Clinical and Echocardiographic Data for the Three MIBG Groups

Group	Number of Patients	Mean Age (years)	Mean Hunt-Hess Score	Peak Troponin I (ug/L)	Mean Initial LVEF	Mean Follow-up LVEF
1 (Normal initial and follow-up)	4	50±5.16	2.5±1	3.5±5.69	0.59±0.08	0.62±0.09
2 (Abnormal initial with normal follow-up)	3	57±10.60	3.67±0.58	1.87±1.25	0.52±0.21	0.70±0.03
3 (Abnormal initial and follow-up)	3	51±12.49	4±0	8.07±13.28	0.37±0.17	0.58±0.18

1142-44 **Prognostic Value of Myocardial Perfusion SPECT Comparing 17-Segment and 20-Segment Scoring Systems**

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Background: A 20-segment (seg), 5-point (0=normal, 4=absent uptake) scoring system has been widely used in semiquantitative visual interpretation of myocardial perfusion SPECT (MPS) and has played important role in risk stratification. However, the prognostic value of MPS by an optimally weighted 17-seg scoring system has not been explored. **Method:** We studied 15,579 consecutive patients (mean age 65±12, 41% females) who had exercise or vasodilator stress Tc-99m sestamibi MPS and were followed up (96%) for 25.4±9.2 months (patients revascularized ≤60 days after MPS excluded). 17-seg scores were derived from 20-seg scores using an algorithm demonstrating excellent agreement between 20- and 17-seg models (Kappa=0.87). Based on the summed stress scores (SSS) of the 20- and 17-seg models, % myocardium (myo) defect was calculated as SSS / max SSS (max SSS=80 for 20 segs, 68 for 17 segs), a variable correlating highly with quantitative analysis (R^2=0.93). **Results:** During follow-up, 353 cardiac deaths (CD) and 616 hard events (HE: CD or MI) occurred. The annual rates of events are shown in Table (*p<0.001 across % myo; p=ns for 17- vs. 20-seg in all comparisons). The areas under the ROC curves by using 20-seg SSS and 17-seg SSS were identical for predicting HE (both 0.75±0.01, p=ns) and for predicting CD (both 0.77±0.02, p=ns). **Conclusion:** When assessed on the basis of % myo, semiquantitative visual interpretations of myocardial perfusion SPECT by 17-seg and 20-seg scoring systems provide similar prognostic value.

% myo	20-seg CD	17-seg CD	20-seg HE	17-seg HE
<5%	0.4% (9985)	0.3% (9685)	0.7% (9985)	0.7% (9685)
5-10%	1.0% (2285)	1.0% (2073)	2.3% (2285)	2.0% (2073)
11-15%	2.3% (988)	1.7% (1225)	3.6% (988)	2.9% (1225)
16-20%	2.4% (676)	2.7% (891)	3.5% (676)	4.3% (891)
>20%	4.2% (1645)*	4.0% (1705)*	6.7% (1645)*	6.3% (1705)*

ORAL CONTRIBUTIONS

835 New Applications of Nuclear Imaging

Monday, March 31, 2003, 4:00 p.m.-5:30 p.m.
McCormick Place, Room S101

4:00 p.m.

835-1 **Imaging Inflammation in Atherosclerotic Lesions by Radiolabeled Chemotactic Peptide: Would Identification of Vulnerable Plaques Become Feasible?**

Artiom Petrov, Dagmar Hartung, Frank Kolodgie, Navneet Narula, Nezam Haider, Andrew Kohut, Renu Virmani, Jagat Narula, Drexel University College of Medicine, Philadelphia, PA, Armed Forces Institute of Pathology, Washington, DC

Background: Chemokines play a key role in the inflammatory process of atherosclerosis. Monocyte Chemoattractant Protein-1 (MCP-1), produced at the site of inflammation, is known to mediate the transendothelial migration of mononuclear cells via CCR-2 receptors. Since atherosclerotic plaques which are prone to rupture and are precursors of acute coronary events harbor significant macrophage infiltration, we propose that the detection of high concentration of CCR-2 receptors (exclusively expressed by the infiltrating cells) should noninvasively determine vulnerable plaques.
Methods: Tc-99m MCP-1 was injected in 7 NZW rabbits with experimental induced atherosclerotic lesions and in 5 unmanipulated control rabbits. Atherosclerotic plaques were induced by deendothelialization of the infradiaphragmatic abdominal aorta followed by hyperlipidemic diet (0.5% cholesterol+6% peanut oil) for 16 weeks. Control rabbits were fed normal chow for 16 weeks. After Tc-99m MCP-1 administration iv, gamma images were obtained until 3H.
Results: Atherosclerotic lesions were clearly visible in all treated animals at 3H. No tracer uptake was seen in the corresponding regions of the control rabbits. Mean %injected dose/g MCP-1 uptake in atherosclerotic lesions was 4 times higher than in the corresponding regions of the control rabbits (0.065+/-0.005 versus 0.016+/-0.006; P<0.05). Histology confirmed a strong correlation between Tc-99m MCP-1 uptake and number of macrophages in AHA type II to IV lesion.
Conclusion: Noninvasive imaging of experimental induced atherosclerotic plaques by radiolabeled MCP-1 is feasible and might be useful for detection of the extent of inflammation in advanced atherosclerotic plaques and identification of plaques vulnerable to rupture.

4:15 p.m.

835-2 **Preferential Uptake of Radiolabeled Oxidation-Specific Antibodies in Lipid-Rich Versus Collagen-Rich Lesions: Implications for Noninvasive Imaging of Vulnerable Plaques**

Sotirios Tsimikas Michael Torzewski, Brian Shortal, Wulf Palinski, Joseph L. Witztum, University of California San Diego, La Jolla, CA

Background: Vulnerable plaques are enriched in lipids and macrophages (Mø), but relatively deficient in collagen. Radiolabeled oxidation-specific antibodies (Ox-AB) targeting Oxidized LDL (OxLDL) in the lipid core may be particularly useful for non-invasive detection of vulnerable plaques. Methods: ^{125}I-MDA2, a prototype Ox-AB, was intravenously injected in 19 Watanabe rabbits of various ages to assess uptake and binding in lipid-rich lesions. Plaque burden was assessed as % atherosclerotic surface area (% Athero) and aortic weight. Aortic plaque uptake of ^{125}I-MDA2, an index of *in vivo* OxLDL content, was determined after 24 hours as % injected dose/gram aortic tissue (%ID/g). Autoradiography was performed and correlated with immunocytochemistry for oxidation-specific epitopes, Mø, smooth muscle cells (SMC) and collagen. Results: In 13/19 rabbits, aortic Sudan staining (neutral lipid) and autoradiographs (reflecting ^{125}I-MDA2 uptake) were nearly identical (Sudan=OxLDL), whereas 6/19 rabbits lacked ^{125}I-MDA2 signal in some areas of Sudan positive lesions (Sudan≠OxLDL). The Sudan≠OxLDL group was older and had greater overall plaque burden (Table). Aortas of older rabbits had reduced ^{125}I-MDA2 uptake, OxLDL immunostaining and Mø, but increased SMCs and collagen. Conclusion: Ox-AB preferentially accumulate in lipid-rich compared to collagen-rich atherosclerotic lesions. These observations suggest that tagged Ox-AB may be useful in non-invasively imaging vulnerable plaques.

	Age (mo)	% Athero	Aortic weight (mg)	125I-MDA2 uptake
Sudan=OxLDL	24 ± 14	63 ± 29	965 ± 408	0.07 ± 0.03
Sudan≠OxLDL	46 ± 11	90 ± 7	1720 ± 452	0.03 ± 0.01
P-Value	0.006	0.04	0.002	0.005

4:30 p.m.

835-3 **^{99M}Tc-Annexin V Imaging for Detection of Atherosclerotic Lesions in Porcine Coronary Artery**

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Background: Apoptosis is an important constituent of unstable atherosclerotic plaques. Whereas apoptosis of smooth muscle cells leads to attenuation of the fibrous cap, apoptosis of macrophages results in enlargement of necrotic core and plaque instability. Imaging apoptosis may allow noninvasive detection of vulnerable plaques.
Methods: To produce a model of coronary atherosclerosis 3 farm pigs underwent vascular injury to the RCA and LAD followed by high fat diet. After average of 47 days, the animals underwent coronary angiography, were injected with 8-10 mCi of Tc-99m annexin V, had blood samples drawn for blood pool clearance and underwent SPECT imaging 3 hr after injection. The animals were sacrificed, the hearts removed, imaged by SPECT ex-vivo and the vessels counted and histopathology performed.
Results: By 50 min after injection the blood pool had cleared to 10% of peak. Two of the 6 vessels were injured by wire abrasion of endothelium and were normal by pathology. Two vessels had AHA type II lesions and 2 had AHA type III lesions. Focal uptake was seen on SPECT reconstructions of in-vivo images in 3 vessels and ex-vivo in 4. Average ratios of cts/gm for injured vs control (LCX) were 1.03 for normal vessels, 1.7 for type II injury, and 2.2 for type III. Macrophage infiltration was prominent in type III lesions. In one experiment focal uptake of annexin V was also seen in the myocardium corresponding to area of myocardial necrosis.
Conclusions: These preliminary studies suggest that Tc-99m annexin may be a non-invasive method to identify vascular plaque apoptosis.

4:45 p.m.

835-4 **Abrogation of Apoptosis in Atherosclerotic Plaques: Feasibility of Noninvasive Detection by Radionuclide Imaging With Annexin-V**

Dagmar Hartung Artiom Petrov, Frank Kolodgie, Navneet Narula, Andrew Kohut, Nezam Haider, Herman K. Gold, Renu Virmani, Jagat Narula, Drexel University College of Medicine, Philadelphia, PA, Armed Forces Institute of Pathology, Washington, DC

Background: Apoptosis occurs commonly in advanced atherosclerotic plaques and potentially contributes to plaque vulnerability and rupture. Specifically, apoptosis of macrophages adds to enlarging lipid cores in vulnerable plaque and overwhelming apoptosis is associated with the site of fibrous cap rupture. It is logical to hypothesize that prevention of apoptosis in advanced atherosclerosis may be of benefit.
Methods: Since Annexin-V has a high affinity for exposed phosphatidylserine on apoptotic cell surfaces, we used radiolabeled Annexin-V for noninvasive imaging of athero-