Nuclear Cardiology in the evaluation of sympathetic innervation

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All heart failure is associated with \( \uparrow \) sympathetic activity leading to malignant arrhythmias causing sudden cardiac death (SCD) and/or progression to pump failure.

Chronic \( \uparrow \) sympathetic activity reduces presynaptic noradrenaline (NA) reuptake in the failing heart due to down regulation of the cardiac NA transporter.

This has been the target of radiolabelled NA analogues in the hope that they can provide unique cost effective clinical information in managing these patients.
Objectives

I-123 MIBG studies: patient preparation, planar imaging, analysis & clinical use.

Potential benefits and limitations of SPECT imaging

PET tracers: Current role and Future directions.
**I-131 (I-123) MIBG**

Developed by Wieland & Beierwaltes to locate Pheochromocytomas in the late 70’s.

A false neuro-transmitter which is taken up in presynapic nerve terminals of sympathetic nerves. Its kinetics and metabolism are complex, influence of perfusion still unclear.

During initial whole body distribution studies I-131 MIBG uptake noted in the heart, liver, spleen, kidneys and salivary glands. Late images were shown to reflect neuronal uptake.

Cardiac uptake correlated inversely with NA & was affected by tricyclic antidepressants.
Early MIBG prospective prognostic studies

Merlet P (France: JNM 1992). 4hr heart/mediastinal ratio (H/M) as indicator of neuronal integrity.
90 CHF pts: independent predictors of survival
H/M: p<0.0001, LVEF: P<0.01, X ray dim: P<0.02

Tamaki S (Japan: JACC, 2009): 20min & 200min images in 106 CHF pts: independent prognostic markers:
SCD: Washout rate (P>0.001) & LVEF (P>0.03) (H/M)

Pump failure: LVEDD: p<0.01, Washout rate : p<0.01, LVEF: <0.02, Cr: <0.03.
Utility of I-123 MIBG in CHF research

Serial H/M or W/R changes correlated with efficacy of many congestive heart failure therapies

- Beta Blockers: Gerson MC, 2002
- ACE inhibitors: Kasama S, 2005
- Sustained CRT benefits: Gould PA, 2007
- Spironolactone & Candesartin: Kasama S, 2007
- Appropriate ICD therapy: Boogers MJ, 2009
- Amiodarone: Toyama T, 2004
- CPAP: Hall AB, 2014

- CRT benefit only if dH/M >1.36: Nishioka SA, 2007
- Statins: Sano H, 2014
- Reduced H/M: HFPEF risk factor: Kato S, 2010
Proposal to Standardize Cardiac I-123 MIBG imaging: EANM & ECNC (EJNM:2010)

Patient preparation important. Medications to be avoided

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of interference (known or expected)</th>
<th>Discontinuation prior to MIBG scan (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioids</td>
<td>Uptake inhibition</td>
<td>7–14</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Uptake inhibition</td>
<td>7–14</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Uptake inhibition</td>
<td>7–14</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Uptake inhibition</td>
<td>7–21</td>
</tr>
<tr>
<td>Amitriptyline and derivatives, imipramine and derivatives, amoxapine, doxepine, others</td>
<td>Uptake inhibition</td>
<td></td>
</tr>
<tr>
<td>Sympathicomimetics&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Depletion of granules</td>
<td>7–14</td>
</tr>
<tr>
<td>Phenylpropanolamine, ephedrine, pseudoephedrine, phenylephrine, amphetamine, dopamine, isoproterenol, salbutamol, terbutaline, phenoterol, xylometazoline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihypertensive/cardiovascular agents</td>
<td>Inhibition uptake and depletion</td>
<td>21</td>
</tr>
<tr>
<td>Labetalol</td>
<td>Depletion and transport inhibition</td>
<td>14</td>
</tr>
<tr>
<td>Reserpine</td>
<td>Depletion and transport inhibition</td>
<td>14</td>
</tr>
<tr>
<td>Bretylium, guanethidine</td>
<td>Increased uptake and retention</td>
<td>14</td>
</tr>
<tr>
<td>Calcium channel blockers (nifedipine, nicardipine, amlodipine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Uptake inhibition</td>
<td>21–28</td>
</tr>
<tr>
<td>Phenothiazines&lt;sup&gt;b&lt;/sup&gt; (chlorpromazine, promethazine, fluphenazine, others)</td>
<td>Uptake inhibition</td>
<td>21–28</td>
</tr>
<tr>
<td>Thioxanthenes (maprotiline, trazolone)</td>
<td>Uptake inhibition</td>
<td>21–28</td>
</tr>
<tr>
<td>Butyrophenones (droperidol, haloperidol)</td>
<td>Uptake inhibition</td>
<td>7–21</td>
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<td>Loxapine</td>
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Flotats A et al, EJNMM! 2010
Proposal to Standardize Cardiac I-123 MIBG imaging: EANM & ECNC (EJNMMI 2010)

Slow IV I-123 MIBG: 110MBq (planar), 370MBq (SPECT).

Imaging: medium energy collimator; @ 15 min (maximal uptake) & 4hrs (max H/M ratio).
10 min/image for anterior chest planar; ~25 min SPECT (CT).

Processing Planar images:
Key measurement: 4hr H/M ratio.
NL ratio >2.0 Interobserver variability: <5%.
Alternative: W/O from 15min & H/M images, but more complex.

Flotats A et al, EJNMMI 2010
ADMIRE-HF : Prospective observational study

906 CHF pts (LVEF<35%), NYHA II to III. Planar & SPECT: MIBG & MPS (tetrofosmin), f/u median 15 months. Composite End-point: NYHA progression, VF/VT or death (SCD or HF). H/M dichotomised ≥1.6 & <1.6

A Composite Primary Endpoint

![Graph showing cumulative rate (%) over months of follow-up between H/M <1.60 and H/M >1.60.]

- 237 CEs
- 165 HF progression
- 50 Arrhythmias
- 24 Cardiac death

Jacobson et al JACC 2010
ADMIRE-HF study: secondary end-points

A. Composite Primary Endpoint

B. Heart Failure Progression

C. Arrhythmic Event

D. Cardiac Death

Jacobson et al JACC 2010
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**Low risk** (ADMIREE-HF score = -3)  
LVEF 30%  
HMR 1.8  
SBP 145 mmHg

**Intermediate risk** (ADMIREE-HF score = 15)  
LVEF34%  
HMR 1.1  
SBP 105 mmHg

**High risk** (ADMIREE-HF score = 20)  
LVEF 24%  
HMR 1.2  
SBP 108 mmHg

Jacobson AF, JACC 2010
ADMIRE-HF study: additional findings

**No added benefit** of 17 segment 5 point SPECT MIBG (± Tc-99 MPS) imaging (issues: low dH/M c/w lung, liver in severe CHF)

Because of this study, MIBG in assessing CHF patients became reimbursable in the U.S.

**Editorial (HW Straus):** May be very useful in patients with high SCD risk being evaluated for ICD therapy. **Main limitation:** Did not directly evaluate the potential benefit of I123 MIBG imaging as an aid to clinical management.

Strauss HW JACC 2010
ADMIRE-HFX study

Extension of Admire-HF: f/u to median 2 yrs

Primary end point, all cause mortality,

Composite: All cause mortality, resuscitated arrest & AICD discharge.

Result:
100 deaths, 131 composite end points.

H/M still significant independent risk factor for all cause mortality and mortality equivalents (treated arrhythmias) in clinical & clinical +BNP + LVEF models.

Narula et al JACC 2015
ADMIRE-HFX study

All Cause Mortality

Sudden cardiac death

Partly explains why SPECT not Significant predictor of SCD

Narula et al JACC 2015
Objectives

I-123 MIBG studies: patient preparation, planar imaging, analysis & clinical use.

Potential benefits and limitations of SPECT imaging.

PET tracers: Current role and future directions.
Semi-automated SPECT (Admire –HF pts)

Tc-99m MPS & I-123 MIBG images. Corrections for level of H/M in quantitating severity & extent of voxel defects & mismatches. MPS used to find heart in low dH/M pts

Image threshold changes as HM fall. High (>1.6), medium (1.6-1.31), low (<1.3)

Pt H/M = 1.31

MIBG  MPS  mismatches

White area: abnormal

Clements IP et al J Nucl card, 2016
MIBG: ischaemic vs non-ischaemic HF pts

(ADMIRE HFX) 691 IHD, 319 Non IHD pts. Analysis now included extent and severity of defects

2 year all cause mortality the same for IHD and non IHD pts being higher in pts with denervation >50%.

In IHD pts mortality highest with 20%-40% myocardial perfusion defect.

In non IHD pts mortality highest when perfusion defects <20% but large MIBG/ Tetrofosmin mismatches (>50%)

Clements IP et al E Heart J, 2016
Intermediate severity innervation defects in Admire HFX IHD pts a/w highest SCD risk

Emory Cardiac Toolbox analysis: only 75% of Admire-HFX IHD pts had adequate SPECT MIBG & MPS studies.

Proportion of pts (%)

- low: 8% (N=12)
- intermediate: 21% (N=52)
- >mildly abnormal: 9% (N=402 pts)

I-123 MIBG Summed SPECT SCORE

H/M=1.2

Travin MI et al J Nucl Card 2016
Potential algorithm for using SPECT

HMR

<1.30
High likelihood of all cardiac events
Poor quality SPECT images probable
SPECT unlikely to be helpful

1.30 – 1.59

≥1.60
Low likelihood of all cardiac events
SPECT unlikely to provide actionable new information

Highest likelihood of arrhythmic events
Consider SPECT if results (specifically intermediate defect score) might influence clinical decisions
SPECT: technical developments: CZT camera

Higher Count statistics, 3D Dynamic imaging
Simultaneous Tc-99m and I-123 window
Better energy windowing
Ability to derive H/M from SPECT images

MIBI

MIBG

Images rated good or better in 85% cases, but needs to be tested in low H/M ratio pts.

Gimelli A et al, EHJ (C’vasc), 2014
Bellevre D et al, EJNMII, 2015
Objectives

I-123 MIBG studies: patient preparation, planar imaging, analysis & clinical use.

Potential benefits and limitations of SPECT imaging.

PET tracers: Current role and Future directions.
PET tracers in sympathetic neuroimaging

Fowler JS: rapid synthesis C-11 Noradrenaline  JNM 1974
C-11 HED (1989*) non-catecholamine  sympathomimetic amine. **High extraction fraction, retention and ½ life of C-11** make W/O assessment not possible

F-18 Dopamine (1990**) to assess striatal dopaminergic innervation and cardiac sympathetic innervation in Parkinson’s disease. Tracer converted to dopamine in sympathetic nerves in heart and other organs. Synthesis and kinetics remain difficult.

F-18 metaraminol *

*Weiland D JNM 1989, **Goldstein Circ 1990
C-11 HED initial studies

Normal vol 1 yr post Tx

Schwaiger et al Circ 1990
C-11 HED reinnervation in heart Tx

Normal vol 1 yr post Tx 4 yrs post Tx

Schwaiger et al Circ 1990
C-11 HED reinnervation in heart Tx

Normal vol 1 yr post Tx 4 yrs post Tx

Schwaiger et al Circ 1990

Toba M JNM 1996
Pivotal PET prospective observational study.

Multicentre Parapet study (Predicting ARrhythmic Events with PET)

204 stable IHD pts, LVEF<35%, eligible for ICD

MPS: N-13 NH4, Viability: F-18 FDG, Innervation: C-11 HED.

1° end point SCA. (sudden cardiac arrhythmia)

Result: 4.1yrs f/u. SCA :16%

Fallavollita JA et al JACC 2014
<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET parameters (per 1% of LV)</td>
<td></td>
</tr>
<tr>
<td>Denervated myocardium</td>
<td>HR (95% CI) 1.057 (1.023–1.092) p Value 0.001</td>
</tr>
<tr>
<td>Viable, denervated myocardium</td>
<td>HR (95% CI) 1.067 (1.008–1.130) p Value 0.025</td>
</tr>
<tr>
<td>Infarcted myocardium</td>
<td>HR (95% CI) 1.029 (0.990–1.069) p Value 0.15</td>
</tr>
<tr>
<td>Hibernating myocardium</td>
<td>HR (95% CI) 0.950 (0.822–1.099) p Value 0.49</td>
</tr>
</tbody>
</table>

Fallavollita JA et al JACC 2014
Parapet Study (Multivariate analysis)

Independent predictors for Sudden cardiac arrhythmia

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denervation size</td>
<td>1.07</td>
<td>0.003</td>
</tr>
<tr>
<td>LVEDV index</td>
<td>1.03</td>
<td>0.003</td>
</tr>
<tr>
<td>Creatinine</td>
<td>2.3</td>
<td>0.023</td>
</tr>
<tr>
<td>No ACE inhibition</td>
<td>4.1</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Fallavollita JA et al JACC 2014
**Note of caution:** Microvascular dysfunction & arrhythmias in IHD. MBF vs C-11 HED.

52 pts LVEF<35% treated with ICD. **MRI:** LGE, LV volumes, C-11 HED, O-15 H₂O (rest & hyperaemic). **EPS:** +ve/-ve VT/VF

### Characteristics (mean±SD)

<table>
<thead>
<tr>
<th>Characteristics (mean±SD)</th>
<th>Total (n=49)</th>
<th>positive (n=23)</th>
<th>negative (n=26)</th>
<th>vs EPS negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting MBF (mL/min/g)*</td>
<td>0.77±0.19</td>
<td>0.75±0.24</td>
<td>0.78±0.14</td>
<td>0.59</td>
</tr>
<tr>
<td>Hyperaemic MBF (mL/min/g)</td>
<td>1.54±0.42</td>
<td>1.36±0.39</td>
<td>1.71±0.39</td>
<td>0.003</td>
</tr>
<tr>
<td>CFR*</td>
<td>2.09±0.67</td>
<td>1.94±0.84</td>
<td>2.21±0.47</td>
<td>0.16</td>
</tr>
<tr>
<td>[¹¹C]HED RI†</td>
<td>2.62±0.77</td>
<td>2.41±0.72</td>
<td>2.81±0.77</td>
<td>0.07</td>
</tr>
<tr>
<td>Defect size</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perfusion defect (MBFₜ) (%)*</td>
<td>18.3±12.0</td>
<td>21.8±12.8</td>
<td>15.3±10.7</td>
<td>0.06</td>
</tr>
<tr>
<td>Innervation defect ([¹¹C]HED RI) (%)†</td>
<td>24.2±12.6</td>
<td>27.9±11.9</td>
<td>20.7±12.6</td>
<td>0.048</td>
</tr>
</tbody>
</table>

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Rijnierse MT, *et al.* Heart 2016;
Why?

Hyperaemic MBF

α

C₁₁HED retention in pts with CM* so C-11 HED's high extraction fraction may limit its use.

Also Implications for MIBG

* Rijnierse MT Eur Heart 2015
New “MIBG”: F-18 LMI1195

Min post inj

52-66 126-147 202-237 237-272  

Very similar pharmacological properties to I-123 MIBG: less dependence on perfusion than C-11 HED. ? Similar washout rate. But better quantitation possible Note: better dH/liver Ratio

Advantages of F-18 over C-11

Yu M, Circ C/V imaging 2011
Sinusas A, JNM 2014
Summary:

I-123 MIBG now approved in USA for heart failure.

Simple planar 4hr H/M ratio: strong prognostic factor for survival & arrhythmias but still lacking prospective trials showing MIBG guidance, is beneficial and cost-effective.

Has potential role in optimizing patient management.

With new technology, SPECT may be useful in managing SCD in CHF but ? limited to intermediate H/M risk pts.

To date C-11 based PET tracers only approved for research. New, more suitable F-18 labeled NA analogues on the way
Acknowledgement: Prof: Don M. Weiland
University of Michigan

1943 - 2014

Responsible for synthesis of:
I-131(I-123) MIBG
C-11 HED (1990)
Appendices
I-123 MIBG: pharmacological properties

**Principle:** Uptake into vesicles Uptake is a complex interplay of delivery, uptake, exocytosis, reverse transport from cytosol. Washout is just as complex.

Injected MIBG: different fate from NA.

1) Not as avidly or selectively taken up by sympathetic nerves as NA nor is it a substrate for Monoamine Oxidase

2) Not metabolized by non-neural cell enzymes thus metabolic fate remains known

Effect of myocardial perfusion on delivery not known but suspected.
Tracers used

18-F-Dopamine

I-123 MIBG
C-11 Hydroxyephedrine
C-11 epinephrine

F-18 “MIBG”
Merlet: I-123 MIBG H/M ratio vs LVEF

90 pts with NYHII-III (LVEF<45%). 10 Nls. f/u 1-27 m

Independent predictors of 22 pt deaths (6 SCD)

H/M = p<0.0001
LVEF: P<0.01
X ray dim: P<0.02

Echo m-mode p= NS

Merlet P, JNM, 1992
Early prospective prognostic studies

90 pts with NYHII-III (LVEF<45%). 10 Nls. f/u 1-27 m
Independent predictors of 22 pt deaths (6 SCD)
H/M: p<0.0001, LVEF, P<0.01, X ray dim: P<0.02

Tamaki S (JACC, 2009).
106 pts: LVEF <40% (NYHA- II). 18 SCD in 65 months of f/u. Independent predictors:
SCD: Washout rate (P>0.001) & LVEF (P>0.03) (H/M)
Pump failure: LVEDD: p<0.01, WR: p<0.01, LVEF: <0.02, Cr: <0.03.
Tamaki: WR: Independent predictor of SCD.

prospective study 106 pts: LVEF <40% (NYHA: II). 18 pts died suddenly in 65 months of f/u.

<table>
<thead>
<tr>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
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<tbody>
<tr>
<td>p Value</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>0.0006</td>
<td>1.052 (1.022-1.082)</td>
</tr>
<tr>
<td>0.0020</td>
<td>0.089 (0.019-0.412)</td>
</tr>
<tr>
<td>0.0045</td>
<td>1.002 (1.001-1.004)</td>
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<tr>
<td>0.0193</td>
<td>1.004 (1.001-1.008)</td>
</tr>
<tr>
<td>0.0202</td>
<td>0.930 (0.875-0.989)</td>
</tr>
<tr>
<td>0.0227</td>
<td>0.125 (0.021-0.747)</td>
</tr>
<tr>
<td>0.0014</td>
<td>1.052 (1.020-1.085)</td>
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<tr>
<td>0.0341</td>
<td>0.930 (0.870-0.995)</td>
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Independent predictors: SCD  WR & LVEF
ADMIRE-HF: independent risk factors

Table 5  Results of Multivariable Cox Proportional Hazards Analysis of Time to Cardiac Events

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A  BNP>140 ng/l and LVEF<30% (n=273)

C  Cardiac Death
Interaction of LVEF, BNP, and H/M
N=Number of variables with most abnormal quartiles
All differences N=2 and N=3 vs N=0 and N=1 p<0.01
N=3 (38 subjects)
N=2 (150 subjects)
N=1 (282 subjects)
N=0 (456 subjects)

Jacobson AF JACC 2010
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Jacobson AF, JACC 2010
MIBG: ischaemic vs non-ischaemic HF pts

(ADMIRE HFX) 691 IHD, 319 Non IHD pts,
2 year all cause mortality the same for IHD and non IHD pts
being higher in pts with dysinnervation >50%.

In non IHD pts mortality highest
when perfusion defects <20%
but large MIBG/ Tetrofosmin mismatches

Clements IP et al EHJ, 2016
intermediate severity innervation defects
In IHD pts a/w highest SCD risk

471/622 Admire-HF IHD pts: adequate SPECT MIBG & Tetrofosmin. Emory Cardiac Toolbox analysis

<table>
<thead>
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<th>Proportion of pts (%)</th>
<th>All ArE</th>
<th>Non fatal ArE</th>
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<tbody>
<tr>
<td>0-13</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>N=12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14/28</td>
<td>21%</td>
<td>14%</td>
</tr>
<tr>
<td>N=52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;29</td>
<td>9%</td>
<td>6%</td>
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<tr>
<td>N=402 pts</td>
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Unclear if findings due to artifacts on SPECT which only correlates moderately with H/M (r=0.4)

I-123 MIBG Summed SPECT SCORE

Travin MI et al J Nucl Card 2016
C-11 HED reinervation in Tx heart

Normal vol

1 yr post Tx

4 yrs post

Schwaiger et al 1990

Schwaiger et al 1991

Bengel et al 1999

Scan2 >3yrs post scan1

Extent of reinn. %

0-1.5yrs  
1.5 - 7 yrs  
>7 yrs post Tx
C/11 HED Diabetic autonomic neuropathy

Early neuropathy

Late neuropathy

Allman K  JACC 1993
Stephens MJ  Metab 1999
C/11 HED Diabetic autonomic neuropathy

Early neuropathy  Late neuropathy

Regression of HED defects after 3 yrs good diabetic control (Gp A) vs progression with poor control (Gp B).

12. Extent of regional HED retention abnormalities detected at line and after 3 years in diabetic subjects with good glycemic rol (group A) versus poor glycemic control (group B). Data are the n ± 1 SEM. *P < .05 v baseline study. †P < .01 v group A.

Allman K JACC 1993
Stephens MJ Metab 1999
### Univariate analysis

<table>
<thead>
<tr>
<th>Other significant parameters</th>
<th>Hazard ratio</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDV index (per ml/m²)</td>
<td>1.021 (1.011–1.032)</td>
<td>&lt;0.0001</td>
</tr>
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</tr>
<tr>
<td>BNP (per ng/L)</td>
<td>1.001 (1.000–1.001)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Creatinine (per mg/dl)</td>
<td>1.53 (1.21–1.95)</td>
<td>0.0005</td>
</tr>
<tr>
<td>LA volume (per ml)</td>
<td>1.011 (1.003–1.019)</td>
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</tr>
<tr>
<td>No angiotensin inhibition therapy</td>
<td>2.88 (1.25–6.67)</td>
<td>0.014</td>
</tr>
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<td>LV ejection fraction (per 1%)</td>
<td>0.951 (0.913–0.990)</td>
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</tr>
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Fallavollita JA et al JACC 2014
### Table 3: Significant Predictors of Time to SCA

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<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>p Value</td>
</tr>
<tr>
<td>PET parameters (per 1% of LV)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Denervated myocardium</td>
<td>1.057 (1.023–1.092)</td>
<td>0.001</td>
</tr>
<tr>
<td>Viable, denervated myocardium</td>
<td>1.067 (1.008–1.130)</td>
<td>0.025</td>
</tr>
<tr>
<td>Infarcted myocardium</td>
<td>1.029 (0.990–1.069)</td>
<td>0.15</td>
</tr>
<tr>
<td>Hibernating myocardium</td>
<td>0.950 (0.822–1.099)</td>
<td>0.49</td>
</tr>
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<tr>
<td>LV mass index (per g/m²)</td>
<td>1.007 (1.000–1.014)</td>
<td>0.038</td>
</tr>
</tbody>
</table>

Fallavollita JA et al JACC 2014
Parapet Study examples

Pt A: SCA,  Pt B: no SCA
Parapet Study: Predictive model for SCA

Optimized cut-offs: Cr: 1.5ml/min (26% pts), No ACE (10% pts), Denervated Ht: >38% (19% pts), LVEDVI: 99m/m2 (34% pts)

Risk Factors
- ≥2: 20% pts
- 1: 36% pts
- 0: 44% pts

Follow-Up (Years)

0 1 2 3 4

p<0.0001

11.7%/yr

3.9%/yr

0.9%/yr
Planar Measurement refinements

Delayed imaging at 2 hours is clinically o.k. for H/M ratio but not for W/O Rates (without corrections).

**Inter observer assessment:** H/M: (95% CI)
experienced: CL -0.1 to 0.05; inexp -0.2 to 0.1

**Cardiac ROI choice:** Fixed oval vs polygonal Heart  SDD:=00.04 ± 0.6

**Washout rates:** best if not decay or bkgd corrected

Dimitriu-Leen AC, EJNMMI, 2016
Veltman C, EJNMMI, 2012
ICM microvascular dysfunction & arrhythmias

52 pts LVEF<35% being assessed for ICD. MRI: LGE LV, volumes, C-11 HED, O-15 H2O MBF (rest & hyperaemic). EPS ± VT/VF

Figure 3  Receiver operating characteristic (ROC) curve analyses

Rijnierse MT, et al. Heart 2016;