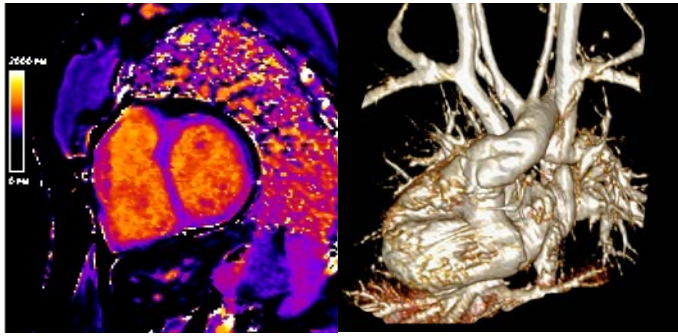
CARDIOLOGY 2023

ADVANCED CARDIAC MRI TECHNIQUES: UTILITY IN CRITICAL DECISION MAKING



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Children's Hospital of Philadelphia® Cardiac Center

Perelman School of Medicine University of Pennsylvania

22CME0420/PPT/01-23

Disclosures

Grants/Industry:

- NIH RO1
- Additional Ventures Grant x 2
- Freidrich's Ataxia Foundation
- Rocket Pharma CMR Core Lab for Danon's Disease

I will be discussing the use of gadolinium and ferumoxytol for the heart.

CARDIOLOGY 2023

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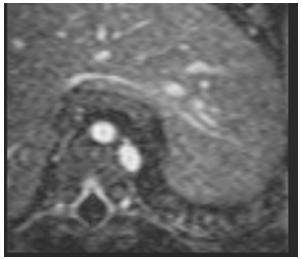
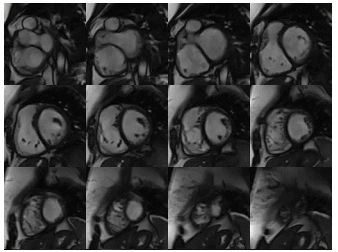
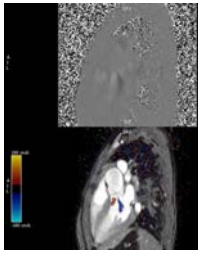
Cardiac Center

Outline

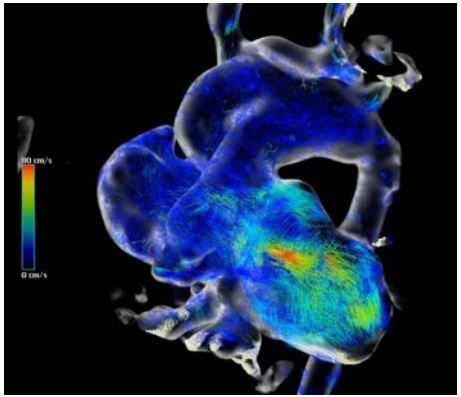
Tissue Characterization

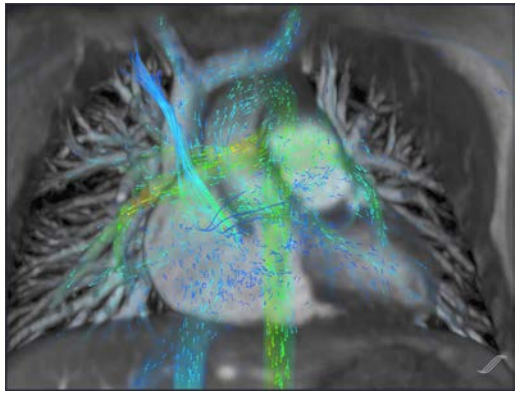




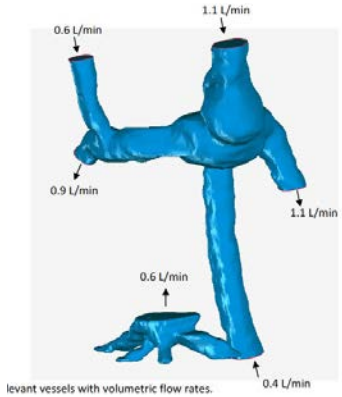


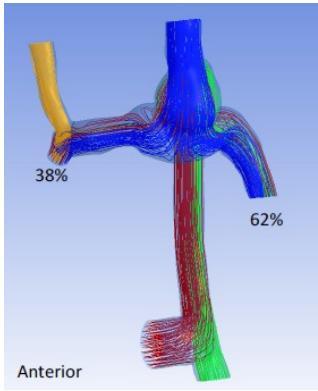
Ferumoxytol Imaging





Courtesy of Dr. Shreyas Vasanawala
Stanford





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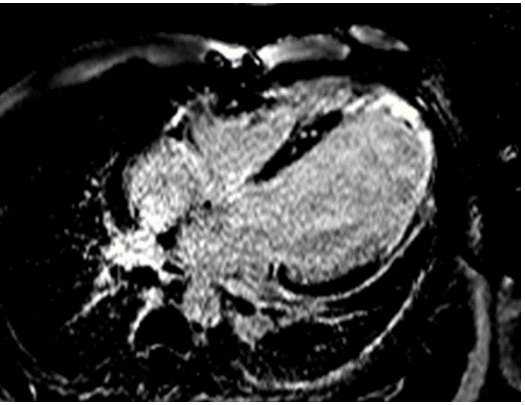
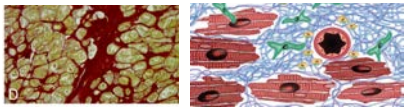
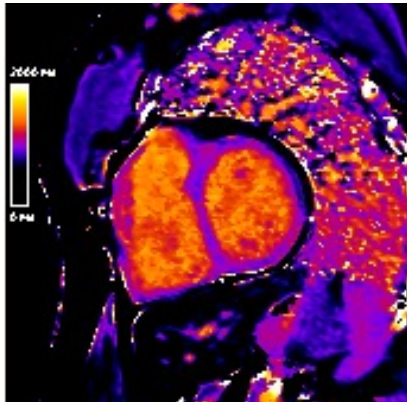
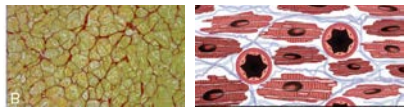
Tissue Characterization



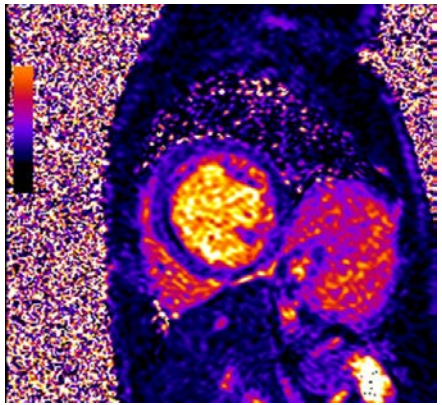


Replacement or discrete fibrosis

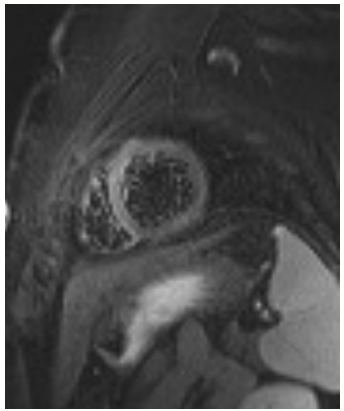




Interstitial or diffuse fibrosis



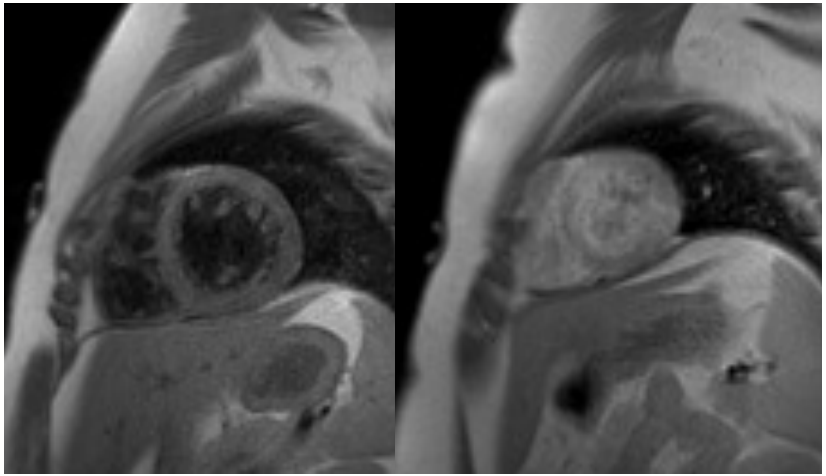
Myocardial edema



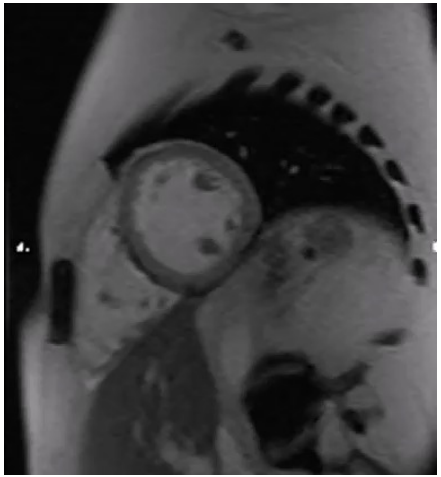
Myocardial edema

Tissue Characterization

Myocardial perfusion



Capillary leak



Myocardial iron

Tissue Characterization: Myocarditis

Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation

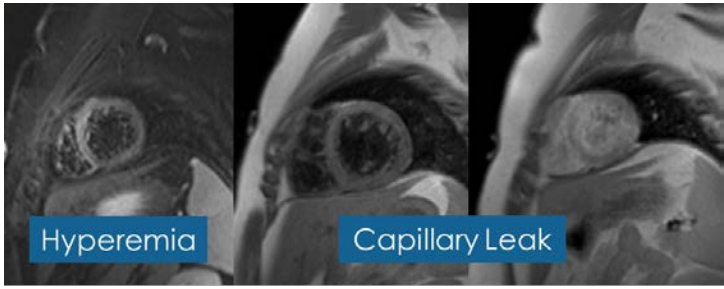
Expert Recommendations

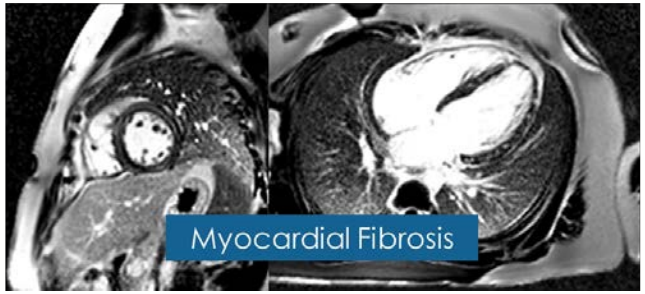
JACC VOL. 72, NO. 24, 2018
DECEMBER 18, 2018:3158–76

Vanessa M. Ferreira, MD, DPhil,[a] Jeanette Schulz-Menger, MD,[b] Godtfred Holmvang, MD,[c] Christopher M. Kramer, MD,[d] Iacopo Carbone, MD,[e] Udo Sechtem, MD,[f] Ingrid Kindermann, MD,[g] Matthias Gutberlet, MD,[h] Leslie T. Cooper, MD,[i] Peter Liu, MD,[j] Matthias G. Friedrich, MD[k,l,m]

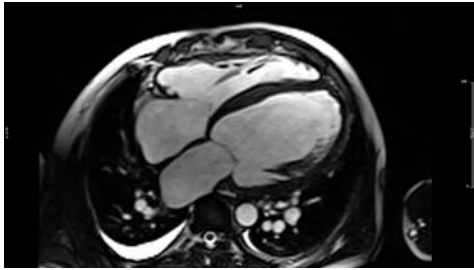
TABLE 3 Updated Recommendations of CMR Criteria of Myocardial Inflammation

Original Lake Louise Criteria I (Any 2 Out of 3)	Updated Lake Louise Criteria II (2 Out of 2)	Diagnostic Targets
Main criteria		
T2-weighted imaging Regional* high T2 SI *or* Global T2 SI ratio ≥2.0† in T2W CMR images	T2-based imaging Regional* high T2 SI *or* Global T2 SI ratio ≥2.0† in T2W CMR images *or* Regional or global increase of myocardial T2 relaxation time†	Myocardial edema
Early gadolinium enhancement SI ratio myocardium/skeletal muscle (EGE ratio) of ≥4.0† in EGE images Late gadolinium enhancement Areas with high SI in a nonischemic distribution pattern in LGE images	T1-based imaging Regional or global increase of native myocardial T1 relaxation time or ECV†‡ *or* Areas with high SI in a nonischemic distribution pattern in LGE images	↑ T1 – edema (intra or extra-cellular), hyperemia/capillary leak, necrosis, fibrosis EGE – hyperemia, capillary leak LGE – necrosis, fibrosis, (extracellular acute edema) ↑ ECV – edema (extracellular), hyperemia/capillary leak, necrosis, fibrosis
Supportive criteria		
Pericardial effusion in cine CMR images	Pericardial effusion in cine CMR images *or* High signal intensity of the pericardium in LGE images, T1-mapping or T2-mapping *or* T1 mapping or T2 mapping	Pericardial inflammation
Systolic LV wall motion abnormality in cine CMR images	Systolic LV wall motion abnormality in cine CMR images	LV dysfunction





4 yo male
Fever, fussy
Troponin:
17 ng/ml



Tissue Characterization:
Diffuse fibrosis predicting Fontan outcome

Diffuse Myocardial Fibrosis, its Distribution and Relationship to Clinical Outcome and Ventricular Function in Single Ventricles Before and After Fontan: A Cardiac Magnetic Resonance Outcome Study

Children's Hospital of Philadelphia Cardiac Center

Jeremiah Joyce, Michael Convery, Elizabeth Donnelly, Andrea Jones, Ivor Asztalos, Cassie Giner, David Biko, Matthew Harris, Kevin Whitehead, Michael Quartermain, Laura Mercer-Rosa, Mark Fogel

Demographics and Comparative Statistics:	LV	RV	p-value
Number of patients	16 (41%)	23 (59%)	
Cardiac Diagnosis			
HLHS	0 (0%)	20 (87%)	
TA	10 (63%)	0 (0%)	
DILV	2 (13%)	0 (0%)	
PA/IVS	2 (13%)	0 (0%)	
Other	2 (13%)	3 (13%)	
Age at Stage II (months)	5.3 (4.5-6.2)	4.3 (4.1-5.5)	0.13
Age at Fontan (years)	3.1 (2.9-3.7)	3.1 (2.8-3.8)	0.93
Number of palliations prior to Fontan	2.06 (0.57)	1.96 (0.47)	0.53
Native T1 time (ms)	1059 (1034-1090)	1047 (1024-1083)	0.66
ECV (%)	33 (31.5-35)	34 (31-36)	0.49
T1 ROI (ms)	1051 (1019-1104)	1028 (1006-1071)	0.27
ECV ROI (%)	33 (31-36)	33 (31-35)	0.93
Coefficient of variation of T1 (%)	**8.3 (6.9-9.9)**	**10.1 (8.4-11.3)**	**0.018**
Coefficient of variation of ECV (%)	**18.9 (17.6-20.6)**	**22.0 (19.3-27.3)**	**0.011**

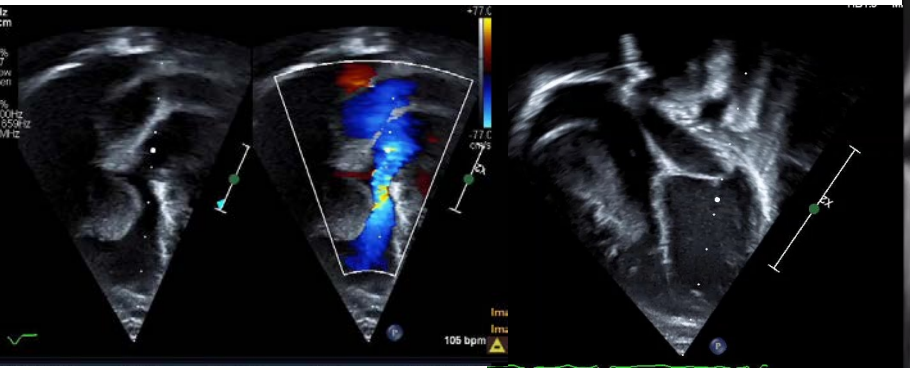
Abstract AHA 2022

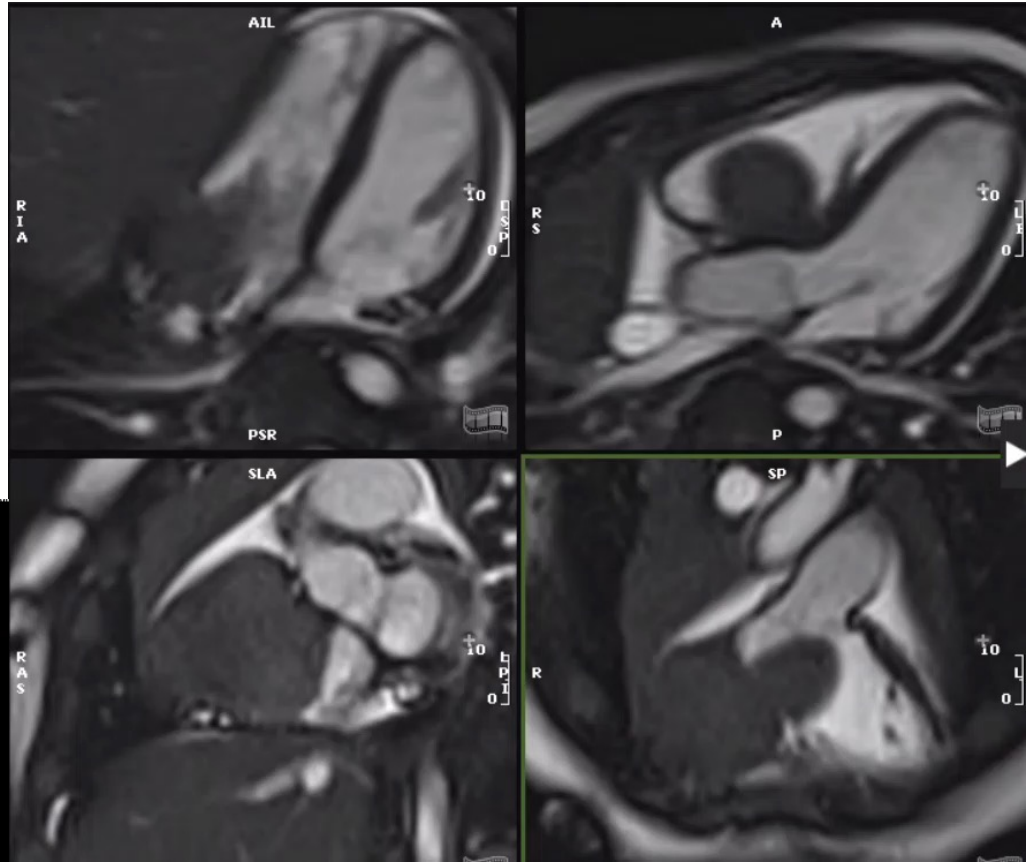
Significant Results from Linear and Logistic Regression Analysis:

Predictor	Outcome	Beta	P-value
Combined Cohort:			
ECV	Duration of ICU stay post-Fontan (Days)	0.563	0.008
	Post-Fontan Longitudinal Systolic Strain	0.266	0.019
	Post-Fontan Longitudinal Systolic Strain Rate	0.031	0.021
	Post-Fontan Circumferential Systolic Strain Rate	0.050	0.017
CV of T1 *	30-day readmission post-discharge after Fontan	0.564	0.008
	Post-Fontan Longitudinal Systolic Strain	0.467	0.044
	Post-Fontan Circumferential Systolic Strain	0.817	0.026
CV of ECV *	Duration of hospitalization after Fontan (Days)	0.526	0.012
	Post-Fontan Longitudinal Systolic Strain	0.244	0.008
	Post-Fontan Circumferential Systolic Strain	0.340	0.015

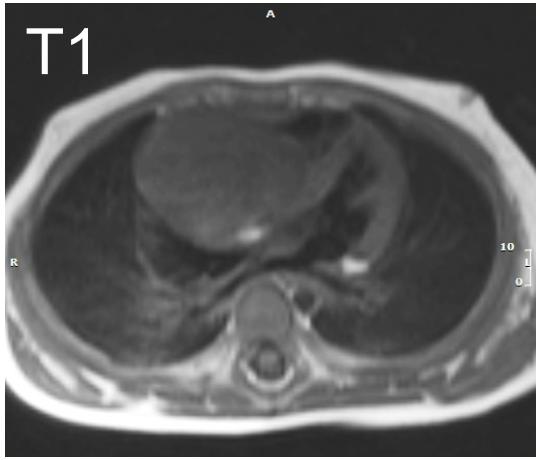
Tumor

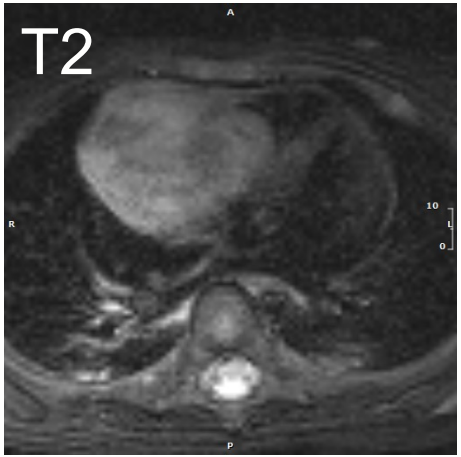
- 8 month old male
- Episode - fussy and then limp, unconscious 1 min

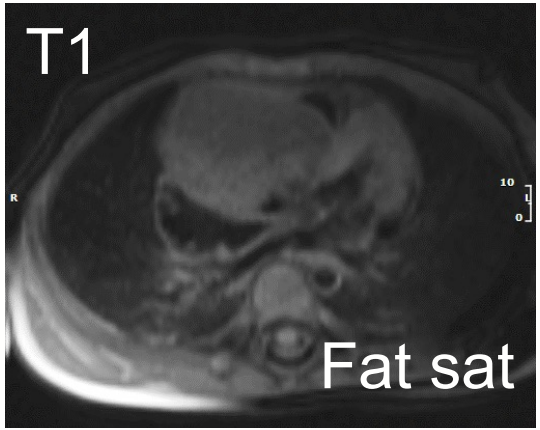




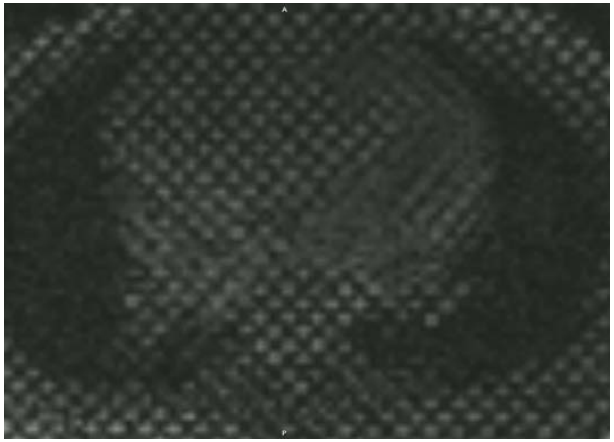
Tumor



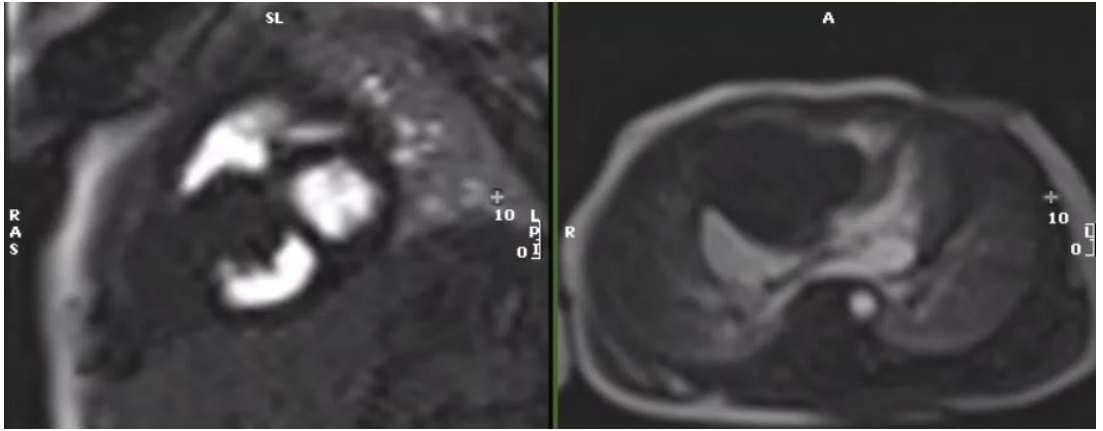




Myocardial tagging



Perfusion



RV Tumor

Predicted:

Component

Case Results

Surgical Pathology — Case: [redacted]
Authorizing Provider: [redacted] — Collected: [redacted]
Ordering Location: Cardiac OR & Imaging — Received:
Pathologist: [redacted]MD
Specimen: Heart, Right Ventricle, Right Ventricular Fibroma

Final Diagnosis

A. Heart, right ventricle, mass, excision:
- Cardiac fibroma, see microscopic description.

Electronically signed by Pogoriler, Jennifer, MD on 1/5/2023 at 1307

Gross Description

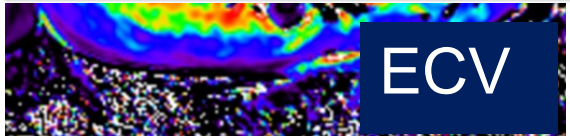
A. Heart, Right Ventricle. Right Ventricular Fibroma

Pre-Procedure Diagnosis

Cardiac mass

Procedure

CARDIAC TUMOR RESECTION, TEE, BIDIRECTIONAL CAVOPULMONARY ANASTOMOSIS (BDCPA) (BIDIRECTIONAL GLENN)



3D

Tumors

ORIGINAL RESEARCH

Accuracy of Cardiac Magnetic Resonance Imaging in Diagnosing Pediatric Cardiac Masses

A Multicenter Study

(J Am Coll Cardiol Img 2022;15:1391-1405)

Rebecca S. Beroukhim, MD,[a] Sunil Ghelani, MD,[a] Ravi Ashwath, MD,[b] Sowmya Balasubramanian, MD,[c] David M. Biko, MD,[d] Sujatha Buddhe, MBBS, MS,[e] M. Jay Campbell, MD, MHA,[f] Russell Cross, MD,[g] Pierluigi Festa, MD,[h] Lindsay Griffin, MD,[i] Heynric Grotenhuis, MD, PhD,[j] Keren Hasbani, MD,[k] Sassan Hashemi, MD,[l] Sanjeet Hegde, MD, PhD,[m] Tarique Hussain, MD, PhD,[n] Supriya Jain, MD,[o] Maria Kiaffas, MD,[p] Shelby Kutty, MD, MS, PhD,[q,r] Christopher Z. Lam, MD,[s] Gabriela Liberato, MD,[t] Anthony Merlocco, MD,[u] Nilanjana Misra, MD,[v] Katie L. Mowers, MD,[c,w] Juan Carlos Muniz, MD,[x] Arni Nutting, MD,[y] David A. Parra, MD,[z] Jyoti K. Patel, MD,[aa] Antonio R. Perez-Atayde, MD, PhD,[a] Deepa Prasad, MD,[bb] Carlos F. Rosental, MD,[cc] Amee Shah, MD,[dd] Margaret M. Samyn, MD,[ee] Lynn A. Sleeper, ScD,[a] Timothy Slesnick, MD,[l] Emanuela Valsangiacomo, MD,[ff] Tal Geva, MD[a]

TABLE 3 CMR-Based Diagnostic Criteria of Cardiac Masses in Children

	Fibroma	Rhabdomyoma	Malignant	Myxoma	Teratoma	Fatty Deposits in TSC[a]	Thrombus
Classification	Fibroblastic	Muscular	Various	Endocardial	Ectopic tissue	Lipomatous	Other
Size, cm	2-10	<1-8	1-10	<1-9[b]	3-7	<1-5	1-2
Location and appearance	• Intramyocardial • Well circumscribed • Solitary ± lobules • Septum, free wall, or both • LV >RV (can be atrium)	• Intracavitary • Attached to LV or RV muscle • Can be atrium or epicardial • Usually multiple[c]	• Commonly SVC/IVC/RA • Epicardial, intra-pericardial, anterior/posterior mediastinal • Infiltrative[d] • May cross tissue plane	• Typically left atrium but can be any chamber • Endocardial, pedunculated, mobile, heterogeneous • Mimics other masses: variable location and appearance	• Usually intra-pericardial, compresses SVC/RA • Multilocular, bosselated, solid, and cystic areas • May be intramyocardial or intracavitary	• Intramyocardial • Commonly ventricular septum • Epicardial • Often multiple	• Intracavitary • SVC/IVC • Endocardial • Often in regions of stasis (lines, infarcts)
Cine SSFP	-	-	±	++	+	± (Rim of chemical shift artifact)	±
T_1	-	-	±	±	-	+	-
T_2	± (Heterogeneous)	±	+	+	+	- (T_2/fat suppression)	-
Fat suppression	No	No	No	No	No	Yes	No
FPP	-	-	±	-	-	-	-
LGE	+++ (Fibroma LGE pattern)	-	±	±	±	-	±
Pericardial effusion	Common	Uncommon	Common	Uncommon	Common	No	Uncommon
Other	• Usually diagnosed prenatally or in infancy • Ventricular arrhythmia • Microscopic calcifications and regions of necrosis • Gorlin syndrome (15% CMR cases)	• Usually diagnosed prenatally or in infancy • Tuberous sclerosis (>80% cases) • Atrial and ventricular arrhythmias	• Pleural effusion • Usually older children • History of malignancy • Chest pain • Multiple • High mortality • Metabolic activity on ^{18}F-FDG PET	• Usually older children • Greater prevalence in female patients • Triad of symptoms: (obstructive, constitutional, and systemic emboli) • Carney complex (30% CMR cases)	• Usually diagnosed prenatally or in infancy • Pericardial/pleural effusion • Respiratory symptoms	• Older children with tuberous sclerosis	• Dark on T_1 scout imaging • Dark on LGE sequence, long inversion time
Differential diagnosis	• Myofibroma	• Thrombus	• Various	• Fibroelastoma • Malignant	• Hemangioma • Pericardial cyst	• Lipoma	• Rhabdomyoma

TABLE 3 Continued

	Infectious/ Inflammatory	IMT	Rosai-Dorfman	Papillary Fibroelastoma	Benign Myofibroblastic Mass	Neurofibroma	Lipoma	Cyst
Classification	Infectious/ inflammatory	Endocardial	Histiocytic	Endocardial	Fibroblastic	Peripheral nerve sheath	Lipomatous	Malformation/ectopic tissue
Size, cm	1-3	<1-6	3-5	<1-2	1-2	5-8	1-5	1-5
Location and appearance	• Variable locations • Endocardial or intramyocardial	• Usually endocardial and intracavitary • Can be intramyocardial or intrapericardial • RA/RV more common • Often polypoid, broad-based	• Variable	• Endocardial • Valve (usually mitral or aortic) • Pedunculated • Mobile	• Outflow tract • Well circumscribed	• Posterior mediastinal • Multiple	• Any location • Commonly intramyocardial or endocardial • May be valvular, pedunculated, mobile	• Pericardium • Posterior mediastinum (bronchogenic or foregut duplication cyst)
Cine SSFP	+	+	±	+	+	±	-	+
T_1	-	±	±	-	-	+	+	±
T_2	+	+	+	+	+	+	+ (T_2/fat suppression)	++
Fat suppression	No	No	No	No	No	No	Yes	No
FPP	-	-	-	±	-	-	-	-
LGE	++	± (Sometimes ++)	++	+	±	-	-	-
Pericardial effusion	Common	Uncommon in infants	Common	Uncommon	Uncommon	Uncommon	Uncommon	Common
Other	• Fever • Anemia • Thrombocytopenia • Chest pain • Inflammatory pseudotumor • Metabolic activity on ^{18}F-FDG-PET	• ALK gene expression • May be locally aggressive with recurrence and metastasis • Heart murmur, fatigue • Metabolic activity on ^{18}F-FDG PET/CT	• Neuro symptoms • Chest pain • Metabolic activity on ^{18}F-FDG PET	• Murmur • Embolic events	• Hemodynamic impact	• Older children • Neurofibromatosis • At risk for malignant degeneration	• Range of clinical presentations—usually benign, but may cause syncope or sudden death depending on location and risk of embolization	• Pericardial cysts may increase in size on repeat imaging
Differential diagnosis	• Endocarditis • IMT • Papillary fibroelastoma	• Low-grade sarcoma • Myxoma • Papillary fibroelastoma • Inflammatory pseudotumor	• Infectious/ inflammatory	• Infectious/ inflammatory • Myxoma	• Papillary fibroelastoma	• Malignant	• Lipomatous hypertrophy of the atrial septum • Fatty deposits in TSC	• Hydatid cyst • Teratoma • Lymphatic malformation

Ferumoxytol

- Iron based contrast agent
- Half life 14-15 hours

Multicenter Safety and Practice for Off-Label Diagnostic Use of Ferumoxytol in MRI

Radiology 2019; 293:554–564

Kim-Lien Nguyen, MD • Takegawa Yoshida, MD • Nikhita Kathuria-Prakash, MD • Islam H. Zaki, MD • Csanad G. Varallyay, MD, PhD • Scott I. Semple, PhD • Rola Saouaf, MD • Cynthia K. Rigsby, MD • Sokratis Stoumpos, MD • Kevin K. Whitehead, MD, PhD • Lindsay M. Griffin, MD • David Saloner, PhD • Michael D. Hope, MD • Martin R. Prince, MD, PhD • Mark A. Fogel, MD • Mark L. Schiebler, MD • Giles H. Roditi, MD • Aleksandra Radjenovic, PhD • David E. Newby, MD, PhD • Edward A. Neuwelt, MD • Mustafa R. Bashir, MD • Peng Hu, PhD • J. Paul Finn, MD

- 3215 pts (409 < 18 yo)
- 4240 injections
- 1.9% AEs related or possibly related
- No life threating or severe AEs
- 1.8% mild AEs

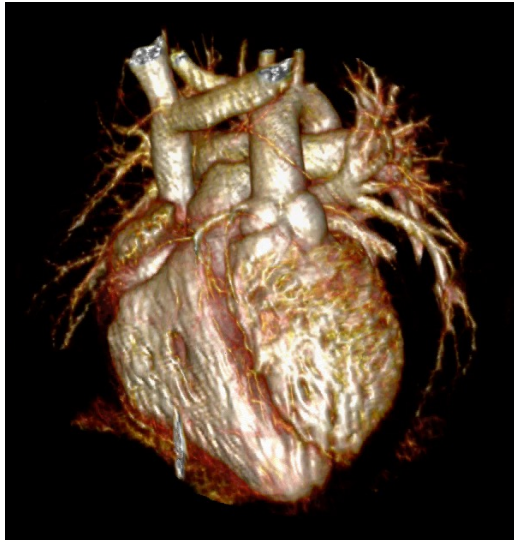
5 day old TOF/PA

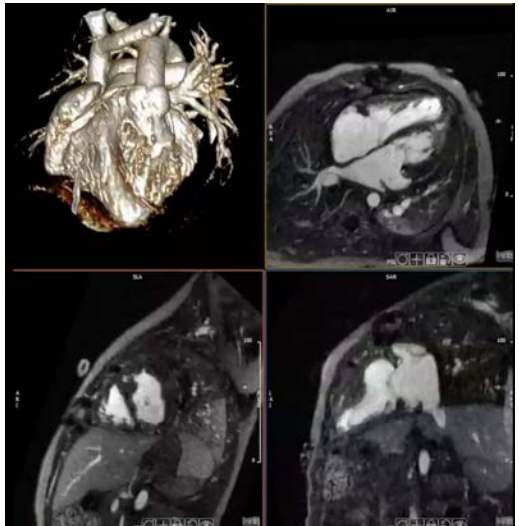
Ferumoxytol

Four-dimensional Multiphase Steady-State MRI with Ferumoxytol Enhancement: Early Multicenter Feasibility in Pediatric Congenital Heart Disease

Radiology 2021; 300:162–173

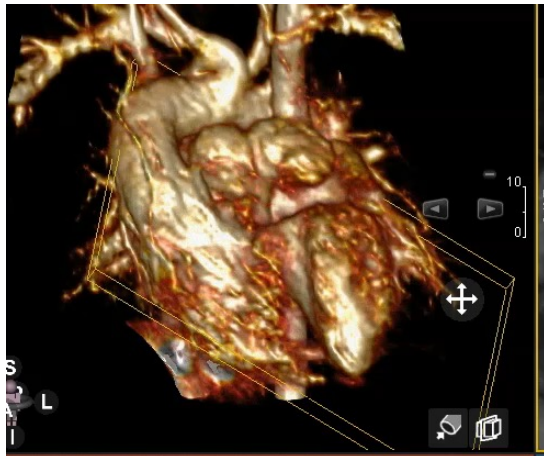
Kim-Lien Nguyen, MD • Reena M. Ghosh, MD • Lindsay M. Griffin, MD • Takegawa Yoshida, MD • Arash Bedayat, MD • Cynthia K. Rigsby, MD • Mark A. Fogel, MD • Kevin K. Whitehead, MD • Peng Hu, MD • J. Paul Finn, MD





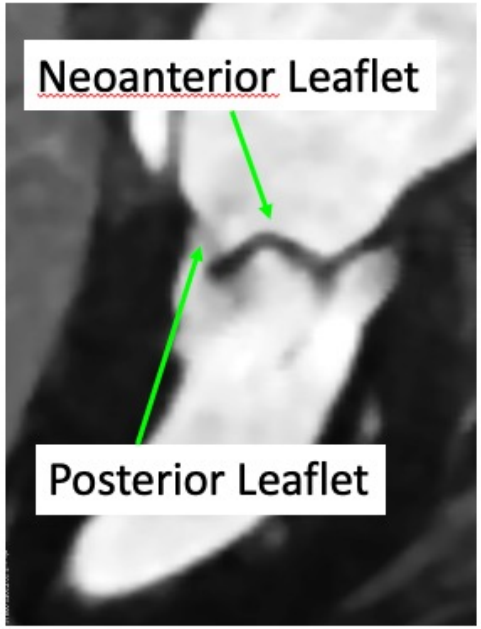
- 3 sites, N = 60
- Ages mean 14.4 mo
- Range of CHD
- Image quality scores: 4.3, 4.6, 4.9 out of 5
- Reduced acquisition time from 44 minutes to 12 minutes

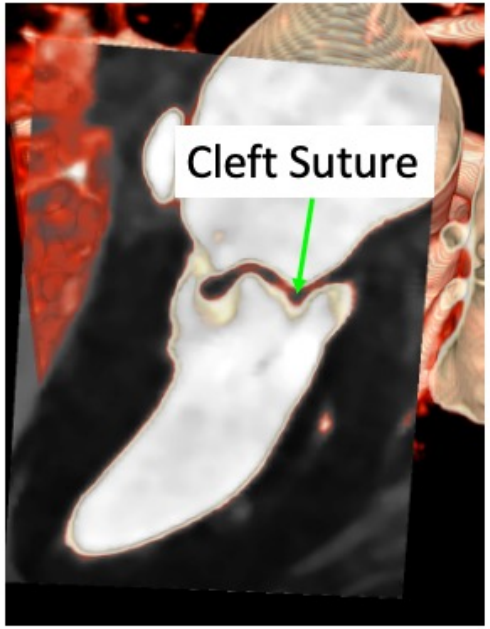
5 month old, 5.5 kg, DORV PS LJAA
Biventricular repair?

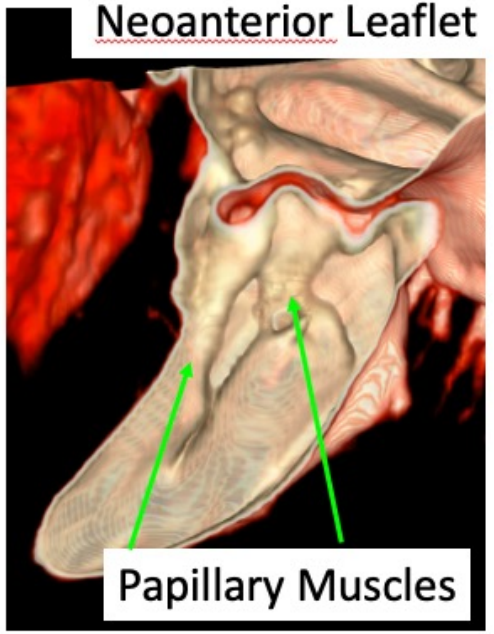


Ferumoxytol – Valve Imaging

- 10 yo with 1^0 ASD, cleft MV & subaortic membrane after repair
- Residual cleft MV & subaortic membrane

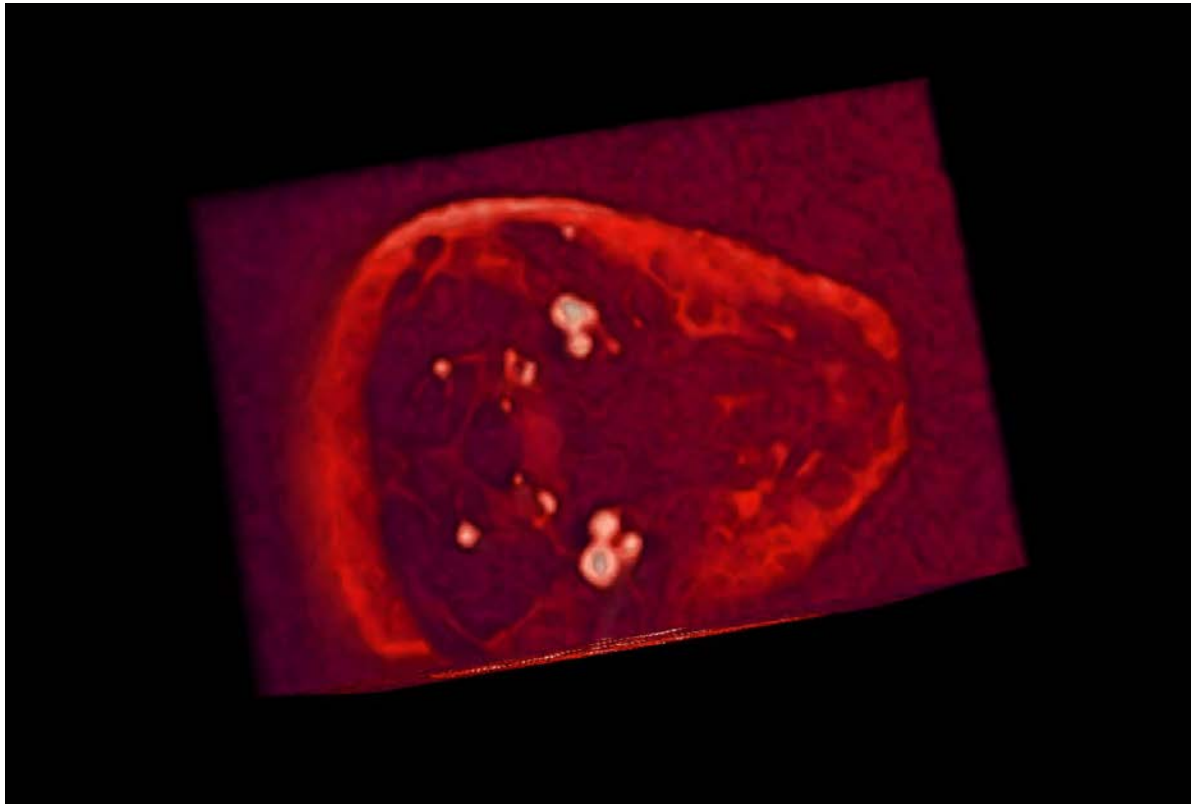






3D creation by Alan Cianciulli, Matt Jolley and the Valve Team

Ferumoxytol – Valve Imaging

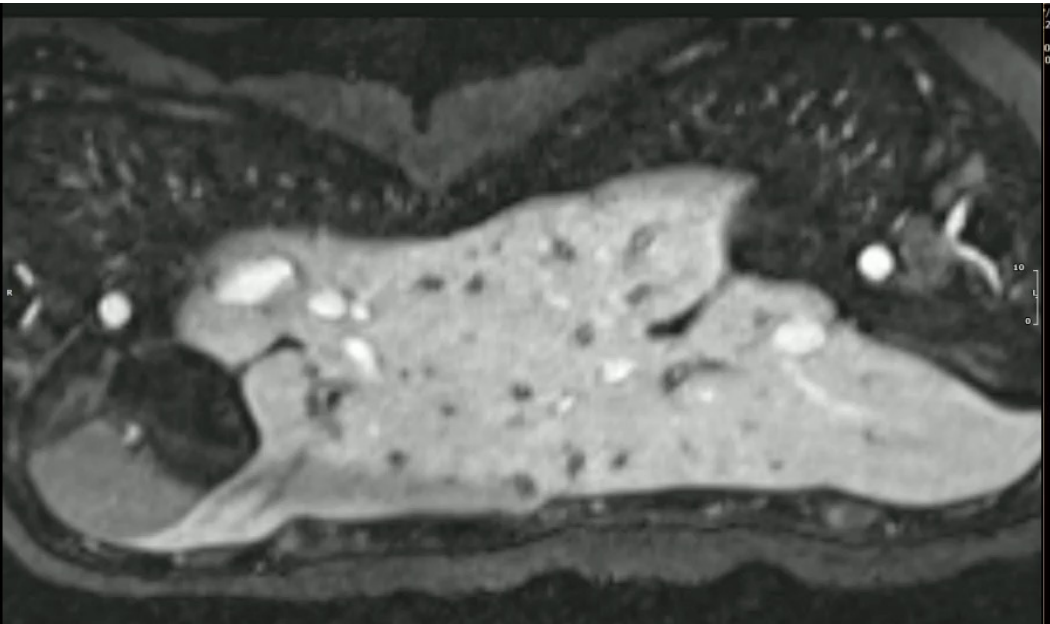


3D creation by Alan Cianciulli, Matt Jolley and the Valve Team

Ferumoxytol And Gad Perfusion Conjoined Twins

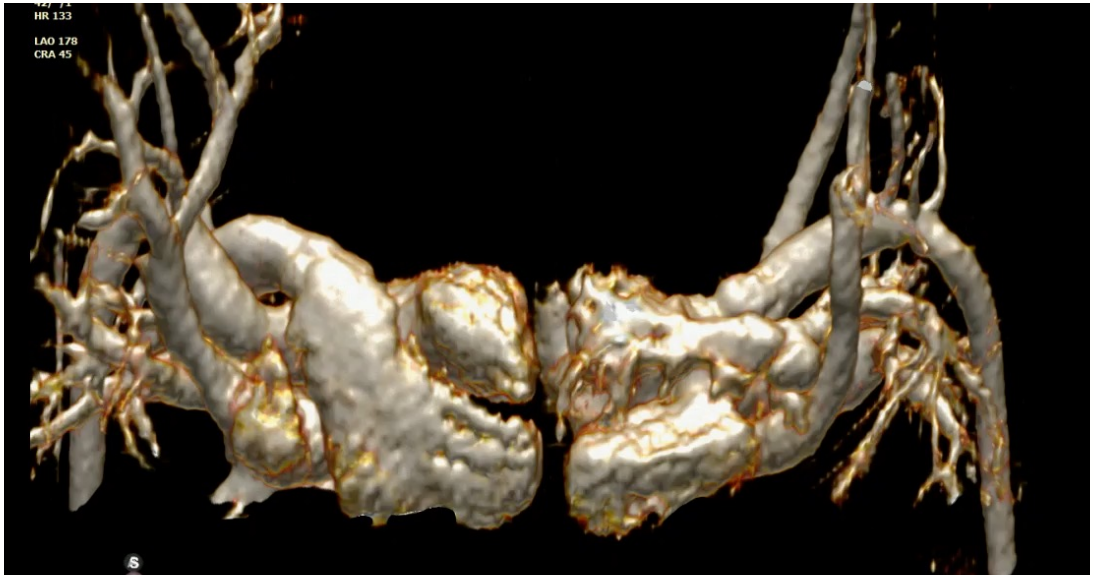
DORV with PS after PDA stent

Normal heart

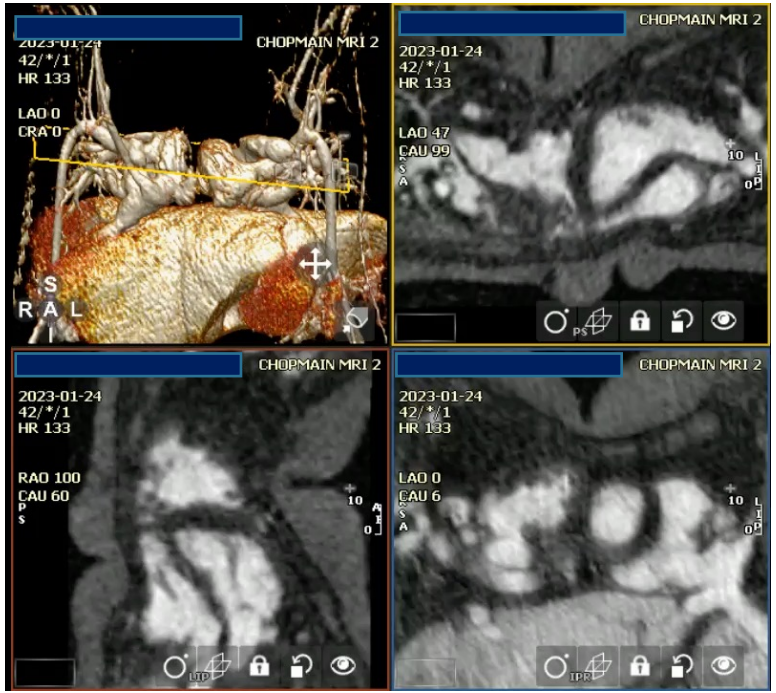


Ferumoxytol And Gad Perfusion Conjoined Twins

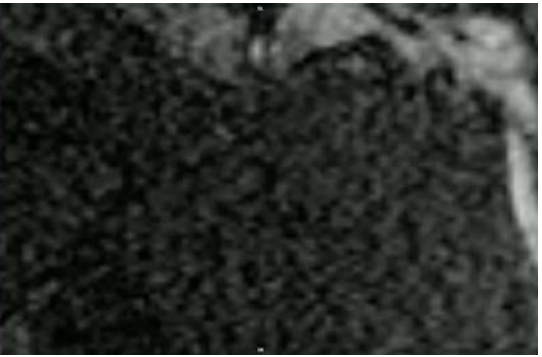
Normal heart

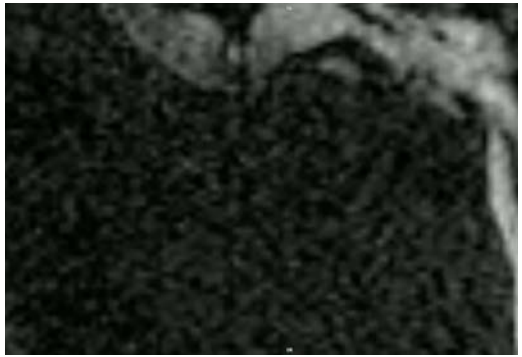


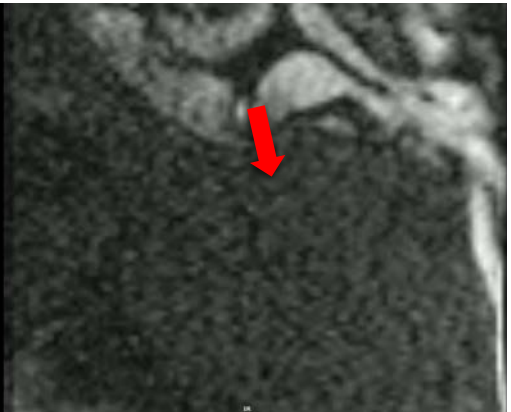
DORV with PS after PDA stent

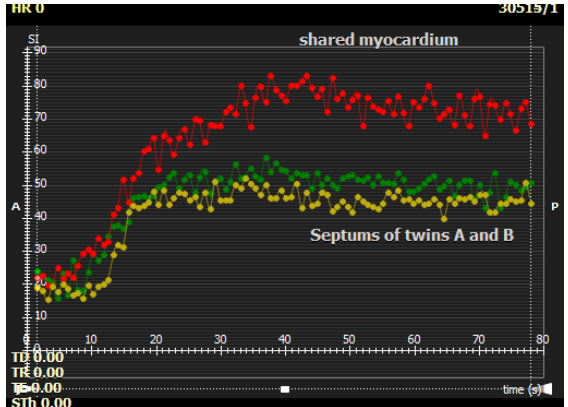


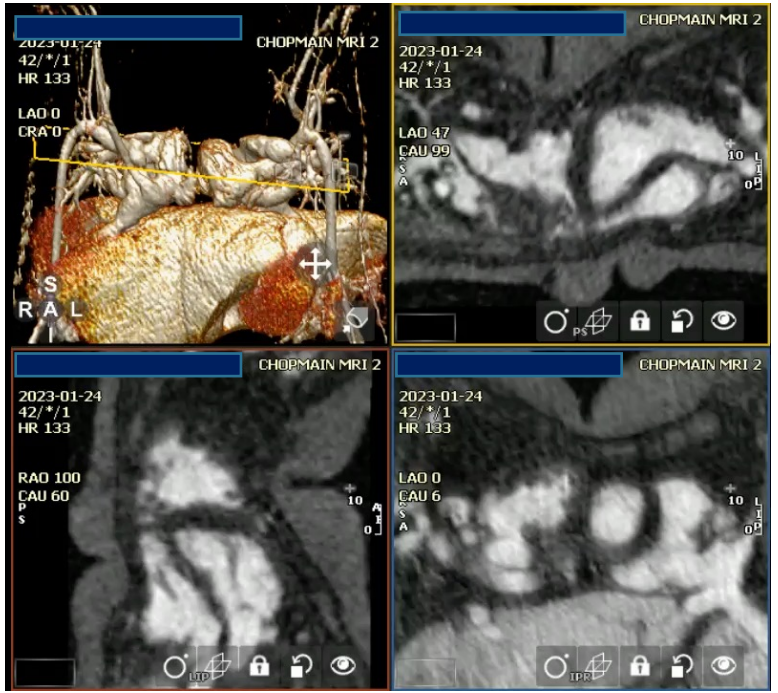
Ferumoxytol And Gad Perfusion Conjoined Twins







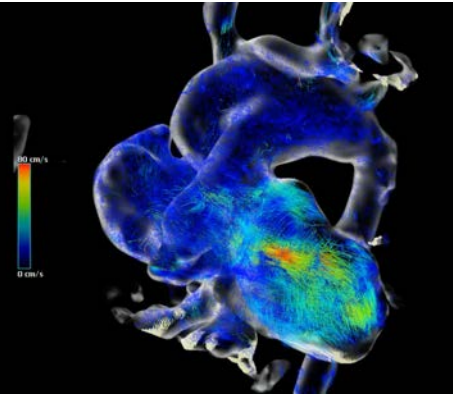


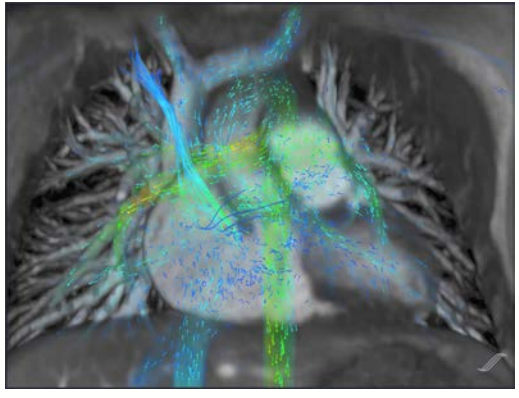


Summary

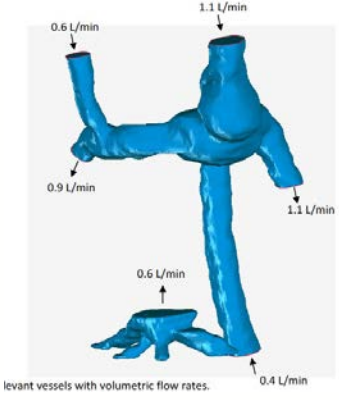
Tissue characterization is a broad category that aids in a myriad of clinical decision making scenarios

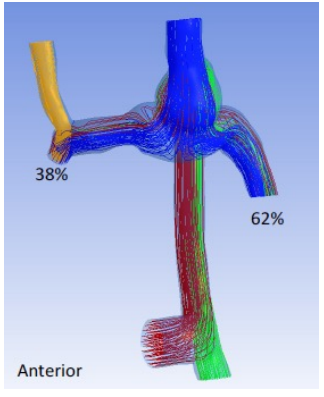
Ferumoxytol imaging allows for high resolution 4D anatomy and function to aid in surgical planning





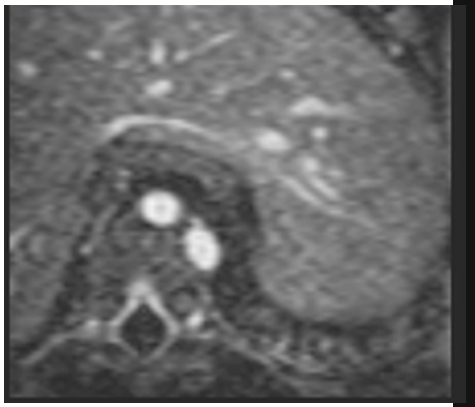
Courtesy of Dr. Shreyas Vasanawala Stanford

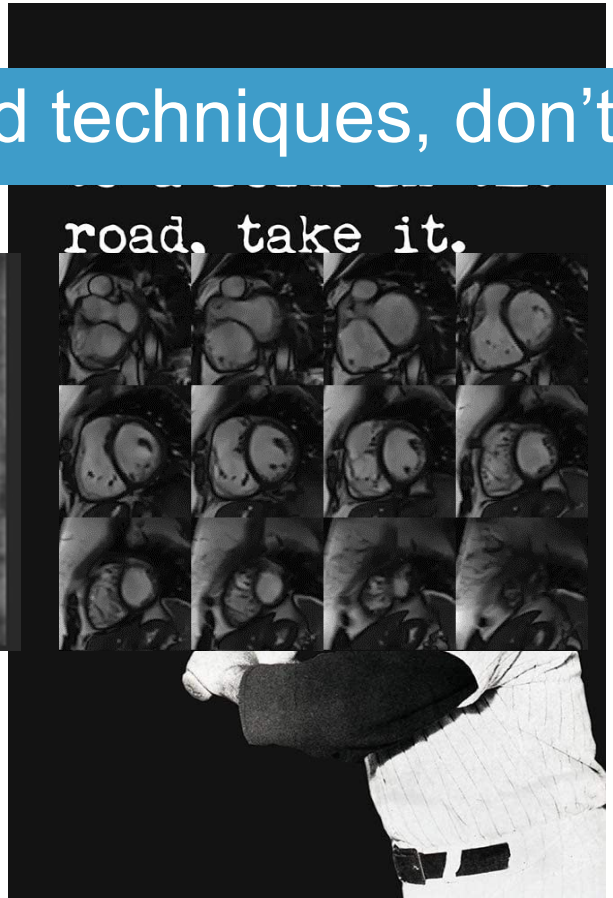


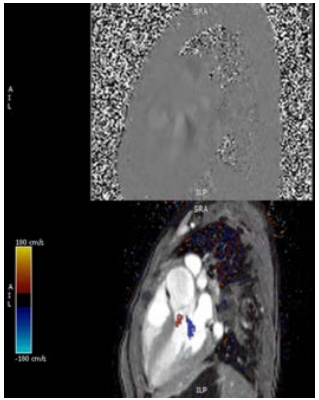


WHEN IT COMES TO CRITICAL DECISIONS…..

Besides advanced techniques, don’t forget about…..







CARDIOLOGY 2023

Children's Hospital of Philadelphia
Cardiac Center

THANK YOU AND CREDITS

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- Jessica Tang

CARDIOLOGY 2023

Children's Hospital of Philadelphia
Cardiac Center

22CME0420/PPT/01-23

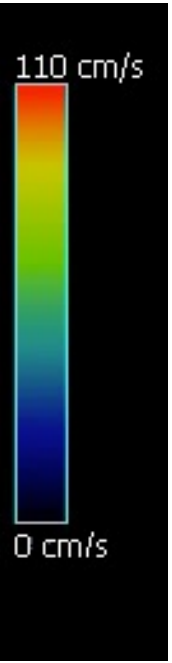
Summary

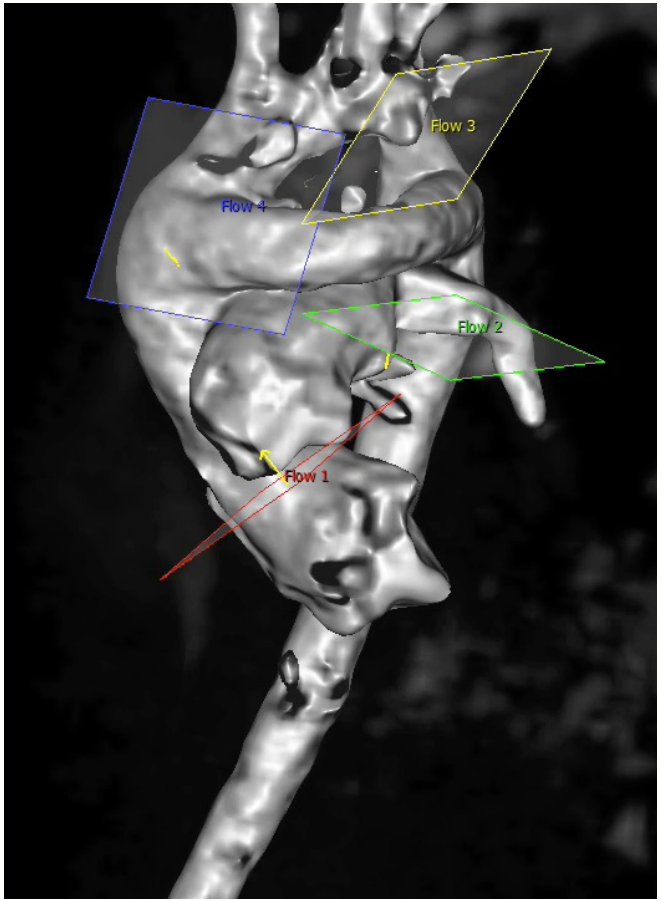
Tissue characterization is a broad category that aids in a myriad of clinical decision making scenarios

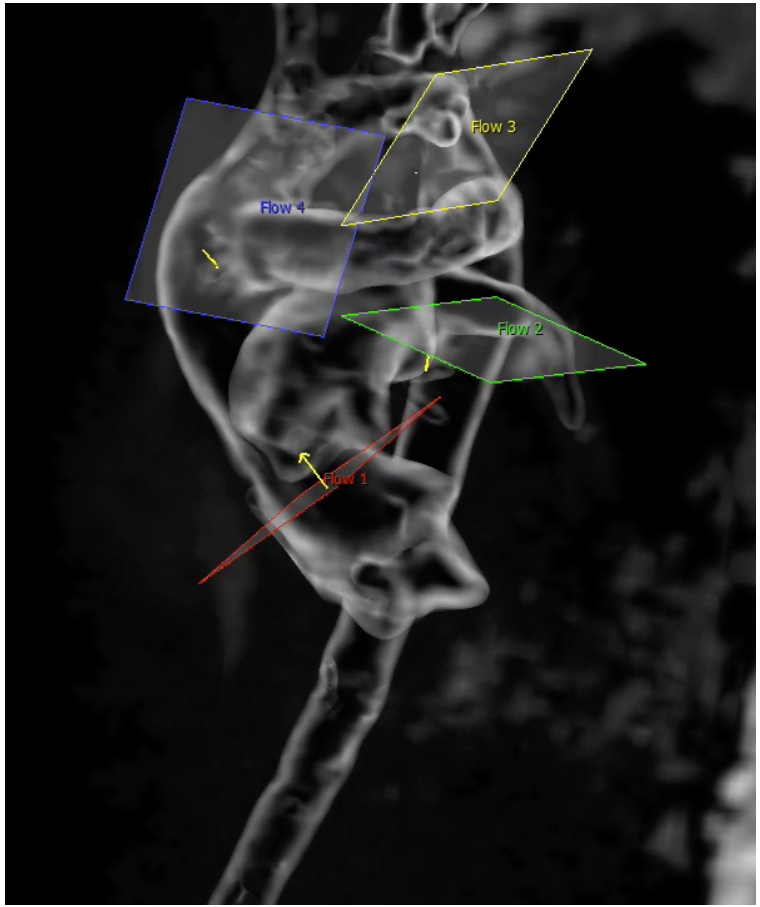
Ferumoxytol imaging allows for high resolution 4D anatomy and function to aid in surgical planning

4D Flow yields much visual and quantitative hemodynamic information

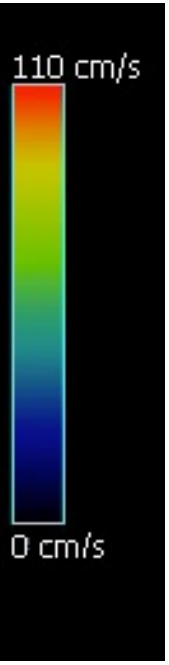
4D Flow: AAo-DAo conduit





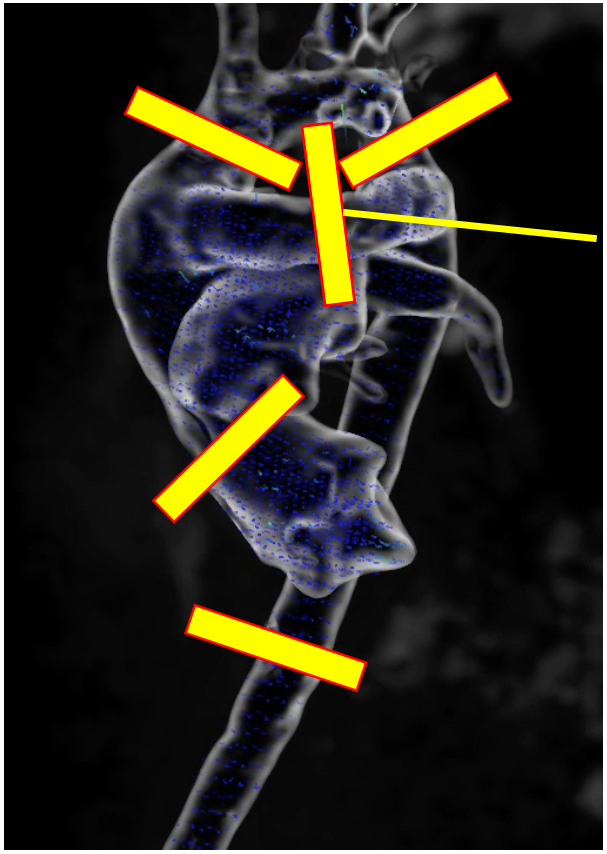


4D Flow



3 l/min

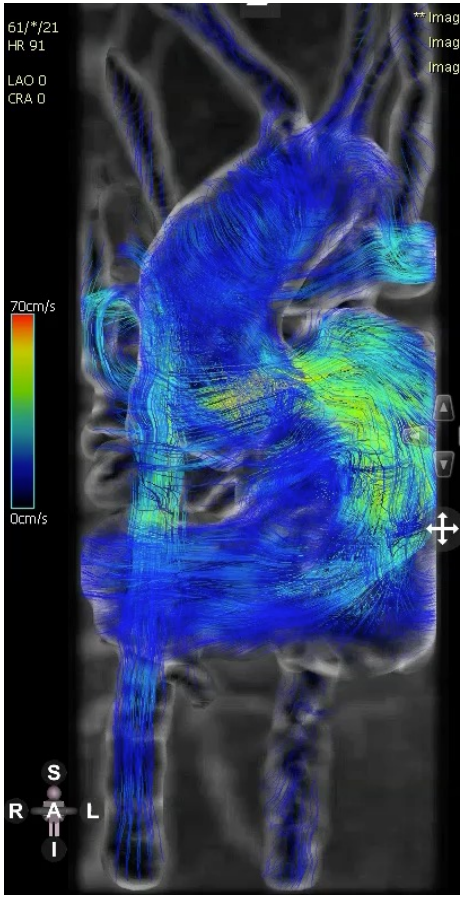
4.5 l/min



1 l/min

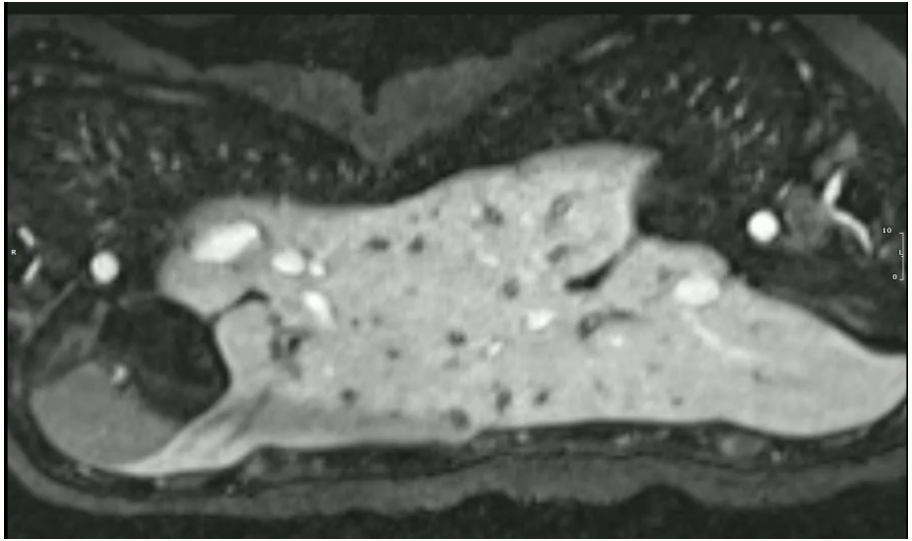
1.5 l/min

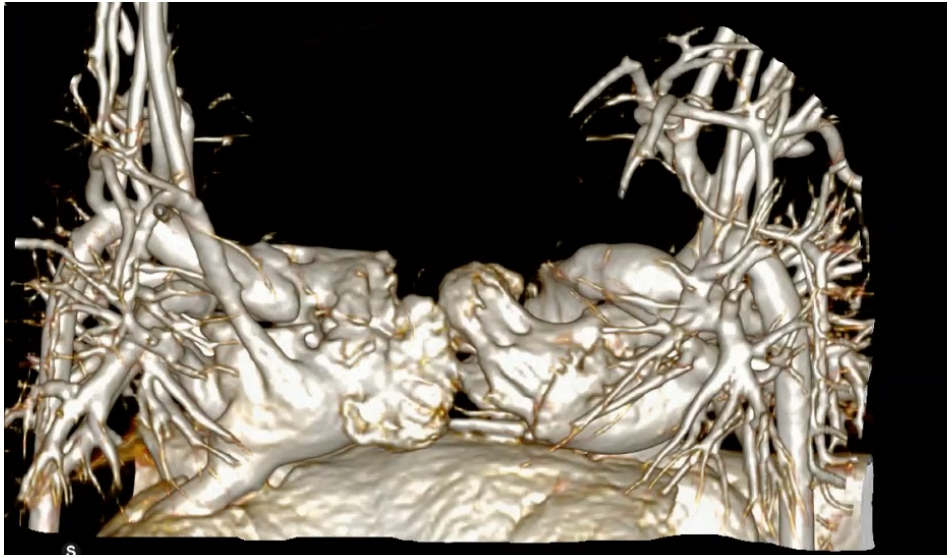
2.5 l/min



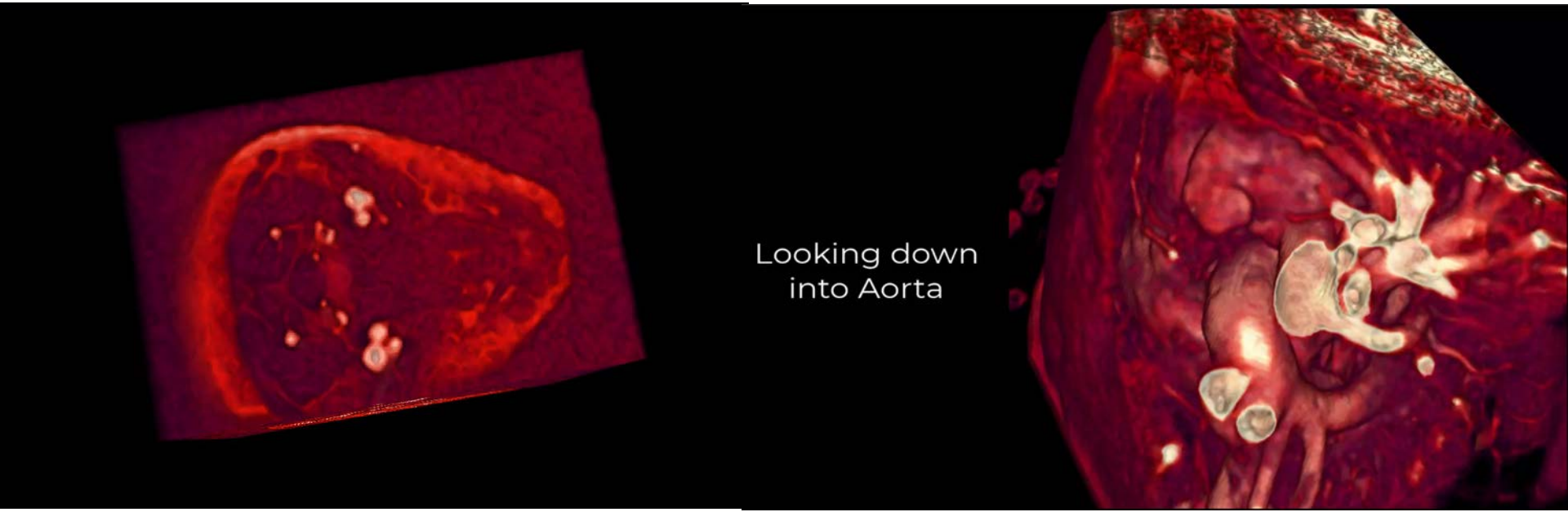
Ferumoxytol And Gadolinium Conjoined Twins

- Normal heart (right), DORV with PS after PDA stent (left)

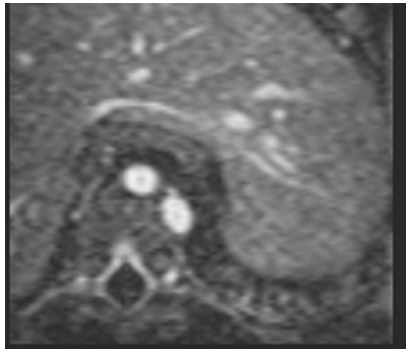


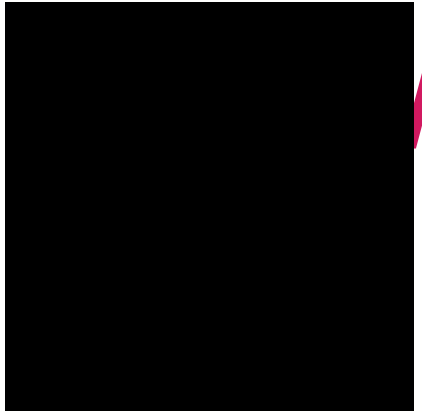


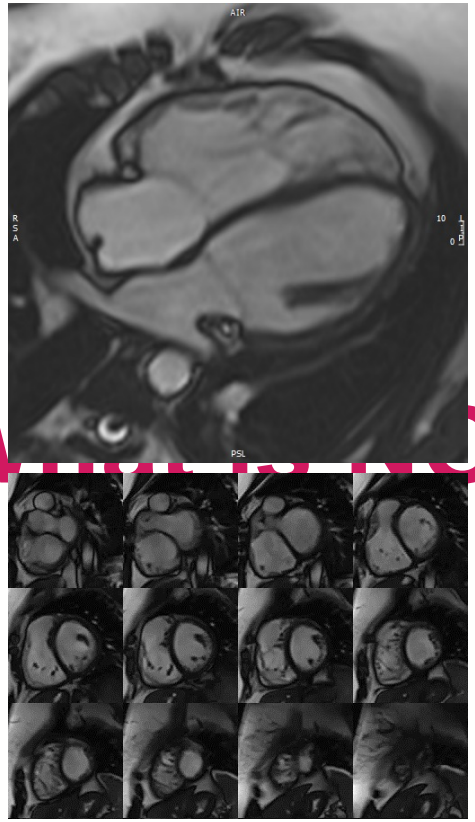
Ferumoxytol – Valve Imaging

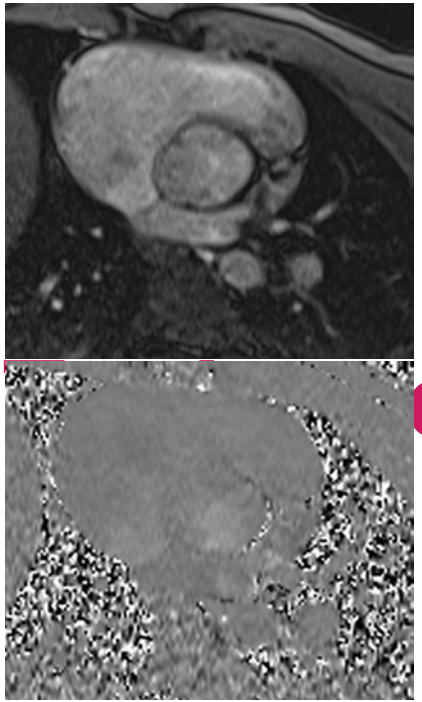


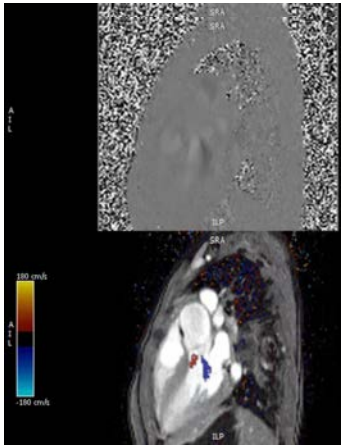
3D creation by Alan Cianciulli, Matt Jolley and the Valve Team

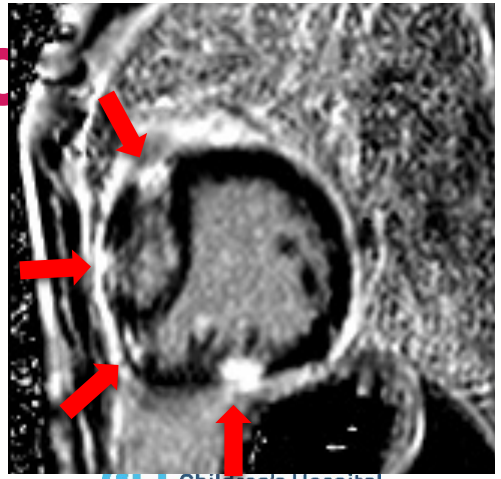












CARDIOLOGY 2023

Children's Hospital of Philadelphia
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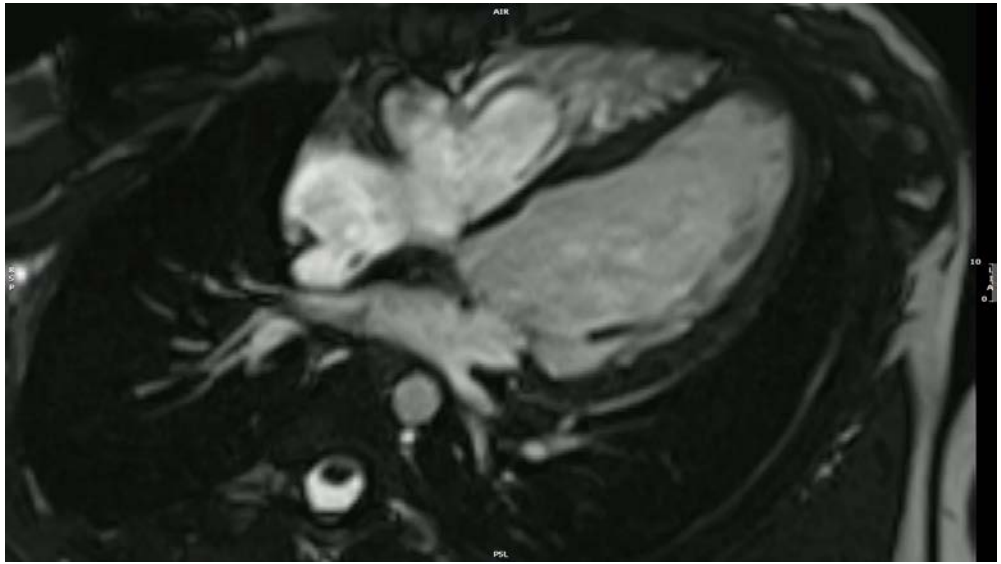
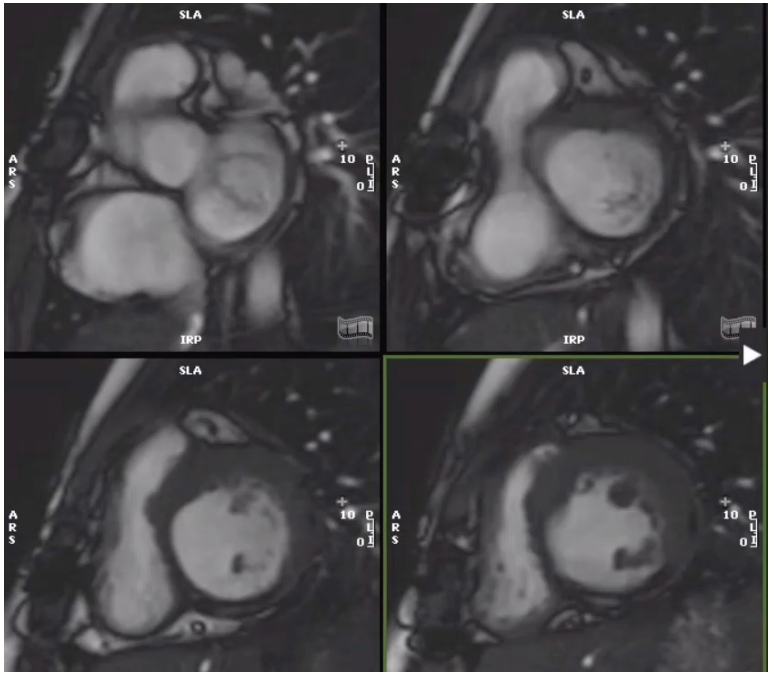
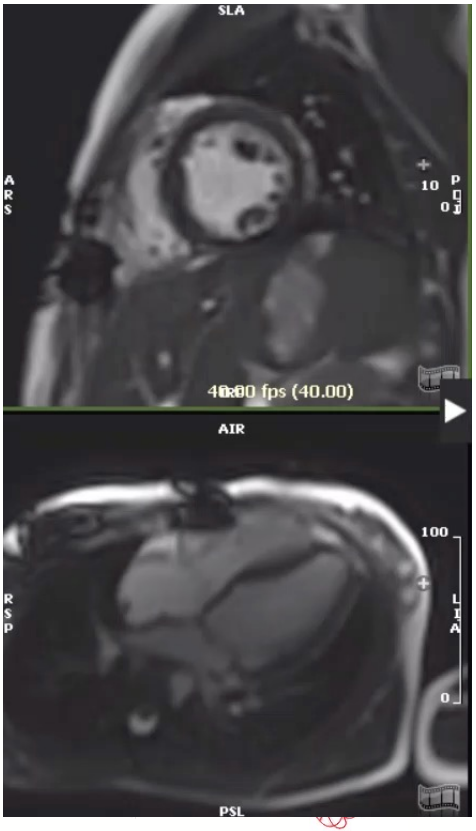
Tissue Characterization: Perfusion

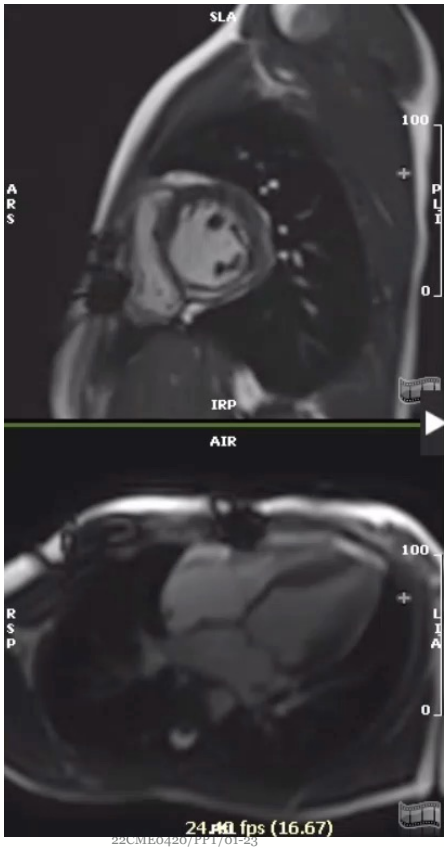
- 14 yo female with FH after Ross, RCA & LCA ostioplasty
- Poor function on echo



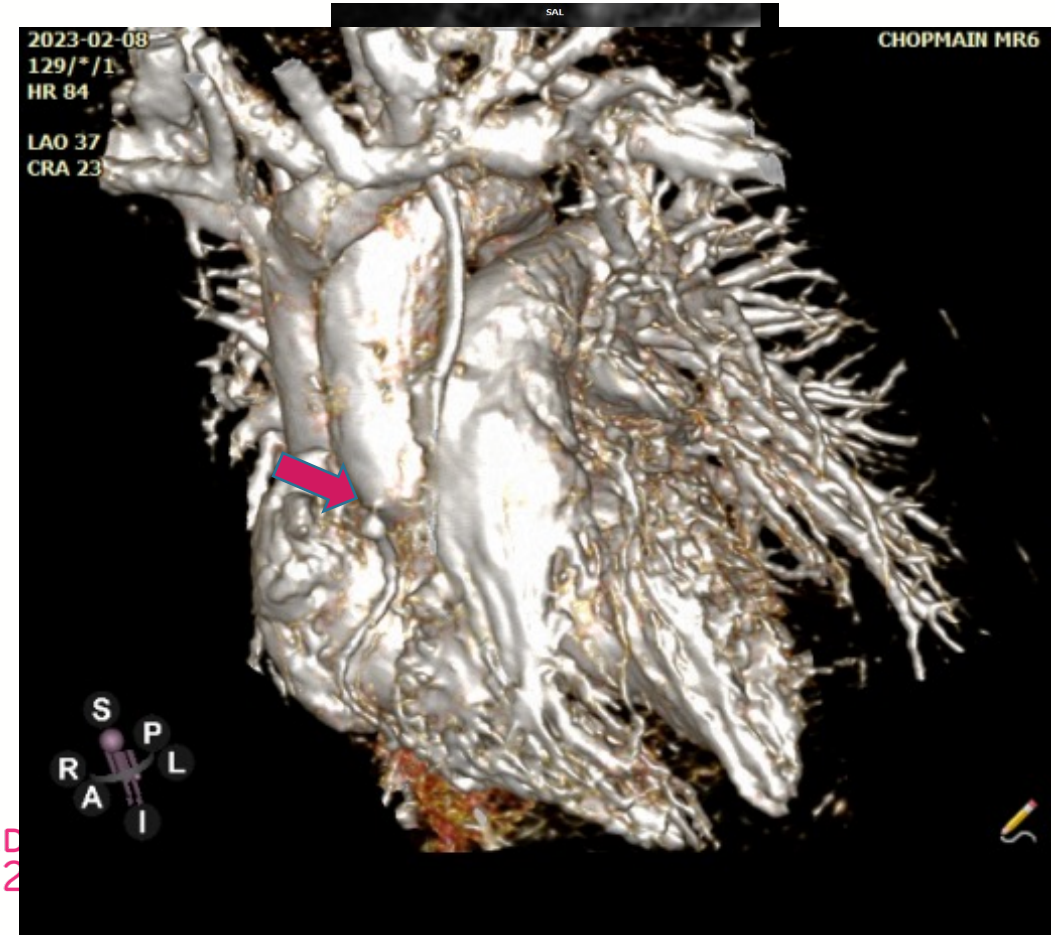


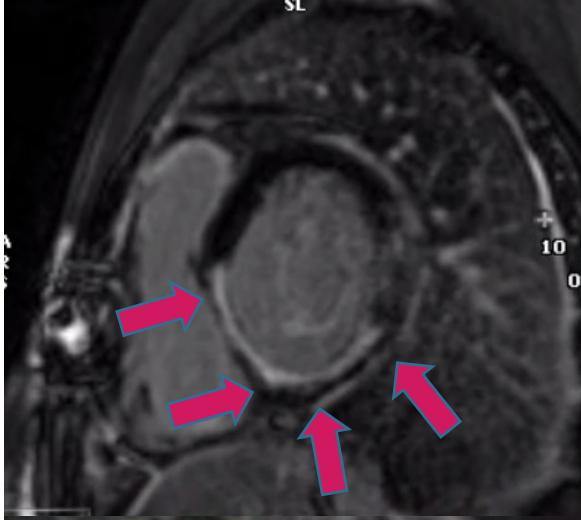
Tissue Characterization - Perfusion

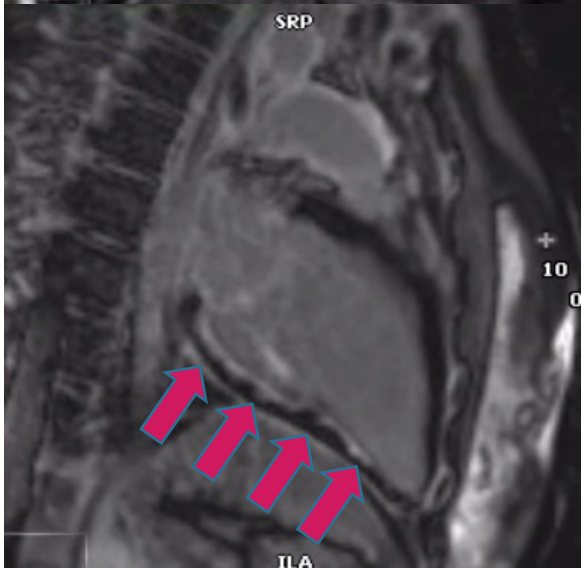




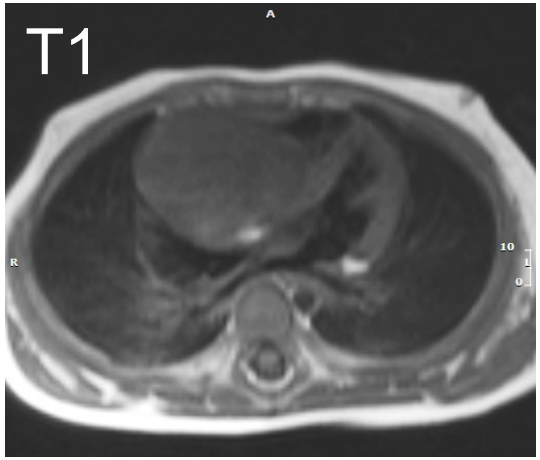
Tissue Characterization

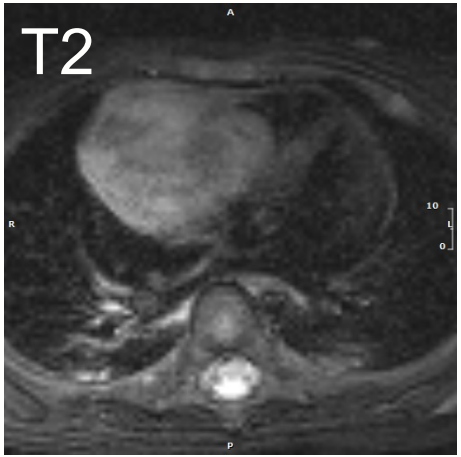


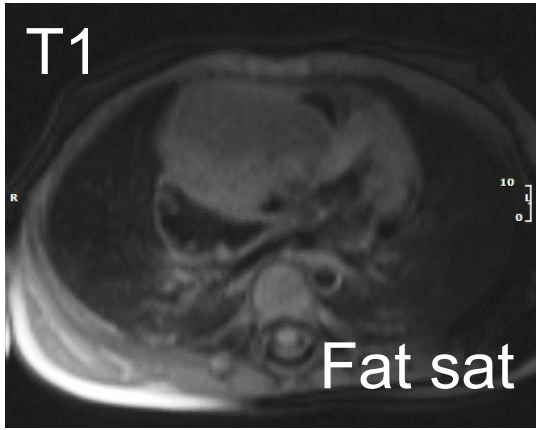


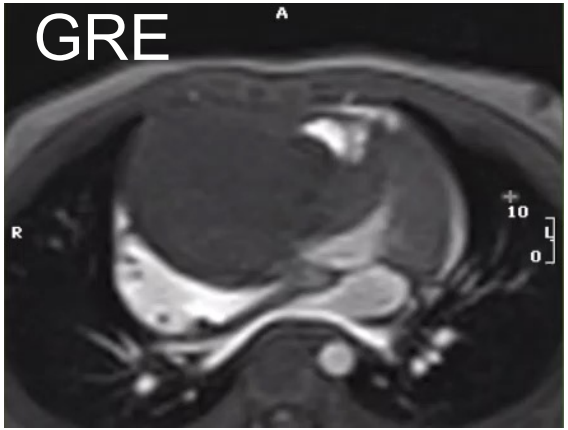


RV Tumor

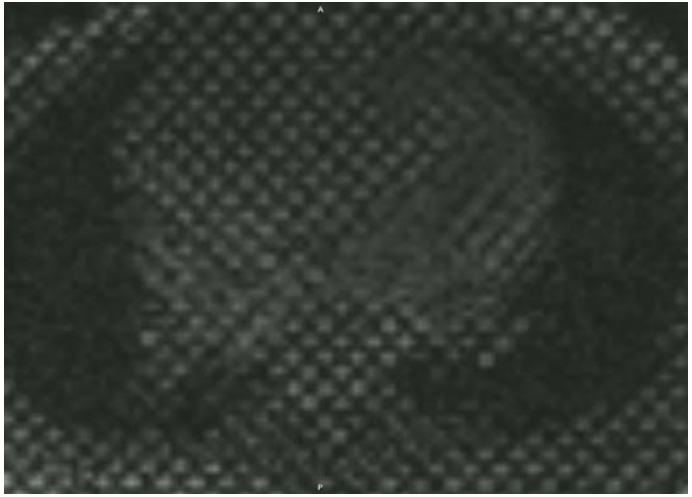






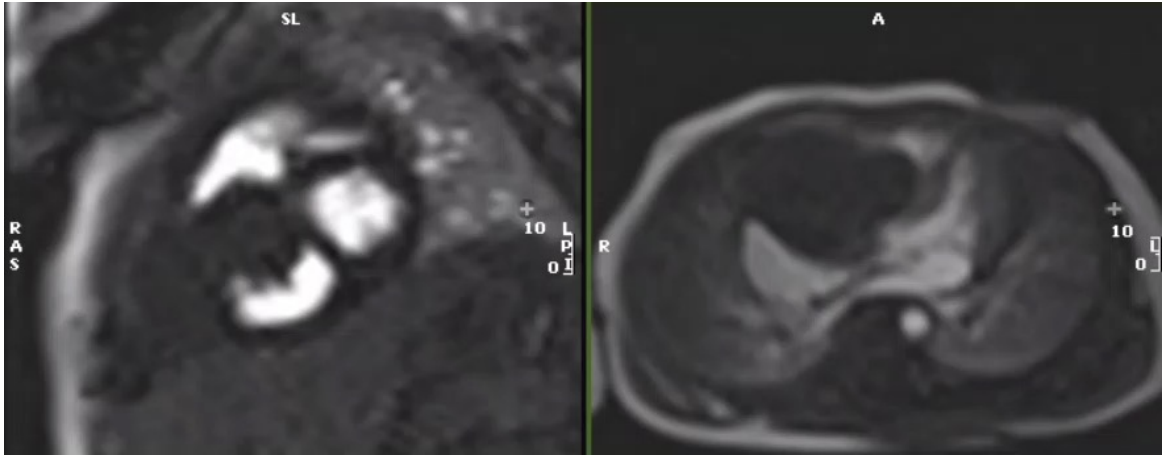


Myocardial tagging

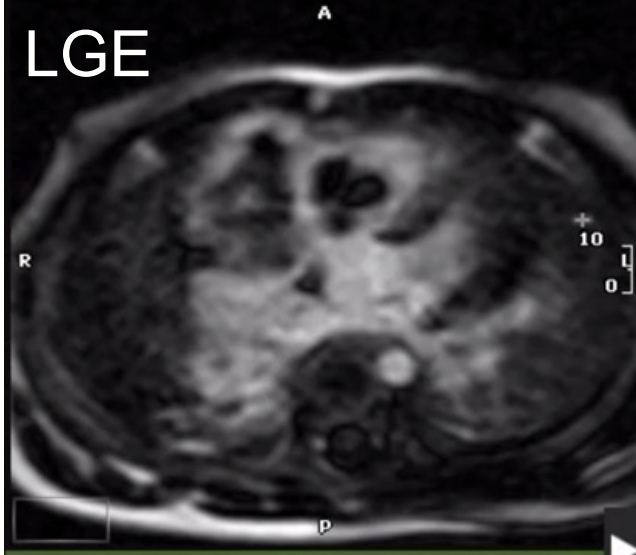


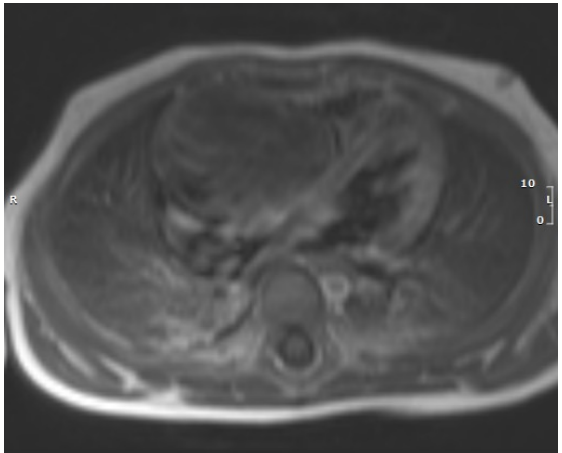
RV Tumor

Perfusion

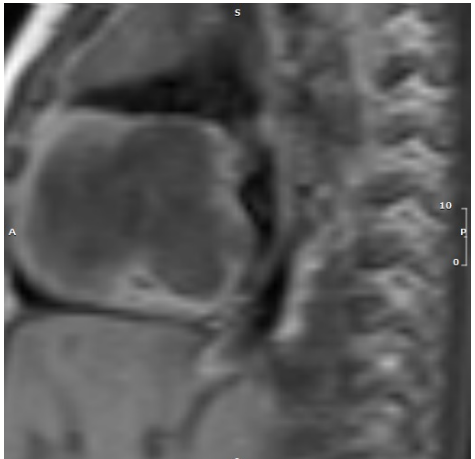


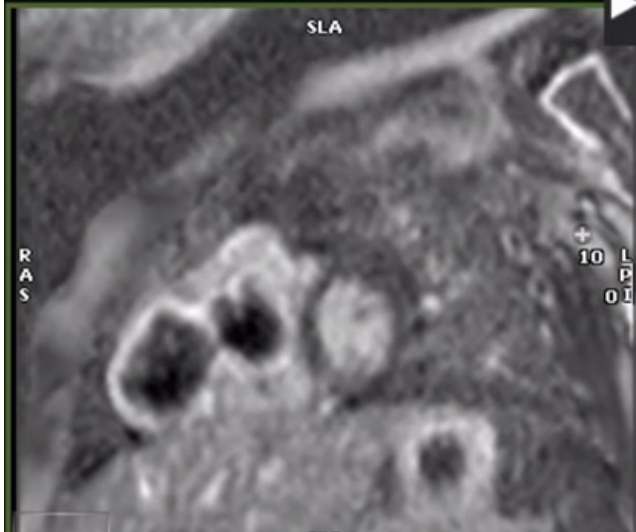
LGE





T1 after gad





RV Tumor

Coronaries

Predicted:

Component

Case Results

Surgical Pathology — Case: [redacted]

Authorizing Provider: [redacted] — Collected: [redacted]

Ordering Location: Cardiac OR & Imaging — Received:

Pathologist: [redacted]MD

Specimen: Heart, Right Ventricle, Right Ventricular Fibroma

Final Diagnosis

A. Heart, right ventricle, mass, excision:
- Cardiac fibroma, see microscopic description.

Electronically signed by Pogoriler, Jennifer, MD on 1/5/2023 at 1307

Note

Reviewed at intradepartmental consensus conference 1/4/2023 with agreement.

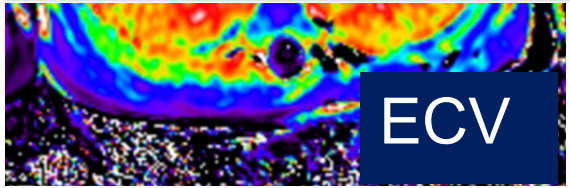
Gross Description

A. Heart, Right Ventricle. Right Ventricular Fibroma

Cardiac mass

Procedure

CARDIAC TUMOR RESECTION, TEE, BIDIRECTIONAL CAVOPULMONARY ANASTOMOSIS (BDCPA) (BIDIRECTIONAL GLENN)



3D