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Centre de

RM Cardiaque



### Sfide in cardiologia clinica

### 10/11 marzo 2017

C : UI

Mantova MaMu, Centro Congressi Mantova Largo di Porta Pradella, 1



# Valore Incrementale della RMN cardiaca nei pazienti con cardiopatia ischemica



Comparative Effective Research (Socio-Economical Impact)

Utility in Risk Stratification & Prognosis Prediction

Diagnostic & Therapeutic Impact

**Diagnostic Performance** 

**IV. Optimized Test Effectiveness Strategy** 

- Compare Effectiveness of 2 or more imaging driven strategies with a RCT
- ✓ Cost-Effectiveness

**III.** Prognostic Utility

 Accuracy of imaging marker in detecting hard clinical end-points with ADDITIVE/INDEPENDENT value respect clinical/other risk algorytms

- II. Diagnostic & Therapeutic Impact
- Relationship between imaging markers of ischemia
  & MD decision making / therapeutic interventions
- I. Diagnostic Performance
- ✓ Technical Aspects
- Accuracy in detecting obstructive CAD





### -PostInfarction Remodeling – - The value of CMR -







- 1. Edema => area-at-risk
- 2. Hemorrhage
- 3. LGE=>Infarct size
- 4. MVO
- 5. Myocardial salvage

Translational & Clinical Research







-PostInfarction Remodeling – - The value of CMR -





T2=58-60 ms

### T2/T1/T2<sup>(\*)</sup>mapping

- 1. Area at risk
- 2. Haemorrhagia



### Post-Gd Img 1. MO [early&late] 2. Infarct burden [late] (IS / transmurality)



**Cine Img** 1. Regional structural & **Functional Remodeling** 

2. Ventricular Geometrical & Functional Remodeling

Translational & Clinical Research



**Chronic Phase** 



1. Infarct burden (IS / transmurality) 2. Viability

### **Cine Img**

1. Regional structural & **Functional Remodeling** 

2. Ventricular Geometrical & Functional Remodeling







### **ACS & Unobstructed Coronaries**

### **Ischemic Causes**

- 'Concealed' Plaque Destabilization
- Coronary Vasospasm
- Distal Embolization

### Coronary Vasospasm



### Plaque destabilization/embolization



### **Diagnostic and Complications**

### **Non-Ischemic Causes**

- Peri(myo)carditis
- Tako-Tsubo (stress) CM
- Cardiomuopathy/Heart Failure

### Acute Myocarditis





### Tako-Tsubo (Stress) CM





### Differential Diagnosis - Clinical Case #1-

### CH

Man 71 y.o. HTA, Hypercholesterolemia during physical activity→ typical CP (8/10→2/10 after nitrate) Labo CK pic 566 U/L (UNL: 190 U/L); HsTnT pic 569 ng/L (UNL: 14 ng/l)





**Diagnostic and Complications** 



### Differential Diagnosis - Clinical Case #1-

Acute ischemic insult of the LV lateral wall likely as a result of vasospasm

About 4-8% of about cardiomyocytes of the lateral wall underwent necrosis (→ CK peak 566 UI)









- Comprehensive CMR @ acute MI -

- PostInfarction Evaluation-











Thrombosis

### **Pseudoaneurysm**

**Septal Defect** 

**RV** infarction



**Diagnostic and Complications** 







□13 of 20 deaths occurred in patients with MO(+) & IS≥19% of LV mass
 □ 1 cardiac death in the group MO(-) & IS<19% of LV mass</li>

**Risk Stratification** 

### 



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EF<43% 255

153

40

7

RM Cardiaque

Baseline Characteristics	Model-1		Model-2		
	HR (95% CI)	P-Value	HR (95% CI)	P-Value	
Model c					
Age≥67years	1.977 (1.272-3.074)	0.002	2.142 (1.381-3.324)	0.001	
Active Smoking	0.628 (0.400-0.985)	0.043	0.659 (0.419-1.037)	0.072	
Killip Class 2,3 vs 1	1.575 (0.882-2.812)	0.125	1.636 (0.922-2.902)	0.092	
CK-MB ≥42*	1.683 (1.084-2.612)	0.020	1.701 (1.099-2.635)	0.017	
MAP<95 mmHg	2.011 (1.281-3.156)	0.002	1.997 (1.271-3.138)	0.003	
Heart rate≥76 bpm	1.141 (0.742-1.756)	0.548	1.191 (0.774-1.833)	0.426	
TIMI flow post PCI	0.714 (0.458-1.114)	0.138	0.713 (0.461-1.103)	0.128	
Rentrop grade 01,s vs 2,3	2.623 (0.639-10.773)	0.181	2.690 (0.658-11.001)	0.168	
LV-EDVi≥81 ml/m2	1.274 (0.824-1.970)	0.275			
LV-ESVi≥39 ml/m2			1.875 (1.137-3.093)	0.014	
LV-EF<43%	1.765 (1.074-2.903)	0.025			
Infarct size≥21% of LV	0.957 (0.546-1.677)	0.877	1.086 (0.644-1.830)	0.758	
MVO extent ≥2.6% of LV	3.185 (1.892-5.362)	<0.001	3.199 (1.915-5.343)	<0.001	
Model d					
Active Smoking	0.667 (0.432-1.029)	0.067	0.675 (0.439-1.040)	0.074	
CK-MB≥42	1.804 (1.175-2.769)	0.007	1.836 (1.197-2.815)	0.005	
TIMI flow post PCI	0.799 (0.509-1.255)	0.329	0.790 (0.505-1.234)	0.300	
Rentrop Grade 0,1 vs 2,3	2.592 (0.633-10.610)	0.185	2.700 (0.661-11.036)	0.167	
LV-EDVi≥81 ml/m²	1.239 (0.809-1.898)	0.324			
LV-ESVi≥39 ml/m2			1.870 (1.144-3.057)	0.013	
LV-EF<43%	1.859 (1.155-2.991)	0.001	- •		
Infarct size≥21% of LV	0.981 (0.577-1.668)	0.943	1.122 (0.684-1.842)	0.648	
MVO extent ≥2.6% of LV	2.896 (1.761-4.761)	< 0.001	2.898 (1.779-4.720)	<0.001	
TIMI Risk Score≥4	2.653 (1.725-4.081)	< 0.001	2.851 (1.865-4.358)	<0.001	



Table 4. Multivariate Cox-Regression Analysis for the primary end-point and chi-squared improvement obtained by the stepwise inclusion of each covariate.

Baseline Characteristics				χ2	
	HR (95% CI)	P-Value	Δ from Previous Step	P-value	Overall
Model a-1					
MVO extent ≥2.6% of LV	3.411 (2.184-5.328)	<0.001	52.883	<0.001	52.883
Age≥67years	2.022 (1.305-3.134)	0.002	19.914	<0.001	72.797
MAP <95 mmHg	1.986 (1.283-3.074)	0.002	10.837	0.001	83.634
LV-EF<43%	1.884 (1.212-2.928)	0.005	8.014	0.005	91.648
CK-MB≥42	1.668(1.083-2.568)	0.020	5.138	0.023	96.786
Active Smoking	0.637 (0.407-0.995)	0.048	3.994	0.046	100.780
Model a-2					
MVO extent≥2.6% of LV	3.505 (2.269-5.415)	<0.001	52.883	<0.001	52.883
Age≥67years	2.612 (1.746-3.909)	<0.001	19.914	<0.001	72.797
MAP <95 mmHg	1.971 (1.275-3.046)	0.002	10.837	0.001	83.634
LV-ESVi≥39ml/m <sup>2</sup>	1.924 (1.189-3.112)	0.008	7.729	0.005	91.363
CK-MB≥42	1.642(1.066-2.528)	0.024	5.239	0.022	96.601
Model b-1					
MVO extent≥2.6% of LV	3.098 (2.007-4.782)	<0.001	54,730	<0.001	54.730
TIMI Risk Score≥4	3.033 (2.015-4.566)	<0.001	32.480	<0.001	87.210
LV-EF<43%	1.929 (1.251-2.975)	0.003	8.948	0.002	96.158
CK-MB≥42	1.743(1.141-2.662)	0.010	6.900	0.009	103.058
Model b-2					
MVO extent ≥2.6% of LV	3.219 (2.101-4.933)	<0.001	57.730	<0.001	54.730
TIMI Risk Score≥4	3.280 (2.186-4.921)	<0.001	32.480	< 0.001	87.210
LV-ESVi≥39ml/m <sup>2</sup>	1.902 (1.186-3.051)	0.008	7.235	0.007	94.445
CK-MB≥42	1.771 (1.159-2.705)	0.008	7.285	0.007	101.730
MAD	the second state of the se				

MAP: mean arterial pressure; other abbreviations as in previous tables.



### Table 5. Multivariate analyses for the secondary end-points end-point based on MVO extent<2.6% or ≥2.6 % of LV

Adverse Events	MVO exten≥2.6% of LV	MVO extent<2.6% of LV	HR (95 CI)	P-value
	(n=215)	(n=595)		
All-Death	15 (7.0%)	24 (4.0%)	2.055 (1.076-3.925)*	0.029
HF Hospitalization	44 (20.5%)	16 (2.7%)	5.999 (3.251-11.069)*	<0.001

\*After correction Age≥67 years; Mean Arterial blood pressure <95 mmHg, LV-EF<43%.; HF: heart failure.











Courtesy of Juerg Schwitter







### Comprehensive Assessment of Ischemic Heart Disease















### Self-navigation enables

1. 100% scan efficiency: the duration of the acquisition is known a priori.

2. No temporal delays and hysteretic effects.

3. No navigator placement and feasibility of whole-heart acquisition: minimal planning effort.

4. Isotropic spatial resolution is enabled.

- Fat Saturated, T2-prepared 3D bSSFP sequence
- FOV (220 mm)<sup>3</sup> Base resolution (192 px)<sup>3</sup>
- Voxel size (0.9 mm)<sup>3</sup> isotropic
- TA = 377 610 Heart Beats = ~ 6 -10 min during free breathing 100% scan efficiency

Diagnosis of CAD

Courtesy of D. Piccini & Pr Stuber



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Diagnosis of CAD

Courtesy of D. Piccini & Pr Stuber



### Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial

John P Greenwood, Neil Maredia, John F Younger, Julia M Brown, Jane Nixon, Colin C Everett, Petra Bijsterveld, John P Ridgway, Aleksandra Radjenovic, Catherine J Dickinson, Stephen G Ball, Sven Plein

### **Study Characteristics**

- 752 consecutive patients with  $\geq$ 1 RF and stable angina (obstructive CAD prevalence 39%)
- Head-to head comparison of CMR and <sup>99m</sup>Tc-gated SPECT (3 weeks apart; identical stress protocol)
- All patients underwent ICA irrespective of CMR / SPECT imaging results (avoidance of referral bias)

### **End-Points**

- Diagnostic accuracy of multiparametric CMR for detection of CAD (primary EP)
- Comparison of multiparametric CMR with <sup>99m</sup>Tc-gated SPECT for detection of CAD
- Comparison of only the equivalent components of CMR with <sup>99m</sup>Tc-gated SPECT













MR-IMPACT: comparison of perfusion-cardiac magnetic resonance with single-photon emission computed tomography for the detection of coronary artery disease in a multicentre, multivendor, randomized trial

Juerg Schwitter<sup>1\*</sup>, Christian M. Wacker<sup>2</sup>, Albert C. van Rossum<sup>3</sup>, Massimo Lombardi<sup>4</sup>, Nidal Al-Saadi<sup>5</sup>, Hakan Ahlstrom<sup>6</sup>, Thorsten Dill<sup>7</sup>, Henrik B.W. Larsson<sup>8</sup>, Scott D. Flamm<sup>9</sup>, Moritz Marquardt<sup>10</sup>, and Lars Johansson<sup>6</sup>

### **Study Characteristics**

- Double-blinded, randomised trial – multivendor (GE & Siemens & Philips)
- 234 pts in 18 centers referred to ICA for clinical reasons (CAD prev 77%)
- MPI-CMR vs MPI-SPECT
- QCA stenosis ≥50% (in vessels> 2mm)



### MR-IMPACT II: Magnetic Resonance Imaging for Myocardial Perfusion Assessment in Coronary artery disease Trial: perfusion-cardiac magnetic

Juerg Schwitter<sup>1\*</sup>, Christian M. Wacker<sup>2</sup>, Norbert Wilke<sup>3</sup>, Nidal Al-Saadi<sup>4</sup>, Ekkehart Sauer<sup>5</sup>, Kalman Huettle<sup>6</sup>, Stefan O. Schönberg<sup>7</sup>, Andreas Luchner<sup>8</sup>, Oliver Strohm<sup>9</sup>, Hakan Ahlstrom<sup>10</sup>, Thorsten Dill<sup>11</sup>, Nadja Hoebel<sup>12</sup>, and Tamas Simor<sup>13</sup>, for the MR-IMPACT Investigators

### **Study Characteristics**

- Multivendor trial
  533 pts in 33 centers (US & EU) (CAD prev 49%)
- ICA, MPI-CMR and SPECT
- QCA stenosis ≥50% (in vessels> 2mm)
   \*0.075 mmol/kg Gd-based CA for perfusion

Modality	Se	Sp	
CMR SPECT	75* 61*	61 § 72 §	
*, § P<0.05			

- 1. Lower CA dose (0.1-0.15 mmol/Kg)
- 2. 33 centers (small centers)
- 3. Lack of quality controls across centers





Fig. 1



Masci et al in press JACC-CVI









Table 4. Multivariate Cox regression analysis for the primary end-point

Baseline Variables	HR (95 CI)	P-Value
Multivariate-analysis-1		
Model a*		
Age (years)	1.038 (1.018-1.058)	<0.001
Presence of LGE	1.892 (1.118-3.014)	0.007
Presence of ischemia	6.855 (4.139-11.354)	<0.001
Model b**		
Age (years)	1.035 (1.015-1.055)	0.001
Presence of LGE	1.894 (1.189-3.017)	0.007
Presence of ischemia	6.841 (4.130-11.331)	<0.001
Model c***		
Age (years)	1.035 (1.015-1.056)	0.001
Presence of LGE	1.894 (1.189-3.017)	0.007
Presence of ischemia	6.855 (4.139-11.354)	<0.001
Multivariate-analysis-2		
Model d°		
Age ≥67 years	2.321 (1.466-3.676)	<0.001
LV-EF ≤40%	1.752 (1.040-2.950)	<mark>0.035</mark>
lschemic burden ≥1.5 segments	8.347 (5.267-13.229)	<0.001
LGE score ≥0.03	1.655 (1.006-2.723)	0.047
Model e <sup>oo</sup>		
Age ≥67 years	2.418 (1.535-3.808)	<0.001
LV-ESVi ≥46 ml/m²	2.195 (1.380-3.491)	0.001
Ischemic burden ≥1.5 segments	8.722 (5.515-13.794)	<0.001
Model f <sup>ooo</sup>		
Age ≥67 years	2.423 (1.542-3.808)	<0.001
LV-EDVi ≥71 ml/m²	1.631 (1.043-2.549)	0.032
Ischemic burden ≥1.5 segments	8.376 (5.286-13.273)	<0.001
LGE score ≥0.03	1.764 (1.098-2.836)	0.019



Table 6. Stepwise inclusion procedure for the multivariate-Analysis-2 (model d)

				$\chi^2$		
Baseline Variables	HR (95% CI)	P-Value	Step	Global Model	P-Value	
Step 1						
Ischemic burden ≥1.5	9.003 (5.692-14.240)	<0.001	95.425	95.425	<0.001	
Step 2						
Ischemic burden ≥1.5	8.644 (5.468-13.665)	<0.001				
Age ≥67 years	2.701 (1.722-4.235)	<0.001	19.511	114.936	<0.001	
Step 3						
Ischemic burden ≥1.5	8.733 (5.521-13.814)	<0.001				
Age ≥67 years	2.557 (1.488-3.735)	<0.001				
LV-EF ≤40%	2.155 (1.320-3.515)	0.002	8.485	123.421	0.004	
Step 4						
Ischemic burden ≥1.5	8.347 (5.267-13.229)	<0.001				
Age ≥67 years	2.321 (1.466-3.676)	<0.001				
LV-EF ≤40%	1.752 (1.040-2.950)	0.035				
LGE score ≥0.03	1.655 (1.006-2.723)	0.047	4.042	127.463	0.044	

Covariates in the model: age ≥67 years; previous coronary revascularization; prior myocardial infarction; history of hypertension; LV-EDVi ≥71ml/m<sup>2</sup>; LV-EF ≤40%; Ischemic burden ≥1.5 segments; LGE score ≥0.03.






C U/



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### **Chronic Ischemic Heart Disease & CMR**

Case #1

Patient 52 y.o, male, HTA & hypercholesteremia Typical chest pain during effort (CCS-II)



Stress-Perfusion



LGE



Whole Heart-CA



**Invasive** CA









**Diagnosis of CAD** 



### **CMR in Acute Ischemic Heart Disease**



### **Chronic Ischemic Heart Disease & CMR**

Comparison of Cardiovascular Magnetic Resonance and Single-Photon Emission Computed Tomography in Women With Suspected Coronary Artery Disease From the Clinical Evaluation of Magnetic Resonance Imaging in Coronary Heart Disease (CE-MARC) Trial

John P. Greenwood, PhD; Manish Motwani, MB, ChB; Neil Maredia, MD; Julia M. Brown, MSc; Colin C. Everett, MSc; Jane Nixon, PhD; Petra Bijsterveld, MA; Catherine J. Dickinson, PhD; Stephen G. Ball, PhD; Sven Plein, PhD



Diagnosis of CAD





### **Myocardial Perfusion Imaging By Cardiovascular MR**



100 pts with intermediate pretest probability for CAD in part for post-test referral bias

	Sensitivity	Specificity	Accuracy			
Interpretation Algorithm	89%	87%	88%			
Perfusion (rest/stress)	84%	54%	68%			
Cine (rest)	49%	73%	63%			
DE-CMR	49%	98%	78%			
Coronary Stenosis ≥ 70% or LMS ≥ 50%						

(obstructive CAD: 40%)

SPECT -> Se/Sp=65-82%/59-67%

Klem et al. J Am Coll Cardiol 2006









### **Improve Acquisition Protocol and Analysis**

- 1) Adequate patient preparation
- 2) Selection of adenosine dose (up to 210 mg/kg/min)
- 3) Acquisition protocol (mistrigerring / respiration artifacts / Valsalva maneuver)



### Time



### Dark-rim

Short-lasting (second-pass)

Starts CM

### **Perfusion-Defect**

Persisting

Starts when CM arrives myocardium

» Hyperemia

arrives in LV cavity

SI < baseline SI

SI> baseline SI

» Hyperemia

may superimpose to true perfusion defect



### **Acute Myocardial Infarction & CMR**

Differential Diagnosis - Clinical Case #1-

### 43 y.o man smoker, typical long-lasting CP, cTnI 3.41 ng/ml, no WM abnormalities at echo



### **Acute Myocardial Infarction & CMR**

### Differential Diagnosis - Ischemic Causes -



#### Plaque disruption and distal embolization

Previous irreversible Ischemic damage

### **Acute Myocardial Infarction & CMR**

63-year old woman with typical chest pain, minimal increment of cTnI, negative T wave in DI & from V2-V5, normal coronary angiograms. Five days after the clinical presentation, the patient was referred to CMR.

### **Coronary Vasospasm ?**



**Cine Imaging** 

T2-w imaging

Late Gd Enhancement





Stress Myocardial Perfusion Imaging by CMR Provides Strong Prognostic Value to Cardiac Events Regardless of Patient's Sex

Otavio R. Coelho-Filho, MD,\* Luciana F. Seabra, MD,\* François-Pierre Mongeon, MD,\* Shuaib M. Abdullah, MD,\* Sanjeev A. Francis, MD,\* Ron Blankstein, MD,\*† Marcelo F. Di Carli, MD,† Michael Jerosch-Herold, PHD,† Raymond Y. Kwong, MD, MPH\* *Boston, Massachusetts* 



#### **Study Characteristics**

- 405 pts (168 women)
- Cine-CMR, MPI-CMR, LGE
- Median FU 30 months (21 cardiac-death, 15 MI)
- Major Adverse Cardiac Events

HR 6.18 (2.07-18.51), P=0.001 For MPI-CMR (+) at multivariate Cox-Regression Analysis

*JACC CVI 2011* 





### Intermediate-Term Prognostic Value of Reversible Perfusion Deficit Diagnosed by Adenosine CMR

A Prospective Follow-Up Study in a Consecutive Patient Population

Dominik Buckert, MD, Patricia Dewes, Thomas Walcher, MD, Wolfgang Rottbauer, MD, Peter Bernhardt, MD

#### **Study Characteristics**

- 1229 pts
- Cine-CMR, MPI-CMR, LGE
- Median FU 4.2 years
- Major Adverse Cardiac Events

Ulm, Germany





 Table 4. Multivariate Analysis of Predictors of the Primary

 Endpoint

Variable	HR	95% Cl	p Value
Age	1.02	1.00-1.05	0.0385
Diabetes mellitus	1.34	1.06-1.67	0.0127
Wall motion score	1.07	0.98-1.09	< 0.0001
Reversible perfusion deficit	3.21	2.06-5.00	< 0.0001

JACC CVI 2013







# obrigado a todos pela vossa atenção

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#### **Practice Guideline**

#### 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease

 Table 11. Stress Testing and Advanced Imaging for Initial Diagnosis in Patients With Suspected SIHD Who Require Noninvasive

 Testing

	Exe	ercise tatus	ECG Interpre	à table	Pretest Probability able of IHD		ty			
Test	Able	Unable	Yes	No	Low	Intermediate	High	COR	LOE	References
Patients able to exercise*										
Exercise ECG	Х		х			Х		1	Α	(114, 145–147)
Exercise with nuclear MPI or Echo	Х			Х		Х	Х	1.1	В	(91, 132, 148-156)
Exercise ECG	Х		х		Х			lla	С	N/A
Exercise with nuclear MPI or Echo	Х		х			Х	Х	lla	В	(91, 132, 148-156)
Pharmacological stress CMR	Х			Х		Х	Х	lla	В	(153, 157, 158)
CCTA	Х		Any	1		Х		llb	В	(158–166)
Exercise Echo	Х		x			Х		llb	С	N/A
Pharmacological stress with nuclear MPI, Echo, or CMR	X		X			Any		III: No Benefit	C	(155, 167, 168)
Exercise stress with nuclear MPI	Х		х		Х			III: No Benefit	С	N/A
Patients unable to exercise										
Pharmacological stress with nuclear MPI or Echo		X	Any	1		X	Х	I.	В	(148–150, 152–156)
Pharmacological stress Echo		х	Апу	1	Х			lla	С	N/A
CCTA		х	Any	1	Х	Х		lla	В	(158–166)
Pharmacological stress CMR		Х	Any	1		Х	Х	lla	В	(153, 157, 158, 169-172)
Exercise ECG		Х		Х		Any		III: No Benefit	С	(91, 132, 148–156, 161)

Circulation 2012







### **Myocardial Perfusion Imaging By Cardiovascular MR**



#### (Se 84% vs 89%)



#### (Sp 58% vs 87%)



Klem et al. J Am Coll Cardiol 2006



Comparative Effective Research (Socio-Economical Impact)

Utility in Risk Stratification & Prognosis Prediction

Diagnostic & Therapeutic Impact

**Diagnostic Performance** 

**IV. Optimized Test Effectiveness Strategy** 

- Compare Effectiveness of 2 or more imaging driven strategies with a RCT
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**III.** Prognostic Utility

 Accuracy of imaging marker in detecting hard clinical end-points with ADDITIVE/INDEPENDENT value respect clinical/other risk algorytms

- II. Diagnostic & Therapeutic Impact
- Relationship between imaging markers of ischemia
   & MD decision making / therapeutic interventions
- I. Diagnostic Performance
- ✓ Technical Aspects
- Accuracy in detecting obstructive CAD





### Myocardial Perfusion Imaging By Cardiovascular MR

### **Semiquantitive Analysis**





p<0.05

### **Myocardial Perfusion Imaging By Cardiovascular MR**



Se: 90 % / Sp: 83% / Acc: 87% (CA stenosis ≥ 75%)

Al-Saadi et al. Circulation 2000





### Myocardial Perfusion Imaging By Cardiovascular MR

Normal (coronary stenosis < 50%) Intermediate (stenosis > 50% & FFR >0.75) Severe (stenosis > 50% & FFR  $\leq$ 0.75) → non-relevant

→ relevant (severe)







#### Assessment of Myocardial Perfusion in Coronary Artery Disease by Magnetic Resonance A Comparison With Positron Emission Tomography and

**Coronary Angiography** 

J. Schwitter, MD; D. Nanz, PhD; S. Kneifel, MD; K. Bertschinger, MD; M. Büchi, MD; P.R. Knüsel, MD; B. Marincek, MD; T.F. Lüscher, MD; G.K. von Schulthess, MD, PhD



Circulation 2001



### MR-MPI vs CXA + FFR

Normal (coronary stenosis < 50%) Intermediate (stenosis > 50% - FFR > 0.75) Severe (stenosis > 50% - FFR ≤ 0.75 or TO)  $\rightarrow \text{ non-relevant}$   $\rightarrow \text{ relevant (severe)}$ 



Rieber et al. Eur Heart J 2006; 27:1465-1471

### -First Pass Perfusion Cardiac MRI--Diagnostic Performance - Orfusion Imaging







### **Diagnostic Performance**



### **MR-IMPACT** trial

234 pts in 18 centers referred to CA for clinical reason

(CMR vs SPECT)

(CA stenosis ≥50% in Vessel > 2mm)

MRI (0.1 mmol/kg) vs SPECT (all)







Coronary Angiography CANNOT provide information about the functional consequences of coronary stenosis



### **Only luminography ('silhouette image')**

The degree of ischemia rather than `anatomical' stenosis herald adverse cardiac events





### -Coronary Function vs Anatomy – - Flow vs Stenosis-



Tonino et al NEJM 2009

Boden et al NEJM 2007

-Coronary Function vs Anatomy – - Flow vs Stenosis -



### -First Pass Perfusion Cardiac MRI-





- 1. Myocardial hyperemia
- 2. Pulse Sequence
- **3. Protocol**
- 4. Image Analysis
- **5. Diagnostic Performance**



Adenosine i.v. (140 µg/kg/minute for 6 min) Adenosine induces vasodilatation A2 receptors on smooth muscle Maximal vasodilation of normal vessels No dilation of stenotic vessels => steal-effect

# **Inducible Myocardial Ischemia**

### **Mechanisms**

### **Side-Effects**

- DIRECT effect inducing maximal hyperemia at 3-4 min of iv infusion 140 mg/kg/min (protocol 6 min)
- Coronary Steal
- Half-life (< 10 sec). No need of antidote</li>
- Modest increase of workload (blood pressure product)

- Facial flushing (35%), chest pain (33%), headache (21%) and dyspnea (19%)
- Transient AV block (III degree in 0.8%)
- Severe bronchospasm (0.08%)
- Myocardial infarction (0.01%)
- Death (0.009%)

Contraindication II-III degree AV block, sick-sinus syndrome & asthma

-First Pass Perfusion Cardiac MRI-- Pulse Sequence -

#### **High Spatial Resolution**

(extent of perfusion defect)

High Temporal Resolution

(SI vs Time curve/motion artficacts)

**Accuracy & Reproducibility** 

High Image Quality

Good coverage of LV

High SNR & CNR (perfusion defect visualization)



5. LV coverage (at least 3 short-axis slices for 16-segment AHA model)

### -First Pass Perfusion Cardiac MRI-- Dark-rim Artifacts -

- 1. Cardiac motion during T<sub>image</sub> (matrix size, SENSE, cardiac phase)
- 2. Gibb's ringing at sub-endocardium (CM dose/infusion rate/spatial res/SSFP)
- 3. Partial Volume effects (blood and myocardium off-resonance)
- 4. Magnetic Susceptibility (» SSFP) & T2\* effect (at high CM dose)

### LAD: stripe-like



LCx: speckled (salt & pepper)

### **RCA**: crescent-like

### -First Pass Perfusion Cardiac MRI-- Dark-rim Artifacts -





### **Dark-rim**

Short-lasting (second-pass)

Starts CM arrives in LV cavity

### Perfusion-Defect

Starts when CM arrives

Persisting



» Hyperemia

» Hyperemia

myocardium

SI < baseline SI

SI> baseline SI

may superimpose to true perfusion defect




(Signal intensity and Gd)

#### -First Pass Perfusion Cardiac MRI-- Pulse Sequences -

	T1-weighted sequence		
Method	SR-SSFP	SR-FLASH	SR-GRE-EPI
TE (ms)	1.1	1.3	1.1 (TE1)
TR (ms)	2.3	2.2	6.1
BW (Hz/pixel)	1400	780	1630
Echotrain length	1	1	4
Readout Flip Angle	50	12	25
Matrix	$128\times80$	128  imes 80	128 × 80
Parallel Imaging	R = 2	R = 2	R = 2
TD (ms) (to 1st line)	39	41	54
TI (ms) (to center)	85	85	85
T <sub>imaging</sub> (ms)	92	88	61
T <sub>slice</sub> (ms) (total)	132	130	117 🛑
Slices per RR @ 60/90/120 bpm	7/5/3	7/5/3	8/5/4

Trade-off spatial/temporal resolution, SNR&CNR and LV coverage (N° slices)

#### -First Pass Perfusion Cardiac MRI-- Diagnostic Performance -

Cardiac MRI versus 99Tc- and 201TI SPECT





#### -First Pass Perfusion Cardiac MRI-- Diagnostic Performance -



1 VD

(14/34)

2 VD

(16/36)

3 VD

(7/27)

0

Overall (37/57)

Schwitter et al. Circulation 2001

-First Pass Perfusion Cardiac MRI-- Image Analysis -

#### **Qualitative visual**

# L 33.7.\*

#### Semi-quantitative Signal-intensity versus time curves



#### **Quantitative** => absolute myocardial blood flow (ml/g/min)



BUSINESS AND ADVOCACY

#### Cardiovascular Imaging Research at the Crossroads

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#### **Comparative Effective Research (CER)**

- Net improvement in health outcomes by comparing 2 imaging modality (imaging vs noimaging ?)
- Randomized controlled studies
- Choice of hard end-points independently assigned (quantitative & rigorously collected)
- ✓ Generalizability of results
- ✓ Costs containment

-First Pass Perfusion Cardiac MRI-- Image Analysis -

**Qualitative visual** 

- DI 33.7 •
- 1. Differentiation between dark-rim artifact vs true perfusion defect
- 2. Severity of Perfusion defect
  - subendocardial
  - transmural
  - number of territory involved



-First Pass Perfusion Cardiac MRI-- Image Analysis -

-First Pass Perfusion Cardiac MRI-- Image Analysis -



#### Fast gradient-echo

 K-lines are acquired after RF pulse with prolonged read-out duration (350-450 ms according to phase-encoding steps) Long acquisition times Suboptimal spatial resolution
 EPI or Hybrid Echo-Planar Pulse Sequence Single excitation (30-70 msec) Susceptibility artifacts / relationship CA concentration - SI not linear Off-resonance - T2\* relaxation
 Steady state free precession (SSFP) Reducing ETL to 8

Multiple RF excitation Improved image quality and image contrast Parallel imaging





## **Search for Ideal Technique**

**Sp 77%** 

**Sp 74%** 

**Exercise ECG** Se 68% SPECT Se 86% Radiation dose (8-20 mSv) Photon scatter / Attenuation artifacts PET **Availibility / Tracer / Expensive**  $= \pm$  SPECT **Stress echocardiography** No radiation Limited : inadequate imaging window **MDCT** Radiation **Only anatomical, no functional information** MRI MR Myocardial Perfusion Imaging (MPI) **Stress Function MRI** 





#### **Myocardial Metabolism**



Oxygen extraction already high in basal circumstances

125

Thus, changes in myocardial oxygen supply result from changes in coronary flow

Primarily caused by coronary atheromatosis

Microvascular disease



#### Flow Profile across a Stenosis Basal Conditions





R = 0 => Flow = normal

R= ++ / P = -- / Cor ++ => Flow = normal (coronary vasodilatory reserve)



MBF (max stress) =  $4 - 6 \times MBF$  (baseline) 0.5 - 1.1 mL/min/g => 3.7 - 6.7 mL/min/g





### Mechanisms



#### Adenosine

#### Dipyridamole

- DIRECT effect : hyperemia
- IV dose of 140 μg/kg/min
- Half-life (< 10 sec)</li>
- 6-min infusion, injection perfusion agent after 3 minutes
- Moderate increase of blood pressure product

- Indirect by increasing interstitial levels of adenosine
- IV: 0.56 mg/kg during 4 min (0.84 mg/kg during 6 min for myocardial perfusion imaging + WM abnormalities
- Half-life 30 min => prolonged side-effects and ischemia
- Injection of perfusion agent 2 minutes after the end of the 4min infusion
- Antidotum: aminophylline



## Mechanisms

5 125

#### Adenosine

#### Dipyridamole

- Facial flushing 35%
- Slight chest pain 33%
  Headache 21% dyspnea 19%
  Nausea / dizziness / sour pain pain in jaw and shoulders
- Important side-effects restricted to heart & lungs
- AV conduction inhibition => AV block
- Severe bronchospasm (0.08%)
- Myocardial infarction (0.01%)
- Death (0.009%)

- Less intense than adenosine
- Chest pain 20%
- Headache 12%
- Dizziness 12%
- Nausea 5%
- Minor dysrhythmias: premature ventricular beats (5-20%)
- Symptomatic bradycardia, AF, VT, VF (very rare)
- Non-fatal MI (0.02%) / Cardiac death (0.01%) / Bronchospasm in asthma patients !!

#### Contraindications: asthma, AV block II-III



**Temporal resolution** 

**Spatial resolution** 

transmural discrimination

LV coverage (apex-base)

High CNR / SNR to discriminate normal from ischemic myocardium

Linear relation signal intensity to contrast dose (ie, input function) for quantification

**Correction for respiration** 



# MRI Perfusion ("First-Pass")



1) Gadolinium-DTPA small particle

231 🔘

2) Diffuse rapidly across into Interstitial space

3) SI ≈ [Gadolinio-DTPA]

Lee et al. Circulation 2004;110:58-65



#### **FAST MR Techniques**

Goal: 1 image per 1-2 RR per slice location, with a sufficient spatial resolution, free of artifacts:

#### Fast gradient-echo

Long acquisition times (500-700 msec/image) Artifacts (cardiac motion - edge blurring)

#### EPI

Single excitation (30-70 msec) Susceptibility artifacts / relationship CA concentration - SI not linear Off-resonance - T2\* relaxation

#### Hybrid EPI-fast gradient-echo

Reducing ETL to 8 Multiple RF excitation Improved image quality and image contrast Steady state free precession (SSFP) Parallel imaging



#### **Contrast Dose and Injection Protocol**

Small homogeneous bolus needed to track first pass of contrast (central venous line)

4 to 5 ml/s followed by 15 ml saline flush (power-injector)

Dose: choice between SNR and relationship linearity CA - SI (input function)

Low CA dose: lower SNR but linear relation High CA dose: higher SNR but nonlinear relation Optimal CA dose dependent on type of MR sequence used

2 IV lines (one for contrast / one for vasodilator)





First European Multicenter Experience 3 centers 0.05-0.1-0.15 mmol/kg Gd-DTPA SI increase : 100-200-280% AUC (ROC): 0.53-0.91-0.86 Pooled (0.1-0.15) Sensitivity: 93% Specificity: 75%

MR-Impact Trial (18 centers) 0.01 to 0.1 mmol/kg Gd-DTPA-BMA 0.1 the best AUC (ROC): 0.85



0.1 mmol/kg Gd is the ideal dose

Schwitter et al. ESC 2005



#### **Coverage of Ventricles - Spatial Resolution**

Optimal compromise between in-plane resolution / LV coverage and temporal resolution

LV coverage at least 3 slices basal / mid / apical => 16 segment

In plane resolution: 2.7 x 2.7mm (or better)

Subendocardial defect detection Artifact reduction



Base

Time



#### **Compensation for Respiratory Motion**

#### **Breath-hold strategies**

1: deep breath-in and breath outs just before myocardial perfusion study / breath-hold as long as possible / shallow breathing afterwards till end of measurement

2: shallow breathing

oxygen mask

Elastic matching for respiratory motion correction



*"two birds (perfusion and function) with a stone (dipyridamole)"* 



#### **MPI** analysis

**Qualitative visual** 

#### **Semi-quantitative**



Signal-intensity versus time curves Parametric perfusion maps, factor analysis Calculation of MPR (myocardial perfusion reserve)

Quantitative => absolute myocardial blood flow (ml blood /g tissue/min)



#### **Analysis - Visual**

**Clinically most often used Perfusion deficit:** Severity / Duration **Transmural** extent Segmental approach (e.g. 16/17 segments) - CA perfusion territory **Perfusion defect:** Stress: yes / rest: no => CAD Stress: yes / rest: yes => artifact (matched defect) **Relation perfusion defect - late enhancement** Match **Mismatch** 



Visible as nonenhancing part of myocardium during first pass of contrast!!

Obeys anatomical borders and respects course of blood supply by coronary arteries

Most pronounced in subendocardium with variable transmural spread

**Duration** of defect ranges from brief to prolonged

Size of perfusion defect is determined by position coronary artery stenosis

Abnormalities are always more pronounced during stress than at rest











#### **Multiple CA lesions: separate perfusion defects**



## **Dark-Rim Artifacts**

Very often present, sequence related Contrast arrival in LV cavity

Difference in relaxivity Susceptibility Edges bloodpool / myocardium



During hyperemia ++ => yielding impression of true defect

Usually darker than nonenhanced myocardium

Rapid decrease in severity / disappear during contrast washout in ventricular cavity / may reappear during second pass

Most pronounced in basal part / septum / papillary muscles

May be superimposed on true defect !!



#### Analysis - Semi-Quantitive



- 1 Time to start
- 2 Upslope
- 3 Signal increase
- 4 Time to peak
- 5 Downslope
- Linear fit
- Gamma variate fit



Se: 90 % / Sp: 83% / Acc: 87% (CA stenosis ≥ 75%)

Al-Saadi et al. Circulation 2000



#### Difficult

Requires deconvolution of the measured myocardial SI curve with the arterial input function SI curve

#### Dual-bolus approach, promising

Tracer-kinetics models based on compartmental analysis of Gd-uptake


### Fondazione Toscana Catende Messeerin

# Myocardial Perfusion Imaging

Clinical implication of adenosine-stress cardiac magnetic resonance imaging as potential gatekeeper prior to invasive examination in patients with AHA/ACC class II indication for coronary angiography



**Fig. 2** CMR stress perfusion and CXA findings in our patients (chi square for CMR and stenosis >70%: 113.7, p<0.0001)



false positive results. Sensitivity of CMR to detect relevant CAD (>70% luminal narrowing) was 0.96. specificity 0.83, positive predictive value 0.92 and negative predictive value 0.92. Of the CMR components, perfusion deficit was the strongest independent predictor (odds ratio 132.3, p<0.0001).



## **MR-MPI versus SPECT**

**No Stenosis** 



MRI

MRI

Severe Stenosis

MRI





SPECT



**Moderate Stenosis** 

ARI Signal Int Time



SPECT



SPECT **ARI Signal Int** 75 RRF 50 Time Sector Number SPECT

Lee et al. Circulation 2004;110:58-65

#### Fondazione Toscana Catrade Manueria

# Myocardial Perfusion Imaging 6175



## Costs Invasive vs. Noninvasive approach (11.249 Pts)



Shaw et al, JACC, 1999



# Myocardial Perfusion Imaging

## 7 122

# Conclusions

Growing scientific evidence that MR-MPI is highly valuable to depict hemodynamically significant coronary stenoses

### STRENGTHS

Easy-to-perform Safe, fast No radiation **Spatial resolution** Part of comprehensive exam CAD + MVDEfficient gate-keeper => risk stratification reduction of medical cost **Prognostic value in predicting CAD-related** events

### LIMITATIONS

Sequence design Compromise between imaging parameters Artifact-free images Interpretation Quantification of absolute MBF







Boden NE et al NEJM 07