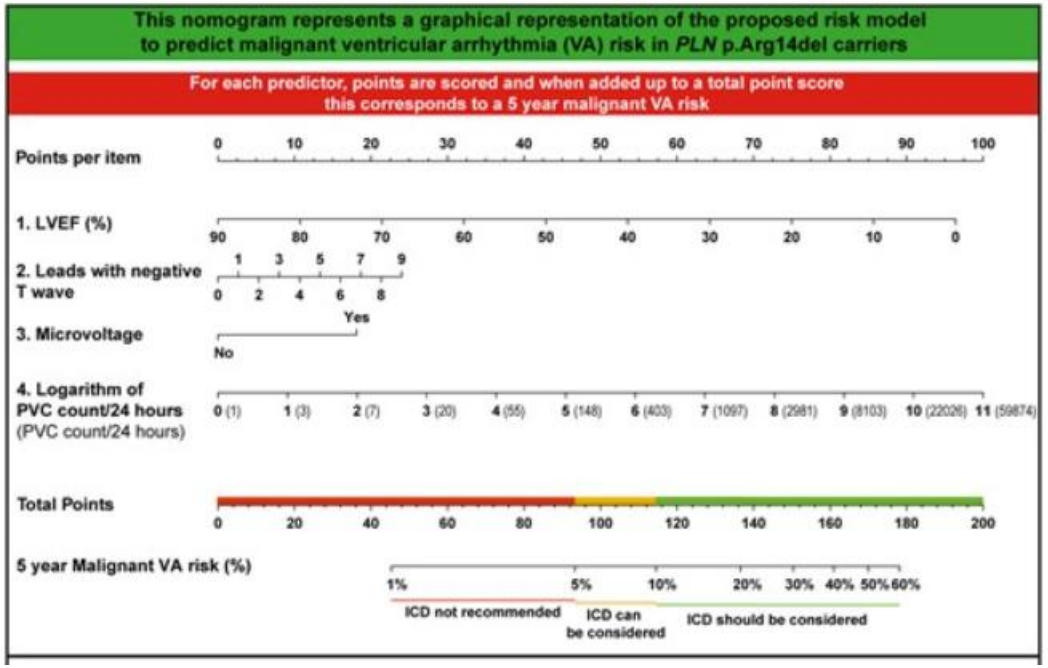
LMNA-risk VTA calculator

Risk Prediction Score for Life-Threatening Ventricular Tachyarrhythmias in Laminopathies

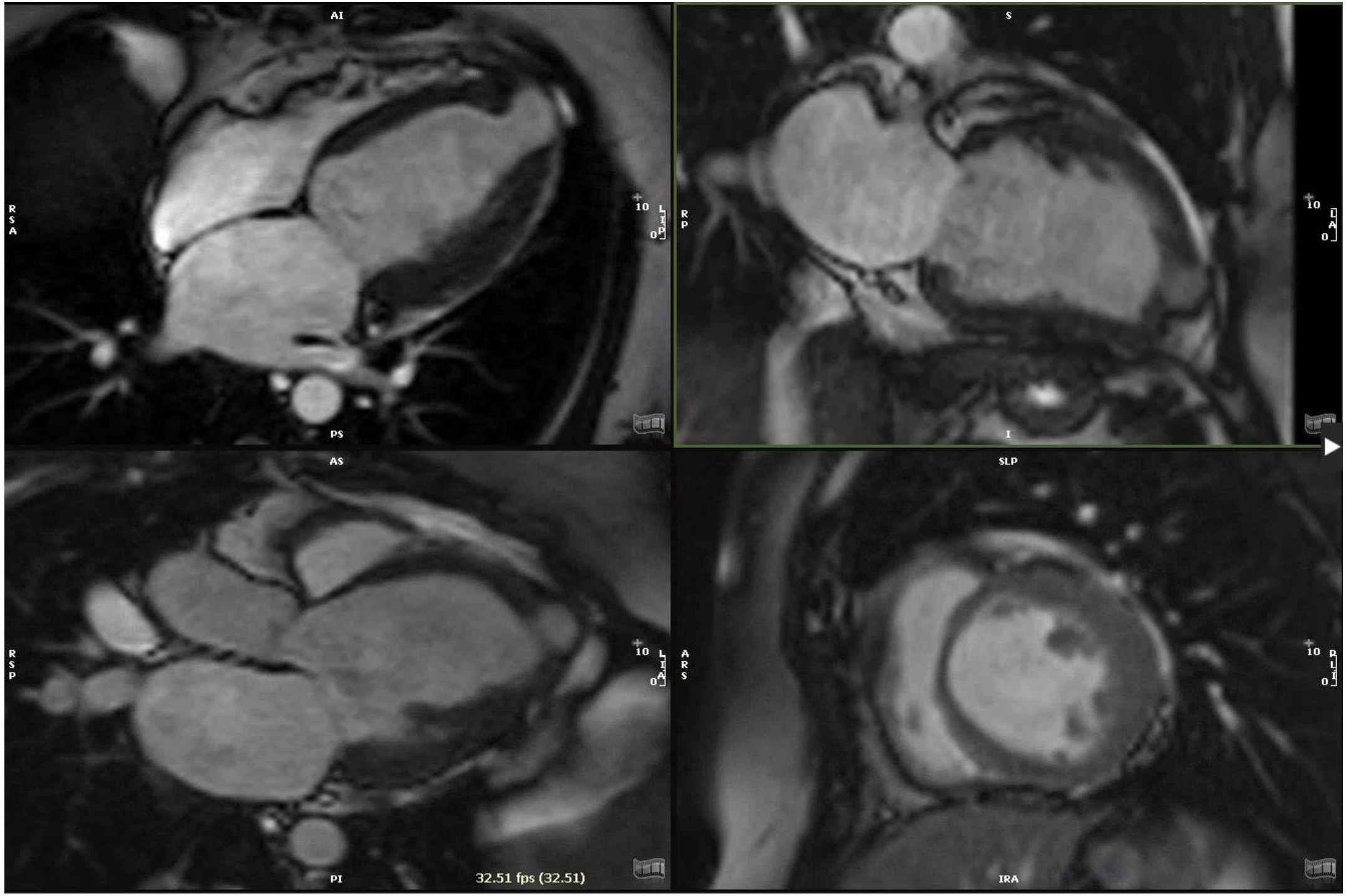
Sex	○ Male ○ Female	
Non-missense LMNA mutation	○ Yes ○ No	*Non-missense mutations include insertions, deletions, truncating mutations or mutations affecting splicing*
Atrio-ventricular block	○ Absent ○ 1st degree ○ High degree	*Please select the highest degree. 1st degree AV block corresponds to ≥0.20 sec PR interval and high degree AV block to type II 2nd degree or 3rd degree (and not type I 2nd degree)*
Non-sustained ventricular tachycardia	○ Yes ○ No	*NSVT corresponds to ≥3 consecutive ventricular complexes at a rate ≥120 bpm on 24-h ambulatory electrocardiographic monitoring*
Left ventricular ejection fraction	%	*Left ventricular ejection fraction measurement derived from echocardiogram*

Risk of Life-Threatening Ventricular Tachyarrhythmias at 5 years



Gene	Annual SCD rate	Predictors of SCD
LMNA[185,186,438,541,865,878,879]	5–10%	Estimated 5-year risk of life-threatening arrhythmia using *LMNA* risk score (https://lmna-risk-vta.fr)
FLNC-truncating variants[866,867,880]	5–10%	LGE on CMR LVEF < 45%
TMEM43[868,881]	5–10%	Male Female and any of the following: LVEF <45%, NSVT, LGE on CMR, >200 VE on 24h Holter ECG
PLN[542,882,883]	3–5%	Estimated 5-year risk of life-threatening arrhythmia using *PLN* risk score (https://plnriskcalculator.shinyapps.io/final_shiny) LVEF < 45% LGE on CMR NSVT
DSP[185,186]	3–5%	LGE on CMR LVEF < 45%
RBM20[869]	3–5%	LGE on CMR LVEF < 45%

Case 2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32.51 fps (32.51)
SLP
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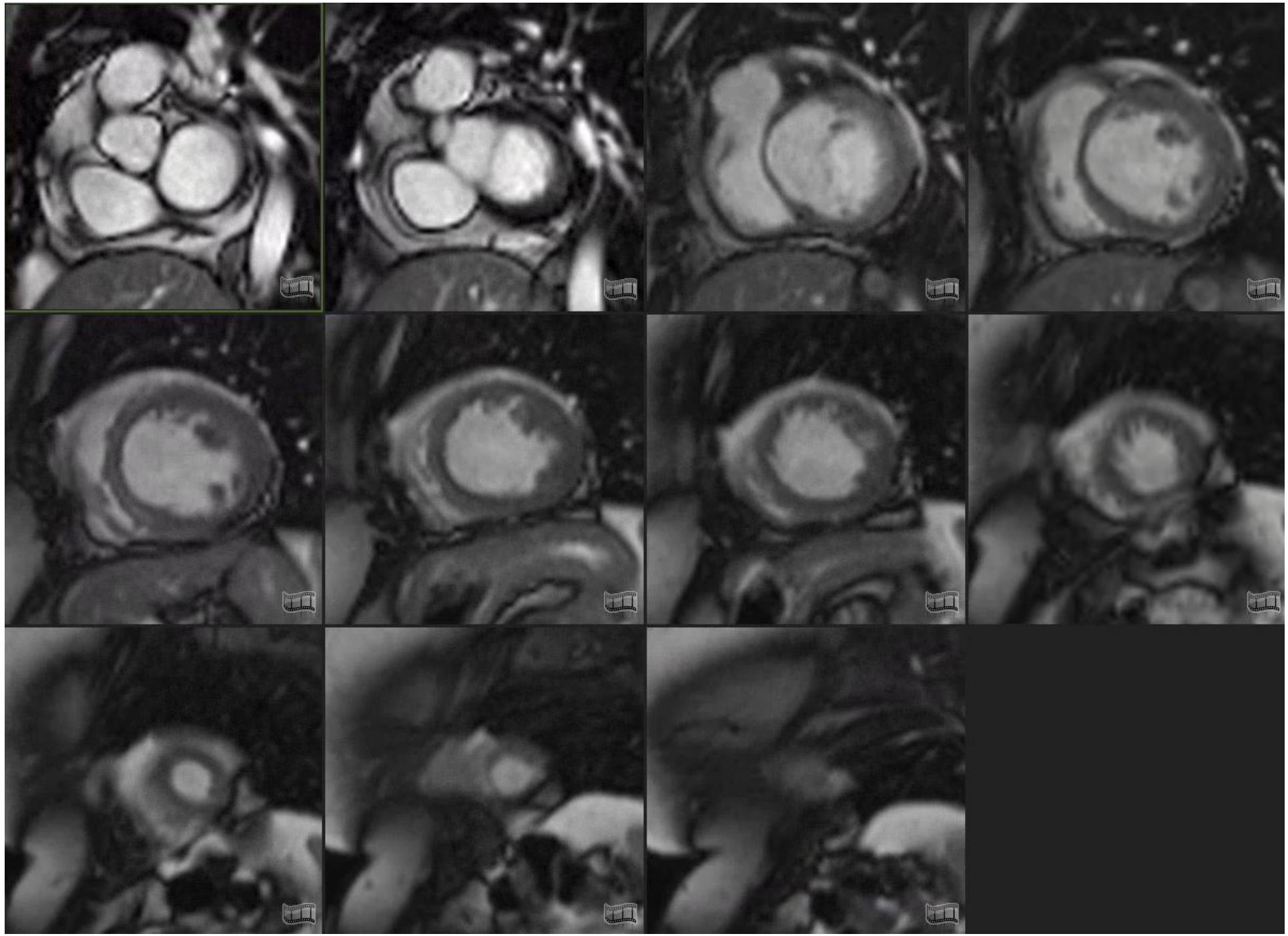
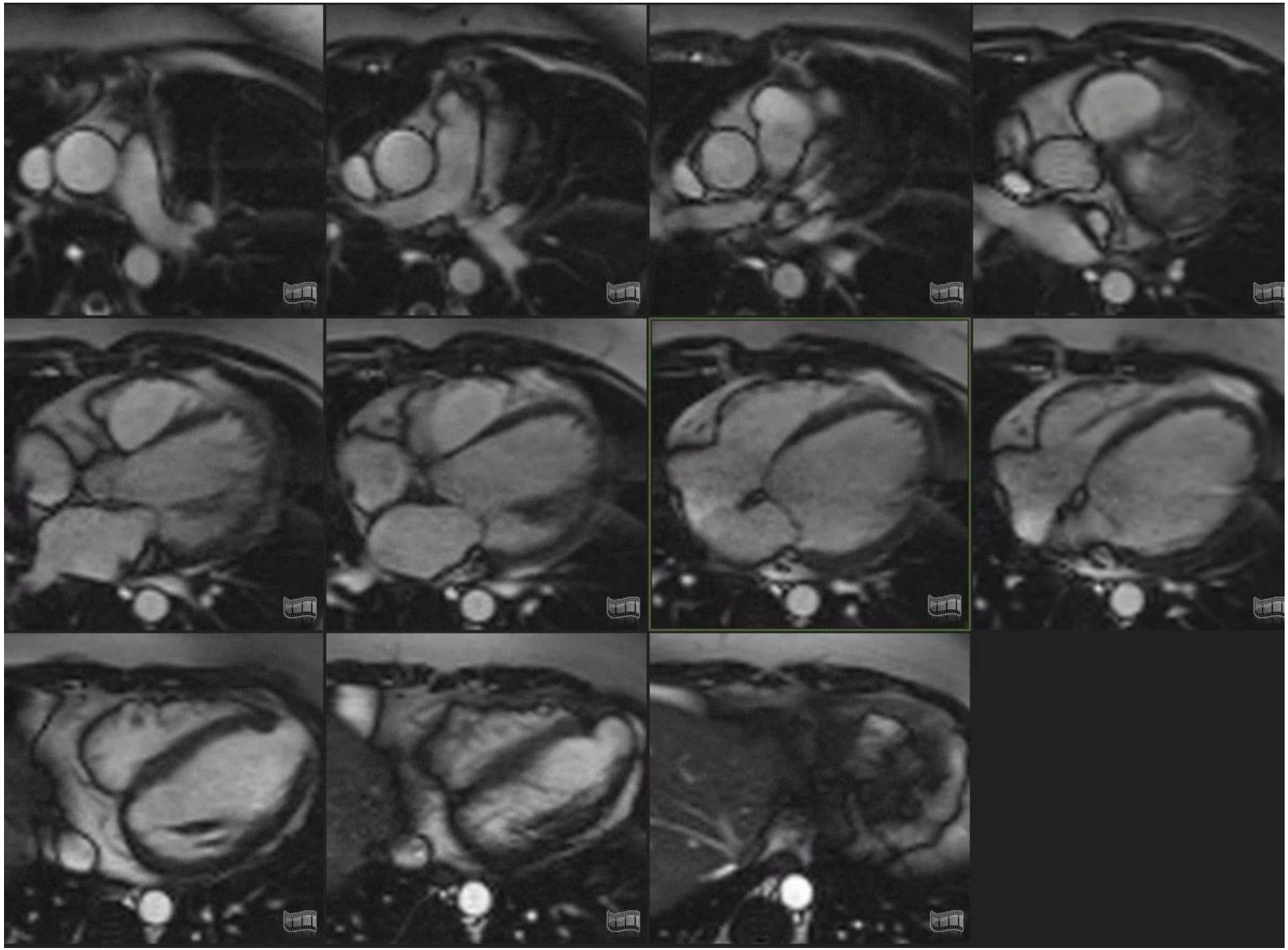
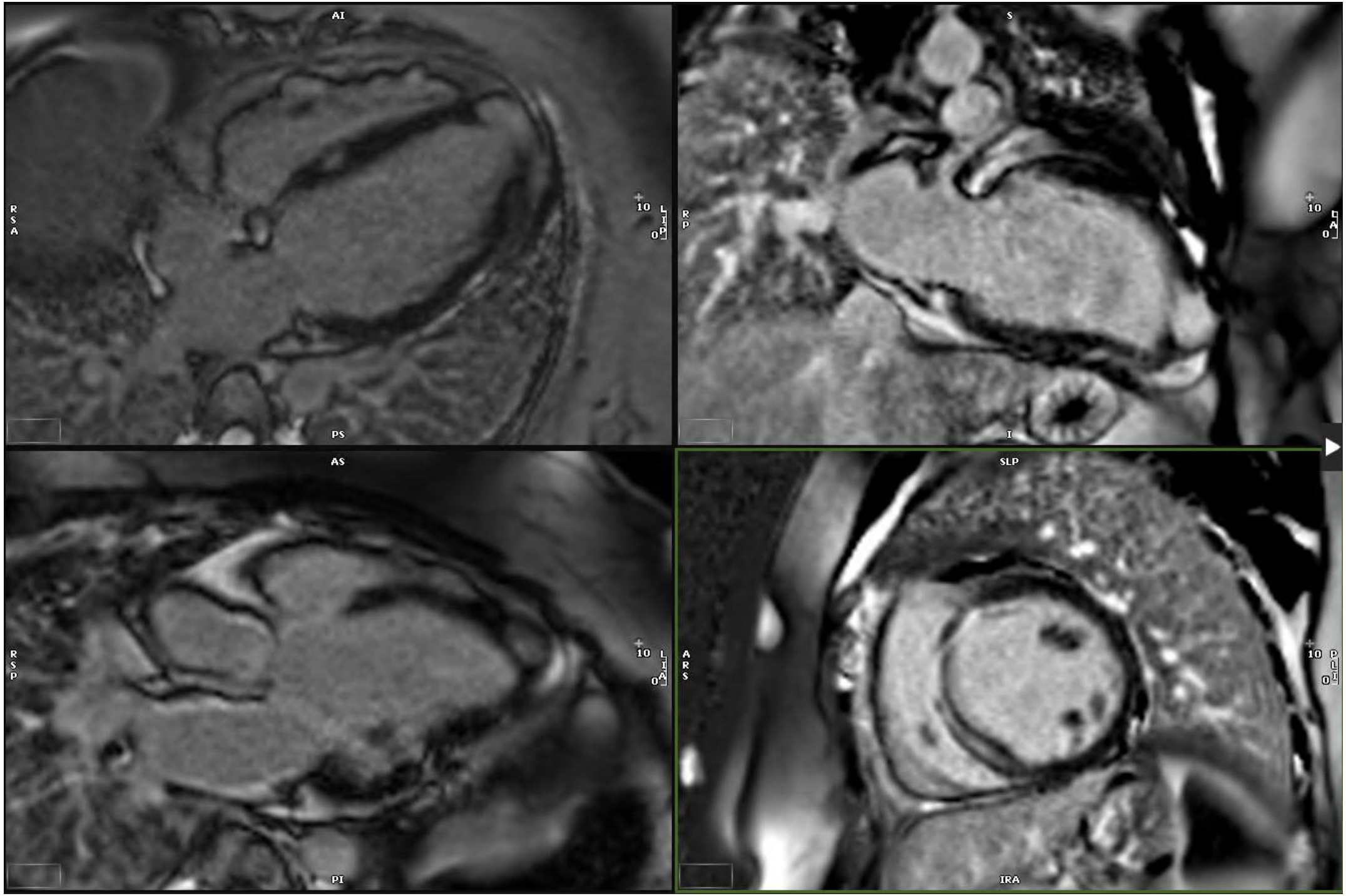
IRA



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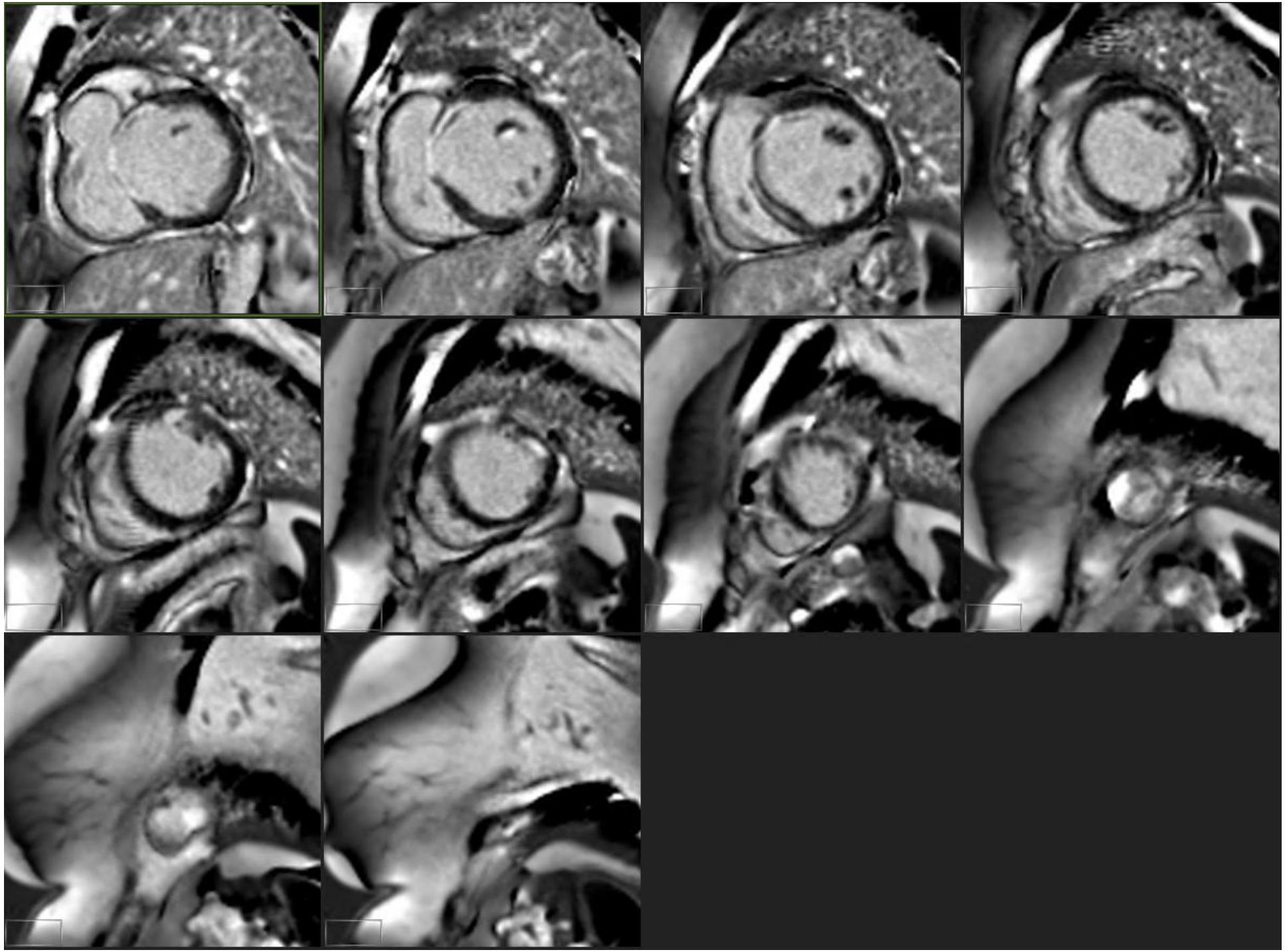
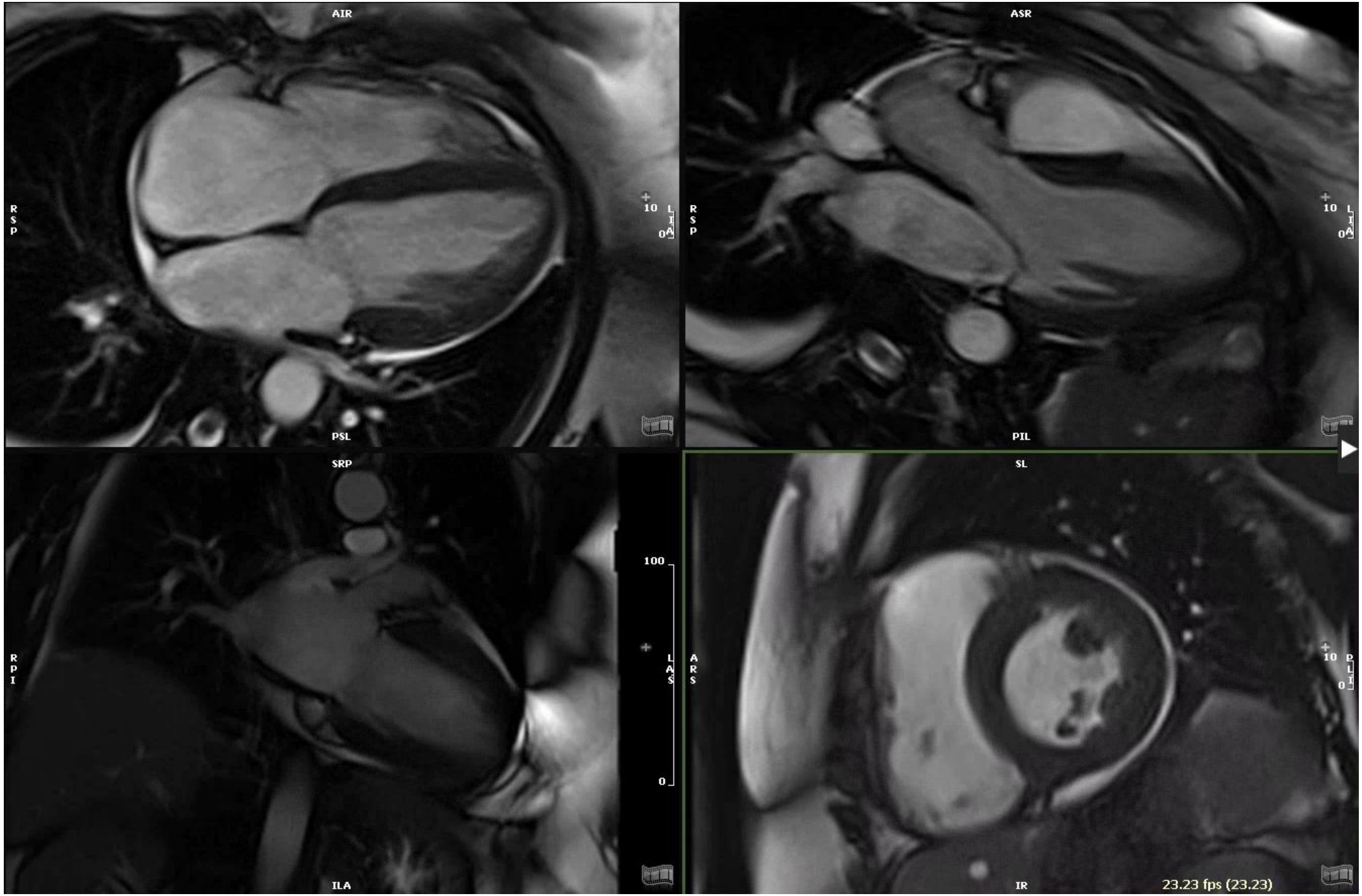


Case 3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L
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PSL
ASR
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PIL
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ILA
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I
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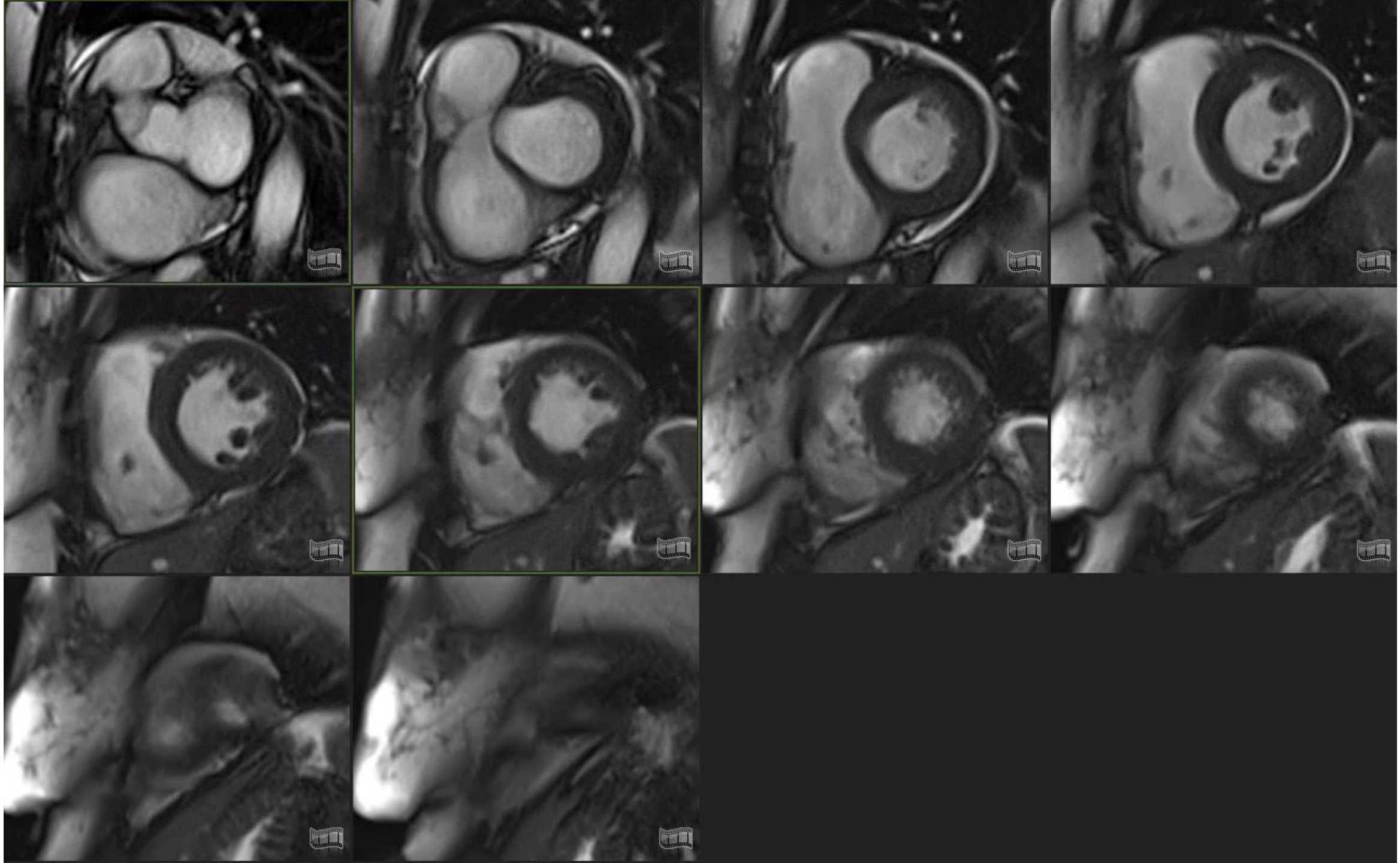
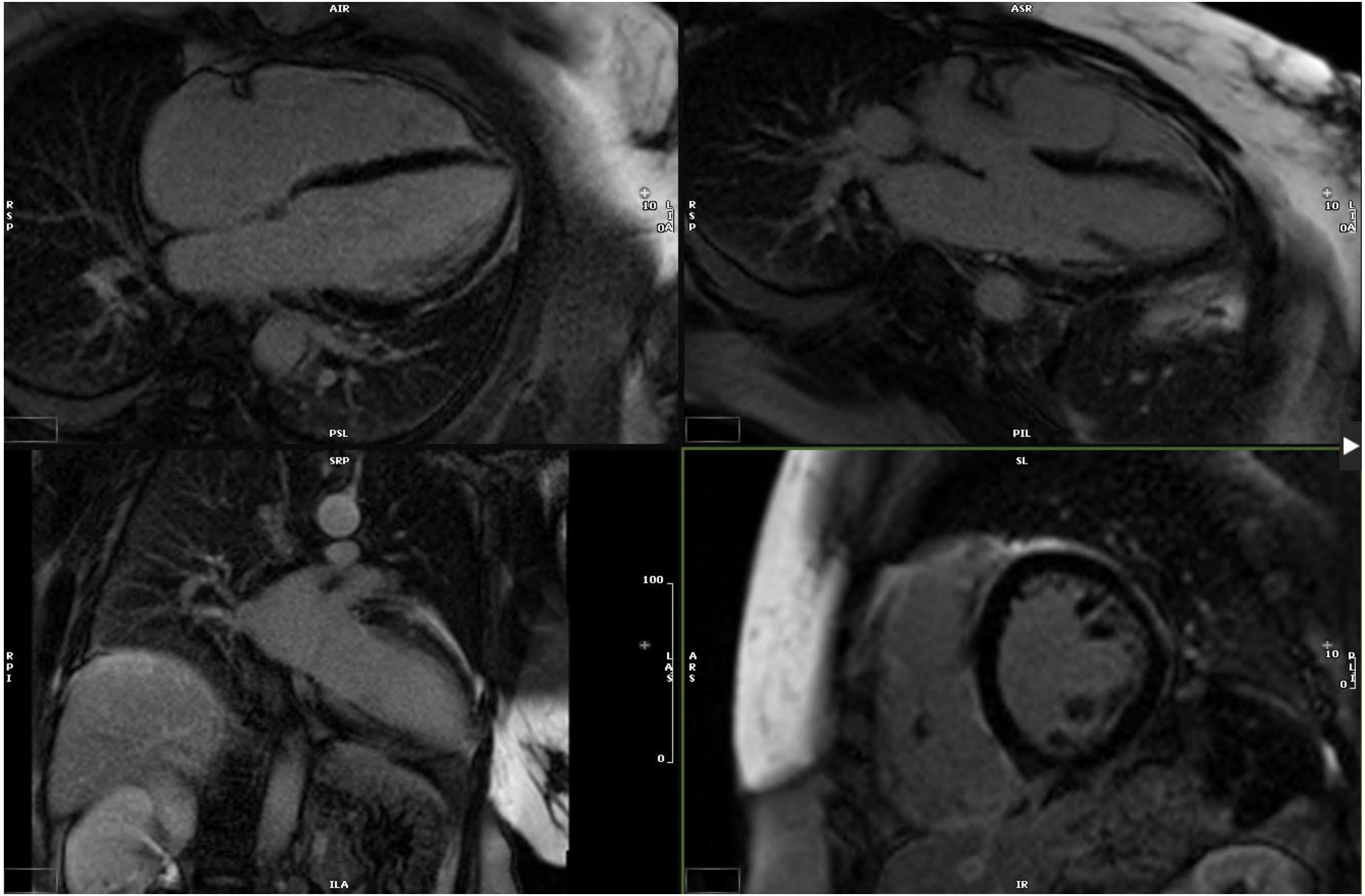
IR
23.23 fps (23.23)




AIR
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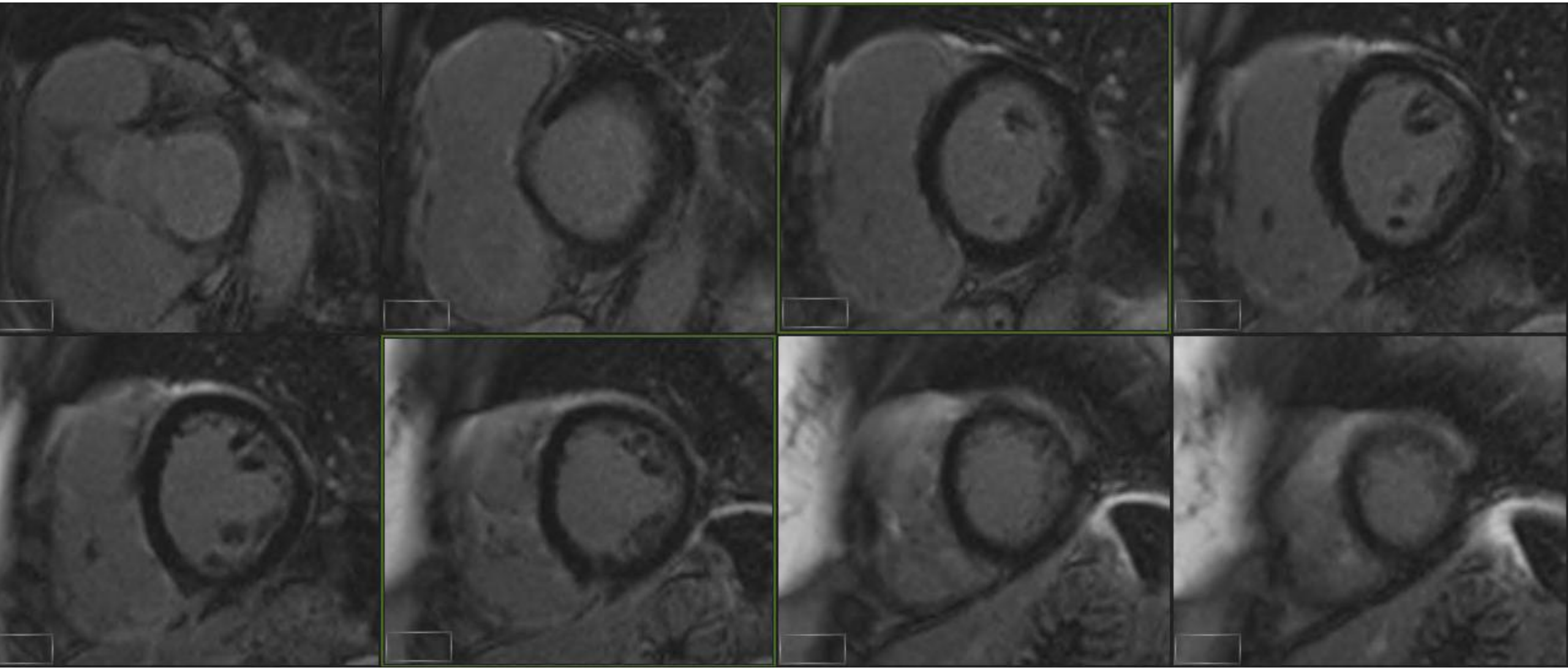
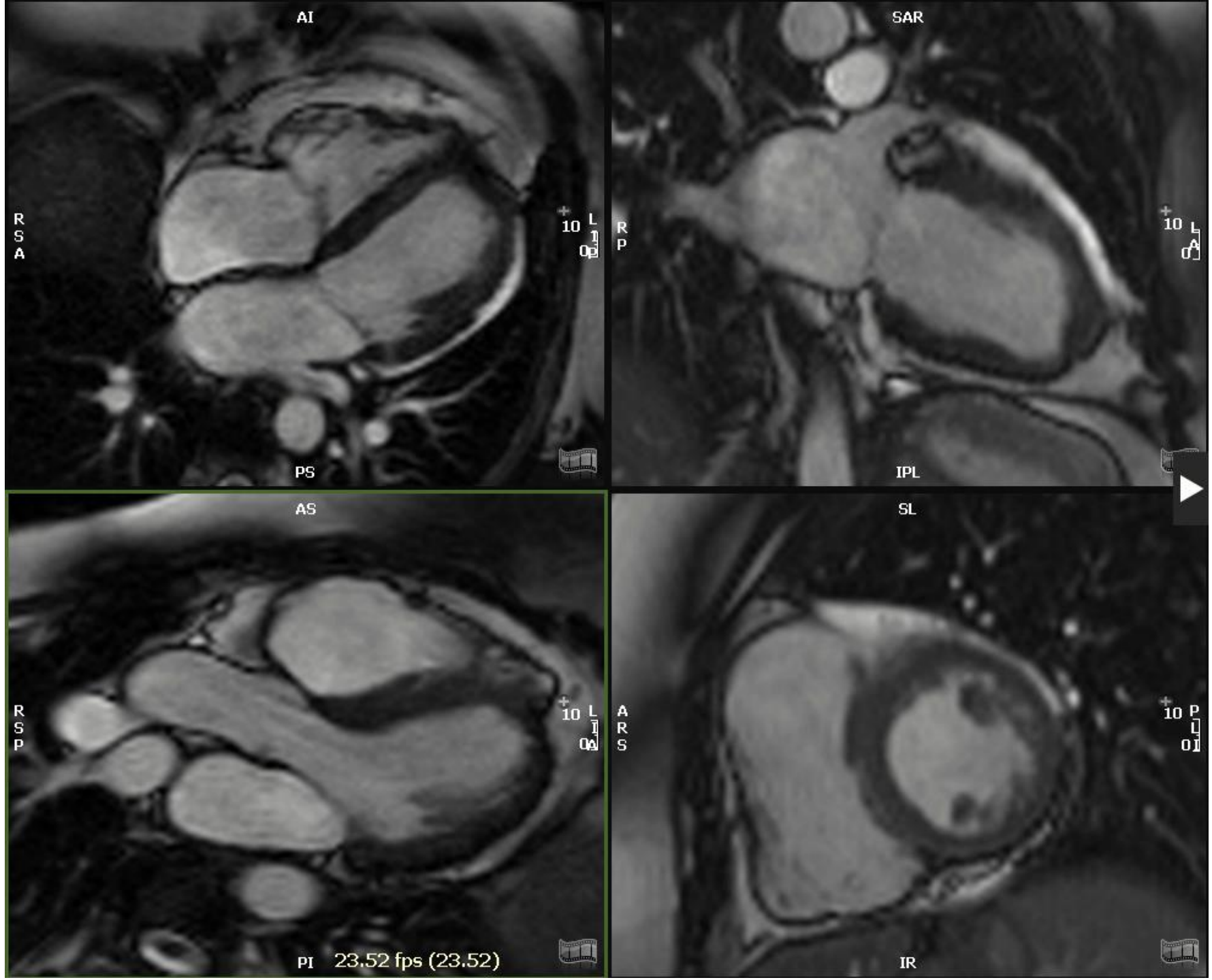


Case 4


AI
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10 L
PS
SAR
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10 L
IPL
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10 L
PI
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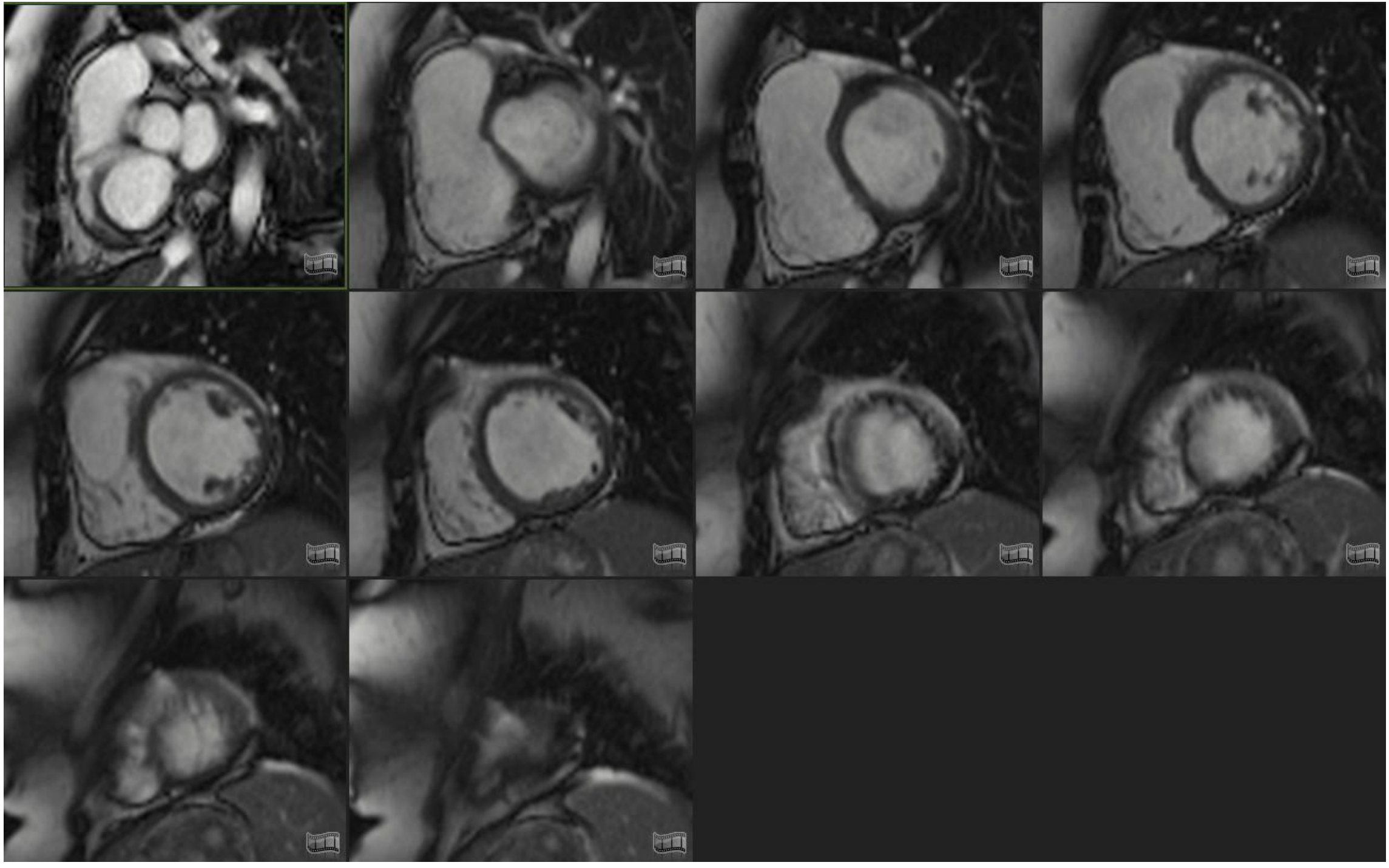
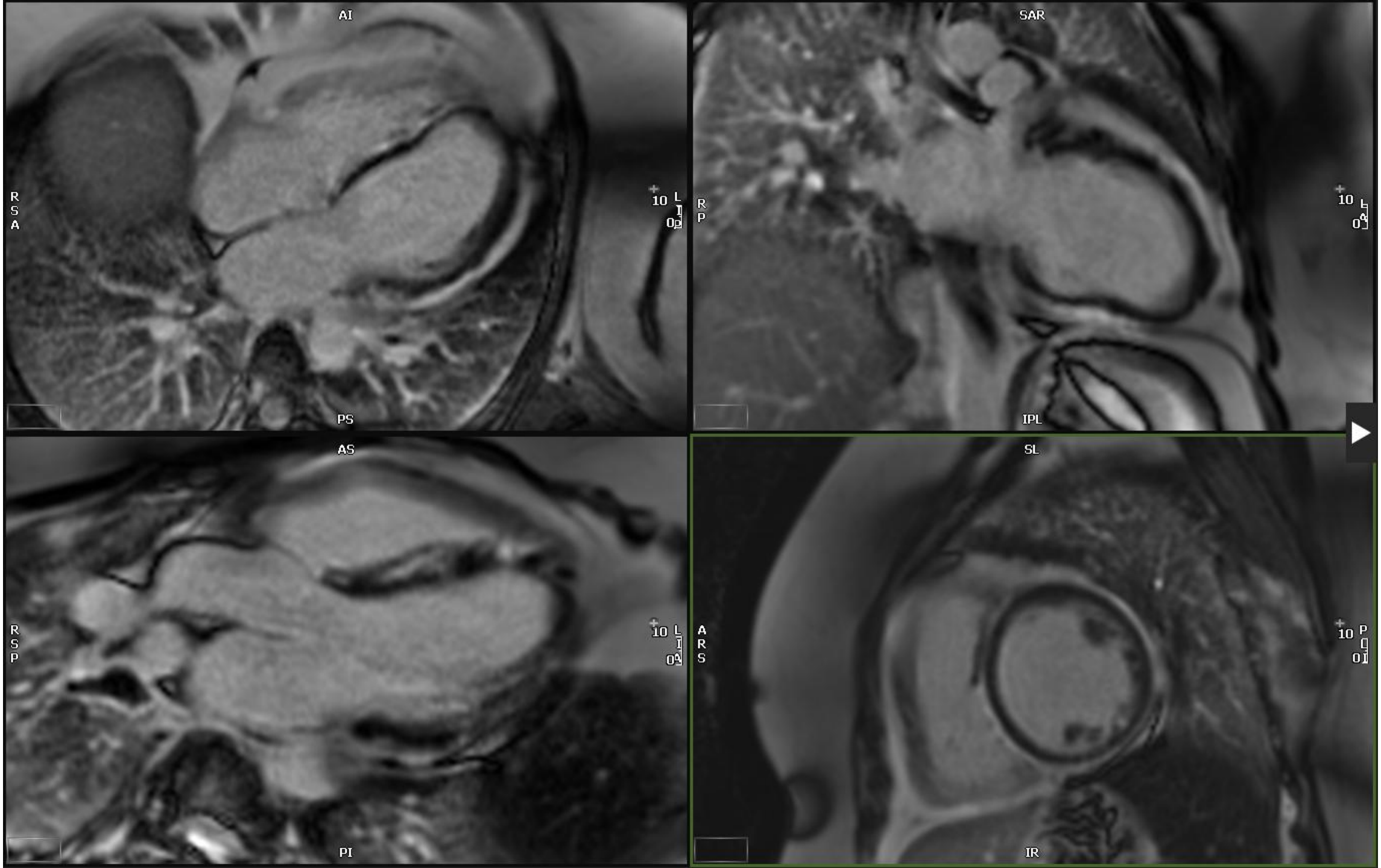
SL
A
R
S
10 P
L
IR

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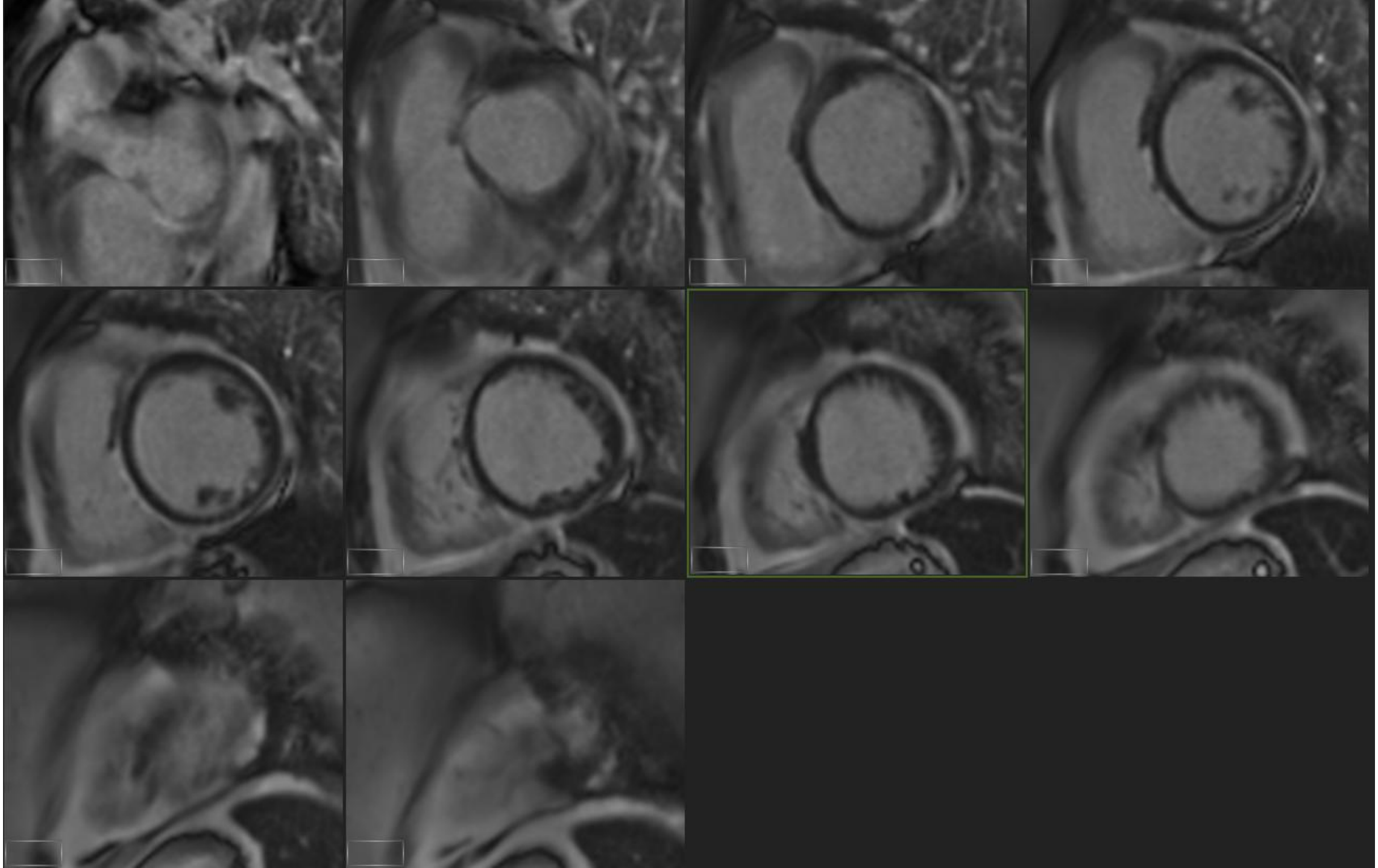
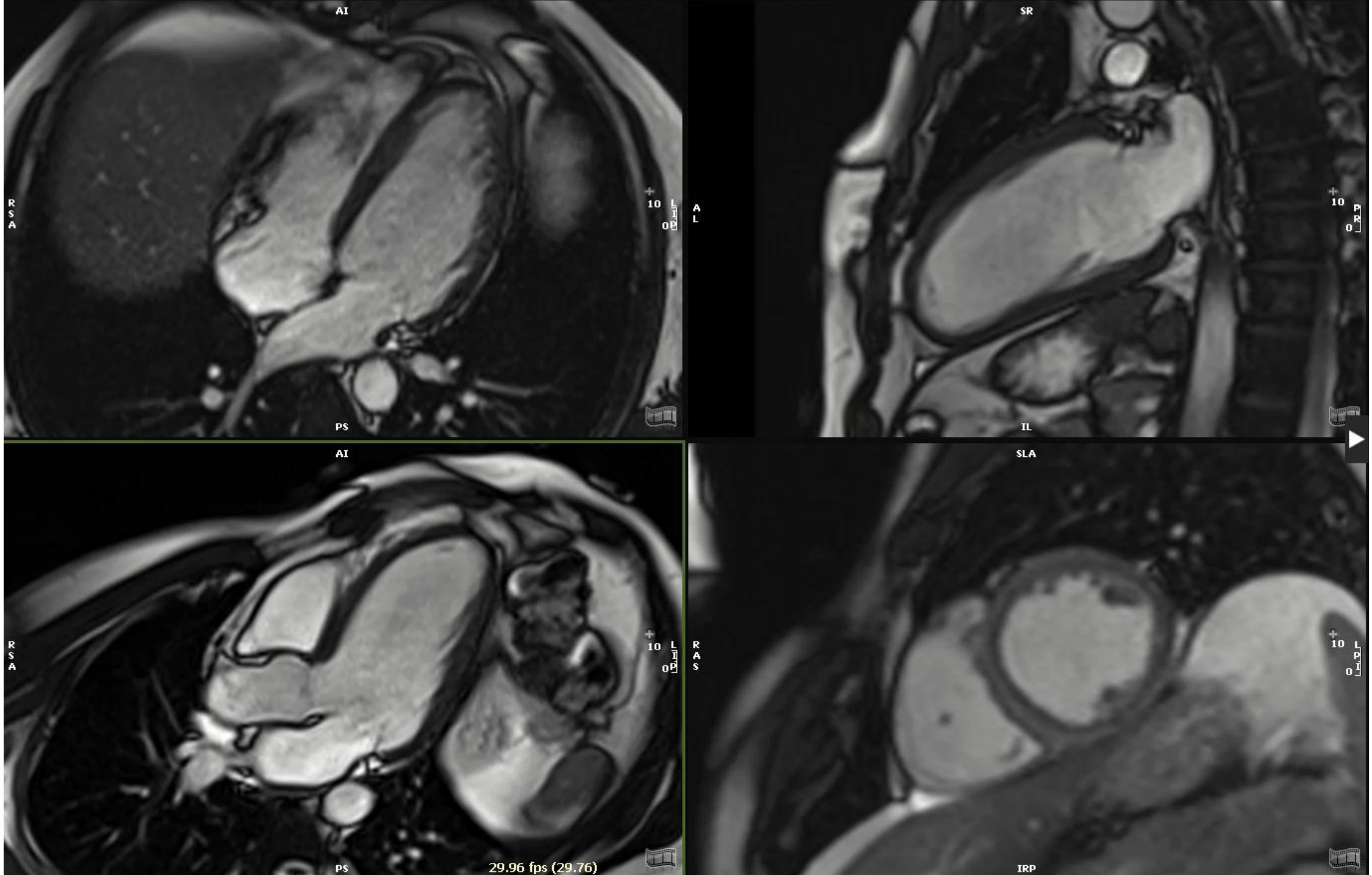


Case 5


AI
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AI
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A
PS
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A
L
SR
IL
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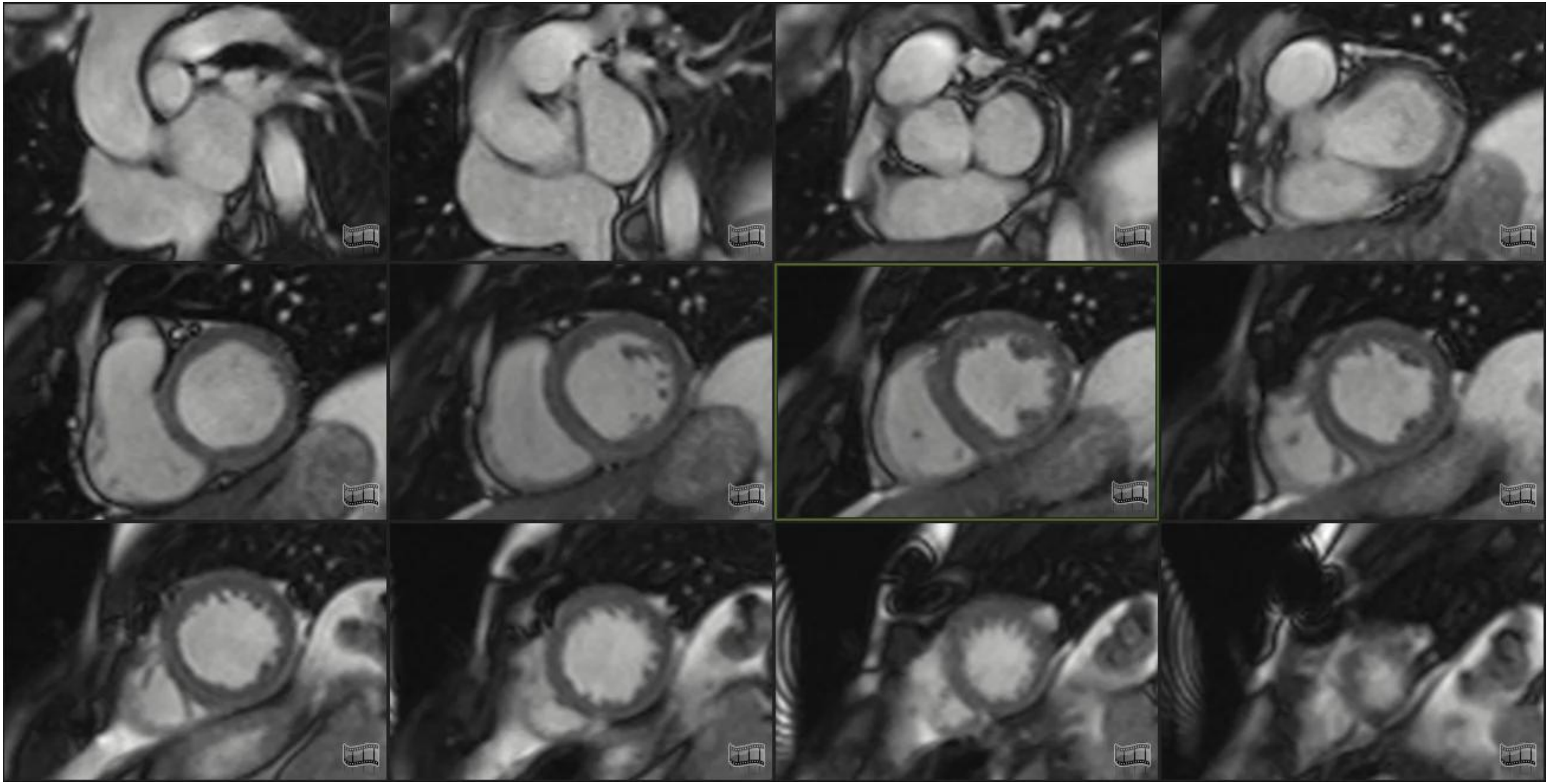

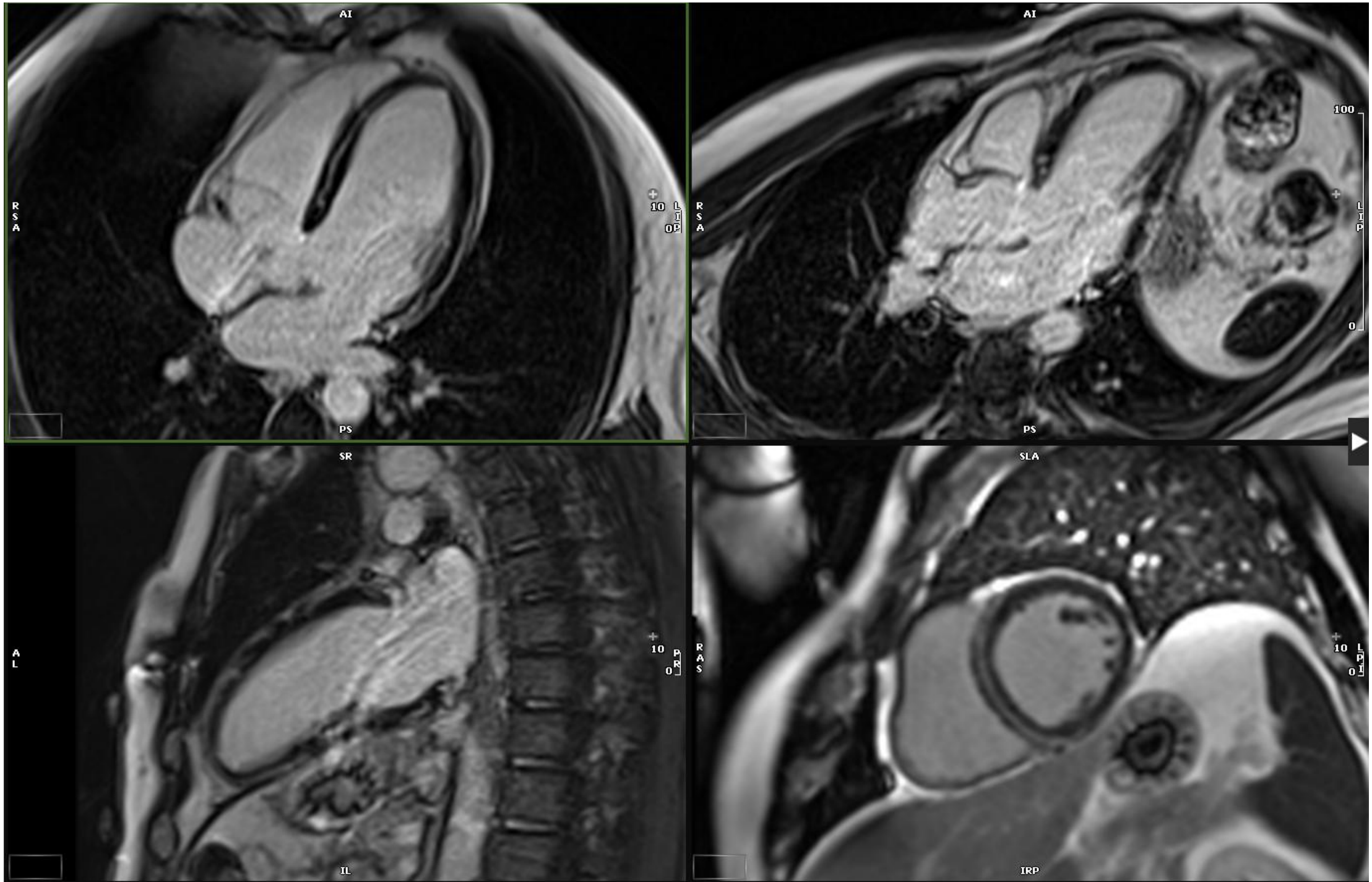
AI
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LDT
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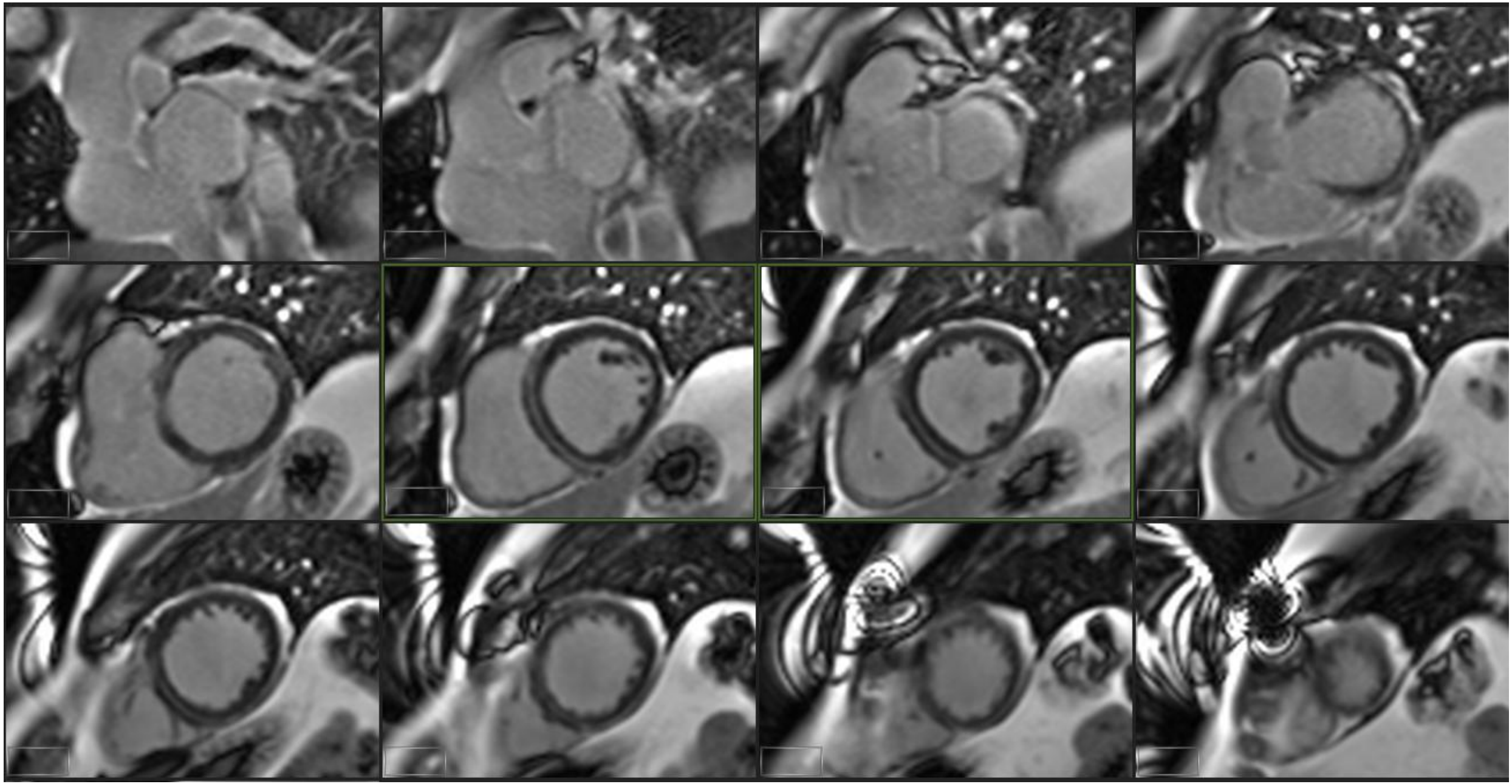
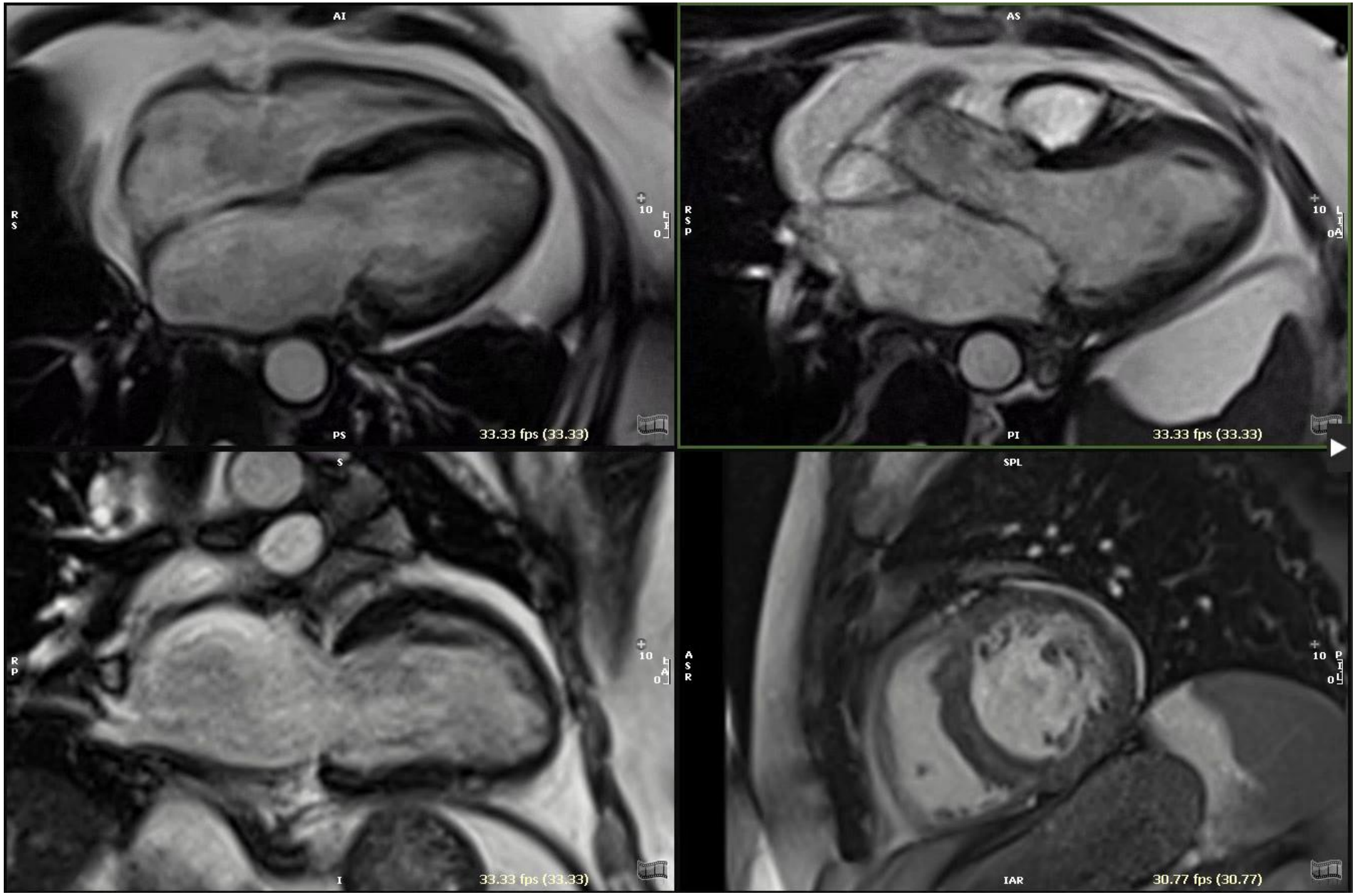


Case 5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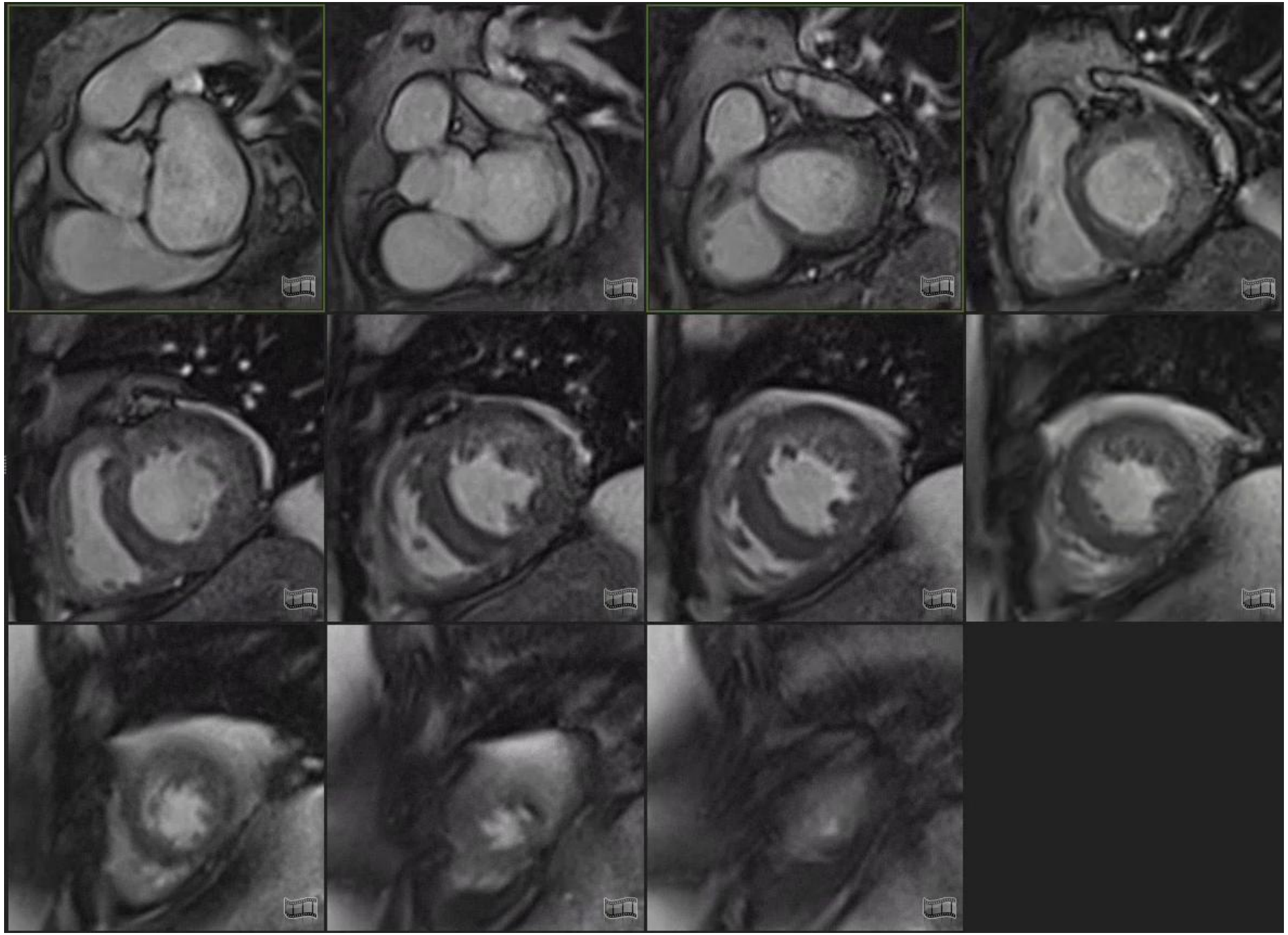

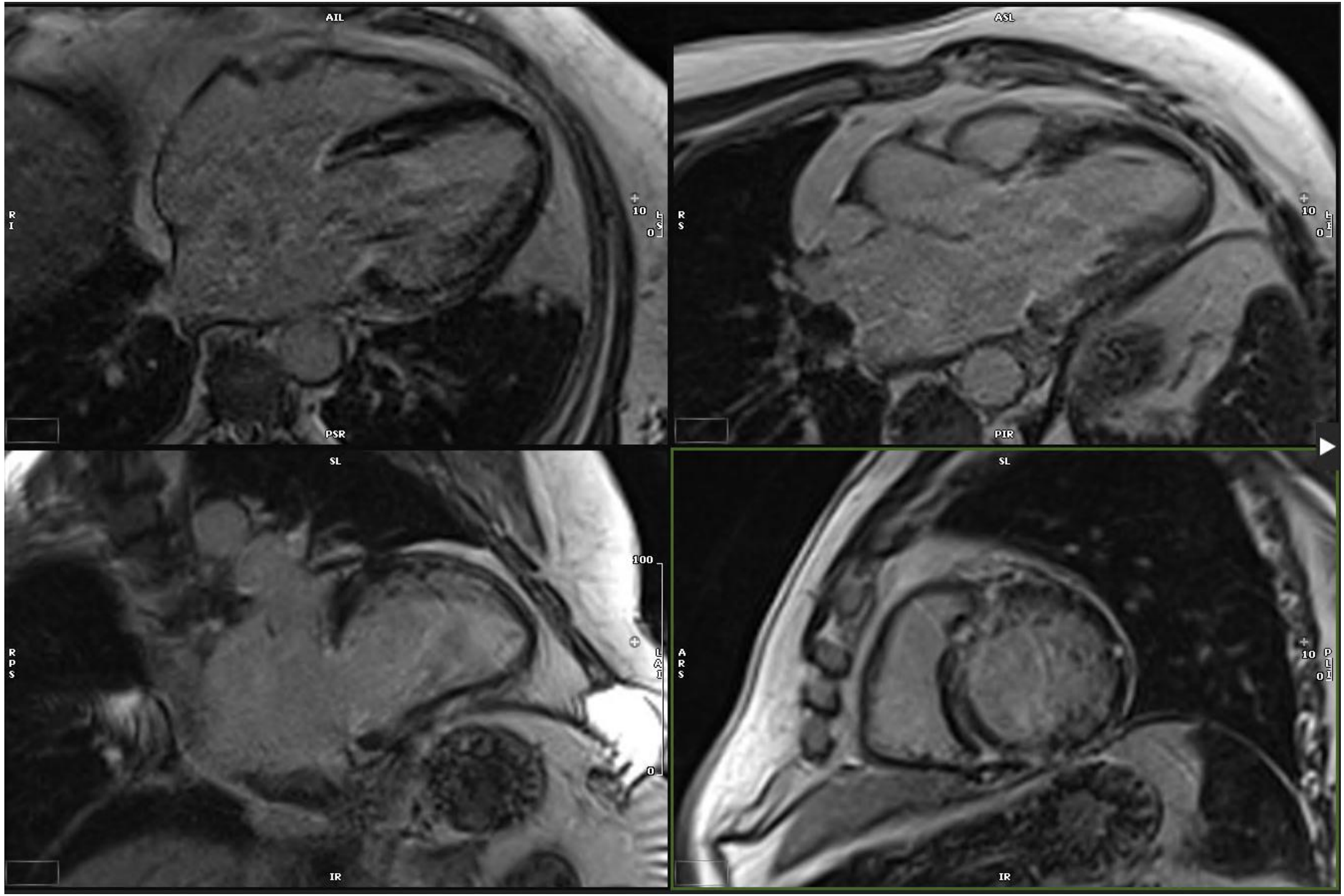
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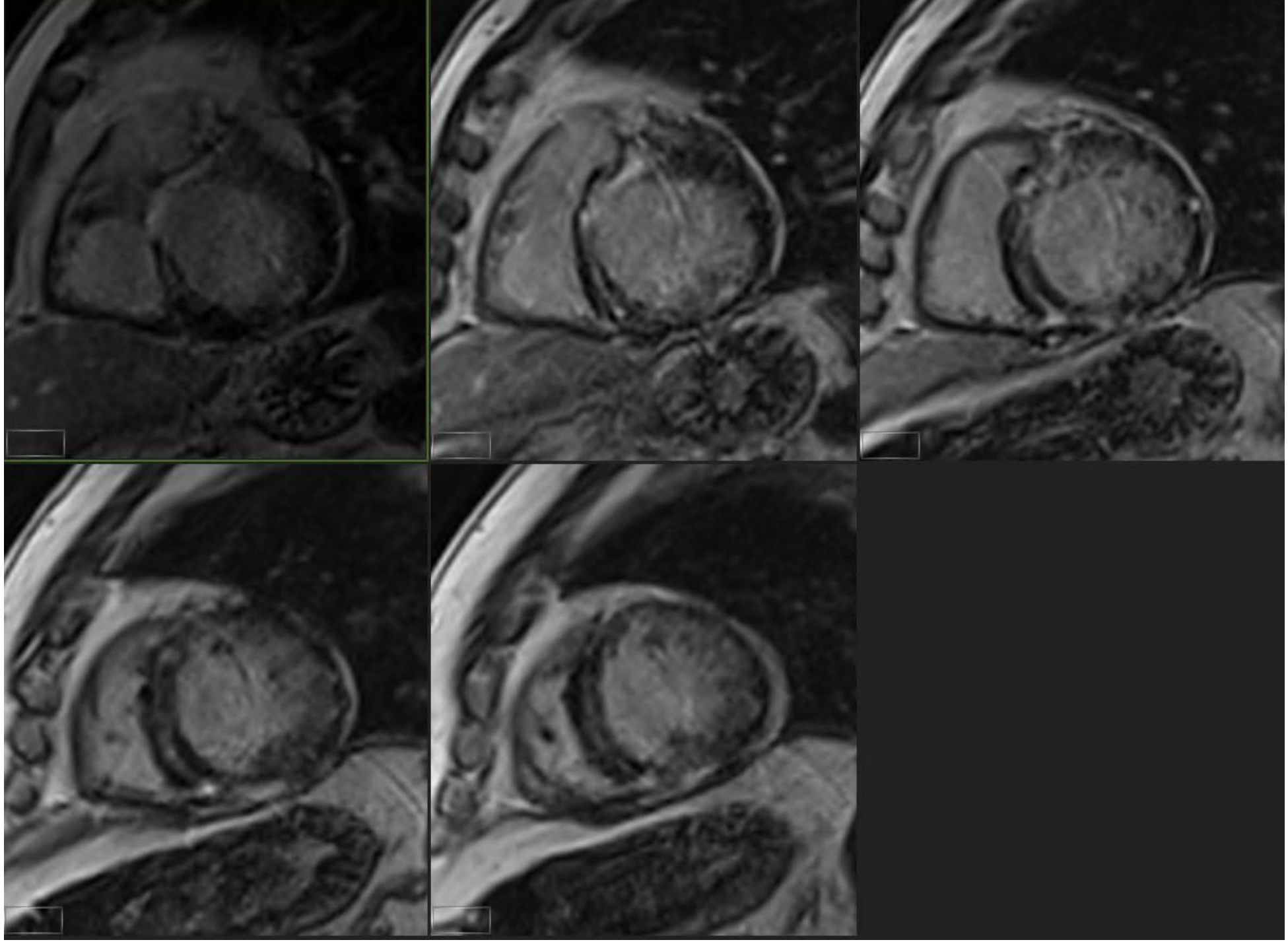
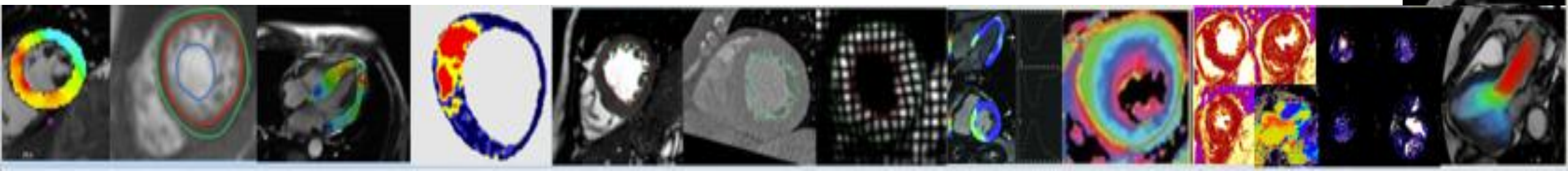


Diseases mimicking ACM

- Myocarditis
- Sarcoidosis
- DCM
- Athlete’s heart
- Uhl’s disease
- Pre tricuspid defects
- TR
- RV infarct
- Ebstein’s anomaly
- Chest deformity
- Pericardial absence
- Chagas

Key messages

- CMR is the gold standard for investigation, diagnosis, management and treatment of heart muscle diseases
- Combine all images and all sequences cardiac and extra cardiac findings
- Remember clinical context, family history and drugs

Thank you