# Young Investigator Award Session
# Oral abstract session

**14:00-15:30**

## 4.1

**Decreased myocardial beta-adrenergic receptor density according to severity of heart failure in patients with left ventricular dysfunction: PET study with C-11-labeled-CGP-12177.**

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**Objectives:** Cardiac sympathetic function plays an important role in regulation of left ventricular (LV) function and pathophysiology of LV dysfunction. C-11-labeled CGP-12177 (CGP) has been used to assess myocardial beta-adrenergic receptor density (Bmax) in vivo using PET. The aim of this study is to measure myocardial Bmax in patients with LV dysfunction and compare obtained Bmax with severity of heart failure.
**Methods:** CGP PET was performed in 16 patients with LV dysfunction (mean LVEF 34.4 ± 10.6%, NYHA class I 2, class II 8, class III 5, class IV 1) and 7 healthy normal volunteers using a double injection method. Following transmission and O-15 labeled carbon monoxide scan, a CGP dynamic scan for 75 min was performed after the initial injection with high specific activity of CGP (201 ± 80 MBq) followed by the second injection of low specific activity of CGP (381 ± 172 MBq) at 30 min. Bmax of LV was calculated based on graphical analysis method introduced by Delforge et al (JNM, 1991).
**Results:** Bmax in patients with LV dysfunction was significantly lower than that in normal volunteers (5.25 ± 1.69 vs. 9.49 ± 2.10 pmol/ml, $p<0.001$). While Bmax in patients did not correlate with left ventricular ejection fraction (LVEF) ($r=0.42$, $p=0.12$), Bmax decreased with the severity of NYHA class (class I: 7.70 ± 1.41 pmol/ml, II: 5.05 ± 1.33 pmol/ml*, III: 4.90 ± 1.82 pmol/ml*, IV: 3.73 pmol/ml, *$p<0.05$ vs. class I).
**Conclusions:** By using C-11-labele-CGP-12177 PET, we could measure Bmax noninvasively. This seems to be a new parameter of heart failure independent of LV systolic function.

## 4.2

**Attenuation correction with CT and its impact on myocardial perfusion imaging in a hybrid SPECT/CT.**

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**Purposes:** Myocardial perfusion imaging (MPI) is widely used to non-invasively detect known or suspected coronary artery disease (CAD) and has been shown to be highly sensitive. However, its accuracy is hampered by attenuation artifacts. A newly developed combined SPECT/CT is now available to correct for attenuation.
**Methods:** We analysed consecutively MPI studies of 265 patients. All studies were performed on a dual-head VG system equipped with a low-end computed tomography (CT) unit (Hawkeye, GE Medical Systems). The study population was divided into three groups according to the dose of radiotracer (99m-Tc-Tetrofosmin) given for the stress study (adenosine) in order to assess any dose-dependent differences in attenuation correction (A:200-300MBq, B:800-900MBq, C:300-400MBq). Non-corrected and CT-corrected images were interpreted for absence or presence of irreversible (scar) or reversible defects (ischemia) and after achieved full consensus between two blinded readers the agreement between non-correction and CT-attenuation correction as well as the sensitivity and specificity were calculated for the diagnosis of scar and ischemia using wall thickening from gated SPECT, PET, coronary angiography or clinical history as gold standard. Furthermore a semiquantitative analysis indicating the relative tracer distribution was performed using polar maps to detect differences in attenuation correction between the three groups.
**Results:** The overall sensitivity for diagnosis of a scar decreased with attenuation correction (96% vs. 82%) whereas specificity increased markedly from 68% to 99%. However, for the diagnosis of a stress-induced ischemia the sensitivity increased from 90% to 100% whereas specificity decreased (95% vs. 93%) with and without attenuation correction. The relative tracer distribution in the inferior segments increased with CTAC in all groups similarly, whereas it decreased in the anterior segments in group A significantly (76% vs. 73%, $p<0.005$) and not at all in group B and C.
**Conclusion:** CTAC by SPECT/CT is useful for compensation of attenuation and helps to improve diagnostic confidence of MPI studies. However, it seems to be strongly dose-dependent for stress studies, especially in the anterior wall. Apparently the dose given for stress studies has to be more than 300 MBq in order not to induce "correction-artifacts" in the anterior wall which would substantially lower the specificity of MPI-studies.

## 4.3

**Rosiglitazone improves myocardial glucose uptake in ischemic regions in patients with type 2 Diabetes. A 16 week randomised, double-blind, placebo-controlled study.**

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**Background:** Rosiglitazone improves insulin sensitivity and skeletal muscle glucose uptake in patients with uncomplicated type 2 diabetes. In patients with ischemic coronary artery disease, glucose is an important source of energy and preserved myocardial glucose uptake is essential for the viability of the jeopardised myocardium. The effect of rosiglitazone on myocardial metabolism in type 2 diabetic patients with coronary artery disease was thus studied.
**Methods:** The study was randomized, double-blind and placebo-controlled. Post-hoc analysis was conducted excluding 4 subjects who were considered violators. 54 patients (38 men, 16 women) with type 2 diabetes (HbA1c 7.2+0.9%) and coronary artery disease were studied with PET and [18F]FDG during hyperinsulinemic euglycemic clamp before and after 16 week intervention period with rosiglitazone ($n=27$) or placebo ($n=27$). Ischemic regions of myocardium were determined with rest-stress 99m Tc-SPECT imaging and coronary angiography.Statistical analysis was carried out using Analysis of Covariance, adjusting for gender and baseline.
**Results:** Myocardial glucose uptake increased by 6.12 [0.89, 11.34] μmol/100g/min in ischemic regions ($P=0.023$) and by 8.40 [2.99, 13.81] μmol/100g/min in non-ischemic regions ($P=0.003$) on rosiglitazone as compared to placebo. The treatment effect of myocardial glucose uptake in ischemic regions based on all subjects was smaller, 4.77 [−0.37, 9.90] μmol/100g/min. In addition, whole body insulin sensitivity and glycemic control were significantly improved on rosiglitazone compared to placebo.
**Conclusion:** Rosiglitazone therapy significantly improves myocardial glucose uptake in type 2 diabetic patients with ischemic coronary artery disease. These results suggest that rosiglitazone therapy may facilitate myocardial glucose storage and utilization in these patients.

## 4.4

**Association between plasma myeloperoxidase levels and ischemic response during stress nuclear perfusion imaging.**

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**Background:** Myeloperoxidase (MPO) is an abundant enzyme secreted from monocytes, neutrophils, and tissue macrophages. Multiple distinct products of MPO are enriched in human atherosclerotic lesions. Elevated MPO levels correlate with an increased risk of future major cardiac events in patients with chest pain and are found in patients with angiographically documented cardiovascular disease.
Objective: The objective of this study was to determine if plasma MPO levels measured by Enzyme Immuno Assay (EIA) correlate with the detection of myocardial ischemia in patients undergoing stress myocardial perfusion imaging (MPI).
**Methods:** Patients undergoing MPI and patients that had recent positive MPI referred for cardiac catheterization were included in the study. Patients with evidence of inflammatory disease by history or abnormal differential blood count and patients with previous myocardial infarction were excluded. Five milliliters of peripheral blood was acquired from each patient and centrifuged. The heparinized plasma was analyzed by EIA (Assay Designs, Inc) using human MPO antibody and the MPO levels were determined photometrically. During laboratory analysis, staff was blinded to the results of MPI and the coronary angiograms.
**Results:** The study comprised of 83 patients. Mean age was 63 years. In control group, 32 patients had a negative MPI (Group 1). Positive MPI was noted in 29 patients, of which 17 had significant stenosis >70% on subsequent coronary angiogram (Group 2, true positives) and the remaining 12 had non-critical CAD or normal coronaries (Group 3, false positives). Patients in Group 1 had a significantly higher mean MPO level (215 ± 22 pM) compared to patients in Group 3 (118 ± 20.9, $p=0.02$). Patients in Group 2 had a significantly higher mean MPO level (320 ± 62.6) than patients in Group 3 ($p=0.006$). Group 2 had a higher MPO level than Group 1, but the difference was not statistically significant (p=NS). Patients who were obese with BMI > 30 had a higher mean MPO level (248 ± 28.7 pM) than patients with BMI < 30 (124 ± 20.6 pM, $p=0.001$).
**Conclusion:** 1)Patients with a true positive MPI and confirmed critical CAD on coronary angiogram (Group 2) have significantly higher MPO levels than patients who have false positive MPI studies (Group 3). MPO levels may help in differentiating true positive from false positive MPI results.
2)Patients with obesity (BMI > 30) have a significantly higher level of MPO than non-obese patients.

## 4.5

**Enhanced imaging of very small experimental atherosclerotic lesions in ApoE−/− mice: Use of bispecific antibody and Tc-99m-labeled polymeric probes.**

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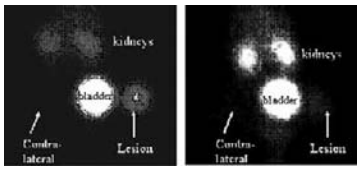
Experimental and clinical (carotid) atherosclerotic lesions were imaged with chimeric Z2D3 antibody. High non-target activities, and substantial lesion size requirement for visualization led us to develop a bispecific antibody (BSAb)-Tc-99m labeled-negative-charged polymeric probes for enhanced imaging of murine atherosclerotic lesions.

**METHODS:** Female ApoE−/− mice were kept 2 weeks on Western Diet. Left and right femoral cut-downs were made under ketamine/xylazine anesthesia. The left femorals were deendothelialized by insertion of a guide wire 3 times. The cut-downs were sterily sutured closed and the animals allowed to recover for 10 days. Then each mouse was injected with 30 μg Z2D3-anti-DTPA (n=7) or control IgG-anti-DTPA BSAb(n=4) intravenously and 24 h later, 6 MBq Tc-99m-DTPA-succinylated polylysine(14.6 KD) were injected intravenously and imaged anteroposteriorly 2-3 h later. 50 μg polymers were radiolabeled with 130 MBq Tc-99m. The pixel density was determined by Adobe photoshop 7.0. BSAb were made by cross-linking Z2D3-F(ab')2 to anti-DTPA-F(ab')2 via disulfide bonds.

**RESULTS:** Atherosclerotic ApoE−/− mice(n=7)injected with Z2D3-BSAb showed accumulation of radioactivity in the lesions ([see picture], 20.6 ± 12.2, mean pixel density ± SD). Sham operated right leg-regions showed no radiotracer accumulation (1.7 ± 0.8, p=0.0015. Atherosclerotic ApoE−/−mice injected with control BSAb showed no radiotracer accumulation in either legs. Images and biodistribution data showed that there was very little non-target organ activity.

**CONCLUSIONS:** Z2D3-anti-DTPA BSAb with Tc-99m-labeled polymeric probes enabeled visualization of very minute atherosclerotic lesions in ApoE−/− mice, with minimal non-target organ activities.




BSAb (left panel) and Cont-BSAb (right)

## 4.6

**Myocardial perfusion imaging: A more powerful predictor than clinical or socioeconomic factors in Hispanic, African-American and Caucasian patients.**

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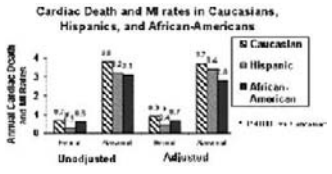
**Background:** Risk factors for coronary disease differ between ethnic groups. Risk stratification of Hispanics (H) and African-Americans (AA) with SPECT MPI is incompletely characterized as many trials enrolled few ethnic minorities.

**Objective:** To determine the role of SPECT MPI in Hispanics and African-Americans compared with Caucasians (C).

**Methods:** We analyzed our prospective database of 15,094 subjects with rest/stress Tc-99m Sestamibi SPECT MPI from 1/1996-6/2003 according to race (H n=2,113, AA n=1,207, C n=11,773) and MPI result. Groups were matched on propensity scores incorporating age, gender, diabetes, cholesterol, hypertension, type of stress, smoking, and socioeconomic status (ethnicity and zip code specific mean per capita income from census 2000).

**Results:** Annual cardiac event rates (MI, cardiac death) were similar for all three groups, although Hispanics with normal MPI were at particularly low risk (p<0.001 vs. C). Annual cardiac event rates were low with normal MPI (H: 0.3, AA: 0.6, C: 0.7; p=n.s. H vs. AA and AA vs. C). Patients with abnormal MPI also had similar event rates in each ethnic group(H: 3.2, AA: 3.1, C: 3.8; p=n.s. all comparisons). Propensity score adjustment made no significant change despite differences in baseline demographics (Adj. annual event rates: Normal MPI H 0.4, AA 0.7, C 0.9 [p<0.001 H vs. C, otherwise p=n.s.]; Abnormal MPI H 3.4, AA 2.8, C 3.7, p=n.s.). Mean follow-up 2.3 years. Follow-up obtained in 81% of patients.

**Conclusion:** Myocardial perfusion imaging is a more powerful indicator of future cardiac events in Hispanic, African-American and Caucasian patients than clinical or socioeconomic factors. MPI result provides similar risk stratification in all three ethnic groups despite baseline differences.




ethnicity specific annual cardiac events