Reste-t-il une place pour l'*Echo* pour la resynchronisation?

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European Heart Journal
doi:10.1093/eurheartj/ehn309

European Journal of Heart Failure
doi:10.1016/j.ejheart.2008.08.005

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008

Cardiac resynchronization therapy (CRT) (*Table 23*)

- CRT-P is recommended to reduce morbidity and mortality in patients in NYHA III–IV class who are symptomatic despite optimal medical therapy, and who have a reduced EF (LVEF ≤35%) and QRS prolongation (QRS width ≥120 ms).

Class of recommendation I, level of evidence A

- CRT with defibrillator function (CRT-D) is recommended to reduce morbidity and mortality in patients in NYHA III–IV class who are symptomatic despite optimal medical therapy, and who have a reduced EF (LVEF ≤35%) and QRS prolongation (QRS width ≥120 ms)

Class of recommendation I, level of evidence A

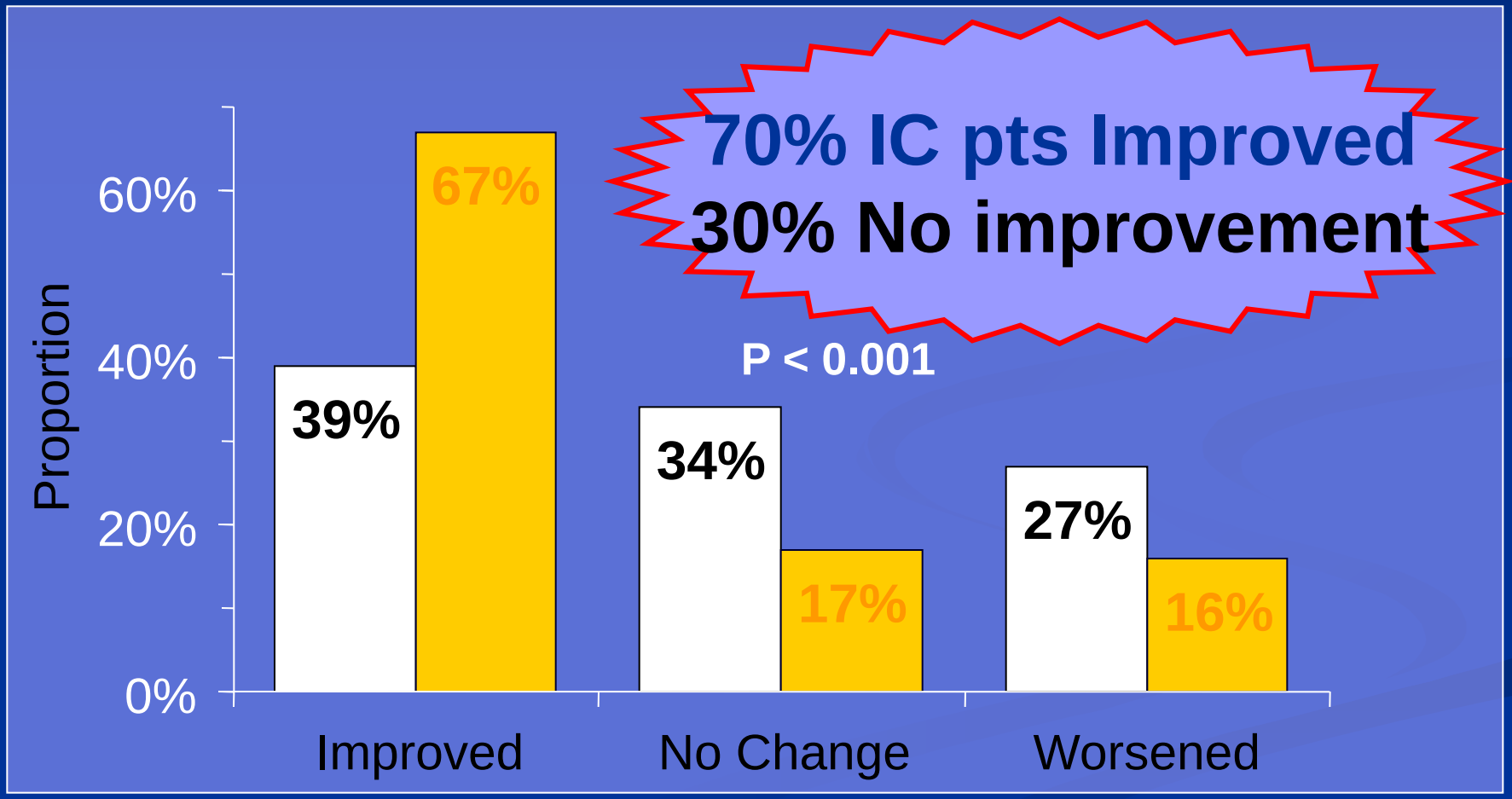
- The survival advantage of CRT-D vs. CRT-P has not been adequately addressed. Due to the documented effectiveness of ICD therapy in the prevention of sudden cardiac death, the use of a CRT-D device is commonly preferred in clinical practice in patients satisfying CRT criteria including an expectation of survival with good functional status for >1 year.

Up-to-date, recognized criteria of dyssynchrony admitted by guidelines…

ELECTRICAL DYSSYNCHRONY

- Severe chronic congestive heart failure(NYHA III or IV class) <u>despite optimal pharmacological treatment</u>
- LV EF < 35%
- LV EDD VG > 55 mm
- QRS > 120 ms

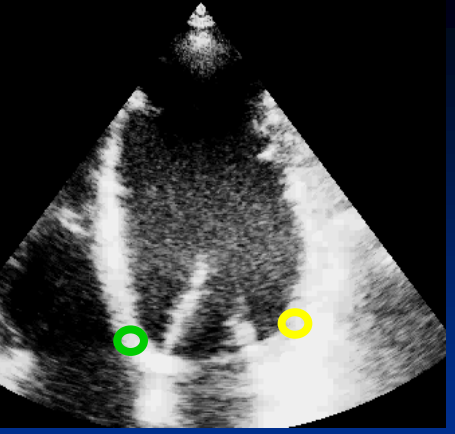
Responders / Non-Responders



MIRACLE TRIAL
NEJM 2002;346:1845-53

Quels Paramètres Mesurer?

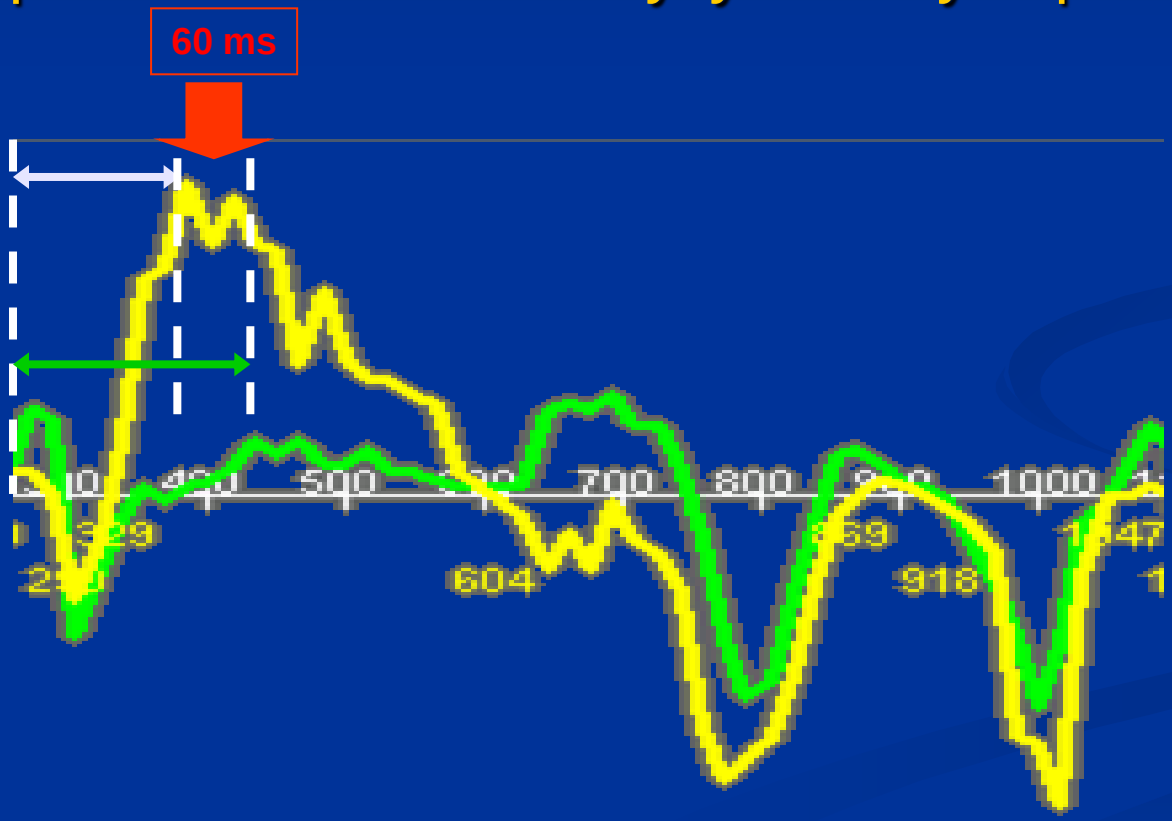
En 20…10…

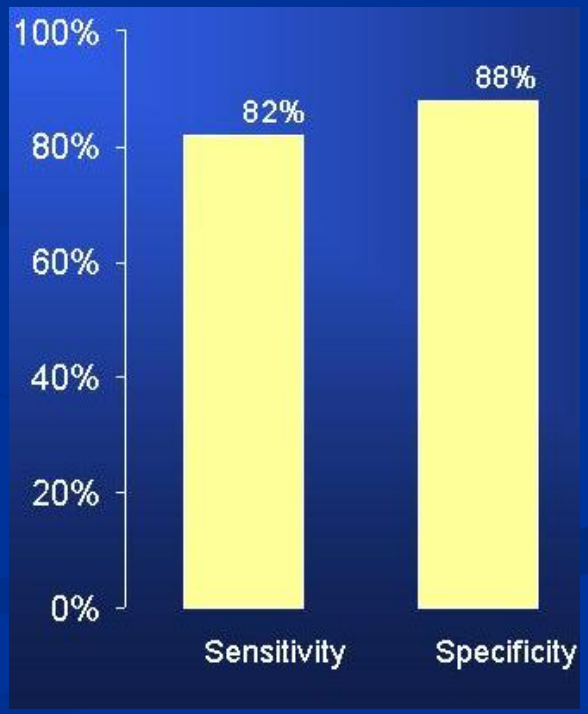


Measure of the time to peak on DTI velocity curves for patient selection

Electro-Systolic Delay

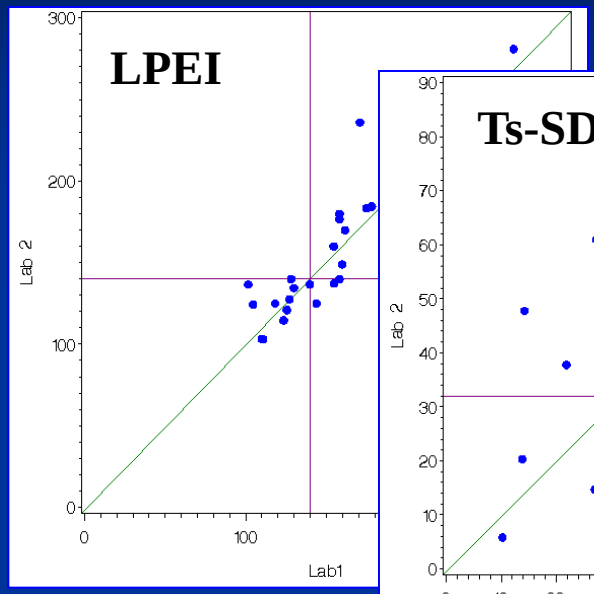
30 pts – measure of the dysynchrony septal vs. Lateral LV wall



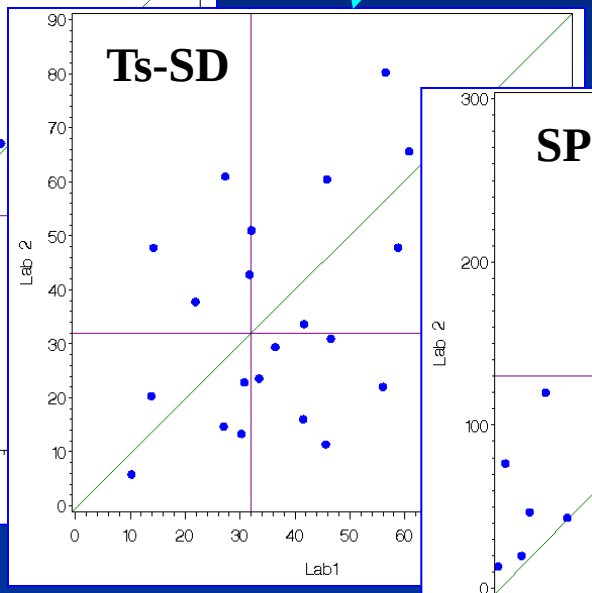


Bax et al. Am J Cardio 2003

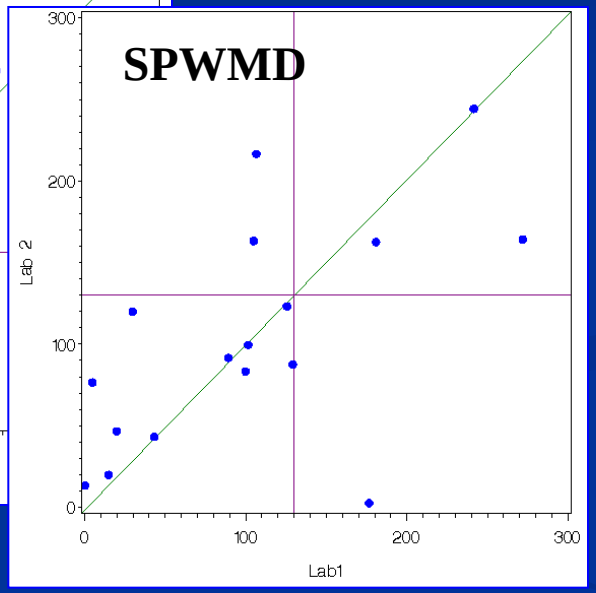
Mesures échocardiographiques: variabilité et faisabilité



Coefficient of Variation: 6.5%



Coefficient of Variation: 33.7%

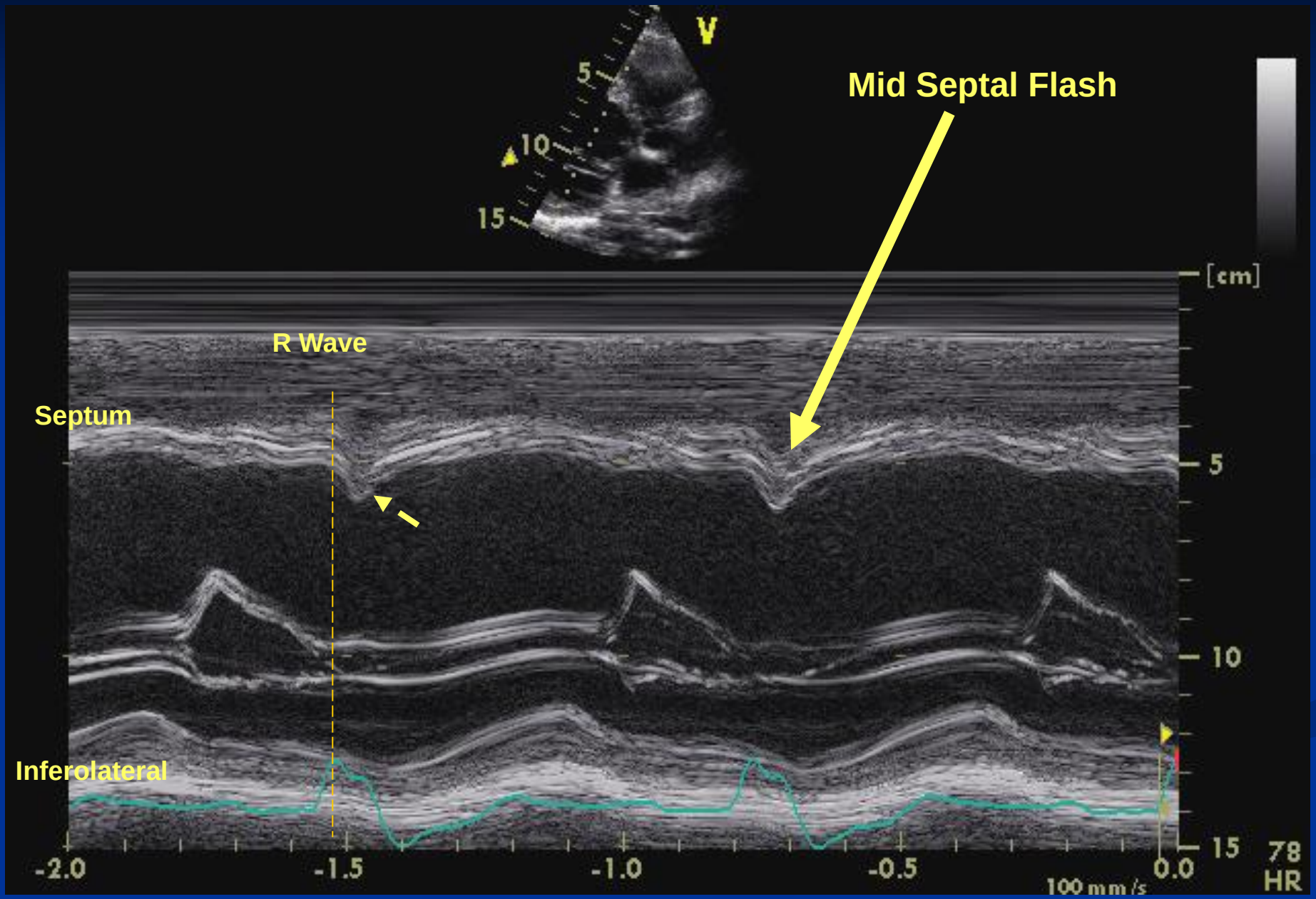


Coefficient of Variation: 72.1%

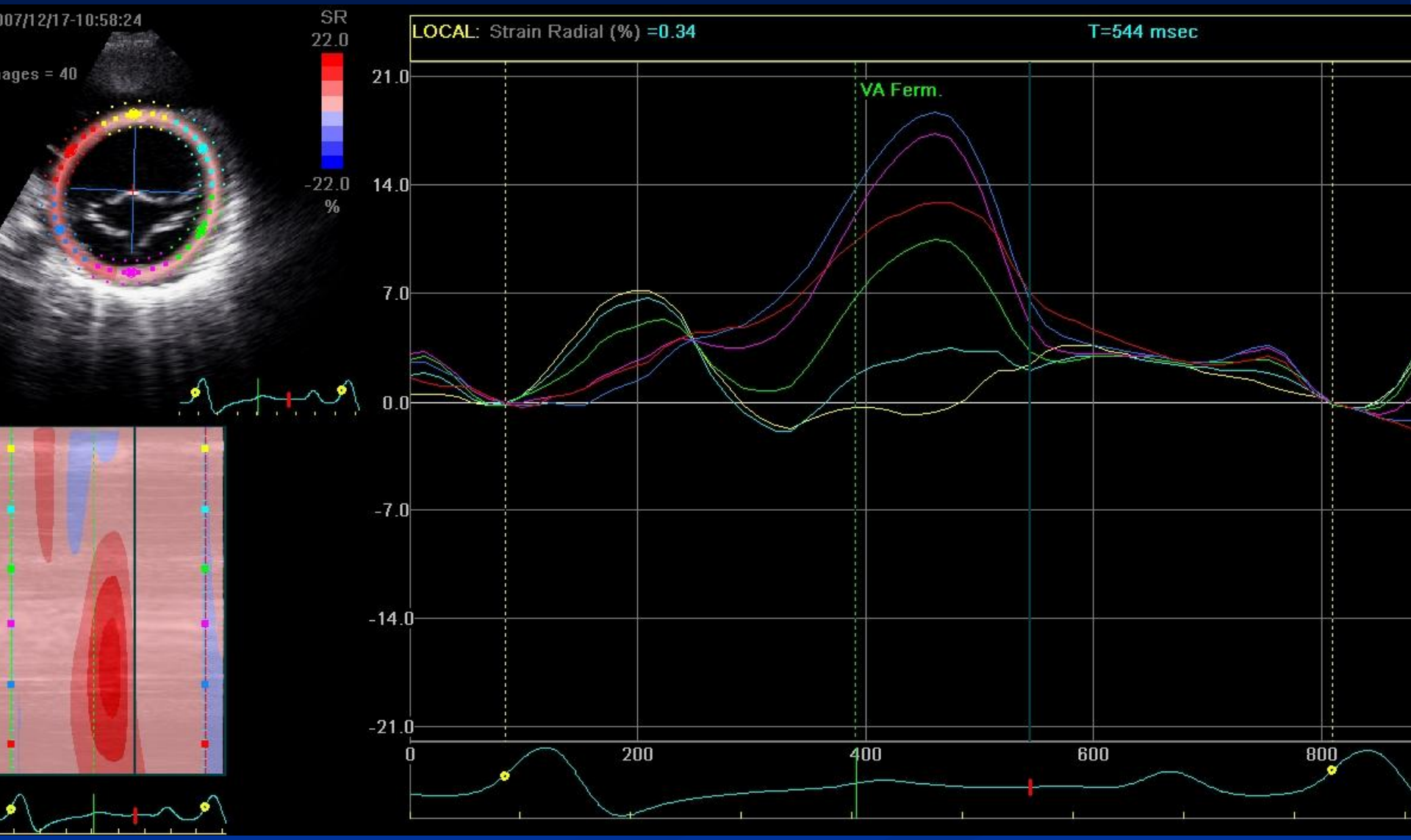
Faisabilité (%)

SPWMD	72
IVMD	92
LVFT/RR	85
LPEI	95
Ts Lat-Se	67
Ts-SD	**50**

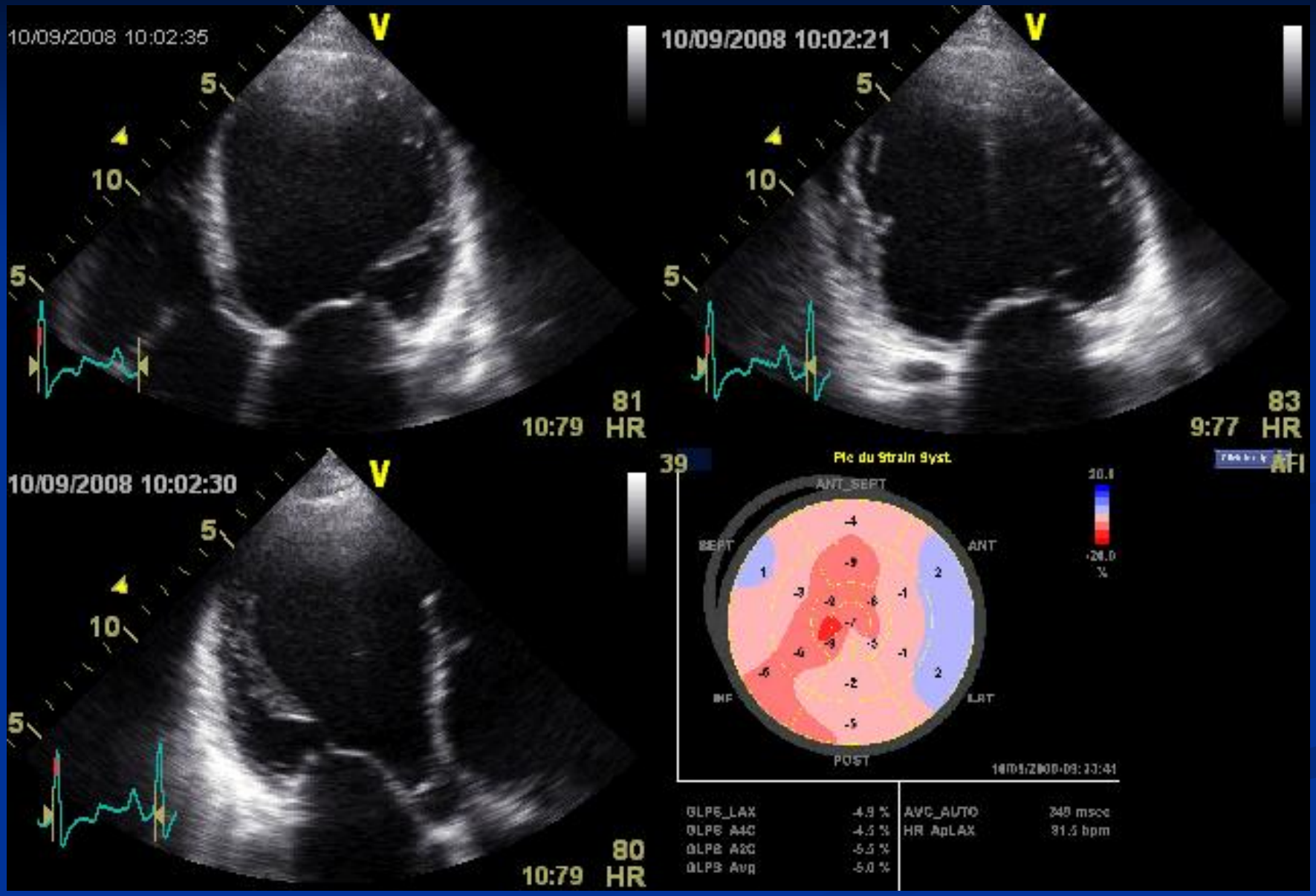
La très grande variabilité entre les CoreLab et la faible faisabilité des mesures nécessitent une Redéfinition méthologique sur comment étudier l'asynchronisme mécanique.


V
5
10
15
Mid Septal Flash
[cm]
R Wave
Septum
5
10
Inferolateral
15
78
HR
-2.0
-1.5
-1.0
-0.5
0.0
100 mm/s

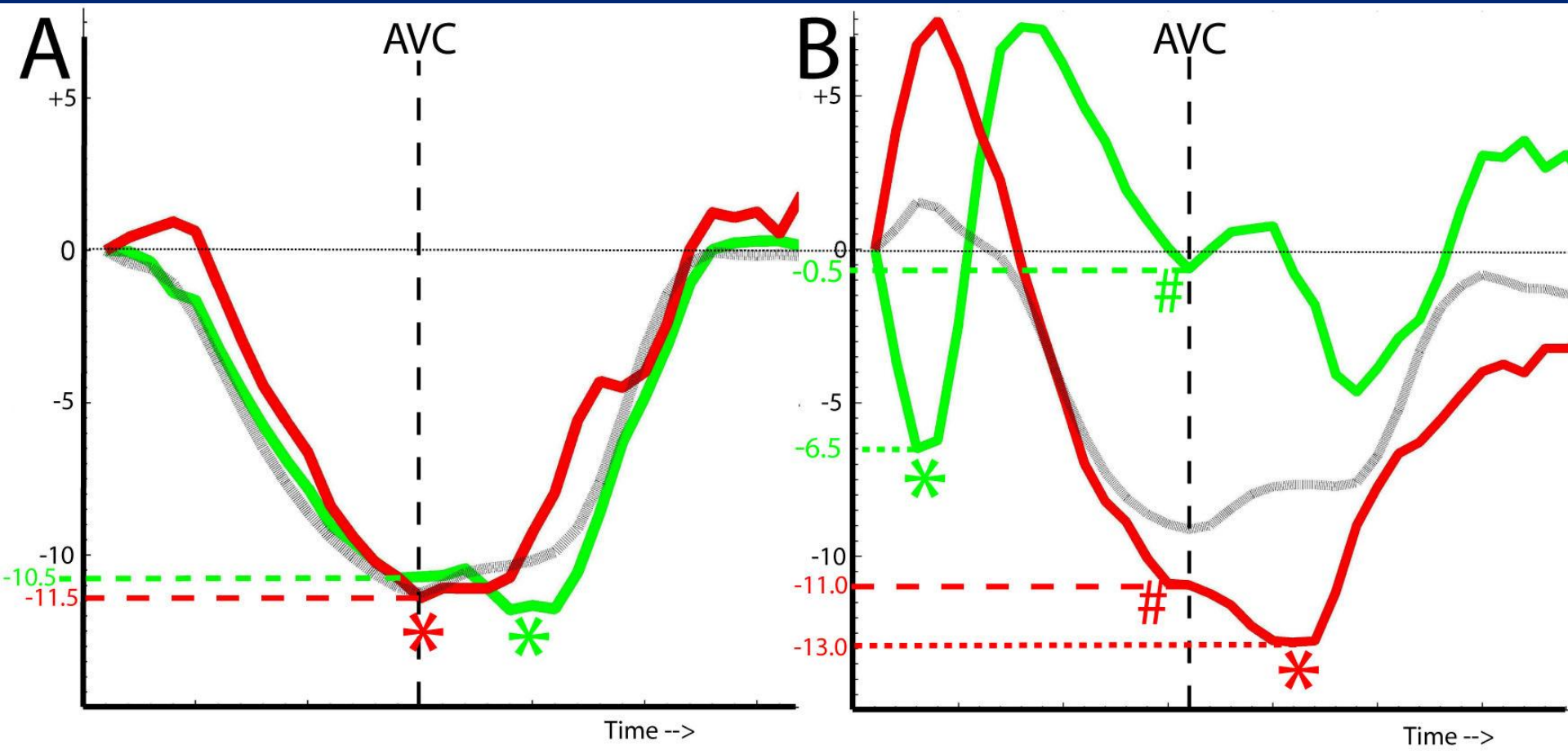
2D-S radial


007/12/17-10:58:24
ages = 40
SR
22.0
-22.0
%
LOCAL: Strain Radial (%) =0.34
T=544 msec
VA Ferm.
21.0
14.0
7.0
0.0
-7.0
-14.0
-21.0
0
200
400
600
800

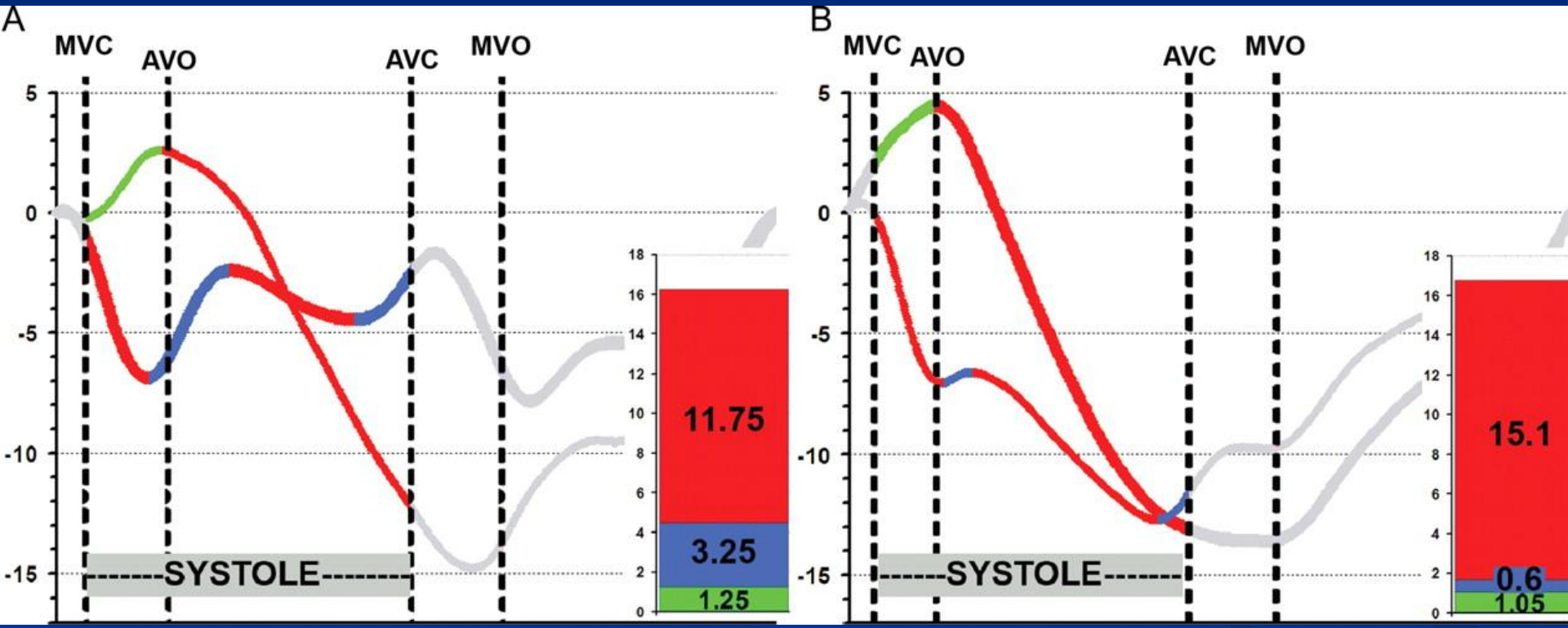
2DS Longitudinal



Longitudinal Strain

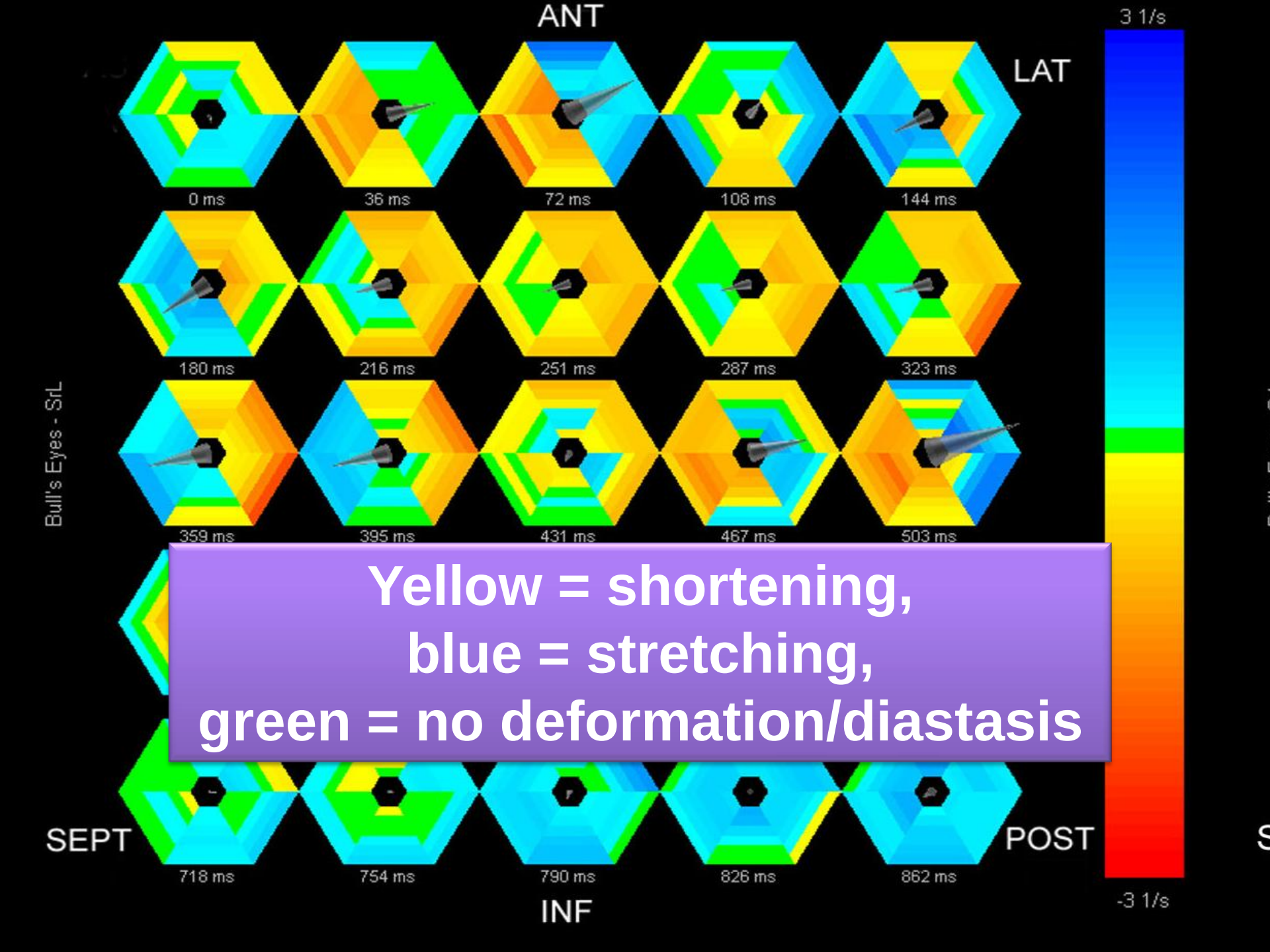


Mesure des déformations efficaces (raccourcissement) et des élongations

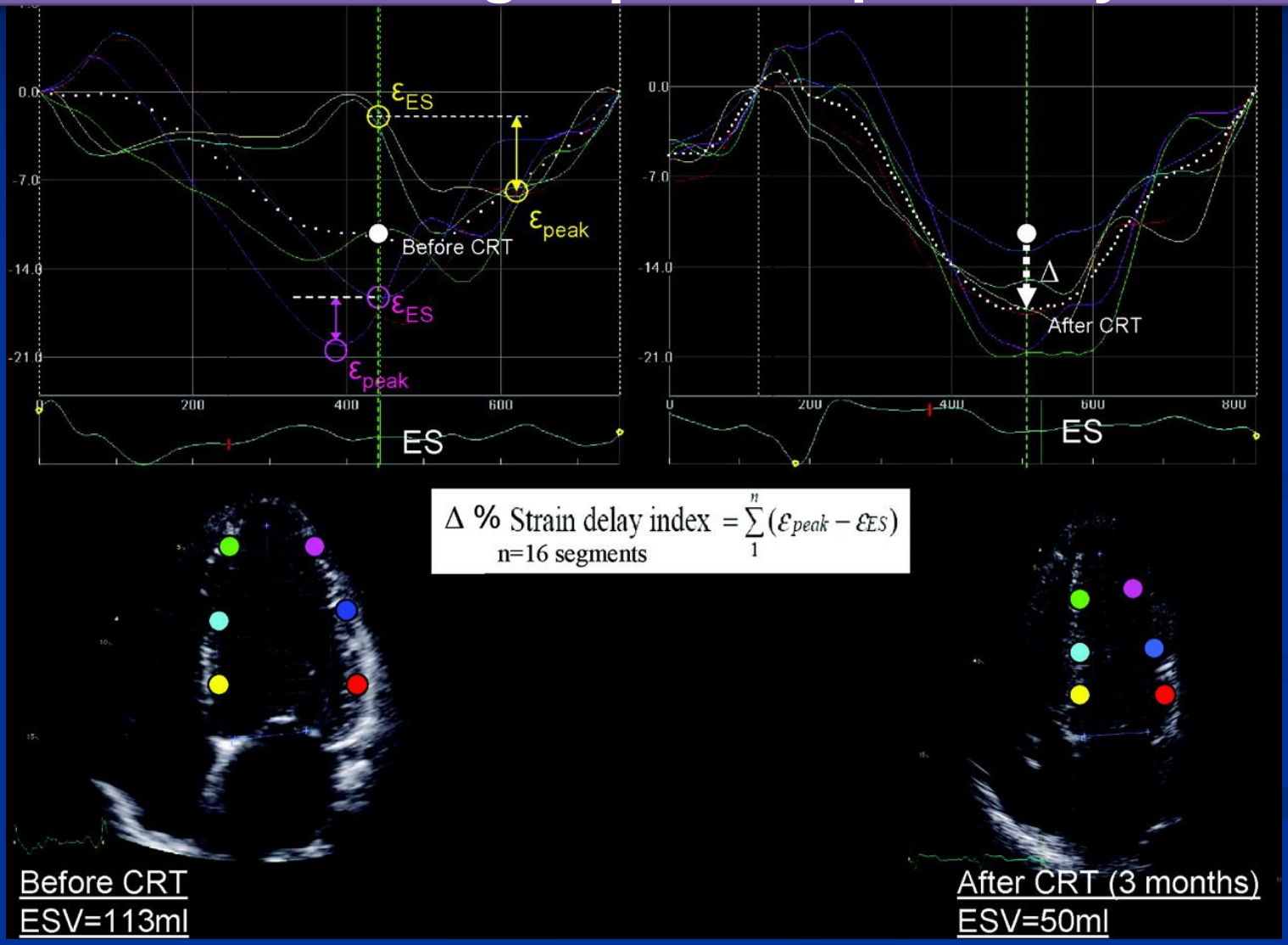


De Boeck, B. W.L. et al. Eur J Heart Fail 2009 11:863-871

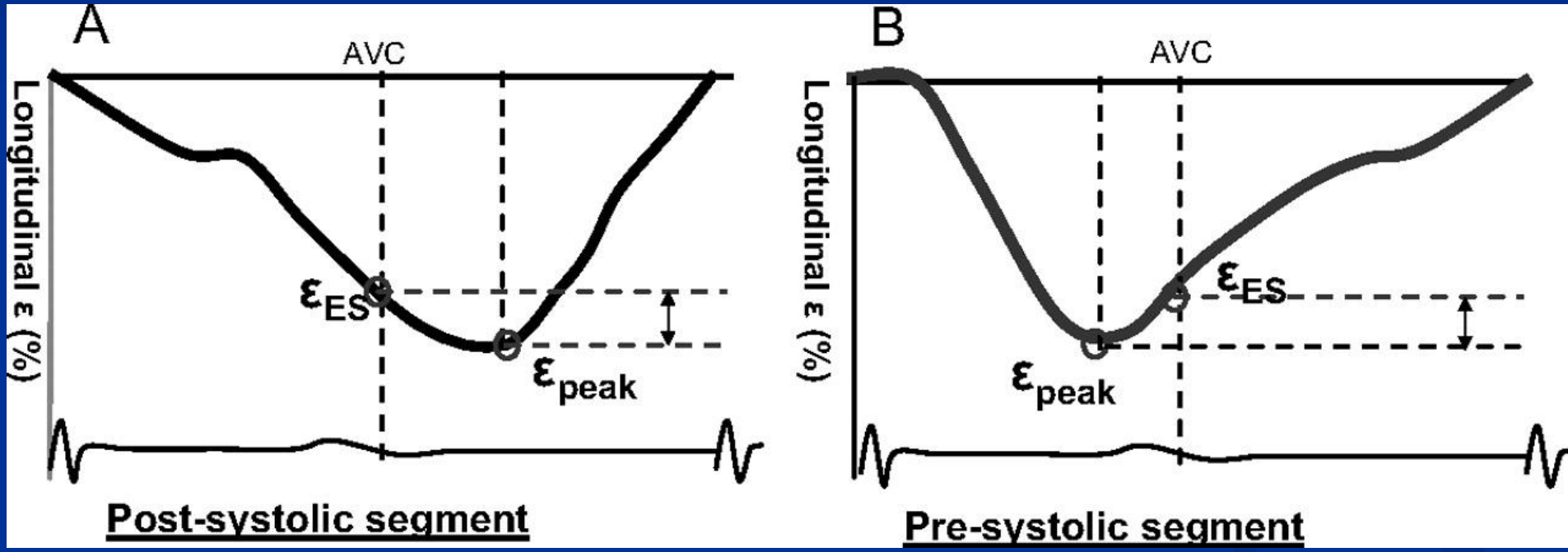
EUROPEAN JOURNAL OF HEART FAILURE


ANT
LAT
SEPT
POST
INF
3 1/s
-3 1/s
Bull's Eyes - SrL
0 ms
36 ms
72 ms
108 ms
144 ms
180 ms
216 ms
251 ms
287 ms
323 ms
359 ms
395 ms
431 ms
467 ms
503 ms
718 ms
754 ms
790 ms
826 ms
862 ms
Yellow = shortening,
blue = stretching,
green = no deformation/diastasis

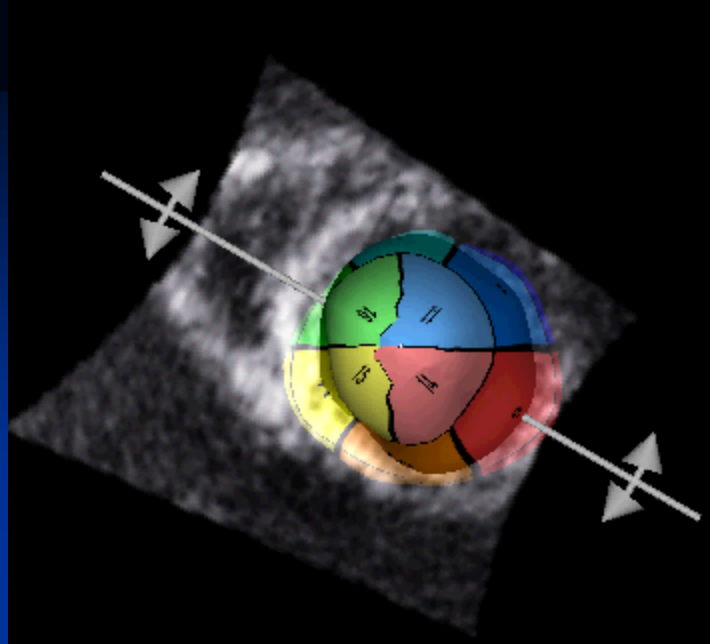
STRAIN DELAY INDEX:
somme de l'energie 'perdue' par le myocarde

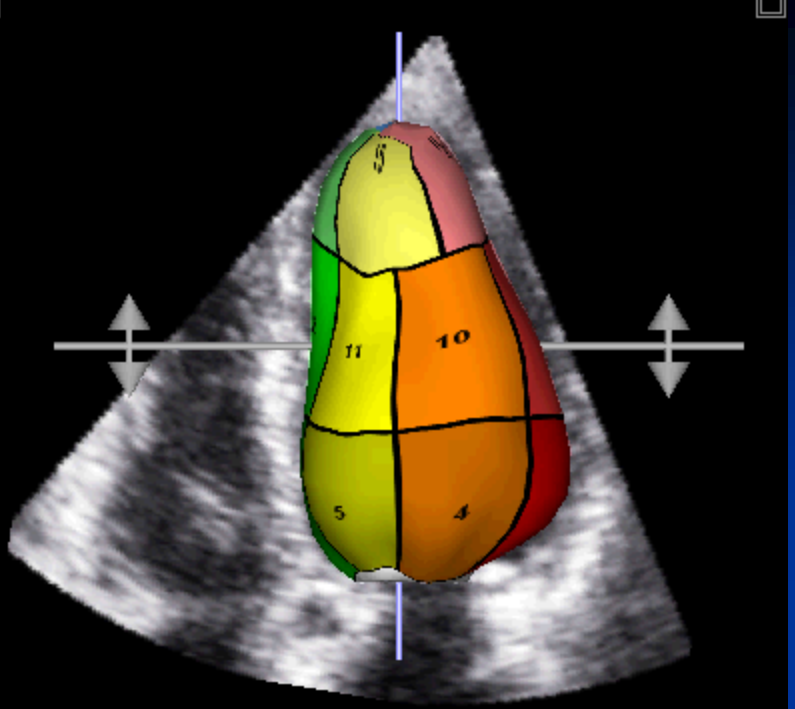


Lim, P. et al. Circulation 2008;118:1130-1137

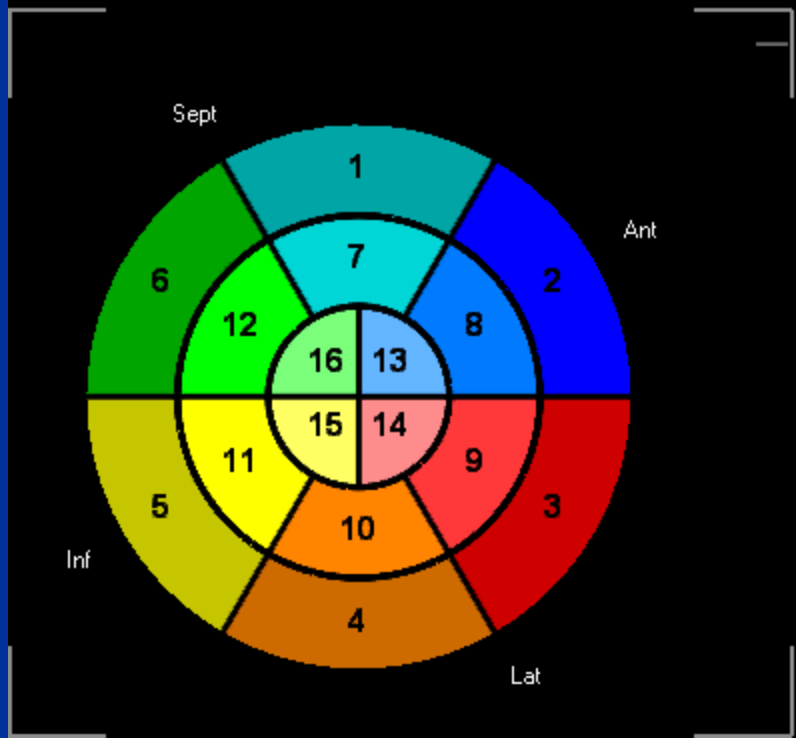


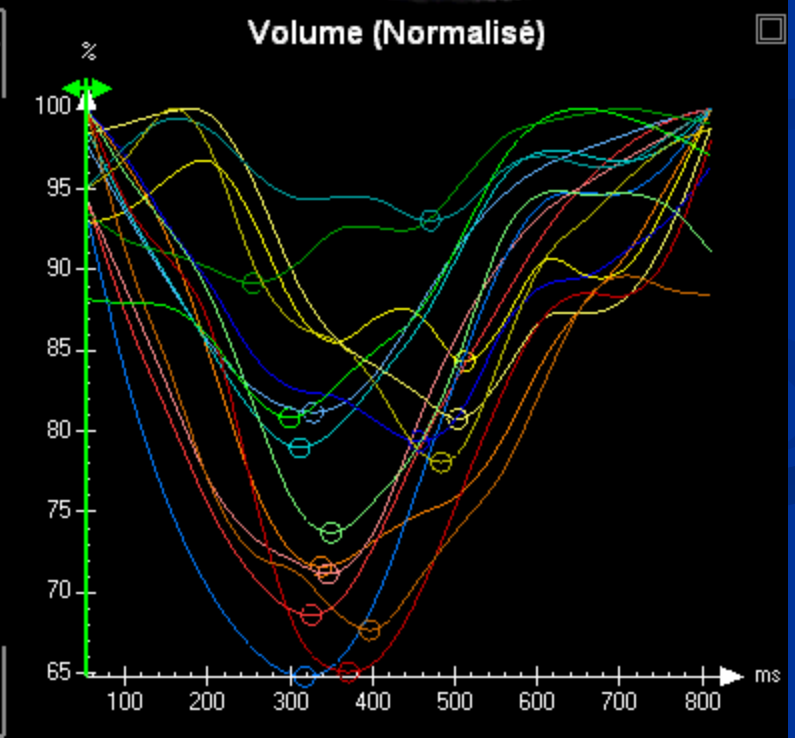
Lim, P. et al. Circulation 2008;118:1130-1137

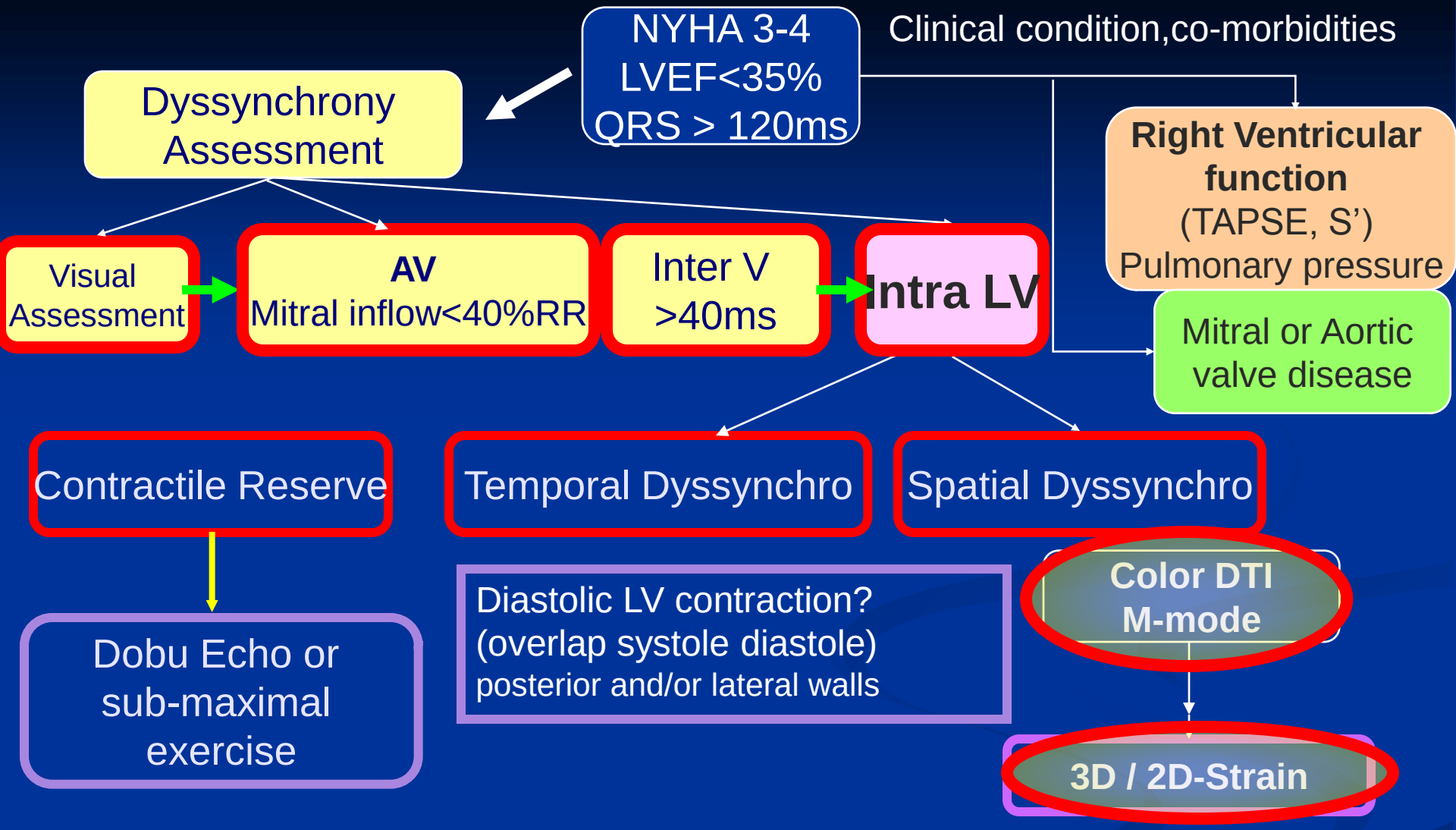




Volume (Normalisé)







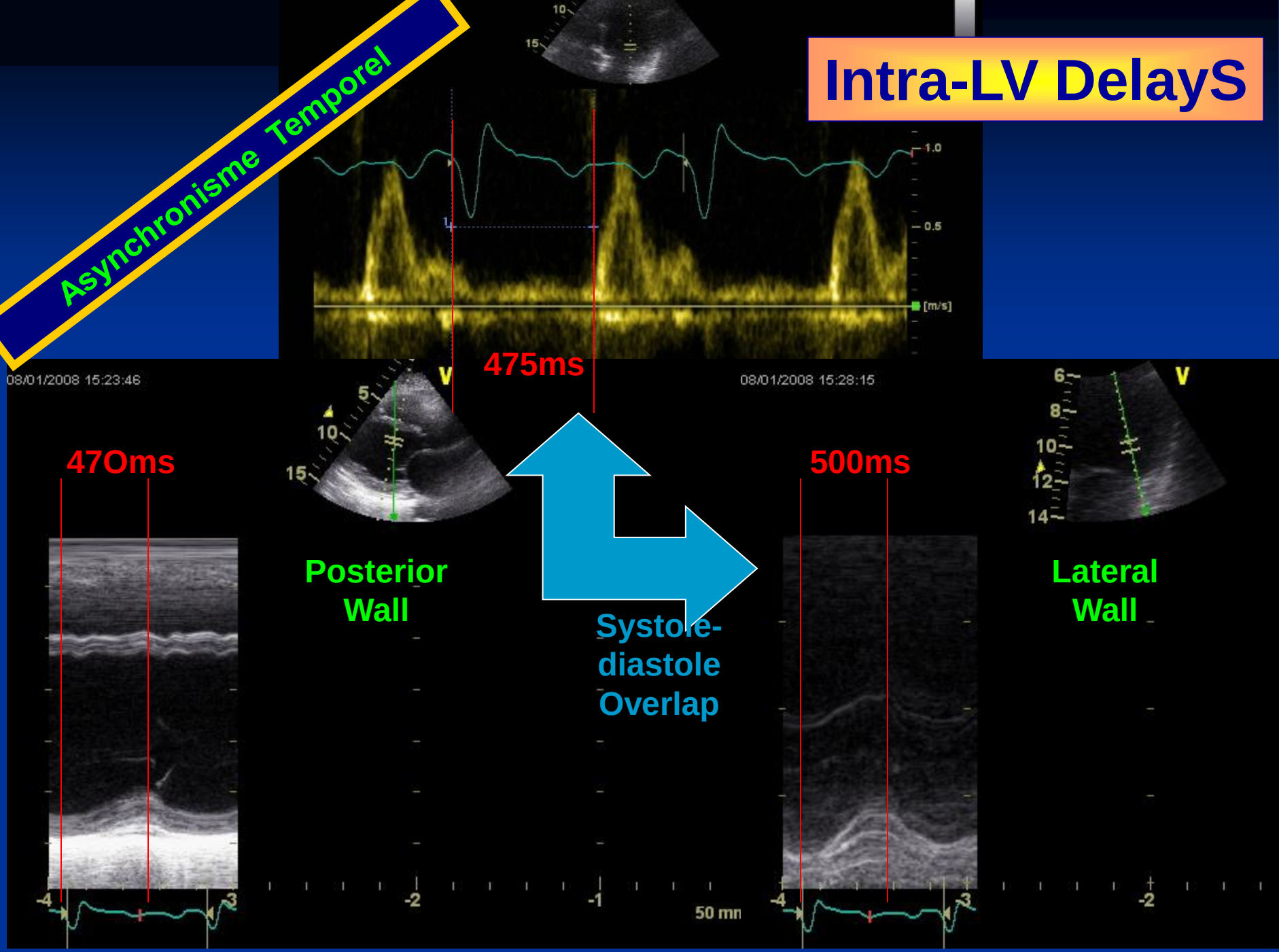
Post-implantation echocardiography is requested to check for the quality of the ressynchronization (especially AV one)

Radial dyssynchrony assessment in parasternal short axis views and **longitudinal** in apical views

Donal et al. Arch Cardio-vasc Dis 2009

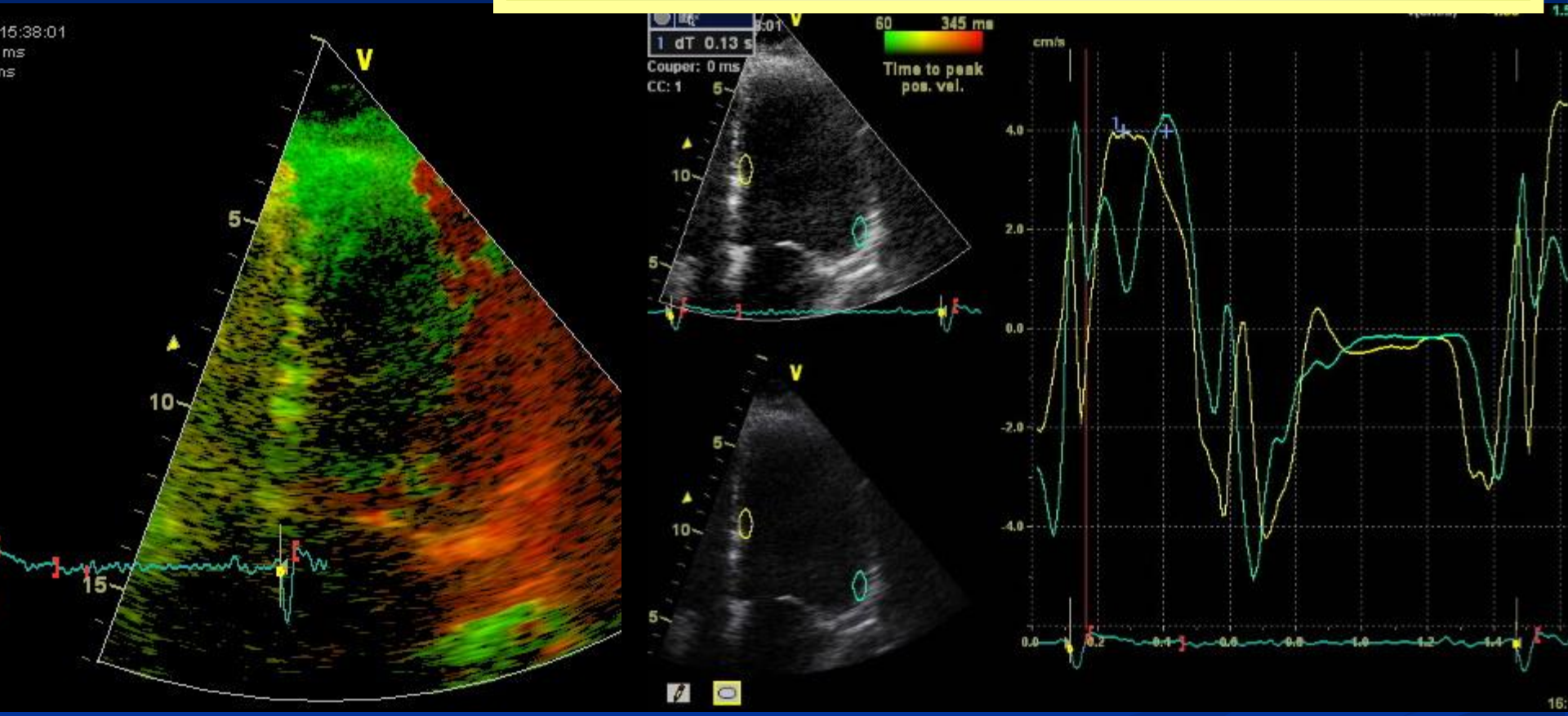
Intra-LV DelayS

Asynchronisme Temporel



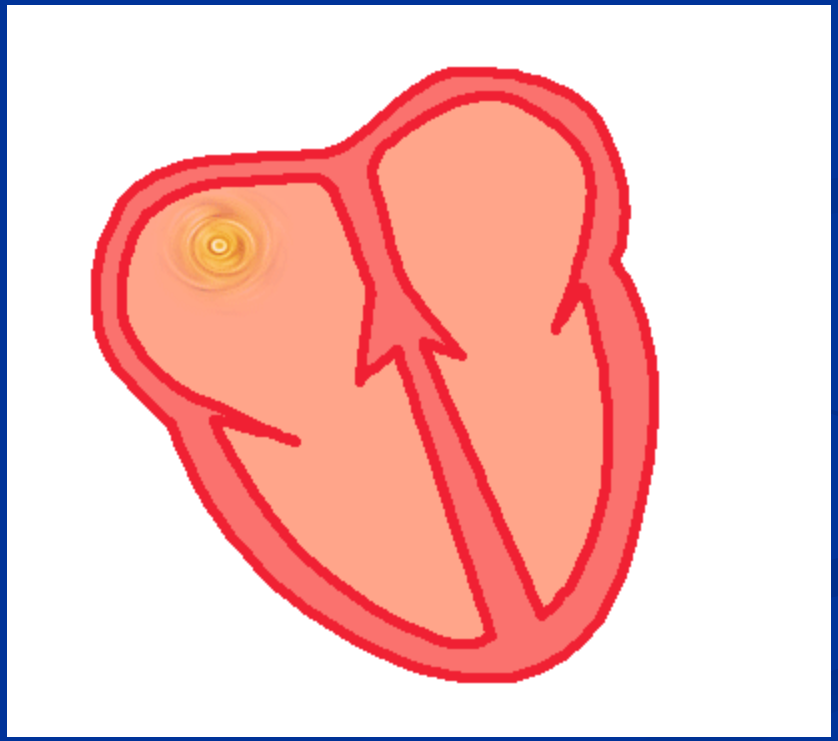
EchoCRT

<u>QRS < 120ms</u>; Asynchronisme intra V avec retard de la paroi lateral, ici de 130ms selon les courbes de vitesses de déplacement longitudinale du septum et de la paroi latérale



TSI: tissue synchronization imaging: colorant en rouge les segments se déplacant après la fermeture de la valve aortique (ici la paroi latérale VG)

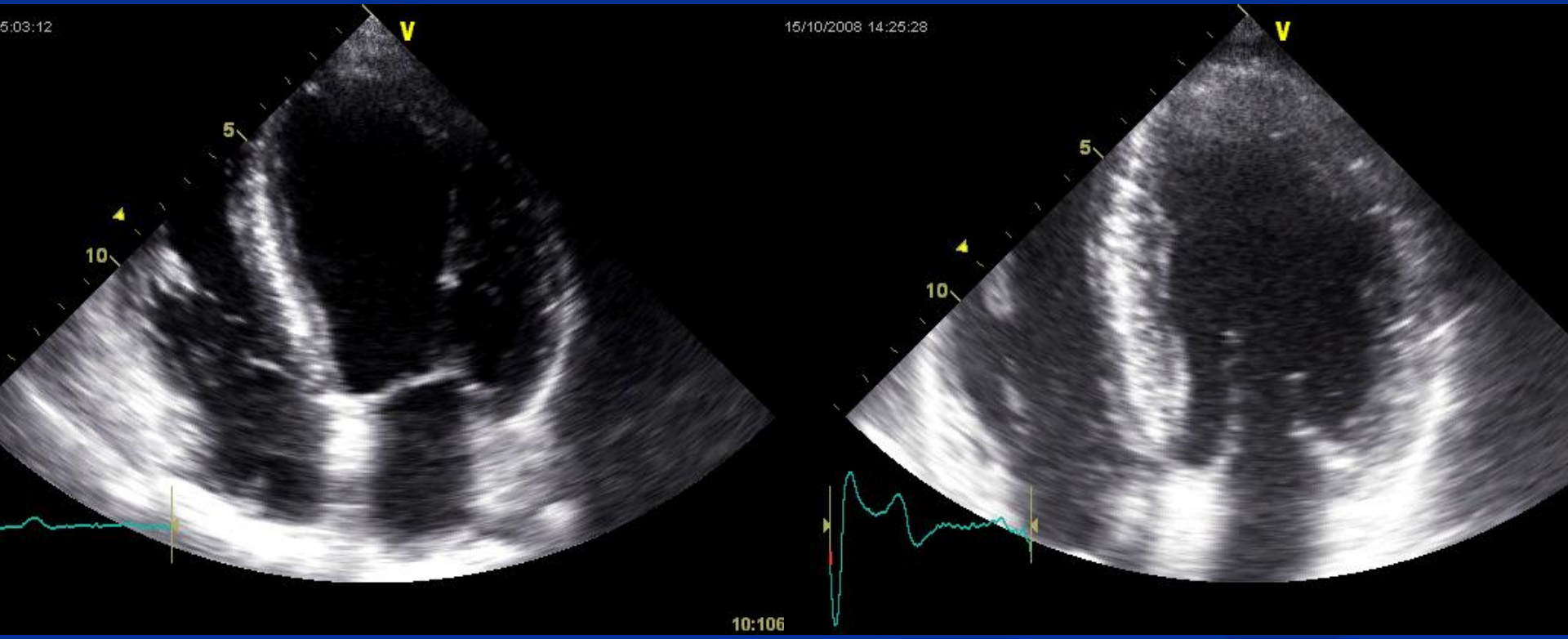
Suivi du patient après CRT



Remodelage VG

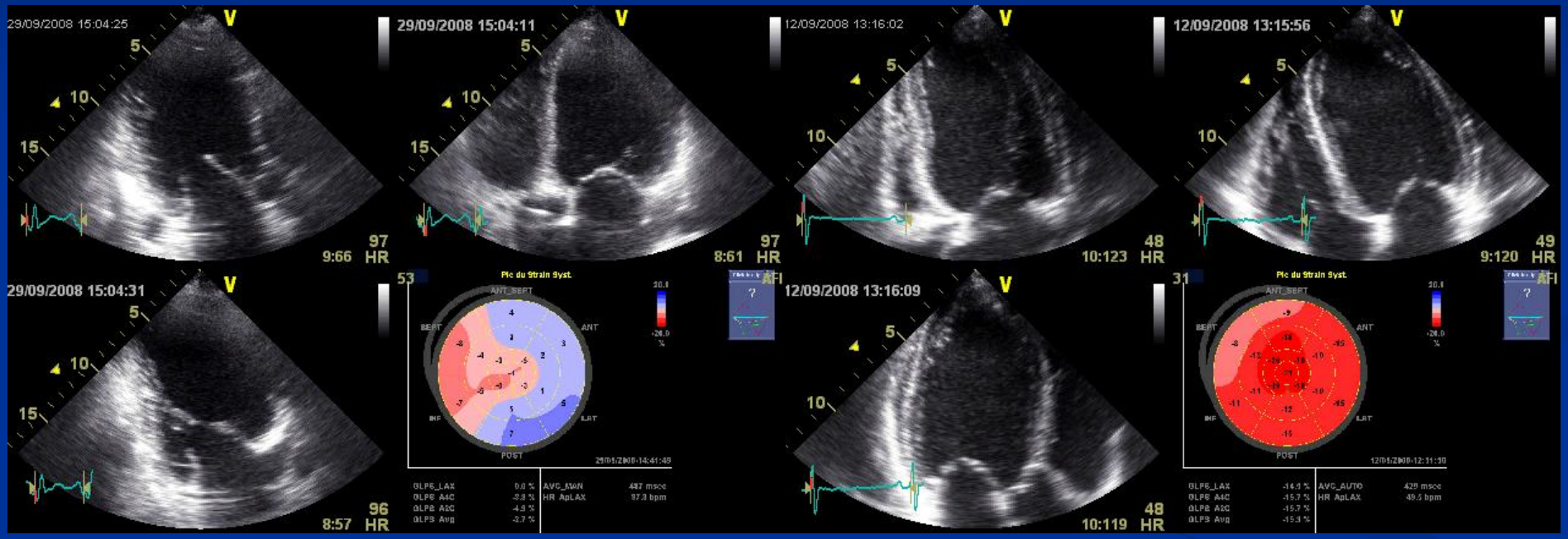
avant

à 3-mois



Par exemple, suivi de CRT

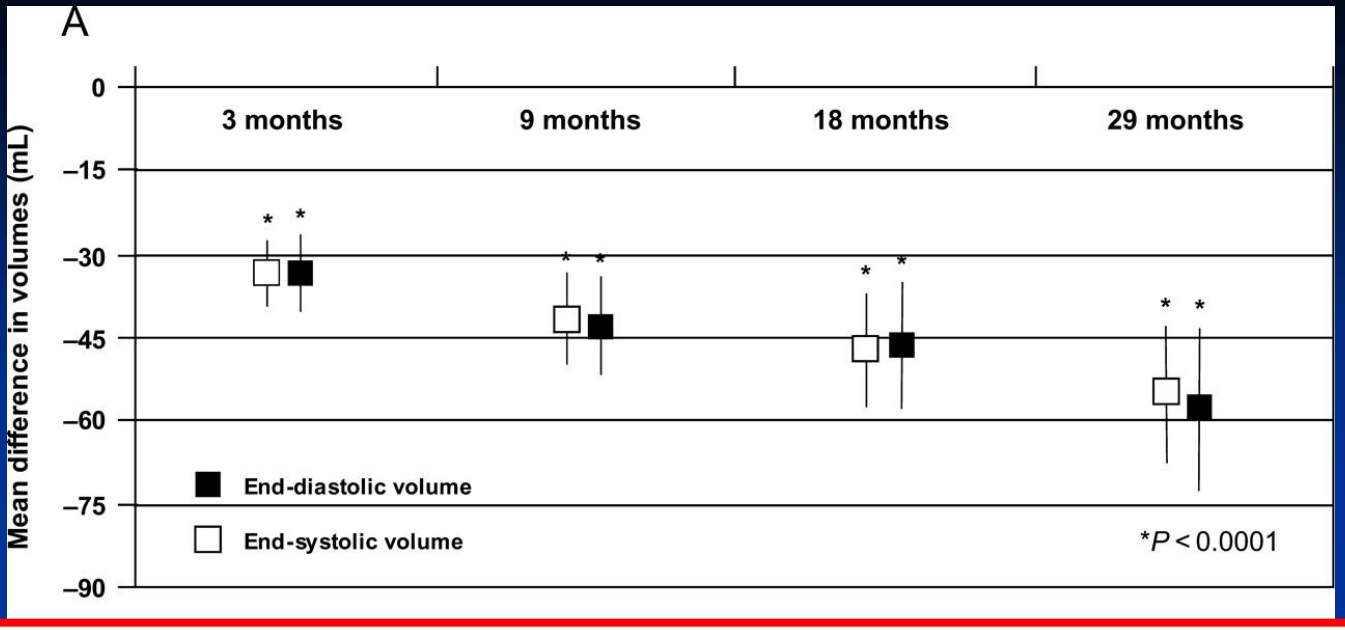
Strain (Déformation) Longitudinale Globale



pre *6-mois*

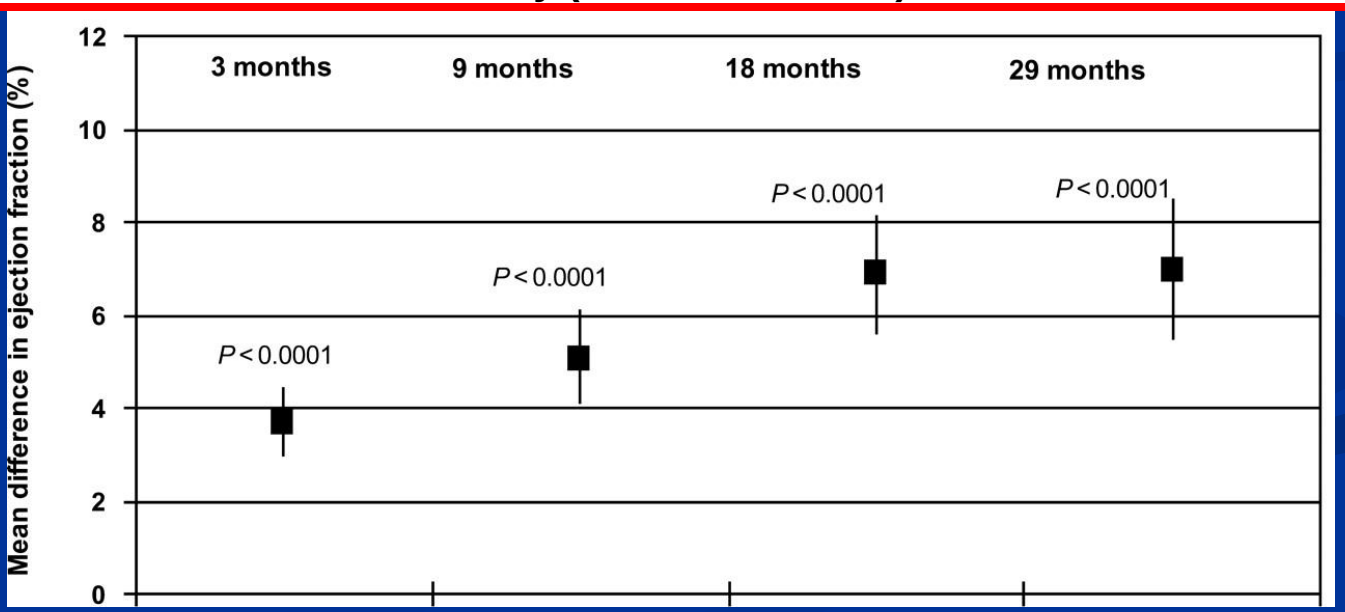
REMODELAGE

LV-volumes



Difference in end-diastolic and end-systolic volumes and ejection fraction at 3, 9, 18 months and the end of the study (mean 29 months)

LV-EF

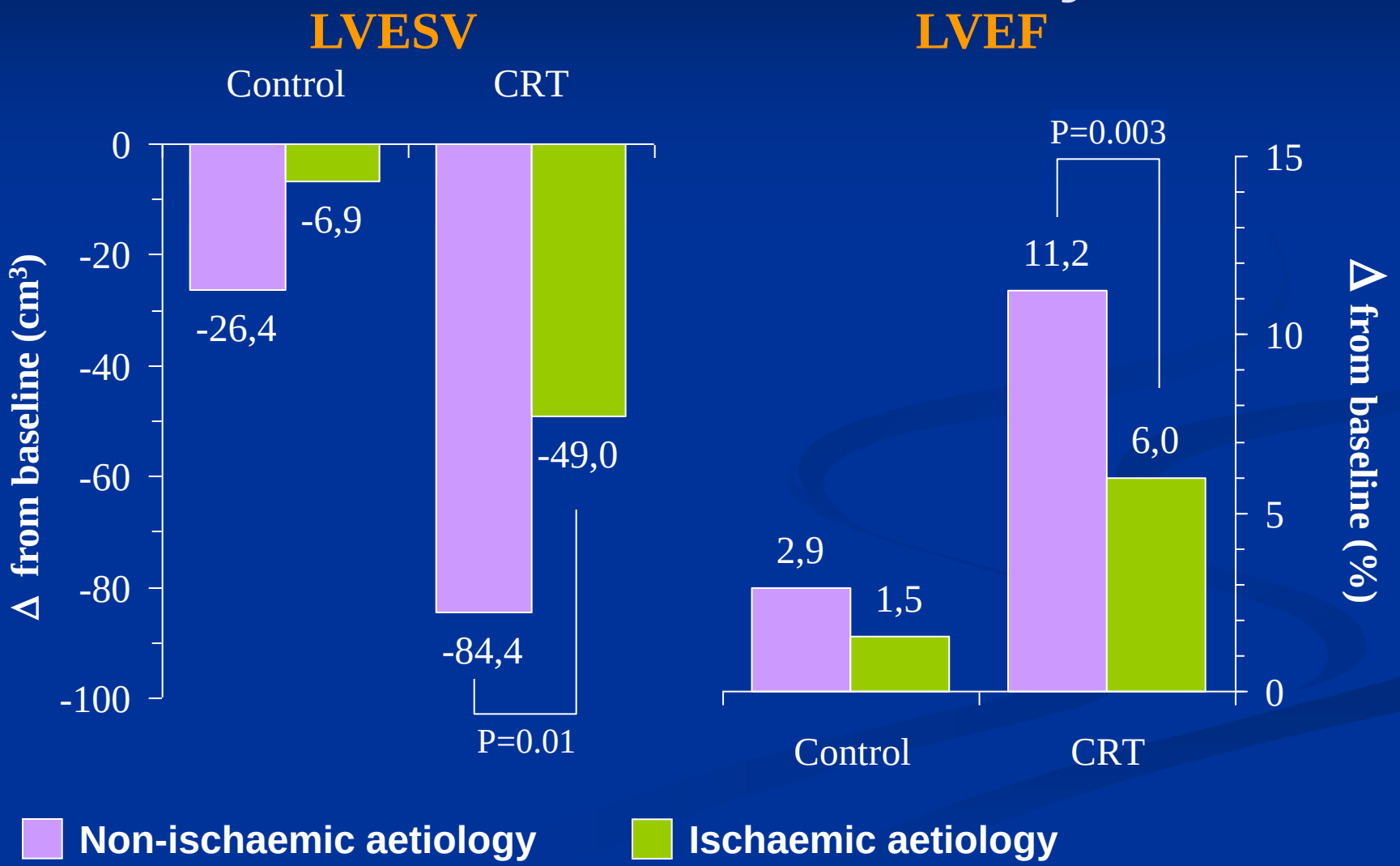


Ghio, S. et al. Eur J Heart Fail 2009 11:480-488

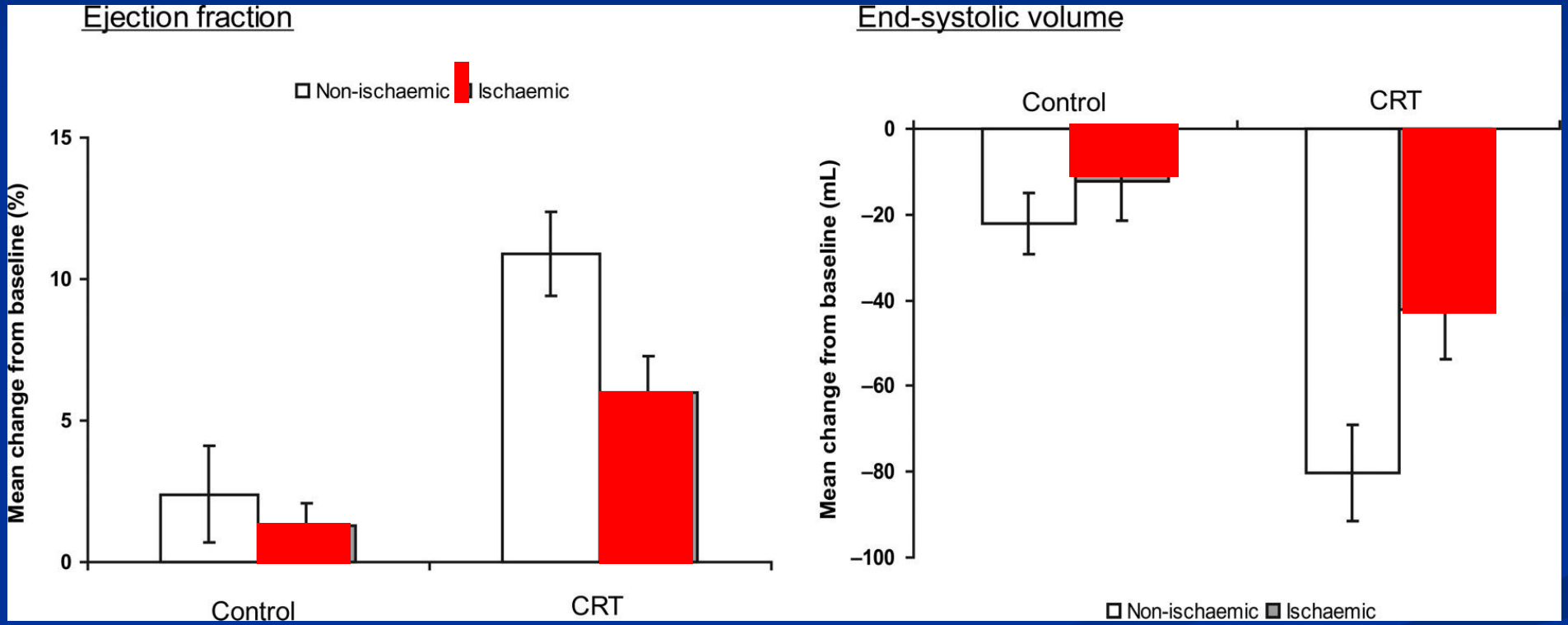
! Points Particuliers !

Problèmes de la cardiopathie Ischémique

CARE-HF extended study

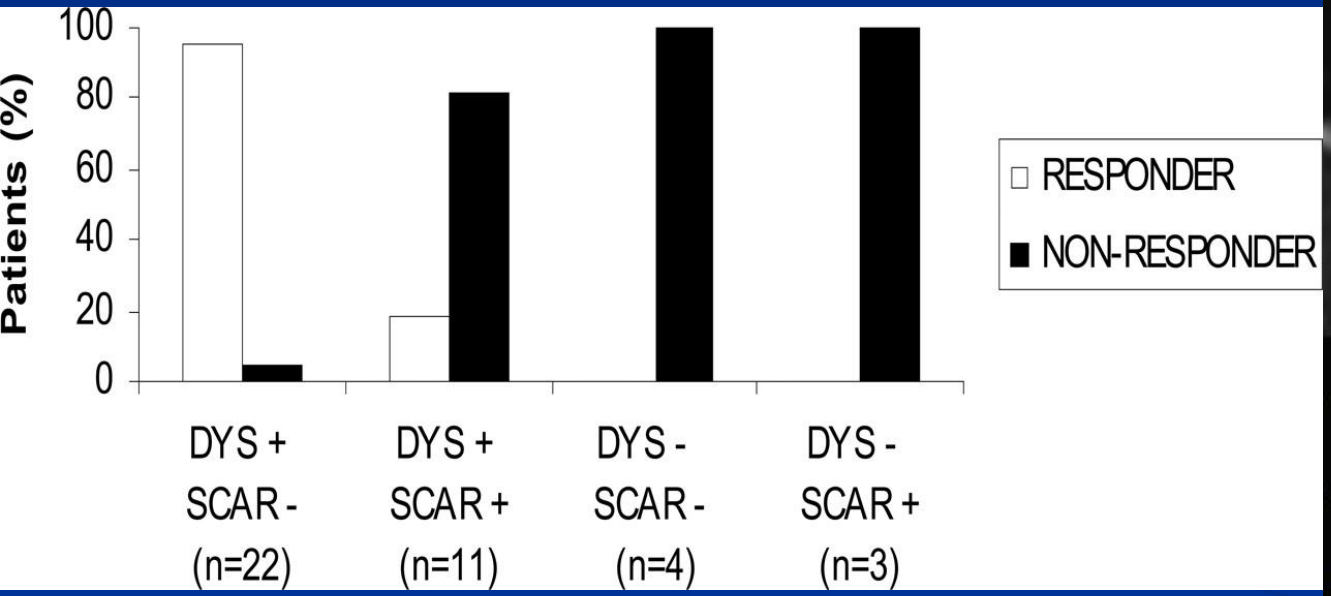


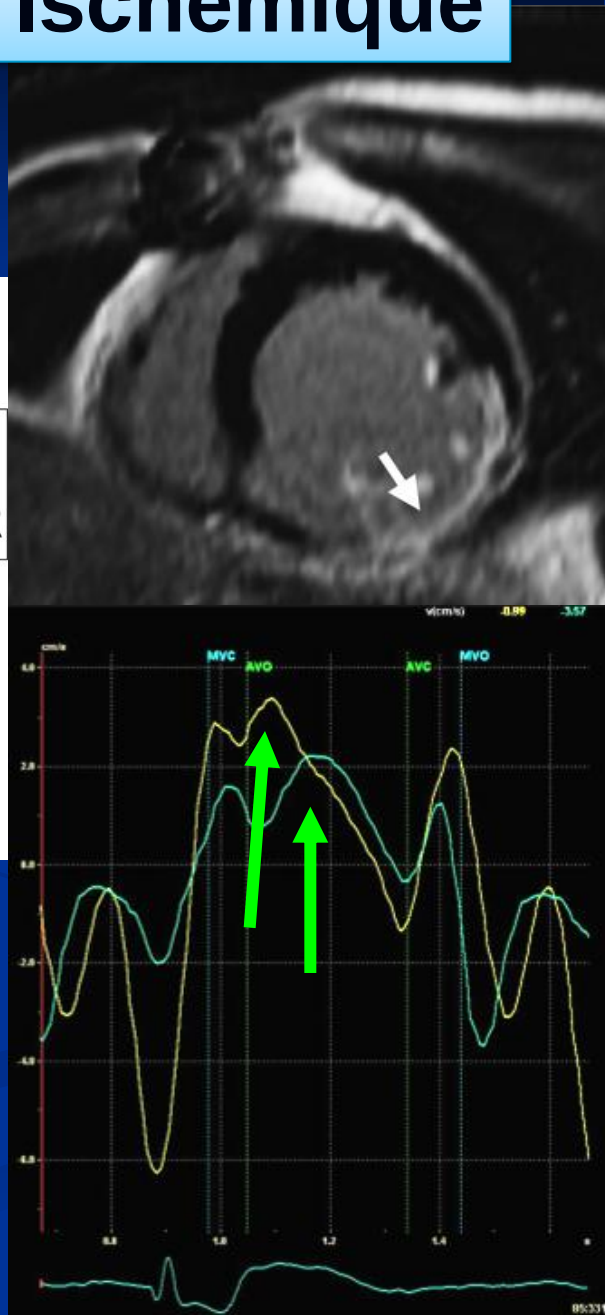
Problèmes de la cardiopathie Ischémique



Ghio, S. et al. Eur J Heart Fail 2009 11:480-488

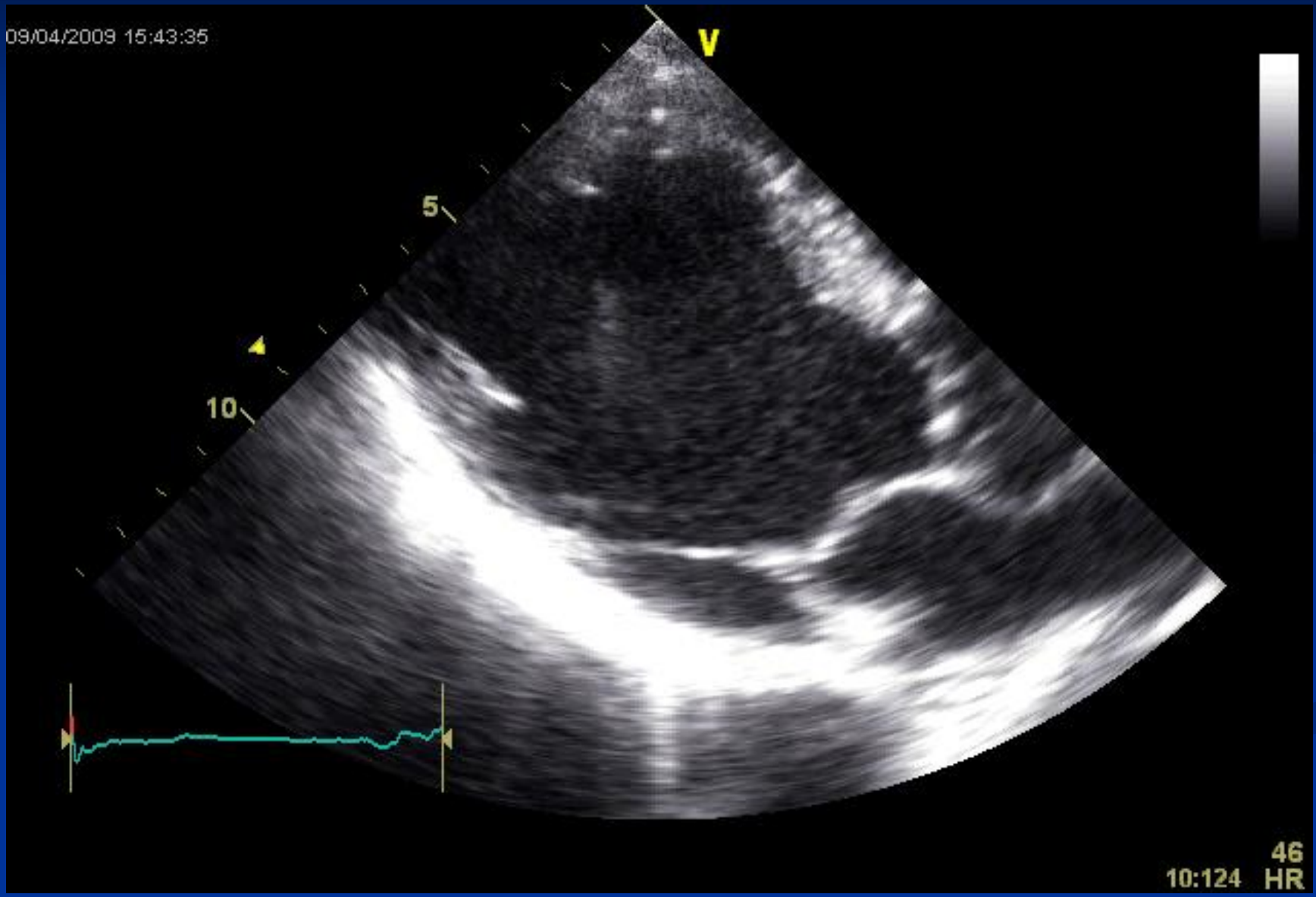
Problèmes de la cardiopathie Ischémique

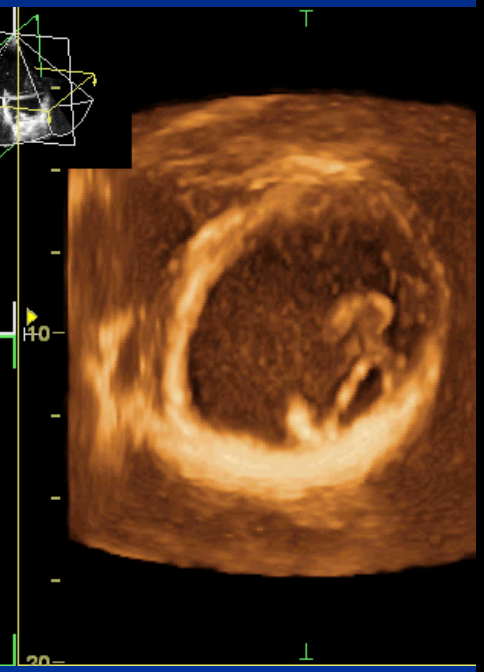


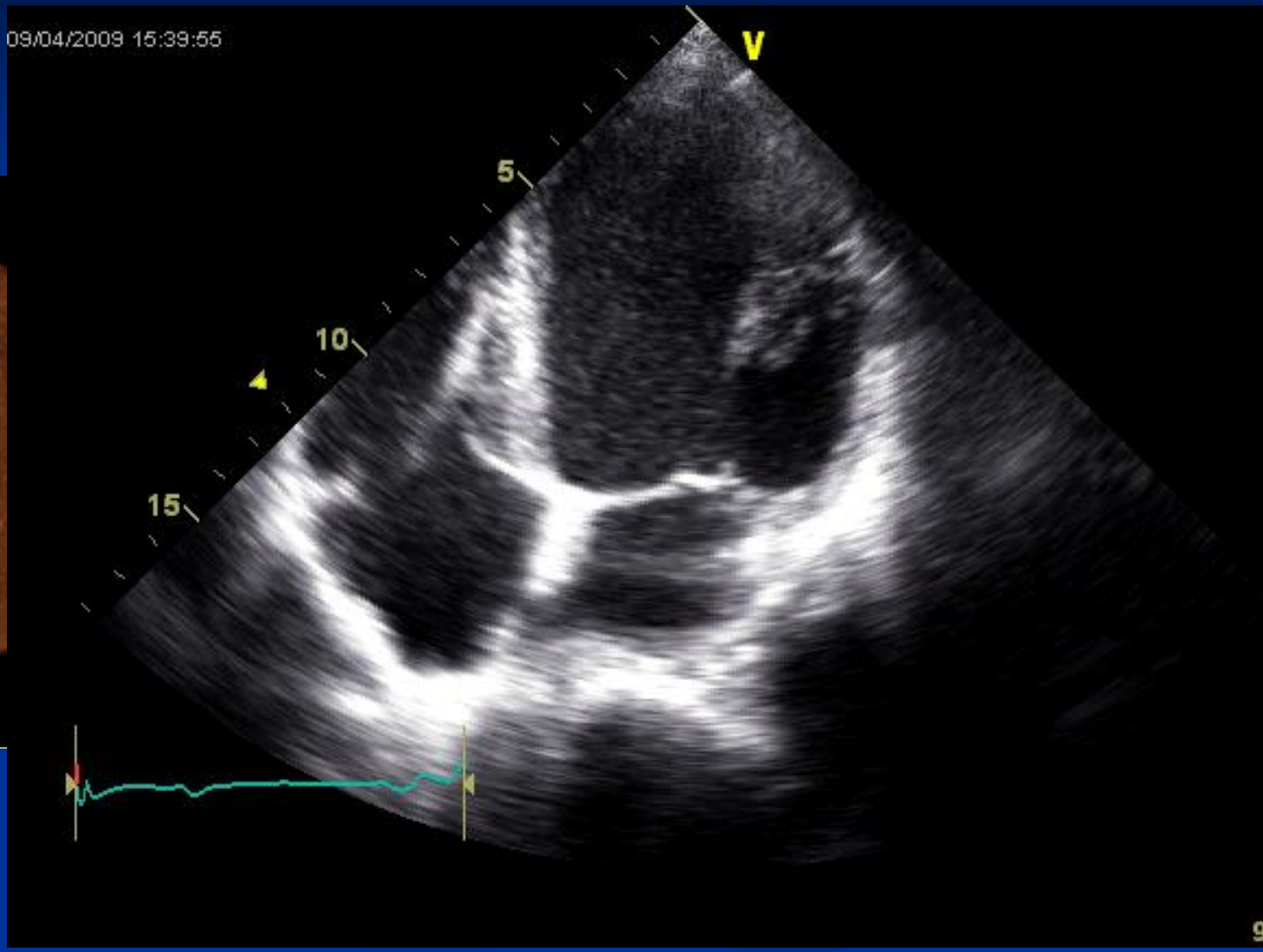


Bleeker et al. Circulation 2006;113:969-976
Cesari, Donal et al. AMC 2007

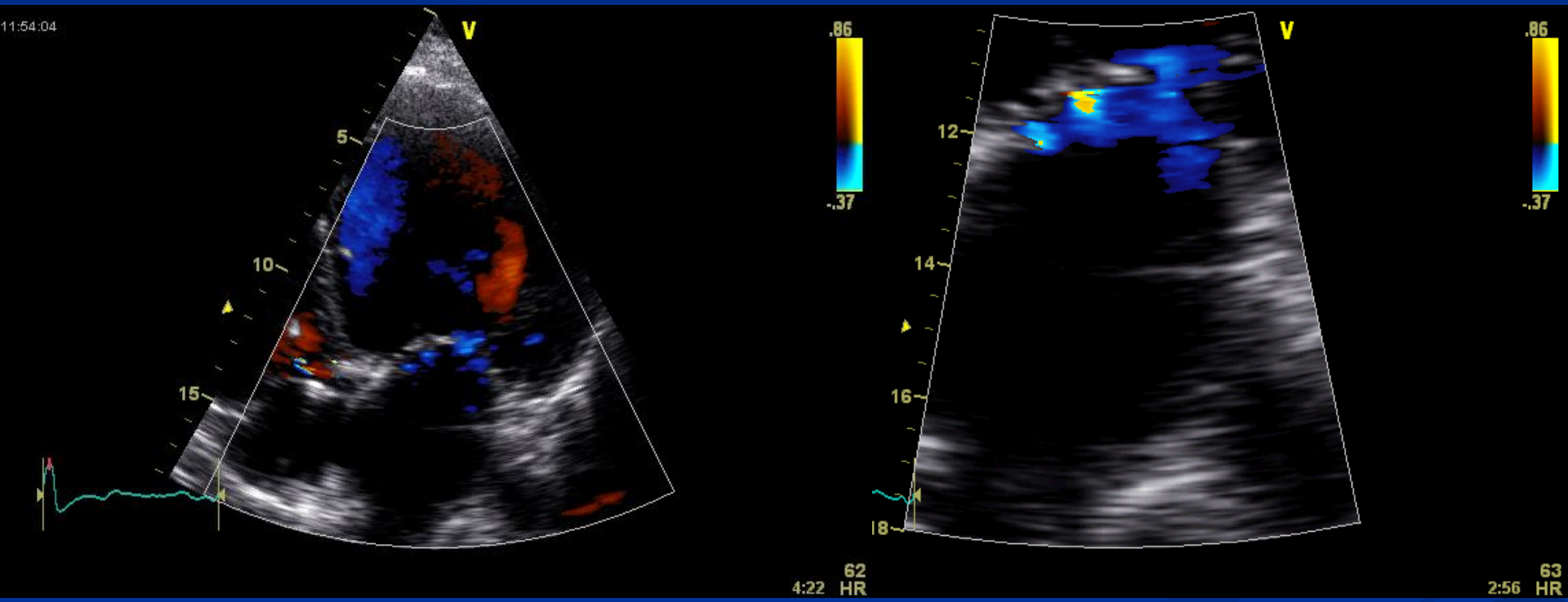
Problèmes de la cardiopathie Ischémique



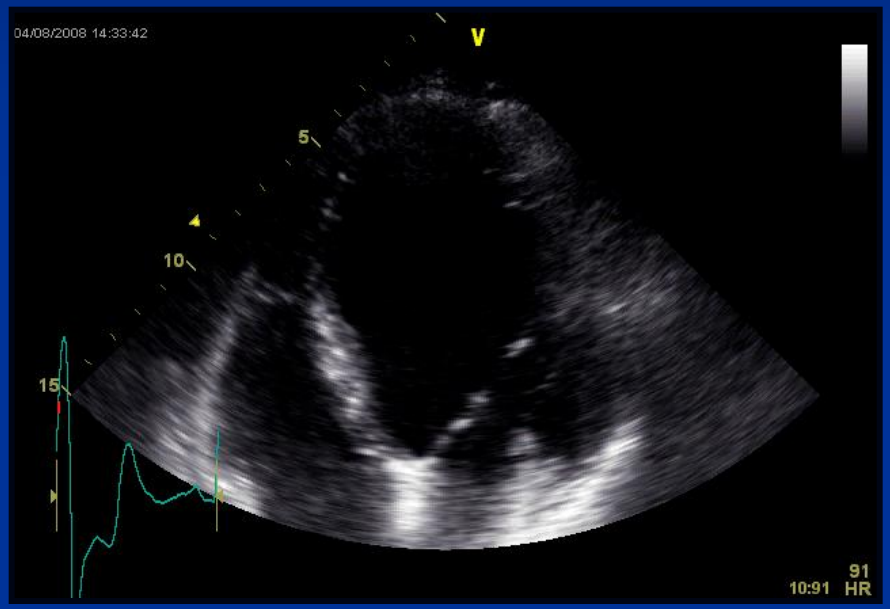


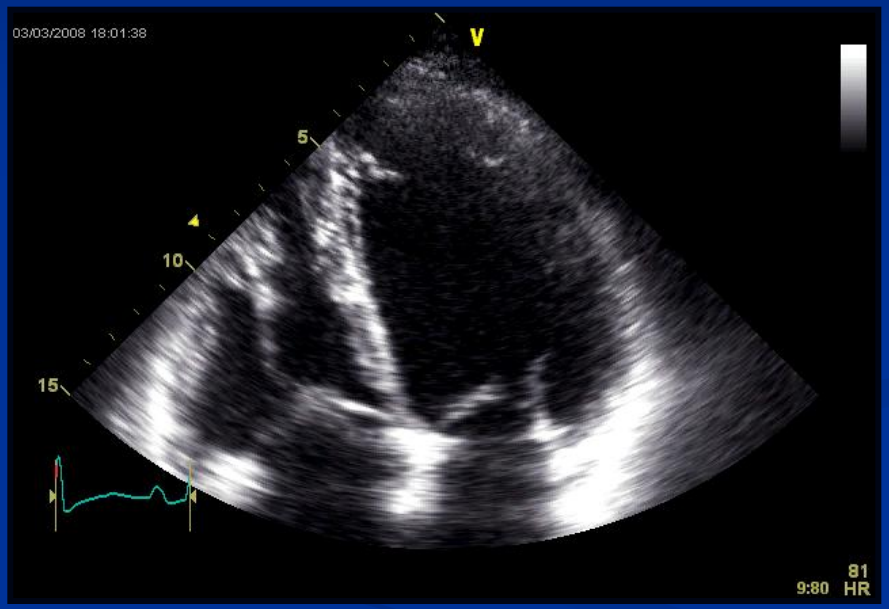

09/04/2009 15:39:55
V
5
10
15

Valvulopathies et Cardiomyopathies



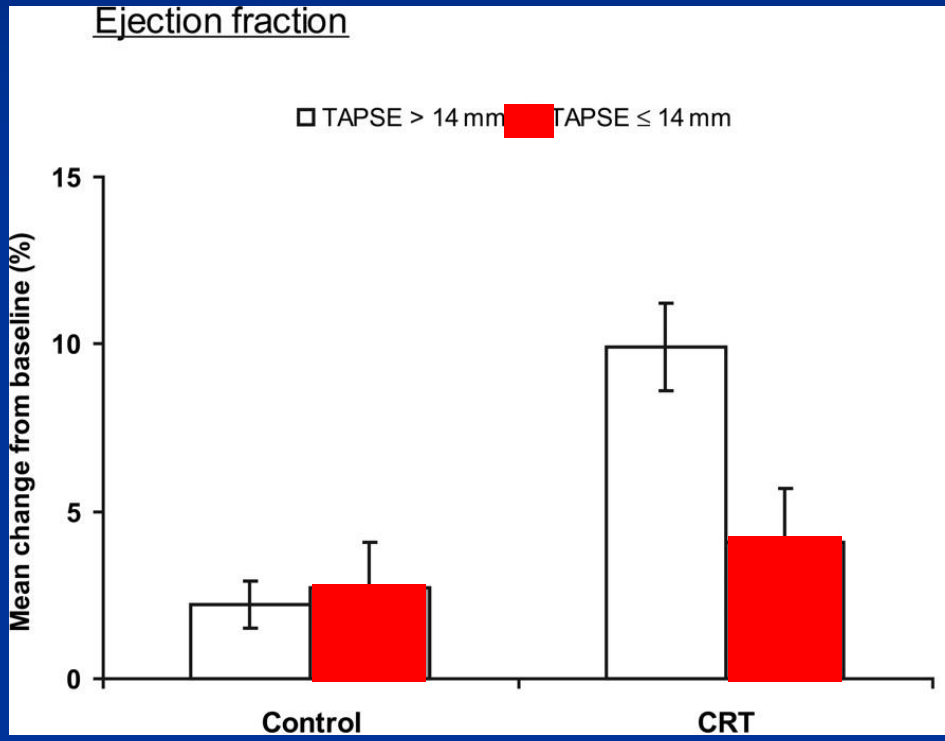
Importance du VD

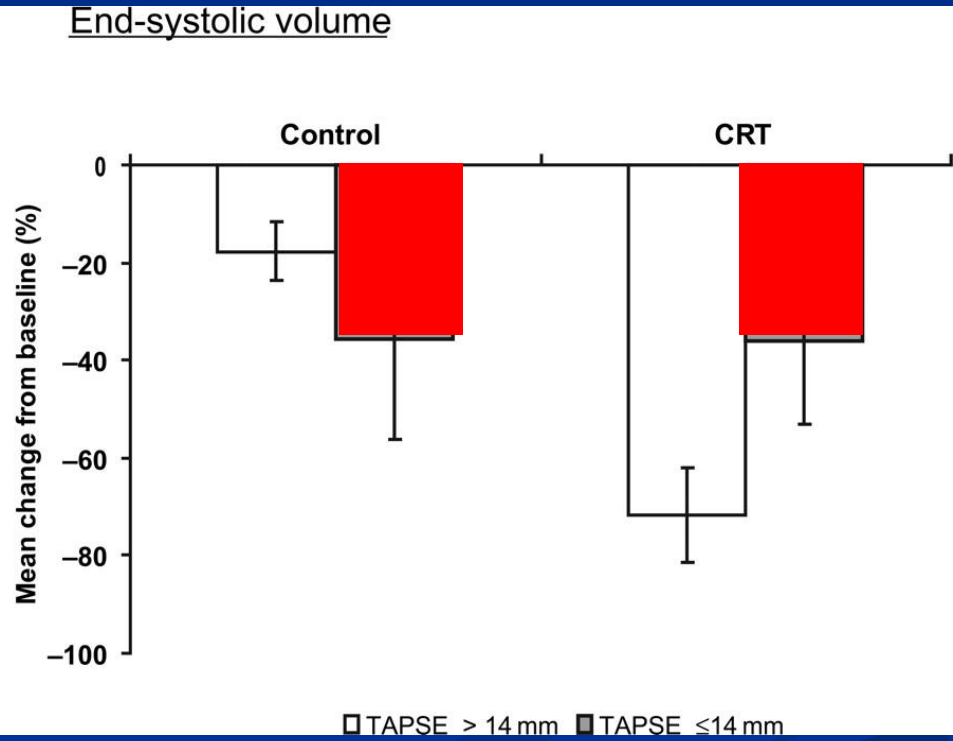




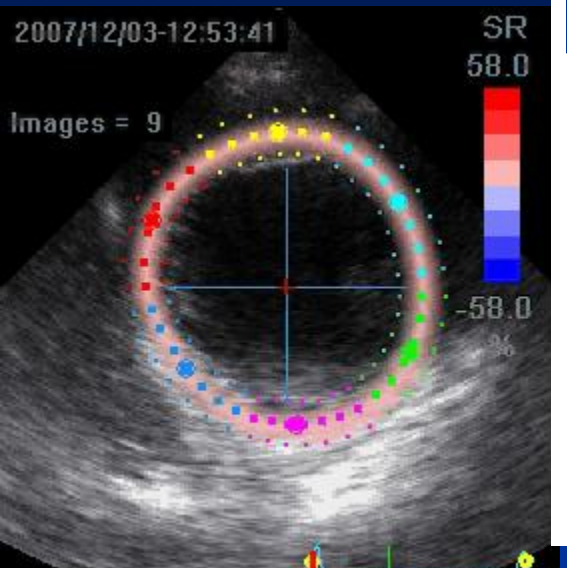
Ghio, S. et al. Eur J Heart Fail 2009 11:480-488
Donal et al. Arch Cardiovasc. 2008
Bernard, Donal et al Int Journal Cardiol (sous presse)

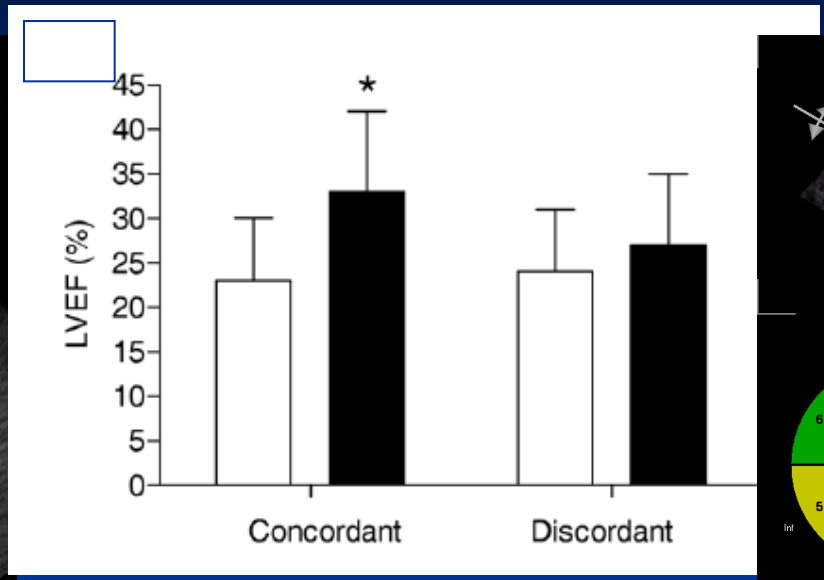
TAPSE <14mm : Mauvaise fonction VD

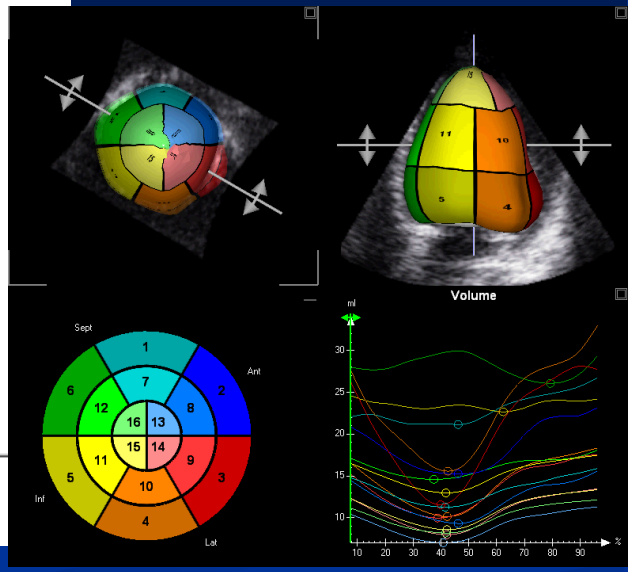


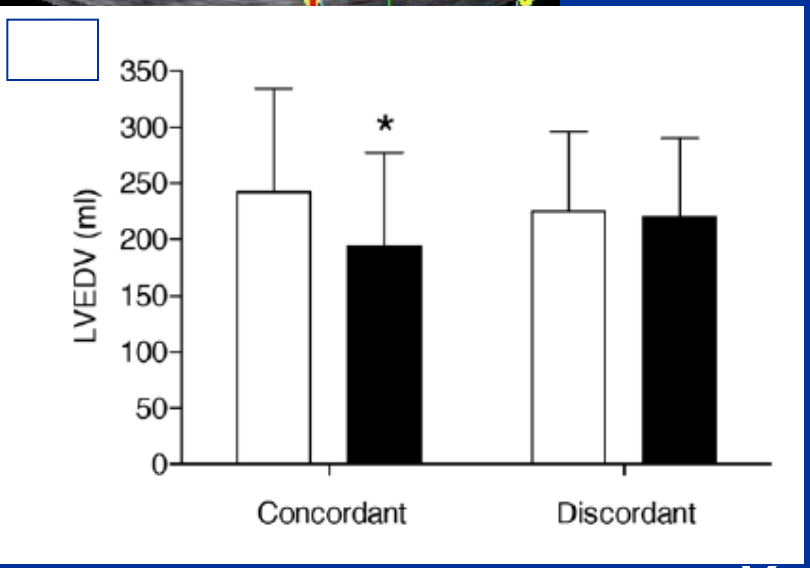


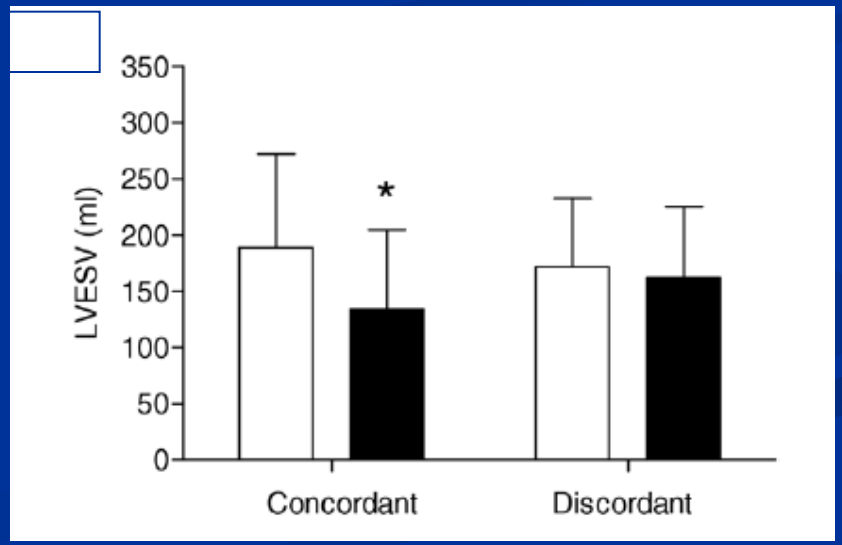
Bénéfice de l'optimisation des sondes





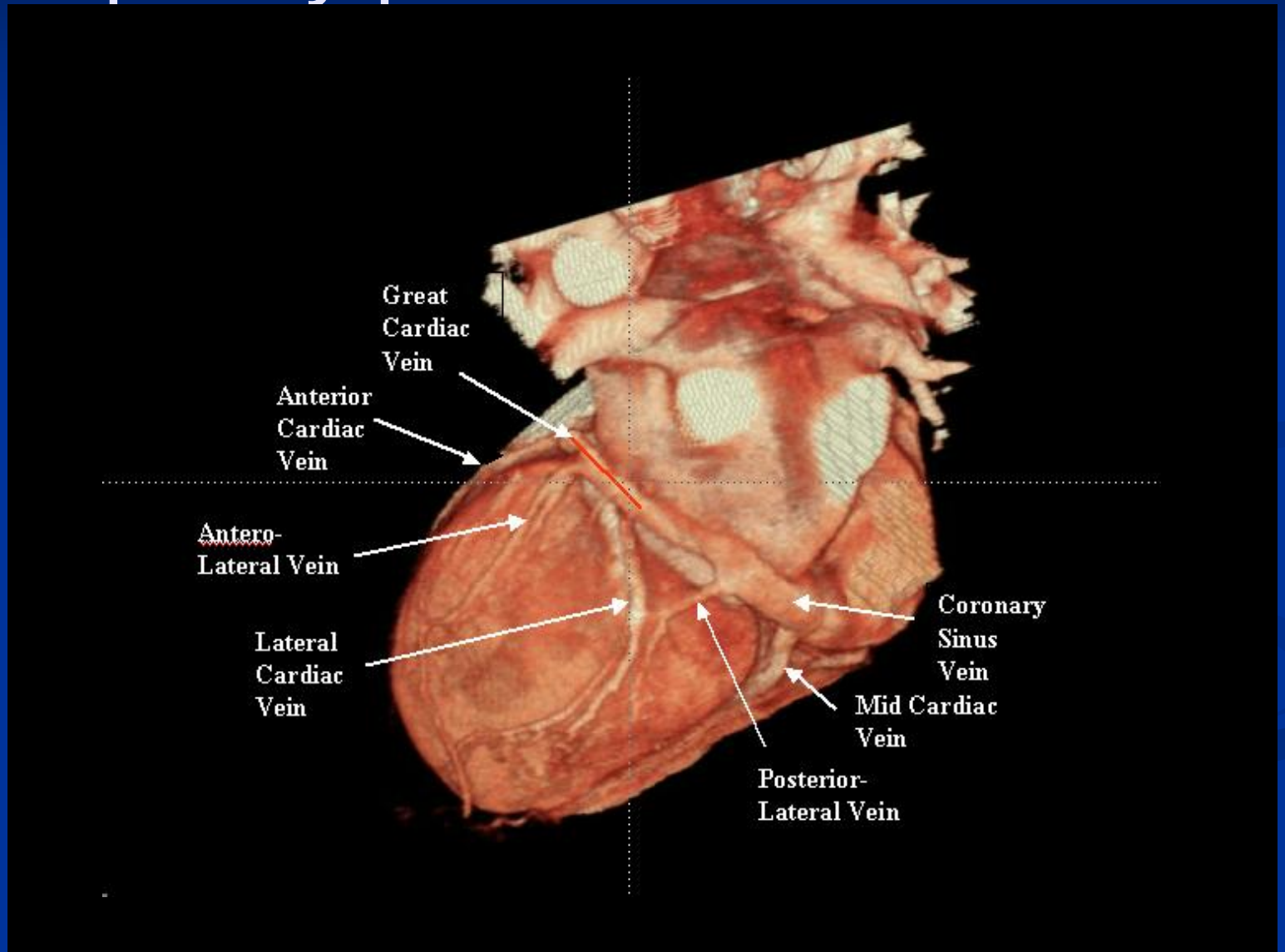






Ypenbrug. J Am Coll Cardiol 2008; 52: 1402-9

Le Territoire asynchrone et la veine pour y positionner la sonde

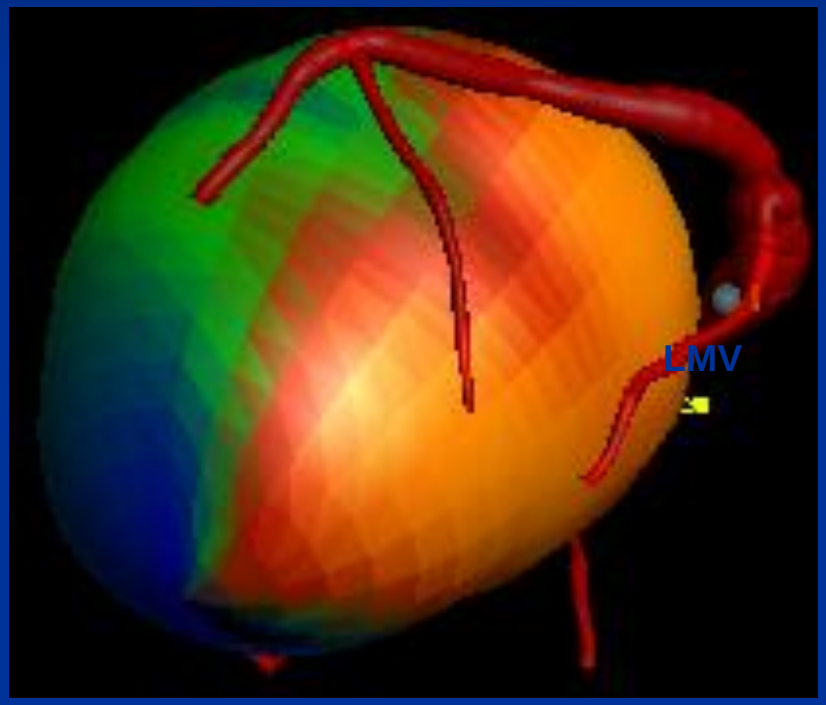


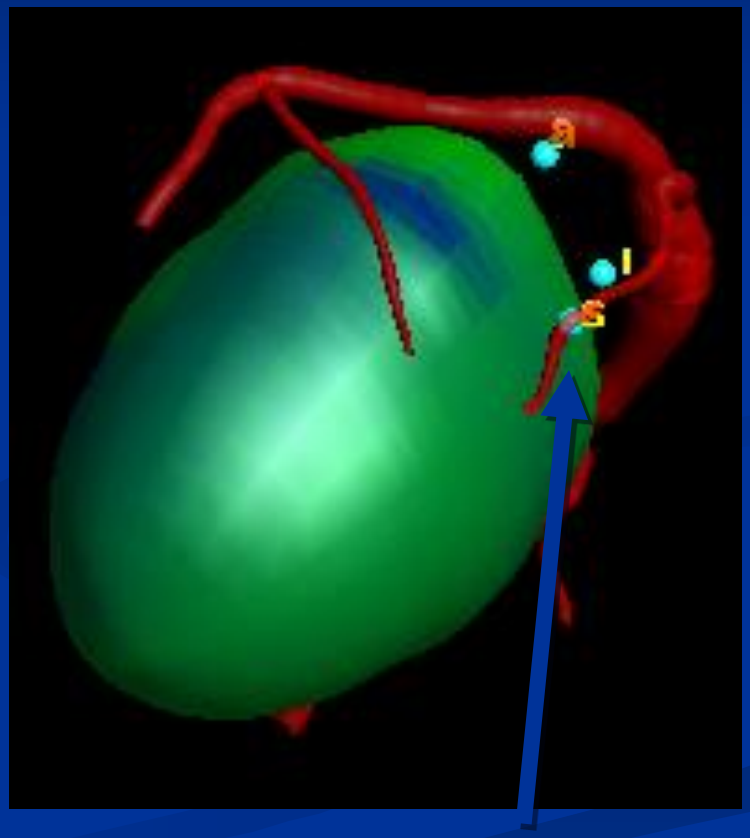
EARLY

BEFORE CRT

AFTER CRT

AIV



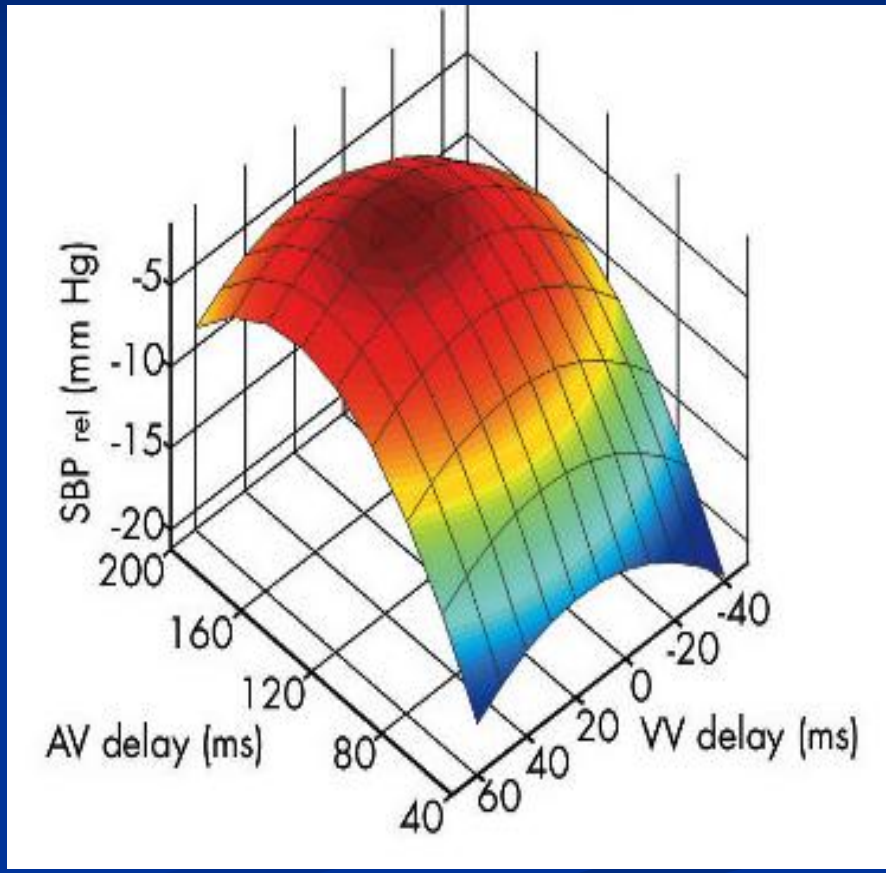


DELAYED

AIV, anterior inter-ventricular vein; LMV, lateral marginal vein;
DOTS: markers for registration; ARROW: LV lead position

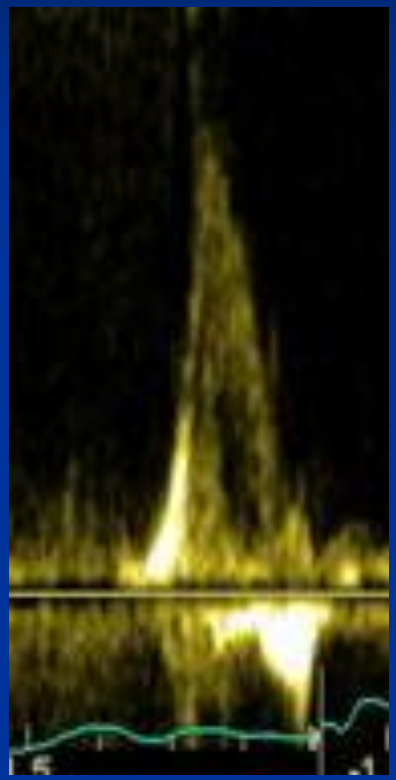
CRT et optimisation

- Configuration optimale de stimulation: propre à chaque patient (1)
- Plusieurs méthodes d'optimisation:
  - Echographiques
  - Non échographique
- Optimum prédit par chaque technique variable (2)
- Courbe parabolique de réponse hémodynamique aux changements de délai atrio ventriculaire (DAV) et inter ventriculaire (VV) (3)



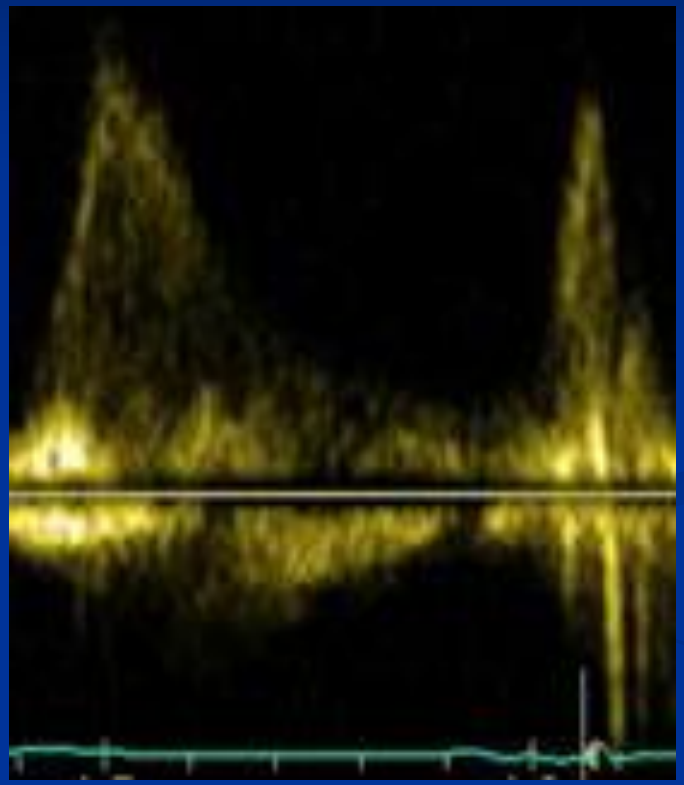
1. *Auricchio et al. EHJ 2008;29:2388-442*
2. *Zuber et al. Europace 2008;10:367-73*
3. *Whinnett et al. Heart 2006;92:1628-34*

La méthode itérative



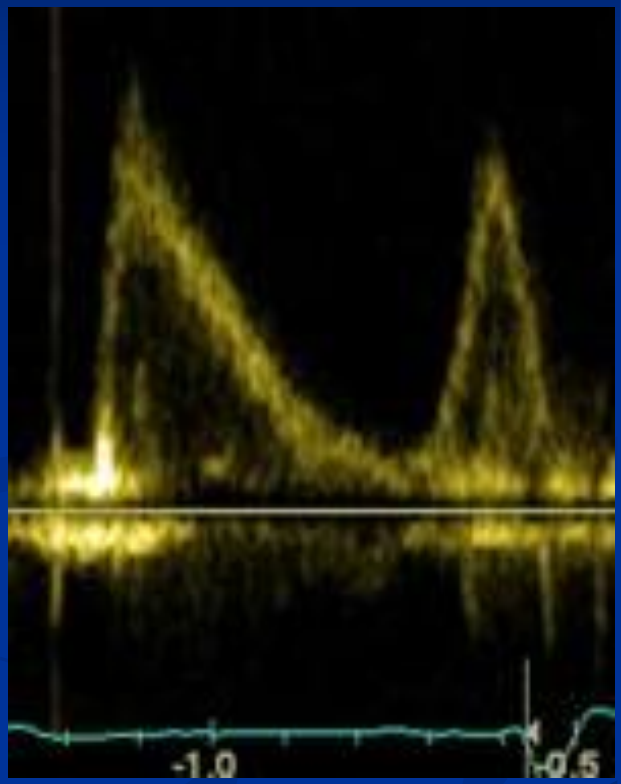
Long AV delay

(E and A fusion)



Decrease by 20 ms steps

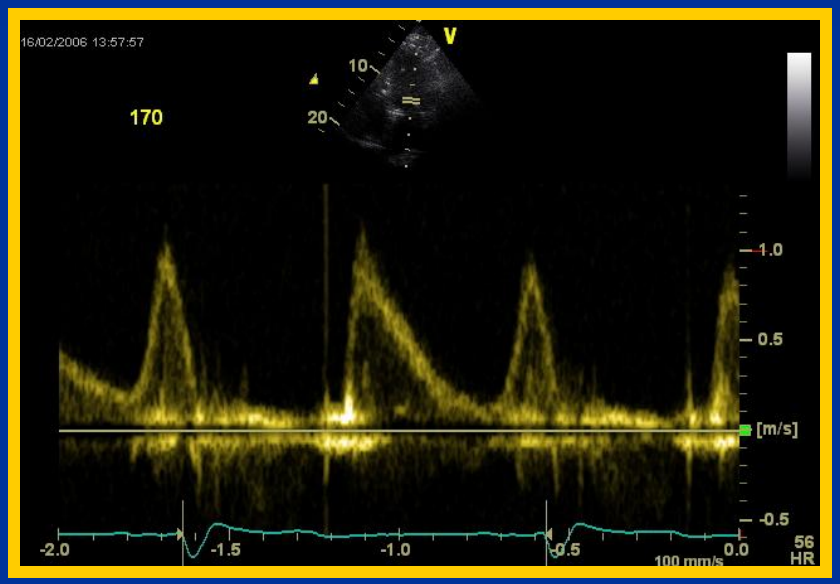
Too short: truncated A-vawe

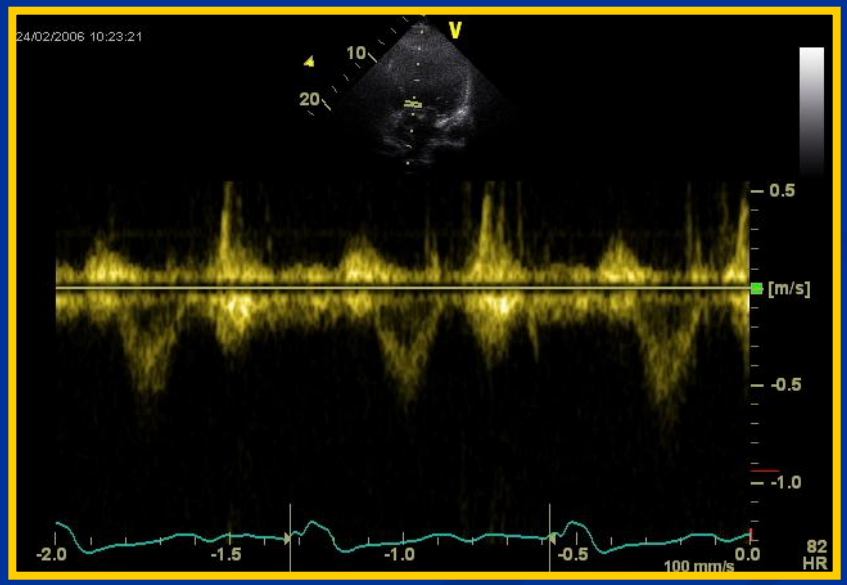


Optimal AV delay

LV filling > 40% RR cycle

Démarche "Pas à Pas"

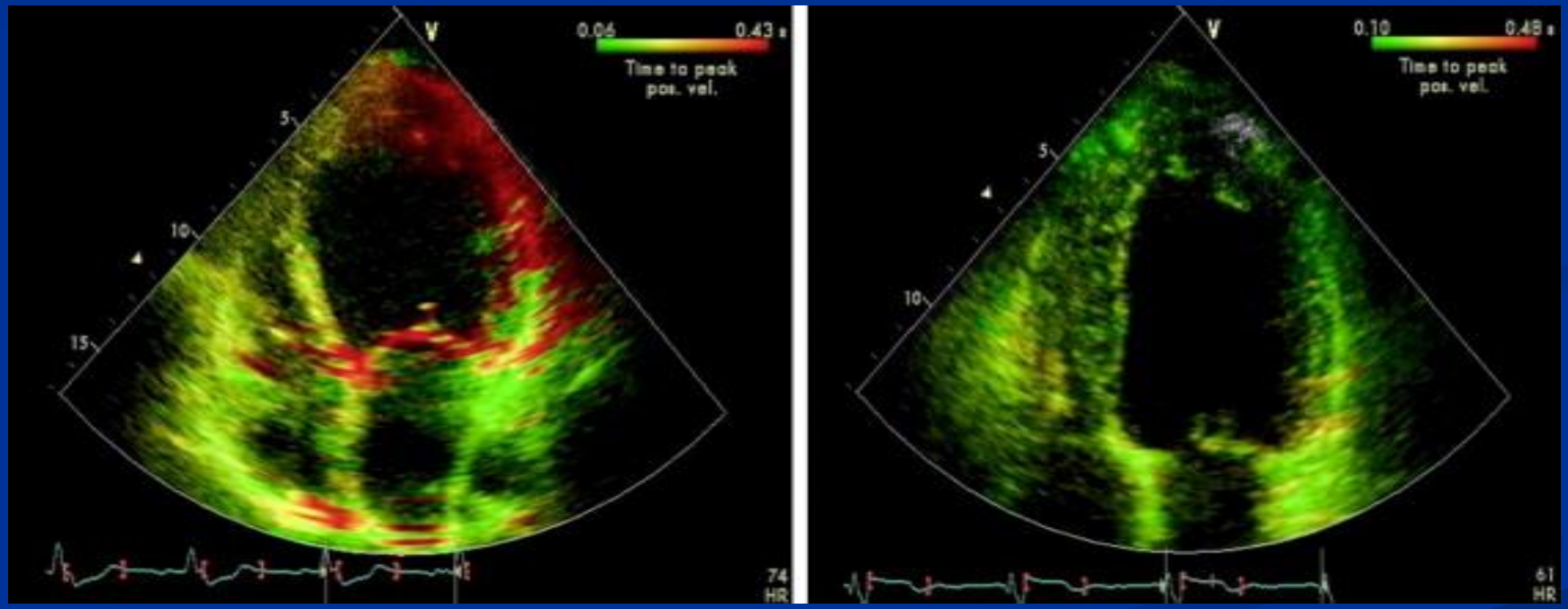




Durée et ITV mitrale et ITV Sous Ao

Jansen et al. Am J Cardiol 2006; 97: 552

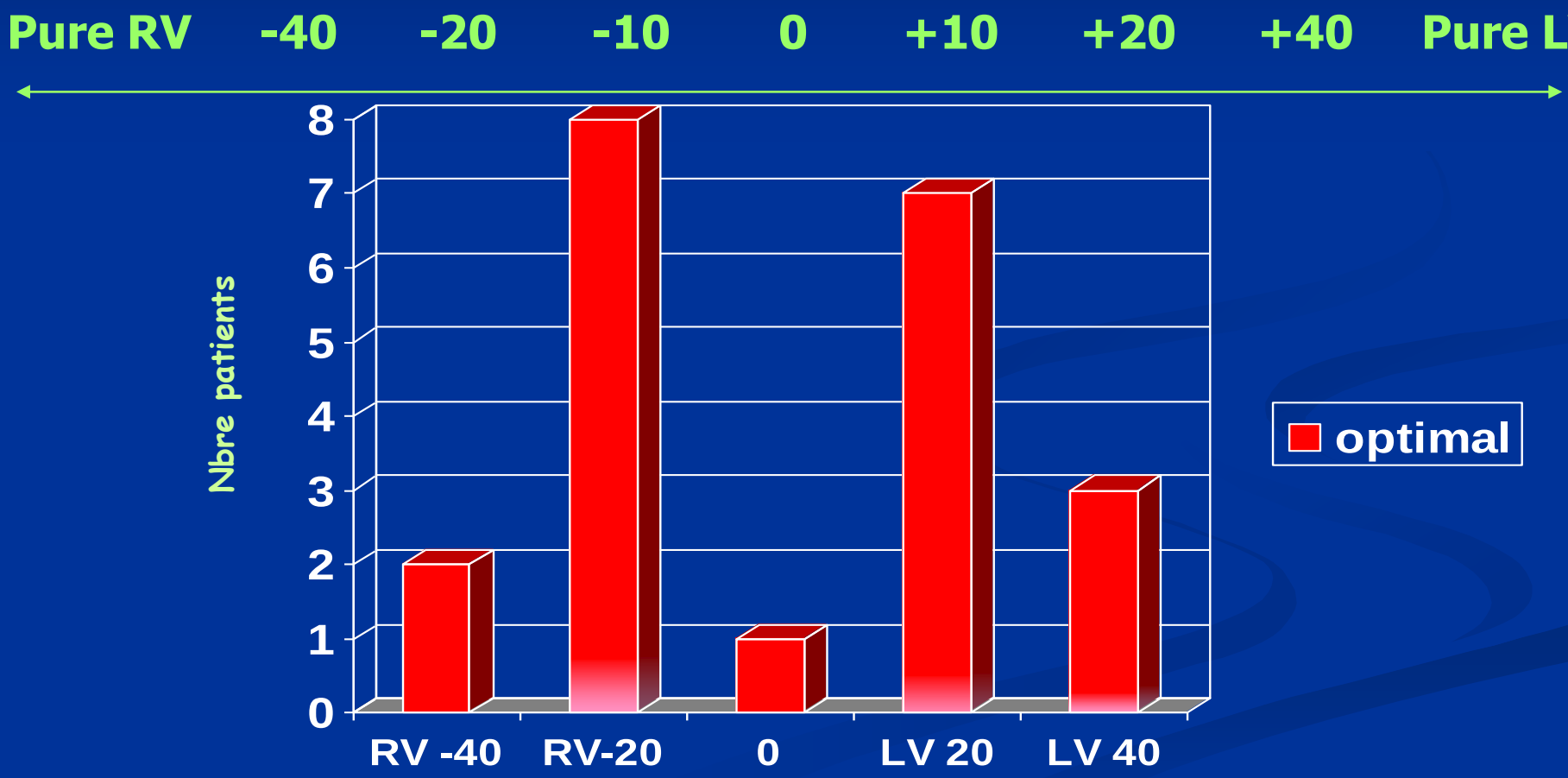
Stimulation séquentielle ou simultanée
intérêt d'optimiser les délais V-V?



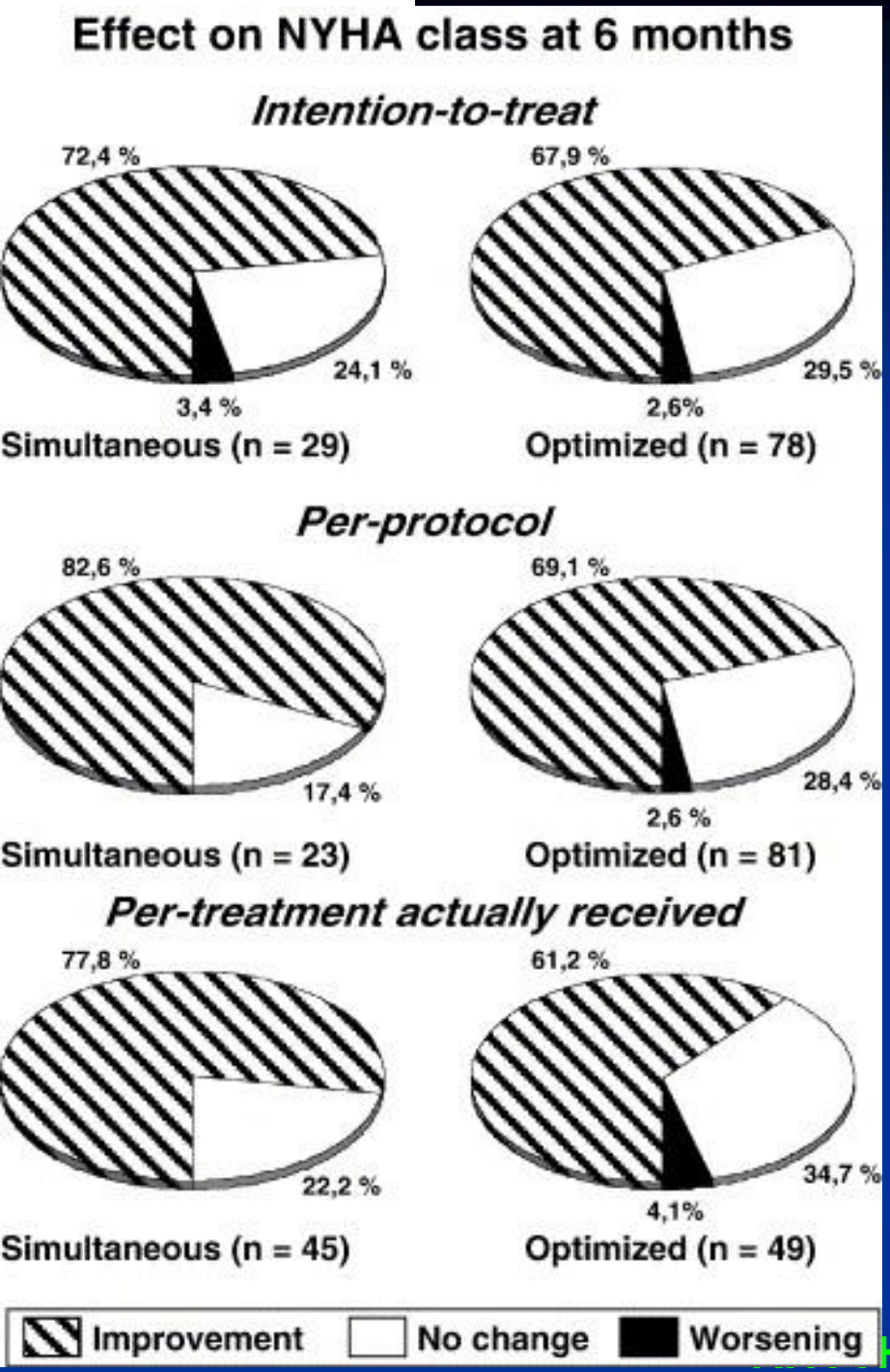
En aigu:

Sogaard et al. Circulation 2002; 106: 2078
Perego et al. Eur J Heart Failure 2003; 5: 303
Van Gelder et al. Am J Cardiol 2004; 93:1500
...

L'Optimisation de VV est à mener pas à pas individuellement



Porciani et al Am J cardio 2005; 95: 1108



Étude multicentrique randomisée en double avoeugle. 126 patients.

Objectif :

délais inter-ventriculaires le plus court possible

Pas d'effet sur

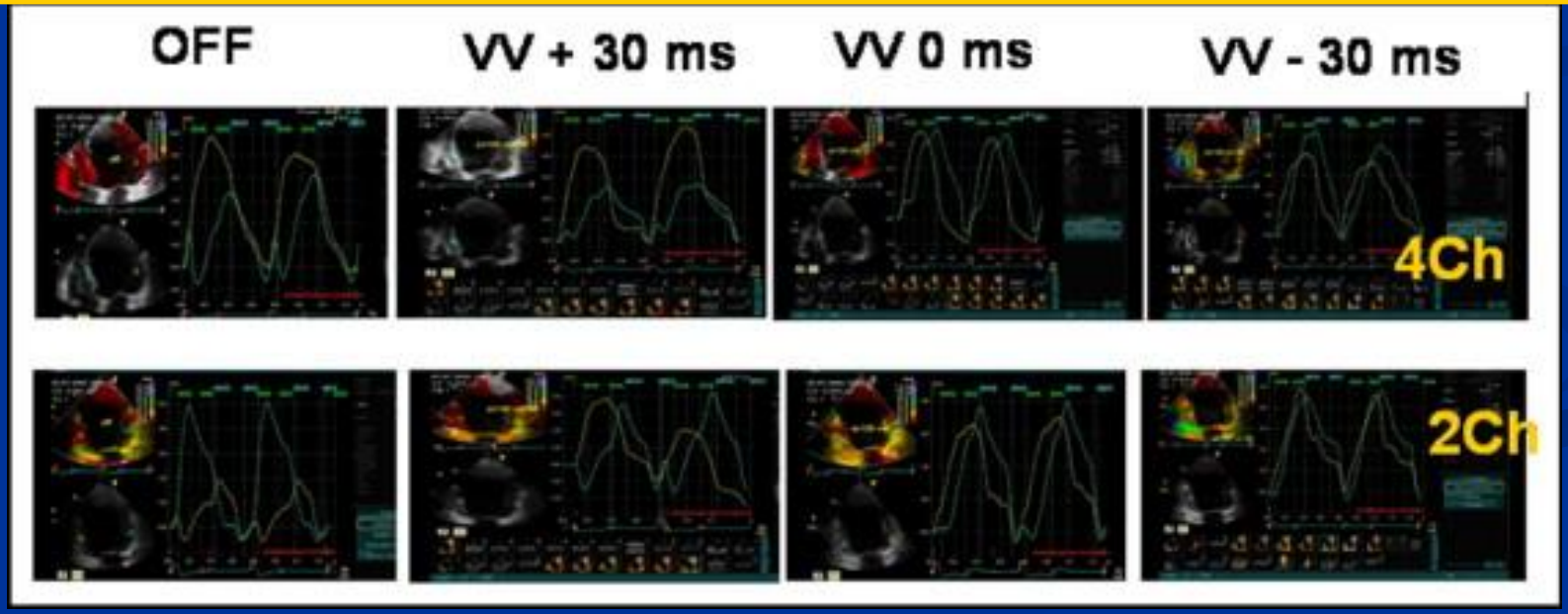
-NYHA,

-Test de marche et

-qualité de vie à 6 mois

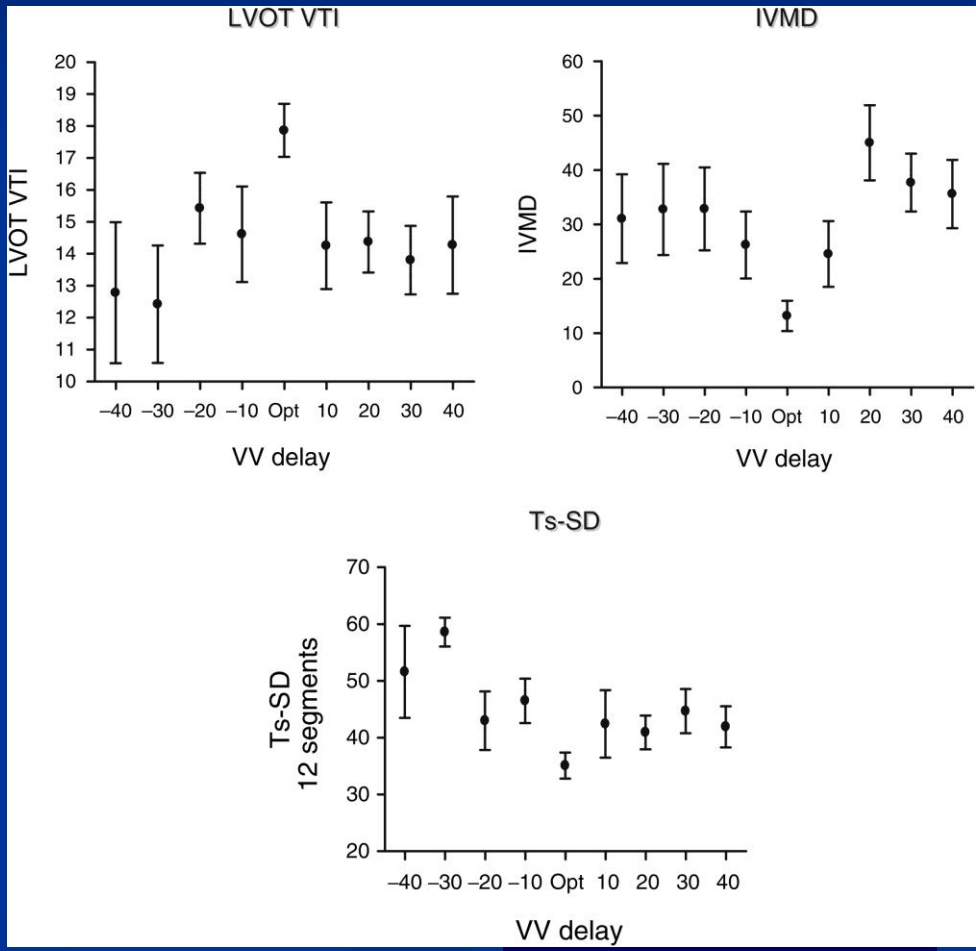
HM II ICD. Am Heart Journal 2006; 151: 1050

- 100 patients
  - 49: AV-delay 120ms & V-V=0
  - 51: optimization with tissue tracking
- ≥ 10% in distance walked in 6’ (6-month)
  - Number of non-responders 27 versus 23% (p=ns)
  - Cardiac output significantly higher in the optimized group (at rest)



Vidal et al. Am J Cardiol 2007; 100: 1002-6

- alteration of AV and/or VV delays in 60% of patients at 3 months
- was associated with a 50% improvement in functional responders between 3 - 6 months



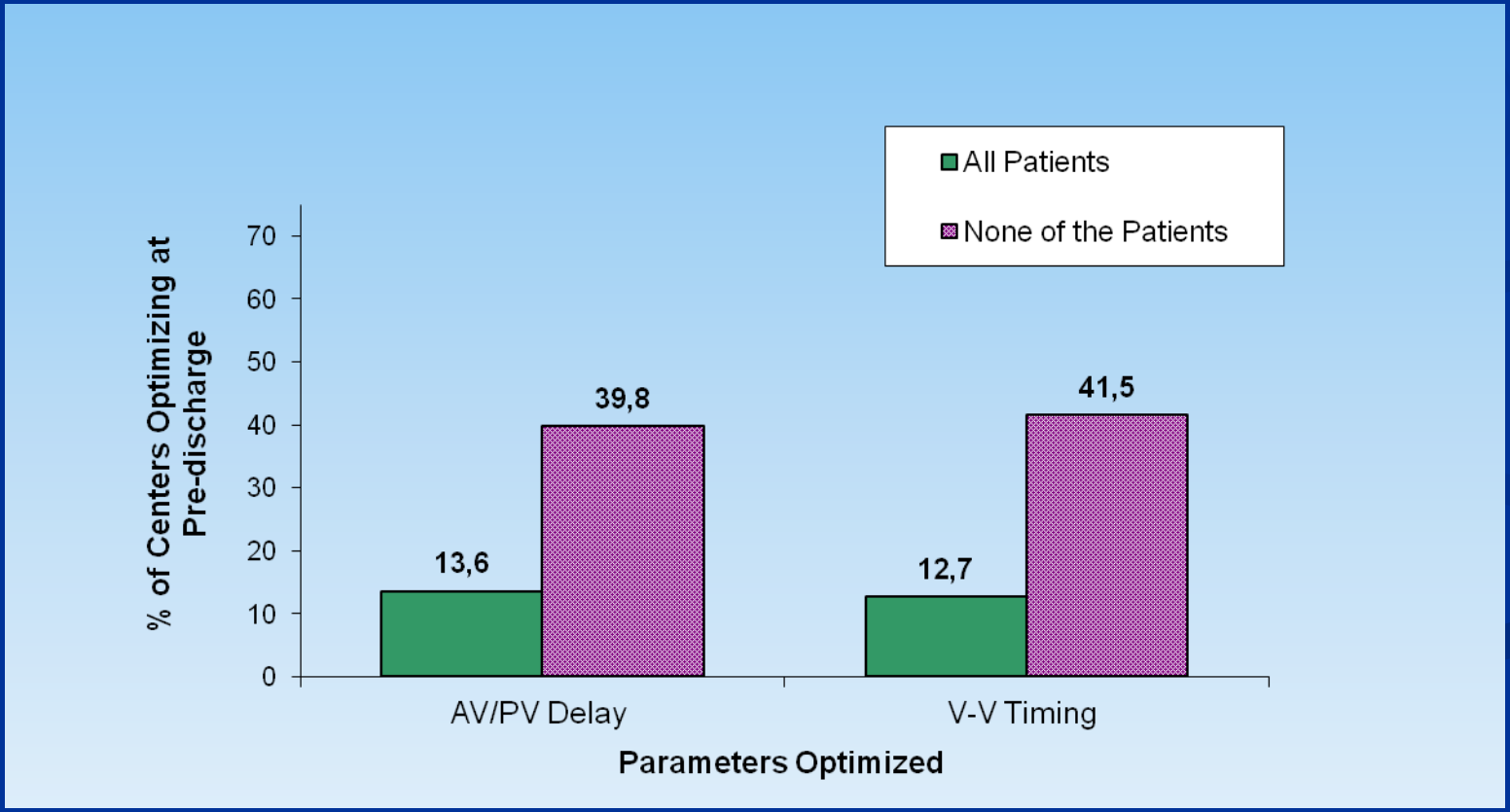
Thomas, D. E. et al. Eur J Heart Fail 2009 11:779-788

EUROPEAN JOURNAL OF HEART FAILURE

Et en pratique ?

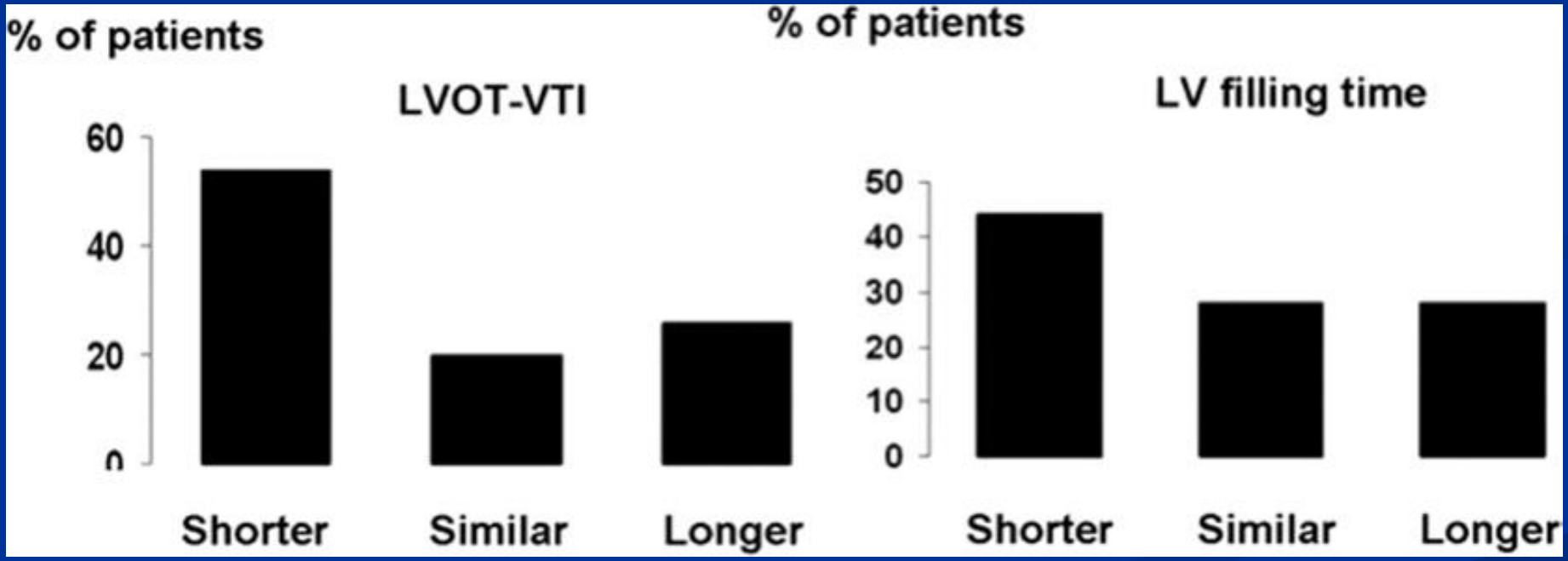
Optimization of CRT Timings at Pre-discharge

- ~13% of the centers optimize CRT timings in all patients
- ~40% of the centers do not optimize CRT timings in any of the patients



Optimization of the AV delay had a positive effect on echocardiographic indices of LV function.

The systematic shortening of the AV delay during exercise is not recommended because, in a high proportion of patients, the optimal AV delay was longer during exercise than at rest



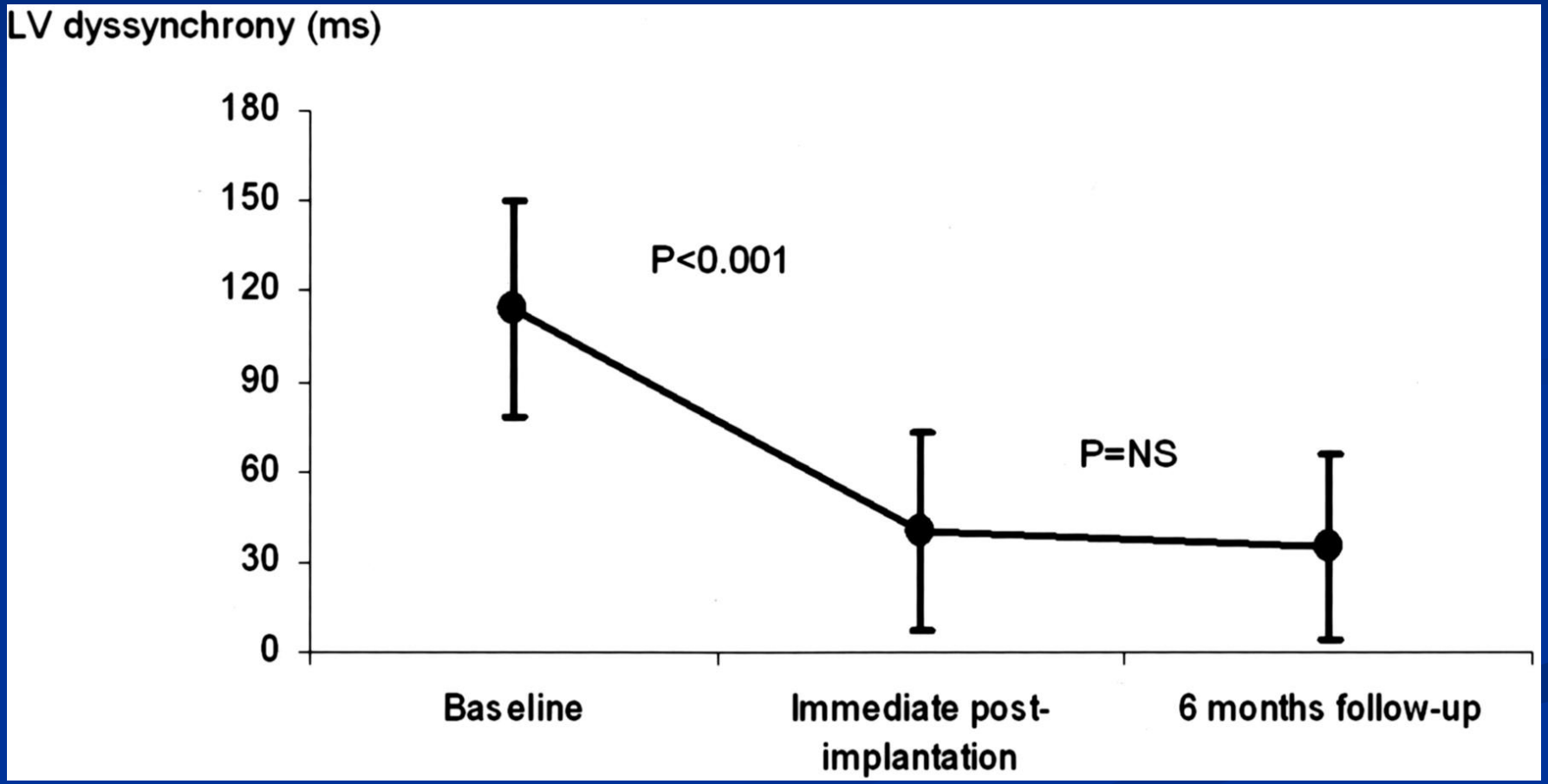
Mokrani et al. Heart Rhythm 2009;6:972–977

Après Implantation

Faut-il étudier les asynchronismes mécaniques…

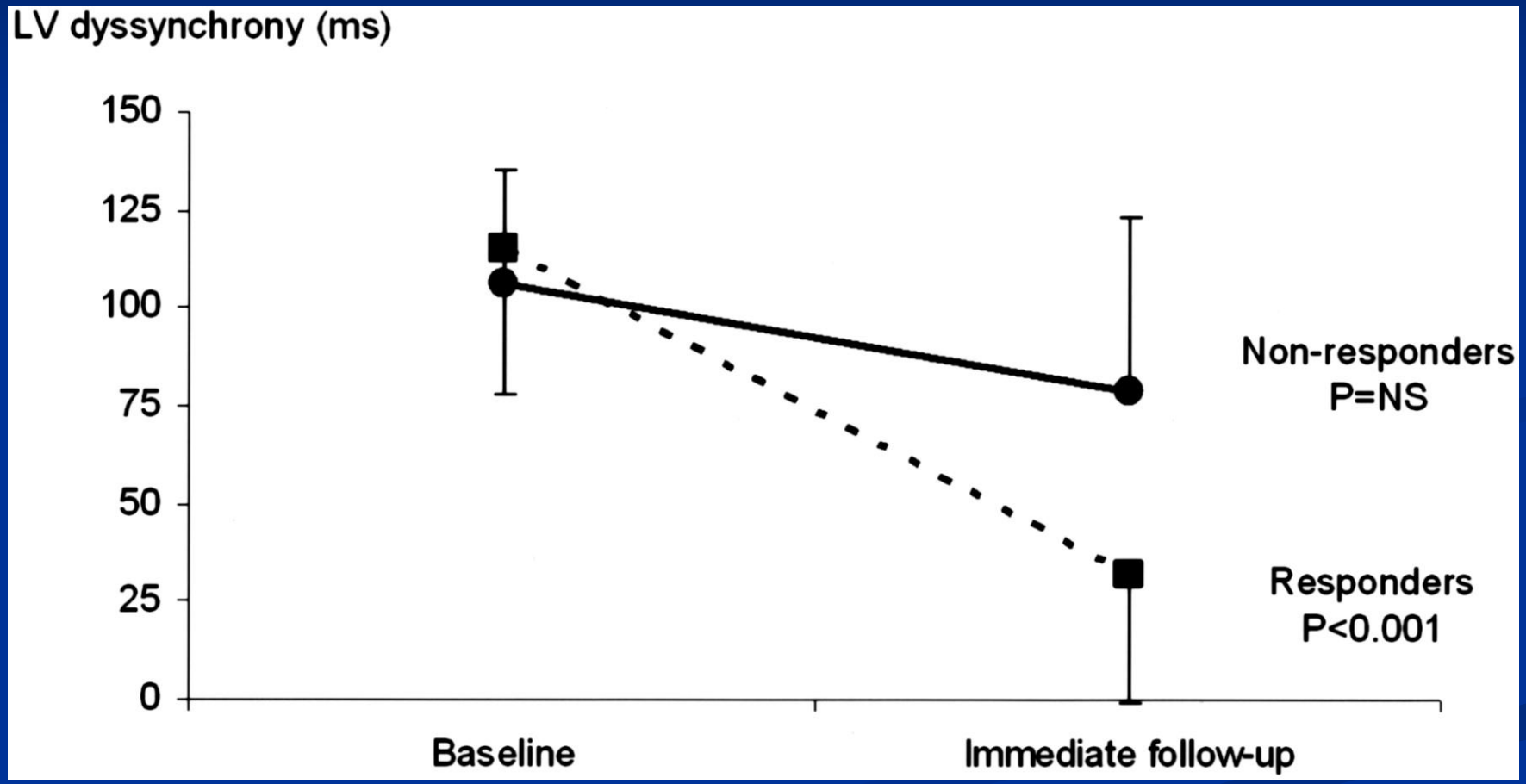
- S’assurer d’un DAV correct
- S’assurer de la Bonne réponse Clinique et en terme de Remodelage

Time course of LV resynchronization after CRT implantation (n=100)



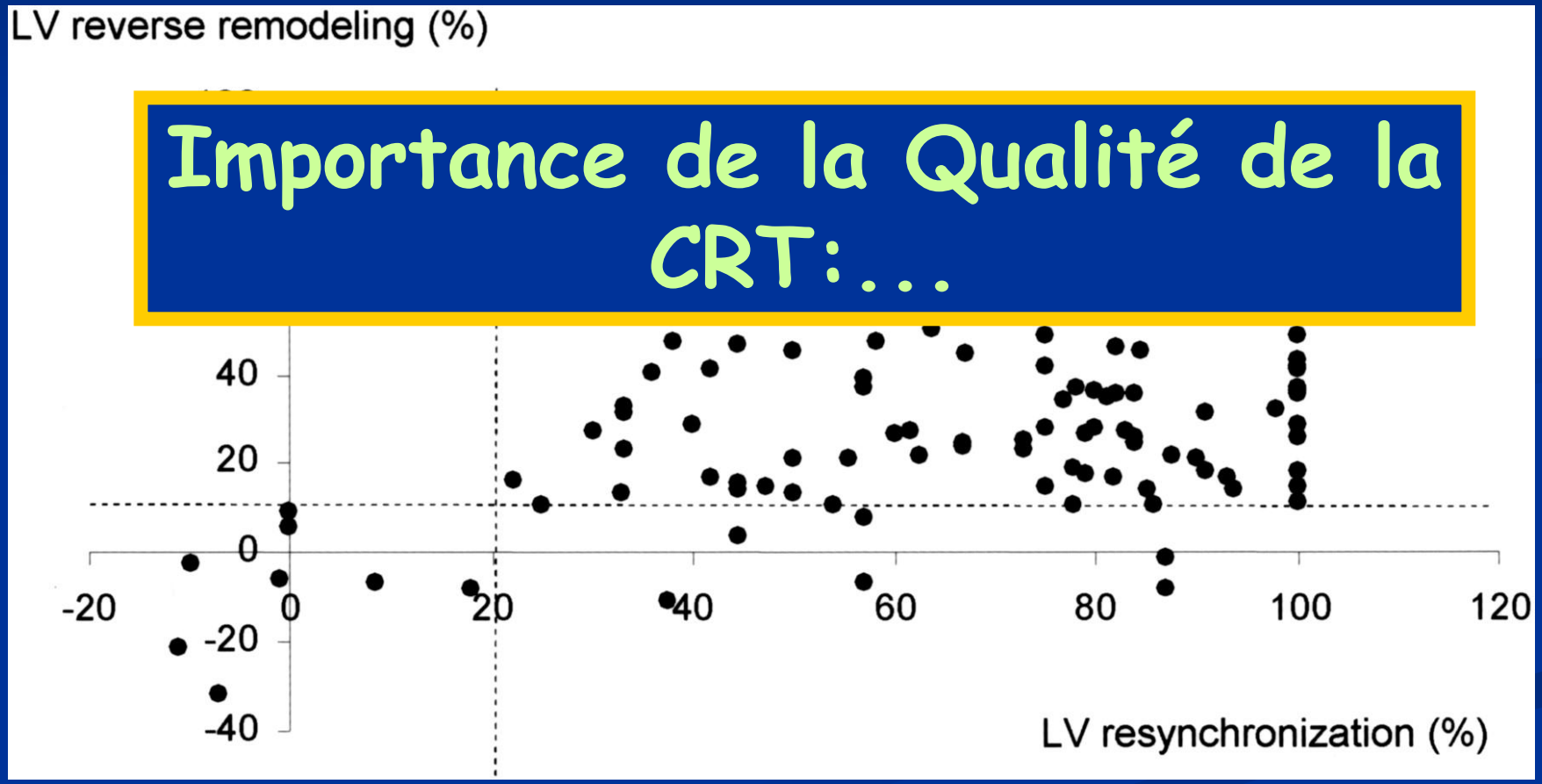
Bleeker, G. B. et al. Circulation 2007;116:1440-1448

Immediate decrease in LV dyssynchrony in the patients with response to CRT (n=85 [85%], defined as >10% reduction in LV end-systolic volume) vs patients without response (n=15 [15%])



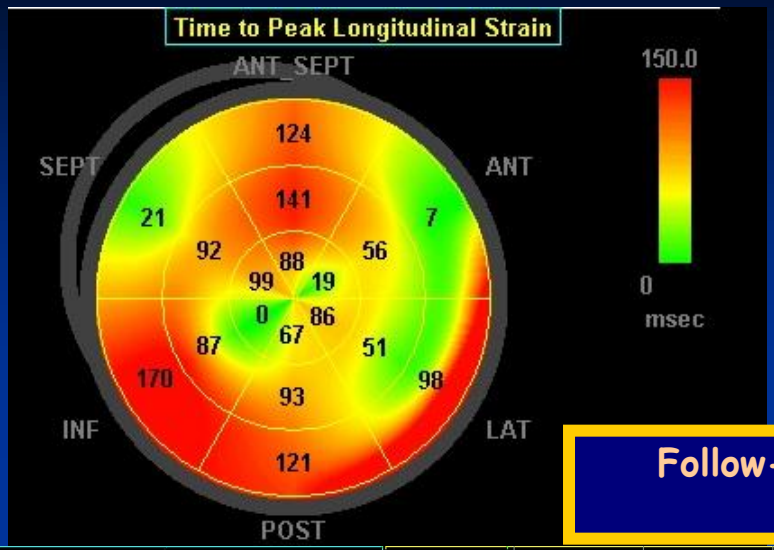
Bleeker, G. B. et al. Circulation 2007;116:1440-1448

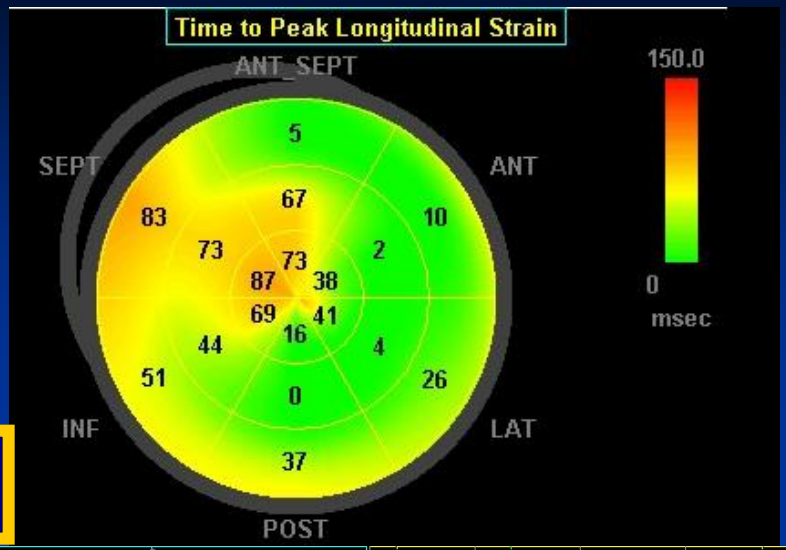
Relationship between immediate LV resynchronization and reduction in LV end-systolic volume at the 6-month follow-up - r=0.41 -



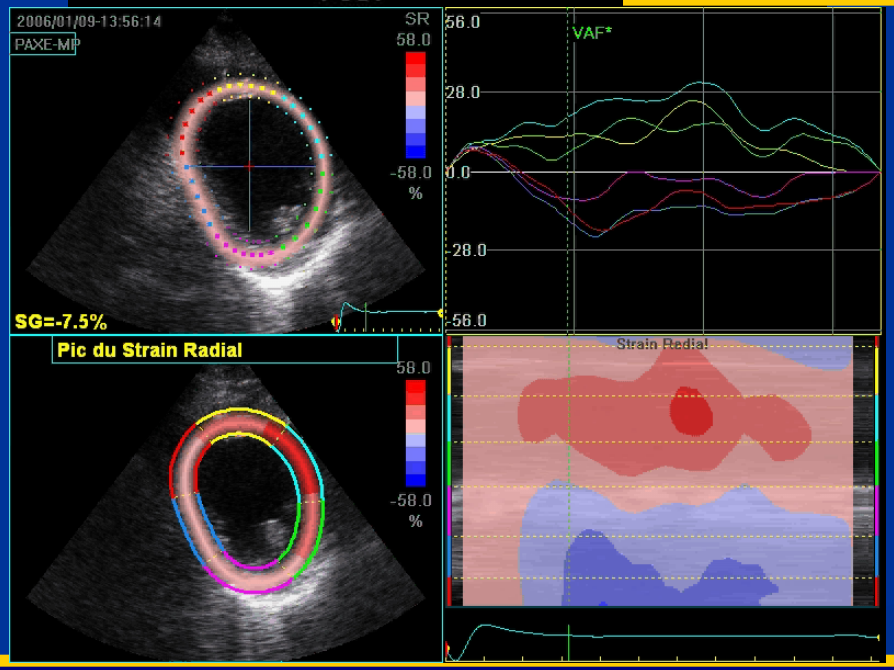
Bleeker, G. B. et al. Circulation 2007;116:1440-1448

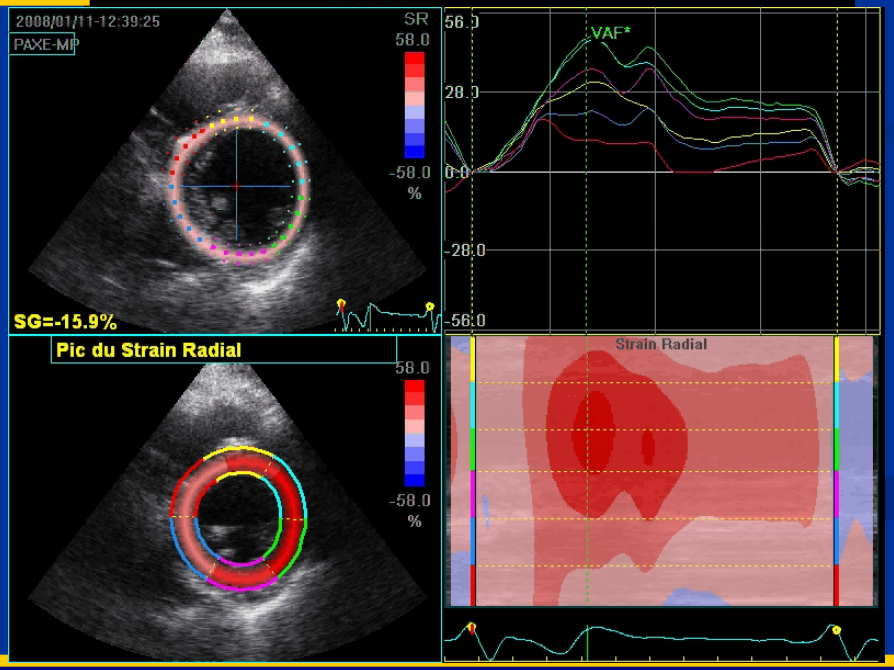
Dyssynchrony Imaging (2D-strain)





Follow-up





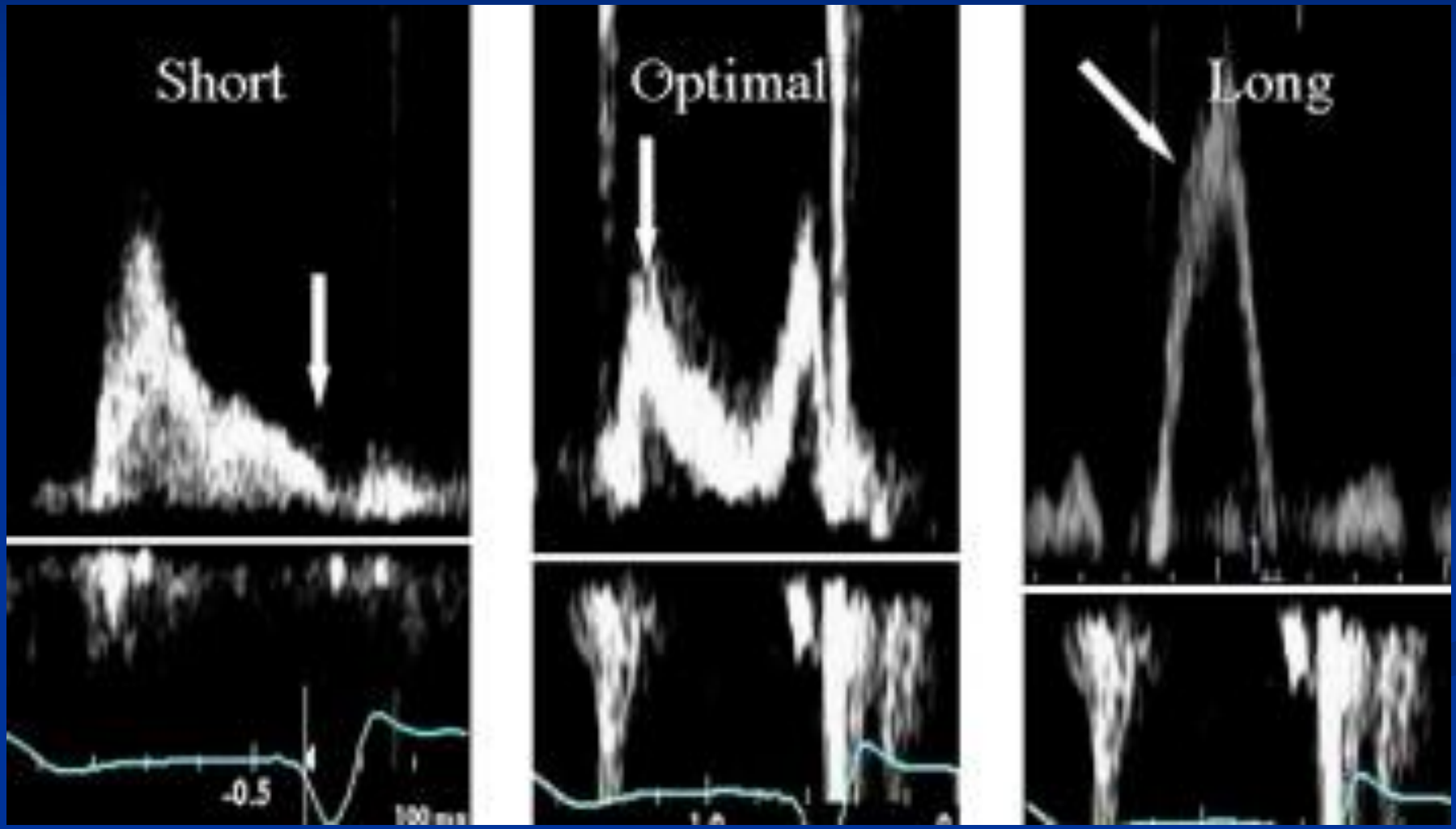
Contractility Imaging (2D-strain)

CONCLUSIONS

- INDICATIONS: pas de cha
  Symptomatique > NYHA 2
- RESULTATS: Remodelage inverse soutenu au cours du temps
- ACTUALITES: place de l'imagerie . Echo et multimodalité à nouveau envisageable (après Prospect)
- Verifier le profil mitral (DAV) et en cas de non réponse: optimiser les délais VV et AV selon l'ITV Sous Ao

Mieux > 150ms

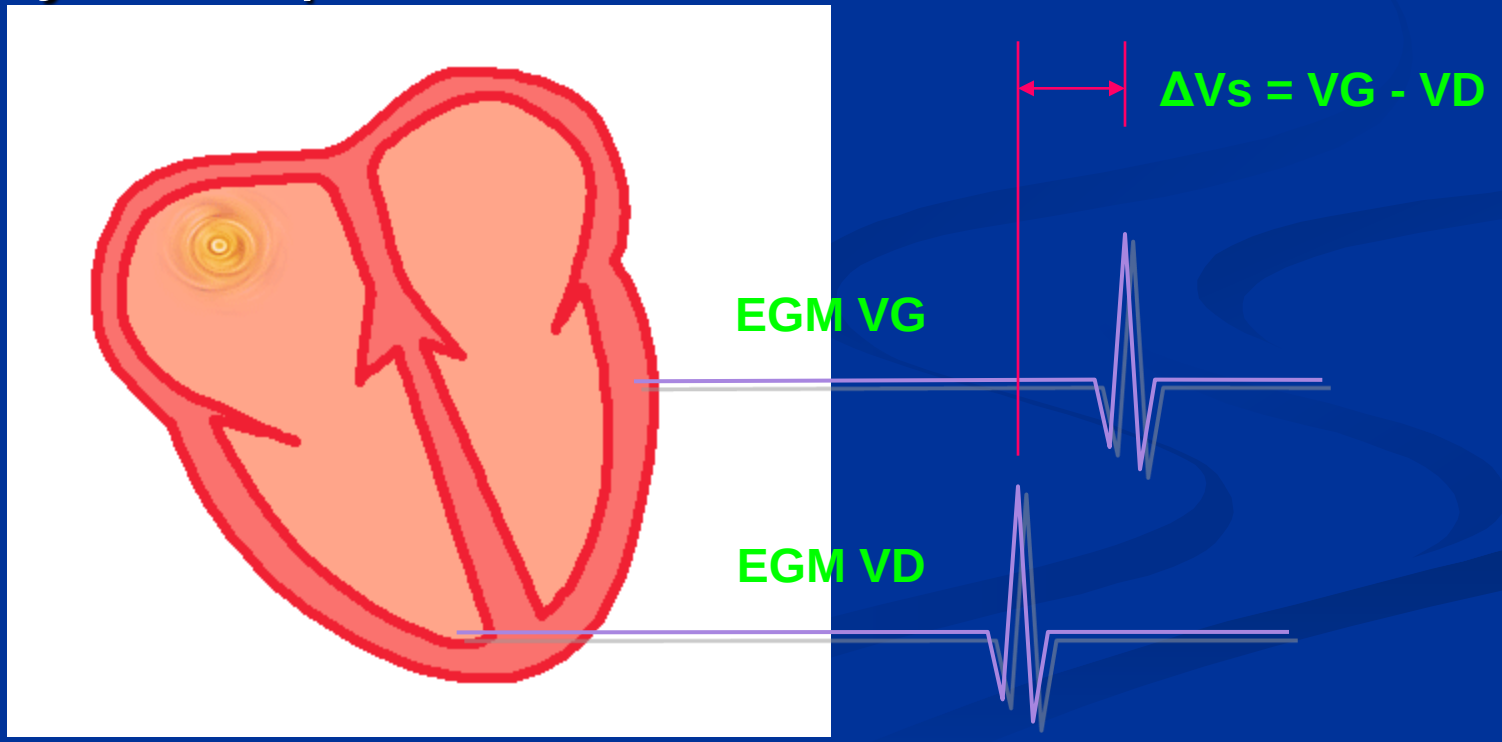
Optimiser le DAV pas à pas avant la sortie de l'hôpital et vérifier à chaque Cs de suivi



QuickOpt™
TIMING CYCLE OPTIMIZATION

Test de détection ventriculaire

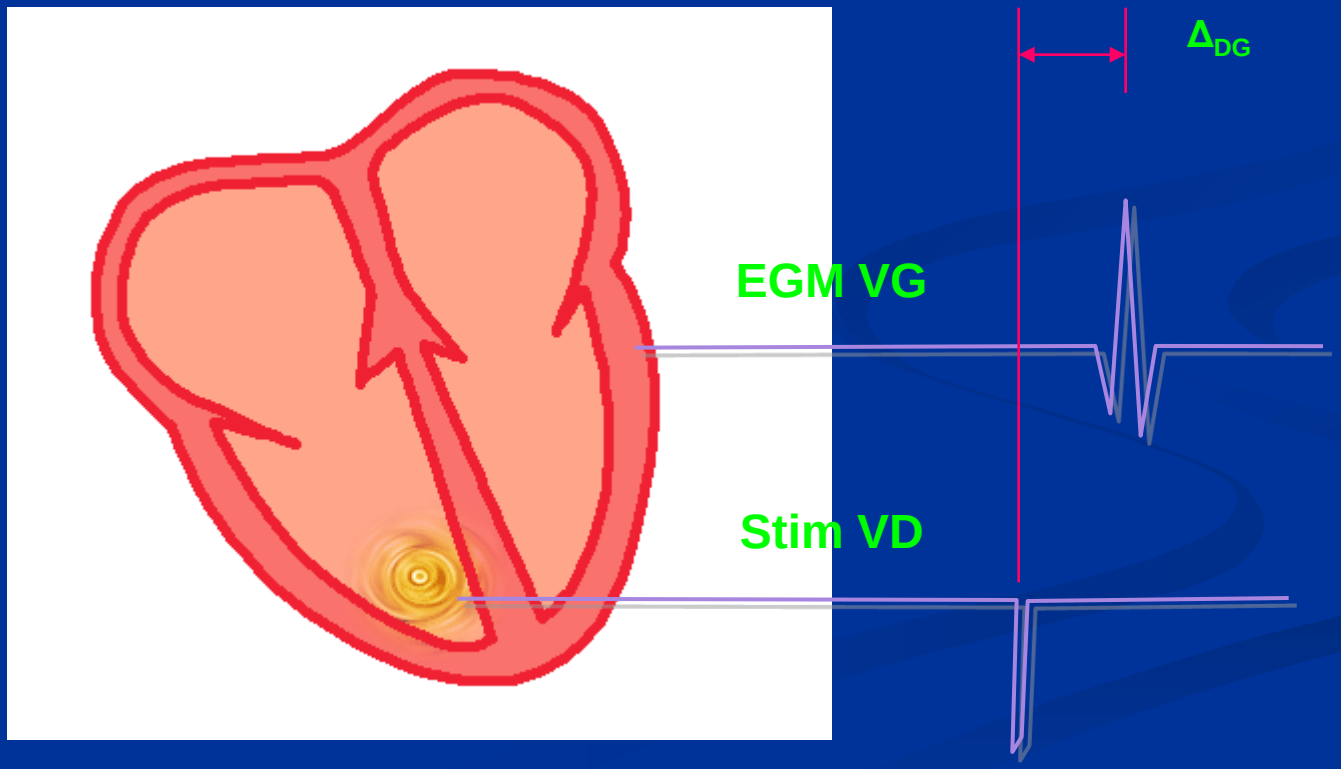
- Mesure du délai moyen de détection inter-ventriculaire
  en rythme spontané



Δ Vs positif si la détection gauche est retardée

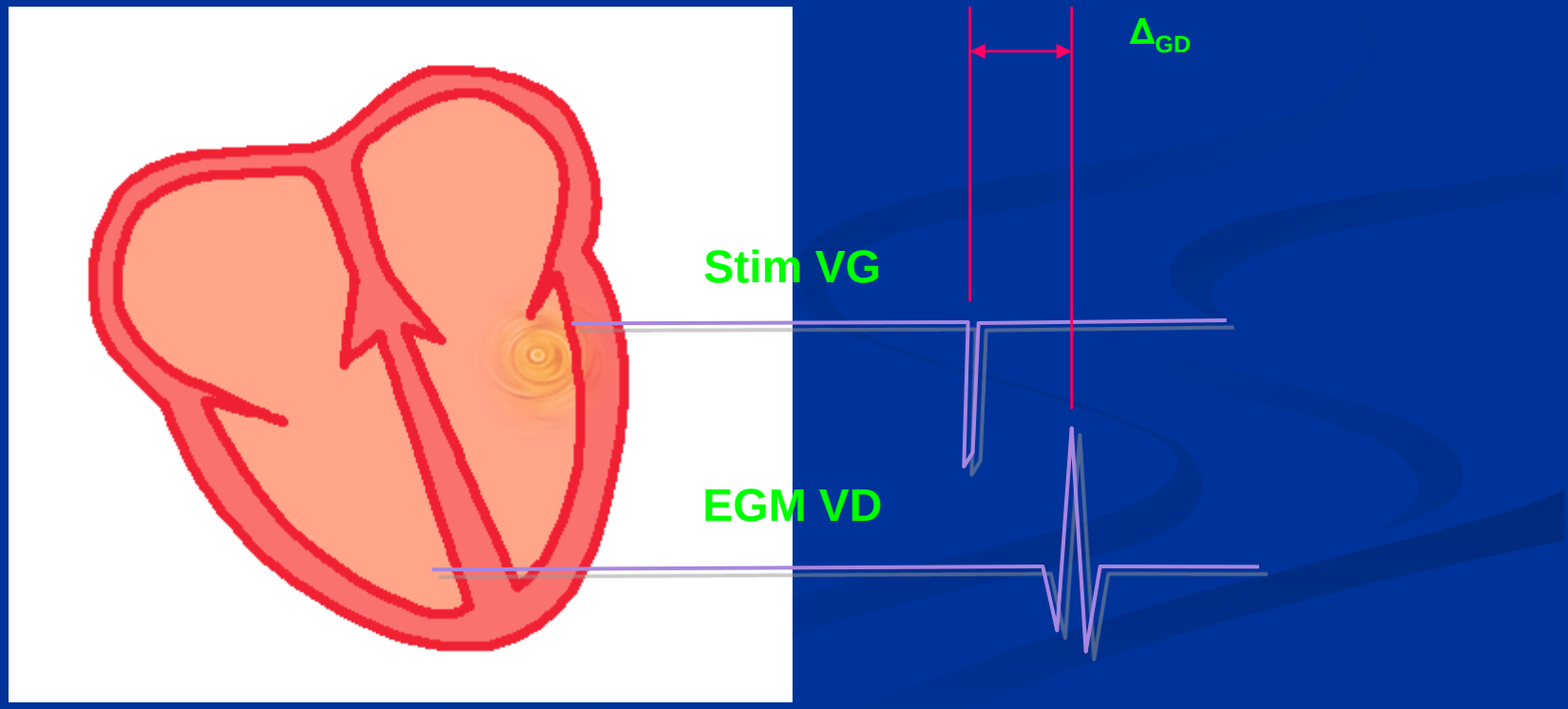
Test de stimulation VD

- Mesure du temps de conduction VD-VG



Test de stimulation VG

- Mesure du temps de conduction VD-VG



Calcul du délai VV optimal

- Délai VV = (ΔV spontané + ($\Delta_{GD} - \Delta_{DG}$)) / 2

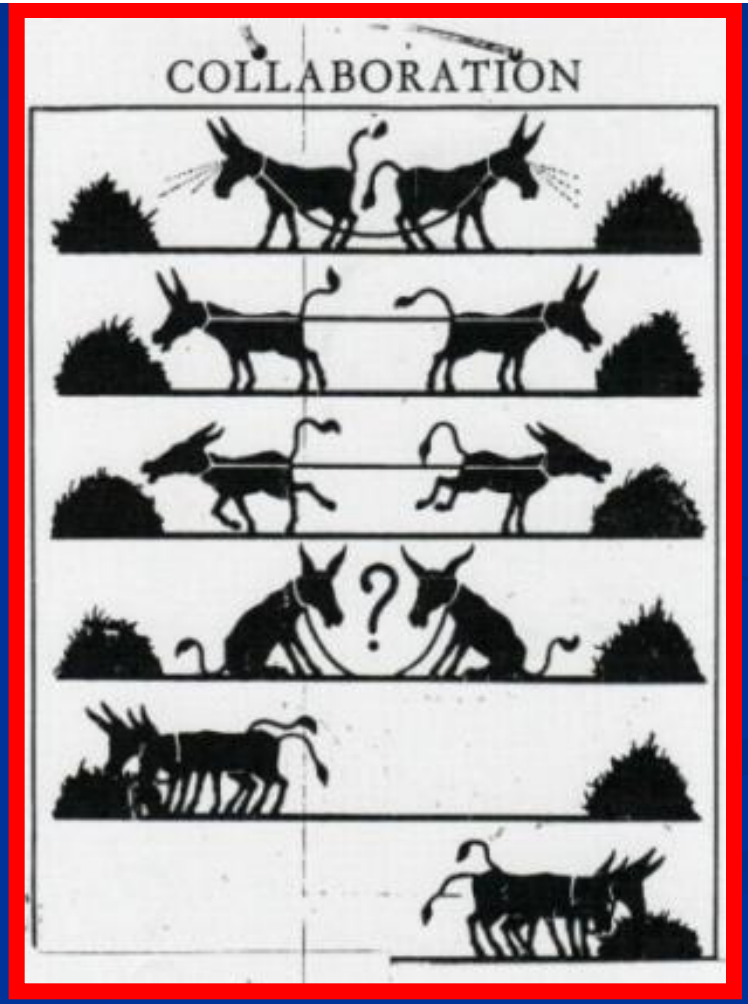
- Exemple :
  - Délai inter-ventriculaire : VG retardé de 60 ms par rapport à VD
  - Délai de conduction VD-VG de 45 ms et VG à VD de 75 ms

  - Délai VV = (60 + (75-45)) / 2 = 45 ms, Stimulation VG en premier

Successful treatment of heart failure with devices requires collaboration

Karl Swedberg [a,*], John Cleland [b], Martin R. Cowie [c], Markku Nieminen [d], Silvia G. Priori [e], Luigi Tavazzi [f], Dirk J. van Veldhuisen [g], Luis Alonso-Pulpon [h], John Camm [i], Kenneth Dickstein [j], Helmut Drexler [k], Gerasimos Filippatos [l], Cecilia Linde [m], José Lopez-Sendon [n], Massimo Santini [o], Faiez Zannad [p]

European Journal of Heart Failure 10 (2008) 1229–1235



Cardiac Resynchronization Therapy Prevents Disease Progression in NYHA Class I and II Heart Failure Patients:

24 month results from the European cohort of the **RE**synchronization re**VE**rses **R**emodeling in **S**ystolic left v**E**ntricular dysfunction trial

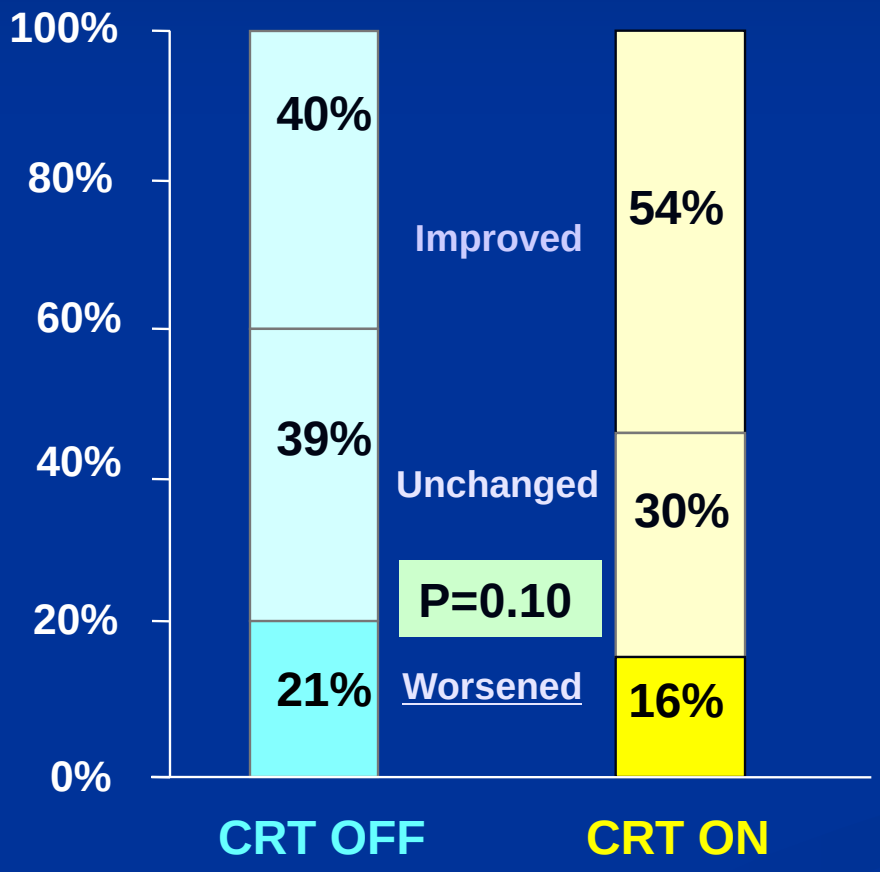
Jean-Claude Daubert, Rennes, France

On Behalf of the **REVERSE** Investigators and Coordinators

Main Study: 12-Month

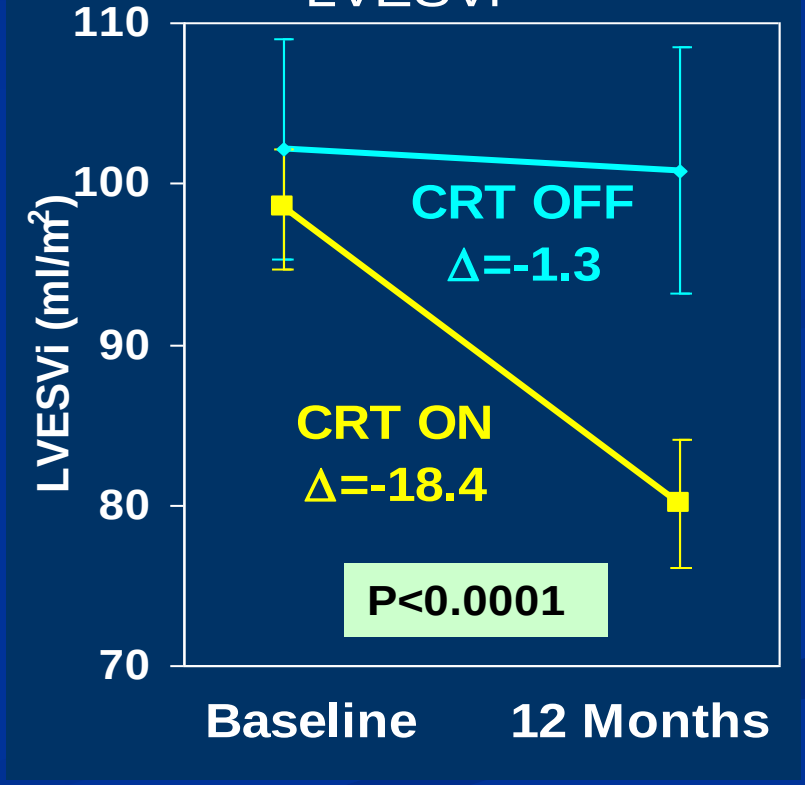
Clinical Composite Response

Pre-Specified Analysis
Proportion Worsened



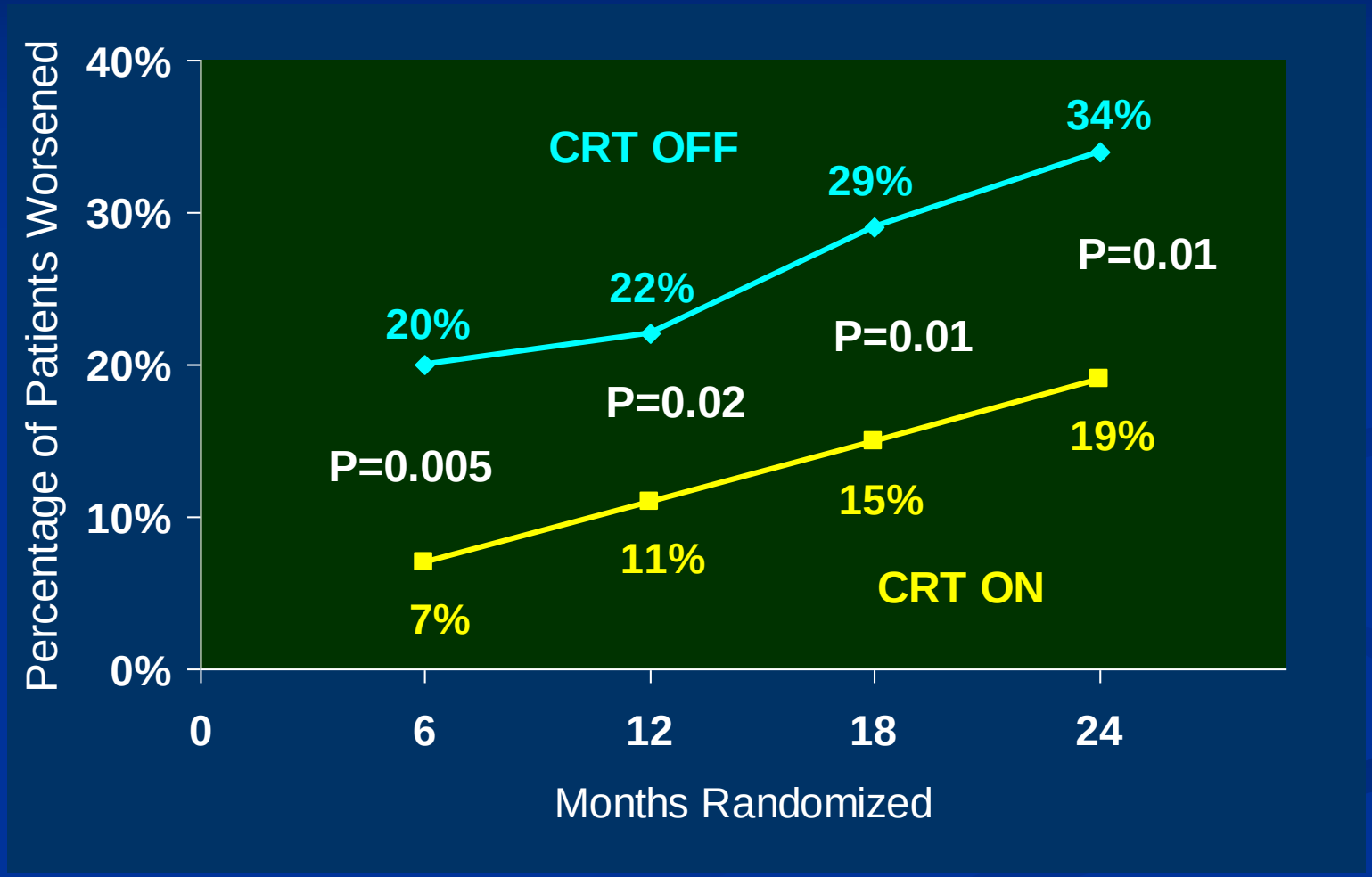
Powered Secondary Objective

12 Month Change in
LVESVi



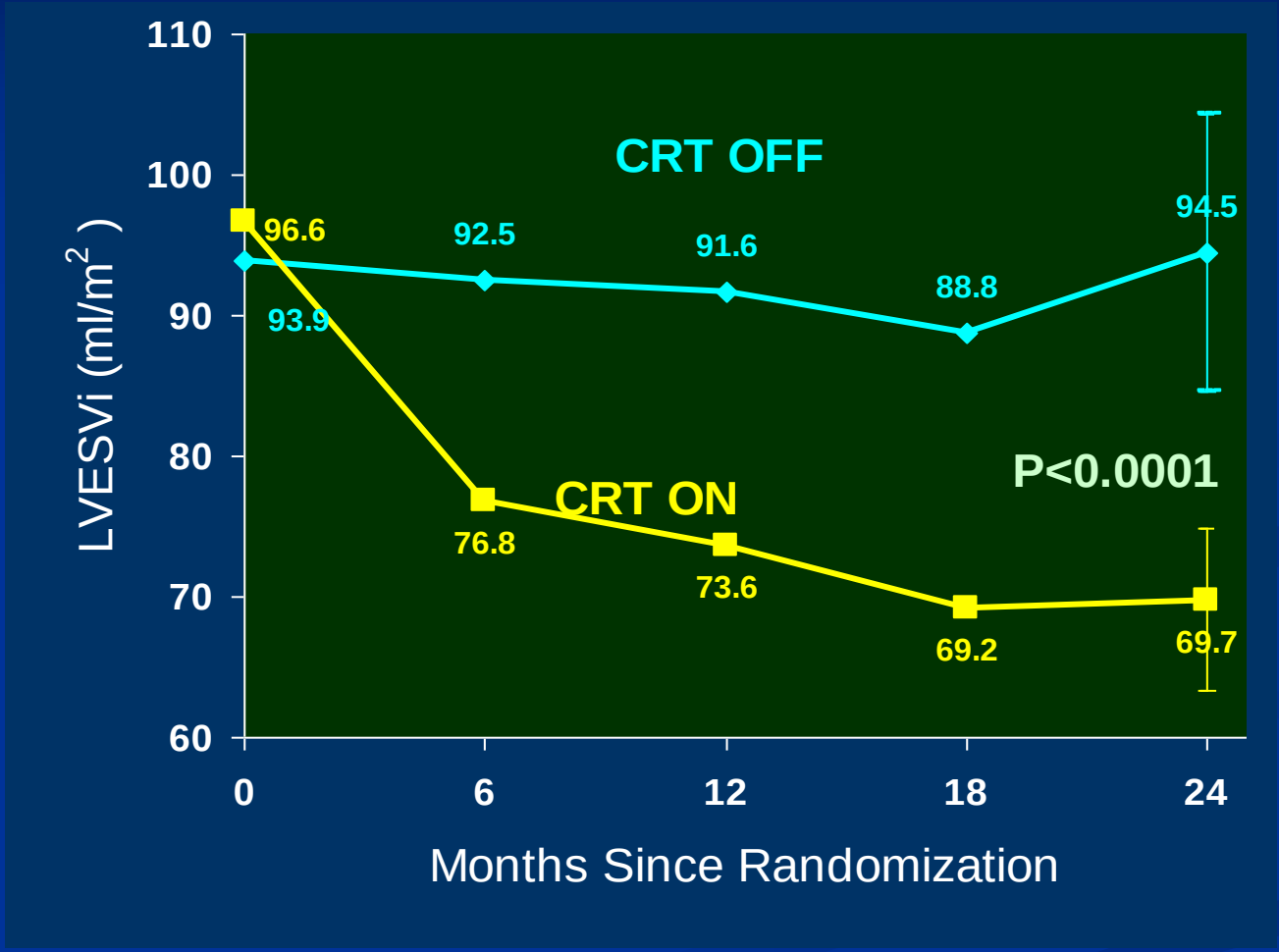
C Linde et Al, JACC 2008; 52: 1834-1843

Primary End Point
Clinical Composite Response
% worsened over time



Worsening attributed to death or HF hospitalization in 68% of worsened patients in the CRT OFF group

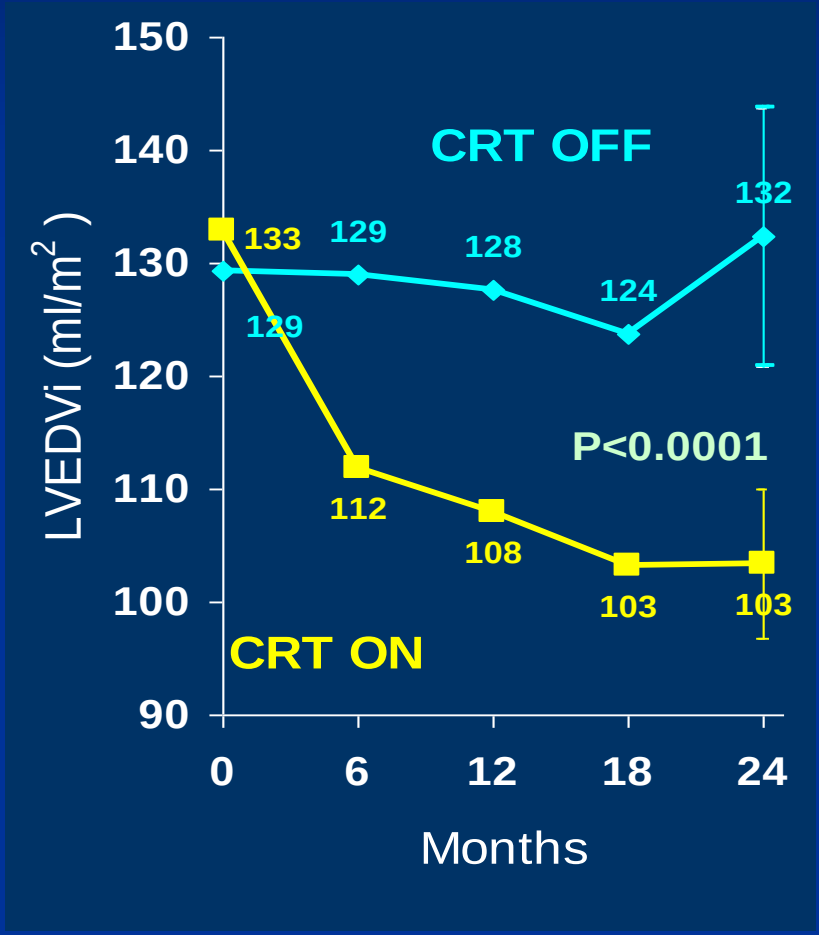
Powered Secondary End Point: LVESVi



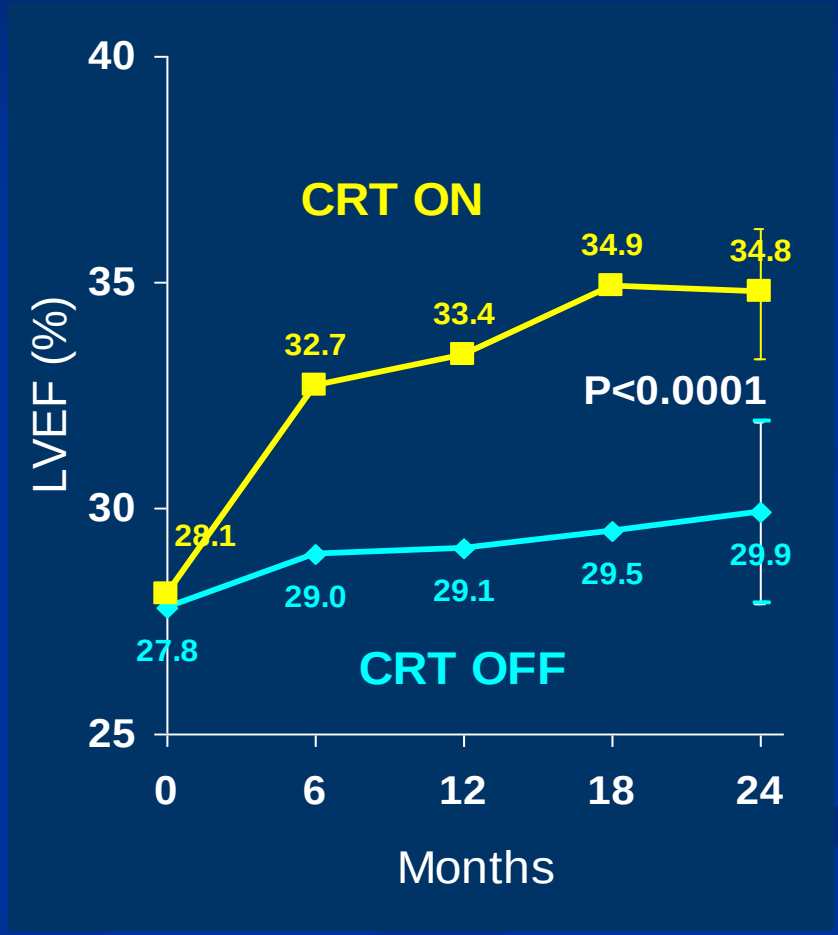
P-value compares 24-month changes.

Other Remodeling Parameters

LVEDVi (ml/m^2)

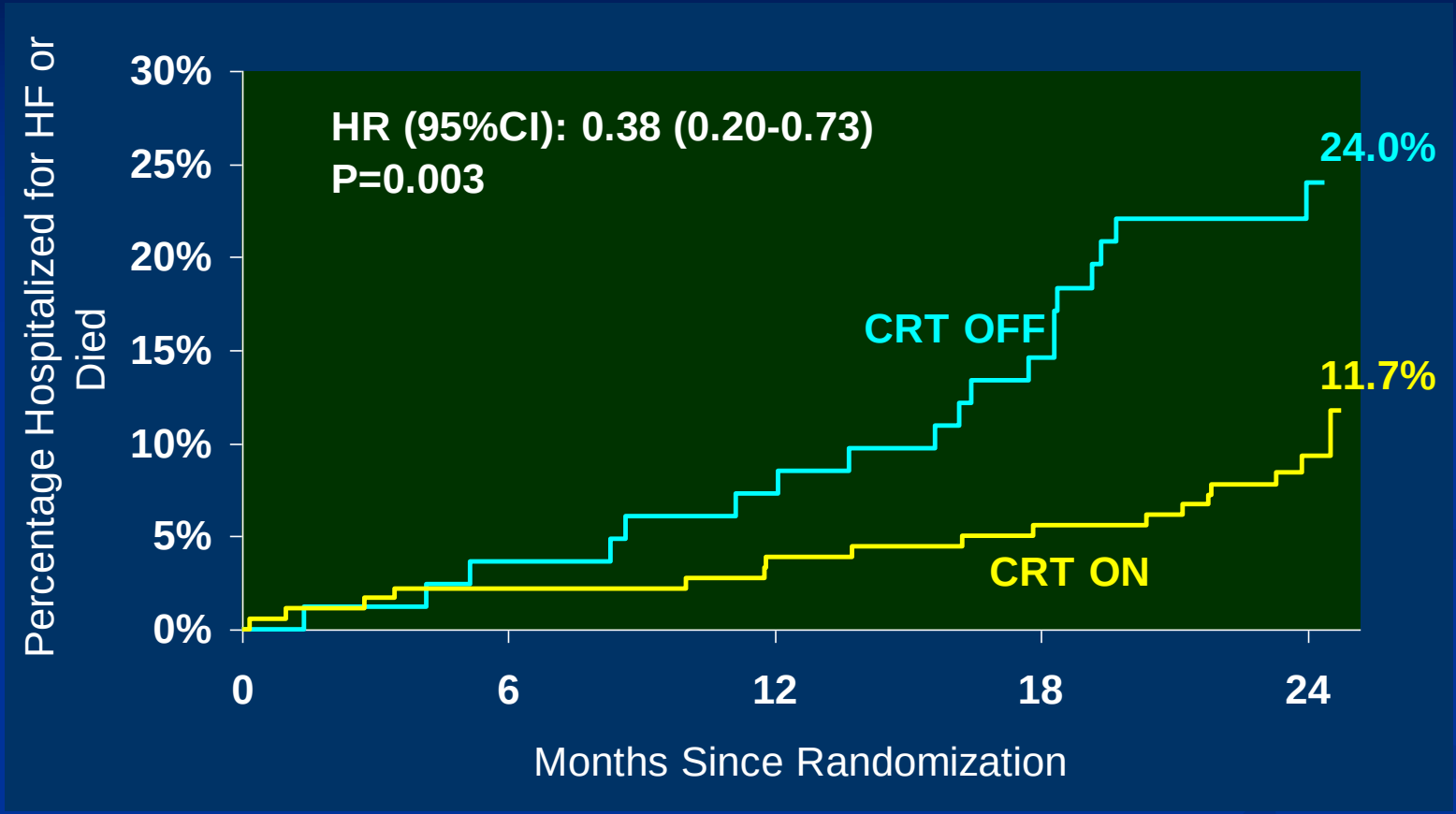


LVEF (%)



P-values compare 24-month changes.

Time to First HF Hospitalization or Death



Number at Risk

CRT OFF	**82**	**79**	**76**	**70**	**39**
CRT ON	**180**	**176**	**173**	**168**	**77**

Conclusion

The 24 month results of the European cohort of REVERSE patients show that CRT in asymptomatic and mildly symptomatic HF patients on optimal medical therapy:

- Improves clinical outcome and
- Improves ventricular structure and function
- CRT thus may modify disease progression in mildly symptomatic HF patients

Note: FDA has not yet reviewed the clinical data to determine whether or not CRT systems are safe and effective in this patient population.

CONCLUSIONS

- INDICATIONS: pas de changement. Symptomatique > NYHA 2 . QRS >120ms
- RESULTATS: Remodelage inverse soutenu au cours du temps
- ACTUALITES: place de l'imagerie . Echo et multimodalité à nouveau envisageable (après Prospect)

Avenir à d'autres indications: stade 2, QRS fins avec asynchronisme mécanique...???

Cardiac Resynchronization Therapy Prevents Disease Progression in NYHA Class I and II Heart Failure Patients:

24 month results from the European cohort of the **RE**synchronization re**VE**rses **R**emodeling in **S**ystolic left v**E**ntricular dysfunction trial

Jean-Claude Daubert, Rennes, France

On Behalf of the **REVERSE** Investigators and Coordinators

Purpose and Design

- To evaluate the long-term benefits of CRT in the 262 European patients included in *REVERSE* and prospectively followed for 24 months

- Randomized, double-blind, parallel-controlled clinical trial

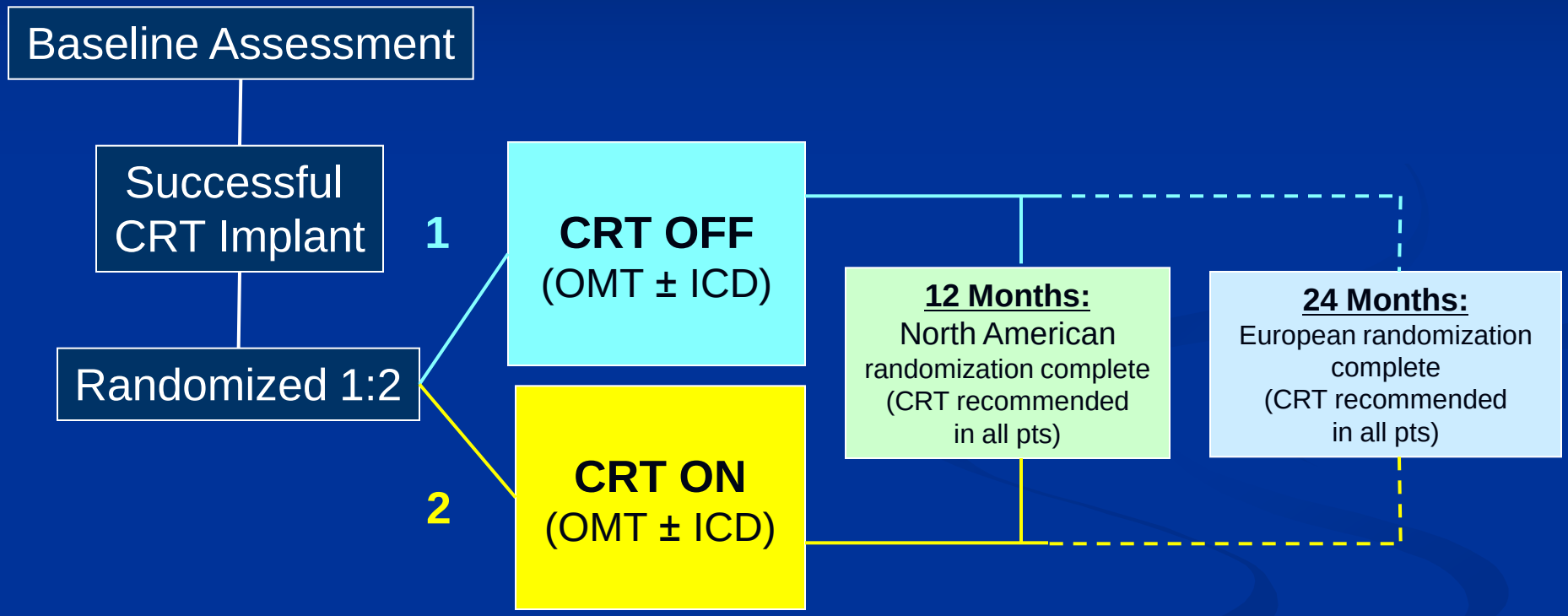
Inclusion Criteria

- NYHA Class II or I (previously symptomatic)
- QRS ≥ 120 ms
- LVEF ≤ 40%; LVEDD ≥ 55 mm
- Optimal medical therapy (OMT)
- Without permanent cardiac pacing
- With or without an ICD indication

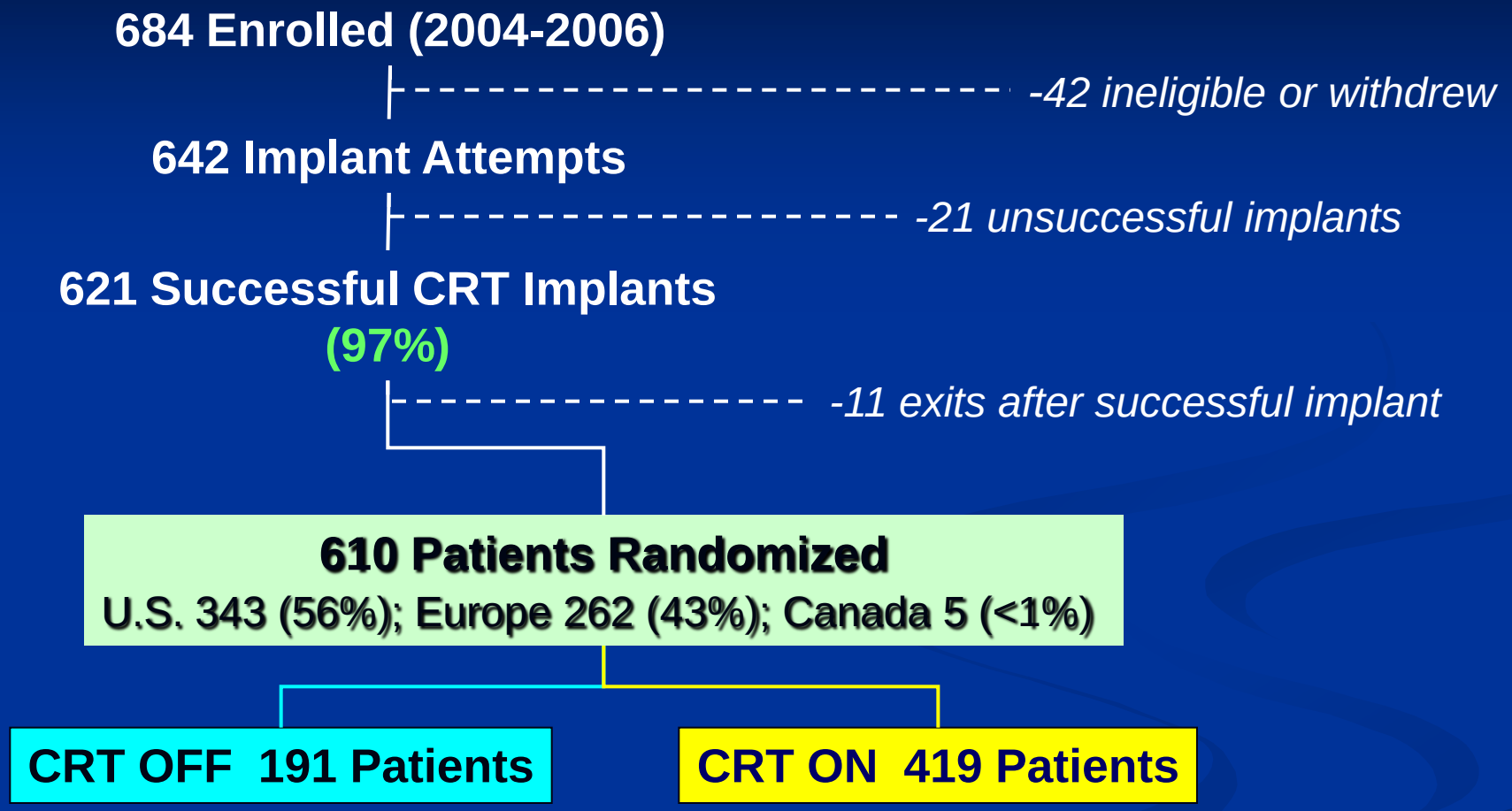
End Points

- Primary: HF Clinical Composite Response,
  comparing the proportion of patients worsened in CRT OFF vs. CRT ON groups
  - Composite includes: all-cause mortality, HF hospitalizations, crossover due to worsening HF, NYHA class, and the patient global assessment assessed in double blind manner
- Prospectively Powered Secondary:
  LV End Systolic Volume Index (LVESVi)
  comparing CRT OFF vs. CRT ON subjects
  - LVESVi assessed by core labs (1 in Europe, 1 in U.S)

Study Schematic



Enrollment and Randomization



C Linde et Al, JACC 2008; 52: 1834-1843

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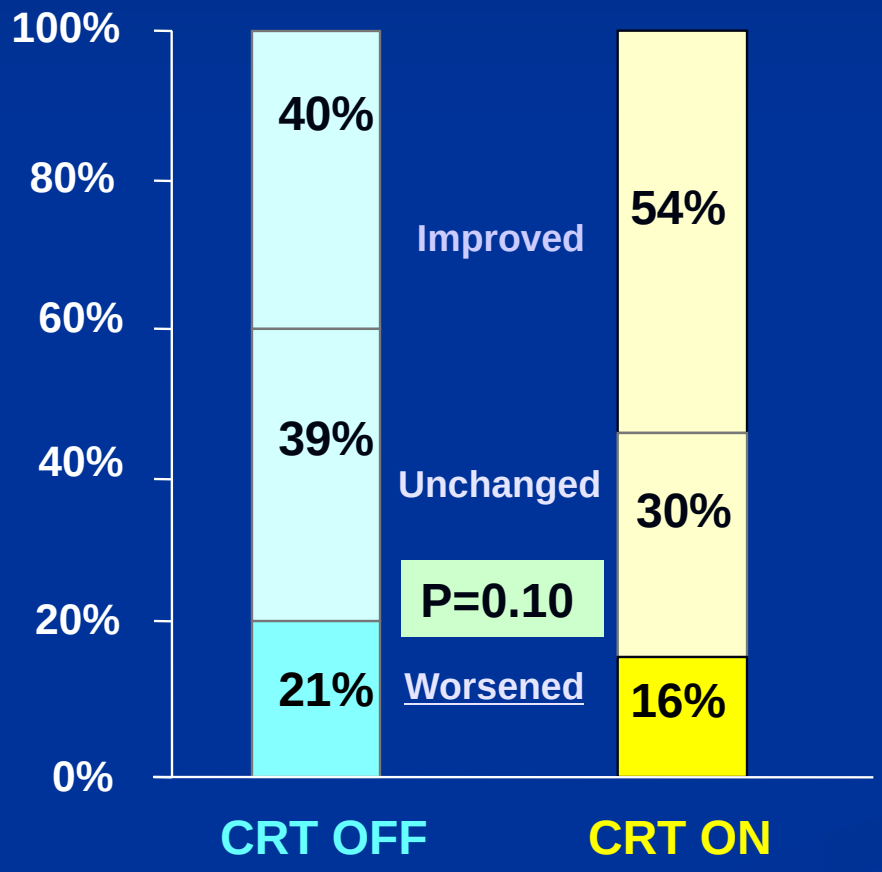
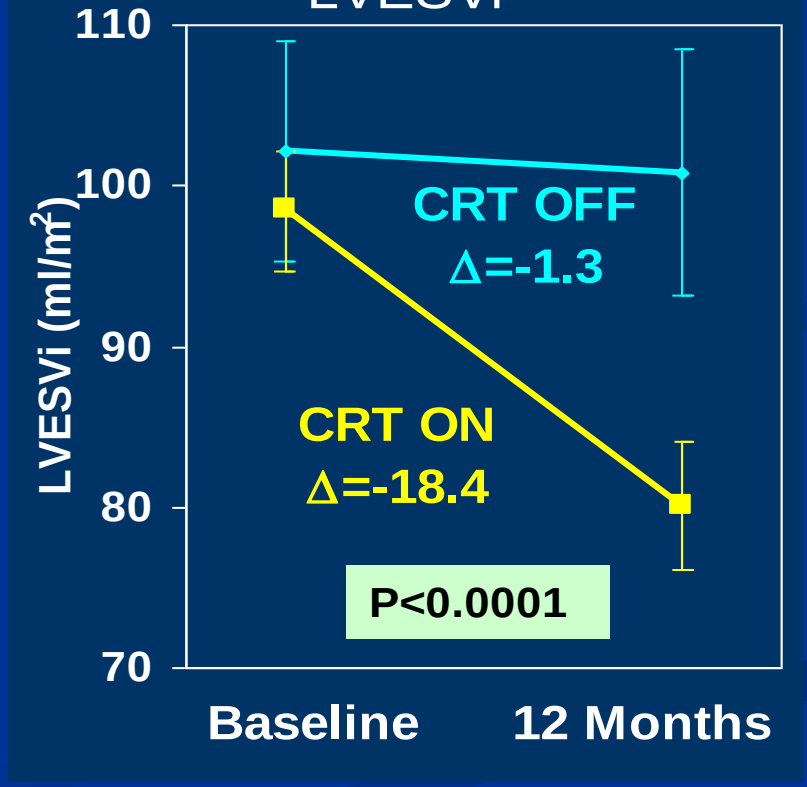


Powered Secondary Objective

12 Month Change in
LVESVi



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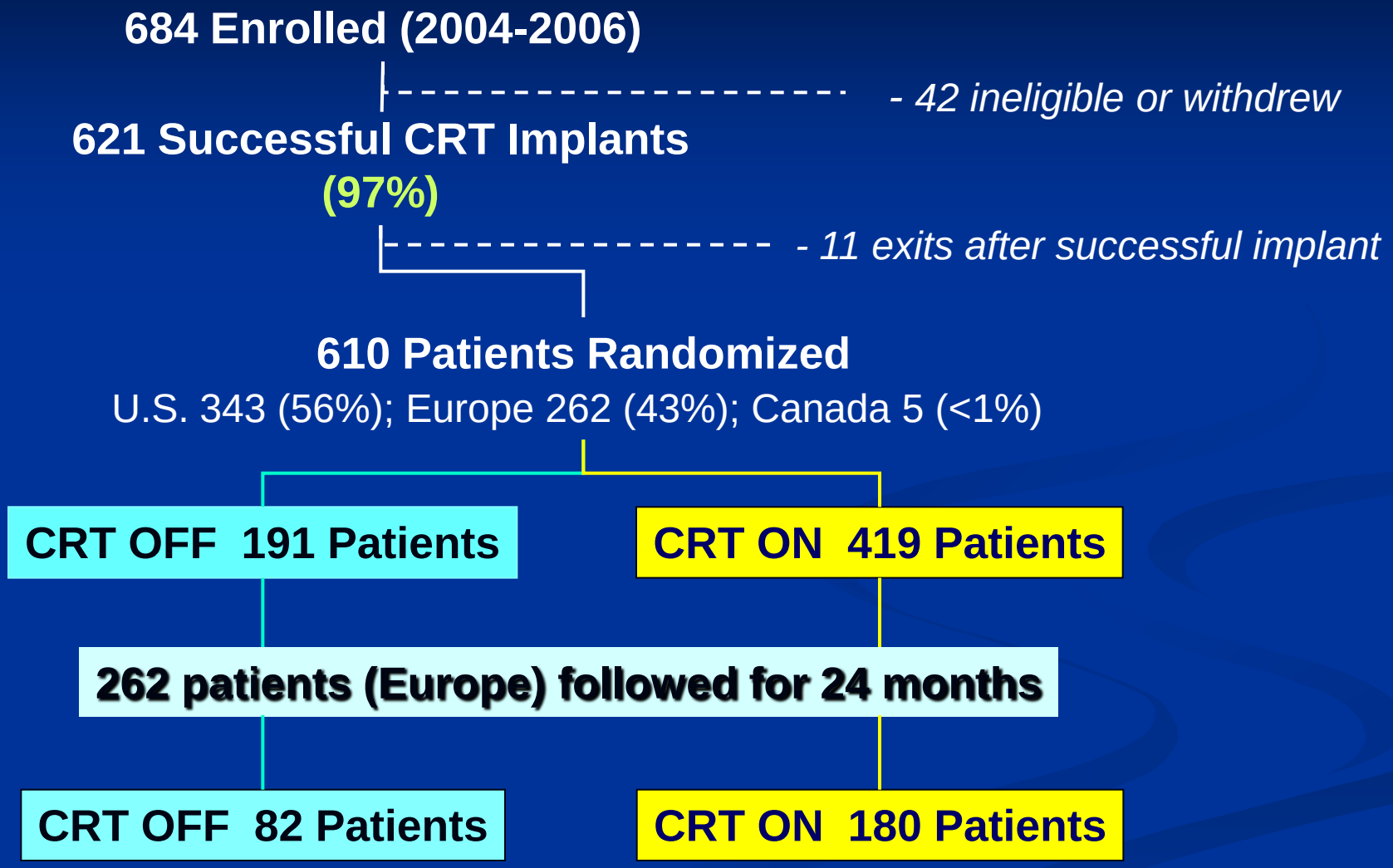
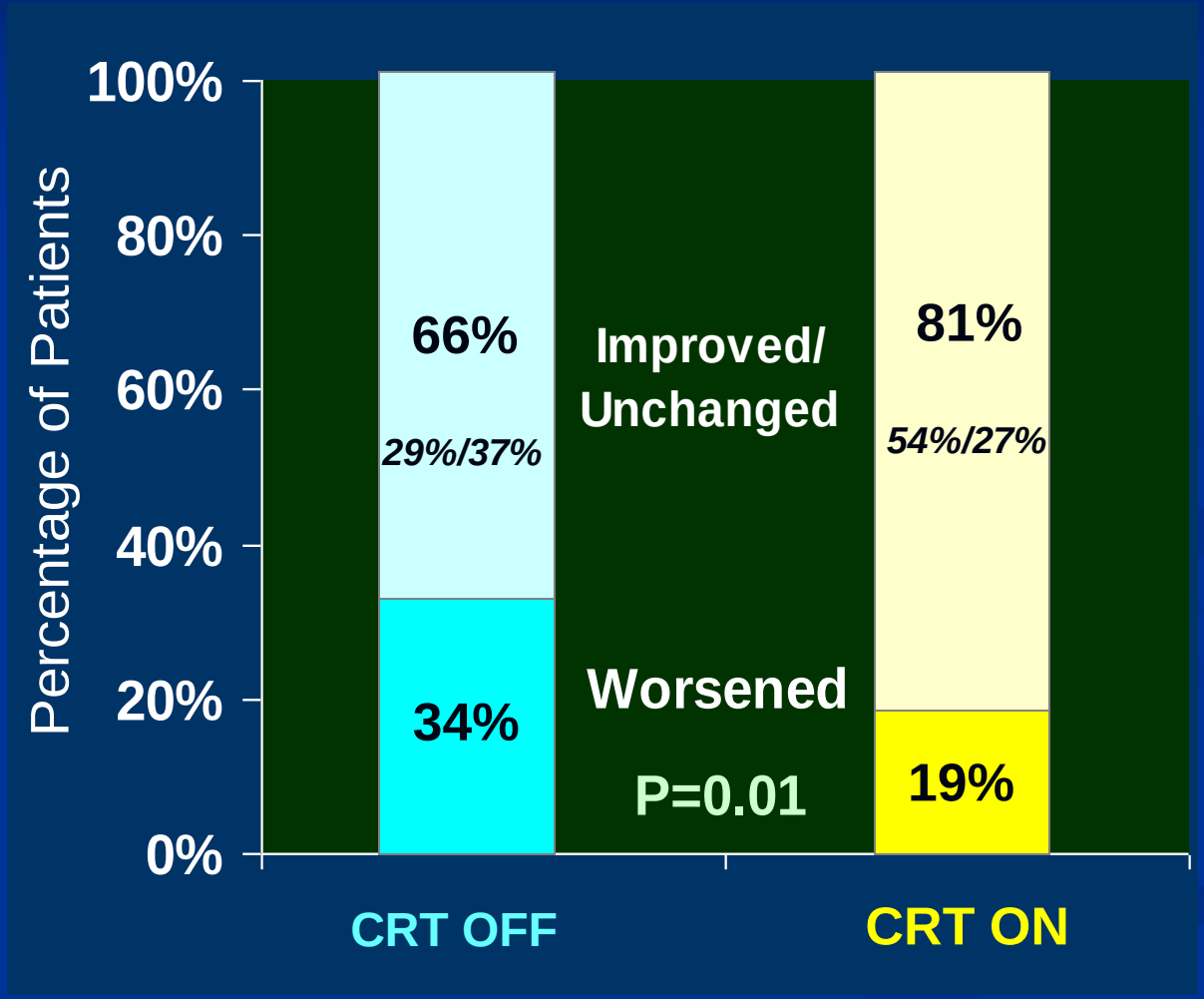


Baseline Characteristics

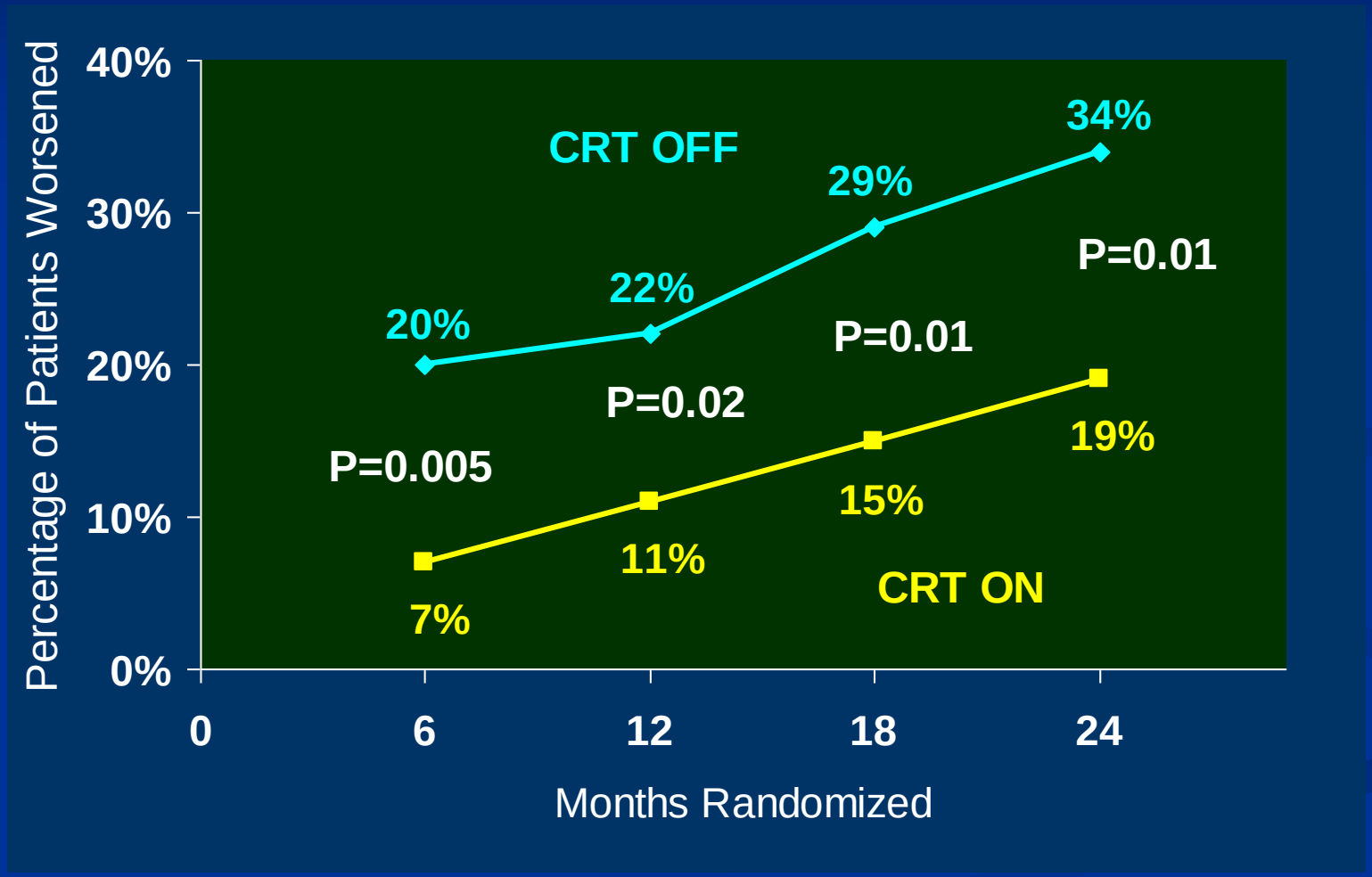
	US/Can N=348	Europe N=262	P-value
Age (mean) yrs	63.4 ± 11.3	61.3 ± 10.4	0.02
Ischemic	63%	44%	<0.0001
NYHA II	82%	83%	0.75
ICD	95%	68%	<0.0001
EF	26.3 ± 7.2	27.1 ± 6.8	0.16
LVEDD (mm)	65.5 ± 8.4	68.8 ± 9.2	<0.0001
QRS (ms)	151 ± 21	156 ± 23	0.008
Beta-blockers	96%	94%	0.13
ACE-i/ ARB	95%	>99%	0.0003
6-min. Walk (m)	363 ± 134	439 ± 103	<0.0001

Primary End Point: Clinical Composite Response



Entire distribution analysis of worsened, unchanged and improved: P=0.0006

Primary End Point
Clinical Composite Response
% worsened over time



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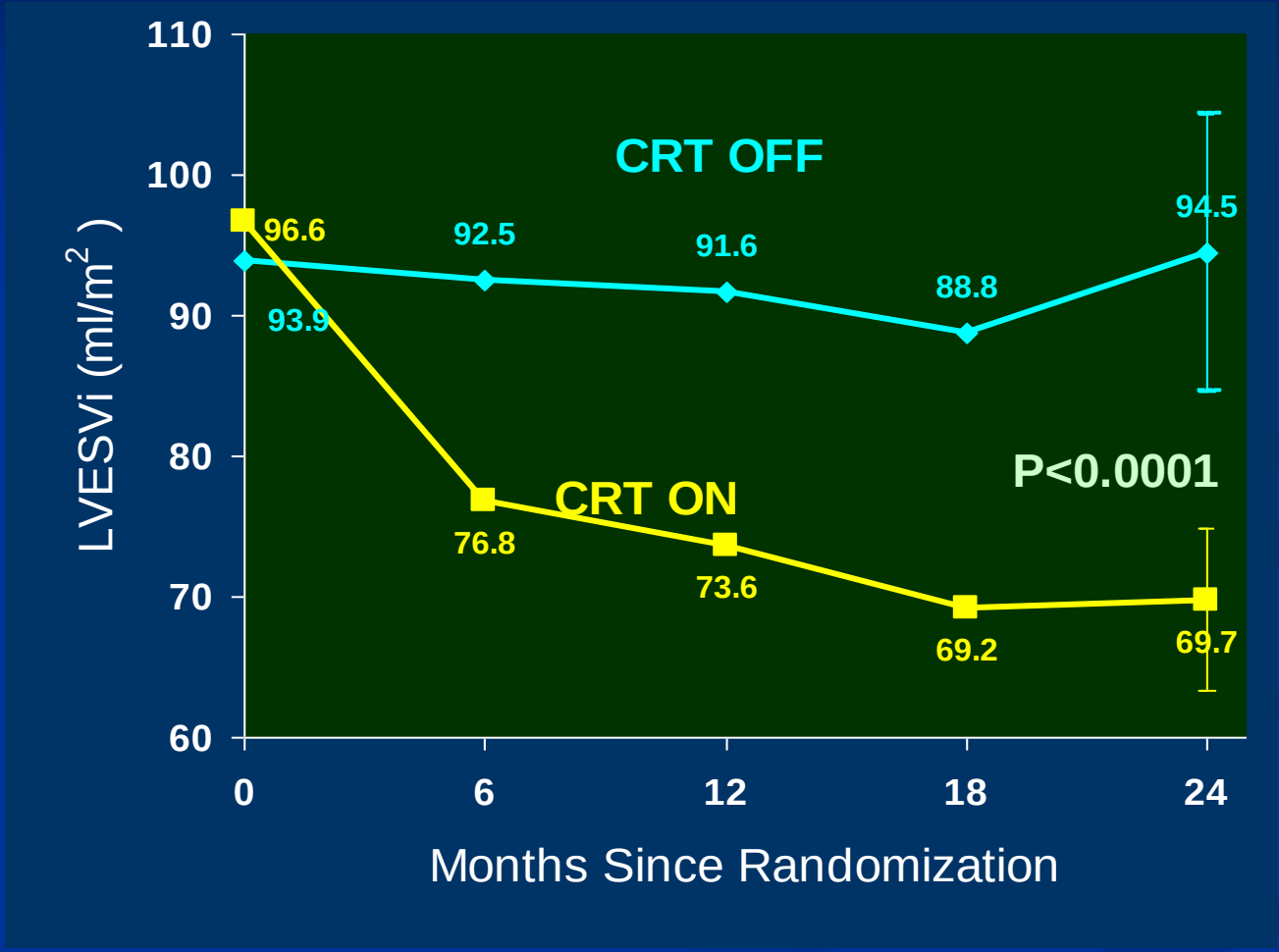
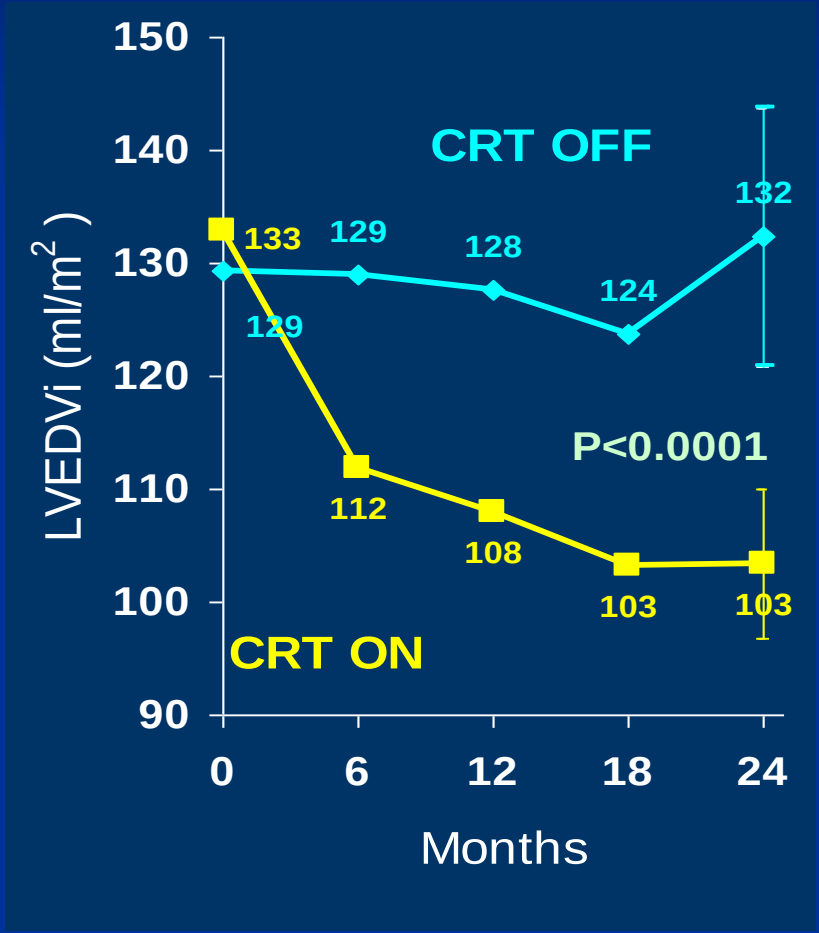


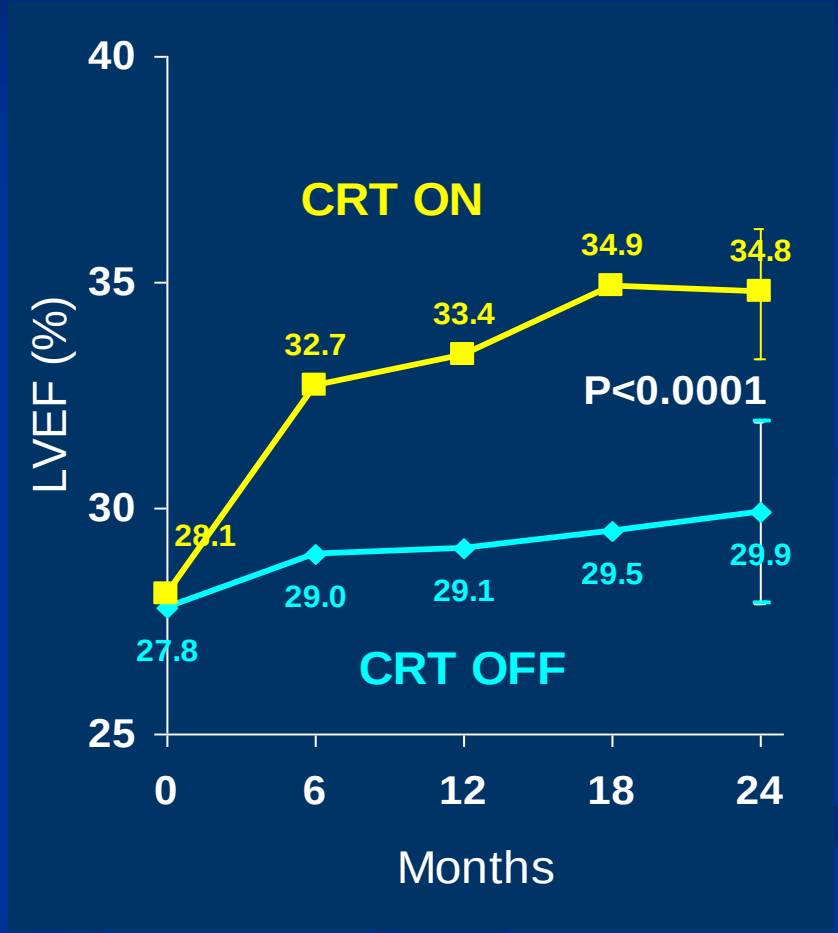
P-value compares 24-month changes.

Other Remodeling Parameters

LVEDVi (ml/m²)

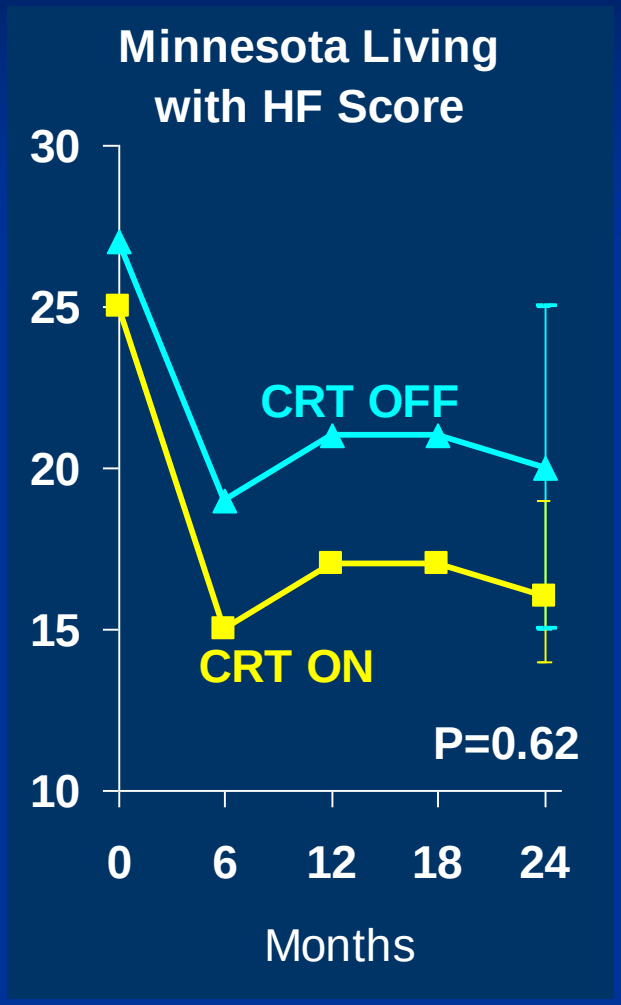


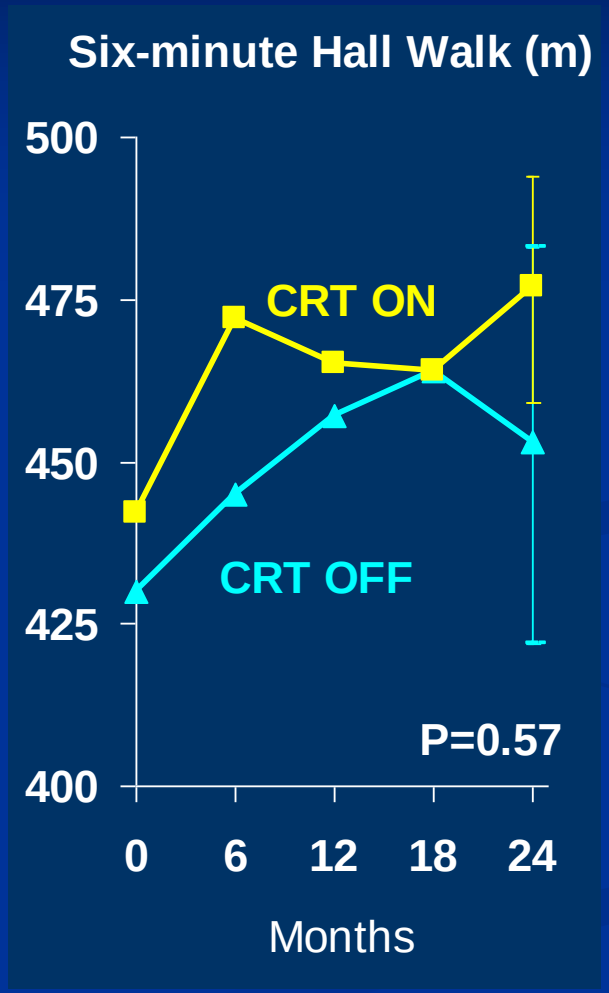
LVEF (%)

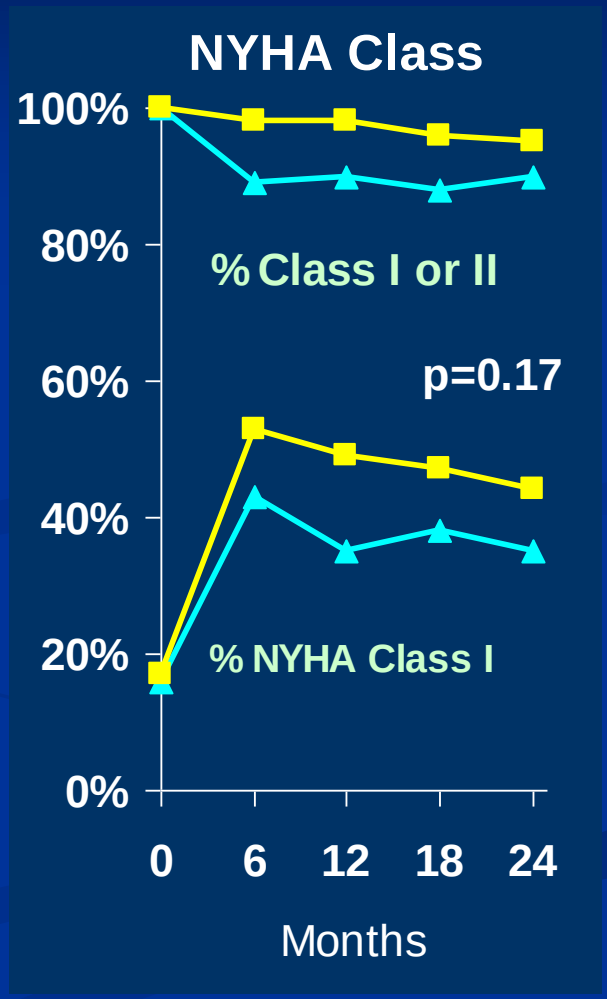


P-values compare 24-month changes.

Other Secondary Endpoints



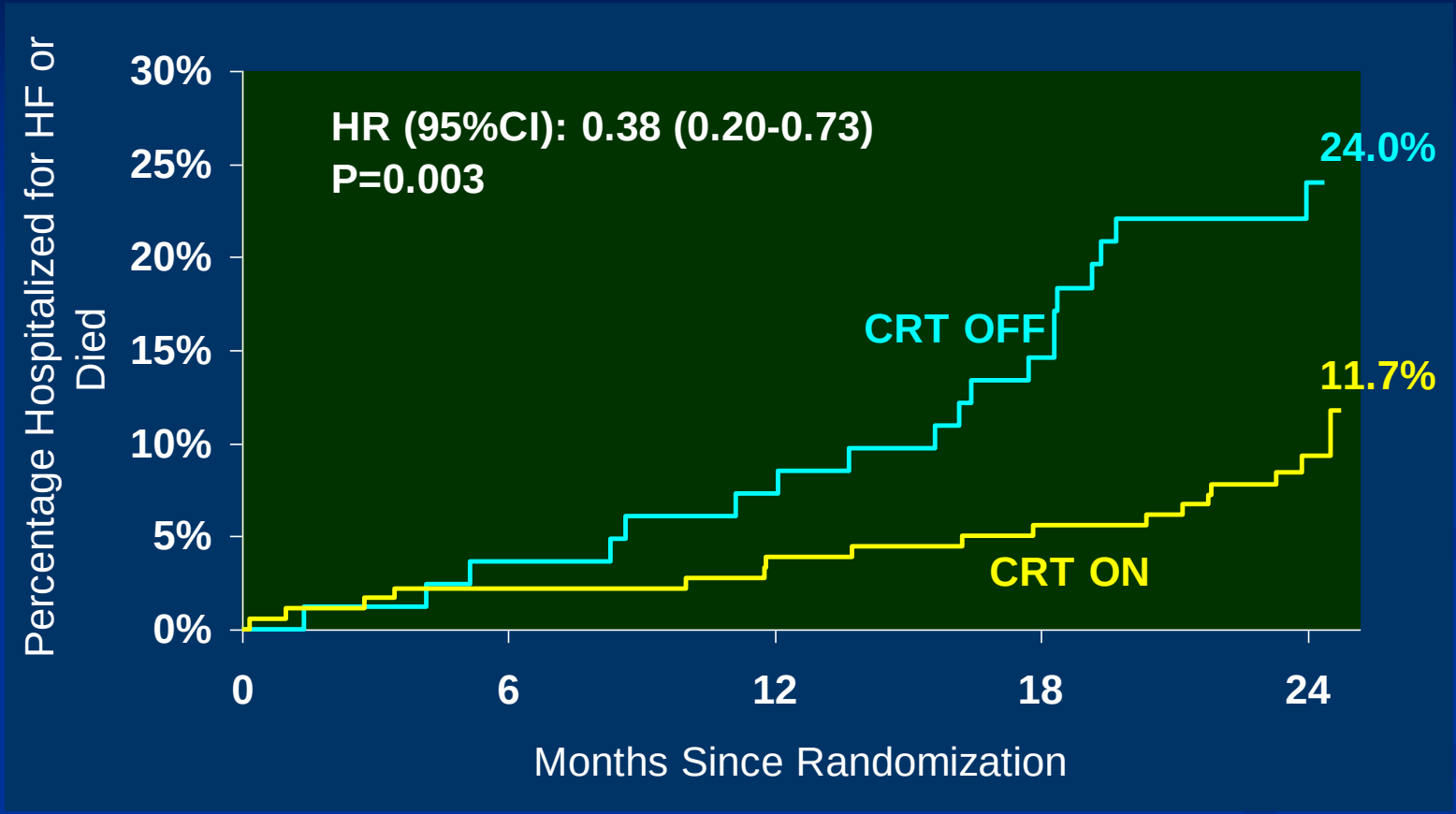




P-values compares 24-month changes.

P-value compares 24-month NYHA.

Time to First HF Hospitalization or Death



Number at Risk

CRT OFF	82	79	76	70	39
CRT ON	180	176	173	168	77

Conclusion

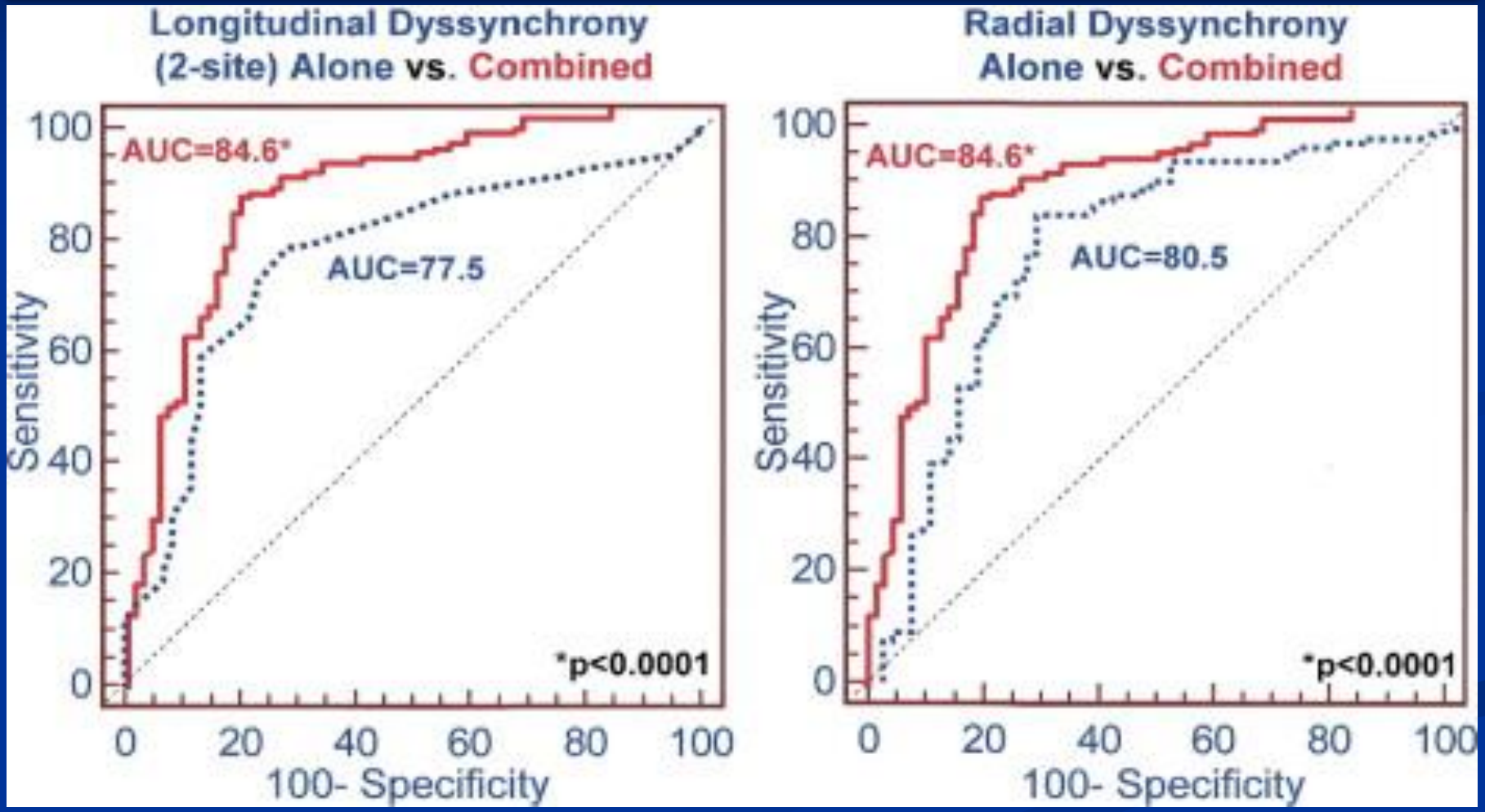
The 24 month results of the European cohort of REVERSE patients show that CRT in asymptomatic and mildly symptomatic HF patients on optimal medical therapy:

- Improves clinical outcome and
- Improves ventricular structure and function
- CRT thus may modify disease progression in mildly symptomatic HF patients

Note: FDA has not yet reviewed the clinical data to determine whether or not CRT systems are safe and effective in this patient population.

Longitudinal dyssynchrony > 60ms + radial dyssynchrony > 130ms:

95% of positive response (≥15% increase in EF)



2 centers, 190 patients

Acknowledgments

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