Beyond ischemia, hibernation and viability…

When to revascularize, implant ICD or CRT?

Role of nuclear cardiology

29th Annual Cardiology for Clinicians Spring Symposium

May 5, 2016

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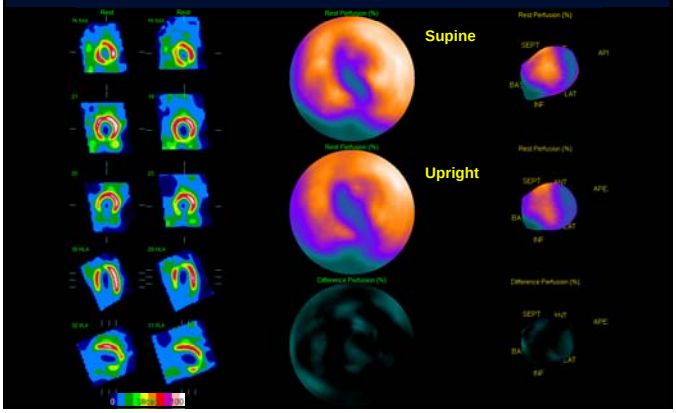
Teaching Goals

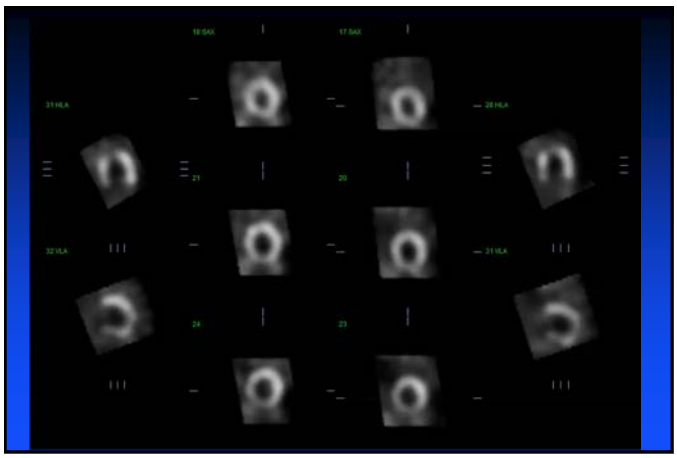
- Identify patients who benefit from revascularization in addition to optimal medical therapy.
- Understand clinical distinctions of hibernating, viable, and stunned myocardium
  - TI-201 Rest and 23 hr Redis imaging
  - FDG PET
- Understand strengths and limitations of STITCH
- Recognize the prognostic power of PET
- Nuclear cardiology to identify high risk patients
  - SCD: Hydroxy-ephedrine
  - Cardiac sarcoid: Fasting FDG
  - Dyssynchrony, benefit of CRT: ERNA and gated SPECT

Case KiSu

- 76 yo college professor who was admitted to OSH complaining of fatigue, nausea, and loss of appetite for one week.
- Transferred to SMH/ED; peak Troponin T level was 5.5.
- While in the hospital he became hypoxic and placed on bipap.
- EF was 10-15.
- PMH: CKD, PE, DM Type I, CVA, peripheral neuropathy, cholecystectomy, and left leg amputation
- His current medications include ASA, Augmentin, atorvastatin, clopidogrel, ferrous sulfate, furosemide, insulin, and metoprolol.
- Major indication for this study is assessing regional myocardial viability.
- AUC indication 62: Assessment of viability / ischemia

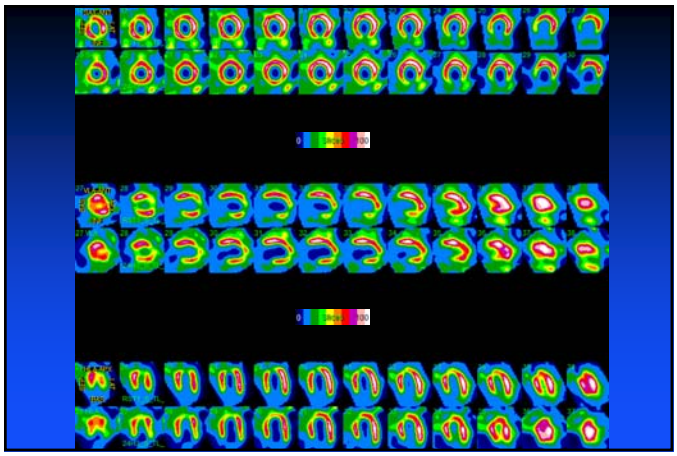
Case KiSu

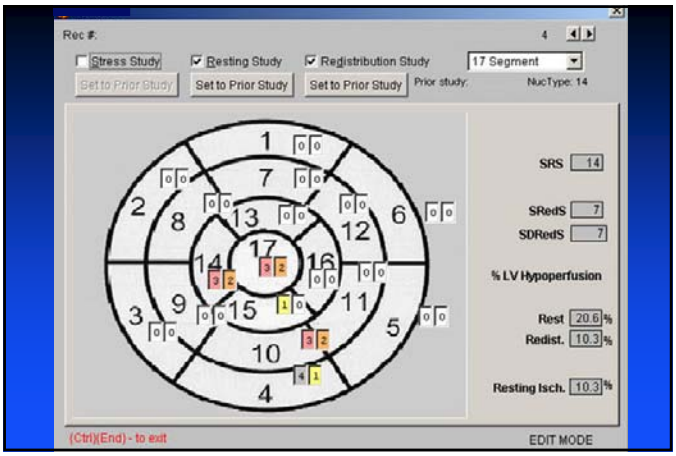




Case KiSu

- Myocardial perfusion SPECT imaging demonstrates: (1) Severe resting perfusion defects (20% LV) of the apex, apical septal, basal inferior and mid-inferior wall regions. (2) Late redistribution imaging is pending to assess regional myocardial hibernation and viability.
- ECG gated myocardial wall motion study shows: (1) Normal LV volume indices; (2) Mild to moderate reduction of LVEF with diffuse dysfunction worst in the apical and apical septal region. LVEF = 41%; EDVI = 47 ml/m^2; ESVI = 28 ml/m^2.
- 24 hr redistribution imaging was performed (AUC indication = 62):





Case KiSu Outcome

- **Stress test cancelled due to 10% myocardial hibernation and viability superimposed on 10% infarction with known severe 2 VD after MI and LVD**
- **The patient underwent successful multivessel PCI with rotational atherectomy assisted DES of LAD and the dominant LCX.**
- **Medical Rx: high-intensity statin, lisinopril and metoprolol succinate.**
- **4 months later, doing well**
  - free of any anginal heart failure symptoms
  - most recent echocardiogram demonstrated ejection fraction ~ 53%
  - remains on appropriate antiplatelet therapy with aspirin and ticagrelor

Case 2: Patient with severe aortic stenosis, LV dysfunction, 3 VD

What can nuclear cardiology offer?

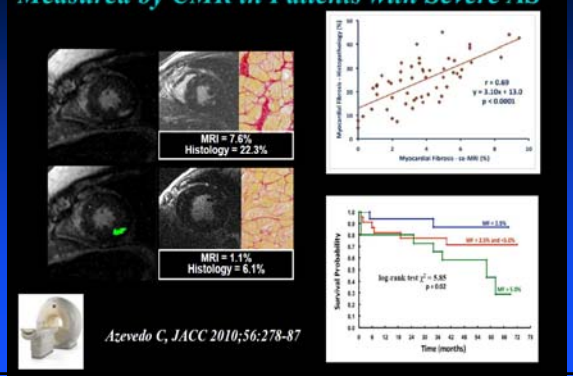
How and Why is the LV Struggling with AS, Low EF, 3 VD?

- AVR: Aortic stenosis or cardiomyopathy?
  - Gradient? Contractile Reserve? Wall stress? LVESVI? LA Volume Index? LV SVI? Regurgitant volume?
- Cardiomyopathy (Low EF + 3VD): Benefit of Revascularization
  - How much scar?
  - How much ischemia?
  - Stress ischemia
  - Rest ischemia
    - Who benefits from device therapy to enhance
    - Mechanical (CRT) ventricular function?
    - Denervated Viable Myocardium (ICD)?

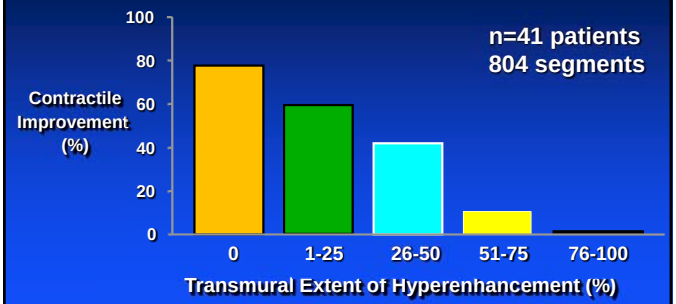
RNI + CMR
RNI
CMR

RNI = Radionuclide Imaging = SPECT + PET ECG Gated Perfusion, Metabolism and / or Function

Prognostic Significance of Myocardial Fibrosis Measured by CMR in Patients with Severe AS



MRI Hyper-enhancement
Contractile Recovery Post-Revascularization



Kim et al NEJM 2000; 343: 1445-53

MRI-Scar predicts outcome, but what about interaction with revascularization?

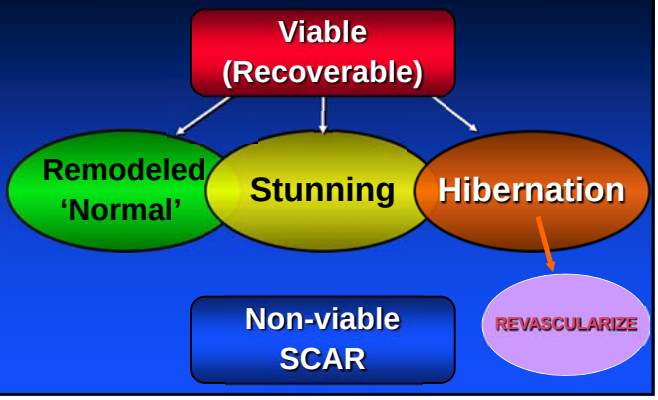
Cox Proportional Hazard Analysis Demonstrating the Association Among Various Factors and Combined Events

	Univariable Analysis		Multivariable Analysis	
	Relative Risk 95% CI	p Value	Relative Risk 95% CI	p Value
Age (yrs)	1.01 (0.99–1.04)	0.29		
Female gender	1.83 (1.06–3.16)	0.03	2.05 (1.18–3.57)	0.01
Diabetes mellitus	0.96 (0.53–1.74)	0.9		
Hypertension	0.73 (0.41–1.29)	0.28		
Statins	0.75 (0.44–1.26)	0.28		
Beta-blockers	0.65 (0.39–1.10)	0.09	0.60 (0.36–1.03)	0.06
ACE inhibitor	0.75 (0.44–1.26)	0.30		
LVEF		0.32		
Post-CMR revascularization	0.98 (0.53–1.79)	0.94		
Post-CMR [CAD] RI				
Quantitative scar (% of total LV myocardium)	1.02 (1.003–1.03)	0.01	1.02 (1.005–1.03)	0.005
Total scar score (semiquantitative)				

Chi-square for the multivariable model = 15.11, p = 0.002. Because of significant correlation between scar percentage (quantitative) and total scar score (semiquantitative), only scar percentage was entered into the multivariable model.
CI = confidence interval; other abbreviations as in Table 1.

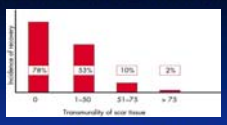
Kwon DH, et al** JACC Cardiovasc Imaging. **2009 Jan;2(1):34-44

Dysfunctional Myocardium



Agreement and disagreement between CE MRI and ^{18}F-FDG

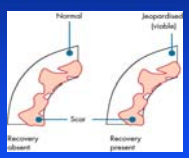
Relationship between contrast enhanced MRI and FDG in dysfunctional myocardial segments

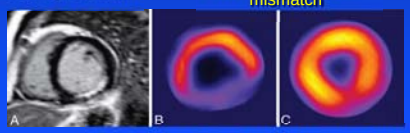


Kaandorp TAM Heart 2005;91:1359

Subendocardial scar by CE MRI

Hibernating, viable myocardium predicts recovery by PET perfusion / ^{18}F-FDG mismatch





Roes SD Eur J Nucl Med Mol Imaging 2009;36:594

The Evidence: Predicting Recovery of Struggling Ischemic LV with Revascularization

Ischemic Jeopardy =
Stress induced ischemia + Hibernating viable myocardium

Functional recovery of stress induced ischemia:
≥ 7% Ischemic jeopardy (Rb-82 PET) — *Taqueti V ACC 2014*
≥ 10% Ischemic jeopardy (Tc-99m MIBI SPECT) — *Hachamovitch R EHJ 2011*
No prior MI (small degree fibrosis) — *Hachamovitch R EHJ 2011*

Functional recovery of Hibernating viable myocardium:
>7% PET Perfusion / FDG metabolism mismatch
D'Egidio et al, JACC Cardiovasc Imaging 2009 Sep;2(9):1060-8

European Heart Journal Advance Access published January 21, 2011

European Heart Journal
doi:10.1093/eurheartj/ehq500

CLINICAL RESEARCH

Impact of ischaemia and scar on the therapeutic benefit derived from myocardial revascularization vs. medical therapy among patients undergoing stress-rest myocardial perfusion scintigraphy

Rory Hachamovitch[1], Alan Rozanski[2], Leslee J. Shaw[3], Gregg W. Stone[4], Louise E. J. Thomson[5,6,7], John D. Friedman[5,6,7], Sean W. Hayes[5,6,7], Ishac Cohen[5,6,7], Guido Germano[5,6,7], and Daniel S. Berman[5,6,7]*

[1]Section of Cardiovascular Imaging, Department of Cardiovascular Medicine, Cleveland Clinic, Cleveland, OH, USA; [2]Department of Medicine, St Luke's Roosevelt Hospital, New York, NY, USA; [3]The Emory Program in CV Outcomes Research and Epidemiology, Emory University School of Medicine, Atlanta, GA, USA; [4]Columbia University Medical Center and the Cardiovascular Research Foundation, New York, NY, USA; [5]Department of Imaging (Division of Nuclear Medicine), Cedars-Sinai Medical Center, 8700 Beverly Boulevard, Room 1258, Los Angeles, CA 90048, USA; [6]Department of Medicine (Division of Cardiology), Cedars-Sinai Medical Center, Los Angeles, CA, USA; and [7]Cedars-Sinai Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA

Received 26 May 2010; revised 20 October 2010; accepted 7 December 2010

SPECT and Risk of Cardiac Death

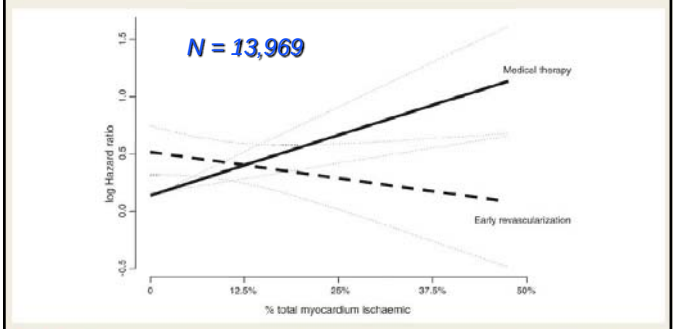
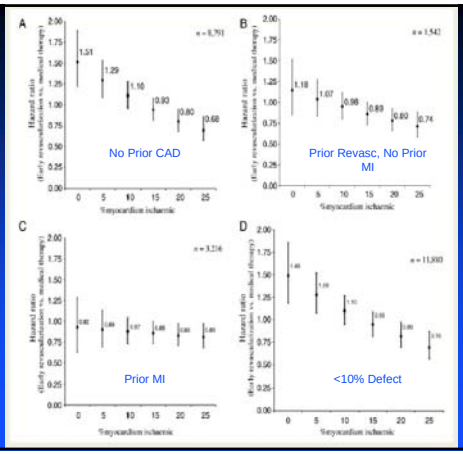


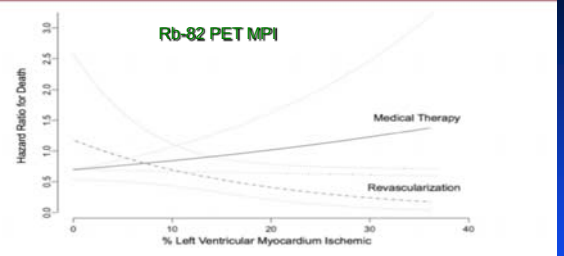
Figure 4 Log hazard ratio for revascularization vs. medical therapy as a function of %myocardium ischaemic in patients with <10% ischaemic myocardium. Graphic representation based on Cox proportional hazards model. Interaction $P < 0.001$.

Hachamovitch R European Heart J 2011

Hachamovitch R et al. Eur Heart J 2011



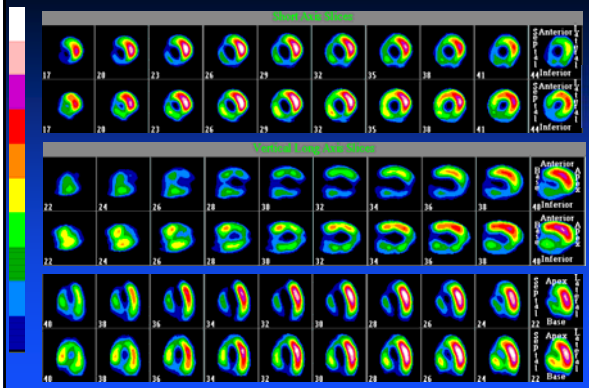
Interaction (1): Ischemia and Revasc



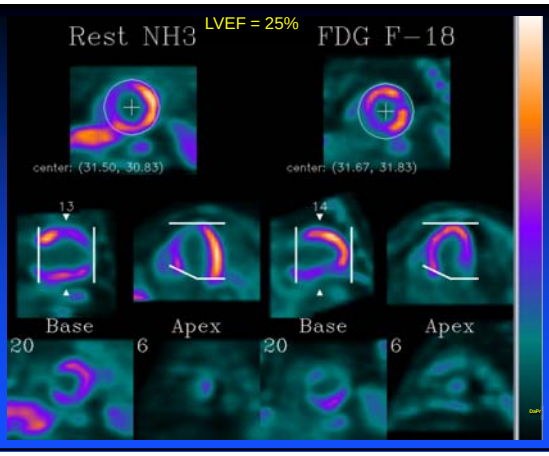
Significant propensity-adjusted interaction seen between LV ischemia and intervention strategy (P =0.03), i.e. pts with increasing ischemia had a survival benefit with revascularization

Source: Taqueti V, et al. ACC 2014

LVEF = 25%



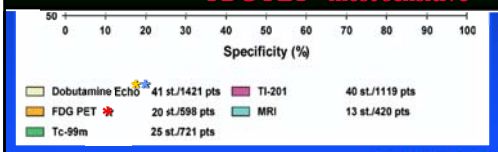
LVEF = 25%



Sensitivity and Specificity of Different Hibernation/Viability Methods

Dobutamine Echo - Contractile Reserve – most specific;

FDG PET - most sensitive



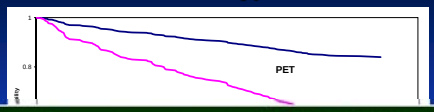
* p< 0.05 vs others

Schinkel et al. Curr Prob Cardiol 2007; 32: 375-410
Buckley O, Di Carli M Circulation 2011;123:444-450

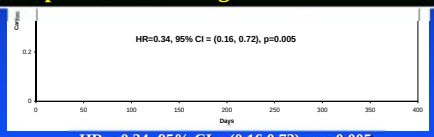
Ottawa-FIVE Subgroup - Composite Event Free Survival

Patients with FDG PET-assisted management vs Standard Care

FDG PET-Guided Therapy vs. Standard Care



Outcome Benefit can be achieved with FDG PET in a centre with access, experience and integration with clinical teams.



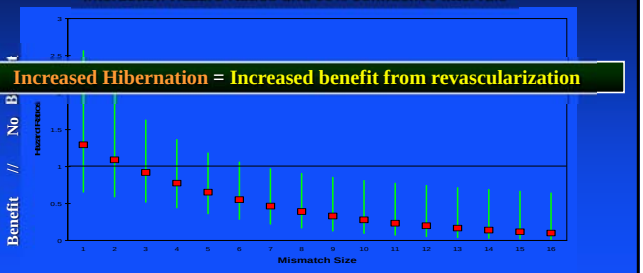
HR = 0.34; 95% CI = (0.16,0.72); p = 0.005

Abraham et al, J Nucl Med 2010;51:567-74.

Revascularization and Mismatch Interaction

Adjusted outcome: Revascularization and Mismatch Interaction Hazard Ratios and 95% confidence intervals

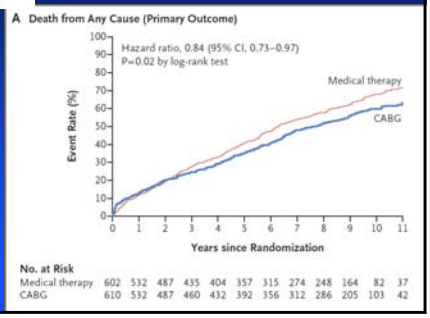
Increased Hibernation = Increased benefit from revascularization



D'Egidio et al, JACC Cardiovasc Imaging 2009 Sep;2(9):1060-8

The NEW ENGLAND JOURNAL of MEDICINE

Coronary-Artery Bypass Surgery in Patients with Ischemic Cardiomyopathy



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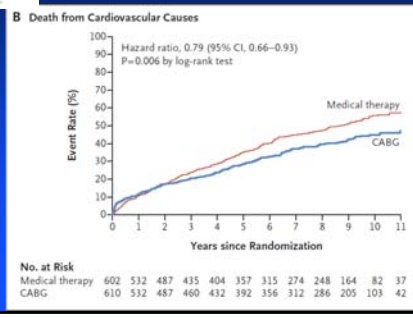

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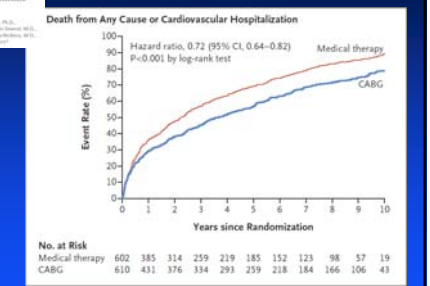
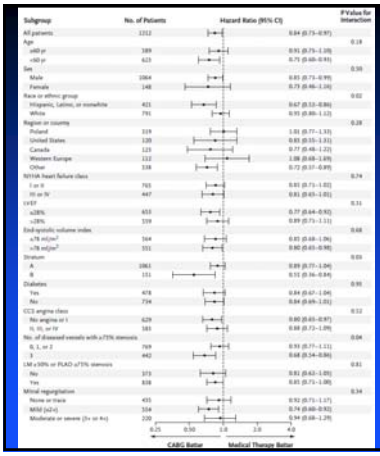


Figure 2. Kaplan–Meier Estimates of the Rates of Death from Any Cause, Death from Cardiovascular Causes, and Death from Any Cause or Hospitalization for Cardiovascular Causes.



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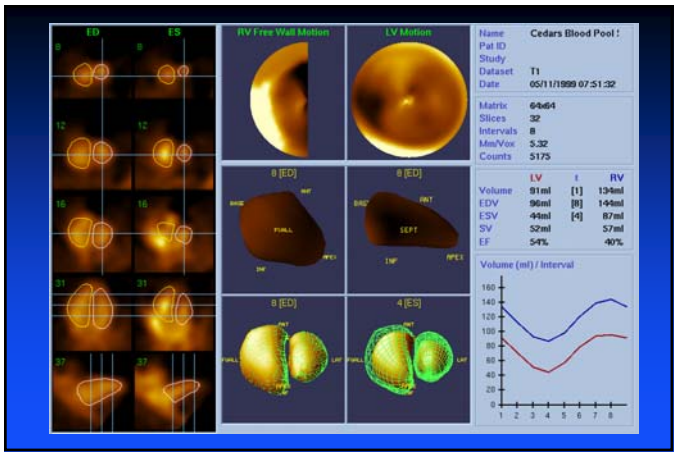
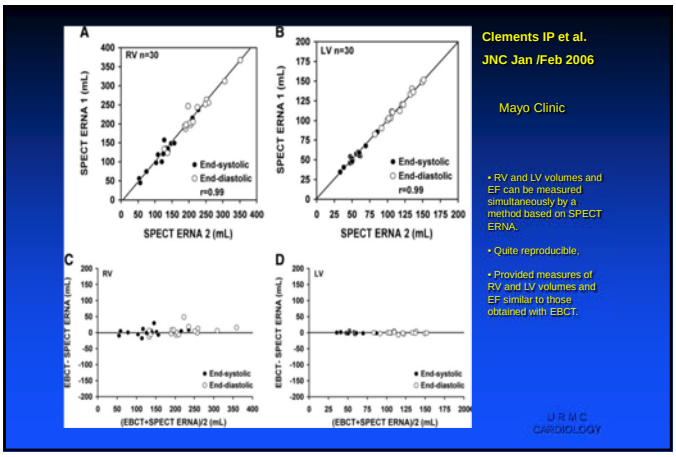




Clements IP et al.

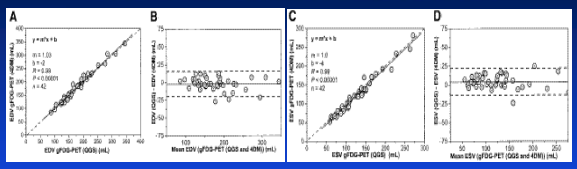
JNC Jan /Feb 2006

Mayo Clinic

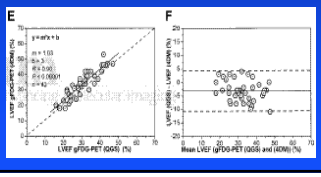
- RV and LV volumes and EF can be measured simultaneously by a method based on SPECT ERNA.
- Quite reproducible,
- Provided measures of RV and LV volumes and EF similar to those obtained with EBCT.

U R M C CARDIOLOGY

Correlation Analysis of LV Volumes and EF: FDG PET vs. Cardiac MRI Schaefer WM. JNM 2004, 45:74-79.



4D-MSPECT



U R M C CARDIOLOGY

ECG-gated SPECT MPI: Risk Adjusted Cardiac Events by Gender

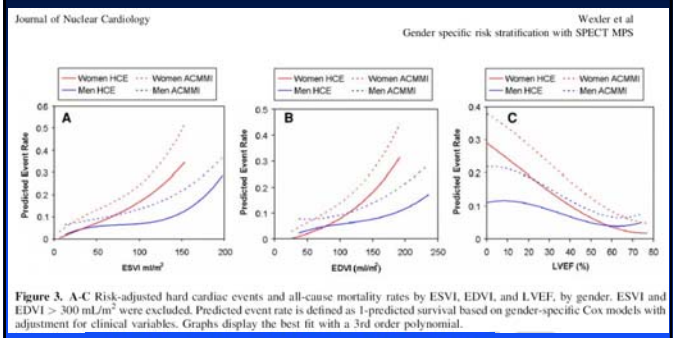
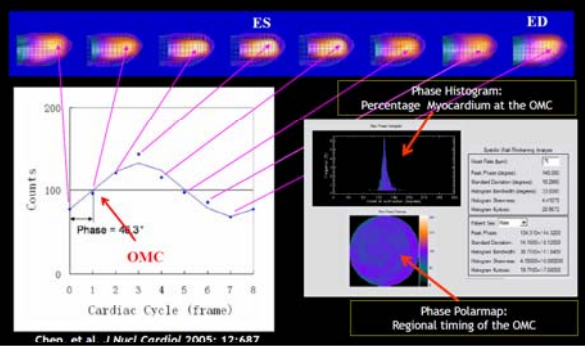


Figure 3. A-C Risk-adjusted hard cardiac events and all-cause mortality rates by ESVI, EDVI, and LVEF, by gender. ESVI and EDVI > 300 mL/m² were excluded. Predicted event rate is defined as 1-predicted survival based on gender-specific Cox models with adjustment for clinical variables. Graphs display the best fit with a 3rd order polynomial.

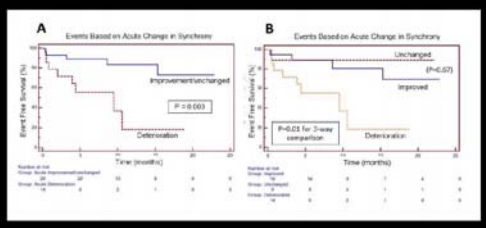
Wexler O et al. J Nucl Cardiol. 2009

SPECT Assessment of LV Synchrony: Technique



Chen, et al. J Nucl Cardiol 2005; 12:687

What Does The Acute Response Mean?



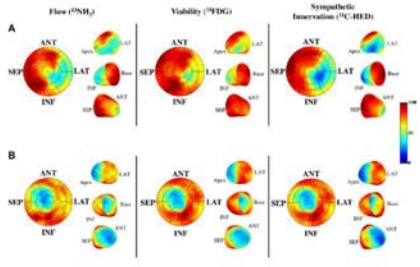
Composite end-point of Death, HF Hospitalization, VT

Soman ACC 2014

Friehling M. *Circ Imaging* 2011
Young Investigator ASNC 2010

Regional Myocardial Sympathetic Denervation Predicts the Risk of Sudden Cardiac Arrest in Ischemic Cardiomyopathy - PAREPET

204 ischemic cardiomyopathy (LVEF≤35%) eligible for primary prevention ICDs.
The primary endpoint was SCA defined as arrhythmic death or ICD discharge for V. Fib or V. Tach >240beats/min.

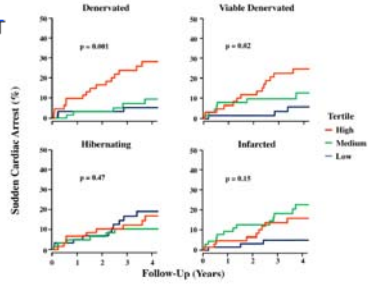


Fallavollita JA et al. J Am Coll Cardiol. 2014;63(2):141-149

Kaplan-Meier Curves Show the Incidence of Sudden Cardiac Arrest for Tertiles of PET-Derived Myocardial Substrates

After 4.1 years, 16.2% (33/204 subjects) had SCA.
Infarct volume and LVEF were not predictors of SCA. However, HED defined viable, denervated myocardium was.

PAREPET



Fallavollita JA et al. J Am Coll Cardiol. 2014;63(2):141-149

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Conclusions: CMR AND SPECT / PET TO SEARCH AND RESCUE THE STRUGGLING (LOW EF, 3VD, AS) VENTRICLE

- Echocardiography *+/- dobutamine to define critical A.S. and value of AVR*
- PET/CMR quantify LV scar: AVR 5 yr survival ~88% MF<2.5%, ~44% MF>2%
- Use SPECT / PET perfusion / metabolism imaging of ischemic cardiomyopathy to assess myocardial ischemic jeopardy = stress ischemia + hibernating viable myocardium >7% LV mass
- Define benefit of device therapy in ischemic cardiomyopathy:
  - ECG-gated SPECT to assess dyssynchrony for CRT *(Friehling Circ Res 2011)*
  - Sympathetic denervation (HED PET) in Viable Myocardium (N13 NH3 + FDG PET) to select optimal ICD candidates *(PAREPET)*

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  - Dyssynchrony, benefit of CRT: ERNA and gated SPECT

UNIVERSITY of ROCHESTER MEDICAL CENTER

URMC CARDIOLOGY