Imaging Congestive Heart Failure: Role of SPECT and PET
Outline

• Myocardial Viability and Revascularization
  - PET/MRI
• Resynchronization Therapy
LV-Function – Risk Stratification

Hachamovitch et al., Circulation 2003
Medical Therapy (M) vs. Revascularisation (R) in patients with reduced ventricular function

Iskander, JACC 1999

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Myocardial Viability and Survival in Ischemic Left Ventricular Dysfunction

Stich Trial Substudy
n=601 (von 1212)
Follow-up: 5.1 yrs: 236 x death

Viability: 17-Segm. Model

**SPECT** n=471
viable: ≥11/17 Segm.;
nonviable: ≥7 Segm.

**DS-ECHO** n=280 (n=150 also SPECT)
Myocardial Viability – SPECT Perfusion

LAD proximal occluded
Injection of 99mTc-Tetrofosmin
5 min before revascularisation

3 days after revascularisation
Gated SPECT Acquisition 2h after revascularisation
Gated SPECT 3 days after revascularisation
Myocardial Stunning

Camici, Circulation 2008
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# Myocardial Tissue Characterization

## Metabolism / Viability

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>LVEF /</th>
<th>Contractility</th>
<th>Perfusion</th>
<th>FDG-PET</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Ischemia</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>≈↑</td>
<td>spontanuous reversibel</td>
</tr>
<tr>
<td>Stunned Myocardium</td>
<td>↓</td>
<td>≈↓</td>
<td>≈</td>
<td></td>
<td>spontanuous reversibel</td>
</tr>
<tr>
<td>Hibernating Myocardium</td>
<td>↓</td>
<td>↓</td>
<td>≈↑</td>
<td></td>
<td>reversibel after revasc.</td>
</tr>
<tr>
<td>Scar</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>irreversibel</td>
</tr>
</tbody>
</table>

Modifiziert nach Camici, Circulation 2008

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Myocardial PET/MRI

**PET:**
- perfusion, viability,
- hibernation,
- LV-function

**DE-MRI:**
- perfusion, scar tissue (extent, transmurality),
- LV-, RV-function, valves,…

**Integrated PET/MRI**
Scar/Viability Diagnostics (LGE)-MRI

Normal myocardium | Acute infarction | Scar

Intact cell membrane | Ruptured cell membrane | Collagen matrix

Marholdt H et al. EHJ 2002, 2006
Methods: PET/MRI Acquisition

Patients:
Twenty two patients (65 ± 12 years) with ICMP (EF: 45% ± 15).

**PET (rest):**
$^{13}\text{N-NH}_3$: 20 min dynamic scan (812 ± 83MBq) followed by
$^{18}\text{F-FDG}$: up to 40 min dynamic scan (342 ± 35 MBq).

**MRI (3T) (rest):**
Axial T2 Haste Cine Sequences in 2, 3, and 4 chamber view, short axis view, LVOT, LGE-sequences: Phase-sensitive inversion recovery (PSIR) sequences during breath-hold 10 min after injection of 0.1mL/kg of gadolinium (Gadovist®).
Example PET/MRI:

Visual agreement

Scar extent-LGE
Perfusion-PET
Viability-PET
Example PET/MRI

Visual agreement with FDG-PET
Disagreement with Perfusion PET and Hibernation

Absence of scar-LGE

Perfusion-PET

Viability-PET
Results PET vs. MRI

Correlations PET parameters with MRI-scar extent

Rasul et al., SNM 2016
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Myocardial Tissue Characterization
Perfusion / Metabolism / Viability / Scar

Kaandorp et al., Heart 2005
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Recovery Prediction after Revascularisation

Anavekar NS et al., JACC 2016
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## Recovery Prediction after Revascularisation

<table>
<thead>
<tr>
<th>Method</th>
<th>Patients, n</th>
<th>Sensitivity, Mean (95% CI)</th>
<th>Specificity, Mean (95% CI)</th>
<th>PPV, Mean (95% CI)</th>
<th>NPV, Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional nuclear</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{99m}$Tc-sestamibi</td>
<td>19</td>
<td>71 (51–91)</td>
<td>40 (18–62)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>SPECT FDG</td>
<td>94</td>
<td>86 (79–93)</td>
<td>93 (88–98)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>$^{201}$TI rest, reinjection</td>
<td>211</td>
<td>84 (79–89)</td>
<td>70 (64–76)</td>
<td>97 (92–100)</td>
<td>93 (86–100)</td>
</tr>
<tr>
<td>$^{201}$TI rest redistribution + FDG</td>
<td>47</td>
<td>86 (76–96)</td>
<td>92 (84–100)</td>
<td>90 (81–99)</td>
<td>89 (80–98)</td>
</tr>
<tr>
<td>Total</td>
<td>371</td>
<td>84 (80–88)</td>
<td>77 (73–81)</td>
<td>94 (89–98)</td>
<td>91 (85–97)</td>
</tr>
<tr>
<td>Echocardiography</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSE</td>
<td>408</td>
<td>76 (71–80)</td>
<td>81 (77–85)</td>
<td>84 (77–91)</td>
<td>91 (85–96)</td>
</tr>
<tr>
<td>DSE + strain rate</td>
<td>55</td>
<td>67 (55–79)</td>
<td>89 (81–97)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>End-diastolic wall thickness</td>
<td>43</td>
<td>63 (49–77)</td>
<td>68 (54–82)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Total</td>
<td>506</td>
<td>74 (70–77)</td>
<td>81 (77–84)</td>
<td>84 (77–91)</td>
<td>91 (85–96)</td>
</tr>
<tr>
<td>PET</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDG</td>
<td>205</td>
<td>81 (75–86)</td>
<td>65 (59–72)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Total</td>
<td>205</td>
<td>81 (75–86)</td>
<td>65 (59–72)</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

PPV indicates positive predictive value; NPV, negative predictive accuracy.
430 patients with severe left ventricular (LV) dysfunction. PET-arm n=218, standard care arm, n=212. Primary outcome: cardiac death, MI, recurrent hospital stay for cardiac cause, within 1 year.
SPECT/PET: Identification and Quantification of hibernating Myokardium

Mismatch (Hibernation): 27%
Scar: 16%

Übleis et al. IJCI 2013
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PARR-2 Substudy

182 patients, severe left ventricular (LV) dysfunction, PET-arm PARR-2

A

% of Patients with Primary Outcome

- Mismatch <7%
  - N=59
  - 31%

- Mismatch ≥7%
  - N=83
  - 29%

B

% of Patients Suffering Cardiac Death

- Mismatch <7%
  - N=59
  - 12%
  - Medical Therapy
  - N=83
  - 11%
  - Protocol Revascularization

- Mismatch ≥7%
  - N=24
  - 13%
  - Medical Therapy
  - N=16
  - 0%

D’Egidio JACC Cardiovasc Imaging 2009

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Heart Failure - Cardiac Resynchronization Therapy

Patient, 74 yrs, advanced stable CAD; stents in LCX and RCA; NYHA III
Left Bundle Branch Block, QRS = 159 ms

LVEF: 24%
LVEF: 39%
Cardiac Resynchronization Therapy

**Recommendation in patients with heart failure in New York Heart Association function class III/IV**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Patient population</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRT-P/CRT-D is recommended to reduce morbidity and mortality (^d)</td>
<td>NYHA function class III/IV LVEF (\leq 35%), QRS (\geq 120\ ms), SR Optimal medical therapy Class IV patients should be ambulatory (^a)</td>
<td>I</td>
<td>A</td>
<td>5–19</td>
</tr>
</tbody>
</table>

**Recommendation in patients with heart failure in New York Heart Association function class II**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Patient population</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRT preferentially by CRT-D is recommended to reduce morbidity or to prevent disease progression (^d)</td>
<td>NYHA function class II LVEF (\leq 35%), QRS (\geq 150\ ms), SR Optimal medical therapy</td>
<td>I</td>
<td>A</td>
<td>9, 20–22</td>
</tr>
</tbody>
</table>
Parameters LVEF $\leq$ 35\% and QRS duration not sufficient for „Response Prediction“!
Resynchronisation Therapy - Response Evaluation

$^{18}$F-FDG PET/IdCT: „Non-Responder“

### Resynchronisation Therapy - Response Evaluation

**18F-FDG PET/IdCT**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All patients ($n = 14$)</th>
<th>Responders ($n = 7$)</th>
<th>Nonresponders ($n = 7$)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>67.9 ± 8.4</td>
<td>68.0 ± 8.8</td>
<td>67.7 ± 8.7</td>
<td>NS</td>
</tr>
<tr>
<td>Men</td>
<td>12 (86)</td>
<td>6 (86)</td>
<td>6 (86)</td>
<td>NS</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitor</td>
<td>13 (93)</td>
<td>7 (100)</td>
<td>6 (86)</td>
<td>NS</td>
</tr>
<tr>
<td>β-blocker</td>
<td>13 (93)</td>
<td>6 (86)</td>
<td>7 (100)</td>
<td>NS</td>
</tr>
<tr>
<td>Diuretics</td>
<td>10 (71)</td>
<td>4 (57)</td>
<td>6 (86)</td>
<td>NS</td>
</tr>
<tr>
<td>Aldosterone receptor antagonist</td>
<td>8 (57)</td>
<td>4 (50)</td>
<td>4 (50)</td>
<td>NS</td>
</tr>
<tr>
<td>Clinical evaluation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA class before CRT</td>
<td>3.0 ± 0.0</td>
<td>3.0 ± 0.0</td>
<td>3.0 ± 0.0</td>
<td>NS</td>
</tr>
<tr>
<td>NYHA class after CRT</td>
<td>2.6 ± 0.6</td>
<td>2.0 ± 0.0</td>
<td>3.1 ± 0.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Δ NYHA class**</td>
<td>-0.4 ± 0.6</td>
<td>-1.0 ± 0.3</td>
<td>+0.1 ± 0.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Brain natriuretic peptide before CRT (pg/mL)</td>
<td>625 ± 514</td>
<td>691 ± 582</td>
<td>560 ± 473</td>
<td>NS</td>
</tr>
<tr>
<td>Brain natriuretic peptide after CRT (pg/mL)</td>
<td>432 ± 533</td>
<td>236 ± 257</td>
<td>628 ± 679</td>
<td>NS</td>
</tr>
<tr>
<td>Δ Brain natriuretic peptide (pg/mL)</td>
<td>193 ± 467</td>
<td>454 ± 416</td>
<td>168 ± 373</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Echocardiographic parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF before CRT (%)</td>
<td>25 ± 8</td>
<td>24 ± 9</td>
<td>27 ± 8</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF after CRT (%)</td>
<td>32 ± 13</td>
<td>39 ± 14</td>
<td>26 ± 8</td>
<td>NS</td>
</tr>
<tr>
<td>Δ LVEF (%)</td>
<td>+7 ± 12</td>
<td>+15 ± 11</td>
<td>-1 ± 7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LVESV before CRT (mL)</td>
<td>219 ± 57</td>
<td>231 ± 64</td>
<td>206 ± 52</td>
<td>NS</td>
</tr>
<tr>
<td>LVESV after therapy (mL)</td>
<td>177 ± 65</td>
<td>150 ± 51</td>
<td>205 ± 70</td>
<td>0.073</td>
</tr>
<tr>
<td>Δ LVESV (mL)**</td>
<td>-41 ± 51</td>
<td>-82 ± 37</td>
<td>+1 ± 24</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Residual dyssynchrony</td>
<td>7 (50)</td>
<td>2 (29)</td>
<td>5 (71)</td>
<td></td>
</tr>
<tr>
<td>PET/CT including phase analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scar burden (%)</td>
<td>20 ± 19</td>
<td>10 ± 8</td>
<td>30 ± 21</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Lead over scar</td>
<td>4 (29)</td>
<td>0 (0)</td>
<td>4 (57)</td>
<td></td>
</tr>
<tr>
<td>Bandwidth (%)</td>
<td>90 ± 38</td>
<td>91 ± 28</td>
<td>89 ± 48</td>
<td>NS</td>
</tr>
<tr>
<td>Phase SD (%)</td>
<td>28 ± 14</td>
<td>42 ± 8</td>
<td>34 ± 14</td>
<td>NS</td>
</tr>
<tr>
<td>Phase entropy (%)</td>
<td>80 ± 5</td>
<td>77 ± 4</td>
<td>83 ± 3</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
Patient Selection CRT

- 44 patients prior to CRT, mean LVEF 25%, mean QRS 178ms

Baseline Dyssynchrony

Yes
n=37

Scar Burden <40%

Yes
n=28

Lead Concordance

Yes
n=22

Improved = 16
Unchanged = 5
Worse = 1

Improved = 1
Unchanged = 1
Worse = 4

No
n=9

Improvement/unchanged

Deterioration

P = 0.003

Events Based on Prediction Model

P = .06

Predicted Responders

Predicted Nonresponders
Multiparametric Quantification

STEP 1
Original QPS and QGS

STEP 2
2 colour mode of original data
- Viable
- Scar
- Synchronous
- Dyssynchronous

STEP 3
Fusion & planimetric quantification

Lehner et al., EJNMMI 2013
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CRT Responder

3D Image fusion: Venous CT Angiography and ECG-gated FDG PET
CRT Non Responder

3D Image fusion: Venous CT Angiography and ECG-gated FDG PET
Patient Selection for ICD Therapy – Imaging Myocardial Innervation with $^{123}$I-MIBG

- Similar chemical structure as Noradrenalin
- Surrogate for sympathetic innervation of the heart

**Methods:**

- Heart-to-mediastinum-ratio (HMR)
- Early- and late Imaging
- SPECT(/CT)

4 h p.i.

HMR: 1,76
$^{123}$I-MIBG Imaging and Outcome

- 961 patients, NYHA II/III, LVEF <35%
- median follow-up 17 months, 237 patients with severe events

Graphs showing cumulative rates of composite primary endpoint and cardiac death over 24 months of follow-up.
PET-Approach Herzinsuffizienz

- 204 patients, LVEF <35%, stable CAD, ICD. 4,1 years follow-up