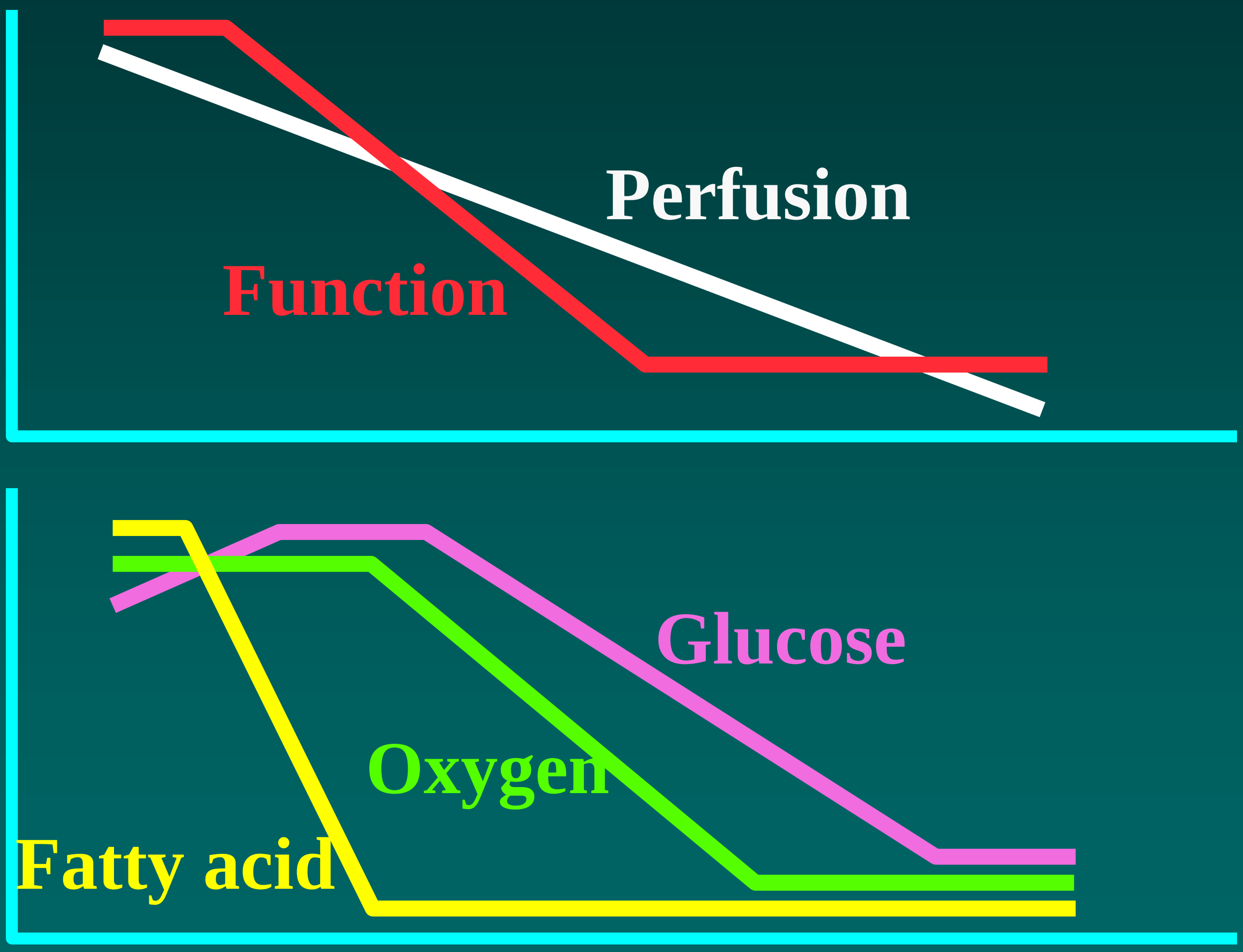
Korean Circulation Society April 15, 2005

Clinical Implication of State-of-Art Cardiac Imaging

Roles of metabolic imaging in the study of coronary artery disease

Nagara Tamaki, M.D.
Department of Nuclear Medicine
Hokkaido University
Graduate School of Medicine
Sapporo, JAPAN

Functional & Metabolic changes in ischemia



Value of metabolic imaging

- Suppression of fatty acid oxidation during ischemia

  → Early detection of ischemia
- Preservation of glucose utilization in severe ischemia

  → Viability assessment
- Persistent metabolic alterations after ischemia

  → Ischemic memory imaging

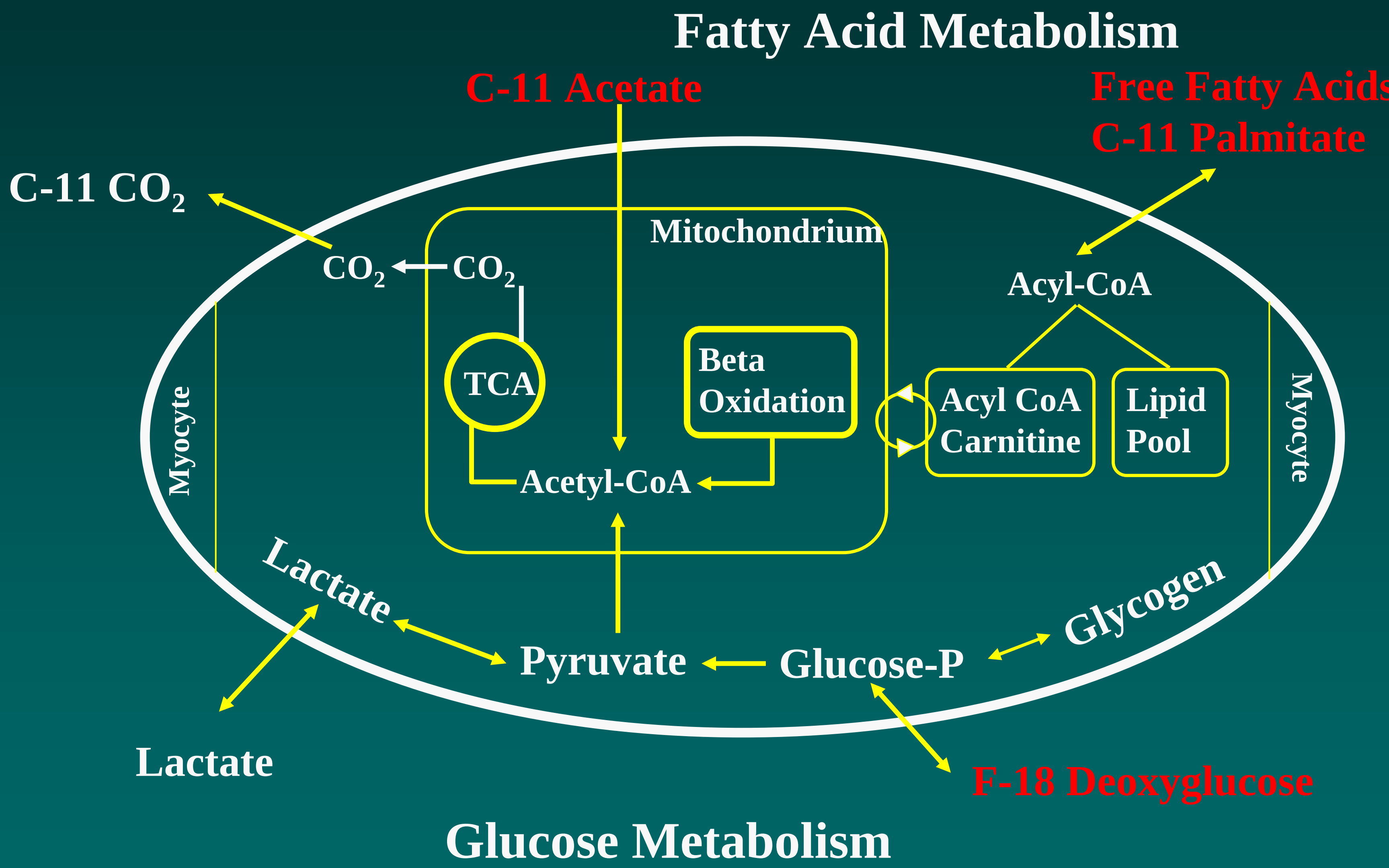
Clinical roles of viability assessment

- Select patients with poor LV function who may benefit by revascularization
- Select high risk group who may have future cardiac events on the medical treatment

→ to improve LV function and QOL

→ to reduce cardiac risk

Myocardial metabolism and PET tracers



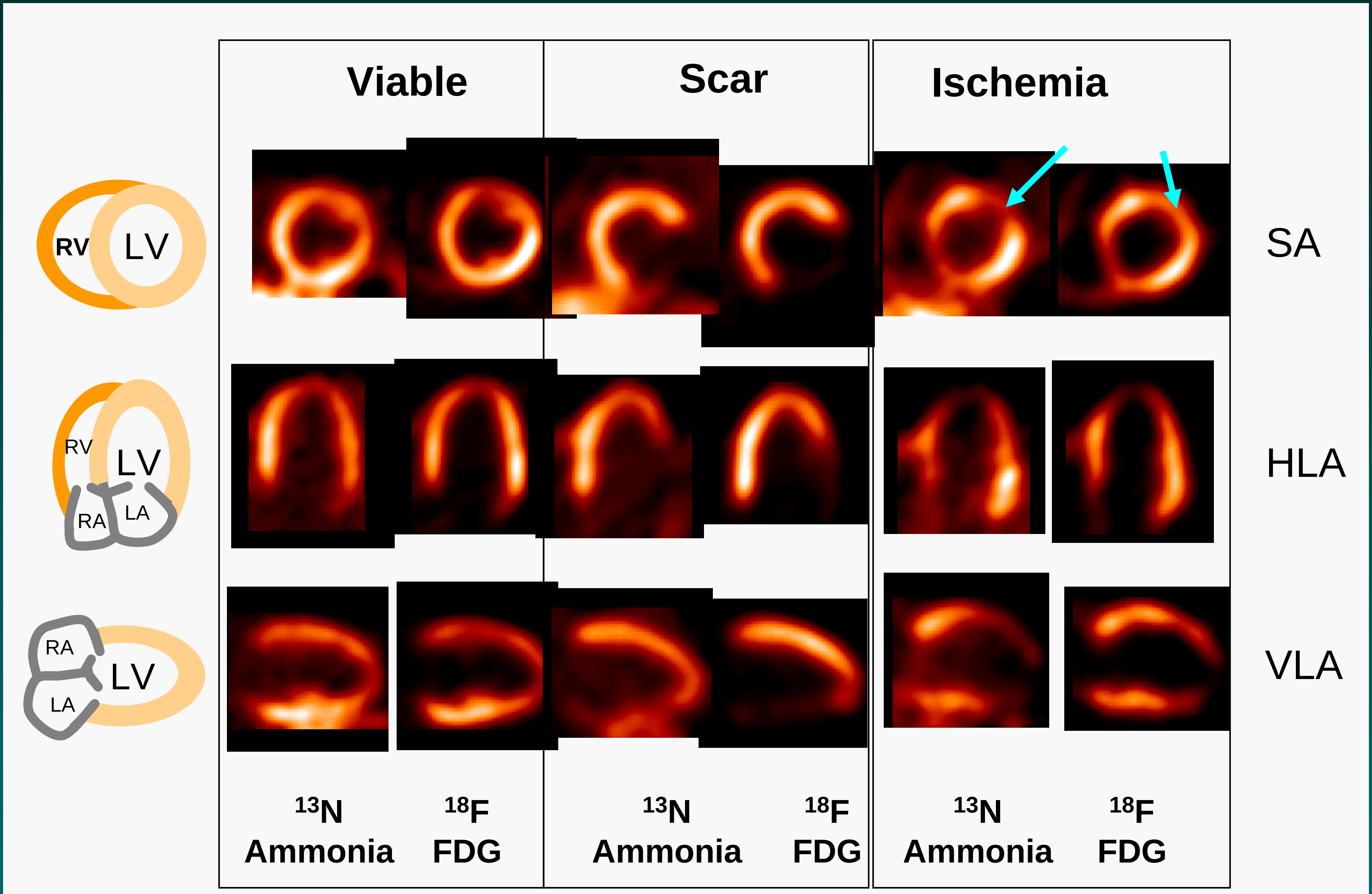
Viability Assessment by PET

Select patients with poor LV function who may benefit by revascularization

- Dysfunctional areas with PET findings

Perfusion	Glucose	Findings
Normal	Normal	PET normal
Reduced	Preserved	PET ischemia (hibernation)
Reduced	Reduced	PET scar

NH3 and FDG PET images



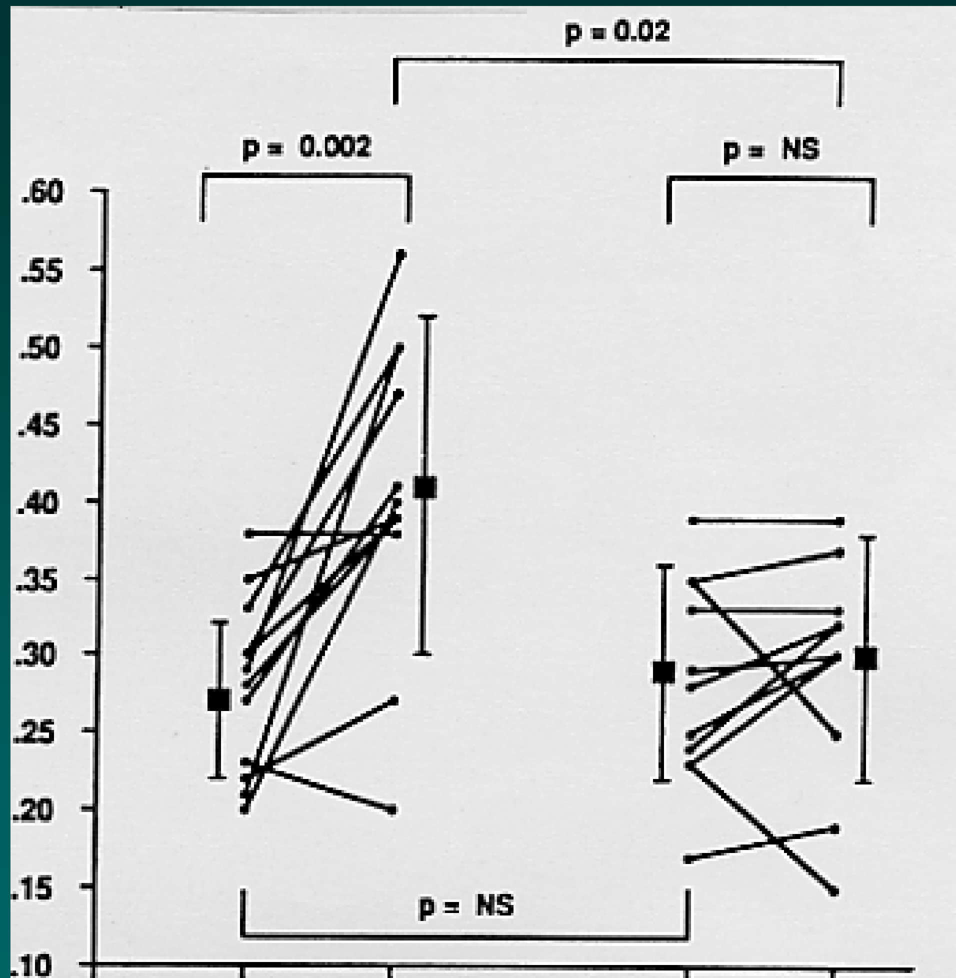
Courtesy of Muenchen Technische Univ. (Muenhen Heart Software)

Predictive value of PET for improvement

Authors	n	PPV	NPV	Methods
Tillisch	17	85%	92%	FDG/NH3
Tamaki	22	78%	78%	FDG/NH3
Lucignani	14	95%	80%	FDG/MIBI
Carrel	23	84%	75%	FDG/Rb
Marwick	16	68%	79%	FDG/Rb
Gropler	34	72%	82%	FDG/Acetate
Vom Dahl	37	48%	86%	FDG/NH3
Knnuti	43	72%	96%	FDG/MIBI or FDG/Tl

LVEF changes in relation to PET findings

LVEF (%)



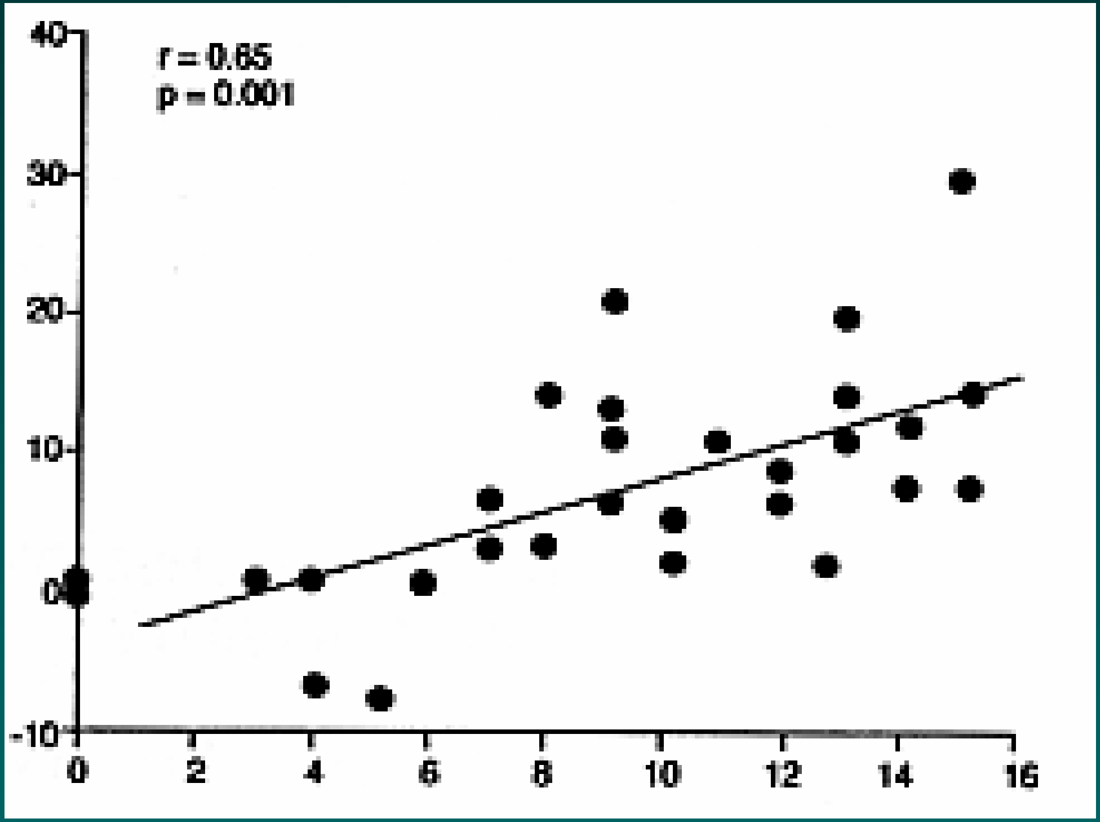
Pre-op Post-op Pre-op Post-op

With ischemia Without ischemia

Ragosta M, Circulation 1993

LVEF changes after TX with PET findings

LVEF change



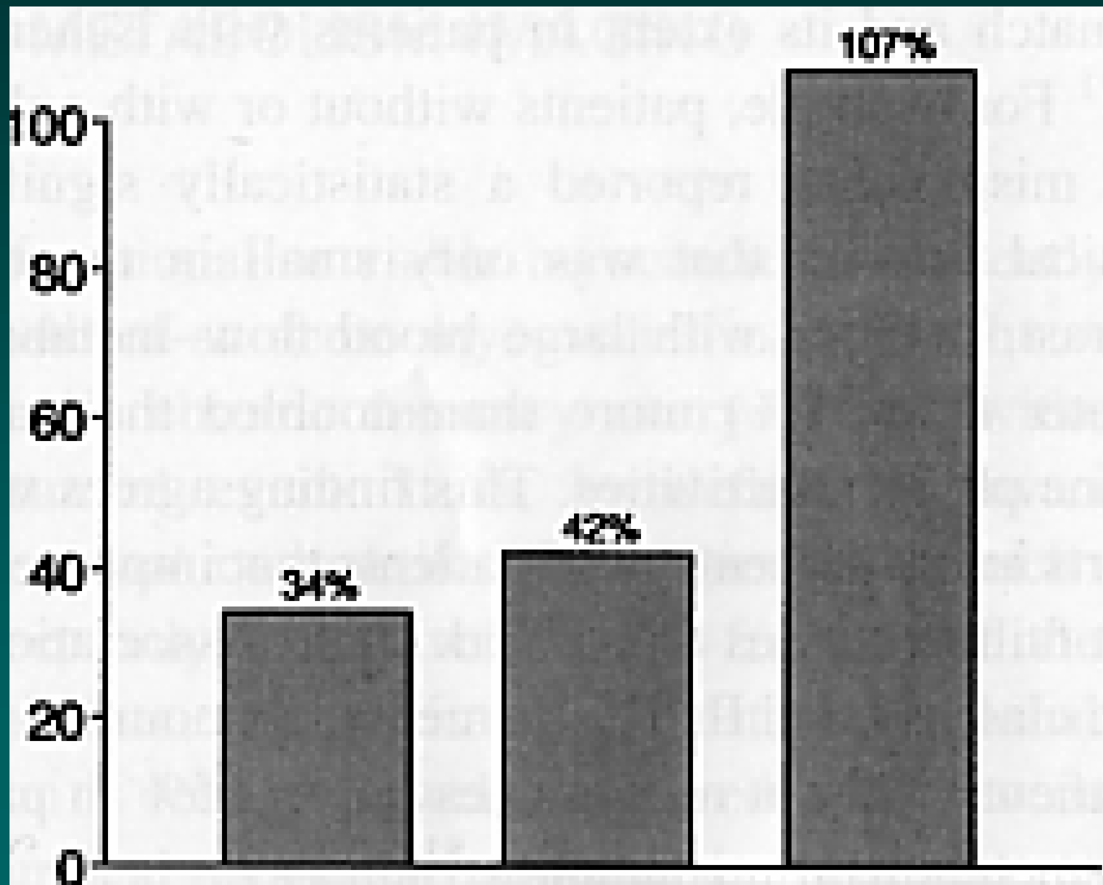
R= 0.65
P=0.001

No of PET viable segments

Schelbert HR. Semin Nucl Med 32: 60-69, 2002

Physical activity change in heart failure

Physical Activity improvement



Ischemia < 5% 5-17% >18%

Schelbert HR. Semin Nucl Med 32: 60-69, 2002

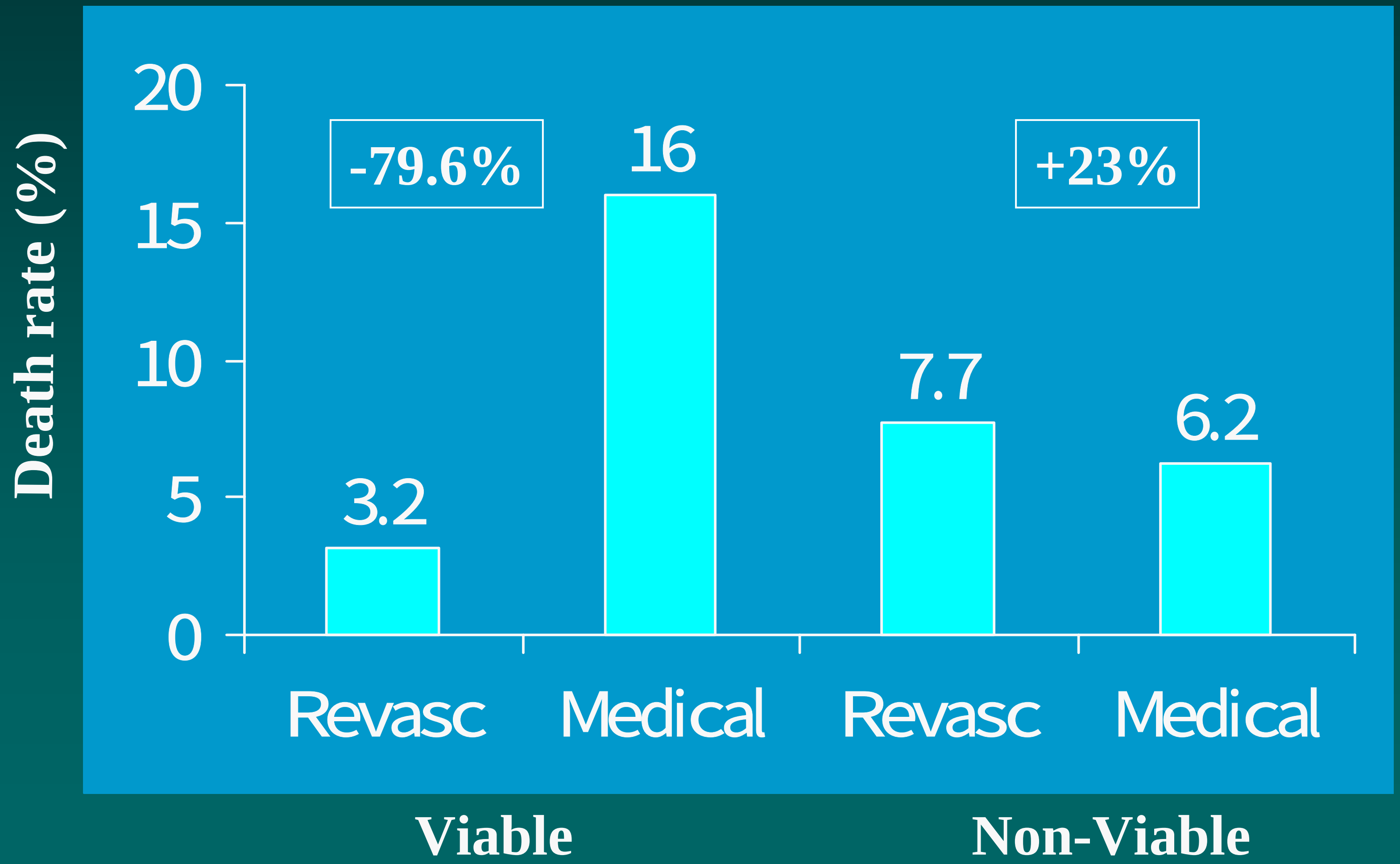
Cardiac event rate with FDG-PET

Author	n	mean follow-up	Event rate (%) FDG+ REV-	FDG- REV-	FDG+ REV+	FDG- REV+
Eitzman	82	12 m	50%	12%	13%	7%
Tamaki	84	23 m	33%	3%	-	-
Yoshida	35	36 m	0%	10%	50%	50%
Di Carli	93	14 m	41%	12%	9%	6%
Lee	129	17 m	62%	16%	18%	11%
Mean	423		29%	11%	15%	13%

(REV = revascularization)

Myocardial Viability and Impact of Revascularisation

Meta- analysis of 24 Studies in 3088 Patients



Allman KC, et al JACC 39:1151-8, 2002

Viability assessment by each method
(Meta-analysis)

Method	No Pts	Sensitivity	Specificity
Tl reinjection	145	90% (87-93)	54% (49-60)
Tl rest RD	209	86% (83-89)	47% (43-51)
^{99m}Tc-MIBI	207	83% (78-87)	69% (63-74)
FDG-PET	332	88% (84-91)	73% (69-77)
LDDE	448	84% (82-90)	81% (79-84)

LDDE=low dose dobutamine echocardiography

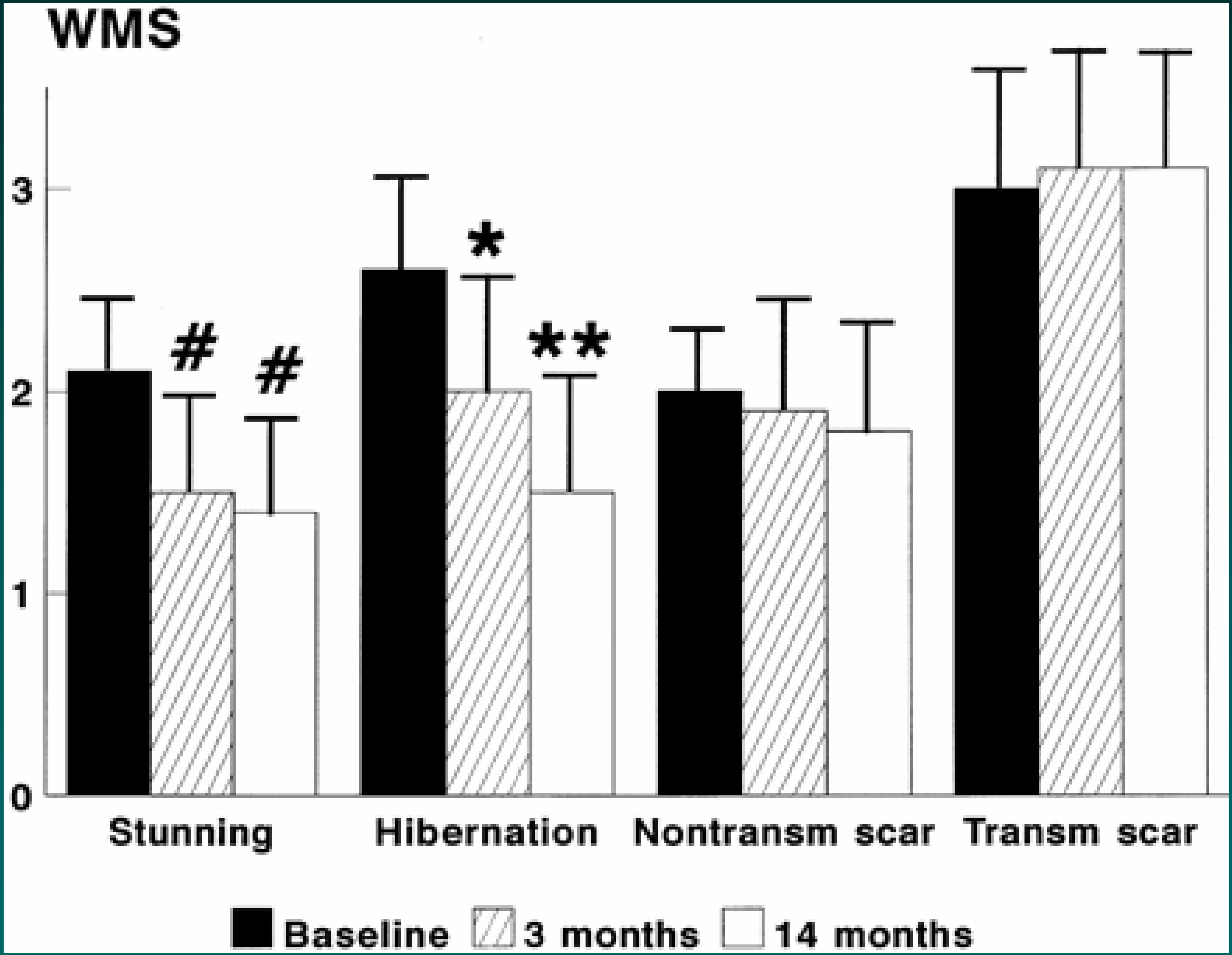
Bax JJ, et al. JACC 30: 1451-1460, 1997

Time course of functional recovery

- Early and late recovery of function was assessed in 26 patients with ischemic cardiomyopathy.
- Regional function was assessed by echo before, 3months and 14 months after revascularization.
- 266 dysfunctional segments were classified as:
  - Stunned myocardium: normal perfusion
  - Hibernating myocardium: reduced perfusion with increased FDG uptake
  - Non-transmural scar: concordant reduction ($\geq$60%)
  - Transmural scar: concordant reduction (<60%)

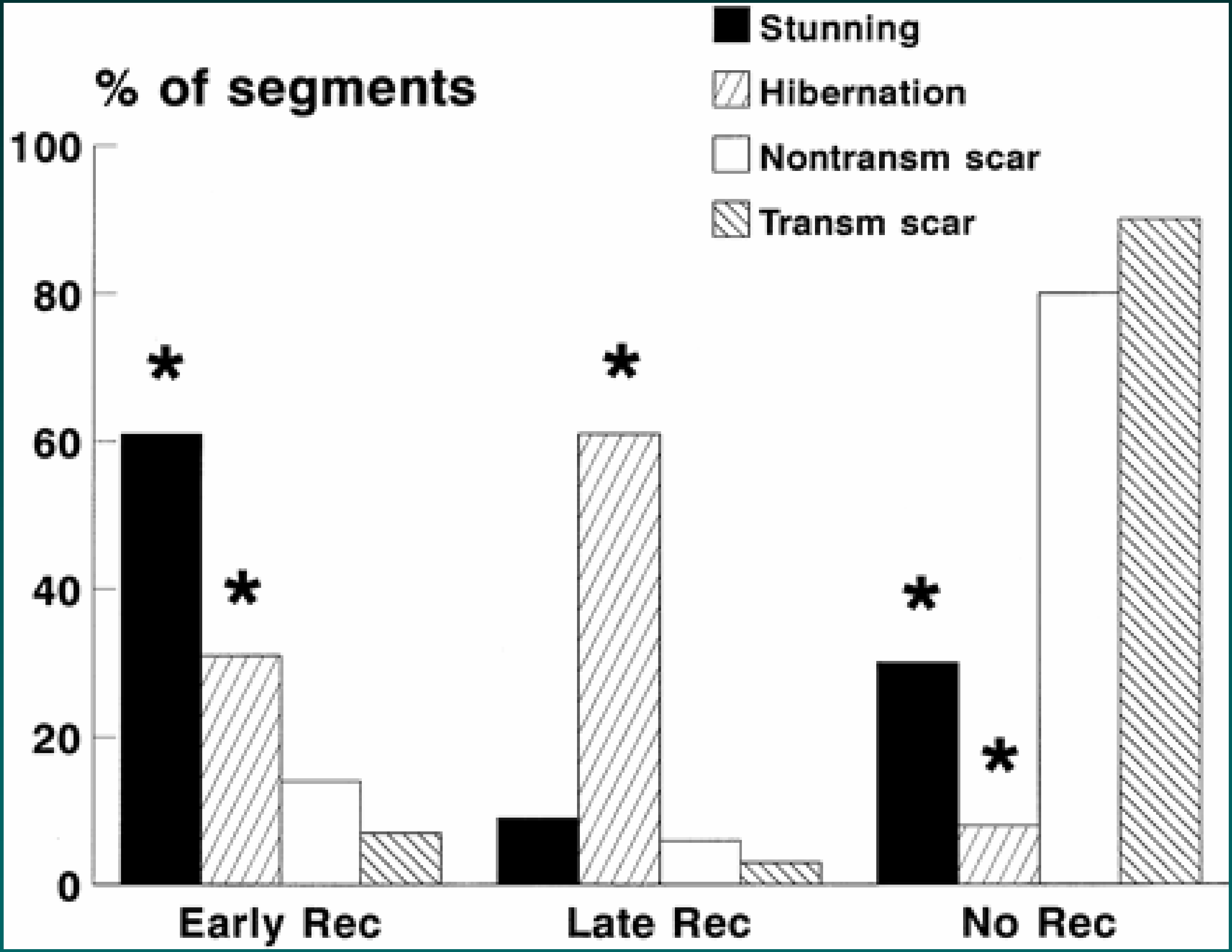
Bax JJ, et al. Circulation 104: I-314-I-318, 2001

Time course of functional recovery



Bax JJ, et al. Circulation 104: I-314-I-318, 2001

Time course of functional recovery



Bax JJ, et al. Circulation 104: I-314-I-318, 2001

Time course of myocardial hibernation

Camici PG, et al.
Am J Physiol 280:H929,2001

Coronary stenosis
↓
CVR ↓
↓
Myocardial ischemia
↓
Stunning(repetitive ischemia) → Enzyme induction
FDG+,DE+
Metabolic adaptation
↓
Functional hibernation → *Revascularization* → Early recovery
FDG+,DE+
Altered gene expression
Protein abnormalities
↓
Structural hibernation → *Revascularization* → Slow recovery
FDG+,DE-
Enzyme induction ↓ Cell-de-differentiation ← Structural hibernation
↓
Cell death
FDG-,DE-

Summary 1

- **FDG-PET is valuable for assessing myocardial viability.**
  - **Select patients with poor LV function who may benefit by revascularization**
  - **Select high risk group who may have future cardiac events on the medical treatment**
- **For better viability assessment, slow recovery after revascularization should be taken into consideration.**

Study of oxidative metabolic response

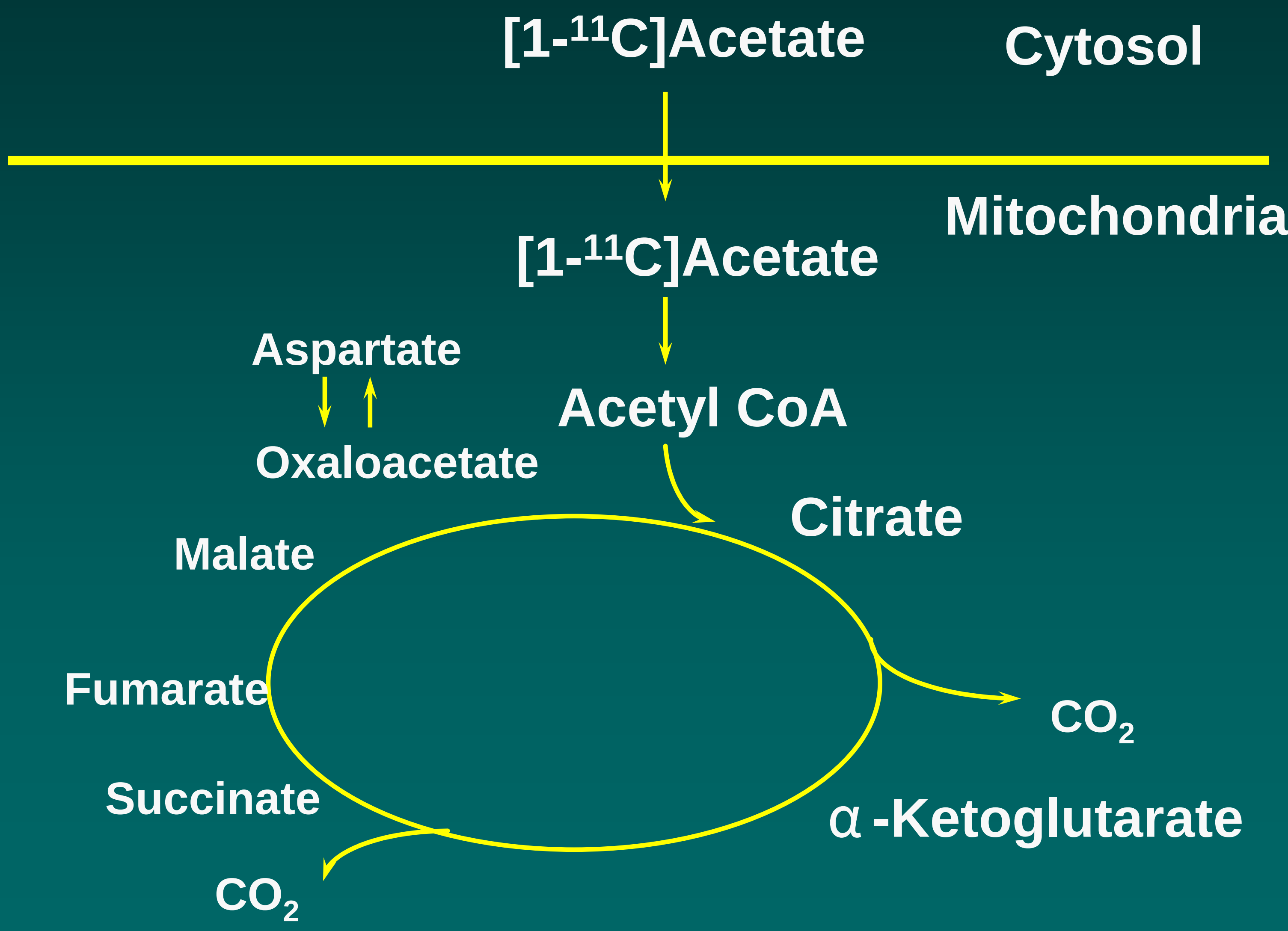
Purposes :

- The aim of this study was to investigate the difference of oxidative metabolic response between the segments with preserved contractile reserve (CR) and those without CR in the segments with preserved FDG uptake (FDG) using carbon-11 acetate PET.

Patients:

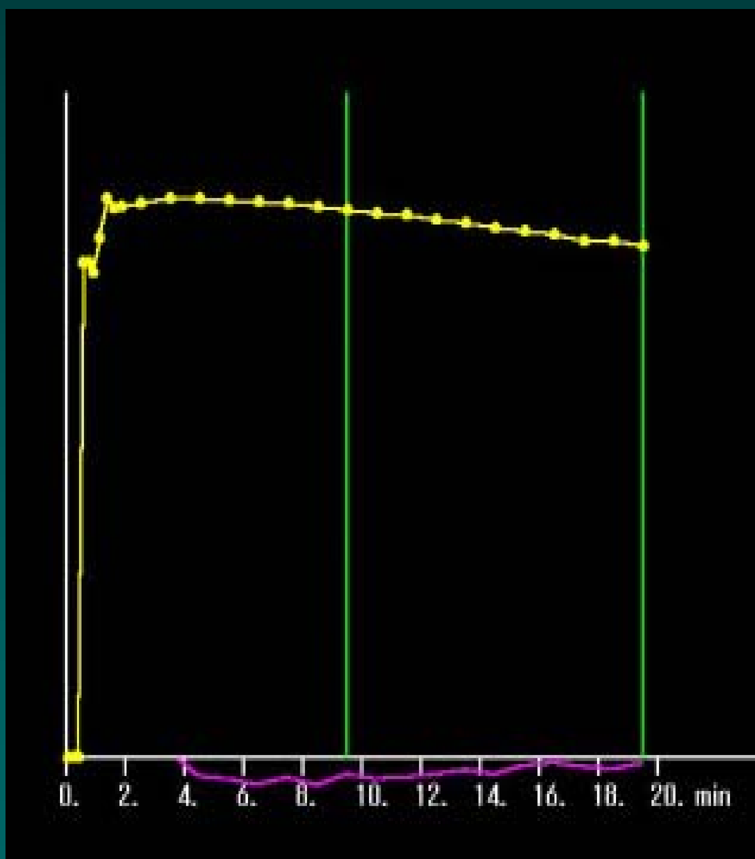
- 18 coronary patients who underwent FDG-PET (rest), acetate PET (rest + dobutamine) and echocardiography (rest + dobutanmine)

^{11}C-Acetate Kinetics

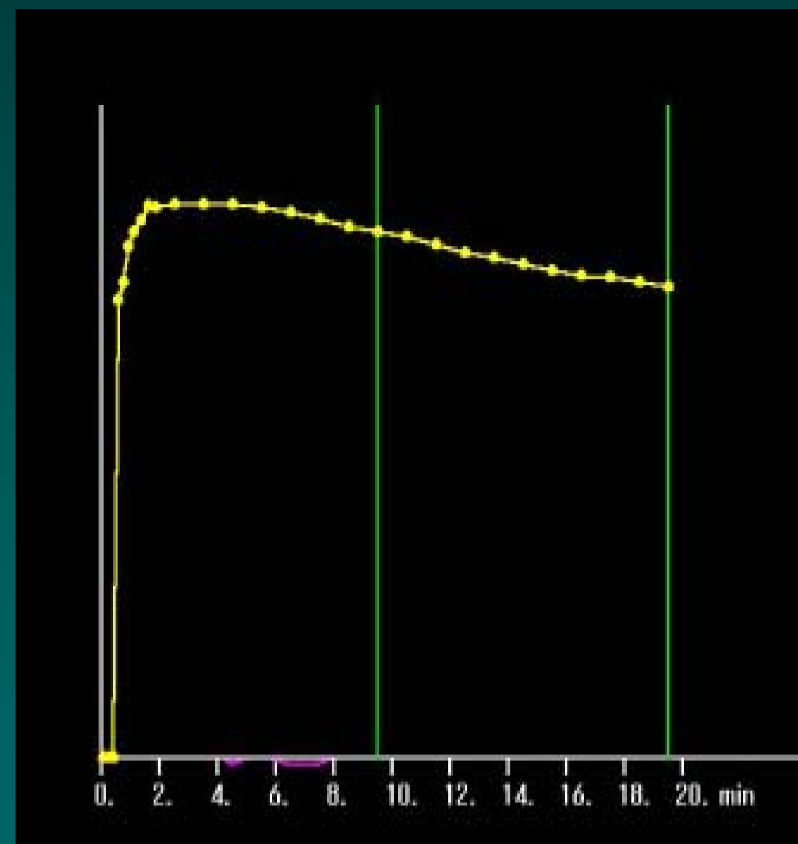


C-11 acetate time activity curves

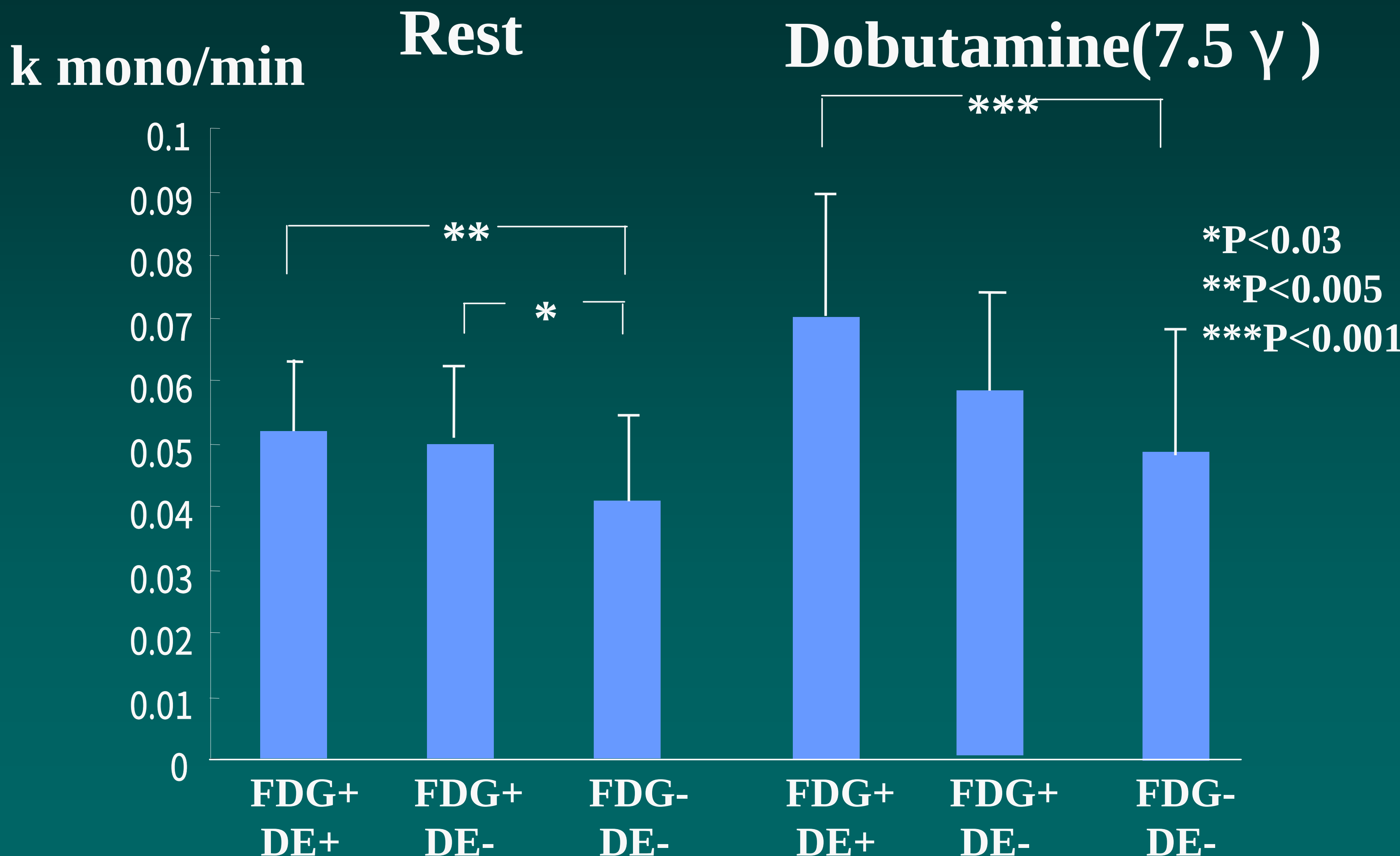
Rest



Dobutamine

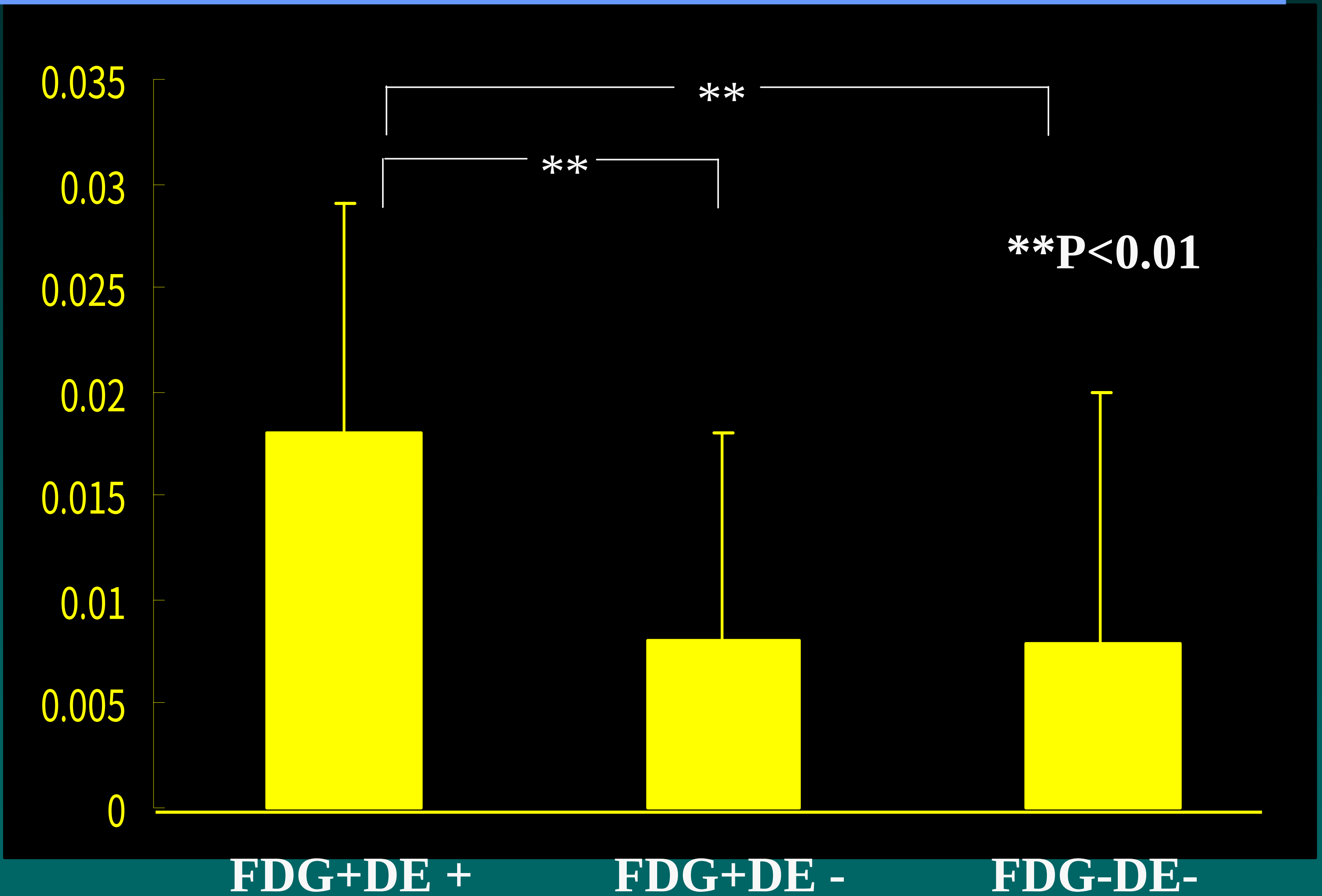


Oxidative metabolism



Yoshinaga K et al. J Nucl Med 45: 1885, 2004

Oxidative metabolic response by DBX



Yoshinaga K et al. J Nucl Med 45: 1885, 2004

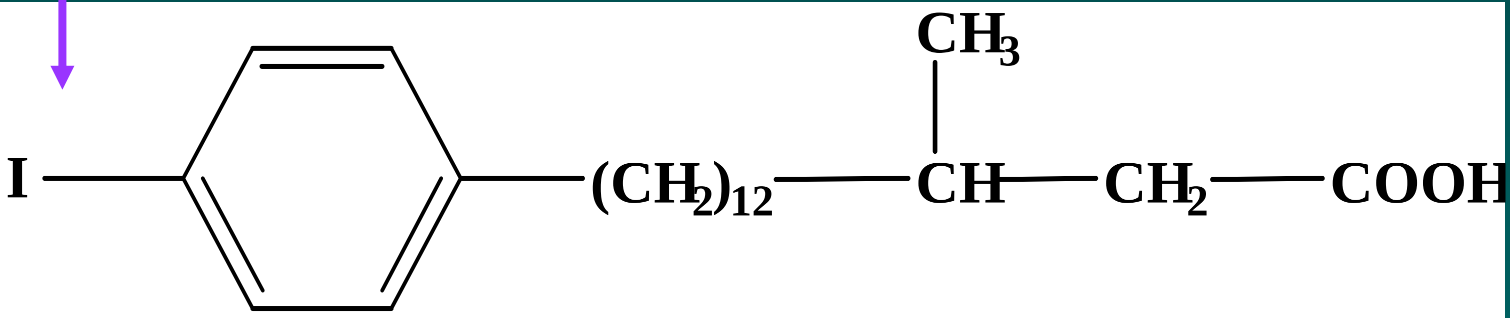
Summary 2

- **C-11 acetate has a potential for viability assessment in terms of preserved oxidative metabolism.**
- **Reduced dobutamine response by echo in the severe ischemia with preserved FDG uptake may be due to reduced oxidative response.**

BMIPP

p-Iodophenyl: metabolically stable

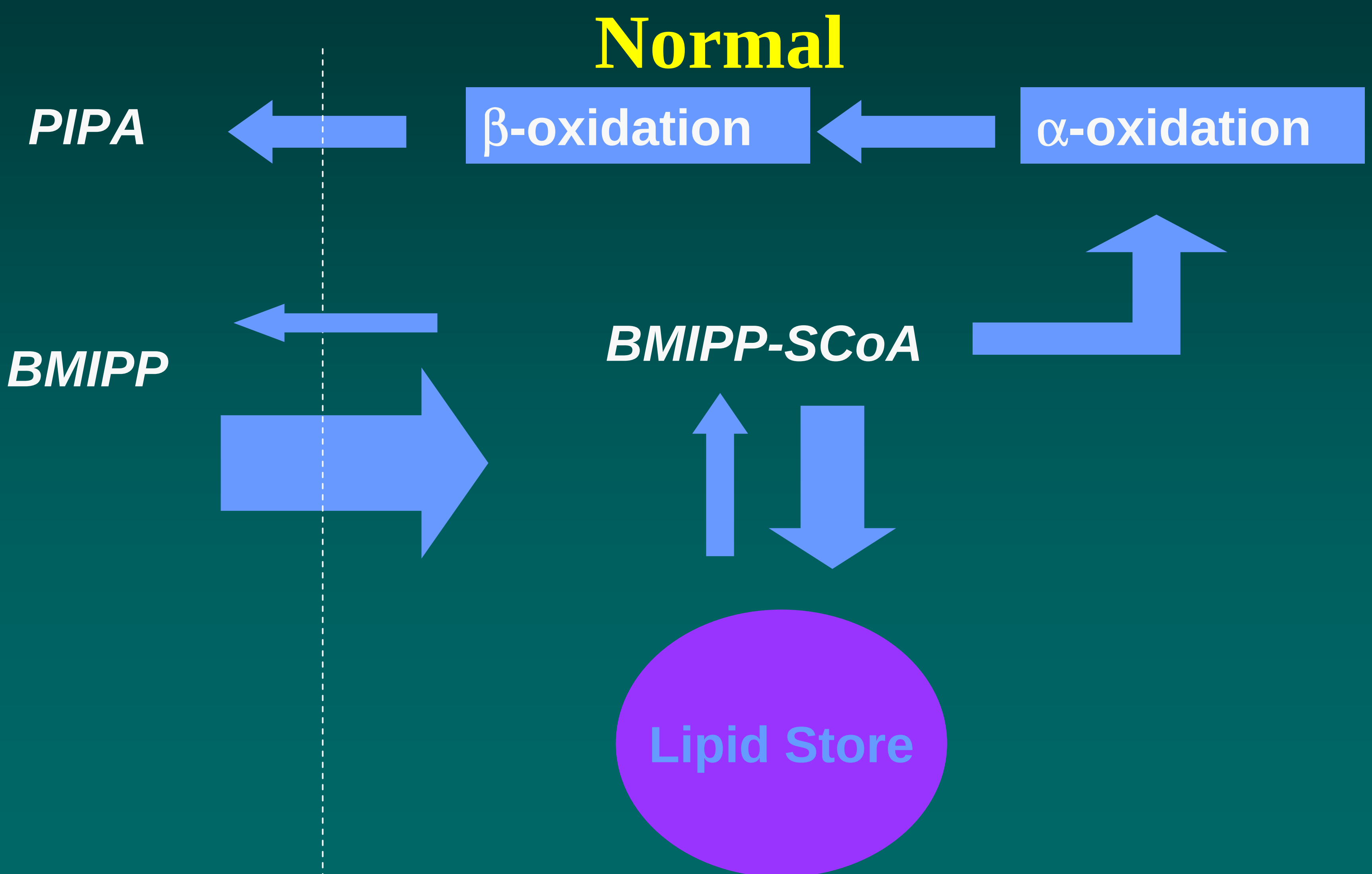
β-methyl: inhibits β-oxidation



15-(*p*-Iodo-phenyl)-3-R,S-methylpentadecanoic acid (BMIPP)

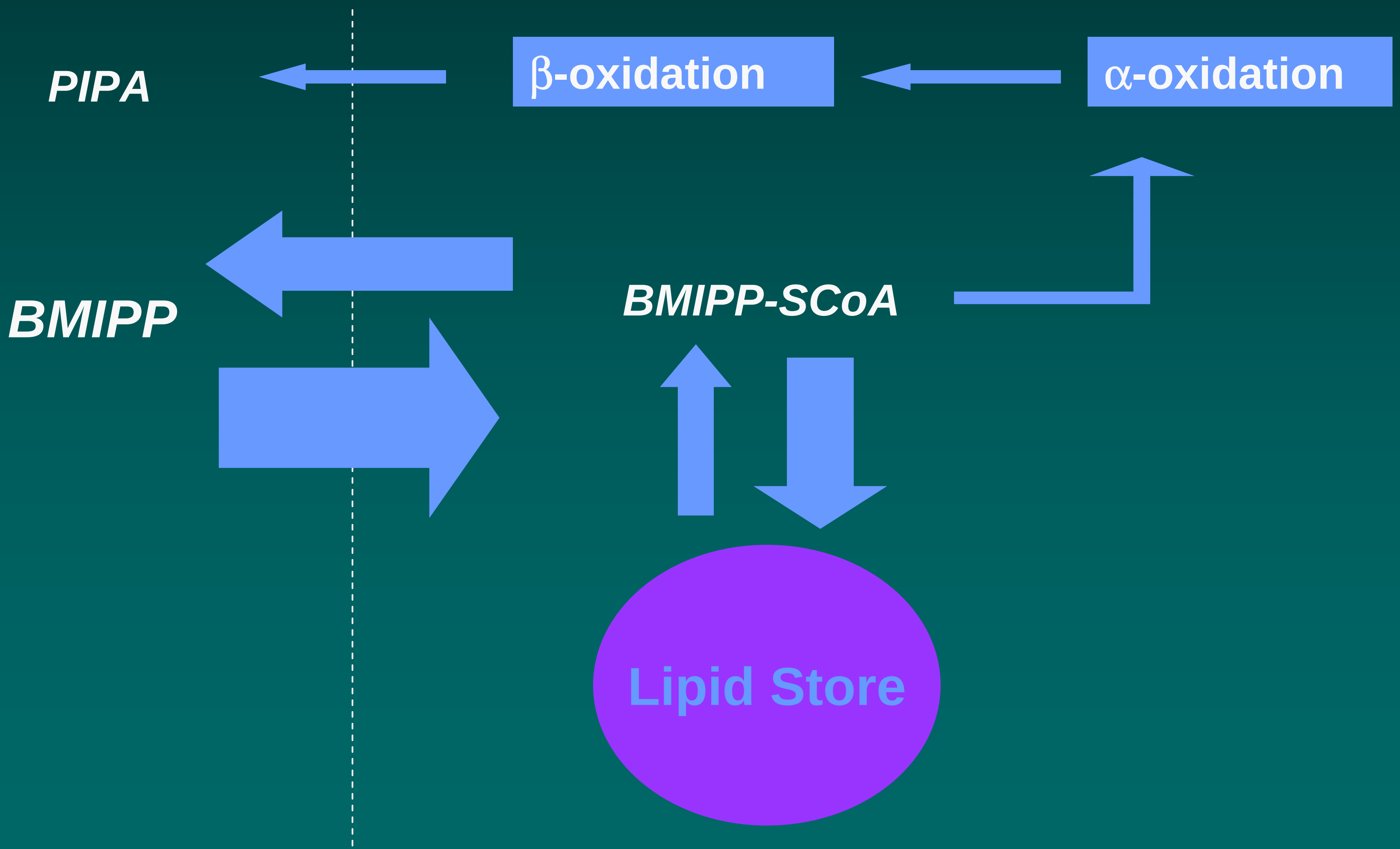
β-methyl iodophenyl pentadecanoic acid (BMIPP)

BMIPP Metabolism

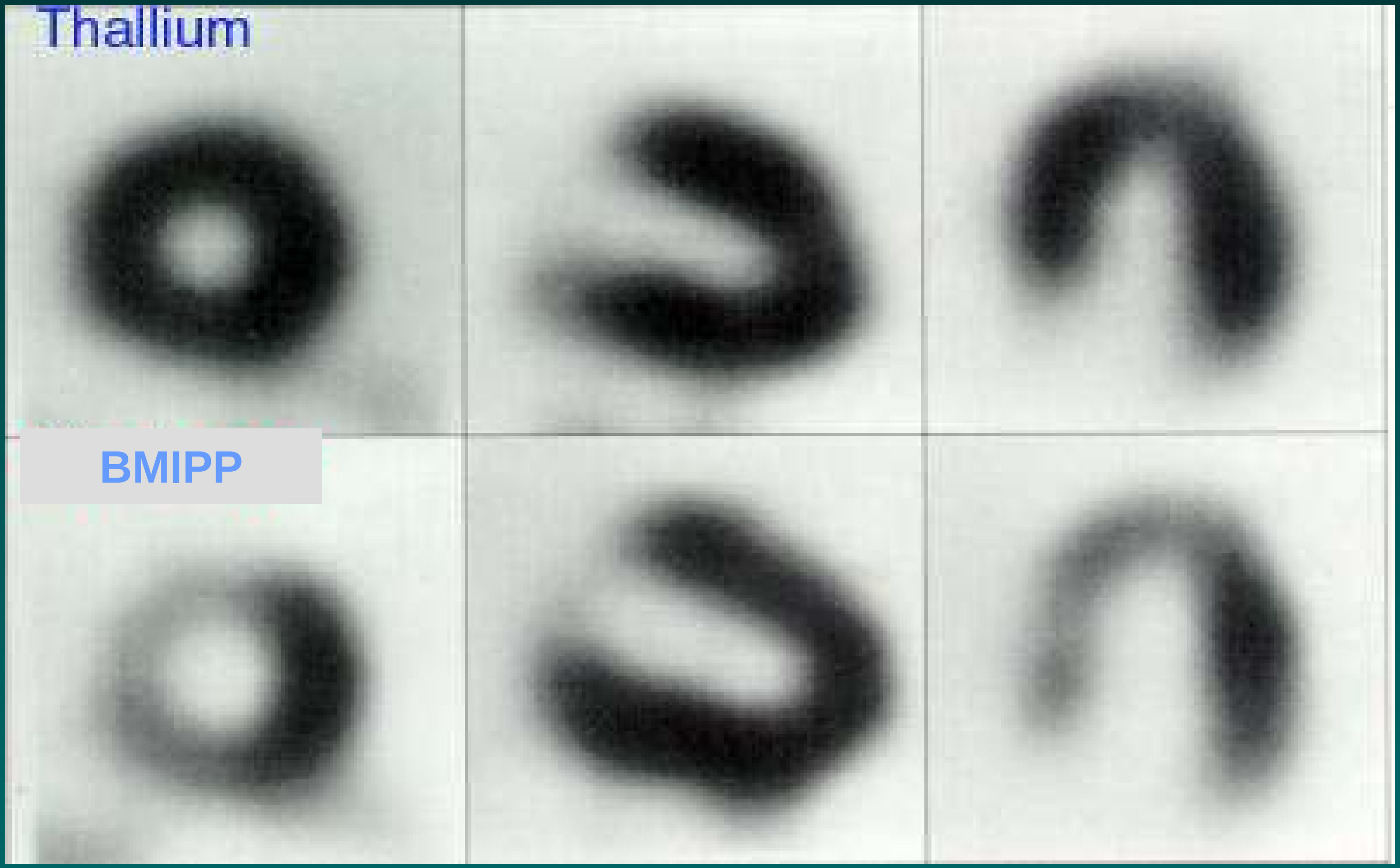


BMIPP Metabolism

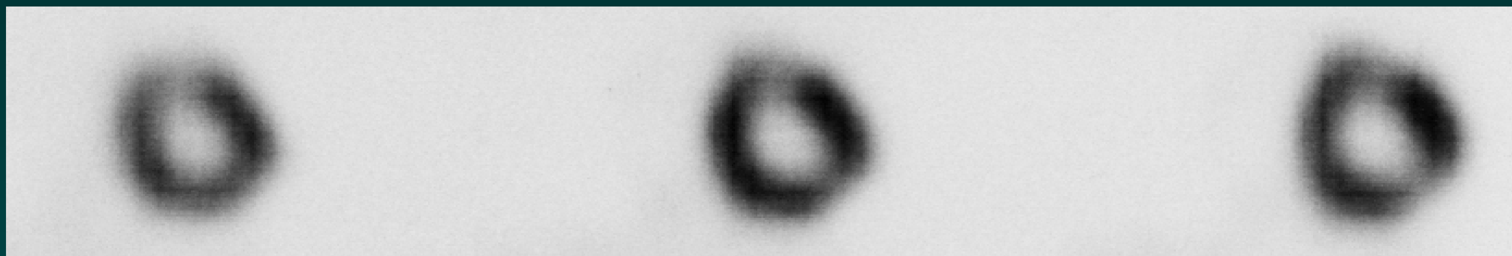
Ischemia



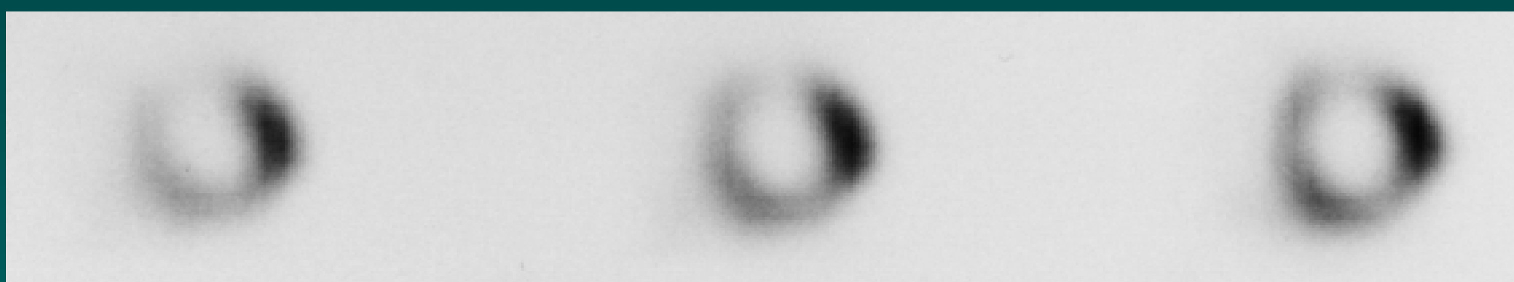
BMIPP and Perfusion Imaging Discordant uptake



BMIPP Detects Ischemia Without Stress Test



Rest Tl-201-SPECT



Stress Tl-201-SPECT

BMIPP SPECT

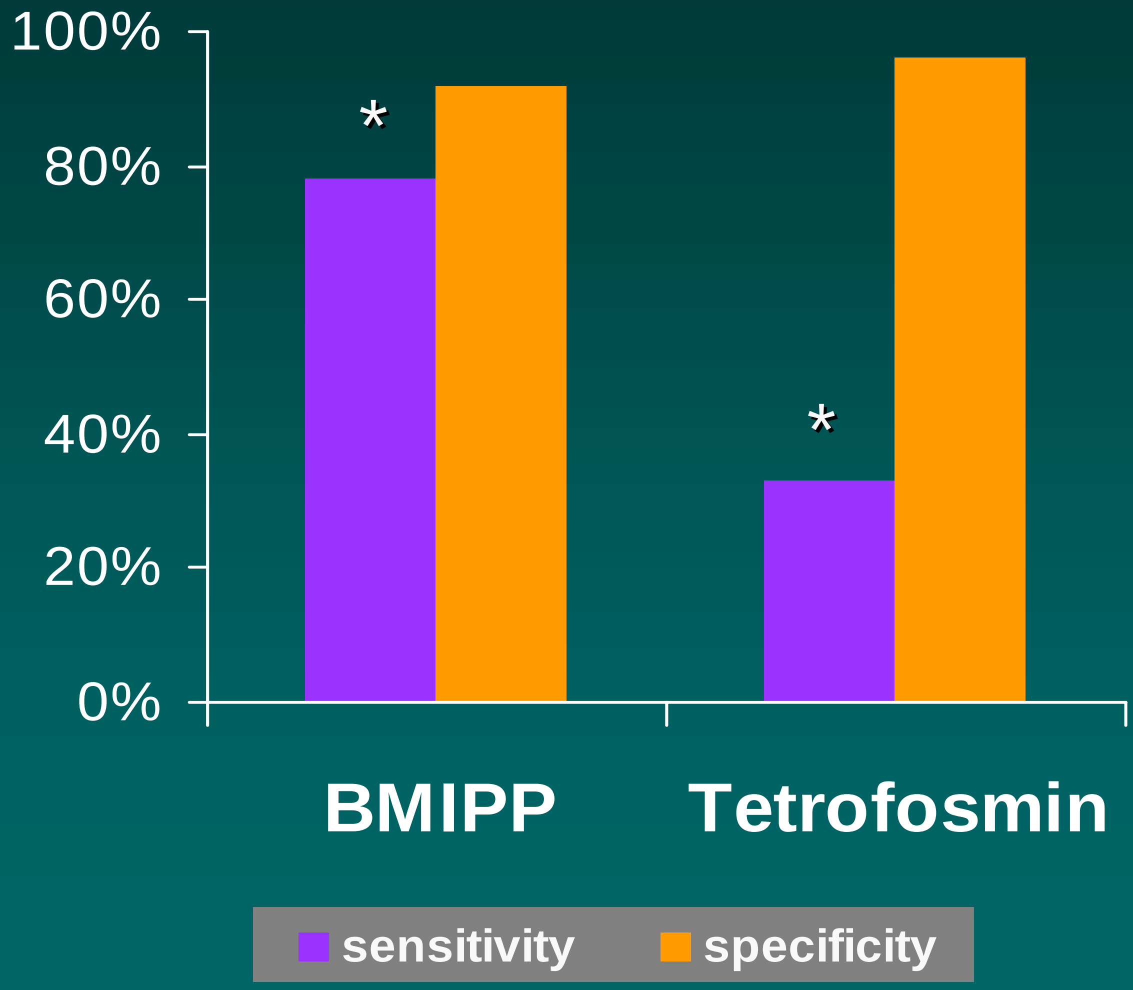
Acute Chest Pain (No evidence of AMI) BMIPP vs Perfusion Imaging at Rest

Tetrofosmin and BMIPP SPECT were obtained in 111 patients with acute chest pain (< 24hr of the last chest pain) and no evidence of AMI

CAG findings	(n)	TF↓ BM↓	TF→ BM↓	TF→ BM→
Organic stenosis	(66)	28	22	16
Coronary spasm	(21)	5	9	7
No abnormalities	(24)	1	1	22
Total	(111)	34	32	45

Kawai Y, et al. JACC 38: 1888-1894, 2001

Acute Chest Pain
BMIPP vs Perfusion Imaging



* p<0.001

Perfusion study <24h of chest pain

BMIPP ~ 48h

Kawai Y, et al. JACC 38: 1888-1894, 2001

Diagnostic accuracy of BMIPP imaging at rest for identifying coronary lesions

Authors	No of patients	Patients	diagnostic accuracy sensitivity	specificity
Nakajima	32	Vasospastic angina	25/32(78%)	NA
Takeishi	78	CAD	28/49(57%)	NA
Fujiwara	29	CAD	15/20(75%)	7/9(78%)
Tateno	31	Angina	27/31(87%)	NA
Suzuki	40	unstable angina	25/28(89%)	12/12(100%)
Yamabe	104	CAD	38/54(84%)	16/20(80%)
Kawai	111	acute chest pain	64/87(74%)	22/24(92%)
Watanabe	75	Vasospastic angina	43/50(86%)	22/25(88%)
Overall	500		265/351(75%)	79/90(88%)

Prognostic analysis of BMIPP SPECT in CAD patients without history of MI

(Follow-up study in 162 patients)

Parameter	Cardiac events (n=50)	No cardiac event (n=112)	P value
Positive BMIPP	41/50 (82%)	57/112 (51%)	0.0004**
Positive MPI	32/50 (64%)	55/112 (49%)	0.113
TDS			
BMIPP	3.8±4.4	1.7±2.8	0.002**
MPI-ex	4.5±5.0	2.1±2.3	0.001**
MPI-rest	2.5±3.4	1.5±2.0	0.049*
MPI-SDS	2.1±3.3	0.6±1.9	0.004**

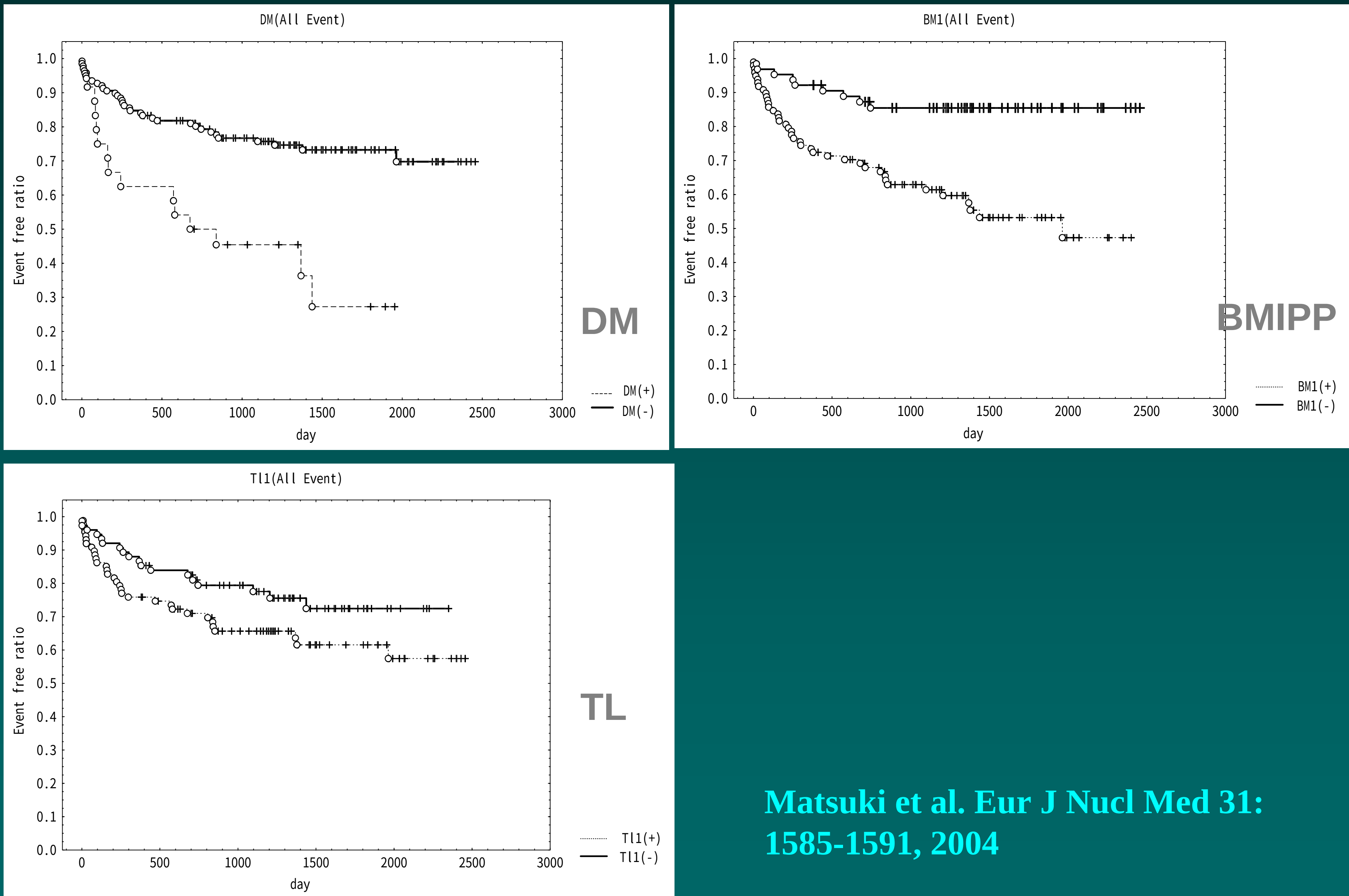
Matsuki et al. Eur J Nucl Med 31: 1585-1591, 2004

Cox's Proportional Hazard Regression for Predicting All Cardiac Events

	Hazard Ratio	95%IC	P value
BMIPP	3.20	1.47-4.33	0.003
Diabetes Mellitus	2.30	1.13-3.09	0.019

Matsuki et al. Eur J Nucl Med 31: 1585-1591, 2004

Event free ratio in patients



Matsuki et al. Eur J Nucl Med 31: 1585-1591, 2004

Summary 3

- BMIPP is a branched fatty acid which trapps in the myocardium reflecting fatty acid utilization.
- BMIPP can identify ischemic myocardium as an area of reduced tracer uptake at rest in patients without history of MI.
- Normal BMIPP may be an excellent prognostic sign in these patients.

Conclusions

- **Nuclear cardiology permits precise tissue characterization with use of suitable radiopharmaceuticals.**
- **Metabolic imaging has a key role for assessing tissue viability and selecting high risk subgroups in patients with coronary artery disease on the basis of metabolic alterations.**