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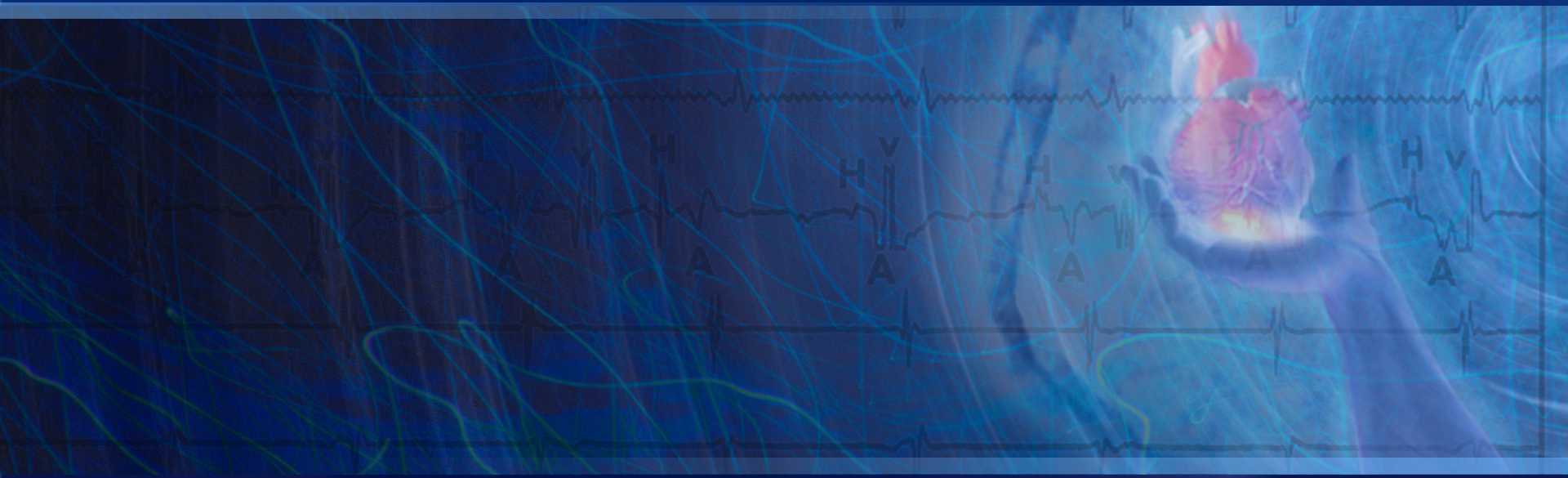
Heart Failure and CRT: Novelties and Controversies



Samuel J. Asirvatham, MD
Professor of Medicine, Professor of Pediatrics
Program Director Cardiac Electrophysiology;
Vice Chair – Innovations Mayo Clinic

Turin, October 26, 2012

Disclosure

I receive royalties for work licensed through Mayo Clinic to a privately held company for contributions related to the use of nerve signal modulation to treat central, autonomic, and peripheral nervous system disorders, including pain. Mayo Clinic receives royalties and owns equity in this company. The company does not currently license or manufacture any drug or device in the medical field.

Co-patent holder for technique to minimize coagulum formation during radiofrequency ablation

Products or techniques related to the above disclosures are not being discussed in this presentation.

Pertains to inventions/startup companies that include Nevro, Aegis, and the Phoenix Corp.

Honoraria/Speakers:	**Consulting:**
Abiomed	**Sanofi**
Biotronik	**Stereotaxis**
Blackwell Futura	
Boston Scientific	
Medtronic	
Sanofi-aventis	
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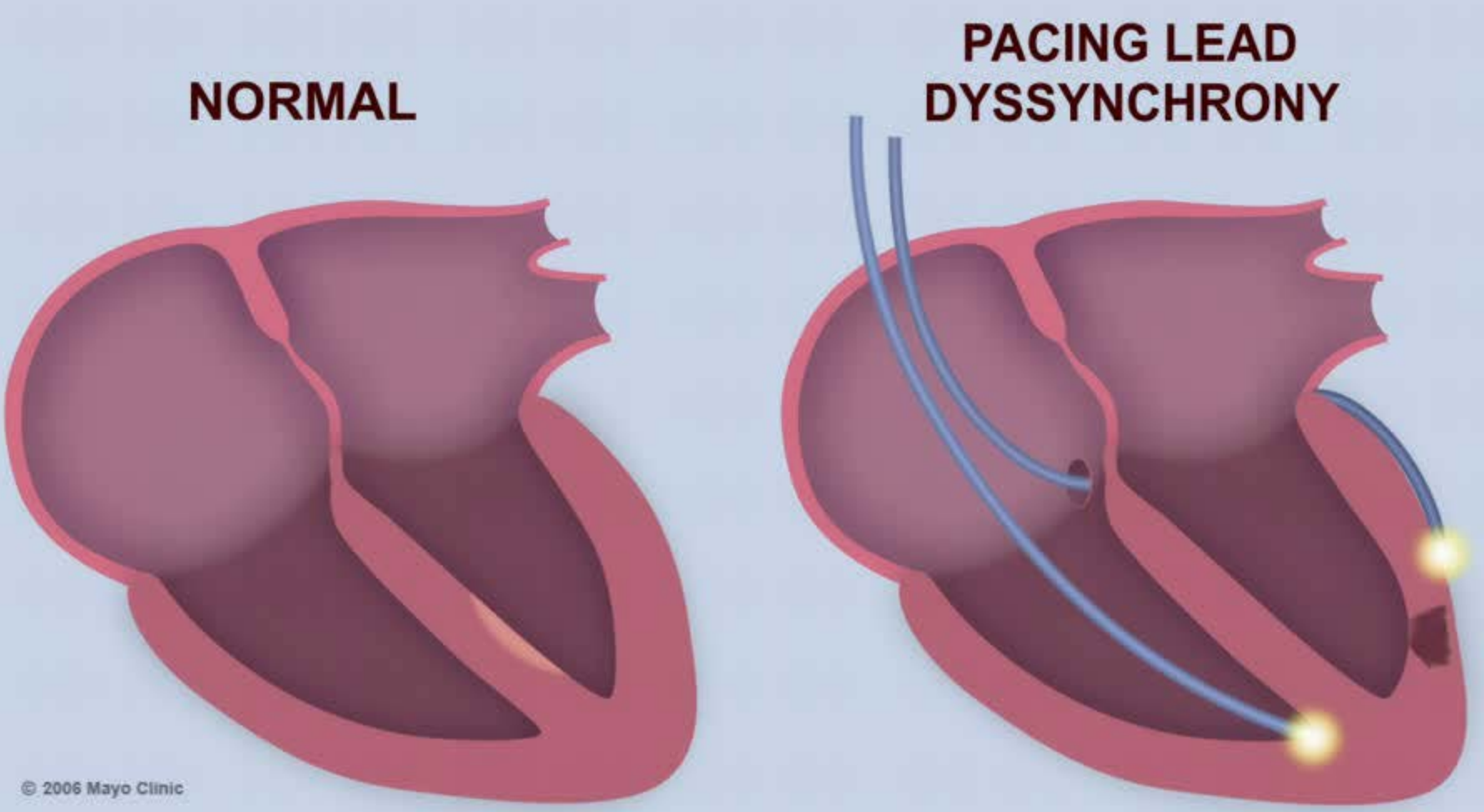
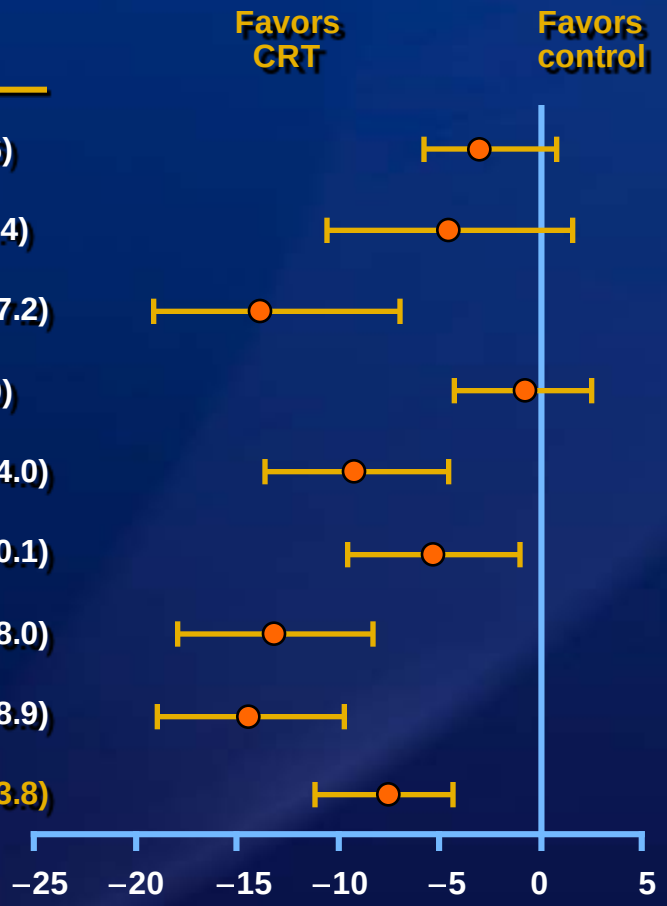
St. Jude	


NORMAL
PACING LEAD
DYSSYNCHRONY
© 2006 Mayo Clinic

QOL Analysis

Study (yr)	Quality of life: CRT group Pt (no.)	CRT group Mean MLWF score±SD	Control group Pt (no.)	Control group Mean MLWF score±SD	Wt mean diff in MLWF score (95% CI)
PATH-CHF, 2002	41	25.2±10.6	41	28.1±11.2	−2.9 (−6.4 to 0.6)
MUSTIC-AF, 2002	39	−9.9±21.3	39	−5.5±21.7	−4.4 (−11.2 to 2.4)
MUSTIC-SR, 2001	45	−17.4±21.6	45	−3.8±22.4	−13.6 (−20.0 to −7.2)
CONTAK-CD, 2003	234	−5.2±19.8	225	−4.5±20.2	−0.7 (−4.4 to 3.0)
MIRACLE, 2002	213	−18.0±28.6	193	−9.0±22.9	−9.0 (−14.0 to −4.0)
MIRACLE-ICD, 2003	162	−18.3±23.2	153	−13.1±22.7	−5.2 (−10.3 to −0.1)
COMPANION, 2004	459	−25.0±−26.0	104	−12.0±23.0	−13.0 (−18.0 to −8.0)
COMPANION-CD, 2004	479	−26.0±28.0	103	−12.0±23.0	−14.0 (−19.1 to −8.9)
Overall					−7.6 (−11.5 to −3.8)



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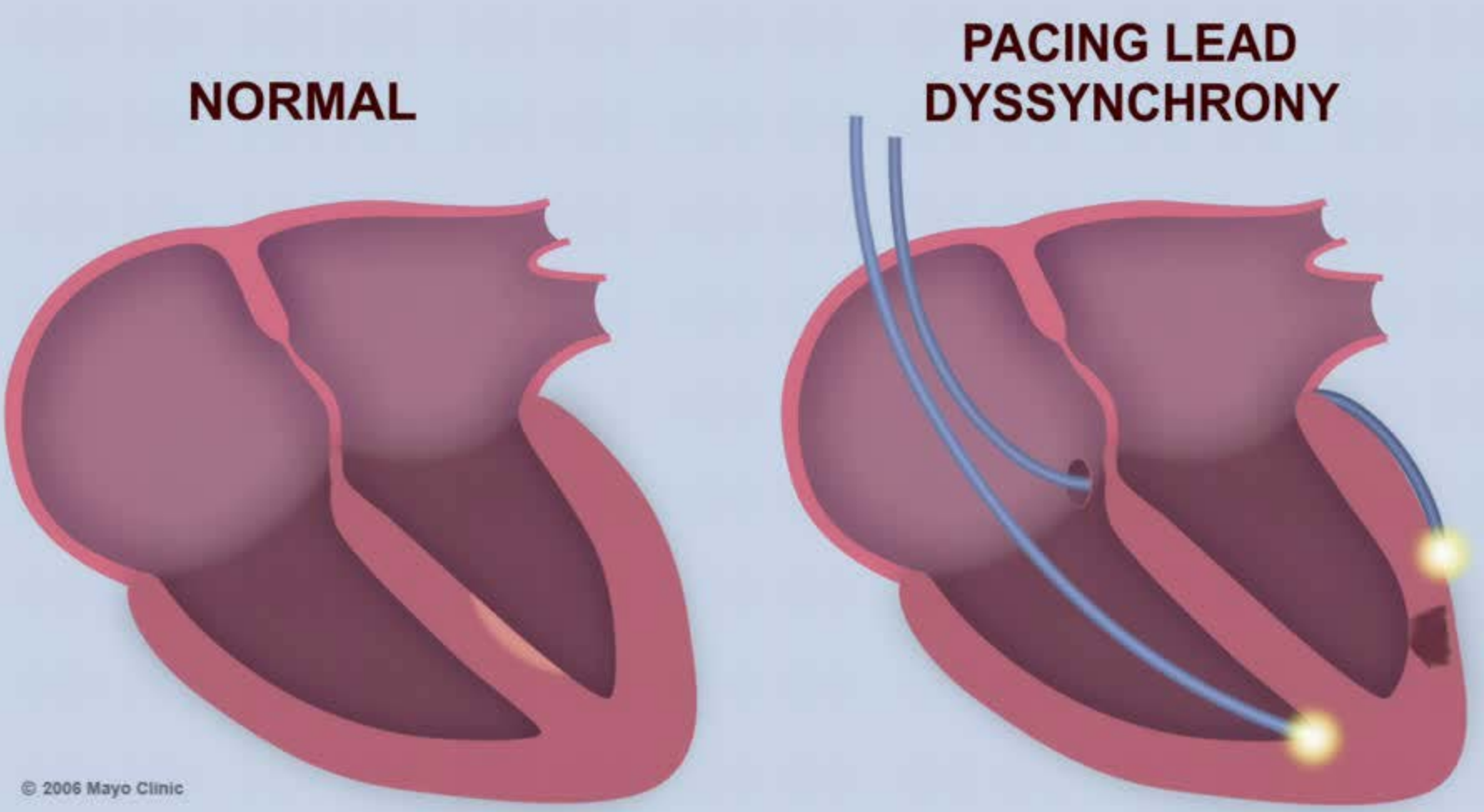
McAlister FA et al: Ann Intern Med 141:381, 2004

Patients In Whom CRT Strongly Supported by Randomized Trials

- Sinus rhythm
- LVEF ≤ 0.35
- Ischemic or nonischemic cardiomyopathy
- QRS complex duration ≥ 120 ms
- NYHA functional class III or IV
- Maximal pharmacological therapy for heart failure

Overview

- CRT – How does it work?
- Normal ventricular function
- Electrical dyssynchrony
- Mechanical dyssynchrony
- Electromechanical coupling
- Arrhythmogenesis
- Resynchronization
  - Electrical
  - Mechanical


NORMAL
PACING LEAD
DYSSYNCHRONY
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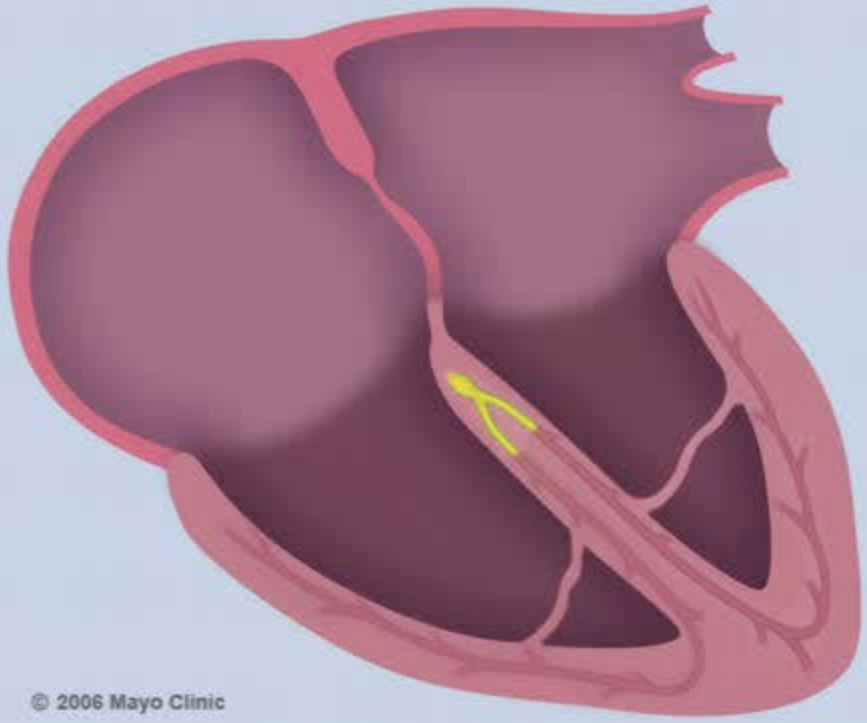
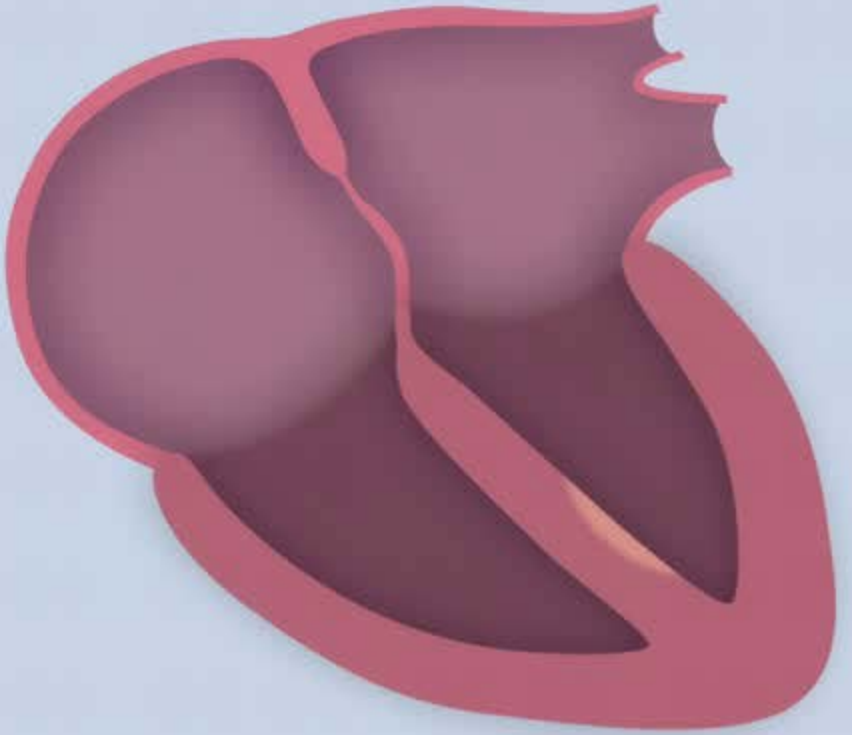
Mechanical Electrical Relationships

- Understand the Electrical Sequela of Mechanical Dysfunction
- Understand the Mechanical Sequela of Electrical Dysfunction
- Restoration of Electrical Synchrony
- Restoration of Mechanical Synchrony
- Application in Heart Failure Management

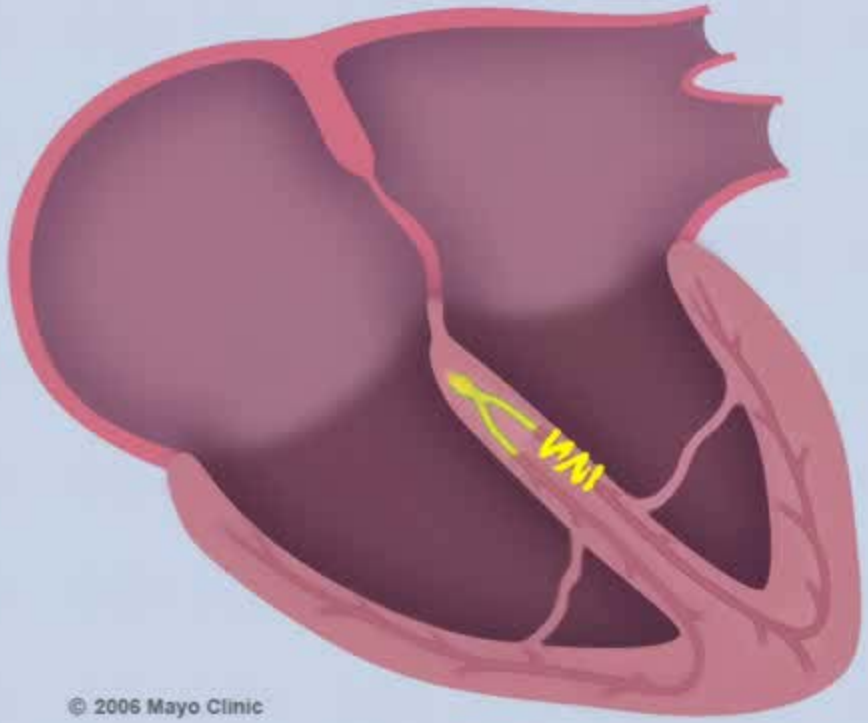
NORMAL ELECTRICAL



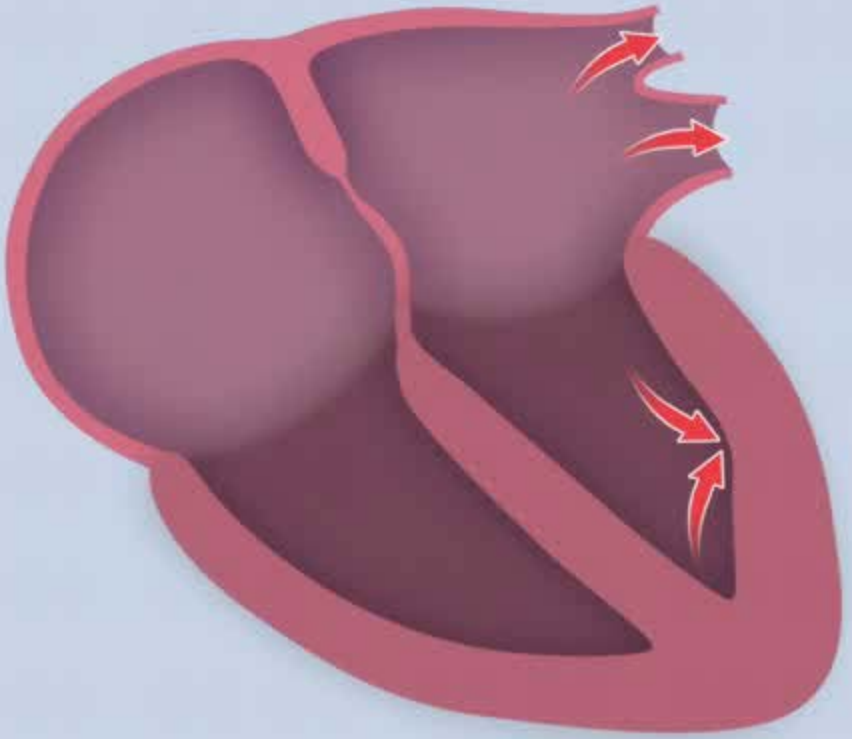
NORMAL MECHANICAL

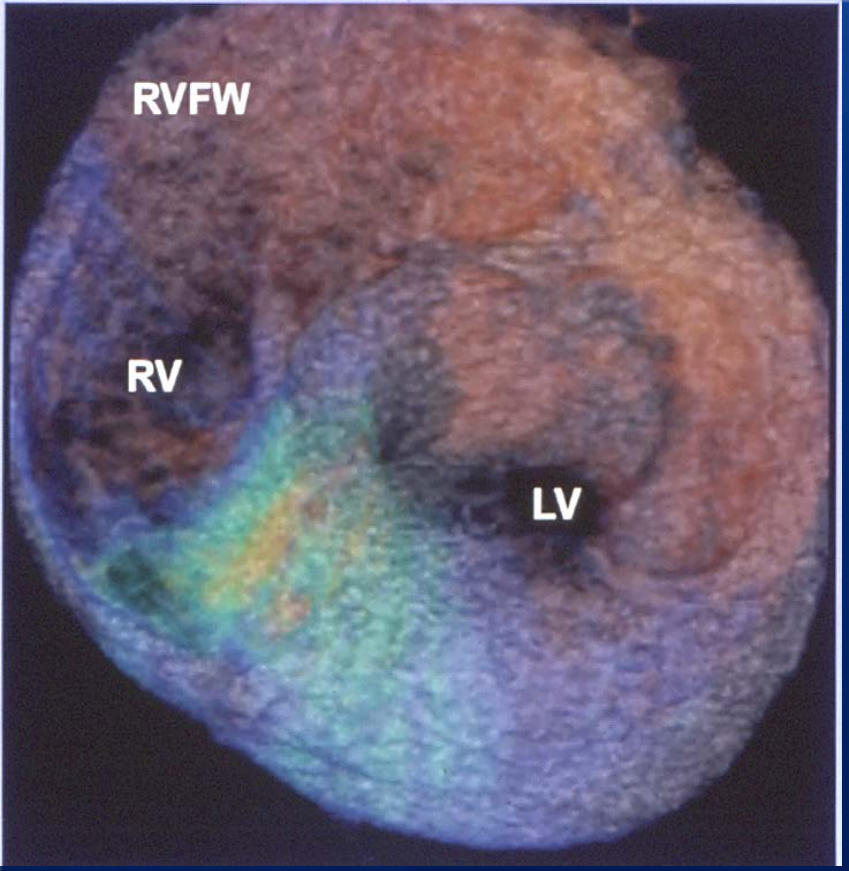


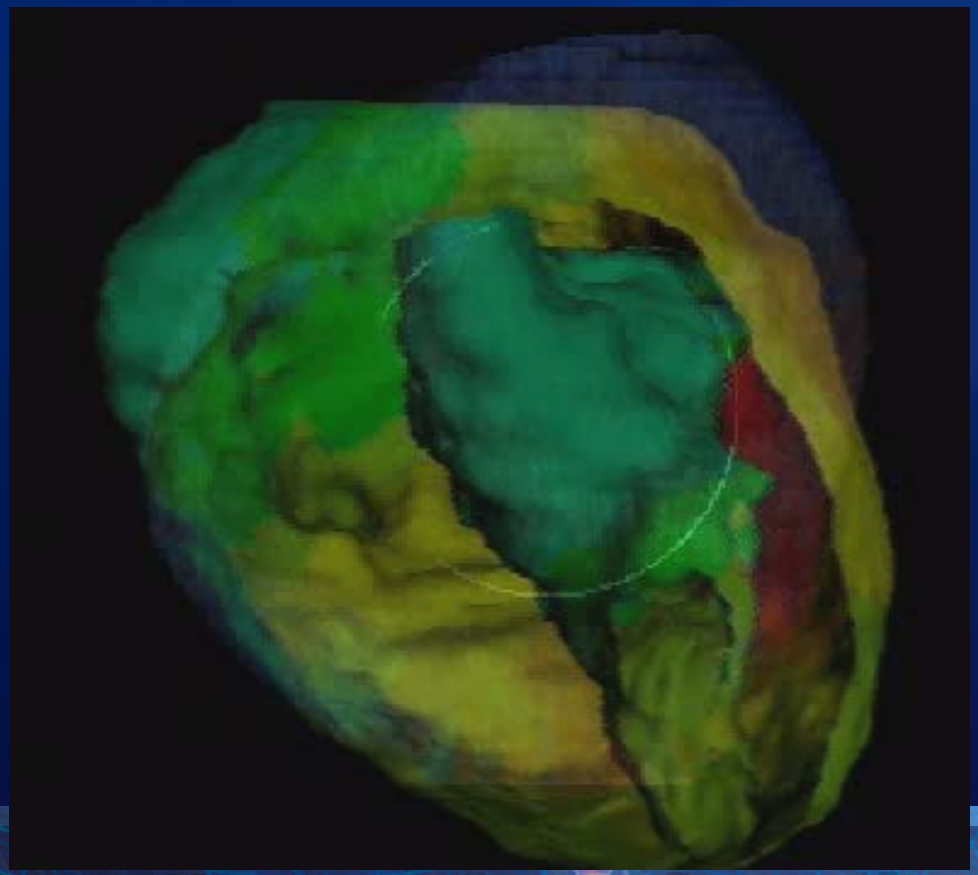
ELECTRICAL DYSSYNCHRONY



MECHANICAL DYSSYNCHRONY







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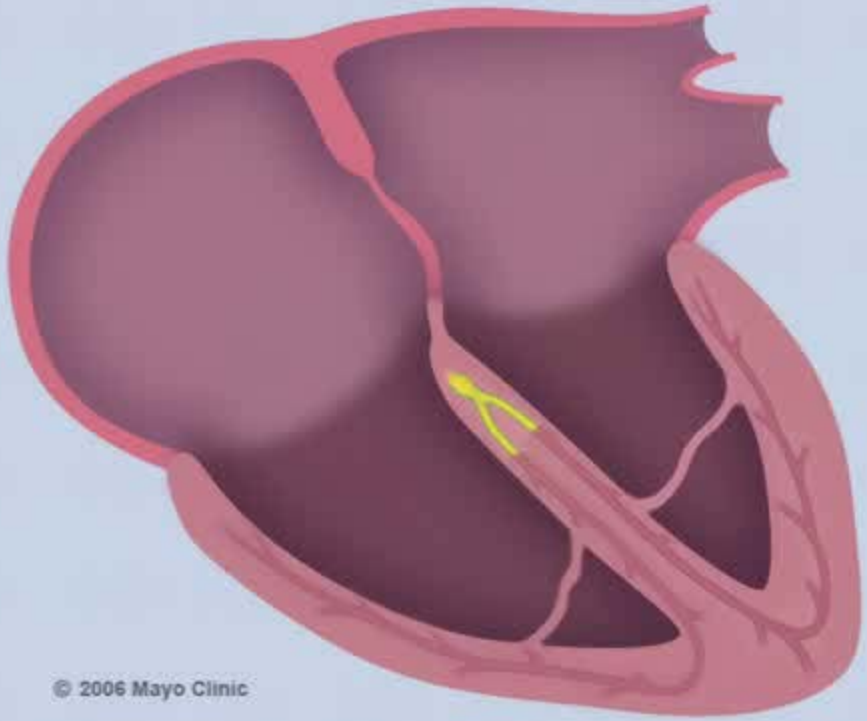
ELECTROMECHANICAL UNCOUPLING



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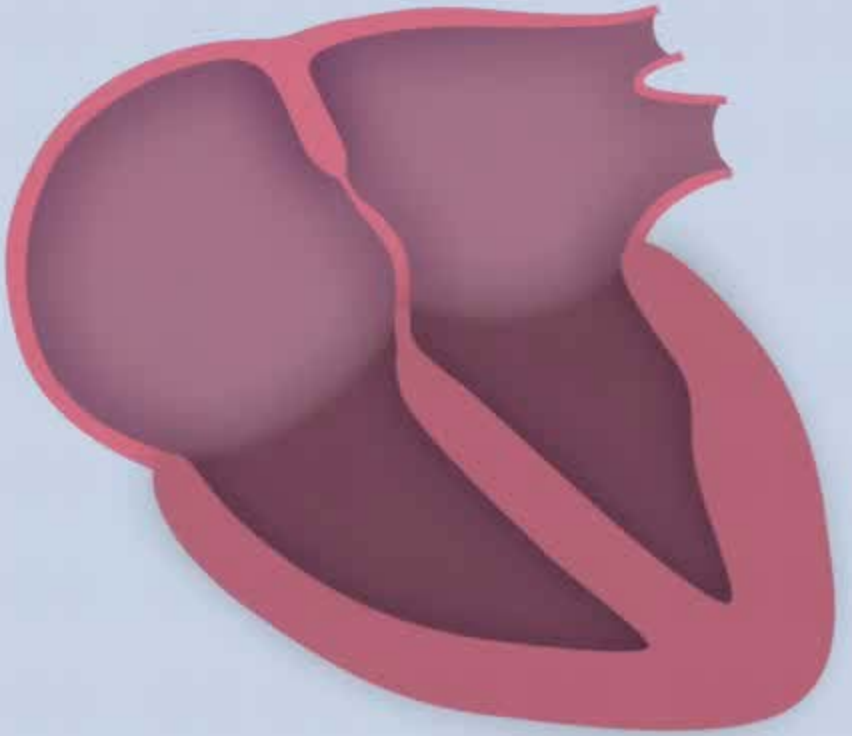
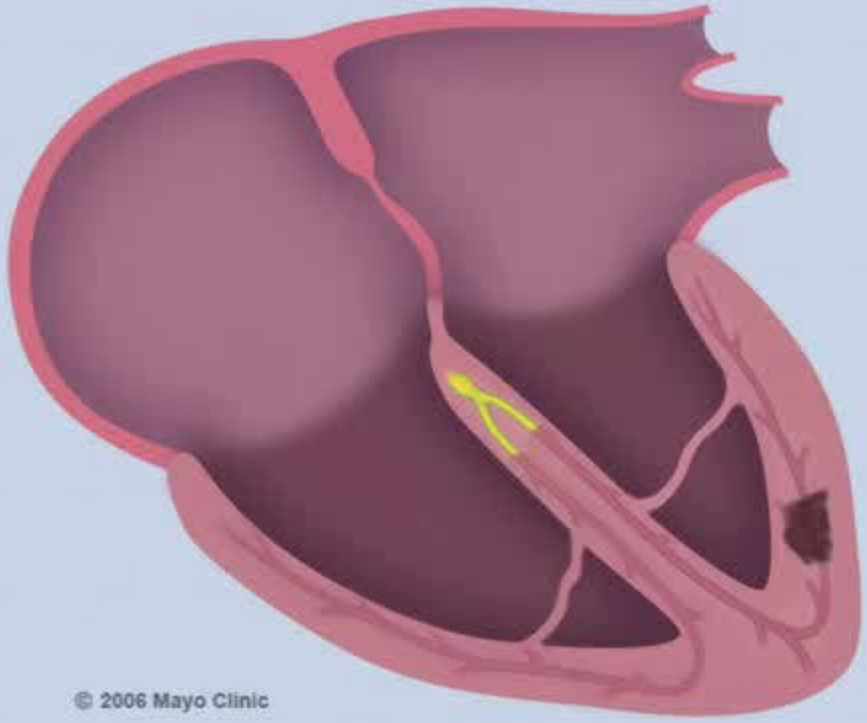


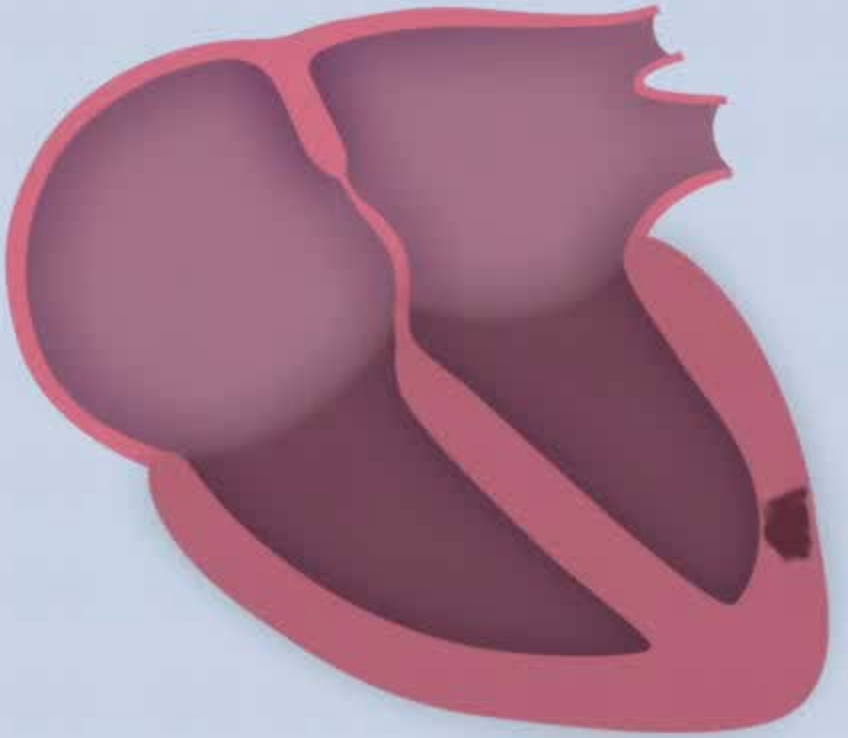
CARDIOMYOPATHY

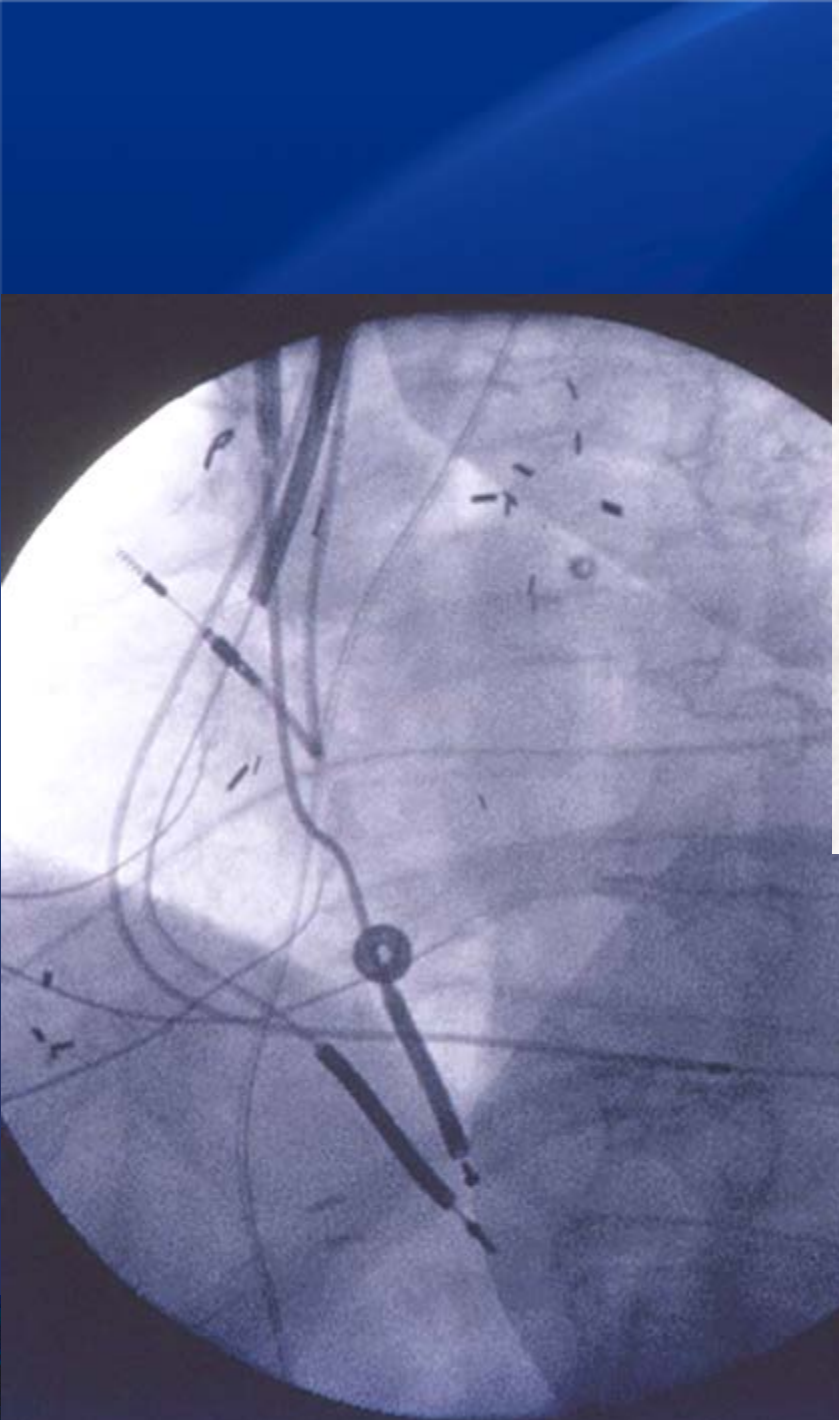
1. CARDIOELECTROPATHY
   - Propensity for arrhythmia
   1. Worsened Myopathy
2. CARDIOMYOPATHY
   - Uncoordinated contraction
   - Negative remodeling
     Electrical dysfunction
3. Thrombogenicity

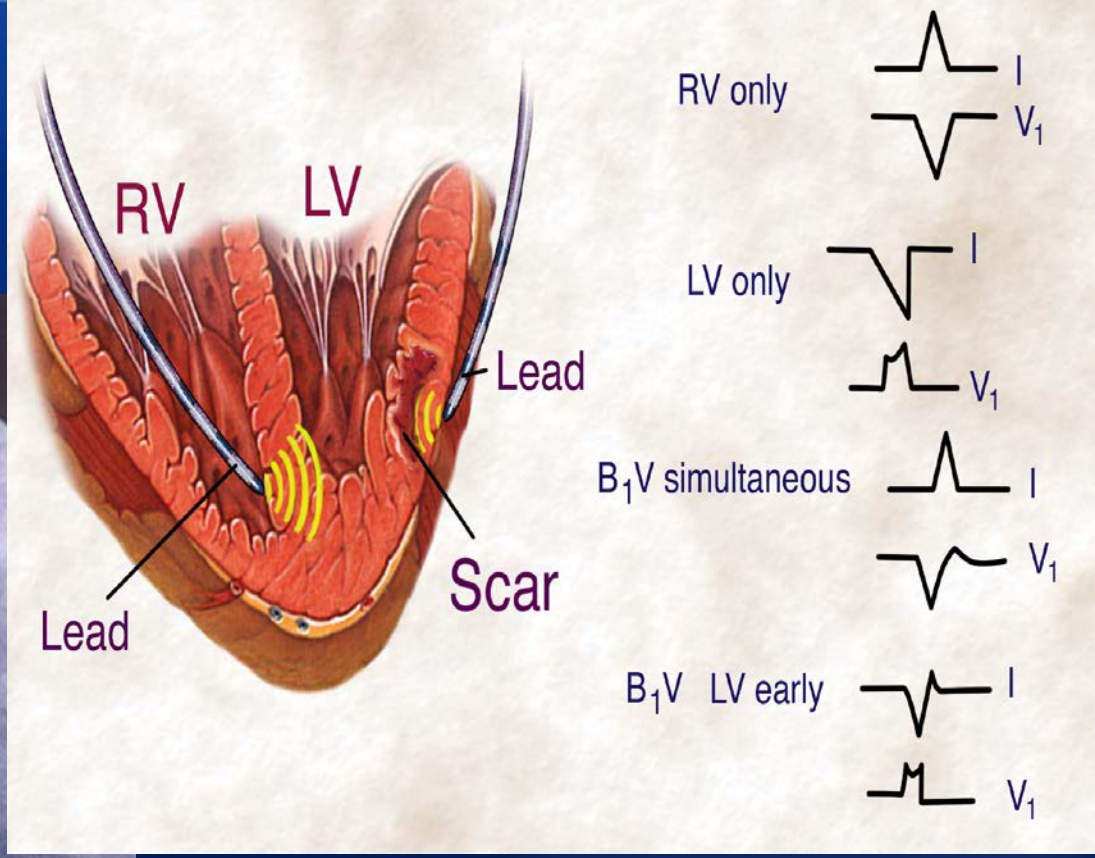
CONDUCTION DISARRAY

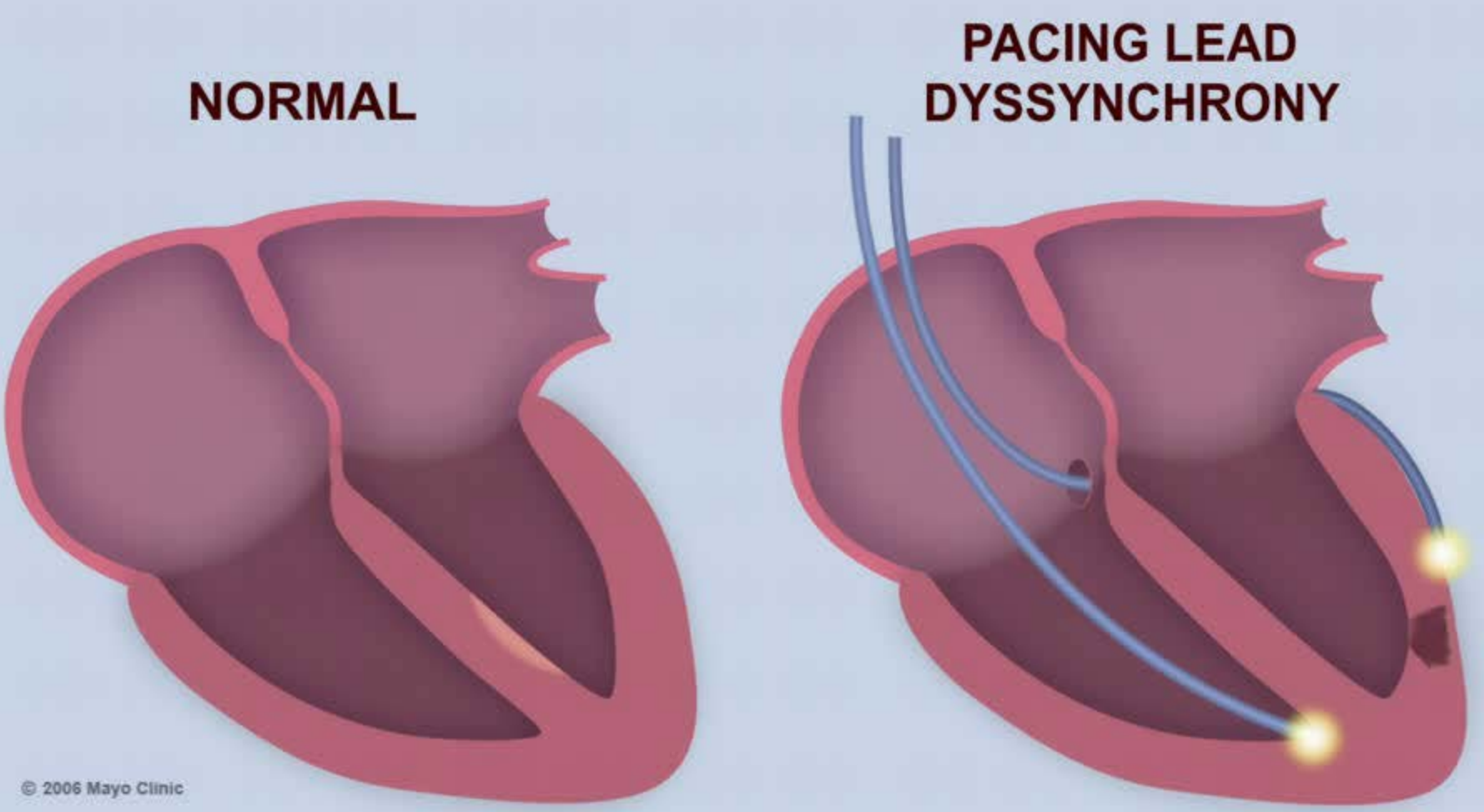
MECHANICAL DYSSYNCHRONY

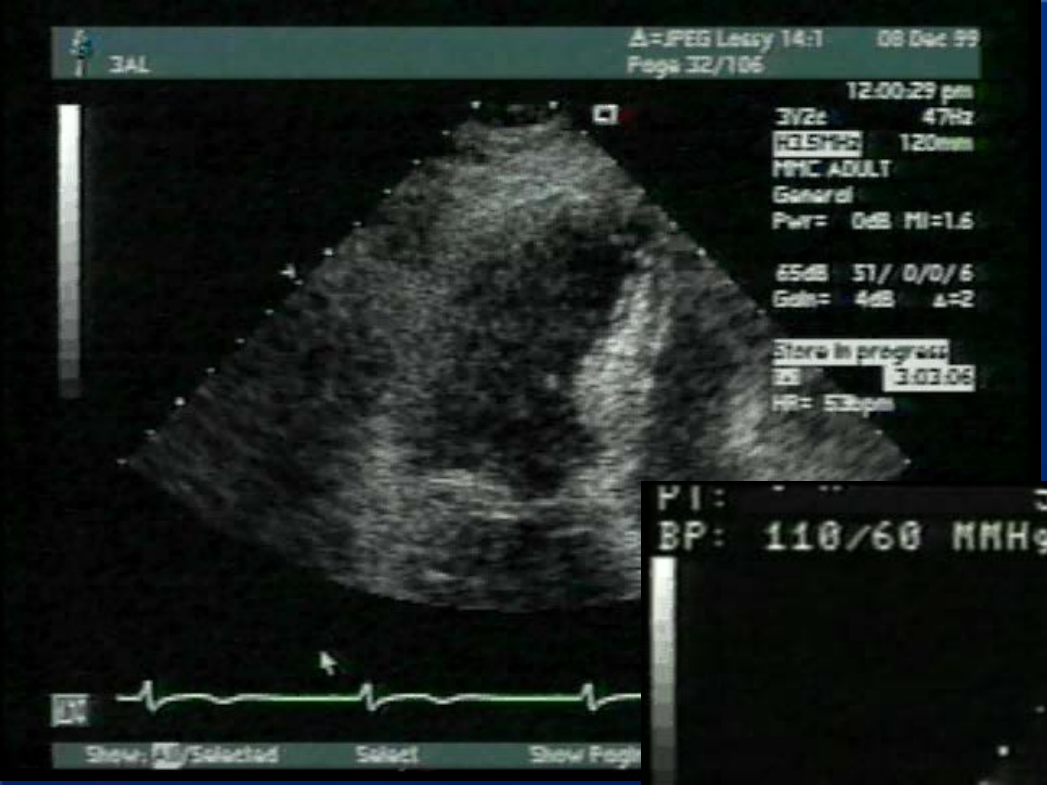








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Show Page


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MAYO /V
PWR = 0dB
44dB B/A/D
GAIN= 19dB
HR= 70bpm
56Hz
28Hz
NORMAL
SLOW

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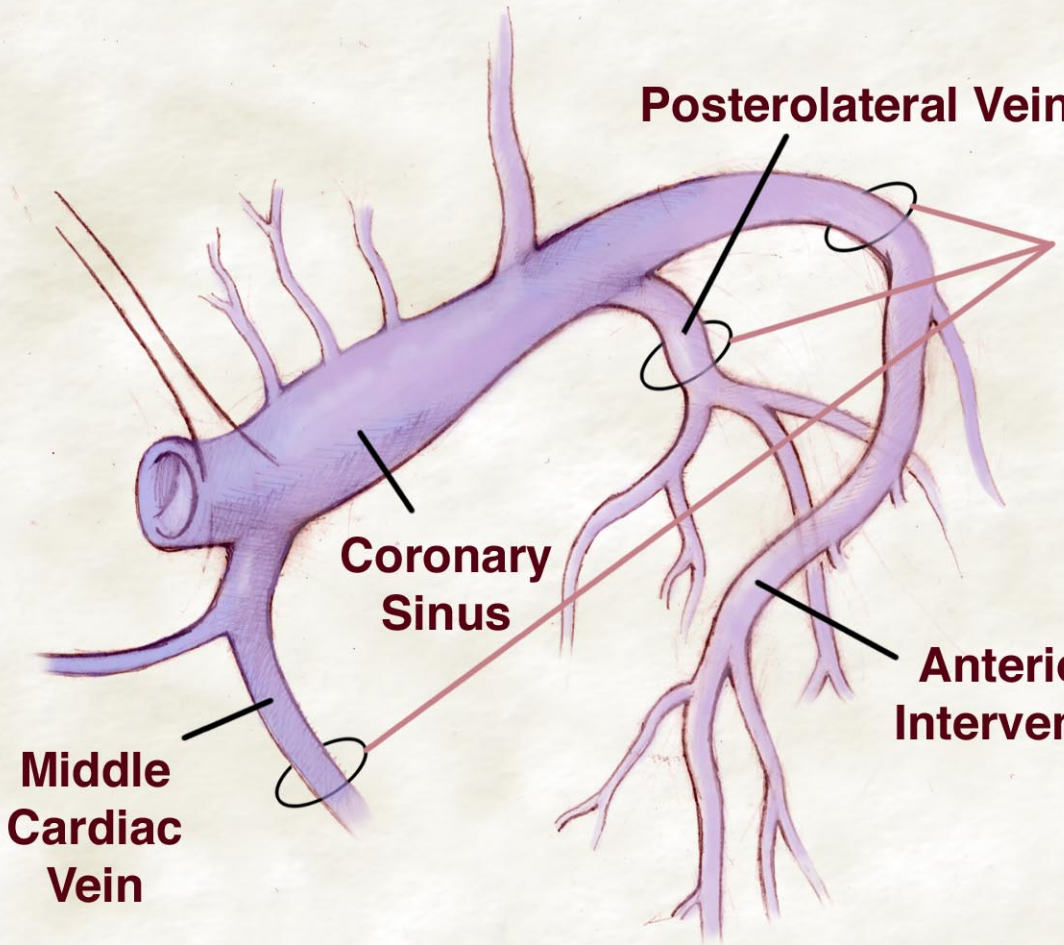
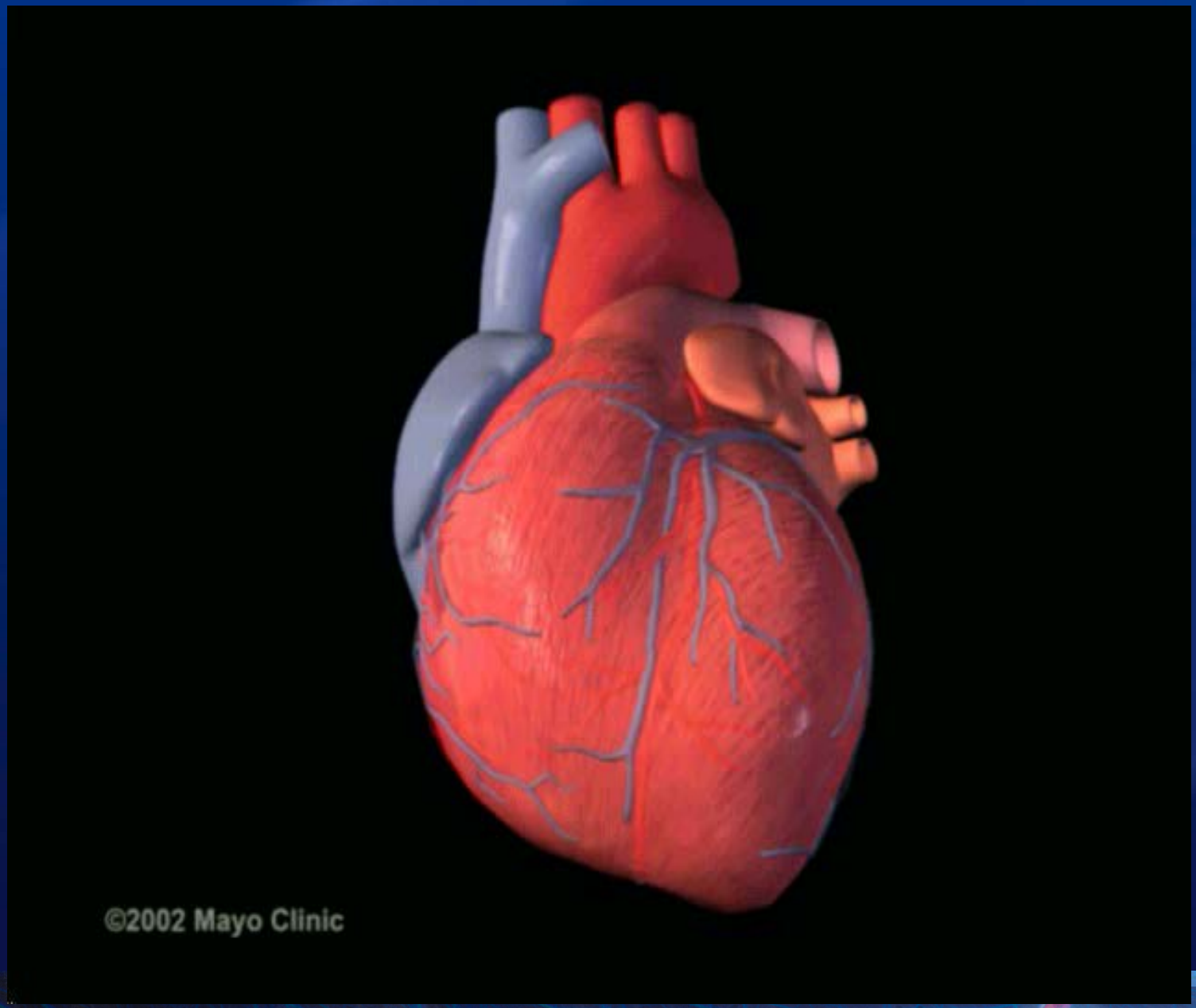
Implant Techniques
What Do You Need?

- Proficiency with standard pacemaker/ICD implant
- Experience finding and negotiating the coronary sinus
- Knowledge of coronary venous anatomy
- Understanding the tools available
- Patience

Ventricular Venous Anatomy





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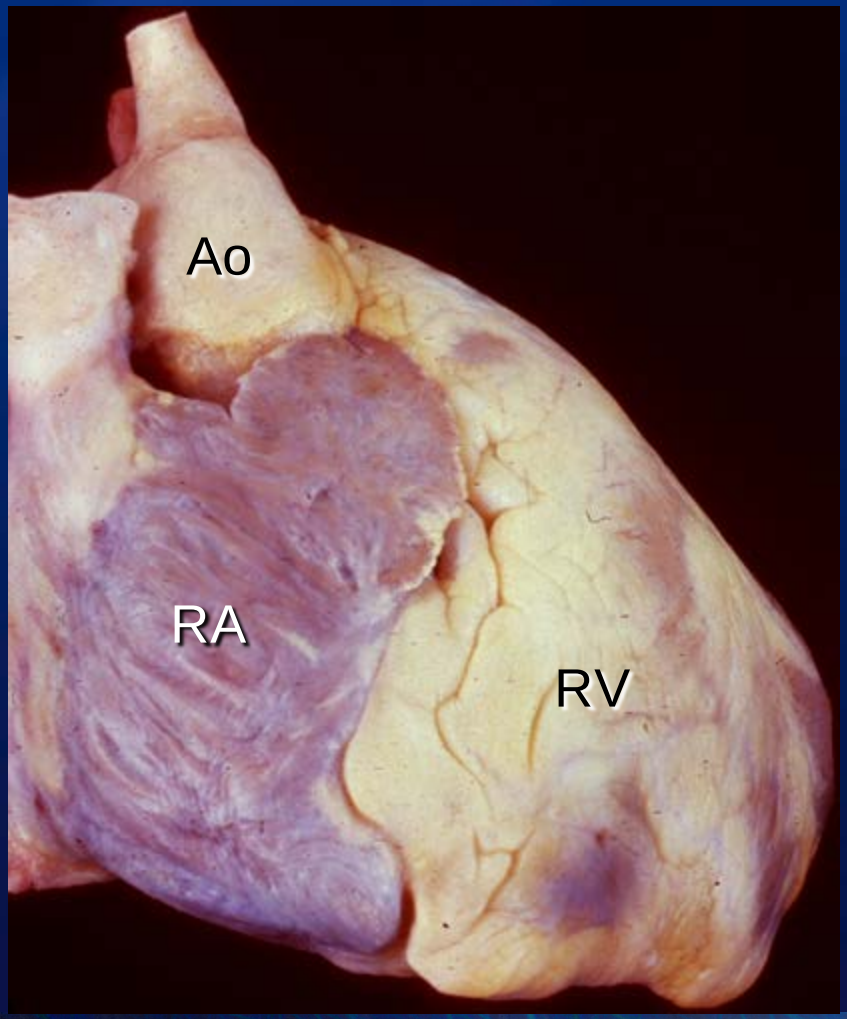
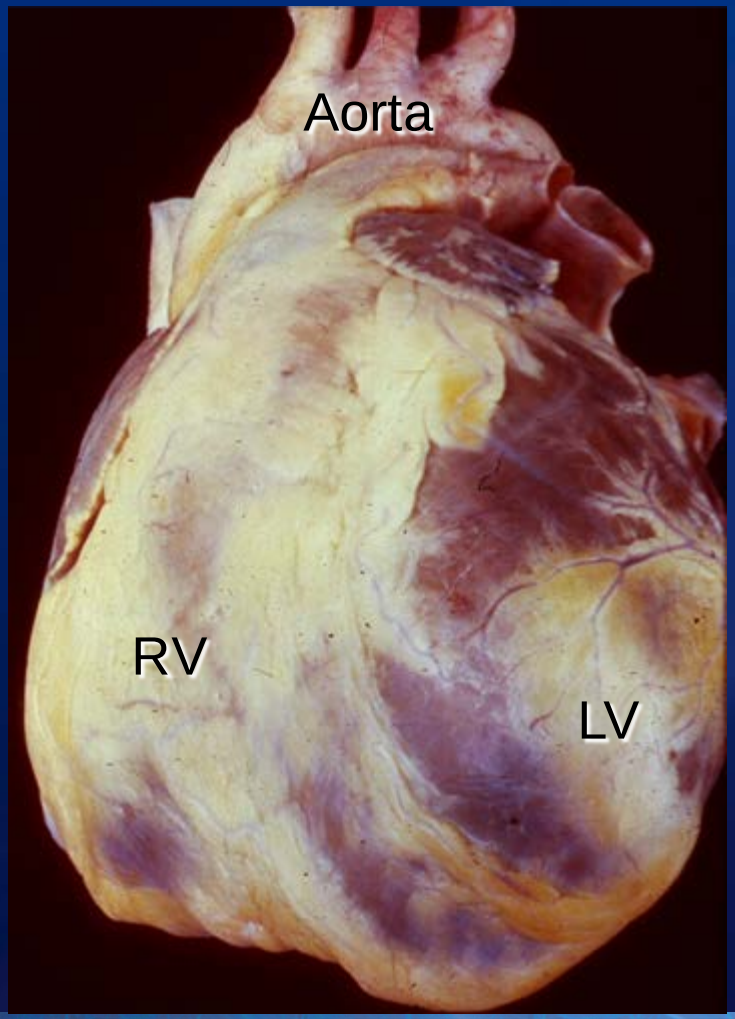
OVERCOMING DIFFICULTIES

- CANNULATING THE CS
- ADVANCING IN THE CS
- GETTING TO THE LATERAL WALL
- AVOIDING MISTAKES
  - COMPLICATIONS
  - EKG
  - FLUOROSCOPIC
  - ECHOCARDIOGRAPHIC

Normal Heart
External Topography





R Ant Oblique

L Ant Oblique

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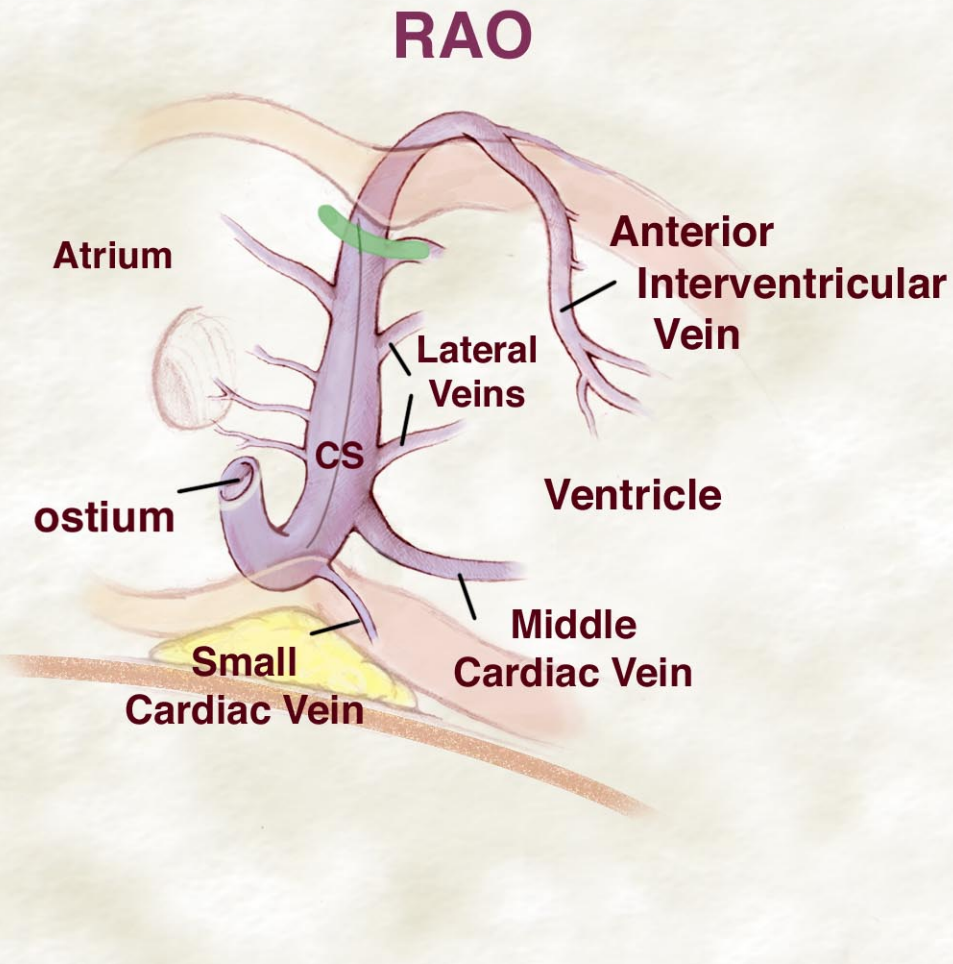
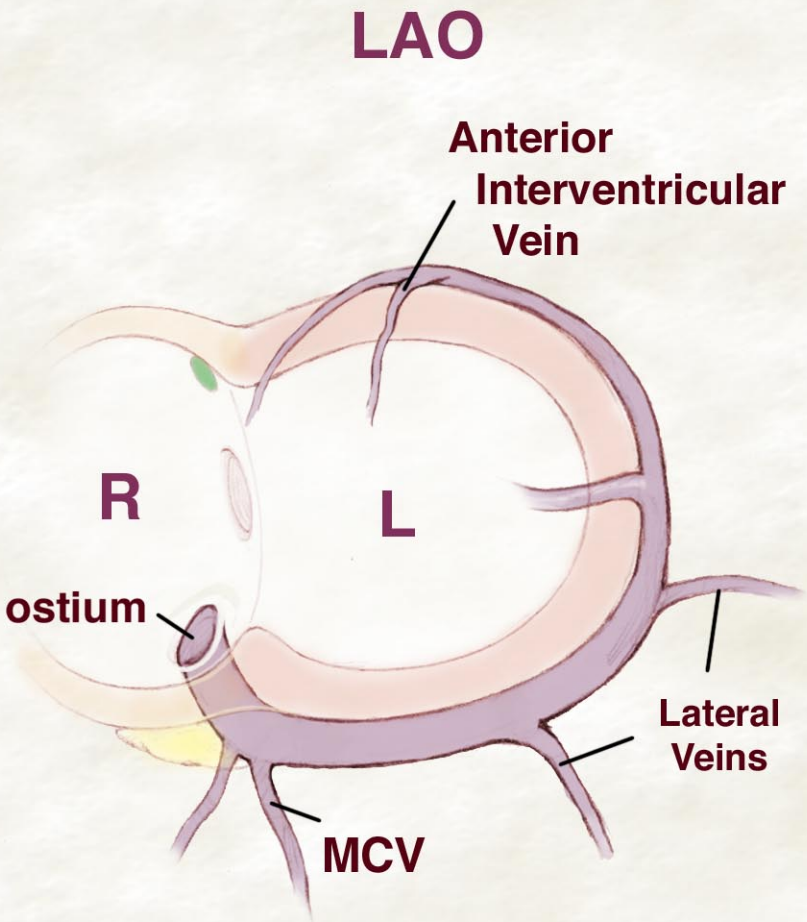
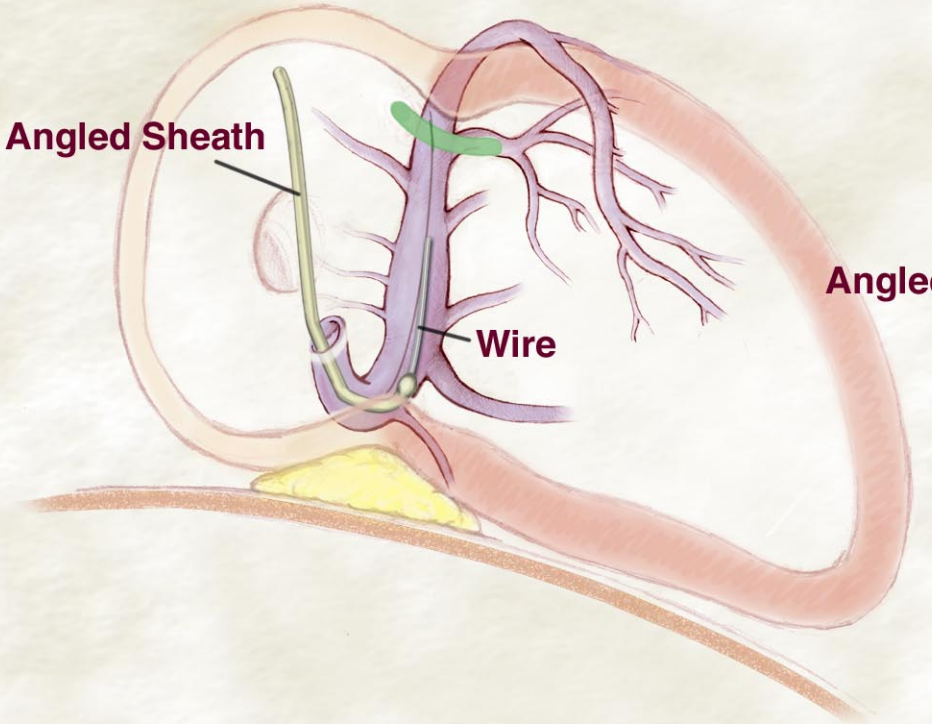
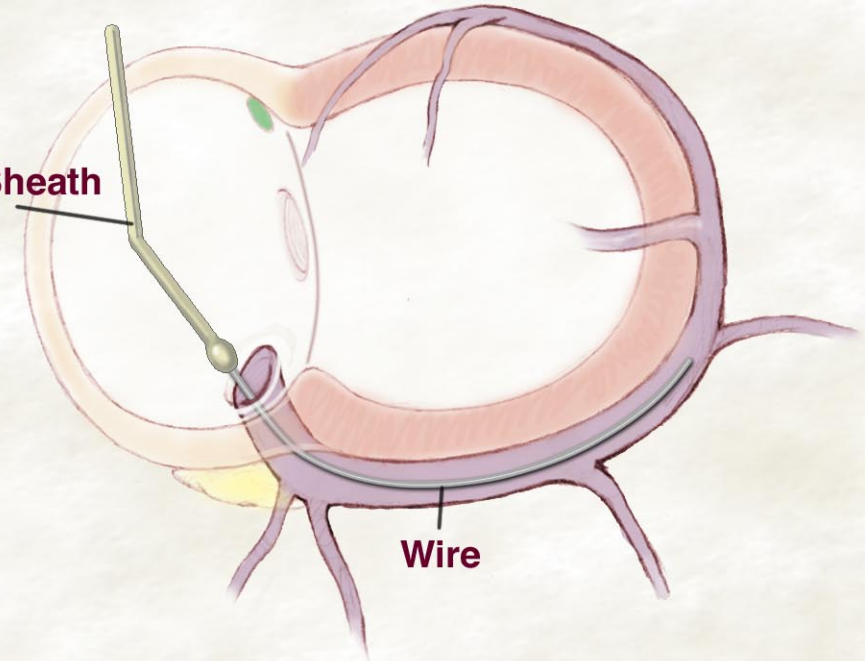
Coronary Sinus and Ventricular Veins

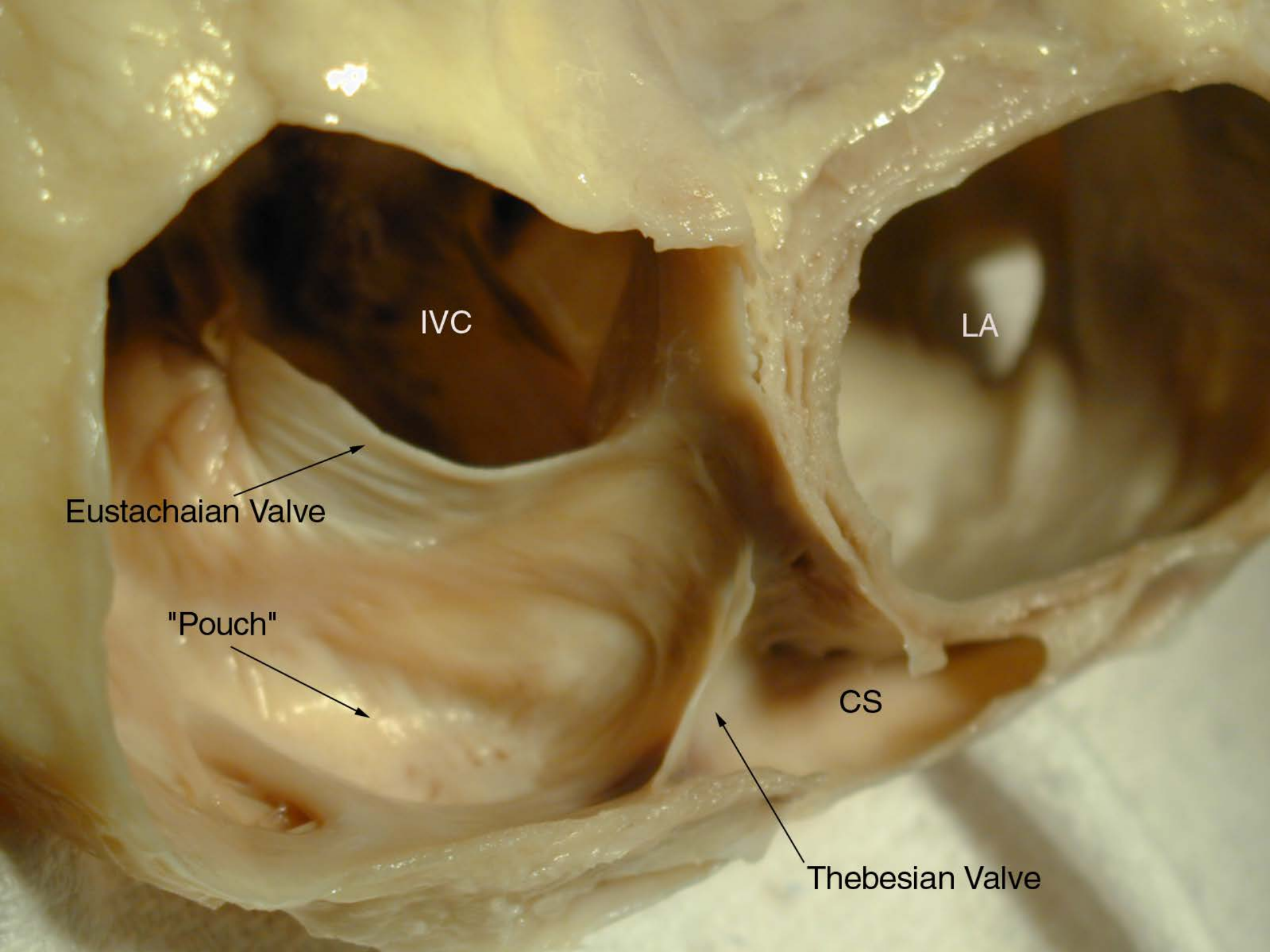


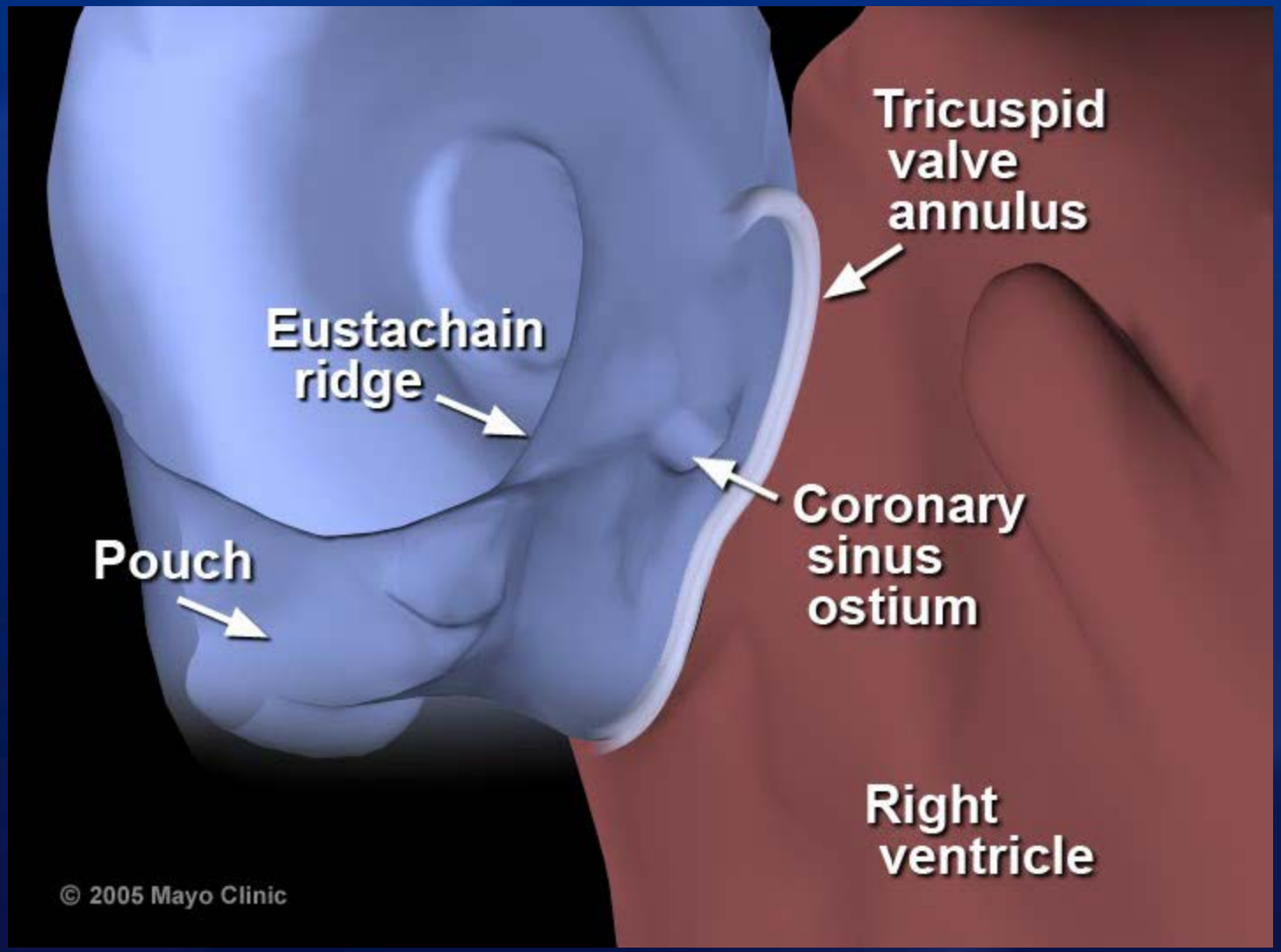


Cannulating the Coronary Sinus with a Guide Wire





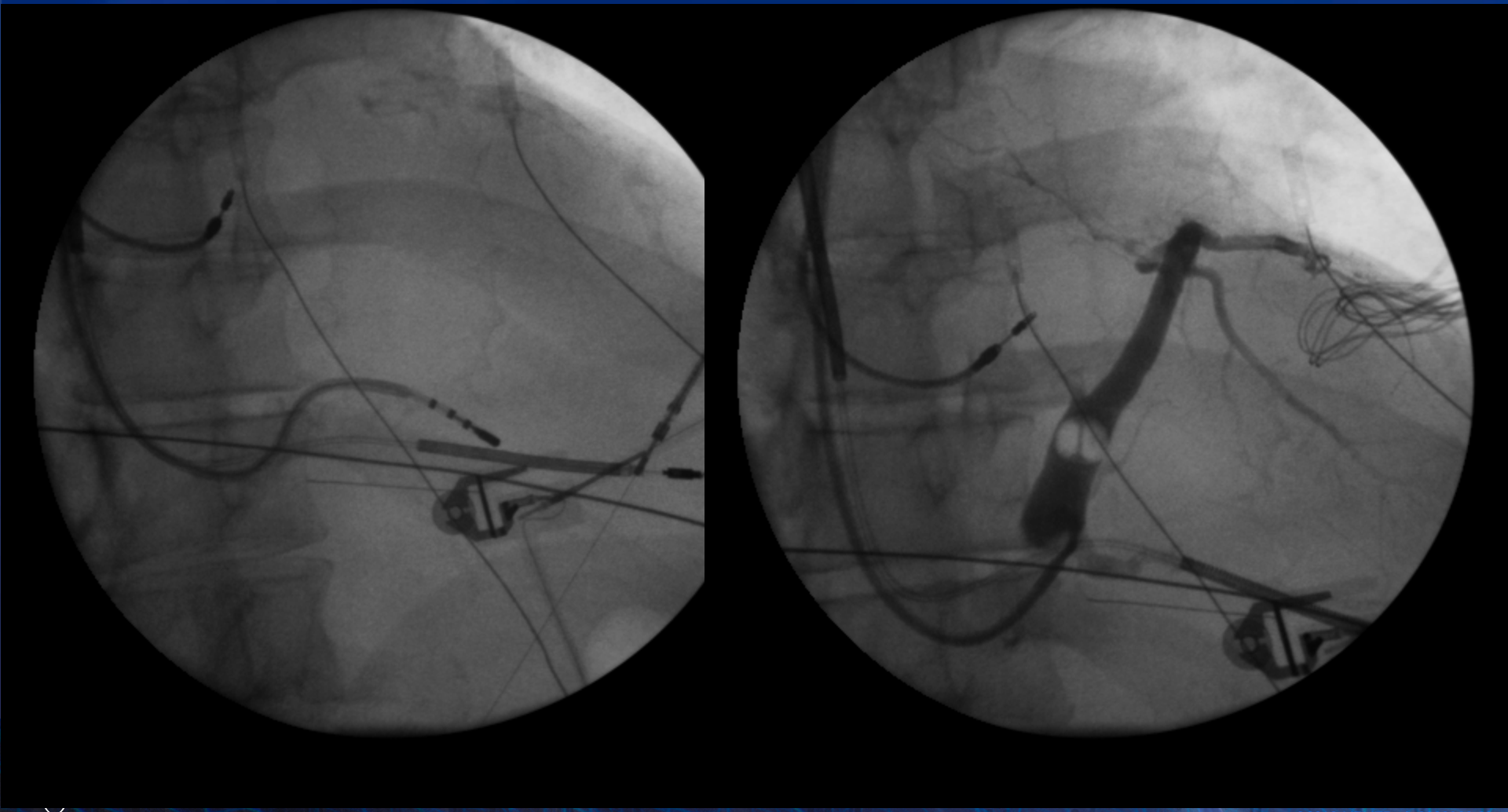

IVC
LA
Eustachaian Valve
"Pouch"
CS
Thebesian Valve

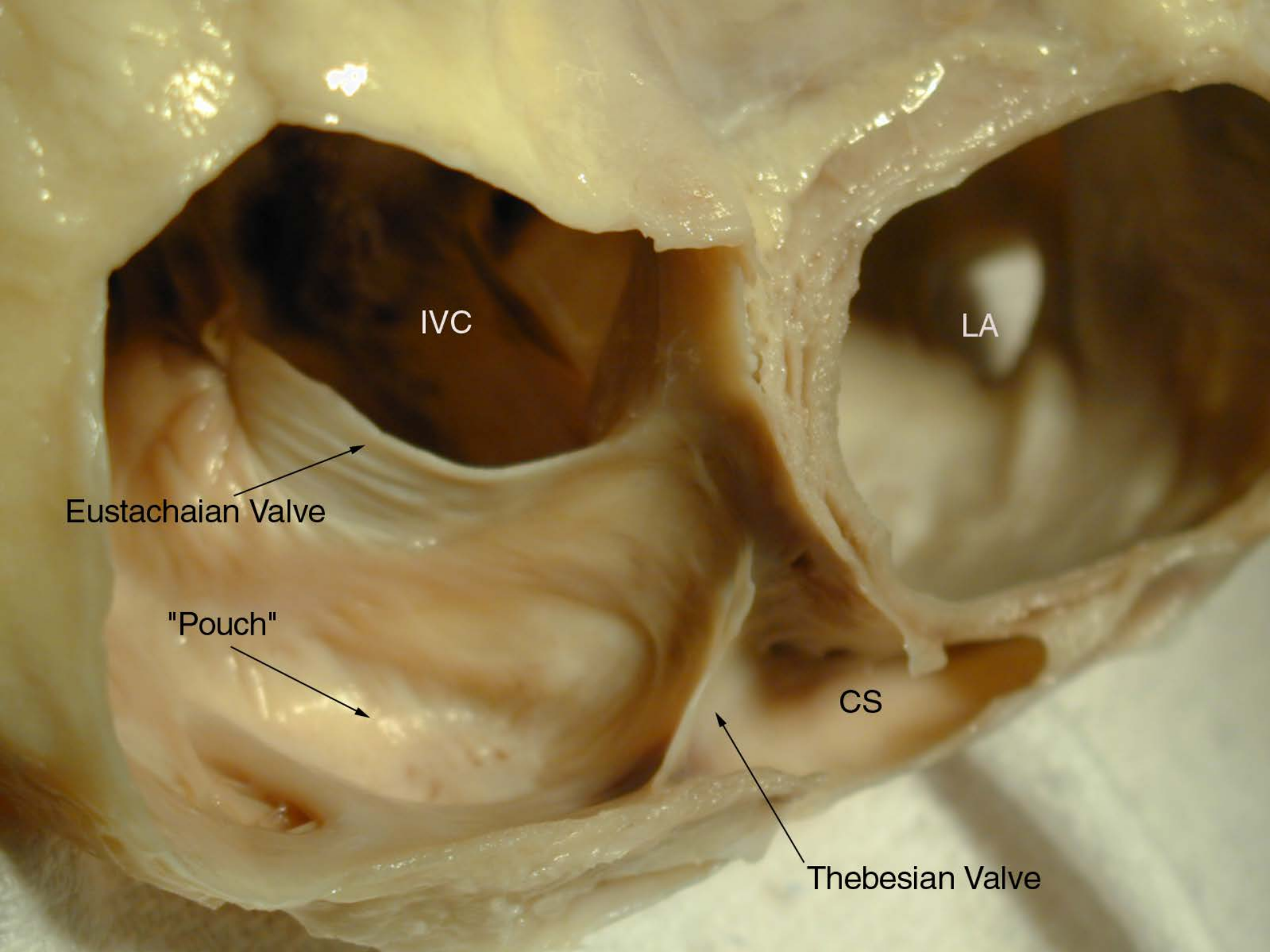


INABILITY TO ADVANCE IN CS

- STENOSIS
- VALVES
- SUBSELECTION
- DISSECTION
- TORTUOSITY

Subselection with catheter




IVC
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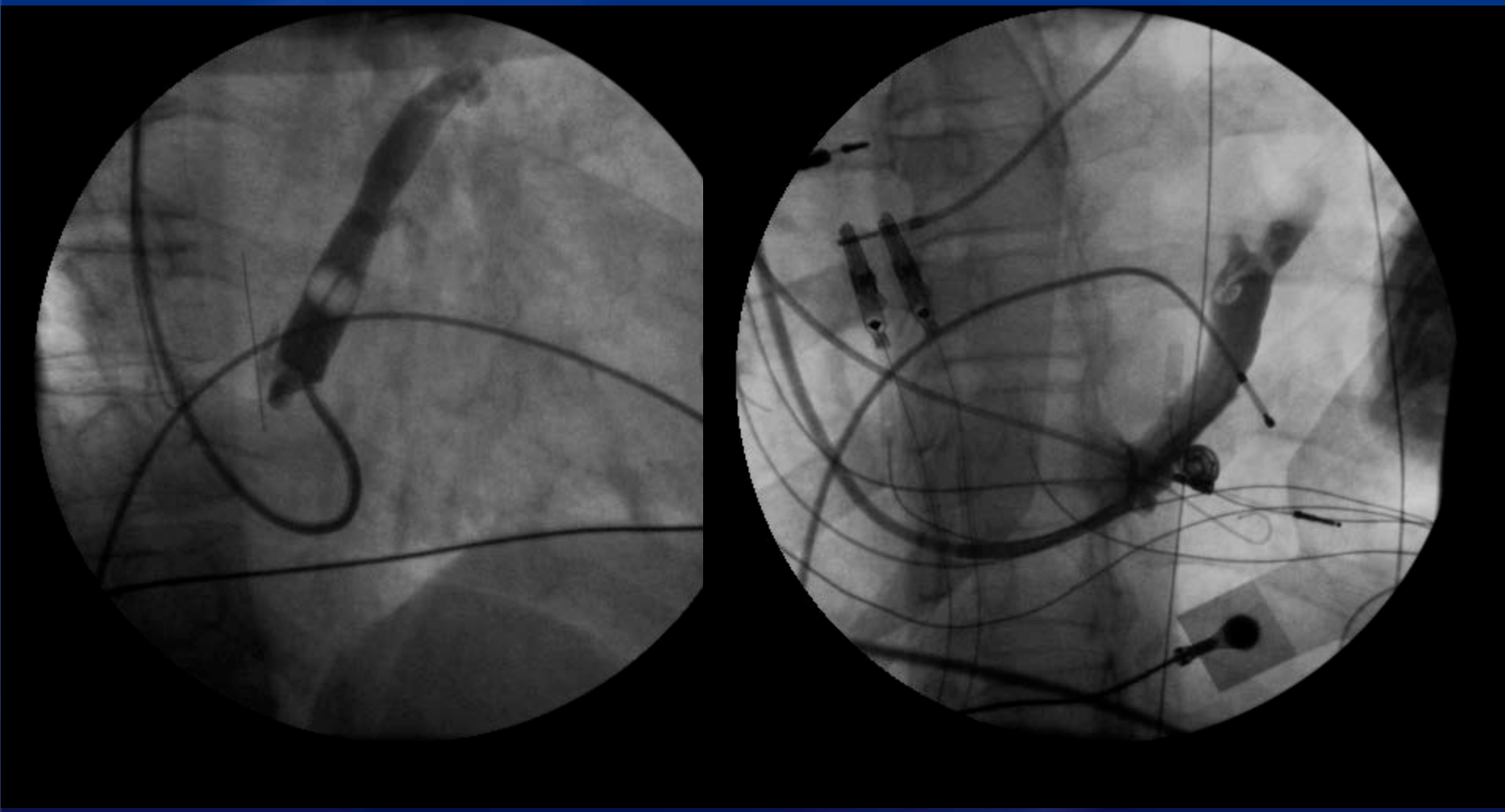
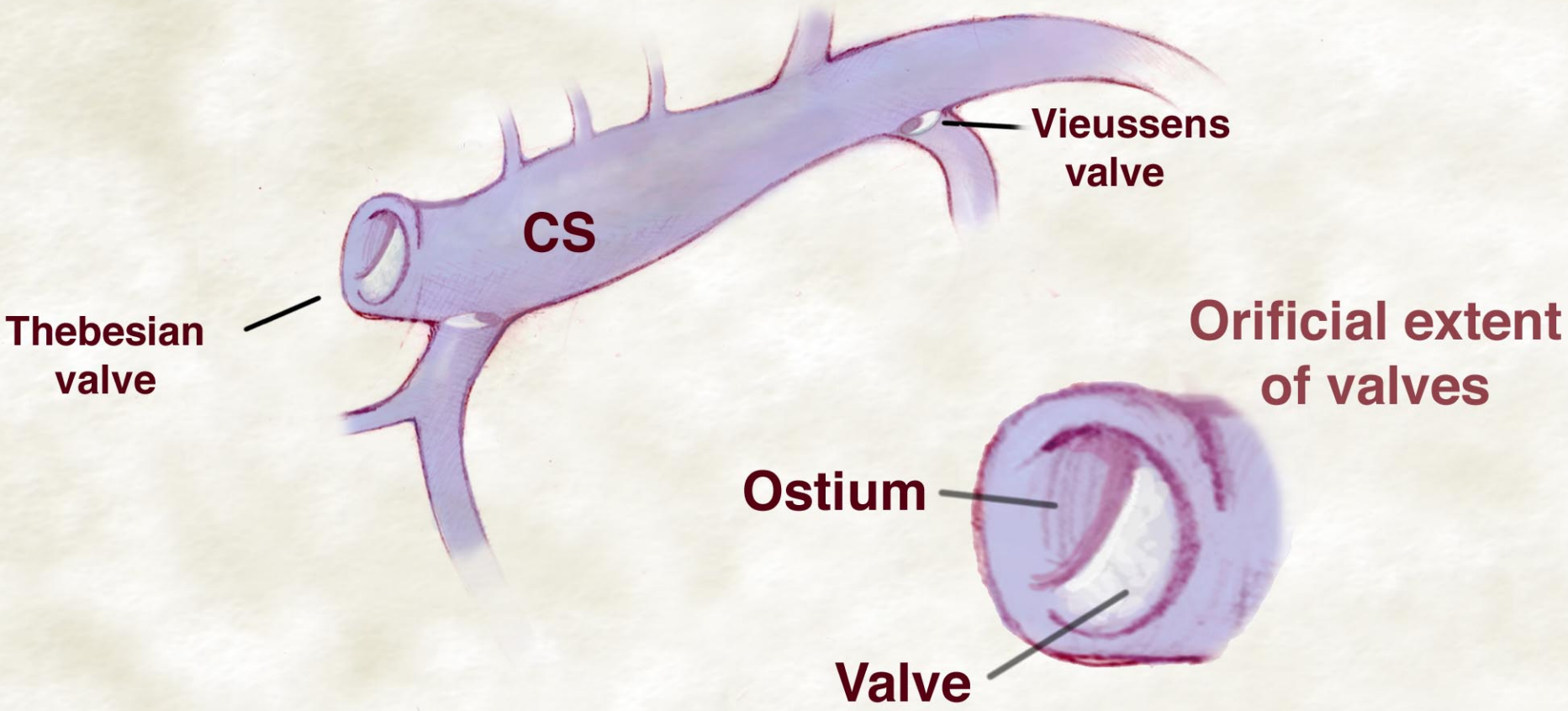
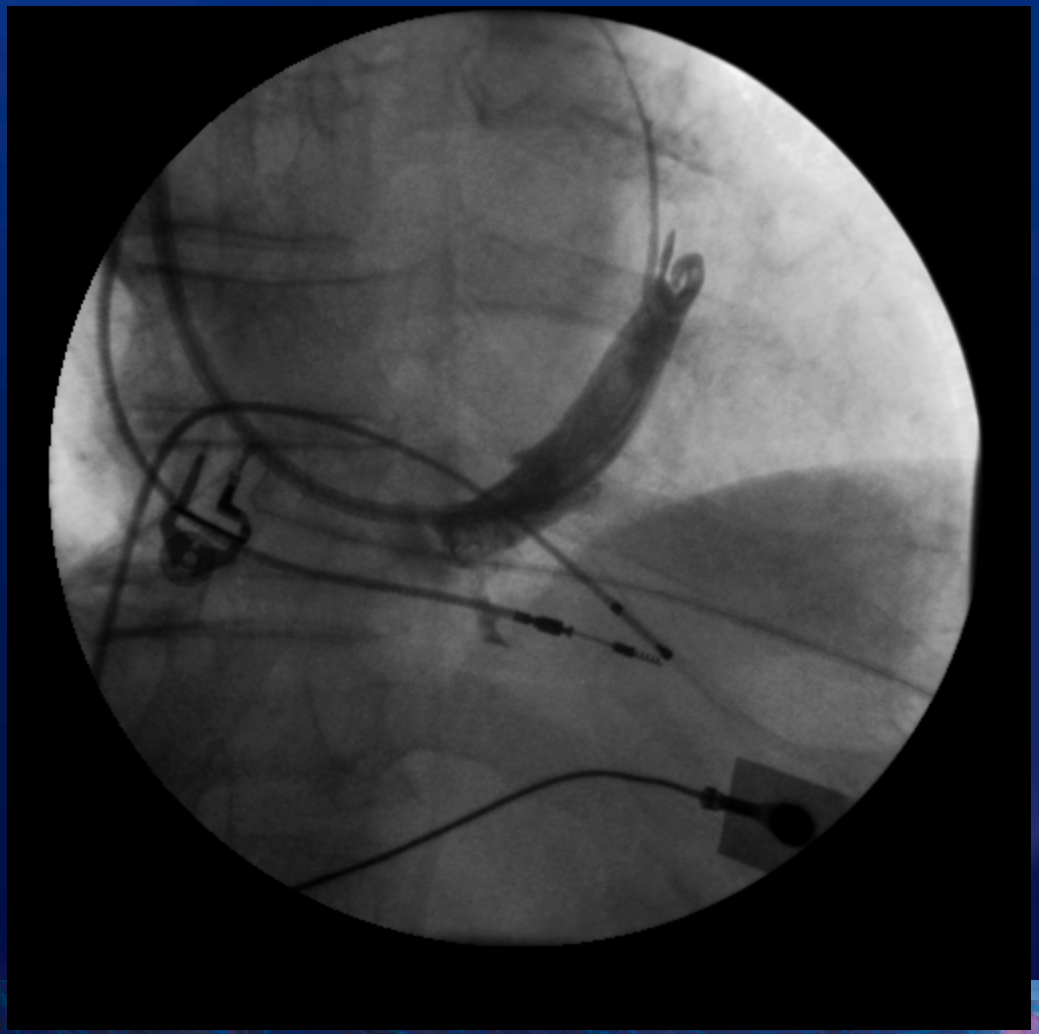


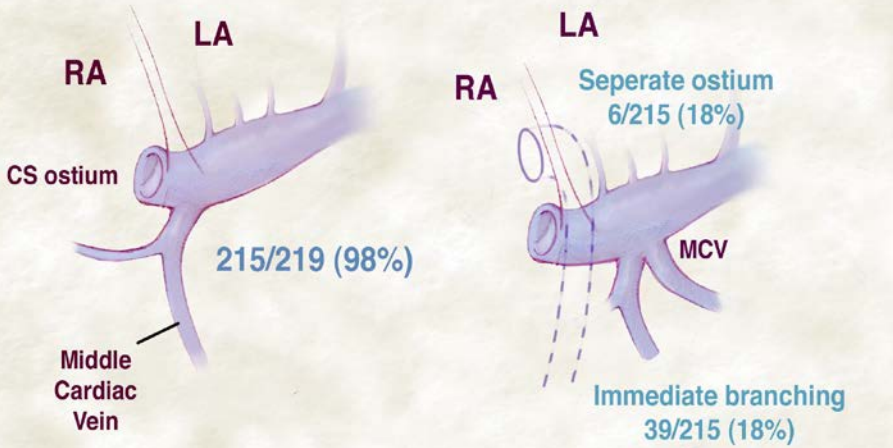
Valves in Ventricular Veins

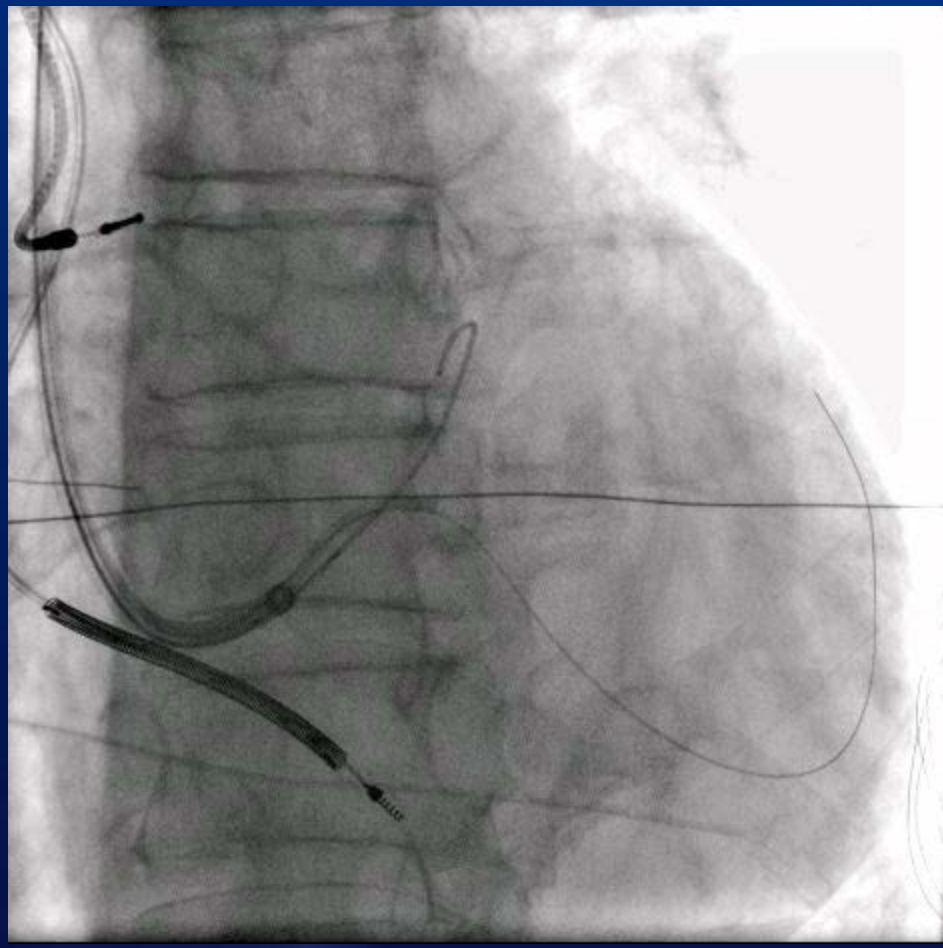


Near occlusive valve

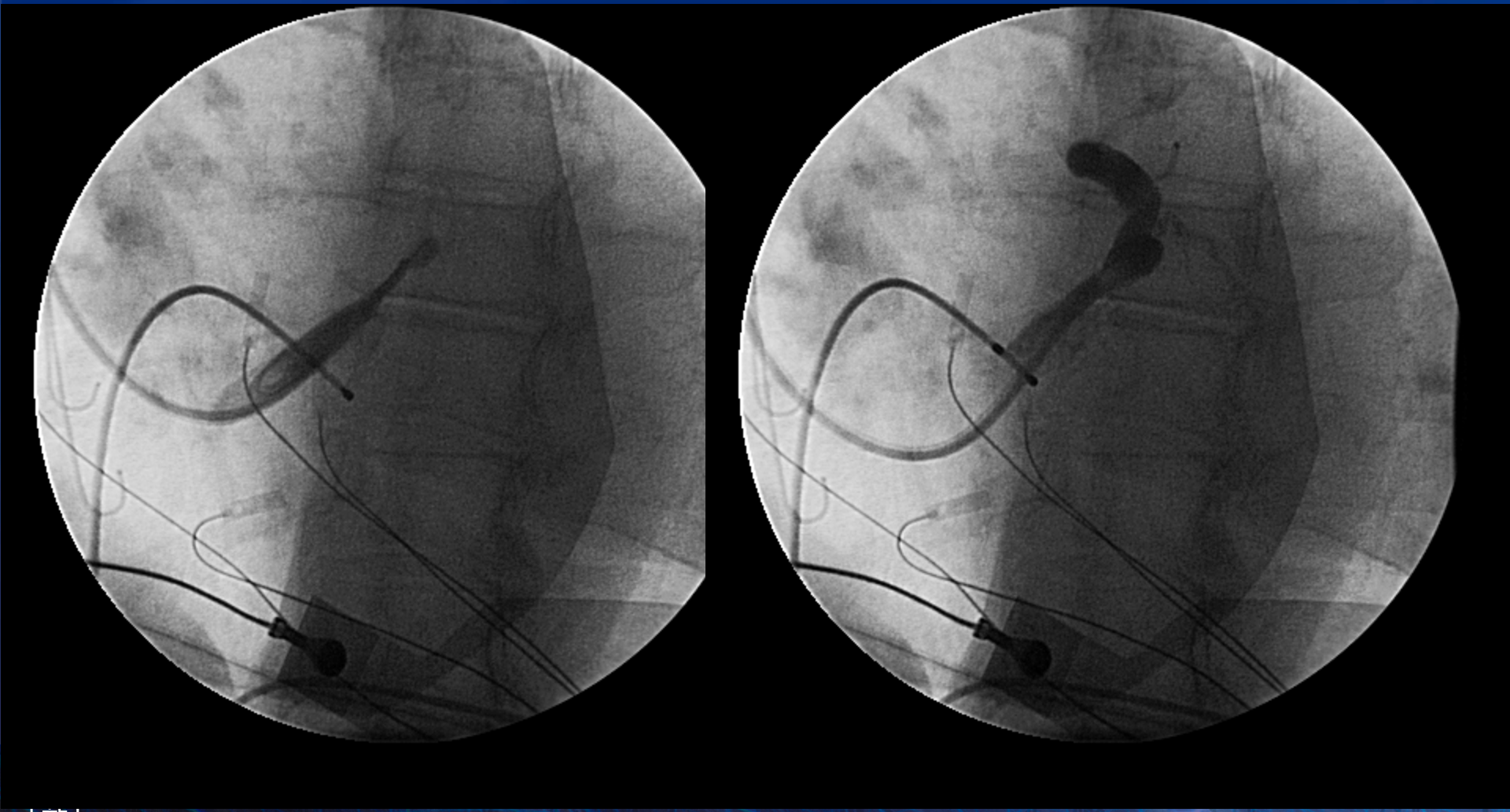


The Middle Cardiac Vein





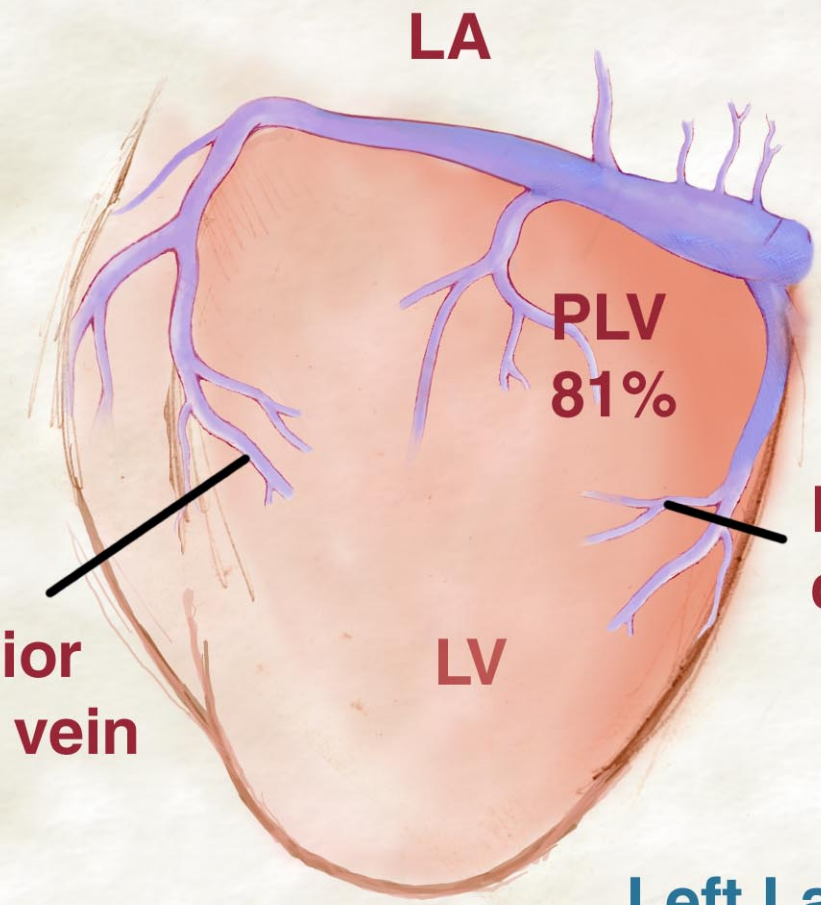
CS Stenosis



INABILITY TO GET TO THE LATERAL WALL

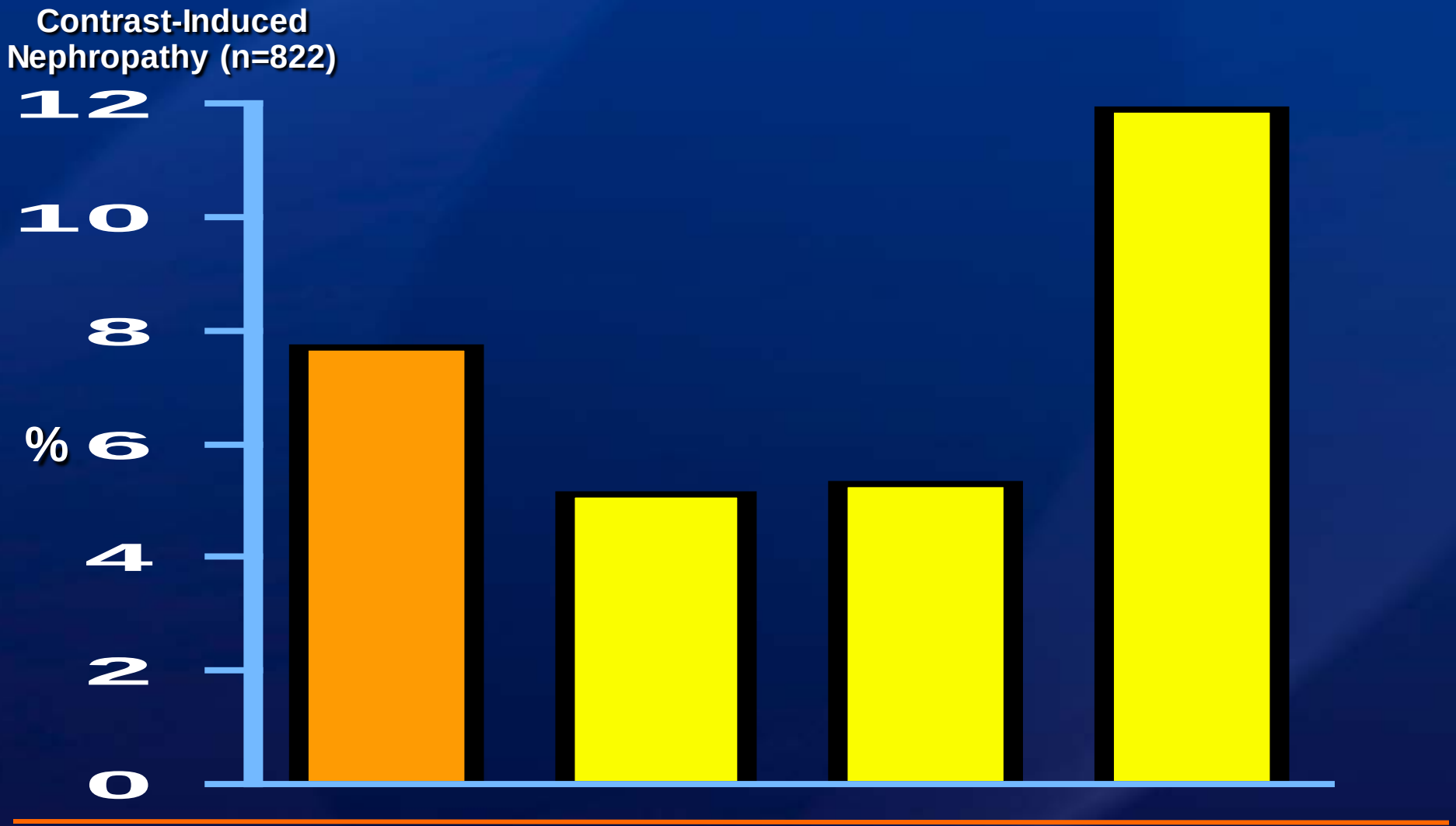
- Middle Cardiac Vein
- Anterior Interventricular Vein
- Venoplasty
- Utilizing Collaterals
- Using Thebesian Vessels

Venous Drainage of the Lateral Left Ventricle

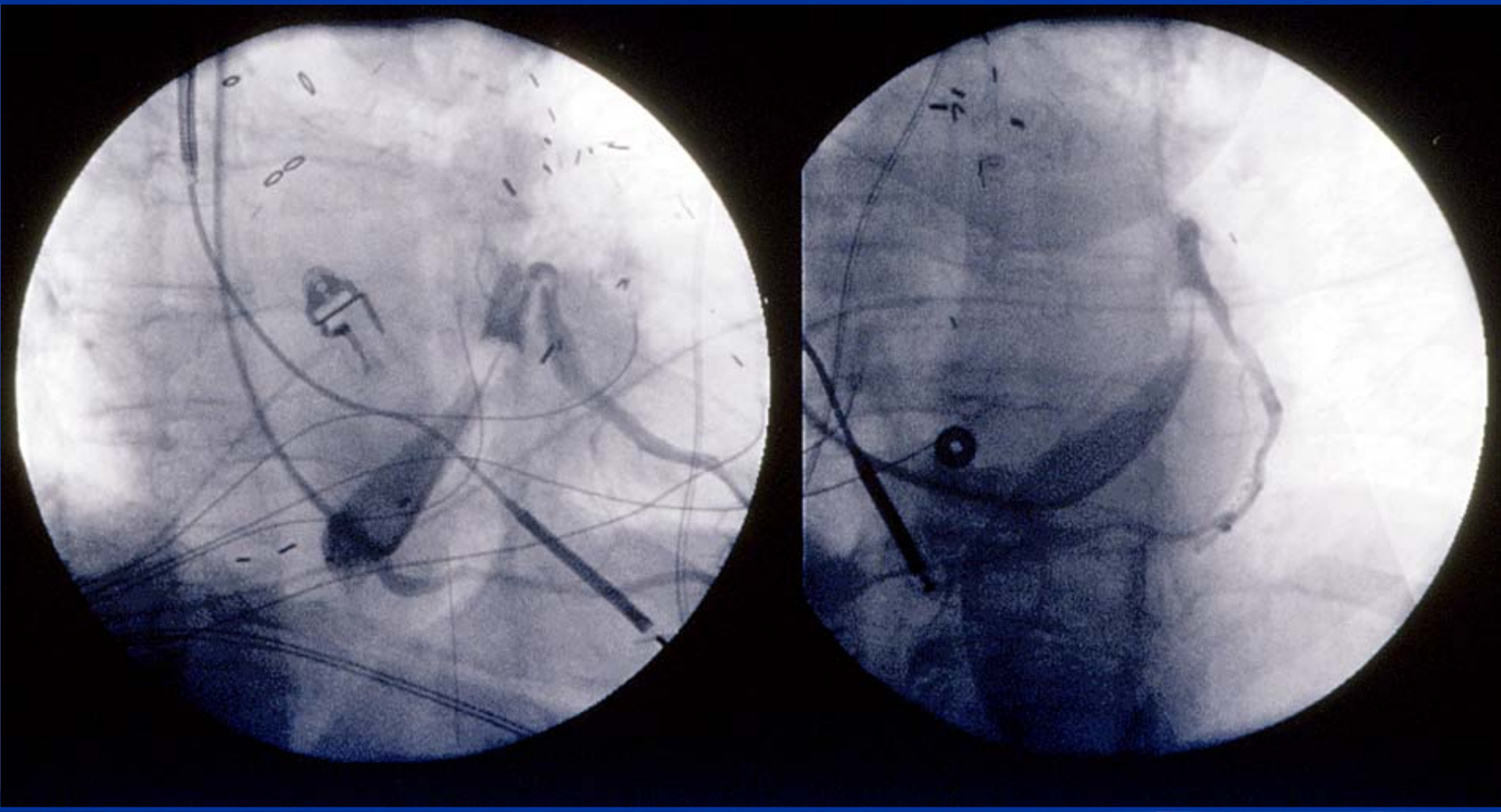


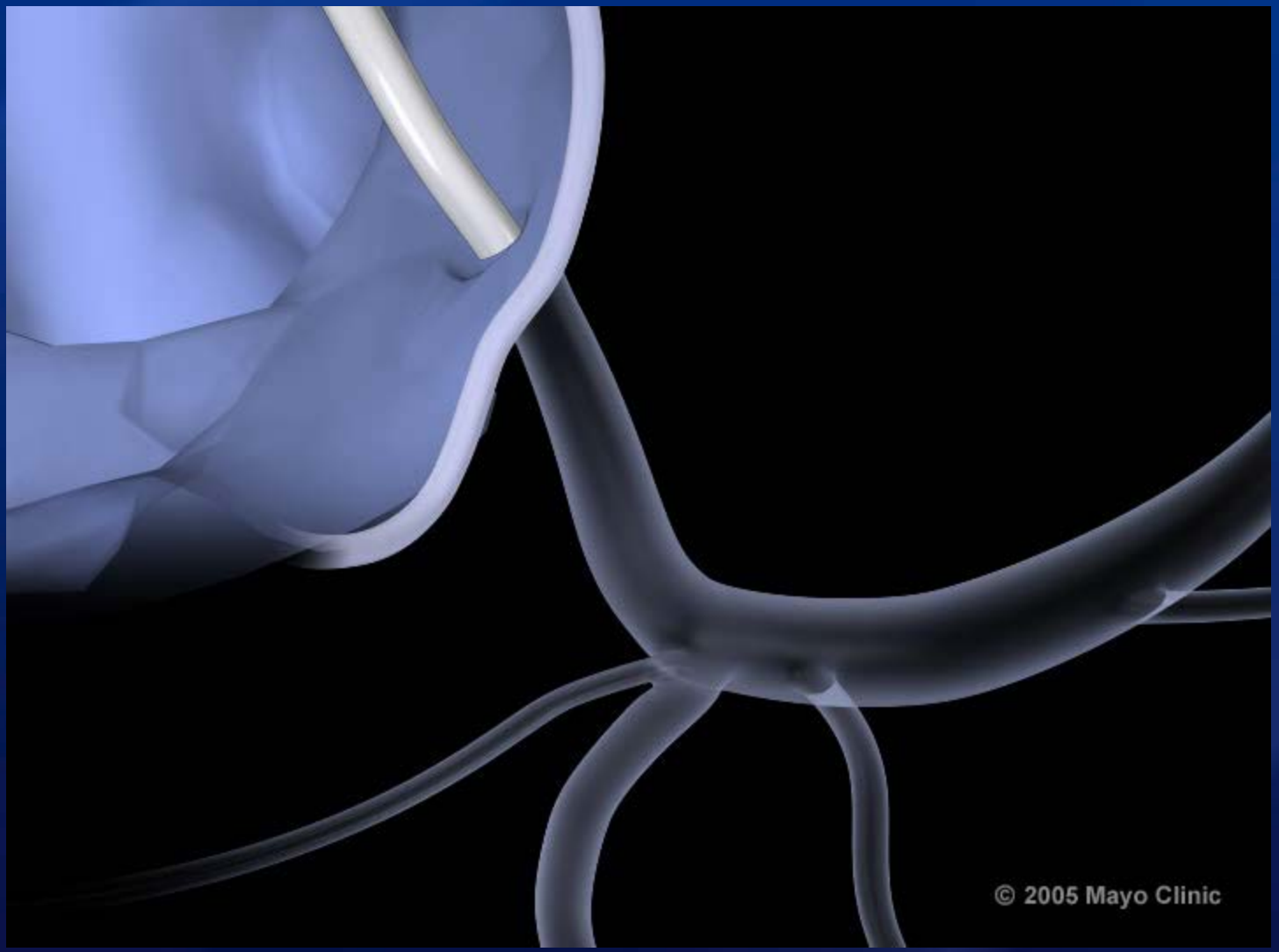
Left Lateral View

The Hazard of Contrast



Posterolateral and Middle Cardiac Veins





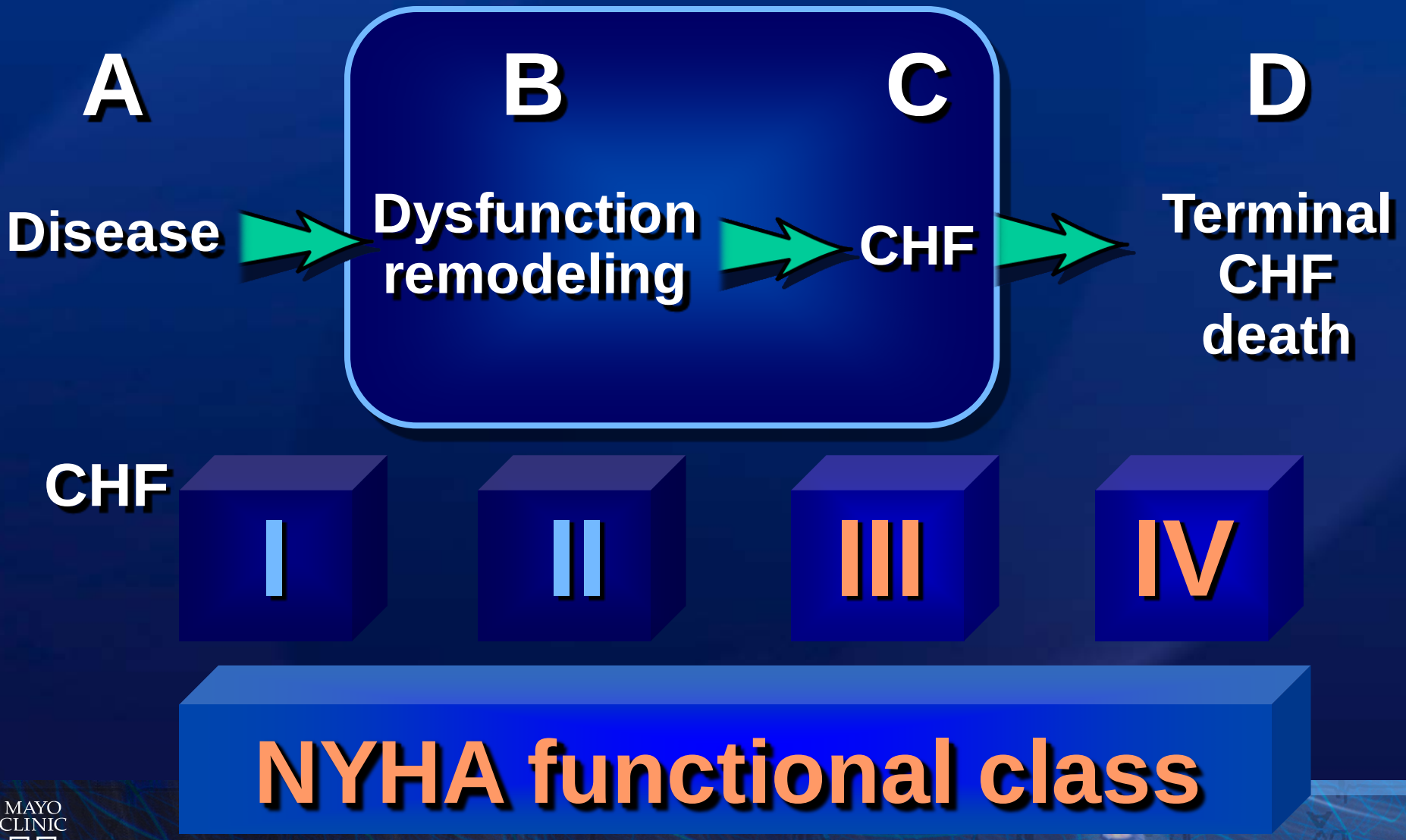
INABILITY TO GET TO THE LATERAL WALL

- Remember it is Where You Wind Up That Matters and Not How You Get There
- Utilize Collaterals and Thebesian Veins to Guide Your Procedure
- When Performing Venoplasty Use as Low an Inflation Pressure as Possible

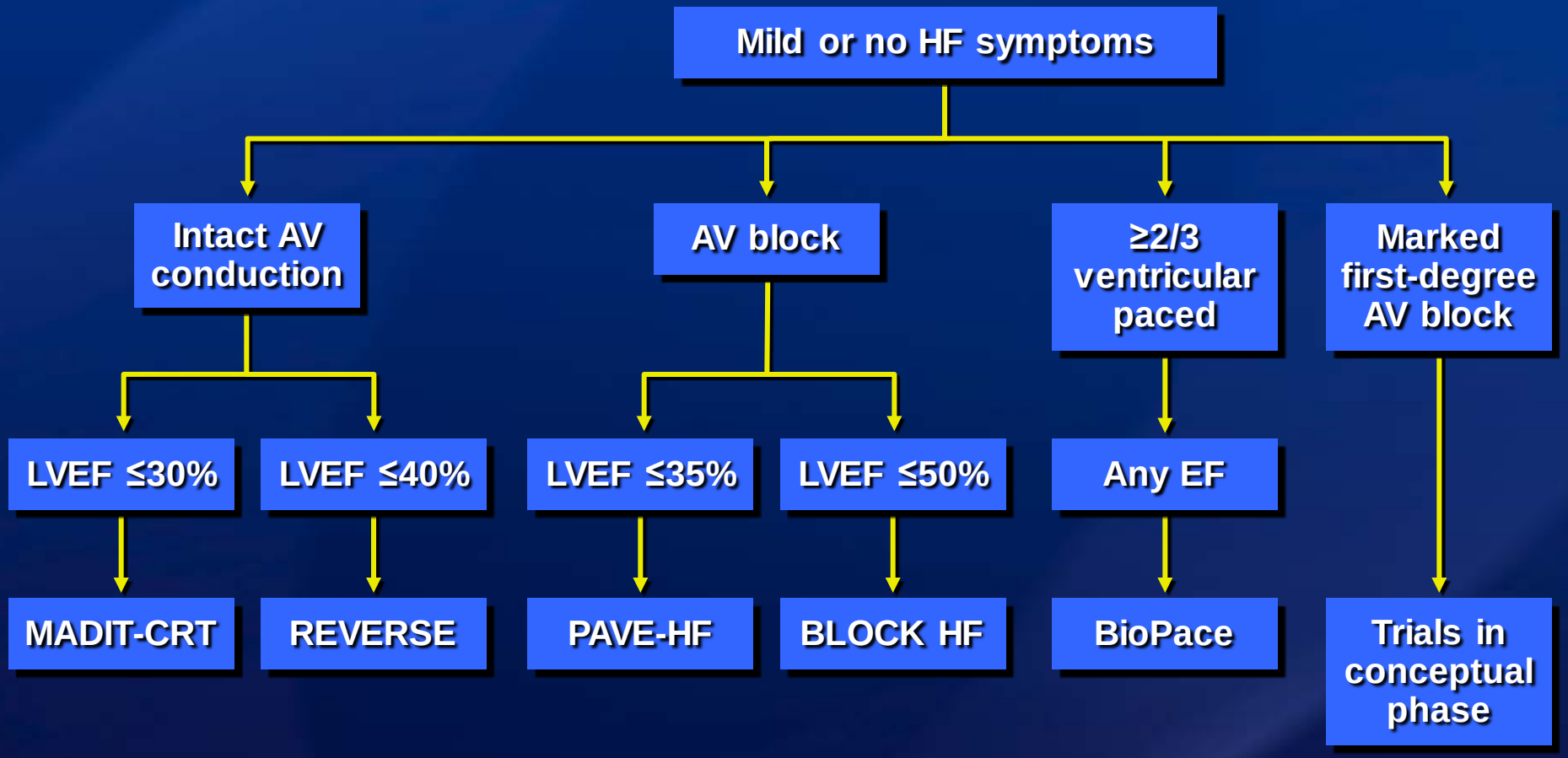
Current "FDA Labeling"
What Should be Challenged

Criteria	Challenge
Opt medical program	No
Fx class III or IV	
QRS > 120 - 130 ms	
LVEF ≤ 35%	Not yet
NSR	?

Point at which CRT Applied is Critical



Recent or Ongoing Trials Expanding the Role of CRT



Reynolds CR and Gold MR: Curr Cardiol Rep 12(5):367, 2010

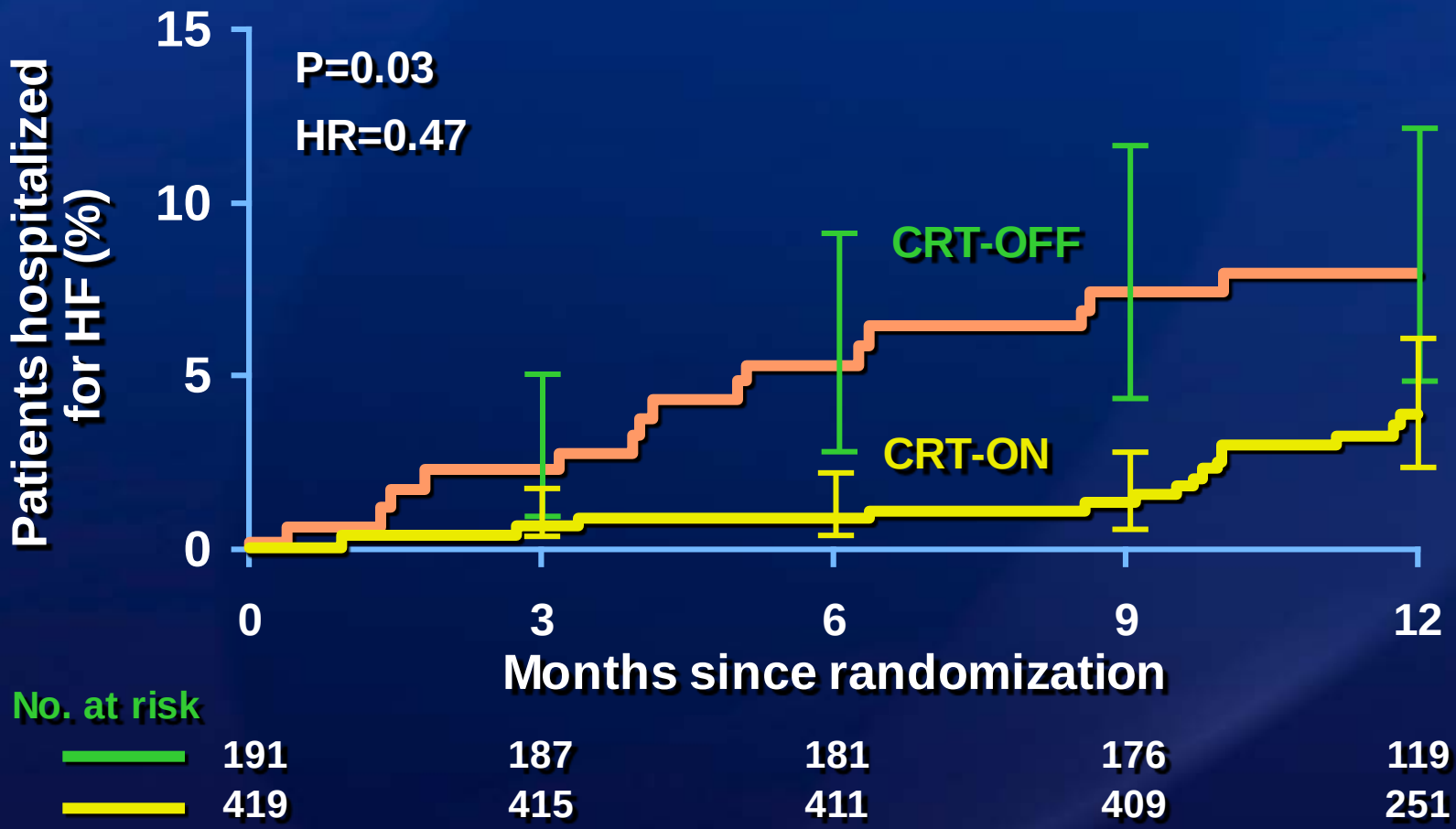
Randomized Trial of Cardiac Resynchronization in Mildly Symptomatic Heart Failure Patients and in Asymptomatic Patients With Left Ventricular Dysfunction and Previous Heart Failure Symptoms

Cecilia Linde, MD, PhD,* William T. Abraham, MD, FACC,† Michael R. Gold, MD, PhD,‡ Martin St. John Sutton, MD,§ Stefano Ghio, MD,¶ Claude Daubert, MD,‖ on behalf of the REVERSE (REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction) Study Group

Stockholm, Sweden; Columbus, Ohio; Charleston, South Carolina; Philadelphia, Pennsylvania; Pavia, Italy; and Rennes, France

Linde et al: JACC 52:1834, 2008

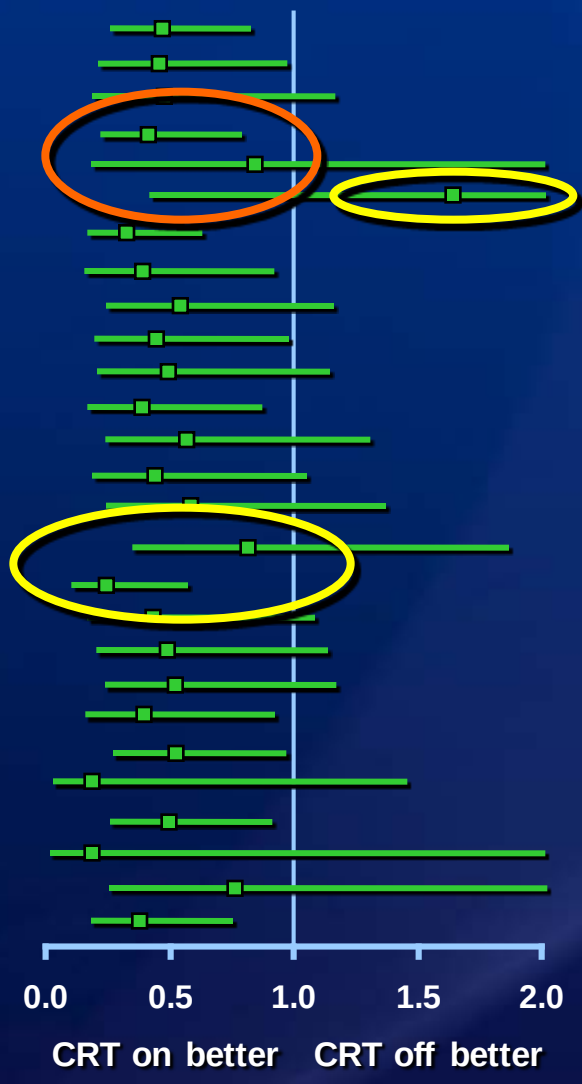
REVERSE*
Time to First Heart Failure Hospitalization
**Similar in 2 other large clinical trials*



Linde et al: JACC 52:1834, 2008

REVERSE European Cohort
Effect of CRT on HF Clinical Composite Response

Group		No.	Odds ratio (95% CI)
Overall		262	0.45 (0.25-0.81)
Age	<63.9 years	149	0.44 (0.20-0.96)
	≥63.9 years	113	0.46 (0.19-1.15)
Gender	Male	213	0.40 (0.21-0.77)
	Female	49	0.83 (0.18-3.80)
NYHA class	I	44	1.63 (0.41-6.44)
	II	218	0.31 (0.16-0.61)
Etiology	Ischemic	114	0.37 (0.15-0.91)
	Nonischemic	148	0.52 (0.24-1.14)
SBP	<122 mm Hg	130	0.43 (0.19-0.97)
	≥122 mm Hg	132	0.48 (0.20-1.13)
EF	<27%	123	0.37 (0.16-0.85)
	≥27%	139	0.55 (0.24-1.29)
ESVI	<92.5 mL/m^2	133	0.43 (0.18-1.03)
	≥92.5 mL/m^2	109	0.57 (0.24-1.36)
QRS interval	<152 ms	120	0.80 (0.35-1.85)
	≥152 ms	142	0.23 (0.10-0.56)
IVMD	<36 ms	103	0.42 (0.16-1.07)
	≥36 ms	126	0.47 (0.20-1.12)
Glomerular filtration rate	<82.7 mL/min	140	0.51 (0.23-1.15)
	≥82.7 mL/min	122	0.38 (0.16-0.91)
Beta-blockers	Yes	245	0.51 (0.27-0.95)
	No	17	0.17 (0.02-1.44)
Diuretics	Yes	223	0.48 (0.26-0.89)
	No	39	0.17 (0.01-2.06)
Device type	CRT	85	0.75 (0.25-2.29)
	CRT + ICD	177	0.36 (0.18-0.74)



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Daubert et al: JACC 54(20):1837, 2009

I “A”

- LVEF ≤35%
- NYHA class III or IV
- QRS ≥120 ms
- Normal sinus rhyt

IIa “B”

- LVEF ≤35%
- NYHA class III or IV
- ORS ≥120 ms
-

Indications for Pacemaker vs CRT may continue to ‘blend’ in years to come

IIa “C”

- LVEF ≤35%
- NYHA class III or IV
- Existing pacemaker or ICD
- Frequent pacing/ dependent

- NYHA class I or II
- Need pacemaker or ICD
- Frequent pacing anticipated

MAYO CLINIC

MUSTIC-AF
24-Month Follow-up

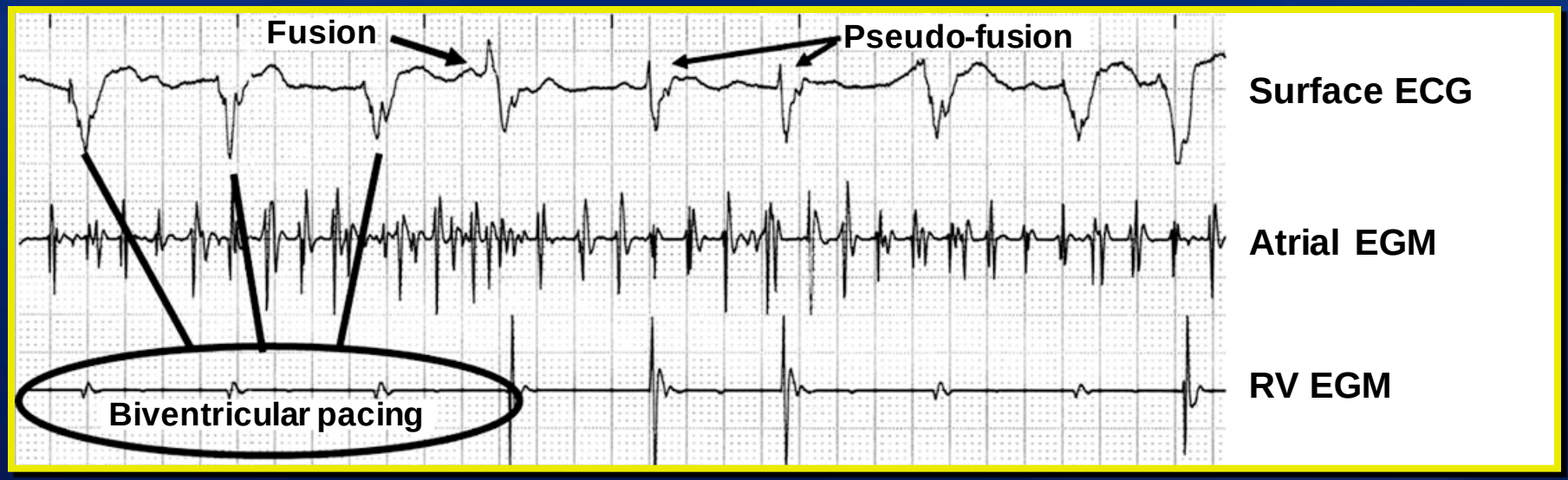
	Baseline	1 yr	
Heart rate	75±15	7[illegible]	
6-min walk	325±82		[illegible]9*
Peak VO_2	13±4		NA
QOL			32±20*
NYHA		[illegible].2±0.5*	2.2±0.5*
LVEF		30±8*	NA

Must be able to maintain ventricular pacing

n=43; 26 completing 2 years FU
*** P<0.01 compared to baseline**
Leclercq et al: ESC, 2002

CRT in the Presence of Atrial Fibrillation

True Biventricular Pacing Must be Maintained



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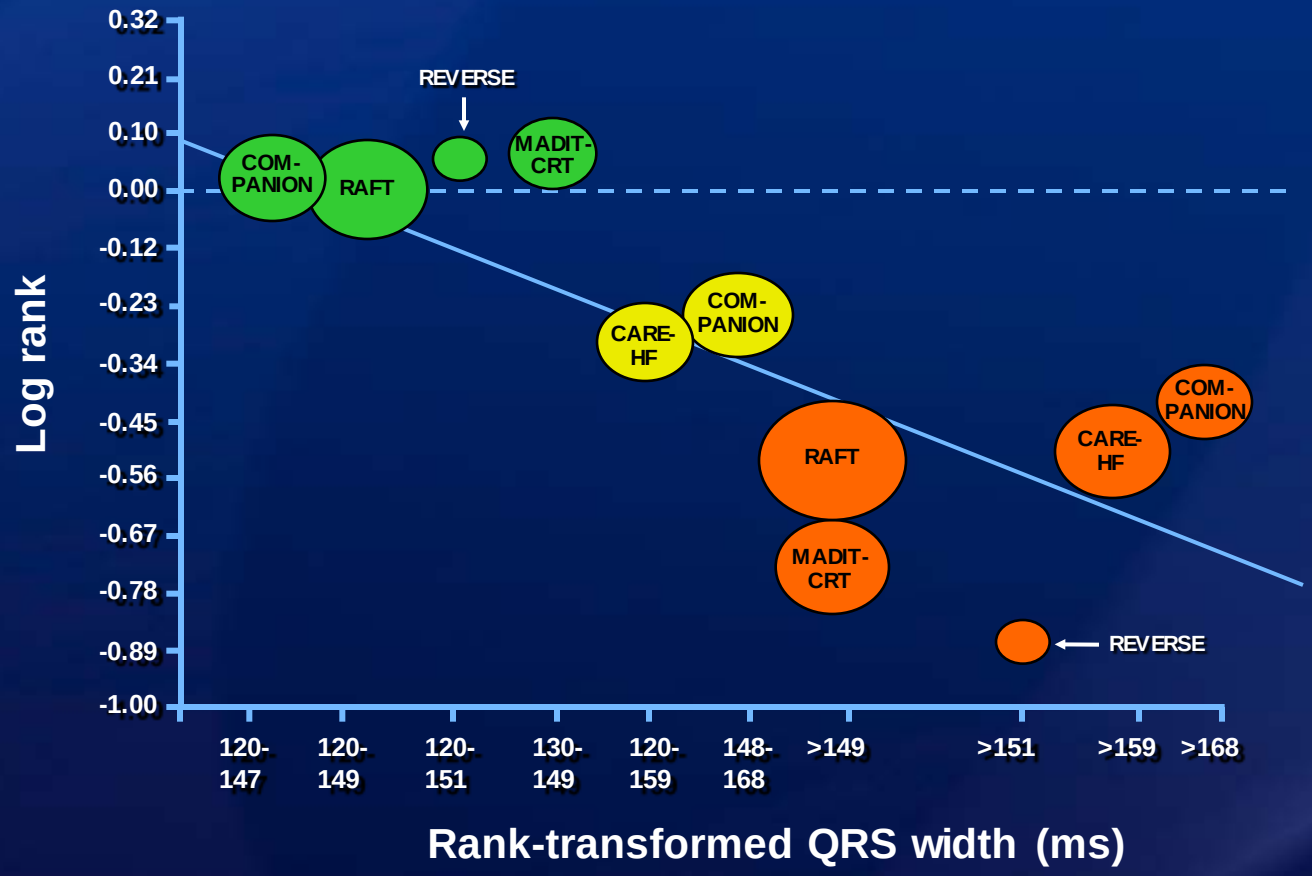
Gasparini M et al: Europace 11:v82, 2009

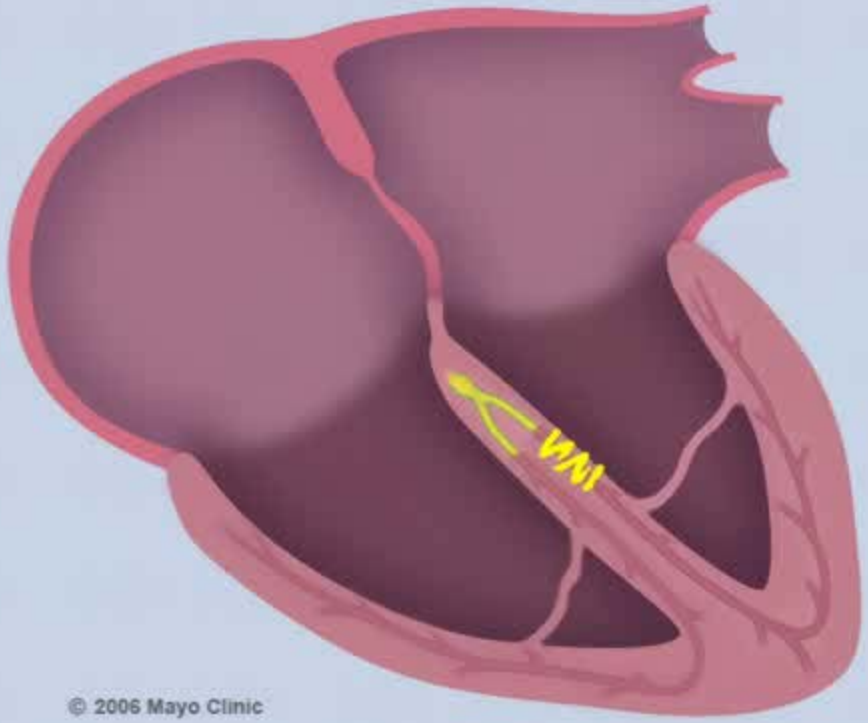
The Greater the QRS Width the More Likely to Have Benefit from CRT



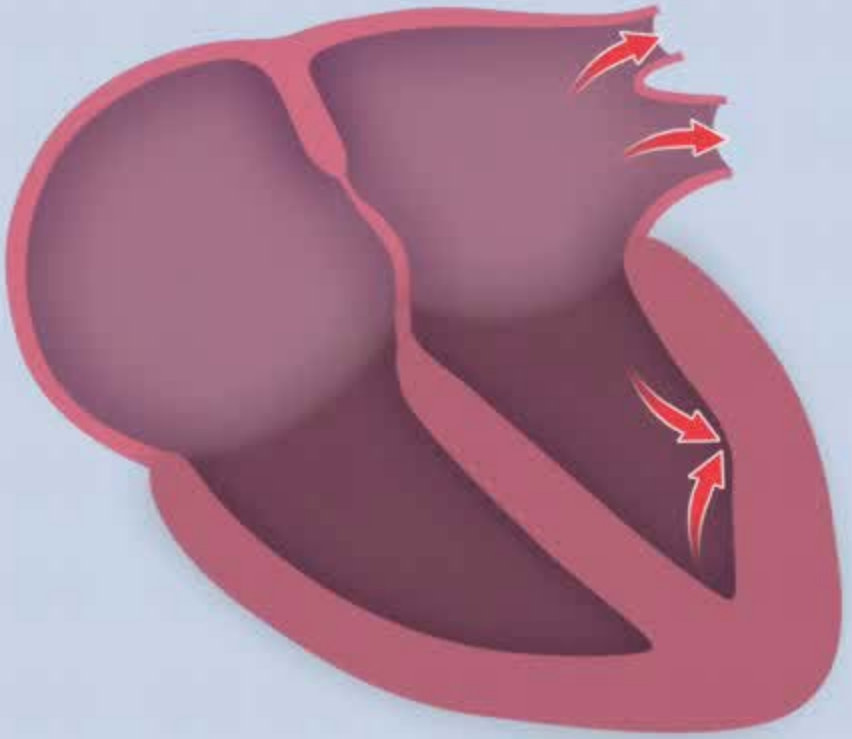
Farther below dashed line indicates greater clinical benefit for prevention of composite of adverse clinical events

Sipahi I et al: Arch Intern Med 171(16), 1454-1462, 2011

ELECTRICAL DYSSYNCHRONY



MECHANICAL DYSSYNCHRONY



Results of the Predictors of Response to CRT (PROSPECT) Trial

Eugene S. Chung, Angel R. Leon, Luigi Tavazzi, Jing-Ping Sun, Petros Nihoyannopoulos, John Merlino, William T. Abraham, Stefano Ghio, Christophe Leclercq, Jeroen J. Bax, Cheuk-Man Yu, John Gorcsan, III, Martin St John Sutton, Johan De Sutter and Jaime Murillo

Circulation 2008;117;2608-2616; originally published online May 5, 2008;
DOI: 10.1161/CIRCULATIONAHA.107.743120
Circulation is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514

 Print ISSN: 0009-7322. Online ISSN: 1524-4539

Chung et al: Circ 117:2608, 2008

Cardiac-Resynchronization Therapy in Heart Failure with Narrow QRS Complexes

John F. Beshai, M.D., Richard A. Grimm, D.O., Sherif F. Nagueh, M.D., James H. Baker II, M.D., Scott L. Beau, M.D., Steven M. Greenberg, M.D., Luis A. Pires, M.D., and Patrick J. Tchou, M.D., for the RethinQ Study Investigators*

Beshai et al: NEJM 374:2461, 2007

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Impact of PROSPECT & ReTHINQ

PROSPECT

- No single measure of mechanical dyssynchrony can be recommended to improve patient selection for CRT
- Methodology to determine mechanical dyssynchrony needs further elaboration

The yield for echo measures varied between 50 – 92 %, the inter core lab variability was relatively great (6.5-72.1%) in view of the expertise of the included centres, indicating the need for simplification of methodology.

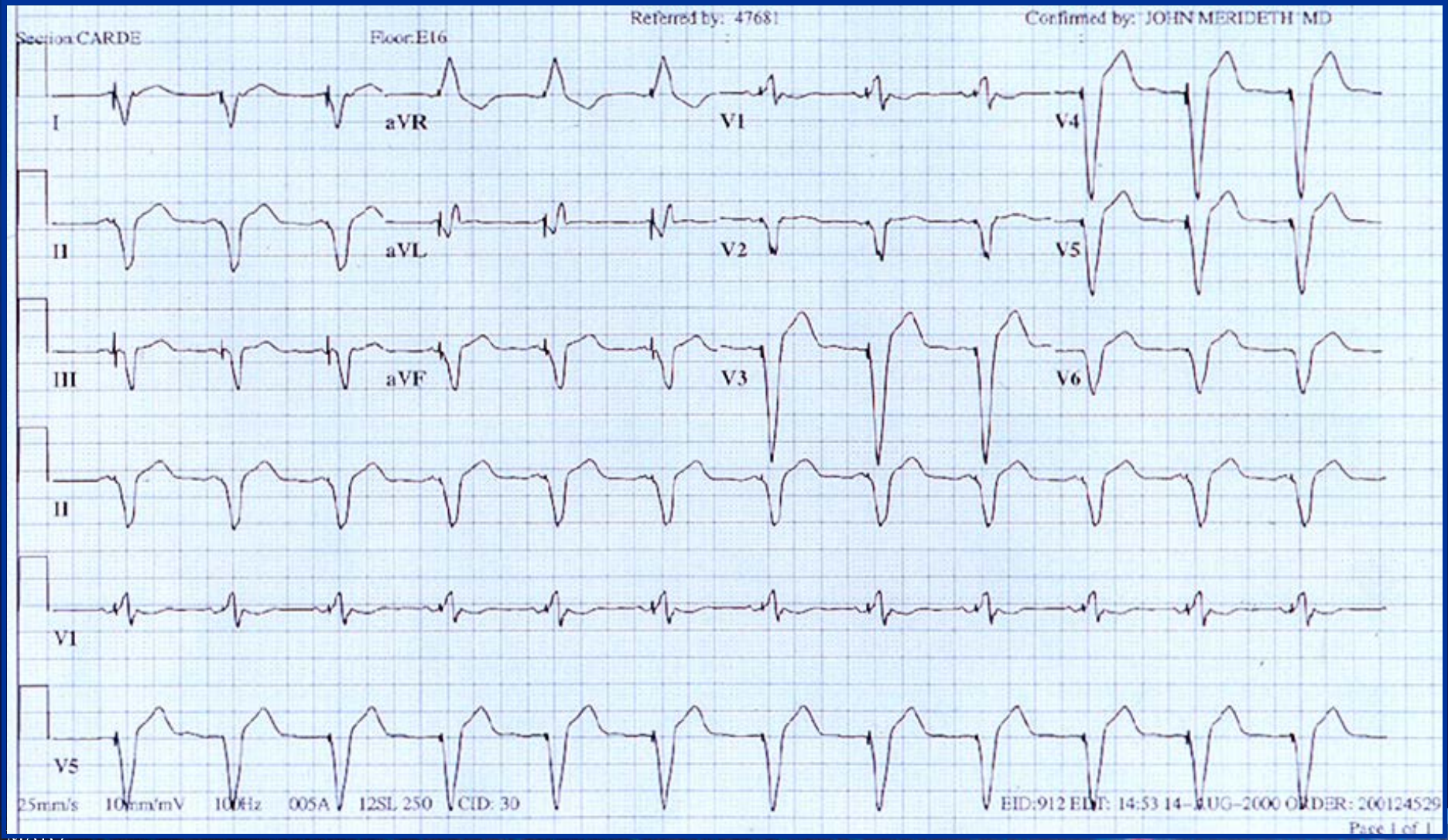
ReTHINQ

- Dyssynchrony variables used in this trial did not predict patient improvement in patients with QRS < 120 ms
- Patients with QRS ≥ 120 and < 130 ms did correlate with dyssynchrony variables; however these patients included in criteria already.

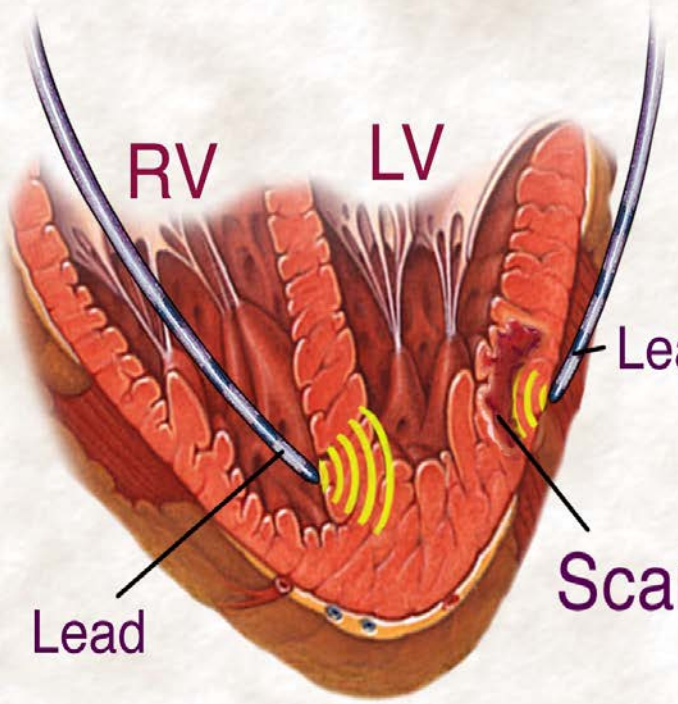
EKG ERRORS

- Failure to Understand Vectors
- Anodal Stimulation
- Lead Placement Errors
  - Phrenic nerve stimulation
  - RV Lead Placement
- Capture Latency Versus Capture Threshold

Postero-Lateral Vein



EKG Vector Fusion



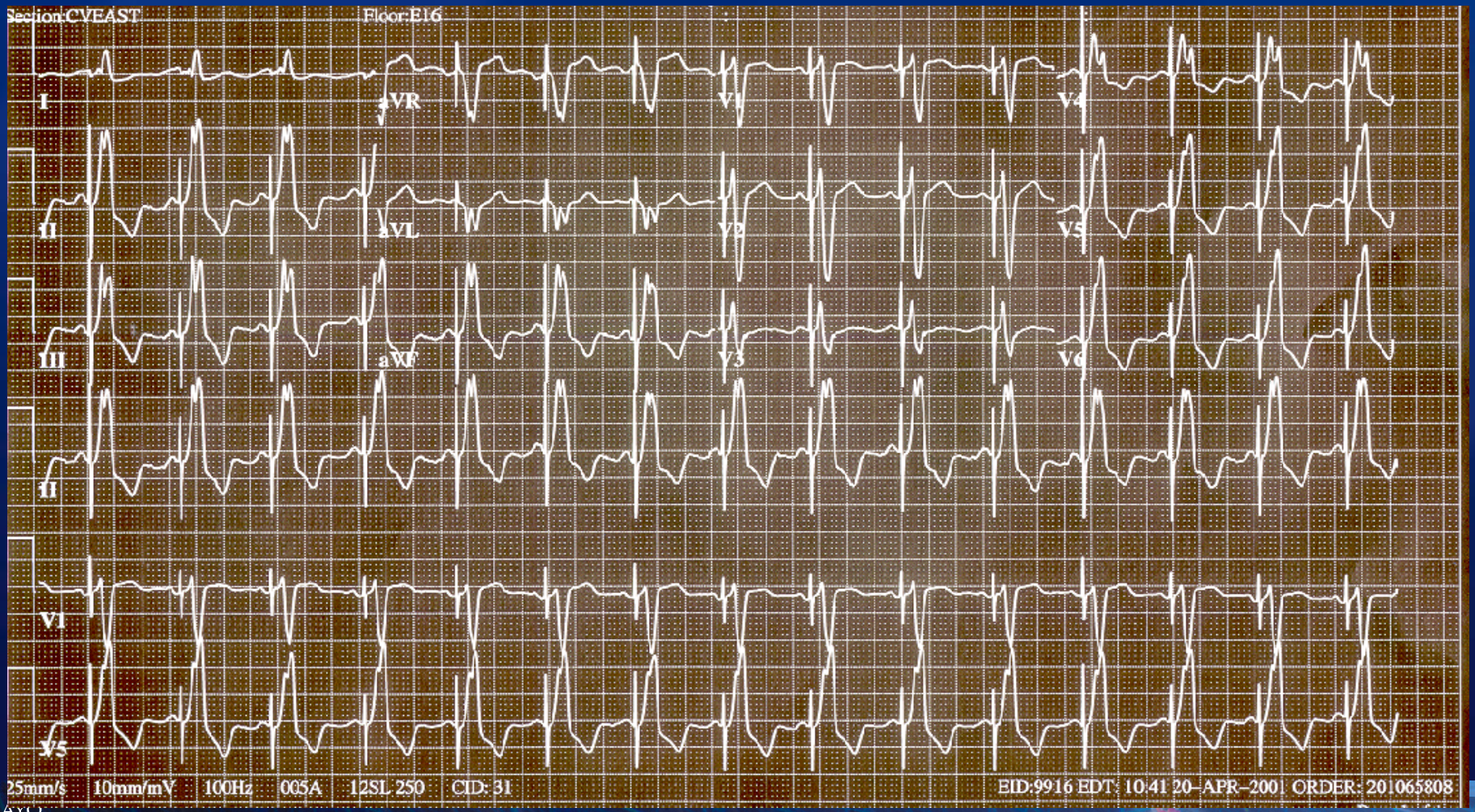
RV only — I, V_1

LV only — I, V_1

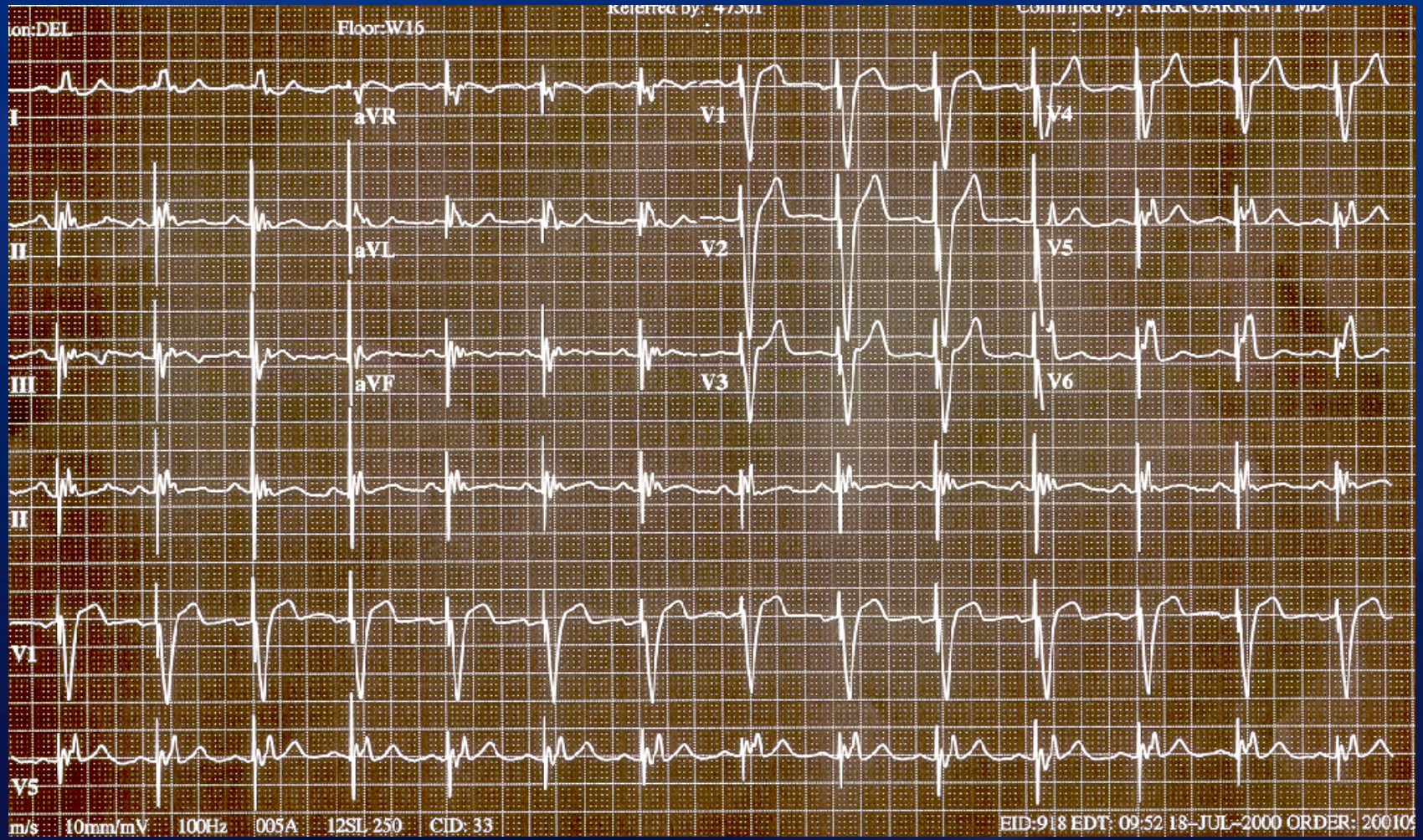
B_1V simultaneous — I, V_1

B_1V LV early — I, V_1

HIGH OUTPUT PACING



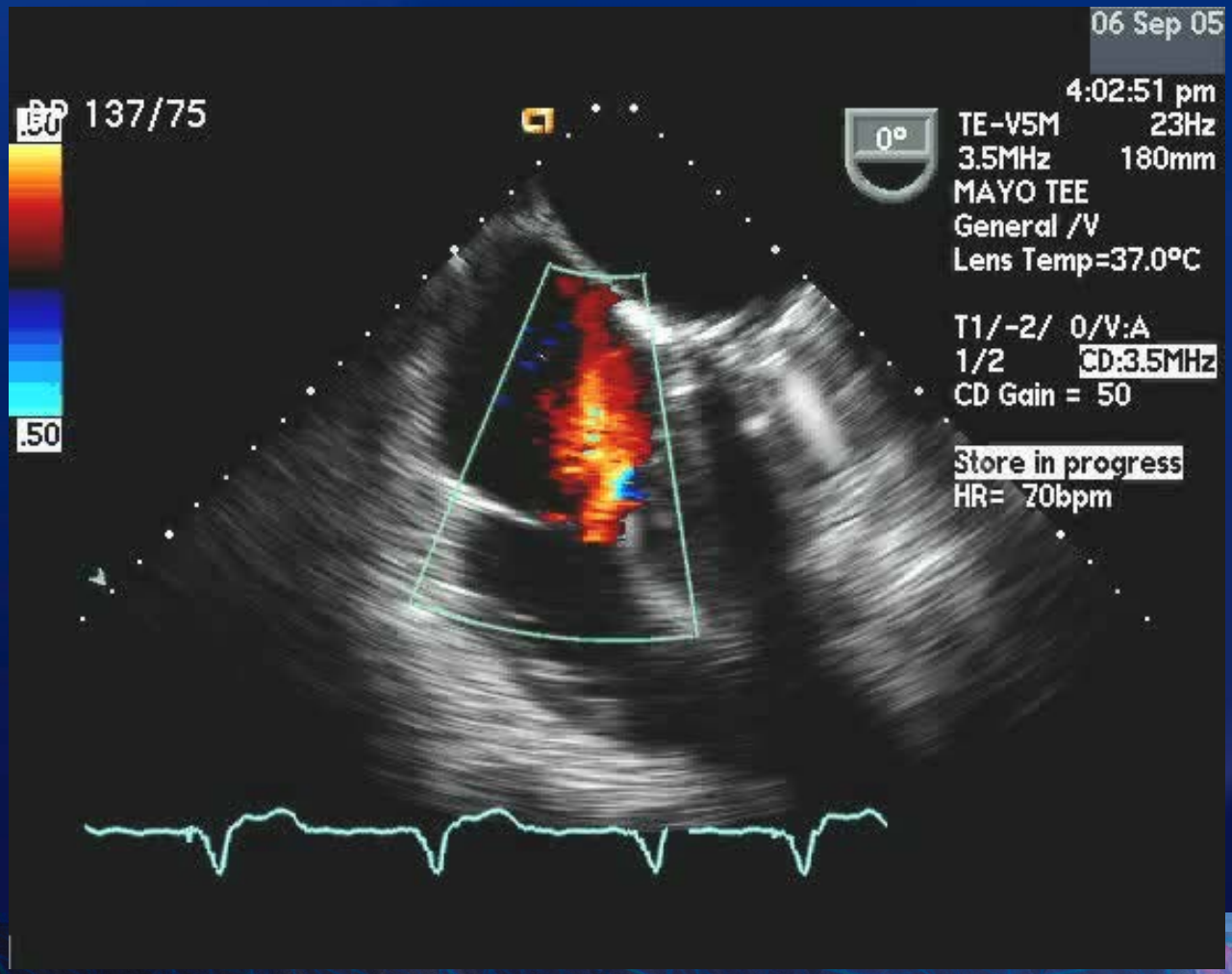
LOW OUTPUT PACING

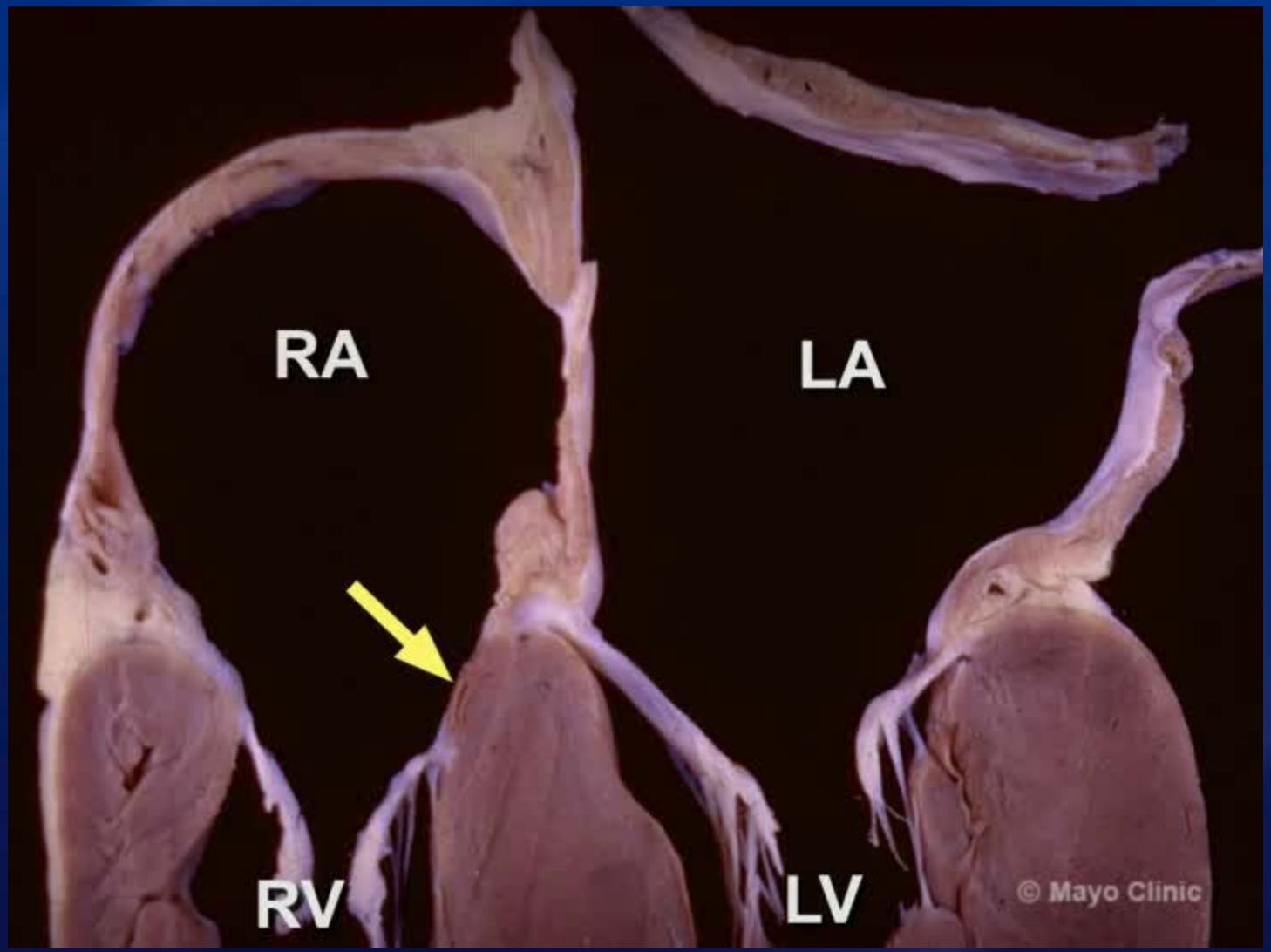


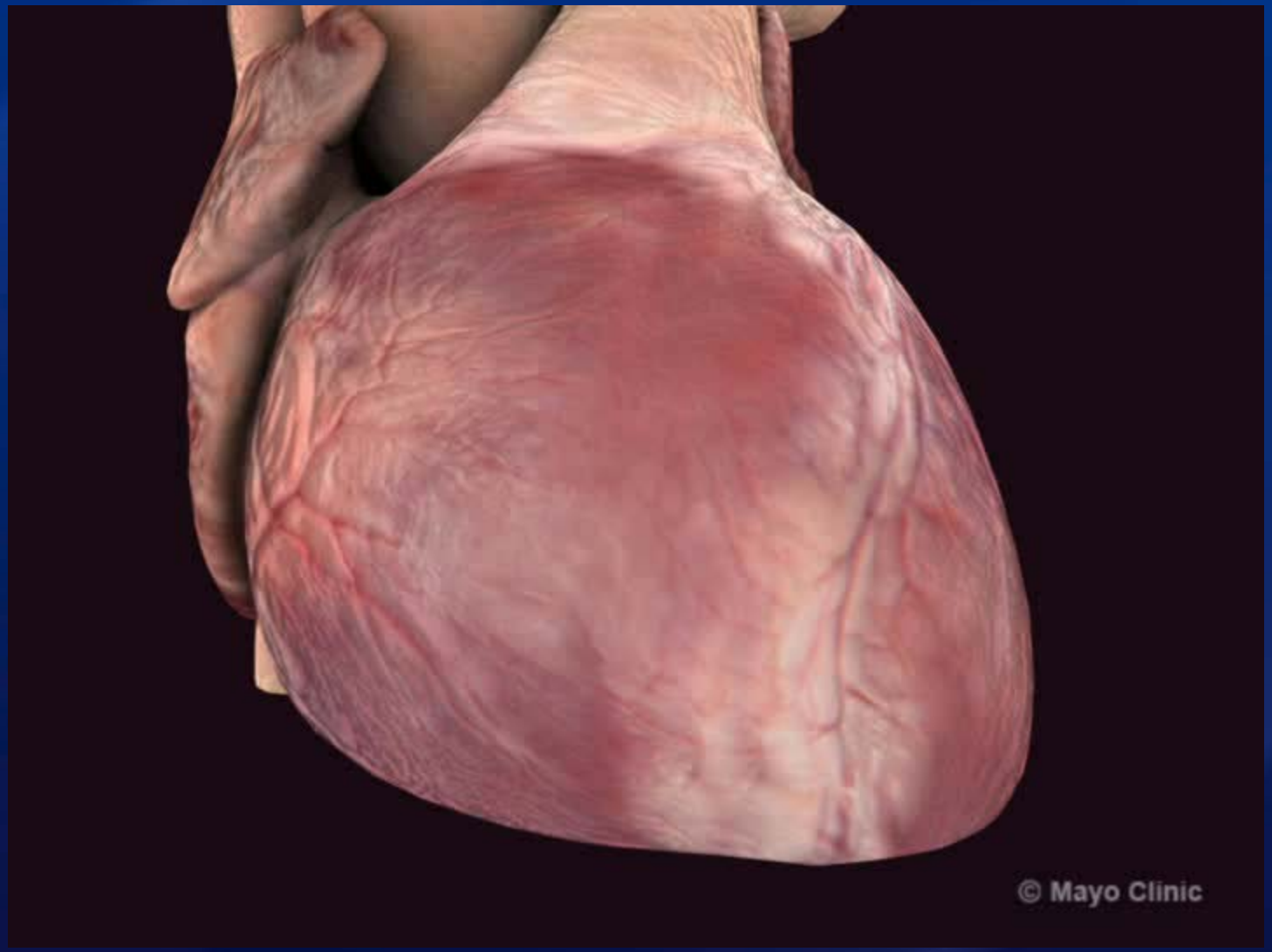
Anodal stimulation

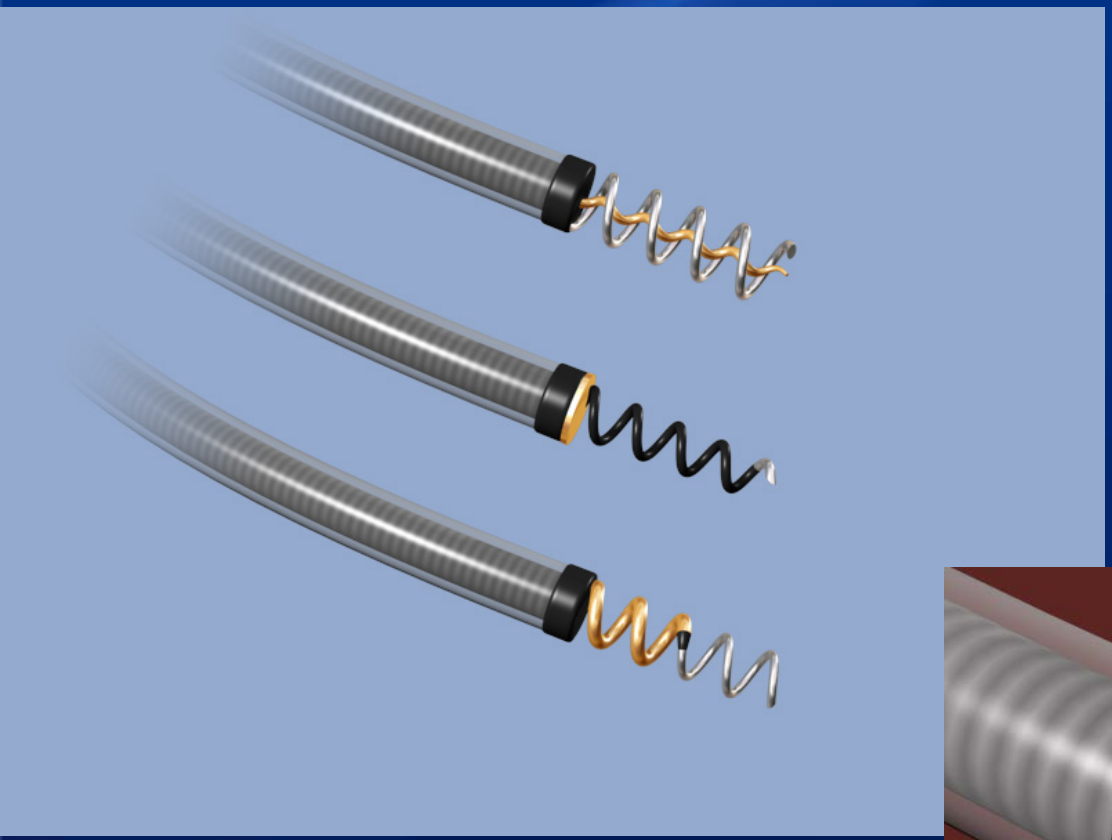
- Usually the stimulation wave front starts from the cathode or negative electrode.
- In certain situations, the stimulation site is reversed.
- More likely to occur with large anodal surface, high or very low output.
- Anodal stimulation may occur along with cathodal stimulation
- May help or harm synchrony.

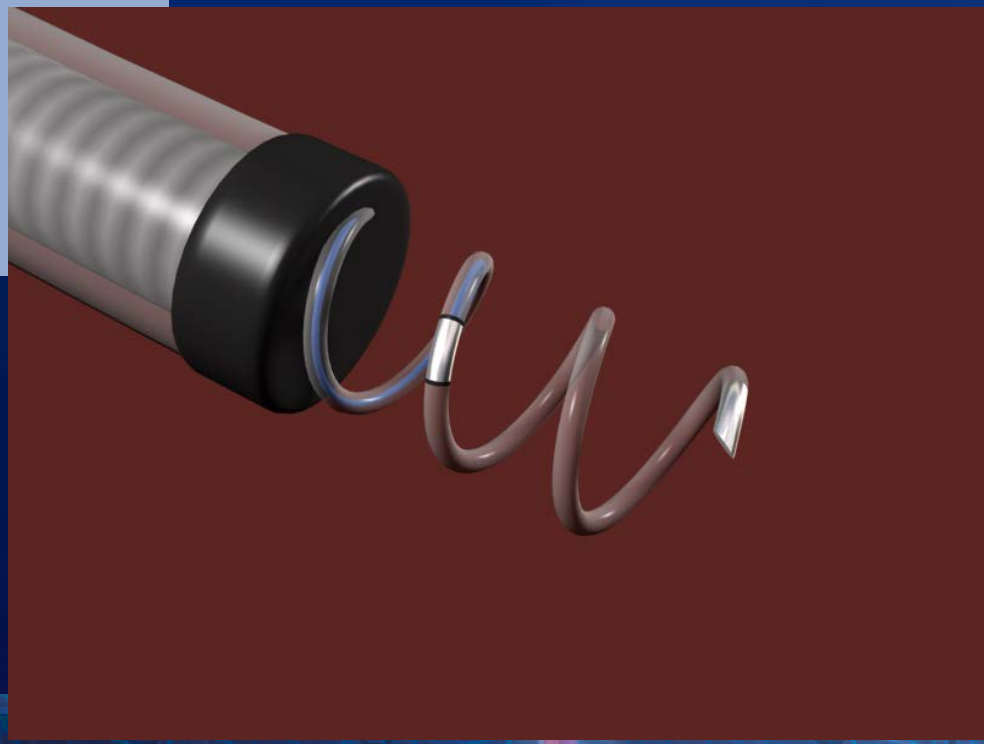
Tricuspid Regurgitation—Problem with Current Leads











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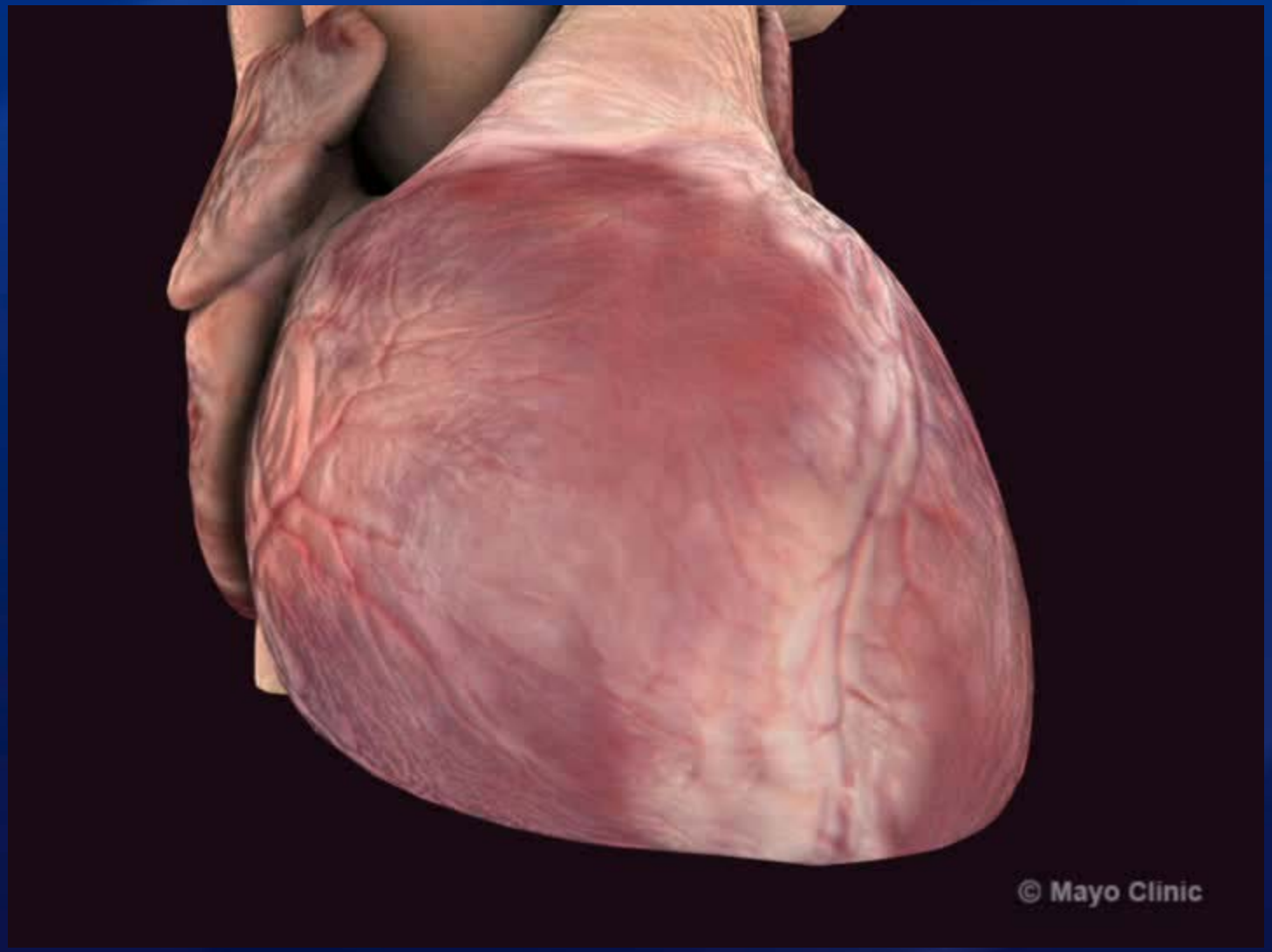

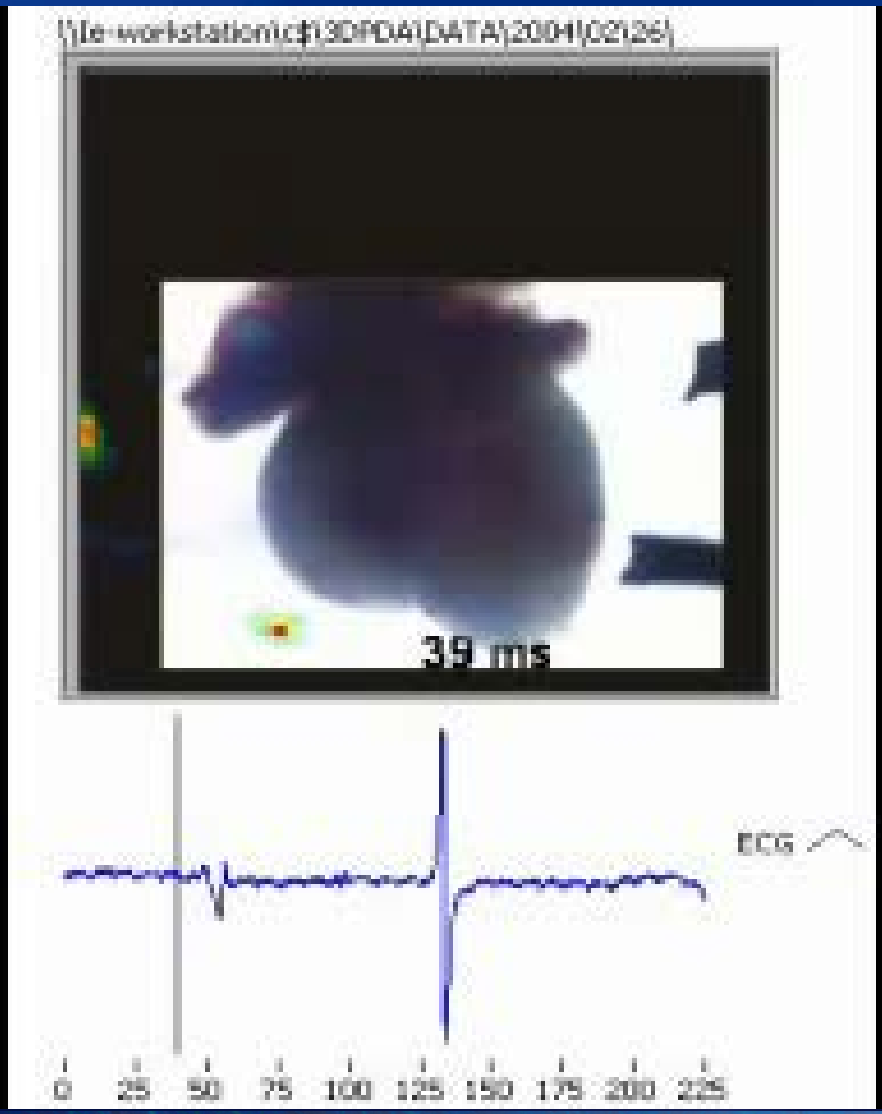

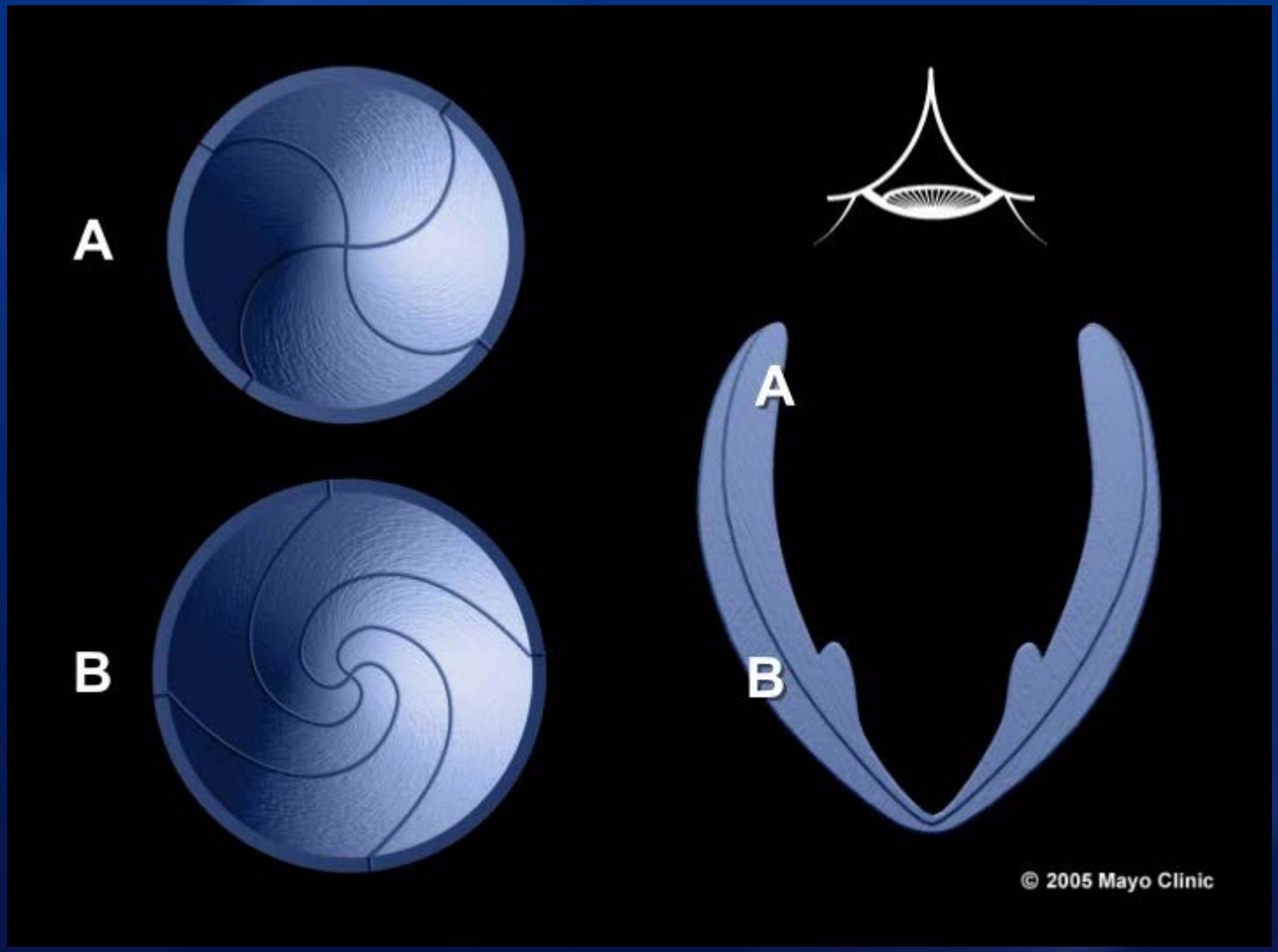

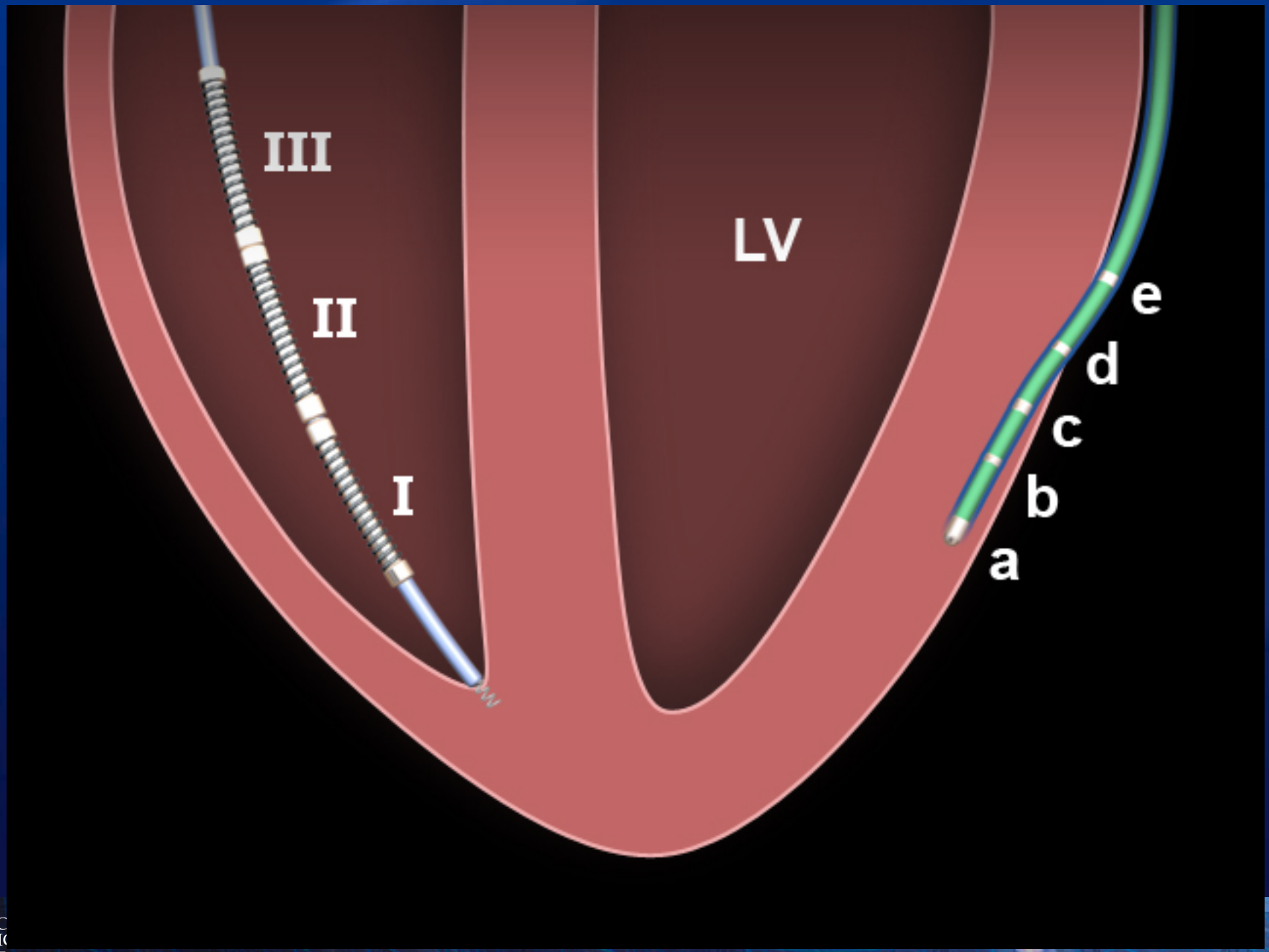

“Normal” LV Synchrony

- Conduction system is on the septum!
- Apex vs. base
- Epicardium vs. endocardium
- Septum vs. free wall
- Papillary muscle activation
- Synchronous relaxation

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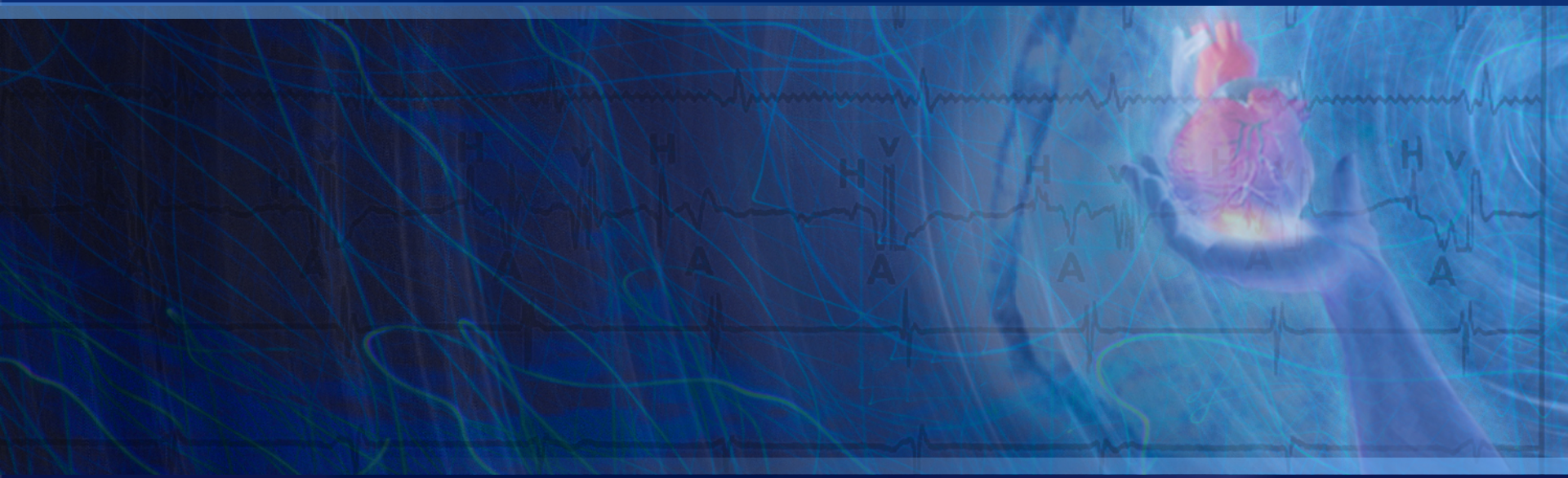
Heart Failure and CRT: Novelties and Controversies



Samuel J. Asirvatham, MD
Professor of Medicine, Professor of Pediatrics
Program Director Cardiac Electrophysiology;
Vice Chair – Innovations Mayo Clinic
Turin, October 26, 2012