

Ποζιτρονική Τομογραφία και μοριακή απεικόνιση στην καρδιολογία

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BIOMEDICAL RESEARCH FOUNDATION

ACADEMY OF ATHENS

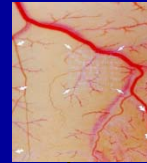


Molecular Imaging Targets for Noninvasive Cardiac Imaging

Microcirculation



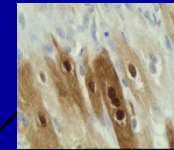
Angiogenesis



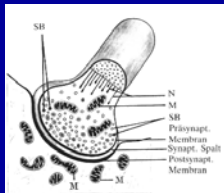
Metabolism



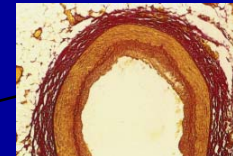
Extracell. Matrix



Autonomic Innervation



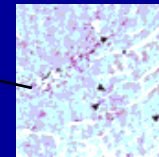
Atherosclerosis /
Plaque Vulnerability



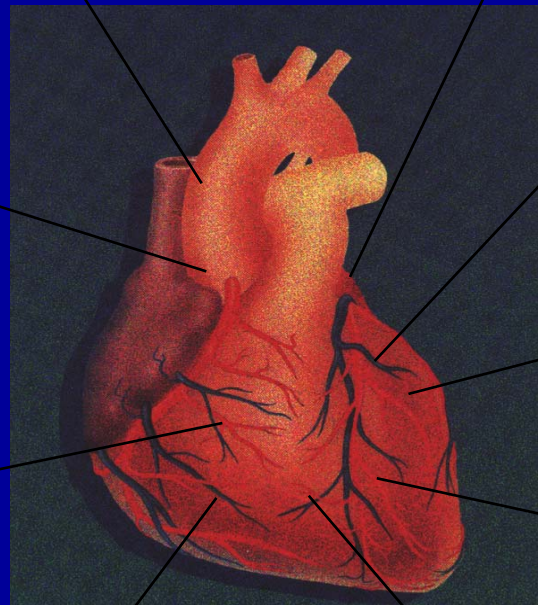
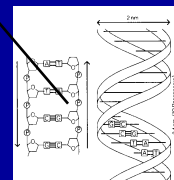
Apoptosis



Stem Cell Migration



Transgene
Expression



Why Molecular Cardiac Imaging?

- Understand mechanisms
- Early diagnosis
- Prognosis
- Sophisticated treatment/personalised
- Monitoring

Tools for molecular imaging with PET

METABOLISM & PERFUSION

Glucose uptake	^{18}F -FDG, ^{11}C -glucose
Perfusion/blood flow	^{15}O -H ₂ O, ^{13}N -NH ₃ /Rubidium-82
Oxygen consumption	^{15}O -O ₂ , ^{11}C -acetate
FFA uptake & oxidation	^{18}F -FTHA, ^{11}C -palmitate
Amino acid uptake & protein synthesis	^{11}C -MeAIB, ^{11}C -methionine
Hypoxia	^{18}F -fluoromiso, ^{18}F -FETNIM

RECEPTOR FUNCTION/APUD

Dopamine system	^{11}C -DOPA, ^{18}F -DOPA; ^{11}C -HTP
Somatostatin receptor	^{18}F -fluoro-octreotide

OTHER

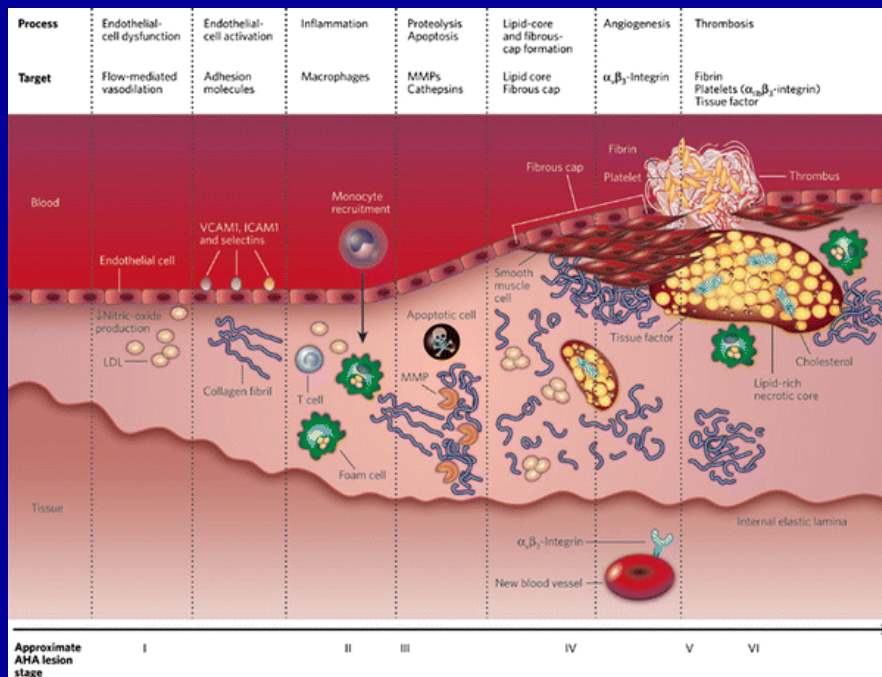
Cortisol synthesis	^{11}C -metomidate
Thyroxin synthesis	^{124}I

$T_{\frac{1}{2}}$

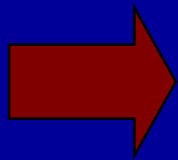
^{18}F 109 min

^{11}C 20 min

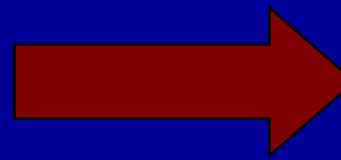
^{15}O 2 min



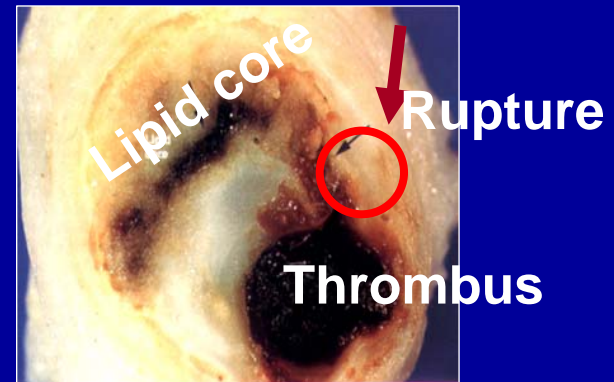
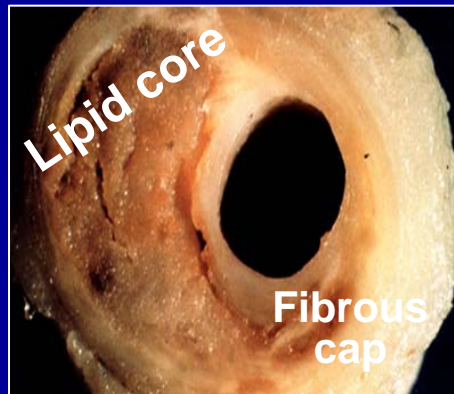
normal



vulnerable



ruptured

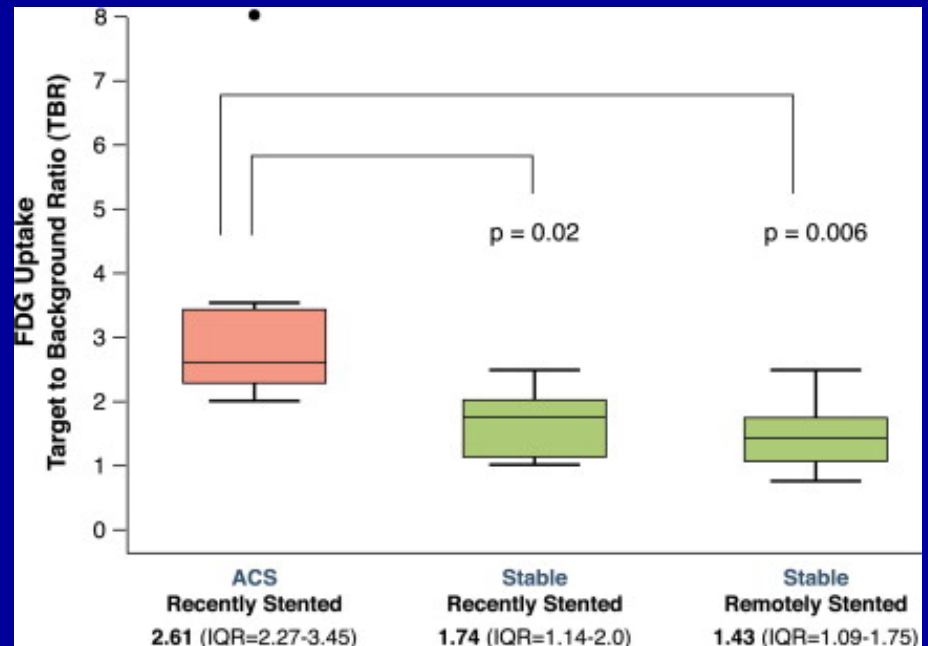
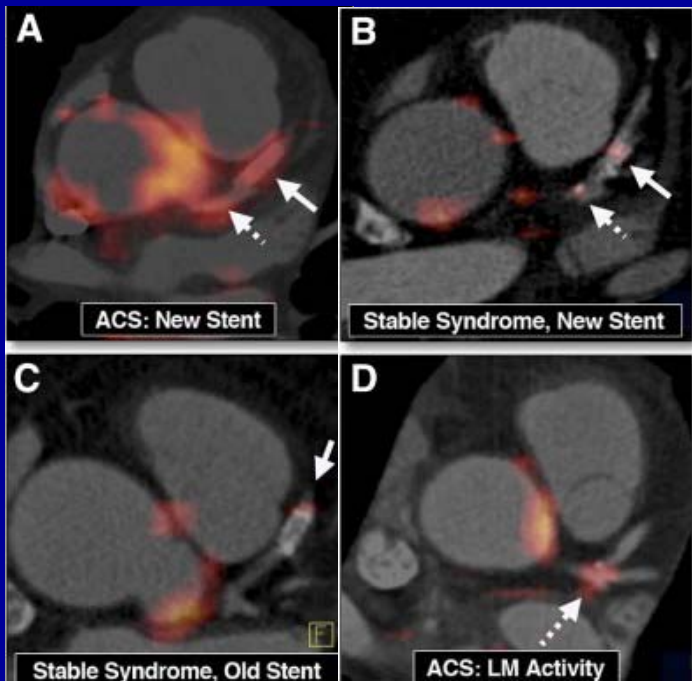


FDG PET imaging of the coronary arteries

25 pts, mean age 57.9 ± 9 y (72% male)

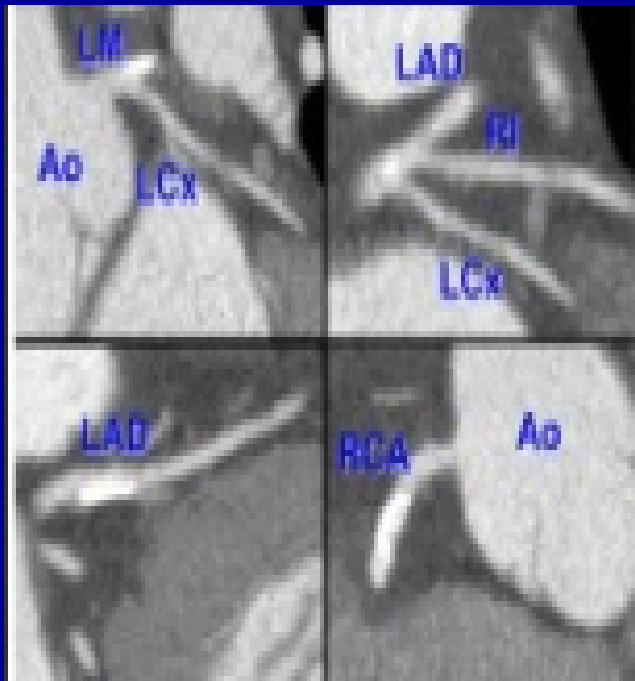
10 ACS treated with PCI

15 with stable angina (5 underwent PCI and 10 ICA only)

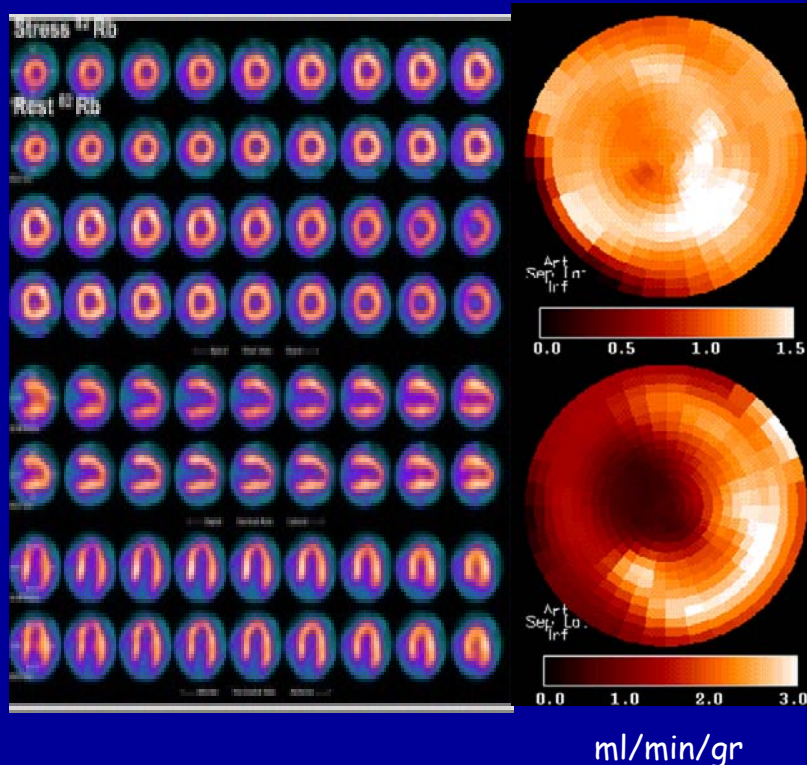


Integrated Imaging of coronary anatomy and function

47 y old male, smoker, overweight, with borderline Hypertension and osteoarthritis

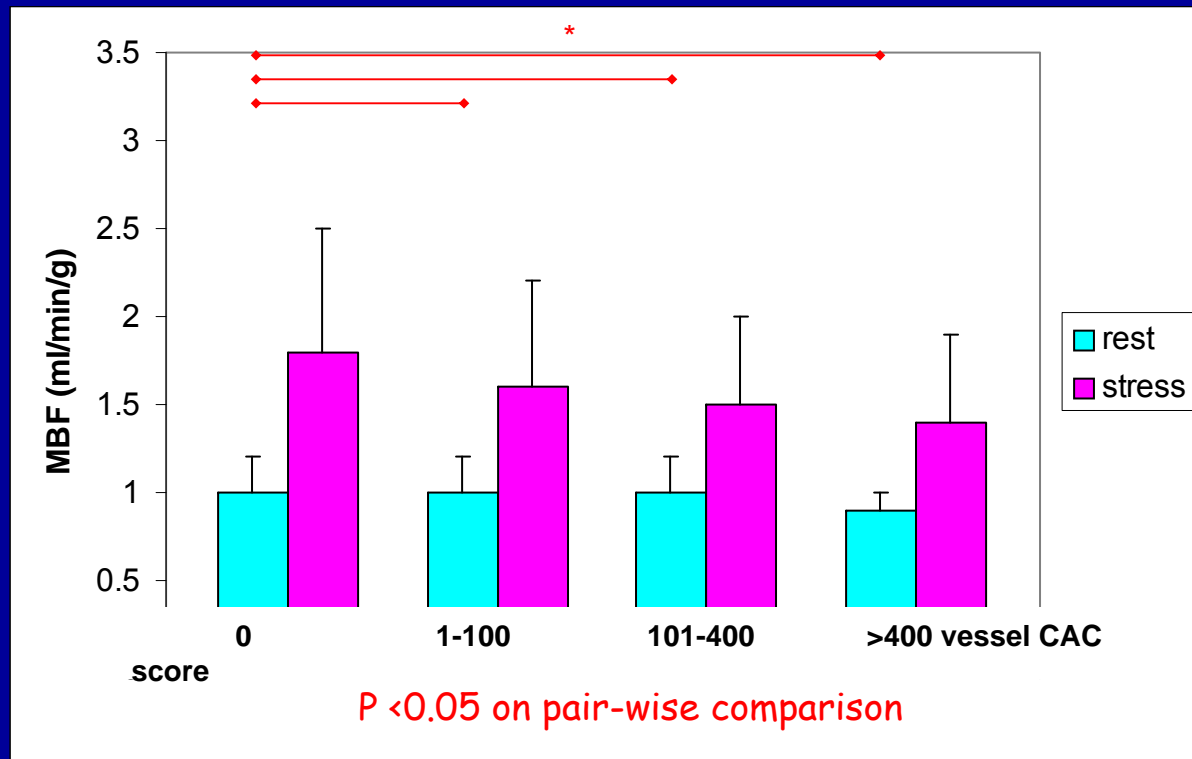


CCS: 186



Interrelation between calcium score and MBF

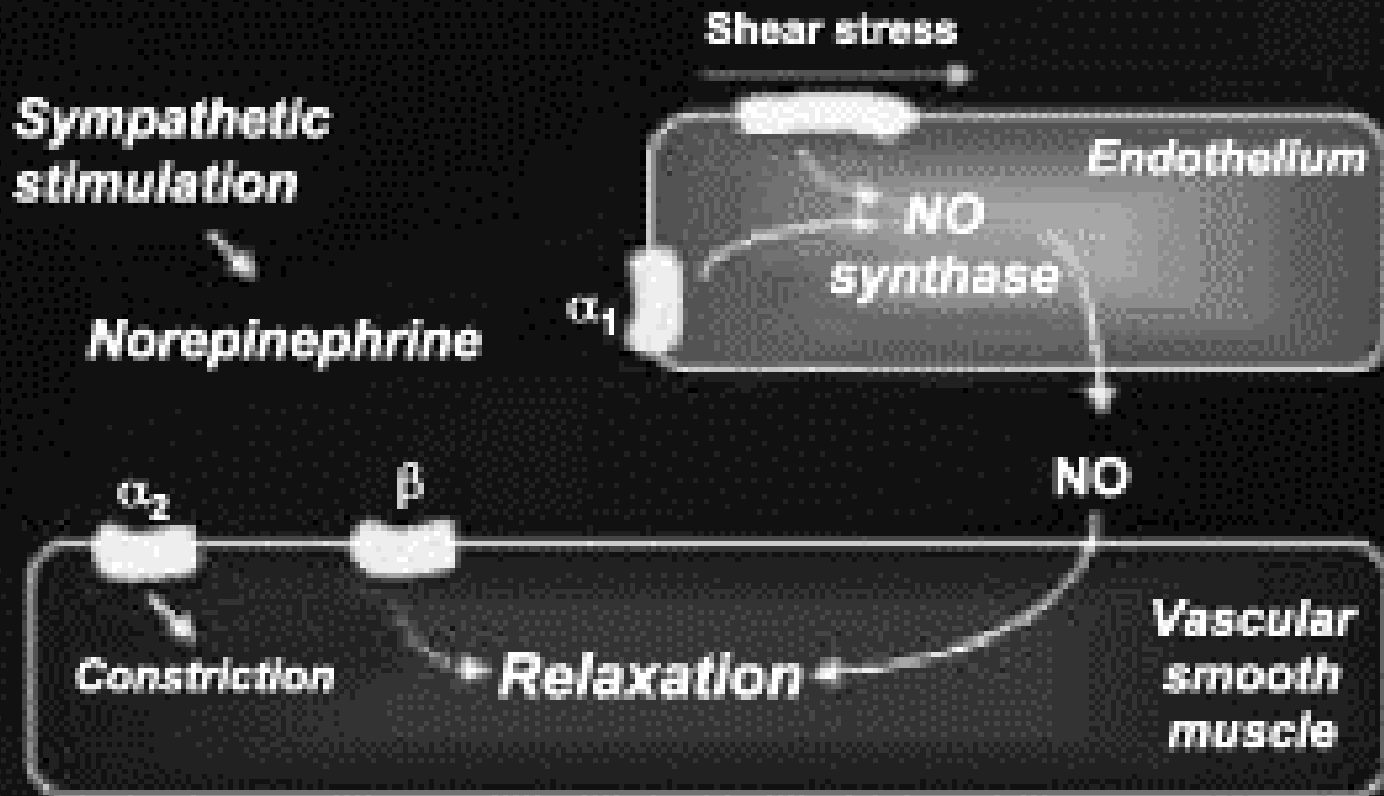
136 consecutive patients without CAD (age 62 ± 12 years, 68 % females) with normal myocardial perfusion using Rb-82 PET
CAD likelihood: 0.31 ± 0.25



Assessment of endothelial function

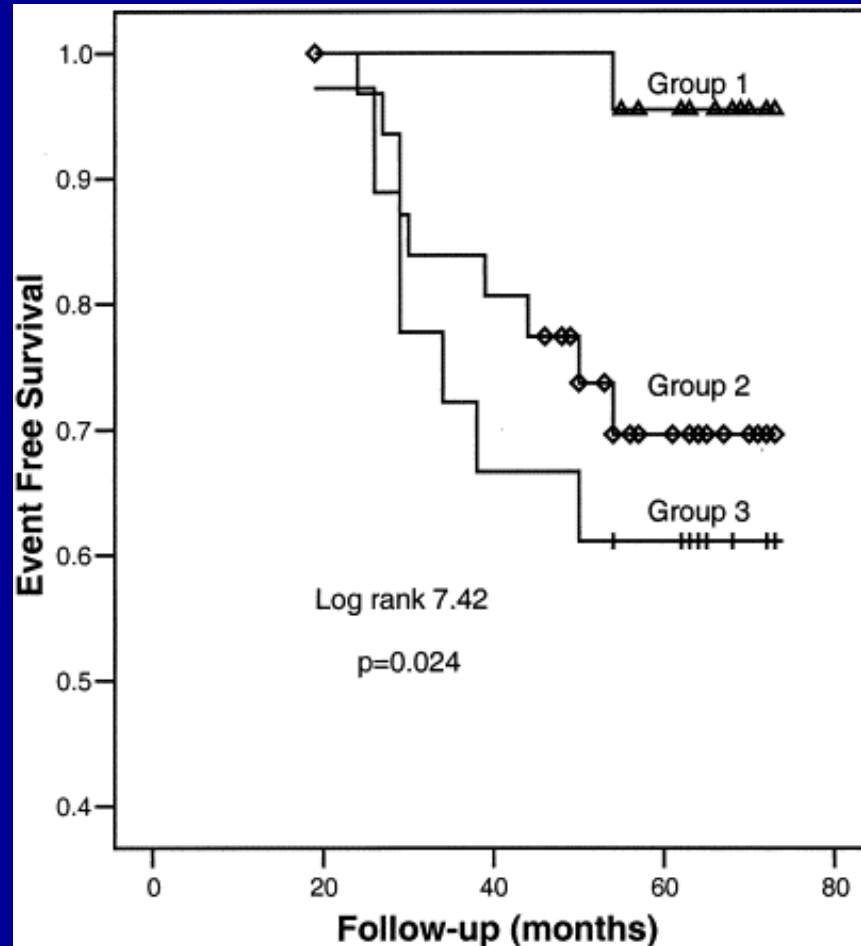
Cold pressor test

(b)



Prognostic value of CPT perfusion measurements

72 patients risk factors for CAD but normal coronary angiography



*CPT:cold pressor test

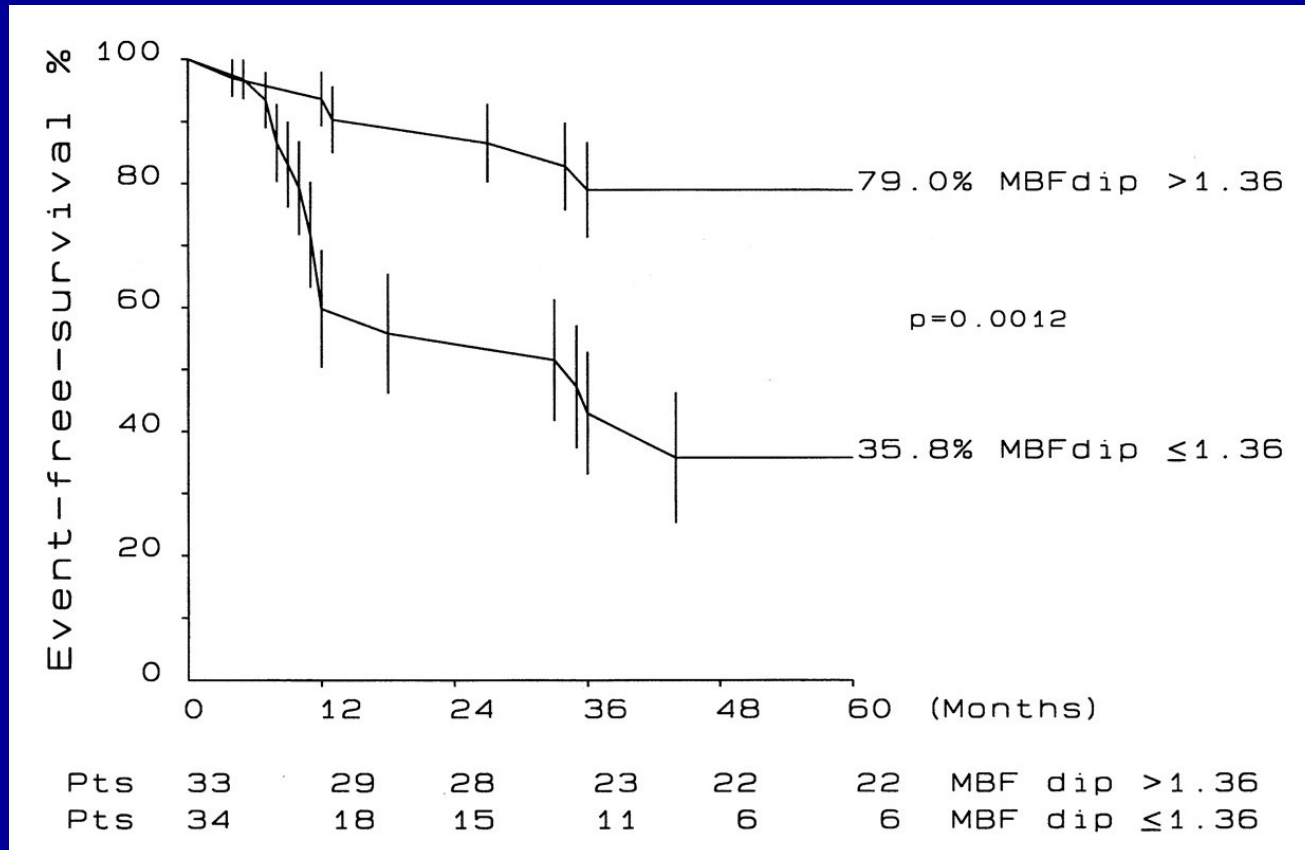
Group 1: patients with $\geq 40\%$ increase in MBF

Group 2, patients with >0 and $<40\%$ increases in MBF

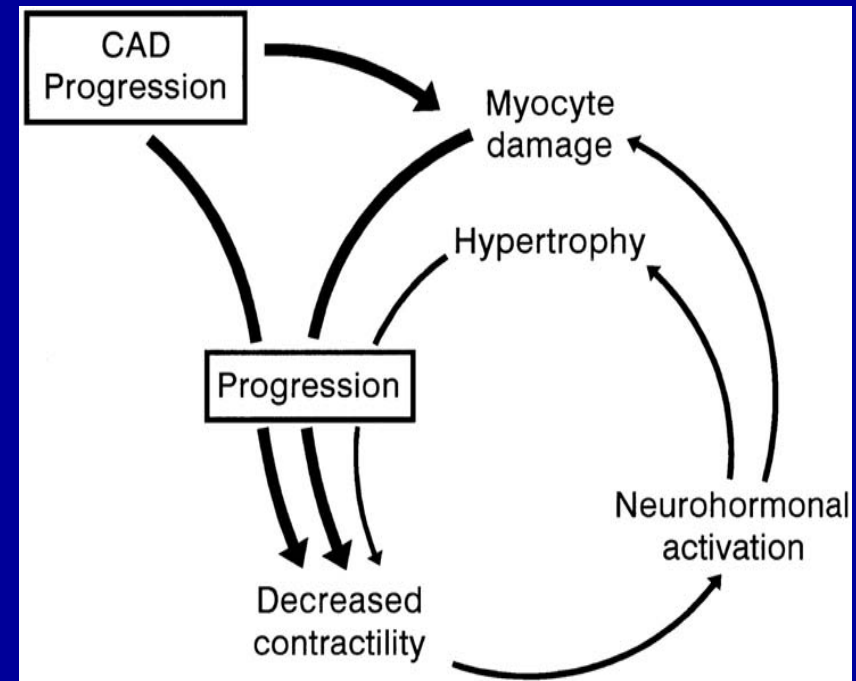
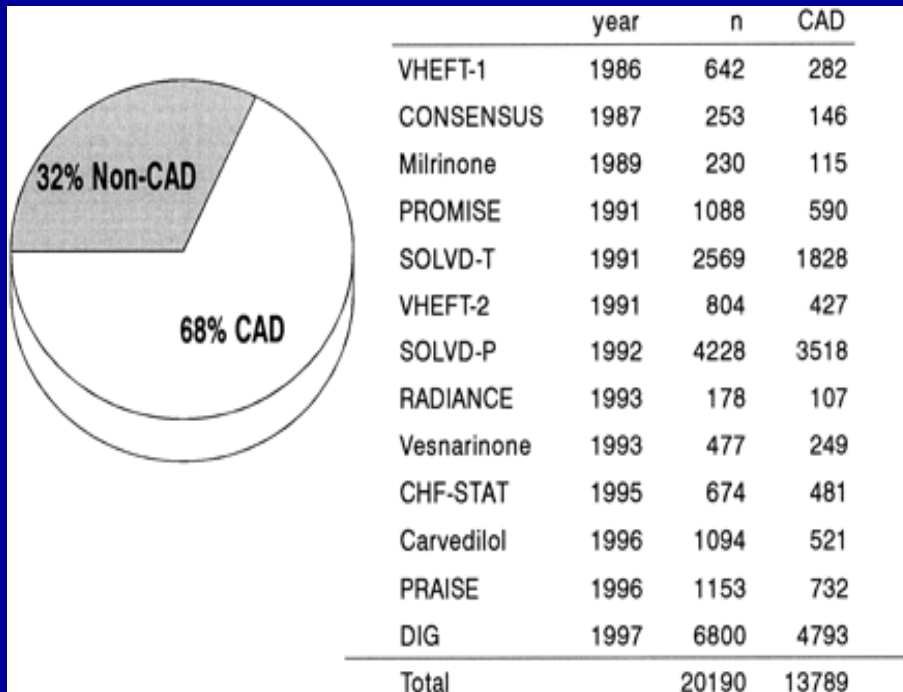
Group 3, patients with decrease in MBF ($\leq 0\%$)

Prognostic Role of Myocardial Blood Flow Impairment in Idiopathic Left Ventricular Dysfunction

- 67 pts (52 male, mean age 52 ± 12 years) with different degrees of idiopathic LV systolic dysfunction: average LVEF 0.34 ± 0.10 ; range, 0.07 to 0.49)
- 34 pts (51%) had no history of heart failure symptoms at enrollment (NYHA class I)



CAD-LV dysfunction and heart failure

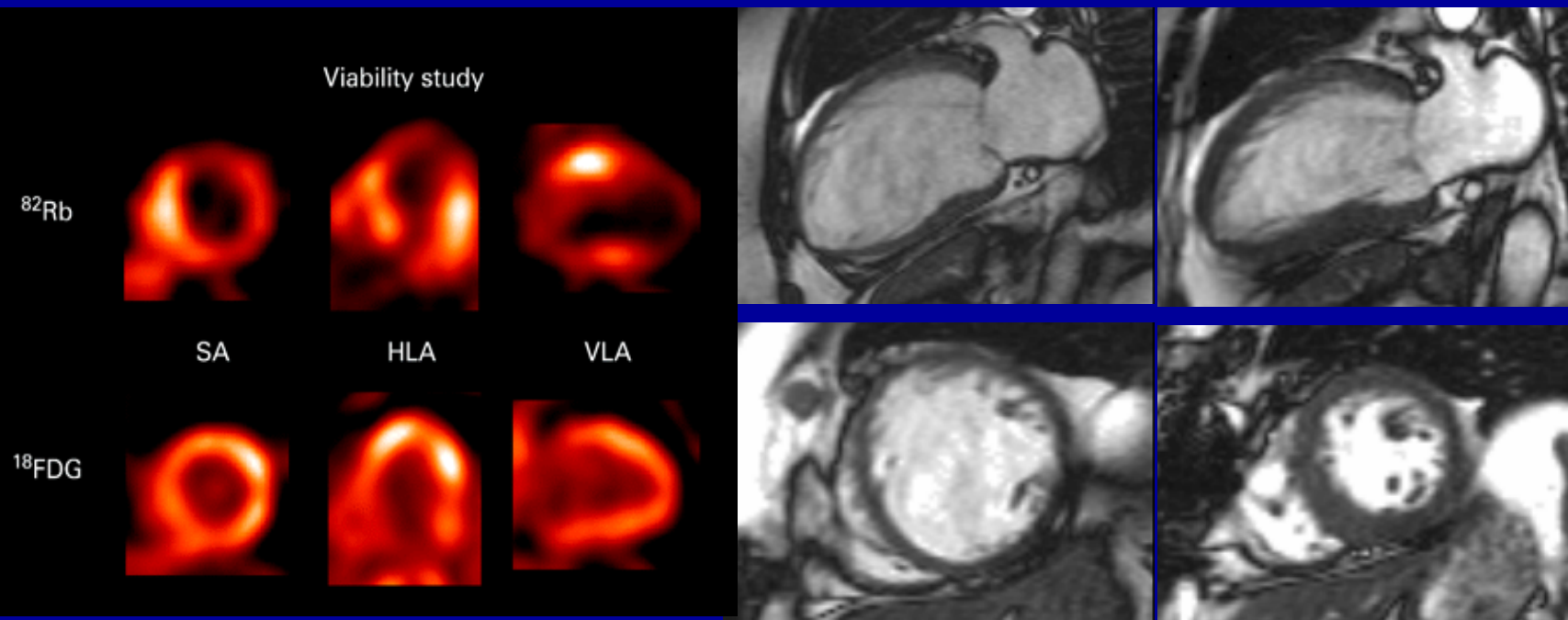


Prevalence of CAD in 13 randomized multicenter heart failure trials

Myocardial Perfusion and metabolism in the ischaemic myocardium

	Mild- moderate ischaemia	Severe ischaemia	Recovery
Metabolism	anaerobic ↑ oxidative ↓	both ↓	anaerobic ↓ oxidative ↑
Preferred substrate	glucose	neither - necrosis	free fatty acid

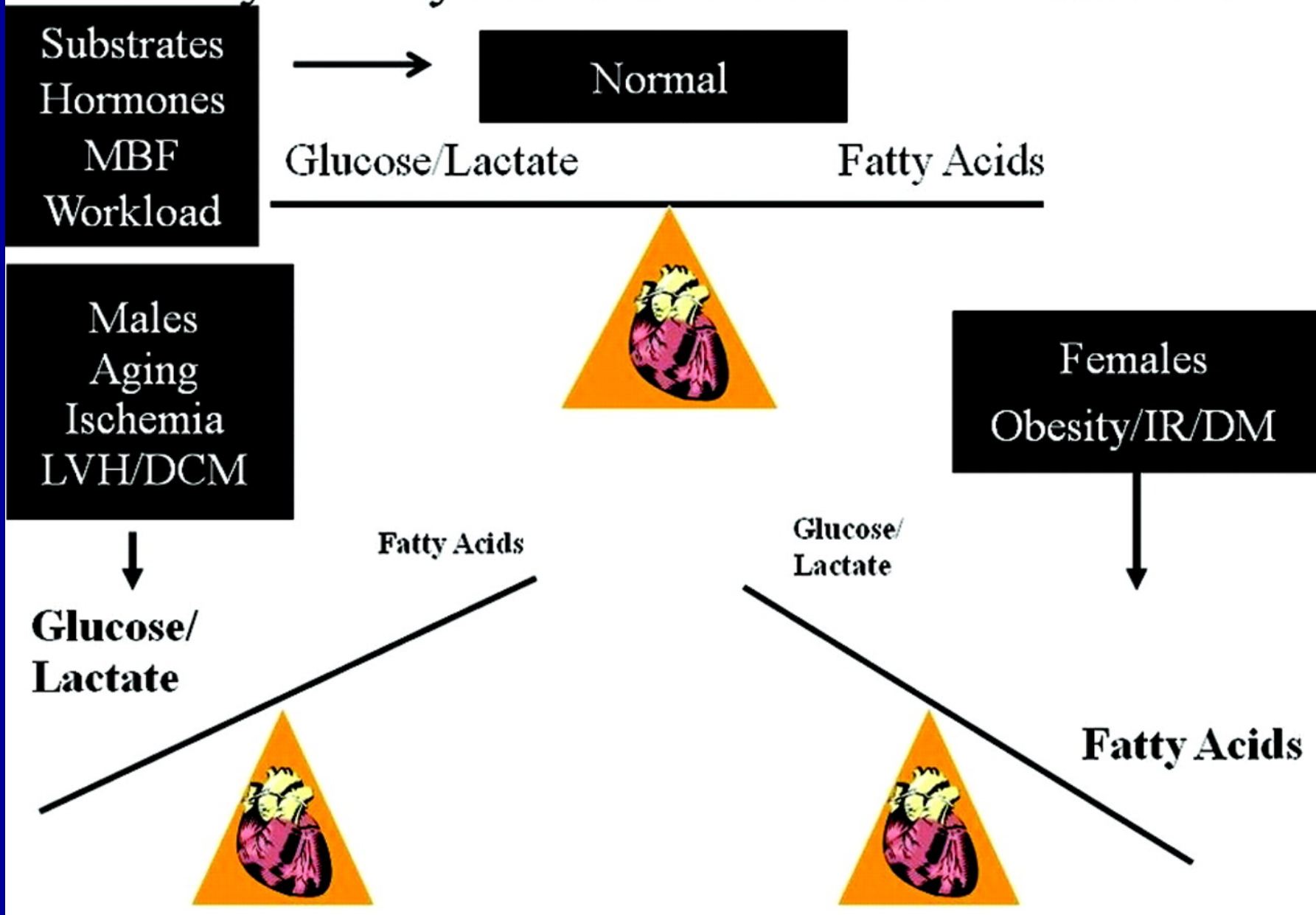
SOB, LVEF <35%



^{82}Rb :Rubidium

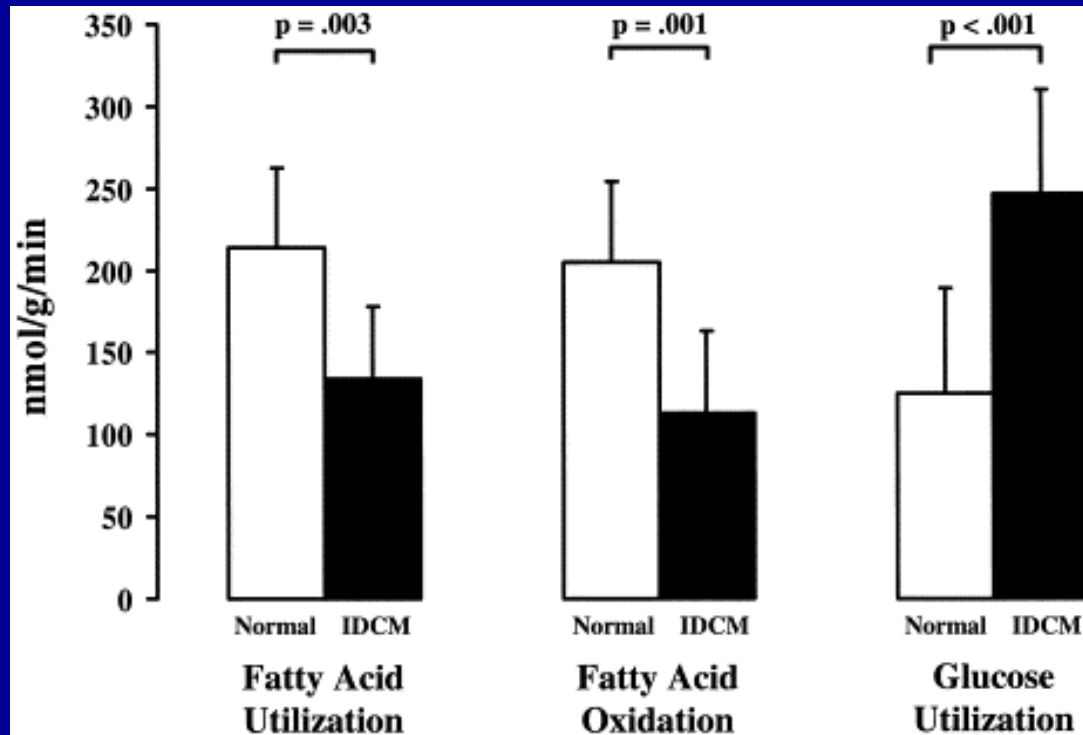
^{18}F -FDG:Fluro-Deoxy-
Glucose

Plasticity in Myocardial Substrate Metabolism



Altered myocardial fatty acid and glucose metabolism in idiopathic dilated cardiomyopathy

17 patients with IDCM (mean LVEF $27 \pm 8\%$) and 12 normal controls underwent dynamic PET to assess myocardial glucose utilization (MGU) with ^{11}C -Glucose and myocardial fatty acid utilization (MFAU) + myocardial fatty acid oxidation (MFAO) using ^{11}C -Palmitate



Neuronal function and chronic Heart Failure

Reduced noradrenaline clearance because of

a) low cardiac output

+

b) Sympathetic nerves of the failing myocardium release more NA and remove it less efficiently by reuptake

↓ uptake 1 mechanism

↑ NA concentration at the myocyte membrane

↑ Myocyte hyperstimulation

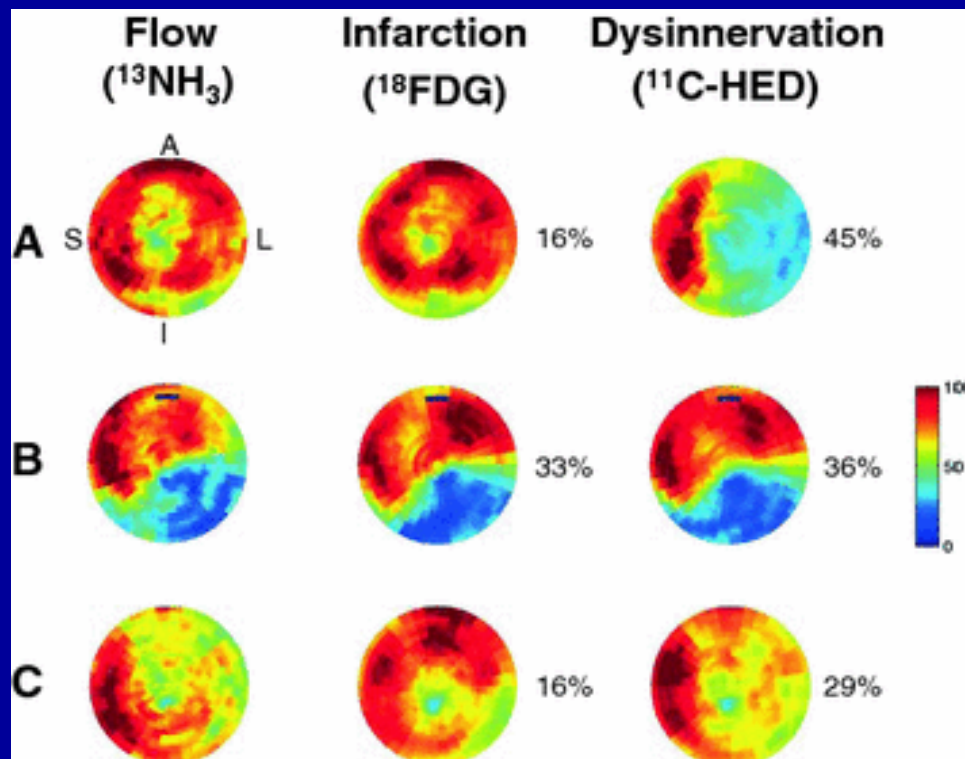
↓
Hypertrophy, remodelling
Disturbed intracellular Ca^{2+} handling
Apoptosis
Arrhythmias

^{11}C hydroxyephedrine (HED) PET in combination with flow and metabolite imaging

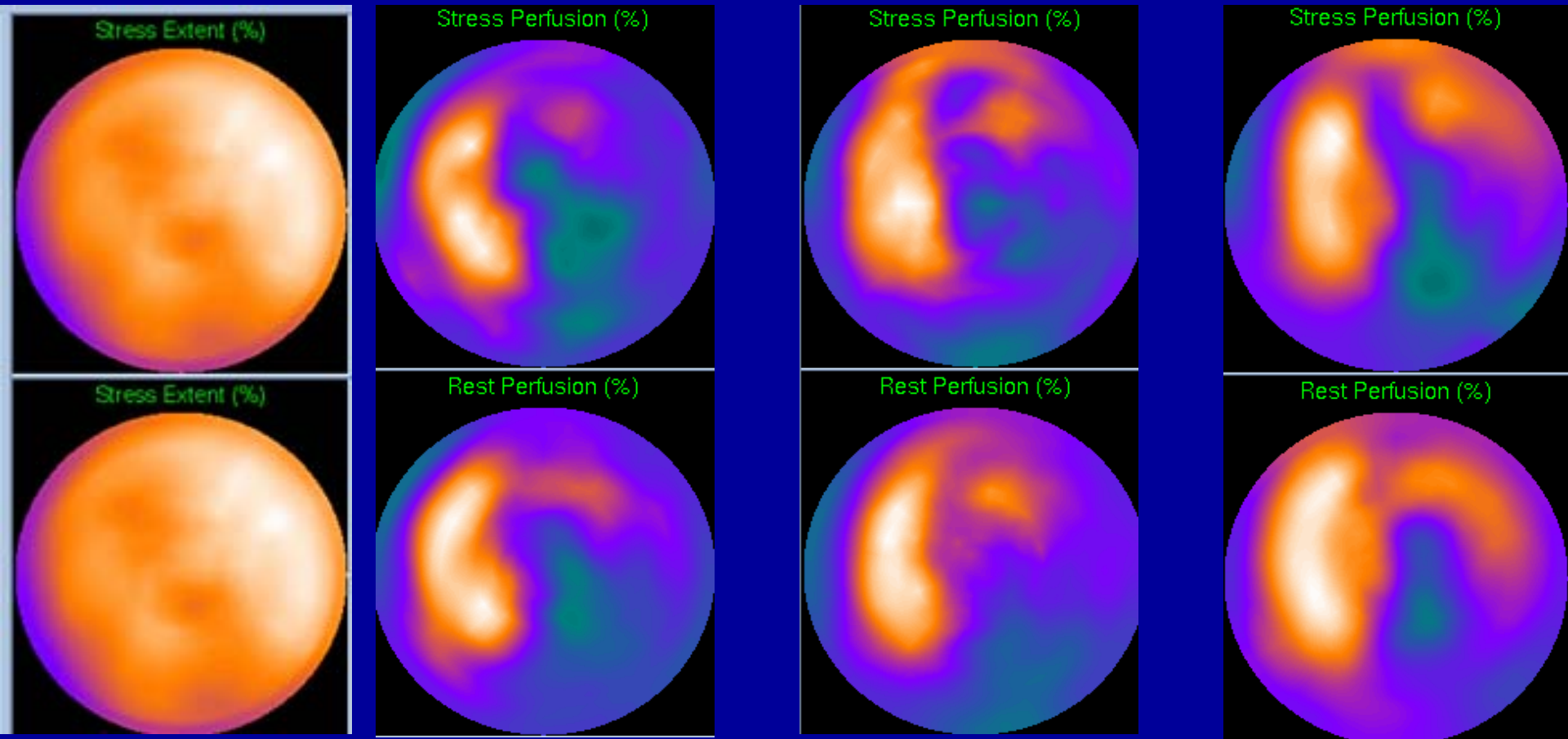
Prediction of ARrhythmic Events with Positron Emission Tomography

Aim: to investigate the clinical utility of assessing regional sympathetic nerve function and its role as a risk factor for sudden cardiac death

200 patients with ischemic LV dysfunction



Monitoring the effect of Stem cell therapy

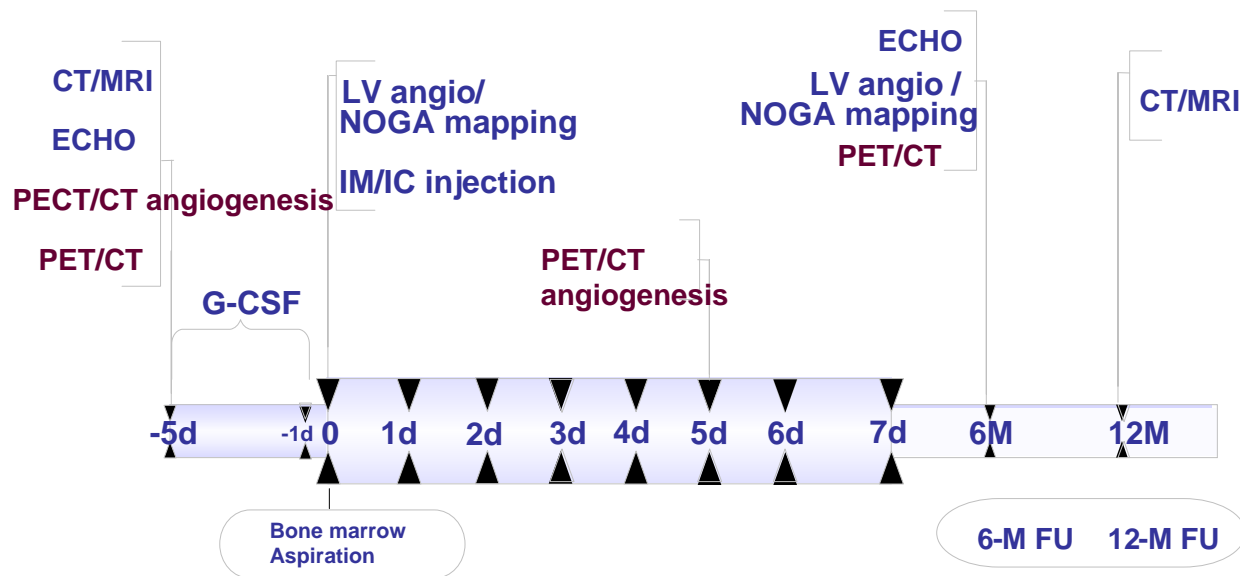


Before

6 months

18 months

Angiogenesis in REGENERATE-IHD Study Flow



PET/CT → Angiogenesis study

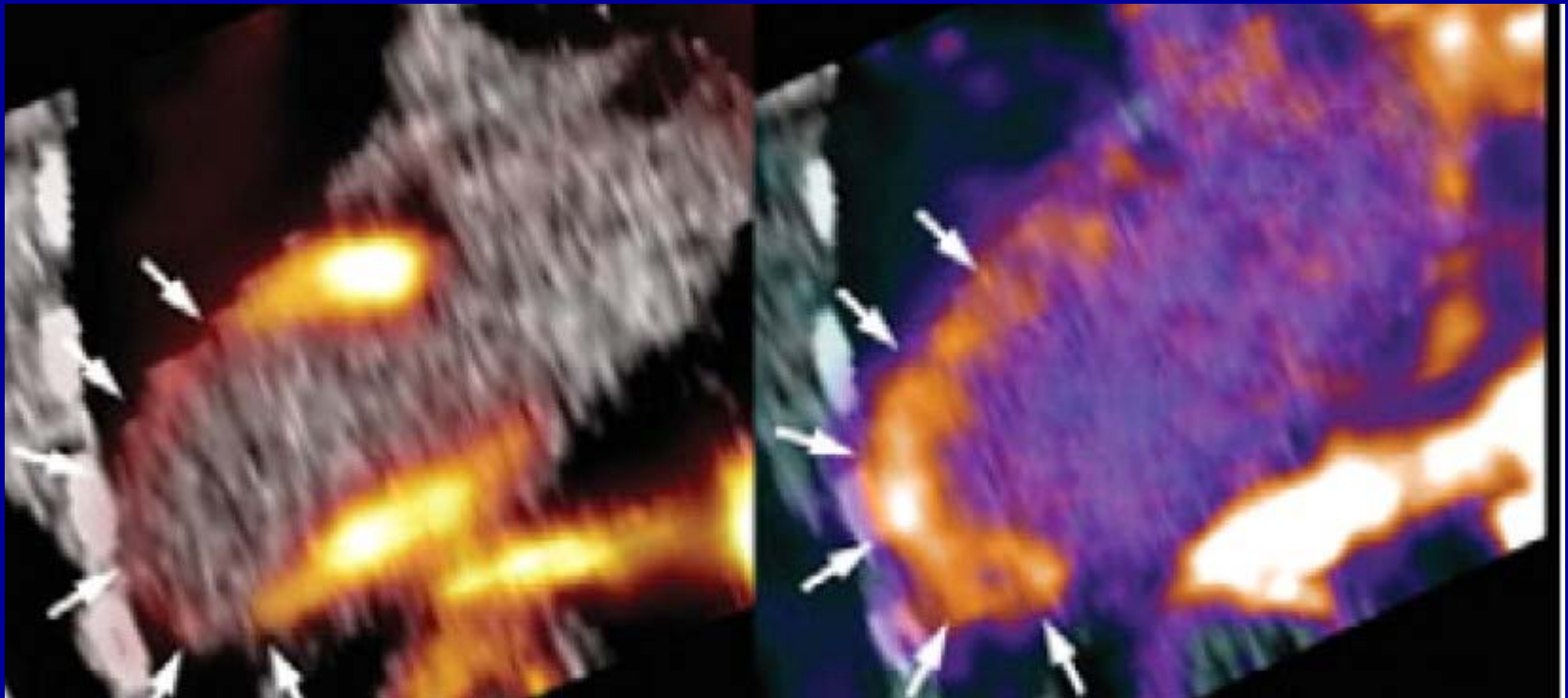
PET/CT → Perfusion study

IM → Intramyocardial; IC → Intracoronary

Time line for Angiogenesis study

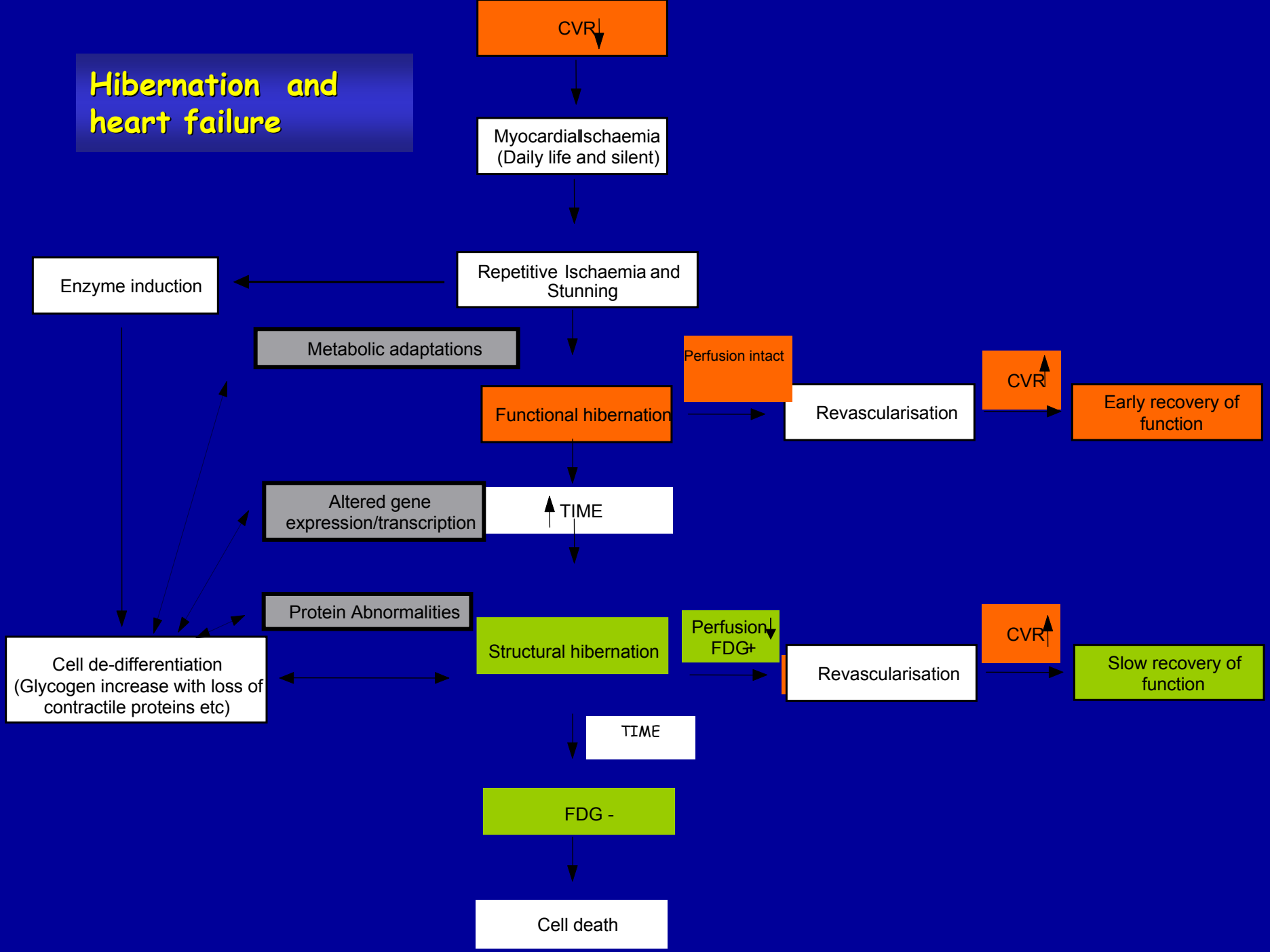
Imaging angiogenesis with F-18-galacto RGD

Arginine-glycine-aspartate (RGD)-binding $\alpha_v\beta_3$ -integrin



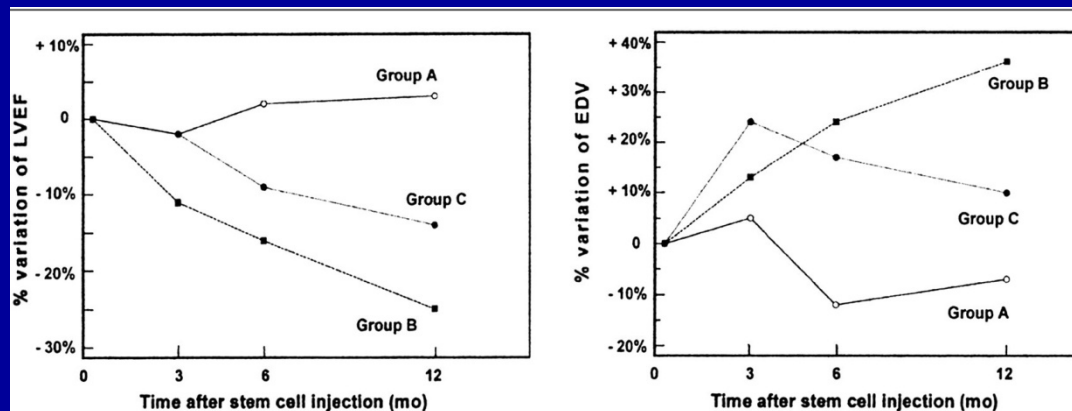
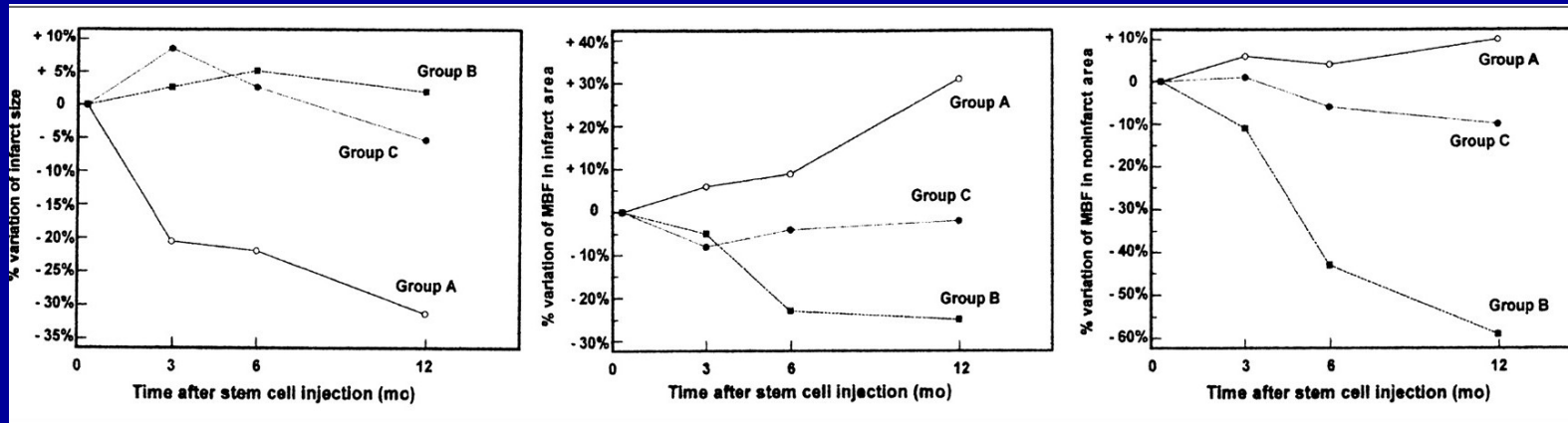
THANK YOU

Hibernation and heart failure

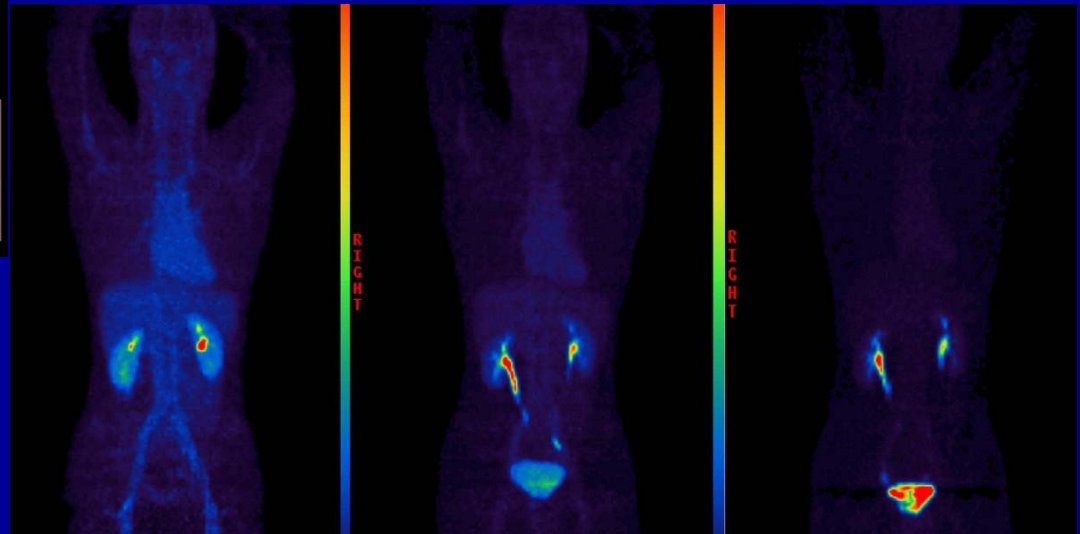
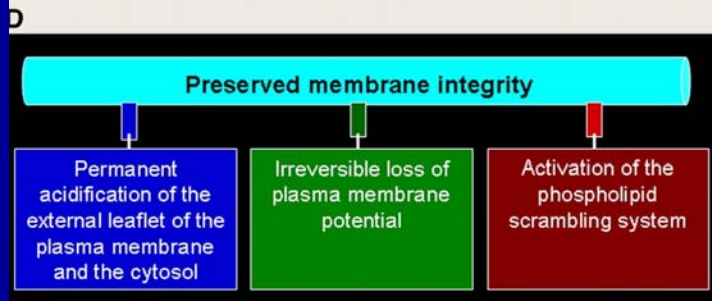
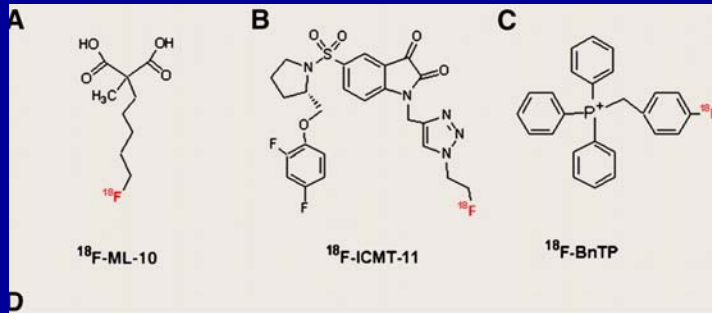


PET with ^{13}N -ammonia and ^{18}F -FDG in the assessment of myocardial perfusion and metabolism in patients with recent AMI and intracoronary stem cell injection

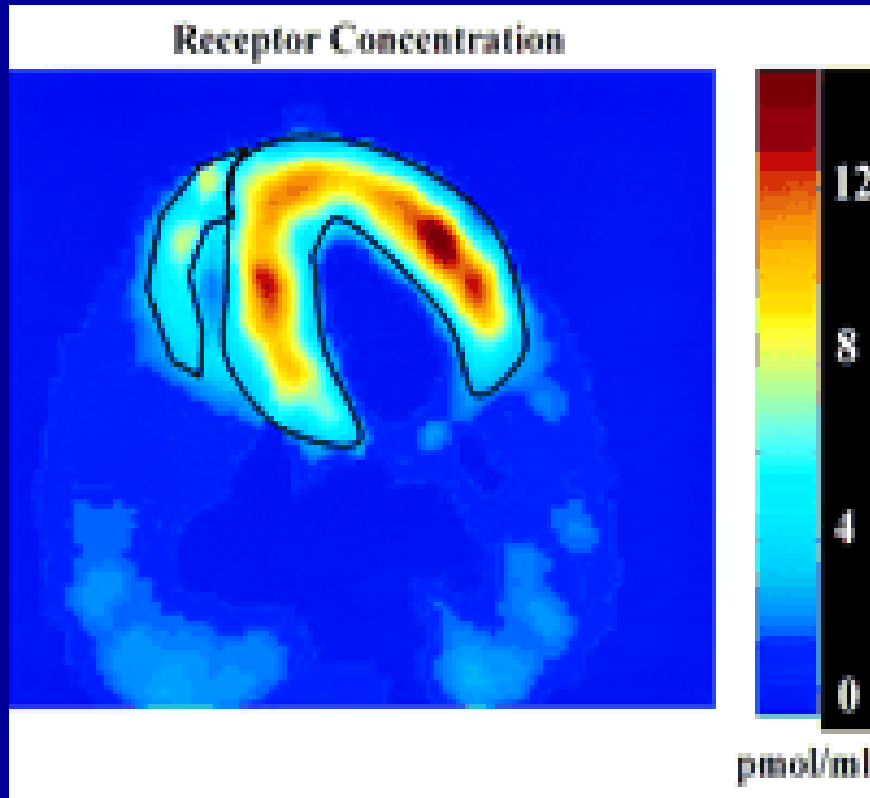
15 patients were randomly assigned to 3 groups based on different treatments
Group A: bone marrow-derived stem cells; Group B: peripheral blood-derived stem cells; group C: standard therapy alone



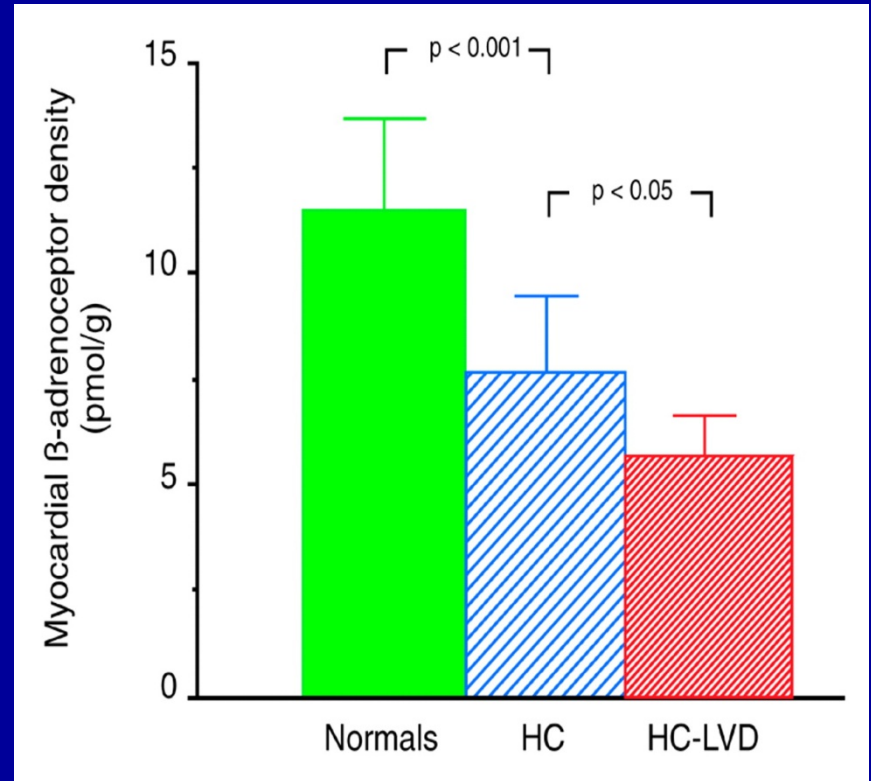
Imaging apoptosis with PET tracers



Adrenoreceptor density assessed by PET



6



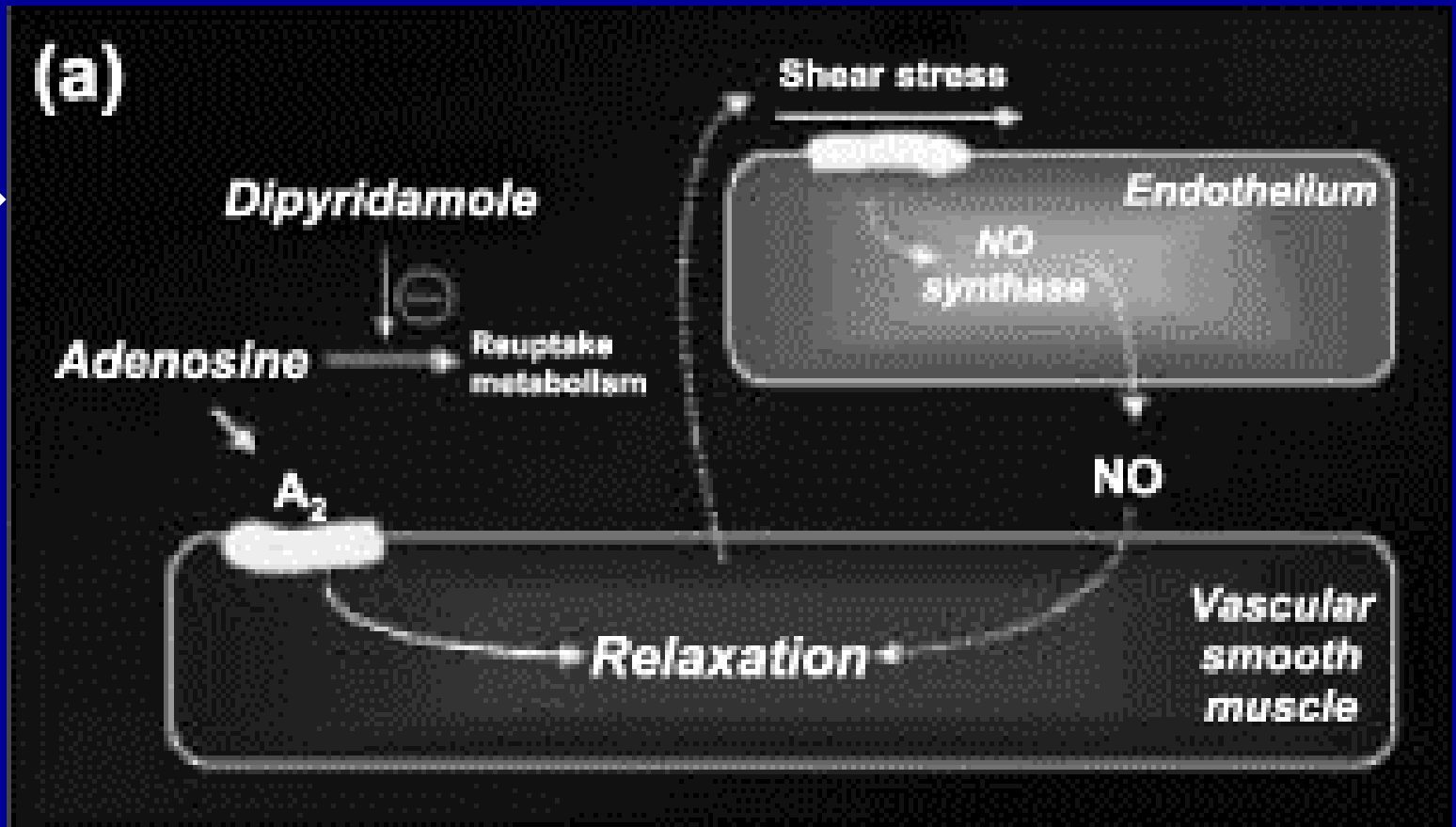
CGP 12177: Non-selective adrenoreceptor antagonist

- Lower Myocardial Perfusion Reserve Is Associated With Decreased Regional Left Ventricular Function in Asymptomatic Participants of the Multi-Ethnic Study of Atherosclerosis (MESA)
B D Rosen et al Circulation 2006

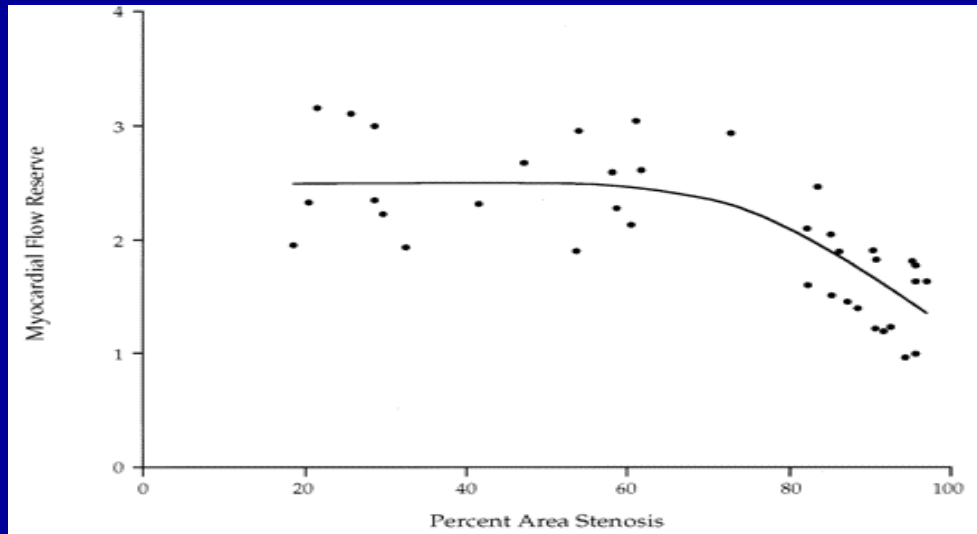
- Among an asymptomatic multiethnic American cohort (MESA), Decreased Regional Left Ventricular Function is an independent predictor beyond traditional risk factors and global LV assessment for incident heart failure and atherosclerotic cardiovascular events (*R T Yan et al J Am. Coll Cardiol 2011*)

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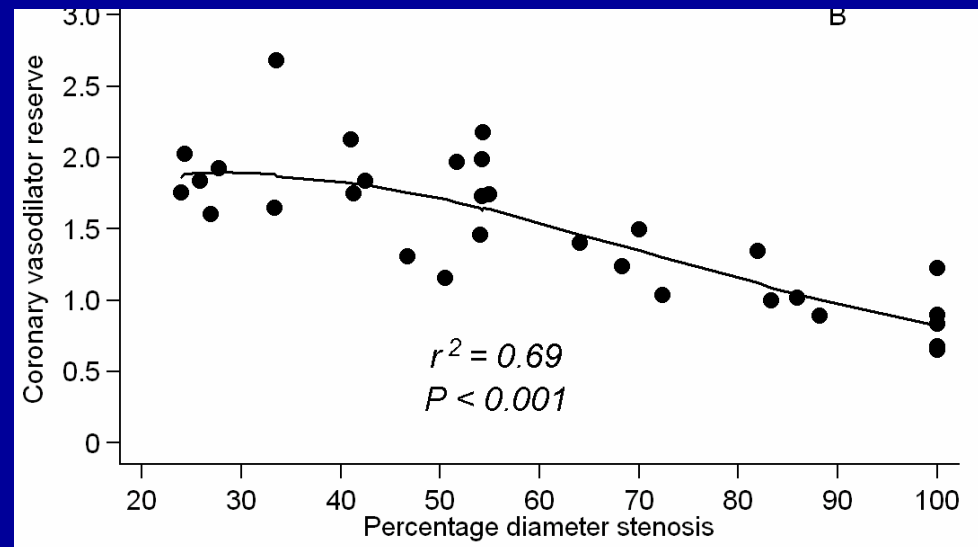
Assessment of total integrated Vasodilator capacity



Coronary Vasodilator Reserve vs. coronary stenosis

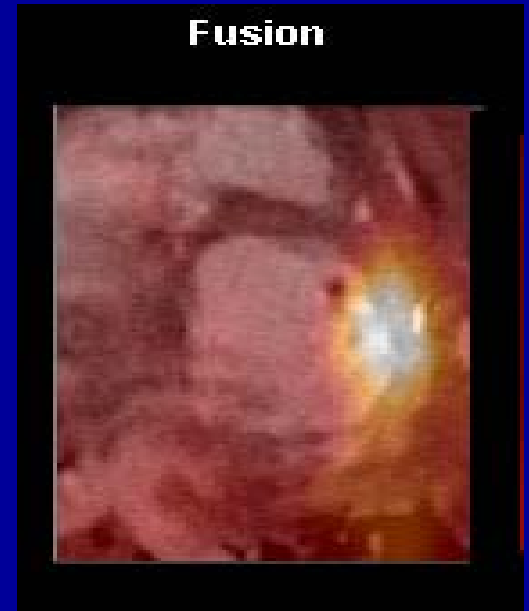
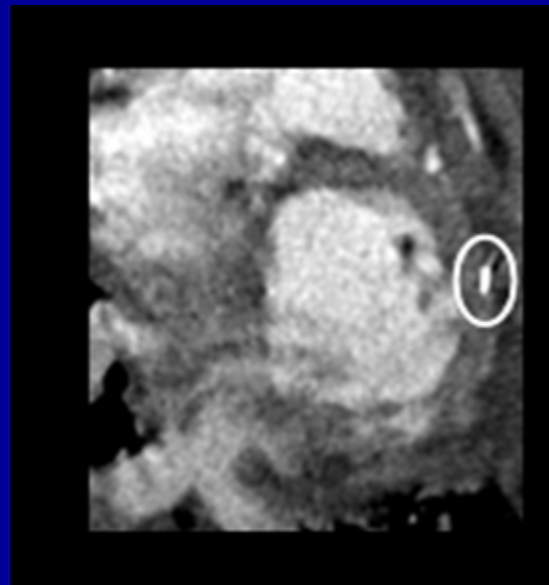
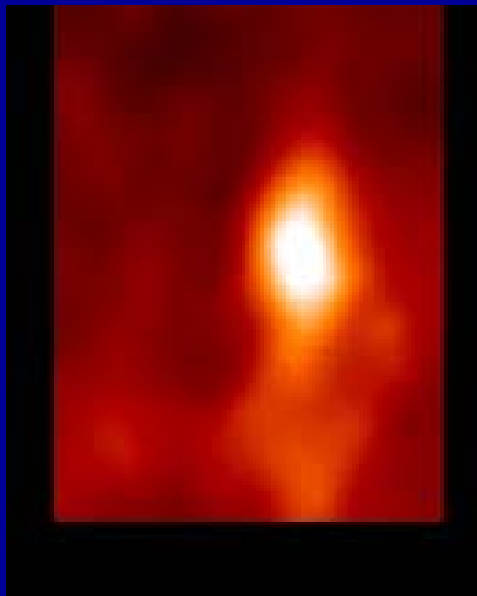


Di Carli et al Circulation 1995



C. Anagnostopoulos et al Eur J Nucl Med MI 2008

Hybrid imaging in Stem cell therapy post MI



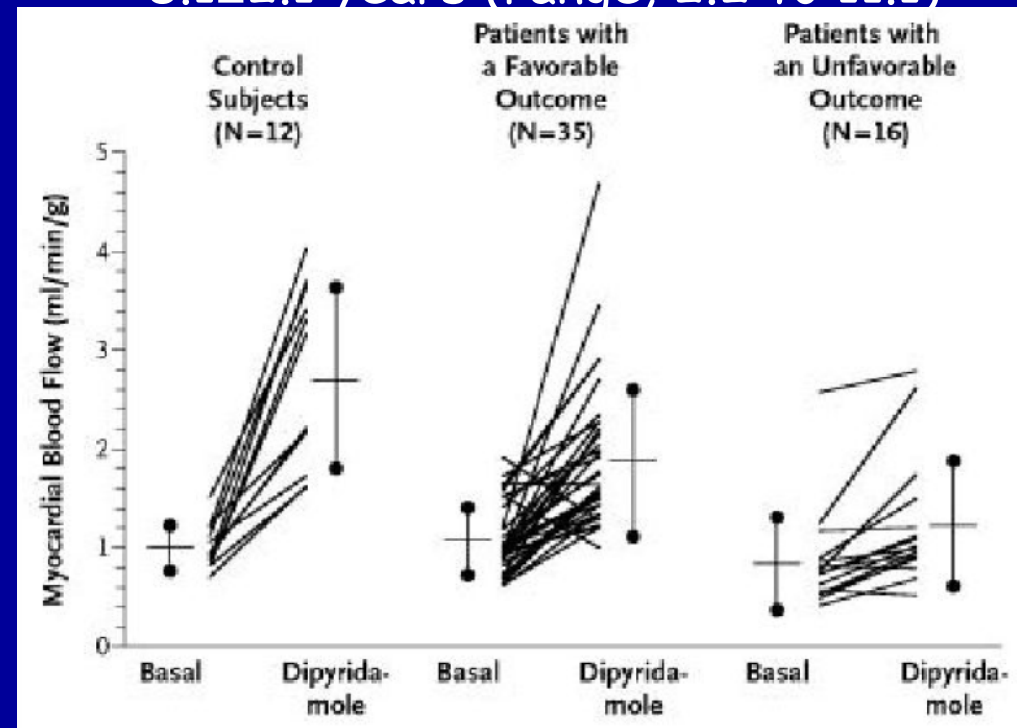
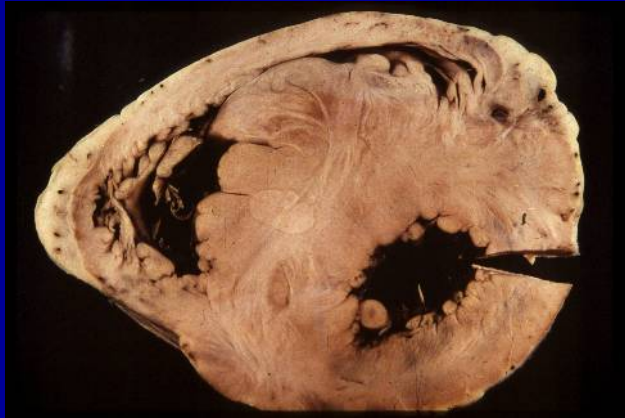
Courtesy F. Bengel

From C. Anagnostopoulos et al. Non Invasive Imaging of myocardial ischaemia-Springer Verlag

Coronary Microvascular Dysfunction and Prognosis in Hypertrophic Cardiomyopathy

51 patients with HCM and normal coronary arteries
f/u

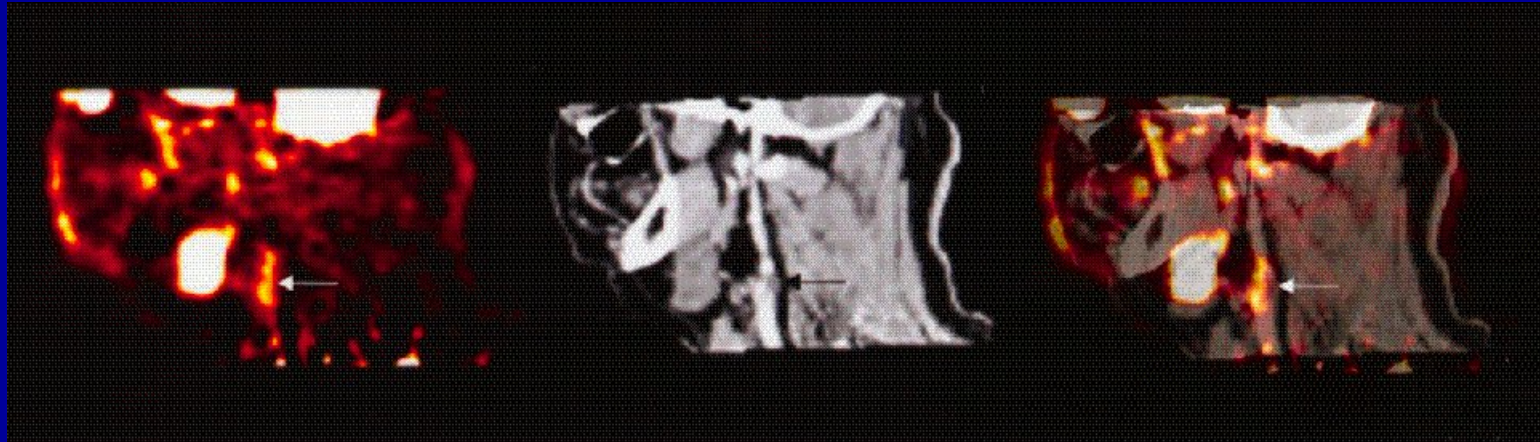
8.1±2.1 years (range, 2.2 to 11.1)



Camici PG et al N Eng J Med 2003

35 patients were stable (NYHA class I or II),
16 patients had an unfavorable outcome: 9 died from cardiovascular causes,
1 developed recurrent sustained VT implantation of a cardioverter-
defibrillator and 6 had progression to NYHA functional class III or IV

PET/CT for imaging of atherosclerosis

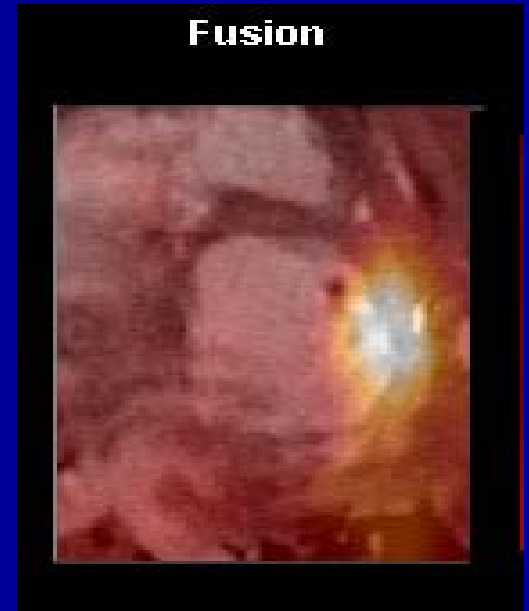
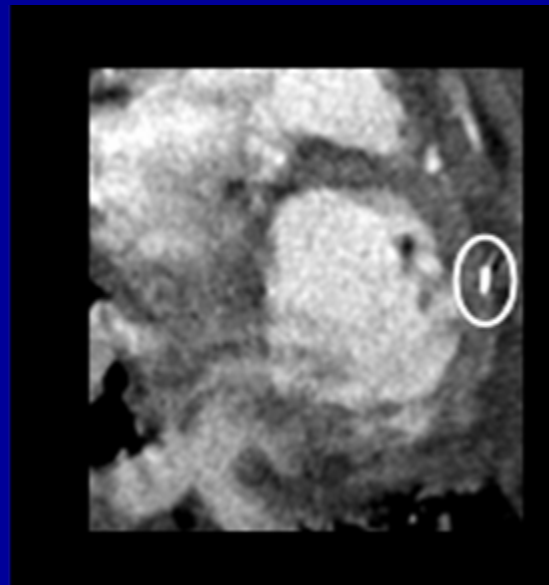
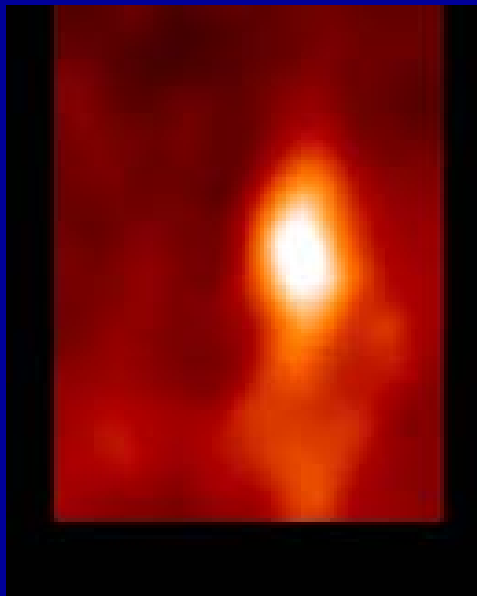


PET, contrast CT, and PET/CT images in the sagittal plane, from a 63-year-old man who had experienced 2 episodes of left-sided hemiparesis

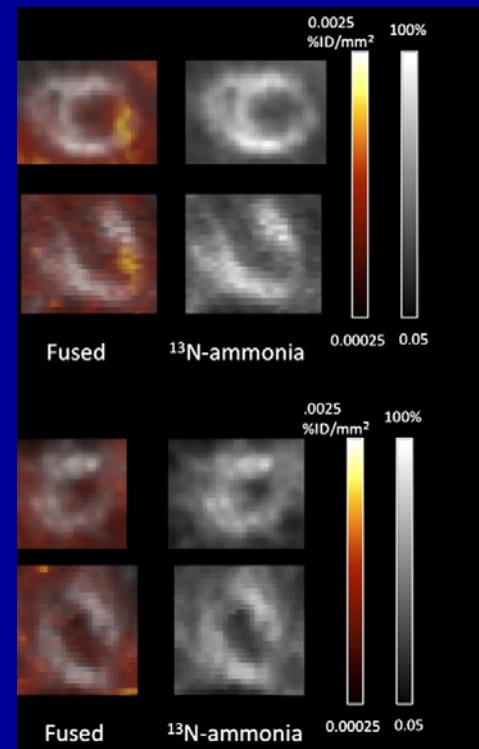


Same views as above depicting an asymptomatic carotid stenosis

Hybrid imaging in Stem cell therapy post MI

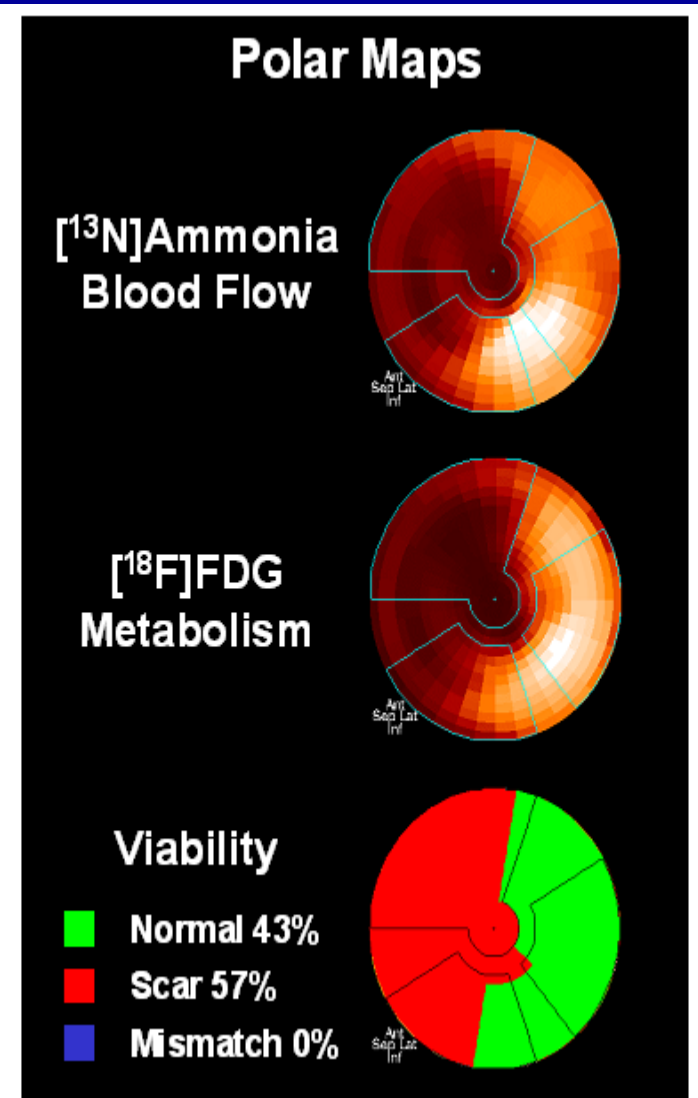
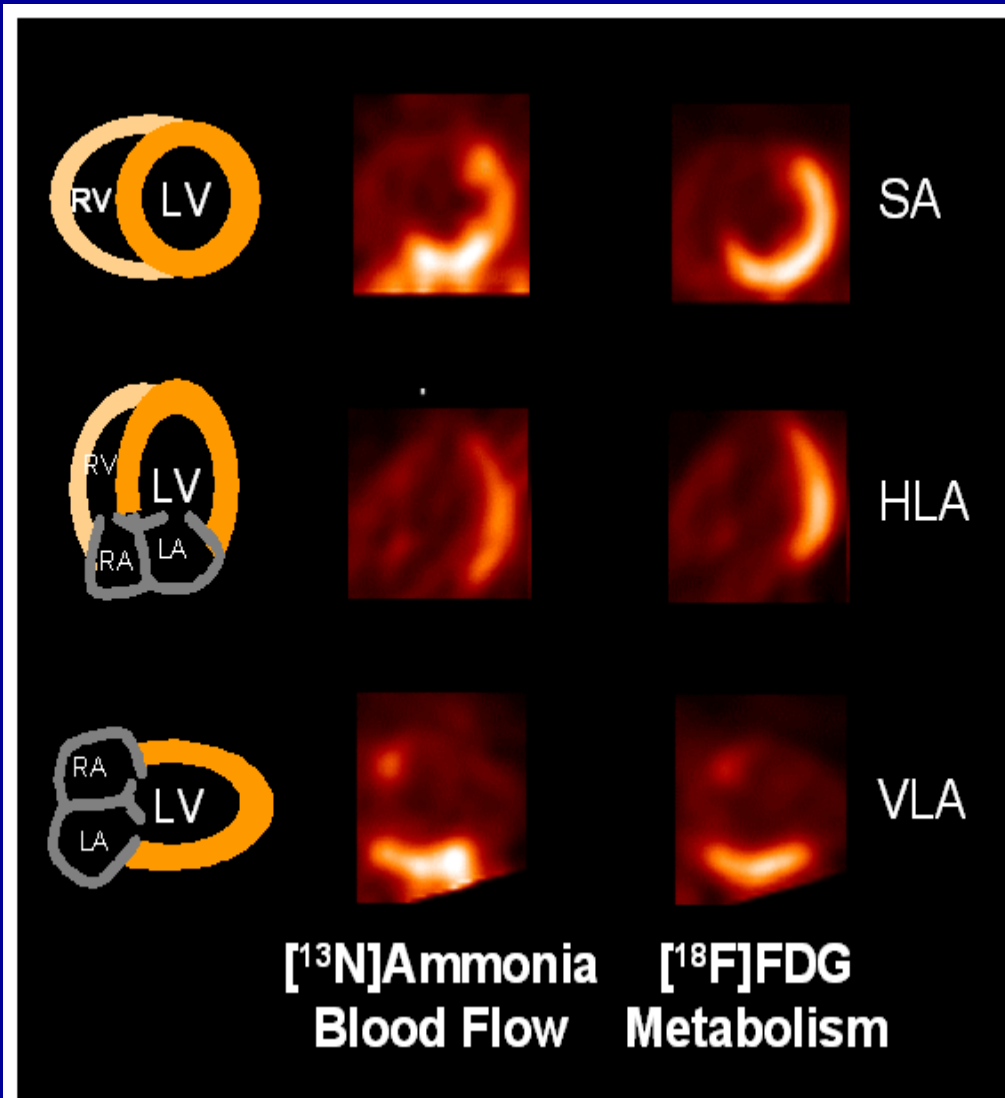


Courtesy F. Bengel

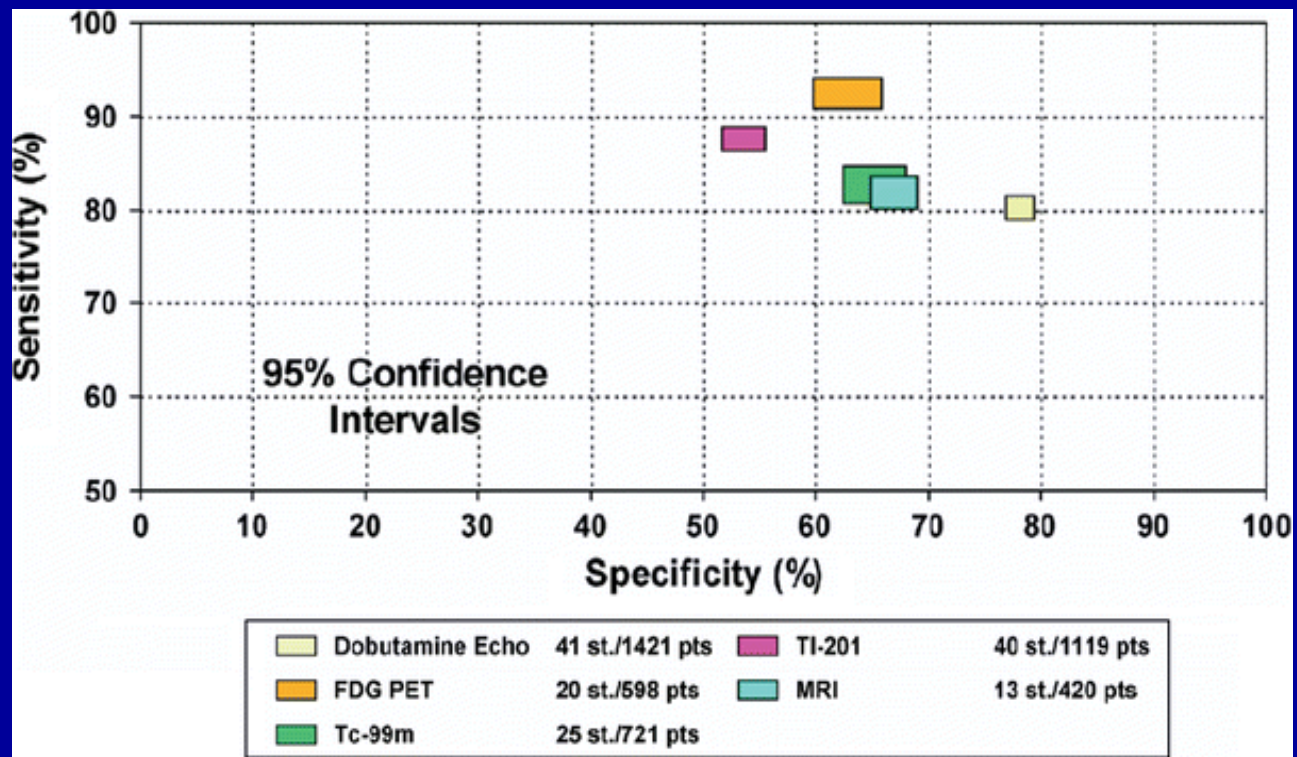


Relationship between perfusion and metabolism

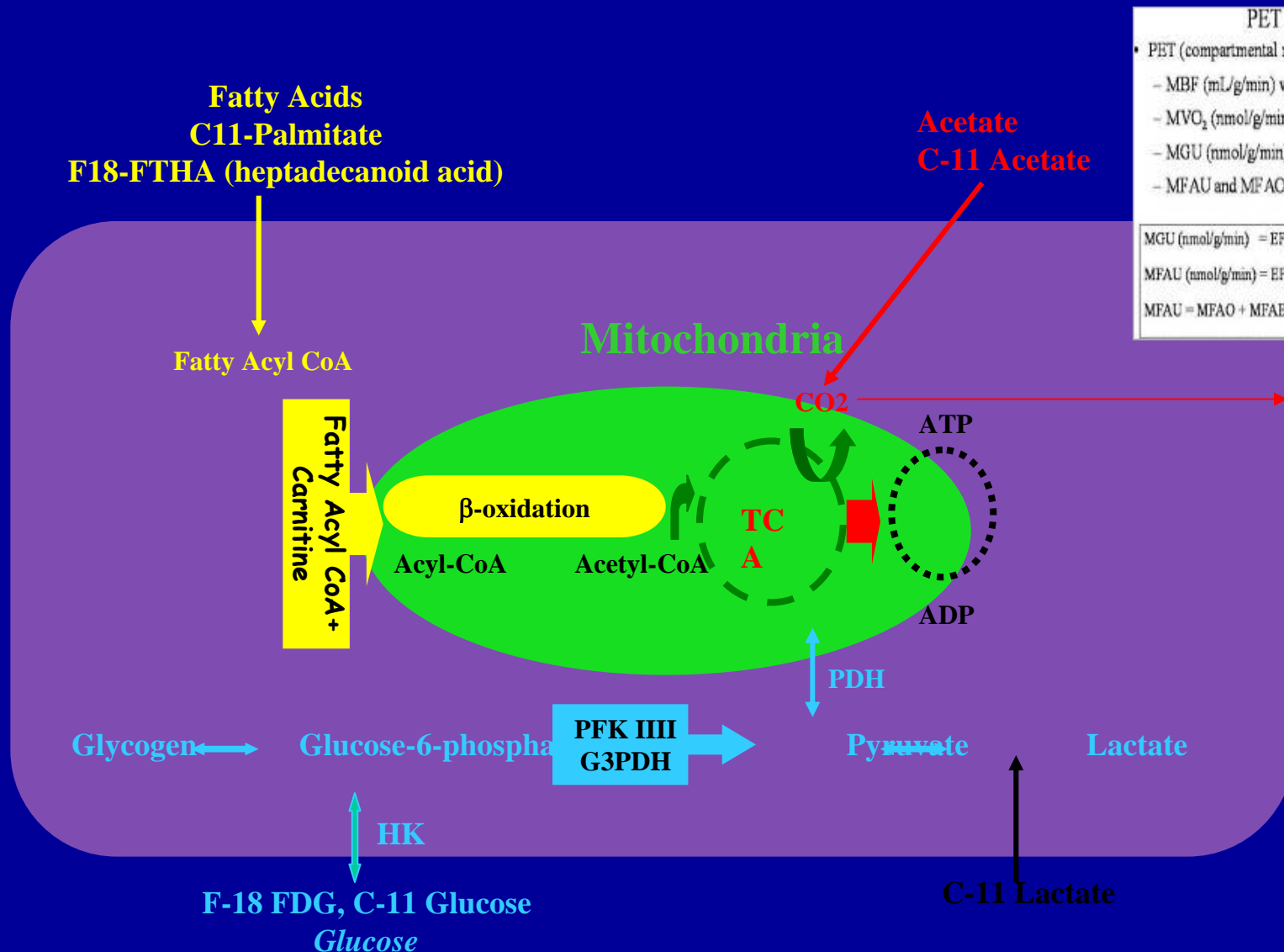
Myocardial infarct



Comparison of non invasive imaging techniques for assessment of myocardial viability/hibernation



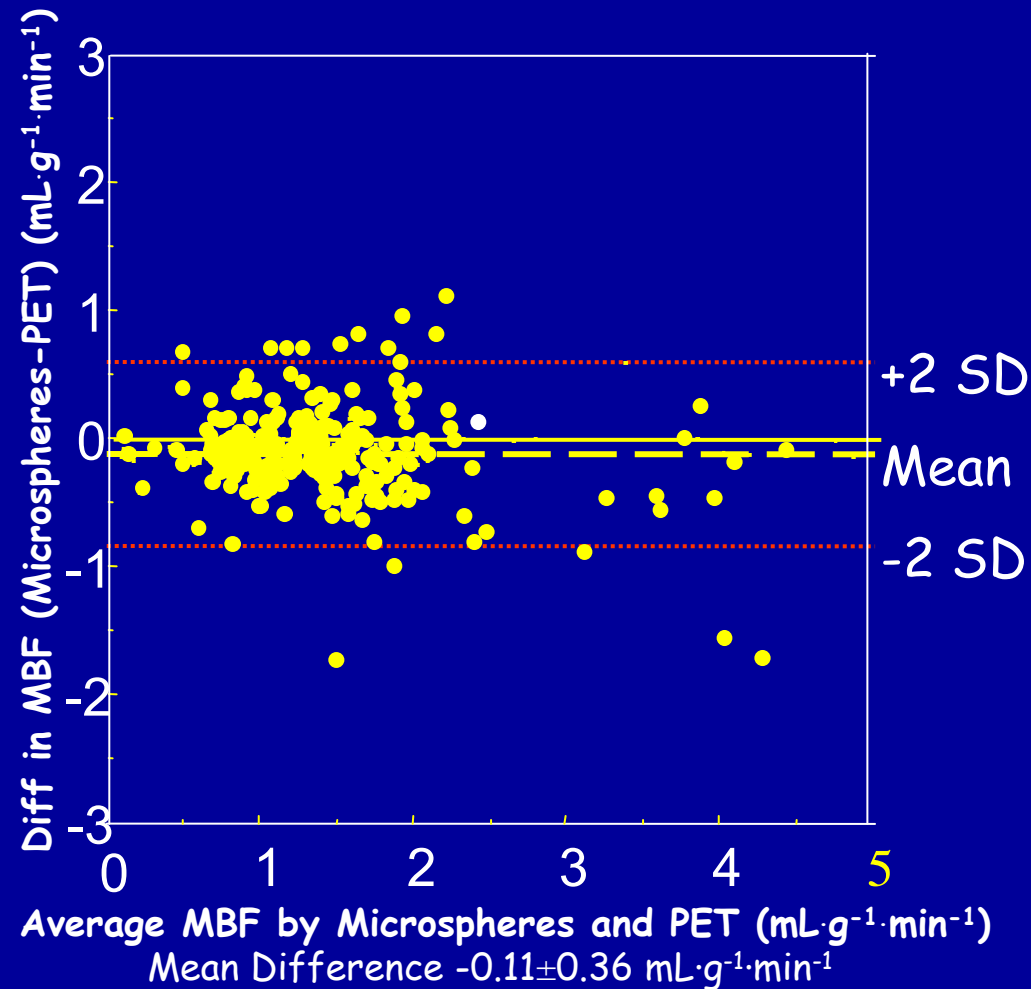
PET tracers of myocardial metabolism



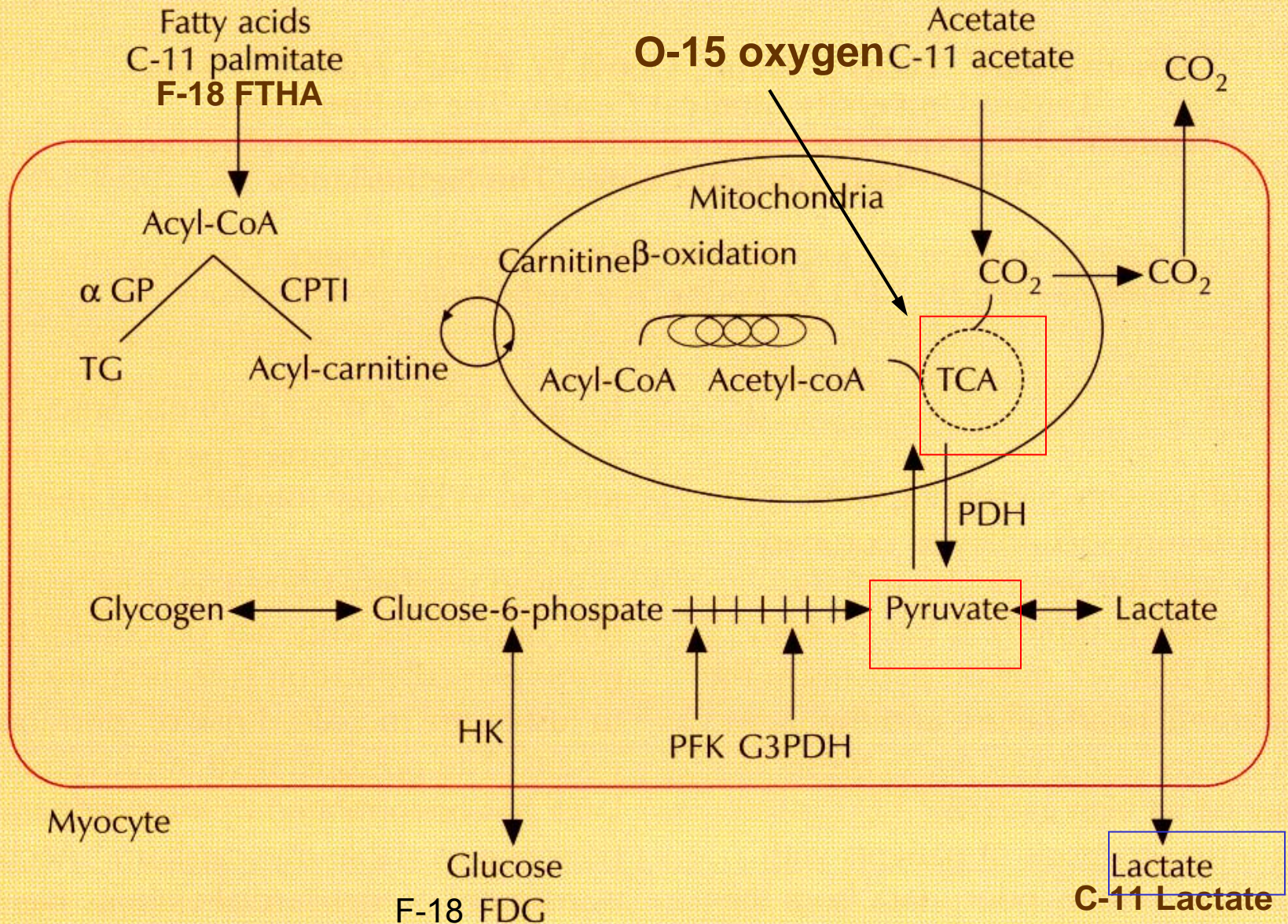
PET Measurements	
• PET (compartmental modeling of tracer kinetics)	
- MBF (mL/g/min) with ^{15}O -water	
- MVO_2 (nmol/g/min) with $1\text{-}^{11}\text{C}$ -acetate	
- MGU (nmol/g/min) with $1\text{-}^{11}\text{C}$ -glucose	
- MFAU and MFAO (nmol/g/min) with $1\text{-}^{11}\text{C}$ -palmitate	
$\text{MGU (nmol/g/min)} = \text{EF}_{\text{glucose}} \cdot \text{MBF} \cdot [\text{Glucose}]_{\text{tissue}}$	
$\text{MFAU (nmol/g/min)} = \text{EF}_{\text{FFA}} \cdot \text{MBF} \cdot [\text{FFA}]_{\text{tissue}}$	
$\text{MFAU} = \text{MFAO} + \text{MFAE} \rightarrow \% \text{MFAO} = 100 \cdot \text{MFAO} / \text{MFAU}$	

Courtesy of P Camici, Hammersmith, Hospital, ICSM

Agreement between PET and microspheres



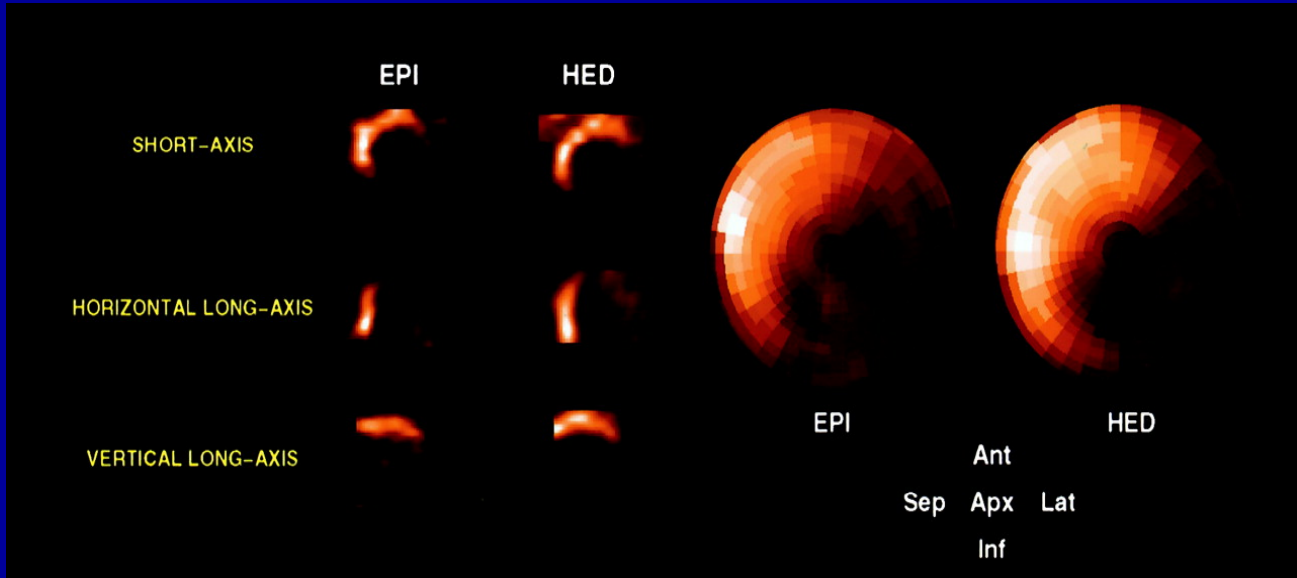
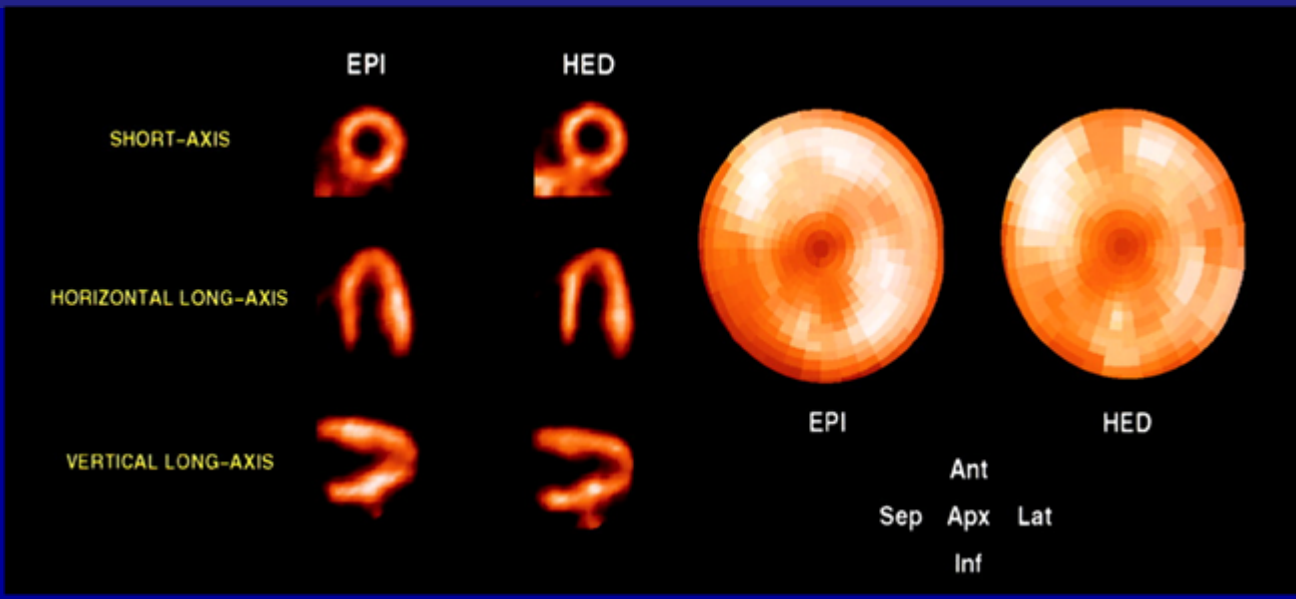
PET: Molecular imaging of metabolic pathways



TCA=tricarballic acid

Similarities of [¹¹C]epinephrine (EPI) and [¹¹C]hydroxyephedrine (HED) using PET

Assessment of presynaptic sympathetic neuronal function



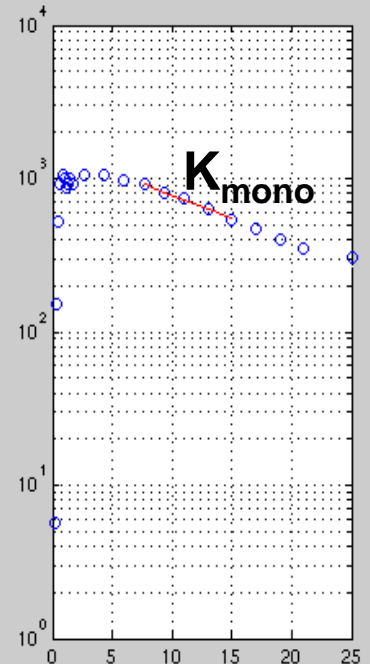
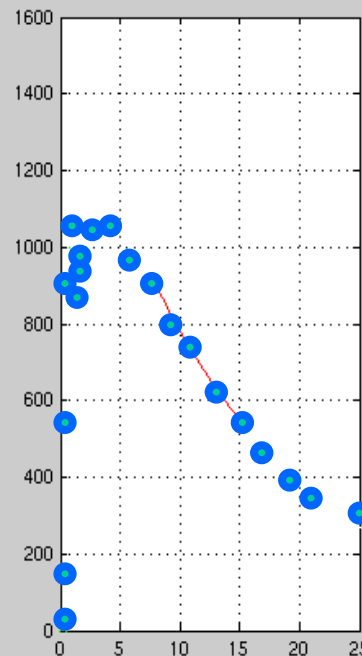
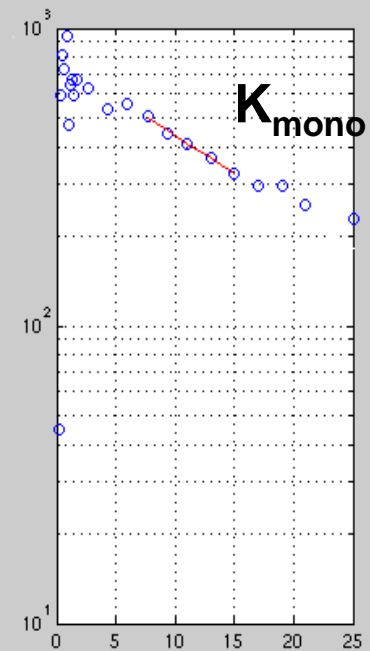
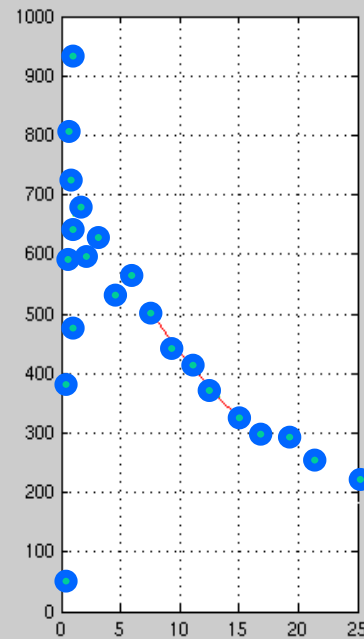
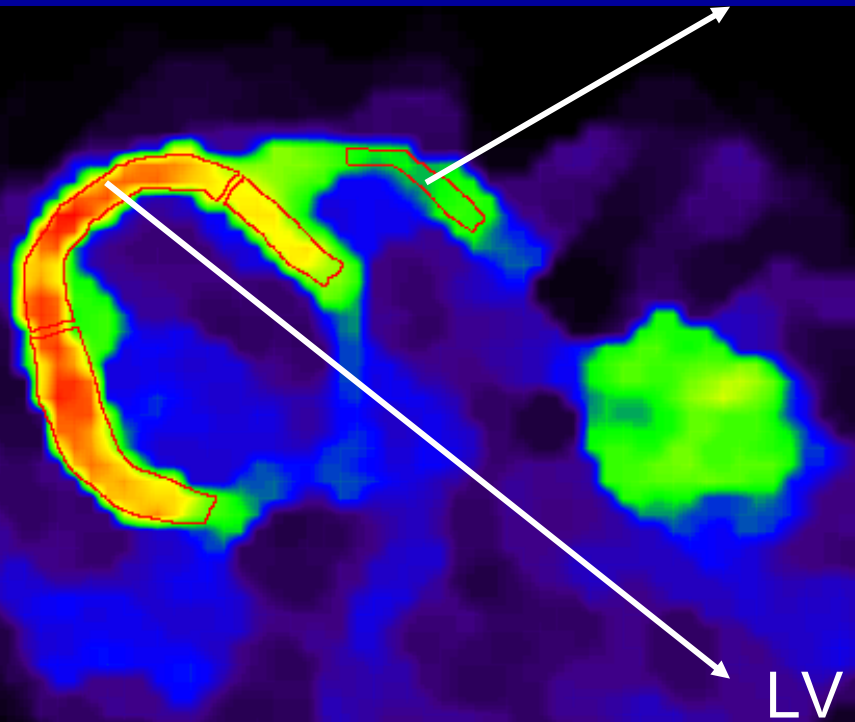
Myocardial Energetics and Efficiency

- The heart relies almost exclusively on the aerobic oxidation of substrates for generation of energy
- There is close coupling between myocardial oxygen consumption (MVO_2) and the main determinants of systolic function: heart rate, contractile state, and wall stress
- Only part of the energy invested is converted to external power
- The ratio of useful energy produced (ie, stroke work [SW]) to oxygen consumed is defined as mechanical efficiency

Myocardial Energetics and Efficiency

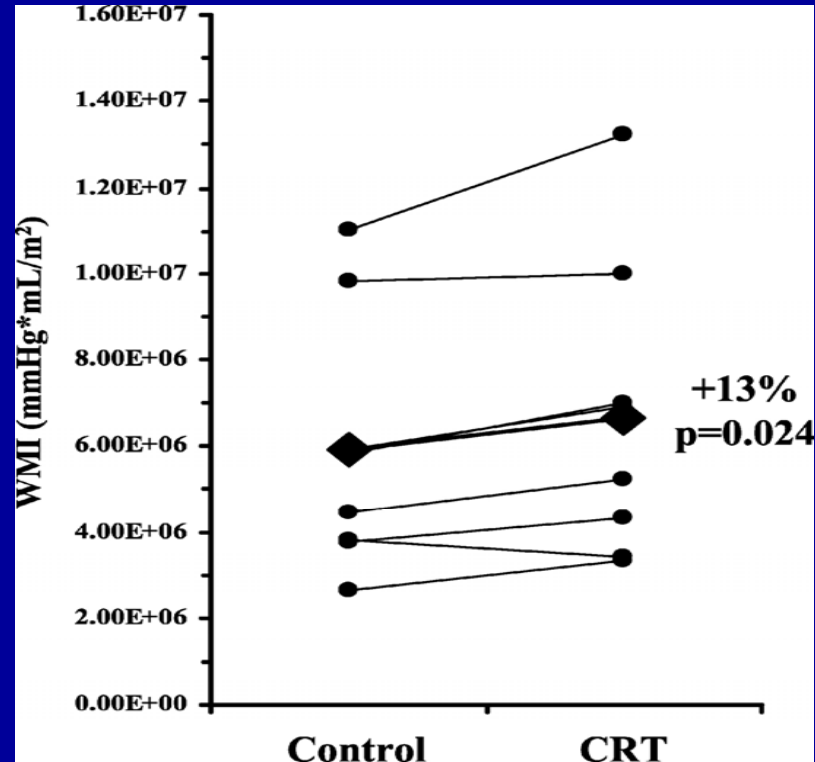
- In pathophysiological disease states, such as heart failure, mechanical efficiency is reduced
- Increased energy expenditure relative to work contributes to progression of the disease
- Quantification of efficiency of the heart to study disease processes and monitor interventions

Cardiac oxidative metabolism: [¹¹C]Acetate PET



Effect of CRT on global LV efficiency

Rest



$$WMI = SWI \times HR / k_{mono}$$

WMI: work metabolic index

Knuuti

- PET sensitive etc..