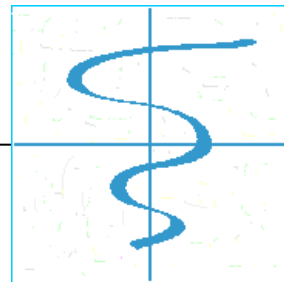

Detection of CAD with MCG Validation Studies – US, Germany, Asia A Metaanalysis

Michael Imhoff, MD PhD

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November 9, 2011

Presentation to the MEDCAC

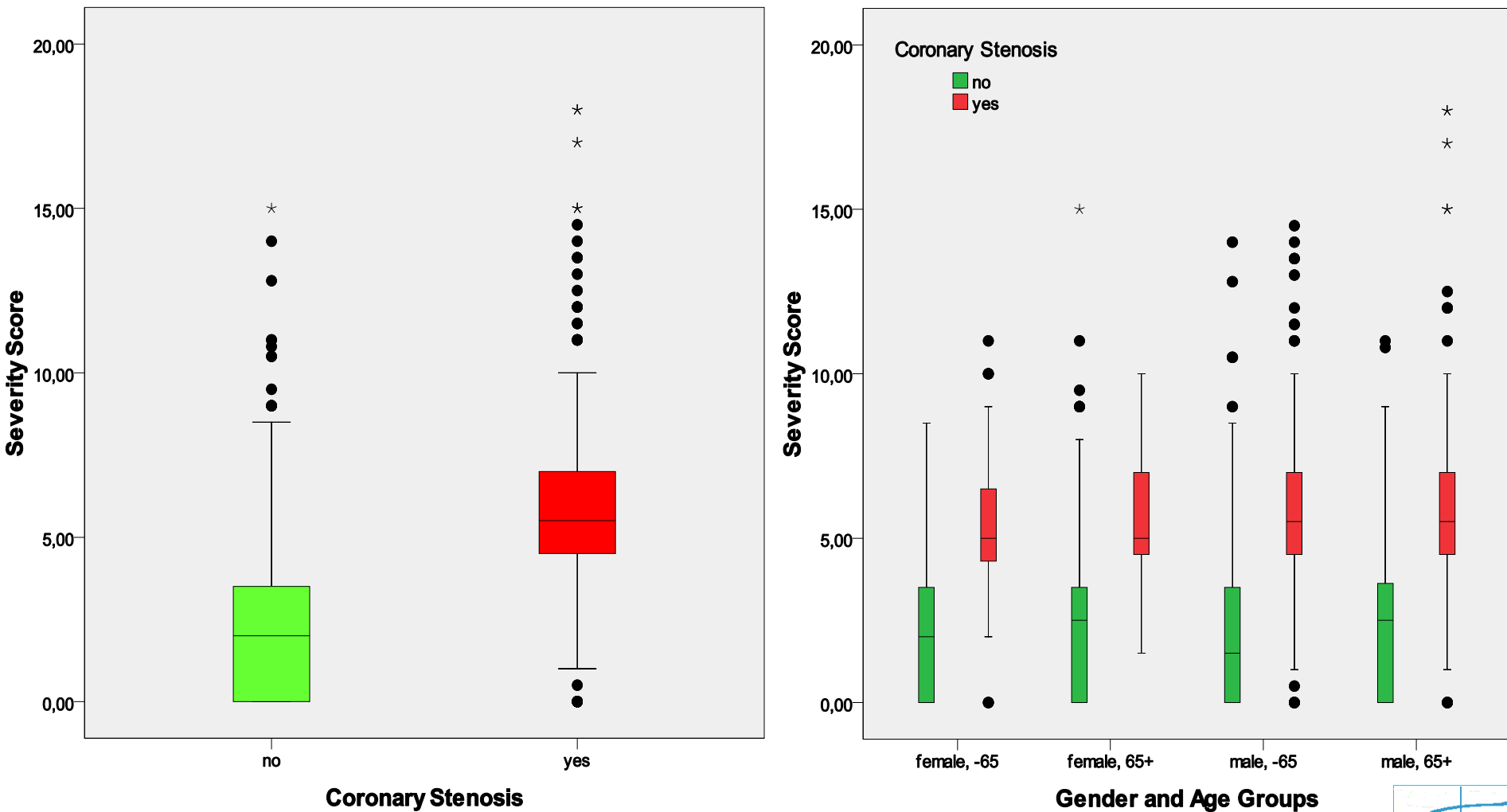


MCG – Clinical Studies

- Prospective clinical studies
- More than 1,000 patients scheduled for angiography
- Comparison of MCG-results to angiography
 - MCG prior to angiography
 - Angiograms verified by two angiographers independently
 - Double-blind
- Independent study monitors
- Westchester Medical Center, Valhalla, NY
 - 136 patients in 2000
- Siegburg Heart Center, Siegburg, Germany
 - 751 patients between Summer 2001 and Summer 2003
- Asian Multicenter Trial (4 sites)
 - 189 patients in Summer/Fall 2004



MCG Severity Score



Prediction of Coronary Stenosis

Angiography

**MCG
Severity
Score**

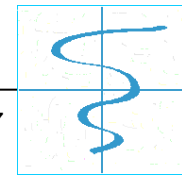
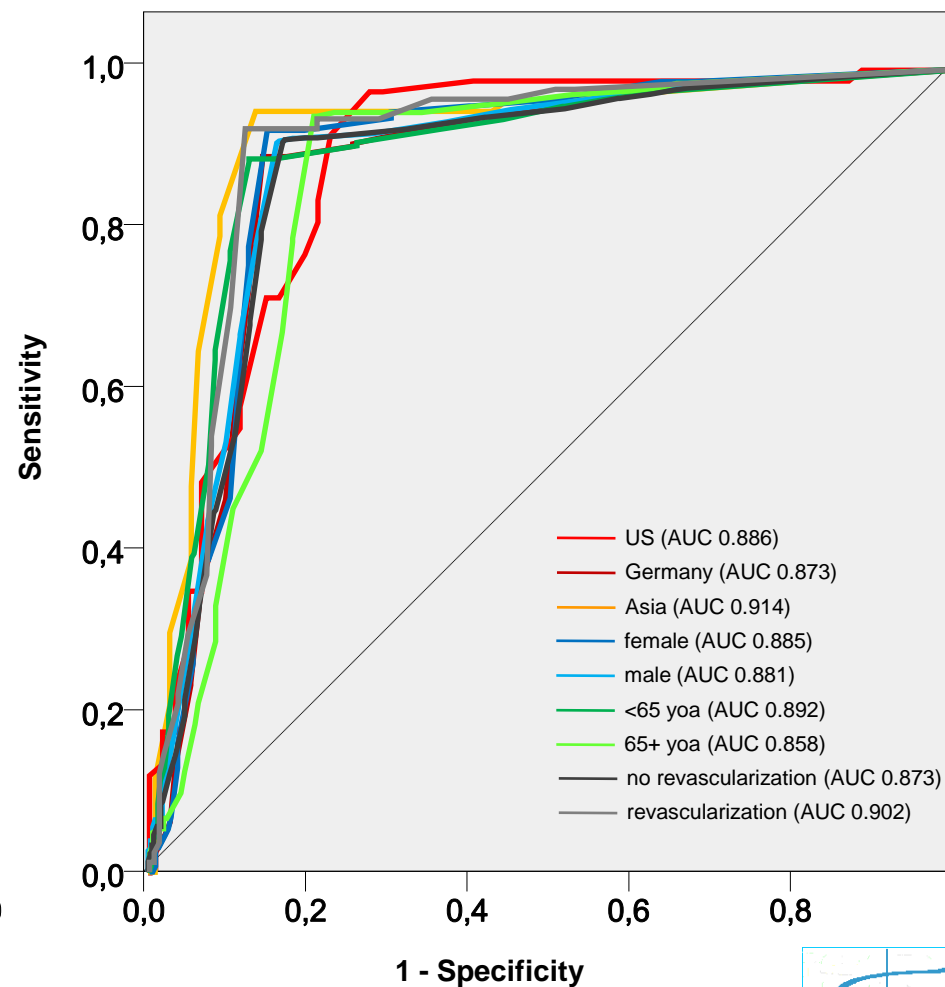
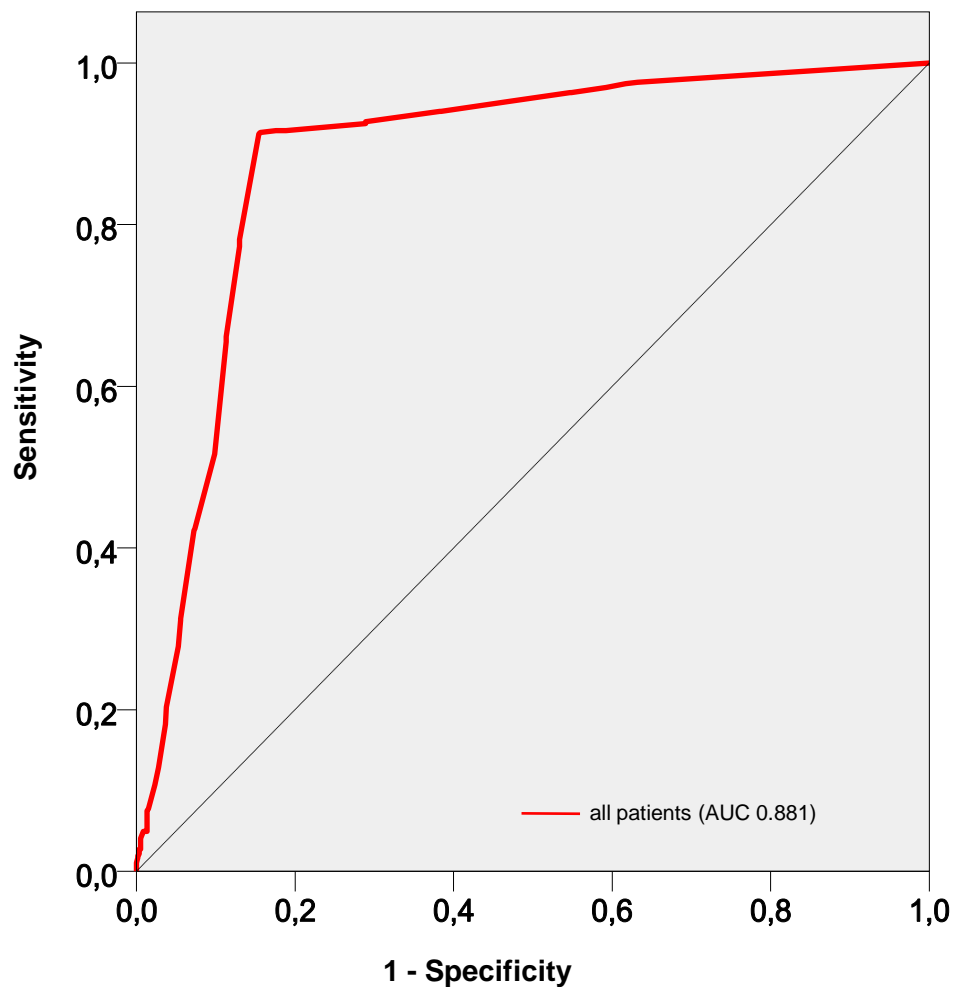
		Angiography	
		No Stenosis	Stenosis
	< 4	515	41
	>= 4	94	426



	n	a priori	Correct	Sens	Spec	PPV	NPV
Total	1076	0,434	0,875	0,912	0,846	0,819	0,926
Female	390	0,336	0,877	0,924	0,853	0,761	0,957
Male	686	0,490	0,873	0,908	0,840	0,845	0,905
< 65 years	623	0,392	0,880	0,885	0,876	0,821	0,922
65+ years	453	0,492	0,868	0,942	0,796	0,817	0,934
No Revasc	827	0,467	0,868	0,909	0,832	0,826	0,913
PCI	188	0,282	0,888	0,887	0,889	0,758	0,952
CABG	61	0,459	0,918	1,000	0,881	0,789	0,961



ROC Curves



Limitations of the Studies

Convenience Sample

- Close match to CAD demographic distribution
- CAD prevalence approx. 50%

Reference standard (coronary angiography)

- Accepted “gold standard”, standard definition of obstructive CAD used in studies
- Underestimation of MCG sensitivity/specificity

Bias because patients were already scheduled for CA

- Close match to CAD demographic distribution
- CAD prevalence approx. 50%
- Similar to data from ACC registry

No direct comparison to stress test modalities



Summary

- Computerized resting ECG analysis
- Prediction of coronary stenosis
 - 88% correct predictions, sensitivity 91%, specificity 85%
 - PPV 82%, NPV 93%
- No significant effects on performance from gender, age, revascularization, study location



Answers to Questions

Question 1:

- MCG was validated against an morphologic reference standard. Therefore, results apply irrespective of clinical presentation. (Q1a, Q1b)
- ACS/AMI was an exclusion criterion in all studies following the same rational as in Patel el al. (NEJM, 2010). (Q1b)

Question 2:

- MCG was validated in patient with indication for coronary angiography including asymptomatic patients. (Q2a).
- MCG was validated against an morphologic reference standard. Therefore, results apply irrespective of clinical presentation. (Q2a, Q2b)



Answers to Questions

Question 3

- Compared to data from the literature the current studies show a much higher sensitivity and specificity of MCG for detection of CAD than 12-lead ECG. (Q3a)
- One study compared MCG against 12-lead ECG and found
- The studies included patients with intermediate risk. (Q3a)
- Prevalence of obstructive CAD similar to ACC registry. (Q3a)
- The studies did not include ACS/AMI patients. (Q3b)

Question 4

- same as question 3



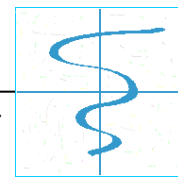
Answers to Questions

Question 5

- As the current studies did not include ACS/AMI patients its performance against Troponin was not assessed. (Q5a)
- Compared to data from the literature the current studies show at least as good sensitivity and specificity of MCG for detection of CAD as stress test modalities. (Q5b)
- MCG was directly compared to coronary angiography. Due its high PPV and NPV for CAD MCG may be suitable to more appropriately select patients for coronary angiography. (Q5c)

Question 6:

- same as Question 5



Answers to Questions

Question 7

- As MCG is a diagnostic method and was studied in comparison to other diagnostic methods. Therefore, inference on its impact on outcomes cannot be made.
- Due to its high PPV and NPV in all patient groups MCG may help to reduce the exposure of patient to unnecessary burdensome or invasive tests.

Question 8

- Same as question 7



Answers to Questions

Question 9

- Impact of MCG on CAD management algorithms and resulting outcomes.
- Direct comparison of MCG to stress test modalities.

Question 10

- Nearly 50% of the study population over 65 years. (Q10a)
- Reference database with large sample from all population strata. (Q10a)
- None of the study centers was an academic medical center. Study population from community based settings. (Q10b)



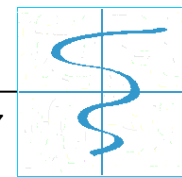
Clinical Studies

- Prospective clinical studies
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Westchester

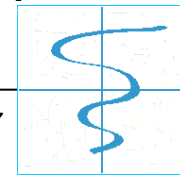
- Total enrollment 200 patients without prior revascularization
- 64 patients excluded because of poor ECG tracings (32%)
- Qualitative MCG diagnosis
- Grading of coronary stenosis with a geometric scoring system (BARI)
- Cut-offs at 40% and 60% coronary stenosis
- Comparison to 12-lead computer-aided ECG diagnosis
- Weiss et al, Heart Dis 2002;4:2-12



Westchester

	n	TP	TN	FP	FN
mf-EMT > 40%	136	84	38	8	6
> 60%	136	76	42	16	2
ECG > 40%	136	68	21	25	22
> 60%	136	59	24	34	19

	Sens	Spec	PPV	NPV	Correct	a priori
mf-EMT > 40%	0,933	0,826	0,954	0,764	0,897	0,662
> 60%	0,974	0,724	0,865	0,940	0,868	0,574
ECG > 40%	0,756	0,457	0,842	0,328	0,654	0,662
> 60%	0,756	0,414	0,700	0,484	0,610	0,574



Siegburg

- Total enrollment 775 patients without and with prior coronary revascularization
- 24 patients excluded because of poor ECG tracings (3%)
- Coronary stenosis at $>70\%$ ($>50\%$ LCA)
- Continuous MCG severity score (cut-off 4.0)
- Complete risk factor model in 595 patients

Grube et al., Int J Med Sci 2007;4:249-263

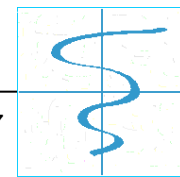
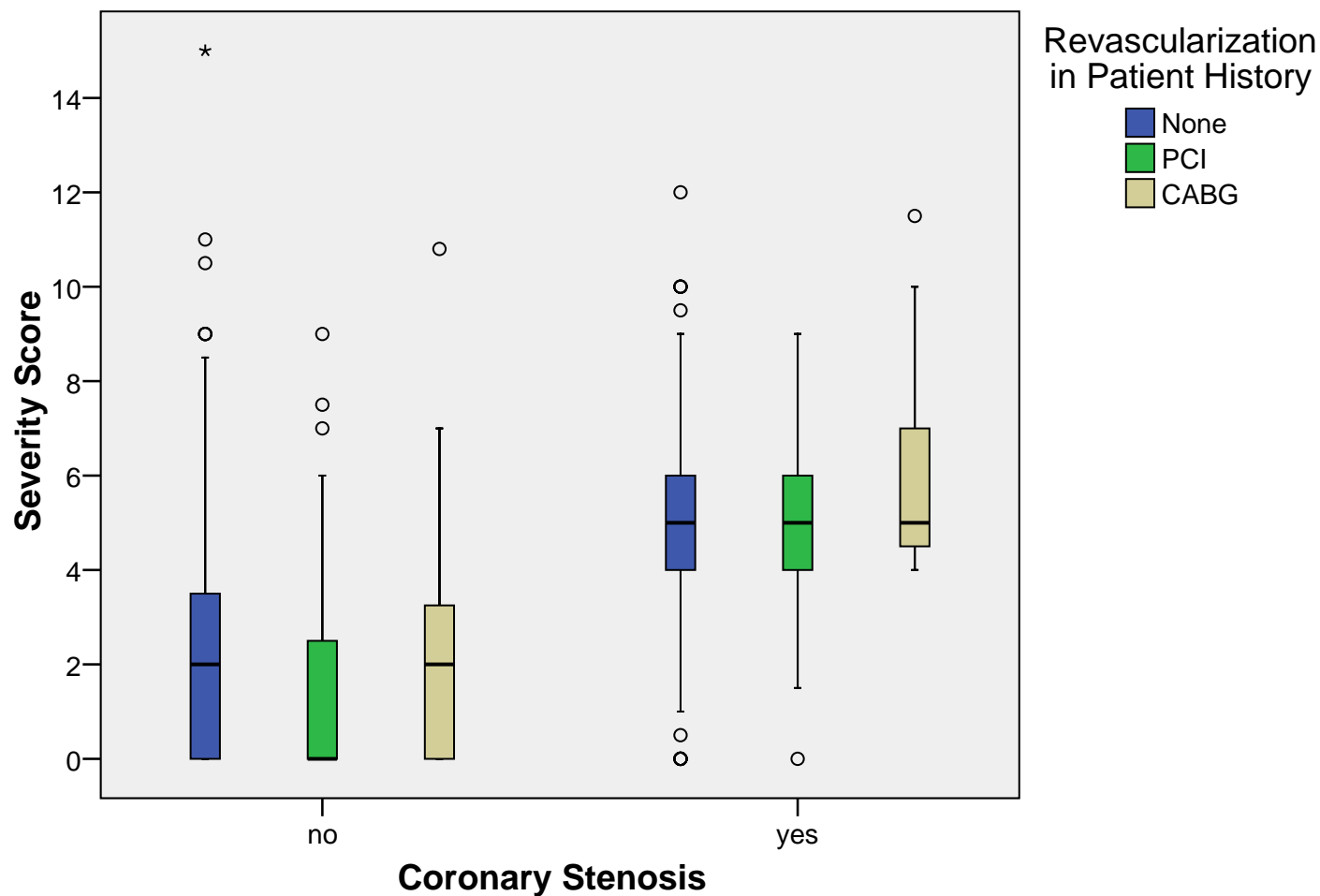
Grube et al., Int J Med Sci 2008;5:50-61

Imhoff et al., Chest 2007

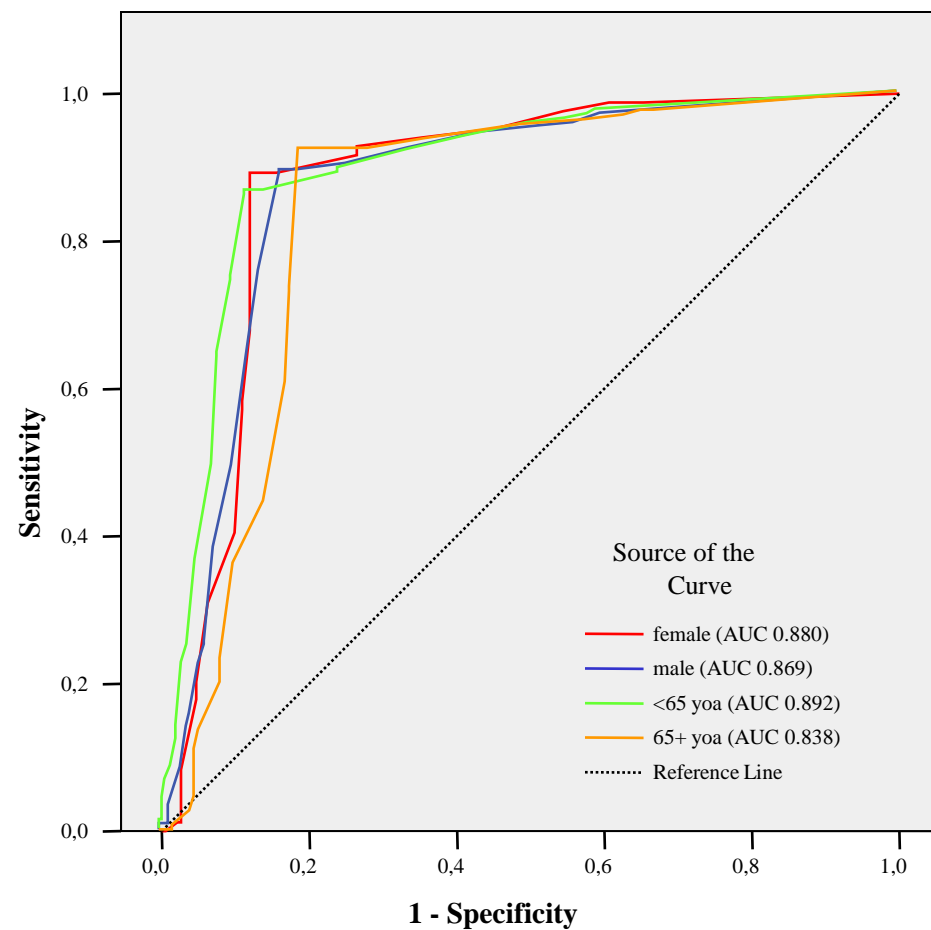
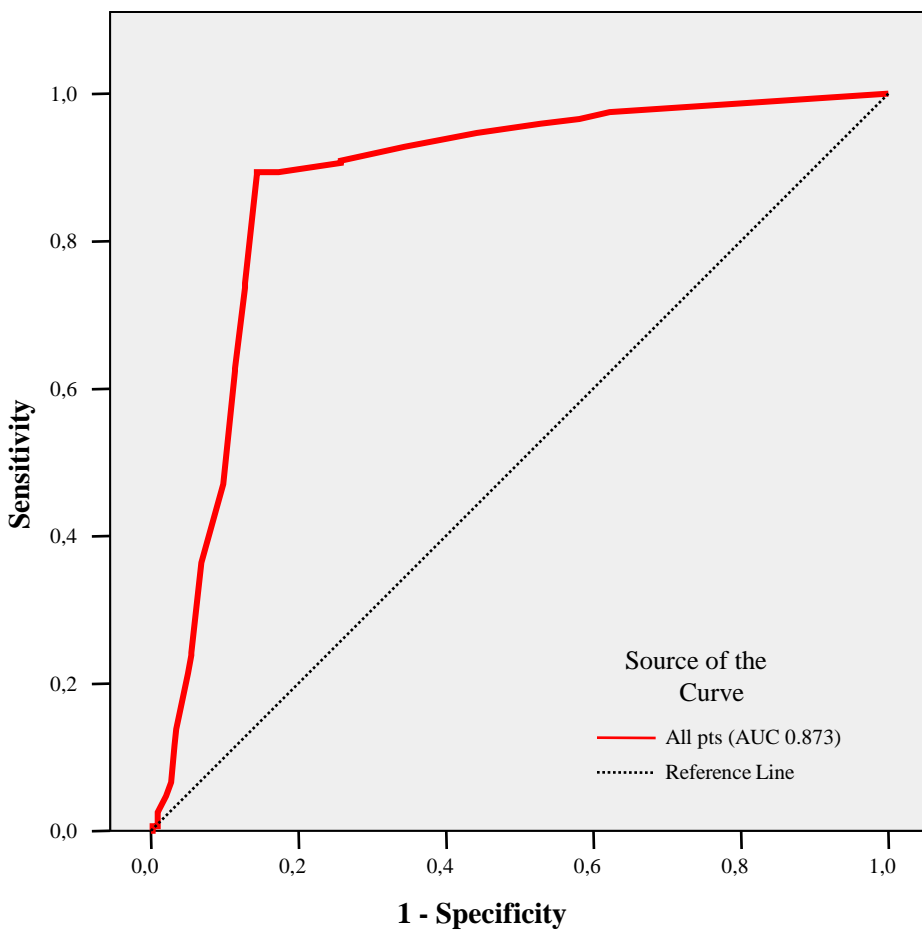
Imhoff et al., AHA Scientific Sessions 2007



Siegburg – Severity Score



Siegburg – ROC Curves



Siegburg – Results Overview

	n	a priori	Correct	Sens	Spec	PPV	NPV
Total	751	0,421	0,871	0,889	0,857	0,767	0,936
Risk factors	595	0,430	0,645	0,469	0,779	0,547	0,719
Female	276	0,304	0,884	0,893	0,880	0,588	0,977
Male	475	0,488	0,863	0,888	0,840	0,835	0,892
< 65 years	429	0,378	0,876	0,858	0,888	0,738	0,944
65+ years	322	0,478	0,863	0,922	0,810	0,803	0,925
No Revasc	545	0,455	0,859	0,879	0,842	0,795	0,909
PCI	145	0,276	0,897	0,875	0,905	0,571	0,980
CABG	61	0,459	0,918	1,000	0,848	0,826	1,000



Asian Multicenter

- Total enrollment 222 patients without and after coronary revascularization in 5 centers in Asia
- 3 patients excluded because of poor ECG tracings (1,6%)
- 30 patients excluded because of legal issues in one center (refusal for second analysis of angiography)
- Continuous MCG severity score (cut-off 4.0)
- Coronary stenosis at $>70\%$ ($>50\%$ LCA)

Hosokawa et al, Congest Heart Fail 2008;14:251-260



Asian Multicenter – Results

	n	TP	TN	FP	FN	a priori	Correct	Sens	Spec	PPV	NPV
Total	189	73	97	15	4	0,407	0,899	0,948	0,866	0,784	0,971
Center A	65	24	34	6	1	0,385	0,892	0,960	0,850	0,730	0,981
Center B	19	9	8	1	1	0,526	0,895	0,900	0,889	0,909	0,878
Center C	44	14	24	6	0	0,318	0,864	1,000	0,800	0,587	1,000
Center D	61	26	31	2	2	0,459	0,934	0,929	0,939	0,917	0,948
Female	57	22	28	6	1	0,404	0,877	0,957	0,824	0,713	0,976
Male	132	51	69	9	3	0,409	0,909	0,944	0,885	0,814	0,969
< 65 yoa	113	43	58	8	4	0,416	0,894	0,915	0,879	0,820	0,943
> 65 yoa	76	30	39	7	0	0,395	0,908	1,000	0,848	0,782	1,000
no revasc	146	61	72	10	3	0,438	0,911	0,953	0,878	0,831	0,968
revasc	43	12	25	5	1	0,302	0,860	0,923	0,833	0,583	0,980



MCG – Clinical Studies

	n	Correct	Sens	Spec	PPV	NPV
Westchester	136	0.868	0.974	0.724	0.865	0.940
Siegburg	751	0.871	0.889	0.857	0.767	0.936
Asia	189	0.899	0.948	0.866	0.784	0.971
Total	1076	0.875	0.913	0.846	0.783	0.941



MCG – Clinical Studies Summary

- Computerized resting ECG analysis
- Clinical studies in three continents with 1000+ patients
- Prediction of coronary stenosis
 - better performance than standard ECG
 - better performance than stress testing
- Similar rule-out performance like stress testing (awaits further study)
- Feasible in patients with contraindications to stress testing
- Diagnostic performance independent of
 - gender, age, ethnic background,
 - type of revascularization, clinical practice patterns,
 - user experience
- Non-invasive screening for coronary artery stenosis
- Simple and fast application in clinical practice

