systolic velocity ratio (DSVR) was 2.3 ± 0.8. Myocardial contrast echocardiography (MCE) was performed before LCX clamping and 15 minutes after release of clamping, with the intracoronary injection of 0.5 ml Albunex. From MCE recordings, post- to pre-clamping gray level ratio (GLR) in contrast enhanced area was determined.

As shown, coronary flow patterns immediately after reperfusion correlated positively with myocardial microvascular injury assessed by MCE in range of DSVR < 4.0. Severe microvascular injury group (lower GLR group; o) was characterized with more decreased systolic flow. Thus, increase in DSVR was influenced mainly by decrease in systolic flow velocity. Conclusion: Coronary flow velocity patterns immediately after reperfusion might indicate well myocardial microcirculatory injury.

## 1040-66 Transient Response Imaging With Intravenous Perfluorocarbon-Exposed Sonicated Dextrose Albumin Detects the Spatial Extent of Ischemia During Dobutamine Stress Echocardiography

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Significantly improved myocardial contrast (MC) following minute intravenous injections (IVI) of perfluorocarbon-exposed sonicated dextrose albumin (PESDA) has occurred when ultrasound pulses are interrupted (transient response imaging (TRI)) and delivered at only one frame per cardiac cycle (1 Hz). TRI is most evident with second harmonic imaging (SHI). It is unknown whether TRI can detect myocardial perfusion abnormalities during stress echocardiography (SE). Accordingly, we performed TRI using SHI following 0.005–0.01 milliliter per kilogram IVI of PESDA during each stage of an incremental dobutamine infusion (DI) (5, 10, 20, and 30 u/kg/min) in eight open chest dogs with a quantitatively significant coronary stenosis (63 ± 6% diameter, range 54–72%) The peak myocardial videointensity (PMVI) in the perfused bed supplied by the stenosis and spatial extent of perfusion abnormality (SEP) as well as % wall thickening (%WT) were measured at each stage. Results are shown (*p < 0.05 compared to base):

| | Base | 5 u | 10 u | 20 u | 30 u |
|---|---|---|---|---|---|
| PMVI | 3 ± 16 | 32 ± 16 | 32 ± 16 | 28 ± 17 | 36 ± 16 |
| SEP(cm$^2$) | 1.6 ± 1.5 | 2.8 ± 1.7 | 4.0 ± 1.5 | 5.5 ± 2.7* | 6.8 ± 4.3* |
| % Wt | 20 ± 10 | 35 ± 25 | 28 ± 23 | 26 ± 25 | 29 ± 36 |

*p < 0.05 compared to base

The SEP was easily visualized earlier using TRI and SHI without myocardial attenuation. These contrast defects were not seen using this dose of IV PESDA and conventional 30 Hertz frame rate imaging. Second harmonic TRI can be utilized during dobutamine SE to detect perfusion abnormalities at earlier stages of infusion.

## 1040-67 Myocardial Contrast Echocardiography: Comparison of Sensitivity and Specificity of FSO69 vs. Thallium-201 in Detecting Myocardial Ischemia and Heterogeneous Perfusion

David R. Richards, Percy J. Colon III, Mario F. Meza, Sameh Mobarek, Carlos A. Moreno, R. Wayne Barbee, Susan Revall, James V. Connaughton III, Stanton E. Shuler, Joseph P. Murgo, Jorge Cheirif. *Ochnser Medical Institutions, New Orleans, LA*

FSO69, a new transpulmonary echocardiographic contrast agent, has been shown to delineate underperfused areas during coronary occlusions. To compare the sensitivity and specificity of FSO69 to nuclear imaging in detecting ischemia, we studied 16 open-chest dogs. IV FSO69 (0.2–0.4 ml) and Tc-99m Sestamibi (20 mCi) were injected during baseline 2D echocardiographic imaging. During short (5 min; n = 5) or long (3 hrs + 3 hrs reperfusion; n = 3) coronary occlusions, coronary stenoses (n = 4), and dipyridamole-stenoses (n = 4), IV FSO69 and Th-201 (1 mCi) were then administered. Planar nuclear imaging and regional blood flow (RBF) determination (radiolabeled microspheres) were performed postmortem. Ischemia was defined as a new wall motion abnormality (WMA) when compared to baseline, and heterogeneous (Heterog) perfusion as a decrease in RBF or in endocardial/epicardial flow ratio in the ischemic zone. Perfusion abnormalities were observed with FSO69 and nuclear, respectively, in 8/8 and 7/8 short occlusions, 3/4 and 2/4 stenoses, 2/5 and 2/5 stenoses + dipyridamole and 3/3 long occlusions by both techniques. Sensitivity (sens) and specificity (spec) follow:

| | Overall | | Ischemia | | Heterog perfusion | |
|---|---|---|---|---|---|---|
| | sens | spec | sens | spec | sens | spec |
| FSO69 | 88% | 50% | 100% | 80% | 86% | 50% |
| Nuclear | 80% | 50% | 81% | 60% | 76% | 50% |

Conclusion: IV FSO69 provides an effective, noninvasive means of detecting ischemic myocardium and RBF abnormalities, with a higher individual sensitivity and specificity than nuclear planar imaging for the detection of ischemia and heterogeneous perfusion.

## 1040-68 Adenosine Reduces Micro-Vascular Damage in the Post-Reperfusion Period: A Myocardial Contrast Echocardiography Study

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It has been suggested that adenosine may attenuate the damage of the microvasculature that occurs after release of a prolonged coronary occlusion. To determine if this effect could be shown in vivo, we used myocardial contrast echocardiography (MCE). Accordingly, we studied 10 open-chest mongrel dogs in which 4–6 hours of coronary occlusion and 3 hours of reperfusion were done. Dogs were given continuous intracoronary saline (placebo, n = 5) or adenosine (n = 5, dose 3 mg/min) infusions 10 minutes pre-reperfusion and for 1 hour after reperfusion. MCE was performed with IV injections of the echo contrast agent, FSO69 (0.1–0.2 ml). Area at risk (% LV) was similar in placebo vs adenosine dogs (32 ± 15 vs 27 ± 89), yet final infarct size (% area at risk) showed a trend in favor of the adenosine group (25 ± 18 vs 6 ± 7). Peak intensity was used as the parameter of myocardial perfusion. Results (ischemic/control region) are shown below:

| Group | Baseline | Occlusion | Early Release | Late Release |
|---|---|---|---|---|
| Placebo | 0.9 ± 0.04 | 0.2 ± 0.08* | 0.2 ± 0.11* | 0.[illegible] ± 0.28* |
| Adenosine | 0.9 ± 0.10 | 0.2 ± 0.18* | 0.9 ± 0.32** | 1.0 ± 0.08** |

*p = < 0.001 vs baseline; **p = 0.001 vs occlusion.

We conclude that adenosine protects the micro-vasculature post-reperfusion as evidenced by smaller infarct size and improved myocardial perfusion. This effect can be demonstrated in vivo by MCE.

# 1041 Metabolic Function and Autonomic Function

Wednesday, March 27, 1996, 3:00 p.m.–5:00 p.m.
Orange County Convention Center, Hall E
Presentation Hour: 3:00 p.m.–4:00 p.m.

## 1041-85 Abnormalities of Cardiac Autonomic Function and $^{11}$C-Hydroxyephedrine PET Coincide in Heart Failure

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Abnormal autonomic nervous function characterizes congestive heart failure (CHF). To study whether these alterations are reflected in myocardial uptake of $^{11}$C-hydroxyephedrine (HED; a false norepinephrine analogue) we performed dynamic HED (metabolite-corrected retention index RI; and $^{15}$O-water PET in 16 patients with stable CHF. Spectral analysis of heart rate (HRV) and blood pressure (BPV) variation and phenylephrine test for baroreflex sensitivity were also performed. HED RI was reduced in the noninfarcted myocardium of CHF patients (0.30 ± 0.09 vs. 0.40 ± 0.10 in age-matched healthy controls, p < 0.05) and correlated significantly with baroreflex sensitivity (r = 0.65, p < 0.01). At rest, we observed an inverse relationship between HED RI and systolic and diastolic mid-to-high frequency BPV ratio (r = −0.60 and −0.50 respectively, p < 0.05). No correlations were observed between HED RI and HRV at rest. During 70 degree head-up tilt (n = 10), total power of systolic BPV and mid-to-high frequency HRV ratio paralleled HED RI (r = 0.75 and 0.70 respectively, p < 0.05). Ability to enhance the mid-to-high frequency HRV ratio from supine to tilt position was better preserved in patients with higher HED RI (r = 0.68, p < 0.05).

We conclude that PET imaging with $^{11}$C-HED probes sympathetic effector organ capacity in CHF. Our results also suggest that autonomic damage in CHF affects both sympathetic and parasympathetic cardiac innervation in a concerted fashion.

## 1041-86 Myocardial Uptake of F-18 Fluoro-Tiiaheptadecanoic Acid (FTHA) Reflects Perfusion and Underestimates Viability

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FTHA is a long-chained fatty acid analog which has been proposed as tracer

of the β-oxidation pathway. To evaluate the diagnostic value of positron emission tomography (PET) with FTHA in patients with coronary artery disease and reduced left ventricular function, 21 patients with multivessel disease and chronic myocardial infarction (EF 33 ± 8%) were studied. Myocardial perfusion and viability were assessed by Tc-99m sestamibi single photon emission computed tomography and by F-18 fluoro-deoxyglucose (FDG) PET imaging.

The relationship between sestamibi defects and regional FDG and FTHA uptake was evaluated by computerized semiquantitative comparison for 33 left ventricular regions with normalization of tracer uptake to the region with highest sestamibi uptake. Regional sestamibi and FTHA uptake showed a good correlation with r = 0.80, whereas sestamibi and FDG demonstrated a weak correlation (r = 0.55). Regions were categorized by the severity of the perfusion defect: group A (normal): sestamibi uptake ≥ normal — 2 SD; B (mild defect): sestamibi < normal — 2 SD; C (severe defect): sestamibi < 0.5 (normal — 2 SD).

| Group/uptake | Sestamibi (%) | FTHA(%) | FDG(%) |
|---|---|---|---|
| A (n = 340) | 85 ± 9 | 87 ± 16 | 86 ± 17 |
| B (n = 163) | 59 ± 6 | 65 ± 19 | 71 ± 22 |
| C (n = 190) | 37 ± 8 | 38 ± 13 | 55 ± 17* |

*p < 0.01 vs sestamibi and vs FTHA

In 85 regions of group C categorized as scar by concordant reduction of sestamibi and FDG uptake, FTHA and FDG uptake was parallel < 50% in all regions. In 52 regions of group C with a significant mismatch between perfusion (sestamibi 40 ± 8%) and glucose metabolism (FDG 87 ± 13%) indicating ischemically compromized myocardium, FTHA uptake (44 ± 20%) was reduced < 50% in 44/52 (85%) regions. These data suggest that regional FTHA uptake predominantly reflects myocardial perfusion and underestimates tissue viability in myocardium with markedly reduced blood flow.

## 1041-87 *In Vivo* Scintillation Imaging of $^{131}$I-Labelled c-Myc Antisense Oligonucleotides After Arterial Transfection

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In considering the use of antisense (AS) oligonucleotides (ODN) for the prevention of restenosis, it is imperative to study the biodistribution of the ODN after transfection. The purpose of this study was to evaluate the *in vivo* fate of ODN transfected to the vessel wall using an $^{131}$I-labelled c-myc AS. To allow the labelling of the AS, an aminolinker was added to the 5' end of the ODN at the end of the synthesis. Isolated portions (1 cm) of denuded carotid artery of New-Zealand white rabbits were transfected for 2 h before blood circulation was reestablished. The transfections were done using either radiolabelled ODN or radioactive sodium iodide (5.55 MBq $^{131}$I). Imaging of the rabbits was done with a gamma camera both during the transfections and 5 min., 30 min., 1, 2, 3, 24, 48, and 72 h after reestablishing the blood circulation. In animals which received sodium iodide, it was eliminated from the denuded artery within the first hour, and accumulated mainly in the liver and the thyroid gland. Conversely, 26.3% of the amount of the labelled AS used for the transfection was detected at the transfection site 5 min. after reestablishing blood circulation. This quantity decreased by 40% over the next 3 h (16.1% of the original 5.55 MBq) which then diminished gradually an additional 15% at 24 h as 11.9% of the initial input still remained within the denuded portion of the carotid. At that time, 21.7% of the total dose remaining in the animal was located in the liver and no focal uptake of ODN was noticed in other organs. After 48 h, the presence of labelled AS at the transfection site was no longer evident and radioactivity accumulation became increasingly visible in the thyroid gland. Conclusions: 1 — *In vivo* arterial penetration of the transfected ODN is relatively limited and long term retention appears to be restricted to the first 48 h post-transfection. 2 — The use of high energy radionuclide to label AS molecules provides a useful tool to follow the *in vivo* distribution of the transfected ODN.

## 1041-88 Metalodobenzylguanadine (MIBG) Imaging or Heart Rate Variability for Assessment of Diabetic Cardiac Autonomic Dysfunction

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Autonomic dysfunction (AD) in diabetics confers a poor prognosis. $I^{123}$-MIBG offers a direct and quantitative (QT) assessment of cardiac efferent sympathetic denervation while heart rate variability (HRV) reflects overall autonomic balance. We therefore studied the relationship between MIBG and HRV in 65 asymptomatic diabetic pts classified with and without AD based on 5 bedside maneuvers (AD if ≥ 2 abnormal responses). HRV was derived from 48 hr Holter monitoring measured as the area under the curve of the low frequency (0.04–0.15 Hz) (LF) and high frequency (0.15–0.40 Hz) (HF) band and standard deviation (SD) of HR, while $I^{123}$-MIBG tomographic defect size, by comparison to a normal data base, was QT measured as % total myocardium ≥ 2 standard deviation below normal and corrected for rest MIBI uptake. The results are shown in the table:

| | LF | HF | SD | MIBG (QT) |
|---|---|---|---|---|
| No AD (n = 19) | 5.9 ± 0.8 | 4.3 ± 0.8 | 46 ± 11 | 4 ± 6 |
| AD (n = 46) | 5.1 ± 1.0 | 4.0 ± 1.1 | 37 ± 13 | 17 ± 17 |
| p | 0.01 | 0.23 | 0.02 | 0.0001 |

MIBG (QT) correlated with LF (r = −0.39, p = 0.006), HF (r = −0.33, p < 0.02) and SD (r = −0.32, p < 0.03). LF correlated with HF (r = 0.86, p < 0.0001). MIBG was the only independent predictor of AD by multiple regression analysis.

Thus, MIBG imaging and heart rate variability are related but MIBG uptake more objectively and directly assesses cardiac sympathetic function.

## 1041-89 HL91-Technetium-99m: Kinetics of a New Hypoxia Avid Imaging Agent in Normal and Ischemic Myocardium as Assessed by Gamma Camera Images

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$^{99m}$Tc-HL91(4,9-diaza-3,3,10,10-tetramethyldodecan-2,11-dione dioxime) is a new hypoxia avid imaging agent which has been shown in preliminary studies to demonstrate increased uptake and retention in globally hypoxic myocardium in vitro. The purpose of the current study was to determine whether these kinetics could be utilized to detect regional ischemia in vivo by gamma camera imaging. Five open-chest dogs were studied. An 85–90% sustained reduction in flow was created by stenosis of the LCx. Injection of 5 mCi of $^{99m}$Tc-HL91 and microspheres was followed by gamma camera imaging over 240 minutes. Myocardial blood flow and tracer activity was determined by well counting. Heart slices were imaged ex vivo. Myocardial clearance was biphasic. Retention at 60 min for LCx was 31.9 ± 6.2% (mean ± SEM), while LAD was 6.5 ± 1.9%; p < 0.05. At 240 min in vivo, LCx was 36.7 ± 10.3%, while LAD was 5.9 ± 1.5%; p < 0.05. LCx/LAD activity ratio in vivo was 4.7 ± 1.2 at 240 min. LCx/LAD activity ratio (ex vivo) ranged from 1.9:1 to 7.0:1 for short axis heart slices. The hypoxic/normoxic activity ratio was 4.5 ± 0.4 (n = 4). Blood activity was 13.8 ± 6.2% at 10 min and 2.5 ± 0.9% at 240 min. Increased LCx activity was qualitatively appreciated on scans from each of the five experiments both in vivo and ex vivo. Images demonstrate increased $^{99m}$Tc-HL91 retention in ischemic myocardium. Thus, $^{99m}$Tc-HL91 may be useful clinically in the positive delineation of low flow myocardial regions which are hypoxic.

## 1041-90 Detection of Myocardial Ischemia With Dynamic SPECT I-123-Iodophenylpentadecanoic Acid (IPPA) Imaging

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We evaluated dynamic IPPA SPECT imaging in an open chest canine model of low flow ischemia as a potential method for detection of ischemic viable myocardium. IPPA (4.0 mCi) was injected in 6 dogs in the presence of a sustained LAD stenosis. Ischemia was confirmed by measures of regional oxygen consumption and lactate balance. Thickening fraction in risk area (RA) was 5.4 ± 1.6%. There was no infarction by histochemical staining. Dynamic SPECT imaging (4 min/acquisition) was performed in all dogs over