of QCA or clinical data. A coronary stenosis ≥70% was considered significant. **Results.** Fourteen patients had no significant disease at QCA, 12 had one vessel, and three had multi-vessel disease. In the 15 patients with disease, 10 were detected by MP at peak stress, 8 were detected by WM with CEBD, and 6 were detected by WM without contrast. MP abnormalities in CAT supplied by >70% diameter stenosis were seen in an additional nine CAT by R1 and four CAT by R2 that were considered to have normal WM with or without CEBD. MP abnormalities were seen during the intermediate stage of the DSE in 9 of the 10 patients with disease at QCA and abnormal MP at peak stress. **Conclusions.** These pilot data indicate that the addition of RTLMII following IV contrast during DSE improves test sensitivity because it detects MP abnormalities that occur in CAT with normal WM even with CEBD.

11:00 a.m.

881-3 Real-Time Contrast Enhanced Ultrasound Imaging of Neovascularization Within the Human Carotid Plaque

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Objective: 1) To review contrast-enhanced ultrasound studies of human carotid artery atherosclerosis to determine incidence of plaque neovascularization, 2) to correlate neovascularization observed during non-invasive imaging to pathologic specimens.
Background: Previous pathologic studies have shown that neovascularization within the human atherosclerotic plaque revealed a far greater incidence of neovascularization from the adventitia relative to the lumen and a correlation between plaque instability and carotid occlusive disease.
Methods:Twenty-one contrast-enhanced carotid examinations were reviewed (criteria for review >50% stenosis). The degree of neovascularization was visually graded.
Results: Neovascularization by contrast-enhanced ultrasound imaging was observed in the carotid artery plaque in 20/21 patients. Four (4) were considered to be extensive; moderate in 5; and minimal in 11 patients. The histology specimens in 2 patients following endarectomy revealed degrees of plaque neovascularization consistent with the images obtained with contrast-enhanced ultrasound imaging.
Conclusion: This is the first report of real-time, contrast-enhanced, ultrasound imaging of the neovascularization within the human carotid plaque. Neovascularization was observed in 95% (20/21) of the carotid images and associated with a perfusion pattern described as "outside-in" (originating in the adventitia and leading to the intima).

Plaque neo-vascularization	Patients	Statin	No Statin	Unknown	MI (Average)
Limited	11	5	3	3	0.12
Moderate	5	2	--	3	0.14
Extensive	4	1	2	1	0.09
None	1	--	--	11	
Totals	21	8	5	7	

11:15 a.m.

881-4 Delivery of Luciferase Enzyme to the Heart Using Ultrasound Targeted Microbubble Destruction

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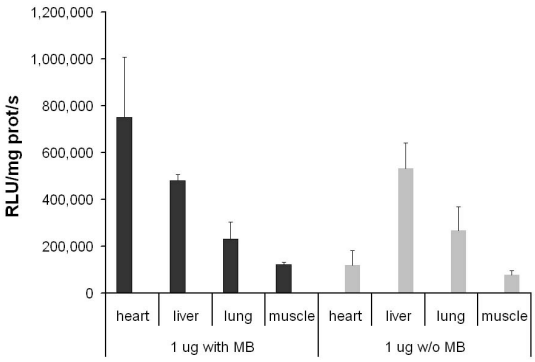
Background: We have previously shown that ultrasound targeted microbubble destruction (UTMD) can direct plasmids to the heart. Other groups have been using this or similar techniques to deliver proteins or drugs to ultrasound accessible organs. The aim of this study was to evaluate UTMD for protein and drug delivery with lipid stabilized microbubbles (MB) using luciferase enzyme as a highly specific and sensitive reporter for quantification.
Methods: 1 μg of luciferase protein was added before assembly of lipid stabilized microbubbles. Microbubbles were infused intravenously over 15 minutes into three rats and high mechanical index ultrasound was applied to destroy intramyocardial microbubbles. Three rats receiving 1 μg of luciferase protein in PBS with ultrasound served as a control. Heart, lung, liver and skeletal muscle were harvested immediately after the experiment and relative luminescence units (RLU) per mg protein per second was determined.
Results: In the microbubble group hearts showed 6-fold augmented luciferase activity compared to the control (751000 vs. 119000 RLU/mg protein/s; p=0.014). The other organs showed comparable activity between these groups.**Conclusion:** This study shows that lipid stabilized microbubbles can be used to deliver proteins to the heart. The 6-fold augmentation of protein uptake in the hearts compares with no change in the uptake of other organs between the groups. This serves as a model for directing proteins and drugs to ultrasound accessible organs using UTMD.



11:30 a.m.

881-5 Comparison of Modified Acoustic Quantification With Echocardiographic Contrast and Radionuclide Ventriculography for Evaluation of Left Ventricular Ejection Fraction

James N. Kirkpatrick, R. Parker Ward, Roberto M. Lang, James E. Bednarz, Jeanne M. DeCara, Kirk T. Spencer, University of Chicago, Chicago, IL

Background. Determination of left ventricular ejection fraction (LVEF) provides one of the most powerful prognostic assessments in cardiovascular medicine.Radionuclide ventriculography (RNV) is considered the gold standard for determination of LVEF because it is quantitative and accurate. However, it is expensive and involves cumbersome preparation and care of radiopharmaceuticals. When combined with echocardiographic contrast infusion, modified acoustic quantification (AQ) can provide real-time quantitative assessment of LVEF, even in patients with poor acoustic windows. We sought to compare the quantitative measurements of LVEF obtained from contrast AQ with LVEF measurements from RNV. **Methods.** Thirty-nine patients scheduled for RNV for assessment of LVEF were recruited. After their nuclear study, patients underwent echocardiographic determination of LVEF using acoustic quantification with a continuous infusion of Definity® contrast agent (Bristol-Meyers Squibb) in apical four chamber (A4C) and apical two chamber (A2C) views. Ultrasound settings were optimized to track the endocardial border. LV volume curves from each cardiac cycle were averaged to form a real-time composite waveform, from which LVEF was calculated. Contrast was titrated to provide optimal opacification of the LV cavity. **Results.** Contrast infusion resulted in uniform LV opacification, allowing accurate endocardial border detection and tracking throughout the cardiac cycle in 38 patients (97%). The mean LVEF by RNV was 50±16% (range, 19-73%). The average LVEF by acoustic quantification with contrast was 49±17% for A4C and 51±18% for A2C. The average difference between LVEF by RNV and LVEF by the mean of A4C and A2C was <1%. **Conclusion.** Echocardiography using acoustic quantification with contrast for quantitative determination of LVEF compared favorably with radionuclide ventriculography. This novel technique shows promise as a relatively inexpensive and easy method for quantitative assessment of LVEF.

11:45 a.m.

881-6 Effect of Attenuation on Intravascular Thrombus Dissolution Using Transcutaneous Ultrasound and Intravenous Microbubbles

Thomas R. Porter, Jeane Mike Tsutsui, Jason M. Johanning, B. Timothy Baxter, John Lof, Terry Matsunaga, Reena Zutshi, Evan Unger, Feng Xie, University of Nebraska Medical Center, Omaha, NE

Although low frequency ultrasound (LFUS) and intravenous (IV) microbubbles (MB) have been used to recanalize arterial thromboses, the effect of ultrasound attenuation (ATT) has not been assessed. We hypothesized that higher intensity LFUS would attenuate more than lower intensities (I), resulting in lower effectiveness. To test this, chronic arteriovenous grafts were repeatedly thrombosed in 3 dogs. One megahertz LFUS at different I and duty cycles (DC) was applied transcutaneously in the presence and absence of a 6 cm thick tissue mimicking phantom (ATT coefficient: 0.49dB/cm/MHz). The different I and DC used were 0.4 Watts/cm2 continuous wave (0.4 CW), 0.8 Watts/cm2 CW (0.8 CW), and 10 W/cm2 pulsed wave at 10% DC (10 PW). IV lipid MB (0.1-0.2 ml bolus) or saline were administered at 3-5 minute intervals during LFUS application. Angiographic reflow (AR) was assessed at 30 and 45 minutes of treatment. Patency score (PS) in each limb of the graft (proximal, mid, and distal) was defined as 0=100% occluded, 1=>10%, 2=>30%, 3=>70%, and 4=>90% recanalized. **Results.** A total of 45 thrombosed grafts were tested (mean age of thrombus 3.8±0.9 hours). In the presence of the phantom, AR in the graft was faster and PS was higher with 0.4 CW LFUS (Table). The PS for 10 PW was significantly lower in the presence of the phantom (Table). **Conclusions.** These findings indicate that LFUS at lower I should be used to recanalize thrombosed vessels where significant ATT is present, such as in acute coronary and cerebral thromboses.